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 proopiomelancortin 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.