

Interleukin-1 family members in the retina of streptozotocin-injected rats

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Diabetic retinopathy (DR) is one of the most common complications of diabetes. It has been demonstrated that pro-inflammatory cytokines are increased in diabetic retina, including interleukin-1 β (IL-1 β) (Joussen et al., 2001), suggesting that this cytokine might play an important role in the pathogenesis of DR (Kowluru and Odenbach, 2004). The principal components of the IL-1 family are two secreted factors, IL-1 α and IL-1 β , two transmembrane receptors (IL-1RI and IL-1RII), and a natural antagonist receptor of IL-1 function (IL-1Ra). To date the molecular mechanisms mediated by IL-1 family members in DR have not been fully characterized. In the present study, to explore the role of IL-1, we analyzed the expression and distribution of IL-1 α and IL-1 β and relative receptors in a model *in vivo* of DR.

Diabetes was induced in adult rats by intraperitoneal injection of streptozotocin (60 mg/kg).

Protein expression and distribution of IL-1 members and relative receptors were analyzed in retinas of nondiabetic and diabetic rats three weeks after induction of diabetes by Western blot and confocal microscopy analyses.

Hyperglycemia induced a significant increase in IL-1 β protein expression levels and distribution as compared to nondiabetic animals. Specifically, IL-1 β retinal immunoreactivity was found not only in the rod and cone layer (RCL), but also in the outer plexiform layer (OPL), inner plexiform (IPL) and in the ganglion cell layer (GCL) of diabetic rats. IL-1 α transcription levels were unchanged in the retinas of both animal groups. Consistent with expression studies, IL-1 α localization did not differ between diabetic and nondiabetic rats. IL-1RI, IL-1RII and IL-1Ra expression was significantly increased in the retina of diabetic rats when compared to controls. Accordingly, IL-1RI positiveness was thoroughly increased in all retinal layers of diabetic rats, while no evident changes were apparent for IL-1RII, which was localized in the RCL layer and in outer nuclear layer (ONL) of both diabetic and nondiabetic rats.

These findings point to IL-1 family members as key elements in the pro-inflammatory cascade after hyperglycemia-induced retinal damage, and therefore support the implementation of novel therapeutic strategies aimed at reducing IL-1 production for the treatment of DR.