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Effects of Epac1 on Diabetic Retinal Inflammation

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Abstract

An ever-growing body of research suggests that inflammation is one of the primary causes of diabetic retinopathy, as the inflammation can lead to insulin resistance. Beta-adrenergic receptor agonists can reduce the inflammation in human retinal endothelial cells (HRECs), but are not a viable treatment due to systemic effects. Epac1 lies downstream of beta-adrenergic receptor signaling, and it may have the capability to reduce inflammation by acting as an alternative pathway for beta-adrenergic receptor agonists to block inflammatory cytokines such as tumor necrosis factor-alpha (TNF-alpha) and interleukin-1 beta (IL-1B). We hypothesized that the Epac1 agonist will decrease cytokine levels, leading to improved insulin signal transduction in the retina.

HRECs were grown in normal (5mM) or high glucose (25mM). Some cells were not treated with the Epac1 agonist and serve as controls. Western blotting was done using primary antibodies for total and phosphorylated insulin receptor substrate-1 (IRS-1), insulin receptor (IR) and Akt, as well as beta actin as a control for loading. Anti-Rabbit IgG/HRP was used for secondary antibodies. ELISA analyses were done for protein levels of TNF-alpha and IL-1B. We are not done with data analyses, but we expect to find that Epac1 will increase insulin receptor and Akt phosphorylation, while reducing TNF-alpha and IL-1B levels.

KEYWORDS: Diabetic retinopathy; Epac1; inflammation; TNF-alpha; Western blot

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ABSTRACT

An ever-growing body of research suggests that inflammation is one of the primary causes of diabetic retinopathy, as the inflammation can lead to insulin resistance. Beta-adrenergic receptor agonists can reduce the inflammation in human retinal endothelial cells (HRECs), but are not a viable treatment due to systemic effects. Epac1 lies downstream of beta-adrenergic receptor signaling, and it may have the capability to reduce inflammation by acting as an alternative pathway for beta-adrenergic receptor agonists to block inflammatory cytokines such as tumor necrosis factor-alpha (TNF-alpha) and interleukin-1 beta (IL-1B). We hypothesized that the Epac1 agonist will decrease cytokine levels, leading to improved insulin signal transduction in the retina.

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