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Use of a reporter iPS cell line to generate RPE tissues

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Retinal degenerations, including Age-related Macular Degeneration (AMD), are a leading cause of vision loss in the US. Several forms of retinal degenerations originate in the back of the eye in the photoreceptor-retinal pigment epithelium (RPE)-choroid complex. Currently there is no effective therapy that reverses or prevents vision loss in patients with such degenrations. The recent use of stem cell-derived RPE as a cell-based therapy has provided hope for a therapeutic intervention. The current methods for RPE differentiation require manual and laborious picking of pigmented colonies from cultures of differentiating stem cells. Such methods are not easily compatible with current Good Manufacturing Protocols (cGMP). To improve RPE differentiation from stem cells, we developed a reporterinduced pluripotent (iPS) cell line.This line expresses a red fluorescent protein (RFP) constitutively and a green fluorescent protein (GFP) when differentiated into RPE-lineage. TheGFP expression marks cells that attain an epithelial morphology, express RPE-specific genes, and become pigmented. Bychangingthe concentrationsofFGF, BMP, NODAL, & WNT pathways we can differentiate up to 92%cells in a dish into RPE-like cells. We have authenticated newly generated RPE cells usingboth molecular and physiological assays. These cells are grown on artificial scaffolds to generate polarized tissue monolayers. In conclusion, the use of the reporter iPS cell line has led aRPE-differentiation protocol that is scalable, cGMP-amenable,and represents a critical first step in the creation of transplantable tissue with fully-differentiated, functional monolayers of polarized RPE cells.

Biography

Kapil Bharti obtained his Ph.D. from Johann Wolfgang Goethe University in Frankfurt, Germany, graduating summa cum laude. His Ph.D. work involved research in the areas of heat stress, chaperones, and epigenetics. He did his postdoc at the NIH, where he published numerous papers in the areas of transcription regulation, pigment cell biology, and developmental biology of the eye. He has won several awards, including, most recently, being a finalist in the prestigious trans-NIH Earl Stadtman Tenure-Track Symposium. His current work as the head of the Unit on Ocular Stem Cells and Translational Research at NEI, NIH involves developing cell-based therapy for retinal degenerative diseases using induced pluripotent stem cell technology.

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