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**Derivation of functional retinal pigmented epithelium from induced pluripotent stem cells.**

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**Authors:** David E Buchholz, Sherry T Hikita, Teisha J Rowland, Amy M Friedrich, Cassidy R Hinman, Lincoln V Johnson, Dennis O Clegg

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**Public Summary:**

Human induced pluripotent stem cells (iPSCs) have great promise for cellular therapy, but it is unclear if they have the same potential as human embryonic stem cells (hESCs) to differentiate into specialized cell types. In this paper, we show that they can make cells in the eye. Ocular cells such as the retinal pigmented epithelium (RPE) are of particular interest because they could be used to treat degenerative eye diseases, including age-related macular degeneration and retinitis pigmentosa. We show here that iPSCs generated using the Thomson factors can spontaneously differentiate into RPE cells, which can then be isolated and cultured to form highly differentiated RPE monolayers. RPE derived from iPSCs (iPS-RPE) were analyzed with respect to gene expression, protein expression, and rod outer segment phagocytosis, and compared with cultured fetal human RPE (fRPE) and RPE derived from hESCs (hESC-RPE). iPS-RPE expression of marker mRNAs was quantitatively similar to that of fRPE and hESC-RPE, and marker proteins were appropriately expressed and localized in polarized monolayers. Levels of rod outer segment phagocytosis by iPS-RPE, fRPE, and hESC-RPE were likewise similar and dependent on integrin alpha v beta 5. This work shows that iPSCs can differentiate into functional RPE that are quantitatively similar to fRPE and hESC-RPE and further supports the finding that iPSCs are similar to hESCs in their differentiation potential. This source of cells might be useful to treat macular degeneration.

**Scientific Abstract:**

Human induced pluripotent stem cells (iPSCs) have great promise for cellular therapy, but it is unclear if they have the same potential as human embryonic stem cells (hESCs) to differentiate into specialized cell types. Ocular cells such as the retinal pigmented epithelium (RPE) are of particular interest because they could be used to treat degenerative eye diseases, including age-related macular degeneration and retinitis pigmentosa. We show here that iPSCs generated using Oct4, Sox2, Nanog, and Lin28 can spontaneously differentiate into RPE cells, which can then be isolated and cultured to form highly differentiated RPE monolayers. RPE derived from iPSCs (iPS-RPE) were analyzed with respect to gene expression, protein expression, and rod outer segment phagocytosis, and compared with cultured fetal human RPE (fRPE) and RPE derived from hESCs (hESC-RPE). iPS-RPE expression of marker mRNAs was quantitatively similar to that of fRPE and hESC-RPE, and marker proteins were appropriately expressed and localized in polarized monolayers. Levels of rod outer segment phagocytosis by iPS-RPE, fRPE, and hESC-RPE were likewise similar and dependent on integrin alpha v beta 5. This work shows that iPSCs can differentiate into functional RPE that are quantitatively similar to fRPE and hESC-RPE and further supports the finding that iPSCs are similar to hESCs in their differentiation potential.

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