CDB SEMINAR

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Wednesday, November 21

16:00~17:00 C1F Auditorium

SOX2 function in retinogenesis

Summary

Our long-term goal is to dissect the transcriptional regulatory circuitry underlying neural progenitor competence. SOX2 is an HMG box transcription factor that acts as a master regulator of stem cell identity. In the vertebrate central nervous system SOX2 is expressed in all neural progenitor cells and is downregulated coincident with cell fate restriction and terminal differentiation of progenitor cells. We focus on the retina as a model system to genetically dissect SOX2 biological functions and mechanisms of action. As an isolated and well-defined structure of the central nervous system, the retina has become a well-characterized model for studies of molecular mechanisms of neurogenesis. Only six major types of neurons develop within the retina, along with a single type of glial cells. These cells are readily distinguished from one another by morphology, laminar position and defined cell-type specific molecular markers. Moreover, the retina is one area of the developing nervous system where SOX2 is expressed in the absence of other SOXB1 sub-family members. Finally, SOX2 mutations have been implicated in several hereditary eye conditions in humans. During the course of retinal development, progenitor cells transition through stages of competence - the process leading to generation of diverse retinal cell types. Most, if not all neural retinal progenitors maintain expression of SOX2 from the onset until the latest stages of retinal differentiation. However the levels of SOX2 vary between subsets of neural retinal progenitor cells. Through the generation of an allelic series of Sox2 mutations in the mouse we demonstrated the molecular and cell biological basis for these hereditary conditions (Taranova et al., 2006). SOX2 is required for proliferation and differentiation of early retinal neural progenitors and lowering expression levels of SOX2 (below 40%) results in aberrant neuronal differentiation leading to anophthalmia and microaphthalmia. We will discuss the use of these genetic tools coupled with a protocol that we have developed of culturing and electroporating embryonic and postnatal mouse retinas in order to: (i) to conditionally inactivate and (ii) reduce the levels of expression of Sox2 in subsets of retinal progenitors at distinct developmental stages.

Host:

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