Research Highlight

Extending Self-Organizing Optic Cups Into Functional Ciliary Epithelium

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Groundbreaking research from the laboratory of the late Yoshiki Sasai captured the world's attention with spontaneous optic cup formation from aggregated embryonic stem cells (ESCs).[1] These ESC-derived optic cups contained both stratified neural retina (NR) with all the major retinal cell types, and an RPE. In this issue, Kinoshita et al.,[2] modified this original protocol with the addition of a GSK-3β inhibitor, CHIR99021, resulting in the production of a double-layered, functional ciliary epithelium at the expense of NR and RPE. The authors demonstrate that both timing and CHIR99021 concentration play an important role in ciliary epithelial formation. Only effective when added at an intermediate (1.2–1.5 μM) concentration during optic vesicle formation, CHIR99021 induced an opposed, double-layered, pigmented (PE) and nonpigmented (NPE) ciliary epithelium, similar to the normal arrangement of these tissues during development. Higher CHIR99021 concentrations resulted only in the formation of pigmented cells. Kinoshita et al.[2] also revealed that GSK-3β inhibition induced accumulation of both cytoplasmic and nuclear β-catenin consistent with canonical Wnt signaling activation. The prevention of CHIR99021 ciliary epithelium induction by XAV939 (an indirect axin activator) strengthens the conclusion that canonical Wnt signaling provides the critical switch to initiate ciliary body development. The authors confirmed the authenticity of their ciliary epithelium both by gene expression and assays testing the transport function necessary for aqueous humor production. Although interesting from a developmental biology perspective, the ability to form functional ciliary epithelia from pluripotent cells offers the real possibility of generating patient-specific tissue for transplant and new hope for people suffering from ciliary body dysfunction and ocular hypotension.

References

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2. Kinoshita H, Suzuma K, Kaneko J, Mandai M, Kitaoka T, Takahashi M. Induction of functional 3D ciliary epithelium–like structure from mouse induced pluripotent cells. *Invest Ophthalmol Vis Sci*. 2016;57:153–161.

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