ARVO 2023

View Abstract

CONTROL ID: 3885337

SUBMISSION ROLE: Abstract Submission

AUTHORS

AUTHORS (LAST NAME, FIRST NAME): Heisler-Taylor, Tyler[1]; Hamadmad, Sumaya[1]; Martini, Dena[1]; Jeng, Yushin[1]; Swindle-Reilly, Katelyn E.[2, 1]; Hill, Kasey[3]; Phelps, Mitch[4]; Cebulla, Colleen M.[1]

INSTITUTIONS (ALL): 1. Ophthalmology and Visual Sciences, The Ohio State University Wexner Medical Center, Columbus, OH, United States.
2. Biomedical Engineering, The Ohio State University, Columbus, OH, United States.
3. CCC - Sponsored Research, The Ohio State University Wexner Medical Center, Columbus, OH, United States.
4. College of Pharmacy, The Ohio State University Wexner Medical Center, Columbus, OH, United States.

Commercial Relationships Disclosure: Tyler Heisler-Taylor: Commercial Relationship: Code N (No Commercial Relationship) | Sumaya Hamadmad: Commercial Relationship: Code N (No Commercial Relationship) | Dena Martini: Commercial Relationship: Code N (No Commercial Relationship) | Yushin Jeng: Commercial Relationship: Code N (No Commercial Relationship) | Katelyn Swindle-Reilly: Commercial Relationship: Code N (No Commercial Relationship) | Kasey Hill: Commercial Relationship: Code N (No Commercial Relationship) | Mitch Phelps: Commercial Relationship: Code N (No Commercial Relationship) | Colleen Cebulla: Commercial Relationship: Code N (No Commercial Relationship)

Study Group: (none)

ABSTRACT

TITLE: MIF targeted neuroprotection through human serum albumin nanoparticle drug delivery

ABSTRACT BODY:

Purpose: Nanoparticles are becoming increasingly popular as a method to enhance drug delivery. We seek to utilize human serum albumin (HSA) and hyaluronic acid (HA) to develop nanoparticles to deliver a small molecule macrophage migration inhibitory factor (MIF) inhibitor ibudilast to treat N-methyl-D-aspartate (NMDA) excitotoxic retinal damage in chicks.

Methods: Blank and ibudilast loaded HSA nanoparticles with or without HA coating were produced and characterized with dynamic light scattering (DLS) and TEM. ARPE-19 cells were used to assess nanoparticle cellular distribution with confocal and toxicity with MTT and TUNEL assay. Under an IACUC approved protocol, *in vivo* experiments were performed in white leghorn chicks (n=39). NMDA (500 nmol) + nanoparticles (20ul total volume) were injected into the left eye while the right eye received nanoparticles and vehicle (sterile saline). Chicks were sacrificed at either one day post-injection (D1) or seven days post-injection (D7). Cell death was determined via TUNEL assay at D1 and nanoparticle distribution was assessed at D1 and D7.

Results: Nanoparticles closely matched the established literature in size, charge (zeta potential), and TEM morphology. Ibudilast concentration was measured as 0.0027mg/ml via HPLC mass spec. Nanoparticles were found to adhere to ARPE-19 cells. Both *in vitro* and *in vivo* experiments showed no cellular or retinal toxicity due to the nanoparticles. Two patterns were found in chick eyes; in undamaged eyes nanoparticles aggregated on the inner limiting membrane, while in damaged eyes they were found distributed across the retina. There was a 75% reduction in cell death due to ibudilast loaded HSA nanoparticles in NMDA damaged eyes compared to NMDA controls (740.8±323.9 cells/mm^2 vs. 2900.1±865.5 cells/mm^2, p = 0.0356).

Conclusions: This study shows preliminary data establishing the potential therapeutic benefits of nanoparticle-based drug delivery of MIF inhibition to treat excitotoxic damage. Additional experiments will be required to optimize the nanoparticle design and drug absorption.

(No Image Selected)

Layman Abstract (optional): Provide a 50-200 word description of your work that non-scientists can understand. Describe the big picture and the implications of your findings, not the study itself and the associated details.: Albumin nanoparticles delivering ibudilast were able to prevent cell death due to excitotoxic damage.

DETAILS

PRESENTATION TYPE: #1 Poster, #2 Paper

CURRENT REVIEWING CODE: 1890 Drug delivery: Iris ciliary body/intraocular fluids/posterior segment - PH

CURRENT SECTION: Physiology/Pharmacology

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): Yes

Support Detail (Abstract): VSRCP core grant P30EY032857 The Ohio Lions Eye Research Foundation (OLERF) This work was supported by The Assistant Secretary of Defense for Health Affairs endorsed by the Department of Defense, through the FY17 Vision Research Program, Technology/Therapeutic Development Award under Award No. W81XWH1810805. Opinions, interpretations, conclusions and recommendations are those of the author and are not necessarily endorsed by the Department of Defense. OSUMC Shared Resource Core Grant P30CA016058

TRAVEL GRANTS and AWARDS APPLICATIONS

AWARDS: