High efficient differentiation of human adipose-derived stem cells into retinal pigment epithelium-like cells in medium containing small molecules inducers with a simple method

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\textbf{A B S T R A C T}

\textbf{Background:} The induction of retinal pigmented epithelium cells (RPE) is one of the most important objectives in research focused on treating retinal degenerative diseases. The present study aims to differentiate human adipose stem cells (hADSCs) into RPE cells for replacement therapies in cases of retinal degenerative diseases.

\textbf{Methods:} Liposomal-derived human adipose stem cells (LA-hADSCs) were obtained from abdominal samples and examined by immunocytochemistry for the expression of mesenchymal adipose stem cell markers. RPE cells were also obtained from human samples and cultured to be used as control after being examined for the expression of their designated markers. hADSCs differentiated into RPE cells after 80 days using chemical inducers in one step. The differentiated cells were then compared to control cells in marker expression. The differentiated cells were also examined under a scanning electron microscope for the presence of apical microvilli and cell connection.

\textbf{Results:} Cultured hADSCs at the fourth passage was shown to express the surface markers CD90 (98 ± 2%), CD11b (96 ± 3%), and CD105 (95 ± 4%). The RPE cells obtained from human samples expressed the marker RPE65 quite well. 80 days after differentiation, the previously hADSCs expressed both RPE65 (100%) and CRALBP (96 ± 1%) and were thus significantly similar to the RPE cells obtained from human samples. Morphologically, differentiated cells appeared to have epithelial and cytoplasmic pigment granules. Observations using a scanning electron microscope recorded clear connections among the differentiated RPE cells and revealed apical microvilli.

\textbf{Conclusion:} Human adipose stem cells can differentiate into retinal pigmented epithelium cells, which can be used in cell replacement therapy for degenerative diseases including age-related macular degeneration (AMD) as well as retinitis pigmentosa (RP).

1. Introduction

Destruction of retinal pigment epithelium layers and photoreceptor cells leads to loss of central and peripheral vision. Degeneration of the retinal pigment epithelium and the photoreceptor cells leads to the loss of central and peripheral vision. Age-related macular degeneration (AMD) is the main cause of irreversible vision loss in industrial countries (Schwart, Nagiel et al. 2017; Chichagova, Hallam et al. 2013). Currently, there is no drug therapy for patients with AMD. Macular translocation and RPE transplantation surgeries lead to decreased visual loss and improvement of vision in some patients. Studies have shown that normal RPE can facilitate the survival and function of photoreceptors, which supports the potential for use of stem cells and RPE derivatives as like resources for AMD treatment (Song, Zhang et al. 2018). Recently, the use of stem cells with the ability to repair and replace damaged tissue in age-related macular degeneration (AMD) and retinitis pigmentosa (RP) has been proposed. The stem cell therapeutic approach can either replace the retinal pigment epithelium (RPE), or the neurosensory retina, or a combination of both (Lee and MacLaren, 2011). Several studies have examined the potential and influence of stem cells and RPE transplantation to treatment of AMD. Stem cell transplantation for AMD can be performed in direct injection...