

# 学位論文要旨

学位論文題目：

Control of adenohypophysis cell differentiation through temporal Notch signaling  
(時間的な Notch シグナルによる脳下垂体細胞分化制御)

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The adenohypophysis (AH) consists of six distinct types of hormone-secreting cells. In zebrafish, while proper differentiation of all AH cell types has been shown to require Notch signaling within a period of 14-16 hours post fertilization (hpf), the mechanisms underlying this process remain to be elucidated. Herein we observed by using the Notch inhibitor dibenzazepine (DBZ) that Notch signaling also contributed to AH cell specification beyond 16 hpf. Specification of distinct cell types was perturbed by DBZ treatment for different time frames, suggesting that AH cells are specified by Notch-dependent and cell-type-specific mechanisms. We also found that two *hes* family genes, *her4.1* and *hey1*, were expressed in the developing AH under the influence of Notch signaling. *her4.1* knockdown reduced expression of *proopiomelanocortin a* (*pomca*), *growth hormone* (*gh*), and *prolactin* (*prl*), while *hey1* was responsible only for *gh* expression. Simultaneous loss of both *Her4.1* and *Hey1* produced milder phenotypes than those of DBZ-treated embryos. Moreover, DBZ treatment from 18 hpf led to a significant downregulation of both *gh* and *pomca* genes only when combined with injection of a subthreshold level of *her4.1*-morpholino. These observations suggest that multiple downstream effectors, including *Her4.1* and *Hey1*, mediate Notch signaling during AH cell specification.