CDB SEMINAR

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Monday, June 8, 2015
16:00~17:00   A7F Seminar Room

Reverse genetics in *Xenopus tropicalis* as a model for understanding human genetic diseases involved in eye and brain formation

Summary

rax (*retina and anterior neural fold homeobox*), *six3* (*SIX homeobox 3*) and *pax6* (*paired box 6*) genes are essential for eye and brain formation in vertebrates. In humans *RAX* mutations result in anophthalmia in compound heterozygotes, *SIX3* mutations cause severe eye and brain defects (holoprosencephaly, HPE), and semi-dominant mutations in *PAX6* cause aniridia (hypoplasia or absence of the iris). While studies of mutants of these genes in other organisms such as rodents and fish demonstrate that their functions are important during early neurula stages, the molecular mechanisms by which they influence eye and brain development are still largely unclear. *Xenopus tropicalis* has several advantages as a model organism, i.e. it is a true diploid (unlike fish), embryos are plentiful, easy to obtain and readily accessible for culture or experimental manipulation from the earliest stages of development (unlike mouse). We have obtained frog mutants of these genes using a Targeting Induced Local Lesions IN Genomes (TILLING) screen (*rax*), or CRISPR- and TALEN-mediated targeted mutagenesis (*six3* and *pax6*, respectively). Briefly, the *rax* mutant revealed that several genes thought to be genetically downstream of *Rax* in mouse are actually not immediate early downstream genes, and losing Rax activity resulted in transformation of presumptive retinal tissue into non-retinal forebrain identities in the *rax* mutant. *six3* mutants showed a HPE-like phenotype, and we could also mimic the human aniridia phenotype in *pax6* mutant frogs. More detailed data and plans for future studies will be presented.
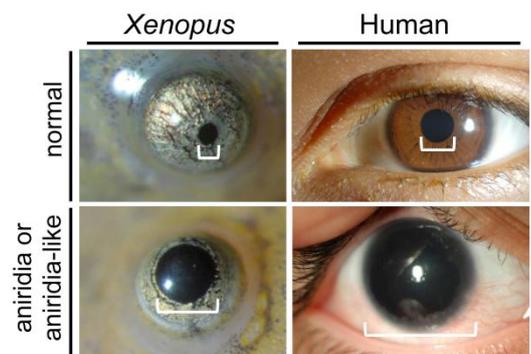
Frog *pax6* hypomorphic mutant mimics human aniridia

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