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A Bioinformatics Approach to Identify Mesenchymal Stem Cells Soluble Factors Regulating Retinal Pigmented Epithelium Cells Development

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Objectives

Human pluripotent stem cells provide a promising cell source for ocular cell replacement therapy, but lack standardized differentiation protocols, yet.
We aimed to develop a defined cell culture system for efficient methods to derive Retinal Pigment Epithelium (RPE) cells from human stem cells.
Our experience, co-culture of mesenchymal stem cells (MSCs) from different parts of the body during differentiation of hESC-RPE cells results in distinct differentiation efficiencies. More specifically, co-culture of MSCs from the head has a significantly higher efficiency enhancement than body-origin. This experimental observation suggests that mesenchymal from head may have secreted factors that play a direct role in the induction of RPE cells.
In the present study, using a bioinformatics approach, we compared expression profiles of MSCs originating from human head and body, in order to find effective factors in RPE induction.

Methods

All data were obtained from the NCBI GEO database, and we included only healthy and untreated adult donor samples. To counterbalance tissue-specific effects, we integrated MSCs from variant tissues in the body, Table 1. Using R/Bioconductor, we performed batch effect removal, quality control, dimension reduction and visualization of the data Fig 1.

Tissue	Type
6 Limbal [1]	Head
3 Bone marrows[1] – 7 Bone marrows – [2] 4 Chondrogenices[3]	Trunk

Table 1 . Details of samples

Results

From 16393 genes present in all samples, we identified 76 genes that were significantly up-regulated in head-derived mesenchymal cells compare than body Fig 2. This narrowed down our candidates to 22 genes Table 2. By scrutinizing pathways and biological functions of these candidates, we selected WNT5B, FBN2, and FBLN1 as the final candidates, to be experimentally validated.

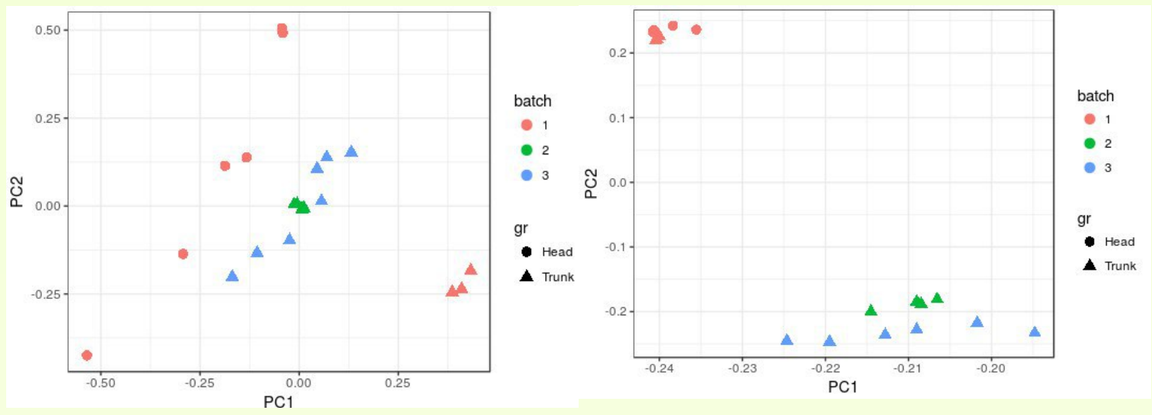

Figure 1. Two principal component of samples before and after removing batch effects.

Secreted	Extra cellular space
TNFRSF11B	TNFRSF11B
WISP2	WISP2
WNT5B	WNT5B
PDPN	ACTG2
ANGPTL2	FBN2
LITAF	THBS1
CPXM2	ANGPTL2
CEMIP	LITAF
DPP4	PDPN
FBN2	FMOD
FMOD	FBLN1
FBLN1	IGFBP2
IGFBP2	PODN
IGFBP5	PCSK9
MRVI	MRVI
NTN1	SEMA3B
PODN	SLIT3
PCSK9	
PRSS12	
RARRES2	
SEMA3B	
SLIT3	

Table 2 . Extra cellular and secreted candid genes

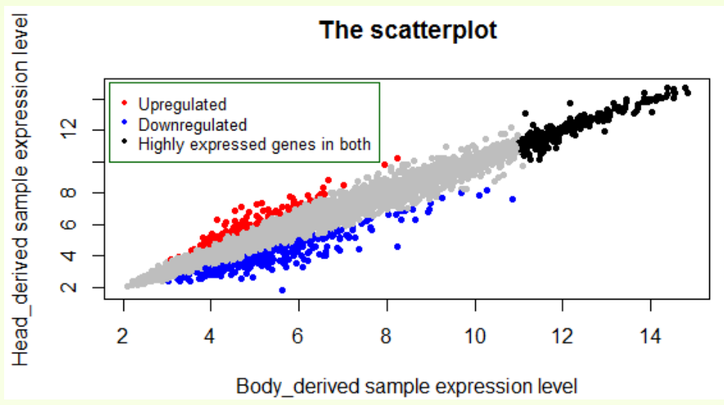

Figure 2. Comparing the gene expression levels in two groups.

Conclusion

Altogether, these data indicate the promising role of bioinformatics analysis in enhancing experimental procedures of cellular differentiation, for regenerative medicine applications.

Reference

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