Toll-like receptor (TLR)-2/4 expression in retinal ganglion cells in a high-glucose environment and its implications

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ABSTRACT. Diabetic retinopathy (DR), a major complication of diabetes mellitus, is the leading cause of adult blindness. The Toll-like receptor (TLR) family is believed to be involved in the pathogenesis and progression of DR. Here, we investigated the expression profiles of TLR-2 and TLR-4 in retinal ganglion cells (RGCs), in an attempt to elucidate the role of these molecules in the etiology of DR. In vitro cultured RGCs were divided into control and high-glucose groups. The mRNA and protein levels of TLR-2, TLR-4, and nuclear factor (NF)-κB were detected by real-time PCR and western blotting. RGCs were further transfected with specific siRNA targeting TLR2/TLR4, the proliferation of transfected RGCs and their tumor necrosis factor (TNF)-α and interleukin (IL)-8 secretory capacity were analyzed by the 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) and enzyme-linked immunosorbent assays (ELISA), respectively. In a high-glucose environment, TLR-2/4 expression was significantly...
upregulated in RGCs (while their viability decreased); additionally, NF-κB expression and secretion of TNF-α and IL-8 were significantly increased. Co-silencing of the TLR-2 and TLR-4 genes inhibited NF-κB expression and TNF-α/IL-8 secretion, while increasing the survival rate of RGCs. Therefore, a high-glucose environment can potentiate the expression of TLR-2 and TLR-4 in RGCs, activate the downstream signaling pathway, and increase the secretion of pro-inflammatory factors, thereby aggravating DR.

**Key words:** Diabetic retinopathy; Retinal ganglion cells; TLR-4; Toll-like receptor-2