INNOVATION PARTNERSHIPS
UNIVERSITY OF MICHIGAN

Modulation of Pyruvate Kinase M2 as a Therapeutic Strategy for Proliferative Vitreoretinopathy

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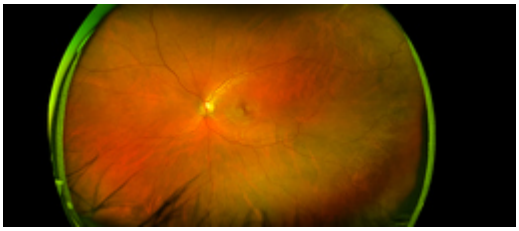

OVERVIEW

A novel therapeutic strategy to circumvent proliferative vitreoretinopathy (PVR)

- Modulation of pyruvate kinase M2 to regulate transcription of proglycolytic genes
- Can both prevent PVR and improve photoreceptor survival

BACKGROUND

Retinal detachment (RD) is an important cause of visual loss, and its treatment commonly includes an attempt at surgical reattachment. About 10% of these surgeries fail due to proliferative vitreoretinopathy (PVR), characterized by a brisk vitreous retraction followed by significant periretinal proliferation. The incidence of PVR correlates with fibrotic membrane production on both surfaces of the retina and portends poor visual outcomes. PVR management currently relies on surgical removal of these membranes, though the resection can incite additional fibrosis and recurrent PVR. The epithelial-to-mesenchymal transition (EMT) of retinal pigment epithelial (RPE) cells is central to PVR pathogenesis, and metabolic reprogramming that increases local tissue glycolysis is a well understood hallmark of RPE EMT. Still, there are currently no available pharmacologic therapies to address PVR, so a need exists for additional research to provide novel treatment methods.

INNOVATION

University of Michigan researchers have discovered that modulation of pyruvate kinase M2 (PKM2) can alter the metabolic profile of retinal pigment epithelial cells undergoing epithelial-to-mesenchymal transition to successfully inhibit EMT induced RPE cell proliferation and contraction. PKM2 is a known regulator of glycolysis that exists in dimer or tetramer forms, the

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Therapeutics and Vaccines
Life Sciences

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latter of which may translocate to cell nuclei and regulate transcription of proglycolytic genes. These researchers have previously shown PKM2 modulation to be a promising strategy for photoreceptor neuroprotection following retinal detachment. The current report is the first to elucidate the importance of PKM2 in RPE EMT and PVR, the effects of which are non-toxic to highly differentiated RPE. Thus, pharmacologic modulation of PKM2 has the potential to both prevent the formation of PVR and improve photoreceptor survival, thereby addressing two major causes of irreversible vision loss after RD.