

Effect of Physical Stimuli on Angiogenic Factor Expression in Retinal Pigment Epithelial Cells | Biological Engineering

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Full Abstract

Retinal function is supported by underlying retinal pigment epithelium (RPE) and choroid. Choroidal neovascularization (CNV) is a major cause of blindness in patients with age-related macular degeneration (AMD). The goal of this dissertation was to determine the effect of mechanical changes of the RPE on the expression of angiogenic factors and the resulting vascularization.

To replicate cell-cell detachment, RPE cells were micropatterned using a stencil patterning method. Different levels of cell-cell detachment were produced by making different sizes of micropatterns. Two novel devices were also developed to expose RPE cells to acute and chronic mechanical stress. An enzyme-linked immunosorbent assay (ELISA) was used to measure vascular endothelial growth factor (VEGF) levels and quantitative real-time polymerase chain reaction (qRT-PCR) was used to measure the expression of angiogenic and inflammatory gene. An in vitro angiogenesis assay was used to determine the effect of mechanical stress on the angiogenic potential of the RPE secretome.

Our results showed that the disruption of intercellular junctions of the RPE can increase VEGF expression. Adding mechanical stress to RPE cells also resulted in an increase in VEGF expression. Moreover, qRT-PCR results showed an increase in the expression of major angiogenic factors, VEGF isoforms, angiopoietin 2 (ANG2) and hypoxia-inducible factor-1# (HIF-1#) and inflammatory genes, interleukin 6 (IL-6), interleukin 8 (IL-8) and tumor necrosis factor # (TNF#). The increase in the expression of angiogenic factors was associated with an increased in vitro angiogenesis.

The results of this work suggest that the physical disruption of the RPE, including cell-cell detachment and mechanical stress, due to different AMD complications may be involved in CNV initiation and development. These findings can be used to develop more effective treatments to control or prevent CNV.