
Molecular signature of primary retinal pigment epithelium and stem-cell-derived RPE cells.

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Public Summary:

Age-related macular degeneration (AMD) is characterized by the loss or dysfunction of retinal pigment epithelium (RPE) and is the most common cause of vision loss among the elderly. Stem-cell-based strategies, using human embryonic stem cells (hESCs) or human-induced pluripotent stem cells (hiPSCs), may provide an abundant donor source for generating RPE cells in cell replacement therapies. Despite a significant amount of research on deriving functional RPE cells from various stem cell sources, it is still unclear whether stem-cell-derived RPE cells fully mimic primary RPE cells. In this report, we demonstrate that functional RPE cells can be derived from multiple lines of hESCs and hiPSCs with varying efficiencies. Stem-cell-derived RPE cells exhibit cobblestone-like morphology, transcripts, proteins and phagocytic function similar to human fetal RPE (fRPE) cells. In addition, we performed global gene expression profiling of stem-cell-derived RPE cells, native and cultured fRPE cells, undifferentiated hESCs and fibroblasts to determine the differentiation state of stem-cell-derived RPE cells. Our data indicate that hESC-derived RPE cells closely resemble human fRPE cells, whereas hiPSC-derived RPE cells are in a unique differentiation state. Furthermore, we identified a set of 87 signature genes that are unique to human fRPE and a majority of these signature genes are shared by stem-cell-derived RPE cells. These results establish a panel of molecular markers for evaluating the fidelity of human pluripotent stem cell to RPE conversion. This study contributes to our understanding of the utility of hESC/hiPSC-derived RPE in AMD therapy.

Scientific Abstract:

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