CDB SEMINAR

Speaker: Veronica van Heyningen

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Title:

"PAX6 and SOX2 in disease, development and evolution"

Date: **Thursday, July 17**

Time: **16:00 P.M.～17:00 P.M.**

Place: **7th floor Conference Room, CDB**

Summary

PAX6 was first associated with the human eye anomaly aniridia, where the iris is hypoplastic or absent, but there are a number of associated anomalies involving the retina lens and cornea as well. Additional abnormalities have been observed in the brain and olfactory system as well, in the heterozygous aniridia patients. SOX2 was recently shown to be mutated in a significant proportion of bilateral and severe anophthalmias.

Small eye, the rodent model system for aniridia and PAX6, the rodent models for Pax6 mutations has revealed many key factors on the role for Pax6, since the homozygous null mutants which are neonatally lethal, can be studied in great detail from the mouse and rat models. In contrast, the heterozygous mouse model for SOX2 knockout has no discernible eye defect and the homozygote null mice are pre-implantation lethals. The human-mouse phenotypic difference is intriguing and requires further work. Following its key role in totipotent ES cells, SOX2 is a major early neural marker, as well as being expressed in mouse lens and retina during development.

We have learnt a lot about PAX6 function from the spectrum of human eye disease-associated mutations, including some chromosomal rearrangements which revealed an extensive set of downstream control elements regulating the spatiotemporal expression pattern of the gene. The existence of this complex control system is further emphasized by studying the evolutionary sequence conservation of vertebrate Pax6 in the 200 kb genomic regions surrounding the gene. It is very likely that SOX2 expression is also controlled by complex long range regulatory elements. Interestingly SOX2 and PAX6 have been shown to interact at the protein level, at least in lens development. All these preliminary observations on function remain to be extended further.

Host **Masatoshi Takeichi** **Cell Adhesion/Tissue Patterning, CDB**

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