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$ANXA1_{Ac2-26}$ peptide, a possible therapeutic approach in inflammatory ocular diseases

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Abstract

The eye is immunologically privileged when inflammatory responses are suppressed. One component responsible for the suppression of inflammatory responses is the blood retinal barrier, which comprises the retinal pigment epithelium. The destruction of this barrier initiates inflammation, which can affect any part of the eye. Therefore, inflammatory response is controlled by the action of anti-inflammatory mediators, among these mediators, annexin A1 (ANXA1) protein acts as a modulator of inflammation. In this study we aimed to improve the knowledge of this area by investigating how a peptide of the ANXA1 protein ($ANXA1_{Ac2-26}$) modulates the morphology, proliferation, migration and expression of genes and proteins in human retinal pigment epithelium cells (ARPE-19). Determining how signaling pathways (NF-κB and UBC) are modulated by the $ANXA1_{Ac2-26}$ peptide could be important for understanding the inflammatory process. ARPE-19 cells were activated by bacterial lipopolysaccharide endotoxin (LPS) and treated with $ANXA1_{Ac2-26}$ peptide, in a concentration of 1.7 μM and 33.8 μM. We observed that the LPS activation diminished the levels of endogenous ANXA1 after 2h and 24h and $ANXA1_{Ac2-26}$ peptide decreased the proliferation and re-establishes the migration of ARPE-19 cells. After using a hybridization approach, 80 differentially expressed genes were found. Five of these genes were selected (*LRAT, CTGF, MAP1B, ALDH1A3* and *SETD7*) and all were down-regulated after treatment with the peptide. The genes *CTGF* and *LRAT* would be considered as potential molecular markers of ophthalmologic inflammation. The expression of pro-inflammatory cytokines was also decreased after the treatment, indicating the efficiency of the anti-inflammatory peptide at high concentrations, since the reduction in the levels of these mediators were observed after the treatment with $ANXA1_{Ac2-26}$ peptide at 33.8 μM. Our results suggest that the retinal pigment epithelial cells are a potential target of the ANXA1 protein and point to possible applications of the $ANXA1_{Ac2-26}$ peptide as an innovative therapy for the treatment of ocular inflammation.