CDB SEMINAR

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16:00~17:00 C1F CDB Auditorium

Regulation of Zebrafish Embryonic Cell Migration and Patterning by Steroids

Summary

Steroids play important roles in sexual differentiation, immune response, salt balance, and organ development. Although being synthesized in large quantities, the functions of steroids during embryogenesis are not fully understood due to the difficulties in dissecting mammalian gastrula embryos. We investigated the functions of embryonic steroids by studying zebrafish early development. Zebrafish possess similar steroidogenic pathways as mammals including enzymes like CYP11A1 and HSD3B, which catalyze the conversion of steroids from a common precursor, cholesterol.

When zebrafish CYP11A1 level is eliminated by the injection of antisense morpholino oligonucleotides, we observed delayed morphogenetic epiboly, convergence, extension, and involution migrations during gastrulation. The epiboly migration can be partially rescued by the injection of *CYP11A1* mRNA or by incubation with pregnenolone, indicating that pregnenolone plays a role in promoting epiboly cell movement. Pregnenolone directly stabilized zebrafish yolk microtubules both *in vitro* and *in vivo*. Another steroid, progesterone, however, opposed the effect of pregnenolone by antagonizing epiboly cell movement.

Zebrafish deficient in CYP11A1 also had ventralization phenotype with more ventral cells and fewer dorsal cells. Fish deficient in *Hsd3b1* expression, however, had the opposite dorsalization phenotype. Thus CYP11A1 and Hsd3b1 appear to have antagonistic effects in their dorsal-ventral cell distribution. Since steroids are small molecules amenable to manipulation for clinical use, their new functions during embryogenesis will provide new ways for drug development in the future.

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