Identification of Potential Factors to Enhance RPE Differentiation from ESC by Bioinformatics Analysis of Mesenchymal Cells

Zeinab Navidi Ghaziani[c], Fatemeh Seyyedsalehi[b], Hadis Abdollahzadeh[a], C. Ali Sharifi-Zarchi[ab], C. Leila Satarian[a]

a Department of Stem Cells and Developmental Biology, Cell Science Research Center, Royan Institute for Stem Cell Biology and Technology, Tehran, 148-16635, Iran

b Department of Computer Engineering Sharif University of Technology, Tehran, 11365-11155, Iran

c Department of Computer Engineering, Iran University of Science and Technology, Tehran, 163-16765, Iran

* asharifi@sharif.ir

Abstract: Disorders like Stargardt disease and macular degeneration are important problems of the eye that are associated with degradation of RPE cells. Hence producing RPE cells is of particular importance for regenerative medicine of these patients. Differentiation of RPE cells from Embryonic Stem Cells (ESCs) or induced Pluripotent Stem Cells (iPSCs) is one of the most promising approaches to generate RPE cells. Despite major advances, the existing experimental protocols have not provided sufficient differentiation efficiency that is essential for producing RPE cells in clinical volume. Hence, finding factors that can enhance differentiation efficiency of RPE cells from pluripotent stem cells is of significant importance. Co-culture of mesenchymal cells from different parts of the body during differentiation of RPE cells from pluripotent stem cells results in distinct differentiation efficiencies. More specifically, co-culture of mesenchymes from the head has a significantly higher efficiency enhancement than body-origin mesenchymes. This experimental observation suggests that mesenchymal from head and neck may have secreted factors that play a direct role in the induction of RPE cells. In the present study, we compared expression profiles of mesenchymal stem cells originating from different parts of human and mouse bodies, in order to find effective factors in RPE induction. All samples were obtained from the NCBI GEO database, and we included only healthy and untreated adult donor samples. To counterbalance tissue-specific effects, we integrated mesenchymal cells from variant tissues in the body. Using R/Bioconductor, we performed batch effect removal, quality control, dimension reduction and visualization of the data. From all 16393 genes present in all samples, we identified 76 genes that were significantly upregulated in head-derived mesenchymal cells. Then, we focused on the genes with extra-cellular and/or secreted functions. This narrowed down our candidates to 22 candidate genes. By scrutinizing pathways and biological functions of these candidates, we selected WNT5B and FBN2 and FBLN1 as the final candidates, to be experimentally validated. Altogether, these data indicate the promising role of bioinformatics analysis in enhancing experimental procedures of cellular reprogramming, for regenerative medicine applications. [1][2][3][4]

Keywords: Mesenchymal cells; Retinal pigment epithelium

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