Expression of *microRNA-29b* and its Potential Target RAX in the Retina of Diabetic Rats: Implications for Apoptosis of Retinal Neurons

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Endoplasmic reticulum(ER) stress induces apoptosis of retinal neurons in diabetic retinopathy, but molecular mechanisms underlying this phenomenon are unclear. RAX, an activator of PKR, is induced by ER stress and activation of PKR signaling pathway leads to apoptosis. MicroRNAs play a pivotal role in regulation of gene expression and our computational analysis predicted that RAX is regulated by *miR-29b*. Here, we investigate the expression of RAX and *miR-29b* and their cellular localization in retina of diabetic rats. Retinas were obtained from normal and streptozotocin-induced diabetic rats. *miR-29b* expression evaluated by qPCR was up-regulated (>3-fold) at 28 and 35 days after injection of streptozotocin. RAX expression monitored by qPCR and Western blot was down-regulated at 28 and 35 days which is consistent with prediction that RAX mRNA is a target of *miR-29b*. *In situ* hybridization revealed that *miR-29b* is highly expressed in ganglionar neurons of retina of diabetic rats. Interestingly, RAX assessed by immunofluorescence displays the same cellular localization of *miR-29b*. Moreover, RAX was up-regulated at 6, 15 and 22 days in retinal ganglionar neurons possibly due to ER stress which activates pro-apoptotic PKR signaling pathway. These findings are relevant since apoptosis of ganglionar neurons is observed in diabetic retinopathy. Our data suggest that RAX is negatively regulated by *miR-29b* which may contribute to develop a new strategy for treatment of diabetic retinopathy by intravitreal injection of *miR-29b*.

Key words: *Apoptosis, Diabetic Retinopathy, microRNA, Neurons, RAX.*
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