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NAP modulates inflammatory cytokines release and counteracts outer blood retinal barrier breakdown in diabetic rat retina

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Diabetic retinopathy (DR) is a common microvascular complication of diabetes. Prolonged hyperglycaemia triggers inflammatory response mediated by release of some cytokines. Combination of these events leads to thinning retinal thickness and blood retinal barrier (BRB) impairment. Many evidences have shown the protective effect played by a small peptide, known as NAP, in some retinal diseases [1]. To this regard, we have recently demonstrated that it reduces apoptotic cell death and interferes with HIFs/VEGF system during early stage of DR [2, 3]. However, the effect of NAP on inflammatory process affecting hyperglycaemic retina has not been identified, yet.

In the present work, we have studied the effect of this peptide in retina of STZ-injected rats, mimicking an in vivo model of diabetes. Furthermore, we have also characterized its role on outer-BRB impairment following exposure of human retinal epithelial cells (ARPE 19) to hyperglycaemic/inflammatory insult.

Results have demonstrated that a single intraocular injection of NAP modulates inflammatory cytokines expression by downregulating IL-1β and related receptors and upregulating IL-1Ra level in diabetic rat retina. These data have been confirmed by immunofluorescence analysis using confocal microscopy. IL-1β immunosignal increased in all retinal layers of diabetic rats as compared to control. NAP treatment reduced cytokine immunoreactivity in inner plexiform layer (IPL), outer plexiform layer (OPL) and rod and cone layer (RCL). We have also evaluated the effect of NAP on the outer-BRB integrity. ARPE19 monolayer hyperpermeability induced by hyperglycaemic/inflammatory insult was significantly reduced after NAP addition in the culture medium. This effect is also mediated through enhancement of tight-junction related proteins expression levels. In conclusion, characterization of NAP action mechanism may be useful to develop a new strategy to prevent retinal damage during DR.

References

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Key words

Diabetic retinopathy, NAP, blood retinal barrier, inflammatory cytokines.

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