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Chronic hyperglycemia inhibits vasoregression in a transgenic model of retinal degeneration

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Diabetic retinopathy is characterized by the retinal vasoregression with the loss of pericytes, the formation of acellular capillaries and neovascularization in animal models and in humans. Recently, diabetic retinopathy is being also recognized as a neurodegenerative disease of the retina with neuronal dysfunction and glial reactivity. However, little is known about the interaction of vascular and neuro-glial cells in diabetic retinas. In our study we superimposed chronic hyperglycemia on a new transgenic rat (PKD) with photoreceptor degeneration and consecutive retinal vasoregression, in which there are some similarities with the changes of diabetic retinopathy.

In order to assess the vascular and neuronal alterations in presence of hyperglycemia we determined the retinal morphometry in retinal digest preparations with several parameters for vasoregression, and quantified the cell numbers and retinal layer thickness for neurodegeneration. Retinal vascular endothelial growth factor (VEGF) levels were measured by enzyme-linked immunosorbent assay (ELISA). We also performed immunofluorescence staining to study the glial activation, the expression and location of heat shock protein 27 (HSP27) in nondiabetic and diabetic PKD retinas.

Different from the expected response to diabetes, the numbers of acellular capillaries und intraretinal microvascular abnormalities (IRMAs) in the diabetic PKD retinas were reduced. The numbers of pericytes and endothelial cells were increased. Furthermore, cell numbers in the inner nuclear layer (INL) of diabetic PKD retinas remained significantly higher at two time-points. Glial activation appeared reduced by diabetes in PKD retinas. VEGF levels were increased compared with the nondiabetic PKD. HSP27 was upregulated in glial cells under hyperglycemia.

The data presented in this study provide evidence that chronic hyperglycemia inhibits vasoregression in this transgenic model of retinal degeneration. The improvement was associated with the up-regulation of survival factors, such as VEGF and HSP 27, which are predominantly expressed in glial cells in the preserved INL. Taken together, hyperglycaemia can play a vascular protective role in the absence of photoreceptors/ hypoxia and the promotion of neuro(cyto)trophins via retinal glia seems to assure the vasoprotection.