# AB043. Long-standing choroidal thinning in oxygen-induced retinopathy

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**Background:** Retinopathy of prematurity (ROP), the most common cause of blindness in premature infants, has long been associated with pathologic retinal vasculature. However, recent studies reveal choroidal involution in adolescent patients formerly afflicted with ROP. We have recently demonstrated that choroidal thinning occurs early in retinopathy and persists into adulthood. Unlike retinal vessels, the damaged choroidal vasculature in ROP is incapably to regenerate. Herein, we investigated the molecular mechanism implicated in the lack of choroidal repair in ischemic retinopathy.

**Methods:** The oxygen-induced retinopathy (OIR) model was used. Newborn Sprague-Dawley (albino) or Long-Evans rats (pigmented) rats were placed under oxygen concentration which cycles at 50%±1% or 10%±1% every 24 hours (hr) from postnatal day (P) 0 to P14. On P14, all rats were returned to room air. Western blotting and qPCR were used to quantify protein and RNA abundances, respectively. The Dual-Luciferase® Reporter Assay System was used to confirm microRNA (miRNA)-mRNA interaction.

**Results:** We detected a substantial oxidative stress in retinal pigment epithelium (RPE) and choroidal tissue, accompanied by a drastic reduction in insulin-like growth factor 1 receptor (IGF1R), a critical player in post-injury revascularization. The mechanism of decreasing IGF1R involves the over-activation of the p53 tumor suppressor that regulates miRNA let-7b, which subsequently silences Igf1r mRNA in the RPE/choroid complex of OIR subjects. Luciferase reporter assay confirmed that let-7b directly targets Igf1r mRNA at its 3' untranslated region (UTR). Indeed, silencing p53 resulted in a decreased let-7b expression, and re-established IGF1R abundance that promoted choroidal regeneration.

**Conclusions:** Together, this study sets forth new mechanistic notion by uncovering the novel p53/let-7b/IGF1R axis; timely intervention of this pathway facilitates healthy choroidal revascularization. Future investigations on anti-angiogenic miRNAs can better our understanding on degenerative choroidopathy, such as geographic atrophy.

**Keywords:** Choroid; retinopathy of prematurity (ROP); p53; microRNA

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