

Effect of NAP in diabetic retinopathy

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Diabetic retinopathy (DR) is a microvascular complication of diabetes leading to vision loss. Hypoxic/hyperglycaemic microenvironment is responsible of outer blood retinal barrier integrity impairment and uncontrolled vascularization typical of this pathology. Activation the hypoxia-inducible factors (HIFs) conduce to aberrant expression of some target genes such as vascular endothelial growth factor (VEGF). Many studies have showed the protective role of a small peptide, known as NAP, in counteract retinal damage induced by different insults (Gozes et al., 2004). In particular, we have previously demonstrated that a single intraocular dose of this peptide is able to protect retina from hyperglycaemic insult (Scuderi et al., 2014). However, the involvement of NAP in the modulation of HIFs and their downstream target genes has not been identified yet. In this work, we have instigated its effect on HIFs /VEGF system both *in vitro* and *in vivo* models of DR. Results have demonstrated that NAP treatment prevents outer BRB breakdown comprising human retinal pigmented epithelial cells (ARPE-19) grown in transwell supports and exposed to high glucose (HG) and low oxygen tension by adding desferoxamine mesylate salt (DFX). Peptide administration also reduced HIF1 α /HIF2 α , VEGF/VEGFRs and increased HIF3 α expression in cells cultured in HG/DFX. Moreover, it reduced apoptotic cells rate by modulating BAX and Bcl2 expression, two genes involved in programmed death.

Furthermore, NAP intraocular administration in STZ-induced diabetic rat reduced retinal expression of HIF-1 α , HIF-2 α and VEGF by increasing HIF-3 α levels. These data have been also confirmed by immunolocalization analysis detected through confocal microscopy showing the different distribution of these factors in retinal layers following hyperglycaemic insult.

Our data suggest that this small peptide may be efficacious in counteract retinal damages during DR.

References

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Keywords

NAP, Diabetic retinopathy, hypoxia, hyperglycaemia.