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View Abstract

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Study Group: (none)

ABSTRACT

TITLE: Modulation of Retinal Inflammatory Macrophages by Sialic-Acid Coated Nanoparticles as Novel mechanism for Nonexudative AMD Treatment

ABSTRACT BODY:

Purpose: Age-related macular degeneration (AMD) is a progressive retinal inflammatory & degenerative disease from chronic innate immunity dysfunction, which causes irreversible blindness. Studies indicate a prominent role of inflammation in the pathogenesis of AMD mediated by macrophages/microglia into the inner layers of the retina. The purpose of this study is to assess the mechanism of action of a novel sialic-acid-coated nanoparticle (NP) construct in dampening the inflammatory response by macrophages by binding specifically to Sialic-acid-binding immunoglobulin-type lectins (Siglecs) on retina macrophages followed by the activation of inhibitory cellular domains and recruiting Src homology region 2 domain-containing Phosphatase-1(SHP1)

Methods: We performed cell-based assays using our proprietary asset in two cell types; THP-1 and PBMC-derived macrophages treated with our AVD-104 to characterize the biological activities. Cellular cytotoxicity of the AVD-104 was evaluated by MTT assay. The cytokines TNF-α, IL-6, IL-1β, IL-10, and VEGF released to the supernatant were measured 24 hours post-treatment by ELISA assay. Src homology region 2 domain-containing Phosphatase-1 (SHP-1) recruitment in macrophages was assessed by Immunoprecipitation (IP) by using anti-Siglec 7/9, followed by western blot analysis for SHP-1, intracellular phosphatase that modulate all key inflammatory and inflammasome pathways

Results: AVD-104 didn't show any significant decrease in cell viability at any of the 5.0 to 0.01 mg/mL dose ranges. AVD-104 showed significant decrease in the production of pro-inflammatory cytokines, TNF-α, IL-6 and IL-1β, VEGF by 1.3-1.4 folds ($p<0.05$), with an increased anti-inflammatory (resolution) cytokine IL-10 by 1.4-fold ($p<0.05$) in macrophages compared to controls. Lastly, LPS-activated macrophages treated with the NPs showed increased recruitment of SHP-1 compared to control

Conclusions: AVD-104, showed significant modulation of macrophage functions by reducing the production of pro-inflammatory cytokines and increasing anti-inflammatory cytokines that promote resolution and re-polarization to "healing" macrophages without any cytotoxicity. Our data supports the use of a novel

engineered NPs as a new potential approach for treatment of non-exudative AMD patients by inhibiting the pro-inflammatory macrophages via binding to Siglecs and SHP-1 recruitment

(No Image Selected)

DETAILS

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CURRENT REVIEWING CODE: 1370 AMD: Translational studies - RE
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TRAVEL GRANTS and AWARDS APPLICATIONS

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