# 博士論文

# Functional analysis of histone deacetylase of *Aspergillus oryzae*

# <sup>「</sup>麴菌 histone deacetylase の機能解析

## 河内 護之

広島大学大学院先端物質科学研究科

2014年3月

### 目次

1. 主論文

Functional analysis of histone deacetylases in *Aspergillus oryzae* (麴菌 histone deacetylase の機能解析) 河内 護之

- 2. 公表論文
  - Fungus-specific sirtuin HstD coordinates secondary metabolism and development through control of LaeA.
    Moriyuki Kawauchi, Mika Nishiura and Kazuhiro Iwashita Eukaryotic Cell, **12** (8), 1087-1096 (2013).
  - (2) Functional analysis of histone deacetylase and its role in stress response, drug resistance and solid-state cultivation in *Aspergillus oryzae.*

Moriyuki Kawauchi and Kazuhiro Iwashita

Journal of Bioscience and Bioengineering, 118(2), 172-176 (2014)



#### CONTENTS

| CONTENTS     | 4 |
|--------------|---|
| SUMMARY      | 7 |
| INTRODUCTION | 9 |

#### **CHAPTER I**

| Phylogenetic analysis of AoHDACs and its role in growth, conidiation and     |
|--|
| secondary metabolism in <i>A. oryzae</i> 12                                  |
| I.1 ABSTRACT13   |
| I.2 INTRODUCTION14   |
| I.3 MATERIALS AND METHODS17  |
| I.3.1 Strains, media, physiological tests17                                  |
| I.3.2 Protein identification, domain prediction, and phylogenetic analysis18 |
| I.3.3 RNA preparation19  |
| I.3.4 Northern hybridization20   |
| I.3.5 Construction of the disruption cassette21                              |
| I.3.6 Complementation of <i>hstD/Aohst4</i> 21                               |
| I.3.7 Construction of overexpression plasmids21                              |
| I.3.8 Transformation of <i>A. oryzae</i> 22                                  |
| I.3.9 Time-lapse imaging22   |
| I.3.10 Secondary metabolite analysis22                                       |
| I.3.11 Microarray analysis23   |
| I.4 RESULTS25  |
| I.4.1 Phylogeny and morphology of AoHDACs25                                  |

| I.4.2 Fungal-specific sirtuin regulates SM production            | 26 |
|--|----|
| I.4.3 <i>hstD/Aohst4</i> regulates the expression of <i>laeA</i> | 28 |
| I.4.4 Genetic interaction of <i>hstD/Aohst4</i> and <i>laeA</i>  | 29 |
| I.5 DISCUSSION   | 31 |
| I.6 FIGURES AND TABLES   |    |

#### **CHAPTER II**

| Comprehensive phenotypic analysis of AoHDAC disruptants55                    |
|--|
| II.1 ABSTRACT  |
| II.2 INTRODUCTION  |
| II.3 MATERIALS AND METHODS59   |
| II.3.1 Strains and media59   |
| II.3.2 Environmental stress resistance assay59                               |
| II.3.3 Drug resistance test59  |
| <b>II.3.4 Measurement of enzyme activity and total proteins production60</b> |
| II.3.5 Measurement of N-acetylglucosamine content in rice- <i>koji</i> 60    |
| II.4 RESULTS62   |
| II.4.1 Stress resistance of AoHDACs62  |
| II.4.2 Drug (inhibitor) resistance of AoHDAC disruptants62                   |
| II.4.3 Effect of AoHDACs disruption on the rice- <i>koji</i> 63              |
| II.5 DISCUSSION  |
| II.6 FIGURES   |

| CONCLUSION REMARKS78 |
|----------------------|
|----------------------|

| ACKNOWLEDGEMENTS    | 80 |
|---------------------|----|
| REFERENCES          | 81 |
| RELATED PUBLICATION | 89 |

#### SUMMARY

The filamentous fungus *Aspergillus oryzae* is used in a number of industries including the manufacturing of pharmaceuticals and the production of traditional Japanese fermented foods. Because histone deacetylases (HDACs) play key roles in the regulation of fundamental cellular processes such as development, metabolism, genome integrity, and the stress response in higher model organisms, I hypothesized that they would also play diverse roles in *A. oryzae*. In this thesis, therefore, I performed a comprehensive analysis of HDACs in *A. oryzae* with the aim of elucidating their function.

I used BLAST analysis to identify HDACs homologs in the *A. oryzae* genome (*A. oryzae* histone deacetylases: AoHDACs) and found 11 AoHDACs. I successfully disrupted 10 of the 11 AoHDACs, but only heterokaryon transformants were obtained in the case of *hdaB/Aorpd3*.

I tested the basic phenotypes of the disruptants such as growth, conidiation. I also tested secondary metabolite (SM) production of AoHDAC disruptants. The *hdaD/Aohos2* and *hstD/Aohst4* disruptants showed defects in conidia formation and a high level of kojic acid production, which is a major SM of *A. oryzae*. I also found that *hstD/Aohst4* coordinates the secondary metabolism and development through the regulation of *laeA*, which is key coordinator of secondary metabolism and development in filamentous fungi.

I also examine the various kinds of phenotypes included stress resistance, drug resistance, and rice-*koji* making using these AoHDAC disruptant. From these results, four AoHDACs, *hdaA/Aohda1*, *hdaB/Aorpd3*, *hdaD/Aohos2*, and *hstD/Aohst4*, were shown to be involved in diverse *A. oryzae* cellular processes such as the stress response,

cell wall synthesis, protein secretion, and genome integrity.

This thesis identified several functions of HDACs in *A. oryzae*. Because many types of HDACs are conserved in diverse organisms, these findings will be useful not only in understanding the function of HDACs in *A. oryzae*, but also in other filamentous fungi and other organisms. In contrast to these conserved HDACs, I showed fugal-specific role of fungal-specific HDAC like *hstD/AohstD*. This finding suggests the importance of fungal-specific HDACs in the fungal specific phenotypes.

#### INTRODUCTION

Eukaryotic DNA is packaged into chromatin, limiting transcriptional activity (Cairns 2009). Histone acetylation is one of the most important modifications to regulate chromatin accessibility. It is controlled by two opposing enzymes, histone acetyltransferases (HATs) and HDACs. These are conserved in a wide range of organisms from yeast to humans and also filamentous fungi (Brosch et al. 2008; Frye 2000; Gregoretti et al. 2004; Nishida 2009; Shahbazian and Grunstein 2007). Acetylation is usually associated with transcriptional activation, while, by contrast, histone deacetylation controls transcriptional repression.

HDACs remove the acetyl moiety from the lysine residue of a histone tail, and also deacetylate many non-histone substrates (Yang and Seto 2008). Protein deacetylation affects diverse cellular processes such as development, metabolism, and stress responses in eukaryotic cells. In mammalian and yeast cells, HDACs are divided into two major families, the sirtuins and the classical HDACs, which are phylogenetically classified into four classes. The sirtuins constitute class III, and the classical HDACs are grouped into classes I, II, and IV (Ekwall 2005; Yang and Seto 2008). With the exception of mammalian specific class IV HDACs, these enzymes are also conserved in the genome of filamentous fungi (Borkovich et al. 2004; Brosch et al. 2008).

Filamentous fungi include a diverse range of species, many of which are important to human life. Some are used in industry to produce fermented foods, commercial enzymes, and useful chemicals, while others are human and plant pathogens (Hoffmeister and Keller 2007; Iwashita 2002; Pagiotti et al. 2011; Raffaele and Kamoun 2012). Recently, the role of HDAC in fungal development, conidiation, the stress response, secondary metabolism, and virulence has been demonstrated in filamentous fungi (Ding et al. 2010; Gacek and Strauss 2012; Li et al. 2010; Shimizu et al. 2012; Tribus et al. 2010; Tribus et al. 2005).

*A. oryzae* is one of useful filamentous fungi. It has been used for more than 1,000 years in the traditional food industries. Because of its long history in food production, it is determined to be generally recognized as safe (GRAS) by the US Food and Drug Administration and its safety is also documented by the World Health Organization (Machida et al. 2008). *A. oryzae* can produce high levels of enzymes and beneficial secondary metabolites (SMs) such as kojic acid and WYK-1 (Christensen et al. 1988; Imamura et al. 2012; Terabayashi et al. 2010). Such commercial importance has resulted in many investigations into its molecular biology and physiology. However, while the regulation of genes involved in *A. oryzae* metabolite or enzyme production is an attractive topic of study, its epigenetic regulation, including histone acetylation, has been not investigated.

In this thesis, therefore, I studied the function of *A. oryzae* HDACs. In Chapter I, I describe the identification of 11 HDAC homologs in the *A. oryzae* genome. I attempted to disrupt these AoHDACs and succeeded for 10 of the AoHDACs and heterokaryon transformants were obtained in the case of *hdaB/Aorpd3*. Using these disruptants, their basic phenotypes, including growth and conidiation, were studied. The SM production of AoHDAC disruptants was also tested, because regulation of SM production is often associated with fungal development (Bayram and Braus 2012). As the result, *hdaD/Aohos2* and *hstD/Aohst4* disruptants were shown to have defective conidia formation and a high production of kojic acid, which is a major SM of *A. oryzae*. Recently, it was reported that *laeA* regulates kojic acid production in *A. oryzae*, so the genetic interaction between *laeA* and *hstD/AohstD* was also focused. As the result, I

concluded that *hstD/Aohst4* regulate SM production and development through the control of *laeA*.

In the higher eukaryote, HDACs play key roles in the regulation of fundamental cellular process such as development regulation, stress response and genome integrity. Therefore, AoHDACs have more divergent role indicated in Chapter I. In the Chapter II, thus, I examine various phenotypes including stress resistance, drug resistance, and rice koji production using the AoHDAC disruptants. This analysis showed that the four AoHDACs *hdaA/Aohda1*, *hdaB/Aorpd3*, *hdaD/Aohos2*, and *hstD/Aohst4* are involved in diverse cellular process such as the stress response, cell wall synthesis, protein secretion, and genome integrity in *A. oryzae*.

#### CHAPTER I Phylogenetic analysis of AoHDACs and its role in growth, conidiation and secondary metabolism in *A. oryzae*

#### I.1 ABSTRACT

The filamentous fungus *A. oryzae* has been used in a number of industries such as the production of traditional Japanese foods and pharmaceutical manufacturing. In higher model organisms, HDACs are concerned with multiple cellular processes such as development, metabolism, and the stress response, so can also be expected to be important in *A. oryzae*. In this chapter, I describe the identification of 11 HDACs homologs in the *A. oryzae* genome (AoHDACs) using BLAST analysis. Ten of these AoHDACs were successfully disrupted, but only heterokaryon transformants were obtained for *hdaB/Aorpd3*.

Basic phenotypes of these disruptants were investigated; including growth and conidiation, as well as SM production because its regulation is often associated with fungal development. The *hdaD/Aohos2* and *hstD/Aohst4* disruptants were defective in conidia formation and produced high levels of the SM kojic acid. I also showed that the gene expression of *laeA*, which is the most studied fungal-specific coordinator for the regulation of secondary metabolism and fungal development, was induced in the *AhstD* strain. Genetic interaction analysis of *hstD/Aohst4* and *laeA* clearly indicated that *hstD/Aohst4* works upstream of *laeA*. Thus, I concluded that the fungal-specific sirtuin *hstD/Aohst4* coordinates fungal development and secondary metabolism via the regulation of *laeA* in filamentous fungi.

#### **I.2 INTRODUCTION**

Histone acetylation plays key roles in the control of chromatin structure and function (Shahbazian and Grunstein 2007). The acetylation state is controlled by two histone modification enzymes with opposing actions, HATs and HDACs. Acetylation is generally associated with transcriptional activation. In contrast, histone deacetylation is generally associated with transcriptional repression. These enzymes are highly conserved from yeast to humans, and they are also conserved in filamentous fungi (Borkovich et al. 2004; Brosch et al. 2008; Ekwall 2005; Nishida 2009).

HDACs remove the acetyl moiety from the lysine residue of a histone tail. In addition to histones, these enzymes deacetylate many non-histone substrates (Yang and Seto 2008). Protein deacetylation affects diverse cellular process such us development, metabolism, and stress responses in eukaryotic cells (Yang and Seto 2008). In mammalian and yeast cells, HDACs are divided into two major families called the sirtuins and the classical HDACs. The HDACs are phylogenetically classified to four classes. The sirtuins constitute class III, and the classical HDACs are grouped into classes I, II, and IV (Ekwall 2005; Yang and Seto 2008). Except for mammalian specific class IV HDACs, these enzymes are also conserved in the genome of filamentous fungi (Borkovich et al. 2004; Brosch et al. 2008).

Recently, HDACs in some filamentous fungi have been investigated for their role in the regulation of histone modification, developmental processes, stress resistance, pathogenesis, metabolism, and other such processes (Brosch et al. 2008; Ding et al. 2010; Izawa et al. 2009; Li et al. 2010; Smith et al. 2008). For example, the homolog of yeast *rpd3* is required for growth and conidiation in several filamentous fungi (Tribus et al. 2010). The class II HDAC *hdaA/Afhda1*, a homolog of yeast *hda1*, is involved in germination and the oxidative stress response in *Aspergillus fumigates* (Lee et al. 2009; Tribus et al. 2005). The yeast *hos2* homolog is required for conidial development, invasive growth, and the production of virulence factors in some plant-pathogenic filamentous fungi (Baidyaroy et al. 2001; Ding et al. 2010; Li et al. 2010).

Filamentous fungi produce wide varieties of SMs, which are small bioactive molecules that include both beneficial medicines and cosmetics, and toxins that are harmful for animals and plants (Hoffmeister and Keller 2007). Therefore, because of the importance of fungal SMs, there has been much research into the mechanisms that regulate their production. *LaeA*, a putative fungal-specific methyltransferase, is implicated in the global regulation of SM production (Bayram and Braus 2012; Sanchez et al. 2012). *LaeA* also has an important role in coordinating fungal development and SM production (Bayram and Braus 2012). Recent studies have shown that histone modification plays key roles in the regulation of SM biosynthetic genes expression (Gacek and Strauss 2012). In *Aspergillus nidulans*, the HDACs *hdaA/Anhda1* and *sirA/Ansir2* regulate carcinogenic sterigmatocystin and antibiotic penicillin production (Shimizu et al. 2012; Shwab 2007). The loss of *hdf1/Fghos2* reduces conidial development and the production of deoxynivalenol, which is the most characterized virulence factor in *Fusarium graminearum* (Li et al. 2010).

However, the importance of fungal HDACs in the regulation of secondary metabolism and fungal development is still not known; studies of these HDACs are limited even though several types of HDACs are found in fungal genomes (Brosch et al. 2008). Moreover, the relationship between the global regulator *laeA* and histone modification is still poorly understood.

In the Chapter I, I examined the phenotypes caused by the disruption of all HDACs

using *A. oryzae*, which is an important filamentous fungus in industry and has potential for the production of pharmaceutical and cosmetic SMs (Abe et al. 2006; Imamura et al. 2012; Machida et al. 2008). My observations indicated that the fungal-specific sirtuin *hstD/Aohst4* regulates conidial development and kojic acid production, which is an important cosmetic material for preventing melanogenesis in skin, as well as antimicrobial penicillin production (Terabayashi et al. 2010). I also performed microarray analysis of *AhstD* to examine the global function of this sirtuin and found that the disruption of this gene affects the expression of many metabolite genes. As described above, *laeA* is an important coordinator for the regulation of secondary metabolism and development. In this context, I also analyzed the genetic interaction between *hstD/Aohst4* and *laeA* and found that *hstD/Aohst4* regulates *laeA* expression. I first describe the function of fungal-specific sirtuin *hstD/Aohst4* in SM production and then on conidial development through the regulation of *laeA* gene expression.

#### **I.3MATERIALS AND METHODS**

#### I.3.1 Strains, media, physiological tests

The strains used in the Chapter I are listed in Table I.6.1. A. oryzae RIB40 was used as the DNA donor. The A. oryzae NSR-ALD2 strain was used as the host for AoHDACs disruption (Maruyama and Kitamoto 2008). M + Met medium or M + Ade medium (M + Ade medium containing 0.5 g of adenine sulfate dihydrate instead of L-methionine was used as the selectable medium for A. oryzae adeA<sup>+</sup> transformants and A. oryzae  $sC^+$  transformants, respectively (Maruyama and Kitamoto 2008). TS medium (6 g of NaNO<sub>2</sub>, 0.52 g of KCl, 1.52 g of KH<sub>2</sub>PO<sub>4</sub>, 0.52 g of MgSO<sub>4</sub>·7H<sub>2</sub>O, 10 g of glucose, 1 ml of trace elements, pH 6.5, in 1 L) was used as the selectable medium for A. orvzae  $adeA^+ sC^+$  transformants. M + Met or M + Ade or TS medium with 0.8 M NaCl added was used for transformation. KAS medium (15 g of Tryptone, 1.52 g of  $K_2$ HPO<sub>4</sub>, 1.5 g of L-methionine, 0.5 g of MgSO<sub>4</sub>  $\cdot$  7H<sub>2</sub>O, 100 g of glucose, 1 ml of trace elements, pH 6.5, in 1 L) was used for screening HDAC-affected kojic acid productivity. KA medium (1 g of yeast extract, 1 g of K<sub>2</sub>HPO<sub>4</sub>, 1.5 g of L-methionine, 0.5 g of MgSO<sub>4</sub> · 7H<sub>2</sub>O, 100 g of glucose, 0.5 g of adenine sulfate dihydrate, pH 6.0, in 1 L) was used to test for KA productivity and RNA preparation. N medium (3 g of L-glutamic acid, 0.52 g of KCl, 1.52 g of K<sub>2</sub>HPO<sub>4</sub>, 0.52 g of MgSO<sub>4</sub>·7H<sub>2</sub>O, 30 g of glucose, 1.5 g of L-methionine, 1 ml of trace elements, pH 6.5, in 1 L) was used for morphological analysis. TSB medium (30 g of Tryptic soy broth, 1.5 g of L-methionine, 3 g of L-glutamic acid, 0.5 g of adenine sulfate dihydrate, pH 7.5, in 1 L) was used for the penicillin bioassay and RNA preparation.

Morphological analysis was performed in 20 ml of 2% agar N plate or 100 ml of N

liquid medium. Three independent disruptants were used for each experiment. For the spore count, conidia suspensions of each strain were point inoculated ( $1 \times 10^5$  conidia) on the center of each plate, and the strain was grown for 5 days at 30°C. Colony diameters were measured at this time, and the spores were harvested in suspension solution (0.025% Tween-80/0.5% NaCl), vortexed vigorously, and counted using a TC10 automated cell counter (Bio-Rad). The conidiation rate was calculated by the conidia number/ radial growth area (cm<sup>2</sup>). For biomass analysis in N liquid medium, 4 cm<sup>2</sup> of full-growth colonies in plate cultures of each strain were cut and homogenized in 1 ml of suspension solution and then used to inoculate each flask. Flasks were incubated for 2 days at 30°C with shaking at 100 rpm. Then, mycelia were harvested, dried at 105°C for 2 h, and weighed.

#### I.3.2 Protein identification, domain prediction, and phylogenetic analysis

HDAC sequences of *Saccharomyces cerevisiae* were obtained from the *Saccharomyces* genome database (<u>http://www.yeastgenome.org/</u>). HDAC sequences of *H. sapiens, Neurospora crassa*, and *A. nidulans* were obtained from the NCBI proteins database (<u>http://www.ncbi.nlm.nih.gov/guide/proteins/</u>), the *Neurospora crassa* database

(http://www.broadinstitute.org/annotation/genome/neurospora/MultiHome.html), and AspGD (http://www.aspgd.org/), respectively. HDAC genes of *A. oryzae* were identified from the Comparative fungal genome database (CFGD; <u>http://nribf2.nrib.go.jp/</u>) by BLAST searching using HDAC sequences of *S. cerevisiae* and *H. sapiens* as the query. The sequence of these HDACs in *A. oryzae* was verified by RNA sequencing using SOLiD3 (Applied Biosystems). The gene structure

18

of all AoHDACs was confirmed by RNA sequence data (details of my RNA-seq data are available in AspGD) (Arnaud et al. 2010). The mapping data of all reads are also available in CFGD. The protein sequence of the HDAC homolog in *A. oryzae* was analyzed for recognizable domains using Interproscan (Quevillon et al. 2005). The protein sequence of the *hstD* homolog in filamentous fungi was identified using NCBI blast with the pezizomycotina genomes (http://www.ncbi.nlm.nih.gov/sutils/genom\_tree.cgi) using the amino acid sequence of *hstD* as a query.

For the classification of HDACs in *A. oryzae*, protein sequences of HDACs in *S. cerevisiae*, *N. crassa*, *A. nidulans*, and *A. oryzae* were aligned with ClustalW software in the Molecular Evolutionary Genetic Analysis 5 (MEGA5) program (Tamura et al. 2011). Phylogenetic analysis was carried out using the neighbor-joining method with 1000 bootstrap replicates by the MEGA5 program. For the classification of *hstD/Aohst4* in filamentous fungi, alignment and phylogenetic analysis was performed as described above. A list of sequence accession numbers used for AoHDACs analysis is in Table 1.6.2, and sequence accession numbers of each *hstD* homolog are described in Fig. I.6.6.

#### **I.3.3 RNA preparation**

KA culture was performed in 20 ml of KA liquid medium inoculated with 200  $\mu$ l of 1 × 10<sup>8</sup> conidia /ml suspension and incubated at 30°C for 4 or 7 days with shaking at 130 rpm. TSB culture was performed in 40 ml of TSB liquid medium inoculated with 400  $\mu$ l of 1 × 10<sup>8</sup> conidia /ml suspension and incubated at 30°C for 1 day with shaking at 200 rpm. After cultivation, mycelia were harvested using Miracloth (Merck). Then, mycelia were immediately frozen in liquid N<sub>2</sub> and ground to a fine powder. Total RNA

was isolated from mycelia from KA or TSB liquid media using Isogen (Nippon Gene) according to the manufacturer's instructions.

#### I.3.4 Northern hybridization

Denatured total RNA (20  $\mu$ g) was electrophoresed on a formaldehyde-agarose gel and transferred in 20 × SSC onto a Hybond N<sup>+</sup>. Northern analysis was performed with a Detection starter kit II (Roche) according to the manufacturer's instructions. DIG-labeled probes were prepared using a PCR digoxigenin probe synthesis kit (Roche) with genomic *A. oryzae* RIB40 DNA as the template and the primers X-probe-F and X-probe-R. The letter X means the respective gene for northern analysis. Each blot was imaged using Luminescent Image Analyzer LAS1000plus (FUJIFILM). A list of the primers used for these PCRs is shown in Table I.6.3.

#### I.3.5 Construction of the disruption cassette

Each disruption cassette was constructed by fusion PCR of three mutually primed DNA fragments, the 5' and 3' flanking region of the target genes and the *adeA* fragment (Szewczyk et al. 2007). About 1 kb of the 5' and 3' flanking region of the target genes and the *adeA* gene were amplified from genomic *A. oryzae* RIB40 DNA with primers X-A and X-B, X-C and X-D, and adeA-F and adeA-R, respectively. Only for the construction of the *AhstDAlaeA*, *A. nidulans sC* gene, amplified from pUSA with sC-F and sC-R, was the gene fused to the flanking region of *laeA* (Yamada et al. 2003). The letter 'X' in the primer names represents the name of each target gene. Each region was amplified by KOD Plus DNA polymerase (TOYOBO). These fragments were combined by a second PCR with KOD Plus DNA polymerase and the primers X-A and X-D or

X-A2 and X-D2. The amplified fragment was purified by the QIAquick PCR purification kit (QIAGEN) and then used as a disruption cassette. A list of the primers used for these PCRs is shown in Table I.6.3.

#### I.3.6 Complementation of hstD/Aohst4

To recover the native locus of *hstD/Aohst4*, I first amplified the same 5' flanking region of the disruption construct of the *hstD/Aohst4* and *adeA* fragments from RIB40 DNA with the primers hstD-A and hstD-compB or adeA fusion sC-F and adeA-R, respectively. I also amplified the *A. nidulans* sC gene from pUSA with sC-F and sC-R as autotrophic markers (Yamada et al. 2003). Then, these fragments were combined by fusion-PCR using nested-adeA-R and hstD-A2 primers (Szewczyk et al. 2007). The amplified fragment was purified by a QIAquick PCR purification kit and used as a complementation cassette. A list of the primers used for these PCRs is shown in Table 1.6.3.

#### I.3.7 Construction of overexpression plasmids

The ORFs of *laeA* or *hstD/Aohst4* were amplified from genomic *A. oryzae* RIB40 with Fusion-laeA-F and Fusion-laeA-R or Fusion-hstD-F and Fusion-hstD-R, respectively. The resulting fragments were fused into *Sma*I-cut pUSA using an In-Fusion HD cloning kit (TAKARA) (Yamada et al. 2003). The *amyB* promoter of pUSA was used to drive the overexpression of *laeA* and *hstD/Aohst4*, respectively (Jin et al. 2011). The resulting plasmids, pUSlaeA and pUShstD, were linearized with one cut restriction enzyme of *BgI*II and *Eco*T22I on *laeA* or *hstD/Aohst4* ORF, respectively. The resulting linearized fragments were used as overexpression cassettes. A list of

primers used for these PCRs is shown in Table I.6.3.

#### I.3.8 Transformation of A. oryzae

Transformation of Α. oryzae strains was performed using the protoplast-polyethylene glycol method (Kitamoto 2002). To verify the disruption of the target gene, direct colony PCR was performed using primers (X-F and X-G; X-A and X-D), KOD-FX (TOYOBO), and a crude DNA sample of each transformant. Primers X-F and X-G were designed at the region of each target gene. The crude DNA sample was prepared as follows: conidia and hyphae from each transformant culture were suspended in 100 µl Buffer A [100 mM Tris-HCl (pH 9.5), 1 M KCl, 10 mM EDTA]. This mycelia suspension was vortexed vigorously and incubated at 95°C for 10 min. Immediately thereafter, this hot solution was vortexed vigorously and centrifuged at 5,000 rpm for 1 min. A total of 1 µl of supernatant was used as the crude DNA sample. A list of primers used for these assays is shown in Table I.6.3.

#### I.3.9 Time-lapse imaging

For time-lapse imaging, conidiophores were germinated in 1.5% agar N medium in 35 mm glass-bottom dishes. Cells were imaged using a real-time cultured cell monitoring system (ASTEC) controlled by CCM software. DIC images of each disruptant were taken every 20 min for approximately 84 h. All imaging was carried out at 30°C. Pictures and movies were edited with CCM software (ASTEC).

#### I.3.10 Secondary metabolite analysis

For the plate assay of kojic acid production, conidia suspensions of each strain

were point inoculated  $(1 \times 10^5 \text{ conidia})$  on the center of 2% agar KAS and KA medium containing 5 mM FeCl<sub>3</sub> and grown for 5 days at 30°C. KAS and KA medium were used for screening and genetic interaction analysis, respectively. Then, a red halo, which indicates the existence of kojic acid, was observed.

For the quantification of kojic acid, 20 ml of KA liquid medium inoculated with 200  $\mu$ l of 1 × 10<sup>8</sup> conidia /ml suspension was incubated at 30°C with shaking at 130 rpm. After cultivation for the appropriate period, mycelia were filtered by Miracloth (Merck), and then the filtrate was collected. Harvested mycelia were dried at 105°C for 1 h and weighed. The collected KA medium was filtered by MillexHV (Millipore), and then the kojic acid concentration was quantified by colorimetric methods.

#### **I.3.11 Microarray analysis**

The *A. oryzae* GeneChip (AoDNAChip; NCBI GEO platform GPL16184) was designed by Affymetrix to refer to the entire genome sequence of *A. oryzae*, and predicted ORFs are published at the Comparative fungal genome database (http://nribf2.nrib.go.jp/, *A. oryzae* RIB40 Ace33v2). The AoDNAchip covered 13,765 ORFs and 6143 promoters of *A. oryzae*. In the Chapter I, I performed transcriptome analysis using probes of 13,765 ORFs set on this microarray.

Total RNA using microarray analysis was purified by using an RNeasy mini kit (QIAGEN). RNA quality was determined by using a BioAnalyzer 2100 (Agilent Technology), and the quantity was determined by using an Ultrospec 3300 pro (Amersham Pharmacia Biotech). Fragmentated biotin labeled cRNA was prepared by using a GeneChip One-cycle Target Labeling and Control Reagent Kit (Affymetrix) according to manufacturer's instructions. The fragmentated cRNA was hybridized to an

AoDNAchip. Then, this GeneChip was washed, stained, and scanned by using a GeneChip Fluidics Station FS-450 (fluidics protocol FS450\_001) and a GeneChip Scanner 3000.

Scanned probe array images were converted into CEL files and normalized by using GCOS v.1.4 (Affymetrix). Calculations of signal intensity and detection p-values were also performed using GCOS v.1.4. The trimmed mean signal of the array was scaled to the target signal of 500 with the All Probe Sets scaling option. Detection call was used in detection of a particular transcript, with a detection p < 0.04 as present (P),  $0.04 \le p < 0.06$  as marginal (M), and  $0.06 \le p$  as absent (A). These calculation data were exported as CHP files. For microarray data analysis, CHP files were imported into GeneSpring7.3 (Agilent Technologies). Expression data were normalized per chip to the 50th percentile. In the Chapter I, I analyzed genes detected as P or M flags. Genes with statistically significant changes in transcript abundance were identified using a cutoff value of 2-fold and Welch's t-test value of less than 5%. FungiFun software was used for FunCat categorization (Priebe et al. 2011; Ruepp et al. 2004). Significantly enriched FunCat categories were extracted using FungiFun software (cut-off p < 0.05; the *p*-value indicates the significance of the number of hits for each category in the dataset taking the number of hits for the whole genome of A. oryzae as a background. The calculation is based on a two-tailed Fisher's exact test). The distribution of whole A. oryzae genes was indicated in Fig. I.6.8. and I.6.9, which was used as a reference of FunCat enrichment analysis. Two biological replicates were used for the microarray analysis. The microarray data have been deposited in NCBIs Gene Expression Omnibus (GEO, http://www.ncbi.nlm.nih.gov/geo/) and are accessible through GEO series accession number GSE41612.

#### **I.4 RESULTS**

#### I.4.1 Phylogeny and morphology of AoHDACs

A total of 11 HDACs (AoHDACs: *A. oryzae* histone deacetylases) were found in the *A. oryzae* genome based on BLAST analysis. I classified AoHDACs according to a previous phylogenetic study of HDACs. These AoHDACs were phylogenetically divided into class I to III HDACs, but the mammal-specific class IV HDACs were not found in the genome. Class III HDACs are generally described as sirtuin-type HDACs, and 6 AoHDACs belonged to this class. The AoSirtuins (*A. oryzae* sirtuins) were classified into classes I to III, but class IV sirtuins were not found in the genome. The class I sirtuins were further categorized into three sub-classes, including the fungal-specific HDACs of sirtuin sub-class C (Fig. I.6.1). I attempted to disrupt these 11 AoHDACs and succeeded for 10 of the AoHDACs. However, only heterokaryon transformants were obtained in the case of *hdaB/Aorpd3* over several trials (data not shown). This result suggests that *hdaB/Aorpd3* is essential in *A. oryzae*, but further experiments are required to confirm this hypothesis. Thus, in this report, the heterokaryon disruptant of *hdaB/Aorpd3* and AoHDACs disruptants were used for subsequent experiments.

I first observed the growth and conidia generation of AoHDAC disruptants and *hdaB/Aorpd3* heterokaryon transformants on the plate culture (Figs. I.6.1-5). Observation of the growth of AoHDACs disruptants revealed an obvious defect of  $\Delta hstD$  and  $\Delta hdaD$  in morphogenesis (Fig. I.6.2A). The conidial formation of these disruptants was significantly decreased and a slight growth effect was observed in plate cultivation (Fig. I.6.2B, C). I additionally observed the growth of AoHDACs disruptants and the *hdaB/Aorpd3* heterokaryon transformant in liquid culture (Fig. S2D). A growth

defect of  $\Delta h daD$  was observed in submerged cultivation (Fig. I.6.4D). Thus, h daD/Aohos2 is required for the growth integrity of *A. oryzae*. These two disruptants were further examined using time-lapse imaging for more detailed observation. As expected,  $\Delta h daD$  showed slow growth but exhibited more crowded aerial hyphae than the wild-type strain (Fig. I.6.4A). However, a few invasive hyphae were detected in the  $\Delta h stD$  strain but not in  $\Delta h daD$ . In this time-lapse imaging analysis, a significant defect of conidial development was also found in both  $\Delta h daD$  and  $\Delta h stD$  strains.

These results indicate that both *hdaD/Aohos2* and *hstD/Aohst4* play an important role in the growth and development of *A. oryzae*, especially in asexual development.

#### I.4.2 Fungal-specific sirtuin regulates SM production

I further examined SM production of AoHDAC disruptants and the *hdaB/Aorpd3* heterokaryon transformant using a plate assay for kojic acid productivity (Fig. I.6.3). High production of kojic acid was observed in  $\Delta hdaB$  and  $\Delta hstA$  (Fig. I.6.3), and significant overproduction was observed in  $\Delta hdaD$  and  $\Delta hstD$  (Fig. I.6.2A). I quantified the kojic acid production of these two HDACs disruptants, and the  $\Delta hstD$  strain showed a 200-fold increased productivity in a 7-day culture (Fig. I.6.2D). In contrast, the  $\Delta hdaD$  strain showed a 30-fold overproduction compared with the control strain (Fig. I.6.2D). The  $\Delta hstD$  strain started to produce kojic acid by 4 days in culture, while kojic acid was not detected in the wild-type strain.

I further analyzed kojic acid production at the gene expression level by examining three key genes in the kojic acid gene cluster (Terabayashi et al. 2010). Northern analysis of 4-day cultures showed extremely high expression of these genes in the  $\Delta hstD$  strain, but no expression was observed in the wild-type strain (Fig. I.6.2E). The kojA gene was also expressed in the  $\Delta hdaD$  strain, but the expression was not as high as in the  $\Delta hstD$  strain. This earlier and higher expression in both disruptants is consistent with the earlier and higher production of kojic acid.

These results indicate the importance of  $\Delta h daD$  and  $\Delta h stD$  in the regulation of kojic acid production. On the basis of phylogenetic classification, hstD/Aohst4 belongs to the fungal-specific class of sirtuins, and this protein is widely conserved in filamentous fungi (Frye 2000) (Fig I.6.6). Interestingly, nst3/Nchst4 is involved in the silencing mechanism of *N. crassa* (Smith et al. 2010). Moreover, the phenotype of  $\Delta hstD$  was reminiscent of the global use of HSTD/AOHST4 for the production of various SMs in *A. oryzae*.

In this context, I examined the regulation of penicillin biosynthesis in the  $\Delta hstD$ strain. As expected, a higher production of penicillin was found in the  $\Delta hstD$  strain, and a higher expression of the penicillin biosynthetic gene was confirmed (Fig. I.6.2F, G). Along with the morphogenetic defect and kojic acid production, these phenotypes were rescued by the complementation of hstD/Aohst4 (Fig. I.6.5).

These results suggest that *hstD/Aohst4* is required for the global regulation of SMs biosynthesis. Thus, I examined  $\Delta hstD$  by microarray analysis to investigate the expression of other SM-related genes. The expression of 388 genes were significantly affected by *hstD/Aohst4* deletion (absolute fold change >2, p < 0.05) (Table I.6.4). These genes were spread across the whole genome; 299 of 388 genes were up-regulated in the  $\Delta hstD$  strain. To reveal the functional distribution of *hstD/Aohst4* affected genes, FunCat enrichment analysis was carried out using FungiFun software (Priebe et al.

2011; Ruepp et al. 2004) (Fig. I.6.7). The "C-compound and carbohydrate metabolism" and "Secondary metabolism" categories were significantly enriched in down-regulated genes. Most of the genes categorized as "Secondary metabolism" overlapped with "C-compound and carbohydrate metabolism" categorized genes. Genes categorized as "C-compound and carbohydrate metabolism" were mainly related to polysaccharide degradation or glycolysis. This result suggested that carbon source degradation related genes were down-regulated in the  $\Delta hstD$  strain. "Secondary metabolism" and "detoxification" categories were significantly enriched in genes up-regulated by hstD deletion. Genes categorized "Secondary metabolism" and "detoxification" were mainly constituted by cytochrome P450 (CYP) genes. Interestingly, three non-ribosomal peptide synthetases (NRPS) and one polyketide synthase (PKS) were also up-regulated in the  $\Delta hstD$  strain. One of three NRPSs encoded wykN (AO080501000008), which is involved in WYK-1 production in A. oryzae (Imamura et al. 2012). PKS and NRPS enzymes generate the general structural scaffolds of most secondary metabolites (Brakhage 2013). Additionally, fungal CYPs have PKS and NRPS associated functions, and generate structural variation of fungal SMs. Thus, hstD/Aohst4 affects many kinds of SM production (at least 6 different SM genes clusters) (Kelly et al. 2009; Podust and Sherman 2012).

#### I.4.3 *hstD/Aohst4* regulates the expression of *laeA*

The LAEA complex coordinates the development and SM biosynthesis in *A. nidulans*, and is conserved in numerous fungal genomes (Bayram and Braus 2012). Recently, it was reported that deleting *laeA* diminishes kojic acid production and gene expression in *A. oryzae* (Oda et al. 2011). Additionally, penicillin production in *A.* 

oryzae is diminished after deletion of veA, which is a member of the LAEA complex (Bayram and Braus 2012; Marui et al. 2010). These reports suggest that the LAEA complex also plays a general role in the induction of the SM genes cluster in A. oryzae. Thus, the SM overproduction phenotype of the hstD/Aohst4 disruptant should be associated with the LAEA complex, and HSTD/AoHST4 may play a role under the control of LAEA. According to this hypothesis, the expression of *laeA* should not be altered in the hstD/Aohst4 disruptant. Thus, I examined the expression of *laeA* in the hstD/Aohst4 disruptant. Surprisingly, *laeA* was highly expressed in the hstD/Aohst4 disruptant, even in the 4-day culture, but remained unexpressed in the wild-type strain (Fig. 1.6.10A). This result suggests that HSTD/AoHST4 is involved in *laeA* gene repression. Thus, both SM overproduction phenotypes and the altered morphological phenotype of the  $\Delta hstD$  strain are caused by the high expression of *laeA*.

#### I.4.4 Genetic interaction of hstD/Aohst4 and laeA

To confirm the above hypothesis, I prepared a  $\Delta laeA$  strain and a  $\Delta hstD\Delta laeA$ double disruptant, and then examined the SM production and conidial development. At first, these strains exhibited the phenotype of the  $\Delta laeA$  strain, including a lack of kojic acid production (Fig. I.6.10A), similar to previous reports (Oda et al. 2011). The production of penicillin and conidial development was also lost in the  $\Delta laeA$  strain (Fig. I.6.10B, C). Next, I observed the effect of *laeA* disruption in the  $\Delta hstD$  background and found that the SM overproduction phenotype of  $\Delta hstD$  was abolished by *laeA* disruption (Fig. I.6.10B, D). I further observed conidial development in the double disruptant, which exhibited a  $\Delta laeA$ -like fluffy phenotype (Fig. 1.6.10B, C). These results clearly indicate a genetic interaction between *hstD/Aohst4* and *laeA* and that HSTD/AoHST4 plays a role upstream of *laeA*.

To confirm this epistatic relationship, I examined the effect of laeA and hstD/Aohst4 overexpression using amyB promoter, respectively. The *laeA*-overexpressed strain exhibited *AhstD*-like phenotypes such as SM overproduction and low conidial formation (Fig. I.6.11). The effects of laeA overexpression were also observed in the *AhstD* background (Fig. I.6.11). Additionally, both the *OE::laeA* strain and  $\Delta hst D$  OE:: laeA strain showed high expression of laeA, kojA, and ipnA, respectively (Fig. I.6.12). These results indicated that laeA is downstream of hstD/Aohst4. Therefore, I overexpressed hstD/Aohst4 in a laeA disruption background. As expected, the overexpression of hstD/Aohst4 resulted in a AlaeA-like phenotype, such as no SM production and a fluffy morphology, in the *AlaeA* background (Fig. I.6.12). Overexpression of hstD/Aohst4 in the wild-type laeA background had no measurable effect on SM production and development (Fig. I.6.12.).

From these results, I suggest that the fungal-specific sirtuin HSTD/AoHST4 controls SM production and fungal development through the regulation of *laeA* gene expression (Fig. I.6.13).

30

#### **I.5 DISCUSSION**

In the past decade, the importance of the role of classical HDACs in filamentous fungi in the regulation of some fungal phenotypes has been revealed (Brosch et al. 2008). For example, *F. graminearum hdf1/fghos2* is important for conidial development and SM production (Li et al. 2010). In the Chapter I, I also determined the importance of *hdaD/Aohos2* in the regulation of hyphal growth, conidiation, and SM production. Compared with the study of classical HDACs, only a few reports have been published for sirtuin-type HDACs in filamentous fungi (Shimizu et al. 2012; Smith et al. 2010). Recently, the *A. nidulans sirA/Ansir2*, which is a homolog of yeast *sir2* and mammalian *sirt1*, was reported to function in secondary metabolism regulation, but no effects on growth, conidiation, and morphogenesis were reported (Shimizu et al. 2012).

The fungal-specific putative methytransferase 'LAEA' coordinates fungal development and SMs in several filamentous fungi (Bayram and Braus 2012). Previously, it was reported that kojic acid production is regulated by LAEA, but I found that *laeA* coordinates both SM production and conidial development (Oda et al. 2011). In general, the production of fungal SMs is coordinated with fungal development, and the LAEA complex coordinates these (Bayram and Braus 2012). In higher eukaryotes, sirtuin affects various physiological functions, such as differentiation, metabolism, and the stress response (Horio et al. 2011; Imai and Guarente 2010; Zhang and Kraus 2010). In the Chapter I, I found that the fungal-specific sirtuin HSTD/AoHST4 affects both fungal development and SM production. Furthermore, the epistatic study revealed that HSTD/AoHST4 is involved in the coordination of fungal development and SM production via *laeA* expression. These results indicate that HSTD/AoHST4 plays a *sirt1*-like central role that coordinates the developmental state and metabolism in

filamentous fungi.

The yeast HST4, which is a homolog of *A. oryzae*'s *hstD/Aohst4*, is a NAD<sup>+</sup>-dependent histone H3K56 deacetylase (Yang et al. 2008). In the northern analysis, deletion of *hstD/Aohst4* affected the gene expression level of *laeA*. Therefore, HSTD/AoHSTD may be involved in the epigenetic regulation of *laeA* gene expression. However, the overexpression of *hstD/Aohst4* did not affect SM production and conidial development. In general, histone acetyltransferase (HAT) is required for gene activation of silenced genes. In budding yeast, it has been reported that the fungal-specific HAT of RTT109 catalyzes H3K56 acetylation and restores the silencing defects of the *Ahst3Δhst4* mutant (D'Arcy and Luger 2011; Yang et al. 2008). I found one *rtt109* homologue of AO090020000581 (*Aortt109*) in the *A. oryzae* genome. This suggests that AoRTT109 is required for the expression of the silenced *laeA* by H3K56 deacetylation and overcomes even *hstD/Aohst4* overexpression. In this context, I will investigate histone H3K56 acetylation of the *laeA* locus and the effect of *Aortt109* on the acetylation and expression of *laeA* in future studies.

In the overexpression analysis of *laeA*, several different phenotypes of kojic acid production were observed compared with the *hstD/Aohst4* mutant. The  $\Delta hstD$  strain showed high kojic acid production in a 4-day liquid culture while the same phenotype was not observed in the *OE::laeA* strain. Compared with the *OE::laeA* strain, interestingly, higher kojic acid production and higher expression of *kojA*, *ipnA*, and *laeA* were observed in the  $\Delta hstD$  *OE::laeA* strain. These results suggested that HSTD/AoHST4 has some LAEA-independent role in the regulation of SM production.

I developed a model of the regulatory system of HSTD/AoHST4 (Fig. I.6.13). The expression of *hstD/Aohst4* may be induced or suppressed by unknown signals. As

described above, an unknown factor like AoRTT109 may compete with HSTD/AoHST4 activity in *hstD/Aohst4*-inducing conditions. In the *hstD/Aohst4* suppressed condition, *laeA* expression was induced. This in turn led to conidiation and secondary metabolism production being induced. However, it is possible that HSTD/AoHST4 directly regulates fungal development and secondary metabolism independent of *laeA*.

The *hstD/Aohst4* gene is fungal-specific but is conserved in the vast family of filamentous fungi (Fig. I.6.6). Furthermore, this gene plays a role in the coordination of fungal development and SM production. These results indicate that *hstD/Aohst4* has great potential as a target to improve the productivity of useful SMs. It is also important in the development of an attractive host for the production of several heterogeneous metabolites.

#### **I.6 FIGURES AND TABLES**



Figure I.6.1. Phylogenetic analysis of histone deacetylase in A. oryzae.

Accession numbers and HDAC names are indicated for each branch. HDAC names of *S. cerevisiae* or *H. sapiens* with the species name indicated followed by a slash. The numbers at the nodes are bootstrap values obtained from 1000 replicates and are indicated as percentages. The scale bar indicates a distance corresponding to 0.2 amino acid substitutions per site. The class or sub-class of HDACs is shown on the right. These classes of HDACs are referred to in previous phylogenetic studies (Ekwall 2005; Frye 2000; Yang and Seto 2008). AoHDACs are indicated by underlines. Abbreviations of AoHDACs gene names are as follows: Hda, Histone deacetylase; Hst, Homolog of sirtuin. The class to which *hstD* belongs is surrounded by a grey border. The gene names and their accession numbers are identified in Table I.6.2. Sc, *Saccharomyces cerevisiae*; An, *Aspergillus nidulans*; Nc, *Neurospora crassa*; Hs, *Homo sapiens*; Ao, *Aspergillus oryzae*.



Figure I.6.2. *hstD/Aohst4* and *hdaD/Aohda1* regulate SM production and development.

(A) The panels for MM and KA show the morphological phenotype and kojic acid production plate assay of the indicated strain, respectively. (B, C) Radial growth and conidiation on MM of the indicated strains. (D) Time-course characteristics of kojic acid production of the indicated disruptants. (E) Expression profiles of kojic acid cluster genes represented by northern hybridization. The culture times of the indicated strains are shown at the top of the panel. The analyzed gene is indicated on the left side of each blot. *rRNA* is shown as the loading control. (F) Penicillin production bioassay of the *AhstD* strain. *rRNA* is shown as the loading control. The *adeA*<sup>+</sup> strain was used as a control in this figure. All data are represented as means  $\pm$  s.d. (n=3); \**p* < 0.01, t-test.



Figure I.6.3. Kojic acid production and developmental phenotype of AoHDACs disruptants and a heterokaryon strain.

MM and KA show the morphological phenotype and kojic acid production plate assays of the indicated strains, respectively.


Figure I.6.4. Phenotypic analysis of AoHDACs disruptants and a heterokaryon strain on plates and submerged cultures.

(A) Time-lapse microscopic analysis of  $\Delta hstD$  and  $\Delta hdaD$ . The pictures were taken at 36, 48, and 84 hr of incubation (black scale bar, 200mm; red scale bar, 500mm). (B-D) Quantification of colony diameter, conidiation rate and mycelial dry cell weight of AoHDACs disruptants or a heterokaryon strain, respectively. The colony diameter and conidiation rate were measured on plate cultures. Dry cell weight was measured on submerged cultures. All data represented as mean ±s.d. (n=3); \*p< 0.01 t-test.



Figure I.6.5. Complementation analysis of hstD/Aohst4.

(A) Analysis of the morphology and SM production of the  $\Delta hstD$  and  $hstD^+$  strains. The panel for MM shows the morphological phenotype of the indicated strain, and the close-up stereomicroscopic images of the strains on MM are shown in adjoining panels (scale bar, 500 µm). Red arrows indicate examples of conidia. The panels for KA and PEN show the plate assay or bioassay of kojic acid and penicillin, respectively. (B, C) Quantification of colony diameter and conidiation rate of  $\Delta hstD$  and  $hstD^+$  strains. (D) Expression profiles of the kojic acid cluster genes were determined by northern hybridization. The culture time of the indicated strain is shown at the top of the panel. The analyzed gene is indicated on the left side of each blot. *rRNA* is shown as the loading control. (E) Quantification of kojic acid production. The *adeA*<sup>+</sup>*sC*<sup>+</sup> strain was used as the control, and the  $\Delta hstDsC^+$  strain represents  $\Delta hstD$  in this figure. All data are represented as means ± s.d. (n=3); \**p* < 0.01, t-test.



0.1

#### Figure I.6.6. Phylogenetic analysis of hstD in filamentous fungi.

The Genebank accession number and species name was indicated each blanches. The number at the nodes is bootstrap values obtained from 1000 and indicated percentage replicates. The scale bar indicates a distance corresponding to 0.1 amino acid substitutions per site. Each class of ascomycetes are shown in the right. The *sirt1* is used us out group of this phylogenetic analysis.



Figure I.6.7. Enrichment analysis of the FunCat categorization of the microarray analysis.

Significantly enriched FunCat level 1 and level 2 categories of genes up-regulated (A, B) or down-regulated (C, D) by *hstD/Aohst4* deletion, respectively. The Functional Catalogue (FunCat) is the organism independent functional description of proteins (Ruepp et al. 2004). FunCat consists of 28 main functional categories (level 1). The level 1 is the most general one, whereas level 2 shows much more detail. The percentage indicated for each category contributes to total mapping. Insignificant FunCat categories are indicated as insignificant in the pie-charts. Significantly enriched categories were extracted by FungiFun software (cut-off p < 0.05, Fisher's exact test) (Priebe et al. 2011). Details of the enrichment analysis are available at the FungiFun website (https://sbi.hki-jena.de/FungiFun/FungiFunHelp.html).





The circular chart indicates the whole genome distribution of indicated categories FunCat level 2. Miner categories (Whole genome distribution < 1%) were indicated as other in pie chart. Percentage indicated each category contributes to total mapping. The data of FunCat categorization of all genes of *A.oryzae* were imported from FungiFun software (https://sbi.hki-jena.de/FungiFun/FungiFun.cgi). Details of each category were available at FunCat Databases (http://mips.helmholtzmuenchen.de/proj/funcatDB/search\_main\_frame.html). This data was referance of FunCat level 2 enrichment analysis of *A. oryzae*.





The circular chart indicates the whole genome distribution of indicated categories FunCat level 2. Miner categories (Whole genome distribution < 1%) were indicated as other in pie chart. Percentage indicated each category contributes to total mapping. The data of FunCat categorization of all genes of *A.oryzae* were imported from FungiFun software (https://sbi.hki-jena.de/FungiFun/FungiFun.cgi). Details of each category were available at FunCat Databases (http://mips.helmholtzmuenchen.de/proj/funcatDB/search\_main\_frame.html). This data was referance of FunCat level 2 enrichment analysis of *A. oryzae*.





(A) Expression profile of *laeA* in the KA-producing condition. The *adeA*<sup>+</sup> strain was used as a control. The culture time of the indicated strain is shown at the top of the panel. *rRNA* is shown as the loading control. (B) Analysis of morphology and SM production of the  $\Delta hstD$ ,  $\Delta laeA$ , and  $\Delta hstD\Delta laeA$  strains. The panel for MM shows the morphological phenotype of the indicated strain, and the close-up stereomicroscopic images of the strains on MM are shown in adjoining panels (scale bar, 500 µm). Red arrows indicate examples of conidia. The panels for KA and PEN show the plate assay or bioassay of kojic acid and penicillin, respectively. (C, D) Quantification of the conidiation rate and kojic acid production of the  $\Delta hstD$ ,  $\Delta laeA$ , and  $\Delta hstD\Delta laeA$  strains. Except for panel (A) the  $adeA^+sC^+$  strain was used as the control, and the  $\Delta hstD sC^+$  and  $\Delta laeA sC^+$  strains represent  $\Delta hstD$  and  $\Delta laeA$  in this figure, respectively. All data are represented as means  $\pm$  s.d. (n=3); \*p < 0.01, t-test.



# Figure I.6.11. Epistatic relationship between *hstD/Aohst4* and *laeA*.

(A) Analysis of the morphology and SM production of the  $\Delta hstD$  OE::laeA and  $\Delta laeA$  OE::hstD strains. The MM panel shows the morphological phenotype of the indicated strain, and the close-up stereomicroscopic images of the strains on MM are shown in the adjoining panels (scale bar, 500 µm). Red arrows indicate examples of conidia. The panels for KA and PEN show the plate assay or bioassay of kojic acid and penicillin, respectively. (**B**, **C**) Quantification of the conidiation rate and kojic acid production of the  $\Delta hstD$  OE::laeA and  $\Delta laeA$  OE::hstD strains. The  $adeA^+$  pUSA<sup>+</sup> strain was used as the control, and  $\Delta hstD$  pUSA<sup>+</sup>, OE::laeA adeA<sup>+</sup>,  $\Delta laeA$  pUSA<sup>+</sup>, and OE::hstD adeA<sup>+</sup> strains represent  $\Delta hstD$ , OE::laeA,  $\Delta laeA$ , and OE::hstD in this figure, respectively. The amyB promoter was used to drive overexpression of laeA and hstD/Aohst4. All data are represented as means  $\pm$  s.d. (n=3); \*p < 0.01, t-test.



# Figure I.6.12. Expression profiling of *laeA*, *kojA*, and *ipnA* in *OE::laeA* and $\Delta hstD$ *OE::laeA* strains, respectively.

(A) Northern hybridization of *laeA* and *kojA*, respectively. The culture time of the indicated strain is shown at the top of the panel. *rRNA* is shown as the loading control. The analyzed gene is indicated on the left side of each blot. (B) Northern hybridization of the penicillin biosynthetic gene *ipnA*. *rRNA* is shown as the loading control. The  $adeA^+ pUSA^+$  strain was used as the control, and the *OE::laeA adeA^+* strain represents *OE::laeA* in this figure.



Figure I.6.13. Schematic model of the regulation of SM production and development by *hstD/Aohst4* through *laeA*.

An unknown signal induces or suppresses the function of HSTD/AoHST4. Suppression of *hstD/Aohst4* leads to expression of *laeA*. This activation stimulates fungal development and SM production. However, there is the possibility of an *hstD/Aohst4* competitive mechanism by an unknown factor (described as FactorX in this figure). SM production: secondary metabolite production.

Table I.6.1. Strains used in the Chapter I

| Name                        | Parental strain  | Genotype <sup>b</sup>   | Reference            |
|-----------------------------|------------------|---|----------------------|
| RIB40                       |                  | wild type   | NRIB <sup>a</sup>    |
| $NSR-\Delta LD2$            | RIB40            | niaD <sup>*</sup> sC <sup>*</sup> adeA <sup>*</sup> argB::adeA <sup>*</sup> ∆ligD::argB   | Maruyama et al. 2008 |
| $adeA$ $^+$                 | NSR-ALD2         | niaD <sup>*</sup> sC <sup>*</sup> adeA <sup>*</sup> argB::adeA <sup>*</sup> <i>AligD::argB</i> adeA <sup>+</sup>  | this study           |
| pUSA +                      | NSR-ALD2         | niaD <sup>*</sup> sC <sup>*</sup> adeA <sup>*</sup> argB::adeA <sup>*</sup> <i>AligD::argB</i> pUSA <sup>+</sup>  | this study           |
| $adeA^+sC^+$                | $adeA$ $^+$      | $niaD^{+}sC^{+}adeA^{+}argB::adeA^{+}\Delta ligD::argBadeA^{+}AnsC^{+}$   | this study           |
| adeA $^+$ pUSA $^+$         | $adeA$ $^+$      | nia $D^+$ s $C^-$ ade $A^+$ arg $B$ ::ade $A^+$ $\Delta$ lig $D$ ::arg $B$ ade $A^+$ pUS $A^+$  | this study           |
| hdaB ht <sup>c</sup>        | NSR-ALD2         | niaD <sup>*</sup> sC <sup>*</sup> adeA <sup>*</sup> argB::adeA <sup>*</sup> AligD::argB AhdaB::adeA hdaB  | this study           |
| $\Delta h da C$             | NSR-ALD2         | niaD <sup>*</sup> sC <sup>*</sup> adeA <sup>*</sup> argB::adeA <sup>*</sup> <i>AligD::argB AhdaC::adeA</i>  | this study           |
| ∆hdaD                       | NSR-ALD2         | niaD <sup>*</sup> sC <sup>*</sup> adeA <sup>*</sup> argB::adeA <sup>*</sup> AligD::argB AhdaD::adeA   | this study           |
| $\Delta h da A$             | NSR-ALD2         | niaD <sup>-</sup> sC <sup>-</sup> adeA <sup>-</sup> argB::adeA <sup>-</sup> <i>AligD::argB AhdaA::adeA</i>  | this study           |
| $\Delta h da E$             | NSR-ALD2         | niaD <sup>*</sup> sC <sup>*</sup> adeA <sup>*</sup> argB::adeA <sup>*</sup> <i>AligD::argB AhdaE::adeA</i>  | this study           |
| $\Delta hstA$               | NSR-ALD2         | niaD <sup>-</sup> sC <sup>-</sup> adeA <sup>-</sup> argB::adeA <sup>-</sup> <i>AligD::argB AhstA::adeA</i>  | this study           |
| $\Delta hst B$              | NSR-ALD2         | niaD <sup>*</sup> sC <sup>*</sup> adeA <sup>*</sup> argB::adeA <sup>*</sup> <i>AligD::argB AhstB::adeA</i>  | this study           |
| $\Delta hstC$               | NSR-ALD2         | niaD <sup>*</sup> sC <sup>*</sup> adeA <sup>*</sup> argB::adeA <sup>*</sup> <i>AligD::argB AhstC::adeA</i>  | this study           |
| ∆hstD                       | NSR-ALD2         | niaD <sup>*</sup> sC <sup>*</sup> adeA <sup>*</sup> argB::adeA <sup>*</sup> <i>AligD::argB AhstD::adeA</i>  | this study           |
| $\Delta hstE$               | NSR-ALD2         | niaD <sup>*</sup> sC <sup>*</sup> adeA <sup>*</sup> argB::adeA <sup>*</sup> <i>AligD::argB AhstE::adeA</i>  | this study           |
| $\Delta hstF$               | NSR-ALD2         | niaD <sup>*</sup> sC <sup>*</sup> adeA <sup>*</sup> argB::adeA <sup>*</sup> <i>AligD::argB AhstF::adeA</i>  | this study           |
| ∆laeA                       | NSR-ALD2         | niaD <sup>*</sup> sC <sup>*</sup> adeA <sup>*</sup> argB::adeA <sup>*</sup> ∆ligD::argB ∆laeA::adeA   | this study           |
| $\Delta hst D sC^+$         | ∆hstD            | $niaD^{+}sC^{+}adeA^{+}argB::adeA^{+}\Delta ligD::argB\Delta hstD::adeAAnsC^{+}$  | this study           |
| $\Delta hstD  pUSA^+$       | ∆hstD            | niaD <sup>*</sup> sC <sup>*</sup> adeA <sup>*</sup> argB::adeA <sup>*</sup> <i>AligD::argB AhstD::adeA</i> pUSA <sup>+</sup>  | this study           |
| ∆hstD OE::laeA              | ∆hstD            | $niaD^{-}sC^{-}adeA^{-}argB::adeA^{-}\Delta ligD::argB\Delta hstD::adeApUSlaeA^{+}$   | this study           |
| $\Delta laeA \ sC^+$        | ∆laeA            | nia $D^*$ s $C^*$ ade $A^*$ arg $B$ ::ade $A^*$ $\Delta$ lig $D$ ::arg $B$ $\Delta$ lae $A$ ::ade $A$ Ans $C^+$   | this study           |
| $\Delta$ lae $A$ pUSA $^+$  | ∆laeA            | nia $D^{+}$ s $C^{+}$ ade $A^{+}$ arg $B$ ::ade $A^{+}$ $\Delta$ lig $D$ ::arg $B$ $\Delta$ lae $A$ ::ade $A$ pUS $A^{+}$   | this study           |
| ∆laeA OE::hstD              | ∆laeA            | $niaD^{+}sC^{-}adeA^{+}argB::adeA^{+}\Delta ligD::argB\Delta laeA::adeApUShstD^{+}$   | this study           |
| OE::laeA                    | NSR-ALD2         | niaD <sup>*</sup> sC <sup>*</sup> adeA <sup>*</sup> argB::adeA <sup>*</sup> $\Delta$ ligD::argB pUSlaeA <sup>+</sup>  | this study           |
| OE::hstD                    | $NSR-\Delta LD2$ | niaD <sup>*</sup> sC <sup>*</sup> adeA <sup>*</sup> argB::adeA <sup>*</sup> <i>AligD</i> ::argB pUShstD <sup>+</sup>  | this study           |
| $\Delta hst D \Delta lae A$ | $\Delta hstD$    | $\textit{niaD}^{-}sC^{-}\textit{adeA}^{-}\textit{argB}::\textit{adeA}^{-}\textit{\Delta}\textit{ligD}::\textit{argB}\textit{\Delta}\textit{hstD}::\textit{adeA}\textit{\Delta}\textit{laeA}::\textit{AnsC}$ | this study           |
| hstD <sup>+</sup>           | ∆hstD            | $niaD^{+}sC^{+}adeA^{+}argB::adeA^{+}\Delta ligD::argB\Delta hstD::adeA::hstD::AnsC$  | this study           |
| OE::laeA adeA +             | OE::laeA         | niaD $^{\circ}$ sC $^{\circ}$ adeA $^{\circ}$ argB::adeA $^{\circ}$ $\Delta$ ligD::argB $$ pUSlaeA $^{+}$ adeA $^{+}$   | this study           |
| OE::hstD adeA +             | OE::hstD         | niaD <sup>-</sup> sC <sup>-</sup> adeA <sup>-</sup> argB::adeA <sup>-</sup> $\Delta$ ligD::argB pUShstD <sup>+</sup> adeA <sup>+</sup>  | this study           |

<sup>a</sup>National Research institute of Brewing

<sup>b</sup>AnsC: Aspergillus nidulans sC

<sup>c</sup>ht: heterokaryon

| Sacchar   | omyces cerviciae  | Homo se  | apience   | Neurosp  | ora crassa                       | Aspergillus                         | nidulans          | Aspergi                          | llus oryzae                      |
|---|---|--|---|--|----------------------------------|-------------------------------------|-------------------|----------------------------------|----------------------------------|
| Gene <sup>a</sup>   | Accession number  | Gene <sup>a</sup>                                  | Accession number  | Gene <sup>ª</sup>                                  | Accession number                 | Gene <sup>a</sup>                   | Accession number  | Gene <sup>a</sup>                | Accession number                 |
| Classical<br>rpd3   | l HDACs familly<br>YNL330C                                      | hdac1 / Hsrpd3<br>hdac2 / Hsrpd3<br>hdac3 / Hsrpd3 | NP_004955<br>NP_001518<br>NP_003874   | hda3 / Ncrpd3                                      | NCU00824                         | rpdA / Anrpd3                       | AN4493            | hdaB / Aorpd3<br>hdaC / Aorpd3   | AB744040<br>AO080525000127       |
| hos2  | YGL194C   |  |   | hda2 / Nchos2                                      | NCU02795                         | hosA / Anhos2                       | AN3806            | hdaD / Aohos2                    | A0080511000459                   |
| hosl  | YPR068C   |  |   |  |                                  |                                     |                   |                                  |                                  |
| hda I   | YRL021W   | hdac6 / Hshda1<br>hdac10 / Hshda1                  | NP_006035<br>NP_114408  | hda1 / Nchda1                                      | NCU01525                         | hdaA / Anhda l                      | AN8024            | hdaA / Aohda I                   | A0080513000236                   |
| hos3  | YPLI16W   | hdac4<br>hdac5<br>hdac7<br>hdac8<br>hdac8          | NP_006028<br>NP_001015053<br>NP_056216<br>NP_066956<br>NP_055522<br>NP_055522 | hda4 / Nchos3                                      | NCU07018                         | hosB / Anhos3                       | AN7019            | hdaE / Aohos3                    | A008057000061                    |
| TheSirtu  | iin familly   | liddel 1   | CU16/0_JN   |  |                                  |                                     |                   |                                  |                                  |
| sir2  | YDL042C   | sirt1 / Hssir2                                     | NP_036370   | nst1 / Ncsir2                                      | NCU04737                         | sirA / Ansir2                       | AN10449           | hstA / Aosir2                    | A0080506000102                   |
| hstl  | YOL068C   |  |   |  |                                  |                                     |                   |                                  |                                  |
| hst2  | YPL015C   | sirt2 / Hshst2<br>sirt3 / Hshst2                   | NP_036369<br>NP_036371  | nst2 / Nchst2                                      | NCU00523                         | AN7461/Anhst2<br>AN11873/Anhst2     | AN7461<br>AN11873 | hstB / Aohst2<br>hstC / Aohst2   | AO08056900094<br>AO080508000293  |
| hst3  | YOR025W   |  |   | nst4 / Nchst3                                      | NCU04859                         |                                     |                   |                                  |                                  |
| hst4  | YDR191W   |  |   | nst3 / Nchst4                                      | NCU03059                         | AN1226 / Anhst4                     | AN1226            | hstD / Aohst4                    | AB744041                         |
|   |   | sirt4<br>sirt5<br>sirt6<br>sirt7                   | NP_036372<br>NP_036373<br>NP_057623<br>NP_057622                              | nst5 / Ncsirt4<br>nst6 / Ncsirt5<br>nst7 / Ncsirt6 | NCU00203<br>NCU05973<br>NCU07624 | hst4 / Ansirt4<br>ANI 782 / Ansirt5 | AN11067<br>AN1782 | hstE / Aosirt4<br>hstF / Aosirt5 | A0080559000113<br>A0080568000195 |
| <sup>a</sup> HDAC (<br><sup>b</sup> Hda : <u>H</u><br><sup>c</sup> Hst : Ho | of Saccharomyces cu<br>jistone DeAcetylase<br>molog of SirTuins | erevisiae or Homo Sa                               | upiens with the speci   | ies name indicated                                 | followed by a slash.             |                                     |                   |                                  |                                  |
| 1011  |   |  |   |  |                                  |                                     |                   |                                  |                                  |

Table 1.6.2. List of sequence accession numbers used in the Chapter I

#### Table I.6.3. PCR primers used in the Chapter I

| Defense  | o (n n n h   | D                                |
|----------|--|----------------------------------|
| adeA_F   | Sequence(5' to 3')""                                   | Region or purpose                |
| adeA-P   | CTGCGCAACAGCATACGAGTCCACAG                             | adeA amplification               |
| hdaB-A   | CAATGGCATGACAAAGAACC                                   |                                  |
| hdaB-B   | CTGACCTATCTTCCTGGACATGACGGCTGTTCCTGCAACATGAGATACA      | 5' flanking region of hdaB       |
| hdaB-C   | CTGTGGACTCGTATGCTGTTGCGCAGAAGATCCGTGCGCAAGTT           |                                  |
| hdaB-D   | CCATGGTGAATTAGGGCTCA                                   | 3'flanking region of hdaB        |
| hdaB-A2  | CAATAGAATATTCCCCGCGT                                   |                                  |
| hdaB-D2  | CCCTTGGGATTAGAGTGCTT                                   | fusion PCR for <i>hdaB</i>       |
| hdaB-F   | GTTGATCGGGATGTCAAAGG                                   |                                  |
| hdaB-G   | AATTCTCGGTTCTGCTGGTG                                   | hdaB ORF                         |
| hdaC-A   | TCTGTGCAAGCCTTATGTGC                                   |                                  |
| hdaC-B   | CTGACCTATCTTCCTGGACATGACGGTCCGTCGAGGTTAGTGACAA         | 5' flanking region of hdaC       |
| hdaC-C   | CTGTGGACTCGTATGCTGTTGCGCAGTCACTTTGACTACGGAGGGCT        | 210 anhing region of hdgC        |
| hdaC-D   | GCCTCGAAATCATGGTCCTA                                   | 3 flanking region of naaC        |
| hdaC-F   | TGAGTGCCTCGTAATGCTTG                                   | hdaC OPE                         |
| hdaC-G   | GTGGGCAGGTTGAAACTCTT                                   | nuue orr                         |
| hdaD-A   | TAACTGGCGCAGACCCATAA                                   | 5' flanking region of hdaD       |
| hdaD-B   | CTGACCTATCTTCCTGGACATGACGGCCCTTCTTCTCTTTCCTTATTGC      | 5 marking region of nuub         |
| hdaD-C   | CTGTGGACTCGTATGCTGTTGCGCAGCTGTACGGTAAATGAAGGTCAGC      | 3'flanking region of hdaD        |
| hdaD-D   | AAGGGGTCAGATCCACAATG                                   | 5 hunding region of hude         |
| hdaD-A2  | CGCAGACCCATAAGAAGGAA                                   | fusion PCR for hdaD              |
| hdaD-D2  | CTGTGTCCACAACTGCCATT                                   |                                  |
| hdaD-F   | GTTGTTTGGTCAGCGTCAGA                                   | hdaD ORF                         |
| hdaD-G   | CCCAAAGGTGACAAGACGAT                                   |                                  |
| hdaA-A   | AACAAAGTGCCCTGTTGACC                                   | 5'flanking region of hdaA        |
| hdaA-B   | CTGACCTATCTTCCTGGACATGACGGCATTGCTATGGCTAGCACCA         | 0 0                              |
| hdaA-C   | CIGIGGACICGIAIGCIGIIGCGCAGITIAGGACGIICAGAIGGGG         | 3'flanking region of hdaA        |
| hdaA-D   |  |                                  |
| hdaA-F   | GIGAIGUCIAIIGUAUAGGA                                   | hdaA ORF                         |
| hdaE A   |  |                                  |
| ndae-A   |  | 5' flanking region of hdaE       |
| hdaE-C   |  |                                  |
| hdaE-D   | AGATCCGGAGTCGTTCCTTT                                   | 3'flanking region of hdaE        |
| hdaE-A2  | AGTCTCTTTTCTTTGGCCGC                                   |                                  |
| hdaE-D2  | ATTGTTCACGTTCTCCACCC                                   | fusion PCR for hdaE              |
| hdaE-F   | GGACCTTTACGCATCCAAGT                                   |                                  |
| hdaE-G   | GATGCGTGTTGGACATTAGC                                   | hdaE ORF                         |
| hstA-A   | ATTACCTGGCGTTCTTGTGG                                   |                                  |
| hstA-B   | CTGACCTATCTTCCTGGACATGACGGGGGTTCTTGTTTGGAGGGTT         | 5'flanking region of hst A       |
| hstA-C   | CTGTGGACTCGTATGCTGTTGCGCAGCGGATTCTTCAACGAAGAGC         |                                  |
| hstA-D   | ACAGCTGCGAACTGATGATG                                   | 3'flanking region of hstA        |
| hstA-F   | GATTTCCGGCTCTTGTGTGT                                   | had ODE                          |
| hstA-G   | GGTATTCCCGATTTTCGGTC                                   | Insta ORF                        |
| hstB-A   | CTTTGCTTTGAGTTCCTGCC                                   | 5'flanking racion of hetP        |
| hstB-B   | CTGACCTATCTTCCTGGACATGACGGTCTAACCTGGCGGAGAGAAA         | 5 manking region of <i>hstb</i>  |
| hstB-C   | CTGTGGACTCGTATGCTGTTGCGCAGTACCGCGAAAAGGAGAGAGA         | 3'flanking region of $hst B$     |
| hstB-D   | AACAGTCGGCGATGTATTCC                                   | 5 Hanking region of hstb         |
| hstB-F   | CTTTTTCAGGGAGAATCCGC                                   | hstB ORF                         |
| hstB-G   | CGCTCCATGTTAATGAGCAC                                   | hsib ord                         |
| hstC-A   | AGTCATGGAAAAGACTGCGG                                   | 5'flanking region of hstC        |
| hstC-B   | CTGACCTATCTTCCTGGACATGACGGATTGGACTCAGCCTGATTGG         | o manual region of more          |
| hstC-C   | CTGTGGACTCGTATGCTGTTGCGCAGAGTGCCCGAATAGGTTTCTG         | 3'flanking region of <i>hstC</i> |
| hstC-D   | AGCCATCGCTGTCAGTTTCT                                   | 0 0                              |
| hstC-F   | GCCTTGCTGGCTAAGAAGAA                                   | hstC ORF                         |
| hstC-G   | TCACACGACCCAAGGATACA                                   |                                  |
| nstD-A   |  | 5'flanking region of hstD        |
| nstD-B   |  |                                  |
| nstD-C   | <u>UTUTUUACTUUTATUUTUTTUUGUAG</u> GGUGTGGTGTAATTUTTUGT | 3'flanking region of hstD        |
| IISTD-D  |  |                                  |
| hstD-A2  |  | fusion PCR for hstD              |
| listD-D2 | ACOTCOODATATIATOOOT                                    |                                  |

| hsD-GAGACATCCATGCCTTCCTTAIND_ORThsE-ATCCATCTGATAGGTTCGGCS*flanking region of hstEhsE-BCTGACCTATCTTCCTGGACATGACGGCAGGGCCTGTCCGAATGTATTAS*flanking region of hstEhsE-DCCATGTGACAATTCCGCCCTfusion PCR for hstEhsE-D2GCCATGATACCTCCGACAGGCGGGGGGGGTGTTGATAATGACTS*flanking region of hstFhsE-D2GCCATGATCACTCCAGCAGAhstF-ChsE-D3GCCATGATCCTCCAAGGCACAfusion PCR for hstFhsE-D4GGCACATTCTCCCAGGCAGGGGGGGGGGTGTTGATAATGACTS*flanking region of hstFhsE-D5CTGACCTATCCTCCGGACGCGGGGGGGGGGGGGGGGGGG  | hstD-F           | ACCATCAAGTCCCAGCAATC                                | herd OPE                               |
|--|------------------|---|--|
| bstE-ATCCATCTGATAAGGTTCGGCSflanking region of <i>hstE</i> bstE-BCTGATCGTATCTTCTCGGACATGACGAGATAATGGGTACGGCGAATGTATTA3flanking region of <i>hstE</i> bstE-CCCATGTACATTCCGCCATfusion PCR for <i>hstE</i> bstE-A2ATAAGGTCGGATGACGAGAGA <i>hstE</i> ORFbstE-D2GCCATGATACATCCAGCAGA <i>hstE</i> ORFbstE-A2ATATAGGTCGCATGACGACGAGA <i>hstE</i> ORFbstE-A2ATTACGTCCAGCAGACACAC <i>hstE</i> ORFbstF-AATTAGCGAACCCTTGGACTGSflanking region of <i>hstF</i> bstF-AATTAGCGAACCCTGGACGACGACGAGGGTATTATGGGGATTGTCGGSflanking region of <i>hstF</i> bstF-CCTGTGGACTCGTATGCTGTGCGCAGGGGGGGGTATTATGGGGATTGTCGGSflanking region of <i>hstF</i> bstF-D2TCTCGCTTCCAAGGCTGCAGAGGCCAGGGGTGTTGATAATGGGGATTGTCGGhstF ORFbstF-GCGCAATGTGGAAGGACATCAG <i>hstF</i> ORFbstF-GCGCAATGTGGAAGGACATCAGhstF ORFbstF-GCGCAATGTGGAAGGACATCAG <i>hstF</i> ORFbstF-GCCGCGTGTCCGCGGTGGCGCGGCGGAGGCCGAGGGG <i>bstF</i> ORFbstF-GCGCACTGTCCCCGGGTGTCCCGAGGCGCAGGGGGAGCGGAGG <i>bstF</i> ORFbstF-GCGCACTGTCCCCGAGTGGCCGGGCGCAGGGCGAGGGGCGAGGGG <i>bstF</i> ORFbstF-GCCGCGCTGTCCGCGGCGGCGGCGGCGGGCGGGGGGGGGG   | hstD-G           | AGACATCCATGCCTCCCTTA                                | ISID ORF                               |
| hst-B       CIGACCTATCTTCCTGGACACIGACCGGAGATAATGGGTACGGCGAGA       Inturing region of hst/         hstB-D       CIGTGGACTCGTATGCGTGTGCGCAGGGCGCGTGTCCGAATGTATA       3'flanking region of hst/         hstB-D       CCACTGTACAATTCCGCCCAT       fusion PCR for hst/         hstB-D2       GCCATGATACATCCAGCAGAGA       hstE-OR         hstB-D2       GCCATGATACATCCAGCAGAGA       hstE-OR         hstB-A       ATTACGGGACAGAGAGA       hstE-OR         hstB-A       ATTACGGGACCACTGGCGACGGGGCGGGGGTGTGATAATGACT       S'flanking region of hst/         hstF-A       ATTACCGAACCCTTGGGACAGGAGAGAGAGACGAGACTGACGGGGGGGTGTGATAATGACT       S'flanking region of hst/         hstF-A       CGCACGGACGAAGGACCAGGGCGGGGGGTGTGATAATGACT       S'flanking region of hst/         hstF-A       CGCACGGGCAGAGGAGACACGAGGACTGACGGGCGGGGGGGG  | hstE-A           | TCCATCTGATAAGGTTCGGC                                |  |
| hstE-CCTGTGGACTCGTATGCTGTTGCGCAGGGGGCGTGTCGAATGTATTA<br>hstE-batE-DJflanking region of hstEhstE-A2ATAAGGTTGGGCATGAGTGGfusion PCR for hstEhstE-A2GCCATGATACATCCCACCAGAhstEhstE-A2GCCATGATACATCCCACCAGAhstEhstE-GGGCACATTCTCAAGAGCACAhstEhstF-AATTGGGGCAGACCGTGGACGGGGGGGTGTTGATAATGACT<br>CTGGGTCTGCAACGCTGGACATGCGGGCGGGGGGTGTTGATAATGACT<br>CTGTGGACTCGTAGCTGTTGCCCAGGGGTATGATGGGGGAGATGTGCGG<br>STIAnking region of hstFhstF-ACTGTGGACTCGTAGCTGTTGCCCAGGGGGGGTGTTGATAATGGACT<br>STIAnking region of hstFhstF-DCTGTGGACTCGTAGCTGTTGCCCAGGGGTGTTGATAATGGACT<br>STIAnking region of hstFhstF-DCTGTGGACTCGTAGCTGTGCCCAGGGGTGTCGCGAGGGGGGTGTTGATAATGGACT<br>STIAnking region of hstFhstF-ACGTCAGCTCACGGATTATGA<br>CTGGGCTGGCGGCGCCGCTGCCGAAGAGGG<br>traison-hstFhstF-AGGACATGGGGAGGACATCAG<br>CCGGCTGTCGGAAGGCGCGCGCGGCTGGCGGCGGCGGCGGCGGGGGGGG   | hstE-B           | CTGACCTATCTTCCTGGACATGACGGAGATAATGGGTACGGCGAGA      | 5 flanking region of <i>nstE</i>       |
| hstE-D     CCAGTGTACAATTCCCGCCAT     Planking region of hstE       hstE-D2     GCCATGATACATCCACCCAGA     fusion PCR for hstE       hstE-D2     GCCATGATACACTCCAGCAGA     hstE       hstE-F     AATAGGTTCCAGAGCGACA     hstE       hstF-A     ATTGACGAACCCTTGGACTG     S*flanking region of hstF       hstF-A     CTGACCTATCCTTCCTGGACATGACCGGCGGGGGTGTGATAATGACT     S*flanking region of hstF       hstF-D     TCTCGTTCCAAGGCTGTGTGCCCAGGGGTATTATGGGGATTGTCGG     S*flanking region of hstF       hstF-D     TCTCGTTGCCTCAGGGCTGTGCCCAGGGTATTATGGGGATTGTGG     S*flanking region of hstF       hstF-D     TCTCGTTGCCTTGCCTGTGCCCAGGGTGCGTGCGGAGG     yean period for pLShstD       hstF-F     AGACATATGGCGCGGCGGGCGGCTGCTGCCGAAGAGG     yeat or construction for pLShstD       Fusion-hstD-F     tegageteggaccaCTGGTGGCAGGTCGCTGCGGTGGGGAC     yeat or construction for pLShstD       Fusion-hastD-R     ctetagaggatccaCTAGGTGCGAGGTCGCTGGCGGCGGGTATTGGGAC     yeat or construction for pLShstD       kacAdach>C     CGGCGGGTGTAAGACGACTGCAGGGGGGGGGACAGGCTGATG     S*flanking region of lacA       kacAdach>C     CGGCGCGGCTGGTTGCCGAGGGGGGGGGGACGGCGAGG     S*flanking region of lacA       kacAdach>C     CGGCGGCGGCTGGTTGCGAGGGGGGGGGGGGGGGGGGGG  | hstE-C           | CTGTGGACTCGTATGCTGTTGCGCAG<br>GGCGCTGTCCGAATGTATTA  | $2^{t}$ flanking region of $hetE$      |
| hstE-A2ATAAGGTTCGGCATGAGTGGfusion PCR for hstEhstE-D2GCCATGATACATCCAGCAGAhstE ORFhstE-FAATAITCGGGGCAGACCGAGAhstE ORFhstE-GGCCACATTCTCAGAGCCGCAS'flanking region of hstFhstF-AATTGACGACCTGTGGACATGACGGGCGGGGGGTGTTGATAATGACTS'flanking region of hstFhstF-CCTGTGGACTCGTATGCTGTTGCGCAGGGGGGGGGTGTTGATAATGACTS'flanking region of hstFhstF-DCTCTGGTCTCCAGGGCTGCCCg'flanking region of hstFhstF-DCTCTGGTCCCCAGGGTTATGCTGTTGCGCAGGGGTGTTGATAATGAGCTfusion PCR for hstFhstF-FAGACATATGGCGCTGAAAGChstF-ORFhstF-GGCAATGTGGAAGGACATCAGhstF-ORFhstF-GCCAATGTGGAAGGCGCGGGCTGGTGTCCGAAGAGGhstF-ORFhstF-GCCACCTCACGGGCCGGGCTGGCTGTCCGGAAGACGhstF-ORFhstF-GCCACCCCACACCCCAAGCCGCGGCTGGATTTAACAACvector construction for <i>PUShaCA</i> Fusion-hstD-RtetgaggetgestacceCTAGTTCGCGACGGCTGGACGGCGGACAGCTGGATg'flanking region of <i>laeA</i> hacAdachACCCGGCGTGTCAAGACCCACGCAGACGGCGAAGCTCCATTACTGGGTATTCGGg'flanking region of <i>laeA</i> hacAdachACCGGCGCGCTGTGCTGTGCGCAGGGCGAAGGCTCATTACTGGGTATTCGGhstP on poch for <i>laeA</i> hacAdachACCGGCGCGCTGTGCTGTGTGCGCAGAGGCGCAGGCTGATGhstP on poch for <i>laeA</i> hacAdachACCGGCGCCTCCGCCCTGACCCAAAhstP on poch for <i>laeA</i> hacAdachACCGGCCCCCAACCCCAAAhstP on poch for <i>laeA</i> hacAdachACCGGCCCCCCCCCCCTGGCGCGCGGGCGCGAGGTGTGCGACGGCTGGTGTGCGAGGGTGThstP on poch for <i>laeA</i> hacAdachACCGGCCCCCCCCCCCCGCGCTGGCGCGCGCGCGCGCGCGGGCGGGGGG  | hstE-D           | CCAGTGTACAATTCCGCCAT                                | 5 Hanking region of <i>hste</i>        |
| hstE-D2       GCCATGATACATCCAGCAGA       Instant PCK No Natz         hstE-F       AATATCTGGGGCAGACGAGAGA       hstE ORF         hstE-G       GGCACATTCTCAGAGCACA       Sflanking region of hstF         hstF-A       ATTGACGAACCCTTGGACTGACGGCGGGGGGTGTTGATAATGACT       Sflanking region of hstF         hstF-D       TCTTCGTTTCAAAGGCTCC       3'flanking region of hstF         hstF-D2       CGTCAGCTCACGGATTATGA       fusion PCR for hstF         hstF-D3       TCTCGTTTGGCAAGGCACACAG       hstF         hstF-F       AGACATATGGCGCGCGCGCGCTGTCCCGAAGAGGG       weetor construction for pUShstD         rsion-hstD-F       tegggeteggtacccATGGTGGCGCGCGGCGCGCGCGCGCGCGCGCGCGCGGCGGAGGGGGAGGGGGAGGGGGAGGGGGAGGGGGAGGGGGAGGGG   | hstE-A2          | ATAAGGTTCGGCATGAGTGG                                | fusion BCP for hetE                    |
| heff-finiteATATCTCGGGCAGACGAGAhstE ORFhstE-GGGCACATTCTCAAGAGCACAS'flanking region of hstFhstF-AATTGACGAACCCTTGGACTGGACGGGGGGGTGTTGATAATGACTS'flanking region of hstFhstF-DCTGTGGACTGGTATGCTGTTGGCAGGGGGGGTGTTGATAATGACTS'flanking region of hstFhstF-DCTCTGGTTCAAAGGCTCCStanking region of hstFhstF-DCTCTGGTTGCATAGCGGTGTGGCAGGGGGGGTGTTAATGAGCGfusion PCR for hstFhstF-DCTCGTTGGCATGGCGGCGCGCGTGTTTCGCAAGAGGhstF ORFhstF-DCCCGTGGGAGGGCGCGCGCGCGGCTGATTTAACAAChstF ORFFusion-hstD-teggeteggtacec4TCGTGGCGGCGCGCGCGGCTGATTAACAACector construction for JUShstDFusion-hstD-teggeteggtacec4TCGTGTGCGCAGGCGGCGGCGGCGGCGGCGGCGGCGGCGGGCG   | hstE-D2          | GCCATGATACATCCAGCAGA                                | TUSION FCR IOI IISIE                   |
| heff-GGGCACATTCTCAAGAGCACAhttp://http:   | hstE-F           | AATATCTGGGGCAGACGAGA                                | hatE OPE                               |
| hstF-AATTGACGAACCCTTGGACTG5'flanking region of hstFhstF-BCTGACCTATCTTCCTGGACATGACGGGGGGGGTGTTGATATGACT3'flanking region of hstFhstF-DTCTTGTCTTCAAAGGCTCCfusion PCR for hstFhstF-D2CGTCAGCTCATGGTGTGCCCAGGGTATTAGGfusion PCR for hstFhstF-D3TCTCGTTTGCCTTAGCTGTGhstF-ORFhstF-G4GCAATGTGGAGGACATCAGhstF-ORFhstGion-hstD-FtegageteggtacccATGGTGGCGCTGCTGCCGAAGAGvector construction for pUShstDFusion-hstD-RtegageteggtacccATGGTGGCGGCTGCCGAAGGCCGGCTGATTAACAACvector construction for pUShaCAFusion-hstD-RtegageteggtacccTCAGTCGCAGCTGGCTGCCGAAGGCGGAGCGGGGTATTGGGGACAGGCGGAAGGCGGAGACGGGGTATTGGGGACGGGGGTGTCGCTGGGGACAGGGGGACAGGGGGACGGGGAGGGGAGAGGGGGACAGGGGGACAGGGGGACAGGGGGACAGGGGGACAGGGGGACAGGGGGACAGGGGGACAGGGGGACAGGGGGACAGGGGGACAGGGGACAGGGGGACAGGGGGACAGGGGGACAGGGGGACAGGGGGACAGGGGGACAGGGGGACAGGGGGACAGGGGGACAGGGGGACAGGGGGACAGGGGGACAGGGGGACAGGGGGACAGGGGGACAGGGGGACGAGGGGGACAGGGGGG   | hstE-G           | GGCACATTCTCAAGAGCACA                                | ISIE ORF                               |
| haff-BCTGACCTATCTTCCTGGACATGACGGCCGGGGTGTTGATAATGACTJahnking region of hat/haff-CCTGTGGACTCGTATGCTGTGCGCAGGGTATTATGGGGATTGTCGG3'flanking region of hat/haff-A2CGTCAGCTCACGGATTATGAfusion PCR for hst/haff-D2TCTCGTTTGCCTTAGCCTGGhatf-D2haff-D2TCTCGTTGGCATGGCGGCGCGCTGATTAAGAhst/haff-GGCAATGTGGAAGGACATCAGhst/haff-D2CCGCGGCGCGCTGGCTGCCGTGCCGCGGCTGATTTAACAACvector construction for pUShst/Dhaff-D3cetagaggatecceTCATGCGGCCGGCTGATTTAACAACvector construction for pUShacAFusion-habA+tetagagatecceTCAGTTCGGAGGGTCGATGTCGCAGGCGGCGGGCGGGGGstflanking region of lacAlacA.acCGGCGTGTCAAGTCCATGGATAGstflanking region of lacAlacA.aCCGGCGTGTCAAGTCCATGGATAGstflanking region of lacAlacA.da(abA)-BCTGACCTATCTTCCTGGACAGGAGGCGCAGGGGGGACAGGCTGATGstflanking region of lacAlacA.da(abA)-CCTGGGACTCGTATGCTGTGGCGAGAGGCTCCATTACTGGGTATTCGstflanking region of lacAlacA.da(abA)-CGGAACCAACCACACACCTfusion PCR for lacAlacA.D2TTACGTTTGGGAACGGAGGCCATATTCGATGGCGACAGGCTGATGstflanking region of lacAlacA.GC-CCAATCGGCCTCCGCACATCACCCClacA ORFlacA.GC-CGGAACCAACCACCACACACCACACACCTlacA ORFlacA.GC-CGAACGAGACGAACGAGGAGCCCATATTCGATGGCGACAGGCTGATGdsruption casette for lacA inlacA.GC-CCAATGGGCACGTATGCCAAGAGAGCCCATATTCAGGGCAACGGCGAGCAGafsruption casette for lacA inlacA.GC-CGGAACCGACGACGAGGAGCCCATATTCAGGGGCACAGGCGCAGAGGCCACAGGGCGCACAGGGCGCACAGGCGCCACATGGCafsruption casette fo   | hstF-A           | ATTGACGAACCCTTGGACTG                                | 5'flenking region of hetE              |
| heff-C<br>hstF-DICITICGIGGACTCCTATGCTGTIGGCGCAGGGTATTATGGGGATTGTCGG<br>TICITGGTCTACAGGCTCC<br>hstF-D2Planking region of hstFhstF-D2CGTCGGTTGCCTAAGGCTGC<br>  | hstF-B           | CTGACCTATCTTCCTGGACATGACGG<br>GCGGGGGTGTTGATAATGACT | 5 Hanking region of <i>hstr</i>        |
| hstF-DTCTTCGTCTTCAAAGGCTCCT halking region of hstPhstF-A2CGTCAGCTCACGGATATGAfusion PCR for hstFhstF-A2CGTCAGTTGGCTAAGCTGTGfusion PCR for hstFhstF-GGCAATGTGGAAGGACATCAGhstF ORFpsion-hstD-RtectagaggatecceTCGTGCGGTGCGCTGTCCCGAAGAGGvector construction for pUShstDreusion-hatA-FtectagaggatecceTCATGCGGCGGGTGATTAACAACvector construction for pUShstDreusion-lacA-FtectagaggatecceTCATGCGGGCGGGTGATTCACGACvector construction for pUShstDlacA/adcAb-BCTGGCCTGTTCGGAGGTGGCGGCGGCGGCGGATGGCGACGGCGGATGGS'flanking region of laeAlacA/adcAb-CCGGGCTGTTCGGAGGGGCGAGAGGCTCCATTACTGGGTATTCGG3'flanking region of laeAlacA/adcAb-CCGGGATACCAACCACACACACCTfusion PCR for laeAlacA/adcAb-CCTGGGGACCGGAGGCCAATTCAGGGCGACAGGCTGATG3'flanking region of laeAlacA-A2GGGATACCAACCACCACACACCCTfusion PCR for laeAlacA-GTTGATGGGAAGGGAGCCAATTCGAGGGGCGACAGGCTGATGdisruption casette for laeAlacA-GTGAACGCCTCCGACTGAClaeA oRFlacA/GCCATACGGCAGGCAATATGCAGAGGAGACCCATTATCGAGGAGCAGGTGATTCGGdisruption casette for laeAlacA/GCCATACGGCAAGGAAGGAGGCCATATTGCAAGGGCACAGGCGGAGTATCGGabstD backgroundsC-FATATGGCTCCTGGTCGGTCGCTGCGTCGTTGCsC amplificationsc-RTCTCTGGCAATAGCGGCAGGAGCCATATTAACCGTGACATGACCCTTGabstD backgroundsc-FATATGGCTCCCGGATACCGATTACCprobe for kajAhstD-comp-BGAACGAGCAGAGGAGGCCATATTAACCGTGCACGTCATGTCAGGAAGATAGGTCAconfirmation of transformationhstD-comp-B </td <td>hstF-C</td> <td>CTGTGGACTCGTATGCTGTTGCGCAGGGTATTATGGGGGATTGTCGG</td> <td>2) flenking region of hetE</td>   | hstF-C           | CTGTGGACTCGTATGCTGTTGCGCAGGGTATTATGGGGGATTGTCGG     | 2) flenking region of hetE             |
| hstF-A2CGTCAGGTCACGGATTATGAfusion PCR for hstFhstF-20TCTCGTTTGCCTTAGCTGTGhstFhstF-7AGACATATGGGCGCTGAAAGCAChstF ORFhstF-6GCAATGTGGAAAGCACTCAGvector construction for pUShstDrusion-hstD-7tegageteggtacecATGGTTGGGACGCTGCTGTCCGAAGAGGvector construction for pUShstDFusion-hacA-FtegageteggtacecATGGTTGGGACGGCTGGTTGCGTGGCGCGCGCGCGGCTGGTTGvector construction for pUShstDlaeAACCGGCTGTTCAAGATCCAGGGCGGCAGGAGGCGCAGACGGCGGATGSflanking region of laeAlaeA(adeA)-CCTGTGGACTCGTATGTCGGACGGCGCAGAGGCTCCATTACTGGGTATTCGG3'flanking region of laeAlaeA(adeA)-CCTGTGGACTCGTATGCTGTGGGCAGAGAGCTCCATTACTGGGTATTCGG3'flanking region of laeAlaeA(adeA)-CCTGTGGACCACACACCACAACCTfusion PCR for laeAlaeA-A2GGGATACCACCACAACACCCCAAAfusion PCR for laeAlaeA-A3CCGCCCCAAACCACCACAACACCCCAAAfusion PCR for laeAlaeA-A5CAGCCCTCGAACGAGGAGGCCATATTCGATGGCGACAGGCTGATGdisruption casette for laeAlaeA-A6TTACGGCCCTCGATTGCCCGTCGTCacA ORFlaeA(sC)-CCATACGGGCAGCATATGCCAAGAGAGAGCCCATATTCGGGGATATCGGafsizuption casette for laeA inlaeA(sC)-CCATACGGGCAGCATAGCGCCCATTGCCacA oRFlaeA(sC)-CGCAACTGCGCTGGTCGTCGTCsC amplificationsC-FATATGGCTCCTCGTCGTCGTCGTCGsC amplificationsC-RTCTCTGGCAATAGCTGGCCGGCGCGCGCGCGTATGCCGGGCAGAGAGAG  | hstF-D           | TCTTCGTCTTCAAAGGCTCC                                | 5 Hanking region of <i>nstr</i>        |
| hstF-D2TCTCGTTTGCCTTAGCTGTGIusion PCR for IntrhstF-FAGACATATGCCCGCTGAAAGChstF ORFhstF-GGCAATGTGGAAGGACATCAGhstF ORFFusion-hstD-FtegageteggtacccATGGTGCGCTGCCCGATTAACAACvector construction for pUShstDFusion-hastD-RetctagaggtaccccTCATGCGGCCGGCTGCATTAACAACvector construction for pUShstDFusion-hastD-RetctagaggtaccccTCGTCGCGGTTCCGCGGCGCGCGCGCGATGGCGAAGACGGCGAAGGCGAAGvector construction for pUShaeAIaeA.acAectagaggtaccccTCGGTGTCGCAGGGCGATGGCGAAGGCGAAGGCTGATGS'flanking region of laeAIaeA(adcA)-BCTGACCTATCTTCTGGACAGAGAGGCCAATGCGGAGGGCGAAGGCTGATGGGAATGGGATTCGG3'flanking region of laeAIaeA.acAGGAATACCAACCAACAACACTfusion PCR for laeAIaeA-A2GGATACCAACCAACAACACCTfusion PCR for laeAIaeA-A2GGATACCAACCACCAAAAfusion PCR for laeAIaeA-A2GGATACCAACCACCAAAAlaeAIaeA-A2GGATACCAACCACCACAAAfusion PCR for laeAIaeA-A2GGATACCAACCACCAAAAlaeAIaeA-A2GGATACCAACCACCACAAAlaeAIaeA-A5CAGCCCTCCAAACCACCAAAAlaeAIaeA-A5GACCGAGAGGAGGGAGGCATATTCGATGGCGACAGGCTGATGdisruption casette for laeAIaeA-A5GACCAGCCTTGGCCCGATTGCafstD backgroundsC-FATATGGGCCAACGAGGGAGGCCATATTCACCGTGACAGGCAGAGAGAG   | hstF-A2          | CGTCAGCTCACGGATTATGA                                | fusion DCD for hot                     |
| hstF-FiAGACATATGGGGCTGAAAGChstF-ORFhstF-GGCAATGTGGAAGGACATCAGhstF ORFhstF-GGCAATGTGGAAGGACATCAGvector construction for pUShaDFusion-hstD-RtettagaggatecceTCATGCGGCGGGTGGATTTAACAACvector construction for pUShaCAFusion-hacA-FtettagaggatecceTCAGTTCGGAAGGGGCCAGACTGGACvector construction for pUShaCAlacA-ACCGGCGTGTTCAAGATCCATGGATAGstillarking region of lacAlacA-ACCGGCGCACATGCTGTGCGGAGGGGCGAGGGCGACAGGCTGATGstillarking region of lacAlacA-ADCGGCCCACACATCAACCACCAfusion PCR for lacAlacA-ADGGATACCACCACAACACCACAACCACCAlacA-ADlacA-ADGGGATACCACCACAACACCACAACCACCAlacA-ADlacA-ADGGATACCACCACAACACCACAACACCAlacA-ADlacA-ADGGATACCACCACAACCACCACAACCACCACAACCACCACAACGAGGAG   | hstF-D2          | TCTCGTTTGCCTTAGCTGTG                                | Iusion PCR for nstr                    |
| hstF-GGCAATGTGGAAGGACATCAGhstF-OKFhstF-GGCAATGTGGAAGGACATCAGhstF-OKFFusion-hstD-FtegageteggtacccATGGTGCGGGCGCGCTGCTCCGAAGAGGvector construction for pUShstDFusion-hacA-FtegageteggtacccATGTTTGGAAACGGCCGGCTGATGACAGCvector construction for pUShacAFusion-hacA-FtegageteggtacccATGTTTGGAAACGGCCAGACTGGACvector construction for pUShacAIacA-ACCGGCTGTTCCAGATCGATGACGGTCGATGGCGACAGGCTGATG5*flanking region of laeAIacA(adeA)-BCTGACCTATCTTCCTGGACATGACGGTCGATGGCGACAGGCTGATG3*flanking region of laeAIacA(adeA)-CCTGTGGACCGCAACACACACACCCfusion PCR for laeAIacA-DGAACCCGCCCAACACCACACACACCfusion PCR for laeAIacA-A2GGGATACCAACCACCACACACACCfusion PCR for laeAIacA-GTTGAACGCCTCCGACTTGAClaeA ORFIaeA(sC)-BGAACGAGGCAGAGGAGCCATATTCGATGGCGACAGGCTGATGdisruption casette for laeA inIacA(sC)-CCATACGGGCAGCGCCGATAGashtD backgroundsC-FATATGGCTCCTGGTCGTCTGTCsC amplificationsC-RTCTCTTGGCAATAGCTGCCCGTATGsC amplificationscC-RCTCTTGGCAATAGCTGCCCGTATTCAAGAGACCCTGGGAGAGTAGGTCAprobe for kajAhstD-comp-BGAACGAGGAACGAGGGAGCCATATTACCGTGACATGACCCTTGcomplementation of hstDscJ-ARGCCTTGGTCTGGGACTGTprobe for kajAkojA-FGGCGCACCTATGCCCAATTGCCAAGAGCCTCATGCCAGGAGCATAGGTCAprobe for kajAkojA-RGGCGTCATGGGGAGAGGTGAACCprobe for kajAkojA-RGGCGTCATGGCAGACCAprobe for kajAkojA-FGGCGCTCAAGACCACCAprobe for k   | hstF-F           | AGACATATGGCGCTGAAAGC                                |  |
| Fusion-hstD-FtcgagetcgateccATGGTGCGGTGCGGTGCGCTGTCCGAAGAGGvector construction for pUShebFusion-hstD-RtctgagetggateccaTGATGTGGAAACGGCCAGACTGGACvector construction for pUShebFusion-lacA-RtctgagetggateccaTGATTCGCAGGTTCGCGGGCGGGCGGACGGGCAvector construction for pUSheblacA.ACCGGCTGTTCAAGATCCATGGATAGftalking region of lacAlacA(adcA)-BCTGACCTGCTCTCTCGGACATGCGGAGAGGCTCATTACTGGGTATTCGGftalking region of lacAlacA.ACGGACTCGTACGGCAACACCAACCTftusion PCR for lacAlacA-D2GGGATACCAACACACACACCAAftusion PCR for lacAlacA-ACGGCCCCAAACCACACACACACACACACACACACACACA  | hstF-G           | GCAATGTGGAAGGACATCAG                                | hstr OKF                               |
| Fusion-hstD-R       ctctagaggateceeTCATGCGGCCGGCTGATTTAACAAC       vector construction for <i>pUShstD</i> Fusion-lacA-F       tegageteggtaceeATGTTTGGAAACGGCCAGACTGGAC       vector construction for <i>pUSlaeA</i> IaeA-R       ctctagaggateceeATGTTCGGAGGTTCCGTGGCTGGCAGGCGGACAGGCTGATG       S'flanking region of <i>laeA</i> IaeA(adeA)-B       CTGACCTATCTTCCTGGACATGACGGTCGATGGCGACAGGCTGATG       S'flanking region of <i>laeA</i> IaeA(adeA)-C       CTGGGACTCGATGCTGTTGCGCAGAGAGCTCCATTACTGGGTATTCGG       3'flanking region of <i>laeA</i> IaeA-AD       GAACCCACACACACCT       fusion PCR for <i>laeA</i> IaeA-A2       TTACGTTTGGGAACGAGGAGCCATATTCGATGGCGACAGGCTGATG       disruption casett for <i>laeA</i> IaeA-G       TTGAACGCCTCCAATTCCCGATGC       disruption casett for <i>laeA</i> IaeA(sC)-C       CATACGGGCAGCTATTGCCCAAGAGAAGAGCTCCATTACTGGGTATTCGG       disruption casett for <i>laeA</i> IaeA(sC)-C       CATACGGGCAGCTATTGCCCAAGAGAAGAGCTCCATTACTGGGTATTCGG       disruption casett for <i>laeA</i> sC-F       ATATGGCTCCTCGTTCGTCTCGTTC <i>a laeA a laeA</i> <t< td=""><td>Fusion-hstD-F</td><td>tcgagetcggtacccATGGTGCGGTCGCTGTCCGAAGAGG</td><td></td></t<>   | Fusion-hstD-F    | tcgagetcggtacccATGGTGCGGTCGCTGTCCGAAGAGG            |  |
| Fusion-lacA-FtegageteggtacccATGTTTGGAAACGGCCAGACTGGACvector construction for pUSlaeAFusion-lacA-RectegaggatcccATGATTCGCAGGTTTCCGTGGCTTGG5'flanking region of laeAlacA/adeA)-BCTGACCTATCTTCCTGGACATGACGGTCGATGGCGACAGGCTGATG5'flanking region of laeAlacA(adeA)-CCTGTGGACTCGTAIGCTGTTGCCCAGAGAGCTCCATTACTGGGTATTCGG3'flanking region of laeAlacA/adeA)-CCTGTGGACTCGTAIGCTGTTGCCCAGAGAGCTCCATTACTGGGTATTCGG3'flanking region of laeAlacA-DGAACCCGCCAACATCAAGCTTCfusion PCR for laeAlacA-A2GGGATACCAACCACACACCACfusion PCR for laeAlacA-F2TTGACGTTTGGGAACGGAGGCCATATTCGATGGCGACAGGCTGATGdisruption casette for laeAlacA-GTTGAACGCCTCCGACTGAClaeA ORFlacA/sC)-BGAACGAGAACGAACGAGGAGCCATATTCGATGGCGACAGGCTGATGdisruption casette for laeA in<br>A hstD backgroundsC-RTTCTTGGCAATAGCTGCCCGTATGsC amplificationsC-RTCTCTTGGCAATAGCTGCCCGTATGsC amplificationsC-RGCACTCGCTTACCGATTACconfirmation of transformationhstD-comp-BGAACGAGACGAACGAGGAGCCATATTACACCGTGACATGACCCTTGcomplementation of hstDscijA-RGGCTTCCAGGGCCAGAACCprobe for kojAkojA-RGGGCTCATGGGAGTGTAprobe for kojAkojA-RGGCGTCATGGGAGTGAACCAprobe for kojAkojR-FCGGCCAGCTATGACCCCATTprobe for kojTkojA-RGGCGTCATGGGAGGTCAACCprobe for kojTkojA-RGGCGTCATGGGAGGTGAACCAprobe for kojTkojA-RGGCATCTCCGGAGGTGAACCAprobe for kojTkojR-RGCCTGGGGTCATGACCA <td< td=""><td>Fusion-hstD-R</td><td>ctctagaggatccccTCATGCGGCCGGCTGATTTAACAAC</td><td>vector construction for <i>pUShstD</i></td></td<>   | Fusion-hstD-R    | ctctagaggatccccTCATGCGGCCGGCTGATTTAACAAC            | vector construction for <i>pUShstD</i> |
| Fusion-lacA-RcitclagaggatecceTCAGTTCGCAGGTTTCCGTGCTTGGvector construction for <i>PDStateA</i> lacA-ACCGGCTGTTCAAGATCCATGGATAGS'flanking region of <i>lacA</i> lacA(adeA)-BCTGACCTATCTTCCTGGACATGACGGTCGATGGCGACAGGCTGATG3'flanking region of <i>lacA</i> lacA(adeA)-BGAACCCGCCAACATCAAGCTTCatalacAlacA(adeA)-CGGGATTCGTTGGGACGGAGGAGCACATGACGGTCCATTACTGGGTATTCGG3'flanking region of <i>lacA</i> lacA-DGAACCGCCCCAACATCAAGCTTCfusion PCR for <i>lacA</i> lacA-D2TTACGTTTGGGACGGAGGCACTATTCGATGGCGACAGGCTGATGdisruption casette for <i>lacA</i> lacA-GTTGAACGCCTCCGACTTGAC <i>lacA</i> ORFlacA(sC)-BGAACGAGAGGAGGAGCCATATTCGATGGCGACAGGCTGATGdisruption casette for <i>lacA</i> inlacA(sC)-CCATACGGGCACCTATGCCCCGTATG <i>disruption</i> casette for <i>lacA</i> inlacA(sC)-CGAACGAGAGGAGCAATGACGCCGTCATG <i>sC</i> amplificationsC-FATATGGCTCCTCGTTCGTCCGTTCsC amplificationsC-RTCTCTGGCAATAGCTGCCCATATCACGGACCGTCATGTCCAGGAAGATAGGTCAconfirmation of transformationhstD-comp-BGAACGAGACGAACGAGGAGGCATATTCAGconfirmation of transformationhstD-comp-BGAACGGCTCCATCAGprobe for <i>kajA</i> kojA-FGGTTTCCAGGGCCAGAACCprobe for <i>kajA</i> kojA-FGGGCGGCAGCTATGGCCAGAACCprobe for <i>kajA</i> kojA-FGGCGTCATGGGAGAGTGTGAprobe for <i>kajA</i> kojA-FGGGCGGCTCATCCAGprobe for <i>kajA</i> kojA-FGGCGGGTCCTCGCCCATTprobe for <i>kajA</i> kojA-FCACCTACTCACGAAACCAprobe for <i>kajA</i> kojA-FCACCTACTCACGAGGGAACCAprob   | Fusion-laeA-F    | tcgagctcggtacccATGTTTGGAAACGGCCAGACTGGAC            |  |
| lacA-ACCGGCTGTTCAAGATCCATGGATAGS'flanking region of lacAlacA(adeA)-BCTGACCTATCTTCCTGGACATGACGGTCGATGGCGACAGGCTGATG3'flanking region of lacAlacA(adeA)-CCTGTGGACTCGTATGCTGTTGCGCAGAGAGCTCCATTACTGGGTATTCGG3'flanking region of lacAlacA-DGAACCCGCCAACAACAACCTfusion PCR for lacAlacA-A2GGGATACCAACCACCCAAAlacAlacA-BCAGCCTCCAAACCACCCAAAlacAlacA-GTTGAACGCCTCCGACTTGAClacAlacA(sC)-BGAACGAGAGGAGGAGCCATATTCGATGGCGACAGGCTGATGdisruption casette for lacA in<br>A hstD backgroundlacA(sC)-CCATACGGGCAGCATTGCCAAGAGAAGAGCCTCCATTACTGGGTATTCGGdisruption casette for lacA in<br>A hstD backgroundlacA(sC)-CCATACGGGCAGCTATTGCCAAGAGAAGAGCCTCCATTACTGGGTATTCGGdisruption casette for lacA in<br>A hstD backgroundsc-FATATGGCTCCTGTTGTCGTCGTCsC amplificationsc-RTCTCTTGGCAATAGCTGCCCGTATGconfirmation of transformationhstD-comp-BGAACGAGAGCAACGAGGAGCCATATTAACCGTGACATGACCCTTGconfirmation of hstDnested adeA-RGCCTTGGTCTGGGAGGTGTprobe for kajAkojA-FGGCTTCCAGGGCCTCATCAGprobe for kajAkojA-RGGCTCATGGGAGAGTGGAprobe for kajAkojR-RGGCGTCATGGGAGGTGAACCAprobe for kajAkojR-RGGCGTCATGGGAAGGAACCAprobe for kajAkojR-RGCACCTCATAGCGGAACCAprobe for kajAkojR-RGCACCTCATCCAGAGGTCAACCprobe for kajAkojR-RGCCTCATGGGAGGTCAACCAprobe for kajAkojR-RGCCTCATCCCAGAGGCAACCAprobe for kajAkojR-R  | Fusion-laeA-R    | ctctagaggatccccTCAGTTCGCAGGTTTCCGTGCTTGG            | vector construction for <i>pUSlaeA</i> |
| lacA(adeA)-BCTGACCTATCTTCCTGGACATGACGGTCGATGGCGACAGGCTGATGSTlanking region of <i>lacA</i> lacA(adeA)-CCTGTGGGACTCGTATGCTGTTGCGCAGAGAGGCTCCATTACTGGGTATTCGG3'flanking region of <i>lacA</i> lacA-DGAACCCGCCAACATCAAGCTTCfusion PCR for <i>lacA</i> lacA-D2TTACGTTTGGGAACGAGAGGAGCCATATfusion PCR for <i>lacA</i> lacA-FCAGCCCTCCAAACCACCACA <i>lacA</i> ORFlacA-FCAGCCCTCCGACTTGAC <i>lacA</i> ORFlacA-FCAGCCCTCCGACTGAC <i>disruption</i> casette for <i>lacA</i> inlacA/SC)-BGAACGAGCAGCAGCTATTGCCAAGGAGAGAGAGCTCCATTACTGGGTATTCGG <i>disruption</i> casette for <i>lacA</i> inlacA(sC)-CCATACGGCCACCTATGCCGTTC <i>sC</i> amplificationsC-FATATGGCTCCTCGTTCGTCTCGTTC <i>sC</i> amplificationsC-RTCTCTTGGCAATAGCTGCCCGTATGconfirmation of transformationhstD-comp-BGAACGAGCGACGAACGAGGAGCCATATTAACCGTGACATGACCCTTGcomplementation of <i>hstD</i> nested adeA-RGCCTTGGTCTGGGCAGGACCprobe for <i>kajA</i> kojA-FCGGCCAGCTATGCCCATAGprobe for <i>kajA</i> kojR-FCGGCCAGCTATGGCAAACCprobe for <i>kajT</i> kojT-FCGAGGTGTCCTTGGAGGGAACCAprobe for <i>kajT</i> kojT-FCACCTACTCACGAGGTCAACCprobe for <i>kajT</i> kojT-FCACCTACTCACGAGGTAGGCGprobe for <i>kajT</i> kojT-FCACCTACTCACGAGGCAACCAprobe for <i>kajT</i> kojT-RGTTCTGGGATAGGCGAACCAprobe for <i>kajT</i> kojT-RGTTCGGCAGCTCGTGGAGGGCAACCAprobe for <i>kajT</i> kojT-RGTTCACCCCCAAAGCCAAACCprobe for <i>kajT</i> ka-A-FAGCCCTCCAAACCACCCAAAAGprobe for <i>in</i>   | laeA-A           | CCGGCTGTTCAAGATCCATGGATAG                           |  |
| lacA(adeA)-CCTGTGGACTCGTATGCTGTTGCGCAGAGAGGCTCCATTACTGGGTATTCGG<br>GAACCCGCCAACATCAAGCTTC3'flanking region of <i>laeA</i> lacA-DGAACCCGCCAACAACAACACCTfusion PCR for <i>laeA</i> lacA-D2TTACGTTTGGGAACGGAGTCAfusion PCR for <i>laeA</i> lacA-D3TTGAACCCTCCAACCACCAACAACCACCAA <i>laeA</i> lacA-D4CAGCCCTCAAACCACCAACAACCACCAA <i>laeA</i> lacA-D5TTGACGTCTGGGAACGGAGGAGCAATA <i>laeA</i> lacA-GTTGAACGCCTCCGACTTGAC <i>laeA</i> ORFlacA(sC)-BGAACGAGACGAACGAAGAGGAGCCATATTCGATGCGCGACAGGCTGATGdisruption casette for <i>laeA</i> inlacA(sC)-CCATACGGGCAGCTATTGCCAAGAGAAGAGAGCTCCATTACTGGGTATTCGG <i>AhstD</i> backgroundsC-RTCTCTTGGCAATAGCTGCCCGTTACsC amplificationsC-RCCTTGGTCAGGAGCAGCATATTACconfirmation of transformationhstD-comp-BGAACGAGCGACGATATTGCCAAGAGACCGTCATGTCCAGGAAGATAGGTCAComplementation of <i>hstD</i> nested adeA-RGCCTTGGTCTGGGAGTGTprobe for <i>kajA</i> kojA-FGAGGAAATCCGGCCCAATAGprobe for <i>kajA</i> kojR-RGGCGCACGTATGGCCAGAACCAprobe for <i>kajT</i> kojR-RGGCGCACGTATGGCAAACCAprobe for <i>kajT</i> kojT-RGTTCTGGGATAGGCGAACCAprobe for <i>kajT</i> ipnA-FAGCCTCCAAACCACCAAAGGprobe for <i>ipnA</i> jacA-FAGCCTCCGACTTGGACGTGGprobe for <i>ipnA</i> jacA-FAGCCCTCGACACCCAAAGGprobe for <i>ipnA</i> jacA-FAGCCCTCGAAACCACCAAAGGprobe for <i>ipnA</i>   | laeA(adeA)-B     | CTGACCTATCTTCCTGGACATGACGGTCGATGGCGACAGGCTGATG      | 5'flanking region of <i>laeA</i>       |
| lack-DGAACCCGCCAACATCAAGCTTC3 Hanking region of <i>lacA</i> lacA-D2GGATACCAACCACAACACCTfusion PCR for <i>lacA</i> lacA-D2TTACGTTTGGGAACGGAGTCA <i>lacA</i> ORFlacA-FCAGCCCTCCAAACCACCCAAA <i>lacA</i> ORFlacA/GTTGAACGGCAGCGAACGAGGAGCCATATTCGATGGCGACAGGCTGATGdisruption casette for <i>lacA</i> inlacA/SC)-BGAACGAGCGAACGAGGAGCACATATTCGATGGCGACAGGCTGATGdisruption casette for <i>lacA</i> inlacA/sC)-CCATACGGGCAGCTATTGCCAAGAGAAGAGCTCCATTACTGGGTATTCGG <i>A hstD</i> backgroundsC-FATATGGCTCCTCGTTCGTCTCGTTCsC amplificationsc-RTCTCTTGGCAATAGCTGCCCGTATGconfirmation of transformationhstD-comp-BGAACGAGACGAACGAGGAGGCCATATTAACCGTGACATGACCCTTGcomplementation of <i>hstD</i> seted adeA-RGCCTTGGTCTGGGCCAGCAGTATcomplementation of <i>hstD</i> kojA-FGGGCTCATGGGCCAGAGTGTprobe for <i>kojA</i> kojA-RGAGAAATCCGGGCCAGAACCprobe for <i>kojA</i> kojR-RGGCGTCATGGGAGAGGTGTGAprobe for <i>kojT</i> kojT-FCACCTACTGGGAAGGTCAACCprobe for <i>kojT</i> kojT-FCACCTACTCAGGAGGAGGGGAACCAprobe for <i>kojT</i> ipnA-FACCCTCCAAACCACCCAAAGprobe for <i>kojT</i> ipnA-FACCCTCCAAACCACCCAAAGGprobe for <i>lacA</i> lacA-FAGCCCTCCAAACCACCCAAAGGprobe for <i>lacA</i>  | laeA(adeA)-C     | CTGTGGACTCGTATGCTGTTGCGCAGAGAGCTCCATTACTGGGTATTCGG  |  |
| lacA-A2GGGATACCAACCAACAACACCTHuson PCR for lacAlacA-D2TTACGTTTGGGAACGGAGTCAlacAlacA-FCAGCCCTCAAACCACCCAAAlacA ORFlacA-GTTGAACGCCTCCGACTTGACdisruption casette for lacA inlacA/SCCATACGGCACGACTATTGCCAAGGAGAGCCATATTCGATGGCGACAGGCTGATGdisruption casette for lacA inlacA(sC)-BGAACGAGCGATTGCCAAGGAGAGCCATATTCGATGGCGACAGGCTGATGdisruption casette for lacA inlacA(sC)-CCATACGGCCCTCGTTCGTCGTCCGTTCSC amplificationsC-FTCTCTTGGCAATAGCTGCCCGTATGsc amplificationsC-RTCTCTTGGCAATAGCTGCCCGTATGconfirmation of transformationhstD-comp-BGAACGAGCGAACGAGGAGCCATATTAACCGTGACATGACCCTTGcomplementation of hstDsctadacA-RGCCTTGGGCAGCTATTGCCAAGAGACCGTCATGTCCAGGAAGATAGGTCAprobe for kajAkojA-FGAGAAATCCGGGCCAGAACCprobe for kajAkojA-RGGCGTCATGGGAGAGTGTGAprobe for kajFkojR-RGGCGTCATGGGAACCAprobe for kajFkojT-FCAGGGTGTCTTTGCAAACCprobe for kajFkojT-FCAGCTACTCACGGGGCAACCAprobe for kajFkojT-RGTTGCGGATAGGCGAACCAprobe for jaAipnA-FCACCTACTCACGAGGTCAACprobe for jaAipnA-FCACCTCGTGAGAGGGGAACCAprobe for jaAlacA-FAGCCCTCCAAACCACCCAAAGprobe for jaAipnA-FCACCTCGTGAGAGGGGAACCAprobe for jaAipnA-FAGCCCTCAAACCACCCAAAGprobe for jaAipnA-FAGCCCTCGAACCACAGGGGGAACCAprobe for jaAipnA-FAGCCCTCAAACCACCCCAAAGprobe for lacA <td>laeA-D</td> <td>GAACCCGCCAACATCAAGCTTC</td> <td>3'flanking region of <i>laeA</i></td>  | laeA-D           | GAACCCGCCAACATCAAGCTTC                              | 3'flanking region of <i>laeA</i>       |
| laeA-D2TTACGTTTGGGAACGGAGTCAIusion PCR for laeAlaeA-FCAGCCTCAAACCACCCAAAlaeA ORFlaeA-GTTGAACGCCTCCGACTTGACdisruption casette for laeA inlaeA(sC)-BGAACGAGACGAACGAGGAGCCATATTCCGATGGCGACAGGCTGATGdisruption casette for laeA inlaeA(sC)-CCATACGGGCAGCTATTGCCCAAGAGAAGAGCTCCATTACTGGGTATTCGG $\Delta hstD$ backgroundsC-FATATGGCTCCTCGTTCGTCCGTTCsC amplificationsC-RTCTCTTGGCAATAGCTGCCCGATGAconfirmation of transformationhstD-comp-BGAACGAGCGAACGAGGAGCCATATTAACCGTGACATGACCCTTGcomplementation of hstDadeA fusion sC-FCATACGGGCAGCTATTGCCAAGAGACCGTCATGTCCAGGAAGATAGGTCAComplementation of hstDhstD-comp-BGAACGAGCGACGTATTGCCAAGAGACCGTCATGTCCAGGAAGATAGGTCAcomplementation of hstDhstD-comp-BGAACGAGGCCTCATCAGprobe for kajAkojA-FGGTTTCCAGGGCCTCATCAGprobe for kajAkojA-FGGCGTCATGGCAGAACCprobe for kajAkojR-RGGGCGTCATGGCGAACCAprobe for kajTkojR-RGGCGGTATGGCGAACCAprobe for ipnAipnA-FCACCTACTCACGAGGTCAACCprobe for ipnAipnA-RGTTGACCTCGTGAGTAGGTGprobe for ipnAiaeA-FAGCCCTCAAACCACCCAAAGprobe for ipnAiaeA-FAGCCCTCAAACCACCCAAAGprobe for ipnAiaeA-FTTGAACGCCTCCGACTGACCprobe for ipnA   | laeA-A2          | GGGATACCAACCACAACACCT                               |  |
| lacA-FCAGCCCTCAAACCACCCAAAlacA ORFlacA-GTTGAACGCCTCCGACTTGACdisruption casette for lacA in<br>(AhstD background)lacA(SC)-BGAACGAGACGAACGAGGAGCCATATTCGATGGCGACAGGCTGATGdisruption casette for lacA in<br>(AhstD background)sc-FATATGGCTCCTCGTTCGTTCGTCCGTTCsC amplificationsc-RTCTCTTGGCAATAGCTGCCCGTATGonfirmation of transformationhstD-comp-BGAACGAGCGAACGAGGAGCCATATTACCGTGACATGACCCTTGconfirmation of transformationhstD-comp-BGAACGAGCGAACGAGGAGCCATATTACCGTGACATGACCCTTGcomplementation of hstDhstD-comp-BGAACGAGCGACGAGTATTGCCAAGAGACCGTCATGTCCAGGAAGATAGGTCAComplementation of hstDhstD-comp-BGAACGAGCGCTCATCGGAGAGCCATATTACCGTGACATGACCCTTGcomplementation of hstDhstD-comp-BGAACGAGCGCCCCAATGCCCCAAGACCprobe for kojAkojA-FGGTTTCCAGGGCCAGAACCprobe for kojAkojA-FGGCGAGCTATGACCCCATTprobe for kojAkojT-FCGGCCAGGTATGGCGAAACCAprobe for kojTkojT-FCACCTACTCACGAGGTCAACCAprobe for ipnAipnA-FCACCTACTCACGAGGTAAGCGprobe for ipnAipnA-FAGCCCTCAAACCACCCAAAGprobe  | laeA-D2          | TTACGTTTGGGAACGGAGTCA                               | fusion PCR for <i>laeA</i>             |
| laeA-GTTGAACGCCTCCGACTTGAClaeA ORFlaeA(sC)-BGAACGAGACGAACGAGGAGCCATATTCGATGGCGACAGGCTGATGdisruption casette for <i>laeA</i> inlaeA(sC)-CCATACGGGCAGCTATTGCCAAGAGAAGAGCTCCATTACTGGGTATTCGGΔhstD backgroundsC-FATATGGCTCCTCGTTCGTCCGTTCsC amplificationsc-RTCTCTTGGCAATAGCTGCCCGTATGconfirmation of transformationhstD-comp-BGAACGAGACGAACGAGGAGCCATATTAACCGTGACATGACCCTTGcomplementation of transformationhstD-comp-BGAACGAGACGACGAGGAGCCATATTAACCGTGACATGACCCTTGcomplementation of hstDadeA fusion sc-FCATACGGGCAGCTATTGCCAAGAGACCGTCATGTCCAGGAAGATAGGTCAcomplementation of hstDnested adeA-RGCCTTGGTCTGGGAGTGTprobe for kojAkojA-FGGGGTCATGGGAGAGTGAprobe for kojAkojR-FCGGCCAGCTATGACCCCATTprobe for kojTkojR-RGGCGTCATGGGAACGAACCAprobe for kojTipnA-FCACCTACTCACGAGGTCAACprobe for ipnAipnA-RGTTGACCTCGTGAGTAGGTGprobe for ipnAlaeA-FAGCCTCCAAACCACCCAAAGprobe for laeAlaeA-RTTGAACGCCTCCGACTTGACprobe for laeA  | laeA-F           | CAGCCCTCAAACCACCCAAA                                |  |
| laeA(sC)-BGAACGAGACGAACGAGGAGCCATATTCGATGGCGACAGGCTGATG<br>ATACGGGCAGCTATTGCCAAGAGAAGAGACCCATTACTGGGTATTCGG<br>AfatGGCTCCTCGTTCGTCCGTC<br>sC-Rdisruption casette for <i>laeA</i> in<br>A <i>hstD</i> background<br>sC amplificationsC-FATATGGCTCCTCGTTCGTCCGTC<br>CGCAATAGCTGCCCGTATGsC amplificationp-amyB-FGGCAACTCGCTTACCGATTAC<br>CATACGGGCAGCACTATTGCCAAGAGACCGTGACATGACCCTTG<br>adeA fusion sC-Fconfirmation of transformationhstD-comp-BGAACGAGCGAACGAGGAGCCATATTCACCGTGACATGACCCTTG<br>adeA fusion sC-FCATACGGGCAGCTATTGCCAAGAGACCGTCATGTCCAGGAAGATAGGTCA<br>GCTTGGTCTGGGAGTGTComplementation of <i>hstD</i> hstD-comp-BGAGAAATCCGGGCCCAGAACC<br>GCTGGTCTGGGAGTGTprobe for <i>kajA</i> hstD-comp-BGACCAGCAGCCCCATCAG<br>GCCTTGGCAAGCCCCATTprobe for <i>kajA</i> hstD-comp-BGGCGTCTGGGAGGTGTGAprobe for <i>kajA</i> hstD-comp-BGGCGTCATGGGCCAGAACCprobe for <i>kajA</i> hstD-comp-BGGCGTCATGGGAGAGTGGAACCAprobe for <i>kajA</i> hstD-comp-BGGCGTCATGGGAGAGTGGAACCAprobe for <i>kajA</i> hstD-comp-BGGCGTCATGGGAACCAprobe for <i>kajA</i> hstD-comp-BGTTCCAGGGCAGAACCAprobe for <i>kajA</i> hstD-comp-BGTTCCAGGGCAGAACCAprobe for <i>ipnA</i> hstD-comp-BGGCGTCATGGGAGGGGAACCAprobe for <i>ipnA</i> hstD-comp-BGTTCCGGAACCACCCAAAGprobe for <i>laeA</i>  | laeA-G           | TTGAACGCCTCCGACTTGAC                                | laeA ORF                               |
| laeA(sC)-C       CATACGGGCAGCTATTGCCAAGAGAAGAGCTCCATTACTGGGTATTCGG       A hstD background         sc-F       ATATGGCTCCTCGTTCGTCCGTTC       sC amplification         sc-R       TCTCTTGGCAATAGCTGCCCGTATG       confirmation of transformation         hstD-comp-B       GAACGAGCAGCTATTGCCAAGAGACCGTCATGTCCAGGAAGACCCTTG       complementation of hstD         adeA fusion sC-F       CATACGGGCAGCTATTGCCAAGAGACCGTCATGTCCAGGAAGATAGGTCA       Complementation of hstD         nested adeA-R       GCCTTGGTCTGGGAGTGT       complementation of hstD         kojA-F       GGTTTCCAGGGCCAGAACC       probe for kojA         kojR-R       GAGAAAATCCGGGCCAGAACC       probe for kojA         kojT-F       CGGCCAGCTATGGCAACCA       probe for kojA         kojT-R       GTTCTGGGATAGGCGAACCA       probe for kojA         ipnA-F       CACCTACTCACGAGGTCAAC       probe for kojA         ipnA-R       GTTGACCTCGTGAGAGAGTGG       probe for ipnA         laeA-F       AGCCCTCAAACCAAAGG       probe for ipnA         laeA-F       AGCCCTCAAACCAAAGG       probe for laeA  | laeA(sC)-B       | GAACGAGACGAACGAGGAGCCATATTCGATGGCGACAGGCTGATG       | disruption casette for <i>laeA</i> in  |
| sC-F       ATATGGCTCCTCGTTCGTTCGTTC       sC amplification         sc-R       TCTCTTGGCAATAGCTGCCCGTATG       confirmation of transformation         hstD-comp-B       GAACGAGACGAACGAGGAGCCATATTAACCGTGACATGACCCTTG       confirmation of transformation         hstD-comp-B       GAACGAGCGACGATTGCCCAGAGAGACCGTCATGTCCAGGAAGATAGGTCA       Complementation of hstD         nested adeA-R       GCCTTGGTCTGGGAGTGT       complementation of hstD         kojA-F       GGTTTCCAGGGCCAGAACC       probe for kojA         kojR-R       GAGAAATCCGGGCCAGAACC       probe for kojA         kojT-F       CGGCCAGCTATGGCAACCA       probe for kojA         kojT-R       GTTCTGGGATAGGCGAACCA       probe for kojA         ipnA-F       CACCTACTCACGAGGTCAAC       probe for ipnA         ipnA-R       GTTGACCTCGTGAGTAGGTG       probe for ipnA         iaeA-F       AGCCCTCAAACCACAAAG       probe for ipnA         iaeA-R       TTGAACGCCTCGACTAGAC       probe for ipnA  | laeA(sC)-C       | CATACGGGCAGCTATTGCCAAGAGAGAGAGCTCCATTACTGGGTATTCGG  | $\Delta hstD$ background               |
| sC-R TCTCTTGGCAATAGCTGCCCGTATG confirmation<br>P-amyB-F GGCAACTCGCTTACCGATTAC confirmation of transformation<br>hstD-comp-B GAACGAGGACGAACGAGGGGGCCATATTAACCGTGACATGACCCTTG<br>adeA fusion sC-F CATACGGGCAGCTATTGCCAAGAGACCGTCATGTCCAGGAAGATAGGTCA<br>nested adeA-R GCCTTGGTCTGGGAGTGT<br>kojA-F GGTTTCCAGGGCCAGAACC<br>kojA-R GAGAAATCCGGGCCAGAACC<br>kojR-R GGCGTCATGGGAGAGTGTGA<br>kojT-F CGGCCAGCTATGACCCCATT<br>kojT-R GTTCTGGGATAGGCGAACCA<br>hacA-F AGCCCTCATCAGGGCCAACC<br>adeA-R TTGAACGCCTCGACTGAC<br>hacA-R TTGAACGCCTCGACTGAC<br>score contained stab<br>score confirmation of transformation<br>confirmation of transformation<br>confirmation of transformation<br>confirmation of transformation<br>score confirmation of transformation of transformation<br>score confirmation of transformation of transformation<br>score confirmation of transformation of transformation of transformation of transformation of transfo | sC-F             | ATATGGCTCCTCGTTCGTCTCGTTC                           |  |
| P-amyB-FGGCAACTCGCTTACCGATTACconfirmation of transformationhstD-comp-BGAACGAACGAACGAAGGAGCCATATTAACCGTGACATGACCCTTGComplementation of hstDadeA fusion SCFCATACGGGCAGCTATTGCCAAGAGACCGTCATGTCCAGGAAGATAGGTCAComplementation of hstDnested adeA-RGCCTTGGTCTGGGAGTGTprobe for kojAkojA-FGGGCAGCTATGACCCCATTprobe for kojAkojA-RGGGCTCATGGGAGAGTGTGAprobe for kojRkojR-RGGCGTCATGGGAGAGTGTGAprobe for kojRkojT-FCGAGGTGTCTCTTGCAAACCprobe for kojTkojT-RGTTCTGGGATAGGCGAACCAprobe for kojTipnA-FCACCTACTCACGAGGTCAACprobe for ipnAipnA-RGTTGACCTCGTGAGTAGGTGprobe for ipnAlaeA-FAGCCCTCAAACCACCCAAAGprobe for laeA   | sC-R             | TCTCTTGGCAATAGCTGCCCGTATG                           | sC amplification                       |
| hstD-comp-BGAACGAGACGAACGAGGAGCCATATTAACCGTGACATGACCCTTGadeA fusion sC-FCATACGGGCAGCTATTGCCAAGAGACCGTCATGTCCAGGAAGATAGGTCAnested adeA-RGCCTTGGTCTGGGAGTGTkojA-FGGTTTCCAGGGCCAGAACCkojA-RGAGAAATCCGGGCCAGAACCkojR-RGGCGTCATGGGAGAGTGTGAgGCGTCATGGGAGAGTGTGAprobe for kojAkojT-FCGAGGTGTCTCTTGCAAACCkojT-RGTTCTGGGATAGGCGAACCAipnA-FCACCTACTCACGAGGTCAACipnA-RGTTGACCTCGTGAGTAGGTGlaeA-FAGCCCTCAAACCCCAAAGlaeA-RTTGAACGCCTCGACTTGAC  | P-amyB-F         | GGCAACTCGCTTACCGATTAC                               | confirmation of transformation         |
| adeA fusion sC-FCATACGGGCAGCTATTGCCAAGAGACCGTCATGTCCAGGAAGATAGGTCAComplementation of hstDnested adeA-RGCCTTGGTCTGGGAGTGTprobe for kojAkojA-FGGTTTCCAGGGCCTCATCAGprobe for kojAkojA-RGAGAAATCCGGGCCAGAACCprobe for kojAkojR-RGGCGTCATGGGAGAGTGTGAprobe for kojRkojT-FCGAGGTGTCTCTTGCAAACCprobe for kojTkojT-RGTTCTGGGATAGGCGAACCAprobe for kojTipnA-FCACCTACTCACGAGGTCAACprobe for ipnAipnA-RGTTGACCTCGTGAGTAGGTGprobe for ipnAlaeA-FAGCCCTCAAACCACCCAAAGprobe for laeA   | hstD-comp-B      | GAACGAGACGAACGAGGAGCCATATTAACCGTGACATGACCCTTG       |  |
| nested adeA-R       GCCTTGGTCTGGGAGTGT         kojA-F       GGTTTCCAGGGCCTATCAG         kojA-R       GAGAAATCCGGGCCAGAACC         kojR-R       GAGCGTCATGACCCCATT         kojR-R       GGCGTCATGGGAGAGTGTGA         kojT-F       CGAGGTGTCTCTTGCAAACC         kojT-R       GTTCTGGGATAGGCGAACCA         ipnA-F       CACCTACTCACGAGGTCAAC         ipnA-R       GTTGACCTCGTGAGTAGGTG         laeA-F       AGCCCTCAAACCACCCAAAG         laeA-R       TTGAACGCCTCCGACTTGAC  | adeA fusion sC-F | CATACGGGCAGCTATTGCCAAGAGACCGTCATGTCCAGGAAGATAGGTCA  | Complementation of hstD                |
| kojA-FGGTTTCCAGGGCCTCATCAGprobe for kojAkojA-RGAGAAATCCGGGCCAGAACCprobe for kojAkojR-FCGGCCAGCTATGACCCCATTprobe for kojRkojR-RGGCGTCATGGGAGAGTGTGAprobe for kojRkojT-FCGAGGTGTCTCTTGCAAACCprobe for kojTipnA-FGACCTACTCACGAGGTCAACprobe for ipnAipnA-RGTTGACCTCGTGAGTAGGTGprobe for ipnAlaeA-FAGCCCTCAAACCACCCAAAGprobe for laeA   | nested adeA-R    | GCCTTGGTCTGGGAGTGT                                  |  |
| kojA-R     GAGAAATCCGGGGCCAGAACC     probe for kojA       kojR-F     CGGCCAGCTATGACCCCATT     probe for kojR       kojR-R     GGCGTCATGGGAGAGTGTGA     probe for kojR       kojT-F     CGAGGTGTCTCTTGCAAACC     probe for kojT       kojT-R     GTTCTGGGATAGGCGAACCA     probe for kojT       ipnA-F     CACCTACTCACGAGGTCAAC     probe for ipnA       laeA-F     AGCCCTCAAACCACCCAAAG     probe for ipnA       laeA-R     TTGAACGCCTCCGACTTGAC     probe for laeA   | kojA-F           | GGTTTCCAGGGCCTCATCAG                                |  |
| kojR-F     CGGCCAGCTATGACCCCATT     probe for kojR       kojR-R     GGCGTCATGGGAGAGTGTGA     probe for kojR       kojT-F     CGAGGTGTCTCTTGCAAACC     probe for kojT       kojT-R     GTTCTGGGATAGGCGAACCA     probe for kojT       ipnA-F     CACCTACTCACGAGGTCAAC     probe for ipnA       laeA-F     AGCCCTCCAAACCACCCAAAG     probe for laeA   | kojA-R           | GAGAAATCCGGGCCAGAACC                                | probe for kojA                         |
| kojR-R     GGCGTCATGGGAGAGTGTGA     probe for kojR       kojT-F     CGAGGTGTCTCTTGCAAACC     probe for kojT       kojT-R     GTTCTGGGATAGGCGAACCA     probe for kojT       ipnA-F     CACCTACTCACGAGGTCAAC     probe for ipnA       ipaA-R     GTTGACCTCGTGAGTAGGTG     probe for ipnA       laeA-F     AGCCCTCCAAACCACCCAAAG     probe for laeA   | kojR-F           | CGGCCAGCTATGACCCCATT                                |  |
| kojT-F     CGAGGTGTCTCTTGCAAACC     probe for kojT       kojT-R     GTTCTGGGATAGGCGAACCA     probe for kojT       ipnA-F     CACCTACTCACGAGGTCAAC     probe for ipnA       ipnA-R     GTTGACCTCGTGAGTAGGTG     probe for ipnA       laeA-F     AGCCCTCAAACCACCCAAAG     probe for laeA   | koiR-R           | GGCGTCATGGGAGAGTGTGA                                | probe for <i>kojR</i>                  |
| kojT-R     GTTCTGGGATAGGCGAACCA     probe for kojT       ipnA-F     CACCTACTCACGAGGTCAAC     probe for ipnA       ipnA-R     GTTGACCTCGTGAGTAGGTG     probe for ipnA       laeA-F     AGCCCTCAAACCACCCAAAG     probe for laeA       laeA-R     TTGAACGCCTCCGACTTGAC     probe for laeA   | koiT-F           | CGAGGTGTCTCTTGCAAACC                                |  |
| ipnA-F     CACCTACTCACGAGGTCAAC     probe for ipnA       ipnA-R     GTTGACCTCGTGAGTAGGTG     probe for ipnA       laeA-F     AGCCCTCAAACCACCCAAAG     probe for laeA       laeA-R     TTGAACGCCTCCGACTTGAC     probe for laeA  | koiT-R           | GTTCTGGGATAGGCGAACCA                                | probe for <i>kojT</i>                  |
| ipnA-R     GTTGACCTCGTGAGTAGGTG     probe for ipnA       laeA-F     AGCCCTCAAACCACCCAAAG     probe for laeA       laeA-R     TTGAACGCCTCCGACTTGAC     probe for laeA   | ipnA-F           | CACCTACTCACGAGGTCAAC                                |  |
| laeA-F AGCCCTCAAACCACCCAAAG probe for <i>laeA</i>  | ipnA-R           | GTTGACCTCGTGAGTAGGTG                                | probe for <i>ipnA</i>                  |
| laeA-R TTGAACGCCTCCGACTTGAC probe for laeA   | laeA-F           | AGCCCTCAAACCACCCAAAG                                |  |
|  | laeA-R           | TTGAACGCCTCCGACTTGAC                                | probe for <i>laeA</i>                  |

<sup>a</sup> Additional nucleotides for fusion PCR are indicated by underlines <sup>b</sup> Additional nucleotides for In-Fusion reaction are indicated in small letters

#### Table I.6.4. Significantly changed genes in $\Delta hstD$

| Gene ID                          | Description  | Fold change                |                   | FunCat categorization <sup>a,b</sup>     |
|----------------------------------|--|----------------------------|-------------------|--|
| AO080553000121                   | KoiT, putative transporter; present in the koiic acid biosynthetic gene cluster  | (AhstD / Control)<br>105.5 | [20][32]          | [20.01][20.03][20.09][32.05][32.07]      |
| AO080550000061                   | Hydroxyindole-O-methyltransferase and related SAM-dependent methyltransferases   | 102.5                      | [01]              | [01.05][01.20]                           |
| AO080501000196<br>AO080563000007 | fleA fucose-specific lectin<br>CpaD. O-dimethylallyltransferase (DMAT); dimethylallylates cAATrp to form beta-cyclopiazonic acid | 61.82                      | #                 | #  |
| AO080554000441                   | Uncharacterized membrane protein, predicted efflux pump  | 38.39                      | [20][32]          | [20.01][32.07]                           |
| AO080563000004                   | Predicted protein  | 32.27                      | [20][32][34]      | [20.01][20.03][20.09][32.05][32.07]      |
| AO080525000393                   | Predicted protein  | 29.96                      | [01][11]          | [34.11]<br>[01.02][11.02]                |
| AO080563000005                   | Cytochrome P450 CYP3 CYP5 CYP6 CYP9 subfamilies  | 27.59                      | [01]              | [01.06][01.20]                           |
| A0080563000006<br>A0080508000254 | Predicted protein Predicted protein  | 25.97                      | #                 | #  |
| A0080511000457                   | Predicted protein  | 21.4                       | #                 | #  |
| AO080522000026                   | Catalase (peroxidase I)  | 20.19                      | [32]              | [32.07]                                  |
| A0080536000097<br>A0080542000015 | Predicted protein Predicted protein  | 19.6                       | [32]              | #<br>[32.05]                             |
| AO080515000039                   | Predicted protein  | 17.93                      | #                 | #  |
| AO080550000056<br>AO080508000512 | Proteins containing the FAD binding domain   | 14.42                      | [01]              | [01.05][01.20]                           |
| A0080515000015                   | Uncharacterized protein, possibly involved in utilization of glycolate and propanediol   | 12.31                      | #                 | #  |
| AO080513000111                   | Predicted protein  | 11.85                      | #                 | #  |
| A0080529000071<br>A0080508000290 | Predicted protein  | 10.43                      | #                 | *  |
| AO080523000388                   | Predicted protein  | 9.984                      | #                 | #  |
| A0080554000006<br>A0080550000062 | Predicted protein<br>Dehydrogenases (flavoproteins)  | 9.951                      | #                 | 24<br>24                                 |
| AO080525000250                   | Predicted protein  | 9.747                      | #                 | #  |
| AO080553000119<br>AO080541000467 | KojA, FAD-dependent oxidoreductase; present in the kojic acid biosynthetic gene cluster  | 9.711                      | #                 | #  |
| A0080550000076                   | Predicted protein  | 9.323                      | #                 | #  |
| AO080539000068                   | Predicted protein  | 9.028                      | #                 | #  |
| A0080510000132<br>A0080529000068 | Predicted protein<br>Predicted protein   | 8.772                      | #                 | #  |
| AO080554000051                   | Predicted protein  | 7.73                       | #                 | #  |
| AO080550000193<br>AO080551000140 | RNA 3 -terminal phosphate cyclase<br>Polykatida synthese modules and related proteins  | 7.67                       | #                 | # [01 20][32 05]                         |
| A0080511000259                   | Predicted protein  | 6.937                      | #                 | #  |
| AO080523000239                   | TPR repeat   | 6.617                      | #                 | #  |
| A0080537000053<br>A0080527000194 | Predicted hydrolases or acyltransferases (alpha beta hydrolase superfamily)<br>Predicted xvlanase chitin deacetvlase             | 6.315                      | #<br>[01][16]     | #<br>[01.05][01.25][16.05]               |
| AO080551000190                   | Beta-lactamase class C and other penicillin binding proteins   | 6,175                      | #                 | #  |
| AO080508000358<br>AO080515000064 | Predicted protein<br>Multiconner oxidases  | 5.923                      | #                 | #<br>[01.05][01.07][01.25][32.07]        |
| A0080527000284                   | Predicted protein  | 5,77                       | #                 | #  |
| A0080549000421                   | Predicted protein  | 5.727                      | #                 | #  |
| A0080523000444                   | Predicted protein  | 5.71                       | #                 | *  |
| AO080567000074                   | Predicted protein  | 5.689                      | #                 | #  |
| AO080541000077<br>AO080523000389 | Predicted protein<br>Cytochrome P450 CVP4 CVP19 CVP26 subfamilies  | 5.673                      | #                 | #<br>[32.07]                             |
| AO080521000213                   | Predicted protein  | 5.575                      | #                 | #  |
| A0080547000015<br>A0080523000405 | Predicted protein Predicted protein  | 5.394                      | #                 | #  |
| A0080527000405<br>A0080527000412 | Predicted protein  | 5.107                      | [32][42]<br>#     | [52.01][42.01][42.04]<br>#               |
| AO080525000701                   | Alkaline phosphatase   | 5.07                       | [01]              | [01.04][01.06][01.07]                    |
| A0080523000550<br>A0080562000080 | afIJ Predicted protein   | 4.932                      | #                 | 14<br>14                                 |
| AO080554000398                   | Predicted protein  | 4.746                      | #                 | #  |
| AO080525000625<br>AO080541000440 | Predicted protein Predicted protein  | 4.693                      | #                 | #  |
| A0080530000095                   | Predicted protein  | 4.602                      | #                 | #  |
| AO080554000103                   | Cytochrome P450 CYP3 CYP5 CYP6 CYP9 subfamilies  | 4.597                      | [01][20][32]      | [01.01][01.02][01.06][01.20][20.01]      |
| 40080547000014                   | Ankarin  | 4.512                      | #                 | [32.07]                                  |
| A0080549000406                   | Predicted dehydrogenases and related proteins  | 4.472                      | [01][11]          | [01.05][11.02]                           |
| A0080508000357                   | Chitin synthase hyaluronan synthase (glycosyltransferases)   | 4.45                       | #                 | #  |
| A0080525000006                   | Predicted protein  | 4.401                      | #                 | #<br>[01.06][01.07][01.20][16.17][16.21] |
| AO080525000059                   | Cytochrome P450 CYP2 subfamily   | 4.37                       | [01][16][20][32]  | [20.01][32.07]                           |
| AO080523000500                   | Predicted protein  | 4.32                       | #                 | #  |
| A0080527000186<br>A0080523000718 | Oxidosqualene-lanosterol cyclase and related proteins<br>Carboxylesterase type B   | 4.272                      | [01]<br>#         | [01.06][01.20]<br>#                      |
| AO080529000067                   | Cytochrome P450 CYP11 CYP12 CYP24 CYP27 subfamilies  | 4.247                      | [01][32]          | [01.01][01.20][32.07]                    |
| AO080515000065<br>AO080532000090 | Predicted protein Predicted protein  | 4.223                      | #                 | #  |
| A0080508000361                   | Predicted protein  | 4.159                      | #                 | 4  |
| AO080551000170                   | Predicted protein  | 4.114                      | [01][16]          | [01.01][01.20][16.17]                    |
| A0080525000706<br>A0080532000546 | Predicted protein<br>Cytochrome P450 CYP2 subfamily  | 4.098                      | #<br>[01][16][20] | #<br>[01.20][16.17][16.21][20.01]        |
| AO080508000305                   | Vesicular amine transporter  | 4.008                      | #                 | #  |
| AO080527000377<br>AO080531000104 | Glucose dehydrogenase choline dehydrogenase mandelonitrile lyase (GMC oxidoreductase family) Predicted protein                   | 4.008                      | [01][16][20]      | [01.01][01.05][01.20][16.21][20.01]<br># |
| A0080525000269                   | Predicted protein  | 3.848                      | #                 | #  |
| AO080557000082                   | Cofilin; actin depolymerisation factor   | 3.847                      | #                 | #  |
| AO080532000337<br>AO080523000512 | Chaperone-dependent E3 ubiquitin protein ligase (contains TPR repeats)<br>Predicted protein                                      | 3.838                      | #                 | 14<br>24                                 |
| AO080523000573                   | Predicted protein  | 3.77                       | #                 | #  |
| A0080536000086                   | ATPases of the AAA <sup>+</sup> class  | 3.719                      | #                 | #  |
| A0080515000151<br>A0080525000687 | Predicted protein<br>Predicted transporter (major facilitator superfamily)   | 3.648                      | [43]              | [43.01]<br>#                             |
| AO080557000045                   | Predicted protein  | 3.624                      | [32]              | [32.05]                                  |
| AO080515000071<br>AO080501000080 | Predicted protein Predicted protein  | 3.604                      | #                 | #  |
| A0080566000093                   | Ankyrin  | 3.555                      | #                 | #  |
| AO080525000026                   | SAM-dependent methyltransferases   | 3.536                      | #                 | #  |
| AO080515000098<br>AO080554000362 | Predicted protein Predicted protein  | 3.503                      | #                 | #<br>#                                   |
| AO080503000171                   | Phosphoenolpyruvate carboxykinase (ATP)  | 3.468                      | [01][02]          | [01.04][01.05][02.01]                    |
| AO080523000572<br>AO080533000276 | Predicted protein<br>Multidrug resistance-associated protein mitoxantrone registance protein ABC superfamily-                    | 3.423                      | #                 | #  |
| A0080508000531                   | Predicted protein  | 3.39                       | #                 | #  |
| AO080549000304                   | Carboxylesterase type B  | 3.38                       | [01]              | [01.06]                                  |
| AO080506000286<br>AO080523000216 | Predicted protein Predicted protein  | 3.315                      | #                 | #  |
| AO080538000066                   | Acyl-CoA synthetase  | 3.298                      | [01]              | [01.01][01.05][01.20]                    |
| AO080523000032                   | Amino acid transporters  | 3.296                      | [01][20][32][34]  | [01.06][20.01][20.03][20.09[32.01]       |
| AO080510000108                   | ATPases of the $AAA^+$ class   | 3,199                      | #                 | [34.01][34.11]<br>#                      |
|                                  | CALL BOAR VILLING COCCE. VIB22   | w14/7                      |                   |  |

| A0080515000095   | Jacalin-like lectin domain-containing protein  | 3.158   | #  | #   |
|--|--|---|--|---|
| AO080525000640   | Predicted protein  | 3.156   | #  | #   |
| A0080527000200<br>A0080553000120   | KoiR, Zn(II)2Cvs6 transcription factor; induced by koiic acid; present in the koiic acid biosynthetic gene clus  | 3.083   | [01]<br>[11][34]   | [11.02][34.11]  |
| 10000525000062   | A satulala lin saturana Distanti dala lin saturana   | 2.076   | (01)(22)   | [01.05][01.06][01.20][01.25][32.05]   |
| A0080525000062   | Acetyicholmesterase Butyryicholmesterase   | 3,076   | [01][32]   | [32.07][32.10]  |
| A0080541000359   | Integral membrane ankyrin-repeat protein Kidins220 (protein kinase D substrate)  | 3.076   | #<br>[20][22]  | #   |
| A0080541000097<br>A0080546000223   | Predicted transporter (major facilitator superfamily) Predicted protein  | 3.039   | [20][32]<br>#  | [20.01][32.07]<br>#   |
| AO080542000014   | Cytochrome P450 CYP4 CYP19 CYP26 subfamilies   | 3.037   | [01][32]   | [01.01][32.05][32.07]   |
| AO080539000029   | Predicted protein  | 3.016   | [11]   | [11.02]   |
| AO080547000070<br>AO080523000242   | Predicted protein Predicted protein  | 2.985   | #  | #   |
| A0080502000014   | Uncharacterized conserved protein  | 2.976   | #  | #   |
| AO080503000338   | NAD <sup>+</sup> ADP-ribosyltransferase Parp, required for poly-ADP ribosylation of nuclear proteins   | 2.959   | [01][10][14][16]   | [01.05][10.01][14.07][16.01][16.03]   |
| AO080506000124   | Predicted protein  | 2.951   | #  | #   |
| AO080542000029<br>AO080521000317   | Conserved protein domain typically associated with flavoprotein oxygenases, DIM6 NTAB family<br>Predicted protein  | 2,943   | #  | #   |
| A0080536000058   | Predicted protein  | 2.901   | #  | #   |
| AO080518000104   | Predicted protein  | 2.888   | #  | #   |
| AO080551000149   | Predicted protein Predicted protein  | 2.88  | #  | #   |
| A0080501000088   | 3-polyprenyl-4-hydroxybenzoate decarboxylase and related decarboxylases  | 2.843   | ü  | ü   |
| AO080509000188   | Predicted aminoglycoside phosphotransferase  | 2.835   | <i>ii</i>  | #   |
| AO080554000077   | Monodehydroascorbate ferredoxin reductase  | 2.835   | [02]   | [02.11]   |
| A0080506000051   | Predicted protein<br>Predicted short chain-type dehydrogenase  | 2.820   | [01][32]   | "<br>[01.05][01.20][32.05]  |
| 1000005100000252   | ATTR dambalance for a fill B L B L B A totachard where here have been been to  | 2.012   | [01][11][12][20]   | [01.04][01.06][11.04][16.17][16.19]   |
| A0080549000355   | ATP adenyiyitransterase (5,5 -P-1, P-4-tetraphosphate phosphorylase II)  | 2.812   | [01][11][10][20]   | [20.01][20.03][20.09]   |
| AO080523000207   | Predicted protein  | 2.766   | #  | #   |
| AO080536000143<br>AO080505000118   | I ellurite resistance protein and related permeases Predicted protein  | 2.745   | #  | #   |
| AO080546000372   | Ornithine aminotransferase   | 2.705   | [01][16]   | [01.01][01.02][01.20][16.21]  |
| AO080505000202   | Methionyl-tRNA formyltransferase   | 2.701   | #  | #   |
| AO080522000033<br>AO080509000132   | Predicted protein Predicted protein  | 2.694   | #  | #   |
| AO080546000363   | Predicted protein  | 2.676   | #  | #   |
| AO080534000002   | Non-ribosomal peptide synthetase modules and related proteins  | 2,663   | #  | #   |
| AO080561000015   | Predicted protein<br>Thransing debutrogeneses and related Zn. dependent debudrogeneses   | 2.659   | #  | #   |
| A0080515000061   | Uncharacterized conserved protein  | 2.644   | #  | #   |
| AO080503000025   | Predicted protein  | 2.631   | <i>ii</i>  | #   |
| AO080525000209   | Dihydrolipoamide succinyltransferase (2-oxoglutarate dehydrogenase, E2 subunit)  | 2.617   | <i>ii</i>  | #   |
| AO080541000475<br>AO080512000001   | Glutathione S-transferase<br>Transposon-encoded proteins with TYA reverse transcriptase integrase domains in various combinations  | 2.593   | 32  40 <br>#   | 32.01  32.07  40.10 <br>#   |
| AO080523000247   | Predicted acyl-CoA transferases carnitine dehydratase  | 2.553   | #  | #   |
| AO080508000270   | RNA polymerase II transcription termination factor TTF2 lodestar, DEAD-box superfamily   | 2.541   | #  | #   |
| AO080523000391<br>AO080527000504   | Cytochrome P450 CYP3 CYP5 CYP6 CYP9 subfamilies<br>Predicted protein   | 2.519   | [16][32]   | [16.21][32.05][32.07]<br>#  |
| A0080525000318   | Predicted protein  | 2.501   | #  | #   |
| AO080566000091   | Predicted protein  | 2.493   | #  | #   |
| AO080503000216   | Predicted protein  | 2,492   | #  | #   |
| A0080523000079<br>A0080532000061   | Uncharacterized conserved protein  | 2.491   | "<br>[20]  | "<br>[20.01][20.03][20.09]  |
| AO080505000203   | Nucleoside-diphosphate-sugar epimerases  | 2,467   | [01][11][42]   | [01.05][11.02][42.10]   |
|  | Prodicted protein  | 2 460   |  |   |
| AO080513000020   | Predicted protein  | 2.459   | 11   | #   |
| AO080513000020<br>AO080505000159   | Alcohol dehydrogenase, class V   | 2.439   | "<br>[01][02][16][42]  | #<br>[01.05][01.20][02.01][02.16][16.17]<br>[42.01]   |
| AO080513000020<br>AO080505000159<br>AO080546000050   | Alcohol dehydrogenase, class V<br>Protein tyrosine serine phosphatase  | 2.439<br>2.446<br>2.442   | n<br>[01][02][16][42]<br>[14]  | #<br>[01.05][01.20][02.01][02.16][16.17]<br>[42.01]<br>[14.07]  |
| AO080513000020<br>AO080505000159<br>AO080546000050<br>AO080531000027   | Alcohol dehydrogenase, class V<br>Protein tyrosine serine phosphatase<br>Dimethylglycine dehydrogenase precursor   | 2.446<br>2.442<br>2.426   | "<br>[01][02][16][42]<br>[14]<br>[01][16][20]  | #<br>[01.05][01.20][02.01][02.16][16.17]<br>[42.01]<br>[14.07]<br>[01.01][01.02][01.05][16.21][20.01]   |
| AO080513000020<br>AO080505000159<br>AO080546000050<br>AO080531000027<br>AO080501000014<br>AO0805670000034  | Alcohol dehydrogenase, class V<br>Protein tyrosine serine phosphatase<br>Dimethylglycine dehydrogenase precursor<br>wykB, FAD-dependent oxidoreductase<br>Predicted notein   | 2,439<br>2,446<br>2,442<br>2,426<br>2,412<br>2,409  | "<br>[01][02][16][42]<br>[14]<br>[01][16][20]<br>[14]<br>#   | μ<br>[01.05][01.20][02.01][02.16][16.17]<br>[42.01]<br>[14.07]<br>[01.01][01.02][01.05][16.21][20.01]<br>[14.07]<br>μ   |
| AO080513000020<br>AO080505000159<br>AO080546000050<br>AO080531000027<br>AO080561000014<br>AO080567000034   | Alcohol dehydrogenase, class V<br>Protein tyrosine serine phosphatase<br>Dimethylgycine dehydrogenase precursor<br>wykB, FAD-dependent oxidoreductase<br>Predicted protein<br>-Xetto-8-miniopelargonate synthetase and related enzymes   | 2.439<br>2.446<br>2.442<br>2.426<br>2.412<br>2.409<br>2.406   | #<br>[01][02][16][42]<br>[14]<br>[01][16][20]<br>[14]<br>#   | и<br>[01.05][01.20][02.01][02.16][16.17]<br>[42.01]<br>[14.07]<br>[01.01][01.02][01.05][16.21][20.01]<br>[14.07]<br>#<br>#  |
| AO080513000020<br>AO080505000159<br>AO080546000050<br>AO080531000027<br>AO08055000014<br>AO080557000034<br>AO080536000139<br>AO080523000390  | Alcohol dehydrogenase, class V<br>Alcohol dehydrogenase, class V<br>Dimethylglycine dehydrogenase precursor<br>wykB; FAD-dependent oxidoreductase<br>Predicted protein<br>7.4eto-8-aminopelargonate symthetase and related enzymes<br>Cytochrome P450 CYP4 CYP19 CYP20 subfamilies   | 2.439<br>2.446<br>2.442<br>2.426<br>2.412<br>2.409<br>2.406<br>2.401  | #<br>[01][02][16][42]<br>[14]<br>[01][16][20]<br>[14]<br>#<br>#<br>[01]  | <pre># [01.05][01.20][02.01][02.16][16.17] [42.01] [14.07] [01.01][01.02][01.05][16.21][20.01] [14.07] # # [01.01]</pre>  |
| AO80513000020<br>AO080505000159<br>AO080546000050<br>AO080531000027<br>AO080501000014<br>AO080567000034<br>AO080556000139<br>AO080523000390  | Producto protein<br>Alcohol dehydrogenase, class V<br>Protein tytosine serine phosphatase<br>Dimethydycine dehydrogenase procursor<br>wykB, FAD-dependen toxidoreductase<br>Predicted protein<br>Predicted protein<br>Predicted protein<br>Predicted protein<br>Predicted protein<br>Predicted protein<br>Predicted protein<br>Predicted protein<br>Predicted protein<br>Protein State<br>Predicted protein<br>Protein State<br>Protein State<br>Predicted protein<br>Protein State<br>Protein Sta | 2.449<br>2.446<br>2.442<br>2.426<br>2.412<br>2.409<br>2.406<br>2.401<br>2.394   | " [01][02][16][42] [14] [01][16][20] [14] # [01] [01] [20][32][34]   | #<br>[01.05][01.20][02.01][02.16][16.17]<br>[42.01]<br>[14.07]<br>[14.07]<br>#<br>#<br>[01.01][01.02][01.05][16.21][20.01]<br>[01.01]<br>[20.01][20.03][20.09][32.05][32.07]  |
| AO80513000020<br>AO80505000159<br>AO80546000050<br>AO80531000027<br>AO80501000014<br>AO805050000139<br>AO80552000030<br>AO80563000003  | Alcohol dehydrogenase, class V<br>Protein tyrosine serine phosphatase<br>Dimethylglycine dehydrogenase precursor<br>wykB, FAD-dependent oxidoreductase<br>Predicted protein<br>7-keto-8-aminopelargonate synthetase and related enzymes<br>Cytochrome P450 CYP4 CYP19 CYP26 subfamilies<br>Synaptic vesicle transporter SVOP and related transporters (major facilitator superfamily)  | 2.4459<br>2.446<br>2.442<br>2.426<br>2.412<br>2.409<br>2.406<br>2.401<br>2.394<br>2.394   | #<br>[01][02][16][42]<br>[14]<br>#<br>[01]<br>[20][32][34]<br>#  | #<br>[01.05][01.20][02.01][02.16][16.17]<br>[42.01]<br>[14.07]<br>[14.07]<br>#<br>#<br>[01.01][01.02][01.05][16.21][20.01]<br>[14.07]<br>#<br>#<br>[01.01]<br>[20.01][20.03][20.09][32.05][32.07]<br>[34.11]  |
| AO80513000020<br>AO80505000159<br>AO80546000050<br>AO80531000027<br>AO80501000014<br>AO80567000034<br>AO80552000039<br>AO80563000039<br>AO80563000003<br>AO8052000001  | Alcohol dehydrogenase, class V<br>Protein tyrosine serine phosphatase<br>Dimethylgylsine dehydrogenase precursor<br>wykB, FAD-dependent oxidoreductase<br>Predicted protein<br>7-keto-8-aminopelargonate symthetase and related enzymes<br>Cytochrome P450 CYP4 CYP19 CYP20 subfamilies<br>Synaptic vesicle transporter SVOP and related transporters (major facilitator superfamily)<br>Reverse transcriptase<br>Predicted protein  | 2.4459<br>2.446<br>2.442<br>2.426<br>2.412<br>2.409<br>2.406<br>2.401<br>2.394<br>2.393<br>2.393<br>2.392   | и<br>[01][02][16][42]<br>[14]<br>[01][16][20]<br>[14]<br>#<br>[01]<br>[20][32][34]<br>#  | #<br>[01.05][01.20][02.01][02.16][16.17]<br>[42.01]<br>[14.07]<br>[14.07]<br>[14.07]<br>#<br>[01.01][01.02][01.05][16.21][20.01]<br>[14.07]<br>#<br>[01.01]<br>[20.01][20.03][20.09][32.05][32.07]<br>[34.11]<br>#  |
| AO080513000020<br>AO080505000159<br>AO080546000050<br>AO080531000027<br>AO080567000034<br>AO080567000034<br>AO08056300003<br>AO080523000390<br>AO08052000001<br>AO08052000001<br>AO08052000001   | Alcohol dehydrogenase, class V<br>Alcohol dehydrogenase, class V<br>Protein tyrosine serine phosphatase<br>Dimethylglycine dehydrogenase precursor<br>wykB; FAD-dependent oxidoreductase<br>Predicted protein<br>7-keto-8-aminopelargonate symhetase and related enzymes<br>Cytochrome P450 CXP4 CYP19 CYP20 subfamilies<br>Synaptic vesicle transporter SVOP and related transporters (major facilitator superfamily)<br>Reverse transcriptase<br>Predicted protein   | 2.4459<br>2.446<br>2.442<br>2.426<br>2.412<br>2.409<br>2.406<br>2.401<br>2.394<br>2.393<br>2.392<br>2.368   | и<br>[01][02][16][42]<br>[14]<br>[01][16][20]<br>[14]<br>#<br>[01]<br>[20][32][34]<br>#<br>#<br>#  | <sup>μ</sup><br>[01.05][01.20][02.01][02.16][16.17]<br>[42.01]<br>[14.07]<br>[14.07]<br><sup>μ</sup><br><sup>μ</sup><br><sup>μ</sup><br><sup>μ</sup><br><sup>μ</sup><br>[01.01]<br>[20.01][20.03][20.09][32.05][32.07]<br>[34.11]<br><sup>μ</sup><br><sup>μ</sup><br><sup>μ</sup><br><sup>μ</sup><br><sup>μ</sup><br><sup>μ</sup><br><sup>μ</sup><br><sup>μ</sup><br><sup>μ</sup><br><sup>μ</sup>   |
| A0080513000020<br>A0080505000159<br>A008054600050<br>A008051000027<br>A0080501000014<br>A0080550000139<br>A0080550000139<br>A008055000010<br>A0080550000010<br>A0080550000010<br>A0080550000010  | Productor protein Alcohol dehydrogenase, class V Protein tyrosine serine phosphatase Dimethydycine dehydrogenase precursor wykB, FAD-dependent oxidoreductase Predicted protein 7-keto-8-aminopelargonate synthetase and related enzymes Cytochrome P450 CYP4 CYP19 CYP26 subfamilies Synaptic vesicle transporter SVOP and related transporters (major facilitator superfamily) Reverse transcriptase Predicted protein Predicted protein Predicted protein Predicted flaxin-nucleotide-binding protein structurally related to pyridoxine 5 -phosphate oxidase   | 2.4459<br>2.446<br>2.442<br>2.426<br>2.412<br>2.409<br>2.406<br>2.401<br>2.394<br>2.393<br>2.392<br>2.368<br>2.363<br>2.363   | и<br>[01][02][16][42]<br>[14]<br>[01][16][20]<br>[14]<br>#<br>#<br>[01]<br>[20][32][34]<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#   | #<br>[01.05][01.20][02.01][02.16][16.17]<br>[42.01]<br>[14.07]<br>[14.07]<br>#<br>#<br>[01.01][01.02][01.05][16.21][20.01]<br>[20.01][20.03][20.09][32.05][32.07]<br>[34.11]<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#  |
| AO080513000020<br>AO0805400050<br>AO08054000050<br>AO08054000027<br>AO08050100001<br>AO08057000034<br>AO08057000034<br>AO08052000039<br>AO080520000010<br>AO080527000001<br>AO080527000001<br>AO080527000001<br>AO080527000001<br>AO08055000003  | Alcohol dehydrogenase, class V<br>Alcohol dehydrogenase, class V<br>Protein tyrosine serine phosphatase<br>Dimethylglycine dehydrogenase precursor<br>wykB, FAD-dependent oxidoreductase<br>Predicted protein<br>Reverse transporters and related enzymes<br>Cytochrome P450 CYP4 CYP19 CYP26 subfamilies<br>Synaptic vesicle transporter SVOP and related transporters (major facilitator superfamily)<br>Reverse transcriptase<br>Predicted protein<br>Predicted protein<br>Predicted protein<br>Predicted protein<br>Predicted protein  | 2,4459<br>2,446<br>2,442<br>2,442<br>2,409<br>2,400<br>2,400<br>2,400<br>2,400<br>2,400<br>2,400<br>2,400<br>2,400<br>2,400<br>2,400<br>2,400<br>2,412<br>2,412<br>2,412<br>2,412<br>2,412<br>2,412<br>2,412<br>2,412<br>2,412<br>2,412<br>2,412<br>2,412<br>2,412<br>2,412<br>2,412<br>2,412<br>2,412<br>2,412<br>2,412<br>2,412<br>2,412<br>2,412<br>2,412<br>2,412<br>2,412<br>2,412<br>2,412<br>2,412<br>2,412<br>2,412<br>2,412<br>2,409<br>2,406<br>2,412<br>2,393<br>2,393<br>2,393<br>2,359<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355<br>2,355    | и<br>[01][02][16][42]<br>[14]<br>[01][16][20]<br>[14]<br>#<br>[01]<br>[20][32][34]<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#  | "<br>[01.05][01.20][02.01][02.16][16.17]<br>[42.01]<br>[14.07]<br>[14.07]<br>#<br>#<br>[01.01][01.02][01.05][16.21][20.01]<br>[14.07]<br>#<br>#<br>[01.01]<br>[20.01][20.03][20.09][32.05][32.07]<br>[34.11]<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#  |
| AO080513000020<br>AO08054000050<br>AO0805400025<br>AO0805400027<br>AO0805300027<br>AO08057000034<br>AO08057000034<br>AO08052000010<br>AO08052000010<br>AO08052000010<br>AO0805200001<br>AO08054000314<br>AO08057000005<br>AO080568000203<br>AO080568000203   | Alcohol dehydrogenase, class V<br>Alcohol dehydrogenase, class V<br>Protein tyrosine serine phosphatase<br>Dimethykglycine dehydrogenase precursor<br>wykB, FAD-dependent oxidoreductase<br>Predicted protein<br>7-keto-8-aminopelargonate symthetase and related enzymes<br>Cytochrome P450 CYP4 CYP19 CYP26 subfamilies<br>Synaptic vesicle transporter SVOP and related transporters (major facilitator superfamily)<br>Reverse transcriptase<br>Predicted protein<br>Predicted protein<br>Protein<br>Protein<br>Protein<br>Protein<br>Protein<br>Protein<br>Protein<br>Protein<br>Protein<br>Protein<br>Protein<br>Protein<br>Protein<br>Protein<br>Protein<br>Protein<br>Protein<br>Protein<br>Protein<br>Protein<br>Protein<br>Protein<br>Protein<br>Protein<br>Protein<br>Protein<br>Protein<br>Protein<br>Protein<br>Protein<br>Protein<br>Protein<br>Protein<br>Protein<br>Protein<br>Protein<br>Protein<br>Protein<br>Protein<br>Protein<br>Protein<br>Protein<br>Protein<br>Protein<br>Protein<br>Protein<br>Protein<br>Protein<br>Protein<br>Protein<br>Protein<br>Protein<br>Protein<br>Protein<br>Protein<br>Protein<br>Protein<br>Protein<br>Protein<br>Protein<br>Protein<br>Protein<br>Protein<br>Protein<br>Protein<br>Protein<br>Protein<br>Protein<br>Protein<br>Protein<br>Protein<br>Pro   | 2,459<br>2,446<br>2,442<br>2,426<br>2,412<br>2,409<br>2,409<br>2,400<br>2,400<br>2,394<br>2,393<br>2,392<br>2,368<br>2,363<br>2,359<br>2,357  | и<br>[01][02][16][42]<br>[14]<br>[01][16][20]<br>[14]<br>и<br>и<br>и<br>и<br>и<br>и<br>и<br>и<br>и<br>и<br>и<br>и<br>и<br>и<br>и<br>и<br>и<br>и<br>и   | "<br>[01.05][01.20][02.01][02.16][16.17]<br>[42.01]<br>[14.07]<br>[14.07]<br>#<br>#<br>[01.01][01.02][01.05][16.21][20.01]<br>[14.07]<br>#<br>#<br>[01.01]<br>[20.01][20.03][20.09][32.05][32.07]<br>[34.11]<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#  |
| A0080513000020<br>A008050500159<br>A008054000050<br>A0080531000027<br>A0080551000027<br>A008055000034<br>A008055000039<br>A008055000039<br>A0080550000010<br>A008055000001<br>A008055000011<br>A008055000011<br>A00805500022<br>A00805500022<br>A00805500022   | Alcohol dehydrogenase, class V<br>Alcohol dehydrogenase, class V<br>Protein tyrosine serine phosphatase<br>Dimethylgycine dehydrogenase precursor<br>wykB; FAD-dependent oxidoreductase<br>Predicted protein<br>7-keto-8-aminopelargonate symhetase and related enzymes<br>Cytochrome P450 CXP4 CYP19 CYP20 subfamilies<br>Synaptic vesicle transporter SVOP and related transporters (major facilitator superfamily)<br>Reverse transcriptase<br>Predicted protein<br>Predicted protein<br>Predicted protein<br>Predicted navin-nucleotide-binding protein structurally related to pyridoxine 5 -phosphate oxidase<br>Predicted protein<br>Predicted protein<br>Predicted protein<br>ATP-dependem RNA helicase<br>ADP-rhose pyrophosphatase   | 2,439<br>2,446<br>2,442<br>2,426<br>2,426<br>2,412<br>2,406<br>2,401<br>2,394<br>2,393<br>2,394<br>2,368<br>2,368<br>2,368<br>2,359<br>2,357<br>2,337<br>2,337<br>2,337   | и<br>[01][02][16][42]<br>[14]<br>[01][16][20]<br>[14]<br>и<br>и<br>и<br>и<br>и<br>и<br>и<br>и<br>и<br>и<br>и<br>и<br>и<br>и<br>и<br>и<br>и<br>и<br>и   | <pre>" " [01.05][01.20][02.01][02.16][16.17] [42.01] [14.07] [01.01][01.02][01.05][16.21][20.01] [14.07] # # # [01.01] [20.01][20.03][20.09][32.05][32.07] [34.11] # # # # # # # # # # # # # # # # # #</pre>  |
| AO080513000020<br>AO08055000159<br>AO08054000050<br>AO080530100014<br>AO08055000034<br>AO08055000034<br>AO08055000034<br>AO08052000001<br>AO08052000001<br>AO08052000001<br>AO08052000001<br>AO080550000125<br>AO080551000212<br>AO080551000212<br>AO080548000025  | Alcohol dehydrogenase, class V<br>Alcohol dehydrogenase, class V<br>Protein tyrosine serine phosphatase<br>Dimethylglycine dehydrogenase procursor<br>wykB, FAD-dependent oxidoreductase<br>Predicted protein<br>7-keto-8-aminopelargonate synthetase and related enzymes<br>Cytochrome P450 CYP4 CYP19 CYP26 subfamilies<br>Synaptic vesicle transporter SVOP and related transporters (major facilitator superfamily)<br>Reverse transcriptase<br>Predicted protein<br>Predicted protein<br>Predicted fortein<br>Predicted fortein<br>Predicted fortein<br>Predicted fortein<br>ATP-dependent RNA helicase<br>ADP-ribose prophosphatase<br>Za-finger<br>Inositio monophosphatase   | 2,4,59<br>2,446<br>2,442<br>2,426<br>2,412<br>2,406<br>2,401<br>2,394<br>2,394<br>2,394<br>2,392<br>2,368<br>2,359<br>2,359<br>2,357<br>2,337<br>2,331<br>2,326   | и<br>[01][02][16][42]<br>[14]<br>[01][16][20]<br>[14]<br>#<br>#<br>[01]<br>[20][32][34]<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#   | <pre>" " [01.05][01.20][02.01][02.16][16.17] [42.01] [42.01] [14.07] [01.01][01.02][01.05][16.21][20.01] [14.07] # # # [01.01] [20.01][20.03][20.09][32.05][32.07] [34.11] # # # # # # # # # # # # # # # # # #</pre>  |
| AO080513000020<br>AO0805400050<br>AO08054600050<br>AO08054000027<br>AO080501000017<br>AO08057000034<br>AO080557000034<br>AO08052000010<br>AO080527000001<br>AO080527000001<br>AO080527000001<br>AO080537000005<br>AO080546000314<br>AO080546000315<br>AO080548000022<br>AO080548000022<br>AO080548000022   | Alcohol dehydrogenase, class V Protein tyrosine serine phosphatase Dimethydycine dehydrogenase precursor wykB, FAD-dependent oxidoreductase Predicted protein 7-keto-8-aminopelargonate synthetase and related enzymes Cytochrome P450 CYP4 CYP19 CYP26 subfamilies Synaptic vesicle transporter SVOP and related transporters (major facilitator superfamily) Reverse transcriptase Predicted protein ATP-dependent RNA helicase ADP-ribose pyrophosphatase Za-finger Inositol monophosphatase Predicted protein  | 2,439<br>2,446<br>2,442<br>2,442<br>2,442<br>2,440<br>2,400<br>2,400<br>2,400<br>2,400<br>2,400<br>2,400<br>2,400<br>2,400<br>2,400<br>2,400<br>2,400<br>2,400<br>2,409<br>2,409<br>2,409<br>2,409<br>2,409<br>2,409<br>2,409<br>2,409<br>2,409<br>2,409<br>2,409<br>2,409<br>2,409<br>2,409<br>2,409<br>2,409<br>2,409<br>2,409<br>2,409<br>2,409<br>2,409<br>2,409<br>2,409<br>2,409<br>2,409<br>2,409<br>2,409<br>2,409<br>2,409<br>2,409<br>2,409<br>2,409<br>2,409<br>2,409<br>2,409<br>2,409<br>2,409<br>2,308<br>2,309<br>2,309<br>2,309<br>2,309<br>2,309<br>2,309<br>2,309<br>2,309<br>2,309<br>2,309<br>2,309<br>2,309<br>2,309<br>2,309<br>2,309<br>2,309<br>2,309<br>2,309<br>2,309<br>2,309<br>2,309<br>2,309<br>2,309<br>2,309<br>2,309<br>2,309<br>2,309<br>2,309<br>2,309<br>2,309<br>2,355<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359     | и<br>[01][02][16][42]<br>[14]<br>[01][16][20]<br>[14]<br>[01]<br>[20][32][34]<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>[01][16][32]<br>#<br>[01][16][32]<br>#   | <pre>" " [01.05][01.20][02.01][02.16][16.17] [42.01] [14.07] [14.07] # # [01.01][01.02][01.05][16.21][20.01] # # [01.01] [20.01][20.03][20.09][32.05][32.07] [34.11] # # # # # # # # # # # # # # # # # #</pre>  |
| AO080513000020<br>AO08054600050<br>AO08054600050<br>AO08051000027<br>AO080551000027<br>AO08055000034<br>AO08055000034<br>AO08052000010<br>AO08052000010<br>AO08052000010<br>AO08052000010<br>AO08052000010<br>AO08052000010<br>AO0805100022<br>AO0805100022<br>AO0805400031<br>AO0805300025  | Alcohol dehydrogenase, class V<br>Alcohol dehydrogenase, class V<br>Protein tyrosine serine phosphatase<br>Dimethylglycine dehydrogenase precursor<br>wykB, FAD-dependent oxidoreductase<br>Predicted protein<br>7-keto-8-aminopelargonate synthetase and related enzymes<br>Cytochrome P450 CYP4 CYP19 CYP20 subfamilies<br>Synaptic vesicle transporter SVOP and related transporters (major facilitator superfamily)<br>Reverse transcriptase<br>Predicted protein<br>Predicted protein  | 2,439<br>2,446<br>2,442<br>2,426<br>2,409<br>2,409<br>2,409<br>2,409<br>2,409<br>2,309<br>2,392<br>2,392<br>2,363<br>2,359<br>2,357<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337<br>2,337     | и<br>[01][02][16][42]<br>[14]<br>[01][16][20]<br>[14]<br>и<br>и<br>[01]<br>[20][32][34]<br>и<br>и<br>и<br>и<br>и<br>и<br>и<br>(01][16][32]<br>и<br>и<br>[01][16][32]<br>и<br>и<br>(01][16][30]<br>и<br>и<br>и  | <pre>" " [01.05][01.20][02.01][02.16][16.17] [42.01] [14.07] [14.07] # # [01.01][01.02][01.05][16.21][20.01] [20.01][20.03][20.09][32.05][32.07] [34.11] # # [01.01] [34.11] # [01.03][16.17][32.01] # [01.04][01.05][01.06][01.20][30.01] # # # # # # # # # # # # # # # # # # #</pre>  |
| AO080513000020<br>AO08050500159<br>AO08054000050<br>AO080551000027<br>AO080551000027<br>AO08055000034<br>AO08055000039<br>AO08055000039<br>AO080550000010<br>AO080550000010<br>AO080550000012<br>AO080551000212<br>AO080551000212<br>AO080551000212<br>AO080551000212<br>AO080550000125<br>AO080550000125<br>AO080550000125<br>AO0805540000125<br>AO0805540000125<br>AO0805540000125<br>AO0805540000125<br>AO08055400000125<br>AO08055400000125<br>AO08055400000125<br>AO08055400000125<br>AO08055400000125<br>AO08055400000125<br>AO08055400000058  | Alcohol dehydrogenase, class V Protein tyrosine serine phosphatase Dimethylycine dehydrogenase precursor wykB; FAD-dependent oxidoreductase Predicted protein 7-keto-8-aminopelargonate symthetase and related enzymes Cytochrome P450 CVP4 CVP10 CVP20 subfamilies Synaptic vesicle transporter SVOP and related transporters (major facilitator superfamily) Reverse transcriptase Predicted protein   | 2,439<br>2,446<br>2,442<br>2,426<br>2,412<br>2,409<br>2,409<br>2,409<br>2,409<br>2,309<br>2,309<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359<br>2,359     | "<br>[01][02][16][42]<br>[14]<br>[01][16][20]<br>[14]<br>#<br>#<br>[01]<br>[20][32][34]<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>[01][16][32]<br>#<br>[01][16][32]<br>#<br>[01][30]<br>#<br>#<br>[01][20][34]<br>#<br>#  | <pre>" " [01.05][01.20][02.01][02.16][16.17] [42.01] [42.01] [14.07] [01.01][01.02][01.05][16.21][20.01] [14.07] # # [01.01] [20.01][20.03][20.09][32.05][32.07] [34.11] # [01.03][16.17][32.01] # [01.03][16.17][30.01] # [01.03][16.17</pre> |
| AO080513000020<br>AO08055000159<br>AO08054000050<br>AO08054000050<br>AO080550100014<br>AO08057000034<br>AO08055000039<br>AO08052000031<br>AO080520000010<br>AO080527000001<br>AO080527000001<br>AO08055000031<br>AO080551000212<br>AO080551000212<br>AO08055400031<br>AO08055400031<br>AO08055400031<br>AO08055400031<br>AO08055400031<br>AO08055400031<br>AO08055400031<br>AO08055400031<br>AO08055400031<br>AO08055400031<br>AO08055400031<br>AO08055400031  | Alcohol dehydrogenase, class V Protein tyrosine serine phosphatase Dimethylycine dehydrogenase precursor wykB, FAD-dependent oxidoreductase Predicted protein 7-keto-8-aminopelargonate synthetase and related enzymes Cytochrome P450 CVP4 CVP10 CVP26 subfamilies Synaptic vesicle transporter SVOP and related transporters (major facilitator superfamily) Reverse transcriptase Predicted protein Predicted protein Predicted protein Predicted frotein Predicted protein ADP-rhose pryothosphatase Za-finger Insoitol monophosphatase Predicted protein Predicted  | 2.439<br>2.446<br>2.442<br>2.446<br>2.412<br>2.409<br>2.400<br>2.394<br>2.393<br>2.392<br>2.35<br>2.35<br>2.35<br>2.35<br>2.331<br>2.326<br>2.331<br>2.322<br>2.315<br>2.329<br>2.299<br>2.298  | и<br>[01][02][16][42]<br>[14]<br>[01][16][20]<br>[14]<br>#<br>[01][20][32][34]<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>[01][16][32]<br>#<br>[01][16][32]<br>#<br>[01][30]<br>#<br>#<br>[01][20][34]<br>#  | <pre>" " [01.05][01.20][02.01][02.16][16.17] [42.01] [42.01] [14.07] [01.01][01.02][01.05][16.21][20.01] [14.07] # # # [01.01] [20.01][20.03][20.09][32.05][32.07] [34.11] # # # # # # # # # # # # # # # # # #</pre>  |
| AO080513000020<br>AO08053000159<br>AO080534000050<br>AO080530100027<br>AO08050100014<br>AO08057000034<br>AO08052000030<br>AO080520000010<br>AO080520000010<br>AO080527000001<br>AO080527000001<br>AO080537000005<br>AO08051000212<br>AO08051000212<br>AO0805480000125<br>AO080548000023<br>AO08055000015<br>AO08055000015<br>AO08055000015<br>AO08055000015<br>AO08055000015<br>AO08056000125<br>AO08056000125<br>AO08056000125<br>AO08056000125<br>AO08056000125<br>AO08056000125<br>AO08056000125<br>AO08056000125<br>AO08056000125<br>AO08056000125<br>AO08056000125<br>AO08056000125<br>AO08056000125<br>AO08056000125<br>AO080560000126<br>AO080560000125<br>AO080560000125<br>AO080560000125<br>AO080560000125<br>AO080500000426   | Alcohol dehydrogenase, class V Protein tyrosine serine phosphatase Dimethydycine dehydrogenase precursor wykB, FAD-dependent oxidoreductase Predicted protein 7-keto-8-aminopelargonate synthetase and related enzymes Cytochrome P450 CYP4 CYP19 CYP26 subfamilies Synaptic vesicle transporter SVOP and related transporters (major facilitator superfamily) Reverse transcriptase Predicted protein Predicted protein Predicted protein Predicted protein ATP-dependent RNA helicase ADP-ribose pyrophosphatase Zn-finger Inositol monophosphatase Predicted protein  | 2,439<br>2,446<br>2,442<br>2,426<br>2,409<br>2,409<br>2,409<br>2,409<br>2,409<br>2,409<br>2,409<br>2,409<br>2,304<br>2,304<br>2,304<br>2,304<br>2,305<br>2,337<br>2,335<br>2,337<br>2,331<br>2,336<br>2,331<br>2,331<br>2,331<br>2,331<br>2,331<br>2,331<br>2,331<br>2,331<br>2,331<br>2,331<br>2,331<br>2,331<br>2,331<br>2,331<br>2,331<br>2,331<br>2,332<br>2,331<br>2,331<br>2,332<br>2,331<br>2,332<br>2,331<br>2,332<br>2,331<br>2,332<br>2,331<br>2,332<br>2,331<br>2,335<br>2,331<br>2,335<br>2,331<br>2,335<br>2,331<br>2,335<br>2,331<br>2,335<br>2,331<br>2,335<br>2,331<br>2,335<br>2,331<br>2,335<br>2,331<br>2,335<br>2,331<br>2,335<br>2,331<br>2,335<br>2,331<br>2,335<br>2,331<br>2,335<br>2,331<br>2,332<br>2,331<br>2,335<br>2,331<br>2,332<br>2,331<br>2,332<br>2,331<br>2,332<br>2,331<br>2,332<br>2,331<br>2,332<br>2,331<br>2,332<br>2,331<br>2,332<br>2,331<br>2,332<br>2,331<br>2,332<br>2,331<br>2,332<br>2,332<br>2,331<br>2,332<br>2,332<br>2,331<br>2,332<br>2,332<br>2,332<br>2,332<br>2,331<br>2,332<br>2,332<br>2,332<br>2,332<br>2,332<br>2,332<br>2,332<br>2,332<br>2,332<br>2,332<br>2,332<br>2,332<br>2,332<br>2,332<br>2,332<br>2,332<br>2,332<br>2,332<br>2,332<br>2,332<br>2,332<br>2,332<br>2,332<br>2,332<br>2,332<br>2,332<br>2,332<br>2,332<br>2,332<br>2,332<br>2,332<br>2,332<br>2,332<br>2,332<br>2,332<br>2,332<br>2,329<br>2,329<br>2,329<br>2,329<br>2,329<br>2,329<br>2,329<br>2,329<br>2,329<br>2,329<br>2,329<br>2,329<br>2,329<br>2,329<br>2,329<br>2,329<br>2,329<br>2,329<br>2,329<br>2,329<br>2,329<br>2,329<br>2,329<br>2,329<br>2,329<br>2,329<br>2,329<br>2,329<br>2,329<br>2,329<br>2,329<br>2,329<br>2,329<br>2,329<br>2,329<br>2,329<br>2,329<br>2,329<br>2,329<br>2,329<br>2,329<br>2,329<br>2,329<br>2,329<br>2,329<br>2,329<br>2,329<br>2,329<br>2,329<br>2,329<br>2,329<br>2,329<br>2,329<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239<br>2,239     | "<br>[01][02][16][42]<br>[14]<br>[01][16][20]<br>[14]<br>[01]<br>[20][32][34]<br>#<br>#<br>[20][32][34]<br>#<br>#<br>[01][16][32]<br>#<br>#<br>[01][20][34]<br>[01][20][34]  | <pre>" " [01.05][01.20][02.01][02.16][16.17] [42.01] [14.07] [14.07] # " [01.01][01.02][01.05][16.21][20.01] [20.01][20.03][20.09][32.05][32.07] [34.11] # # [01.01] [20.01][20.03][20.09][32.05][32.07] [34.11] # [01.03][16.17][32.01] # # [01.03][16.17][32.01] # [01.04][01.05][01.06][01.20][30.01] # [01.04][01.05][01.06][01.20][30.01] # [01.04][01.05][01.06][01.20][30.01] # [01.04][20.01][20.01][34.01] # [01.05][20.01][20.03][20.09][34.01] [34.11]</pre>   |
| A0080513000020<br>A008050500159<br>A008054000050<br>A008054000050<br>A008057000034<br>A008057000034<br>A008052000034<br>A008052000030<br>A0080520000010<br>A0080520000010<br>A008052000010<br>A008052000010<br>A008055000012<br>A0080530000254<br>A0080530000254<br>A0080554000031<br>A0080554000031<br>A0080554000035<br>A0080551000053<br>A008050000055<br>A0080551000005<br>A0080551000005<br>A008050000055<br>A00805000005<br>A00805000005<br>A00805000005<br>A00805000005<br>A00805000005<br>A00805000005<br>A00805000005<br>A00805000005<br>A00805000005<br>A00805000005<br>A00805000005<br>A00805000005<br>A00805000005<br>A00805000005<br>A00805000005<br>A00805000005<br>A00805000005<br>A00805000005<br>A00805000005<br>A00805000005<br>A0080500005<br>A0080500005<br>A0080500005<br>A0080500005<br>A0080500005<br>A0080500005<br>A0080500005<br>A0080500005<br>A0080500005<br>A0080500005<br>A0080500005<br>A0080500005<br>A0080500005<br>A0080500005<br>A0080500005<br>A0080500005<br>A0080500005<br>A0080500005<br>A0080500005<br>A008050005<br>A008050005<br>A008050005<br>A0080520005<br>A0080520005<br>A0080520005<br>A0080520005<br>A0080520005<br>A0080520005<br>A0080520005<br>A0080520005<br>A0080520005<br>A0080520005<br>A0080520005<br>A0080520005<br>A0080520005<br>A0080520005<br>A0080520005<br>A0080520005<br>A0080520005<br>A0080520005<br>A0080520005<br>A0080520005<br>A0080550005<br>A0080550005<br>A0080550005<br>A0080550005<br>A0080550005<br>A0080550005<br>A0080550005<br>A0080550005<br>A0080550005<br>A0080550005<br>A0080550005<br>A0080550005<br>A0080550005<br>A0080550005<br>A0080550005<br>A0080550005<br>A0080550005<br>A0080550005<br>A0080550005<br>A0080550005<br>A0080550005<br>A0080550005<br>A0080550005<br>A0080550005<br>A0080550005<br>A0080550005<br>A0080550005<br>A0080550005<br>A0080550005<br>A0080550005<br>A0080550005<br>A0080550005<br>A0080550005<br>A0080550005<br>A0080550005<br>A0080550005<br>A0080550005<br>A0080550005<br>A0080550005<br>A0080550005<br>A0080550005<br>A0080550005<br>A0080550005<br>A0080550005<br>A0080550005<br>A0080550005<br>A0080550005<br>A0080550005<br>A0080550005<br>A0080550005<br>A0080550005<br>A0080550005<br>A0080550005<br>A0080550005<br>A0080550005<br>A0080550005<br>A0080550005<br>A0080550005<br>A0080550005<br>A0080550005<br>A0080550005<br>A0080550005<br>A0080550005<br>A0080550005<br>A0080550005<br>A0080550005<br>A0080550005<br>A0080550005<br>A0080550005<br>A0080550005<br>A0080550005<br>A0080550005<br>A0080550005<br>A0080550005<br>A0080550005<br>A0080550005<br>A0080550005<br>A0080550005<br>A0080550005<br>A005 | Alcohol dehydrogenase, class V<br>Alcohol dehydrogenase, class V<br>Protein tyrosine serine phosphatase<br>Dimethylglycine dehydrogenase precursor<br>wykB, FAD-dependent oxidoreductase<br>Predicted protein<br>7-keto-8-aminopelargonate synthetase and related enzymes<br>Cytochrome P450 CYP4 CYP19 CYP20 subfamilies<br>Synaptic vesicle transporter SVOP and related transporters (major facilitator superfamily)<br>Reverse transcriptase<br>Predicted protein<br>Predicted prote   | 2.446<br>2.442<br>2.426<br>2.409<br>2.400<br>2.401<br>2.394<br>2.393<br>2.392<br>2.368<br>2.363<br>2.359<br>2.35<br>2.337<br>2.331<br>2.332<br>2.315<br>2.326<br>2.315<br>2.329<br>2.315<br>2.329<br>2.315<br>2.329<br>2.315<br>2.329<br>2.315<br>2.329<br>2.325<br>2.329<br>2.325<br>2.329<br>2.325<br>2.329<br>2.325<br>2.329<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.325<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.355<br>2.3555<br>2.355<br>2.355<br>2.355<br>2.355<br>2.3555<br>2.3555<br>2.3555<br>2.3555<br>2.    | "<br>[01][02][16][42]<br>[14]<br>[01][16][20]<br>[14]<br>[01]<br>[20][32][34]<br>#<br>#<br>#<br>#<br>[01][16][32]<br>#<br>[01][16][32]<br>#<br>[01][16][32]<br>#<br>[01][20][34]<br>#<br>[01][20][34]<br>#   | <pre>// [01.05][01.20][02.01][02.16][16.17]<br/>[42.01]<br/>[14.07]<br/>[01.01][01.02][01.05][16.21][20.01]<br/>[14.07]<br/>#<br/>#<br/>[01.01]<br/>[20.01][20.03][20.09][32.05][32.07]<br/>[34.11]<br/>#<br/>#<br/>[01.03][16.17][32.01]<br/>#<br/>[01.03][16.17][32.01]<br/>#<br/>[01.03][16.17][32.01]<br/>#<br/>[01.03][16.17][32.01]<br/>#<br/>[01.03][16.17][32.01]<br/>#<br/>[01.03][16.17][32.01]<br/>#<br/>[01.03][16.17][32.01]<br/>#<br/>[01.03][16.17][32.01]<br/>#<br/>[01.03][16.17][32.01]<br/>#<br/>[01.03][16.17][32.01]<br/>#<br/>[01.03][16.17][32.01]<br/>#<br/>[01.03][16.17][32.01]<br/>#<br/>[01.03][16.17][32.01]<br/>#<br/>[01.03][16.17][32.01]<br/>#<br/>[01.03][16.17][32.01]<br/>#<br/>[01.03][16.17][32.01]<br/>#<br/>[01.03][10.01][20.03][20.09][34.01]<br/>#<br/>#</pre>   |
| AO080513000020<br>AO08050500159<br>AO08054000050<br>AO080551000027<br>AO080551000027<br>AO08055000034<br>AO08055000034<br>AO080520000010<br>AO080520000010<br>AO080520000010<br>AO080520000012<br>AO080521000212<br>AO080551000223<br>AO080551000212<br>AO080551000212<br>AO0805510000125<br>AO0805510000125<br>AO0805510000012<br>AO0805510000012<br>AO0805510000012<br>AO0805510000012<br>AO0805510000012<br>AO0805510000012<br>AO080521000014<br>AO080521000014<br>AO080521000014<br>AO080520000048<br>AO080520000048<br>AO080520000148<br>AO080520000148<br>AO080520000148<br>AO080520000148   | Alcohol dehydrogenase, class V Protein tyrosine serine phosphatase Dimethylycine dehydrogenase precursor wykB; FAD-dependent oxidoreductase Predicted protein 7-keto-8-aminopelargonate synthetase and related enzymes Cytochrome P450 CVP4 CVP10 CVP20 subfamilies Synaptic vesicle transporter SVOP and related transporters (major facilitator superfamily) Reverse transcriptase Predicted protein   | 2.439<br>2.446<br>2.442<br>2.426<br>2.412<br>2.409<br>2.400<br>2.304<br>2.393<br>2.392<br>2.393<br>2.392<br>2.358<br>2.359<br>2.35<br>2.331<br>2.326<br>2.331<br>2.329<br>2.331<br>2.329<br>2.331<br>2.329<br>2.331<br>2.329<br>2.331<br>2.329<br>2.331<br>2.329<br>2.331<br>2.329<br>2.331<br>2.329<br>2.331<br>2.329<br>2.331<br>2.329<br>2.331<br>2.329<br>2.331<br>2.329<br>2.331<br>2.329<br>2.331<br>2.329<br>2.331<br>2.329<br>2.331<br>2.329<br>2.331<br>2.329<br>2.331<br>2.329<br>2.331<br>2.329<br>2.331<br>2.329<br>2.331<br>2.329<br>2.331<br>2.329<br>2.331<br>2.329<br>2.331<br>2.329<br>2.331<br>2.329<br>2.331<br>2.329<br>2.329<br>2.329<br>2.329<br>2.329<br>2.329<br>2.329<br>2.329<br>2.329<br>2.329<br>2.329<br>2.329<br>2.329<br>2.329<br>2.329<br>2.329<br>2.329<br>2.329<br>2.329<br>2.329<br>2.329<br>2.329<br>2.329<br>2.329<br>2.329<br>2.329<br>2.329<br>2.329<br>2.329<br>2.329<br>2.329<br>2.329<br>2.329<br>2.329<br>2.329<br>2.329<br>2.329<br>2.329<br>2.329<br>2.329<br>2.329<br>2.329<br>2.329<br>2.329<br>2.329<br>2.329<br>2.329<br>2.329<br>2.329<br>2.329<br>2.329<br>2.329<br>2.329<br>2.329<br>2.329<br>2.329<br>2.329<br>2.329<br>2.329<br>2.329<br>2.329<br>2.329<br>2.329<br>2.329<br>2.329<br>2.329<br>2.329<br>2.329<br>2.329<br>2.329<br>2.329<br>2.329<br>2.329<br>2.329<br>2.329<br>2.329<br>2.329<br>2.329<br>2.329<br>2.329<br>2.329<br>2.329<br>2.329<br>2.329<br>2.329<br>2.329<br>2.329<br>2.329<br>2.329<br>2.2298<br>2.2298<br>2.2298<br>2.2299<br>2.2298<br>2.2299<br>2.2298<br>2.2299<br>2.2298<br>2.2299<br>2.2298<br>2.2299  | "<br>[01][02][16][42]<br>[14]<br>[01][16][20]<br>[14]<br>[01]<br>[20][32][34]<br>#<br>[20][32][34]<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>[01][16][32]<br>#<br>[01][16][32]<br>#<br>[01][16][32]<br>#<br>[01][20][34]<br>#<br>[01][20][34]<br>#<br>[20]<br>[20][20][34]   | <pre>" " [01.05][01.20][02.01][02.16][16.17] [42.01] [42.01] [14.07] [01.01][01.02][01.05][16.21][20.01] [14.07] # # # [01.01] [20.01][20.03][20.09][32.05][32.07] [34.11] # [01.03][16.17][32.01] # [01.03][16.17][32.01] # [01.03][16.17][32.01] # [01.20][20.01][34.01] # [01.20][20.01][34.01] # [01.20][20.01][20.03][20.09][34.01] [34.11] # [20.01][20.03][20.09] # [20.01][20.03][20.09][34.01] # [20.01][20.03][20.09] # [20.01][20.03][20.09][20.09][20.09][20.09][20.09][20.00][20.09][</pre> |
| AO080513000020<br>AO08055000159<br>AO08054000050<br>AO08054000050<br>AO080550100014<br>AO08055000034<br>AO08055000034<br>AO08052000010<br>AO080520000010<br>AO080520000010<br>AO08054000023<br>AO080550000125<br>AO080550000125<br>AO080551000202<br>AO080551000026<br>AO080551000031<br>AO080551000031<br>AO080551000031<br>AO080551000031<br>AO080551000031<br>AO080551000046<br>AO080551000046<br>AO080551000046<br>AO080551000046<br>AO080552000732  | Alcohol dehydrogenase, class V Protein tyrosine serine phosphatase Dimethylycine dehydrogenase precursor wykB, FAD-dependent oxidoreductase Predicted protein 7-keto-8-aminopelargonate synthetase and related enzymes Cytochrome P450 CVP4 CVP10 CVP26 subfamilies Synaptic vesicle transporter SVOP and related transporters (major facilitator superfamily) Reverse transcriptase Predicted protein Predicted protein Predicted protein Predicted protein Predicted protein Predicted frotein Predicted frotein Predicted frotein Predicted protein   | 2.439<br>2.446<br>2.442<br>2.446<br>2.449<br>2.440<br>2.400<br>2.394<br>2.393<br>2.392<br>2.35<br>2.35<br>2.35<br>2.331<br>2.326<br>2.35<br>2.331<br>2.326<br>2.331<br>2.329<br>2.315<br>2.329<br>2.299<br>2.299<br>2.299<br>2.293<br>2.287<br>2.284<br>2.283   | "<br>[01][02][16][42]<br>[14]<br>[01][16][20]<br>[14]<br>#<br>[01][20][32][34]<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>[01][10][32]<br>#<br>[01][10][32]<br>#<br>[01][20][34]<br>#<br>[01][20][34]<br>#<br>[20]<br>#<br>[20]  | <pre>" " [01.05][01.20][02.01][02.16][16.17] [42.01] [42.01] [14.07] [01.01][01.02][01.05][16.21][20.01] [14.07] # # # [01.01] [20.01][20.03][20.09][32.05][32.07] [34.11] # # # # # # # # # # # # # # # # # #</pre>  |
| AO080513000020<br>AO08053000159<br>AO08053000027<br>AO08053000027<br>AO080530100014<br>AO08057000034<br>AO08052000030<br>AO08052000010<br>AO08052000001<br>AO080527000001<br>AO080527000001<br>AO080527000005<br>AO08055000022<br>AO080550000125<br>AO080540000125<br>AO080540000125<br>AO080540000125<br>AO080550000045<br>AO08055000045<br>AO08055000045<br>AO08055000045<br>AO08055000045<br>AO08055000045<br>AO08055000045<br>AO08055000045<br>AO080523000735<br>AO08055000045   | Alcohol dehydrogenase, class V Protein tyrosine serine phosphatase Dimethydycine dehydrogenase precursor wykB, FAD-dependent oxidoreductase Predicted protein 7-keto-8-aminopelargonate synthetase and related enzymes Cytochrome P450 CYP4 CYP19 CYP26 subfamilies Synaptic vesicle transporter SVOP and related transporters (major facilitator superfamily) Reverse transcriptase Predicted protein Predicted protein Predicted protein Predicted protein ATP-dependent RNA helicase ADP-ribous pryophosphatase Predicted protein   | 2.439<br>2.446<br>2.442<br>2.426<br>2.409<br>2.409<br>2.409<br>2.409<br>2.409<br>2.409<br>2.409<br>2.409<br>2.303<br>2.302<br>2.303<br>2.302<br>2.363<br>2.35<br>2.331<br>2.35<br>2.331<br>2.326<br>2.321<br>2.319<br>2.319<br>2.319<br>2.319<br>2.319<br>2.319<br>2.329<br>2.299<br>2.299<br>2.298<br>2.299<br>2.284<br>2.282<br>2.285   | и<br>[01][02][16][42]<br>[14]<br>[01][16][20]<br>[14]<br>#<br>#<br>[01]<br>[20][32][34]<br>#<br>#<br>#<br>#<br>[01][30]<br>#<br>#<br>[01][20][34]<br>#<br>[01][20][34]<br>#<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[2  | <pre>" " [01.05][01.20][02.01][02.16][16.17] [42.01] [14.07] [14.07] # " [01.01][01.02][01.05][16.21][20.01] [14.07] # " [01.01] [20.01][20.03][20.09][32.05][32.07] [34.11] # [01.03][16.17][32.01] # [01.03][16.17][32.01] # [01.04][01.05][01.06][01.20][30.01] # [01.04][01.05][01.06][01.20][30.01] # [01.04][01.05][01.06][01.20][30.01] # [01.04][01.05][01.06][01.20][30.01] # [01.04][01.05][01.06][01.20][30.01] # [01.04][20.01][20.03][20.09][34.01] [20.01][20.03][20.09] # [20.01][20.03][20.00] # [20.01][20.03][20.00] # [20.01][20.0</pre> |
| A0080513000020<br>A008050500159<br>A008054000050<br>A008054000050<br>A0080551000014<br>A008055000034<br>A008055000034<br>A008055000039<br>A0080520000010<br>A0080520000010<br>A008054000314<br>A0080550000125<br>A0080540000125<br>A0080540000125<br>A0080550000053<br>A0080550000053<br>A0080550000053<br>A0080550000053<br>A0080553000026<br>A008055000025<br>A0080550000053<br>A008055000025<br>A008055000025<br>A008055000025<br>A008055000025<br>A008055000025<br>A008055000025<br>A008055000025<br>A008055000025<br>A008055000025<br>A008055000025<br>A008055000025<br>A008055000025<br>A008055000025<br>A008055000025<br>A008055000025<br>A008055000025<br>A008055000025<br>A008055000025<br>A008055000025<br>A008055000025<br>A008055000025<br>A008055000025<br>A008055000025<br>A008055000025<br>A008055000025<br>A008055000025<br>A008055000025<br>A008055000025<br>A008055000025<br>A008055000025<br>A008055000025<br>A008055000025<br>A008055000025<br>A008055000025<br>A008055000025<br>A008055000025<br>A008055000025<br>A008055000025<br>A008055000025<br>A008055000025<br>A008055000025<br>A008055000025<br>A008055000025<br>A008055000025<br>A008055000025<br>A008055000025<br>A008055000025<br>A008055000025<br>A008052000005<br>A008055000025<br>A008055000025<br>A008055000025<br>A008055000025<br>A008055000025<br>A008055000025<br>A008055000025<br>A008055000025<br>A008055000025<br>A008055000025<br>A008055000025<br>A008055000025<br>A008055000025<br>A008055000025<br>A008055000025<br>A008055000025<br>A008055000025<br>A008055000025<br>A008055000025<br>A008055000025<br>A008055000025<br>A008055000025<br>A008055000025<br>A008055000025<br>A008055000025<br>A008055000025<br>A008055000025<br>A008055000025<br>A008055000025<br>A008055000025<br>A008055000025<br>A008055000025<br>A008055000025<br>A008055000025<br>A008055000025<br>A008055000025<br>A008055000025<br>A008055000025<br>A008055000025<br>A008055000025<br>A008055000025<br>A008055000025<br>A008055000025<br>A008055000025<br>A008055000025<br>A008055000025<br>A008055000025<br>A008055000025<br>A008055000025<br>A008055000025<br>A008055000025<br>A008055000025<br>A008055000025<br>A008055000025<br>A008055000025<br>A008055000025<br>A008055000025<br>A00805500005<br>A00805500005<br>A00805500005<br>A00805500005<br>A00805500005<br>A00805500005<br>A00805500005<br>A00805500005<br>A00805500005<br>A00805500005<br>A00805500005<br>A00805500005<br>A00805500005<br>A00805500005<br>A00805500005<br>A00805500005<br>A00805500005<br>A00805500005<br>A00805500005<br>A0080550   | Alcohol dehydrogenase, class V Alcohol dehydrogenase, class V Protein tyrosine serine phosphatase Dimethylgycine dehydrogenase precursor wykB, FAD-dependent oxidoreductase Predicted protein Cytochrome P450 CVP4 CVP10 CVP20 subfamilies Synaptic vesicle transporter SVOP and related transporters (major facilitator superfamily) Reverse transcriptase Predicted protein Predic   | 2.446<br>2.442<br>2.426<br>2.409<br>2.400<br>2.401<br>2.394<br>2.393<br>2.392<br>2.368<br>2.363<br>2.359<br>2.35<br>2.337<br>2.331<br>2.326<br>2.327<br>2.321<br>2.315<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2.288<br>2 | "<br>[01][02][16][42]<br>[14]<br>[01][16][20]<br>[14]<br>[01]<br>[20][32][34]<br>#<br>#<br>#<br>[01][32][34]<br>#<br>[01][16][32]<br>#<br>#<br>[01][16][32]<br>#<br>[01][20][34]<br>#<br>[01][20][34]<br>#<br>[20]<br>#<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]<br>[20]  | <pre>" " [01.05][01.20][02.01][02.16][16.17] [14.07] [14.07] [14.07] [14.07] [14.07] # # [01.01] [20.01][20.03][20.09][32.05][32.07] [34.11] # # [01.03][16.17][32.01] # [01.03][16.17][32.01] # [01.03][16.17][32.01] # [01.03][16.17][32.01] # [01.03][16.17][32.01] # [01.03][16.17][32.01] # [01.03][16.17][32.01] # [01.03][16.17][32.01] # [01.03][16.17][32.01] # [01.03][16.17][32.01] # [01.03][16.17][32.01] # [01.03][16.17][32.01] # [01.03][16.17][32.01] # [01.03][16.17][32.01] # [01.03][16.17][32.01] # [01.03][16.17][32.01] # [01.03][10.03][20.09][34.01] [34.11] # [20.01][20.03][20.09] [34.01] [34.11] # [10.03][120.03][20.09] [34.01] [34.11] # [10.03][120.03][20.09] [34.01] [34.11] # [34.1</pre> |
| AO080513000020<br>AO08050500159<br>AO08054000050<br>AO080550100017<br>AO080551000027<br>AO08055000034<br>AO08055000034<br>AO080520000010<br>AO080520000010<br>AO080520000010<br>AO080520000010<br>AO080521000212<br>AO080551000212<br>AO080551000212<br>AO0805510000125<br>AO080551000012<br>AO080551000012<br>AO080551000012<br>AO080551000012<br>AO080551000012<br>AO080520000048<br>AO08052000013<br>AO08052000013<br>AO08052000013<br>AO08052000013<br>AO08052000013<br>AO08052000013<br>AO08052000013<br>AO08052000013<br>AO08052000013<br>AO08052000013<br>AO08052000013<br>AO08052000013<br>AO08052000013<br>AO08052000013  | Alcohol dehydrogenase, class V Protein tyrosine serine phosphatase Dimethylycine dehydrogenase precursor wykB; FAD-dependent oxidoreductase Predicted protein 7-keto-8-aminopelargonate synthetase and related enzymes Cytochrome P450 CVP4 CVP10 CVP20 subfamilies Synaptic vesicle transporter SVOP and related transporters (major facilitator superfamily) Reverse transcriptase Predicted protein   | 2.439<br>2.446<br>2.442<br>2.426<br>2.412<br>2.409<br>2.400<br>2.394<br>2.393<br>2.392<br>2.393<br>2.392<br>2.393<br>2.392<br>2.383<br>2.359<br>2.357<br>2.331<br>2.329<br>2.331<br>2.329<br>2.331<br>2.329<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.2281   | <pre>" " [01][02][16][42] [14] [01][16][20] [14] " [01] [20][32][34] " " [20][32][34] " " [4] # # # [01][16][32] # [01][16][32] # [01][20][34] # [01][20][34] # [20] # [20] [10][11][42] # # #</pre>   | <pre>" " [01.05][01.20][02.01][02.16][16.17] [42.01] [42.01] [14.07] [01.01][01.02][01.05][16.21][20.01] [14.07] # # [01.01] [20.01][20.03][20.09][32.05][32.07] [34.11] # [01.03][16.17][32.01] # [01.03][16.17][32.01] # [01.03][16.17][32.01] # [01.03][16.17][32.01] # [01.03][16.17][32.01] # [01.03][16.17][32.01] # [01.03][16.17][32.01] # [01.03][20.01][20.03][20.09][34.01] [34.11] # [20.01][20.03][20.03][20.09][34.01] [34.11] # [20.01][20.03][20.09] [10.03][1.04][11.06][42.16] # #</pre>  |
| AO080513000020<br>AO08055300159<br>AO08054000050<br>AO08054000050<br>AO080551000014<br>AO08055000034<br>AO08055000034<br>AO08052000010<br>AO080520000010<br>AO080520000010<br>AO080540000314<br>AO080540000314<br>AO080540000314<br>AO080551000022<br>AO080551000030<br>AO080551000031<br>AO080551000031<br>AO080551000031<br>AO080551000031<br>AO080551000031<br>AO080551000031<br>AO080551000034<br>AO080551000034<br>AO080551000034<br>AO080551000034<br>AO08055200073<br>AO08052300073<br>AO080553000126<br>AO080553000126<br>AO080553000126<br>AO080553000126<br>AO080553000126<br>AO080553000126<br>AO080553000126<br>AO080553000126<br>AO080553000126<br>AO080553000126<br>AO080553000126<br>AO080553000126<br>AO080553000126<br>AO080553000126<br>AO080553000129<br>AO080553000129<br>AO080557000056   | Alcohol dehydrogenase, class V Protein tyrosine serine phosphatase Dimethylycine dehydrogenase precursor wykB, FAD-dependent oxidoreductase Predicted protein 7-keto-8-aminopelargonate synthetase and related enzymes Cytochrome P450 CVP4 CVP10 CVP26 subfamilies Synaptic vesicle transporter SVOP and related transporters (major facilitator superfamily) Reverse transcriptase Predicted protein   | 2.439<br>2.446<br>2.442<br>2.446<br>2.442<br>2.440<br>2.400<br>2.394<br>2.393<br>2.392<br>2.35<br>2.331<br>2.326<br>2.331<br>2.325<br>2.331<br>2.326<br>2.331<br>2.329<br>2.299<br>2.299<br>2.299<br>2.299<br>2.293<br>2.284<br>2.284<br>2.284<br>2.283<br>2.2251<br>2.2251<br>2.231<br>2.2251<br>2.231<br>2.231<br>2.231<br>2.231<br>2.231<br>2.235<br>2.235<br>2.235<br>2.235<br>2.235<br>2.235<br>2.235<br>2.235<br>2.235<br>2.235<br>2.235<br>2.235<br>2.235<br>2.235<br>2.235<br>2.235<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.2281<br>2.229   | <pre>// [01][02][16][42]<br/>[14]<br/>[01][16][20]<br/>[14]<br/>// (01][16][20]<br/>[14]<br/>// (01][20][34]<br/>// (01][30]<br/>// (01][30]</pre>   | <pre>" " [01.05][01.20][02.01][02.16][16.17] [42.01] [42.01] [14.07] [01.01][01.02][01.05][16.21][20.01] [14.07] # # # [01.01] [20.01][20.03][20.09][32.05][32.07] [34.11] # # # # # # # # # # # # # # # # # #</pre>  |
| AO080513000020<br>AO080531000020<br>AO080534000050<br>AO080531000027<br>AO080530100014<br>AO08057000034<br>AO08057000034<br>AO08052000031<br>AO080527000001<br>AO080527000001<br>AO080527000001<br>AO08053000022<br>AO080515000222<br>AO080530000125<br>AO080540000125<br>AO080540000125<br>AO080551000042<br>AO080551000042<br>AO080550000133<br>AO080550000133<br>AO080550000133<br>AO080550000133<br>AO080550000133<br>AO080550000133<br>AO080550000133<br>AO080550000133<br>AO080550000133<br>AO080550000133<br>AO080550000133<br>AO080551000005<br>AO080551000005<br>AO080551000005   | Alcohol dehydrogenase, class V Protein tyrosine serine phosphatase Dimethylycine dehydrogenase precursor wykB, FAD-dependent oxidoreductase Predicted protein 7-keto-8-aminopelargonate symhetase and related enzymes Cytochrome P450 CYP4 CYP19 CYP26 subfamilies Synaptic vesicle transporter SVOP and related transporters (major facilitator superfamily) Reverse transcriptase Predicted protein  | 2.439<br>2.446<br>2.442<br>2.442<br>2.400<br>2.401<br>2.394<br>2.392<br>2.392<br>2.392<br>2.392<br>2.392<br>2.392<br>2.392<br>2.392<br>2.392<br>2.392<br>2.392<br>2.393<br>2.359<br>2.357<br>2.399<br>2.357<br>2.399<br>2.395<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.299<br>2.298<br>2.299<br>2.298<br>2.299<br>2.299<br>2.299<br>2.299<br>2.299<br>2.299<br>2.299<br>2.299<br>2.299<br>2.299<br>2.299<br>2.299<br>2.299<br>2.299<br>2.299<br>2.299<br>2.299<br>2.299<br>2.299<br>2.299<br>2.299<br>2.299<br>2.299<br>2.299<br>2.299<br>2.299<br>2.299<br>2.299<br>2.299<br>2.299<br>2.299<br>2.299<br>2.299<br>2.299<br>2.299<br>2.299<br>2.299<br>2.299<br>2.299<br>2.299<br>2.299<br>2.299<br>2.299<br>2.299<br>2.299<br>2.299<br>2.299<br>2.299<br>2.299<br>2.299<br>2.299<br>2.299<br>2.299<br>2.299<br>2.299<br>2.299<br>2.299<br>2.299<br>2.299<br>2.299<br>2.299<br>2.299<br>2.299<br>2.299<br>2.299<br>2.299<br>2.299<br>2.299<br>2.299<br>2.299<br>2.299<br>2.299<br>2.299<br>2.299<br>2.299<br>2.299<br>2.299<br>2.299<br>2.299<br>2.299<br>2.299<br>2.299<br>2.299<br>2.299<br>2.299<br>2.299<br>2.299<br>2.299<br>2.299<br>2.299<br>2.299<br>2.299<br>2.299<br>2.299<br>2.299<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.292<br>2.291<br>2.292<br>2.293<br>2.292<br>2.293<br>2.292<br>2.293<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291     | <pre>// [01][02][16][42]<br/>[14]<br/>[01][16][20]<br/>[14]<br/>[01][16][20]<br/>[14]<br/>////////////////////////////////////</pre>   | <pre>" " [01.05][01.20][02.01][02.16][16.17] [42.01] [4.07] [4.01] [14.07] # " [01.01][01.02][01.05][16.21][20.01] [20.01][20.03][20.09][32.05][32.07] [34.11] # [01.01] [01.03][16.17][32.01] # # [01.03][16.17][32.01] # [01.04][01.05][01.06][01.20][30.01] # [01.04][01.05][01.06][01.20][30.01] # [01.04][01.05][01.06][01.20][30.01] # [01.04][01.05][01.06][01.20][30.01] # [01.04][01.05][01.06][01.20][30.01] # [01.05][20.01][20.03][20.09][34.01] [34.11] # [01.03][10.03][20.09][31.01] [10.03][10.03][20.09] # [20.01][20.03][20.00] # [20.01][20.03][20.00] # [20.01][20.03][20.00] # [20.01][20.03][20.00] # #</pre> |
| A0080513000020<br>A008050500159<br>A008054000050<br>A0080531000027<br>A008055000034<br>A008055000034<br>A008055000034<br>A0080520000010<br>A0080520000010<br>A0080520000010<br>A0080520000115<br>A008054000314<br>A008055000022<br>A0080550000125<br>A0080550000053<br>A0080550000053<br>A008055000053<br>A008055300024<br>A008055300024<br>A008055300024<br>A008055300024<br>A008055300024<br>A008055300024<br>A008055300024<br>A008055300024<br>A008055300024<br>A008055300024<br>A008055300024<br>A008055300024<br>A008055300024<br>A008055300024<br>A008055300024<br>A008055300024<br>A008055300024<br>A008055300024<br>A008055300024<br>A008055300024<br>A008055300024<br>A008055300024<br>A008055300024<br>A008055300024<br>A008055300024<br>A008055300024<br>A008055300024<br>A008055300025<br>A0080551000015<br>A008055100005  | Alcohol dehydrogenase, class V Protein tyrosine serine phosphatase Dimethylycine dehydrogenase precursor wykB, FAD-dependent oxidoreductase Predicted protein 7-keto-8-aminopelargonate synthetase and related enzymes Cytochrome F450 CYP4 CYP19 CYP20 subfamilies Synaptic vesicle transporter SVOP and related transporters (major facilitator superfamily) Reverse transcriptase Predicted protein   | 2.446<br>2.442<br>2.426<br>2.409<br>2.400<br>2.401<br>2.394<br>2.393<br>2.392<br>2.368<br>2.363<br>2.359<br>2.35<br>2.337<br>2.331<br>2.320<br>2.337<br>2.331<br>2.320<br>2.321<br>2.329<br>2.326<br>2.327<br>2.287<br>2.288<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.2287<br>2.288<br>2.2287<br>2.288<br>2.2287<br>2.288<br>2.2281<br>2.228<br>2.2281<br>2.2281<br>2.2291<br>2.2211<br>2.2114<br>2.212  | <pre>" " [01][02][16][42] [14] [01][16][20] [14] " [01][16][20] [20][32][34] # " [01][20][32][34] # [01][16][32] # [01][10][11][42] # [10][11][4] # " " " " " " " " " " " " " " " " " "</pre>  | <pre>" " [01.05][01.20][02.01][02.16][16.17] [14.07] [14.07] [14.07] [14.07] [14.07] [14.07] [14.07] [20.01][20.03][20.09][32.05][32.07] [34.11] # # # # # [01.03][16.17][32.01] # [01.03][16.17][32.01] # [01.04][01.05][01.06][01.20][30.01] # [10.04][11.04][11.06][42.16] # [10.04][11.04][11.06][42.16] # [10.04][11.04][11.06][42.16] # [10.04][11.04][11.06][42.16] # [10.04][11.04][11.06][42.16] # [10.04][11.04][11.06][42.16] # [10.04][11.04][11.06][42.16] # [10.04][11.04][11.06][42.16] # [10.04][11.04][11.06][42.16] # [10.04][11.04][11.06][42.16] # [10.04][11.04][11.06][42.16] # [10.04][11.04][11.06][42.16] # [10.04][11.04][11.06][42.16] # [10.04][11.04][11.06][42.16] # [10.04][11.04][11.06][42.16] # [10.04][11.04][11.06][42.16] # [10.04][11.04][11.06][42.16] # [10.04][11.04][11.06][40.16] # [10.04][11.04][11.04][11.06][40.16] # [10.04][11</pre> |
| AO080513000020<br>AO08050500159<br>AO08054000050<br>AO080550100014<br>AO080551000027<br>AO080551000027<br>AO08055000034<br>AO08055000034<br>AO08055000001<br>AO08055000001<br>AO080550000125<br>AO08056000125<br>AO080551000025<br>AO080551000025<br>AO080551000015<br>AO080551000015<br>AO08052000014<br>AO08052000014<br>AO08052000014<br>AO08052000014<br>AO08052000014<br>AO08052000014<br>AO08052000014<br>AO08052000014<br>AO08052000014<br>AO08052000014<br>AO08052000014<br>AO08052000014<br>AO08052000014<br>AO08052000014<br>AO08052000014<br>AO08052000014<br>AO08052000014<br>AO08052000014<br>AO08052000014<br>AO08052000014<br>AO08052000014<br>AO08052000014<br>AO08052000014<br>AO08052000014<br>AO08052000014<br>AO08052000014<br>AO08052000014<br>AO08052000014<br>AO08052000014<br>AO08052000014<br>AO08052000014<br>AO08052000014<br>AO08052000014<br>AO08052000014  | Alcohol dehydrogenase, class V Protein tyrosine serine phosphatase Dimethylycine dehydrogenase precursor wykB; FAD-dependent oxidoreductase Predicted protein 7-keto-8-aminopelargonate synthetase and related enzymes Cytochrome P450 CVP4 CVP10 CVP20 subfamilies Synaptic vesicle transporter SVOP and related transporters (major facilitator superfamily) Reverse transcriptase Predicted protein   | 2,446<br>2,442<br>2,446<br>2,442<br>2,409<br>2,400<br>2,400<br>2,401<br>2,394<br>2,393<br>2,392<br>2,393<br>2,392<br>2,393<br>2,392<br>2,383<br>2,359<br>2,357<br>2,331<br>2,326<br>2,331<br>2,329<br>2,331<br>2,329<br>2,239<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,299<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,298<br>2,299<br>2,299<br>2,299<br>2,299<br>2,299<br>2,299<br>2,299<br>2,299<br>2,299<br>2,299<br>2,299<br>2,299<br>2,299<br>2,299<br>2,299<br>2,299<br>2,299<br>2,299<br>2,299<br>2,299<br>2,299     | <pre>// [01][02][16][42]<br/>[14]<br/>[00][16][20]<br/>[14]<br/>// (01][16][20]<br/>[14]<br/>// (01]<br/>(01][20][34]<br/>// (01][10][32]<br/>// (01][10][32]<br/>// (01][10][32]<br/>// (01][20][34]<br/>// (01][20][34]<br/>//</pre>   | <pre>" " [01.05][01.20][02.01][02.16][16.17] [42.01] [42.01] [14.07] [01.01][01.02][01.05][16.21][20.01] [14.07] # # [01.01] [20.01][20.03][20.09][32.05][32.07] [34.11] # [01.03][16.17][32.01] # [01.03][16.17][32.01] # [01.03][16.17][32.01] # [01.03][16.17][32.01] # [01.03][16.17][32.01] # [01.03][10.05][01.06][01.20][30.01] # [01.03][20.01][34.01] # [01.03][20.01][20.03][20.09][34.01] [34.11] # [20.01][20.03][20.09] [10.03][10.03][20.09] [10.03][10.03][10.04][11.06][42.16] # [01.04][11.02] # [01.05][11.02][30.01]</pre>   |
| AO080513000020<br>AO08050500159<br>AO08054000050<br>AO08054000050<br>AO080551000027<br>AO08055000034<br>AO08055000034<br>AO080520000010<br>AO080520000010<br>AO080520000010<br>AO08054000314<br>AO08054000314<br>AO08054000314<br>AO08054000314<br>AO080551000022<br>AO080551000025<br>AO080554000031<br>AO080554000031<br>AO080554000031<br>AO080554000031<br>AO080554000033<br>AO080551000005<br>AO08052000046<br>AO08052000045<br>AO08052000045<br>AO08052000045<br>AO08052000045<br>AO08052000045<br>AO08052000045<br>AO08052000045<br>AO08052000045<br>AO08052000045<br>AO08052000045<br>AO08052000045<br>AO08052000045<br>AO08052000045<br>AO08052000045<br>AO08052000045<br>AO08052000045<br>AO08052000045<br>AO08052000045<br>AO08052000045<br>AO08052000045<br>AO08052000045<br>AO08052000045<br>AO08052000045<br>AO08052000045<br>AO08052000045<br>AO08052000045<br>AO08052000045<br>AO08052000045<br>AO08052000045<br>AO08052000045<br>AO08052000045<br>AO08052000045<br>AO08052000045<br>AO08052000045<br>AO08052000045<br>AO08052000045<br>AO08052000045<br>AO08052000045<br>AO08052000045<br>AO08052000045<br>AO08052000045<br>AO08052000045<br>AO08052000045<br>AO08052000045<br>AO08052000045<br>AO08052000045<br>AO08052000045<br>AO08052000045<br>AO08052000045<br>AO08052000045<br>AO08052000045<br>AO08052000045<br>AO08052000045<br>AO08052000045<br>AO08052000045<br>AO08052000045<br>AO08052000045<br>AO08052000045<br>AO08052000045<br>AO08052000045<br>AO08052000045<br>AO08052000045<br>AO08052000045<br>AO08052000045<br>AO08052000045<br>AO08052000045<br>AO08052000045<br>AO08052000045<br>AO08052000045<br>AO08052000045<br>AO08052000045<br>AO08052000045<br>AO08052000045<br>AO08052000045<br>AO08052000045<br>AO0805200045<br>AO0805200045<br>AO0805200045<br>AO0805200045<br>AO0805200045<br>AO0805200045<br>AO0805200045<br>AO0805200045<br>AO0805200045<br>AO0805200045<br>AO0805200045<br>AO0805200045<br>AO0805200045<br>AO0805200045<br>AO0805200045<br>AO0805200045<br>AO0805200045<br>AO0805200045<br>AO0805200045<br>AO0805200045<br>AO0805200045<br>AO0805200045<br>AO0805200045<br>AO0805200045<br>AO0805200045<br>AO0805200045<br>AO0805200045<br>AO0805200045<br>AO0805200045<br>AO0805200045<br>AO0805200045<br>AO0805200045<br>AO0805200045<br>AO0805200045<br>AO0805200045<br>AO0805200045<br>AO0805200045<br>AO0805200045<br>AO0805200045<br>AO0805200045<br>AO0805200045<br>AO0805200045<br>AO0805200045<br>AO0805200045<br>AO0805200045<br>AO0805200045<br>AO0805200045<br>AO0805200045<br>AO0805200045<br>AO0805200045<br>AO080520004   | Alcohol dehydrogenase, class V Protein tyrosine serine phosphatase Dimethylycine dehydrogenase precursor wykB, FAD-dependent oxidoreductase Predicted protein 7-keto-8-aminopelargonase synthetase and related enzymes Cytochrome P450 CVP4 CVP10 CVP20 subfamilies Synaptic vesicle transporter SVOP and related transporters (major facilitator superfamily) Reverse transcriptase Predicted protein   | 2.439<br>2.446<br>2.442<br>2.426<br>2.412<br>2.409<br>2.400<br>2.394<br>2.393<br>2.393<br>2.393<br>2.393<br>2.393<br>2.393<br>2.393<br>2.393<br>2.393<br>2.393<br>2.393<br>2.393<br>2.393<br>2.393<br>2.393<br>2.393<br>2.393<br>2.393<br>2.393<br>2.393<br>2.393<br>2.393<br>2.393<br>2.393<br>2.393<br>2.393<br>2.393<br>2.393<br>2.393<br>2.393<br>2.393<br>2.393<br>2.393<br>2.393<br>2.393<br>2.393<br>2.393<br>2.393<br>2.393<br>2.395<br>2.299<br>2.299<br>2.299<br>2.284<br>2.263<br>2.253<br>2.231<br>2.212<br>2.2284<br>2.263<br>2.238<br>2.231<br>2.212<br>2.2284<br>2.2284<br>2.2284<br>2.2284<br>2.2284<br>2.2284<br>2.2284<br>2.2284<br>2.2284<br>2.2284<br>2.2284<br>2.2284<br>2.2284<br>2.2284<br>2.2284<br>2.2284<br>2.2284<br>2.2284<br>2.2284<br>2.2284<br>2.2284<br>2.2284<br>2.2284<br>2.2284<br>2.2284<br>2.2284<br>2.2284<br>2.2284<br>2.2284<br>2.2284<br>2.2284<br>2.2284<br>2.2284<br>2.2284<br>2.2284<br>2.2284<br>2.2284<br>2.2284<br>2.2284<br>2.2284<br>2.2284<br>2.2284<br>2.2284<br>2.2284<br>2.2284<br>2.2284<br>2.2284<br>2.2284<br>2.2284<br>2.2284<br>2.2284<br>2.2284<br>2.2284<br>2.2284<br>2.2284<br>2.2284<br>2.2284<br>2.2284<br>2.2284<br>2.2284<br>2.2284<br>2.2284<br>2.2284<br>2.2284<br>2.2284<br>2.2284<br>2.2284<br>2.2284<br>2.2284<br>2.2284<br>2.2284<br>2.2284<br>2.2284<br>2.2284<br>2.2297<br>2.214<br>2.212<br>2.112<br>2.112<br>2.112<br>2.112<br>2.112<br>2.112<br>2.112<br>2.112<br>2.112<br>2.112<br>2.112<br>2.112<br>2.112<br>2.112<br>2.112<br>2.112<br>2.112<br>2.112<br>2.112<br>2.112<br>2.112<br>2.112<br>2.112<br>2.112<br>2.112<br>2.112<br>2.112<br>2.112<br>2.112<br>2.112<br>2.112<br>2.112<br>2.112<br>2.112<br>2.112<br>2.112<br>2.112<br>2.112<br>2.112<br>2.115<br>2.115<br>2.115<br>2.115<br>2.115<br>2.115<br>2.115<br>2.115<br>2.115<br>2.115<br>2.115<br>2.115<br>2.115<br>2.115<br>2.115<br>2.115<br>2.115<br>2.115<br>2.115<br>2.115<br>2.115<br>2.115<br>2.115<br>2.115<br>2.115<br>2.115<br>2.115<br>2.115<br>2.115<br>2.115<br>2.115<br>2.115<br>2.115<br>2.115<br>2.115<br>2.115<br>2.115<br>2.115<br>2.115<br>2.115<br>2.115<br>2.115<br>2.115<br>2.115<br>2.115<br>2.115<br>2.115<br>2.115<br>2.115<br>2.115<br>2.115<br>2.115<br>2.115<br>2.115<br>2.115<br>2.115<br>2.115<br>2.115<br>2.115<br>2.115<br>2.115<br>2.115<br>2.115<br>2.115<br>2.115<br>2.115<br>2.115<br>2.115<br>2.115<br>2.115<br>2.115<br>2.115<br>2.115<br>2.115<br>2.115<br>2.115<br>2.115<br>2.115<br>2.115<br>2.115<br>2.115<br>2.115<br>2.115<br>2.115<br>2.115<br>2.115<br>2.115<br>2.115<br>2.115<br>2.115<br>2.115<br>2.115<br>2.115<br>2.115<br>2.115<br>2.115<br>2.115<br>2.115<br>2.115<br>2.115<br>2.115<br>2.115<br>2.115<br>2.115<br>2.1  | "<br>[01][02][16][42]<br>[14]<br>[01][16][20]<br>[13]<br>#<br>[01]<br>[20][32][34]<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>[01][16][32]<br>#<br>[01][10][32]<br>#<br>[01][20][34]<br>#<br>[01][20][34]<br>#<br>#<br>[20]<br>[10][11][42]<br>#<br>#<br>[10][11][42]<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>[10][11][42]<br>#<br>#<br>[10][11][30]<br>#<br>#<br>#<br>[10][11][30]<br>#<br>#<br>#<br>[10][11][30]<br>#<br>#<br>#<br>[10][11][30]<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#   | <pre></pre>   |
| AO080513000020<br>AO080513000027<br>AO08053000159<br>AO080531000027<br>AO080530100014<br>AO08053000027<br>AO08050100014<br>AO08053000033<br>AO08052000001<br>AO080527000001<br>AO080527000001<br>AO08053000005<br>AO08051000212<br>AO08051000012<br>AO08055000003<br>AO080551000024<br>AO080551000024<br>AO080551000024<br>AO080551000024<br>AO080551000024<br>AO080551000024<br>AO080551000024<br>AO080551000024<br>AO080551000024<br>AO080551000024<br>AO080551000024<br>AO080551000005<br>AO080551000005<br>AO080551000013<br>AO080551000005<br>AO080551000005<br>AO080551000013<br>AO080551000005<br>AO080551000005<br>AO080551000005<br>AO080551000005<br>AO080551000005<br>AO080551000005<br>AO080551000005<br>AO080551000005<br>AO080551000005<br>AO080551000005<br>AO080551000005<br>AO080551000005<br>AO080551000005  | Alcohol dehydrogenase, class V Protein tyrosine serine phosphatase Dimethylycine dehydrogenase precursor wykB, FAD-dependent oxidoreductase Predicted protein 7-keto-8-aminopelargonate synthetase and related enzymes Cytochrome P450 CYP4 CYP19 CYP20 subfamilies Synaptic vesicle transporter SVOP and related transporters (major facilitator superfamily) Reverse transcriptase Predicted protein   | 2.446<br>2.442<br>2.442<br>2.440<br>2.440<br>2.440<br>2.394<br>2.394<br>2.392<br>2.392<br>2.392<br>2.392<br>2.392<br>2.392<br>2.392<br>2.392<br>2.392<br>2.392<br>2.392<br>2.392<br>2.393<br>2.337<br>2.337<br>2.337<br>2.337<br>2.337<br>2.337<br>2.337<br>2.337<br>2.337<br>2.337<br>2.337<br>2.337<br>2.337<br>2.337<br>2.337<br>2.337<br>2.337<br>2.337<br>2.337<br>2.337<br>2.337<br>2.337<br>2.337<br>2.337<br>2.337<br>2.337<br>2.337<br>2.337<br>2.337<br>2.337<br>2.337<br>2.337<br>2.337<br>2.337<br>2.337<br>2.337<br>2.337<br>2.337<br>2.337<br>2.337<br>2.328<br>2.329<br>2.325<br>2.329<br>2.228<br>2.2283<br>2.2284<br>2.2284<br>2.2282<br>2.2284<br>2.2284<br>2.2284<br>2.2281<br>2.2212<br>2.229<br>2.2212<br>2.2212<br>2.2212<br>2.2212<br>2.2212<br>2.2212<br>2.2212<br>2.2212<br>2.2212<br>2.2212<br>2.2212<br>2.2212<br>2.2212<br>2.2212<br>2.2212<br>2.2212<br>2.2212<br>2.2212<br>2.2212<br>2.2212<br>2.2212<br>2.2212<br>2.2212<br>2.2212<br>2.2212<br>2.2212<br>2.2212<br>2.2212<br>2.2212<br>2.2212<br>2.2212<br>2.2212<br>2.2212<br>2.2212<br>2.2212<br>2.2212<br>2.2212<br>2.2212<br>2.2212<br>2.2212<br>2.2212<br>2.2212<br>2.2212<br>2.2212<br>2.2212<br>2.2212<br>2.2212<br>2.2212<br>2.2212<br>2.2212<br>2.2212<br>2.2212<br>2.2212<br>2.2212<br>2.2212<br>2.2212<br>2.2212<br>2.2212<br>2.2212<br>2.2212<br>2.2212<br>2.2212<br>2.2212<br>2.2212<br>2.2212<br>2.2212<br>2.2212<br>2.2212<br>2.2212<br>2.2212<br>2.2212<br>2.2212<br>2.2212<br>2.2212<br>2.2212<br>2.2212<br>2.2212<br>2.2212<br>2.2212<br>2.2212<br>2.2212<br>2.2212<br>2.2212<br>2.2212<br>2.2212<br>2.2212<br>2.2212<br>2.2212<br>2.2212<br>2.2212<br>2.2212<br>2.2212<br>2.2212<br>2.2212<br>2.2212<br>2.2212<br>2.2212<br>2.2212<br>2.2212<br>2.2212<br>2.2212<br>2.2212<br>2.2212<br>2.2212<br>2.2212<br>2.2212<br>2.2212<br>2.2212<br>2.2212<br>2.2212<br>2.2212<br>2.2212<br>2.2212<br>2.2212<br>2.2212<br>2.2212<br>2.2212<br>2.2212<br>2.2212<br>2.2212<br>2.2212<br>2.2212<br>2.2212<br>2.2212<br>2.2212<br>2.2212<br>2.2212<br>2.2212<br>2.2212<br>2.2212<br>2.2212<br>2.2212<br>2.2212<br>2.2212<br>2.2212<br>2.212<br>2.212<br>2.212  | "         [01][02][16][42]         [14]         [01][16][20]         [14]         [01]         [20][32][34]         #         #         #         #         #         #         #         #         #         #         #         #         #         #         #         #         #         [01][20][34]         #         [20]         [20]         [20]         [20]         [10][11]         #         #         [10][11][30]         #         [10][11][30]         #         #         [10][11][30]         #         [43]  | <pre> // (01.05][01.20][02.01][02.16][16.17] [42.01] [4.07] [4.01] [14.07] // (14.07] /</pre> |
| A0080513000020<br>A008050500159<br>A008054000050<br>A008054000050<br>A0080551000027<br>A008055000034<br>A008055000034<br>A008055000039<br>A0080520000010<br>A0080520000010<br>A0080520000010<br>A008054000314<br>A0080550000125<br>A0080550000125<br>A0080550000125<br>A0080550000125<br>A0080550000125<br>A0080550000125<br>A0080550000125<br>A0080550000125<br>A0080550000125<br>A0080550000125<br>A0080550000125<br>A0080553000246<br>A0080553000246<br>A0080553000245<br>A0080553000245<br>A0080553000245<br>A0080553000245<br>A0080553000245<br>A0080553000245<br>A0080553000245<br>A0080553000125<br>A0080553000125<br>A0080553000125<br>A0080553000125<br>A0080553000125<br>A0080551000015<br>A0080551000015<br>A0080551000015<br>A0080551000015  | Alcohol dehydrogenase, class V Protein tyrosine serine phosphatase Dimethylycine dehydrogenase precursor wykB, FAD-dependent oxidoreductase Predicted protein 7-keto-8-aminopelargonate synthetase and related enzymes Cytochrome FASO CYP4 CYP19 CYP20 subfamilies Synaptic vesicle transporter SVOP and related transporters (major facilitator superfamily) Reverse transcriptase Predicted protein   | 2.446<br>2.442<br>2.446<br>2.442<br>2.406<br>2.401<br>2.394<br>2.393<br>2.394<br>2.393<br>2.394<br>2.393<br>2.358<br>2.357<br>2.331<br>2.326<br>2.327<br>2.341<br>2.329<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.291<br>2.298<br>2.291<br>2.298<br>2.298<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.291<br>2.211<br>2.212<br>2.217<br>2.107<br>2.107<br>2.107<br>2.107<br>2.108  | <pre>" " [01][02][16][42] [14] [01][16][20] [14] " [01][16][20] [20][32][34] # " [01][32][34] # [01][30] # # [01][30] # [01][20][34] # [01][20][34] # [20] [10][11][42] # [4] [10][11][42] # [4] [4] [4] [4] [4] [4] [4] [4] [4] [4]</pre>   | <pre>" " [01.05][01.20][02.01][02.16][16.17] [14.07] [14.07] [14.07] [14.07] [14.07] [14.07] [20.01][20.03][20.09][32.05][32.07] [34.11] # # # # # # # [01.03][16.17][32.01] # # [01.03][16.17][32.01] # # [01.03][16.17][32.01] # # [01.03][16.17][32.01] # # [01.03][16.17][32.01] # # [01.03][16.17][32.01] # [01.03][10.03][20.09][34.01] [34.11] # [20.01][20.03][20.09][34.01] [34.11] # [20.01][20.03][20.09] # [20.01][20.03][20.00] # [20.01][20.03][20.00] # [20.01][20.03][20.00] # [20.01][20.03][20.00] # [20.01][20.03][20.00] # [20.01][20.01][20.01] # # [20.01][20.01][20.01] # # [20.01][20.01][20.01] # # # [20.01][20.01][20.01][20.01] # # # [20.01][20.01][20.01] # # # [20.01][20.01][20.01] # # # # # # # # # # # # # # # # # # #</pre>   |
| A0080513000020<br>A008050500159<br>A0080550100014<br>A0080551000027<br>A0080551000027<br>A008055000034<br>A008055000034<br>A008052000001<br>A008052000001<br>A008052000001<br>A008052000001<br>A0080521000212<br>A008051000022<br>A0080551000023<br>A0080551000023<br>A0080551000042<br>A0080520000048<br>A0080520000048<br>A0080520000048<br>A0080520000048<br>A0080520000048<br>A008052000048<br>A008052000048<br>A008052000048<br>A008052000048<br>A008052000048<br>A008052000048<br>A008052000048<br>A008052000048<br>A008052000048<br>A008052000048<br>A008052000048<br>A008052000048<br>A008052000048<br>A008052000048<br>A008052000048<br>A008052000048<br>A008052000048<br>A008052000048<br>A008052000048<br>A008052000048<br>A008052000048<br>A008052000048<br>A008052000048<br>A008052000048<br>A008052000048<br>A008052000048<br>A008052000048<br>A008052000048<br>A008052000048<br>A008052000048<br>A008052000048<br>A008052000048<br>A008052000048<br>A008052000048<br>A008052000048<br>A008052000048<br>A008051000048<br>A008051000048<br>A008051000048<br>A008051000048<br>A008051000048<br>A008051000048<br>A008051000048  | Alcohol dehydrogenase, class V Protein tyrosine serine phosphatase Dimethylycine dehydrogenase precursor wykB; FAD-dependent oxidoreductase Predicted protein 7-keto-8-aminopelargonate synthetase and related enzymes Cytochrome P450 CVP4 CVP10 CVP20 subfamilies Synaptic vesicle transporter SVOP and related transporters (major facilitator superfamily) Reverse transcriptase Predicted protein   | 2.446<br>2.442<br>2.446<br>2.442<br>2.409<br>2.400<br>2.401<br>2.394<br>2.393<br>2.393<br>2.394<br>2.393<br>2.393<br>2.395<br>2.357<br>2.331<br>2.329<br>2.331<br>2.329<br>2.331<br>2.329<br>2.335<br>2.337<br>2.332<br>2.331<br>2.329<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.228<br>2.238<br>2.238<br>2.238<br>2.231<br>2.299<br>2.298<br>2.298<br>2.238<br>2.238<br>2.231<br>2.298<br>2.228<br>2.238<br>2.238<br>2.238<br>2.238<br>2.239<br>2.298<br>2.298<br>2.228<br>2.238<br>2.238<br>2.238<br>2.238<br>2.239<br>2.298<br>2.298<br>2.228<br>2.238<br>2.238<br>2.238<br>2.238<br>2.238<br>2.238<br>2.238<br>2.238<br>2.238<br>2.238<br>2.238<br>2.238<br>2.2298<br>2.228<br>2.228<br>2.238<br>2.238<br>2.238<br>2.238<br>2.238<br>2.238<br>2.238<br>2.238<br>2.238<br>2.239<br>2.298<br>2.238<br>2.238<br>2.231<br>2.298<br>2.238<br>2.231<br>2.215<br>2.298<br>2.238<br>2.231<br>2.216<br>2.228<br>2.231<br>2.217<br>2.218<br>2.218<br>2.218<br>2.218<br>2.218<br>2.218<br>2.218<br>2.218<br>2.218<br>2.218<br>2.218<br>2.218<br>2.218<br>2.218<br>2.218<br>2.218<br>2.218<br>2.218<br>2.218<br>2.218<br>2.218<br>2.218<br>2.218<br>2.218<br>2.218<br>2.218<br>2.218<br>2.218<br>2.218<br>2.218<br>2.218<br>2.218<br>2.218<br>2.218<br>2.218<br>2.218<br>2.218<br>2.218<br>2.218<br>2.218<br>2.218<br>2.218<br>2.218<br>2.218<br>2.218<br>2.219<br>2.219<br>2.219<br>2.217<br>2.219<br>2.217<br>2.217<br>2.117<br>2.117<br>2.1168<br>2.168<br>2.168<br>2.168<br>2.168<br>2.168<br>2.168<br>2.168<br>2.168<br>2.168<br>2.168<br>2.168<br>2.168<br>2.168<br>2.168<br>2.168<br>2.168<br>2.168<br>2.168<br>2.168<br>2.168<br>2.168<br>2.168<br>2.168<br>2.168<br>2.168<br>2.168<br>2.168<br>2.168<br>2.168<br>2.168<br>2.168<br>2.168<br>2.168<br>2.168<br>2.168<br>2.168<br>2.168<br>2.168<br>2.168<br>2.168<br>2.168<br>2.168<br>2.168<br>2.168<br>2.168<br>2.168<br>2.168<br>2.168<br>2.168<br>2.168<br>2.168<br>2.168<br>2.168<br>2.168<br>2.168<br>2.168<br>2.168<br>2.168<br>2.168<br>2.168<br>2.168<br>2.168<br>2.168<br>2.168<br>2.168<br>2.168<br>2.168<br>2.168<br>2.168<br>2.168<br>2.168<br>2.168<br>2.168<br>2.168<br>2.168<br>2.168<br>2.168<br>2.168<br>2.168<br>2.168<br>2.168<br>2.168<br>2.168<br>2.168<br>2.168<br>2.168<br>2.168<br>2.168<br>2.168<br>2.168<br>2.168<br>2.168<br>2.168<br>2.168<br>2.168<br>2.168<br>2.168<br>2.168<br>2.168<br>2.168<br>2.168<br>2.168<br>2.168<br>2.168<br>2.168<br>2.168<br>2.168<br>2.168<br>2.168<br>2.168<br>2.168<br>2.168<br>2.168<br>2.168<br>2.168<br>2.168<br>2.168<br>2.168<br>2.168<br>2.168<br>2.168<br>2.168<br>2.168<br>2.168<br>2.168<br>2.168<br>2.168<br>2.168<br>2.168<br>2.168<br>2.168<br>2.168<br>2.168<br>2.168<br>2.168<br>2.168  | <pre>" " [01][02][16][42] [14] [01][16][20] [14] " [01][16][20] [14] " " [20][32][34] " " [20][32][34] " " [01][16][32] " " [01][16][32] " [01][10][4] " [01][20][34] " " [20] " [10][11][42] " " " [43] " [</pre>  | <pre>" " [01.05][01.20][02.01][02.16][16.17] [42.01] [42.01] [14.07] [01.01][01.02][01.05][16.21][20.01] [14.07] # # [01.01] [20.01][20.03][20.09][32.05][32.07] [34.11] # [01.03][16.17][32.01] # [01.03][16.17][32.01] # [01.03][16.17][32.01] # [01.03][16.17][32.01] # [01.03][10.05][01.06][01.20][30.01] # [01.03][20.01][20.03][20.09][34.01] [34.11] # [01.05][20.01][20.03][20.09][34.01] # [01.05][20.01][20.03][20.09][34.01] # [01.03][10.01][20.03][20.09][34.01] # [01.03][10.03][20.09] [10.03][10.03][10.04][01.06][42.16] # [01.05][11.02][30.01] # [01.05][11.02][30.01] # [14.01][11.02] # [14.01][11.02][30.01] # [14.01][34.01] # [10.01][11.02][30.01] # [14.01][34.01] # [10.02][34.01] # [10.02][34.01] # [10.02][34.01] # [10.02][34.01] # [10.02][34.01] # [10.02][34.01] # [10.02][34.01] # [10.02][34.01] # [10.02][34.01] # [10.02][34.01] # [10.02][34.01] # [10.02][34.01] # [10.02][34.01] # [10.02][34.01] # [10.02][34.01] # [10.02][34.01] # [10.02][34.01</pre> |
| A0080513000020<br>A008050500159<br>A00805000050<br>A0080530100014<br>A0080530100014<br>A008053000027<br>A008053000034<br>A008052000010<br>A0080520000010<br>A0080520000010<br>A0080520000014<br>A008053000031<br>A0080540000314<br>A008051000022<br>A008051000022<br>A008051000022<br>A0080554000012<br>A0080554000012<br>A0080554000012<br>A0080554000034<br>A0080521000046<br>A0080521000046<br>A008052000023<br>A0080554000031<br>A0080554000031<br>A0080554000031<br>A0080554000032<br>A0080554000034<br>A0080554000033<br>A008055000046<br>A0080551000005<br>A0080551000005<br>A0080551000005<br>A0080551000013<br>A0080551000013<br>A0080551000013<br>A0080551000013<br>A0080551000013<br>A0080551000013<br>A0080551000013<br>A0080551000013<br>A0080551000013<br>A0080551000013<br>A0080551000013<br>A0080551000013<br>A0080551000013<br>A0080551000013<br>A0080551000013<br>A0080551000013<br>A0080551000013<br>A0080551000013<br>A0080511000146<br>A008052000071<br>A0080551000013<br>A0080511000146<br>A0080511000146<br>A0080511000146<br>A0080511000146<br>A0080511000146<br>A0080511000146<br>A0080511000146<br>A0080511000146<br>A0080511000146<br>A0080511000146<br>A0080511000146<br>A0080511000146<br>A0080511000146<br>A0080511000146<br>A0080511000146<br>A0080511000146<br>A0080511000146<br>A0080511000146<br>A0080511000146<br>A0080511000146<br>A0080511000146<br>A0080511000146<br>A0080511000146<br>A0080511000146<br>A0080511000146<br>A0080511000146<br>A0080511000146<br>A0080511000146<br>A0080511000146<br>A0080511000146<br>A0080511000146<br>A0080511000146<br>A0080511000146<br>A008052000014<br>A0080511000146<br>A008052000014<br>A0080511000146<br>A008052000014<br>A0080511000146<br>A0080520000146<br>A0080520000046<br>A0080520000046<br>A008052000046<br>A008052000046<br>A008052000046<br>A008052000046<br>A008052000046<br>A008052000046<br>A008052000046<br>A008052000046<br>A008052000046<br>A008052000046<br>A008052000046<br>A008052000046<br>A008052000046<br>A008052000046<br>A008052000046<br>A008052000046<br>A008052000046<br>A008052000046<br>A008052000046<br>A008052000046<br>A008052000046<br>A008052000046<br>A008052000046<br>A008052000046<br>A00805200046<br>A00805200046<br>A00805200046<br>A00805200046<br>A00805200046<br>A00805200046<br>A00805200046<br>A00805200046<br>A00805200046<br>A00805200046<br>A00805200046<br>A00805200046<br>A00805200046<br>A00805200046<br>A00805200046<br>A00805200046<br>A00805200046<br>A00805200046<br>A00805200046<br>A00805200046<br>A00805200046<br>A00805200046   | Alcohol dehydrogenase, class V Protein tyrosine serine phosphatase Dimethylycine dehydrogenase precursor wykB, FAD-dependent oxidoreductase Predicted protein 7-keto-8-aminopelargonate synthetase and related enzymes Cytochrome P450 CVP4 CVP10 CVP20 subfamilies Synaptic vesicle transporter SVOP and related transporters (major facilitator superfamily) Reverse transcriptase Predicted protein   | 2.439<br>2.446<br>2.442<br>2.446<br>2.442<br>2.440<br>2.400<br>2.394<br>2.393<br>2.392<br>2.393<br>2.392<br>2.393<br>2.392<br>2.35<br>2.337<br>2.331<br>2.320<br>2.331<br>2.320<br>2.331<br>2.320<br>2.331<br>2.320<br>2.299<br>2.299<br>2.299<br>2.299<br>2.299<br>2.299<br>2.299<br>2.299<br>2.299<br>2.299<br>2.299<br>2.299<br>2.299<br>2.293<br>2.2284<br>2.263<br>2.263<br>2.263<br>2.263<br>2.263<br>2.263<br>2.263<br>2.263<br>2.263<br>2.263<br>2.263<br>2.263<br>2.263<br>2.263<br>2.263<br>2.263<br>2.263<br>2.263<br>2.263<br>2.263<br>2.263<br>2.263<br>2.263<br>2.263<br>2.263<br>2.263<br>2.263<br>2.263<br>2.263<br>2.263<br>2.263<br>2.263<br>2.263<br>2.263<br>2.263<br>2.263<br>2.263<br>2.263<br>2.263<br>2.263<br>2.263<br>2.263<br>2.263<br>2.263<br>2.263<br>2.263<br>2.214<br>2.212<br>2.212<br>2.212<br>2.214<br>2.212<br>2.217<br>2.217<br>2.217<br>2.217<br>2.217<br>2.217<br>2.217<br>2.218<br>2.217<br>2.218<br>2.218<br>2.218<br>2.215<br>2.228<br>2.231<br>2.217<br>2.228<br>2.231<br>2.217<br>2.228<br>2.231<br>2.217<br>2.228<br>2.231<br>2.217<br>2.228<br>2.231<br>2.217<br>2.228<br>2.231<br>2.217<br>2.228<br>2.228<br>2.231<br>2.217<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.228<br>2.217<br>2.217<br>2.217<br>2.217<br>2.217<br>2.217<br>2.217<br>2.217<br>2.217<br>2.217<br>2.217<br>2.217<br>2.217<br>2.217<br>2.217<br>2.217<br>2.217<br>2.217<br>2.217<br>2.217<br>2.217<br>2.217<br>2.217<br>2.217<br>2.217<br>2.217<br>2.217<br>2.217<br>2.217<br>2.217<br>2.217<br>2.217<br>2.217<br>2.217<br>2.217<br>2.217<br>2.217<br>2.217<br>2.217<br>2.217<br>2.217<br>2.217<br>2.217<br>2.217<br>2.217<br>2.217<br>2.217<br>2.217<br>2.217<br>2.217<br>2.217<br>2.217<br>2.217<br>2.217<br>2.217<br>2.217<br>2.217<br>2.217<br>2.217<br>2.217<br>2.217<br>2.217<br>2.217<br>2.217<br>2.217<br>2.217<br>2.217<br>2.217<br>2.217<br>2.217<br>2.217<br>2.217<br>2.217<br>2.2172<br>2.175<br>2.216<br>2.216<br>2.2175<br>2.2162<br>2.2162<br>2.2162<br>2.2175<br>2.2162<br>2.2175<br>2.2162<br>2.2162<br>2.2175<br>2.2162<br>2.162<br>2.162  | <pre>// [01][02][16][42]<br/>[14]<br/>[01][16][20]<br/>[13]<br/>////////////////////////////////////</pre>   | <pre>" " [01.05][01.20][02.01][02.16][16.17] [42.01] [42.01] [14.07] [01.01][01.02][01.05][16.21][20.01] [14.07] # " [01.01] [20.01][20.03][20.09][32.05][32.07] [34.11] # # # # # # # # # # # # # # # # # #</pre>  |
| A0080513000020<br>A008054000050<br>A008054000050<br>A008054000050<br>A0080551000014<br>A008055000034<br>A008055000034<br>A008052000001<br>A008052000001<br>A008052000001<br>A008054000014<br>A008054000014<br>A008054000014<br>A0080540000154<br>A0080550000153<br>A0080550000053<br>A0080550000153<br>A0080550000153<br>A0080550000127<br>A0080550000127<br>A0080550000127<br>A0080550000127<br>A0080550000127<br>A0080550000127<br>A0080550000127<br>A0080550000127<br>A0080550000127<br>A0080550000127<br>A0080550000127<br>A0080550000127<br>A0080550000127<br>A0080550000127<br>A0080550000127<br>A0080550000127<br>A0080550000127<br>A0080550000127<br>A0080550000127<br>A0080550000127<br>A0080550000127<br>A0080550000127<br>A0080550000127<br>A00805510000127<br>A00805510000127<br>A00805510000127<br>A00805510000127<br>A00805510000127<br>A00805510000127<br>A00805510000127<br>A00805510000127<br>A00805510000127<br>A00805510000127<br>A00805510000127<br>A00805510000127<br>A00805510000127<br>A00805510000127<br>A00805510000028<br>A0080511000029<br>A00805110000149<br>A0080511000149<br>A0080511000149  | Alcohol dehydrogenase, class V Protein tyrosine serine phosphatase Dimethylgycine dehydrogenase precursor wykB, FAD-dependent oxidoreductase Predicted protein 7-keto-8-aminopelargonate synthetase and related enzymes Cytochrome P450 CVP4 CVP19 CVP20 subfamilies Synaptic vesicle transporter SVOP and related transporters (major facilitator superfamily) Reverse transcriptase Predicted protein Predicted protei   | 2.446<br>2.442<br>2.426<br>2.400<br>2.401<br>2.394<br>2.393<br>2.392<br>2.368<br>2.363<br>2.359<br>2.35<br>2.337<br>2.337<br>2.337<br>2.337<br>2.337<br>2.337<br>2.337<br>2.337<br>2.337<br>2.337<br>2.337<br>2.337<br>2.337<br>2.337<br>2.337<br>2.337<br>2.337<br>2.337<br>2.337<br>2.337<br>2.337<br>2.337<br>2.337<br>2.337<br>2.337<br>2.337<br>2.337<br>2.337<br>2.337<br>2.337<br>2.337<br>2.337<br>2.337<br>2.337<br>2.337<br>2.337<br>2.337<br>2.337<br>2.337<br>2.337<br>2.337<br>2.337<br>2.337<br>2.337<br>2.337<br>2.337<br>2.337<br>2.337<br>2.337<br>2.337<br>2.337<br>2.337<br>2.337<br>2.337<br>2.326<br>2.239<br>2.239<br>2.235<br>2.239<br>2.235<br>2.239<br>2.235<br>2.239<br>2.235<br>2.239<br>2.235<br>2.239<br>2.235<br>2.239<br>2.232<br>2.231<br>2.231<br>2.231<br>2.2284<br>2.2284<br>2.2281<br>2.2281<br>2.221<br>2.219<br>2.219<br>2.219<br>2.219<br>2.219<br>2.219<br>2.219<br>2.219<br>2.229<br>2.229<br>2.229<br>2.229<br>2.229<br>2.229<br>2.229<br>2.229<br>2.229<br>2.229<br>2.229<br>2.229<br>2.229<br>2.229<br>2.229<br>2.229<br>2.229<br>2.229<br>2.229<br>2.229<br>2.229<br>2.229<br>2.229<br>2.229<br>2.229<br>2.229<br>2.229<br>2.229<br>2.229<br>2.229<br>2.229<br>2.229<br>2.229<br>2.229<br>2.229<br>2.229<br>2.229<br>2.229<br>2.229<br>2.229<br>2.229<br>2.229<br>2.229<br>2.229<br>2.229<br>2.229<br>2.229<br>2.229<br>2.229<br>2.229<br>2.229<br>2.229<br>2.229<br>2.229<br>2.229<br>2.229<br>2.229<br>2.229<br>2.219<br>2.229<br>2.219<br>2.229<br>2.219<br>2.219<br>2.219<br>2.219<br>2.219<br>2.219<br>2.219<br>2.219<br>2.219<br>2.219<br>2.219<br>2.219<br>2.219<br>2.219<br>2.219<br>2.219<br>2.219<br>2.219<br>2.219<br>2.219<br>2.219<br>2.219<br>2.219<br>2.219<br>2.219<br>2.219<br>2.219<br>2.219<br>2.219<br>2.219<br>2.219<br>2.219<br>2.219<br>2.219<br>2.219<br>2.219<br>2.219<br>2.219<br>2.219<br>2.219<br>2.219<br>2.219<br>2.219<br>2.219<br>2.219<br>2.219<br>2.219<br>2.219<br>2.219<br>2.219<br>2.219<br>2.219<br>2.219<br>2.219<br>2.219<br>2.219<br>2.219<br>2.219<br>2.219<br>2.219<br>2.219<br>2.219<br>2.219<br>2.219<br>2.219<br>2.219<br>2.219<br>2.219<br>2.219<br>2.219<br>2.219<br>2.219<br>2.219<br>2.219<br>2.219<br>2.219<br>2.219<br>2.219<br>2.219<br>2.219<br>2.219<br>2.219<br>2.219<br>2.219<br>2.219<br>2.219<br>2.219<br>2.219<br>2.219<br>2.219<br>2.219<br>2.219<br>2.219<br>2.219   | "         [01][02][16][42]         [14]         [01][16][20]         [14]         [01]         [20][32][34]         #         #         #         #         [01][16][32]         #         [01][16][32]         #         [01][20][34]         #         [01][20][34]         #         [10][10][11][42]         #         #         #         [10][11][43]         #         [01][11][43]         #         [43]         #         [01]         #         [01]         #         [01]         #         #         #         #         [01]         #         #         #         #         #         #         #         #         #         #         #         #         #  | <pre>     [01.05][01.20][02.01][02.16][16.17] [42.01] [44.07] [14.07] [14.07] [01.01][01.02][01.05][16.21][20.01] [14.07] # # [01.01] [20.01][20.03][20.09][32.05][32.07] [34.11] # # [01.03][16.17][32.01] # [01.03][16.17][32.01] # [01.03][16.17][32.01] # [01.03][16.17][32.01] # [01.03][16.17][32.01] # [01.03][16.17][32.01] # [01.03][20.01][20.03][20.09][34.01] [34.11] # [20.01][20.03][20.09] [34.11] # [20.01][20.03][20.09] [4 [10.03][20.03][20.09] [4 [10.03][20.03][20.09] [4 [10.03][20.03][20.09] [4 [10.03][20.03][20.09] [4 [10.01][20.03][20.00] [4 [10.01][20.03][20.00] [4 [10.01][20.03][20.00] [4 [10.01][20.03][20.00] [4 [10.01][20.03][20.00] [4 [10.01][20.03][20.00] [4 [10.01][20.03][20.00] [4 [10.01][20.03][20.00] [4 [10.01][20.03][20.00] [4 [10.01][20.03][20.00] [4 [10.01][20.03][20.00] [4 [10.01][20.03][20.00] [4 [10.01][20.03][20.00] [4 [10.01][20.03][20.00] [4 [10.01][20.03][20.00] [4 [10.01][20.03][20.00] [4 [10.01][20.03][20.00] [4 [10.01][20.03][20.00] [4 [10.01][20.03][20.00] [4 [10.01][20.03][2</pre> |
| A0080513000020<br>A008050500159<br>A008055000159<br>A008055000050<br>A0080551000027<br>A008055000034<br>A008055000039<br>A008055000039<br>A008055000031<br>A0080520000010<br>A0080520000010<br>A0080520000012<br>A008055000022<br>A008055000022<br>A008055000055<br>A008055000055<br>A008055000055<br>A008055000053<br>A0080520000125<br>A008055000053<br>A0080520000125<br>A008055000053<br>A0080520000125<br>A008055000053<br>A0080520000125<br>A008055000053<br>A0080520000125<br>A008055000053<br>A0080520000125<br>A008055000053<br>A0080550000153<br>A008055000053<br>A008055000055<br>A008055000055<br>A008055000055<br>A008055000015<br>A008055000015<br>A008055000015<br>A008055000055<br>A008055000055<br>A008055000055<br>A008055000055<br>A008055000055<br>A008055000055<br>A008055000055<br>A008055000055<br>A008055000055<br>A008055000055<br>A008055000055<br>A008055000055<br>A008055000055<br>A008055000055<br>A008055000055<br>A008055000055<br>A008055000055<br>A008055000055<br>A008051000054<br>A0080551000054<br>A0080551000054<br>A0080551000054<br>A0080551000054<br>A0080551000054<br>A0080551000054<br>A0080551000054<br>A0080551000054<br>A0080551000054<br>A0080551000054<br>A0080551000054<br>A0080551000054<br>A0080551000055<br>A008051100054<br>A0080551000054<br>A0080551000054<br>A0080551000054<br>A0080551000054<br>A0080551000054<br>A0080551000054<br>A0080551000054<br>A0080551000054<br>A0080551000054<br>A0080551000054<br>A0080551000054<br>A0080551000054<br>A008055200055<br>A008055000155<br>A008055000155<br>A008055000155<br>A008055000155<br>A008055000155<br>A008055000155<br>A008055000155<br>A008055000155<br>A008055000155<br>A008055000155<br>A008055000155<br>A008055000155<br>A008055000155<br>A008055000155<br>A008055000155<br>A008055000155<br>A008055000155<br>A008055000155<br>A008055000155<br>A008055000155<br>A008055000155<br>A008055000155<br>A008055000155<br>A008055000155<br>A008055000155<br>A008055000155<br>A008055000155<br>A008055000155<br>A008055000155<br>A008055000155<br>A008055000155<br>A008055000155<br>A008055000155<br>A008055000155<br>A008055000155<br>A008055000155<br>A008055000155<br>A008055000155<br>A008055000155<br>A00805500055<br>A00805500055<br>A00805500055<br>A00805500055<br>A00805500055<br>A00805500055<br>A00805500055<br>A00805500055<br>A00805500055<br>A00805500055<br>A00805500055<br>A00805500055<br>A00805500055<br>A00805500055<br>A00805500055<br>A00805500055<br>A00805500055<br>A00805500055<br>A00805500055<br>A00805500055<br>A00805500055<br>A00805500055<br>A  | Alcohol dehydrogenase, class V Protein tyrosine serine phosphatase Dimethylycine dehydrogenase precursor wykB, FAD-dependent oxidoreductase Predicted protein 7-keto-8-aminopelargonate synthetase and related enzymes Cytochrome F450 CVP4 CVP10 CVP20 subfamilies Synaptic vesicle transporter SVOP and related transporters (major facilitator superfamily) Reverse transcriptase Predicted protein   | 2.446<br>2.442<br>2.446<br>2.442<br>2.440<br>2.406<br>2.401<br>2.394<br>2.393<br>2.393<br>2.394<br>2.393<br>2.394<br>2.368<br>2.368<br>2.359<br>2.357<br>2.331<br>2.329<br>2.337<br>2.331<br>2.329<br>2.329<br>2.337<br>2.331<br>2.329<br>2.329<br>2.299<br>2.298<br>2.293<br>2.298<br>2.293<br>2.298<br>2.293<br>2.298<br>2.293<br>2.298<br>2.293<br>2.298<br>2.293<br>2.298<br>2.293<br>2.298<br>2.293<br>2.298<br>2.293<br>2.298<br>2.231<br>2.298<br>2.231<br>2.298<br>2.231<br>2.298<br>2.231<br>2.298<br>2.231<br>2.298<br>2.231<br>2.298<br>2.231<br>2.298<br>2.231<br>2.298<br>2.231<br>2.298<br>2.231<br>2.298<br>2.231<br>2.298<br>2.231<br>2.298<br>2.231<br>2.298<br>2.231<br>2.298<br>2.231<br>2.298<br>2.231<br>2.298<br>2.231<br>2.298<br>2.231<br>2.299<br>2.298<br>2.231<br>2.298<br>2.231<br>2.299<br>2.298<br>2.231<br>2.299<br>2.298<br>2.231<br>2.299<br>2.298<br>2.212<br>2.214<br>2.212<br>2.217<br>2.214<br>2.212<br>2.219<br>2.216<br>2.219<br>2.216<br>2.219<br>2.211<br>2.219<br>2.211<br>2.219<br>2.211<br>2.219<br>2.211<br>2.219<br>2.211<br>2.219<br>2.211<br>2.219<br>2.211<br>2.219<br>2.211<br>2.219<br>2.211<br>2.219<br>2.211<br>2.219<br>2.211<br>2.219<br>2.211<br>2.219<br>2.211<br>2.219<br>2.211<br>2.219<br>2.211<br>2.219<br>2.219<br>2.216<br>2.115<br>2.175<br>2.175<br>2.175<br>2.175<br>2.175<br>2.175<br>2.168<br>2.161<br>2.167<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.155<br>2.  | <pre>" " [01][02][16][42] [14] [01][16][20] [14] " [01][16][20] [20][32][34] # " [01][20][32][34] # [01][20][34] # [01][20][34] # [20][ [10][11][42] # # [43] % [43] % # # # # # # # # # # # # # # # # # #</pre>   | <pre>" " [01.05][01.20][02.01][02.16][16.17] [14.07] [14.07] [14.07] [14.07] [14.07] # # [01.01] [20.01][20.03][20.09][32.05][32.07] [34.11] # # [01.03][16.17][32.01] # [01.03][16.17][32.01] # [01.03][16.17][32.01] # [01.04][01.05][01.06][01.20][30.01] # [01.04][01.05][01.06][01.20][30.01] # [01.04][01.05][01.06][01.20][30.01] # [01.04][01.05][01.06][01.20][30.01] # [01.05][20.01][20.03][20.09][34.01] [34.11] # [20.01][20.03][20.09] [10.03][11.04][11.06][42.16] # [10.03][11.02][30.01] # [10.03][11.02][30.01] # [10.03][11.02][30.01] # [14.01] [11.02][30.01] # [14.01] [11.02][30.01] # [14.01] [11.02][30.01] # [14.01] [14.01</pre> |
| A0080513000020<br>A008050500159<br>A0080550100014<br>A0080550100014<br>A0080551000027<br>A008055000034<br>A008055000034<br>A008052000001<br>A008052000001<br>A008052000001<br>A008052000012<br>A0080521000212<br>A008051500022<br>A0080551000023<br>A008055000038<br>A008052000004<br>A008052000004<br>A008052000004<br>A008052000004<br>A008052000004<br>A00805200004<br>A00805200004<br>A00805200004<br>A00805200004<br>A00805200004<br>A00805200004<br>A00805200004<br>A00805200004<br>A00805200004<br>A00805200004<br>A00805200004<br>A00805200004<br>A00805200004<br>A00805200004<br>A00805200004<br>A00805200004<br>A00805200004<br>A00805200004<br>A00805200004<br>A00805200004<br>A00805200004<br>A00805200004<br>A00805200004<br>A00805200004<br>A00805200004<br>A00805200004<br>A00805200004<br>A00805200004<br>A00805200004<br>A00805200004<br>A00805200004<br>A00805200004<br>A00805200004<br>A00805200004<br>A00805200004<br>A00805200004<br>A00805200004<br>A00805200004<br>A00805200004<br>A00805200004<br>A00805200004<br>A00805200004<br>A00805200004<br>A00805200004<br>A00805200004<br>A00805200004<br>A00805200004<br>A00805200004<br>A00805200004<br>A00805200004<br>A00805200004<br>A00805200004<br>A00805200004<br>A00805200004<br>A00805200004<br>A00805200004<br>A00805200004<br>A00805200004<br>A00805200004<br>A00805200004<br>A00805200004<br>A00805200004<br>A00805200004<br>A00805200004<br>A00805200004<br>A00805200004<br>A00805200004<br>A00805200004<br>A00805200004<br>A00805200004<br>A00805200004<br>A00805200004<br>A00805200004<br>A00805200004<br>A00805200004<br>A00805200004<br>A00805200004<br>A00805200004<br>A00805200004<br>A00805200004<br>A00805200004<br>A00805200004<br>A00805200004<br>A00805200004<br>A0080520004<br>A0080520004<br>A0080520004<br>A0080520004<br>A0080520004<br>A0080520004<br>A0080520004<br>A0080520004<br>A0080520004<br>A0080520004<br>A0080520004<br>A0080520004<br>A0080520004<br>A0080520004<br>A0080520004<br>A0080520004<br>A0080520004<br>A0080520004<br>A0080520004<br>A0080520004<br>A0080520004<br>A0080520004<br>A0080520004<br>A0080520004<br>A0080520004<br>A0080520004<br>A0080520004<br>A0080520004<br>A0080520004<br>A0080520004<br>A0080520004<br>A0080520004<br>A0080520004<br>A0080520004<br>A0080520004<br>A0080520004<br>A0080520004<br>A0080520004<br>A0080520004<br>A0080520004<br>A0080520004<br>A0080520004<br>A0080520004<br>A0080520004<br>A0080520004<br>A0080520004<br>A0080520004<br>A0080520004<br>A0080520004<br>A0080520004<br>A0080520004<br>A0080520004<br>A008054<br>A008054<br>A008054<br>A008054<br>A008054<br>A008          | Alcohol dehydrogenase, class V Protein tyrosine serine phosphatase Dimethylycine dehydrogenase precursor wykB; FAD-dependent oxidoreductase Predicted protein 7-keto-8-aminopelargonate synthetase and related enzymes Cytochrome P450 CVP4 CVP10 CVP20 subfamilies Synaptic vesicle transporter SVOP and related transporters (major facilitator superfamily) Reverse transcriptase Predicted protein   | 2.446<br>2.442<br>2.446<br>2.442<br>2.440<br>2.409<br>2.400<br>2.401<br>2.394<br>2.393<br>2.392<br>2.393<br>2.392<br>2.393<br>2.353<br>2.359<br>2.357<br>2.331<br>2.329<br>2.331<br>2.329<br>2.335<br>2.337<br>2.332<br>2.315<br>2.299<br>2.298<br>2.298<br>2.298<br>2.298<br>2.298<br>2.228<br>2.231<br>2.219<br>2.228<br>2.231<br>2.219<br>2.228<br>2.231<br>2.219<br>2.228<br>2.231<br>2.219<br>2.228<br>2.231<br>2.219<br>2.228<br>2.231<br>2.219<br>2.228<br>2.231<br>2.219<br>2.228<br>2.231<br>2.219<br>2.228<br>2.231<br>2.219<br>2.228<br>2.231<br>2.219<br>2.228<br>2.231<br>2.219<br>2.228<br>2.231<br>2.219<br>2.228<br>2.231<br>2.219<br>2.228<br>2.231<br>2.219<br>2.216<br>2.217<br>2.217<br>2.216<br>2.166<br>2.166<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.165<br>2.  | "         [01][02][16][42]         [14]         [01][16][20]         [14]         [01]         [20][32][34]         #         #         #         #         #         #         #         #         #         #         #         [01][16][32]         #         [01][20][34]         #         [01][20][34]         #         [01][20][34]         #         [01][20][34]         #         [01][20][34]         #         [01][20][34]         #         [01][11][42]         #         [01][11][30]         #         [01][11][30]         #         [01][11][30]         #         [01][11][30]         #         [01][11][30]         #         [01][30][4]         #         [01][30][4]         #         [30][34][4]          [30][34][4] <td><pre>" " [01.05][01.20][02.01][02.16][16.17] [42.01] [14.07] [01.01][01.02][01.05][16.21][20.01] [14.07] # # [01.01] [20.01][20.03][20.09][32.05][32.07] [34.11] # [01.03][16.17][32.01] # [01.03][16.17][32.01] # [01.03][16.17][32.01] # [01.03][16.17][32.01] # [01.03][10.05][01.06][01.20][30.01] # [01.03][20.01][20.03][20.09][34.01] [34.11] # [01.05][20.01][20.03][20.09][34.01] # [01.05][20.01][20.03][20.09][34.01] [34.11] # [01.03][10.03][20.09][34.01] # [01.03][10.03][20.09] [10.03][10.03][10.04][01.20][30.01] # [01.05][20.01][20.03][20.09] [10.03][10.03][10.04][11.06][42.16] # [01.05][11.02][30.01] # [01.05][11.02][30.01] # [01.05][11.02][30.01] # [01.05][11.02][30.01] # [01.03][11.04][11.06][42.16] # [01.05][11.02][30.01] # [01.05][30.01][30.01] # [01.05][30.01][30.01] # [01.05][30.01][30.01] # [01.05][30.01][30.01] # [01.05][30.01][30.01] # [01.00][30.01][30.01] # [01.00][30.01][30.01] # [01.00][30.01][30.01][30.01] # [01.00][30.01][30.01][30.01][30.01] # [01.00][30.01][</pre></td> | <pre>" " [01.05][01.20][02.01][02.16][16.17] [42.01] [14.07] [01.01][01.02][01.05][16.21][20.01] [14.07] # # [01.01] [20.01][20.03][20.09][32.05][32.07] [34.11] # [01.03][16.17][32.01] # [01.03][16.17][32.01] # [01.03][16.17][32.01] # [01.03][16.17][32.01] # [01.03][10.05][01.06][01.20][30.01] # [01.03][20.01][20.03][20.09][34.01] [34.11] # [01.05][20.01][20.03][20.09][34.01] # [01.05][20.01][20.03][20.09][34.01] [34.11] # [01.03][10.03][20.09][34.01] # [01.03][10.03][20.09] [10.03][10.03][10.04][01.20][30.01] # [01.05][20.01][20.03][20.09] [10.03][10.03][10.04][11.06][42.16] # [01.05][11.02][30.01] # [01.05][11.02][30.01] # [01.05][11.02][30.01] # [01.05][11.02][30.01] # [01.03][11.04][11.06][42.16] # [01.05][11.02][30.01] # [01.05][30.01][30.01] # [01.05][30.01][30.01] # [01.05][30.01][30.01] # [01.05][30.01][30.01] # [01.05][30.01][30.01] # [01.00][30.01][30.01] # [01.00][30.01][30.01] # [01.00][30.01][30.01][30.01] # [01.00][30.01][30.01][30.01][30.01] # [01.00][30.01][</pre> |
| AO080513000020<br>AO08050500159<br>AO08050500159<br>AO080550100014<br>AO080551000027<br>AO08055000034<br>AO08055000034<br>AO08052000010<br>AO08052000010<br>AO08052000011<br>AO080550000314<br>AO080550000314<br>AO080550000125<br>AO080551000022<br>AO080551000024<br>AO080551000026<br>AO080551000026<br>AO080551000026<br>AO080551000026<br>AO080551000026<br>AO080551000026<br>AO08052000008<br>AO08052000008<br>AO08052000008<br>AO08052000008<br>AO080551000005<br>AO080551000013<br>AO080551000013<br>AO080551000013<br>AO080551000013<br>AO080551000013<br>AO080551000013<br>AO080551000013<br>AO080520000128<br>AO080520000128<br>AO080520000128<br>AO080520000128<br>AO080520000128<br>AO080520000128<br>AO080520000128<br>AO080520000128<br>AO080520000128<br>AO080520000128<br>AO080520000128<br>AO080520000128<br>AO080520000128<br>AO080520000128<br>AO080520000128<br>AO080520000128<br>AO080520000128<br>AO080520000128<br>AO080520000128<br>AO080520000128<br>AO080520000128<br>AO080520000128<br>AO080520000128<br>AO080520000128<br>AO080520000128<br>AO080520000128<br>AO080501000028  | Alcohol dehydrogenase, class V Protein tyrosine serine phosphatase Dimethylycine dehydrogenase precursor wykB, FAD-dependent oxidoreductase Predicted protein 7-keto-8-aminopelargonate synthetase and related enzymes Cytochrome P450 CVP4 CVP10 CVP20 subfamilies Synaptic vesicle transporter SVOP and related transporters (major facilitator superfamily) Reverse transcriptase Predicted protein   | 2.439<br>2.446<br>2.442<br>2.446<br>2.442<br>2.440<br>2.400<br>2.394<br>2.393<br>2.393<br>2.394<br>2.393<br>2.393<br>2.393<br>2.393<br>2.393<br>2.393<br>2.393<br>2.393<br>2.393<br>2.393<br>2.393<br>2.393<br>2.393<br>2.393<br>2.393<br>2.393<br>2.393<br>2.393<br>2.393<br>2.393<br>2.393<br>2.393<br>2.393<br>2.393<br>2.393<br>2.393<br>2.393<br>2.393<br>2.393<br>2.393<br>2.393<br>2.393<br>2.393<br>2.393<br>2.393<br>2.393<br>2.393<br>2.393<br>2.393<br>2.393<br>2.393<br>2.393<br>2.393<br>2.393<br>2.393<br>2.393<br>2.393<br>2.299<br>2.298<br>2.293<br>2.284<br>2.263<br>2.253<br>2.231<br>2.215<br>2.214<br>2.212<br>2.217<br>2.1175<br>2.1175<br>2.162<br>2.162<br>2.161<br>2.161<br>2.145  | "         [01][02][16][42]         [14]         [01][16][20]         [14]         [01]         [01]         [20][32][34]         #         #         #         [01][16][32]         #         [01][16][32]         #         [01][20][34]         #         [01][20][34]         #         [01][20][34]         #         [10][11]         #         [10][11]         #         [10][11]         #         [10][11]         #         [10][11]         #         [10][11]         #         [10][11]         #         [10]         #         [10]         #         [30][34][43]         [01][20]   | #           [01.05][01.20][02.01][02.16][16.17]           [42.01]           [14.07]           [01.01][01.02][01.05][16.21][20.01]           [14.07]           #           #           #           [01.01]           [20.01][20.03][20.09][32.05][32.07]           [34.11]           #           #           #           #           [01.03][16.17][32.01]           #           #           [01.03][16.17][32.01]           #           [01.03][16.05][01.06][01.20][30.01]           #           [01.05][20.01][20.03][20.09][34.01]           [34.11]           #           [01.05][20.01][20.03][20.09]           [10.03][11.04][11.06][42.16]           #           [10.01][11.02][30.01]           #           [10.01][11.02][30.01]           #           [10.03][11.02][30.01]           #           [10.03][11.02][30.01]           #           [10.03][20.03][20.09]           [10.03][20.03][20.03]   |
| A0080513000020<br>A00805400050<br>A008054000050<br>A008054000050<br>A0080551000014<br>A008055000034<br>A008055000034<br>A008052000001<br>A008052000001<br>A008052000001<br>A008054000014<br>A008054000014<br>A008054000015<br>A008054000000<br>A008054000000<br>A008055000005<br>A008055000000<br>A0080550000127<br>A0080550000127<br>A0080550000013<br>A0080550000127<br>A0080550000127<br>A0080550000127<br>A0080550000127<br>A0080550000127<br>A0080550000127<br>A0080550000127<br>A0080550000127<br>A0080550000127<br>A0080550000127<br>A0080550000127<br>A0080550000127<br>A0080550000127<br>A0080550000127<br>A0080550000127<br>A0080550000127<br>A0080550000127<br>A00805510000127<br>A00805510000127<br>A00805510000127<br>A00805510000127<br>A00805510000127<br>A00805510000127<br>A00805510000127<br>A00805510000127<br>A00805510000127<br>A00805510000127<br>A00805510000127<br>A00805510000127<br>A00805510000127<br>A00805510000127<br>A00805510000127<br>A00805510000127<br>A00805510000127<br>A00805510000127<br>A00805510000127<br>A00805510000127<br>A00805510000127<br>A00805510000127<br>A00805510000127<br>A00805510000127<br>A00805510000127<br>A00805510000125<br>A008050000290<br>A0080570001025<br>A0080500000127<br>A008051000015<br>A0080500000127<br>A0080500000127<br>A0080500000127<br>A0080500000127<br>A0080500000127<br>A0080500000127<br>A00805000000127<br>A0080500000127<br>A008051000015<br>A0080500000127<br>A0080500000127<br>A00805000000000000000000000000000000000  | Alcohol dehydrogenase, class V Protein tyrosine serine phosphatase Dimethylgycine dehydrogenase precursor wykB, FAD-dependent oxidoreductase Predicted protein 7-keto-8-aminopelargonate synthetase and related enzymes Cytochrome P450 CVP4 CVP19 CVP20 subfamilies Synaptic vesicle transporter SVOP and related transporters (major facilitator superfamily) Reverse transcriptase Predicted protein Predicted protei   | 2.446<br>2.442<br>2.446<br>2.442<br>2.406<br>2.401<br>2.394<br>2.393<br>2.392<br>2.368<br>2.353<br>2.35<br>2.35<br>2.35<br>2.35<br>2.35<br>2.35<br>2.35<br>2.35<br>2.35<br>2.35<br>2.35<br>2.35<br>2.35<br>2.35<br>2.35<br>2.35<br>2.35<br>2.35<br>2.35<br>2.35<br>2.35<br>2.35<br>2.35<br>2.35<br>2.35<br>2.35<br>2.35<br>2.35<br>2.35<br>2.35<br>2.35<br>2.35<br>2.35<br>2.35<br>2.35<br>2.35<br>2.35<br>2.35<br>2.35<br>2.35<br>2.35<br>2.35<br>2.35<br>2.35<br>2.35<br>2.298<br>2.287<br>2.287<br>2.287<br>2.287<br>2.287<br>2.287<br>2.282<br>2.268<br>2.255<br>2.293<br>2.211<br>2.211<br>2.212<br>2.212<br>2.211<br>2.211<br>2.212<br>2.211<br>2.211<br>2.211<br>2.211<br>2.211<br>2.211<br>2.211<br>2.211<br>2.211<br>2.211<br>2.215<br>2.219<br>2.215<br>2.219<br>2.215<br>2.219<br>2.211<br>2.211<br>2.211<br>2.211<br>2.211<br>2.211<br>2.211<br>2.211<br>2.211<br>2.211<br>2.211<br>2.211<br>2.211<br>2.211<br>2.211<br>2.211<br>2.211<br>2.211<br>2.211<br>2.211<br>2.211<br>2.211<br>2.211<br>2.211<br>2.211<br>2.211<br>2.211<br>2.211<br>2.211<br>2.211<br>2.211<br>2.211<br>2.211<br>2.211<br>2.211<br>2.211<br>2.211<br>2.211<br>2.211<br>2.211<br>2.211<br>2.211<br>2.211<br>2.211<br>2.211<br>2.211<br>2.211<br>2.211<br>2.211<br>2.211<br>2.211<br>2.211<br>2.211<br>2.211<br>2.211<br>2.211<br>2.211<br>2.211<br>2.211<br>2.211<br>2.211<br>2.211<br>2.115<br>2.157<br>2.151<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145<br>2.145  | "         [01][02][16][42]         [14]         [01][16][20]         [14]         [01]         [20][32][34]         #         #         #         #         [01][16][32]         #         [01][10][30]         #         [01][20][34]         #         [01][20][34]         #         [01][20][34]         #         [10][11]         #         #         #         [01][11]         #         #         [01][11]         #         #         [01][11][30]         #         #         [01][11][30]         #         #         #         [30][34][43]         [01][20]         #         #         #         [30][34][43]         #         #         #         #         #         #         #         # <td><pre>" " [01.05][01.20][02.01][02.16][16.17] [42.01] [14.07] [14.07] [14.07] [14.07] [14.07] [20.01][20.03][20.09][32.05][32.07] [34.11] [20.01][20.03][20.09][32.05][32.07] [34.11] [4] [4] [4] [4] [4] [4] [4] [4] [4] [4</pre></td>  | <pre>" " [01.05][01.20][02.01][02.16][16.17] [42.01] [14.07] [14.07] [14.07] [14.07] [14.07] [20.01][20.03][20.09][32.05][32.07] [34.11] [20.01][20.03][20.09][32.05][32.07] [34.11] [4] [4] [4] [4] [4] [4] [4] [4] [4] [4</pre>   |
| A0080513000020<br>A008050500159<br>A008055000159<br>A008055000050<br>A0080551000027<br>A008055000034<br>A008055000039<br>A008055000039<br>A008055000039<br>A008055000011<br>A008055000012<br>A0080550000125<br>A008055000053<br>A008055000053<br>A008055000053<br>A008055000053<br>A008055000053<br>A008055000053<br>A008055000053<br>A008055000053<br>A008055000053<br>A008055000053<br>A008055000053<br>A008055000053<br>A008055000053<br>A008055000053<br>A008055000053<br>A008055000053<br>A008055000053<br>A008055000053<br>A008055000053<br>A008055000053<br>A008055000055<br>A008055000055<br>A008055000055<br>A008055000055<br>A008055000055<br>A008055000055<br>A008055000055<br>A008055000055<br>A008055000055<br>A008055000055<br>A008055000055<br>A008055000055<br>A008055000055<br>A008055000055<br>A008055000055<br>A008055000055<br>A008055000055<br>A008055000055<br>A008055000055<br>A008055000055<br>A008055000055<br>A008055000055<br>A008055000055<br>A008055000055<br>A008055000055<br>A008055000055<br>A008055000057<br>A008055000057<br>A008055000057<br>A008055000057<br>A008055000057<br>A008055000057<br>A008055000057<br>A008055000057<br>A008055000057<br>A008055000057<br>A008055000057<br>A008055000057<br>A008055000057<br>A008055000057<br>A008055000057<br>A008055000057<br>A008055000057<br>A008055000057<br>A008055000057<br>A008055000057<br>A008055000057<br>A008055000057<br>A008055000057<br>A008055000057<br>A008055000057<br>A008055000057<br>A008055000057<br>A008055000057<br>A008055000057<br>A00805500057<br>A00805500057<br>A00805500057<br>A00805500057<br>A00805500057<br>A00805500057<br>A00805500057<br>A00805500057<br>A00805500057<br>A00805500057<br>A00805500057<br>A00805500057<br>A00805500057<br>A00805500057<br>A00805500057<br>A00805500057<br>A00805500057<br>A00805500057<br>A00805500057<br>A00805500057<br>A00805500057<br>A00805500057<br>A00805500057<br>A00805500057<br>A00805500057<br>A0080550057<br>A0080550057<br>A0080550057<br>A0080550057<br>A0080550057<br>A0080550057<br>A0080550057<br>A0080550057<br>A0080550057<br>A0080550057<br>A0080550057<br>A0080550057<br>A0080550057<br>A0080550057<br>A0080550057<br>A0080550057<br>A0080550057<br>A0080550057<br>A0080550057<br>A0080550057<br>A0080550057<br>A0080550057<br>A0080550057<br>A0080550057<br>A0080550057<br>A0080550057<br>A0080550057<br>A0080550057<br>A0080550057<br>A0080550057<br>A0080550057<br>A0080550057<br>A0080550057<br>A0080550057<br>A0080550057<br>A0080550057<br>A0080550057<br>A0080550057<br>A00805550057<br>A00805550057<br>A00805550057<br>A0085                                  | Alcohol dehydrogenase, class V Protein tyrosine serine phosphatase Dimethylgycine dehydrogenase precursor wykB, FAD-dependent oxidoreductase Predicted protein 7-keto-8-aminopelargonate synthetase and related enzymes Cytochrome FASO CYP4 CYP10 CYP20 subfamilies Synaptic vesicle transporter SVOP and related transporters (major facilitator superfamily) Reverse transcriptase Predicted protein Predicted protei   | 2.446<br>2.442<br>2.446<br>2.442<br>2.440<br>2.440<br>2.394<br>2.393<br>2.393<br>2.394<br>2.393<br>2.394<br>2.393<br>2.394<br>2.368<br>2.368<br>2.359<br>2.357<br>2.331<br>2.329<br>2.337<br>2.331<br>2.329<br>2.329<br>2.337<br>2.331<br>2.329<br>2.329<br>2.329<br>2.329<br>2.329<br>2.329<br>2.329<br>2.329<br>2.329<br>2.329<br>2.329<br>2.329<br>2.329<br>2.329<br>2.329<br>2.329<br>2.329<br>2.329<br>2.329<br>2.329<br>2.329<br>2.329<br>2.329<br>2.329<br>2.329<br>2.329<br>2.329<br>2.329<br>2.329<br>2.329<br>2.329<br>2.329<br>2.329<br>2.329<br>2.329<br>2.329<br>2.329<br>2.293<br>2.293<br>2.293<br>2.293<br>2.293<br>2.293<br>2.214<br>2.212<br>2.217<br>2.147<br>2.168<br>2.161<br>2.167<br>2.157<br>2.147<br>2.147<br>2.142<br>2.151<br>2.147<br>2.142<br>2.151<br>2.147<br>2.142<br>2.151<br>2.147<br>2.142<br>2.151<br>2.147<br>2.142<br>2.151<br>2.147<br>2.142<br>2.151<br>2.147<br>2.142<br>2.151<br>2.147<br>2.142<br>2.151<br>2.147<br>2.142<br>2.151<br>2.147<br>2.142<br>2.152<br>2.151<br>2.147<br>2.142<br>2.152<br>2.151<br>2.147<br>2.142<br>2.152<br>2.151<br>2.147<br>2.142<br>2.152<br>2.151<br>2.147<br>2.142<br>2.152<br>2.151<br>2.147<br>2.142<br>2.152<br>2.151<br>2.147<br>2.142<br>2.152<br>2.151<br>2.147<br>2.142<br>2.152<br>2.151<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.142<br>2.  | "         [01][02][16][42]         [14]         [01][16][20]         [14]         [01][16][20]         [14]         [01]         [20][32][34]         #         #         #         [01][16][32]         #         [01][10][30]         #         [01][20][34]         #         [01][20][34]         #         [10][11][#         #         [01][11][#         #         [01][11][#         #         [01][11]         #         [10][11]         #         [01][11][30]         #         [01][11][30]         #         [01][11][30]         #         [01][11]         #         [01][11]         #         [01][11]         #         [01][120]         #         [01][20]         #         [01][20]         #         [01]         #  | <pre>" " [01.05][01.20][02.01][02.16][16.17] [14.07] [14.07] [14.07] [14.07] [14.07] [14.07] [14.07] [14.07] [20.01][20.03][20.09][32.05][32.07] [34.11] # # # # [01.03][16.17][32.01] # [01.03][16.17][32.01] # [01.04][01.05][01.06][01.20][30.01] # [10.04][01.05][01.06][01.20][30.01] # [10.04][01.05][01.06][01.20][30.01] # [10.04][01.05][01.06][01.20][30.01] # [10.04][01.05][01.06][01.20][30.01] # [10.04][01.05][01.06][01.20][30.01] # [10.04][10.05][01.06][01.20][30.01] # [10.04][10.05][20.04][20.09] [10.04][11.02][20.09] # [10.05][11.02][20.09] # [10.05][11.02][30.01] # [10.05][11.02][30.01] # [10.05][11.02][30.01] # [10.05][11.02][30.01] # [10.05][11.02][30.01] # [10.05][11.02][30.01] # [10.05][11.02][30.01] # [10.01][34.11][43.01] [10.05][20.09] # [10.01][34.11][43.01] [10.05][30.01][34.01] [10.05][30.00] # [10.01][34.11][43.01] [10.05][30.00] # [10.01][34.11][43.01] [10.05][30.00] # [10.01][34.01][34.01] [10.05][30.00] # [10.01][34.01][34.01] [10.05][30.00] # [10.01][34.01][34.01] [10.05][30.00] # [10.01][34.01][34.01] # [10.05][30.00][30.00] # [10.01]</pre> |

| AO080539000074<br>AO080518000037   |  |  |   |  |
|--|--|--|---|--|
| AO080518000037   | Predicted protein  | 2.097  | #   | #  |
|  | Predicted transporter (major facilitator superfamily)  | 2.073  | [20][32]  | [20.01][20.03][20.09][32.05][32.07]  |
| AO080541000154   | Carboxypeptidase C (cathepsin A)   | 2.062  | [14]  | [14.13]  |
| AO080567000053   | Predicted protein  | 2,062  | #   | #  |
| AO080550000102   | Predicted acyl esterases   | 2.055  | #   | #  |
| AO080505000097   | Transthyretin and related proteins   | 2.053  | [01]  | [01.02][01.03]   |
| AO080546000347   | Catalase (nerovidase I)  | 2.051  | [20][32][42]  | [20.01][32.01][32.07][42.16]   |
| 1000005100000047   | Cardinate (provinite 1)  | 2.046  | [=0][0=][4=]  | #  |
| A0080551000123   | Productor protein  | 2.030  | #   | 4  |
| A0080551000125   | Predicted protein  | 2.039  | #   | #  |
| A0080562000073   | Predicted protein  | 2.036  | #   | #  |
| A0080551000142   | Predicted protein  | 2.034  | #   | #  |
| AO080532000609   | Predicted protein  | 2.032  | #   | #  |
| 10080522000202   | Jeonizate iconserving late data decompos   | 2.021  | [01][02][16][20]  | [01.01][01.05][02.01][02.10][16.21]  |
| AQ080327000203   | isocritate isopropyinalate denyal ogenase  | 2,021  | [01][02][10][20]  | [20.01]  |
| 40080525000648   | Producted protein  | 2.02   | #   | #  |
| 10080523000012   | Relevator protein  | 2.014  | #   |  |
| A0080571000012   | Notecular endperone (Diab superiannity)  | 2.014  | #<br>#  | 11<br>11   |
| A0080525000419   | Predicted protein  | 2.007  | #   | #  |
| AO080531000318   | 2-polyprenyl-6-methoxyphenol hydroxylase and related FAD-dependent oxidoreductases   | 2.004  | [01]  | [01.05][01.20]   |
| AO080504000029   | Phospholipase C  | 2.002  | #   | #  |
|  |  |  | TO LY ON THE YEAR OF THE YEAR   | [01.04][01.05][02.19][10.01][10.03]  |
| 100006222000100  | Descriptions DOTATOR and allowed   | 2 001  |   | [11.02][14.07][16.01][16.03][16.19]  |
| A0080555000108   | Protein kinase PC I AIKE and related kinases   | 2.001  | [10][18][50][54][40]  | [18.01][18.02][30.01][30.05][34.05]  |
|  |  |  | [42][43]  | [34 11][40 01][42 10][43 01]   |
| 1000005050000101   | Characterization   | 0.402  | 1011[02][22][24][42]  | [01.05][02.10][22.01][24.11][42.01]  |
| A0080503000131   | Orycosyntansienase   | 0.496  | [01][02][52][54][45]  | [01.05][02.15][52.01][54.11][45.01]  |
| A0080503000128   | Predicted protein  | 0.496  | #   | #  |
| AO080521000172   | Predicted membrane protein   | 0.496  | <b>1</b> 4  | 11   |
| AO080514000015   | Transcription factor PRD and related proteins, contain PAX and HOX domains   | 0.495  | #   | #  |
| AO080531000179   | Predicted protein  | 0.494  | #   | #  |
| AO080503000252   | Predicted protein  | 0.492  | #   | #  |
| AO080546000219   | Predicted protein  | 0.492  | #   | <i>ii</i>  |
| AO080560000080   | Predicted protein  | 0.492  | #   | 11   |
| AO080513000270   | Predicted protein  | 0.491  | #   | #  |
| AO080508000004   | Predicted protein  | 0.487  | #   | #  |
| AO080503000123   | Predicted protein  | 0.486  | #   | #  |
| A00805130000125  | Alaba-amilaza  | 0.485  | [01]  | //<br>[01.05]  |
| A0080513000000   | Alpha-anylase<br>Device device   | 0.481  | [01]<br>#   | [01:00]  |
| A0080552000307   | Predicted protein  | 0.481  | #   | #<br>[0] 053(0] 203(16 173   |
| A0080554000482   | NADPH:quinone reductase and related Zn-dependent oxidoreductases   | 0.481  | [01][16]  | 01.05 01.20 16.17  |
| AO080523000408   | Dehydrogenases with different specificities (related to short-chain alcohol dehydrogenases)  | 0.48   | #   | #  |
| AO080550000156   | Predicted protein  | 0.479  | #   | #  |
| AO080513000204   | Predicted protein  | 0.478  | #   | #  |
| AO080560000087   | Predicted protein  | 0.478  | <i>li</i>   | 11   |
| AO080505000104   | Predicted protein  | 0.476  | #   | #  |
| AO080568000096   | Cytochrome P450 CYP4 CYP19 CYP26 subfamilies   | 0.474  | [01][02]  | [01.06][01.20][02.45]  |
| 40080523000182   | A cetudo la inectera ce Buturul cholinectera ce  | 0.47   | #   | #  |
| A0080523000182   | Accepted associate as a busylytenonnesterase<br>Deviated associate   | 0.460  | (11)(14)  | //<br>[11.06][14.07][14.13]  |
| A0080532000189   | Producted protein  | 0.469  | [11][14]  | [11.00][14.07][14.15]  |
| A0080570000072   | Cytochrome P450 CYP4 CYP19 CYP26 subfamilies   | 0.469  | [01][32]  | [01.01][32.05][32.07]  |
| AO080561000074   | Endopolygalacturonase  | 0.468  | #   | #  |
| AO080511000067   | Predicted protein  | 0.466  | #   | #  |
| AO080533000118   | Predicted protein  | 0.464  | #   | #  |
| AO080508000310   | Ketopantoate hydroxymethyltransferase  | 0.463  | [01][42]  | [01.07][42.01]   |
| AO080523000640   | Sorbin and SH3 domain-containing protein   | 0.463  | [10]  | [10.03]  |
| AO080536000108   | Predicted protein  | 0.459  | #   | #  |
| AO080508000430   | Predicted protein  | 0.457  | #   | #  |
| AO080521000200   | Provinted protein  | 0.456  | [20][24]  | [20.01][34.11]   |
| 10080522000004   | Contraction protein  | 0.456  | 12011341  | 120.01 [[ 54.11 ]]   |
| A0080522000004   | Cytochronic 1450   | 0.455  | #   |  |
| A0080500000272   | Predicted protein  | 0.455  | #<br>#  | 17<br>14   |
| A0080557000027   | Predicted protein  | 0.455  | #<br>   | #<br>  |
| A0080555000231   | Predicted protein  | 0.454  | #   | #  |
| AO080523000128   | Predicted protein  | 0.453  | #   | #  |
| AO080533000173   | Predicted protein  | 0.453  | #   | #  |
| AO080508000082   | Predicted protein  | 0.451  | #   | 11   |
| AO080515000125   | Permeases of the major facilitator superfamily   | 0.449  | [20]  | [20.01][20.03][20.09]  |
| AO080542000184   | Cytochrome P450 CYP4 CYP19 CYP26 subfamilies   | 0.448  | #   | #  |
| AO080533000250   | Predicted protein  | 0.447  | #   | #  |
|  |  |  |   | [01 02][10 01][16 02][16 17][16 21]  |
| AO080549000362   | Endonuclease III   | 0.447  | [01][10][16][32]  |  |
|  |  |  |   | [32.01]  |
| AO080523000306   | Predicted protein  | 0.442  | #   | #  |
| AO080532000098   | beta-1,6-N-acetylglucosaminyltransferase, contains WSC domain  | 0.442  | #   | #  |
| AO080536000028   | Predicted protein  | 0.442  | #   | #  |
| AO080550000149   | Predicted protein  | 0.441  | #   | #  |
|  | Amidases   | 0.44   | 1011  |  |
| AO080513000148   |  | 0.130  | 101   | [01.02]  |
| AO080513000148<br>AO080508000396   | Acetylornithine aminotransferase   | 0.438  | [01]  | [01.02]<br>[01.07][01.20]  |
| AO080513000148<br>AO080508000396<br>AO080501000092   | Acetylomithine aminotransferase<br>Nucleoside phosphorylase  | 0.438  | [01]<br>#   | [01.02]<br>[01.07][01.20]<br>#   |
| AO080513000148<br>AO080508000396<br>AO080501000092<br>AO080521000357   | Acetylornithine aminotransferase<br>Nucleoside phosphorylase<br>Prodicted protein  | 0.438<br>0.437<br>0.437  | [01]<br>#<br>#  | [01.02]<br>[01.07][01.20]<br>#<br>#  |
| AO080513000148<br>AO080508000396<br>AO080501000092<br>AO080521000357<br>AO080536000070   | Acetylornithine aminotransferase<br>Nucleoside phosphorylase<br>Predicted protein<br>Predicted protein   | 0.438<br>0.437<br>0.437<br>0.437   | [01]<br>#<br>#<br>[01](20](32](34]  | [01.02]<br>[01.07][01.20]<br>#<br>#<br>[01.07][20.01][20.09][32.07][34.01]   |
| AO080513000148<br>AO080508000396<br>AO080501000092<br>AO080521000357<br>AO080536000070<br>AO080532000519   | Acetylornithine aminotransferase<br>Nucleoside phosphorylase<br>Predicted protein<br>Predicted transporter (major facilitator superfamily)<br>Predicted protein  | 0.438<br>0.437<br>0.437<br>0.437<br>0.435  | [01]<br>[01]<br>#<br>[01][20][32][34]<br>#  | [01.02]<br>[01.07][01.20]<br>#<br>[01.07][20.01][20.09][32.07][34.01]  |
| AO080513000148<br>AO080508000396<br>AO080501000092<br>AO080521000357<br>AO080536000070<br>AO080532000519   | Acetylornithine aminotransferase<br>Nucleoside phosphorylase<br>Predicted protein<br>Predicted protein<br>Scienchreneine entrie Manage   | 0.438<br>0.437<br>0.437<br>0.437<br>0.435<br>0.435   | [01]<br>[01]<br>#<br>[01][20][32][34]<br>#  | [01.02]<br>[01.07][01.20]<br>#<br>[01.07][20.01][20.09][32.07][34.01]<br>#   |
| AO080513000148<br>AO080508000396<br>AO080501000092<br>AO080521000357<br>AO080536000070<br>AO080532000519<br>AO08050800049<br>AO08050800049   | Acetylonrithine anninotransferase<br>Nucleoside phosphorylase<br>Predicted protein<br>Predicted transporter (major facilitator superfamily)<br>Predicted protein<br>Serine threcome protein kinase   | 0.438<br>0.437<br>0.437<br>0.437<br>0.435<br>0.435<br>0.434  | [01]<br>[01]<br>#<br>#<br>[01][20][32][34]<br>#<br>#<br>[01]  | [01.02]<br>[01.07][01.20]<br>#<br>[01.07][20.01][20.09][32.07][34.01]<br>#<br>[01.04]  |
| AO080513000148<br>AO080508000396<br>AO080501000092<br>AO080521000357<br>AO080536000070<br>AO080532000519<br>AO080503000049<br>AO080508000367   | Acetylornithine aminotransferase<br>Nucleoside phosphorylase<br>Predicted protein<br>Predicted protein<br>Predicted protein<br>Serine threonine protein kinase<br>Predicted protein  | 0.438<br>0.437<br>0.437<br>0.437<br>0.435<br>0.435<br>0.434<br>0.433   | 01]<br>[01]<br>#<br>#<br>[01][20][32][34]<br>#<br>#<br>[01]<br>#  | [01.02]<br>[01.07][01.20]<br>#<br>[01.07][20.01][20.09][32.07][34.01]<br>#<br>#<br>[01.04]   |
| AO080513000148<br>AO080508000396<br>AO080501000092<br>AO080521000357<br>AO080536000070<br>AO080532000519<br>AO080503000049<br>AO080541000303   | Acetylornithine anninotransferase<br>Nucleoside phosphorylase<br>Predicted protein<br>Predicted transporter (major facilitator superfamily)<br>Predicted protein<br>Serine threonine protein kinase<br>Predicted protein<br>Predicted protein  | 0.438<br>0.437<br>0.437<br>0.437<br>0.435<br>0.434<br>0.433<br>0.433   | [01]<br>#<br>#<br>[01][20][32][34]<br>#<br>[01]<br>#<br>[01]<br>#   | [01.02]<br>[01.07][01.20]<br>#<br>[01.07][20.01][20.09][32.07][34.01]<br>#<br>[01.04]<br>#<br>-  |
| AO080513000148<br>AO080508000396<br>AO080501000092<br>AO080521000357<br>AO080532000519<br>AO08050300049<br>AO080508000367<br>AO080541000303<br>AO080525000618  | Acetylornithine aminotransferase<br>Nucleoside phosphorylase<br>Predicted protein<br>Predicted protein<br>Predicted protein kinase<br>Predicted protein<br>Predicted protein<br>Predicted protein<br>Predicted protein   | 0.438<br>0.437<br>0.437<br>0.437<br>0.435<br>0.435<br>0.434<br>0.433<br>0.433<br>0.432   | [01]<br>μ<br>μ<br>[01][20][32][34]<br>μ<br>[01]<br>μ<br>μ<br>[01]<br>μ<br>μ<br>μ<br>[01]<br>μ<br>μ<br>μ<br>μ<br>μ<br>μ<br>μ<br>μ<br>μ<br>μ<br>μ<br>μ<br>μ   | [01.02]<br>[01.07][01.20]<br>#<br>[01.07][20.01][20.09][32.07][34.01]<br>#<br>[01.04]<br>#<br>=<br>=   |
| AO080513000148<br>AO080508000396<br>AO080501000092<br>AO080521000357<br>AO08052000519<br>AO08052000519<br>AO080508000367<br>AO080508000367<br>AO08052000018<br>AO080525000618  | Acetylornithine anninotransferase<br>Nucleoside phosphorylase<br>Predicted protein<br>Predicted transporter (major facilitator superfamily)<br>Predicted protein<br>Serine threonine protein kinase<br>Predicted protein<br>Predicted protein<br>Predicted protein<br>Predicted protein  | 0.438<br>0.437<br>0.437<br>0.437<br>0.435<br>0.434<br>0.433<br>0.433<br>0.433<br>0.432<br>0.432  | 01]<br> 01]<br>   | [01.02]<br>[01.07][01.20]<br>#<br>#<br>[01.07][20.01][20.09][32.07][34.01]<br>#<br>#<br>[01.04]<br>#<br>#<br>#   |
| AO080513000148<br>AO080508000396<br>AO080501000092<br>AO080521000357<br>AO080532000519<br>AO08053000049<br>AO080503000049<br>AO080541000303<br>AO080529000144<br>AO080529000044  | Acetylornithine aminotransferase<br>Nucleoside phosphorylase<br>Predicted protein<br>Predicted protein<br>Predicted protein<br>Serine threonine protein kinase<br>Predicted protein<br>Predicted protein<br>Predicted protein<br>Predicted protein<br>Predicted protein<br>Predicted protein<br>Predicted protein  | 0.438<br>0.437<br>0.437<br>0.437<br>0.435<br>0.434<br>0.433<br>0.433<br>0.433<br>0.432<br>0.432<br>0.432   | 101]<br>#<br>#<br>101][20][32][34]<br>#<br>#<br>[01]<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#   | [01.02]<br>[01.07][01.20]<br>#<br>[01.07][20.01][20.09][32.07][34.01]<br>#<br>[01.04]<br>#<br>[01.04]<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#   |
| AO080513000148<br>AO080508000396<br>AO08050100092<br>AO080521000357<br>AO080532000519<br>AO08053000070<br>AO08053000049<br>AO0805030000367<br>AO08052000033<br>AO0805250000111<br>AO080508000204   | Acetylornithine anninotransferase<br>Nucleoside phosphorylase<br>Predicted protein<br>Predicted transporter (major facilitator superfamily)<br>Predicted protein<br>Serine threonine protein kinase<br>Predicted protein<br>Predicted protein<br>Predicted protein<br>Predicted protein<br>Predicted protein<br>Predicted protein  | 0.438<br>0.437<br>0.437<br>0.437<br>0.435<br>0.434<br>0.433<br>0.433<br>0.433<br>0.432<br>0.432<br>0.432<br>0.432<br>0.431   | [01]<br>μ<br>μ<br>[01][20][32][34]<br>μ<br>[01]<br>μ<br>μ<br>μ<br>μ<br>μ<br>μ<br>μ<br>μ<br>μ<br>μ<br>μ<br>μ<br>μ  | [01.02]<br>[01.07][01.20]<br>#<br>[01.07][20.01][20.09][32.07][34.01]<br>#<br>[01.04]<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#   |
| AO080513000148<br>AO080508000396<br>AO080501000092<br>AO080521000357<br>AO08053000070<br>AO080532000519<br>AO080503000049<br>AO080508000367<br>AO080525000618<br>AO080550000141<br>AO080550000141<br>AO080550000111  | Acetylomithine aminotransferase<br>Nucleoside phosphorylase<br>Predicted protein<br>Predicted protein<br>Serine threonine protein kinase<br>Predicted protein<br>Predicted protein<br>Predicted protein<br>Predicted protein<br>Predicted protein<br>Predicted protein<br>Predicted protein<br>Predicted dehydrogenase<br>Predicted dehydrogenase  | 0.438<br>0.437<br>0.437<br>0.437<br>0.435<br>0.434<br>0.433<br>0.433<br>0.432<br>0.432<br>0.432<br>0.431   | [01]<br>μ<br>[01](20](32](34]<br>μ<br>[01]<br>μ<br>μ<br>μ<br>μ<br>μ<br>μ<br>μ<br>μ<br>μ<br>[01](16]   | [01.02]<br>[01.07][01.20]<br>#<br>[01.07][20.01][20.09][32.07][34.01]<br>#<br>[01.04]<br>#<br>[01.04]<br>#<br>[1.04]<br>#<br>[1.001][16.03]  |
| AO080513000148<br>AO080508000396<br>AO080501000092<br>AO080521000357<br>AO080536000070<br>AO080532000019<br>AO080508000049<br>AO080508000049<br>AO080520000111<br>AO080520000111<br>AO080520000111<br>AO080520000114<br>AO080520000114   | Acetylornithine aminotransferase<br>Nucleoside phosphorylase<br>Predicted protein<br>Predicted transporter (major facilitator superfamily)<br>Predicted transporten<br>Predicted protein<br>Predicted protein<br>Aspart/ proteiase   | 0.438<br>0.437<br>0.437<br>0.437<br>0.435<br>0.435<br>0.434<br>0.433<br>0.432<br>0.432<br>0.432<br>0.432<br>0.432<br>0.431<br>0.431<br>0.43  | [01]<br>μ<br>[01][20][32][34]<br>μ<br>[01]<br>μ<br>μ<br>[01]<br>μ<br>μ<br>[10][16]<br>[01][14]  | [01.02]<br>[01.07][01.20]<br>#<br>#<br>[01.07][20.01][20.09][32.07][34.01]<br>#<br>#<br>[01.04]<br>[01.04]<br>[01.04]<br>#<br>#<br>[10.01][16.03]<br>[01.25][14.13]  |
| A0080513000148<br>A0080508000396<br>A0080508000396<br>A0080521000357<br>A0080532000519<br>A008053000070<br>A0080532000519<br>A008052000044<br>A008052000044<br>A008052000044<br>A008052000044<br>A0080523000678<br>A0080515000221  | Acetylonithine aminotransferase<br>Nucleoside phosphorylase<br>Predicted protein<br>Predicted protein<br>Serine threonine protein kinase<br>Predicted protein<br>Predicted protein<br>Aspartyl protease<br>I-Acyd Hidwtowacetone phosphate reductase and related dehydrogenases   | 0.438<br>0.437<br>0.437<br>0.437<br>0.435<br>0.433<br>0.433<br>0.433<br>0.433<br>0.432<br>0.432<br>0.431<br>0.431<br>0.431<br>0.427  | [01]<br>#<br>[01][20][32][34]<br>#<br>[01]<br>#<br>#<br>#<br>#<br>[01][43]<br>[01][43]  | [01.02]<br>[01.07][01.20]<br>#<br>#<br>[01.07][20.01][20.09][32.07][34.01]<br>#<br>[01.04]<br>#<br>#<br>[01.04]<br>#<br>#<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[ |
| A00805130001148<br>A0080508000396<br>A0080501000092<br>A0080521000357<br>A008053000019<br>A008053000019<br>A008053000019<br>A008055000011<br>A008055000011<br>A008055000011<br>A008055000011<br>A008055000011<br>A008055000011<br>A008055000011<br>A008055000011<br>A008051000221  | Acetylornithine aminotransferase<br>Nucleoside phosphorylase<br>Predicted protein<br>Predicted transporter (major facilitator superfamily)<br>Predicted transporten<br>Serine threonine protein kinase<br>Predicted protein<br>Predicted protein<br>Predicted protein<br>Predicted protein<br>Predicted protein<br>Predicted protein<br>Predicted protein<br>Predicted protein<br>Predicted protein<br>Aspartyl protease<br>I-Acyl dihydroxyacetone phosphate reductase and related dehydrogenases   | 0.438<br>0.437<br>0.437<br>0.437<br>0.437<br>0.435<br>0.434<br>0.433<br>0.433<br>0.432<br>0.432<br>0.432<br>0.432<br>0.431<br>0.431<br>0.43<br>0.427<br>0.426  | [01]<br>μ<br>[01][20][32][34]<br>μ<br>[01]<br>μ<br>μ<br>μ<br>μ<br>μ<br>μ<br>[01]<br>μ<br>μ<br>[01]<br>μ<br>μ<br>[01]<br>μ<br>μ<br>[01]<br>μ<br>μ<br>[01]<br>[01][20][32][34]<br>μ<br>μ<br>μ<br>[01][20][32][34]<br>μ<br>μ<br>[01][20][32][34]<br>μ<br>μ<br>[01][20][32][34]<br>μ<br>μ<br>[01][20][32][34]<br>μ<br>μ<br>[01][20][32][34]<br>μ<br>μ<br>[01][20][32][34]<br>μ<br>μ<br>[01][20][32][34]<br>μ<br>μ<br>μ<br>[01][20][32][34]<br>μ<br>μ<br>μ<br>[01][20][32][34]<br>μ<br>μ<br>μ<br>μ<br>μ<br>[01][20][32][34]<br>μ<br>μ<br>μ<br>μ<br>μ<br>μ<br>μ<br>[01][20][32][34]<br>μ<br>μ<br>μ<br>μ<br>μ<br>μ<br>μ<br>μ<br>μ<br>μ<br>μ<br>μ<br>μ  | [01.02]<br>[01.07][01.20]<br>#<br>#<br>[01.07][20.01][20.09][32.07][34.01]<br>#<br>#<br>[01.04]<br>[01.04]<br>#<br>#<br>#<br>[10.01][16.03]<br>[01.25][14.13]<br>[01.05][01.06][43.01]<br>#  |
| A0088513000148<br>A008850800336<br>A008951000032<br>A0089521000357<br>A008053600037<br>A0080536000170<br>A0080536000170<br>A008053000049<br>A0080550000111<br>A0080550000111<br>A0080550000111<br>A0080550000171<br>A008051000254<br>A008051000254<br>A0080523000411<br>A008052300041  | Acetylonithine aminotransferase<br>Nucleoside phosphorylase<br>Predicted protein<br>Predicted transporter (major facilitator superfamily)<br>Predicted protein<br>Serine threcome protein kinase<br>Predicted protein<br>Predicted protein<br>Predicted protein<br>Predicted protein<br>Predicted protein<br>Predicted protein<br>Predicted protein<br>Predicted protein<br>Asparty   protease<br>I-Acyl dhiydroyacetone phosphate reductase and related dehydrogenases<br>Predicted protein   | 0.438<br>0.437<br>0.437<br>0.437<br>0.435<br>0.434<br>0.433<br>0.433<br>0.433<br>0.432<br>0.432<br>0.432<br>0.432<br>0.431<br>0.43<br>0.43<br>0.43<br>0.43<br>0.427<br>0.426   | [01]<br>μ<br>[01](20)[32][34]<br>μ<br>[01]<br>μ<br>μ<br>μ<br>μ<br>μ<br>[10][16]<br>[01][14]<br>[01][14]<br>[01][13]<br>μ<br>μ<br>μ<br>μ<br>μ<br>μ<br>μ<br>μ<br>μ<br>μ<br>μ<br>μ<br>μ  | [0102]<br>[01.07][01.20]<br>#<br>#<br>[01.07][20.01][20.09][32.07][34.01]<br>#<br>[01.04]<br>#<br>#<br>[01.04]<br>#<br>#<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.04]<br>[01.05][01.06][43.01]<br>#<br>#   |
| AO080513000148<br>AO080508000396<br>AO080501000092<br>AO080521000357<br>AO08053600070<br>AO08053000049<br>AO080503000049<br>AO08052000014<br>AO08052000014<br>AO08052000014<br>AO08052000014<br>AO080521000254<br>AO080521000254<br>AO080521000254<br>AO080521000254<br>AO080521000254   | Acetylornithine aminotransferase<br>Nucleoside phosphorylase<br>Predicted protein<br>Predicted transporter (major facilitator superfamily)<br>Predicted protein<br>Predicted protein<br>Aspartyl protease<br>1-Acyl dihydroxyacetone phosphate reductase and related dehydrogenases<br>Predicted protein<br>Predicted protein   | 0.438<br>0.437<br>0.437<br>0.437<br>0.435<br>0.434<br>0.433<br>0.433<br>0.433<br>0.432<br>0.432<br>0.432<br>0.432<br>0.432<br>0.432<br>0.431<br>0.431<br>0.421<br>0.426<br>0.426   | [01]<br>μ<br>[01][20][32][34]<br>μ<br>[01]<br>μ<br>μ<br>μ<br>μ<br>μ<br>μ<br>μ<br>μ<br>[01][4]<br>[01][4]<br>μ<br>μ<br>μ<br>μ<br>μ<br>μ<br>μ<br>μ<br>μ<br>μ<br>μ<br>μ<br>μ   | [01.02]<br>[01.07][01.20]<br>#<br>[01.07][20.01][20.09][32.07][34.01]<br>#<br>[01.04]<br>#<br>[01.04]<br>#<br>[01.04]<br>#<br>[01.04]<br>[01.04]<br>[01.05][10.03]<br>[01.25][14.13]<br>[01.05][10.06][43.01]<br>#<br>#  |
| A0080513000148<br>A0080508000396<br>A008051000032<br>A0080521000357<br>A008053000037<br>A008053000049<br>A00805080010<br>A008053000049<br>A008052000011<br>A008052000011<br>A008055000011<br>A008055000011<br>A008051000254<br>A0080523000478<br>A0080523000478<br>A0080523000475<br>A0080523000478  | Acetylonithine aminotransferase<br>Nucleoside phosphorylase<br>Predicted protein<br>Predicted transporter (major facilitator superfamily)<br>Predicted transporter<br>Predicted protein<br>Predicted protein<br>Predicted protein<br>Predicted protein<br>Predicted protein<br>Predicted protein<br>Predicted protein<br>Predicted protein<br>Asparty   protease<br>Predicted protein<br>Asparty   protease<br>Predicted protein<br>Predicted protein  | 0.438<br>0.437<br>0.437<br>0.437<br>0.435<br>0.434<br>0.433<br>0.433<br>0.432<br>0.432<br>0.432<br>0.432<br>0.431<br>0.431<br>0.43<br>0.431<br>0.43<br>0.427<br>0.426<br>0.426   | [01]<br>μ<br>[01](20](32](34)<br>μ<br>[01]<br>μ<br>μ<br>μ<br>μ<br>μ<br>[01](10]<br>μ<br>μ<br>μ<br>[10][16]<br>[01][14]<br>[01][14]<br>[01][13]<br>μ<br>μ<br>μ<br>μ<br>μ<br>μ<br>μ<br>μ<br>μ<br>μ<br>μ<br>μ<br>μ   | [0102]<br>[01.07][01.20]<br>#<br>#<br>[01.07][20.01][20.09][32.07][34.01]<br>#<br>[01.04]<br>#<br>#<br>[01.04]<br>#<br>#<br>[01.04]<br>[01.04]<br>#<br>#<br>#<br>[01.01][16.03]<br>[01.05][14.13]<br>[01.05][14.01]<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#   |
| AO080513000148<br>AO080508000396<br>AO080501000092<br>AO080521000357<br>AO08053600070<br>AO08053000049<br>AO080503000049<br>AO08052000018<br>AO080525000011<br>AO08052000018<br>AO08052000018<br>AO080515000221<br>AO080515000221<br>AO080515000221<br>AO080521000156<br>AO0805300011<br>AO080521000156<br>AO0805300011  | Acetylornithine aminotransferase<br>Nucleoside phosphorylase<br>Predicted protein<br>Predicted transporter (major facilitator superfamily)<br>Predicted protein<br>Predicted protein<br>Aspartyl protease<br>1-Acyl dihydroxyacetone phosphate reductase and related dehydrogenases<br>Predicted protein<br>Predicted protein<br>Predicted protein<br>Predicted protein<br>Predicted protein<br>Predicted protein<br>Predicted protein  | 0.438<br>0.437<br>0.437<br>0.437<br>0.435<br>0.435<br>0.434<br>0.433<br>0.433<br>0.432<br>0.432<br>0.432<br>0.432<br>0.431<br>0.431<br>0.431<br>0.431<br>0.431<br>0.427<br>0.426<br>0.426<br>0.424<br>0.419  | [01]<br>μ<br>[01][20][32][34]<br>μ<br>[01]<br>μ<br>μ<br>μ<br>μ<br>μ<br>μ<br>μ<br>μ<br>μ<br>μ<br>μ<br>μ<br>μ   | [0102]<br>[0107][01.20]<br>#<br>[0107][20.01][20.09][32.07][34.01]<br>#<br>[0104]<br>#<br>[0104]<br>#<br>[0104]<br>#<br>[0104]<br>#<br>[0105][16.03]<br>[01.25][14.13]<br>[01.25][14.13]<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#  |
| A00880513000148<br>A008805000396<br>A008951000032<br>A0089521000357<br>A0080532000519<br>A0080532000519<br>A008053000049<br>A008052000014<br>A008052000014<br>A008052000014<br>A0080520000111<br>A008052000015<br>A008051000251<br>A008051000255<br>A008051000254<br>A0080521000254<br>A0080523000411<br>A008051000255<br>A008051000055<br>A0080510000156<br>A0080510000156  | Acetylonithine aminotransferase<br>Nucleoside phosphorylase<br>Predicted protein<br>Predicted protein<br>Serine threonine protein kinase<br>Predicted protein<br>Predicted protein   | 0.437<br>0.437<br>0.437<br>0.437<br>0.435<br>0.435<br>0.434<br>0.433<br>0.433<br>0.432<br>0.432<br>0.432<br>0.432<br>0.432<br>0.432<br>0.432<br>0.432<br>0.431<br>0.43<br>0.426<br>0.426<br>0.426<br>0.424<br>0.419<br>0.418   | [01]<br>μ<br>[01](20](32](34)<br>μ<br>[01](20](32](34)<br>μ<br>μ<br>μ<br>μ<br>μ<br>[01](16]<br>[01](14]<br>[01](14]<br>μ<br>μ<br>μ<br>μ<br>μ<br>μ<br>μ<br>μ<br>μ<br>μ<br>μ<br>μ<br>μ  | [01.02]<br>[01.07][01.20]<br>#<br>[01.07][20.01][20.09][32.07][34.01]<br>#<br>[01.04]<br>#<br>[01.04]<br>#<br>[10.01][16.03]<br>[01.25][14.13]<br>[01.25][14.13]<br>#<br>#<br>[01.05][01.06][43.01]<br>#<br>#<br>[01.20]   |
| AO080513000148<br>AO080508000396<br>AO080501000025<br>AO080510000357<br>AO080530000357<br>AO08053000049<br>AO080503000049<br>AO08052000018<br>AO080525000618<br>AO0805250000111<br>AO080520000718<br>AO080520000718<br>AO080520000718<br>AO08052000011<br>AO080520000186<br>AO080520000186<br>AO08052000118<br>AO08052000118<br>AO08052000118<br>AO08052000118<br>AO08052000118<br>AO08052000118<br>AO08052000118<br>AO08052000118<br>AO08052000118<br>AO08052000118   | Acetylomithine aminotransferase<br>Nucleoside phosphorylase<br>Predicted protein<br>Predicted protein<br>Serine threonine protein kinase<br>Predicted protein<br>Predicted protein<br>Predicted protein<br>Predicted protein<br>Predicted protein<br>Predicted protein<br>Predicted protein<br>Predicted protein<br>Predicted protein<br>Predicted protein<br>Asparty protease<br>I - Acyl dihydroxyacetone phosphate reductase and related dehydrogenases<br>Predicted protein<br>Predicted pro   | $\begin{array}{c} 0.438\\ 0.437\\ 0.437\\ 0.437\\ 0.435\\ 0.435\\ 0.434\\ 0.433\\ 0.432\\ 0.432\\ 0.432\\ 0.432\\ 0.431\\ 0.431\\ 0.431\\ 0.427\\ 0.426\\ 0.424\\ 0.418\\ 0.418\\ 0.416\\ \end{array}$   | [01]<br>μ<br>[01][20][32][34]<br>μ<br>[01]<br>μ<br>μ<br>μ<br>μ<br>μ<br>μ<br>μ<br>μ<br>μ<br>μ<br>μ<br>μ<br>μ   | [0102]<br>[0107][01.20]<br>#<br>[0107][20.01][20.09][32.07][34.01]<br>#<br>[01.04]<br>#<br>[01.04]<br>#<br>[01.04]<br>#<br>[01.04]<br>#<br>[01.05][16.03]<br>[01.05][16.03]<br>[01.05][16.03]<br>#<br>[01.05][16.03]<br>[01.05][16.03]<br>#<br>[01.05][16.03]<br>[01.05][16.03]<br>[01.05][16.03]<br>[01.05][16.03]<br>[01.05][16.03]<br>[01.05][16.03]<br>[01.05][16.03]<br>[01.05][16.03]<br>[01.05][16.03]<br>[01.05][16.03]<br>[01.05][16.03]<br>[01.05][16.03]<br>[01.05][16.03]<br>[01.05][16.03]<br>[01.05][16.03]<br>[01.05][16.03]<br>[01.05][16.03]<br>[01.05][16.03]<br>[01.05][16.03]<br>[01.05][16.03]<br>[01.05][16.03]<br>[01.05][16.03]<br>[01.05][16.03]<br>[01.05][16.03]<br>[01.05][16.03]<br>[01.05][16.03]<br>[01.05][16.03]<br>[01.05][16.03]<br>[01.05][16.03]<br>[01.05][16.03]<br>[01.05][16.03]<br>[01.05][16.03]<br>[01.05][16.03]<br>[01.05][16.03]<br>[01.05][16.03]<br>[01.05][16.03]<br>[01.05][16.03]<br>[01.05][16.03]<br>[01.05][16.03]<br>[01.05][16.03]<br>[01.05][16.03]<br>[01.05][16.03]<br>[01.05][16.03]<br>[01.05][16.03]<br>[01.05][16.03]<br>[01.05][16.03]<br>[01.05][16.03]<br>[01.05][16.03]<br>[01.05][16.03]<br>[01.05][16.03]<br>[01.05][16.03]<br>[01.05][16.03]<br>[01.05][16.03]<br>[01.05][16.03]<br>[01.05][16.03]<br>[01.05][16.03]<br>[01.05][16.03]<br>[01.05][16.03]<br>[01.05][16.03]<br>[01.05][16.03]<br>[01.05][16.03]<br>[01.05][16.03]<br>[01.05][16.03]<br>[01.05][16.03]<br>[01.05][16.03]<br>[01.05][16.03]<br>[01.05][16.03]<br>[01.05][16.03]<br>[01.05][16.03]<br>[01.05][16.03]<br>[01.05][16.03]<br>[01.05][16.03]<br>[01.05][16.03]<br>[01.05][16.03]<br>[01.05][16.03]<br>[01.05][16.03]<br>[01.05][16.03]<br>[01.05][16.03]<br>[01.05][16.03]<br>[01.05][16.03]<br>[01.05][16.03]<br>[01.05][16.03]<br>[01.05][16.03]<br>[01.05][16.05][   |
| A0080513000148<br>A0080508000396<br>A008051000032<br>A008051000032<br>A008051000037<br>A008053000049<br>A008050300049<br>A0080508000049<br>A008052000014<br>A008052000014<br>A008052000014<br>A008052000015<br>A0080515000221<br>A008051000055<br>A008051000055<br>A0080501000155<br>A0080501000155<br>A0080501000155  | Acetylonithine aminotransferase<br>Nucleoside phosphorylase<br>Predicted protein<br>Predicted protein<br>Protein<br>Predicted protein<br>Protein<br>Protein<br>Protein<br>Protein<br>Protein<br>Protein<br>Protein<br>Protein<br>Protein<br>Protein<br>Protein<br>Protein<br>Protein<br>Protein<br>Protein<br>Protein<br>Protein<br>Protein<br>Protein<br>Protein<br>Protein<br>Protein<br>Protein<br>Protein<br>Protein<br>Protein<br>Protein<br>Protein<br>Protein<br>Protein<br>Protein<br>Prote | $\begin{array}{c} 0.438\\ 0.437\\ 0.437\\ 0.437\\ 0.435\\ 0.434\\ 0.433\\ 0.432\\ 0.432\\ 0.432\\ 0.432\\ 0.432\\ 0.431\\ 0.43\\ 0.426\\ 0.426\\ 0.426\\ 0.426\\ 0.426\\ 0.424\\ 0.419\\ 0.418\\ 0.416\\ 0.416\end{array}$   | [01]<br>μ<br>[01](20](32](34)<br>μ<br>[01](20](32](34)<br>μ<br>μ<br>μ<br>μ<br>[01]<br>[16]<br>[01](16]<br>[01](16]<br>[01](43]<br>μ<br>μ<br>[01]<br>[01]<br>[01](20](20](20)(20)(20)(20)(20)(20)(20)(20)(20)(20)  | [01.02]<br>[01.07][01.20]<br>#<br>[01.07][20.01][20.09][32.07][34.01]<br>#<br>[01.04]<br>[01.04]<br>#<br>#<br>[01.04]<br>[01.05][01.06][43.01]<br>#<br>#<br>[01.05][01.06][43.01]<br>#<br>[01.05][01.06][43.01]<br>#<br>[01.05][01.06][43.01]<br>#<br>[01.05][01.06][43.01]<br>#<br>[01.05][01.06][43.01]<br>#<br>[01.05][01.06][43.01]<br>#<br>[01.05][01.06][43.01]<br>#<br>[01.05][01.06][43.01]<br>#<br>[01.05][01.06][43.01]<br>#<br>[01.05][01.06][43.01]<br>#<br>[01.05][01.06][43.01]<br>#<br>[01.05][01.06][43.01]<br>#<br>[01.05][01.06][43.01]<br>#<br>[01.05][01.06][43.01]<br>#<br>[01.05][01.06][43.01]<br>#<br>[01.05][01.06][43.01]<br>#<br>[01.05][01.06][43.01]<br>#<br>[01.05][01.06][43.01]<br>#<br>[01.05][01.06][43.01]<br>#<br>[01.05][01.06][43.01]<br>#<br>[01.05][01.06][43.01]<br>#<br>[01.05][01.06][43.01]<br>#<br>[01.05][01.06][43.01]<br>#<br>[01.05][01.06][43.01]<br>#<br>[01.05][01.06][43.01]<br>#<br>[01.05][01.06][43.01]<br>#<br>[01.05][01.06][43.01]<br>#<br>[01.05][01.06][43.01]<br>#<br>[01.05][01.06][43.01]<br>#<br>[01.05][01.06][43.01]<br>#<br>[01.05][01.06][43.01]<br>#<br>[01.05][01.06][43.01]<br>#<br>[01.05][01.06][43.01]<br>#<br>[01.05][01.06][43.01]<br>#<br>[01.05][01.06][43.01]<br>#<br>[01.05][01.06][43.01]<br>#<br>[01.05][01.06][43.01]<br>#<br>[01.05][01.06][43.01]<br>#<br>[01.05][01.06][43.01]<br>#<br>[01.05][01.06][43.01]<br>#<br>[01.05][01.06][43.01]<br>#<br>[01.05][01.06][43.01]<br>#<br>[01.05][01.06][43.01]<br>#<br>[01.05][01.06][43.01]<br>#<br>[01.05][01.06][43.01]<br>#<br>[01.05][01.06][43.01]<br>#<br>[01.05][01.06][43.01]<br>#<br>[01.05][01.06][43.01]<br>#<br>[01.05][01.06][43.01]<br>#<br>[01.05][01.06][43.01]<br>#<br>[01.05][01.06][43.01][43.01]<br>#<br>[01.05][01.06][43.01][4   |
| AO080513000148<br>AO080508000396<br>AO080501000025<br>AO080510000357<br>AO080530000357<br>AO08053000049<br>AO080503000049<br>AO080508000367<br>AO080520000111<br>AO08052000018<br>AO08052000018<br>AO08052000018<br>AO08052000018<br>AO08052000018<br>AO0805200011<br>AO0805200018<br>AO0805200018<br>AO0805200011<br>AO0805200011<br>AO0805200018<br>AO08052000118<br>AO08052000118<br>AO08052000118<br>AO08050100018<br>AO08052000115<br>AO08050100014<br>AO08052000115  | Acetylornithine aminotransferase<br>Nucleoside phosphorylase<br>Predicted protein<br>Predicted transporter (major facilitator superfamily)<br>Predicted protein<br>Predicted protein<br>Predicted protein<br>Predicted protein<br>Predicted Zn-dependent hydrolases of the beta-lactamase fold<br>Predicted protein<br>Predicted protein<br>P   | 0.438<br>0.437<br>0.437<br>0.437<br>0.435<br>0.434<br>0.433<br>0.433<br>0.432<br>0.432<br>0.432<br>0.432<br>0.432<br>0.432<br>0.432<br>0.432<br>0.431<br>0.432<br>0.424<br>0.424<br>0.424<br>0.418<br>0.413  | [01]<br>μ<br>[01](20](32](34]<br>μ<br>μ<br>μ<br>μ<br>μ<br>μ<br>μ<br>μ<br>μ<br>μ<br>μ<br>μ<br>μ  | [0102]<br>[0107][01.20]<br>#<br>[0107][20.01][20.09][32.07][34.01]<br>#<br>[0104]<br>#<br>[01.04]<br>#<br>[01.04]<br>#<br>[01.04]<br>#<br>[01.05][16.03]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][10.06][43.01]<br>#<br>[01.20]<br>[01.06][10.06][43.01]<br>#<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.20]<br>[01.               |
| A0080513000148<br>A0080508000396<br>A008051000032<br>A0080510000357<br>A0080512000357<br>A008053000049<br>A008050300049<br>A0080508000367<br>A008051000033<br>A008052000014<br>A008052000014<br>A008052000015<br>A0080515000221<br>A0080515000221<br>A008051000055<br>A008051000055<br>A008051000055<br>A0080501000155<br>A0080501000155<br>A0080501000155<br>A0080501000155<br>A0080501000155<br>A0080501000155<br>A0080501000155<br>A0080501000155<br>A0080501000155<br>A0080501000155<br>A0080501000155<br>A0080501000155<br>A0080501000155<br>A0080501000155<br>A0080501000155<br>A0080501000155<br>A0080501000155<br>A0080501000155<br>A0080501000155<br>A0080501000155<br>A0080501000155<br>A0080501000155<br>A008051000058  | Acetylonithine aminotransferase<br>Nucleoside phosphorylase<br>Predicted protein<br>Predicted protein<br>Aspartyl protease<br>Predicted protein<br>Predicted protein<br>Stable Protein<br>Predicted protein<br>Stable Protein<br>Predicted protein<br>Predicted protein<br>Predicted protein<br>Stable Protein<br>Predicted protein<br>Predicted protein<br>Predicted protein<br>Stable Protein<br>Predicted protein<br>Pre  | 0.438<br>0.437<br>0.437<br>0.437<br>0.435<br>0.434<br>0.435<br>0.433<br>0.433<br>0.432<br>0.432<br>0.432<br>0.432<br>0.432<br>0.432<br>0.432<br>0.432<br>0.431<br>0.431<br>0.431<br>0.426<br>0.426<br>0.426<br>0.426<br>0.419<br>0.418<br>0.416<br>0.411<br>0.4113   | [01]<br>μ<br>[01](20](32](34)<br>μ<br>[01](20](32](34)<br>μ<br>μ<br>μ<br>μ<br>[01]<br>[16]<br>[01](16]<br>[01](16]<br>[01](16]<br>μ<br>μ<br>μ<br>[01](20](32)(32)(34)<br>μ<br>μ<br>μ<br>μ<br>μ<br>μ<br>μ<br>μ<br>μ<br>μ<br>μ<br>μ<br>μ  | [01.02]<br>[01.07][01.20]<br>#<br>#<br>[01.07][20.01][20.09][32.07][34.01]<br>#<br>#<br>[01.04]<br>[01.04]<br>#<br>#<br>[01.04]<br>[01.04]<br>[01.05][01.06][43.01]<br>#<br>#<br>[01.05][01.06][43.01]<br>#<br>[01.05][01.06][43.01]<br>#<br>[01.05][01.06][43.01]<br>#<br>#<br>[01.05][01.06][43.01]<br>#<br>#<br>[01.05][01.06][43.01]<br>#<br>#<br>[01.05][01.06][43.01]<br>#<br>#<br>[01.05][01.06][43.01]<br>#<br>#<br>[01.05][01.06][43.01]<br>#<br>#<br>[01.05][01.06][40.01][40.01]<br>#<br>[01.05][01.06][40.01][40.01]<br>#<br>#<br>[01.05][01.06][40.01][40.01]<br>#<br>[01.05][40.01][40.01][40.01][40.01][40.01]<br>#<br>[01.05][40.01]   |
| A0080513000148<br>A0080508000396<br>A008051000035<br>A008051000035<br>A008053000037<br>A008053000049<br>A008053000049<br>A008053000049<br>A008053000048<br>A008052000018<br>A008052000018<br>A00805200018<br>A00805200078<br>A008051000254<br>A00805200078<br>A008051000255<br>A008051000156<br>A008051000156<br>A008051000156<br>A008051000156<br>A008051000174<br>A008051000174<br>A0080515000085<br>A0080515000085<br>A0080515000085<br>A0080515000037  | Acetylonithine aminotransferase<br>Nucleoside phosphorylase<br>Predicted protein<br>Predicted protein<br>Aspartyl protease<br>I-Acyl dihytoxyacetone phosphate reductase and related dehydrogenases<br>Predicted protein<br>Predicted protein<br>Premases of the major facilitator superfamily<br>Signal transduction histidine kinase<br>Carboxylesterase and related proteins<br>Fuctose tagatose bisphosphate adolase  | 0.438<br>0.437<br>0.437<br>0.437<br>0.435<br>0.434<br>0.433<br>0.433<br>0.433<br>0.432<br>0.433<br>0.432<br>0.431<br>0.431<br>0.431<br>0.431<br>0.431<br>0.427<br>0.426<br>0.424<br>0.418<br>0.413<br>0.412  | [01]<br>#<br>[01](20)(32](34)<br>#<br>[01]<br>#<br>#<br>#<br>[01][16]<br>[01][14]<br>[01][14]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01  | [0102]<br>[0107][01.20]<br>#<br>[0107][20.01][20.09][32.07][34.01]<br>#<br>[01.04]<br>#<br>[01.04]<br>#<br>[01.04]<br>#<br>[1001][16.03]<br>[01.25][14.13]<br>101.05][01.06][43.01]<br>#<br>#<br>[01.20]<br>[01.03]<br>[01.03][20.01][20.03]<br>#<br>[01.05][20.01][20.03]<br>#  |
| A0080513000148<br>A0080508000396<br>A008051000032<br>A008051000032<br>A008051000037<br>A008053000049<br>A00805080000519<br>A0080508000051<br>A008052000014<br>A008052000014<br>A008052000014<br>A008052000015<br>A008051000254<br>A008052000058<br>A008051000055<br>A008051000055<br>A008051000055<br>A0080501000155<br>A0080501000155<br>A0080501000155<br>A0080501000155<br>A0080501000155<br>A0080501000155<br>A008051000055<br>A008051000055<br>A008051000055<br>A008051000055<br>A008051000058<br>A008051000055<br>A008051000058<br>A008051000058<br>A008051000058<br>A008051000058<br>A008051000058<br>A008051000058<br>A008051000058<br>A008051000058<br>A008051000058  | Acetylonithine aminotransferase<br>Nucleoside phosphorylase<br>Predicted protein<br>Predicted protein<br>Aspartyl protease<br>Predicted protein<br>Predicted protein<br>Standard Conserved protein<br>FAD FMN-containing dehydrogenases<br>nuc5 nuclease S1 precursor<br>Permeases of the major facilitator superfamily<br>Signal transduction histidne kinase<br>Carbox/yesterases and related proteins<br>Fructose tagatose bisphosphate aldolase<br>Proteined protein  | 0.438<br>0.437<br>0.437<br>0.437<br>0.435<br>0.434<br>0.435<br>0.433<br>0.433<br>0.432<br>0.432<br>0.432<br>0.432<br>0.432<br>0.432<br>0.432<br>0.432<br>0.431<br>0.431<br>0.431<br>0.426<br>0.426<br>0.426<br>0.426<br>0.419<br>0.418<br>0.416<br>0.411<br>0.412<br>0.412   | [01]<br>μ<br>[01](20](32](34)<br>μ<br>[01](20](32](34)<br>μ<br>μ<br>μ<br>μ<br>[01]<br>[16]<br>[01][43]<br>μ<br>μ<br>[01][43]<br>μ<br>μ<br>[01]<br>[01][20]<br>μ<br>μ<br>[01](20](32](34)<br>μ<br>μ<br>μ<br>μ<br>μ<br>[01](20](32)(34)<br>μ<br>μ<br>μ<br>μ<br>μ<br>μ<br>μ<br>μ<br>μ<br>μ<br>μ<br>μ<br>μ  | [01.02]<br>[01.07][01.20]<br>#<br>[01.07][20.01][20.09][32.07][34.01]<br>#<br>[01.04]<br>[01.04]<br>#<br>#<br>[01.04]<br>[01.04]<br>[01.05][01.06][43.01]<br>#<br>[01.05][01.06][43.01]<br>#<br>[01.05][01.06][43.01]<br>#<br>[01.05][00.01][20.03]<br>#<br>[01.05][20.01][20.03]<br>#<br>[01.05][02.01][20.07]<br>#   |
| A0080513000148<br>A0080508000396<br>A008051000035<br>A008051000035<br>A008053000037<br>A008053000049<br>A008053000049<br>A008053000049<br>A00805200018<br>A00805200018<br>A00805200018<br>A00805200018<br>A00805200018<br>A00805200018<br>A00805200018<br>A00805200018<br>A00805200018<br>A00805200018<br>A00805200018<br>A00805200018<br>A00805100025<br>A00805100018<br>A00805100018<br>A00805100018<br>A00805100018<br>A00805100018<br>A00805100018<br>A00805100018<br>A008051500008<br>A008051500008<br>A008051500008<br>A008051500008   | Acetylonithine aminotransferase<br>Nucleoside phosphorylase<br>Predicted protein<br>Predicted protein<br>Serine threconine protein kinase<br>Predicted protein<br>Predicted protein<br>Predicted protein<br>Predicted protein<br>Predicted protein<br>Predicted protein<br>Predicted protein<br>Predicted protein<br>Predicted protein<br>Predicted protein<br>Aspartyl protease<br>I-Acyl dhydroyacetone phosphate reductase and related dehydrogenases<br>Predicted protein<br>Predicted protein<br>Premases of the major facilitator superfamily<br>Signal transduction histidine kinase<br>Carboxylesterase and related proteins<br>Fructose tagatose bisphosphate adolase<br>Predicted protein<br>Predicted protein<br>Predicted protein<br>Predices bisphosphate adolase<br>Predicted protein<br>Predicted protein<br>Predicted protein<br>Predicted protein<br>Predicted protein<br>Predicted protein<br>Premeases of the major facilitator superfamily<br>Signal transduction histidine kinase<br>Carboxylesterase and related proteins<br>Predicted protein<br>Predicted protein<br>Predicted protein<br>Predicted protein<br>Premeases of the major facilitator superfamily<br>Signal transduction histidine kinase<br>Carboxylesterase and related proteins<br>Predicted protein<br>Predicted pro  | 0.438<br>0.437<br>0.437<br>0.437<br>0.435<br>0.434<br>0.433<br>0.433<br>0.433<br>0.433<br>0.433<br>0.432<br>0.432<br>0.432<br>0.431<br>0.431<br>0.426<br>0.426<br>0.426<br>0.424<br>0.418<br>0.411<br>0.412<br>0.412   | [01]<br>#<br>[01][20][32][34]<br>#<br>[01]<br>#<br>#<br>#<br>[01][06]<br>[01][14]<br>[01][14]<br>[01][13]<br>#<br>#<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#  | [0102]<br>[0107][01.20]<br>#<br>[0107][20.01][20.09][32.07][34.01]<br>#<br>[01.04]<br>#<br>[01.04]<br>#<br>[01.04]<br>#<br>[1001][16.03]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][12.01][20.01]<br>#<br>#<br>[01.25][20.01][20.03]<br>#<br>[01.25][20.01][20.03]<br>#<br>#<br>[01.25][20.01][20.03]<br>#<br>#<br>[01.25][20.01][20.03]<br>#<br>[01.25][20.01][20.03]<br>#<br>[01.25][20.01][20.03]<br>#<br>[01.25][20.01][20.03]<br>#<br>[01.25][20.01][20.03]<br>#<br>[01.25][20.01][20.03]<br>#<br>[01.25][20.01][20.03]<br>#<br>[01.25][20.01][20.03]<br>#<br>[01.25][20.01][20.03]<br>#<br>[01.25][20.01][20.03]<br>#<br>[01.25][20.01][20.03]<br>#<br>[01.25][20.01][20.03]<br>#<br>[01.25][20.01][20.03]<br>#<br>[01.25][20.01][20.03]<br>#<br>[01.25][20.01][20.03]<br>#<br>[01.25][20.01][20.03]<br>#<br>[01.25][20.01][20.03]<br>#<br>[01.25][20.01][20.03]<br>#<br>[01.25][20.01][20.03]<br>#<br>[01.25][20.01][20.03]<br>#<br>[01.25][20.01][20.03]<br>#<br>[01.25][20.01][20.03]<br>#<br>[01.25][20.01][20.03]<br>#<br>[01.25][20.01][20.03]<br>#<br>[01.25][20.01][20.03]<br>#<br>[01.25][20.01][20.03]<br>#<br>[01.25][20.01][20.03]<br>#<br>[01.25][20.01][20.03]<br>#<br>[01.25][20.01][20.03]<br>[01.25][20.01][20.03]<br>#<br>[01.25][20.01][20.03]<br>#<br>[01.25][20.01][20.03]<br>#<br>[01.25][20.01][20.03]<br>#<br>[01.25][20.01][20.03]<br>#<br>[01.25][20.01][20.03]<br>#<br>[01.25][20.01][20.01][20.03]<br>#<br>[01.25][20.01][20.01][20.03]<br>#<br>[01.25][20.01][20.01][20.01][20.03]<br>#<br>[01.25][20.01   |
| A0080513000148<br>A008050000396<br>A008051000032<br>A008051000037<br>A008051000037<br>A008053000049<br>A00805000049<br>A008051000049<br>A008052000014<br>A008052000014<br>A008052000014<br>A008052000014<br>A008052000015<br>A0080515000221<br>A008051000254<br>A008052000015<br>A008051000055<br>A0080501000155<br>A0080501000155<br>A0080501000155<br>A0080501000155<br>A0080510000155<br>A0080510000155<br>A0080510000155<br>A0080510000155<br>A0080510000155<br>A0080510000155<br>A0080510000155<br>A0080510000155<br>A0080510000155<br>A0080510000155<br>A0080510000155<br>A0080515000155<br>A0080515000155<br>A0080515000155<br>A0080515000155<br>A0080515000155<br>A0080515000155<br>A0080515000155<br>A0080515000155<br>A0080515000155<br>A0080515000155<br>A0080515000155<br>A0080515000155<br>A0080515000155<br>A0080515000155<br>A0080515000155<br>A0080515000155<br>A0080515000155<br>A0080515000155<br>A0080515000155<br>A0080515000155<br>A0080515000155<br>A0080515000155<br>A0080515000155<br>A0080515000155<br>A0080515000155<br>A0080515000155<br>A0080515000155<br>A0080515000155<br>A0080515000155<br>A0080515000155<br>A0080515000155<br>A0080515000155<br>A0080515000155<br>A008051500055<br>A008051500055<br>A008051500055<br>A008051500055<br>A008051500055<br>A008051500055<br>A008051500055<br>A008051500055<br>A008051500055<br>A008051500055<br>A008051500055<br>A008051500055<br>A008051500055<br>A008051500055<br>A008051500055<br>A008051500055<br>A008051500055<br>A008051500055<br>A008051500055<br>A008051500055<br>A008051500055<br>A008051500055<br>A008051500055<br>A008051500055<br>A008051500055<br>A008051500055<br>A008051500055<br>A008051500055<br>A008051500055<br>A008051500055<br>A008051500055<br>A008051500055<br>A008051500055<br>A008051500055<br>A008051500055<br>A008051500055<br>A008051500055<br>A008051500055<br>A008051500055<br>A00805150055<br>A00805150055<br>A008051500055<br>A008051500055<br>A008051500055<br>A00805150055<br>A00805150055<br>A008051500055<br>A008051500055<br>A008051500055<br>A00805150055<br>A00805150055<br>A00805150055<br>A00805150055<br>A00805150055<br>A00805150055<br>A00805150055<br>A00805150055<br>A00805150055<br>A00805150055<br>A00805150055<br>A00805150055<br>A00805150055<br>A00805150055<br>A00805150055<br>A00805150055<br>A00805150055<br>A00805150055<br>A00805150055<br>A00805150055<br>A00805150055<br>A00805150055<br>A00805150055<br>A00805150055<br>A00805150055<br>A00805150055<br>A00805150055<br>A00805150055<br>A00805150055<br>A00805150055<br>A00805150055<br>A0  | Acetylonithine aminotransferase<br>Nucleoside phosphorylase<br>Predicted protein<br>Predicted protein<br>Pructose tagatose bisphosphate aldolase<br>Predicted protein   | 0.438<br>0.437<br>0.437<br>0.437<br>0.435<br>0.434<br>0.433<br>0.433<br>0.432<br>0.432<br>0.432<br>0.432<br>0.432<br>0.432<br>0.432<br>0.432<br>0.431<br>0.431<br>0.431<br>0.426<br>0.426<br>0.424<br>0.419<br>0.416<br>0.4112<br>0.412<br>0.412<br>0.412<br>0.412<br>0.412  | [01]<br>#<br>[01][20][32][34]<br>#<br>[01]<br>#<br>#<br>#<br>[01]<br>[10][4]<br>[01][4]<br>[01][4]<br>[01][4]<br>[01][4]<br>[01][4]<br>[01][02]<br>#<br>#<br>[01][20]<br>#<br>#<br>#<br>#<br>[01][20][20][20][20]<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#  | [01.02]<br>[01.07][01.20]<br>#<br>[01.07][20.01][20.09][32.07][34.01]<br>#<br>[01.04]<br>[01.04]<br>#<br>#<br>[01.04]<br>[01.04]<br>[01.05][01.06][43.01]<br>#<br>[01.05][01.06][43.01]<br>#<br>[01.05][01.06][43.01]<br>#<br>[01.05][01.06][43.01]<br>#<br>[01.05][01.06][43.01]<br>#<br>[01.05][01.06][43.01]<br>#<br>[01.05][01.06][43.01]<br>#<br>[01.05][01.06][43.01]<br>#<br>[01.05][01.06][43.01]<br>#<br>[01.05][01.06][43.01]<br>#<br>[01.05][01.06][43.01]<br>[01.05][40.01][40.00][   |
| A0080513000148<br>A008050000396<br>A008051000035<br>A008051000035<br>A008053000037<br>A008053000049<br>A008053000049<br>A008053000049<br>A00805200014<br>A00805200014<br>A00805200014<br>A00805200014<br>A00805200014<br>A00805200014<br>A00805200015<br>A008051000254<br>A00805200015<br>A00805100025<br>A008051000156<br>A008051000156<br>A008051000174<br>A008052000175<br>A008051000174<br>A008052000175<br>A008051000035<br>A008051000035<br>A008051000035<br>A008051000035<br>A008051000035<br>A008051000035<br>A008051000035<br>A008051000035<br>A008051000035<br>A008051000035<br>A008055000015<br>A008055000015<br>A008055000015<br>A008055000015<br>A008055000015<br>A008055000015<br>A008055000015<br>A008055000015<br>A008055000015<br>A008055000015<br>A008055000015<br>A008055000015<br>A008055000015<br>A008055000015<br>A008055000015<br>A008055000015<br>A008055000015<br>A008055000015<br>A008055000015<br>A008055000015<br>A008055000015<br>A008055000015<br>A008055000015<br>A008055000015<br>A008055000015<br>A008055000015<br>A008055000015<br>A008055000015<br>A008055000015<br>A008055000015<br>A008055000015<br>A008055000015<br>A008055000015<br>A008055000015<br>A008055000015<br>A008055000015<br>A008055000015<br>A008055000015<br>A008055000015<br>A008055000015<br>A008055000015<br>A008055000015<br>A008055000015<br>A008055000015<br>A00805500005<br>A008055000005<br>A008055000005<br>A008055000005<br>A008055000005<br>A008055000005<br>A008055000005<br>A008055000005<br>A00805500005<br>A00805500005<br>A00805500005<br>A00805500005<br>A00805500005<br>A00805500005<br>A00805500005<br>A00805500005<br>A00805500005<br>A00805500005<br>A00805500005<br>A00805500005<br>A00805500005<br>A00805500005<br>A0080550005<br>A00805500005<br>A00805500005<br>A00805500005<br>A0080550005<br>A0080550005<br>A0080550005<br>A0080550005<br>A0080550005<br>A0080550005<br>A0080550005<br>A0080550005<br>A0080550005<br>A0080550005<br>A0080550005<br>A0080550005<br>A0080550005<br>A0080550005<br>A0080550005<br>A0080550005<br>A0080550005<br>A0080550005<br>A008055005<br>A0080550005<br>A0080550005<br>A0080550005<br>A0080550005<br>A008055005<br>A008055005<br>A008055005<br>A008055005<br>A008055005<br>A008055005<br>A008055005<br>A008055005<br>A008055005<br>A008055005<br>A008055005<br>A008055005<br>A008055005<br>A008055005<br>A008055005<br>A008055005<br>A008055005<br>A008055005<br>A008055005<br>A008055005<br>A008055005<br>A008055005<br>A008055005<br>A008055005<br>A008055005<br>A008055005<br>A008055005<br>A008055005<br>A008055005<br>A008055005<br>A008055005<br>A0       | Acetylonithine aminotransferase<br>Nucleoside phosphorylase<br>Predicted protein<br>Predicted protein<br>Serine threconine protein kinase<br>Predicted protein<br>Predicted protein<br>Premeases of the major facilitator superfamily<br>Signal transduction histidine kinase<br>Carboxylesterase and related proteins<br>Predicted protein<br>Predicted protei  | 0.438<br>0.437<br>0.437<br>0.437<br>0.435<br>0.434<br>0.433<br>0.433<br>0.433<br>0.433<br>0.433<br>0.432<br>0.432<br>0.432<br>0.432<br>0.431<br>0.431<br>0.426<br>0.426<br>0.426<br>0.424<br>0.418<br>0.411<br>0.411<br>0.412<br>0.412<br>0.412<br>0.412   | [01]<br>#<br>[01][20][32][34]<br>#<br>[01][20][32][34]<br>#<br>#<br>#<br>[01][01]<br>[01][14]<br>[01][14]<br>[01][13]<br>#<br>#<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>[01]<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#  | [0102]<br>[0107][01.20]<br>#<br>[0107][20.01][20.09][32.07][34.01]<br>#<br>[01.04]<br>#<br>[01.04]<br>#<br>[01.04]<br>#<br>[1001][16.03]<br>[01.25][14.13]<br>[01.25][01.06][43.01]<br>#<br>#<br>[01.05][01.06][43.01]<br>#<br>[01.02]<br>[01.03]<br>[01.03][20.01][20.03]<br>#<br>#<br>[01.05][20.01][20.03]<br>#<br>#<br>[01.05][20.01][20.03]<br>#<br>#<br>[01.05][20.01][20.03]<br>#<br>#<br>[01.05][20.01][20.03]<br>#<br>[01.05][20.01][20.03]<br>#<br>[01.05][20.01][20.03]<br>#<br>[01.05][20.01][20.03]<br>#<br>[01.05][20.01][20.03]<br>#<br>[01.05][20.01][20.03]<br>#<br>[01.05][20.01][20.03]<br>#<br>[01.05][20.01][20.03]<br>#<br>[01.05][20.01][20.03]<br>#<br>[01.05][20.01][20.03]<br>[01.05][20.01][20.03]<br>#<br>[01.05][20.01][20.03]<br>#<br>[01.05][20.01][20.03]<br>#<br>[01.05][20.01][20.03]<br>#<br>[01.05][20.01][20.03]<br>#<br>[01.05][20.01][20.03]<br>#<br>[01.05][20.01][20.03]<br>#<br>[01.05][20.01][20.03]<br>#<br>[01.05][20.01][20.03]<br>#<br>[01.05][20.01][20.03]<br>#<br>[01.05][20.01][20.03]<br>#<br>[01.05][20.01][20.03]<br>#<br>[01.05][20.01][20.03]<br>#<br>[01.05][20.01][20.03]<br>#<br>[01.05][20.01][20.03]<br>#<br>[01.05][20.01][20.03]<br>#<br>[01.05][20.01][20.03]<br>#<br>[01.05][20.01][20.03]<br>#<br>[01.05][20.01][20.03]<br>#<br>[01.05][20.01][20.03]<br>#<br>[01.05][20.01][20.03]<br>#<br>[01.05][20.01][20.03]<br>#<br>[01.05][20.01][20.03]<br>#<br>[01.05][20.01][20.03]<br>[01.05][20.01][20.03]<br>#<br>[01.05][20.01][20.03]<br>#<br>[01.05][20.01][20.03]<br>#<br>[01.05][20.01][20.03]<br>#<br>[01.05][20.01][20.03]<br>#<br>[01.05][20.01][20.03]<br>#<br>[01.05][20.01][20.01][20.03]<br>#<br>[01.05][20.01][20.01][20.03]<br>#<br>[01.05][20.01][20.01][20.01][20.03]<br>#<br>[01.05][20.01][20.01][20.01][20.01][20.01][20.01][20.01][20.02]<br>#<br>[01.05][20.01   |
| A0080513000148<br>A008050000396<br>A008051000032<br>A008051000037<br>A008051000037<br>A008051000037<br>A008051000049<br>A008051000049<br>A008052000014<br>A008052000014<br>A008052000014<br>A008052000014<br>A008052000015<br>A00805100025<br>A008051000055<br>A008051000055<br>A008050100015<br>A008052000171<br>A008052000172<br>A008051000055<br>A008051000055<br>A008051000055<br>A008051000055<br>A008051000055<br>A008051000055<br>A008051000055<br>A008051000055<br>A008051000055<br>A008051000055<br>A008051000055<br>A008051000055<br>A008051000055<br>A008051000055<br>A008051000055<br>A008051000055<br>A008051000055<br>A008051000055<br>A008051000055<br>A008051000055<br>A008051000055<br>A008051000055<br>A008051000055<br>A008051000055<br>A008051000055<br>A008051000055<br>A008051000055<br>A008051000055<br>A008051000055<br>A008051000055<br>A00805100005<br>A00805100005<br>A00805100005<br>A00805100005<br>A00805100005<br>A00805100005<br>A00805100005<br>A00805100005<br>A00805100005<br>A00805100005<br>A00805100005<br>A00805100005<br>A00805100005<br>A00805100005<br>A00805100005<br>A00805100005<br>A00805100005<br>A00805100005<br>A00805100005<br>A00805100005<br>A00805100005<br>A00805100005<br>A00805100005<br>A0080510005<br>A0080510005<br>A0080510005<br>A0080510005<br>A0080510005<br>A0080510005<br>A0080510005<br>A0080510005<br>A0080510005<br>A0080510005<br>A0080510005<br>A0080510005<br>A0080510005<br>A0080510005<br>A0080510005<br>A0080510005<br>A0080510005<br>A0080510005<br>A0080510005<br>A0080510005<br>A0080510005<br>A0080510005<br>A0080510005<br>A0080510005<br>A0080510005<br>A0080510005<br>A0080510005<br>A0080510005<br>A0080510005<br>A0080510005<br>A0080510005<br>A0080510005<br>A0080510005<br>A0080510005<br>A0080510005<br>A0080510005<br>A0080510005<br>A0080510005<br>A0080510005<br>A0080510005<br>A0080510005<br>A0080510005<br>A0080510005<br>A0080510005<br>A0080510005<br>A0080510005<br>A0080510005<br>A0080510005<br>A0080510005<br>A0080510005<br>A0080510005<br>A0080510005<br>A0080510005<br>A0080510005<br>A0080510005<br>A0080510005<br>A0080510005<br>A0080510005<br>A0080510005<br>A0080510005<br>A0080510005<br>A0080510005<br>A0080510005<br>A0080510005<br>A0080510005<br>A0080510005<br>A0080510005<br>A0080510005<br>A0080510005<br>A0080510005<br>A0080510005<br>A0080510005<br>A0080510005<br>A0080510005<br>A0080510005<br>A0080510005<br>A0080510005<br>A0080510005<br>A0080510005<br>A0080510005<br>A0080510005<br>A0080510005<br>A0080510005<br>A0080510005<br>A0080510005<br>A0080510005<br>A0080510005<br>A008050005<br>A00805 | Acetylornithine aminotransferase<br>Nucleoside phosphorylase<br>Predicted protein<br>Predicted protein<br>FAD FNN-containing dehydrogenases<br>Inco Suclease S I precursor<br>Permeases of the major facilitator superfamily<br>Signal transduction histidine kinase<br>Carbox/yesterase and related proteins<br>Fructose tagatose bisplosphate aldolase<br>Predicted protein<br>Permeases of the major facilitator superfamily<br>Amino acid transporters<br>SAM-dependent methyltransferases   | 0.438<br>0.437<br>0.437<br>0.437<br>0.438<br>0.434<br>0.433<br>0.433<br>0.432<br>0.432<br>0.432<br>0.432<br>0.432<br>0.432<br>0.431<br>0.431<br>0.431<br>0.431<br>0.431<br>0.431<br>0.426<br>0.426<br>0.426<br>0.424<br>0.416<br>0.416<br>0.4112<br>0.412<br>0.412<br>0.412<br>0.412<br>0.412<br>0.412<br>0.412  | [01]<br>#<br>[01][20][32][34]<br>#<br>[01]<br>#<br>#<br>[01]<br>[10][6]<br>[01][16]<br>[01][16]<br>[01][16]<br>[01][16]<br>[01][16]<br>[01][10]<br>#<br>#<br>[01]<br>[01]<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#  | [01.02]<br>[01.07][01.20]<br>#<br>#<br>[01.07][20.01][20.09][32.07][34.01]<br>#<br>#<br>[01.04]<br>#<br>#<br>[01.04]<br>#<br>[01.04]<br>[01.04]<br>[01.05][01.03]<br>[01.05][01.06][43.01]<br>#<br>#<br>[01.05][01.06][43.01]<br>#<br>[01.05][01.01]<br>[01.05][01.01][02.01]<br>[01.05][02.01][02.03]<br>#<br>#<br>[01.05][20.01][02.07]<br>#<br>#<br>[01.05][20.01][02.07]<br>#<br>#<br>[01.05][20.01][02.07]<br>#<br>#<br>[01.05][20.01][02.07]<br>#<br>#<br>[01.05][20.01][02.07]<br>[01.05][20.01][02.07]<br>#<br>#<br>[01.05][20.01][02.07]<br>#<br>#<br>[01.05][20.01][02.07]<br>[01.05][20.01][02.07]<br>[01.05][20.01][02.07]<br>#<br>[01.05][20.01][02.07]<br>[01.05][20.01][02.07]<br>[01.05][20.01][02.07]<br>[01.05][20.01][02.07]<br>[01.05][20.01][02.07]<br>[01.05][20.01][02.07]<br>[01.05][20.01][02.07]<br>[01.05][20.01][02.07]<br>[01.05][02.01][02.07]<br>[01.05][02.01][02.07]<br>[01.05][02.01][02.07]<br>[01.05][02.01][02.07]<br>[01.05][02.01][02.07]<br>[01.05][02.01][02.07]<br>[01.05][02.01][02.07]<br>[01.05][02.01][02.07]<br>[01.05][02.01][02.07]<br>[01.05][02.01][02.07]<br>[01.05][02.01][02.07]<br>[01.05][02.01][02.07]<br>[01.05][02.01][02.07]<br>[01.05][02.01][02.07]<br>[01.05][02.01][02.07]<br>[01.05][02.01][02.07]<br>[01.05][02.01][02.07]<br>[01.05][02.01][02.07]<br>[01.05][02.01][02.07]<br>[01.05][02.01][02.07][02.07]<br>[01.05][02.01][02.07]   |
| A0080513000148<br>A008050000396<br>A008051000032<br>A008051000035<br>A008053000037<br>A008053000049<br>A008053000049<br>A008053000049<br>A00805200011<br>A00805200014<br>A00805200014<br>A00805200014<br>A00805200015<br>A008051000254<br>A008051000254<br>A00805300015<br>A008051000254<br>A00805300015<br>A008051000025<br>A008051000035<br>A008051000035<br>A0080515000035<br>A0080515000035<br>A0080515000035<br>A0080515000035<br>A0080515000035<br>A0080515000035<br>A0080530000154<br>A0080531000035<br>A0080531000035<br>A0080551000035<br>A0080551000035<br>A0080551000035<br>A0080551000035<br>A0080551000035<br>A0080551000015<br>A0080551000035<br>A0080551000035<br>A0080551000035<br>A0080551000035<br>A0080551000035<br>A0080551000035<br>A0080551000035<br>A0080551000035<br>A0080551000035<br>A0080551000035<br>A0080551000035<br>A0080551000035<br>A0080551000035<br>A0080551000035<br>A0080551000035<br>A0080551000035<br>A0080551000035<br>A0080551000035<br>A0080551000035<br>A0080551000035<br>A0080551000035<br>A0080550000154<br>A0080550000154<br>A0080551000035<br>A0080550000154<br>A0080550000032<br>A0080550000154<br>A008055000035<br>A008055000035<br>A008055000035<br>A008055000035<br>A008055000035<br>A008055000035<br>A008055000035<br>A008055000035<br>A008055000035<br>A008055000035<br>A008055000035<br>A008055000035<br>A008055000035<br>A008055000035<br>A008055000035<br>A008055000035<br>A008055000035<br>A008055000035<br>A008055000035<br>A008055000035<br>A008055000035<br>A008055000035<br>A008055000035<br>A008055000035<br>A008055000035<br>A008055000035<br>A008055000035<br>A008055000035<br>A008055000035<br>A008055000035<br>A008055000035<br>A008055000035<br>A008055000035<br>A008055000035<br>A008055000035<br>A008055000035<br>A00805500035<br>A00805500035<br>A00805500035<br>A00805500035<br>A00805500035<br>A00805500035<br>A00805500035<br>A00805500035<br>A00805500035<br>A00805500035<br>A00805500035<br>A00805500035<br>A00805500035<br>A00805500035<br>A00805500035<br>A00805500035<br>A00805500035<br>A00805500035<br>A00805500035<br>A00805500035<br>A00805500035<br>A00805500035<br>A00805500035<br>A00805500035<br>A00805500035<br>A00805500035<br>A00805500035<br>A00805500035<br>A00805500055<br>A00805500055<br>A00805500055<br>A00805500055<br>A00805500055<br>A00805500055<br>A0080550055<br>A0080550055<br>A0080550055<br>A0080550055<br>A0080550055<br>A0080550055<br>A0080550055<br>A0080550055<br>A0080550055<br>A0080550055<br>A0080550055<br>A0080550055<br>A0080550055<br>A0080550055<br>A0080550055<br>A0                                     | Acetylonithine aminotransferase<br>Nucleoside phosphorylase<br>Predicted protein<br>Predicted protein<br>Serine threonine protein kinase<br>Predicted protein<br>Predicted protein<br>Asparty   protease<br>Predicted protein<br>Predicted protein<br>Signal transduction histidine kinase<br>Carboxylesterase and related proteins<br>Predicted protein<br>Predicted protein<br>Protein<br>Predicted protein<br>Protein<br>Predicted protein<br>Predicted protein<br>Predicted protein<br>Predicted protein<br>Predicted protein<br>Predicted protein<br>Predicted protein<br>Protein<br>Predicted protein<br>Protein<br>Predicted protein<br>Predicted protein<br>Predicted protein<br>Protein<br>Protein<br>Predicted protein<br>Protein<br>Protein<br>Protein<br>Protein<br>Protein<br>Protein<br>Protein<br>Protein<br>Protein<br>Protein<br>Protein<br>Protein<br>Protein<br>Protein<br>Protein<br>Protein<br>Protein<br>Protein<br>Protein<br>Protein<br>Protein<br>Protein<br>Protein<br>Protein<br>Protein<br>Protein<br>Prote          | 0.438<br>0.437<br>0.437<br>0.437<br>0.435<br>0.433<br>0.433<br>0.433<br>0.433<br>0.433<br>0.432<br>0.432<br>0.432<br>0.431<br>0.432<br>0.431<br>0.426<br>0.426<br>0.426<br>0.426<br>0.418<br>0.416<br>0.411<br>0.412<br>0.412<br>0.412<br>0.412<br>0.412<br>0.412<br>0.412   | [01]         #         [01]/20](32](34)         #         [01]         #         #         #         [01][14]         [01][14]         [01][13]         #         [01]         [01]         [01]         [01]         [01]         [01]         [01]         [01]         [01]         [01]         # <td< td=""><td>[0102]<br/>[0107][01.20]<br/>#<br/>[0107][20.01][20.09][32.07][34.01]<br/>#<br/>[01.04]<br/>#<br/>[01.04]<br/>#<br/>[01.04]<br/>#<br/>[01.05][01.06][43.01]<br/>#<br/>[01.25][01.06][43.01]<br/>#<br/>[01.02]<br/>[01.03]<br/>[01.03][20.01][20.03]<br/>#<br/>#<br/>[01.04]<br/>[01.05][20.01][20.03]<br/>#<br/>#<br/>[01.05][20.01][20.03]<br/>#<br/>#<br/>[01.05][20.01][20.03]<br/>#<br/>#<br/>[01.05][20.01][20.03]<br/>#<br/>#<br/>[01.05][20.01][20.03]<br/>#<br/>#<br/>[01.05][20.01][20.03]<br/>#<br/>#<br/>[01.05][20.01][20.03]<br/>#<br/>#<br/>[01.05][20.01][20.03]<br/>#<br/>#<br/>[01.05][20.01][20.03]<br/>#<br/>#<br/>[01.05][20.01][20.03]<br/>#<br/>#<br/>[01.05][20.01][20.03]<br/>#<br/>#<br/>[01.05][20.01][20.03]<br/>#<br/>#<br/>[01.05][20.01][20.03]<br/>#<br/>#<br/>[01.05][20.01][20.03]<br/>#<br/>#<br/>#<br/>#<br/>#<br/>#<br/>#<br/>#<br/>#<br/>#<br/>#<br/>#<br/>#</td></td<>   | [0102]<br>[0107][01.20]<br>#<br>[0107][20.01][20.09][32.07][34.01]<br>#<br>[01.04]<br>#<br>[01.04]<br>#<br>[01.04]<br>#<br>[01.05][01.06][43.01]<br>#<br>[01.25][01.06][43.01]<br>#<br>[01.02]<br>[01.03]<br>[01.03][20.01][20.03]<br>#<br>#<br>[01.04]<br>[01.05][20.01][20.03]<br>#<br>#<br>[01.05][20.01][20.03]<br>#<br>#<br>[01.05][20.01][20.03]<br>#<br>#<br>[01.05][20.01][20.03]<br>#<br>#<br>[01.05][20.01][20.03]<br>#<br>#<br>[01.05][20.01][20.03]<br>#<br>#<br>[01.05][20.01][20.03]<br>#<br>#<br>[01.05][20.01][20.03]<br>#<br>#<br>[01.05][20.01][20.03]<br>#<br>#<br>[01.05][20.01][20.03]<br>#<br>#<br>[01.05][20.01][20.03]<br>#<br>#<br>[01.05][20.01][20.03]<br>#<br>#<br>[01.05][20.01][20.03]<br>#<br>#<br>[01.05][20.01][20.03]<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#   |
| A0080513000148<br>A008050000396<br>A008051000032<br>A008051000032<br>A008051000037<br>A008053000049<br>A008051000049<br>A008051000049<br>A008052000014<br>A008052000014<br>A008052000014<br>A008052000014<br>A008052000015<br>A008051000254<br>A008052000015<br>A008051000055<br>A008051000055<br>A008051000015<br>A008052000015<br>A008051000015<br>A008051000015<br>A008051000015<br>A008051000015<br>A008051000015<br>A008051000015<br>A008051000015<br>A008051000015<br>A008051000015<br>A008051000015<br>A008051000015<br>A008051000015<br>A008051000015<br>A008051000015<br>A008051000015<br>A008051000015<br>A008051000015<br>A008051000015<br>A008051000015<br>A008051000015<br>A008051000015<br>A008051000015<br>A008051000015<br>A008051000015<br>A008051000015<br>A008051000015   | Acetylornithine aminotransferase<br>Nucleoside phosphorylase<br>Predicted protein<br>Predicted protein<br>Premeases of the major facilitator superfamily<br>Signal transduction histidine kinase<br>Carbox/yestrase and related proteins<br>Fructose tagatose bisplosphate aldolase<br>Predicted protein<br>Permeases of the major facilitator superfamily<br>Amino acid transporters<br>SAM-dependent methyltransferases<br>NADPH?quinone reductase and related Zn-dependent oxidoreductases<br>Proteicted metal-dependent hydrolase with the TIM-barrel fold   | 0.438<br>0.437<br>0.437<br>0.437<br>0.437<br>0.434<br>0.433<br>0.433<br>0.433<br>0.432<br>0.432<br>0.432<br>0.432<br>0.432<br>0.432<br>0.431<br>0.431<br>0.431<br>0.431<br>0.431<br>0.426<br>0.426<br>0.426<br>0.424<br>0.416<br>0.416<br>0.4112<br>0.4112<br>0.412<br>0.412<br>0.412<br>0.412<br>0.409<br>0.409<br>0.409<br>0.409<br>0.409<br>0.409<br>0.409<br>0.409<br>0.409<br>0.409<br>0.409<br>0.409<br>0.409<br>0.409<br>0.409<br>0.409<br>0.409<br>0.409<br>0.409<br>0.409<br>0.409<br>0.409<br>0.409<br>0.409<br>0.409<br>0.409<br>0.409<br>0.409<br>0.409<br>0.409<br>0.409<br>0.409<br>0.409<br>0.409<br>0.401<br>0.413<br>0.413<br>0.413<br>0.413<br>0.425<br>0.425<br>0.425<br>0.425<br>0.425<br>0.425<br>0.425<br>0.425<br>0.425<br>0.425<br>0.425<br>0.425<br>0.425<br>0.425<br>0.425<br>0.425<br>0.425<br>0.425<br>0.425<br>0.425<br>0.425<br>0.425<br>0.425<br>0.425<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.427<br>0.427<br>0.427<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.427<br>0.427<br>0.427<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.427<br>0.427<br>0.427<br>0.427<br>0.427<br>0.427<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.427<br>0.427<br>0.427<br>0.427<br>0.427<br>0.427<br>0.427<br>0.427<br>0.427<br>0.427<br>0.427<br>0.427<br>0.427<br>0.427<br>0.427<br>0.427<br>0.427<br>0.427<br>0.427<br>0.427<br>0.427<br>0.427<br>0.427<br>0.427<br>0.427<br>0.427<br>0.427<br>0.427<br>0.427<br>0.427<br>0.427<br>0.427<br>0.427<br>0.427<br>0.427<br>0.427<br>0.427<br>0.427<br>0.427<br>0.427<br>0.427<br>0.427<br>0.427<br>0.427<br>0.427<br>0.427<br>0.427<br>0.427<br>0.427<br>0.427<br>0.427<br>0.427<br>0.427<br>0.427<br>0.427<br>0.427<br>0.427<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.447<br>0.44 | [01]       μ       [01]/20][32][34]       μ       [01]       μ       μ       [01]       μ       [10]       μ       [10]       [10]       [11]       [01]    <  | [01.02]<br>[01.07][01.20]<br>#<br>#<br>[01.07][20.01][20.09][32.07][34.01]<br>#<br>#<br>[01.04]<br>#<br>[01.04]<br>#<br>[01.04]<br>#<br>[01.05][01.03]<br>[01.25][14.13]<br>[01.05][01.06][43.01]<br>#<br>#<br>[01.05][01.06][43.01]<br>#<br>[01.05][01.01][02.01]<br>[01.05][02.01][02.03]<br>#<br>#<br>[01.05][20.01][02.03]<br>#<br>#<br>[01.05][20.01][02.03]<br>#<br>#<br>[01.05][20.01][02.03]<br>#<br>#<br>[01.05][20.01][02.03]<br>#<br>#<br>[01.05][20.01][02.03]<br>#<br>#<br>[01.05][20.01][02.03]<br>#<br>#<br>[01.05][20.01][02.03]<br>#<br>#<br>[01.05][20.01][02.03]<br>#<br>#<br>[01.05][20.01][02.03]<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#  |
| A0080513000148<br>A008050000396<br>A008051000032<br>A008051000037<br>A008053600037<br>A008053600037<br>A008053000049<br>A008053000049<br>A008053000049<br>A0080530000111<br>A008053000011<br>A008053000011<br>A008053000011<br>A008053000011<br>A008053000011<br>A008053000011<br>A008053000011<br>A008053000011<br>A008053000011<br>A008053000012<br>A008053000012<br>A008053000012<br>A008053000012<br>A008053000012<br>A008053000012<br>A008053000012<br>A008053000012<br>A008053000012<br>A008053000012<br>A008053000012<br>A008053000012<br>A008053000012<br>A008053000012<br>A008053000012<br>A008053000012<br>A008053000012<br>A008053000012<br>A008052000013<br>A008052000013<br>A0080522000057<br>A0080522000057  | Acetylonithine aminotransferase<br>Nucleoside phosphorylase<br>Predicted protein<br>Predicted protein<br>Serine threonine protein kinase<br>Predicted protein<br>Predicted protein<br>Asparty   protease<br>Predicted protein<br>Predicted pr  | 0.438<br>0.437<br>0.437<br>0.437<br>0.435<br>0.433<br>0.433<br>0.433<br>0.433<br>0.433<br>0.432<br>0.432<br>0.432<br>0.431<br>0.432<br>0.431<br>0.427<br>0.426<br>0.426<br>0.426<br>0.418<br>0.416<br>0.416<br>0.411<br>0.412<br>0.412<br>0.412<br>0.412<br>0.412<br>0.412<br>0.412<br>0.412<br>0.4399<br>0.399<br>0.399   | [01]         #         [01](20)[32][34]         #         [01]         #         #         #         [10][16]         [01][14]         [01][13]         #         [10]         [01]   | [0102]<br>[0107][01.20]<br>#<br>[0107][20.01][20.09][32.07][34.01]<br>#<br>[01.04]<br>#<br>[01.04]<br>#<br>[1001][16.03]<br>[0125][14.13]<br>[0125][14.13]<br>[0125][14.13]<br>[0125][14.13]<br>[0125][14.13]<br>[0125][14.13]<br>[0125][14.13]<br>[0125][14.13]<br>[0125][14.13]<br>[0125][14.13]<br>[0125][14.13]<br>[0125][14.13]<br>[0125][14.13]<br>[0125][14.13]<br>[0125][14.13]<br>[0125][14.13]<br>[0125][14.13]<br>[0125][14.13]<br>[0125][14.13]<br>[0125][14.13]<br>[0125][14.13]<br>[0125][14.13]<br>[0125][14.13]<br>[0125][14.13]<br>[0125][14.13]<br>[0125][14.13]<br>[0125][14.13]<br>[0125][14.13]<br>[0125][14.13]<br>[0125][14.13]<br>[0125][14.13]<br>[0125][14.13]<br>[0125][14.13]<br>[0125][14.13]<br>[0125][14.13]<br>[0125][14.13]<br>[0125][14.13]<br>[0125][14.13]<br>[0125][14.13]<br>[0125][14.13]<br>[0125][14.13]<br>[0125][14.13]<br>[0125][14.13]<br>[0125][14.13]<br>[0125][14.13]<br>[0125][14.13]<br>[0125][14.13]<br>[0125][14.13]<br>[0125][14.13]<br>[0125][14.13]<br>[0125][14.13]<br>[0125][14.13]<br>[0125][14.13]<br>[0125][14.13]<br>[0125][14.13]<br>[0125][14.13]<br>[0125][14.13]<br>[0125][14.13]<br>[0125][14.13]<br>[0125][14.13]<br>[0125][14.13]<br>[0125][14.13]<br>[0125][14.13]<br>[0125][14.13]<br>[0125][14.13]<br>[0125][14.13]<br>[0125][14.13]<br>[0125][14.13]<br>[0125][14.13]<br>[0125][14.13]<br>[0125][14.13]<br>[0125][14.13]<br>[0125][14.13]<br>[0125][14.13]<br>[0125][14.13]<br>[0125][14.13]<br>[0125][14.13]<br>[0125][14.13]<br>[0125][14.13]<br>[0125][14.13]<br>[0125][14.13]<br>[0125][14.13]<br>[0125][14.13]<br>[0125][14.13]<br>[0125][14.13]<br>[0125][14.13]<br>[0125][14.13]<br>[0125][14.13]<br>[0125][14.13]<br>[0125][14.13]<br>[0125][14.13]<br>[0125][14.13]<br>[0125][14.13]<br>[0125][14.13]<br>[0125][14.13]<br>[0125][14.13]<br>[0125][14.13]<br>[0125][14.13]<br>[0125][14.13]<br>[0125][14.13]<br>[0125][14.13]<br>[0125][14.13]<br>[0125][14.13]<br>[0125][14.13]<br>[0125][14.13]<br>[0125][14.13]<br>[0125][14.13]<br>[0125][14.13]<br>[0125][14.13]<br>[0125][14.13]<br>[0125][14.13]<br>[0125][14.13]<br>[0125][14.13]<br>[0125][14.13]<br>[0125][14.13]<br>[0125][14.13]<br>[0125][14.13]<br>[0125][14.13]<br>[0125][14.13]<br>[0125][14.13]<br>[0125][14.13]<br>[0125][14.13]<br>[0125][14.13]<br>[0125][14.13]<br>[0125][14.13]<br>[0125][14.13]<br>[0125][14.13]<br>[0125][14.13]<br>[0125][14.13]<br>[0125][   |
| A0080513000148<br>A0080508000396<br>A008051000032<br>A008051000035<br>A008051000035<br>A008051000035<br>A008051000049<br>A008051000049<br>A008052000014<br>A008052000014<br>A008052000014<br>A008052000015<br>A00805100025<br>A00805100025<br>A008051000055<br>A00805100005<br>A008052000017<br>A008052000017<br>A008052000017<br>A008052000017<br>A008052000017<br>A008052000017<br>A008052000017<br>A008052000017<br>A008052000017<br>A008052000017<br>A008052000017<br>A008052000017<br>A008052000017<br>A008052000017<br>A008052000017<br>A008052000017<br>A008052000017<br>A008052000017<br>A008052000017<br>A008052000017<br>A008052000015<br>A008052000017<br>A008052000015<br>A008052000015<br>A008052000017<br>A008052000015<br>A008052000015<br>A008052000015<br>A008052000015<br>A008052000015<br>A008052000015<br>A008052000015<br>A008052000015<br>A008052000015<br>A008052000015<br>A008052000015<br>A008052000015<br>A008052000015<br>A008052000015<br>A008052000015<br>A008052000015<br>A008052000015<br>A008052000015<br>A008052000015<br>A008052000015<br>A008052000015<br>A008052000015<br>A008052000015<br>A008052000015<br>A008052000015<br>A008052000015<br>A008052000015<br>A008052000015<br>A008052000015<br>A008052000015<br>A008052000015<br>A008052000015<br>A008052000015<br>A008052000015<br>A008052000015<br>A008052000015<br>A008052000015<br>A008052000015<br>A008052000015<br>A008052000015<br>A008052000015<br>A008052000015<br>A008052000015<br>A008052000015<br>A008052000015<br>A008052000015<br>A008052000015<br>A008052000015<br>A008052000015<br>A008052000015<br>A008052000015<br>A008052000015<br>A008052000015<br>A008052000015<br>A00805200005<br>A00805200005<br>A00805200005<br>A00805200005<br>A00805200005<br>A00805200005<br>A00805200005<br>A0080520005<br>A0080520005<br>A0080520005<br>A0080520005<br>A0080520005<br>A0080520005<br>A0080520005<br>A0080520005<br>A0080520005<br>A00805<br>A0080520005<br>A0080520005<br>A0080520005<br>A0080520005<br>A0080520005<br>A0080520005<br>A0080520005<br>A0080520005<br>A0080520005<br>A0080520005<br>A0080520005<br>A0080520005<br>A0080520005<br>A0080520005<br>A0080520005<br>A0080520005<br>A0080520005<br>A0080520005<br>A0080520005<br>A0080520005<br>A0080520005<br>A0080520005<br>A0080520005<br>A0080520005<br>A0080520005<br>A0080520005<br>A0080520005<br>A0080520005<br>A0080520005<br>A0080520005<br>A0080520005<br>A0080520005<br>A0080520005<br>A0080520005<br>A008052005<br>A008052005<br>A008052005<br>A008052005<br>A008052005<br>A008052005<br>A008052005<br>A008052005<br>A008052005<br>A008                | Acetylornithine aminotransferase<br>Nucleoside phosphorylase<br>Predicted protein<br>Predicted protein<br>Premeases of the major facilitator superfamily<br>Signal transduction histidine kinase<br>Carbox/pelsterse and related protein<br>Prucisce tagatose bisplosphate aldolase<br>Premeases of the major facilitator superfamily<br>Permeases of the major facilitator superfamily<br>Premeases of the major facilitator superfamily<br>Premeases of the major facilitator superfamily<br>Permeases of the major facilitator superfamily<br>Permease of the major facilitator superfamily<br>Permease of the major facilitator supe   | 0.438<br>0.437<br>0.437<br>0.437<br>0.437<br>0.435<br>0.434<br>0.433<br>0.433<br>0.432<br>0.432<br>0.432<br>0.432<br>0.431<br>0.431<br>0.431<br>0.431<br>0.431<br>0.431<br>0.432<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.424<br>0.411<br>0.411<br>0.4112<br>0.4112<br>0.412<br>0.412<br>0.412<br>0.412<br>0.412<br>0.412<br>0.412<br>0.412<br>0.413<br>0.412<br>0.413<br>0.412<br>0.413<br>0.412<br>0.413<br>0.412<br>0.413<br>0.413<br>0.413<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.427<br>0.431<br>0.433<br>0.433<br>0.427<br>0.436<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.427<br>0.431<br>0.431<br>0.431<br>0.432<br>0.432<br>0.432<br>0.432<br>0.432<br>0.432<br>0.432<br>0.432<br>0.432<br>0.432<br>0.432<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.431<br>0.431<br>0.431<br>0.432<br>0.432<br>0.432<br>0.432<br>0.432<br>0.433<br>0.432<br>0.433<br>0.432<br>0.433<br>0.432<br>0.433<br>0.432<br>0.433<br>0.432<br>0.433<br>0.432<br>0.433<br>0.432<br>0.433<br>0.432<br>0.433<br>0.432<br>0.433<br>0.432<br>0.433<br>0.432<br>0.433<br>0.432<br>0.433<br>0.432<br>0.433<br>0.432<br>0.433<br>0.432<br>0.433<br>0.432<br>0.433<br>0.433<br>0.432<br>0.433<br>0.432<br>0.433<br>0.433<br>0.433<br>0.433<br>0.433<br>0.433<br>0.433<br>0.433<br>0.433<br>0.433<br>0.433<br>0.433<br>0.433<br>0.433<br>0.433<br>0.433<br>0.433<br>0.433<br>0.433<br>0.433<br>0.433<br>0.433<br>0.433<br>0.433<br>0.3399   | [01]       μ       [01](20](32](34)       μ       [01]       μ       μ       [01]       μ       [10]       μ       [10][16]       [01][14]       [01][14]       [01]   | [0102]<br>[0107][01.20]<br>#<br>#<br>[0107][20.01][20.09][32.07][34.01]<br>#<br>[01.04]<br>#<br>[01.04]<br>#<br>[01.04]<br>#<br>[01.05][01.05][01.06][43.01]<br>#<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][12.01][20.03]<br>#<br>[01.05][20.01][20.03]<br>#<br>[01.05][20.01][20.03]<br>#<br>[01.05][20.01][20.03]<br>#<br>[01.05][20.01][20.03]<br>#<br>[01.05][20.01][20.03]<br>#<br>[01.05][20.01][20.03]<br>#<br>[01.05][20.01][20.03]<br>#<br>[01.05][20.01][20.03]<br>#<br>[01.05][20.01][20.03]<br>#<br>[01.05][20.01][20.03]<br>#<br>[01.05][20.01][20.03]<br>#<br>[01.05][20.01][20.03]<br>#<br>[01.05][20.01][20.03]<br>#<br>[01.05][20.01][20.03]<br>#<br>[01.05][20.01][20.03]<br>#<br>[01.05][20.01][20.03]<br>#<br>[01.05][20.01][20.03]<br>#<br>[01.05][20.01][20.03]<br>#<br>[01.05][20.01][20.03]<br>#<br>[01.05][20.01][20.03]<br>#<br>[01.05][20.01][20.03]<br>#<br>[01.05][20.01][20.03]<br>#<br>[01.05][20.01][20.03]<br>#<br>[01.05][20.01][20.03]<br>#<br>[01.05][20.01][20.03]<br>#<br>[01.05][20.01][20.03]<br>#<br>[01.05][20.01][20.03]<br>#<br>[01.05][20.01][20.03]<br>#<br>[01.05][20.01][20.03]<br>#<br>[01.05][20.01][20.03]<br>#<br>[01.05][20.01][20.03]<br>#<br>[01.05][20.01][20.03]<br>#<br>[01.05][20.01][20.03]<br>#<br>[01.05][20.01][20.03]<br>#<br>[01.05][20.01][20.03]<br>#<br>[01.05][20.01][20.03]<br>#<br>[01.05][20.01][20.03]<br>#<br>[01.05][20.01][20.03]<br>#<br>[01.05][20.01][20.03]<br>#<br>[01.05][20.01][20.03]<br>#<br>[01.05][20.01][20.03]<br>#<br>[01.05][20.01][20.03]<br>#<br>[01.05][20.01][20.03]<br>#<br>[01.05][20.01][20.03]<br>#<br>[01.05][20.01][20.03]<br>#<br>[01.05][20.01][20.03]<br>#<br>[01.05][20.01][20.03]<br>#<br>[01.05][20.01][20.03]<br>#<br>[01.05][20.01][20.03]<br>#<br>[01.05][20.01][20.01][20.03]<br>#<br>[01.05][20.01][20.03]<br>#<br>[01.05][20.01   |
| A0080513000148<br>A008050000396<br>A008051000032<br>A008051000037<br>A008053600037<br>A0080536000170<br>A008053000049<br>A008053000049<br>A008053000048<br>A0080530000111<br>A008053000018<br>A008053000018<br>A008053000018<br>A008053000018<br>A008053000018<br>A008053000018<br>A008053000018<br>A008053000018<br>A008053000018<br>A008053000018<br>A008053000018<br>A008053000018<br>A008053000018<br>A008053000018<br>A008053000018<br>A0080515000038<br>A0080515000038<br>A0080515000038<br>A0080515000038<br>A0080515000038<br>A0080515000038<br>A0080515000038<br>A0080515000038<br>A0080515000038<br>A0080515000038   | Acetylonithine aminotransferase<br>Nucleoside phosphorylase<br>Predicted protein<br>Predicted protein<br>Serine fluctomic protein kinase<br>Predicted protein<br>Predicted protein   | 0.438<br>0.437<br>0.437<br>0.437<br>0.435<br>0.433<br>0.433<br>0.433<br>0.433<br>0.433<br>0.432<br>0.432<br>0.432<br>0.431<br>0.432<br>0.431<br>0.427<br>0.426<br>0.426<br>0.426<br>0.418<br>0.416<br>0.416<br>0.411<br>0.412<br>0.412<br>0.412<br>0.412<br>0.412<br>0.412<br>0.412<br>0.412<br>0.4399<br>0.399<br>0.399<br>0.399  | [01]         #         [01](20)[32][34]         #         [01]         #         #         #         [10][16]         [01][14]         [01][13]         #         #         #         [01] <t< td=""><td>[0102]<br/>[0107][01.20]<br/>#<br/>[0107][20.01][20.09][32.07][34.01]<br/>#<br/>[01.04]<br/>#<br/>[01.04]<br/>#<br/>[1001][16.03]<br/>[0125][14.13]<br/>[01.25][14.13]<br/>[01.25][14.13]<br/>[01.25][14.13]<br/>[01.25][14.13]<br/>[01.25][14.13]<br/>[01.25][14.13]<br/>[01.25][14.13]<br/>[01.25][14.13]<br/>[01.25][14.13]<br/>[01.25][14.13]<br/>[01.25][14.13]<br/>[01.25][14.13]<br/>[01.25][14.13]<br/>[01.25][14.13]<br/>[01.25][14.13]<br/>[01.25][14.13]<br/>[01.25][14.13]<br/>[01.25][14.13]<br/>[01.25][14.13]<br/>[01.25][14.13]<br/>[01.25][14.13]<br/>[01.25][14.13]<br/>[01.25][14.13]<br/>[01.25][14.13]<br/>[01.25][14.13]<br/>[01.25][14.13]<br/>[01.25][14.13]<br/>[01.25][14.13]<br/>[01.25][14.13]<br/>[01.25][14.13]<br/>[01.25][14.13]<br/>[01.25][14.13]<br/>[01.25][14.13]<br/>[01.25][14.13]<br/>[01.25][14.13]<br/>[01.25][14.13]<br/>[01.25][14.13]<br/>[01.25][14.13]<br/>[01.25][14.13]<br/>[01.25][14.13]<br/>[01.25][14.13]<br/>[01.25][14.13]<br/>[01.25][14.13]<br/>[01.25][14.13]<br/>[01.25][14.13]<br/>[01.25][14.13]<br/>[01.25][14.13]<br/>[01.25][14.13]<br/>[01.25][14.13]<br/>[01.25][14.13]<br/>[01.25][14.13]<br/>[01.25][14.13]<br/>[01.25][14.13]<br/>[01.25][14.13]<br/>[01.25][14.13]<br/>[01.25][14.13]<br/>[01.25][14.13]<br/>[01.25][14.13]<br/>[01.25][14.13]<br/>[01.25][14.13]<br/>[01.25][14.13]<br/>[01.25][14.13]<br/>[01.25][14.13]<br/>[01.25][14.13]<br/>[01.25][14.13]<br/>[01.25][14.13]<br/>[01.25][14.13]<br/>[01.25][14.13]<br/>[01.25][14.13]<br/>[01.25][14.13]<br/>[01.25][14.13]<br/>[01.25][14.13]<br/>[01.25][14.13]<br/>[01.25][14.13]<br/>[01.25][14.13]<br/>[01.25][14.13]<br/>[01.25][14.13]<br/>[01.25][14.13]<br/>[01.25][14.13]<br/>[01.25][14.13]<br/>[01.25][14.13]<br/>[01.25][14.13]<br/>[01.25][14.13]<br/>[01.25][14.13]<br/>[01.25][14.13]<br/>[01.25][14.13]<br/>[01.25][14.13]<br/>[01.25][14.13]<br/>[01.25][14.13]<br/>[01.25][14.13]<br/>[01.25][14.13]<br/>[01.25][14.13]<br/>[01.25][14.13]<br/>[01.25][14.13]<br/>[01.25][14.13]<br/>[01.25][14.13]<br/>[01.25][14.13]<br/>[01.25][14.13]<br/>[01.25][14.13]<br/>[01.25][14.13]<br/>[01.25][14.13]<br/>[01.25][14.13]<br/>[01.25][14.13]<br/>[01.25][14.13]<br/>[01.25][14.13]<br/>[01.25][14.13]<br/>[01.25][14.13]<br/>[01.25][14.13]<br/>[01.25][14.13]<br/>[01.25][14.13]<br/>[01.25][14.13]<br/>[01.25][14.13]<br/>[01.25][14.13]<br/>[01.25][14.13]<br/>[01.25][14.13]<br/>[01.25][14.13]<br/>[01.25][14.13]<br/>[01.25][14.13]<br/>[01.25][14.13]<br/>[01.25][14.13]<br/>[01.25]</td></t<> | [0102]<br>[0107][01.20]<br>#<br>[0107][20.01][20.09][32.07][34.01]<br>#<br>[01.04]<br>#<br>[01.04]<br>#<br>[1001][16.03]<br>[0125][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25]   |
| A0080513000148<br>A008050000396<br>A008051000032<br>A008051000037<br>A008051000037<br>A008051000037<br>A008051000049<br>A008051000049<br>A008052000014<br>A008052000014<br>A008052000014<br>A008052000014<br>A008052000015<br>A00805100025<br>A00805100025<br>A008051000055<br>A00805100005<br>A008052000017<br>A008052000017<br>A008052000017<br>A008052000017<br>A008052000017<br>A008052000017<br>A008052000017<br>A008052000017<br>A008052000017<br>A008052000017<br>A008052000017<br>A008052000017<br>A008052000017<br>A008052000017<br>A008052000017<br>A008052000017<br>A008052000017<br>A008052000017<br>A008052000017<br>A008052000017<br>A008052000017<br>A008052000017<br>A008052000017<br>A008052000017<br>A008052000017<br>A008052000017<br>A008052000017<br>A008052000017<br>A008052000017<br>A008052000017<br>A008052000017<br>A008052000017<br>A008052000017<br>A008052000017<br>A008052000017<br>A008052000017<br>A008052000017<br>A008052000017<br>A008052000017<br>A008052000017<br>A008052000017<br>A008052000017<br>A008052000017<br>A008052000017<br>A008052000017<br>A008052000017<br>A008052000017<br>A008052000017<br>A008052000017<br>A008052000017<br>A008052000017<br>A008052000017<br>A008052000017<br>A008052000017<br>A008052000017<br>A008052000017<br>A008052000017<br>A008052000017<br>A008052000017<br>A008052000017<br>A008052000017<br>A008052000017<br>A008052000017<br>A008052000017<br>A008052000017<br>A008052000017<br>A008052000017<br>A008052000017<br>A008052000017<br>A008052000017<br>A008052000017<br>A008052000017<br>A008052000017<br>A008052000017<br>A008052000017<br>A008052000017<br>A008052000017<br>A008052000017<br>A008052000017<br>A008052000017<br>A008052000017<br>A008052000017<br>A008052000017<br>A008052000017<br>A008052000017<br>A008052000017<br>A008052000017<br>A008052000017<br>A008052000017<br>A008052000017<br>A008052000017<br>A008052000017<br>A008052000017<br>A008052000017<br>A008052000017<br>A008052000017<br>A008052000017<br>A008052000017<br>A008052000017<br>A008052000017<br>A008052000017<br>A008052000017<br>A008052000017<br>A008052000017<br>A008052000017<br>A008052000017<br>A008052000017<br>A008052000017<br>A008052000017<br>A008052000017<br>A008052000017<br>A008052000017<br>A008052000017<br>A008052000000000000000000000000000000000   | Acetylornithine aminotransferase<br>Nucleoside phosphorylase<br>Predicted protein<br>Predicted protein<br>Premeases of the major facilitator superfamily<br>Signal transduction histidine kinase<br>Predicted protein<br>Predicted protein<br>Predicted protein<br>Predicted protein<br>Predicted protein<br>Predicted protein<br>Predicted protein<br>Predicted protein<br>Premeases of the major facilitator superfamily<br>Premeases of the major facilitator superfamily<br>Predicted metal-dependent hydrolose with the TIM-barrel fold<br>Predicted protein<br>Predicted protein Conserved in bacteria<br>Predicted protein<br>Predicted protein<br>Pr   | 0.438<br>0.437<br>0.437<br>0.437<br>0.437<br>0.435<br>0.434<br>0.433<br>0.433<br>0.433<br>0.432<br>0.432<br>0.432<br>0.432<br>0.431<br>0.431<br>0.431<br>0.431<br>0.432<br>0.432<br>0.433<br>0.426<br>0.426<br>0.426<br>0.426<br>0.412<br>0.411<br>0.411<br>0.411<br>0.412<br>0.412<br>0.412<br>0.412<br>0.412<br>0.412<br>0.412<br>0.412<br>0.412<br>0.413<br>0.412<br>0.413<br>0.412<br>0.413<br>0.412<br>0.413<br>0.412<br>0.413<br>0.413<br>0.413<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.427<br>0.433<br>0.433<br>0.433<br>0.433<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.427<br>0.433<br>0.433<br>0.433<br>0.433<br>0.427<br>0.433<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.427<br>0.433<br>0.433<br>0.433<br>0.433<br>0.427<br>0.433<br>0.426<br>0.426<br>0.426<br>0.431<br>0.427<br>0.433<br>0.433<br>0.433<br>0.427<br>0.433<br>0.427<br>0.433<br>0.426<br>0.426<br>0.426<br>0.431<br>0.412<br>0.431<br>0.412<br>0.433<br>0.432<br>0.433<br>0.433<br>0.433<br>0.433<br>0.433<br>0.433<br>0.433<br>0.433<br>0.433<br>0.433<br>0.433<br>0.433<br>0.433<br>0.433<br>0.433<br>0.433<br>0.433<br>0.433<br>0.433<br>0.433<br>0.433<br>0.433<br>0.433<br>0.433<br>0.433<br>0.433<br>0.433<br>0.433<br>0.433<br>0.433<br>0.433<br>0.433<br>0.433<br>0.433<br>0.433<br>0.433<br>0.433<br>0.433<br>0.433<br>0.433<br>0.433<br>0.433<br>0.433<br>0.433<br>0.433<br>0.433<br>0.433<br>0.433<br>0.433<br>0.433<br>0.433<br>0.433<br>0.433<br>0.433<br>0.433<br>0.433<br>0.433<br>0.433<br>0.433<br>0.433<br>0.433<br>0.433<br>0.433<br>0.433<br>0.3399<br>0.3395   | [01]         #         [01][20][32][34]         #         [01]         #         #         [10][10]         #         [01][14]         [01][14]         [01][14]         [01][14]         [01][10]         #         #         #         [01]         [01][20]         # <t< td=""><td>[0102]<br/>[0107][01.20]<br/>#<br/>[0107][20.01][20.09][32.07][34.01]<br/>#<br/>[01.04]<br/>#<br/>[01.04]<br/>#<br/>[01.04]<br/>#<br/>[01.04]<br/>#<br/>[01.05][01.05][01.06][43.01]<br/>#<br/>[01.05][01.06][43.01]<br/>#<br/>[01.05][01.01][20.03]<br/>[01.05][02.01][20.03]<br/>#<br/>[01.05][02.01][02.07]<br/>#<br/>[01.05][02.01][02.07]<br/>#<br/>[01.05][02.01][02.07]<br/>#<br/>[01.05][02.01][02.07]<br/>#<br/>[01.05][02.01][02.07]<br/>#<br/>[01.05][02.01][02.07]<br/>#<br/>[01.05][02.01][02.07]<br/>#<br/>[01.05][02.01][02.07]<br/>#<br/>[01.05][02.01][02.07]<br/>#<br/>[01.05][02.01][02.07]<br/>#<br/>[01.05][02.01][02.07]<br/>[01.05][02.01][02.07]<br/>#<br/>[01.05][02.01][02.07]<br/>#<br/>[01.05][02.01][02.07][03.07]<br/>[01.05][03.01][03.07]<br/>[01.05][03.01][03.07]<br/>[01.05][03.01][03.07]<br/>[01.05][03.01][03.07]<br/>[01.05][03.01][03.07]<br/>[01.05][03.01][03.07]<br/>[01.05][03.01][03.07]<br/>[01.05][03.01][03.07]<br/>[01.05][03.07]<br/>[01.05][03.07]<br/>[01.05][03.07]<br/>[01.05][03.07]<br/>[01.05][03.07]<br/>[01.05][03.07]<br/>[01.05][03.07]<br/>[01.05][03.07]<br/>[01.05][03.07]<br/>[01.05][03.07]<br/>[01.05][03.07]<br/>[01.05][03.07]<br/>[01.05][03.07]<br/>[01.05][03.07]<br/>[01.05][03.07]<br/>[01.05][03.07]<br/>[01.05][03.07]<br/>[01.05][03.07]<br/>[01.05][03.07]<br/>[01.05][03.07]<br/>[01.05][03.07]<br/>[01.05][03.07]<br/>[01.05][03.07]<br/>[01.05][03.07]<br/>[01.05][03.07]<br/>[01.05][03.07]<br/>[01.05][03.07]<br/>[01.05][03.07]<br/>[01.05][03.07]<br/>[01.05][03.07]<br/>[01.05][03.07]<br/>[01.05][03.07]<br/>[01.05][03.07]<br/>[01.05][03.07]<br/>[01.05][03.07]<br/>[01.05][03.07]<br/>[01.05][03.07]<br/>[01.05][03.07]<br/>[01.05][03.07]<br/>[01.05][03.07]<br/>[01.05][03.07]<br/>[01.05][03.07]<br/>[01.05][03.07]<br/>[01.05][03.07]<br/>[01.05][03.07]<br/>[01.05][03.07]<br/>[01.05][03.07]<br/>[01.05][03.07]<br/>[01.05][03.07]<br/>[01.05][03.07]<br/>[01.05][03.07]<br/>[01.05][03.07]<br/>[01.05][03.07]<br/>[01.05][03.07]<br/>[01.05][03.07]<br/>[01.05][03.07]<br/>[01.05][03.07]<br/>[01.05][03.07]<br/>[01.05][03.07]<br/>[01.05][03.07]<br/>[01.05][03.07]<br/>[01.05][03.07]<br/>[01.05][03.07]<br/>[01.05][03.07]<br/>[01.05][03.07]<br/>[01.05][03.07]<br/>[01.05][03.07]<br/>[01.05][03.07]<br/>[01.05][03.07]<br/>[01.05][03.07]<br/>[01.05][03.07]<br/>[01.05][03.07]<br/>[01.05][03.07]<br/>[01.05][03.07]<br/>[01.05][03.07]<br/>[01.05][03.07]<br/>[01.05][03.07]<br/>[01.05][03.07]<br/>[01.05][03.07]<br/>[01.05][03.0</td></t<>  | [0102]<br>[0107][01.20]<br>#<br>[0107][20.01][20.09][32.07][34.01]<br>#<br>[01.04]<br>#<br>[01.04]<br>#<br>[01.04]<br>#<br>[01.04]<br>#<br>[01.05][01.05][01.06][43.01]<br>#<br>[01.05][01.06][43.01]<br>#<br>[01.05][01.01][20.03]<br>[01.05][02.01][20.03]<br>#<br>[01.05][02.01][02.07]<br>#<br>[01.05][02.01][02.07]<br>#<br>[01.05][02.01][02.07]<br>#<br>[01.05][02.01][02.07]<br>#<br>[01.05][02.01][02.07]<br>#<br>[01.05][02.01][02.07]<br>#<br>[01.05][02.01][02.07]<br>#<br>[01.05][02.01][02.07]<br>#<br>[01.05][02.01][02.07]<br>#<br>[01.05][02.01][02.07]<br>#<br>[01.05][02.01][02.07]<br>[01.05][02.01][02.07]<br>#<br>[01.05][02.01][02.07]<br>#<br>[01.05][02.01][02.07][03.07]<br>[01.05][03.01][03.07]<br>[01.05][03.01][03.07]<br>[01.05][03.01][03.07]<br>[01.05][03.01][03.07]<br>[01.05][03.01][03.07]<br>[01.05][03.01][03.07]<br>[01.05][03.01][03.07]<br>[01.05][03.01][03.07]<br>[01.05][03.07]<br>[01.05][03.07]<br>[01.05][03.07]<br>[01.05][03.07]<br>[01.05][03.07]<br>[01.05][03.07]<br>[01.05][03.07]<br>[01.05][03.07]<br>[01.05][03.07]<br>[01.05][03.07]<br>[01.05][03.07]<br>[01.05][03.07]<br>[01.05][03.07]<br>[01.05][03.07]<br>[01.05][03.07]<br>[01.05][03.07]<br>[01.05][03.07]<br>[01.05][03.07]<br>[01.05][03.07]<br>[01.05][03.07]<br>[01.05][03.07]<br>[01.05][03.07]<br>[01.05][03.07]<br>[01.05][03.07]<br>[01.05][03.07]<br>[01.05][03.07]<br>[01.05][03.07]<br>[01.05][03.07]<br>[01.05][03.07]<br>[01.05][03.07]<br>[01.05][03.07]<br>[01.05][03.07]<br>[01.05][03.07]<br>[01.05][03.07]<br>[01.05][03.07]<br>[01.05][03.07]<br>[01.05][03.07]<br>[01.05][03.07]<br>[01.05][03.07]<br>[01.05][03.07]<br>[01.05][03.07]<br>[01.05][03.07]<br>[01.05][03.07]<br>[01.05][03.07]<br>[01.05][03.07]<br>[01.05][03.07]<br>[01.05][03.07]<br>[01.05][03.07]<br>[01.05][03.07]<br>[01.05][03.07]<br>[01.05][03.07]<br>[01.05][03.07]<br>[01.05][03.07]<br>[01.05][03.07]<br>[01.05][03.07]<br>[01.05][03.07]<br>[01.05][03.07]<br>[01.05][03.07]<br>[01.05][03.07]<br>[01.05][03.07]<br>[01.05][03.07]<br>[01.05][03.07]<br>[01.05][03.07]<br>[01.05][03.07]<br>[01.05][03.07]<br>[01.05][03.07]<br>[01.05][03.07]<br>[01.05][03.07]<br>[01.05][03.07]<br>[01.05][03.07]<br>[01.05][03.07]<br>[01.05][03.07]<br>[01.05][03.07]<br>[01.05][03.07]<br>[01.05][03.07]<br>[01.05][03.07]<br>[01.05][03.07]<br>[01.05][03.07]<br>[01.05][03.07]<br>[01.05][03.0   |
| A0080513000148<br>A00805000396<br>A008051000032<br>A008051000037<br>A00805300037<br>A008053000170<br>A008053000170<br>A008053000049<br>A008053000044<br>A0080520000111<br>A008052000014<br>A008052000014<br>A0080520000150<br>A008051000254<br>A008051000254<br>A0080510000156<br>A0080510000156<br>A0080510000156<br>A0080510000156<br>A0080510000156<br>A0080510000156<br>A0080510000156<br>A0080510000157<br>A0080510000157<br>A008052000171<br>A008052000171<br>A008052000171<br>A008052000173<br>A008051000153<br>A008052000173<br>A008052000175<br>A008052000175<br>A008052000175<br>A008052000175<br>A008052000175<br>A008052000175<br>A008052000175<br>A008052000175<br>A008052000175<br>A008052000175<br>A008052000175<br>A008052000175<br>A008052000175<br>A008052000175<br>A008052000175<br>A008052000175<br>A008052000175<br>A008052000175<br>A008052000175<br>A008052000175<br>A008052000175<br>A008052000175<br>A008052000175<br>A008052000175<br>A008052000175<br>A008052000175<br>A008052000175<br>A008052000175<br>A008052000175<br>A008052000175<br>A008052000175<br>A008052000175<br>A008052000175<br>A008052000175<br>A008052000175<br>A008052000175<br>A008052000175<br>A008052000175<br>A008052000175<br>A008052000175<br>A008052000175<br>A008052000175<br>A008052000175<br>A008052000175<br>A008052000175<br>A008052000175<br>A008052000175<br>A008052000175<br>A008052000175<br>A008052000175<br>A008052000175<br>A008052000175<br>A008052000175<br>A008052000175<br>A008052000175<br>A008052000175<br>A008052000175<br>A008052000175<br>A008052000175<br>A008052000175<br>A008052000175<br>A008052000175<br>A008052000175<br>A008052000175<br>A008052000175<br>A008052000175<br>A008052000175<br>A008052000175<br>A008052000175<br>A008052000175<br>A008052000175<br>A008052000175<br>A008052000175<br>A008052000175<br>A008052000175<br>A008052000175<br>A008052000175<br>A008052000175<br>A008052000175<br>A008052000075<br>A008052000075<br>A00805200075<br>A00805200075<br>A00805200075<br>A00805200075<br>A00805200075<br>A00805200075<br>A00805200075<br>A00805200075<br>A00805200075<br>A00805200075<br>A00805200075<br>A00805200075<br>A00805200075<br>A00805200075<br>A00805200075<br>A00805200075<br>A00805200075<br>A00805200075<br>A00805200075<br>A00805200075<br>A00805200075<br>A00805200075<br>A00805200075<br>A00805200075<br>A00805200075<br>A00805200075<br>A00805200075<br>A00805200075<br>A00805200075<br>A00805200075<br>A00805200075<br>A00805200075<br>A00805200075<br>A00805200075<br>A00805200075<br>A00805200075<br>A00805200075<br>A                                     | Acetylonithine aminotransferase<br>Nucleoside phosphorylase<br>Predicted protein<br>Predicted protein<br>NADPHFuguinone reductase and related Zn-dependent oxidoreductases<br>Predicted protein<br>Predicted protein<br>Predicted protein<br>Predicted protein<br>Predicted protein<br>Predicted protein<br>Predicted protein<br>Predicted protein<br>Predicted transporter (major facilitator superfamily)<br>Predicted transporter (major facilitator superfamily)   | 0.438<br>0.437<br>0.437<br>0.437<br>0.435<br>0.433<br>0.433<br>0.433<br>0.433<br>0.433<br>0.432<br>0.432<br>0.432<br>0.431<br>0.432<br>0.431<br>0.432<br>0.431<br>0.427<br>0.426<br>0.426<br>0.419<br>0.410<br>0.411<br>0.412<br>0.412<br>0.412<br>0.412<br>0.412<br>0.412<br>0.412<br>0.412<br>0.412<br>0.412<br>0.4399<br>0.399<br>0.399<br>0.399<br>0.399<br>0.399<br>0.399<br>0.399<br>0.395   | [01]         μ         [01](20](32](34)         μ         [01]         μ         μ         [01]         μ         μ         [01]         μ         [01]         μ         [01] <t< td=""><td>[0102]<br/>[0107][01.20]<br/>#<br/>[0107][20.01][20.09][32.07][34.01]<br/>#<br/>[01.04]<br/>#<br/>[01.04]<br/>#<br/>[01.04]<br/>#<br/>[0101][16.03]<br/>[0125][14.13]<br/>[01.25][14.13]<br/>[01.25][14.13]<br/>[01.25][14.13]<br/>[01.25][14.13]<br/>[01.05][00.01][20.03]<br/>#<br/>#<br/>[01.05][20.01][20.03]<br/>#<br/>#<br/>[01.05][20.01][20.03]<br/>#<br/>#<br/>[01.05][20.01][20.03]<br/>#<br/>#<br/>[01.05][20.01][20.03]<br/>#<br/>#<br/>[01.05][20.01][20.03][20.09][34.01]<br/>#</td></t<>   | [0102]<br>[0107][01.20]<br>#<br>[0107][20.01][20.09][32.07][34.01]<br>#<br>[01.04]<br>#<br>[01.04]<br>#<br>[01.04]<br>#<br>[0101][16.03]<br>[0125][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.05][00.01][20.03]<br>#<br>#<br>[01.05][20.01][20.03]<br>#<br>#<br>[01.05][20.01][20.03]<br>#<br>#<br>[01.05][20.01][20.03]<br>#<br>#<br>[01.05][20.01][20.03]<br>#<br>#<br>[01.05][20.01][20.03][20.09][34.01]<br>#   |
| A0080513000148<br>A00805000396<br>A008051000032<br>A008051000037<br>A008051000037<br>A008051000037<br>A008051000037<br>A008051000149<br>A008052000149<br>A008052000014<br>A008052000014<br>A008052000014<br>A008052000014<br>A008052000015<br>A00805100025<br>A008051000075<br>A008051000075<br>A008051000075<br>A008051000075<br>A008051000071<br>A0080520000174<br>A00805230000172<br>A008051000074<br>A00805230000174<br>A00805230000174<br>A0080515000015<br>A0080510000074<br>A00805230000174<br>A00805230000174<br>A00805230000174<br>A008051000005<br>A008051000005<br>A008051000005<br>A008051000005<br>A008051000005<br>A008051000005<br>A008051000005<br>A008051000005<br>A008051000005<br>A008051000005<br>A008051000005<br>A008051000005<br>A008051000005<br>A008051000005<br>A0080510000005<br>A008051000005<br>A0080510000007<br>A0080520000070<br>A0080520000070<br>A008052000007<br>A0080520000070<br>A008051000000000000000000000000000000000   | Acetylornithine aminotransferase<br>Nucleoside phosphorylase<br>Predicted protein<br>Predicted protein<br>Permeases of the major facilitator superfamily<br>Signal transduction histidine kinase<br>Carboxylesterase and related proteins<br>Fructose tagatose bisplosphate adolase<br>Predicted protein<br>Permeases of the major facilitator superfamily<br>Annino acid transporters<br>SAM-dependent methylransferases<br>NADPH quinone reductase and related Zn-dependent oxidoreductases<br>Predicted protein<br>Predicted protein<br>Predicted protein<br>Predicted protein conserved in bacteria<br>Predicted protein<br>Predicted protein  | 0.438<br>0.437<br>0.437<br>0.437<br>0.437<br>0.435<br>0.434<br>0.433<br>0.433<br>0.433<br>0.432<br>0.432<br>0.432<br>0.432<br>0.432<br>0.432<br>0.432<br>0.431<br>0.431<br>0.431<br>0.433<br>0.426<br>0.426<br>0.426<br>0.426<br>0.419<br>0.411<br>0.411<br>0.412<br>0.412<br>0.412<br>0.412<br>0.412<br>0.412<br>0.412<br>0.412<br>0.412<br>0.412<br>0.413<br>0.413<br>0.413<br>0.413<br>0.413<br>0.426<br>0.426<br>0.426<br>0.424<br>0.413<br>0.413<br>0.413<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.413<br>0.413<br>0.413<br>0.426<br>0.426<br>0.426<br>0.413<br>0.413<br>0.413<br>0.413<br>0.413<br>0.426<br>0.426<br>0.426<br>0.416<br>0.416<br>0.416<br>0.416<br>0.416<br>0.413<br>0.437<br>0.433<br>0.427<br>0.431<br>0.433<br>0.433<br>0.426<br>0.426<br>0.416<br>0.416<br>0.416<br>0.416<br>0.416<br>0.417<br>0.417<br>0.431<br>0.437<br>0.437<br>0.437<br>0.437<br>0.437<br>0.437<br>0.437<br>0.437<br>0.437<br>0.426<br>0.419<br>0.416<br>0.416<br>0.416<br>0.417<br>0.417<br>0.417<br>0.417<br>0.417<br>0.417<br>0.417<br>0.418<br>0.417<br>0.417<br>0.417<br>0.417<br>0.417<br>0.417<br>0.417<br>0.417<br>0.417<br>0.417<br>0.417<br>0.417<br>0.417<br>0.417<br>0.417<br>0.417<br>0.417<br>0.417<br>0.437<br>0.437<br>0.437<br>0.437<br>0.437<br>0.437<br>0.437<br>0.437<br>0.437<br>0.437<br>0.437<br>0.437<br>0.437<br>0.437<br>0.437<br>0.437<br>0.437<br>0.437<br>0.437<br>0.437<br>0.437<br>0.437<br>0.437<br>0.437<br>0.437<br>0.437<br>0.437<br>0.437<br>0.437<br>0.437<br>0.437<br>0.437<br>0.437<br>0.437<br>0.437<br>0.437<br>0.437<br>0.437<br>0.437<br>0.437<br>0.437<br>0.437<br>0.437<br>0.437<br>0.4399<br>0.399<br>0.395<br>0.393<br>0.375  | [01]         #         [01][20][32][34]         #         [01]         #         #         [10][16]         [01][14]         [01][14]         [01][14]         [01][16]         [01][10]         #         #         #         #         #         [01][20]         #   | [0102]<br>[0107][01.20]<br>#<br>[0107][20.01][20.09][32.07][34.01]<br>#<br>[01.04]<br>#<br>[01.04]<br>#<br>[01.04]<br>#<br>[01.04]<br>#<br>[01.05][01.05][01.06][43.01]<br>#<br>[01.05][01.06][43.01]<br>#<br>[01.05][01.06][43.01]<br>#<br>[01.05][02.01][20.03]<br>[01.05][20.01][20.03]<br>#<br>#<br>[01.05][02.01][02.07]<br>#<br>#<br>[01.05][02.01][02.07]<br>#<br>[01.05][02.01][02.07]<br>#<br>[01.05][02.01][02.07]<br>#<br>[01.05][02.01][02.07]<br>#<br>[01.05][02.01][02.07]<br>#<br>[01.05][02.01][02.07]<br>#<br>[01.05][02.01][02.07]<br>#<br>[01.05][02.01][02.07][03.07]<br>#<br>[01.05][02.01][02.07][03.07]<br>#<br>[01.05][02.01][02.07][03.07]   |
| A0080513000148<br>A008050000396<br>A008051000032<br>A008051000037<br>A008053000037<br>A0080530000170<br>A0080530000170<br>A0080530000170<br>A008052000018<br>A0080520000111<br>A008052000014<br>A0080520000111<br>A0080520000171<br>A008051000251<br>A008051000251<br>A008051000257<br>A008051000057<br>A0080510000186<br>A0080530000186<br>A0080510000186<br>A0080510000186<br>A0080510000186<br>A0080510000186<br>A0080510000186<br>A0080510000186<br>A0080510000186<br>A0080510000186<br>A0080510000186<br>A0080510000186<br>A0080510000186<br>A0080510000186<br>A0080510000186<br>A0080510000186<br>A0080510000186<br>A0080510000186<br>A0080510000186<br>A0080510000186<br>A0080510000186<br>A0080510000186<br>A0080510000186<br>A0080510000186<br>A0080510000186<br>A0080510000186<br>A0080510000186<br>A0080510000186<br>A0080510000186<br>A0080510000180<br>A0080520000176<br>A0080510000180<br>A008052000076<br>A0080510000083<br>A008053000076<br>A0080510000082<br>A008053000076<br>A008053000078<br>A008053000078<br>A008053000078<br>A008053000078<br>A008053000078<br>A008053000078<br>A008053000078<br>A008053000078<br>A008053000078<br>A008053000078<br>A008053000078<br>A008053000078<br>A008053000078<br>A008053000078<br>A008053000078<br>A008053000078<br>A008053000078<br>A008053000078<br>A008053000078<br>A008053000078<br>A008053000078<br>A008053000078<br>A008053000078<br>A008053000078<br>A008053000078<br>A008053000078<br>A008053000078<br>A008053000078<br>A008053000078<br>A008053000078<br>A008053000078<br>A008053000078<br>A008053000078<br>A008053000078<br>A008053000078<br>A008053000078<br>A008053000078<br>A008053000078<br>A008053000078<br>A008053000078<br>A008053000078<br>A008053000078<br>A008053000078<br>A008053000078<br>A008053000078<br>A008053000078<br>A008053000078<br>A008053000078<br>A008053000078<br>A008053000078<br>A008053000078<br>A008053000078<br>A008053000078<br>A008053000078<br>A00805300078<br>A008053000078<br>A008053000078<br>A008053000078<br>A00805300078<br>A008053000078<br>A008053000078<br>A008053000078<br>A008053000078<br>A008053000078<br>A008053000078<br>A008053000078<br>A00805300078<br>A008053000078<br>A008053000078<br>A00805300078<br>A008053000078<br>A008053000078<br>A008053000078<br>A008053000078<br>A008053000078<br>A008053000078<br>A008053000078<br>A008053000078<br>A008053000078<br>A008053000078<br>A008053000078<br>A008053000078<br>A008053000078<br>A008053000078<br>A008053000078<br>A008053000078<br>A008053000078<br>A008053000078<br>A008053000078<br>A008050  | Acetylonithine aminotransferase<br>Nucleoside phosphorylase<br>Predicted protein<br>Predicted   | 0.438<br>0.437<br>0.437<br>0.437<br>0.437<br>0.433<br>0.433<br>0.433<br>0.433<br>0.433<br>0.432<br>0.432<br>0.431<br>0.432<br>0.431<br>0.432<br>0.431<br>0.432<br>0.431<br>0.432<br>0.432<br>0.431<br>0.426<br>0.412<br>0.416<br>0.411<br>0.412<br>0.412<br>0.412<br>0.412<br>0.412<br>0.412<br>0.412<br>0.43<br>0.433<br>0.426<br>0.413<br>0.412<br>0.412<br>0.412<br>0.412<br>0.43<br>0.433<br>0.427<br>0.434<br>0.426<br>0.413<br>0.412<br>0.412<br>0.412<br>0.412<br>0.412<br>0.412<br>0.412<br>0.412<br>0.413<br>0.412<br>0.413<br>0.412<br>0.413<br>0.412<br>0.413<br>0.412<br>0.413<br>0.412<br>0.413<br>0.412<br>0.413<br>0.412<br>0.413<br>0.412<br>0.413<br>0.412<br>0.433<br>0.426<br>0.413<br>0.412<br>0.413<br>0.412<br>0.412<br>0.412<br>0.431<br>0.433<br>0.433<br>0.426<br>0.433<br>0.433<br>0.427<br>0.433<br>0.426<br>0.433<br>0.433<br>0.433<br>0.427<br>0.433<br>0.426<br>0.418<br>0.412<br>0.412<br>0.431<br>0.432<br>0.433<br>0.433<br>0.427<br>0.433<br>0.426<br>0.418<br>0.412<br>0.431<br>0.432<br>0.433<br>0.432<br>0.433<br>0.427<br>0.433<br>0.426<br>0.426<br>0.418<br>0.412<br>0.431<br>0.432<br>0.432<br>0.433<br>0.432<br>0.433<br>0.432<br>0.433<br>0.432<br>0.433<br>0.432<br>0.433<br>0.433<br>0.432<br>0.433<br>0.432<br>0.433<br>0.432<br>0.433<br>0.432<br>0.434<br>0.412<br>0.3399<br>0.3395<br>0.335<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.375<br>0.   | [01]         μ         [01](20](32](34)         μ         [01]         μ         μ         [01]         μ         μ         [10][16]         [01][14]         [01][14]         [01][14]         [01]         [01]         [01][02]         μ         μ         μ         [01][02]         μ <t< td=""><td>[0102]<br/>[01.07][01.20]<br/>#<br/>1<br/>[01.07][20.01][20.09][32.07][34.01]<br/>#<br/>[01.04]<br/>#<br/>[01.04]<br/>#<br/>[1001][16.03]<br/>[01.25][14.13]<br/>[01.25][14.13]<br/>[01.25][14.13]<br/>[01.25][14.13]<br/>[01.05][01.06][43.01]<br/>#<br/>#<br/>[01.05]<br/>[01.05]<br/>[01.05]<br/>[01.05][20.01][20.03]<br/>#<br/>[01.05][20.01][20.03]<br/>#<br/>[01.05][20.01][20.03]<br/>#<br/>[01.05][20.01][20.03][20.09][34.01]<br/>#<br/>[01.05][20.01][20.03][20.09][34.01]<br/>#<br/>[01.05][20.01][20.03][20.09][34.01]<br/>#</td></t<>   | [0102]<br>[01.07][01.20]<br>#<br>1<br>[01.07][20.01][20.09][32.07][34.01]<br>#<br>[01.04]<br>#<br>[01.04]<br>#<br>[1001][16.03]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.25][14.13]<br>[01.05][01.06][43.01]<br>#<br>#<br>[01.05]<br>[01.05]<br>[01.05]<br>[01.05][20.01][20.03]<br>#<br>[01.05][20.01][20.03]<br>#<br>[01.05][20.01][20.03]<br>#<br>[01.05][20.01][20.03][20.09][34.01]<br>#<br>[01.05][20.01][20.03][20.09][34.01]<br>#<br>[01.05][20.01][20.03][20.09][34.01]<br>#  |
| A0080513000148<br>A0080508000396<br>A008051000032<br>A008051000035<br>A008051000035<br>A008051000035<br>A008051000036<br>A008051000149<br>A008052000149<br>A008052000014<br>A008052000014<br>A008052000014<br>A008052000015<br>A008051000025<br>A008051000055<br>A008051000055<br>A00805100005<br>A008052000015<br>A00805100007<br>A008052000017<br>A008052000017<br>A008052000015<br>A008051000007<br>A00805100007<br>A00805100007<br>A00805100007<br>A00805100007<br>A00805100007<br>A00805100007<br>A00805100007<br>A00805100007<br>A00805100007<br>A00805100007<br>A00805100007<br>A008051000007<br>A008051000007<br>A008051000007<br>A008051000007<br>A008051000007<br>A008051000007<br>A008051000007<br>A008051000000<br>A008051000000<br>A008051000000<br>A008051000000<br>A008051000000<br>A008051000000<br>A008051000000<br>A008051000000<br>A008051000000<br>A008051000000<br>A008051000000000000000000000000000000000   | Acetylornithine aminotransferase<br>Nucleoside phosphorylase<br>Predicted protein<br>Predicted protein<br>Serine threonine protein kinase<br>Predicted protein<br>Predicted pr  | 0.438<br>0.437<br>0.437<br>0.437<br>0.437<br>0.435<br>0.434<br>0.433<br>0.433<br>0.433<br>0.432<br>0.432<br>0.432<br>0.432<br>0.432<br>0.432<br>0.431<br>0.431<br>0.43<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.419<br>0.418<br>0.412<br>0.413<br>0.412<br>0.413<br>0.412<br>0.413<br>0.412<br>0.413<br>0.412<br>0.413<br>0.412<br>0.413<br>0.412<br>0.413<br>0.412<br>0.413<br>0.412<br>0.413<br>0.412<br>0.413<br>0.413<br>0.413<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.426<br>0.431<br>0.433<br>0.433<br>0.433<br>0.433<br>0.437<br>0.433<br>0.437<br>0.436<br>0.432<br>0.431<br>0.437<br>0.436<br>0.432<br>0.436<br>0.436<br>0.437<br>0.437<br>0.437<br>0.437<br>0.437<br>0.437<br>0.437<br>0.437<br>0.437<br>0.437<br>0.437<br>0.437<br>0.437<br>0.437<br>0.437<br>0.437<br>0.437<br>0.437<br>0.437<br>0.437<br>0.437<br>0.437<br>0.437<br>0.437<br>0.426<br>0.4419<br>0.416<br>0.416<br>0.412<br>0.430<br>0.437<br>0.437<br>0.437<br>0.437<br>0.437<br>0.437<br>0.437<br>0.437<br>0.437<br>0.437<br>0.437<br>0.437<br>0.437<br>0.437<br>0.437<br>0.437<br>0.437<br>0.437<br>0.437<br>0.437<br>0.437<br>0.437<br>0.437<br>0.437<br>0.437<br>0.437<br>0.437<br>0.437<br>0.437<br>0.437<br>0.437<br>0.437<br>0.437<br>0.437<br>0.437<br>0.437<br>0.437<br>0.437<br>0.437<br>0.437<br>0.437<br>0.437<br>0.437<br>0.437<br>0.437<br>0.437<br>0.437<br>0.437<br>0.437<br>0.437<br>0.437<br>0.437<br>0.437<br>0.437<br>0.437<br>0.437<br>0.437<br>0.4399<br>0.398<br>0.395<br>0.397<br>0.377<br>0.377<br>0.377<br>0.377<br>0.377<br>0.377<br>0.377<br>0.377<br>0.377<br>0.377<br>0.377<br>0.377<br>0.377<br>0.377<br>0.377<br>0.377<br>0.377<br>0.377<br>0.377<br>0.377<br>0.377<br>0.377<br>0.377<br>0.377<br>0.377<br>0.377<br>0.37700<br>0.3770000000000   | [01]         #         [01][20][32][34]         #         [01]         #         #         [10][16]         [01][14]         [01][14]         [01][14]         [01][16]         [01][10]         #         #         #         #         [01]         [01][20]         # <t< td=""><td>[0102]<br/>[0107][01.20]<br/>#<br/>[0107][20.01][20.09][32.07][34.01]<br/>#<br/>[01.04]<br/>#<br/>[01.04]<br/>#<br/>[01.04]<br/>#<br/>[01.04]<br/>#<br/>[01.05][01.05][01.06][43.01]<br/>#<br/>[01.05][01.06][43.01]<br/>#<br/>[01.05][01.06][43.01]<br/>#<br/>[01.05][02.01][20.03]<br/>[01.05][20.01][20.03]<br/>#<br/>#<br/>[01.05][02.01][02.07]<br/>#<br/>#<br/>[01.05][02.01][02.07]<br/>#<br/>#<br/>[01.05][02.01][02.07]<br/>#<br/>#<br/>[01.05][02.01][02.07]<br/>#<br/>#<br/>#<br/>#<br/>#<br/>#<br/>#<br/>#<br/>#<br/>#<br/>#<br/>#<br/>#</td></t<>   | [0102]<br>[0107][01.20]<br>#<br>[0107][20.01][20.09][32.07][34.01]<br>#<br>[01.04]<br>#<br>[01.04]<br>#<br>[01.04]<br>#<br>[01.04]<br>#<br>[01.05][01.05][01.06][43.01]<br>#<br>[01.05][01.06][43.01]<br>#<br>[01.05][01.06][43.01]<br>#<br>[01.05][02.01][20.03]<br>[01.05][20.01][20.03]<br>#<br>#<br>[01.05][02.01][02.07]<br>#<br>#<br>[01.05][02.01][02.07]<br>#<br>#<br>[01.05][02.01][02.07]<br>#<br>#<br>[01.05][02.01][02.07]<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#  |

| AO080521000073                   | Aldo keto reductase family proteins   | 0,369  | [01][02][16][32][34]                 | [01.01][01.05][01.06][01.07][01.20]<br>[02.01][02.16][16.21][32.01][32.10] |
|----------------------------------|---|--------|--------------------------------------|--|
|                                  |   |        | ()(.=)()(.=)()                       | [34.11]<br>[01.05][01.07][01.20][02.01][32.01]                             |
| AO080521000107                   | Flavonol reductase cinnamoyl-CoA reductase  | 0.369  | [01][02][32][42]                     | [32.07][42.01]   |
| AO080567000015                   | Predicted protein   | 0.369  | #                                    | #  |
| AO080505000144                   | Predicted protein   | 0.368  | #                                    | #  |
| AO080503000326                   | Predicted protein   | 0.367  | #                                    | #  |
| AO080508000394                   | Predicted protein   | 0.366  | #                                    | #  |
| AO080515000088                   | Dehydrogenases with different specificities (related to short-chain alcohol dehydrogenases)                                 | 0.366  | [01][02][43]                         | [01.05][01.06][01.20][02.25][43.01]  |
| AO080508000236                   | Predicted protein   | 0.363  | #                                    | #  |
| AO080531000178                   | Predicted protein   | 0.362  | #                                    | #  |
| A0080522000018                   | Fatty acid desaturase   | 0,356  | [01]                                 | [01.06]  |
| AO080533000203                   | Cytochrome P450 CYP3 CYP5 CYP6 CYP9 subfamilies   | 0.355  | [01][20][32]                         | [01.06][01.20][20.01][32.05][32.07]  |
| A0080508000166                   | Synaptic vesicle transporter SVOP and related transporters (major facilitator superfamily)                                  | 0.354  | [20]                                 | [20.01]  |
| A0080541000328                   | 1-animocyciopropane-1-carboxylate synthase, and related proteins  | 0.333  | [01][30][40]<br>#                    | u  |
| A0080502000005                   | Freukteu protein<br>Endo, 1.4-heta-alueanace IV   | 0.345  |                                      | "<br>[0] 05][0] 25]  |
| A0080554000005                   | Predicted protein   | 0.338  | #                                    | #  |
|                                  |   | 01000  |                                      | 10 0110 03104 07100 011032 011   |
| AO080539000025                   | Predicted protein   | 0.332  | [10][14][20][32][42]                 | [32.07][42.25]   |
| AO080515000066                   | Permease of the major facilitator superfamily   | 0.331  | [20]                                 | [20.01][20.03][20.09]  |
| AO080523000164                   | Predicted protein   | 0.328  | [32]                                 | [32.07]  |
| AO080525000600                   | Ma <sup>2+</sup> and Ca <sup>2+</sup> transportant  | 0.325  | #                                    | #  |
| AO080530000035                   | Predicted protein   | 0.325  | #                                    | #  |
| AO080536000027                   | manD Endo-beta-mannanase  | 0.319  | [01]                                 | [0] 05]  |
| AO080541000084                   | Predicted protein   | 0.316  | [01]                                 | [01.05]  |
| AO080521000262                   | Predicted protein   | 0.314  | #                                    | #  |
| AO080525000417                   | Predicted protein   | 0.314  | #                                    | #  |
| AO080551000032                   | Predicted protein   | 0.314  | #                                    | #  |
| AO080541000430                   | Dehydrogenases with different specificities (related to short-chain alcohol dehydrogenases)                                 | 0.309  | #                                    | #  |
| AO080503000237                   | Predicted protein   | 0.308  | #                                    | #  |
| AO080525000729                   | Probable taurine catabolism dioxygenase   | 0.308  | [01]                                 | [01.02]  |
| AO080521000084                   | 2,4-dihydroxyhept-2-ene-1,7-dioic acid aldolase   | 0.302  | [01]                                 | [01.20]  |
| AO080513000199                   | Predicted protein   | 0.299  | #                                    | #  |
| AO080523000583                   | Predicted protein   | 0.299  | #                                    | #  |
| AO080523000582                   | Predicted transporter (major facilitator superfamily)   | 0.289  | [01][20][34][41]                     | [01.05][20.01][20.03][20.09][34.01]  |
|                                  | Beelf and seconds   | 0.000  |                                      | [34.11][41.01]   |
| A0080523000410                   | Predicted protein   | 0.288  | #                                    | #<br>#   |
| A0080528000012                   | n 2 <sup>+</sup> h <sup>+</sup>   | 0.285  | #                                    | #<br>#   |
| A0080532000211                   | Ca <sup>+</sup> Na antiporter<br>Debute senses with different energificities (related to short sheir cleaked debute senses) | 0.28   | #<br>[01][16]                        | "<br>[0] 05][0] 20][16 21]   |
| A0080503000406                   | Denydrogenases with different specificities (related to short-chain alconol denydrogenases)                                 | 0.276  | [01][16]                             | [01.05][01.20][16.21]  |
| A0080513000058                   | A mine acid transporters  | 0.275  | #<br>[20]                            | #<br>[20.01][20.03][20.09]   |
| A0080525000086                   | Predicted protein   | 0.274  | [20]                                 | [01.05][01.25]   |
| 110000722000000                  | r runnu protein   | 0.271  | forl                                 | [01.05][01.06][01.07][01.20][02.07]  |
| AO080508000345                   | Dehydrogenases with different specificities (related to short-chain alcohol dehydrogenases)                                 | 0.269  | [01][02][10][16][20]<br>[30][32][34] | [10.03][16.01][16.21][20.01][30.05]<br>[32.05][34.01]                      |
|                                  |   |        |                                      | [01.01][01.05][01.07][01.20][02.16]  |
| AO080549000389                   | Sorbitol dehydrogenase  | 0.269  | [01][02][16]                         | [16 17][16 21]   |
| AO080536000095                   | Predicted protein   | 0.266  | #                                    | #  |
| AO080532000017                   | Phenylpropionate dioxygenase and related ring-hydroxylating dioxygenases, large terminal subunit                            | 0.263  | #                                    | #  |
| AO080554000001                   | H <sup>+</sup> oligopeptide symporter   | 0.259  | [20]                                 | [20.01][20.03][20.09]  |
| AO080532000023                   | Predicted protein   | 0.258  | #                                    | #  |
| AO080525000588                   | 1-aminocyclopropane-1-carboxylate synthase, and related proteins  | 0.251  | [01]                                 | [01.02][01.05][01.20]  |
| AO080510000163                   | Predicted protein   | 0.244  | #                                    | #  |
| AO080541000142                   | WD40 repeat   | 0.243  | #                                    | #  |
| AO080513000202                   | Chitinase   | 0.24   | 4                                    | #  |
| AO080531000064                   | Predicted protein   | 0.24   | #                                    | #  |
| A0080531000061                   | Predicted protein   | 0.238  | #                                    | #<br>#   |
| A0080541000150<br>A0080540000222 | Predicted protein<br>Predicted protein  | 0.228  | #                                    | #<br>#   |
| A0080525000018                   | Predicted protein   | 0.224  | #                                    | #  |
| AO080532000465                   | Predicted protein   | 0.221  | #                                    | #  |
|                                  |   |        |                                      | [20.01][20.03][20.09][32.05][32.07]  |
| AO080532000197                   | Synaptic vesicle transporter SVOP and related transporters (major facilitator superfamily)                                  | 0.216  | [20][32][34]                         | [34.11]  |
| AO080530000022                   | Predicted protein   | 0.208  | #                                    | #  |
| AO080523000427                   | Permease of the major facilitator superfamily   | 0.193  | #                                    | #  |
| AO080513000203                   | Predicted protein   | 0.19   | #                                    | #  |
| AO080521000112                   | Dehydrogenases with different specificities (related to short-chain alcohol dehydrogenases)                                 | 0.172  | [01]                                 | [01.05][01.06][01.20]  |
| A0080501000148                   | Hydroxyindoie-O-methyltransferase and related SAM-dependent methyltransferases  | 0.162  | [01]                                 | [01.05][01.20]   |
| A0080501000144                   | Giutaminyi cyclase  | 0.155  | [01][14]                             | [01.01][14.07][14.13]  |
| A0080532000466                   | Predicted protein   | 0.142  | #                                    | #  |
| AO080554000025                   | Amino acid transporters   | 0.14   | [20]                                 | [20.01][20.09]   |
| AO080501000146                   | Predicted protein   | 0.136  | #                                    | #  |
| AO080501000145                   | Predicted protein   | 0.135  | #                                    | #  |
| AO080561000089                   | Endo-1,4-beta-xylanase G2   | 0.111  | [01]                                 | [01.05]  |
| AO080536000049                   | Predicted protein   | 0.0778 | #                                    | #  |
| AO080508000347                   | Dehydrogenases with different specificities (related to short-chain alcohol dehydrogenases)                                 | 0.0748 | #                                    | #  |
| AO080522000002                   | Predicted protein   | 0.0479 | #                                    | #  |
| AO080513000200                   | Predicted protein   | 0.0336 | #                                    | #  |
| A0080501000141                   | Predicted protein   | 0.0322 | #                                    | #  |

AO080501000141 Predicted protein 0.0322 # # # <sup>a</sup> FunCat (http://www.webcitation.org/getfile?fileid=be4936ae25ebb5dfb89b687842ea640f8acf7790) is the organism independent functional description of proteins. FunCat consists of 28 main functional categories (level 1). The level 1 is the most general one, whereas level 2 shows much more detail. <sup>b</sup> #: Unclassified gene <sup>c</sup> Detailed descriptions of each category are available at the MIPS Functional Catalogue Database (http://mips.helmholtz-muenchen.de/proj/funcatDB/)

# CHAPTER II Comprehensive phenotypic analysis of AoHDAC disruptants

### **II.1 ABSTRACT**

In the eukaryotic cell, HDACs play key roles in the regulation of fundamental cellular process such as development regulation, stress response, secondary metabolism and genome integrity. Thus, it was expected that AoHDAC also have divergent functions in *A. oryzae*. In the Chapter II, I provide a comprehensive phenotypic analysis using HDAC disruptants in *A. oryzae*. My study revealed that four AoHDACs, *hdaA/Aohda1*, *hdaB/Aorpd3*, *hdaD/Aohos2* and *hst4/AohstD* were involved in stress response, cell wall synthesis and chromatin integrity in *A. oryzae*. Osmotic stress sensitivity of HDAC disruptants differed between plate cultures and liquid cultures, suggesting that HDACs adapt to the difference environmental conditions. Using a common *A.oryzae* fermentation medium, rice-*koji*, I also characterized HDACs will be required for adaptation to environmental conditions and stress resistances. Because HDACs are widely conserved, my study has broad applications and may inform work with filamentous fungi and other eukaryote.

#### **II.2 INTRODUCTION**

In the past decade, the importance of HDACs have been recognized as important to multiple cellular processes, including development, stress response and genome integrity (Horio et al. 2011; Yang and Seto 2008).

The filamentous fungi are a diverse group with important economical applications, including the production of fermented foods, commercial enzymes and useful chemicals (Hoffmeister and Keller 2007; Iwashita 2002). Others are human or plant pathogens and virulence has even been reported in some filamentous fungi (Ding et al. 2010; Gacek and Strauss 2012; Pagiotti et al. 2011; Raffaele and Kamoun 2012). Recently, attention has been drawn to HDACs and their industrial applications as regulators of fungal development, conidiation, stress response and secondary metabolite production (Li et al. 2010; Shimizu et al. 2012; Tribus et al. 2010; Tribus et al. 2005). As described in introduction of Chapter I, HDACs have been suggested their role in multiple fungal processes in some filamentous fungi. Thus, AoHDACs will concern with diverse cellular processes in *A. oryzae*.

The filamentous fungus *A. oryzae* has been used for more than 1000 years in the traditional food industry and is listed as a GRAS species (i.e., generally recognized as safe) by the Food and Drug Administration in the United States. Its safety is also confirmed by the World Health Organization (Machida et al. 2008). *A. oryzae* has the ability to produce high quantities of enzymes and beneficial secondary metabolites, such as kojic acid and WYK-1 (Christensen et al. 1988; Imamura et al. 2012; Terabayashi et al. 2010). Thus, it was attractive to understand the relationship between these beneficial phenotypes of *A. oryzae* and functions of AoHDACs.

In the chapter II, I more closely examine the phenotypic expression of HDAC in A.

*oryzae*, specifically in response to several types of stress and drugs and its role in growth and production of protein in rice-*koji*.

#### **II.3 MATERIALS AND METHODS**

#### **II.3.1 Strains and media**

All *A. oryzae* strains used in the Chapter II are listed in Table I.6.1 (Kawauchi et al. 2013). N medium was used as the basic medium for all stress and drug-resistance analyses (Kawauchi et al. 2013). For rice-*koji* making, 15g  $\alpha$ -rice (70% polished *Akihikari*) was used. Distilled water suspending the conidia of disruptants was added to the  $\alpha$ -rice as 30% initial water content and 1 × 10<sup>5</sup> conidia/g  $\alpha$ -rice. The inoculum was incubated at 35 °C for 42h in 100% humidity.

#### **II.3.2 Environmental stress resistance assay**

For the stress test on plates, 1  $\mu$ l of conidia suspension (1 × 10<sup>5</sup> conidia) of each strain was point inoculated on the center of the plate and grown for five days at 30°C. N medium containing 1.6 M NaCl was used for the osmotic stress resistance test and 20mM H<sub>2</sub>O<sub>2</sub> was used for the oxidative stress resistance test. For the heat resistance test, the plate was incubated at 37°C. For hypoxic growth test, the plate was incubated in a 2% O<sub>2</sub> concentration using the Multi Gas Incubator APM-50DR (Astec, Fukuoka, Japan). After these incubations, Colony diameter was measured after the incubation period. For biomass analysis in the liquid culture, a 4 cm<sup>2</sup> plug of each strain were cut from the full-growth plate cultures and homogenized in 1 ml of suspension solution and then inoculated with 100 ml of N liquid medium containing 0.8 M NaCl. Flasks were incubated for two days at 30°C with shaking at 100 rpm. Mycelia were harvested, dried at 105°C for 1 h and weighed.

#### **II.3.3 Drug resistance test**

For drug resistance tests, conidia suspensions of each strain were point inoculated an incubated as outlined in the stress test above. The following chemicals were tested: calcofluor white (300 µg/ml), Congo red (50 µg/ml), micafungin (2 ng/ml), hydroxy urea (10 mM), camptothecin (1 µM), methyl methane sulfonate (MMS; 0.1%), tunicamycin (5 µg/ml), nocodazole (500 ng/ml), dithiothreitol (10mM), brefeldin A (5 µg/ml). Congo red, dithiothreitol, camptothecin, MMS, brefeldin A and nocodazole were purchased from Wako Chemicals (Osaka, Japan); tunicamycin were purchased from Calbiochem (La Jolla, CA, USA); and the hydroxy urea and calcofluor white were purchased from Sigma Aldrich (St. Louis, MO, USA). The micafungin (Astellas, Tokyo, Japan) was gifted. A stock solution of was prepared by dissolving 100 mg/ml calcofluor white, 10mg/ml Congo red, 1mg/ml micafungin, 1M hydroxyl urea, and 1M dithiothreitol (1M) in water. The camptothecin (10 mM), nocodazole (1 mg/ml), brefeldin A (1 mg/ml) and tunicamycin (2 mg/ml) were dissolved in dimethyl sulfoxide.

#### **II.3.4** Measurement of enzyme activity and total proteins production

Enzymes were extracted from 5 g of rice-*koji* after incubation with 25 ml acetate buffer (10 mM, pH 5.0, 0.5% NaCl) at 4°C for 3 h with shaking at 80 rpm followed by filtration. Enzyme activities of  $\alpha$ -amylase, glucoamylase and acid carboxypeptidase were measured using enzyme assay kits (Kikkoman, Chiba, Japan). Acidic protease activity was assayed according to a previous report (Iemura et al. 1999). Total protein was measured by using the Bio-Rad Protein Assay Kit II.

#### II.3.5 Measurement of N-acetylglucosamine content in rice-koji

The rice-koji (5g) was dried at 105°C for 1h, then homogenized in 12.5 ml

phosphate buffer (50 mM, pH 6.8) using physcotron (Microtec, Chiba, Japan), and centrifuged. The pellet was washed with a 10-ml phosphate buffer more than five times then suspended in a 20-ml phosphate buffer. A 2-ml of suspension was mixed with 7 ml phosphate buffer and 1 ml Yatalase (TaKaRa, Kyoto, Japan) solution (10 mg /ml in phosphate buffer). This mixture was shaking at 80rpm at 37°C for 3 h. The N-acetylglucosamine composition was determined with a pulse high-performance anion-exchange chromatography with a pulse electrochemical detector (DX500 chromatography system, Dionex, Sunnyvale, CA, USA) and an anion exchange column (Carbo PAC PA-1, 4×250 mm, Dionex) at a flow rate of 1 mL/min. Isocratic elution was performed with 16mM NaOH. The column was stabilized for 20min before injection and washed with 100mM NaOH / 600mM CH<sub>3</sub>COONa for 10 min after elution. To quantify the N-acetylglucosamine, I used N-acetyl-D (+)-glucosamine (Wako) as a standard and D-fucose as an internal standard.

#### **II.4 RESULTS**

#### **II.4.1 Stress resistance of AoHDACs**

In the previous chapter, I identified 11 HDACs homologs in *A. oryzae* genome and construct 10 AoHDAC disruptants and one AoHDAC heterokaryon disruptant as listed in Table I.6.1 (Kawauchi et al. 2013).

The osmotic, oxidative, heat and hypoxia stress tolerances of all AoHDAC disruptants were quantified to analyze the importance of HDACs in environmental adaptations (Figs. II.6.1-3). Three AoHDAC disruptants showed sensitivity against these stresses (Fig. II.6.1A, B). The  $\Delta hstD$  strain was sensitive to the osmotic stress; the hdaB/Aorpd3 heterokaryon disruptant (hdaB ht strain) showed significant sensitivity against osmotic, oxidative and heat stress; the  $\Delta hdaD$  strain showed significant sensitivity against the low oxygen and osmotic stress. These results suggest that hdaB/Aorpd3, hdaD/Aohos2 and hstD/Aohst4 are required for stress tolerance in A. oryzae.

In the liquid culture of the osmotic-stress test, I found a unique phenotype of  $\Delta h daA$  strain (Fig. II.6.1C). This strain showed significant sensitivity against osmotic stress in liquid culture, but not in plate culture. This result suggests that h daA/Aoh da1 plays a role in liquid culture specific osmotic stress response. I also found that the h daB ht and  $\Delta h daD$  strain were more osmo-sensitive in liquid culture (Fig. II.6.1C). These findings suggest that different osmotic stress resistance mechanisms between the plate and liquid culture conditions, and h daB/Aorpd3, h daA/Aoh da1 and h daD/Aohos2 will be included in these mechanisms.

#### **II.4.2 Drug (inhibitor) resistance of AoHDAC disruptants**

I examined AoHDAC disruptants' resistance to several chemicals on plate culture and, at first, the cell wall integrity was tested using cell wall synthesis inhibitors (Figs. II.6.4-5). The *hdaB ht* strain was significantly sensitive to micafungin, a  $\beta$ -1,3-glucan synthesis inhibitor (Free 2013). The deletion of *hdaD/Aohos2* showed the greatest sensitivity against the calcofluor white, which is a chitin synthesis inhibitor. The  $\Delta hstA$ strain also showed the slight sensitivity to calcofluor white (Fig. II.6.4.5). These results suggest that there is variation in how different AoHDACs affect cell wall integrity, and *hdaB/Aorpd3* and *hdaD/Aohos2* will be concerned with these mechanisms.

HDACs are also relevant to genome integrity (Huertas et al. 2009); thus, I examined the genotoxin tolerances of all AoHDAC disruptants (Figs. II.6.6-7). As expected, the *hdaB ht*,  $\Delta hdaD$  and  $\Delta hstD$  strains showed defects against methyl methane sulfonate, which methylates DNA predominantly on N7-deoxyguanosine and N3-deoxyadenosine and is believed to cause double-stranded DNA breaks. Additionally, the  $\Delta hstD$  strain showed the strongest sensitivity to camptothecin, a topoisomerase inhibitor. These results suggested *hdaB/Aorpd3*, *hdaD/Aohos2* and *hstD/Aohst4* are involved in genome integrity.

No obvious sensitivity to protein secretion inhibitors was observed when tested dithiothreitol, tunicamycin or brefeldin A (Fig. II.6.8). A slight sensitivity was observed with nocodazole, which depolymerizes microtubules, in the  $\Delta hstD$  and hdaB ht strain.

#### II.4.3 Effect of AoHDACs disruption on the rice-koji

A distinctive feature of the *koji* fermentation process is the use of solid-state culture where *A. oryzae* is grown on steamed cereals such as rice and soybean. The resulting material contains abundant hydrolytic enzymes and metabolites that are

important for the quality of the final products (Kitamoto 2002). I analyzed the effect of AoHDACs disruption on the growth and protein production of rice-*koji* (Figs. II.6.9-10).

It is difficult to separate the mycelia from rice-*koji* to measure exact fungal biomass, so instead I measured N-acetylglucosamine, which has been shown strongly correlated with biomass (Arima and Uozumi 1967). I found significant decreases in N-acetylglucosamine on rice-*koji* made by the *hdaB ht* and *ΔhdaD* strains (Fig. II.6.9A). The *ΔhdaA* strain also decreased N-acetylglucosamine, but the results were not significant. The disruptant strains also decreased total protein production, but enzyme activity differed by disruptant (Fig. II.6.9B, C). The *hdaB ht* strain showed significant decreases in all measured enzyme activity, while the *ΔhdaA* and *ΔhdaD* strains only showed a significant decrease in glycoside hydrolase activity and a slight increased acid carboxypeptidase activity. In these strains, the low glycoside hydrolase productivity or growth defect might cause low protein productivity. Compared with these three strains, the *ΔhstD* strain showed no decrease in N-acetylglucosamine but had lowered protein production. I also found significant decreased in glycoside hydrolase and acid protease. These results suggest that *hstD/Aohst4* can affect many types of protein production even when it does not affect growth.

#### **II.5 DISCUSSION**

HDACs play diverse roles in higher eukaryote development, stress response, and genome integrity (Horio et al. 2011; Yang and Seto 2008). In some filamentous fungi, HDACs are important to growth, conidia formation, and secondary metabolism (Brosch et al. 2008). The results of ChapterII strongly suggest that functional divergence of HDACs in *A. oryzae* with important industrial implications for HDAC deletion.

The modes of development and enzyme production in *A. oryzae* are significantly different when it grows in solid-state or liquid culture conditions (Biesebeke et al. 2002). This supports recent omics studies of *A. oryzae* that revealed how the transcriptome and proteome were altered depending on culture type (Oda et al. 2006; Wang et al. 2010). However, a detailed molecular investigation is needed to understand the underlying mechanisms.

HDACs widely affected gene expression through the structural modification of chromatin by the deacetylation of histones. I found phenotypic differences between disruptants grown on the liquid culture as opposed to the plate culture. The  $\Delta h daA$  strain did not show any significant effect against osmotic stress on the plate culture, but an obvious defect was observed in liquid culture. Additionally, the h daB ht strain and  $\Delta h daD$  strains had a more sensitive phenotypic response to osmotic stress in the liquid culture on the osmotic adaptation and these three HDACs would play a role in the adaptation mechanisms in *A. oryzae*.

I also found a significant decrease in the amount of N-acetylglucosamine in rice-*koji* produced by the *hdaB ht*,  $\Delta hdaD$  and  $\Delta hdaA$  strains. N-acetylglucosamine is a key constituent saccharide of chitin, the major glycan composing fungal cell walls and a

good surrogate for measuring fungal growth on rice-*koji* (Arima and Uozumi 1967). The lack of growth effects in these three HDACs in the solid-state cultures suggests the importance of the role of other compounds stabilizing the fungal cell wall. In this experiment I only measured the amount of N-acetylglucosamine whereas fungal cell walls also contain  $\beta$ - and  $\alpha$ -1,3-glucan, chitin and galactomannan (Latgé 2010). Thus, it is not clear whether the disruption of *hdaB/Aorpd3* and *hdaD/Aohos2* affects the overall glycan construction of cell wall. Future work should examine the detailed role of AoHDACs on the cell wall synthesis mechanisms and the relationship of AoHDAC disruption to fungal biomass.

The *hstD/AoHst4* HDAC has been phylogenetically classified in the fungal specific sirtuin class but its function is still poorly understood (Frye 2000). I indicated that *hstD/Aohst4* coordinates fungal specific phenotypes of secondary metabolite production and conidia formation and a separate study using *S. cerevisiae*, found that *hst4* (a homolog of *hstD* in *A.oryzae*) was important for genome integrity and resistance to genotoxin (Kawauchi et al. 2013; Miller et al. 2006). In my work, I reveal an additional function. The deletion of *hstD/Aohst4* led to MMS- and CPT-sensitive phenotypes suggests that this family of proteins plays a conserved role in the genome integrity among fungi.

I also found a novel effect on enzyme production in rice-*koji* produced by the disruptant strains. The  $\Delta hstD$  strain decreased enzyme production despite the growth of mycelia being unchanged. This was surprising because, in general, alteration of the protein secretion pathway affects filamentous growth of *A. oryzae* (Shoji et al. 2008). The lack of sensitive phenotypes when I tested protein secretion pathway inhibitors suggests that *hstD/Aohst4* may not affect the protein secretion pathway. In general,

HDACs affect transcriptional regulation, so it is possible *hstD/Aohst4* affects extracellular enzyme expression. This would have significant industrial applications and future work should investigate the expression, histone modification and chromatin structure of these genes.

This work reveals novel phenotypes of four AoHDAC disruptants in *A. oryzae*: *hdaA/Aohda1, hdaB/Aorpd3, hdaD/Aohos2,* and *hstD/Aohst4* with diverse cellular process that include stress response, cell wall synthesis, protein secretion, and genome integrity. Because HDACs are highly conserved among filamentous fungi and other eukaryote, my study is broadly applicable to understanding the function of HDACs.

#### **II.6 FIGURES**





(A) Morphological phenotypes of disruptants on stress plate culture on day five. (B) Comparison of stress sensitivity on plate culture. Graphs represent radial growth relative to the no-stress plate culture (corresponding to 1.0). (C) Comparison of osmotic stress sensitivity on liquid culture. Graphs represent mycelia dry weight relative to the no-stress liquid culture (corresponding to 1.0). The *adeA*<sup>+</sup> strain was used as a control in this figure. All data are represented as means  $\pm$  s.d. (n=3); \* p < 0.05, t-test.



Figure II.6.2. Phenotypes of AoHDAC disruptants on stress plate culture at day five.

The  $adeA^+$  strain was used as a control.



Figure II.6.3. Stress sensitivity test of AoHDAC disruptants.

(A) Comparison of stress sensitivity on plate culture. Graphs represent radial growth relative to the no stress plate culture (corresponding to 1.0). (B) Comparison of osmotic stress sensitivity on liquid culture. Graphs represent mycelia dry weight relative to the no stress liquid culture (corresponding to 1.0). The *adeA*<sup>+</sup> strain was used as a control. All data are represented as means  $\pm$  s.d. (n=3); \* p < 0.05, t-test.



Figure II.6.4. Cell wall synthesis inhibitor sensitivity of AoHDAC disruptants. (A) Morphological phenotypes of indicated strain on cell wall synthesis inhibitor treated culture on day five. (B) Comparison of inhibitors sensitivity on plate culture. Graphs represent radial growth relative to the plate culture lacking an inhibitor (corresponding to 1.0). The *adeA*<sup>+</sup> strain was used as a control. All data are represented as means  $\pm$  s.d. (n=3); \* p < 0.05, t-test. Abbreviations: CFW, calcofluor white; CR, Congo red; MF, micafungin.



## Figure II.6.5. Cell wall synthesis inhibitor sensitivity of AoHDAC disruptants.

(A) Morphological phenotypes of indicated strain on cell wall synthesis inhibitor treated culture on day five. (B) Comparison of inhibitor sensitivity on plate culture. Graphs represent radial growth relative to the plate culture lacking an inhibitor (corresponding to 1.0). The *adeA*<sup>+</sup> strain was used as a control. All data are represented as means  $\pm$  s.d. (n=3); \* *p* < 0.05, t-test. Abbreviations: CFW, calcofluor white; CR, Congo red; MF, micafungin.


### Figure II.6.6. Genotoxin sensitivity of AoHDAC disruptants.

(A) Morphological phenotypes of indicated strain on genotoxin treated culture. The picture of 5 days colony was shown. (B) Comparison of genotoxin sensitivity on plate culture. In order to minimize the effect of different growth on no genotoxin treated plate culture among the strain, each graph represent relative radial growth to that on no genotoxin treated plate culture (corresponding to 1.0). The *adeA*<sup>+</sup> strain was used as a control in this figure. All data are represented as means  $\pm$  s.d. (n=3); \* *p* < 0.05, t-test. Abbreviations: HU, hydroxy urea; CPT, Camptothecin; MMS, Methyl methane sulfonate.



## Figure II.6.7. Genotoxin sensitivity of AoHDAC disruptants.

(A) Morphological phenotypes of indicated strain on cell wall synthesis genotoxin treated culture on day five. (B) Comparison of inhibitors sensitivity on plate culture. Graphs represent radial growth relative to the no genotoxin treated plate culture (corresponding to 1.0). The  $adeA^+$  strain was used as a control. All data are represented as means  $\pm$  s.d. (n=3); \* p < 0.05, t-test. Abbreviations: HU, hydroxy urea; CPT, camptothecin; MMS, methyl methane sulfonate.







### Figure II.6.9 Phenotypes of AoHDACs on rice-koji.

(A) N-acetylglucosamine amounts in rice-*koji*. (B) Total protein equivalent in rice-*koji*. (C) Activity of enzymes in rice-*koji*. Enzyme activities represented as the activity relative to the control strain (corresponding to 1.0). The  $adeA^+$  strain functions as a control. All data are represented as means  $\pm$  s.d. (n=3); \* p < 0.05, t-test.





(A) N-acetylglucosamine amounts in rice-*koji*. (B) Total protein equivalent in rice-*koji*. (C) Activity of indicated enzyme in rice-*koji*. Enzyme activities represent activity relative to the  $adeA^+$  control strain (corresponding to 1.0). All data are represented as means  $\pm$  s.d. (n=3); \* p < 0.05, t-test.

## **CONCLUSION REMARKS**

HDACs are concerned with multiple cellular process (Horio et al. 2011; Yang and Seto 2008), and the importance of the role of classical HDACs in the regulation of filamentous fungal phenotypes has been appreciated during the past decade (Brosch et al. 2008). While the molecular biology of *A. oryza*e has been widely studied because of its industrial importance in many fields (Machida et al. 2008), an investigation of its epigenetic regulation has yet to be performed. In this work, we showed the diverse functions of AoHDACs.

In the Chapter I, I identified 11 AoHDACs and constructed these disruptants. In the case of *hdaB/Aorpd3* disruption, we only obtained a heterokaryon disruptant, suggested that *hdaB/Aorpd3* is essential in *A. oryzae*. The *hdaD/Aohos2* and *hstD/Aohst4* disruptants were shown to have defective conidia formation and to produce high levels of the SM kojic acid. The *hstD/Aohst4* was also found to coordinate secondary metabolism and development through the regulation of *laeA*, which is a key coordinator in filamentous fungi. The *hstD/Aohst4* gene is fungal-specific and is conserved throughout the filamentous fungi. It also has great potential to be a target for the improvement of SM productivity, and could be useful in the development of an attractive host for the production of heterogeneous metabolites.

In the Chapter II, we also examine the various kinds of phenotypes included stress resistance, drug resistance, and rice-*koji* making using these AoHDAC disruptant. As the result, I suggest that 4 AoHDACs named *hdaA/Aohda1*, *hdaB/Aorpd3*, *hdaD/Aohos2*, and *hstD/Aohst4* will relate diverse cellular process such as stress

response, cell wall synthesis, protein secretion, and genome integrity.

To my knowledge, this is the first study of *A. oryzae* HDACs, and also the first comprehensive analysis of HDACs in filamentous fungi. This work will be of great value in helping to understand HDACs in all filamentous fungi because of the high level of HDAC conservation. It will also contribute to the improvement of SMs and enzymes production of filamentous fungi, and the development of drugs against pathogenic filamentous fungi.

## AKNOWLEDGEMENTS

I would like to express my hearty thanks to vice director Kazuhiro Iwashita, National Research Institute of Brewing (NRIB), for his invaluable suggestion and encouragement throughout this work

I am indebted to my committee members, Vice director Kazuhiro Iwashita, Researcher Ken Oda, Director Nami Goto, Senior Researcher Atsuko Isogai, Senior Researcher Ken Akao, Director Osamu Yamada, Director Hisashi Fukuda, NRIB.

I am grateful to Professor Katsuhiko Kitamoto at Tokyo University for gifting *A*. *oryzae* NSR-ΔLD2 strain and Associate Professor Masatoshi Goto at Kyushu University for gifting micafungin.

I am also grateful to Professor Hitoshi Shimoi, Iwate University, Assistant Professor Daisuke Watanabe, at Nara Institute of Science and Technology, Assistant Professor Masafumi Tokuoka, Tokyo University of Agriculture, Dr. Toru Takahashi, Gifu Shellac MFG, Ms. Mika Nishiura at Nippon Maruten Shouyu Co. Ltd., and all the member of my laboratory.

Finally, I would like to be deeply grateful to all my families and my friends for their continuous encouragement and behind-the-scenes support.

## REFERENCE

Abe K, Gomi K, Hasegawa F, Machida M (2006) Impact of *Aspergillus oryzae* genomics on industrial production of metabolites. *Mycopathologia* **162**:143-153

Arima K, Uozumi T (1967) A new method for estimation of the mycelial weight in *koji. Agri. Biol. Chem.* **31**:119-123

Arnaud MB, Chibucos MC, Costanzo MC, Crabtree J, Inglis DO, Lotia A, Orvis J, Shah P, Skrzypek MS, Binkley G, Miyasato SR, Wortman JR, Sherlock G (2010) The *Aspergillus* Genome Database, a curated comparative genomics resource for gene, protein and sequence information for the *Aspergillus* research community. *Nucleic Acids Res.* **38**:D420-427

Baidyaroy D, Brosch G, Ahn J-h, Graessle S, Wegener S, Tonukari NJ, Caballero O, Loidl P, Walton JD (2001) A gene related to yeast HOS2 histone deacetylase affects extracellular depolymerase expression and virulence in a plant pathogenic fungus. *Plant Cell* **13**:1609-1624

Bayram Ö, Braus GH (2012) Coordination of secondary metabolism and development in fungi: the velvet family of regulatory proteins. *FEMS Microbiol. Rev.* **36**:1-24

Biesebeke R, Ruijter G, Rahardjo YSP, Hoogschagen MJ, Heerikhuisen M, Levin A, Driel KGA, Schutyser MAI, Dijksterhuis J, Zhu Y, Weber FJ, Vos WM, Hondel KAMJJ, Rinzema A, Punt PJ (2002) *Aspergillus oryzae* in solid-state and submerged fermentations. *FEMS Yeast Res.* **2**:245-248

Borkovich KA, Alex LA, Yarden O, Freitag M, Turner GE, Read ND, Seiler S, Bell-Pedersen D, Paietta J, Plesofsky N, Plamann M, Goodrich-Tanrikulu M, Schulte U, Mannhaupt G, Nargang FE, Radford A, Selitrennikoff C, Galagan JE, Dunlap JC, Loros JJ, Catcheside D, Inoue H, Aramayo R, Polymenis M, Selker EU, Sachs MS, Marzluf GA, Paulsen I, Davis R, Ebbole DJ, Zelter A, Kalkman ER, O'Rourke R, Bowring F, Yeadon J, Ishii C, Suzuki K, Sakai W, Pratt R (2004) Lessons from the genome sequence of *Neurospora crassa*: tracing the path from genomic blueprint to multicellular organism. *Microbiol. Mol. Biol. Rev.* **68**:1-108

Brakhage AA (2013) Regulation of fungal secondary metabolism. *Nat. Rev. Microbiol.* **11**:21-32

Brosch G, Loidl P, Graessle S (2008) Histone modifications and chromatin dynamics: a focus on filamentous fungi. *FEMS Microbiol. Rev.* **32**:409-439

Cairns BR (2009) The logic of chromatin architecture and remodelling at promoters. *Nature* **461**:193-198

Christensen T, Woeldike H, Boel E, Mortensen SB, Hjortshoej K, Thim L, Hansen MT (1988) High level expression of recombinant genes in *Aspergillus oryzae. Nat. Biotechol.* **6**:1419-1422

Ding S-L, Liu W, Iliuk A, Ribot C, Vallet J, Tao A, Wang Y, Lebrun M-H, Xu J-R (2010) The *tig1* histone deacetylase complex regulates infectious growth in the rice blast fungus *Magnaporthe oryzae*. *Plant Cell* **22**:2495-2508

D'Arcy S, Luger K (2011) Understanding histone acetyltransferase *Rtt109* structure and function: how many chaperones does it take? *Curr. Opin. Struct. Biol.* **21**:728-734

Ekwall K (2005) Genome-wide analysis of HDAC function. *Trends Genet*. **21**:608-615

Free SJ (2013) Chapter Two - Fungal Cell Wall Organization and Biosynthesis. P.32-82 In: Freedman T, Dunlap JC, Goodwin SF(ed.) *Adv. Genet.*, vol. 81. Academic Press, Waltham, MA

Frye RA (2000) Phylogenetic classification of prokaryotic and eukaryotic *Sir2*-like proteins. *Bioche. Biophys. Res. Commun.* **273**:793-798

Gacek A, Strauss J (2012) The chromatin code of fungal secondary metabolite gene clusters. *Appl. Microbiol. Biotech.* **95**:1389-1404

Gregoretti I, Lee Y-M, Goodson HV (2004) Molecular evolution of the histone deacetylase family: Functional implications of phylogenetic analysis. *J. Mol. Biol.* **338**:17-31

Hoffmeister D, Keller NP (2007) Natural products of filamentous fungi: enzymes, genes, and their regulation. *Nat. Prod. Rep.* **24**:393-416

Horio Y, Hayashi T, Kuno A, Kunimoto R (2011) Cellular and molecular effects of sirtuins in health and disease. *Clin. Sci.(Lond.)* **121**:191-203

Huertas D, Sendra R, Muñoz P (2009) Chromatin dynamics coupled to DNA repair. *Epigenetics* **4**:31-42

Iemura Y, Yamada T, Takahashi T, Furukawa K, Hara S (1999) Properties of the peptides liberated from rice protein in *Sokujo-moto*. *J. Biosci. Bioeng.* **88**:276-280

Imai S-i, Guarente L (2010) Ten years of NAD-dependent SIR2 family deacetylases: implications for metabolic diseases. *Trends. Pharmacol. Sci.* **31**:212-220

Imamura K, Tsuyama Y, Hirata T, Shiraishi S, Sakamoto K, Yamada O, Akita O, Shimoi H (2012) Identification of a gene involved in the synthesis of a Dipeptidyl Peptidase IV Inhibitor in *Aspergillus oryzae*. *Appl. Environ. Microbiol.* **78**:6996-7002

Iwashita K (2002) Recent studies of protein secretion by filamentous fungi. J. Biosci. Bioeng. 94:530-535

Izawa M, Takekawa O, Arie T, Teraoka T, Yoshida M, Kimura M, Kamakura T

(2009) Inhibition of histone deacetylase causes reduction of appressorium formation in the rice blast fungus *Magnaporthe oryzae*. J. Gen. Appl. Microbiol. **55**:489-498

Jin FJ, Takahashi T, Matsushima K, Hara S, Shinohara Y, Maruyama J, Kitamoto K, Koyama Y (2011) SclR, a basic helix-loop-helix transcription factor, regulates hyphal morphology and promotes sclerotial formation in *Aspergillus oryzae. Eukaryotic Cell* **10**:945-955

Kawauchi M, Nishiura M, Iwashita K (2013) Fungal-specific sirtuin HstD coordinates secondary metabolism and development through control of LaeA. *Eukaryotic Cell* **12**:1087-1096

Kelly DE, Kraševec N, Mullins J, Nelson DR (2009) The CYPome (Cytochrome P450 complement) of *Aspergillus nidulans*. *Fungal Genet*. *Biol*. **46**:S53-S61

Kitamoto K (2002) Molecular biology of the Koji molds. p. 129-153, *Adv. Appl. Microbiol.*, vol. 51. Academic Press, Waltham, MA

Latgé J-P (2010) Tasting the fungal cell wall. Cell. Microbiol. 12:863-872

Lee I, Oh J-H, Keats Shwab E, Dagenais TRT, Andes D, Keller NP (2009) *HdaA*, a class 2 histone deacetylase of *Aspergillus fumigatus*, affects germination and secondary metabolite production. *Fungal Genet. Biol.* **46**:782-790

Li Y, Wang C, Liu W, Wang G, Kang Z, Kistler HC, Xu J-R (2010) The *HDF1* histone deacetylase gene is important for conidiation, sexual reproduction and pathogenesis in *Fusarium graminearum*. *Mol. Plant Microbe Interact.* **24**:487-496

Machida M, Yamada O, Gomi K (2008) Genomics of *Aspergillus oryzae*: Learning from the history of *koji* mold and exploration of its future. *DNA Res.* **15**:173-183

Marui J, Ohashi-Kunihiro S, Ando T, Nishimura M, Koike H, Machida M (2010) Penicillin biosynthesis in *Aspergillus oryzae* and its overproduction by genetic engineering. J. Biosci. Bioeng. 110:8-11

Maruyama J, Kitamoto K (2008) Multiple gene disruptions by marker recycling with highly efficient gene-targeting background ( $\Delta ligD$ ) in Aspergillus oryzae. Biotech. Lett. **30**:1811-1817

Miller K, Maas N, Toczyski D (2006) Taking it off: regulation of H3 K56 acetylation by *Hst3* and *Hst4*. *Cell Cycle* **5**:2561-2565

Nishida H (2009) Evolutionary conservation levels of subunits of histone-modifying protein complexes in fungi. *Comp. Funct. Genomics.* **2009**:379317

Oda K, Kakizono D, Yamada O, Iefuji H, Akita O, Iwashita K (2006) Proteomic analysis of extracellular proteins from *Aspergillus oryzae* grown under submerged and solid-state culture conditions. *Appl. Environ. Microbiol.* **72**:3448-3457

Oda K, Kobayashi A, Ohashi S, Sano M (2011) *Aspergillus oryzae laeA* regulates kojic acid synthesis genes. *Biosci. Biotechnol. Biochem.* **75**:1832-1834

Pagiotti R, Angelini P, Rubini A, Tirillini B, Granetti B, Venanzoni R (2011) Identification and characterisation of human pathogenic filamentous fungi and susceptibility to *Thymus schimperi* essential oil. *Mycoses* **54**:e364-e376

Podust LM, Sherman DH (2012) Diversity of P450 enzymes in the biosynthesis of natural products. *Nat. Prod. Rep.* **29**:1251-1266

Priebe S, Linde J, Albrecht D, Guthke R, Brakhage AA (2011) FungiFun: a web-based application for functional categorization of fungal genes and proteins. *Fungal Genet. Biol.* **48**:353-358

Quevillon E, Silventoinen V, Pillai S, Harte N, Mulder N, Apweiler R, Lopez R (2005) InterProScan: protein domains identifier. *Nucleic Acids Res.* **33**:W116-120

Raffaele S, Kamoun S (2012) Genome evolution in filamentous plant pathogens:

why bigger can be better. Nat. Rev. Microbiol. 10:417-430

Ruepp A, Zollner A, Maier D, Albermann K, Hani J, Mokrejs M, Tetko I, Güldener U, Mannhaupt G, Münsterkötter M, Mewes HW (2004) The FunCat, a functional annotation scheme for systematic classification of proteins from whole genomes. *Nucleic Acids Res.* **32**:5539-5545

Sanchez JF, Somoza AD, Keller NP, Wang CCC (2012) Advances in *Aspergillus* secondary metabolite research in the post-genomic era. *Nat. Prod. Rep.* **29**:351-371

Shahbazian MD, Grunstein M (2007) Functions of site-specific histone acetylation and deacetylation. *Annu. Rev. Biochem.* **76**:75-100

Shimizu M, Masuo S, Fujita T, Doi Y, Kamimura Y, Takaya N (2012) Hydrolase controls cellular NAD, sirtuin and secondary metabolites. *Mol. Cell. Biol.* **32**:3743-3755

Shoji J, Arioka M, Kitamoto K (2008) Dissecting cellular components of the secretory pathway in filamentous fungi: insights into their application for protein production. *Biotech. Lett.* **30**:7-14

Shwab EK (2007) Histone deacetylase activity regulates chemical diversity in *Aspergillus. Eukaryotic Cell* **6**:1656-1664

Smith K, Kothe G, Matsen C, Khlafallah T, Adhvaryu K, Hemphill M, Freitag M, Motamedi M, Selker E (2008) The fungus *Neurospora crassa* displays telomeric silencing mediated by multiple sirtuins and by methylation of histone H3 lysine 9. *Epigenetics Chromatin* **1**:5

Smith KM, Dobosy JR, Reifsnyder JE, Rountree MR, Anderson DC, Green GR, Selker EU (2010) H2B- and H3-specific histone deacetylases are required for DNA methylation in *Neurospora crassa. Genetics* **186**:1207-1216

Szewczyk E, Nayak T, Oakley CE, Edgerton H, Xiong Y, Taheri-Talesh N,

Osmani SA, Oakley BR (2007) Fusion PCR and gene targeting in *Aspergillus nidulans*. *Nat. Protoc.* **1**:3111-3120

Tamura K, Peterson D, Peterson N, Stecher G, Nei M, Kumar S (2011) MEGA5: Molecular Evolutionary Genetics Analysis using maximum likelihood, evolutionary distance, and maximum parsimony methods. *Mol. Biol. Evol.* **28**:2731-2739

Terabayashi Y, Sano M, Yamane N, Marui J, Tamano K, Sagara J, Dohmoto M, Oda K, Ohshima E, Tachibana K, Higa Y, Ohashi S, Koike H, Machida M (2010) Identification and characterization of genes responsible for biosynthesis of kojic acid, an industrially important compound from *Aspergillus oryzae*. *Fungal Genet. Biol.* **47**:953-961

Tribus M, Bauer I, Galehr J, Rieser G, Trojer P, Brosch G, Loidl P, Haas H, Graessle S (2010) A novel motif in fungal Class 1 histone deacetylases is essential for growth and development of *Aspergillus*. *Mol. Biol. Cell* **21**:345-353

Tribus M, Galehr J, Trojer P, Brosch G, Loidl P, Marx F, Haas H, Graessle S (2005) *HdaA*, a major class 2 histone deacetylase of *Aspergillus nidulans*, affects growth under conditions of oxidative stress. *Eukaryotic Cell* **4**:1736-1745

Wang B, Guo G, Wang C, Lin Y, Wang X, Zhao M, Guo Y, He M, Zhang Y, Pan L (2010) Survey of the transcriptome of *Aspergillus oryzae* via massively parallel mRNA sequencing. *Nucleic Acids Res.* **38**:5075-5087

Yamada O, Na Nan S, Akao T, Tominaga M, Watanabe H, Satoh T, Enei H, Akita O (2003) *dffA* gene from *Aspergillus oryzae* encodesl-ornithineN5-oxygenase and is indispensable for deferriferrichrysin biosynthesis. *J. Biosci. Bioeng.* **95**:82-88

Yang B, Miller A, Kirchmaier AL (2008) HST3/HST4-dependent deacetylation of lysine 56 of histone H3 in silent chromatin. *Mol. Biol. Cell.* **19**:4993-5005

Yang X-J, Seto E (2008) The *Rpd3/Hda1* family of lysine deacetylases: from bacteria and yeast to mice and men. *Nat. Rev. Mol. Cell. Biol.* **9**:206-218

Zhang T, Kraus WL (2010) SIRT1-dependent regulation of chromatin and transcription: Linking NAD<sup>+</sup> metabolism and signaling to the control of cellular functions. *Biochim. Biophys. Acta* **1804**:1666-1675

## **RELATED PUBLICATION**

- Fungus-specific sirtuin HstD coordinates secondary metabolism and development through control of LaeA.
  <u>Morivuki Kawauchi</u>, Mika Nishiura, Kazuhiro Iwashita Eukaryotic Cell, **12** (8), 1087-1096 (2013).
- (2) Functional analysis of histone deacetylase and its role in stress response, drug resistance and solid-state cultivation in *Aspergillus oryzae*.

Moriyuki Kawauchi, Kazuhiro Iwashita

Journal of Bioscience and Bioengineering, **118** (2), 172-176 (2014)



- Fungus-specific sirtuin HstD coordinates secondary metabolism and development through control of LaeA.
  Moriyuki Kawauchi, Mika Nishiura and Kazuhiro Iwashita Eukaryotic Cell, **12** (8), 1087-1096 (2013).
- (2) Functional analysis of histone deacetylase and its role in stress response, drug resistance and solid-state cultivation in *Aspergillus oryzae.* Moriyuki Kawauchi and Kazuhiro Iwashita

Journal of Bioscience and Bioengineering, 118(2), 172-176 (2014)



## Fungus-Specific Sirtuin HstD Coordinates Secondary Metabolism and Development through Control of LaeA

#### Moriyuki Kawauchi,<sup>a,b</sup> Mika Nishiura,<sup>a,b</sup> Kazuhiro Iwashita<sup>a,b</sup>

Department of Molecular Biotechnology, Graduate School of Advanced Science of Matter, Hiroshima University, Kagamiyama, Higashi-Hiroshima, Hiroshima, Japan<sup>a</sup>; National Research Institute of Brewing, Higashi-Hiroshima, Hiroshima, Japan<sup>b</sup>

The sirtuins are members of the NAD<sup>+</sup>-dependent histone deacetylase family that contribute to various cellular functions that affect aging, disease, and cancer development in metazoans. However, the physiological roles of the fungus-specific sirtuin family are still poorly understood. Here, we determined a novel function of the fungus-specific sirtuin HstD/Aspergillus oryzae Hst4 (AoHst4), which is a homolog of Hst4 in *A. oryzae* yeast. The deletion of all histone deacetylases in *A. oryzae* demonstrated that the fungus-specific sirtuin HstD/AoHst4 is required for the coordination of fungal development and secondary metabolite production. We also show that the expression of the *laeA* gene, which is the most studied fungus-specific coordinator for the regulation of secondary metabolism and fungal development, was induced in a  $\Delta hstD$  strain. Genetic interaction analysis of *hstD*/*Aohst4* and *laeA* genes are fungus specific but conserved in the vast family of filamentous fungi. Thus, we conclude that the fungus-specific sirtuin HstD/AoHst4 coordinates fungal development and secondary metabolism via the regulation of LaeA in filamentous fungi.

istone acetylation plays key roles in the control of chromatin structure and function (1). The acetylation state is controlled by two histone modification enzymes with opposing actions, histone acetyltransferases (HATs) and deacetylases (HDACs). Acetylation is generally associated with transcriptional activation. In contrast, histone deacetylation is generally associated with transcriptional repression. These enzymes are highly conserved from yeasts to humans, and they are also conserved in filamentous fungi (2–5).

HDACs remove the acetyl moiety from the lysine residue of a histone tail. In addition to histones, these enzymes deacetylate many nonhistone substrates (6). Protein deacetylation affects diverse cellular processes, such us development, metabolism, and stress responses in eukaryotic cells (6). In mammalian and yeast cells, HDACs are divided into two major families called the sirtuins and the classical HDACs. The HDACs are phylogenetically classified into four classes. The sirtuins constitute class III, and the classical HDACs are grouped into classes I, II, and IV (4, 6). Except for mammal-specific class IV HDACs, these enzymes are also conserved in the genome of filamentous fungi (2, 5).

Recently, histone deacetylases in some filamentous fungi have been investigated for their role in the regulation of histone modification, developmental processes, stress resistance, pathogenesis, metabolism, and other such processes (2, 7–10). For example, the homolog of yeast Rpd3 is required for growth and conidiation in several filamentous fungi (11). The class II HDAC HdaA/*Aspergillus fumigatus* Hda1 (AfHda1), a homolog of yeast Hda1, is involved in germination and the oxidative stress response in *Aspergillus fumigatus* (12, 13). The yeast Hos2 homolog is required for conidial development, invasive growth, and the production of virulence factors in some plant-pathogenic filamentous fungi (7, 8, 14).

Filamentous fungi produce wide varieties of secondary metabolites (SMs), which are small bioactive molecules that include both beneficial medicines and cosmetics and toxins that are harmful for animals and plants (15, 16). Therefore, because of the importance of fungal SMs, there has been much research into the mechanisms that regulate their production. LaeA, a putative fungus-specific methyltransferase, is implicated in the global regulation of SM production (16, 17). LaeA also has an important role in coordinating fungal development and SM production (17). Recent studies have shown that histone modification plays key roles in the regulation of SM biosynthetic gene expression (18). In *Aspergillus nidulans*, the HDACs HdaA/*Aspergillus nidulans* Hda1 (AnHda1) and SirA/*A. nidulans* Sir2 (AnSir2) regulate carcinogenic sterigmatocystin and production of the antibiotic penicillin (19, 20). The loss of Hdf1/*Fusarium graminearum* Hos2 (FgHos2) reduces conidial development and the production of deoxynivalenol, which is the most characterized virulence factor in *Fusarium graminearum* (7).

However, the importance of fungal HDACs in the regulation of secondary metabolism and fungal development is still not known; studies of these HDACs are limited, even though several types of HDACs are found in fungal genomes (2). Moreover, the relationship between the global regulator *laeA* and histone modification is still poorly understood.

In this study, we examined the phenotypes caused by the disruption of all HDACs using *Aspergillus oryzae*, which is an important filamentous fungus in industry and has potential for the production of pharmaceutical and cosmetic SMs (21–23). Our observations indicated that the fungus-specific sirtuin HstD/ *Aspergillus oryzae* Hst4 (AoHst4) regulates conidial development

Received 10 January 2013 Accepted 28 May 2013

Published ahead of print 31 May 2013

Address correspondence to Kazuhiro Iwashita, iwashitact@nrib.go.jp.

Supplemental material for this article may be found at http://dx.doi.org/10.1128 /EC.00003-13.

Copyright © 2013, American Society for Microbiology. All Rights Reserved. doi:10.1128/EC.00003-13

and production of kojic acid (KA), which is an important cosmetic material for preventing melanogenesis in skin, as well as production of the antimicrobial penicillin (24). We also performed microarray analysis of the  $\Delta hstD$  strain to examine the global function of this sirtuin and found that the disruption of this gene affects the expression of many metabolite genes. As described above, *laeA* is an important coordinator for the regulation of secondary metabolism and development. In this context, we also analyzed the genetic interaction between *hstD/Aohst4* and *laeA* and found that *hstD/Aohst4* regulates *laeA* expression. We describe the function of the fungus-specific sirtuin HstD/AoHst4 first in SM production and then in conidial development through the regulation of *laeA* gene expression.

#### MATERIALS AND METHODS

Strains, media, and physiological tests. The strains used in this study are listed in Table S1 in the supplemental material. Aspergillus oryzae RIB40 was used as the DNA donor. The A. oryzae NSR-ΔLD2 strain was used as the host for A. oryzae HDAC (AoHDAC) disruption (25). M+Met medium [2 g NH<sub>4</sub>Cl, 1 g (NH<sub>4</sub>)2SO<sub>4</sub>, 0.5 g KCl, 1 g KH<sub>2</sub>PO<sub>4</sub>, 0.5 g  $\rm MgSO_4\cdot 7H_2O,\, 0.02$ g FeSO\_4, 20 g glucose, 1.5 g L-methionine, pH 5.5, in 1 liter] or M+Ade medium (M+Met medium containing 0.5 g of adenine sulfate dihydrate instead of L-methionine) was used as the selection medium for A. oryzae adeA<sup>+</sup> transformants and A. oryzae sC<sup>+</sup> transformants, respectively (25). TS medium (6 g of NaNO<sub>2</sub>, 0.52 g of KCl, 1.52 g of KH<sub>2</sub>PO<sub>4</sub>, 0.52 g of MgSO<sub>4</sub>·7H<sub>2</sub>O, 10 g of glucose, 1 ml of trace elements, pH 6.5, in 1 liter) was used as the selectable medium for A. oryzae adeA<sup>+</sup>  $sC^+$  transformants. M+Met, M+Ade, or TS medium with 0.8 M NaCl added was used for transformation. KAS medium (10 g of tryptone, 1.52 g of K<sub>2</sub>HPO<sub>4</sub>, 1.5 g of L-methionine, 0.5 g of MgSO<sub>4</sub>·7H<sub>2</sub>O, 1 ml of trace elements, pH 6.5, in 1 liter) was used for screening for HDAC-affected kojic acid productivity. KA medium (1 g of yeast extract, 0.5 g of KCl, 1 g of K<sub>2</sub>HPO<sub>4</sub>, 1.5 g of L-methionine, 0.5 g of MgSO<sub>4</sub>·7H<sub>2</sub>O, 100 g of glucose, 0.5 g of adenine sulfate dihydrate, pH 6.0, in 1 liter) was used to test for KA production and RNA preparation. N medium (3 g of L-glutamic acid, 0.52 g of KCl, 1.52 g of K<sub>2</sub>HPO<sub>4</sub>, 0.52 g of MgSO<sub>4</sub>·7H<sub>2</sub>O, 30 g of glucose, 1.5 g of L-methionine, 1 ml of trace elements, pH 6.5, in 1 liter) was used for morphological analysis. TSB medium (20 g of tryptic soy broth, 1.5 g of L-methionine, 3 g of L-glutamic acid, 0.5 g of adenine sulfate dihydrate, pH 7.5, in 1 liter) was used for the penicillin bioassay and RNA preparation.

Morphological analysis was performed in 20 ml of N 2% agar medium or 100 ml of N liquid medium. Three independent disruptants were used for each experiment. For the spore count, suspensions of conidia of each strain were point inoculated ( $1 \times 10^5$  conidia) on the center of each plate, and the strain was grown for 5 days at 30°C. Colony diameters were measured at this time, and the spores were harvested in suspension solution (0.025% Tween 80, 0.5% NaCl), vortexed vigorously, and counted using a TC10 automated cell counter (Bio-Rad). The conidiation rate was calculated by the conidium number/radial growth area (cm<sup>2</sup>). For biomass analysis in N liquid medium, 4 cm<sup>2</sup> of full-growth colonies in plate cultures of each strain were cut out, homogenized in 1 ml of suspension solution, and then used to inoculate each flask. Flasks were incubated for 2 days at 30°C with shaking at 100 rpm. Then, mycelia were harvested, dried at 105°C for 2 h, and weighed.

Protein identification, domain prediction, and phylogenetic analysis. HDAC sequences of *Saccharomyces cerevisiae* were obtained from the *Saccharomyces* genome database (http://www.yeastgenome.org/). HDAC sequences of *Homo sapiens*, *Neurospora crassa*, and *A. nidulans* were obtained from the NCBI proteins database (http://www.ncbi.nlm .nih.gov/guide/proteins/), the *Neurospora crassa* database (http://www .broadinstitute.org/annotation/genome/neurospora/MultiHome .html), and AspGD (http://www.aspgd.org/), respectively. The HDAC genes of *A. oryzae* were identified from the Comparative Fungal Genome Database (CFGD; http://nribf2.nrib.go.jp/) by BLAST searching using the HDAC sequences of *S. cerevisiae* and *H. sapiens* as the query. The sequences of these HDACs in *A. oryzae* were verified by RNA sequencing using the SOLiD3 system (Applied Biosystems). The gene structures of all AoHDACs were confirmed from the RNA sequence data (details of our RNA sequence data are available in AspGD [accession no. ASPL0000367586; http://www.aspergillusgenome.org /download/large\_scale\_data/Iwashita\_2012/]) (26). The mapping data for all reads are also available in CFGD. For recognizable domains, the protein sequence of the HDAC homolog in *A. oryzae* was analyzed using the InterProScan tool (27). The protein sequence of the HstD homolog in filamentous fungi was identified using an NCBI blast search with Pezizomycotina genomes (http://www.ncbi.nlm.nih.gov /sutils/genom\_tree.cgi) and the amino acid sequence of HstD as a query.

For the classification of HDACs in *A. oryzae*, protein sequences of HDACs in *S. cerevisiae*, *N. crassa*, *A. nidulans*, and *A. oryzae* were aligned with the ClustalW software in the Molecular Evolutionary Genetic Analysis, v.5 (MEGA5), program (28). Phylogenetic analysis was carried out by the MEGA5 program using the neighbor-joining method with 1,000 bootstrap replicates. For the classification of HstD in filamentous fungi, alignment and phylogenetic analysis were performed as described above. A list of sequence accession numbers used for AoHDAC analysis is provided in Table S2 in the supplemental material, and the sequence accession numbers of each HstD homolog are provided in Fig. S3 in the supplemental material.

**RNA preparation.** KA culture was performed in 20 ml of KA liquid medium inoculated with 200  $\mu$ l of 1  $\times$  10<sup>8</sup> conidia/ml suspension, and incubation was at 30°C for 4 or 7 days with shaking at 130 rpm. TSB culture was performed in 40 ml of TSB liquid medium inoculated with 400  $\mu$ l of 1  $\times$  10<sup>8</sup> conidia/ml suspension, and incubation was at 30°C for 1 day with shaking at 200 rpm. After cultivation, mycelia were harvested using Miracloth (Merck). Then, mycelia were immediately frozen in liquid N<sub>2</sub> and ground to a fine powder. Total RNA was isolated from mycelia from KA or TSB liquid medium using the Isogen reagent (Nippon Gene) according to the manufacturer's instructions.

Northern hybridization. Denatured total RNA (20  $\mu$ g) was electrophoresed on a formaldehyde-agarose gel and transferred in 20× SSC (1× SSC is 0.15 M NaCl plus 0.015M sodium citrate) onto a Hybond N<sup>+</sup> membrane. Northern analysis was performed with a Detection starter kit II (Roche) according to the manufacturer's instructions. Digoxigeninlabeled probes were prepared using a PCR digoxigenin probe synthesis kit (Roche) with genomic *A. oryzae* RIB40 DNA as the template and the primers X-probe-F and X-probe-R. The letter X means the respective gene used for Northern analysis. Each blot was imaged using an LAS1000plus luminescent image analyzer (Fujifilm). A list of the primers used for these PCRs is shown in Table S3 in the supplemental material.

Construction of the disruption cassette. Each disruption cassette was constructed by fusion PCR of three mutually primed DNA fragments, the 5' and 3' flanking regions of the target genes and the *adeA* fragment (29). About 1 kb of the 5' and 3' flanking regions of the target genes and the adeA gene was amplified from genomic A. oryzae RIB40 DNA with primers X-A and X-B, X-C and X-D, and adeA-F and adeA-R, respectively. Only for the construction of the  $\Delta hstD$  and  $\Delta laeA$  genes and the A. nidulans sC gene, amplified from pUSA with primers sC-F and sC-R, was the gene fused to the flanking region of *laeA* (30). The letter X in the primer names represents the name of each target gene. Each region was amplified by KOD Plus DNA polymerase (Toyobo). These fragments were combined by a second PCR with KOD Plus DNA polymerase and the primers X-A and X-D or X-A2 and X-D2. The amplified fragment was purified by a QIAquick PCR purification kit (Qiagen) and then used as a disruption cassette. A list of the primers used for these PCRs is shown in Table S3 in the supplemental material.

**Complementation of** *hstD***.** To recover the native locus of *hstD*, we first amplified the same 5' flanking region of the disruption construct of the *hstD* and *adeA* fragments from RIB40 DNA with primers hstD-A and



FIG 1 Phylogenetic analysis of histone deacetylase in *A. oryzae*. Accession numbers and HDAC names are indicated for each branch. The HDAC names of *S. cerevisiae* or *H. sapiens* with the species name indicated are followed by a slash. The numbers at the nodes are bootstrap values obtained from 1,000 replicates and are indicated as percentages. Scale bar, a distance corresponding to 0.2 amino acid substitution per site. The class or subclass of HDACs is shown on the right. These classes of HDACs are referred to in previous phylogenetic studies (4, 6, 34). AoHDACs are indicated by underlines. Abbreviations of AoHDAC gene names are as follows: *hda*, <u>histone deacetylase</u>; *hst*, <u>homolog of sirt</u>uin. The class to which *hstD* belongs is surrounded by a gray border. The gene names and their accession numbers are identified in Table S2 in the supplemental material. Sc, *Saccharomyces cerevisiae*; An, *Aspergillus nidulans*; Nc, *Neurospora crassa*; Hs, *Homo sapiens*; Ao, *Aspergillus nidulans*; Nc, *Neurospora crassa*; Hs, *Homo sapiens*; Ao, *Aspergillus nidulans*; Nc, *Neurospora crassa*; Hs, *Homo sapiens*; Ao, *Aspergillus nidulans*; Nc, *Neurospora crassa*; Hs, *Homo sapiens*; Ao, *Aspergillus nidulans*; Nc, *Neurospora crassa*; Hs, *Homo sapiens*; Ao, *Aspergillus nidulans*; Nc, *Neurospora crassa*; Hs, *Homo sapiens*; Ao, *Aspergillus nidulans*; Nc, *Neurospora crassa*; Hs, *Homo sapiens*; Ao, *Aspergillus nidulans*; Nc, *Neurospora crassa*; Hs, *Homo sapiens*; Ao, *Aspergillus nidulans*; Nc, *Neurospora crassa*; Hs, *Homo sapiens*; Ao, *Aspergillus nidulans*; Nc, *Neurospora crassa*; Hs, *Homo sapiens*; Ao, *Aspergillus nidulans*; Nc, *Neurospora crassa*; Hs, *Homo sapiens*; Ao, *Aspergillus nidulans*; Nc, *Neurospora crassa*; Hs, *Homo sapiens*; Ao, *Aspergillus nidulans*; Nc, *Neurospora crassa*; Hs, *Homo sapiens*; Ao, *Aspergillus nidulans*; Nc, *Neurospora crassa*; Hs, *Homo sapiens*; Ao, *Aspergillus nidulans*; Nc, *Neurospora crassa*; Hs, *Homo sapiens*; Ao, *Aspergillus nidulans*; Nc, *Neurospor* 



FIG 2 *hstD*/Aohst4 and *hdaD*/Aohos2 regulate SM production and development. (A) The morphological phenotype on N agar medium (MM) and results of the kojic acid production plate assay (KA) are provided for the indicated strains. (B, C) Radial growth and conidiation of the indicated strains on N agar medium, respectively. (D) Time course characteristics of kojic acid production of the indicated disruptants. (E) Expression profiles of kojic acid cluster genes represented by Northern hybridization. The culture times of the indicated strains are shown at the top of the panel. The analyzed gene is indicated on the left side of each blot. The results for rRNA, used as the loading control, are shown. (F) Bioassay of penicillin production of the  $\Delta hstD$  strain. (G) Northern hybridization of the experiment whose results are presented in this figure. All data are represented as means  $\pm$  SDs (n = 3); \*, P < 0.01, t test.

hstD-compB or *adeA* fusion primers sC-F and adeA-R, respectively. We also amplified the *A. nidulans sC* gene from pUSA with sC-F and sC-R as autotrophic markers (30). Then, these fragments were combined by fusion PCR using nested primers adeA-R and hstD-A2 (29). The amplified fragment was purified by a QIAquick PCR purification kit and used as a complementation cassette. A list of the primers used for these PCRs is shown in Table S3 in the supplemental material.

**Construction of overexpression plasmids.** The open reading frames (ORFs) of *laeA* or *hstD/Aohst4* were amplified from the genomic DNA of *A. oryzae* RIB40 with Fusion-laeA-F and Fusion-laeA-R or Fusion-hstD-F and Fusion-hstD-R, respectively. The resulting fragments were fused into SmaI-cut pUSA using an In-Fusion HD cloning kit (TaKaRa) (30). The *amyB* promoter of pUSA was used to drive the overexpression of *laeA* and *hstD/Aohst4*, respectively. The resulting plasmids, pUSlaeA and pUShstD, were linearized with one cut of restriction enzyme BgIII and EcoT22I on the *laeA* ORF and *hstD/Aohst4* ORF, respectively. The resulting linearized fragments were used as overexpression cassettes. A list of the primers used for these PCRs is shown in Table S3 in the supplemental material.

**Transformation of** *A. oryzae.* Transformation of *A. oryzae* strains was performed using the protoplast-polyethylene glycol method (31). To verify the disruption of the target gene, direct colony PCR was performed using primers (X-F and X-G, X-A and X-D), KOD-FX (Toyobo), and a crude DNA sample of each transformant. Primers X-F and X-G were designed at the region of each target gene. The crude DNA sample was prepared as follows: conidia and hyphae from each transformant culture were suspended in 100 µl buffer A (100 mM Tris-HCl [pH 9.5], 1 M KCl, 10 mM EDTA). This mycelial suspension was vigorously vortexed and incubated at 95°C for 10 min. Immediately thereafter, this hot solution was vigorously vortexed and centrifuged at 5,000 rpm for 1 min. A total of 1 µl of supernatant was used as the crude DNA sample. A list of the

primers used for these assays is shown in Table S3 in the supplemental material.

**Time-lapse imaging.** For time-lapse imaging, conidiophores were germinated in 1.5% agar N medium in 35-mm glass-bottom dishes. Cells were imaged using a real-time culture cell monitoring system (Astec) controlled by CCM software. Differential interference contrast images of each disruptant were taken every 20 min for approximately 84 h. All imaging was carried out at 30°C. Pictures and movies were edited with CCM software (Astec).

Secondary metabolite analysis. For the plate assay of kojic acid production, KAS medium and KA medium containing 5 mM FeCl<sub>3</sub> were used for screening and genetic interaction analysis, respectively. Suspensions of conidia of each strain were point inoculated ( $1 \times 10^5$  conidia) on the center of the 2% agar medium and grown for 5 days at 30°C. Then, a red halo, which indicates the existence of kojic acid, was observed.

For the quantification of kojic acid, 20 ml of KA liquid medium inoculated with 200  $\mu$ l of 1  $\times$  10<sup>8</sup> conidia/ml suspension was incubated at 30°C with shaking at 130 rpm. After cultivation for the appropriate period, mycelia were filtered through Miracloth (Merck), and then the filtrate was collected. Harvested mycelia were dried at 105°C for 1 h and weighed. The collected KA medium was filtered through a MillexHV filter (Millipore), and then the kojic acid concentration was quantified by colorimetric methods.

**Microarray analysis.** The *A. oryzae* GeneChip microarray (AoDNAChip; NCBI Gene Expression Omnibus [GEO] platform GPL16184) was designed by Affymetrix to refer to the entire genome sequence of *A. oryzae*, and predicted ORFs are published at the Comparative Fungal Genome Database (http://nribf2.nrib.go.jp/, accession number *A. oryzae* RIB40 Ace33v2). The AoDNAChip covered 13,765 ORFs and 6,143 promoters of *A. oryzae*. In this



FIG 3 Complementation analysis of *hstD*. (A) Analysis of the morphology and SM production of the  $\Delta hstD$  and  $hstD^+$  strains. MM, morphological phenotype of the indicated strain on N agar medium; ×100, closeup stereomicroscopic images of the strains on N agar medium (magnification, ×100; bar, 500 µm; red arrows, examples of conidia); KA and PEN, plate assay or bioassay of kojic acid and penicillin, respectively. (B, C) Quantification of colony diameter and rate of conidiation of  $\Delta hstD$  and  $hstD^+$  strains, respectively. (D) The expression profiles of the kojic acid cluster genes were determined by Northern hybridization. The culture time of the indicated strain is shown at the top. The analyzed gene is indicated on the left side of each blot. The results for rRNA, used as the loading control, are shown. (E) Quantification of kojic acid production. The *adeA*<sup>+</sup> *sC*<sup>+</sup> strain was used as the control, and the  $\Delta hstD sC^+$  strain represents the  $\Delta hstD$ strain. All data are represented as means ± SDs (n = 3); \*, P < 0.01, t test.

study, we performed transcriptome analysis using probes of 13,765 ORFs set on this microarray.

Total RNA was purified for microarray analysis by using an RNeasy minikit (Qiagen). RNA quality was determined by using a BioAnalyzer 2100 system (Agilent Technology), and the quantity was determined by using an Ultrospec 3300 pro spectrophotometer (Amersham Pharmacia Biotech). Fragmented biotin-labeled cRNA was prepared by using a GeneChip one-cycle target labeling and control reagent kit (Affymetrix) according to the manufacturer's instructions. The fragmented cRNA was hybridized to an AoDNAChip. Then, this GeneChip was washed, stained, and scanned by using a GeneChip FS-450 fluidics station (fluidics protocol FS450\_001) and a GeneChip 3000 scanner.

Scanned probe array images were converted into CEL files and normalized by using the GCOS v.1.4 program (Affymetrix). Calculations of signal intensity and detection P values were also performed using GCOS v.1.4. The trimmed mean signal of the array was scaled to the target signal of 500 with the all probe sets scaling option. The detection call was used for detection of a particular transcript, with a detection P value of <0.04considered present (P),  $0.04 \le P < 0.06$  considered marginal (M), and a *P* value of  $\geq$ 0.06 considered absent (A). These calculation data were exported as CHP files. For microarray data analysis, CHP files were imported into GeneSpring v.7.3 (Agilent Technologies). Expression data were normalized per chip to the 50th percentile. In this study, we analyzed genes detected as P or M flags. Genes with statistically significant changes in transcript abundance were identified using a cutoff value of 2-fold and a Welch's t test value of less than 5%. FungiFun software was used for functional catalogue (FunCat) categorization (32, 33). Significantly enriched FunCat categories were extracted using FungiFun software (cutoff P value, <0.05; the P value indicates the significance of the number of hits for each category in the data set, taking the number of hits for the whole genome of A. oryzae as the background). The calculation is based on a two-tailed Fisher's exact test). The distribution of whole A. oryzae genes is

indicated in Fig. S4 and S5 in the supplemental material and was used as a reference for FunCat enrichment analysis. Two biological replicates were used for the microarray analysis.

Accession numbers. The microarray data have been deposited in the NCBI Gene Expression Omnibus (GEO) database (http://www.ncbi.nlm .nih.gov/geo/) and are accessible through GEO series accession number GSE41612. The coding sequences of *hdaB* and *hstD* were deposited in DDBJ under accession no. AB744040 and AB744041, respectively.

#### RESULTS

Phylogeny and morphology of AoHDACs. A total of 11 AoHDACs were found in the A. oryzae genome on the basis of a BLAST analysis. We classified the AoHDACs according to a previous phylogenetic study of HDACs. These AoHDACs were phylogenetically divided into class I to III HDACs, but the mammal-specific class IV HDACs were not found in the genome. Class III HDACs are generally described as sirtuin-type HDACs, and 6 AoHDACs belonged to this class. The A. oryzae sirtuins (AoSirtuins) were classified into classes I to III, but class IV sirtuins were not found in the genome. The class I sirtuins were further categorized into three subclasses, including the fungus-specific HDACs of sirtuin subclass C (Fig. 1). We attempted to disrupt these 11 AoHDACs and succeeded for 10 of the AoHDACs. However, only heterokaryon transformants were obtained in the case of *hdaB/A. oryzae rpd3* (Aorpd3) over several trials (data not shown). This result suggests that hdaB/Aorpd3 is essential in A. oryzae, but further experiments are required to confirm this hypothesis. Thus, in this report, the heterokaryon disruptant of hdaB/Aorpd3 and AoHDAC disruptants were used for subsequent experiments.

We first observed the growth and generation of conidia of AoHDAC disruptants and *hdaB/Aorpd3* heterokaryon transfor-



FIG 4 Enrichment analysis of the FunCat categorization of the microarray analysis. Significantly enriched FunCat level 1 and level 2 categories of genes upregulated (A, B) or downregulated (C, D) by *hstD*/*Aohst4* deletion are shown. The FunCat is the organism-independent functional description of proteins (33). FunCat consists of 28 main functional categories (level 1). Level 1 is the most general one, whereas level 2 shows much more detail. The percentage indicated for each category contributes to the total mapping. Insignificant FunCat categories are indicated as insignificant in the pie charts. Significantly enriched categories were extracted by FungiFun software (cutoff *P* value, <0.05; Fisher's exact test) (32). Details of the enrichment analysis are available at the FungiFun website (https://sbi.hki-jena.de/FungiFun/FungiFunHelp.html).

mants on the plate culture (see Fig. S1 and S2B and C in the supplemental material). Observation of the growth of AoHDAC disruptants revealed an obvious defect of the  $\Delta hstD$  and  $\Delta hdaD$ strains in morphogenesis (Fig. 2A). The conidial formation of these disruptants was significantly decreased, and a slight growth effect was observed in plate cultivation (Fig. 2B and C). We additionally observed the growth of AoHDAC disruptants and the hdaB/Aorpd3 heterokaryon transformant in liquid culture (see Fig. S2D in the supplemental material). A growth defect of the  $\Delta h daD$  strain was observed in submerged cultivation (see Fig. S2D in the supplemental material). Thus, hdaD/Aohos2 is required for the growth integrity of A. oryzae. These two disruptants were further examined using time-lapse imaging for more detailed observation. As expected, the  $\Delta h daD$  strain showed slow growth but exhibited more crowded aerial hyphae than the wild-type strain (see Fig. S2A in the supplemental material). However, a few invasive hyphae were detected in the  $\Delta hstD$  strain but not in the  $\Delta h daD$  strain. In this time-lapse imaging analysis, a significant defect of conidial development was also found in both the  $\Delta h daD$ and  $\Delta hst D$  strains.

These results indicate that both HdaD/AoHos2 and HstD/ AoHst4 play an important role in the growth and development of *A. oryzae*, especially in asexual development.

**Fungus-specific sirtuin regulates SM production.** We further examined SM production of AoHDAC disruptants and the *hdaB*/ *Aorpd3* heterokaryon transformant using a plate assay for kojic acid productivity (see Fig. S1 in the supplemental material). High levels of production of kojic acid were observed in the  $\Delta hdaB$  and  $\Delta hstA$  strains (see Fig. S1 in the supplemental material), and significant overproduction was observed in the  $\Delta hdaD$  and  $\Delta hstD$ strains (Fig. 2A). We quantified the kojic acid production of these two HDAC disruptants, and the  $\Delta hstD$  strain showed a 200-fold increased productivity in a 7-day culture (Fig. 2D). In contrast, the  $\Delta hdaD$  strain showed a 30-fold overproduction compared with the level of production for the control strain (Fig. 2D). The  $\Delta hstD$ strain started to produce kojic acid by 4 days in culture, while kojic acid was not detected in the wild-type strain culture.

We further analyzed kojic acid production at the gene expression level by examining three key genes in the kojic acid gene cluster (24). Northern analysis of 4-day-old cultures showed extremely high levels of expression of these genes in the  $\Delta hstD$  strain, but no expression was observed in the wild-type strain (Fig. 2E). The *kojA* gene was also expressed in the  $\Delta hdaD$  strain, but the expression was not as high as that in the  $\Delta hstD$  strain. This earlier and higher expression in both disruptants is consistent with the earlier and higher production of kojic acid.

These results indicate the importance of  $\Delta hdaD$  and  $\Delta hstD$  in the regulation of kojic acid production. On the basis of phylogenetic classification, HstD/AoHst4 belongs to the fungus-specific class of sirtuins, and this protein is widely conserved in filamentous fungi (34) (see Fig. S3 in the supplemental material). Interestingly, *nst3/N. crassa hst4* (*Nchst4*) is involved in the silencing mechanism of *N. crassa* (35). Moreover, the phenotype of the  $\Delta hstD$  strain was reminiscent of the global use of HstD/AoHst4 for the production of various SMs in *A. oryzae*.

In this context, we examined the regulation of penicillin biosynthesis in the  $\Delta hstD$  strain. As expected, a higher level of production of penicillin was found in the  $\Delta hstD$  strain, and a higher level of expression of the penicillin biosynthetic gene was confirmed (Fig. 2F and G). Along with the morphogenetic defect and kojic acid production, these phenotypes were rescued by the complementation of *hstD*/*Aohst4* (Fig. 3).



FIG 5 Genetic interaction between *hstD* and *laeA*. (A) Expression profile of *laeA* under the KA-producing condition. The *adeA*<sup>+</sup> strain was used as a control. The culture time of the indicated strain is shown at the top of the panel. The results for rRNA, used as the loading control, are shown. (B) Analysis of morphology and SM production of the  $\Delta hstD$ ,  $\Delta laeA$ , and  $\Delta hstD$   $\Delta laeA$  strains. MM, morphological phenotype of the indicated strain on N agar medium; ×100, closeup stereomicroscopic images of the strains on N agar medium (magnification, ×100; bar, 500 µm; red arrows, examples of conidia); KA and PEN, plate assay or bioassay of kojic acid and penicillin, respectively. (C, D) Quantification of the conidiation rate and kojic acid production of the  $\Delta hstD$ ,  $\Delta laeA$ , and  $\Delta hstD$   $\Delta laeA$  strains, respectively. Except for panel A, the *adeA*<sup>+</sup> sC<sup>+</sup> strain was used as the control, and the  $\Delta hstD$  sC<sup>+</sup> and  $\Delta laeA$  sC<sup>+</sup> strains represent the  $\Delta hstD$  and  $\Delta laeA$  strains, respectively, in this figure. All data are represented as means ± SDs (n = 3); \*, P < 0.01, t test.

These results suggest that *hstD*/*Aohst4* is required for the global regulation of SM biosynthesis. Thus, we examined the  $\Delta hstD$ strain by microarray analysis to investigate the expression of other SM-related genes. The expression of 388 genes was significantly affected by *hstD*/*Aohst4* deletion (absolute fold change, >2; *P* < 0.05) (see Table S4 in the supplemental material). These genes were spread across the whole genome; 299 of 388 genes were upregulated in the  $\Delta hstD$  strain. To reveal the functional distribution of genes affected by hstD/Aohst4, FunCat enrichment analysis was carried out using FungiFun software (32, 33) (Fig. 4). The C-compound and carbohydrate metabolism and the secondary metabolism categories were significantly enriched in downregulated genes. Most of the genes categorized as secondary metabolism overlapped with the genes categorized as C-compound and carbohydrate metabolism. Genes categorized as C-compound and carbohydrate metabolism were mainly related to polysaccharide degradation or glycolysis. This result suggests that carbon source degradation-related genes are downregulated in the  $\Delta hstD$  strain. The secondary metabolism and detoxification categories were significantly enriched in genes upregulated by hstD deletion. Genes categorized as secondary metabolism and detoxification were mainly constituted by cytochrome P450 (CYP) genes. Interestingly, three nonribosomal peptide synthetases (NRPSs) and one polyketide synthase (PKS) were also upregulated in the  $\Delta hstD$ strain. One of three NRPSs encoded wykN (AO080501000008), which is involved in Wyk-1 production in A. oryzae (23). PKS and NRPS enzymes generate the general structural scaffolds of most secondary metabolites (36). Additionally, fungal CYPs have PKS-

and NRPS-associated functions and generate structural variation of fungal SMs. Thus, *hstD*/*Aohst4* affects many kinds of SM production (at least 6 different SM gene clusters) (37, 38).

hstD/Aohst4 regulates expression of laeA. The LaeA complex coordinates the development and SM biosynthesis in A. nidulans and is conserved in numerous fungal genomes (17). Recently, it was reported that deleting *laeA* diminishes kojic acid production and gene expression in A. oryzae (39). Additionally, penicillin production in A. oryzae is diminished after deletion of veA, which is a member of the LaeA complex (17, 40). These reports suggest that the LaeA complex also plays a general role in the induction of the SM gene cluster in A. oryzae. Thus, the SM overproduction phenotype of the hstD/Aohst4 disruptant should be associated with the LaeA complex, and HstD/AoHst4 may play a role under the control of LaeA. According to this hypothesis, the expression of laeA should not be altered in the hstD/Aohst4 disruptant. Thus, we examined the expression of laeA in the hstD/Aohst4 disruptant. Surprisingly, laeA was highly expressed in the hstD/Aohst4 disruptant, even in the 4-day culture, but remained unexpressed in the wild-type strain (Fig. 5A). This result suggests that HstD/ AoHst4 is involved in laeA gene repression. Thus, both SM overproduction phenotypes and the altered morphological phenotype of the  $\Delta hstD$  strain are caused by the high level of expression of laeA.

Genetic interaction of *hstD* and *laeA*. To confirm the hypothesis presented above, we prepared a  $\Delta laeA$  strain and a  $\Delta hstD$   $\Delta laeA$  double disruptant and then examined the strains for SM production and conidial development. At first, these strains ex-



FIG 6 Epistatic relationship between *hstD* and *laeA*. (A) Analysis of the morphology and SM production of the  $\Delta hstD$  *OE::laeA* and  $\Delta laeA$  *OE::hstD* strains. MM, morphological phenotype of the indicated strain on N agar medium; ×100, closeup stereomicroscopic images of the strains on N agar medium (magnification, ×100; bar, 500 µm; red arrows, examples of conidia); KA and PEN, plate assay or bioassay of kojic acid and penicillin, respectively. (B, C) Quantification of the conidiation rate and kojic acid production of the  $\Delta hstD$  *OE::laeA* and  $\Delta laeA$  *OE::hstD* strains, respectively. The *adeA*<sup>+</sup> *pUSA*<sup>+</sup> strain was used as the control, and the  $\Delta hstD$  *pUSA*<sup>+</sup>, *OE::laeA adeA*<sup>+</sup>,  $\Delta laeA$  *pUSA*<sup>+</sup>, and *OE::hstD adeA*<sup>+</sup> strains represent the  $\Delta hstD$ , *OE::laeA*, and *OE::hstD* strains, respectively, in this figure. The *amyB* promoter was used to drive overexpression of *laeA* and *hstD*. All data are represented as means ± SDs (*n* = 3); \*, *P* < 0.01, *t* test.

hibited the phenotype of the  $\Delta laeA$  strain, including a lack of kojic acid production (Fig. 5B and D), similar to previous reports (39). The production of penicillin and conidial development were also lost in the  $\Delta laeA$  strain (Fig. 5B and C). Next, we observed the



FIG 7 Schematic model of the regulation of SM production and development by HstD/AoHst4 through LaeA. An unknown signal induces or suppresses the function of HstD/AoHst4. Suppression of HstD/AoHst4 leads to expression of LaeA. This activation stimulates fungal development and secondary metabolite production. However, there is the possibility of an HstD/AoHst4 competitive mechanism by an unknown factor (described as factor X in this figure).

effect of *laeA* disruption in the  $\Delta hstD$  strain background and found that the SM overproduction phenotype of the  $\Delta hstD$  strain was abolished by *laeA* disruption (Fig. 5B and D). We further observed conidial development in the double disruptant, which exhibited a  $\Delta laeA$  strain-like fluffy phenotype (Fig. 5B and C). These results clearly indicate a genetic interaction between *hstD*/ *Aohst4* and *laeA* and that HstD/AoHst4 plays a role upstream of LaeA.

To confirm this epistatic relationship, we examined the effect of *laeA* and *hstD*/*Aohst4* overexpression using the *amyB* promoter. The strain overexpressing *laeA* exhibited a  $\Delta hstD$  strain-like phenotype, such as SM overproduction and low levels of conidial formation (Fig. 6). The effects of laeA overexpression were also observed in the  $\Delta hstD$  strain background (Fig. 6). Additionally, both the *OE*::*laeA* strain and  $\Delta hstD$  *OE*::*laeA* strain showed high levels of expression of laeA, kojA, and ipnA (see Fig. S6 in the supplemental material). These results indicate that laeA is downstream of hstD/Aohst4. Therefore, we overexpressed hstD/Aohst4 in a *laeA* disruption background. As expected, the overexpression of *hstD*/*Aohst4* resulted in a  $\Delta laeA$  strain-like phenotype, such as no SM production and a fluffy morphology, in the  $\Delta laeA$  background (Fig. 6). Overexpression of hstD/Aohst4 in the wild-type laeA background had no measurable effect on SM production and development (Fig. 6).

From these results, we suggest that the fungus-specific sirtuin HstD/AoHst4 controls SM production and fungal development through the regulation of *laeA* gene expression.

#### DISCUSSION

In the past decade, the importance of the role of classical HDACs in filamentous fungi in the regulation of some fungal phenotypes has been revealed (2). For example, *F. graminearum hdf1/F. graminearum hos2* is important for conidial development and SM production (7). In this study, we also determined the importance of *hdaD/Aohos2* in the regulation of hyphal growth, conidiation, and SM production. Compared with the study of classical HDACs, only a few reports have been published for sirtuin-type HDACs in filamentous fungi (20, 35). Recently, *sirA/A. nidulans sir2 (Ansir2)*, which is a homolog of yeast *sir2* and mammalian *sirt1*, was reported to function in secondary metabolism regulation, but no effects on growth, conidiation, or morphogenesis were reported (20).

The fungus-specific putative methyltransferase LaeA coordinates fungal development and SMs in several filamentous fungi (17). It was previously reported that kojic acid production is regulated by LaeA, but we found that laeA coordinates both SM production and conidial development (39). In general, the production of fungal SMs is coordinated with fungal development, and the LaeA complex coordinates these (17). In higher eukaryotes, sirtuin affects various physiological functions, such as differentiation, metabolism, and the stress response (41-43). In this study, we found that the fungus-specific sirtuin HstD/AoHst4 affects both fungal development and SM production. Furthermore, the epistatic study revealed that HstD/AoHst4 is involved in the coordination of fungal development and SM production via LaeA expression. These results indicate that HstD/AoHst4 plays a Sirt1like central role that coordinates the developmental state and metabolism in filamentous fungi.

The yeast Hst4, which is a homolog of hstD/Aohst4 of A. oryzae, is a NAD<sup>+</sup>-dependent histone H3K56 deacetylase (44). In the Northern analysis, deletion of hstD/Aohst4 affected the level of laeA gene expression. Therefore, HstD/AoHstD may be involved in the epigenetic regulation of laeA gene expression. However, the overexpression of hstD/Aohst4 did not affect SM production or conidial development. In general, histone acetyltransferase (HAT) is required for activation of silenced genes. In budding yeast, it has been reported that the fungus-specific HAT of RTT109 catalyzes H3K56 acetylation and restores the silencing defects of the  $\Delta hst3 \Delta hst4$  mutant (44, 45). We found one *rtt109* homologue of AO090020000581 (A. oryzae rtt109 [Aortt109]) in the A. oryzae genome. This suggests that Aortt109 is required for the expression of the silenced laeA by H3K56 deacetylation and overcomes even hstD/Aohst4 overexpression. In this context, we will investigate histone H3K56 acetylation of the laeA locus and the effect of Aortt109 on the acetylation and expression of laeA in future studies.

In the overexpression analysis of *laeA*, several different phenotypes of kojic acid production were observed compared with the phenotype of the *hstD*/*Aohst4* mutant. The  $\Delta hstD$  strain showed high levels of kojic acid production in a 4-day liquid culture, while the same phenotype was not observed in the *OE::laeA* strain. Compared with the *OE::laeA* strain, interestingly, higher levels of kojic acid production and higher levels of expression of *kojA*, *ipnA*, and *laeA* were observed in the  $\Delta hstD$  *OE::laeA* strain. These results suggested that HstD/AoHst4 has some LaeA-independent role in the regulation of SM production.

We developed a model of the regulatory system of HstD/ AoHst4 (Fig. 7). The expression of *hstD/Aohst4* may be induced or suppressed by unknown signals. As described above, an unknown factor like AoRtt109 may compete with HstD/AoHst4 activity under *hstD/Aohst4*-inducing conditions. Under the *hstD/Aohst4*suppressed condition, *laeA* expression was induced. This in turn led to conidiation and induction of secondary metabolite production. However, it is possible that HstD/AoHst4 directly regulates fungal development and secondary metabolism independently of LaeA.

The *hstD*/Aohst4 gene is fungus specific but is conserved in the vast family of filamentous fungi (see Fig. S3 in the supplemental material). Furthermore, this gene plays a role in the coordination of fungal development and SM production. These results indicate that HstD/AoHst4 has great potential as a target to improve the productivity of useful SMs. It will also be important in the development of an attractive host for the production of several heterogeneous metabolites.

#### ACKNOWLEDGMENTS

We thank Ken Oda for great discussions, Katsuhiko Kitamoto for the gift of the *A. oryzae* NSR- $\Delta$ LD2 strain, Ryoko Hamada for technical help with the microarray analysis, and Kanae Koike (Electron Microscopy Service, Center for Gene Science, Hiroshima University) for technical help with electron microscopic analysis.

#### REFERENCES

- 1. Shahbazian MD, Grunstein M. 2007. Functions of site-specific histone acetylation and deacetylation. Annu. Rev. Biochem. **76**:75–100.
- Brosch G, Loidl P, Graessle S. 2008. Histone modifications and chromatin dynamics: a focus on filamentous fungi. FEMS Microbiol. Rev. 32: 409–439.
- Nishida H. 2009. Evolutionary conservation levels of subunits of histonemodifying protein complexes in fungi. Comp. Funct. Genomics 2009: 379317. doi:10.1155/2009/379317.
- Ekwall K. 2005. Genome-wide analysis of HDAC function. Trends Genet. 21:608–615.
- 5. Borkovich KA, Alex LA, Yarden O, Freitag M, Turner GE, Read ND, Seiler S, Bell-Pedersen D, Paietta J, Plesofsky N, Plamann M, Goodrich-Tanrikulu M, Schulte U, Mannhaupt G, Nargang FE, Radford A, Selitrennikoff C, Galagan JE, Dunlap JC, Loros JJ, Catcheside D, Inoue H, Aramayo R, Polymenis M, Selker EU, Sachs MS, Marzluf GA, Paulsen I, Davis R, Ebbole DJ, Zelter A, Kalkman ER, O'Rourke R, Bowring F, Yeadon J, Ishii C, Suzuki K, Sakai W, Pratt R. 2004. Lessons from the genome sequence of *Neurospora crassa*: tracing the path from genomic blueprint to multicellular organism. Microbiol. Mol. Biol. Rev. 68:1–108.
- Yang X-J, Seto E. 2008. The Rpd3/Hda1 family of lysine deacetylases: from bacteria and yeast to mice and men. Nat. Rev. Mol. Cell Biol. 9:206– 218.
- Li Y, Wang C, Liu W, Wang G, Kang Z, Kistler HC, Xu J-R. 2011. The HDF1 histone deacetylase gene is important for conidiation, sexual reproduction, and pathogenesis in *Fusarium graminearum*. Mol. Plant Microbe Interact. 24:487–496.
- Ding S-L, Liu W, Iliuk A, Ribot C, Vallet J, Tao A, Wang Y, Lebrun M-H, Xu J-R. 2010. The tig1 histone deacetylase complex regulates infectious growth in the rice blast fungus *Magnaporthe oryzae*. Plant Cell 22: 2495–2508.
- Izawa M, Takekawa O, Arie T, Teraoka T, Yoshida M, Kimura M, Kamakura T. 2009. Inhibition of histone deacetylase causes reduction of appressorium formation in the rice blast fungus *Magnaporthe oryzae*. J. Gen. Appl. Microbiol. 55:489–498.
- 10. Smith K, Kothe G, Matsen C, Khlafallah T, Adhvaryu K, Hemphill M, Freitag M, Motamedi M, Selker E. 2008. The fungus *Neurospora crassa* displays telomeric silencing mediated by multiple sirtuins and by methyl-

ation of histone H3 lysine 9. Epigenetics Chromatin 1:5. doi:10.1186/1756 -8935-1-5.

- Tribus M, Bauer I, Galehr J, Rieser G, Trojer P, Brosch G, Loidl P, Haas H, Graessle S. 2010. A novel motif in fungal class 1 histone deacetylases is essential for growth and development of *Aspergillus*. Mol. Biol. Cell 21: 345–353.
- 12. Tribus M, Galehr J, Trojer P, Brosch G, Loidl P, Marx F, Haas H, Graessle S. 2005. HdaA, a major class 2 histone deacetylase of *Aspergillus nidulans*, affects growth under conditions of oxidative stress. Eukaryot. Cell 4:1736–1745.
- Lee I, Oh J-H, Keats Shwab E, Dagenais TRT, Andes D, Keller NP. 2009. HdaA, a class 2 histone deacetylase of *Aspergillus fumigatus*, affects germination and secondary metabolite production. Fungal Genet. Biol. 46:782–790.
- 14. Baidyaroy D, Brosch G, Ahn J-H, Graessle S, Wegener S, Tonukari NJ, Caballero O, Loidl P, Walton JD. 2001. A gene related to yeast *HOS2* histone deacetylase affects extracellular depolymerase expression and virulence in a plant pathogenic fungus. Plant Cell **13**:1609–1624.
- 15. Hoffmeister D, Keller NP. 2007. Natural products of filamentous fungi: enzymes, genes, and their regulation. Nat. Prod. Rep. 24:393–416.
- Sanchez JF, Somoza AD, Keller NP, Wang CCC. 2012. Advances in Aspergillus secondary metabolite research in the post-genomic era. Nat. Prod. Rep. 29:351–371.
- Bayram Ö, Braus GH. 2012. Coordination of secondary metabolism and development in fungi: the velvet family of regulatory proteins. FEMS Microbiol. Rev. 36:1–24.
- Gacek A, Strauss J. 2012. The chromatin code of fungal secondary metabolite gene clusters. Appl. Microbiol. Biotechnol. 95:1389–1404.
- Shwab EK, Bok JW, Tribus M, Galehr J, Graessle S, Keller NP. 2007. Histone deacetylase activity regulates chemical diversity in *Aspergillus*. Eukaryot. Cell 6:1656–1664.
- Shimizu M, Masuo S, Fujita T, Doi Y, Kamimura Y, Takaya N. 2012. Hydrolase controls cellular NAD, sirtuin, and secondary metabolites. Mol. Cell. Biol. 32:3743–3755.
- 21. Machida M, Yamada O, Gomi K. 2008. Genomics of *Aspergillus oryzae*: learning from the history of koji mold and exploration of its future. DNA Res. 15:173–183.
- Abe K, Gomi K, Hasegawa F, Machida M. 2006. Impact of Aspergillus oryzae genomics on industrial production of metabolites. Mycopathologia 162:143–153.
- 23. Imamura K, Tsuyama Y, Hirata T, Shiraishi S, Sakamoto K, Yamada O, Akita O, Shimoi H. 2012. Identification of a gene involved in the synthesis of a dipeptidyl peptidase IV inhibitor in *Aspergillus oryzae*. Appl. Environ. Microbiol. 78:6996–7002.
- 24. Terabayashi Y, Sano M, Yamane N, Marui J, Tamano K, Sagara J, Dohmoto M, Oda K, Ohshima E, Tachibana K, Higa Y, Ohashi S, Koike H, Machida M. 2010. Identification and characterization of genes responsible for biosynthesis of kojic acid, an industrially important compound from *Aspergillus oryzae*. Fungal Genet. Biol. 47:953–961.
- 25. Maruyama J-I, Kitamoto K. 2008. Multiple gene disruptions by marker recycling with highly efficient gene-targeting background ( $\Delta ligD$ ) in *Aspergillus oryzae*. Biotechnol. Lett. **30**:1811–1817.
- 26. Arnaud MB, Chibucos MC, Costanzo MC, Crabtree J, Inglis DO, Lotia A, Orvis J, Shah P, Skrzypek MS, Binkley G, Miyasato SR, Wortman JR, Sherlock G. 2010. The *Aspergillus* Genome Database, a curated comparative genomics resource for gene, protein and sequence information for the *Aspergillus* research community. Nucleic Acids Res. 38:D420–D427. doi:10.1093/nar/gkp751.

- Quevillon E, Silventoinen V, Pillai S, Harte N, Mulder N, Apweiler R, Lopez R. 2005. InterProScan: protein domains identifier. Nucleic Acids Res. 33:W116–W120. doi:10.1093/nar/gki442.
- Tamura K, Peterson D, Peterson N, Stecher G, Nei M, Kumar S. 2011. MEGA5: molecular evolutionary genetics analysis using maximum likelihood, evolutionary distance, and maximum parsimony methods. Mol. Biol. Evol. 28:2731–2739.
- Szewczyk E, Nayak T, Oakley CE, Edgerton H, Xiong Y, Taheri-Talesh N, Osmani SA, Oakley BR. 2007. Fusion PCR and gene targeting in *Aspergillus nidulans*. Nat. Protoc. 1:3111–3120.
- 30. Yamada O, Na Nan S, Akao T, Tominaga M, Watanabe H, Satoh T, Enei H, Akita O. 2003. *dffA* gene from *Aspergillus oryzae* encodes L-ornithine N5-oxygenase and is indispensable for deferriferrichrysin biosynthesis. J. Biosci. Bioeng. **95**:82–88.
- Kitamoto K. 2002. Molecular biology of the koji molds. Adv. Appl. Microbiol. 51:129–153.
- Priebe S, Linde J, Albrecht D, Guthke R, Brakhage AA. 2011. FungiFun: a web-based application for functional categorization of fungal genes and proteins. Fungal Genet. Biol. 48:353–358.
- 33. Ruepp A, Zollner A, Maier D, Albermann K, Hani J, Mokrejs M, Tetko I, Güldener U, Mannhaupt G, Münsterkötter M, Mewes HW. 2004. The FunCat, a functional annotation scheme for systematic classification of proteins from whole genomes. Nucleic Acids Res. 32:5539–5545.
- Frye RA. 2000. Phylogenetic classification of prokaryotic and eukaryotic Sir2-like proteins. Biochem. Biophys. Res. Commun. 273:793–798.
- Smith KM, Dobosy JR, Reifsnyder JE, Rountree MR, Anderson DC, Green GR, Selker EU. 2010. H2B- and H3-specific histone deacetylases are required for DNA methylation in *Neurospora crassa*. Genetics 186: 1207–1216.
- Brakhage AA. 2013. Regulation of fungal secondary metabolism. Nat. Rev. Microbiol. 11:21–32.
- Podust LM, Sherman DH. 2012. Diversity of P450 enzymes in the biosynthesis of natural products. Nat. Prod. Rep. 29:1251–1266.
- Kelly DE, Kraševec N, Mullins J, Nelson DR. 2009. The CYPome (cytochrome P450 complement) of *Aspergillus nidulans*. Fungal Genet. Biol. 46:S53–S61.
- Oda K, Kobayashi A, Ohashi S, Sano M. 2011. Aspergillus oryzae laeA regulates kojic acid synthesis genes. Biosci. Biotechnol. Biochem. 75: 1832–1834.
- Marui J, Ohashi-Kunihiro S, Ando T, Nishimura M, Koike H, Machida M. 2010. Penicillin biosynthesis in *Aspergillus oryzae* and its overproduction by genetic engineering. J. Biosci. Bioeng. 110:8–11.
- Zhang T, Kraus WL. 2010. SIRT1-dependent regulation of chromatin and transcription: linking NAD<sup>+</sup> metabolism and signaling to the control of cellular functions. Biochim. Biophys. Acta 1804:1666–1675.
- Imai S-I, Guarente L. 2010. Ten years of NAD-dependent SIR2 family deacetylases: implications for metabolic diseases. Trends Pharmacol. Sci. 31:212–220.
- 43. Horio Y, Hayashi T, Kuno A, Kunimoto R. 2011. Cellular and molecular effects of sirtuins in health and disease. Clin. Sci. 121:191–203.
- Yang B, Miller A, Kirchmaier AL. 2008. HST3/HST4-dependent deacetylation of lysine 56 of histone H3 in silent chromatin. Mol. Biol. Cell 19:4993–5005.
- D'Arcy S, Luger K. 2011. Understanding histone acetyltransferase Rtt109 structure and function: how many chaperones does it take? Curr. Opin. Struct. Biol. 21:728–734.

## Figure S1. Kojic acid production and developmental phenotype of AoHDACs disruptants and heterokaryon strain



MM and KA show the morphological phenotype and kojic acid production plate assays of the indicated strains, respectively.





(A) Time-lapse microscopic analysis of  $\Delta hstD$  and  $\Delta hdaD$ . The pictures were taken at 36, 48, and 84 hr of incubation (black scale bar, 200 µm; red scale bar, 500 µm). (B-D) Quantification of colony diameter, conidiation rate, and mycelial dry cell weight of AoHDACs disruptants or the heterokaryon strain, respectively. The colony diameter and conidiation rates were measured on plate cultures. Dry cell weight was measured on submerged cultures. All data are represented as means  $\pm$  s.d. (n=3); \**p* < 0.01, t-test

## Figure S3. Phylogenetic analysis of *hstD* in filamentous fungi



The Genebank accession numbers and species names are indicated for each branch. The numbers at the nodes are bootstrap values obtained from 1000 replicates and are indicated as percentages. The scale bar indicates a distance corresponding to 0.1 amino acid substitutions per site. Each class of ascomycetes is shown at the right. *Sirt1* is used as the out-group in this phylogenetic analysis.

## Figure S4. Whole genome distribution of FunCat level 1 categories



The pie-chart indicates the whole genome distribution of the indicated categories of FunCat level 1. Percentages indicate each category that contributes to total mapping. The data of FunCat categorization of all genes of *A. oryzae* were imported from FungiFun software. Details of each category are available at the FunCat Database

(<u>http://mips.helmholtzmuenchen.de/proj/funcatDB/search\_main\_frame.html</u>). This data was reference of FunCat level 1 enrichment analysis of *A. oryzae*.

## Figure S5. Whole genome distribution of FunCat level 2 categories



The circular chart indicates the whole genome distribution of indicated categories FunCat level 2. Miner categories(Whole genome distribution < 1%) were indicated as other in pie chart. Percentage indicated each category contributes to total mapping. The data of FunCat categorization of all genes of *A.oryzae* were imported from FungiFun software (https://sbi.hki-jena.de/FungiFun/FungiFun.cgi). Details of each categories were available at FunCat Databases

(<u>http://mips.helmholtzmuenchen.de/proj/funcatDB/search\_main\_frame.html</u>). This data was referance of FunCat level 2 enrichment analysis of *A. oryzae*.

# Figure S6. Expression profiling of *laeA*, *kojA*, and *ipnA* in *OE::laeA* and *AhstD OE::laeA* strains, respectively



(A) Northern hybridization of *laeA and kojA*, respectively. The culture time of the indicated strain is shown at the top of the panel. *rRNA* is shown as the loading control. The analyzed gene is indicated on the left side of each blot (B) Northern hybridization of the penicillin biosynthetic gene *ipnA*. *rRNA* is shown as the loading control. The *adeA*<sup>+</sup> *pUSA*<sup>+</sup> strain was used as the control, and the *OE:laeA* adeA<sup>+</sup>strain represents *OE::laeA* in this figure.

## Table S1. Strain used in this study

| Name  | Parental strain | <sup>n</sup> Genotype <sup>b</sup>   | Reference         |
|---|-----------------|--|-------------------|
| RIB40                                       |                 | wild type  | NRIB <sup>a</sup> |
| $NSR-\Delta LD2$                            | RIB40           | niaD sC adeA argB::adeA AligD::argB  | (25)              |
| adeA +                                      | NSR-ALD2        | niaD sC adeA argB::adeA AligD::argB adeA +   | this study        |
| $pUSA^+$                                    | NSR-ALD2        | niaD <sup>-</sup> sC <sup>-</sup> adeA <sup>-</sup> argB::adeA <sup>-</sup> AligD::argB pUSA <sup>+</sup>                                | this study        |
| $adeA^+sC^+$                                | $adeA$ $^+$     | niaD <sup>-</sup> sC <sup>-</sup> adeA <sup>-</sup> argB::adeA <sup>-</sup> AligD::argB adeA <sup>+</sup> AnsC <sup>+</sup>              | this study        |
| $adeA^+ pUSA^+$                             | $adeA$ $^+$     | niaD <sup>-</sup> sC <sup>-</sup> adeA <sup>-</sup> argB::adeA <sup>-</sup> AligD::argB adeA <sup>+</sup> pUSA <sup>+</sup>              | this study        |
| $hdaB ht^{c}$                               | NSR-ALD2        | niaD sC adeA argB::adeA AligD::argB AhdaB::adeA hdaB   | this study        |
| $\Delta h da C$                             | NSR-ALD2        | niaD <sup>-</sup> sC <sup>-</sup> adeA <sup>-</sup> argB::adeA <sup>-</sup> AligD::argB AhdaC::adeA                                      | this study        |
| ∆hdaD                                       | NSR-ALD2        | niaD <sup>-</sup> sC <sup>-</sup> adeA <sup>-</sup> argB::adeA <sup>-</sup> AligD::argB AhdaD::adeA                                      | this study        |
| $\Delta h da A$                             | NSR-ALD2        | niaD <sup>-</sup> sC <sup>-</sup> adeA <sup>-</sup> argB::adeA <sup>-</sup> AligD::argB AhdaA::adeA                                      | this study        |
| $\Delta h da E$                             | NSR-ALD2        | niaD <sup>-</sup> sC <sup>-</sup> adeA <sup>-</sup> argB::adeA <sup>-</sup> AligD::argB AhdaE::adeA                                      | this study        |
| $\Delta hstA$                               | NSR-ALD2        | niaD <sup>-</sup> sC <sup>-</sup> adeA <sup>-</sup> argB::adeA <sup>-</sup> AligD::argB AhstA::adeA                                      | this study        |
| $\Delta hst B$                              | NSR-ALD2        | niaD <sup>-</sup> sC <sup>-</sup> adeA <sup>-</sup> argB::adeA <sup>-</sup> AligD::argB AhstB::adeA                                      | this study        |
| $\Delta hstC$                               | NSR-ALD2        | niaD <sup>-</sup> sC <sup>-</sup> adeA <sup>-</sup> argB::adeA <sup>-</sup> AligD::argB AhstC::adeA                                      | this study        |
| $\Delta hstD$                               | NSR-ALD2        | niaD <sup>-</sup> sC <sup>-</sup> adeA <sup>-</sup> argB::adeA <sup>-</sup> $\Delta$ ligD::argB $\Delta$ hstD::adeA                      | this study        |
| $\Delta hstE$                               | NSR-ALD2        | niaD <sup>-</sup> sC <sup>-</sup> adeA <sup>-</sup> argB::adeA <sup>-</sup> AligD::argB AhstE::adeA                                      | this study        |
| $\Delta hstF$                               | NSR-ALD2        | niaD <sup>-</sup> sC <sup>-</sup> adeA <sup>-</sup> argB::adeA <sup>-</sup> AligD::argB AhstF::adeA                                      | this study        |
| ∆laeA                                       | NSR-ALD2        | niaD sC adeA argB::adeA AligD::argB AlaeA::adeA  | this study        |
| $\Delta hst D s C^+$                        | ∆hstD           | niaD <sup>-</sup> sC <sup>-</sup> adeA <sup>-</sup> argB::adeA <sup>-</sup> $\Delta$ ligD::argB $\Delta$ hstD::adeA AnsC <sup>+</sup>    | this study        |
| $\Delta hstD  pUSA^+$                       | ∆hstD           | niaD <sup>-</sup> sC <sup>-</sup> adeA <sup>-</sup> argB::adeA <sup>-</sup> $\Delta$ ligD::argB $\Delta$ hstD::adeA pUSA <sup>+</sup>    | this study        |
| ∆hstD OE∷laeA                               | ∆hstD           | niaD <sup>-</sup> sC <sup>-</sup> adeA <sup>-</sup> argB::adeA <sup>-</sup> <i>AligD::argB AhstD::adeA</i> pUSlaeA <sup>+</sup>          | this study        |
| $\Delta laeA \ sC^+$                        | ∆laeA           | $niaD^{-}sC^{-}adeA^{-}argB::adeA^{-}\Delta ligD::argB\Delta laeA::adeAAnsC^{+}$   | this study        |
| ${\it \Delta}$ lae ${\it A}$ ${\it pUSA}^+$ | ∆laeA           | nia $D^{-}$ s $C^{-}$ ade $A^{-}$ arg $B$ ::ade $A^{-}$ $\Delta$ lig $D$ ::arg $B$ $\Delta$ lae $A$ ::ade $A$ pUS $A^{+}$                | this study        |
| ∆laeA OE∷hstD                               | ∆laeA           | niaD <sup>-</sup> sC <sup>-</sup> adeA <sup>-</sup> argB::adeA <sup>-</sup> $\Delta$ ligD::argB $\Delta$ laeA::adeA pUShstD <sup>+</sup> | this study        |
| OE::laeA                                    | NSR-ALD2        | niaD <sup>-</sup> sC <sup>-</sup> adeA <sup>-</sup> argB::adeA <sup>-</sup> AligD::argB pUSlaeA <sup>+</sup>                             | this study        |
| OE::hstD                                    | NSR-ALD2        | niaD <sup>-</sup> sC <sup>-</sup> adeA <sup>-</sup> argB::adeA <sup>-</sup> $\Delta$ ligD::argB pUShstD <sup>+</sup>                     | this study        |
| $\Delta hst D \Delta lae A$                 | ∆hstD           | niaD <sup>-</sup> sC <sup>-</sup> adeA <sup>-</sup> argB::adeA <sup>-</sup> AligD::argB AhstD::adeA AlaeA::AnsC                          | this study        |
| hstD <sup>+</sup>                           | ∆hstD           | niaD <sup>-</sup> sC <sup>-</sup> adeA <sup>-</sup> argB::adeA <sup>-</sup> $\Delta$ ligD::argB $\Delta$ hstD::adeA::hstD::AnsC          | this study        |
| <i>OE::laeA adeA</i> <sup>+</sup>           | OE::laeA        | $niaD^{-}sC^{-}adeA^{-}argB::adeA^{-}\Delta ligD::argB^{-}pUSlaeA^{+}adeA^{+}$   | this study        |
| OE::hstD adeA +                             | OE::hstD        | $niaD^{-}sC^{-}adeA^{-}argB::adeA^{-}\Delta ligD::argB pUShstD^{+}adeA^{+}$  | this study        |

<sup>a</sup>National Research institute of Brewing <sup>b</sup>AnsC: Aspergillus nidulans sC

<sup>c</sup>ht: heterokaryon

## Table S2. List of sequence accession numbers used in this study

| Saccharomyces cerviciae |                            | Homo sapience                                       |   | Neurospora crassa                                  |                                  | Aspergillus nidulans               |                   | Aspergillus oryzae               |                                  |
|-------------------------|----------------------------|---|---|--|----------------------------------|------------------------------------|-------------------|----------------------------------|----------------------------------|
| Gene <sup>a</sup>       | Accession number           | Gene <sup>a</sup>                                   | Accession number  | Gene <sup>a</sup>                                  | Accession number                 | Gene <sup>a</sup>                  | Accession number  | Gene <sup>a</sup>                | Accession number                 |
| Classica<br>rpd3        | I HDACs familly<br>YNL330C | hdac1 / Hsrpd3<br>hdac2 / Hsrpd3<br>hdac3 / Hsrpd3  | NP_004955<br>NP_001518<br>NP_003874   | hda3 / Ncrpd3                                      | NCU00824                         | rpdA / Anrpd3                      | AN4493            | hdaB / Aorpd3<br>hdaC / Aorpd3   | AB744040<br>AO080525000127       |
| hos2                    | YGL194C                    |   |   | hda2 / Nchos2                                      | NCU02795                         | hosA / Anhos2                      | AN3806            | hdaD / Aohos2                    | AO080511000459                   |
| hos1                    | YPR068C                    |   |   |  |                                  |                                    |                   |                                  |                                  |
| hda l                   | YRL021W                    | hdac6 / Hshda1<br>hdac10 / Hshda1                   | NP_006035<br>NP_114408  | hda1 / Nchda1                                      | NCU01525                         | hdaA / Anhda1                      | AN8024            | hdaA / Aohda1                    | AO080513000236                   |
| hos3<br>TheSirt         | YPL116W<br>uin familly     | hdac4<br>hdac5<br>hdac7<br>hdac8<br>hdac9<br>hdac11 | NP_006028<br>NP_001015053<br>NP_056216<br>NP_060956<br>NP_055522<br>NP_079103 | hda4 / Nchos3                                      | NCU07018                         | hosB / Anhos3                      | AN7019            | hdaE / Aohos3                    | AO080570000061                   |
| sir2                    | YDL042C                    | sirt1 / Hssir2                                      | NP_036370   | nst1 / Ncsir2                                      | NCU04737                         | sirA / Ansir2                      | AN10449           | hstA / Aosir2                    | AO080506000102                   |
| hst1                    | YOL068C                    |   |   |  |                                  |                                    |                   |                                  |                                  |
| hst2                    | YPL015C                    | sirt2 / Hshst2<br>sirt3 / Hshst2                    | NP_036369<br>NP_036371  | nst2 / Nchst2                                      | NCU00523                         | AN7461/ Anhst2<br>AN11873/ Anhst2  | AN7461<br>AN11873 | hstB / Aohst2<br>hstC / Aohst2   | AO080569000094<br>AO080508000293 |
| hst3                    | YOR025W                    |   |   | nst4 / Nchst3                                      | NCU04859                         |                                    |                   |                                  |                                  |
| hst4                    | YDR191W                    |   |   | nst3 / Nchst4                                      | NCU03059                         | AN1226 / Anhst4                    | AN1226            | hstD / Aohst4                    | AB744041                         |
|                         |                            | sirt4<br>sirt5<br>sirt6<br>sirt7                    | NP_036372<br>NP_036373<br>NP_057623<br>NP_057622                              | nst5 / Ncsirt4<br>nst6 / Ncsirt5<br>nst7 / Ncsirt6 | NCU00203<br>NCU05973<br>NCU07624 | hstA / Ansirt4<br>AN1782 / Ansirt5 | AN11067<br>AN1782 | hstE / Aosirt4<br>hstF / Aosirt5 | AO080559000113<br>AO080568000195 |

<sup>a</sup> HDAC names of *Saccharomyces cerevisiae* or *Homo Sapiens* with the species name indicated followed by a slash.

<sup>b</sup> Hda : <u>H</u>istone <u>D</u>e<u>A</u>cetylase

<sup>c</sup> Hst : <u>H</u>omolog of <u>SirT</u>uins
# Table S3. PCR primers used in this study

| Primer name | Sequence(5' to 3') <sup>a,b</sup>                 | Region or purpose                 |
|-------------|---|-----------------------------------|
| adeA-F      | CCGTCATGTCCAGGAAGATAGGTCAG                        | ada ( amplification               |
| adeA-R      | CTGCGCAACAGCATACGAGTCCACAG                        | adeA amplification                |
| hdaB-A      | CAATGGCATGACAAAGAACC                              | 5! floring racian of hdgp         |
| hdaB-B      | CTGACCTATCTTCCTGGACATGACGGCTGTTCCTGCAACATGAGATACA | 5 Hanking legion of haab          |
| hdaB-C      | CTGTGGACTCGTATGCTGTTGCGCAGAAGATCCGTGCGCAAGTT      | 2'flonking region of hdgR         |
| hdaB-D      | CCATGGTGAATTAGGGCTCA                              | 5 mailking region of naab         |
| hdaB-A2     | CAATAGAATATTCCCCGCGT                              | fusion DCD for hdaB               |
| hdaB-D2     | CCCTTGGGATTAGAGTGCTT                              | Iusion FCK for huud               |
| hdaB-F      | GTTGATCGGGATGTCAAAGG                              | hdaR ORE                          |
| hdaB-G      | AATTCTCGGTTCTGCTGGTG                              | nuub OKI                          |
| hdaC-A      | TCTGTGCAAGCCTTATGTGC                              | 5' flanking region of hdaC        |
| hdaC-B      | CTGACCTATCTTCCTGGACATGACGGTCCGTCGAGGTTAGTGACAA    | 5 Hanking region of have          |
| hdaC-C      | CTGTGGACTCGTATGCTGTTGCGCAGTCACTTTGACTACGGAGGGCT   | 3'flanking region of <i>hdaC</i>  |
| hdaC-D      | GCCTCGAAATCATGGTCCTA                              | 5 Hunking region of mute          |
| hdaC-F      | TGAGTGCCTCGTAATGCTTG                              | hdaC ORF                          |
| hdaC-G      | GTGGGCAGGTTGAAACTCTT                              | nuue on                           |
| hdaD-A      | TAACTGGCGCAGACCCATAA                              | 5' flanking region of <i>hdaD</i> |
| hdaD-B      | CTGACCTATCTTCCTGGACATGACGGCCCTTCTTCTCTTTCCTTATTGC | e manking region of made          |
| hdaD-C      | CTGTGGACTCGTATGCTGTTGCGCAGCTGTACGGTAAATGAAGGTCAGC | 3'flanking region of hdaD         |
| hdaD-D      | AAGGGGTCAGATCCACAATG                              | 5 Humang region of haub           |
| hdaD-A2     | CGCAGACCCATAAGAAGGAA                              | fusion PCR for <i>hdaD</i>        |
| hdaD-D2     | CTGTGTCCACAACTGCCATT                              |                                   |
| hdaD-F      | GTTGTTTGGTCAGCGTCAGA                              | hdaD ORF                          |
| hdaD-G      | CCCAAAGGTGACAAGACGAT                              | mul old                           |
| hdaA-A      | AACAAAGTGCCCTGTTGACC                              | 5'flanking region of <i>hdaA</i>  |
| hdaA-B      | CTGACCTATCTTCCTGGACATGACGGCATTGCTATGGCTAGCACCA    | 5 Hunking region of huuri         |
| hdaA-C      | CTGTGGACTCGTATGCTGTTGCGCAGTTTAGGACGTTCAGATGGGG    | 3'flanking region of <i>hdaA</i>  |
| hdaA-D      | TAGGTTTTCTGATGGCCCAG                              |                                   |
| hdaA-F      | GTGATGCCTATTGCACAGGA                              | hdaA ORF                          |
| hdaA-G      | GCTTTCGGGTACATGCAACT                              | 11111 OIN                         |

| hdaE-A  | TCCGAAGTCCACTTTCTTGC                              | 5' flanking region of hdgE        |
|---------|---|-----------------------------------|
| hdaE-B  | CTGACCTATCTTCCTGGACATGACGGCAAATAGTAGGTTCATTTGGGGG | 3 Hanking region of <i>naal</i>   |
| hdaE-C  | CTGTGGACTCGTATGCTGTTGCGCAGAGTCTATCGGACTTTTGGTCG   | 2'flanking region of hdgF         |
| hdaE-D  | AGATCCGGAGTCGTTCCTTT                              | 5 manking region of naal          |
| hdaE-A2 | AGTCTCTTTTCTTTGGCCGC                              | fusion PCR for hdaF               |
| hdaE-D2 | ATTGTTCACGTTCTCCACCC                              | Tusion I CIX IOI nuul             |
| hdaE-F  | GGACCTTTACGCATCCAAGT                              | hdaE OBE                          |
| hdaE-G  | GATGCGTGTTGGACATTAGC                              | nuul on                           |
| hstA-A  | ATTACCTGGCGTTCTTGTGG                              | 5'flanking region of hst A        |
| hstA-B  | CTGACCTATCTTCCTGGACATGACGGGGGTTCTTGTTTGGAGGGTT    | 5 Hanking region of <i>hst</i> 21 |
| hstA-C  | CTGTGGACTCGTATGCTGTTGCGCAGCGGATTCTTCAACGAAGAGC    | 3'flanking region of hst 4        |
| hstA-D  | ACAGCTGCGAACTGATGATG                              | 5 manking region of <i>hstri</i>  |
| hstA-F  | GATTTCCGGCTCTTGTGTGT                              | hstA ORF                          |
| hstA-G  | GGTATTCCCGATTTTCGGTC                              |                                   |
| hstB-A  | CTTTGCTTTGAGTTCCTGCC                              | 5'flanking region of <i>hstB</i>  |
| hstB-B  | CTGACCTATCTTCCTGGACATGACGGTCTAACCTGGCGGAGAGAAA    |                                   |
| hstB-C  | CTGTGGACTCGTATGCTGTTGCGCAGTACCGCGAAAAGGAGAGAGA    | 3'flanking region of <i>hstB</i>  |
| hstB-D  | AACAGTCGGCGATGTATTCC                              | 5 mainting region of <i>hsib</i>  |
| hstB-F  | CTTTTTCAGGGAGAATCCGC                              | hst BORF                          |
| hstB-G  | CGCTCCATGTTAATGAGCAC                              | histid Old                        |
| hstC-A  | AGTCATGGAAAAGACTGCGG                              | 5'flanking region of hstC         |
| hstC-B  | CTGACCTATCTTCCTGGACATGACGGATTGGACTCAGCCTGATTGG    | 5 manking region of histe         |
| hstC-C  | CTGTGGACTCGTATGCTGTTGCGCAGAGTGCCCGAATAGGTTTCTG    | 3'flanking region of hstC         |
| hstC-D  | AGCCATCGCTGTCAGTTTCT                              | 5 manking region of <i>hst</i> e  |
| hstC-F  | GCCTTGCTGGCTAAGAAGAA                              | hstC OPE                          |
| hstC-G  | TCACACGACCCAAGGATACA                              | hsie ora                          |
| hstD-A  | TGCGGAAATGGGTTGTTT                                | 5'flanking ragion of hetD         |
| hstD-B  | CTGACCTATCTTCCTGGACATGACGGATGGCACTTGTCGCATGTC     | 5 Hanking region of hstD          |
| hstD-C  | CTGTGGACTCGTATGCTGTTGCGCAGGGCGTGGTGTAATTCTTCGT    | 2'flanking ragion of hatD         |
| hstD-D  | TAACCGTGACATGACCCTTG                              | 5 Haliking region of <i>hstD</i>  |
| hstD-A2 | TGAAAGGATTACCTCCTCCC                              | fusion DCD for hat D              |
| hstD-D2 | ACGTCCGGGATATTATGGGT                              | IUSION PCK IOI <i>MSID</i>        |
| hstD-F  | ACCATCAAGTCCCAGCAATC                              | hat DODE                          |
| hstD-G  | AGACATCCATGCCTCCCTTA                              | nsid OKr                          |

| hstE-A        | TCCATCTGATAAGGTTCGGC                                   | 5'florking region of hetE               |
|---------------|--|---|
| hstE-B        | CTGACCTATCTTCCTGGACATGACGGGAGATAATGGGTACGGCGAGA        | 5 Hanking region of <i>nstE</i>         |
| hstE-C        | <u>CTGTGGACTCGTATGCTGTTGCGCAG</u> GGCGCTGTCCGAATGTATTA | 2!florking region of hetE               |
| hstE-D        | CCAGTGTACAATTCCGCCAT                                   | 5 Hanking region of <i>nstE</i>         |
| hstE-A2       | ATAAGGTTCGGCATGAGTGG                                   | fusion DCD for hatE                     |
| hstE-D2       | GCCATGATACATCCAGCAGA                                   | IUSIOII FCK IOI <i>NSIE</i>             |
| hstE-F        | AATATCTGGGGCAGACGAGA                                   | hatE ODE                                |
| hstE-G        | GGCACATTCTCAAGAGCACA                                   | ISIE OKF                                |
| hstF-A        | ATTGACGAACCCTTGGACTG                                   | 5! floring region of hetE               |
| hstF-B        | CTGACCTATCTTCCTGGACATGACGGGCGGGGGGTGTTGATAATGACT       | 5 manking region of <i>nstr</i>         |
| hstF-C        | CTGTGGACTCGTATGCTGTTGCGCAGGGTATTATGGGGGATTGTCGG        | 2!florking region of hetE               |
| hstF-D        | TCTTCGTCTTCAAAGGCTCC                                   | 5 Hanking legion of <i>nstr</i>         |
| hstF-A2       | CGTCAGCTCACGGATTATGA                                   | fusion DCD for hat                      |
| hstF-D2       | TCTCGTTTGCCTTAGCTGTG                                   | IUSIOII PCK IOI <i>NSIF</i>             |
| hstF-F        | AGACATATGGCGCTGAAAGC                                   | hatE ODE                                |
| hstF-G        | GCAATGTGGAAGGACATCAG                                   | nstr Okf                                |
| Fusion-hstD-F | tcgagetcggtacccATGGTGCGGTCGCTGTCCGAAGAGG               | votor construction for pUShatD          |
| Fusion-hstD-R | ctctagaggatccccTCATGCGGCCGGCTGATTTAACAAC               | vector construction for <i>p</i> USAStD |
| Fusion-laeA-F | tcgagctcggtacccATGTTTGGAAACGGCCAGACTGGAC               | votor construction for nUSLack          |
| Fusion-laeA-R | ctctagaggatccccTCAGTTCGCAGGTTTCCGTGCTTGG               | vector construction for <i>pOsideA</i>  |
| laeA-A        | CCGGCTGTTCAAGATCCATGGATAG                              | 5'floring region of last                |
| laeA(adeA)-B  | CTGACCTATCTTCCTGGACATGACGGTCGATGGCGACAGGCTGATG         | 5 manking region of <i>tueA</i>         |
| laeA(adeA)-C  | CTGTGGACTCGTATGCTGTTGCGCAGAGAGCTCCATTACTGGGTATTCGG     | 2!flanking region of last               |
| laeA-D        | GAACCCGCCAACATCAAGCTTC                                 | 5 manking region of <i>tueA</i>         |
| laeA-A2       | GGGATACCAACAACACCT                                     | fusion DCD for last                     |
| laeA-D2       | TTACGTTTGGGAACGGAGTCA                                  | IUSION PCK IOI IdeA                     |
| laeA-F        | CAGCCCTCAAACCACCCAAA                                   | lact ODE                                |
| laeA-G        | TTGAACGCCTCCGACTTGAC                                   | IdeA ORF                                |
| laeA(sC)-B    | <u>GAACGAGACGAACGAGGAGCCATAT</u> TCGATGGCGACAGGCTGATG  | disruption casette for <i>laeA</i> in   |
| laeA(sC)-C    | CATACGGGCAGCTATTGCCAAGAGAGAGAGCTCCATTACTGGGTATTCGG     | $\Delta hstD$ background                |
| sC-F          | ATATGGCTCCTCGTTCGTCTCGTTC                              |   |
| sC-R          | TCTCTTGGCAATAGCTGCCCGTATG                              | sC amplification                        |

| P-amyB-F         | GGCAACTCGCTTACCGATTAC                                      | confirmation of transformation<br>of over expression construct |
|------------------|--|--|
| hstD-comp-B      | GAACGAGACGAACGAGGAGCCATATTAACCGTGACATGACCCTTG              |  |
| adeA fusion sC-F | <u>CATACGGGCAGCTATTGCCAAGAGA</u> CCGTCATGTCCAGGAAGATAGGTCA | Complementation of <i>hstD</i>                                 |
| nested adeA-R    | GCCTTGGTCTGGGAGTGT   |  |
| kojA-F           | GGTTTCCAGGGCCTCATCAG                                       | probe for kail   |
| kojA-R           | GAGAAATCCGGGCCAGAACC                                       | probe for kojA   |
| kojR-F           | CGGCCAGCTATGACCCCATT                                       | probe for kaiP   |
| kojR-R           | GGCGTCATGGGAGAGTGTGA                                       | probe for kojk   |
| kojT-F           | CGAGGTGTCTCTTGCAAACC                                       | proba for kaiT   |
| kojT-R           | GTTCTGGGATAGGCGAACCA                                       |  |
| ipnA-F           | CACCTACTCACGAGGTCAAC                                       | probe for inn 1  |
| ipnA-R           | GTTGACCTCGTGAGTAGGTG                                       | probe for <i>ipnA</i>  |
| laeA-F           | AGCCCTCAAACCACCCAAAG                                       | probe for last   |
| laeA-R           | TTGAACGCCTCCGACTTGAC                                       | probe for <i>tueA</i>  |

<sup>a</sup> Additional nucleotides for fusion PCR are indicated by underlines <sup>b</sup> Additional nucleotides for In-Fusion reaction are indicated in small letters

#### Table S4. Significantly changed genes in $\Delta hstD$

| Gene ID                                      | Description  | Fold change               |              | FunCat categorization <sup>a,b</sup>           |
|--|--|---------------------------|--------------|--|
|  |  | ( <i>AhstD</i> / Control) | level 1      | level 2  |
| AO080553000121 KojT, putative transporter; p | resent in the kojic acid biosynthetic gene cluster                     | 105.5                     | [20][32]     | [20.01][20.03][20.09][32.05][32.07]            |
| AO080550000061 Hydroxyindole-O-methyltrar    | sferase and related SAM-dependent methyltransferases                   | 102.5                     | [01]         | [01.05][01.20]                                 |
| AO080501000196 fleA fucose-specific lectin   |  | 61.82                     | #            | #  |
| AO080563000007 CpaD, O-dimethylallyltransf   | erase (DMAT); dimethylallylates cAATrp to form beta-cyclopiazonic acid | 49.39                     | #            | #  |
| AO080554000441 Uncharacterized membrane      | protein, predicted efflux pump   | 38.39                     | [20][32]     | [20.01][32.07]                                 |
| AO080563000004 Predicted protein             |  | 32.27                     | [20][32][34] | [20.01][20.03][20.09][32.05][32.07]<br>[34.11] |
| AO080525000393 Predicted protein             |  | 29.96                     | [01][11]     | [01.02][11.02]                                 |
| AO080563000005 Cytochrome P450 CYP3 CY       | P5 CYP6 CYP9 subfamilies   | 27.59                     | [01]         | [01.06][01.20]                                 |
| AO080563000006 Predicted protein             |  | 25.97                     | #            | #  |
| AO080508000254 Predicted protein             |  | 24.93                     | [01]         | [01.05]  |
| AO080511000457 Predicted protein             |  | 21.4                      | #            | #  |
| AO080522000026 Catalase (peroxidase I)       |  | 20.19                     | [32]         | [32.07]  |
| AO080536000097 Predicted protein             |  | 19.6                      | #            | #  |
| AO080542000015 Predicted protein             |  | 19.4                      | [32]         | [32.05]  |
| AO080515000039 Predicted protein             |  | 17.93                     | #            | #  |
| AO080550000056 Proteins containing the FAD   | binding domain   | 14.42                     | [01]         | [01.05][01.20]                                 |
| AO080508000512 mleA lectin                   | C  | 12.87                     | #            | #  |
| AO080515000015 Uncharacterized protein, pos  | sibly involved in utilization of glycolate and propanediol             | 12.31                     | #            | #  |
| AO080513000111 Predicted protein             | 5 65 11  | 11.85                     | #            | #  |
| AO080529000071 Predicted protein             |  | 10.43                     | #            | #  |
| AO080508000290 Predicted protein             |  | 10.11                     | #            | #  |
| AO080523000388 Predicted protein             |  | 9.984                     | #            | #  |
| AO080554000006 Predicted protein             |  | 9.951                     | #            | #  |
| AO080550000062 Dehydrogenases (flavoprotei   | ns)  | 9.86                      | #            | #  |
| AO080525000250 Predicted protein             |  | 9.747                     | #            | #  |
| AO080553000119 KojA, FAD-dependent oxido     | preductase; present in the kojic acid biosynthetic gene cluster        | 9.711                     | #            | #  |
| AO080541000467 Predicted protein             | , i j j č  | 9.668                     | #            | #  |
| AO080550000076 Predicted protein             |  | 9.323                     | #            | #  |
| AO080539000068 Predicted protein             |  | 9.028                     | #            | #  |
| AO080510000132 Predicted protein             |  | 8.772                     | #            | #  |
| AO080529000068 Predicted protein             |  | 8.053                     | #            | #  |
| AO080554000051 Predicted protein             |  | 7.73                      | #            | #  |
| AO080550000193 RNA 3 -terminal phosphate     | cvclase  | 7.67                      | #            | #  |
| AO080551000140 Polyketide synthase modules   | and related proteins   | 7.028                     | [01][32]     | [01.20][32.05]                                 |
| AO080511000259 Predicted protein             | I  | 6.937                     | #            | #  |
| AO080523000239 TPR repeat                    |  | 6.617                     | #            | #  |
| AO080537000053 Predicted hydrolases or acvit | transferases (alpha beta hydrolase superfamily)                        | 6.315                     | #            | #  |
| AO080527000194 Predicted xylanase chitin dea | acetylase  | 6.251                     | [01][16]     | [01.05][01.25][16.05]                          |
| AO080551000190 Beta-lactamase class C and c  | other penicillin binding proteins                                      | 6.175                     | #            | #  |
| AO080508000358 Predicted protein             | r r r r r r r r r r r r r r r r r r r                                  | 5,923                     | #            | #  |
| AO080515000064 Multicopper oxidases          |  | 5.855                     | [01][32]     | [01.05][01.07][01.25][32.07]                   |
| AO080527000284 Predicted protein             |  | 5.77                      | #            | #  |

| AO080549000421 Predicted protein  | 5.727 | #                          | #  |
|---|-------|----------------------------|--|
| AO080550000107 Predicted protein  | 5.723 | #                          | #  |
| AO080523000444 Predicted protein  | 5.71  | #                          | #  |
| AO080567000074 Predicted protein  | 5.689 | #                          | #  |
| AO080541000077 Predicted protein  | 5.673 | #                          | #  |
| AO080523000389 Cytochrome P450 CYP4 CYP19 CYP26 subfamilies   | 5 589 | [32]                       | [32.07]  |
| AO080521000213 Predicted protein  | 5 575 | [ <i>3</i> <b>_</b> ]<br># | [32:07]<br>#                                   |
| A O080547000015 Predicted protein   | 5 394 | #                          | #  |
| A OD80523000405 Predicted protein   | 5 171 | [32][42]                   | [32 01][42 01][42 04]                          |
| A O0805257000412 Predicted protein  | 5 107 | [JZ][TZ]<br>#              | #  |
| A OD805270007121 Alkalina phoenhataca   | 5.07  | π<br>[01]                  | $\pi^{-1}$                                     |
| AO080525000/01 Aikanie pilospialase   | 4.022 | [01]<br>#                  | [01.04][01.00][01.07]<br>#                     |
| A0080525000550 Fieldeted protein  | 4.932 | #<br>#                     | н<br>ц   |
| A0080552000080 and Fredicide protein  | 4.922 | #<br>#                     | #<br>#   |
| A0080534000398 Predicted protein  | 4./46 | #                          | #<br>  |
| AO080525000625 Predicted protein  | 4.693 | #                          | #  |
| AO080541000440 Predicted protein  | 4.676 | #                          | #  |
| AO080530000095 Predicted protein  | 4.602 | #                          | #  |
| AO080554000103 Cytochrome P450 CYP3 CYP5 CYP6 CYP9 subfamilies  | 4.597 | [01][20][32]               | [01.01][01.02][01.06][01.20][20.01]<br>[32.07] |
| AO080547000014 Ankyrin  | 4.512 | #                          | #  |
| AO080549000406 Predicted dehydrogenases and related proteins  | 4.472 | [01][11]                   | [01.05][11.02]                                 |
| AO080508000357 Chitin synthase hvaluronan synthase (glycosyltransferases)                                   | 4.45  | #                          | #  |
| AO080523000006 Predicted protein  | 4 401 | #                          | #  |
|   |       |                            |  |
| AO080525000059 Cytochrome P450 CYP2 subfamily   | 4.37  | [01][16][20][32]           | [20.01][32.07]                                 |
| AO080523000500 Predicted protein  | 4.32  | #                          | #  |
| AO080527000186 Oxidosqualene-lanosterol cyclase and related proteins  | 4.272 | [01]                       | [01.06][01.20]                                 |
| AO080523000718 Carboxylesterase type B  | 4.266 | #                          | #  |
| AO080529000067 Cytochrome P450 CYP11 CYP12 CYP24 CYP27 subfamilies  | 4.247 | [01][32]                   | [01.01][01.20][32.07]                          |
| AO080515000065 Predicted protein  | 4.223 | #                          | #  |
| AO080532000090 Predicted protein  | 4.183 | #                          | #  |
| AO080508000361 Predicted protein  | 4.159 | #                          | #  |
| AO080551000170 Predicted protein  | 4.114 | [01][16]                   | [01.01][01.20][16.17]                          |
| AO080525000706 Predicted protein  | 4.098 | #                          | #  |
| AO080532000546 Cytochrome P450 CYP2 subfamily   | 4.046 | [01][16][20]               | [01.20][16.17][16.21][20.01]                   |
| AO080508000305 Vesicular amine transporter  | 4.008 | #                          | #  |
| AO080527000377 Glucose dehydrogenase choline dehydrogenase mandelonitrile lyase (GMC oxidoreductase family) | 4.008 | [01][16][20]               | [01.01][01.05][01.20][16.21][20.01]            |
| AO080531000104 Predicted protein  | 3.951 | #                          | #  |
| AO080525000269 Predicted protein  | 3.848 | #                          | #  |
| A0080557000082 Cofilin: actin depolymerisation factor   | 3 847 | #                          | #  |
| AO080532000337 Chaperone-dependent E3 ubiquitin protein ligase (contains TPR repeats)                       | 3 838 | #                          | <br>#  |
| AO080523000512 Predicted protein  | 3 774 | #                          | <br>#  |
| A O080523000573 Predicted protein   | 3 77  | #                          | #  |
| $\Delta O080536000086 \wedge TDecose of the \Lambda \Lambda \Lambda^+ along$                                | 3 710 | <br>#                      | <br>#  |
| A COROUS SOUCHOUS A Frazes of life AAA Class  | 2 707 | π<br>[42]                  | π<br>[42.01]                                   |
| AU000515000151 FIGUEIGU PIOLEIII  | 5./0/ | [45]<br>#                  | [43.01]<br>#                                   |
| A0080525000087 Fredicted transporter (major facilitator superfamily)  | 3.648 | #<br>[22]                  | #  |
| AU08055 / 000045 Predicted protein  | 3.024 | 32                         | [32.03]  |

| AO080515000071 Predicted protein  | 3.604   | #   | #   |
|---|---|---|---|
| AO080501000080 Predicted protein  | 3.559   | #   | #   |
| AO080566000093 Ankyrin  | 3.555   | #   | #   |
| AO080525000026 SAM-dependent methyltransferases   | 3.536   | #   | #   |
| AO080515000098 Predicted protein  | 3.503   | #   | #   |
| AO080554000362 Predicted protein  | 3.493   | #   | #   |
| AO080503000171 Phosphoenolpyruvate carboxykinase (ATP)  | 3.468   | [01][02]  | [01.04][01.05][02.01]   |
| AO080523000572 Predicted protein  | 3.423   | #   | #   |
| AO080533000376 Multidrug resistance-associated protein mitoxantrone resistance protein, ABC superfamily   | 3.391   | [01][16][20][32]  | [01.04][16.19][20.03][32.07]  |
| AO080508000531 Predicted protein  | 3.39  | #   | #   |
| AO080549000304 Carboxylesterase type B  | 3.38  | [01]  | [01.06]   |
| AO080506000286 Predicted protein  | 3.315   | #   | #   |
| AO080523000216 Predicted protein  | 3.303   | #   | #   |
| AO080538000066 AcvI-CoA synthetase  | 3.298   | [01]  | [01.01][01.05][01.20]   |
| AO080523000032 Amino acid transporters  | 3.296   | [01][20][32][34]  | [01.06][20.01][20.03][20.09[32.01]<br>[34.01][34.11]  |
| AO080510000108 ATPases of the $AAA^+$ class   | 3.199   | #   | #   |
| AO080513000093 Jacalin-like lectin domain-containing protein  | 3.158   | #   | #   |
| AO080525000640 Predicted protein  | 3.156   | #   | #   |
| AQ080527000200 Chitinase  | 3.085   | [01]  | [01 05][01 25]  |
| AO080553000120 KoiR, Zn(II)2Cys6 transcription factor; induced by kojic acid; present in the kojic acid biosynthetic gene cl  | 3.083   | [11][34]  | [11.02][34.11]  |
| AO080525000062 Acetylcholinesterase Butyrylcholinesterase   | 3.076   | [01][32]  | [01.05][01.06][01.20][01.25][32.05]<br>[32.07][32.10]   |
|   |   |   | 32.0, 32.10   |
| AO080541000359 Integral membrane ankvrin-repeat protein Kidins220 (protein kinase D substrate)  | 3.076   | #   | #   |
| AO080541000359 Integral membrane ankyrin-repeat protein Kidins220 (protein kinase D substrate)<br>AO080541000097 Predicted transporter (major facilitator superfamily)  | 3.076<br>3.063  | #<br>[20][32]   | #<br>[20.01][32.07]   |
| AO080541000359 Integral membrane ankyrin-repeat protein Kidins220 (protein kinase D substrate)<br>AO080541000097 Predicted transporter (major facilitator superfamily)<br>AO080546000223 Predicted protein  | 3.076<br>3.063<br>3.039   | #<br>[20][32]<br>#  | #<br>[20.01][32.07]<br>#  |
| AO080541000359 Integral membrane ankyrin-repeat protein Kidins220 (protein kinase D substrate)<br>AO080541000097 Predicted transporter (major facilitator superfamily)<br>AO080546000223 Predicted protein<br>AO080542000014 Cytochrome P450 CYP4 CYP19 CYP26 subfamilies   | 3.076<br>3.063<br>3.039<br>3.037  | #<br>[20][32]<br>#<br>[01][32]  | #<br>[20.01][32.07]<br>#<br>[01.01][32.05][32.07]   |
| AO080541000359 Integral membrane ankyrin-repeat protein Kidins220 (protein kinase D substrate)<br>AO080541000097 Predicted transporter (major facilitator superfamily)<br>AO080546000223 Predicted protein<br>AO080542000014 Cytochrome P450 CYP4 CYP19 CYP26 subfamilies<br>AO080539000029 Predicted protein   | 3.076<br>3.063<br>3.039<br>3.037<br>3.016   | #<br>[20][32]<br>#<br>[01][32]<br>[11]  | #<br>[20.01][32.07]<br>#<br>[01.01][32.05][32.07]<br>[11.02]  |
| AO080541000359 Integral membrane ankyrin-repeat protein Kidins220 (protein kinase D substrate)<br>AO080541000097 Predicted transporter (major facilitator superfamily)<br>AO080546000223 Predicted protein<br>AO080542000014 Cytochrome P450 CYP4 CYP19 CYP26 subfamilies<br>AO080539000029 Predicted protein<br>AO080547000070 Predicted protein   | 3.076<br>3.063<br>3.039<br>3.037<br>3.016<br>2.985  | #<br>[20][32]<br>#<br>[01][32]<br>[11]<br>#   | #<br>[20.01][32.07]<br>#<br>[01.01][32.05][32.07]<br>[11.02]<br>#   |
| AO080541000359 Integral membrane ankyrin-repeat protein Kidins220 (protein kinase D substrate)<br>AO080541000097 Predicted transporter (major facilitator superfamily)<br>AO080546000223 Predicted protein<br>AO080542000014 Cytochrome P450 CYP4 CYP19 CYP26 subfamilies<br>AO080539000029 Predicted protein<br>AO080547000070 Predicted protein<br>AO080523000242 Predicted protein   | 3.076<br>3.063<br>3.039<br>3.037<br>3.016<br>2.985<br>2.977   | #<br>[20][32]<br>#<br>[01][32]<br>[11]<br>#<br>#  | #<br>[20.01][32.07]<br>#<br>[01.01][32.05][32.07]<br>[11.02]<br>#<br>#  |
| AO080541000359 Integral membrane ankyrin-repeat protein Kidins220 (protein kinase D substrate)<br>AO080541000097 Predicted transporter (major facilitator superfamily)<br>AO080546000223 Predicted protein<br>AO080542000014 Cytochrome P450 CYP4 CYP19 CYP26 subfamilies<br>AO080539000029 Predicted protein<br>AO080547000070 Predicted protein<br>AO080523000242 Predicted protein<br>AO080502000014 Uncharacterized conserved protein   | 3.076<br>3.063<br>3.039<br>3.037<br>3.016<br>2.985<br>2.977<br>2.976  | #<br>[20][32]<br>#<br>[01][32]<br>[11]<br>#<br>#  | #<br>[20.01][32.07]<br>#<br>[01.01][32.05][32.07]<br>[11.02]<br>#<br>#  |
| AO080541000359 Integral membrane ankyrin-repeat protein Kidins220 (protein kinase D substrate)<br>AO080541000097 Predicted transporter (major facilitator superfamily)<br>AO080546000223 Predicted protein<br>AO080542000014 Cytochrome P450 CYP4 CYP19 CYP26 subfamilies<br>AO08053900029 Predicted protein<br>AO080547000070 Predicted protein<br>AO080523000242 Predicted protein<br>AO080502000014 Uncharacterized conserved protein<br>AO080502000014 Uncharacterized conserved protein  | 3.076<br>3.063<br>3.039<br>3.037<br>3.016<br>2.985<br>2.977<br>2.976<br>2.959   | #<br>[20][32]<br>#<br>[01][32]<br>[11]<br>#<br>#<br>#<br>[01][10][14][16]   | #<br>[20.01][32.07]<br>#<br>[01.01][32.05][32.07]<br>[11.02]<br>#<br>#<br>#<br>[01.05][10.01][14.07][16.01][16.03]  |
| AO080541000359 Integral membrane ankyrin-repeat protein Kidins220 (protein kinase D substrate)<br>AO080541000097 Predicted transporter (major facilitator superfamily)<br>AO080546000223 Predicted protein<br>AO080542000014 Cytochrome P450 CYP4 CYP19 CYP26 subfamilies<br>AO08053900029 Predicted protein<br>AO080547000070 Predicted protein<br>AO080523000242 Predicted protein<br>AO080502000014 Uncharacterized conserved protein<br>AO080503000338 NAD <sup>+</sup> ADP-ribosyltransferase Parp, required for poly-ADP ribosylation of nuclear proteins<br>AO080506000124 Predicted protein   | 3.076<br>3.063<br>3.039<br>3.037<br>3.016<br>2.985<br>2.977<br>2.976<br>2.959<br>2.951  | #<br>[20][32]<br>#<br>[01][32]<br>[11]<br>#<br>#<br>[01][10][14][16]<br>#   | #<br>[20.01][32.07]<br>#<br>[01.01][32.05][32.07]<br>[11.02]<br>#<br>#<br>#<br>[01.05][10.01][14.07][16.01][16.03]<br>#   |
| AO080541000359 Integral membrane ankyrin-repeat protein Kidins220 (protein kinase D substrate)<br>AO080541000097 Predicted transporter (major facilitator superfamily)<br>AO080546000223 Predicted protein<br>AO08054200014 Cytochrome P450 CYP4 CYP19 CYP26 subfamilies<br>AO08053900029 Predicted protein<br>AO080547000070 Predicted protein<br>AO080523000242 Predicted protein<br>AO080502000014 Uncharacterized conserved protein<br>AO080503000338 NAD <sup>+</sup> ADP-ribosyltransferase Parp, required for poly-ADP ribosylation of nuclear proteins<br>AO080542000124 Predicted protein<br>AO080502000124 Predicted protein  | 3.076<br>3.063<br>3.039<br>3.037<br>3.016<br>2.985<br>2.977<br>2.976<br>2.959<br>2.951<br>2.943   | #<br>[20][32]<br>#<br>[01][32]<br>[11]<br>#<br>#<br>[01][10][14][16]<br>#<br>#  | #<br>[20.01][32.07]<br>#<br>[01.01][32.05][32.07]<br>[11.02]<br>#<br>#<br>[01.05][10.01][14.07][16.01][16.03]<br>#<br>#   |
| AO080541000359 Integral membrane ankyrin-repeat protein Kidins220 (protein kinase D substrate)<br>AO080541000097 Predicted transporter (major facilitator superfamily)<br>AO080546000223 Predicted protein<br>AO080542000014 Cytochrome P450 CYP4 CYP19 CYP26 subfamilies<br>AO08053900029 Predicted protein<br>AO080547000070 Predicted protein<br>AO080523000242 Predicted protein<br>AO080502000014 Uncharacterized conserved protein<br>AO080503000338 NAD <sup>+</sup> ADP-ribosyltransferase Parp, required for poly-ADP ribosylation of nuclear proteins<br>AO08054200029 Conserved protein<br>AO080542000029 Conserved protein domain typically associated with flavoprotein oxygenases, DIM6 NTAB family<br>AO080521000317 Predicted protein   | 3.076<br>3.063<br>3.039<br>3.037<br>3.016<br>2.985<br>2.977<br>2.976<br>2.959<br>2.951<br>2.943<br>2.904  | #<br>[20][32]<br>#<br>[01][32]<br>[11]<br>#<br>#<br>[01][10][14][16]<br>#<br>#  | #<br>[20.01][32.07]<br>#<br>[01.01][32.05][32.07]<br>[11.02]<br>#<br>#<br>[01.05][10.01][14.07][16.01][16.03]<br>#<br>#<br>#  |
| AO080541000359 Integral membrane ankyrin-repeat protein Kidins220 (protein kinase D substrate)<br>AO080541000097 Predicted transporter (major facilitator superfamily)<br>AO080546000223 Predicted protein<br>AO080542000014 Cytochrome P450 CYP4 CYP19 CYP26 subfamilies<br>AO08053900029 Predicted protein<br>AO080547000070 Predicted protein<br>AO080523000242 Predicted protein<br>AO080502000014 Uncharacterized conserved protein<br>AO080503000338 NAD <sup>+</sup> ADP-ribosyltransferase Parp, required for poly-ADP ribosylation of nuclear proteins<br>AO08054200029 Conserved protein domain typically associated with flavoprotein oxygenases, DIM6 NTAB family<br>AO080521000317 Predicted protein   | 3.076<br>3.063<br>3.039<br>3.037<br>3.016<br>2.985<br>2.977<br>2.976<br>2.959<br>2.951<br>2.943<br>2.904<br>2.901   | #<br>[20][32]<br>#<br>[01][32]<br>[11]<br>#<br>#<br>[01][10][14][16]<br>#<br>#<br>#   | #<br>[20.01][32.07]<br>#<br>[01.01][32.05][32.07]<br>[11.02]<br>#<br>#<br>[01.05][10.01][14.07][16.01][16.03]<br>#<br>#<br>#<br>#   |
| AO080541000359 Integral membrane ankyrin-repeat protein Kidins220 (protein kinase D substrate)<br>AO080541000097 Predicted transporter (major facilitator superfamily)<br>AO080546000223 Predicted protein<br>AO080542000014 Cytochrome P450 CYP4 CYP19 CYP26 subfamilies<br>AO08053900029 Predicted protein<br>AO080547000070 Predicted protein<br>AO080523000242 Predicted protein<br>AO080502000014 Uncharacterized conserved protein<br>AO080502000014 Uncharacterized conserved protein<br>AO080503000338 NAD <sup>+</sup> ADP-ribosyltransferase Parp, required for poly-ADP ribosylation of nuclear proteins<br>AO08054200029 Conserved protein domain typically associated with flavoprotein oxygenases, DIM6 NTAB family<br>AO080521000317 Predicted protein<br>AO080518000104 Predicted protein   | 3.076<br>3.063<br>3.039<br>3.037<br>3.016<br>2.985<br>2.977<br>2.976<br>2.959<br>2.951<br>2.943<br>2.904<br>2.901<br>2.888  | #<br>[20][32]<br>#<br>[01][32]<br>[11]<br>#<br>#<br>[01][10][14][16]<br>#<br>#<br>#<br>#  | #<br>[20.01][32.07]<br>#<br>[01.01][32.05][32.07]<br>[11.02]<br>#<br>#<br>[01.05][10.01][14.07][16.01][16.03]<br>#<br>#<br>#<br>#<br>#<br>#   |
| AO080541000359 Integral membrane ankyrin-repeat protein Kidins220 (protein kinase D substrate)<br>AO080541000097 Predicted transporter (major facilitator superfamily)<br>AO080546000223 Predicted protein<br>AO080542000014 Cytochrome P450 CYP4 CYP19 CYP26 subfamilies<br>AO08053900029 Predicted protein<br>AO080547000070 Predicted protein<br>AO080523000242 Predicted protein<br>AO080502000014 Uncharacterized conserved protein<br>AO080502000014 Uncharacterized conserved protein<br>AO080503000338 NAD <sup>+</sup> ADP-ribosyltransferase Parp, required for poly-ADP ribosylation of nuclear proteins<br>AO08054200029 Conserved protein domain typically associated with flavoprotein oxygenases, DIM6 NTAB family<br>AO080521000317 Predicted protein<br>AO080536000058 Predicted protein<br>AO080518000104 Predicted protein   | 3.076<br>3.063<br>3.039<br>3.037<br>3.016<br>2.985<br>2.977<br>2.976<br>2.959<br>2.951<br>2.943<br>2.904<br>2.901<br>2.888<br>2.88  | #<br>[20][32]<br>#<br>[01][32]<br>[11]<br>#<br>#<br>[01][10][14][16]<br>#<br>#<br>#<br>#  | #<br>[20.01][32.07]<br>#<br>[01.01][32.05][32.07]<br>[11.02]<br>#<br>#<br>[01.05][10.01][14.07][16.01][16.03]<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#  |
| AO080541000359 Integral membrane ankyrin-repeat protein Kidins220 (protein kinase D substrate)<br>AO080541000097 Predicted transporter (major facilitator superfamily)<br>AO08054000023 Predicted protein<br>AO080542000014 Cytochrome P450 CYP4 CYP19 CYP26 subfamilies<br>AO08053900029 Predicted protein<br>AO080547000070 Predicted protein<br>AO080523000242 Predicted protein<br>AO080502000014 Uncharacterized conserved protein<br>AO080502000014 Uncharacterized conserved protein<br>AO080503000338 NAD <sup>+</sup> ADP-ribosyltransferase Parp, required for poly-ADP ribosylation of nuclear proteins<br>AO080542000029 Conserved protein domain typically associated with flavoprotein oxygenases, DIM6 NTAB family<br>AO080521000317 Predicted protein<br>AO080518000104 Predicted protein<br>AO080518000149 Predicted protein<br>AO080518000149 Predicted protein   | 3.076<br>3.063<br>3.039<br>3.037<br>3.016<br>2.985<br>2.977<br>2.976<br>2.959<br>2.951<br>2.943<br>2.904<br>2.901<br>2.888<br>2.88<br>2.88<br>2.853   | #<br>[20][32]<br>#<br>[01][32]<br>[11]<br>#<br>#<br>[01][10][14][16]<br>#<br>#<br>#<br>#<br>#   | #<br>[20.01][32.07]<br>#<br>[01.01][32.05][32.07]<br>[11.02]<br>#<br>#<br>[01.05][10.01][14.07][16.01][16.03]<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#  |
| AO080541000359 Integral membrane ankyrin-repeat protein Kidins220 (protein kinase D substrate)<br>AO080541000097 Predicted transporter (major facilitator superfamily)<br>AO080540000223 Predicted protein<br>AO080542000014 Cytochrome P450 CYP4 CYP19 CYP26 subfamilies<br>AO08053900029 Predicted protein<br>AO080547000070 Predicted protein<br>AO080523000242 Predicted protein<br>AO080502000014 Uncharacterized conserved protein<br>AO080503000338 NAD <sup>+</sup> ADP-ribosyltransferase Parp, required for poly-ADP ribosylation of nuclear proteins<br>AO080542000029 Conserved protein domain typically associated with flavoprotein oxygenases, DIM6 NTAB family<br>AO080518000104 Predicted protein<br>AO080551000149 Predicted protein<br>AO080551000149 Predicted protein<br>AO080551000149 Predicted protein  | 3.076<br>3.063<br>3.039<br>3.037<br>3.016<br>2.985<br>2.977<br>2.976<br>2.959<br>2.951<br>2.943<br>2.904<br>2.901<br>2.888<br>2.888<br>2.883<br>2.843   | #<br>[20][32]<br>#<br>[01][32]<br>[11]<br>#<br>#<br>[01][10][14][16]<br>#<br>#<br>#<br>#<br>#   | #<br>#<br>[20.01][32.07]<br>#<br>[01.01][32.05][32.07]<br>[11.02]<br>#<br>#<br>#<br>[01.05][10.01][14.07][16.01][16.03]<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#  |
| AO080541000359 Integral membrane ankyrin-repeat protein Kidins220 (protein kinase D substrate)<br>AO080541000097 Predicted transporter (major facilitator superfamily)<br>AO080546000223 Predicted protein<br>AO080542000014 Cytochrome P450 CYP4 CYP19 CYP26 subfamilies<br>AO080539000029 Predicted protein<br>AO080547000070 Predicted protein<br>AO080523000242 Predicted protein<br>AO080502000014 Uncharacterized conserved protein<br>AO080503000338 NAD <sup>+</sup> ADP-ribosyltransferase Parp, required for poly-ADP ribosylation of nuclear proteins<br>AO080506000124 Predicted protein<br>AO080506000124 Predicted protein domain typically associated with flavoprotein oxygenases, DIM6 NTAB family<br>AO08053600058 Predicted protein<br>AO080518000104 Predicted protein<br>AO080518000104 Predicted protein<br>AO080551000149 Predicted protein<br>AO080551000149 Predicted protein<br>AO080551000149 Predicted protein<br>AO0805500001018 Predicted protein<br>AO08055000010188 Predicted aprotein  | 3.076<br>3.063<br>3.039<br>3.037<br>3.016<br>2.985<br>2.977<br>2.976<br>2.959<br>2.951<br>2.943<br>2.904<br>2.901<br>2.888<br>2.883<br>2.883<br>2.853<br>2.843<br>2.835                                     | #<br>[20][32]<br>#<br>[01][32]<br>[11]<br>#<br>#<br>[01][10][14][16]<br>#<br>#<br>#<br>#<br>#<br>#  | #<br>[20.01][32.07]<br>#<br>[01.01][32.05][32.07]<br>[11.02]<br>#<br>#<br>[01.05][10.01][14.07][16.01][16.03]<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#  |
| AO080541000359 Integral membrane ankyrin-repeat protein Kidins220 (protein kinase D substrate)<br>AO080541000097 Predicted transporter (major facilitator superfamily)<br>AO080546000223 Predicted protein<br>AO080542000014 Cytochrome P450 CYP4 CYP19 CYP26 subfamilies<br>AO080539000029 Predicted protein<br>AO080547000070 Predicted protein<br>AO080523000242 Predicted protein<br>AO08052000014 Uncharacterized conserved protein<br>AO0805000014 Uncharacterized conserved protein<br>AO08050000124 Predicted protein<br>AO08050000124 Predicted protein<br>AO080502000014 Uncharacterized conserved protein<br>AO080502000014 Uncharacterized conserved protein<br>AO080542000029 Conserved protein domain typically associated with flavoprotein oxygenases, DIM6 NTAB family<br>AO080521000317 Predicted protein<br>AO080518000104 Predicted protein<br>AO0805518000104 Predicted protein<br>AO080551000149 Predicted protein<br>AO080550000110 Predicted protein<br>AO080550000110 Predicted protein<br>AO080550000188 Predicted protein  | 3.076<br>3.063<br>3.039<br>3.037<br>3.016<br>2.985<br>2.977<br>2.976<br>2.959<br>2.951<br>2.943<br>2.904<br>2.901<br>2.888<br>2.888<br>2.883<br>2.853<br>2.843<br>2.835<br>2.835                            | #<br>[20][32]<br>#<br>[01][32]<br>[11]<br>#<br>#<br>[01][10][14][16]<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#   | #<br>[20.01][32.07]<br>#<br>[01.01][32.05][32.07]<br>[11.02]<br>#<br>#<br>[01.05][10.01][14.07][16.01][16.03]<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>[02.11]  |
| AO080541000359 Integral membrane ankyrin-repeat protein Kidins220 (protein kinase D substrate)<br>AO080541000097 Predicted transporter (major facilitator superfamily)<br>AO080546000223 Predicted protein<br>AO080542000014 Cytochrome P450 CYP4 CYP19 CYP26 subfamilies<br>AO080539000029 Predicted protein<br>AO080547000070 Predicted protein<br>AO080523000242 Predicted protein<br>AO080502000014 Uncharacterized conserved protein<br>AO080502000014 Uncharacterized conserved protein<br>AO0805020000124 Predicted protein<br>AO0805020000124 Predicted protein<br>AO0805020000124 Predicted protein<br>AO0805020000124 Predicted protein<br>AO080542000029 Conserved protein domain typically associated with flavoprotein oxygenases, DIM6 NTAB family<br>AO08053600058 Predicted protein<br>AO080551000149 Predicted protein<br>AO080551000149 Predicted protein<br>AO080551000149 Predicted protein<br>AO080550000101 Predicted protein<br>AO080550000101 Predicted protein<br>AO0805500001018 Predicted protein<br>AO080550000188 Predicted aminoglycoside phosphotransferase<br>AO080554000077 Monodehydroascorbate ferredoxin reductase<br>AO080554000077 Monodehydroascorbate ferredoxin reductase<br>AO080554000077 Monodehydroascorbate ferredoxin reductase<br>AO080554000077 Monodehydroascorbate ferredoxin reductase  | 3.076<br>3.063<br>3.039<br>3.037<br>3.016<br>2.985<br>2.977<br>2.976<br>2.959<br>2.951<br>2.943<br>2.904<br>2.901<br>2.888<br>2.883<br>2.883<br>2.843<br>2.835<br>2.835<br>2.835<br>2.835                   | #<br>[20][32]<br>#<br>[01][32]<br>[11]<br>#<br>#<br>[01][10][14][16]<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>[02]<br>#   | #<br>[20.01][32.07]<br>#<br>[01.01][32.05][32.07]<br>[11.02]<br>#<br>#<br>[01.05][10.01][14.07][16.01][16.03]<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#  |
| AO080541000359 Integral membrane ankyrin-repeat protein Kidins220 (protein kinase D substrate)<br>AO08054100097 Predicted transporter (major facilitator superfamily)<br>AO080546000223 Predicted protein<br>AO080542000014 Cytochrome P450 CYP4 CYP19 CYP26 subfamilies<br>AO08053900029 Predicted protein<br>AO0805300029 Predicted protein<br>AO080523000242 Predicted protein<br>AO080502000014 Uncharacterized conserved protein<br>AO080502000014 Uncharacterized conserved protein<br>AO0805020000124 Predicted protein<br>AO0805020000124 Predicted protein<br>AO0805020000124 Predicted protein<br>AO080502000124 Predicted protein<br>AO080502000124 Predicted protein<br>AO080510000124 Predicted protein<br>AO080551000137 Predicted protein<br>AO080551000149 Predicted protein<br>AO080551000149 Predicted protein<br>AO080551000149 Predicted protein<br>AO080551000119 Predicted protein<br>AO080550000101 Predicted protein<br>AO080550000101 Predicted protein<br>AO0805500000188 3-polyprenyl-4-hydroxybenzoate decarboxylase and related decarboxylases<br>AO080550000188 Predicted aminoglycoside phosphotransferase<br>AO080554000077 Monodehydroascorbate ferredoxin reductase<br>AO080554000077 Monodehydroascorbate ferredoxin reductase<br>AO08059000018 Predicted protein  | 3.076<br>3.063<br>3.039<br>3.037<br>3.016<br>2.985<br>2.977<br>2.976<br>2.959<br>2.951<br>2.943<br>2.904<br>2.901<br>2.888<br>2.883<br>2.843<br>2.843<br>2.835<br>2.835<br>2.835<br>2.835<br>2.826<br>2.821 | #<br>[20][32]<br>#<br>[01][32]<br>[11]<br>#<br>#<br>[01][10][14][16]<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>[01][0][14][16]<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br># | #<br>[20.01][32.07]<br>#<br>[01.01][32.05][32.07]<br>[11.02]<br>#<br>#<br>[01.05][10.01][14.07][16.01][16.03]<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>[01.05][10.01][14.07][16.01][16.03]<br>#<br>#<br>#<br>#<br>#<br>[01.05][10.01][14.07][16.01][16.03]<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#      |
| AO080541000359 Integral membrane ankyrin-repeat protein Kidins220 (protein kinase D substrate)<br>AO080541000097 Predicted transporter (major facilitator superfamily)<br>AO080546000223 Predicted protein<br>AO080542000014 Cytochrome P450 CYP4 CYP19 CYP26 subfamilies<br>AO08053900029 Predicted protein<br>AO08053900029 Predicted protein<br>AO080523000242 Predicted protein<br>AO080502000014 Uncharacterized conserved protein<br>AO080502000014 Uncharacterized conserved protein<br>AO0805020000124 Predicted protein<br>AO0805020000124 Predicted protein<br>AO0805020000124 Predicted protein<br>AO0805020000124 Predicted protein<br>AO0805020000124 Predicted protein<br>AO08051200029 Conserved protein domain typically associated with flavoprotein oxygenases, DIM6 NTAB family<br>AO080512000317 Predicted protein<br>AO080518000104 Predicted protein<br>AO080518000104 Predicted protein<br>AO080518000104 Predicted protein<br>AO080550000101 Predicted protein<br>AO080550000101 Predicted protein<br>AO080550000101 Predicted protein<br>AO080550000101 Predicted protein<br>AO0805500000188 Predicted protein<br>AO080554000077 Monodehydroascorbate ferredoxin reductase<br>AO080554000071 Predicted protein<br>AO080506000051 Predicted short chain-type dehydrogenase | 3.076<br>3.063<br>3.039<br>3.037<br>3.016<br>2.985<br>2.977<br>2.976<br>2.959<br>2.951<br>2.943<br>2.904<br>2.901<br>2.888<br>2.883<br>2.843<br>2.835<br>2.835<br>2.835<br>2.835<br>2.826<br>2.821          | #<br>[20][32]<br>#<br>[01][32]<br>[11]<br>#<br>#<br>[01][10][14][16]<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>[01][0][14][16]<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br># | #<br>[20.01][32.07]<br>#<br>[01.01][32.05][32.07]<br>[11.02]<br>#<br>#<br>#<br>[01.05][10.01][14.07][16.01][16.03]<br>#<br>#<br>#<br>#<br>#<br>#<br>[01.05][01.01][14.07][16.01][16.03]<br>#<br>#<br>#<br>#<br>#<br>#<br>[01.05][10.01][14.07][16.01][16.03]<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br>#<br># |

| AO080523000207 Predicted protein  | 2.766 | #                | #  |
|---|-------|------------------|--|
| AO080536000143 Tellurite resistance protein and related permeases   | 2.743 | #                | #  |
| AO080505000118 Predicted protein  | 2.726 | #                | #  |
| AO080546000372 Ornithine aminotransferase   | 2.705 | [01][16]         | [01.01][01.02][01.20][16.21]                   |
| AO080505000202 Methionyl-tRNA formyltransferase   | 2.701 | #                | #  |
| AO080522000033 Predicted protein  | 2.694 | #                | #  |
| AO080509000132 Predicted protein  | 2.686 | #                | #  |
| AO080546000363 Predicted protein  | 2.676 | #                | #  |
| AO080534000002 Non-ribosomal peptide synthetase modules and related proteins  | 2.663 | #                | #  |
| AO080561000015 Predicted protein  | 2.659 | #                | #  |
| AO080532000416 Threonine dehydrogenase and related Zn-dependent dehydrogenases  | 2.657 | [01][02][16]     | [01.01][01.05][02.16][16.17]                   |
| AO080515000061 Uncharacterized conserved protein  | 2.644 | #                | #  |
| AO080503000025 Predicted protein  | 2.631 | #                | #  |
| AO080525000209 Dihydrolipoamide succinvltransferase (2-oxoglutarate dehydrogenase. E2 subunit)  | 2.617 | #                | #  |
| AO080541000475 Glutathione S-transferase  | 2.593 | [32][40]         | [32.01][32.07][40.10]                          |
| AO080512000001 Transposon-encoded proteins with TYA, reverse transcriptase, integrase domains in various combinations   | 2.561 | #                | #  |
| AO080523000247 Predicted acvI-CoA transferases carnitine dehvdratase  | 2.553 | #                | #  |
| AO080508000270 RNA polymerase II transcription termination factor TTF2 lodestar. DEAD-box superfamily   | 2.541 | #                | #  |
| AO080523000391 Cytochrome P450 CYP3 CYP5 CYP6 CYP9 subfamilies  | 2.519 | [16][32]         | [16.21][32.05][32.07]                          |
| AO080527000504 Predicted protein  | 2.503 | #                | #  |
| AO080525000318 Predicted protein  | 2.501 | #                | #  |
| AO080566000091 Predicted protein  | 2.493 | #                | #  |
| AO080503000216 Predicted protein  | 2,492 | #                | #  |
| AO080523000079 Beta-lactamase class C and other penicillin binding proteins   | 2.491 | #                | #  |
| AO080532000061 Uncharacterized conserved protein  | 2.483 | [20]             | [20.01][20.03][20.09]                          |
| AO080505000203 Nucleoside-diphosphate-sugar enimerases  | 2.467 | [01][11][42]     | [01.05][11.02][42.10]                          |
| AO080513000020 Predicted protein  | 2.459 | #                | #  |
|   |       |                  | [01 05][01 20][02 01][02 16][16 17]            |
| AO080505000159 Alcohol dehydrogenase, class V   | 2.446 | [01][02][16][42] | [42 01]  |
| A 0080546000050 Protein twosine serine phosphatase  | 2 442 | [14]             | [12.01]  |
| A 0080531000077 Dimethylolycine dehydrogenase precursor   | 2.112 | [01][16][20]     | [01,01][01,02][01,05][16,21][20,01]            |
| A 008050100001/ wwkB. FAD-dependent oxidoreductase  | 2.420 | [14]             | [14 07]  |
| A OD80567000034 Wykb, 1 AD-dependent of Adreaded as a construction of the second | 2.412 | [17]<br>#        | [14.07]<br>#                                   |
| A 008053600134 7-keto. S-aminonelargonate synthetase and related enzymes  | 2.405 | #                | #  |
| A OD005/2000/2007 Citoshrama D450 CVD4 CVD10 CVD16 subfamilias  | 2.400 | π<br>[01]        | π<br>[01 01]                                   |
| A0080325000590 Cytochronic F450 C1F4 C1F19 C1F20 Subtainines  | 2.401 | [01]             |  |
| AO080563000003 Synaptic vesicle transporter SVOP and related transporters (major facilitator superfamily)   | 2.394 | [20][32][34]     | [20.01][20.03][20.09][32.05][32.07]<br>[34.11] |
| AO080520000010 Reverse transcriptase  | 2.393 | #                | #  |
| AO080527000001 Predicted protein  | 2.392 | #                | #  |
| AO080546000314 Predicted protein  | 2.368 | #                | #  |
| AO080537000005 Predicted flavin-nucleotide-binding protein structurally related to pyridoxine 5 -phosphate oxidase  | 2.363 | #                | #  |
| AO080568000203 Predicted protein  | 2.359 | #                | #  |
| AO080521000212 Predicted protein  | 2.35  | #                | #  |
| AO080515000262 ATP-dependent RNA helicase   | 2.337 | #                | #  |
| AO080506000125 ADP-ribose pyrophosphatase   | 2.331 | [01][16][32]     | [01.03][16.17][32.01]                          |
| AO080548000022 Zn-finger  | 2.326 | #                | #  |
| AO080533000254 Inositol monophosphatase   | 2.32  | [01][30]         | [01.04][01.05][01.06][01.20][30.01]            |

| AO080554000301 Predicted protein  | 2.319 | #            | #                                      |
|---|-------|--------------|--|
| AO080509000068 Predicted protein  | 2.315 | #            | #                                      |
| AO080521000046 Putative dehydrogenase domain of multifunctional non-ribosomal peptide synthetases and related enzymes | 2.299 | [01][20][34] | [01.20][20.01][34.01]                  |
| AO080561000093 Predicted protein  | 2.298 | #            | #                                      |
| A 0080503000246 Predicted transporter (major facilitator superfamily)   | 2 203 | [01][20][24] | [01.05][20.01][20.03][20.09][34.01]    |
| A00805050002401 redicted transporter (major racintator superraining)  | 2.295 | [01][20][34] | [34.11]                                |
| AO080523000538 Predicted glutamine synthetase   | 2.287 | #            | #                                      |
| AO080528000042 Permease of the major facilitator superfamily  | 2.284 | [20]         | [20.01][20.03][20.09]                  |
| AO080523000723 Acetyltransferases, including N-acetylases of ribosomal proteins                                       | 2.282 | #            | #                                      |
| AO080570000066 Permease of the major facilitator superfamily  | 2.263 | [20]         | [20.01][20.03][20.09]                  |
| AO080569000133 Predicted protein  | 2.255 | [10][11][42] | [10.03][11.04][11.06][42.16]           |
| AO080523000499 Predicted protein  | 2.238 | #            | #                                      |
| AO080527000070 Lactoylgutathione lyase and related lyases   | 2.231 | #            | #                                      |
| AO080553000127 Predicted protein  | 2.231 | #            | #                                      |
| AO080567000088 Predicted protein  | 2.219 | #            | #                                      |
| AO080551000005 Spt6 ortholog, DNA-binding subunit of a DNA-dependent protein kinase (Ku70 autoantigen)                | 2.214 | [10][11]     | [10.01][11.02]                         |
| AO080515000013 Predicted protein  | 2.212 | #            | #                                      |
| AO080537000052 Predicted protein  | 2.212 | #            | #                                      |
| AO080550000146 Exopolyphosphatase   | 2.207 | [01][11][30] | [01.05][11.02][30.01]                  |
| AO080527000050 Predicted protein  | 2.19  | #            | #                                      |
| AO080511000186 Predicted protein  | 2,175 | #            | #                                      |
| AO080509000038 Predicted protein  | 2.172 | [43]         | [43.01]                                |
| AO080515000014 Predicted protein  | 2.168 | #            | #                                      |
| A0080532000091 Cysteine desulfurase NFS1  | 2.162 | [01]         | [01.20]                                |
| AO080511000049 Predicted protein  | 2.161 | #            | #                                      |
| AO080511000294 Predicted protein  | 2.16  | #            | #                                      |
| AO080523000130 Predicted protein  | 2.157 | #            | #                                      |
| AO080536000059 Predicted protein  | 2.152 | #            | #                                      |
| AO080508000090 Predicted protein  | 2.151 | #            | #                                      |
| AO080527000162 Predicted protein  | 2.147 | [30][34][43] | [30 01][34 11][43 01]                  |
| AO080501000155 Predicted transporter (major facilitator superfamily)  | 2.145 | [01][20]     | $[01 \ 05][20 \ 01][20 \ 03][20 \ 09]$ |
| AO080505000279 Predicted protein  | 2.142 | #            | #                                      |
| AO080508000097 3-deoxy-D-arabino-heptulosonate 7-phosphate (DAHP) synthase  | 2.139 | [01]         | [01.01][01.05][01.20]                  |
| A0080523000024 Glycerol uptake facilitator and related permeases (Maior Intrinsic Protein Family)                     | 2.129 | #            | #                                      |
| AO080501000008 wykN_Non-ribosomal peptide synthetase modules and related proteins                                     | 2.117 | #            | #                                      |
| AO080539000074 Predicted protein  | 2.097 | #            | #                                      |
| AO080518000037 Predicted transporter (major facilitator superfamily)  | 2.073 | [20][32]     | [20 01][20 03][20 09][32 05][32 07]    |
| A0080541000154 Carboxynentidase C (carboxin A)  | 2.062 | [14]         | [14 13]                                |
| AO080567000053 Predicted protein  | 2.062 | #            | #                                      |
| AO080550000102 Predicted acyl esterases   | 2.055 | #            | #                                      |
| AO080505000097 Transflyretin and related proteins   | 2.053 | [01]         | [01 02][01 03]                         |
| AO080546000347 Catalase (neroxidase D   | 2.051 | [20][32][42] | [20, 01][32, 01][32, 07][42, 16]       |
| AO080533000188 Predicted protein  | 2.046 | #            | #                                      |
| AO080551000123 Predicted protein  | 2.039 | #            | #                                      |
| AO080562000073 Predicted protein  | 2.036 | #            | #                                      |
| AO080551000142 Predicted protein  | 2.034 | #            | #                                      |
| AO080532000609 Predicted protein  | 2.032 | #            | #                                      |
| · · · · · · <b>r</b>  |       |              |  |

| AO080527000203 Isocitrate isopropylmalate dehydrogenase  | 2.021 | [01][02][16][20]               | [01.01][01.05][02.01][02.10][16.21]<br>[20.01]  |
|--|-------|--------------------------------|---|
| AO080525000648 Predicted protein   | 2.02  | #                              | #   |
| AO080571000012 Molecular chaperone (DnaJ superfamily)  | 2.014 | #                              | #   |
| AO080523000419 Predicted protein   | 2.007 | #                              | #   |
| AO0805310003182-notwnerwl-6-methoxynhenol hydroxylase and related FAD-dependent oxidoreductases                        | 2 004 | [01]                           | [01 05][01 20]  |
| A O0805510000192 Phospholipase C   | 2.007 | [01]<br>#                      | #   |
|  | 2.002 | [01][02][10][11][1             | [01.04][01.05][02.19][10.01][10.03]   |
| AO080533000108 Protein kinase PCTAIRE and related kinases  | 2.001 | 4]<br>[16][18][30][34][4<br>0] | $ \begin{bmatrix} 11.02 \end{bmatrix} \begin{bmatrix} 14.07 \end{bmatrix} \begin{bmatrix} 16.01 \end{bmatrix} \begin{bmatrix} 16.03 \end{bmatrix} \begin{bmatrix} 16.19 \end{bmatrix} \\ \begin{bmatrix} 18.01 \end{bmatrix} \begin{bmatrix} 18.02 \end{bmatrix} \begin{bmatrix} 30.01 \end{bmatrix} \begin{bmatrix} 30.05 \end{bmatrix} \begin{bmatrix} 34.05 \end{bmatrix} \\ \begin{bmatrix} 34.11 \end{bmatrix} \begin{bmatrix} 40.01 \end{bmatrix} \begin{bmatrix} 42.10 \end{bmatrix} \begin{bmatrix} 43.01 \end{bmatrix} $ |
| AO080505000181 Glycosyltransferase   | 0.498 | [01][02][32][34][43            | [01.05][02.19][32.01][34.11][43.01]   |
| AO080503000128 Predicted protein   | 0 496 | #                              | #   |
| AO080521000172 Predicted membrane protein  | 0.496 | #                              | #   |
| AO080514000015 Transcription factor PRD and related proteins contain PAX and HOX domains                               | 0.495 | #                              | #   |
| AO080531000179 Predicted protein   | 0.494 | #                              | #   |
| A O080551000752 Predicted protein  | 0.492 | #                              | #   |
| AO080546000212 Fredicted protein   | 0.492 | #                              | #   |
| A O0805400002191 Pradicted protein   | 0.492 | #                              | #   |
| A OD00512000270 Pradicted protein  | 0.492 | #<br>#                         | #<br>#  |
| A O00051000004 Producted protein   | 0.491 | #<br>#                         | #<br>#  |
| AO080503000004 Fredicted protein   | 0.487 | #<br>#                         | #<br>#  |
|  | 0.480 | #<br>[01]                      | #<br>[01.05]  |
| AO000515000000 Aphila-aniyase  | 0.485 | [01]<br>#                      | [01.05]<br>#  |
| A0000552000507 Fledicited protein<br>A0000552000402 NA DBUtaviaene reductore and related Zn. dependent evidereductores | 0.481 | #<br>[01][16]                  | #<br>[01 05][01 20][16 17]  |
| AO000534000462 NADE IN. quinone reductase and related 21-dependent oxforte ductases                                    | 0.461 |                                |   |
| A00005250000166 Denditional anothing   | 0.46  | н<br>4                         | #<br>#  |
| A0080530000150 Predicted protein   | 0.479 | #<br>#                         | #<br>#  |
| A0080515000204 Predicted protein   | 0.478 | #                              | #<br>//   |
| AO08056000008 / Predicted protein  | 0.478 | #                              | #   |
| AO080505000104 Predicted protein   | 0.476 | #                              |   |
| AO080568000096 Cytochrome P450 CYP4 CYP19 CYP26 subfamilies  | 0.474 | [01][02]                       | [01.06][01.20][02.45]   |
| AO080523000182 Acetylcholinesterase Butyrylcholinesterase  | 0.47  | #                              | #   |
| A0080532000189 Predicted protein   | 0.469 |                                | [11.06][14.07][14.13]   |
| AO080570000072 Cytochrome P450 CYP4 CYP19 CYP26 subfamilies  | 0.469 | [01][32]                       | [01.01][32.05][32.07]   |
| AO080561000074 Endopolygalacturonase   | 0.468 | #                              | #   |
| AO080511000067 Predicted protein   | 0.466 | #                              | #   |
| AO080533000118 Predicted protein   | 0.464 | #                              | #   |
| AO080508000310 Ketopantoate hydroxymethyltransferase   | 0.463 | [01][42]                       | [01.07][42.01]  |
| AO080523000640 Sorbin and SH3 domain-containing protein  | 0.463 | [10]                           | [10.03]   |
| AO080536000108 Predicted protein   | 0.459 | #                              | #   |
| AO080508000430 Predicted protein   | 0.457 | #                              | #   |
| AO080521000200 Predicted protein   | 0.456 | [20][34]                       | [20.01][34.11]  |
| A0080522000004 Cytochrome P450   | 0.456 | #                              | #   |
| AO080506000272 Predicted protein   | 0.455 | #                              | #   |
| AO080557000027 Predicted protein   | 0.455 | #                              | #   |
| AO080555000231 Predicted protein   | 0.454 | #                              | #   |
| AO080523000128 Predicted protein   | 0.453 | #                              | #   |

| AO080533000173 Predicted protein   | 0.453 | #                | #  |
|--|-------|------------------|--|
| AO080508000082 Predicted protein   | 0.451 | #                | #  |
| AO080515000125 Permeases of the major facilitator superfamily                        | 0.449 | [20]             | [20.01][20.03][20.09]                          |
| AO080542000184 Cytochrome P450 CYP4 CYP19 CYP26 subfamilies                          | 0.448 | #                | #  |
| AO080533000250 Predicted protein   | 0.447 | #                | #  |
| AO080549000362 Endonuclease III  | 0.447 | [01][10][16][32] | [01.03][10.01][16.03][16.17][16.21]<br>[32.01] |
| AO080523000306 Predicted protein   | 0.442 | #                | #  |
| AO080532000098 beta-1,6-N-acetylglucosaminyltransferase, contains WSC domain         | 0.442 | #                | #  |
| AO080536000028 Predicted protein   | 0.442 | #                | #  |
| AO080550000149 Predicted protein   | 0.441 | #                | #  |
| AO080513000148 Amidases  | 0.44  | [01]             | [01.02]  |
| AO080508000396 Acetylornithine aminotransferase                                      | 0.438 | [01]             | [01.07][01.20]                                 |
| AO080501000092 Nucleoside phosphorylase  | 0.437 | #                | #  |
| AO080521000357 Predicted protein   | 0.437 | #                | #  |
| AO080536000070 Predicted transporter (major facilitator superfamily)                 | 0.437 | [01][20][32][34] | [01.07][20.01][20.09][32.07][34.01]            |
| AO080532000519 Predicted protein   | 0.435 | #                | #  |
| AO080503000049 Serine threonine protein kinase                                       | 0.434 | #                | #  |
| AO080508000367 Predicted protein   | 0.433 | [01]             | [01.04]  |
| AO080541000303 Predicted protein   | 0.433 | #                | #  |
| AO080525000618 Predicted protein   | 0.432 | #                | #  |
| AO080529000044 Predicted Zn-dependent hydrolases of the beta-lactamase fold          | 0.432 | #                | #  |
| AO080550000111 Predicted protein   | 0.432 | #                | #  |
| AO080508000204 Predicted dehydrogenase   | 0.431 | #                | #  |
| AO080523000678 Predicted protein   | 0.431 | [10][16]         | [10.01][16.03]                                 |
| AO080515000221 Aspartyl protease   | 0.43  | [01][14]         | [01.25][14.13]                                 |
| AO0805210002541-Acyl dihydroxyacetone phosphate reductase and related dehydrogenases | 0.427 | [01][43]         | [01.05][01.06][43.01]                          |
| AO080523000411 Predicted protein   | 0.426 | #                | #  |
| AO080541000075 Predicted protein   | 0.426 | #                | #  |
| AO080501000186 Predicted protein   | 0.424 | #                | #  |
| AO080538000052 Uncharacterized conserved protein                                     | 0.419 | #                | #  |
| AO080508000165 FAD FMN-containing dehydrogenases                                     | 0.418 | [01]             | [01.20]  |
| AO080501000074 nucS nuclease S1 precursor  | 0.416 | [01]             | [01.03]  |
| AO080523000712 Permeases of the major facilitator superfamily                        | 0.416 | [01][20]         | [01.05][20.01][20.03]                          |
| AO080530000037 Signal transduction histidine kinase                                  | 0.413 | #                | #  |
| AO080515000068 Carboxylesterase and related proteins                                 | 0.412 | #                | #  |
| AO080515000315 Fructose tagatose bisphosphate aldolase                               | 0.412 | [01][02]         | [01.05][02.01][02.07]                          |
| AO080539000047 Predicted protein   | 0.412 | #                | #  |
| AO080558000032 Permeases of the major facilitator superfamily                        | 0.41  | #                | #  |
| AO080550000154 Amino acid transporters   | 0.409 | #                | #  |
| AO080531000003 SAM-dependent methyltransferases                                      | 0.402 | #                | #  |
| AO080502000037 NADPH:quinone reductase and related Zn-dependent oxidoreductases      | 0.399 | #                | #  |
| AO080523000067 Predicted metal-dependent hydrolase with the TIM-barrel fold          | 0.399 | #                | #  |
| AO080525000576 Predicted protein   | 0.398 | #                | #  |
| AO080515000209 Uncharacterized protein conserved in bacteria                         | 0.395 | #                | #  |
| AO080553000093 Predicted protein   | 0.394 | #                | #  |
| AO080549000130 Predicted transporter (major facilitator superfamily)                 | 0.393 | [01][20][34]     | [01.05][20.01][20.03][20.09][34.01]            |

| AO080530000032 Predicted protein   | 0.385 | #                        | #  |
|--|-------|--------------------------|--|
| AO080533000073 Predicted protein   | 0.379 | #                        | #  |
| AO080503000122 Predicted protein   | 0.371 | #                        | #  |
| AO080513000198 Cytochrome P450 CYP2 subfamily  | 0.369 | #                        | #  |
| AO080521000073 Aldo keto reductase family proteins   | 0.369 | [01][02][16][32][3<br>4] | [01.01][01.05][01.06][01.07][01.20]<br>[02.01][02.16][16.21][32.01][32.10]<br>[34.11]                                    |
| AO080521000107 Flavonol reductase cinnamoyl-CoA reductase  | 0.369 | [01][02][32][42]         | [01.05][01.07][01.20][02.01][32.01]<br>[32.07][42.01]  |
| AO080567000015 Predicted protein   | 0.369 | #                        | #  |
| AO080505000144 Predicted protein   | 0.368 | #                        | #  |
| AO080503000326 Predicted protein   | 0.367 | #                        | #  |
| AO080508000394 Predicted protein   | 0.366 | #                        | #  |
| AO080515000088 Dehydrogenases with different specificities (related to short-chain alcohol dehydrogenases) | 0.366 | [01][02][43]             | [01.05][01.06][01.20][02.25][43.01]  |
| AO080508000236 Predicted protein   | 0.363 | #                        | #  |
| AO080531000178 Predicted protein   | 0.362 | #                        | #  |
| AO080522000018 Eatty acid desaturase   | 0.356 | [01]                     | [01.06]  |
| AO080533000203 Cytochrome P450 CYP3 CYP5 CYP6 CYP9 subfamilies   | 0.355 | [01][20][32]             |  |
| AO080508000166 Synaptic vesicle transporter SVOP and related transporters (major facilitator superfamily)  | 0.354 | [20]                     | [20.01]  |
| AO080541000328 Laminocyclonronane-Learboxylate synthase and related motions                                | 0.353 | [01][36][40]             | $[01 \ 02][01 \ 05][01 \ 20][36 \ 02][40 \ 02]$  |
| A CORRECTION OF Predicted protein  | 0.343 | #                        | #  |
| AO08050200006 Endo 1.4 heta ducanase IV  | 0.34  | π<br>[01]                | [01 05][01 25]   |
| AC080552000005 Prodictor protein   | 0.34  | [01]<br>#                | [01.05][01.25]<br>#  |
| A0080000000000000000000000000000000000   | 0.558 | π                        | $\pi$  |
| AO080539000025 Predicted protein   | 0.332 | [10][14][20][32][42      | [10.01][10.03][14.07][20.01][32.01]<br>[32.07][42.25]  |
| AO080515000066 Permease of the major facilitator superfamily   | 0.331 | [20]                     | [20.01][20.03][20.09]  |
| AO080523000164 Predicted protein   | 0.328 | [32]                     | [32.07]  |
| AO080525000600 Mg <sup>2+</sup> and Co <sup>2+</sup> transporters  | 0.325 | #                        | #  |
| AO080530000035 Predicted protein   | 0.325 | #                        | #  |
| AO080536000027 manD Endo-heta-mannanase  | 0.319 | [01]                     | [01 05]  |
| AO080541000084 Predicted protein   | 0.316 | [01]                     | [01.05]  |
| AC080521000262 Predicted protein   | 0.314 | [01]<br>#                | <u>#</u>   |
| AO080525000417 Predicted protein   | 0.314 | #                        | #<br>#   |
| AO0805251000027 Producted protein  | 0.314 | #                        | π<br>#   |
| A00805/1000/32 Debudrogeneses with different specificities (related to short chain alcohol debudrogeneses) | 0.314 | #                        | π<br>#   |
| A Operson 2000 27 Predicted protein  | 0.309 | #                        | π<br>#   |
| A0080555007257 Fredered pittering attability disturgence   | 0.308 | #<br>[01]                | #<br>[01.02]   |
| AO0005251000029 Filobable taumie catabolism dioxygenase  | 0.308 | [01]                     |  |
| AO080521000084 2,4-diriydroxynepi-2-ene-1,7-dioic acid aidolase  | 0.302 | [01]<br>#                | [01.20]  |
| AO080513000199 Predicted protein   | 0.299 | #                        | #<br>//  |
| AO080523000583 Predicted protein   | 0.299 | #                        | #  |
| AO080523000582 Predicted transporter (major facilitator superfamily)                                       | 0.289 | [01][20][34][41]         | $\begin{bmatrix} 01.05 \\ 20.01 \\ 20.03 \\ 20.09 \\ 34.01 \end{bmatrix}$ $\begin{bmatrix} 34.11 \\ 41.01 \end{bmatrix}$ |
| AO080523000410 Predicted protein   | 0.288 | #                        | #  |
| AO080528000012 Predicted protein   | 0.283 | #                        | #  |
| AO080532000211 $Ca^{2+} Na^+$ antiporter   | 0.28  | #                        | #  |
| AO080503000406 Dehydrogenases with different specificities (related to short-chain alcohol dehydrogenases) | 0.276 | [01][16]                 | [01.05][01.20][16.21]  |
| AO080513000058 Predicted protein   | 0.275 | #                        | #  |

| AO080562000011 Amino acid transporters  | 0.274  | [20]         | [20.01][20.03][20.09]                                   |
|---|--------|--------------|---|
| AO080525000086 Predicted protein  | 0.271  |              |   |
|   | 0.00   |              | [01.05][01.06][01.07][01.20][02.07]                     |
| AO0805080000345 Dehydrogenases with different specificities (related to short-chain alcohol dehydrogenases)     | 0.269  | 0]           | [10.03][16.01][16.21][20.01][30.05]                     |
|   |        | [30][32][34] | [32.05][34.01]  |
| AO080549000389 Sorbitol dehydrogenase   | 0.269  | [01][02][16] | $[01.01][01.05][01.07][01.20][02.16] \\ [16.17][16.21]$ |
| AO080536000095 Predicted protein  | 0.266  | #            | #   |
| AO080532000017 Phenylpropionate dioxygenase and related ring-hydroxylating dioxygenases, large terminal subunit | 0.263  | #            | #   |
| AO080554000001 H <sup>+</sup> oligopeptide symporter  | 0.259  | [20]         | [20.01][20.03][20.09]                                   |
| AO080532000023 Predicted protein  | 0.258  | #            | #   |
| AO080525000588 1-aminocyclopropane-1-carboxylate synthase, and related proteins                                 | 0.251  | [01]         | [01.02][01.05][01.20]                                   |
| AO080510000163 Predicted protein  | 0.244  | #            | #   |
| A0080541000142 WD40 repeat  | 0.243  | #            | #   |
| A0080513000202 Chitinase  | 0.24   | #            | #   |
| AO080531000064 Predicted protein  | 0.24   | #            | #   |
| AO080531000061 Predicted protein  | 0.238  | #            | #   |
| AO080541000150 Predicted protein  | 0.228  | #            | #   |
| AO080549000322 Protocatechuate 3,4-dioxygenase beta subunit   | 0.225  | #            | #   |
| AO080525000018 Predicted protein  | 0.224  | #            | #   |
| AO080532000465 Predicted protein  | 0.221  | #            | #   |
| AO080532000197 Synaptic vesicle transporter SVOP and related transporters (major facilitator superfamily)       | 0.216  | [20][32][34] | [20.01][20.03][20.09][32.05][32.07]<br>[34.11]          |
| AO080530000022 Predicted protein  | 0.208  | #            | #   |
| AO080523000427 Permease of the major facilitator superfamily  | 0.193  | #            | #   |
| AO080513000203 Predicted protein  | 0.19   | #            | #   |
| AO080521000112 Dehydrogenases with different specificities (related to short-chain alcohol dehydrogenases)      | 0.172  | [01]         | [01.05][01.06][01.20]                                   |
| AO080501000148 Hydroxyindole-O-methyltransferase and related SAM-dependent methyltransferases                   | 0.162  | [01]         | [01.05][01.20]  |
| AO080501000144 Glutaminyl cyclase   | 0.155  | [01][14]     | [01.01][14.07][14.13]                                   |
| AO080501000147 Predicted protein  | 0.151  | #            | #   |
| AO080532000466 Predicted protein  | 0.142  | #            | #   |
| AO080554000025 Amino acid transporters  | 0.14   | [20]         | [20.01][20.09]  |
| AO080501000146 Predicted protein  | 0.136  | #            | #   |
| AO080501000145 Predicted protein  | 0.135  | #            | #   |
| AO080561000089 Endo-1,4-beta-xylanase G2  | 0.111  | [01]         | [01.05]   |
| AO080536000049 Predicted protein  | 0.0778 | #            | #   |
| AO080508000347 Dehydrogenases with different specificities (related to short-chain alcohol dehydrogenases)      | 0.0748 | #            | #   |
| AO080522000002 Predicted protein  | 0.0479 | #            | #   |
| AO080513000200 Predicted protein  | 0.0336 | #            | #   |
| AO080501000141 Predicted protein  | 0.0322 | #            | #   |

<sup>a</sup> FunCat (http://www.webcitation.org/getfile?fileid=be4936ae25ebb5dfb89b687842ea640f8acf7790) is the organism independent functional description of proteins. FunCat consists of 28 main functional categories (level 1). The level 1 is the most general one, whereas level 2 shows much more detail.

<sup>b</sup>#: Unclassified gene

<sup>c</sup> Detailed descriptions of each category are available at the MIPS Functional Catalogue Database (http://mips.helmholtz-muenchen.de/proj/funcatDB/)

| 2        | http://dx.doi.org/10.1016/j.jbiosc.2014.02.004   |
|----------|--|
| 3        | Copyright © 2014 The Society for Biotechnology, Japan. All rights reserved.                |
| 4        |  |
| <b>5</b> | Title: Functional analysis of histone deacetylase and its role in stress response, drug    |
| 6        | resistance and solid-state cultivation in Aspergillus oryzae                               |
| 7        |  |
| 8        | Running title: Function of histone deacetylase in A. oryzae                                |
| 9        |  |
| 10       | Moriyuki Kawauchi <sup>1, 2</sup> and Kazuhiro Iwashita <sup>1, 2*</sup>                   |
| 11       | Department of Molecular Biotechnology, Graduate School of Advanced Science of              |
| 12       | Matter, Hiroshima University, 1-3-1 Kagamiyama, Higashi-hiroshima, Hiroshima               |
| 13       | 739-8530, Japan <sup>1</sup> and National Research Institute of Brewing, 3-7-1 Kagamiyama, |
| 14       | Higashi-hiroshima, Hiroshima 739-0046, Japan <sup>2</sup>                                  |
| 15       | [Keywords: Histone deacetylase, Aspergillus oryzae, Stress response, Drug resistance,      |
| 16       | Rice- <i>koji</i> ]  |
| 17       | *Corresponding author. E-mail: <u>iwashitact@nrib.go.jp</u>                                |
| 18       | Phone: +81-(0)82-420-0824, Fax: +81-(0)82-420-0808   |
|          |  |

Journal of Bioscience and Bioengineering, VOL. 118 No. 2, 172-176 (2014)

#### 19 Abstract

In the eukaryotic cell, histone deacetylases (HDACs) play key roles in the regulation of 20fundamental cellular process such as development regulation, stress response, secondary 21metabolism and genome integrity. Here, we provide a comprehensive phenotypic 22analysis using HDAC disruptants in Aspergillus oryzae. Our study revealed that four 23HDACs, hdaA/Aohda1, hdaB/Aorpd3, hdaD/Aohos2 and hst4/AohstD were involved in 2425stress response, cell wall synthesis and chromatin integrity in A. oryzae. Osmotic stress sensitivity of HDAC disruptants differed between plate cultures and liquid cultures, 2627suggesting that HDACs adapt to the difference environmental conditions. Using a common A.oryzae fermentation medium, rice-koji, we also characterized HDACs 2829related to growth and enzyme production to investigate which HDACs will be required for adaptation to environmental conditions and stress resistances. Because HDACs are 30 widely conserved, our study has broad applications and may inform work with 31filamentous fungi and other eukaryote. 32

33

 $\mathbf{2}$ 

### 34 Introduction

Eukaryotic DNA is packaged into chromatin, limiting transcriptional activity (1). 35Histone acetylation is one of the most important modifications to regulate chromatin 36 37 accessibility. It is controlled by two opposing enzymes, histone acetyltransferases (HATs) and histone deacetylases (HDACs), both of which were conserved in wide range 38of taxa. Deacetylated histories that are intermediated by HDACs lead to transcriptional 39inactivation (2-5). HDACs are divided into two major types, sirtuins and the classical 40 HDACs. Sirtuins are NAD<sup>+</sup>-dependent, while classical HDACs are zinc-dependent 41 42HDAC family (6). In the past decade, the importance of sirtuins and classical HDACs 43have been recognized as important to multiple cellular processes, including development, stress response and genome integrity (6). 44 The filamentous fungi are a diverse group with important economical applications, 45including the production of fermented foods, commercial enzymes and useful chemicals 46 (7, 8). Others are human or plant pathogens and virulence has even been reported in 47some filamentous fungi (9-13). Recently, attention has been drawn to HDACs and their 48industrial applications as regulators of fungal development, conidiation, stress response 4950and secondary metabolite production (12-16). The filamentous fungus Aspergillus oryzae has been used for more than 1000 years in 51

| 52 | the traditional food industry and is listed as a GRAS species (i.e., generally recognized |
|----|---|
| 53 | as safe) by the Food and Drug Administration in the United States. Its safety is also     |
| 54 | confirmed by the World Health Organization (17). A. oryzae has the ability to produce     |
| 55 | high quantities of enzymes and beneficial secondary metabolites, such as kojic acid and   |
| 56 | WYK-1 (18-20).  |
| 57 | In a previous study, we identified 11 HDACs homolog (AoHDACs) in A. oryzae                |
| 58 | genome and attempt the disruption of all of them (21). We isolated 10 AoHDAC              |
| 59 | disruptants, and one heterokaryon disruptant for hdaB/Aorpd3 disruption. Using, these     |
| 60 | disruptants, we revealed the effects of HDACs on the growth, conidiation, and             |
| 61 | secondary metabolite production. In the present study, we more closely examine the        |
| 62 | phenotypic expression of HDAC in A. oryzae, specifically in response to several types     |
| 63 | of stress and drugs and its role in growth and production of protein in rice-koji.        |
|    |   |

### 65 Materials and methods

## 66 Strains and media

- 67 All *A. oryzae* strains used in this study were derived from previous work and are listed
- in Table 1 (21). N medium was used as the basic medium for all stress and
- 69 drug-resistance analyses (21). For rice-*koji* making, 15g α-rice (70% polished *Akihikari*)
- 70 was used. Distilled water suspending the conidia of disruptants was added to the  $\alpha$ -rice
- as 30% initial water content and  $1 \times 10^5$  conidia/g  $\alpha$ -rice. The inoculum was incubated

72 at 35 °C for 42h in 100% humidity.

73

#### 74 Environmental stress resistance assay

| 75 | For the stress test on plates, 1 $\mu$ l of conidia suspension (1 × 10 <sup>5</sup> conidia) of each strain         |
|----|---|
| 76 | was point inoculated on the center of the plate and grown for five days at 30°C. N                                  |
| 77 | medium containing 1.6 M NaCl was used for the osmotic stress resistance test and                                    |
| 78 | 20mM H <sub>2</sub> O <sub>2</sub> was used for the oxidative stress resistance test. For the heat resistance test, |
| 79 | the plate was incubated at 37°C. For hypoxic growth test, the plate was incubated in a                              |
| 80 | 2% O <sub>2</sub> concentration using the Multi Gas Incubator APM-50DR (Astec, Fukuoka,                             |
| 81 | Japan). After these incubations, Colony diameter was measured after the incubation                                  |
| 82 | period. For biomass analysis in the liquid culture, a 4 cm <sup>2</sup> plug of each strain were cut                |

| 83 | from the full-growth plate cultures and homogenized in 1 ml of suspension solution and |
|----|--|
| 84 | then inoculated with 100 ml of N liquid medium containing 0.8 M NaCl. Flasks were      |
| 85 | incubated for two days at 30°C with shaking at 100 rpm. Mycelia were harvested, dried  |
| 86 | at 105°C for 1 h and weighed.  |
|    |  |

# 88 Drug resistance test

| 89  | For drug resistance tests, conidia suspensions of each strain were point inoculated an      |
|-----|---|
| 90  | incubated as outlined in the stress test above. The following chemicals were tested:        |
| 91  | calcofluor white (300 $\mu$ g/ml), Congo red (50 $\mu$ g/ml), micafungin (2 ng/ml), hydroxy |
| 92  | urea (10 mM), camptothecin (1 $\mu$ M), methyl methane sulfonate (MMS; 0.1%),               |
| 93  | tunicamycin (5 µg/ml), nocodazole (500 ng/ml), dithiothreitol (10mM), brefeldin A (5        |
| 94  | $\mu$ g/ml). Congo red, dithiothreitol, camptothecin, MMS, brefeldin A and nocodazole       |
| 95  | were purchased from Wako Chemicals (Osaka, Japan); tunicamycin were purchased               |
| 96  | from Calbiochem (La Jolla, CA, USA); and the hydroxy urea and calcofluor white were         |
| 97  | purchased from Sigma Aldrich (St. Louis, MO, USA). The micafungin (Astellas, Tokyo,         |
| 98  | Japan) was gifted. A stock solution of was prepared by dissolving 100 mg/ml calcofluor      |
| 99  | white, 10mg/ml Congo red, 1mg/ml micafungin, 1M hydroxyl urea, and 1M                       |
| 100 | dithiothreitol (1M) in water. The camptothecin (10 mM), nocodazole (1 mg/ml),               |

brefeldin A (1 mg/ml) and tunicamycin (2 mg/ml) were dissolved in dimethyl sulfoxide.

| 103        | Measurement of enzyme activity and total proteins production  |
|------------|---|
| 104        | Enzymes were extracted from 5 g of rice-koji after incubation with 25 ml acetate buffer   |
| 105        | (10 mM, pH 5.0, 0.5% NaCl) at 4°C for 3 h with shaking at 80 rpm followed by  |
| 106        | filtration. Enzyme activities of $\alpha$ -amylase, glucoamylase and acid carboxypeptidase  |
| 107        | were measured using enzyme assay kits (Kikkoman, Chiba, Japan). Acidic protease   |
| 108        | activity was assayed according to a previous report (22). Total protein was measured by   |
| 109        | using the Bio-Rad Protein Assay Kit II.   |
| 110        |   |
| 111        | Measurement of N-acetylglucosamine content in rice-koji   |
| 112        | The rice-koji (5g) was dried at 105°C for 1h, then homogenized in 12.5 ml phosphate   |
| 113        | buffer (50 mM, pH 6.8) using physcotron (Microtec, Chiba, Japan), and centrifuged. The  |
| 114        | pellet was washed with a 10-ml phosphate buffer more than five times then suspended   |
| 115        | in a 20-ml phosphate buffer. A 2-ml of suspension was mixed with 7 ml phosphate   |
|            |   |
| 116        | buffer and 1 ml Yatalase (TaKaRa, Kyoto, Japan) solution (10 mg /ml in phosphate  |
| 116<br>117 | buffer and 1 ml Yatalase (TaKaRa, Kyoto, Japan) solution (10 mg/ml in phosphate buffer). This mixture was shaking at 80rpm at 37°C for 3 h. The N-acetylglucosamine |

| 119 | chromatography with a pulse electrochemical detector (DX500 chromatography system, |
|-----|--|
| 120 | Dionex, Sunnyvale, CA, USA) and an anion exchange column (Carbo PAC PA-1,          |
| 121 | 4×250 mm, Dionex) at a flow rate of 1 ml/min. Isocratic elution was performed with |
| 122 | 16mM NaOH. The column was stabilized for 20min before injection and washed with    |
| 123 | 100mM NaOH / 600mM CH <sub>3</sub> COONa for 10 min after elution. To quantify the |
| 124 | N-acetylglucosamine, we used N-acetyl-D (+)-glucosamine (Wako) as a standard and   |
| 125 | D-fucose as an internal standard.  |

#### 127 **Results**

## 128 Stress resistance of AoHDACs

- 129 In the previous study, we identified 11 HDACs homologs in *A. oryzae* genome and
- 130 construct 10 AoHDAC disruptants and one AoHDAC heterokaryon disruptant as listed
- in Table 1 with the phylogenetic classification (21).
- 132 The osmotic, oxidative, heat and hypoxia stress tolerances of all AoHDAC disruptants
- 133 were quantified to analyze the importance of HDACs in environmental adaptations

134 (Figs. 1, S1 and S2). Three AoHDAC disruptants showed sensitivity against these

135 stresses (Fig. 1A and B). The  $\Delta hstD$  strain was sensitive to the osmotic stress; the

136 *hdaB/Aorpd3* heterokaryon disruptant (*hdaB ht* strain) showed significant sensitivity

- 137 against osmotic, oxidative and heat stress; the  $\Delta h daD$  strain showed significant
- 138 sensitivity against the low oxygen and osmotic stress. These results suggest that
- 139 *hdaB/Aorpd3*, *hdaD/Aohos2* and *hstD/Aohst4* are required for stress tolerance in A.
- 140 *oryzae*.
- 141 In the liquid culture of the osmotic-stress test, we found a unique phenotype of  $\Delta h daA$
- 142 strain (Fig. 1C). This strain showed significant sensitivity against osmotic stress in
- 143 liquid culture, but not in plate culture. This result suggests that *hdaA/Aohda1* plays a
- 144 role in liquid culture specific osmotic stress response. We also found that the *hdaB ht*

| 145 | and $\Delta h daD$ strain were more osmo-sensitive in liquid culture (Fig. 1C). These findings     |
|-----|--|
| 146 | suggest that different osmotic stress resistance mechanisms between the plate and liquid           |
| 147 | culture conditions, and hdaB/Aorpd3, hdaA/Aohda1 and hdaD/Aohos2 will be included                  |
| 148 | in these mechanisms.   |
| 149 |  |
| 150 | Drug (inhibitor) resistance of AoHDACs disruptants   |
| 151 | We examined AoHDAC disruptants' resistance to several chemicals on plate culture and,              |
| 152 | at first, the cell wall integrity was tested using cell wall synthesis inhibitors (Figs. 2 and     |
| 153 | S3). The <i>hdaB ht</i> strain was significantly sensitive to micafungin, a $\beta$ -1,3-glucan    |
| 154 | synthesis inhibitor (23). The deletion of <i>hdaD/Aohos2</i> showed the greatest sensitivity       |
| 155 | against the calcofluor white, which is a chitin synthesis inhibitor. The $\Delta hstA$ strain also |
| 156 | showed the slight sensitivity to calcofluor white (Fig. S3). These results suggest that            |
| 157 | there is variation in how different AoHDACs affect cell wall integrity, and                        |
| 158 | <i>hdaB/Aorpd3</i> and <i>hdaD/Aohos2</i> will be concerned with these mechanisms.                 |
| 159 | HDACs are also relevant to genome integrity (24); thus, we examined the genotoxin                  |
| 160 | tolerances of all AoHDAC disruptants (Figs. 3 and S4). As expected, the hdaB ht,                   |
| 161 | $\Delta h daD$ and $\Delta h stD$ strains showed defects against methyl methane sulfonate, which   |
| 162 | methylates DNA predominantly on N7-deoxyguanosine and N3-deoxyadenosine and is                     |

| 163 | believed to cause double-stranded DNA breaks. Additionally, the $\Delta hstD$ strain showed             |
|-----|---|
| 164 | the strongest sensitivity to camptothecin, a topoisomerase inhibitor. These results                     |
| 165 | suggested hdaB/Aorpd3, hdaD/Aohos2 and hstD/Aohst4 are involved in genome                               |
| 166 | integrity.  |
| 167 | No obvious sensitivity to protein secretion inhibitors was observed when tested                         |
| 168 | dithiothreitol, tunicamycin or brefeldin A (Fig. S5). A slight sensitivity was observed                 |
| 169 | with nocodazole, which depolymerizes microtubules, in the $\Delta hstD$ and $hdaB$ ht strain.           |
| 170 |   |
| 171 | Effect of AoHDACs disruption on rice-koji   |
| 172 | A distinctive feature of the <i>koji</i> fermentation process is the use of solid-state culture         |
| 173 | where A. oryzae is grown on steamed cereals such as rice and soybean. The resulting                     |
| 174 | material contains abundant hydrolytic enzymes and metabolites that are important for                    |
| 175 | the quality of the final products (25). We analyzed the effect of AoHDACs disruption on                 |
| 176 | the growth and protein production of rice-koji (Figs. 4 and S6).  |
| 177 | It is difficult to separate the mycelia from rice-koji to measure exact fungal biomass, so              |
| 178 | instead we measured N-acetylglucosamine, which has been shown strongly correlated                       |
| 179 | with biomass (26). We found significant decreases in N-acetylglucosamine on rice-koji                   |
| 180 | made by the <i>hdaB ht</i> and $\Delta hdaD$ strains (Fig. 4A). The $\Delta hdaA$ strain also decreased |

| 181 | N-acetylglucosamine, but the results were not significant. The disruptant strains also              |
|-----|---|
| 182 | decreased total protein production, but enzyme activity differed by disruptant (Fig. 4B             |
| 183 | and C). The hdaB ht strain showed significant decreases in all measured enzyme activity,            |
| 184 | while the $\Delta h daA$ and $\Delta h daD$ strains only showed a significant decrease in glycoside |
| 185 | hydrolase activity and a slight increased acid carboxypeptidase activity. In these strains,         |
| 186 | the low glycoside hydrolase productivity or growth defect might cause low protein                   |
| 187 | productivity. Compared with these three strains, the $\Delta hstD$ strain showed no decrease in     |
| 188 | N-acetylglucosamine but had lowered protein production. We also found significant                   |
| 189 | decrease in glycoside hydrolase and acid protease. These results suggest that                       |
| 190 | <i>hstD/Aohst4</i> can affect many types of protein production even when it does not affect         |
| 191 | growth.   |
| 192 |   |
| 193 | Discussion  |
| 194 | HDACs play diverse roles in higher eukaryote development, stress response, and                      |
| 195 | genome integrity (6, 27). In some filamentous fungi, HDACs are important to growth,                 |
| 196 | conidia formation, and secondary metabolism (28). This study, strongly suggests that                |
| 197 | functional divergence of HDACs in A. oryzae with important industrial implications for              |
| 198 | HDAC deletion.  |

| 199 | The modes of development and enzyme production in A. oryzae are significantly                          |
|-----|--|
| 200 | different when it grows in solid-state or liquid culture conditions (29, 30). This supports            |
| 201 | recent omics studies of A. oryzae that revealed how the transcriptome and proteome                     |
| 202 | were altered depending on culture type (30, 31). However, a detailed molecular                         |
| 203 | investigation is needed to understand the underlying mechanisms.                                       |
| 204 | HDACs widely affected gene expression through the structural modification of                           |
| 205 | chromatin by the deacetylation of histones. We found phenotypic differences between                    |
| 206 | disruptants grown on the liquid culture as opposed to the plate culture. The $\Delta h daA$ strain     |
| 207 | did not show any significant effect against osmotic stress on the plate culture, but an                |
| 208 | obvious defect was observed in liquid culture. Additionally, the hdaB ht strain and                    |
| 209 | $\Delta h da D$ strains had a more sensitive phenotypic response to osmotic stress in the liquid       |
| 210 | culture. These results indicated some difference between the liquid and plate culture                  |
| 211 | on the osmotic adaptation and these three HDACs would play a role in the adaptation                    |
| 212 | mechanisms in A. oryzae.   |
| 213 | We also found a significant decrease in the amount of N-acetylglucosamine in rice-koji                 |
| 214 | produced by the <i>hdaB ht</i> , $\Delta hdaD$ and $\Delta hdaA$ strains. N-acetylglucosamine is a key |
| 215 | constituent saccharide of chitin, the major glycan composing fungal cell walls and a                   |
| 216 | good surrogate for measuring fungal growth on rice-koji (26). The growth effects of                    |

| 217 | these three HDACs in the solid-state cultures suggests the importance of the compound                  |
|-----|--|
| 218 | stabilizing the fungal cell wall. In this experiment we only measured the amount of                    |
| 219 | N-acetylglucosamine whereas fungal cell walls also contain $\beta$ - and $\alpha$ -1,3-glucan, chitin, |
| 220 | galactomannan (32). Thus, it is not clear whether the disruption of hdaB/Aorpd3 and                    |
| 221 | hdaD/Aohos2 affects the overall glycan construction of cell wall. Future work should                   |
| 222 | examine the detailed role of AoHDACs on the cell wall synthesis mechanisms and the                     |
| 223 | relationship of AoHDAC disruption to fungal biomass.   |
| 224 | The hstD/AoHst4 HDAC has been phylogenetically classified in the fungal specific                       |
| 225 | sirtuin class but its function is still poorly understood (4). We previously reported that             |
| 226 | hstD/Aohst4 coordinates fungal specific phenotypes of secondary metabolite production                  |
| 227 | and conidia formation, and a separate study using Saccharomyces cerevisiae found that                  |
| 228 | hst4 (a homolog of hstD in A.oryzae) was important for genome integrity and resistance                 |
| 229 | to genotoxin (21, 33). In our work, we reveal an additional function. The deletion of                  |
| 230 | hstD/Aohst4 led to MMS- and CPT-sensitive phenotypes suggests that this family of                      |
| 231 | proteins plays a conserved role in the genome integrity among fungi.                                   |
| 232 | We also found a novel effect on enzyme production in rice-koji produced by the                         |
| 233 | disruptant strains. The $\Delta hstD$ strain decreased enzyme production despite the growth of         |
| 234 | mycelia being unchanged. This was surprising because, in general, alteration of the                    |

| 235 | protein secretion pathway affects filamentous growth of A. oryzae (34). The lack of      |
|-----|--|
| 236 | sensitive phenotypes when we tested protein secretion pathway inhibitors suggests that   |
| 237 | hstD/Aohst4 may not affect the protein secretion pathway. In general, HDACs affect       |
| 238 | transcriptional regulation, so it is possible hstD/Aohst4 affects extracellular enzyme   |
| 239 | expression. This would have significant industrial applications and future work should   |
| 240 | investigate the expression, histone modification and chromatin structure of these genes. |
| 241 | This work reveals novel phenotypes of four AoHDAC disruptants in A. oryzae:              |
| 242 | hdaA/Aohda1, hdaB/Aorpd3, hdaD/Aohos2, and hstD/Aohst4 with diverse cellular             |
| 243 | process that include stress response, cell wall synthesis, protein secretion, and genome |
| 244 | integrity. Because HDACs are highly conserved among filamentous fungi and other          |
| 245 | eukaryote, our study is broadly applicable to understanding the function of HDACs.       |
| 246 |  |
| 247 | Acknowledgments  |
| 248 | We thank Dr. Masatoshi Goto for gifting micafungin.                                      |
| 249 |  |

## **Reference**

| 252 | 1. | Cairns, B. R.: The logic of chromatin architecture and remodelling at promoters, |
|-----|----|--|
| 253 |    | Nature, <b>461</b> ,193-198 (2009).  |
| 254 | 2. | Shahbazian, MD. and Grunstein, M.: Functions of site-specific histone            |
| 255 |    | acetylation and deacetylation, Annu. Rev. Biochem., 76, 75-100 (2007).           |
| 256 | 3. | Nishida, H.: Evolutionary conservation levels of subunits of histone-modifying   |
| 257 |    | protein complexes in fungi, Comp. Funct. Genomics, 379317 (2009).                |
| 258 | 4. | Frye, R. A.: Phylogenetic Classification of prokaryotic and eukaryotic Sir2-like |
| 259 |    | proteins, Biochem. Biophys. Res. Commun., 273, 793-798 (2000).                   |
| 260 | 5. | Gregoretti, I., Lee. Y-M., and Goodson, H. V.: Molecular evolution of the        |
| 261 |    | histone deacetylase family: Functional implications of phylogenetic analysis, J. |
| 262 |    | Mol. Biol., <b>338</b> , 17-31 (2004).   |
| 263 | 6. | Yang, X-J. and Seto, E.: The Rpd3/Hda1 family of lysine deacetylases: from       |
| 264 |    | bacteria and yeast to mice and men, Nat. Rev. Mol. Cell. Biol., 9, 206-218       |
| 265 |    | (2008).  |
| 266 | 7. | Iwashita, K.: Recent studies of protein secretion by filamentous fungi, J.       |
| 267 |    | Biosci. Bioeng., <b>94</b> , 530-535 (2002).                                     |
| 268 | 8. | Hoffmeister, D. and Keller, N. P.: Natural products of filamentous fungi:        |

| 269 |     | enzymes, genes, and their regulation, Nat. Prod. Rep., 24, 393-416 (2007).                      |
|-----|-----|---|
| 270 | 9.  | Raffaele, S. and Kamoun, S.: Genome evolution in filamentous plant                              |
| 271 |     | pathogens: why bigger can be better, Nat. Rev. Micro., 10, 417-430 (2012).                      |
| 272 | 10. | Pagiotti, R., Angelini, P., Rubini, A., Tirillini, B., Granetti, B., Venanzoni, R.,             |
| 273 |     | Identification and characterisation of human pathogenic filamentous fungi and                   |
| 274 |     | susceptibility to <i>Thymus schimperi</i> essential oil, Mycoses, <b>54</b> , e364-e376 (2011). |
| 275 | 11. | Gacek, A. and Strauss, J.: The chromatin code of fungal secondary metabolite                    |
| 276 |     | gene clusters, Appl. Microbiol. Biotechnol., 95, 1389-1404 (2012).                              |
| 277 | 12. | Ding, S-L., Liu, W., Iliuk, A., Ribot, C., Vallet, J., Tao, A., Wang, Y., Lebrun,               |
| 278 |     | M-H., and Xu, J-R., The Tig1 histone deacetylase complex regulates infectious                   |
| 279 |     | growth in the rice blast fungus Magnaporthe oryzae, Plant Cell, 22, 2495-2508                   |
| 280 |     | (2010).   |
| 281 | 13. | Li, Y., Wang, C., Liu, W., Wang, G., Kang, Z., Kistler, H. C., and Xu, J-R.:                    |
| 282 |     | The HDF1 histone deacetylase gene is important for conidiation, sexual                          |
| 283 |     | reproduction, and pathogenesis in Fusarium graminearum, Mol. Plant Microbe                      |
| 284 |     | Interact, <b>24</b> , 487-496 (2010).   |
| 285 | 14. | Tribus, M., Bauer, I., Galehr, J., Rieser, G., Trojer, P., Brosch, G., Loidl, P.,               |
| 286 |     | Haas, H., and Graessle, S.: A novel motif in fungal class 1 histone deacetylases                |

288

is essential for growth and development of *Aspergillus*, Mol. Biol. Cell., **21**, 345-353 (2010).

- Tribus, M., Galehr, J., Trojer, P., Brosch, G., Loidl, P., Marx, F., Haas, H.,
   and Graessle, S.: HdaA, a major class 2 histone deacetylase of *Aspergillus nidulans*, affects growth under conditions of oxidative stress, Eukaryotic Cell, 4,
- 292 1736-1745 (2005).
- Shimizu, M., Masuo S., Fujita, T., Doi, Y., Kamimura, Y., and Takaya, N.:
  Hydrolase controls cellular NAD, sirtuin, and secondary metabolism, Mol. Cell.
- 295 Biol., 32, 3743-3755 (2012).
- 296 17. Machida, M., Yamada, O., and Gomi, K.: Genomics of Aspergillus oryzae:
- learning from the history of koji mold and exploration of its future. DNA Res.,
- **15**, 173-183 (2008).
- 299 18. Christensen, T., Woeldike, H., Boel, E., Mortensen, S. B., Hjortshoej, K.,
- Thim, L., and Hansen, M. T.: High level expression of recombinant genes in
   *Aspergillus oryzae*, Nat. Biotechnol., 6, 1419-1422 (1988).
- 302 19. Imamura, K., Tsuyama, Y., Hirata, T., Shiraishi, S., Sakamoto, K., Yamada,
- 303 O., Akita, O., and Shimoi, H.: Identification of a gene involved in the synthesis
- 304 of a dipeptidyl peptidase IV inhibitor in Aspergillus oryzae, Appl. Environ.

305 Microbiol., **78**, 6996-7002 (2012).

| 306 | 20. | Terabayashi, Y., Sano, M., Yamane, N., Marui, J., Tamano, K., Sagara, J.,          |
|-----|-----|--|
| 307 |     | Dohmoto, M., Oda, K., Ohshima, E., Tachibana, K., and other 4 authors:             |
| 308 |     | Identification and characterization of genes responsible for biosynthesis of kojic |
| 309 |     | acid, an industrially important compound from Aspergillus oryzae, Fungal Genet.    |
| 310 |     | Biol., 47, 953-961, (2010).  |
| 311 | 21. | Kawauchi, M., Nishiura, M., and Iwashita, K.: Fungas-specific sirtuin HstD         |
| 312 |     | coordinates secondary metabolism and development through control of LaeA,          |
| 313 |     | Eukaryotic Cell, <b>12</b> , 1087-1096 (2013).                                     |
| 314 | 22. | Iemura, Y., Yamada, T., Takahashi, T., Furukawa, K., and Hara S.:                  |
| 315 |     | Properties of the peptides liberated from rice protein in Sokujo-moto, J. Biosci.  |
| 316 |     | Bioeng., <b>88</b> , 276-280 (1999).   |
| 317 | 23. | Free, S. J.: Chapter Two - Fungal Cell Wall Organization and Biosynthesis, p.      |
| 318 |     | 33-82. In Freedman, T., Dunlap, J. C., and Goodwin S. F. (ed.), Advances in        |
| 319 |     | Genetics, vol. 81. Academic Press, Waltham, MA. (2013).                            |
| 320 | 24. | Huertas, D., Sendra, R., and Muñoz, P.: Chromatin dynamics coupled to DNA          |
| 321 |     | repair, Epigenetics, 4, 31-42 (2009).  |
| 322 | 25. | Kitamoto, K.: Molecular biology of the Koji molds, Adv. Appl. Microbiol., 51,      |

323 129-153 (2002) Academic Press., Waltham, MA.

| 324 | 26. | Arima, K., and Uozumi, T.: A new method for estimation of mycelial weight in       |
|-----|-----|--|
| 325 |     | koji, Agr. Biol. Chem., <b>31</b> , 119-123 (1967)                                 |
| 326 | 27. | Horio, Y., Hayashi, T., Kuno, A., and Kunimoto, R.: Cellular and molecular         |
| 327 |     | effects of sirtuins in health and disease, Clin. Sci.(Lond.), 121, 191-203 (2011). |
| 328 | 28. | Brosch, G., Loidl, P., and Graessle, S.: Histone modifications and chromatin       |
| 329 |     | dynamics: a focus on filamentous fungi, FEMS Microbiol. Rev., 32, 409-439          |
| 330 |     | (2008).  |
| 331 | 29. | Biesebeke, R., Ruijter, G., Rahardjo, Y. S. P., Hoogschagen, M. J.,                |
| 332 |     | Heerikhuisen, M., Levin, A., Driel, K. G. A., Schutyser, M. A. I.,                 |
| 333 |     | Dijksterhuis, J., Zhu, Y., and other 4 authors.: Aspergillus oryzae in             |
| 334 |     | solid-state and submerged fermentations, FEMS Yeast Res., 2, 245-248 (2002).       |
| 335 | 30. | Oda, K., Kakizono, D., Yamada, O., Iefuji, H., Akita, O., Iwashita, K.:            |
| 336 |     | Proteomic Analysis of Extracellular Proteins from Aspergillus oryzae Grown         |
| 337 |     | under Submerged and Solid-state Culture Conditions, Appl. Environ. Microbiol.,     |
| 338 |     | 72, 3448-3457 (2006).  |
| 339 | 31. | Wang, B., Guo, G., Wang, C., Lin, Y., Wang, X., Zhao, M., Guo, Y., He, M.,         |
| 340 |     | Zhang, Y., Pan, L.: Survey of the transcriptome of Aspergillus oryzae via          |

- massively parallel mRNA sequencing, Nucleic Acids Res., 38, 5075-5087
  (2010).
- 343 32. Latgé J.P.: Tasting the fungal cell wall., Cell Microbiol., 12, 863-72 (2010)
- 344 32. **Miller, K., Maas, N., Toczyski, D.:** Taking it off: regulation of H3 K56 345 acetylation by *Hst3* and *Hst4*, Cell Cycle, **5**, 2561-2565 (2006).
- 346 33. Shoji, J., Arioka, M., Kitamoto, K.: Dissecting cellular components of
- 347 secretory pathway in filamentou fungi: insights into their application for protein
- 348 production, Biotecnol. Lett., **30**, 7-14 (2008).
- 349

## 351 Figure legends

- 352 FIG. 1. Stress sensitivity test of AoHDAC disruptants.
- 353 (A) Morphological phenotypes of disruptants on stress plate culture on day five. (B)
- 354 Comparison of stress sensitivity on plate culture. Graphs represent radial growth
- relative to the no-stress plate culture (corresponding to 1.0). (C) Comparison of osmotic
- 356 stress sensitivity on liquid culture. Graphs represent mycelia dry weight relative to the
- no-stress liquid culture (corresponding to 1.0). The  $adeA^+$  strain was used as a control in

this figure. All data are represented as means  $\pm$  s.d. (n=3); \* p < 0.05, t-test.

359

360 FIG. 2. Cell wall synthesis inhibitor sensitivity of AoHDAC disruptants.

- 361 (A) Morphological phenotypes of indicated strain on cell wall synthesis inhibitor treated
- 362 culture on day five. (B) Comparison of inhibitors sensitivity on plate culture. Graphs
- 363 represent radial growth relative to the plate culture lacking an inhibitor (corresponding
- to 1.0). The *adeA*<sup>+</sup> strain was used as a control. All data are represented as means  $\pm$
- s.d. (n=3); \* p < 0.05, t-test. Abbreviations: CFW, calcofluor white; CR, Congo red; MF,
- 366 micafungin.

367

368 FIG. 3. Genotoxin sensitivity of AoHDAC disruptants.

| 369 | (A) Morphological phenotypes of indicated strain on genotoxin treated culture on day           |
|-----|--|
| 370 | five. (B) Comparison of genotoxin sensitivity on plate culture. Graphs represent radial        |
| 371 | growth relative to the no genotoxin treated plate culture (corresponding to 1.0). The          |
| 372 | $adeA^+$ strain was used as a control. All data are represented as means ± s.d. (n=3); * $p <$ |
| 373 | 0.05, t-test. Abbreviations: HU, hydroxy urea; CPT, camptothecin; MMS, methyl                  |
| 374 | methane sulfonate.   |
| 375 |  |
| 376 | FIG. 4. Phenotypes of AoHDACs on rice-koji.  |
| 377 | (A) N-acetylglucosamine amounts in rice-koji. (B) Total protein equivalent in rice-koji.       |
| 378 | (C) Activity of enzymes in rice-koji. Enzyme activities represented as the activity            |
| 379 | relative to the $adeA^+$ control strain (corresponding to 1.0). All data are represented as    |
| 380 | means $\pm$ s.d. (n=3); * $p < 0.05$ , t-test.   |
|     |  |
## 382 Supplementary figure legends

383

FIG. S1. Phenotypes of AoHDAC mutants on stress plate culture at day five.

385 The  $adeA^+$  strain was used as a control.

386

- 387 FIG. S2. Stress sensitivity test of AoHDAC disruptants.
- 388 (A) Comparison of stress sensitivity on plate culture. Graphs represent radial growth
- relative to the no stress plate culture (corresponding to 1.0). (B) Comparison of osmotic
- 390 stress sensitivity on liquid culture. Graphs represent mycelia dry weight relative to the
- no stress liquid culture (corresponding to 1.0). The  $adeA^+$  strain was used as a control.
- All data are represented as means  $\pm$  s.d. (n=3); \* p < 0.05, t-test.
- 393
- FIG. S3. Cell wall synthesis inhibitor sensitivity of AoHDAC disruptants.
- (A) Morphological phenotypes of indicated strain on cell wall synthesis inhibitor treated
- 396 culture on day five. (B) Comparison of inhibitor sensitivity on plate culture. Graphs
- 397 represent radial growth relative to the plate culture lacking an inhibitor (corresponding
- to 1.0). The *adeA*<sup>+</sup> strain was used as a control. All data are represented as means  $\pm$  s.d.
- (n=3); \* p < 0.05, t-test. Abbreviations: CFW, calcofluor white; CR, Congo red; MF,

400 micafungin.

401

- 403 (A) Morphological phenotypes of indicated strain on cell wall synthesis genotoxin
- 404 treated culture on day five. (B) Comparison of inhibitors sensitivity on plate culture.
- 405 Graphs represent radial growth relative to the no genotoxin treated plate culture
- 406 (corresponding to 1.0). The  $adeA^+$  strain was used as a control. All data are represented

407 as means  $\pm$  s.d. (n=3); \* p < 0.05, t-test. Abbreviations: HU, hydroxy urea; CPT,

408 camptothecin; MMS, methyl methane sulfonate.

409



411 (A) Morphological phenotypes of indicated strain on protein synthesis or secretion

- treated culture on day five. (B) Comparison of inhibitors sensitivity on plate culture.
- 413 Graphs represent radial growth relative to the plate culture lacking an inhibitor
- 414 (corresponding to 1.0). The  $adeA^+$  strain was used as a control. All data are represented
- 415 as means  $\pm$  s.d. (n=3); \* p < 0.05, t-test. Abbreviations: TM, tunicamycin; DTT,
- 416 dithiothreitol; BFA, brefeldin A; NC, nocodazole.
- 417

- 418 FIG. S6. Phenotypes of AoHDAC disruptants on rice-*koji*.
- 419 (A) N-acetylglucosamine amounts in rice-*koji*. (B) Total protein equivalent in rice-*koji*.
- 420 (C) Activity of indicated enzyme in rice-*koji*. Enzyme activities represent activity
- 421 relative to the  $adeA^+$  control strain (corresponding to 1.0). All data are represented as
- 422 means  $\pm$  s.d. (n=3); \* p < 0.05, t-test.

TABLE 1. Strains used in this study.

| Name                 | Genotype   | Disrupted gene (accession) <sup>b</sup> | HDAC type (HDAC Class)   | Reference |
|----------------------|--|---|--------------------------|-----------|
| $adeA^+$             | $niaD^*sC^*adeA^*argB::adeA^*\Delta ligD::argB adeA^+$   |   |                          | (22)      |
| hdaB ht <sup>a</sup> | niaD <sup>*</sup> sC <sup>*</sup> adeA <sup>*</sup> argB::adeA <sup>*</sup> AligD::argB AhdaB::adeA hdaB | hdaB / Aorpd3(AO080554000240)           | Classical HDAC (Class 1) | (22)      |
| $\Delta h da C$      | niaD <sup>*</sup> sC <sup>*</sup> adeA <sup>*</sup> argB::adeA <sup>*</sup> AligD::argB AhdaC::adeA      | hdaC / Aorpd3(AO080525000127)           | Classical HDAC (Class 1) | (22)      |
| ∆hdaD                | niaD sC adeA argB::adeA AligD::argB AhdaD::adeA  | hdaD / Aohos2(AO080511000459)           | Classical HDAC (Class 1) | (22)      |
| ∆hdaA                | niaD <sup>*</sup> sC <sup>*</sup> adeA <sup>*</sup> argB::adeA <sup>*</sup> AligD::argB AhdaA::adeA      | hdaA / Aohda1(AO080513000236)           | Classical HDAC (Class 2) | (22)      |
| $\Delta h da E$      | niaD <sup>-</sup> sC <sup>-</sup> adeA <sup>-</sup> argB::adeA <sup>-</sup> AligD::argB AhdaE::adeA      | hdaE / Aohos3 (AO080570000061)          | Classical HDAC (Class 2) | (22)      |
| $\Delta hstA$        | niaD <sup>-</sup> sC <sup>-</sup> adeA <sup>-</sup> argB::adeA <sup>-</sup> AligD::argB AhstA::adeA      | hstA / Aosir2 (AO080506000102)          | Sirtuin (Class3)         | (22)      |
| ∆hstB                | niaD <sup>-</sup> sC <sup>-</sup> adeA <sup>-</sup> argB::adeA <sup>-</sup> AligD::argB AhstB::adeA      | hstB / Aohst2 (AO080569000094)          | Sirtuin (Class3)         | (22)      |
| $\Delta hstC$        | niaD <sup>-</sup> sC <sup>-</sup> adeA <sup>-</sup> argB::adeA <sup>-</sup> AligD::argB AhstC::adeA      | hstC / Aohst2 (AO080508000293)          | Sirtuin (Class3)         | (22)      |
| ∆hstD                | niaD' sC' adeA' argB::adeA' AligD::argB AhstD::adeA  | hstD / Aohst4 (AO080533000358)          | Sirtuin (Class3)         | (22)      |
| $\Delta hstE$        | niaD <sup>*</sup> sC <sup>*</sup> adeA <sup>*</sup> argB::adeA <sup>*</sup> AligD::argB AhstE::adeA      | hstE / Aosirt4 (AO080559000113)         | Sirtuin (Class3)         | (22)      |
| $\Delta hstF$        | niaD <sup>*</sup> sC <sup>*</sup> adeA <sup>*</sup> argB::adeA <sup>*</sup> \DeltaligD::argB             | hstF / Aosirt5(AO080568000195)          | Sirtuin (Class3)         | (22)      |

<sup>a</sup> ht: heterokaryon

<sup>b</sup> HDAC homolog of Saccharomyces cerevisiae or Homo Sapiens with the species name (Ao: Aspergillus oryzae) indicated followed by a slash.

Fig.1





С

Relative mycelial dry weight



### Fig.2







Fig.3 Α No treatment 10mM HU 1µM CPT 0.1%MMS Control

∆hdaD

hdaB ht

∆hstD







■α-amylase ■glucoamylase ■α-glucosidase ■acid carboxypeptidase ■acid protease



Fig. S2











С



