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Oxidative stress and inflammation in diabetic retinopathy and retinal vascular diseases: Modulation by Nrf2

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Inflammation and oxidative stress play an important role in the development and progression of diabetic retinopathy and Lother retinal vascular diseases. These processes contribute significantly to retinal damage and dysfunction in these conditions, including vascular permeability, neuronal impairment, and capillary degeneration. It is therefore critical to gain further insights into the mechanisms governing oxidative stress and inflammation in the retina, as well as approaches for modulating these processes. The transcription factor nuclear factor erythroid-2-related factor 2 (also known as NFE2L2 or NRF2) is an important regulator of oxidative stress and also has anti-inflammatory effects. It is well-known to play a cytoprotective role in many tissues systemically, but its effects in the retina have been less clear. Our lab has shown that Nrf2 is expressed in the retina in multiple cell types. In order to determine the role of Nrf2, we are examining the effects of Nrf2 deficiency in mouse models of retinal vascular disease, including ischemia-reperfusion injury and diabetic retinopathy. We find that Nrf2 knockout mice (Nrf2 -/-) exhibit significant exacerbation of oxidative stress and inflammation in these models. In addition, Nrf2 knockout mice exhibit increase in pathological endpoints in these models, including retinal vascular permeability, neuronal impairment, and capillary degeneration. With systemic administration of a triterpenoid, we are able to activate Nrf2 in the retina and thereby ameliorate retinal damage. Together, this indicates that Nrf2 plays a protective role in the retina, and pharmacologic modulation of Nrf2 represents a potential therapeutic strategy for retinal vascular disease processes.

Biography

Elia J. Duh is Associate Professor of Ophthalmology at the Wilmer Eye Institute in the Johns Hopkins School of Medicine. He specializes in retinal vascular diseases such as diabetic retinopathy. He received his bachelor degree in molecular biophysics and biochemistry from Yale University. He subsequently earned his medical degree at Harvard Medical School. Duh completed his ophthalmology residency and fellowship in medical retina at the Wilmer Eye Institute.

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