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EFFECT OF BASIC FIBROBLAST GROWTH FACTOR ON SIGNALING PATHWAYS IN ADULT HUMAN RETINAL PIGMENT EPITHELIAL CELLS

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Retinal pigment epithelium (RPE) plays a key role in the development of many eye diseases, manifested by visual impairment and even blindness. The use of cell cultures to model changes in RPE makes it possible to study the factors that stimulate them and signaling pathways that coordinate the cellular and molecular mechanisms of intercellular interactions under conditions of pathology. In addition, it is possible to identify targets and develop specific therapy that is effectively aimed at eliminating pathological changes in the retina. Based on the results of previously obtained experimental data on a decrease in the level of differentiation of RPE cells in the direction of neuroepithelium after a single exposure to basic fibroblast growth factor (bFGF), research in this direction was continued and the changes in Wnt-, BMP- and Notch-signaling pathways were studied, which is necessary for a deeper understanding of the mechanisms that lower the level of differentiation of RPE cells. So, after adding the factor in culture, a decrease in immunocytochemical staining for β -catenin was observed, an increase in staining for Wnt7a, BMP2 and BMP7, as well as a change in the localization of staining for BMP4. In addition, quantitative real-time PCR in

RPE cells treated with bFGF revealed an increase in the expression of mRNA of *BMP2*, a decrease in the expression of mRNA genes, such as *CTNNA1*, *BMP4*, *BMP2*, and a decrease in the expression of mRNA of Notch signaling genes, such as *JAG1*, *NOTCH1*, *HES1* and *HEY1*. Analysis of the data indicates inactivation of the Wnt/ β -catenin and Notch signaling pathways, activation of the non-canonical Wnt/PCP signaling pathway, and modulating of BMP-signaling with a decrease in the level of differentiation of adult RPE cells after a single (short-term) exposure of bFGF to them. Thus, the results obtained clarify the mechanisms of dedifferentiation of RPE cells under the influence of bFGF.

Keywords: adult human retinal pigment epithelium cells, basic fibroblast growth factor, Wnt, BMP, Notch