AB008. Cellular senescence and retinal angiogenesis

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Abstract: Pathological retinal neovascularization is the hallmark of primary blinding diseases across all age groups, yet surprisingly little is known about the causative factors. These diseases include diabetic retinopathy and retinopathy of prematurity where progressive decay of retinal vasculature yields zones of neural ischemia. These avascular zones and the hypoxic neurons and glia that reside in them are the source of pro-angiogenic factors that mediate destructive pre-retinal angiogenesis. Central neurons such as retinal ganglion cells (RGCs), which are directly apposed to degenerating vasculature in ischemic retinopathies, require stable metabolic supply for proper function. However, we unexpectedly found that RGCs are resilient to hypoxia/ischemia and a generally compromised metabolic supply and instead of degenerating, trigger protective mechanisms of cellular senescence. Paradoxically, while potentially favoring neuronal survival, the senescent state of RGCs is incompatible with vascular repair as they adopt a senescence-associated secretory phenotype (SASP) that provokes release of a secretome of inflammatory cytokines that drives paracrine senescence and further exacerbates pathological angiogenesis. The mechanisms that lead to retinal cellular senescence and dormancy as well as the therapeutic potential of targeting these pathways will be discussed.

Keywords: Cellular senescence; age-related macular degeneration

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