ARVO 2023

View Abstract

CONTROL ID: 3876317

SUBMISSION ROLE: Abstract Submission

AUTHORS

AUTHORS (LAST NAME, FIRST NAME): Patel, Diyan[1]; Lad, Amit[1]; Callanan, David[1]; Hassan, Tarek[1]; Tolentino, Michael[1]; Scott, Christopher[1]; Genead, Mohamed[1]; Krishnan, Anitha[1]

INSTITUTIONS (ALL): 1. Opthalmics, Aviceda Therapeutics, Cambridge, MA, United States.

Commercial Relationships Disclosure: Diyan Patel: Commercial Relationship(s);Code E (Employment):Aviceda Therapeutics | Amit Lad: Commercial Relationship(s);Code E (Employment):Aviceda Therapeutics | David Callanan: Commercial Relationship(s);Code E (Employment):Aviceda Therapeutics | Tarek Hassan: Commercial Relationship(s);Code E (Employment):Aviceda Therapeutics | Michael Tolentino: Commercial Relationship(s);Code E (Employment):Aviceda Therapeutics;Code P (Patent):Aviceda Therapeutics | Christopher Scott: Commercial Relationship(s);Code E (Employment):Aviceda Therapeutics | Mohamed Genead: Commercial Relationship(s);Code P (Patent):Aviceda Therapeutics;Code E (Employment):Aviceda Therapeutics | Anitha Krishnan: Commercial Relationship(s);Code E (Employment):Aviceda Therapeutics;Code P (Patent):Aviceda Therapeutics

Study Group: (none)

ABSTRACT

TITLE: Targeting Self-Recognition Pattern Receptors on Retina Immune Cells with an Engineered Glycan-coated Nanoparticle as a Novel Therapy for Nonexudative AMD

ABSTRACT BODY:

Purpose: Age-related macular degeneration (AMD) is a progressive retinal inflammatory disease, which causes irreversible blindness. AVD-104, an optimized sialic-acid (glycan) coated nanoparticle (Aviceda Therapeutics, Cambridge, MA) was engineered to directly agonize the self-pattern recognition receptors on retina immune cells called Siglecs (sialic-acid binding immunoglobulin-like lectins). Siglecs are members of the Ig superfamily that recognize sialic-acid residues of glycoproteins. Siglecs 7,9, and 11 are expressed on monocytes, macrophages, and microglia which are key innate immune cells implicated in AMD pathobiology. Sialic-acid recognizes ITIMS (immunoreceptor tyrosine-based inhibitory motifs) bearing Sigelcs that modulate inflammation. Therefore, our therapeutic strategy was to show high binding affinity of our lead nanoparticles to Siglecs involved in dampened activity of inflammatory cells in AMD.

Methods: Binding affinity towards Siglecs 7, 9, and 11, was demonstrated using an ELISA-based assay to obtain a dose-response curve, and an Octet red system to measure the binding kinetics, in comparison to our blank nanoparticle. qRT-PCR and western blot were used to analyze the Siglec 7, 9, and 11 receptor expression on retina immune cells (macrophages & microglia) in human exudative and nonexudative AMD donors.

Results: AMD donors exhibited an increase in Siglecs 7, 9, and 11 gene expression by 90-, 64-, and 58-fold, respectively, compared with normal donors. AVD-104 elicited a dose-response binding to Siglec 7 (3-fold) and Siglec 9 (2.5-fold) compared to our blank nanoparticle. The dissociation constants (Kd) of AVD-104 to Siglecs 7, 9, and 11 indicated that 50% of the complex formed dissociates in 26.9 to 1.52 seconds, 24.5 to 6.21 seconds, and 69.3 to 58.3 seconds, respectively, in contrast to the blank nanoparticle which showed very unstable, weak, and non-specific binding.

Conclusions: Our glycan-coated nanoparticle (AVD-104) bound significantly to Siglecs 7, 9, and 11 on retina macrophages & microglia. These findings support our previous study results that the decreased immune responses treated with our nanoparticles, is due to binding to Siglecs on retina immune cells, and thereby activating the ITIMS. This study provides evidence that targeting Siglecs in patients with AMD is a novel

promising effective therapeutic strategy.

(No Image Selected)

DETAILS

PRESENTATION TYPE: Poster Only
CURRENT REVIEWING CODE: 1360 AMD: Preclinical studies - RC
CURRENT SECTION: Retinal Cell Biology
Clinical Trial Registration (Abstract): No
Other Registry Site (Abstract): (none)
Registration Number (Abstract): (none)
Date Trial was Registered (MM/DD/YYYY) (Abstract): (none)
Date Trial Began (MM/DD/YYYY) (Abstract): (none)
Grant Support (Abstract): No
Support Detail (Abstract): None

TRAVEL GRANTS and AWARDS APPLICATIONS

AWARDS: