THE NUCLEAR LEVELS OF THIOREDOXIN REDUCTASE 1, GAMMA-H2AX, AND YAP ARE MODULATED BY PRIMARY CILIA IN RESPONSE TO HIGH GLUCOSE LEVELS.

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Diabetes is a condition characterized by impaired regulation of blood glucose levels, leading to various complications such as hypertension, cardiovascular disease, and retinopathy. Diabetic retinopathy (DR), caused by a disrupted retinal blood barrier, is associated with oxidative stress resulting from dysregulated glucose levels in the retina. The primary cilium, an organelle involved in energy balance and glucose homeostasis, has been implicated in the development of various diseases known as ciliopathies, which include overlapping phenotypes such as obesity, diabetes, and retinopathy.

This study aims to investigate the impact of high glucose levels on primary cilia assembly in retinal pigment epithelium (RPE-1) cell cultures and explore the role of cilia in the cellular response to high glucose levels. RPE-1 cells were grown in media supplemented with different glucose concentrations (5 mM, 25 mM, and 5 mM glucose + 20 mM mannitol), and cilia assembly was induced before or after glucose supplementation. The results revealed that glucose supplementation did not affect the number of ciliated cells, but cells supplemented with 25 mM glucose exhibited shorter cilia. To understand the role of cilia in response to high glucose levels, the nuclear levels of thioredoxin reductase 1 (TRXR1), a key enzyme involved in combating oxidative stress triggered by hyperglycemia, were evaluated. Additionally, γH2AX, a marker of DNA breaks and cellular senescence, and YAP, a Hippo pathway effector, were examined. It was observed that glucose supplementation, particularly at high levels (25 mM), influenced the nuclear levels of TRXR1, γH2AX, and YAP. Notably, the presence of cilia modulated the cellular response to high glucose levels, modulating the levels of these proteins. These preliminary findings indicate that primary cilia significantly influence the cellular response to high glucose concentrations, which are known to induce oxidative stress and potentially contribute to the development of DR.

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