AB006. The co-receptor CD36 as a target in regulation of subretinal inflammation

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Abstract: Subretinal inflammation plays a critical role in retinal degenerative diseases. Although activated macrophages have been shown to play a key role in the progression of retinopathies and specifically in age-related macular degeneration, little is known about the mechanisms involved in the loss of photoreceptors leading to vision impairment. In our study on retinal damages induced by photo-oxidative stress, we have observed that CD36-deficient mice featured less subretinal macrophage accumulation with attenuated photoreceptor degeneration compared to wild-type (WT) mice. Treatment with CD36-selective azapeptide ligand (labelled MPE-001) as modulator of the inflammatory environment of the retina reduced subretinal macrophage/activated microglia accumulation with preservation of photoreceptor layers and function assessed by ERG in WT, in a CD36-dependent manner. The azapeptide modulated the transcriptome of subretinal macrophage/activated microglia by reducing pro-inflammatory markers. In isolated macrophages, the CD36-selective azapeptide induced dissociation of the CD36-TLR2/6 heterodimer complex (using FRET) altering the TLR2 signaling pathway, thus decreasing NF-KB activation and inflammasome activity. The azapeptide also incurred cytoprotection against photoreceptor apoptosis elicited by activated macrophages. These findings suggest that the azapeptide as ligand of co-receptor CD36 decreases the inflammatory response by modulating CD36-TLR2/6 complex signaling pathway in macrophages, and suggests its potential application in the treatment of retinal degenerative diseases.

Keywords: CD36; subretinal inflammation; age-related macular degeneration

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