CDB SEMINAR

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Symmetrical divisions dedicated to generating distinct cone photoreceptor types

Summary

In the vertebrate retina, color information is transmitted by cone photoreceptors with different spectral sensitivities. Although much is known about the transcriptional regulation underlying cone development and the timing of their generation relative to other retinal cell types during development, the location and nature of cell divisions that produce cones remained largely unknown. We thus chose zebrafish that has four distinct cone subtypes as our model animal and used *in vivo* multiphoton time-lapse microscopy to image the generation of cone. Time-lapse imaging of cells labeled using the *thyroid hormone receptor β2* (*trβ2*) promoter revealed cone precursors dedicated to production of Long wavelength sensitive-cones (L-cones). The L-cone precursor underwent symmetric division at the apical surface without attaching the basal surface to give rise to a pair of L-cones. To examine the role of *trβ2* in L-cone genesis, we knocked down *trβ2* by morpholino oligonucleotide. Consistent with mouse *trβ2* function, knockdown of *trβ2* resulted in a loss of L-cone associated with a corresponding increase of UV light sensitive cones. Interestingly, almost all of the cones became L-cones when *trβ2* was overexpressed around the time of precursor division. Furthermore *trβ2* overexpression after cell division also caused L-opsin expression ectopically, but such late expression of *trβ2* could not completely suppress expression of other opsins, giving rise to cones with expression of mixed cone opsins. Our findings suggest that *trβ2* expression at around the precursor stage is sufficient to confer L-cone fate, preventing emergence of mixed cone types. Finally, we also observed symmetric divisions resulting in pairs of non-L cones, and divisions generating different cone types occur concurrently within an area. Thus, there exist dedicated precursors whose symmetric divisions produce each cone type. Our study demonstrates the first example of symmetrical divisions to generate a functionally distinct subtype in a single neuronal type.

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