線虫 *Caenorhabditis elegans* の2種類のAAA族ペルオキシンの遺伝子 *pex-1* と *pex-6*

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Two AAA-family peroxin genes, *pex-1* and *pex-6* of the nematode *Caenorhabditis elegans*

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Peroxins are proteins that play essential roles in peroxisome biogenesis and are encoded by a large number of *pex* genes. Among peroxins, Pex1p (yeast protein)/PEX1 (mammalian protein) and Pex6p/PEX6 constitute the subfamily 2 (SF2) of AAA (ATPases associated with diverse cellular activities) protein family. SF2 presents two AAA modules of which the one located closest to the C-terminus is highly conserved, while the other diverges considerably from the consensus sequence. The genes encoding these two proteins are mutated in 80% of patients with peroxisomal biogenesis disorders (e.g. Zellweger cerebro-hepato-renal syndrome); the effect of defective peroxisomes on neuronal cells could be studied with the model organism *Caenorhabditis elegans,* whose full cell lineage has been completely determined. However, none of the peroxins of this organism has been identified and although the *C. elegans* genome sequence is completely read, PEX-1 is not predicted from any open reading frame (ORF). The only ORF with a significant similarity to PEX-1 was c11h1.6, but it encoded only the highly conserved AAA module; this raised the question if c11h1.6 alone is sufficient to fulfill the Pex1p/PEX1 function. Here, I describe the cloning of the complete cDNAs encoding two AAA peroxin from *C. elegans* in an attempt to analyze their physiological function in this organism.

The complete cDNA sequence of *pex-1* and *pex-6* agreed well with the size of the respective mRNA and carried no spliced leader sequence. The *pex-1* cDNA was composed of 24 exons, which were encoded by a genomic region containing three ORFs, c11h1.4, c11h1.5, and c11h1.6. Although many exon-intron borders in *pex-1* were inconsistent with those predicted for ORFs, those in *pex-6* coincided with those for the ORF f39g3.7. The *pex-1* and *pex-6* genes encoded proteins with 996 and 720 amino acids residue, respectively. PEX-1 and PEX-6 showed a high degree of similarity to the respective cognate proteins not only in the motifs sequences of AAA modules but also in distances between the motifs. In addition to these similarities, three crucial residues identified PEX-1 and PEX-6 as genuine orthologs of Pex1p/PEX1 and Pex6p/PEX6, respectively.

Both *pex-1* mRNA and *pex-6* mRNA were detectable throughout the life cycle of *C. elegans* in an appar-

広島大学総合科学部紀要Ⅳ理系編、第28巻（2002）
*広島大学審査学位論文
口頭発表日：2002年2月7日、学位取得日：2002年3月21日
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ently parallel manner; the amount relative to that of the mRNA used as the internal standard was higher at the larval stage L3 and lower at the young adult stage than the other stages: embryo, larvae (L1, L2 and L4), or egg-lying adult. Whole-mount *in situ* hybridization of L4 larva using antisense RNA probes suggested that both *pex-1* and *pex-6* mRNA accumulated mainly in intestinal cells. Tissue localization of *pex-1* and *pex-6* mRNA is similar to that of the peroxisomal P-44, which is *C. elegans* type-II 3-oxoacyl-CoA thiolase. The RNA interference of the *pex-6* expression using *in vivo* synthesis of double-stranded RNA provided a line that developed to the adult stage and showed an unusual moving behavior.