Role of inflammation pathways in retinal degeneration

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The retina is a layered tissue lining the interior part of the eye that enables the conversion of incoming light into a neural signal that is suitable for further processing in the visual cortex of the brain. Retinal degeneration, including age-related macular degeneration and retinitis pigmentosa (RP), is the most common form of neural degenerative disease in the world, is known as progressive neuronal cell death. Although several genetic and biochemical factors are associated with the pathogenesis of retinal degeneration, it has yet to be determined role of many different impairments such as inflammation on progression of degenerative phenotypes. Inflammation mediator amounts are evaluated under receptor interacting protein kinase (RIP presence and also RIP’s inhibitors by western blot in rd1 mice (retinitis pigmentosa), any other treated mice and age matched mice (normal control). In addition cell death has been detected by TUNEL assay. Genes was examined with the aid of real-time PCR. Immunocytochemistry was used to visualize changes in the retina for some of the genes-products. The results showed that necrosis is activated in the retina as well as apoptosis. The necroptotic microglia released various pro-inflammatory cytokines and chemokines, which orchestrated the retinal inflammation in the retinal degeneration rd1 mice, and also, in the acute retinal neural injury mice. Importantly, necroptosis blockade using necrostatin-1 could suppress microglia-mediated inflammation, rescue retinal degeneration or prevent neural injury in vivo. Toll like receptor (TLR4) deficiency ameliorated microglia necroptosis with decreased expression levels of machinery molecules RIP1 and RIP3, suggesting that TLR4 signaling was required in microglia necroptosis mediated inflammation. Also in apoptosis pathway genes encoded inflammasome components as well as inflammasome substrates along with their receptors, are upregulated. In fact, results point out to upregulated immune response accompanying disease progression in animal models of retinal degeneration and to potential benefits of early anti-inflammatory therapy.

References
