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ISER 2024
PROGRAM ABSTRACTS

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Abstract ID: 157

Intranasal biologic therapy for Optic Neuritis: Peclinical studies and implications for clinical translation

Section: Ocular Physiology, Pharmacology and Therapeutics

Kenneth Shindler[1]
[1]*University of Pennsylvania, Ophthalmology and Neurology, Philadelphia, United States*

Introduction
Retinal ganglion cell (RGC) loss occurs following acute inflammatory demyelinating optic neuritis and corresponds with permanent visual dysfunction that develops in 60% of patients. While steroids hasten visual recover, no treatment improves the final visual outcome after optic neuritis.

Objectives
Evaluate potential therapies to reduce RGC loss induced by optic neuritis.

Methods
Experimental autoimmune encephalomyelitis (EAE), a model of multiple sclerosis with high incidence of optic neuritis, is induced in C57BL6/J mice by immunization with myelin peptide. Visual function is assessed weekly by optokinetic responses, and RGC survival is assessed by Brn3a immunostaining 6-8 weeks after immunization.

Results
Daily intranasal treatment with a secretome therapy derived from amniotic progenitor cells, or with small molecule activators of the SIRT1 deacetylase, attenuate RGC loss in EAE mice. Treatments are effective when initiated before or at varying time points after disease onset.

Conclusion
Biologic and pharmacologic therapies can reduce RGC loss in EAE optic neuritis. The ability to assess new therapies delivered by novel routes of administration in an acute disease model that includes a measurable window of time to successfully initiate treatment holds important implications for future clinical translation.

Retinal function, diagnosis, and potential therapeutics in ocular and non-ocular diseases

Abstract ID: 316

The Phospholipase D2 (PLD2) as a potential therapeutic target for the treatment of uveitis

Section: Ocular Physiology, Pharmacology and Therapeutics

Paula Estefania Tenconi[1 2], Bo Man Ho[3], Lin Du[3], Vicente Bermudez[1 2], Wai Kit Chu[3], Melina Valeria Mateos[1 2]
[1]*Instituto de Investigaciones Bioquímicas de Bahía Blanca (INIBIBB)-Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET), Bahia Blanca, Argentina,* [2]*UNIVERSIDAD NACIONAL DEL SUR (UNS), BIOLOGIA, BIOQUIMICA Y FARMACIA (BByF), Bahia Blanca, Argentina,* [3]*The Chinese University of Hong Kong, Department of Ophthalmology and Visual Sciences, Hong Kong, China*

Introduction
Uveitis is a common, sight-threatening inflammatory ocular disease. If left untreated, uveitis can cause irreversible ocular tissue damage and eventually impaired vision and is estimated to account for ~25 % of blindness in developed countries. We previously demonstrated that the phospholipase D (PLD) pathway mediates the inflammatory response of retinal pigment epithelium (RPE)

cells induced by lipopolysaccharide (LPS).

Objectives
This work aims to study the effects of PLD2 inhibition in ocular inflammation using an endotoxin-induced uveitis (EIU) animal model.

Methods
Female Sprague Dawley rats (~250 g, 6–8 weeks old) were used and EIU was induced by the injection of 0.1 mL of 1 mg/kg LPS of Salmonella typhimurium solution into one footpad. After 2 or 4 h of LPS injection, (1, 4 or 8 mg/kg) of PLD2i (VU0285655-1) were injected intraperitoneally (IP) in 200 µl solution. 6 % DMSO was used as a PLD2i vehicle. PBS was injected instead of LPS in the negative control group of animals and dexamethasone was used as an anti-inflammatory positive control. Ethics approval for this study was obtained from the Animal Experimentation Ethics Committee of the CUHK. To evaluate clinical manifestations of EIU and the effects of PLD2i, rats were quantified using a score from 0 to 4 based in the presence of hyperemia, edema and synachesia, at baseline and 24 h after LPS injection. EIU were considered positive when clinical score >1 in at least one eye. To characterize the influxes of proteins into the aqueous humor (AH) in the different experimental conditions, protein concentrations were measured by the BCA Protein assay.

Results
After 24 h LPS injection, we observed ocular inflammation indicated by the presence of hyperemia and edema in the iris. The quantitative evaluation of clinical scoring showed a significant reduction by 30 % ($p < 0.0001$) in animals treated with 8 mg/kg PLD2i at after 2 h of LPS injection. The protein concentration in AH from LPS-treated rats was increased by 116 % ($p < 0.001$) compared to the negative control animals. Additionally, the elevated AH protein levels were significantly reduced by 33 % ($p < 0.01$) and by 49 % ($p < 0.0001$) in rats treated with 4 mg/kg or 8 mg/kg PLD2i, respectively. No statistically significance was observed between the 2 PLD2i treated groups and the negative control group.

Conclusion
Our study reports for first time the promising role of PLD2 inhibition as a potential early treatment for inflammatory ocular diseases.

Abstract ID: 472

Sphingosine-1-phosphate: Potential mediator in retinal proliferative disorders?

Section: Retinal Degeneration

MARIA VICTORIA SIMON[1 2 3], Camila Torlaschi[1 3], Gabriela Gutiérrez Jofré[1 2 3], Nora Rotstein[1 2]
[1]Instituto de Investigaciones Bioquímicas de Bahía Blanca, Lipids in retinal development, Bahía Blanca, Argentina, [2]Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET), Argentina, [3]Universidad Nacional del Sur (UNS), Argentina

Introduction
Fibrosis is a common feature of retina proliferative diseases, as diabetic retinopathy and proliferative vitreoretinopathy, which lead to vision loss. Dysregulation of cell attachment, migration and de-differentiation of Müller glial cells (MGC) and retinal pigment epithelium (RPE) cells, which provide structural and metabolic support in the retina contribute to the fibrotic process. Modulation of this process might hold the key to prevent the development of proliferative retinopaties. Sphingolipids such as sphingosine-1- phosphate (S1P), which regulates critical cellular functions, like proliferation, inflammation, migration, survival and differentiation, advance fibrosis in different tissues, but their role in the retina is still unclear.

Objectives
To study the role of S1P in the regulation of processes leading to fibrosis in the retina.

Methods
Primary MGC cultures and RPE cell line cultures (ARPE-19 and D407) were exposed to 5 uM S1P for 24 h. We incubated cell cultures with sphingosine kinase inhibitors SphKI2 and PF-543, to study the role of endogenous S1P, with W146, JTE-013 and BML241, specific S1P1, S1P2 and S1P3 antagonists, respectively, to analyze the involvement of S1P receptors . The ERK/MAPK