

5<sup>th</sup> International Conference on

# Clinical & Experimental Ophthalmology

August 04-06, 2015 Valencia, Spain

## Endoplasmic reticulum homeostasis and inflammation in retinal müller cells

Joshua J Wang

State University of New York, USA

Increasing evidence suggests that endoplasmic reticulum (ER) stress and inflammation contributes to the pathogenesis of diabetic retinopathy (DR), a leading cause of blindness in working-age population. Muller glia cells which constitute the major glial component of the retina are considered major source of inflammatory factors in DR. In the present study, we investigated the role of ER stress in Muller cell inflammation using conditional knockout (Xbp1Muller<sup>-/-</sup>) mice that lack X-box binding protein 1 (XBP1) in Muller cells. Diabetes was induced by streptozotocin in male adult Xbp1Muller<sup>-/-</sup> mice and their littermate controls (Xbp1Muller<sup>+/+</sup>). Expression of retinal ER stress markers and inflammatory cytokines was examined by real-time qPCR, Western blotting and immunostaining. Retinal vascular permeability was measured by FITC-conjugated dextran method after 2 months of diabetes. Xbp1Muller<sup>-/-</sup> mice exhibit normal retinal development and retinal function determined by ERG. In diabetic mice, mRNA and protein levels of major inflammatory cytokines (VEGF and TNF- $\alpha$ ) were significantly increased in retinas of Xbp1Muller<sup>-/-</sup> mice compared to control mice. In addition, XBP1 deficiency resulted in greater ER stress in diabetic retinas as evidenced by enhanced expression of GRP78, p-eIF2 $\alpha$ , ATF4, CHOP, ATF6 and p-JNK. Consistently, retinal vascular permeability was significantly increased in diabetic Xbp1Muller<sup>-/-</sup> mice compared to the control. Increased ER stress and inflammatory gene expression was confirmed in retinal Muller cells isolated from Xbp1Muller<sup>-/-</sup> mice. Taken together, our results indicate that increased ER stress in Muller cell is an important contributing factor in inflammatory cytokine production and inflammation-related vascular damage in diabetic retinopathy (DR).

### Biography

Joshua J Wang holds MD and MS degrees and is currently an Assistant Professor in Department of Ophthalmology and Department of Medicine at University at Buffalo, the State University of New York. His research interest includes molecular mechanisms of diabetic vascular complications such as diabetic retinopathy, diabetic vascular disease, insulin resistance and diabetic nephropathy.

[jianxinw@buffalo.edu](mailto:jianxinw@buffalo.edu)

### Notes: