



LPS-INDUCED ACUTE OCULAR INFLAMMATION IN RABBITS AND MICE

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COMPARATIVE BIOSCIENCES, INC.
A TRANSLATIONAL APPROACH TO PRECLINICAL RESEARCH

COMPARATIVE BIOSCIENCES, INC.

Premier Preclinical Contract Research Organization

- **20 years** of experience
- Conveniently **located in the heart of Silicon Valley**, amidst many biotech companies
- **State of the art, purpose-built facility**
- Approximately **30 employees**
- **Highly experienced staff**
- **GLP, OECD, FDA, USDA, OLAW**
- **AAALAC Accreditation**



Scientific Overview

We specialize in developing a custom study plan in order to best meet your pre-clinical research needs and prepare for regulatory submission.

- GLP and Non-GLP
- Toxicology
- Efficacy
- Pharmacokinetics
- Pharmacology
- Oncology Studies
- In-house histopathology, immunohistochemistry & TCR



LPS-induced acute ocular inflammation in rabbits and mice

- CBI provides a validated model of endotoxin (LPS) induced acute ocular inflammation in rabbits and mice. In this model, LPS is injected into the vitreous.
- Acute inflammation develops and persists over about 3 days with a peak at about 24 hours.
- Responsive to dexamethasone treatment. The inflammation is characterized by neutrophilic and proteinic effusion into the aqueous humor and an acute ophthalmitis histopathologically.



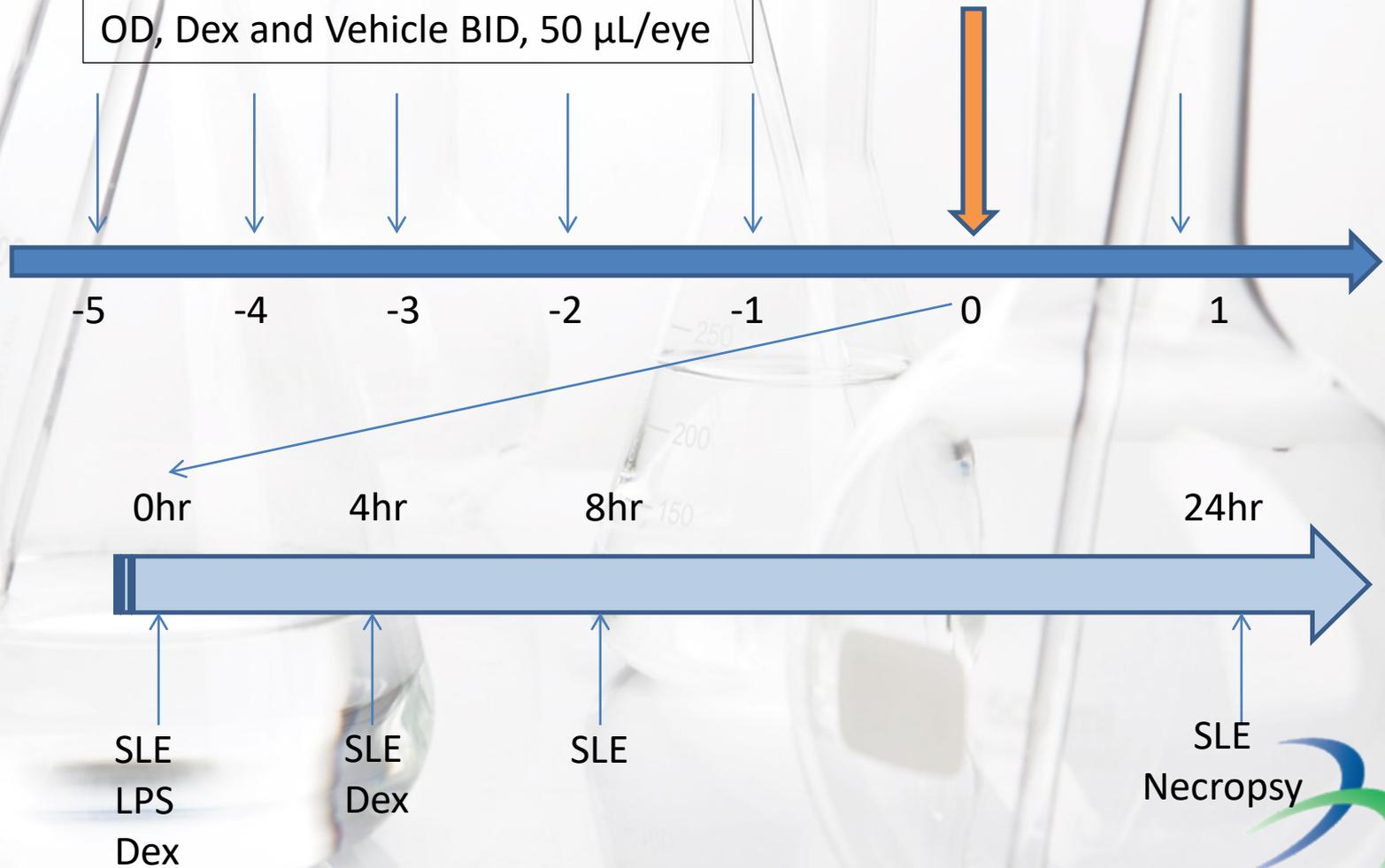
Study Design

- A typical study design includes:
 - Groups with at least 6 NZW rabbits or mice/group recommended
 - Vehicle, positive control and 2-3 test article doses or more
 - LPS (100 ng) is injected into 1 eye, other eye untreated
 - Test article administration either topically or systemically for up to 3 days
 - Topical dexamethasone is an appropriate positive control
 - Slit lamp and funduscopic examination
 - Histopathology on eye and adenexal structures



Typical Study Design

OD, Dex and Vehicle BID, 50 μ L/eye

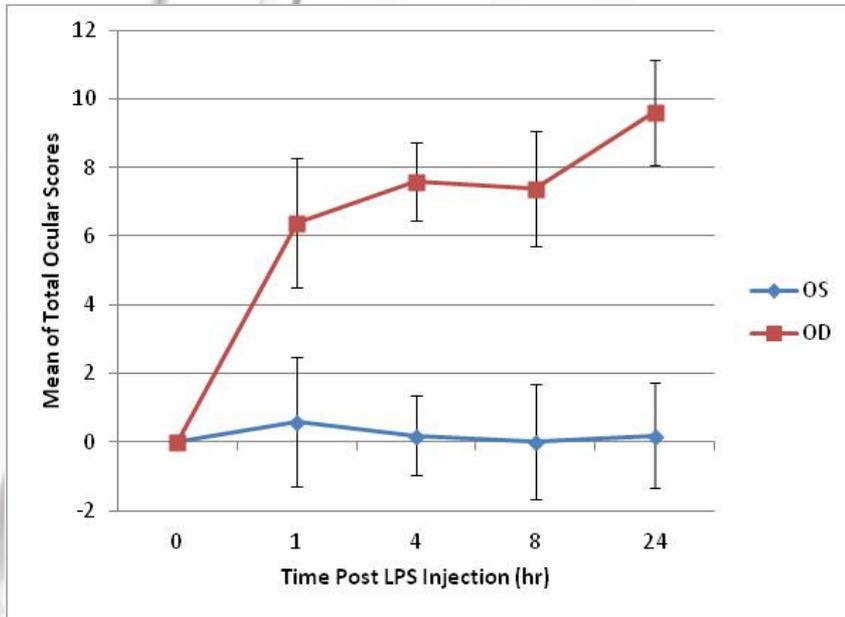


Results

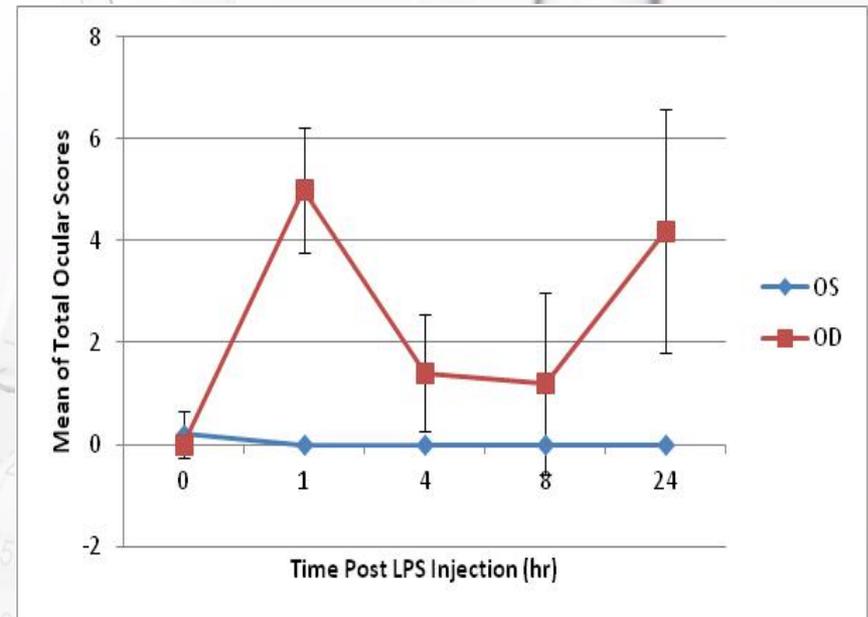
- A brisk acute inflammatory response occurs
- Inflammation located in iris, anterior segment, vitreous, and sometimes extending to retina and optic nerve
- Increases in McDonald-Shadduck scoring
- Increases in neutrophilic infiltration and protein in the anterior chamber
- Histology: Acute uveitis with cellular infiltration, and proteinic effusion



Ocular scores following LPS administration in rabbits



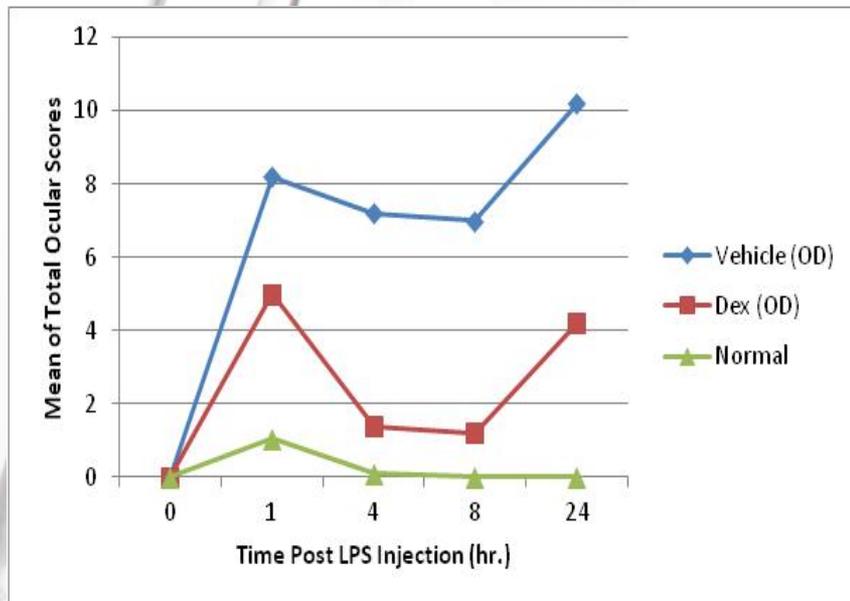
Vehicle-Treated Rabbits



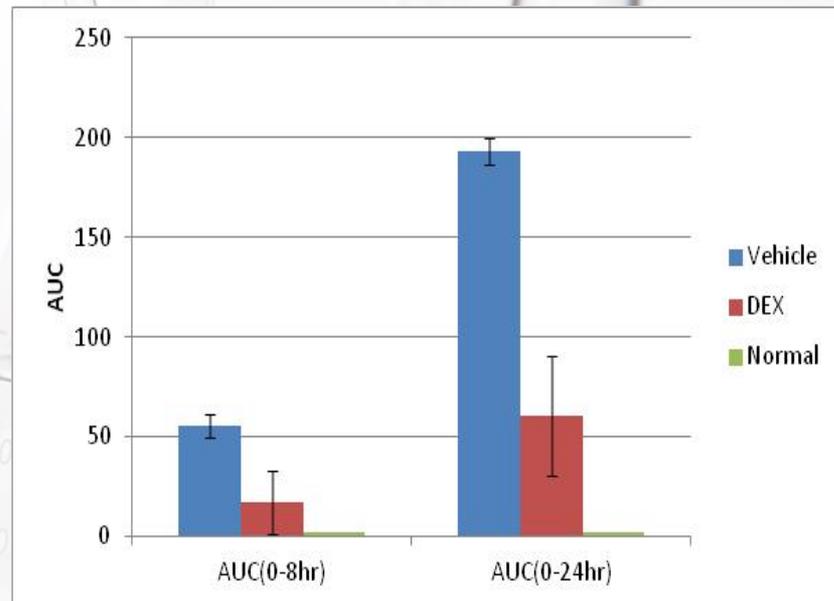
Dexamethasone-Treated Rabbits



Effect of dexamethasone on LPS-induced ocular inflammation in rabbits



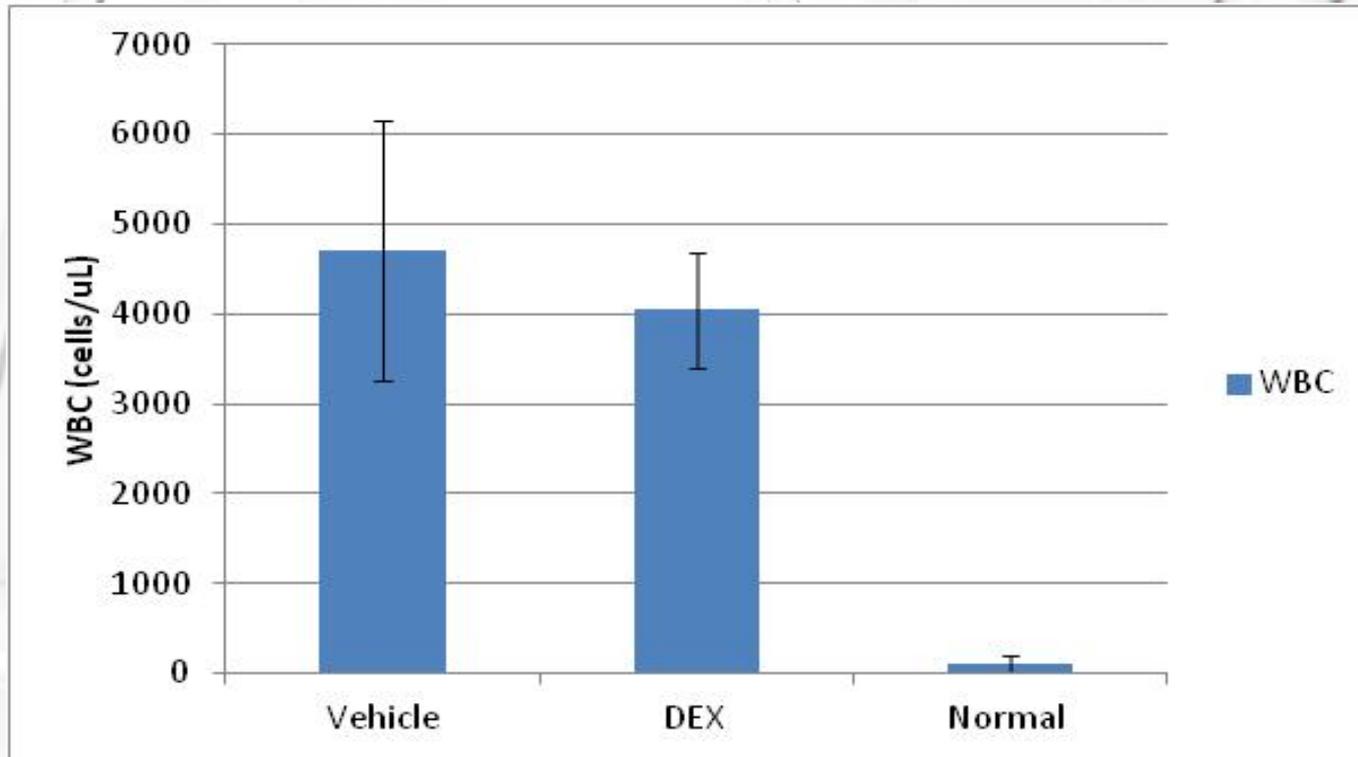
Total Scores Over 24 hr



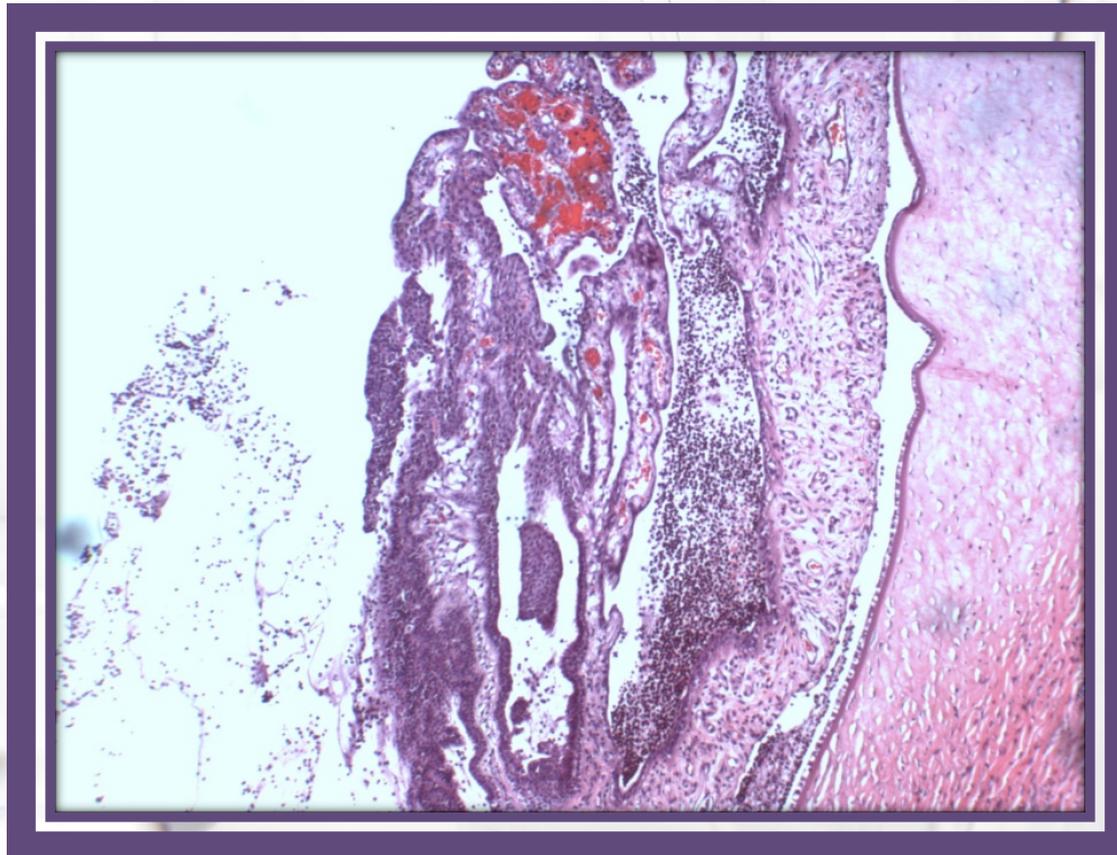
AUC calculated for 8 and 24 hr.



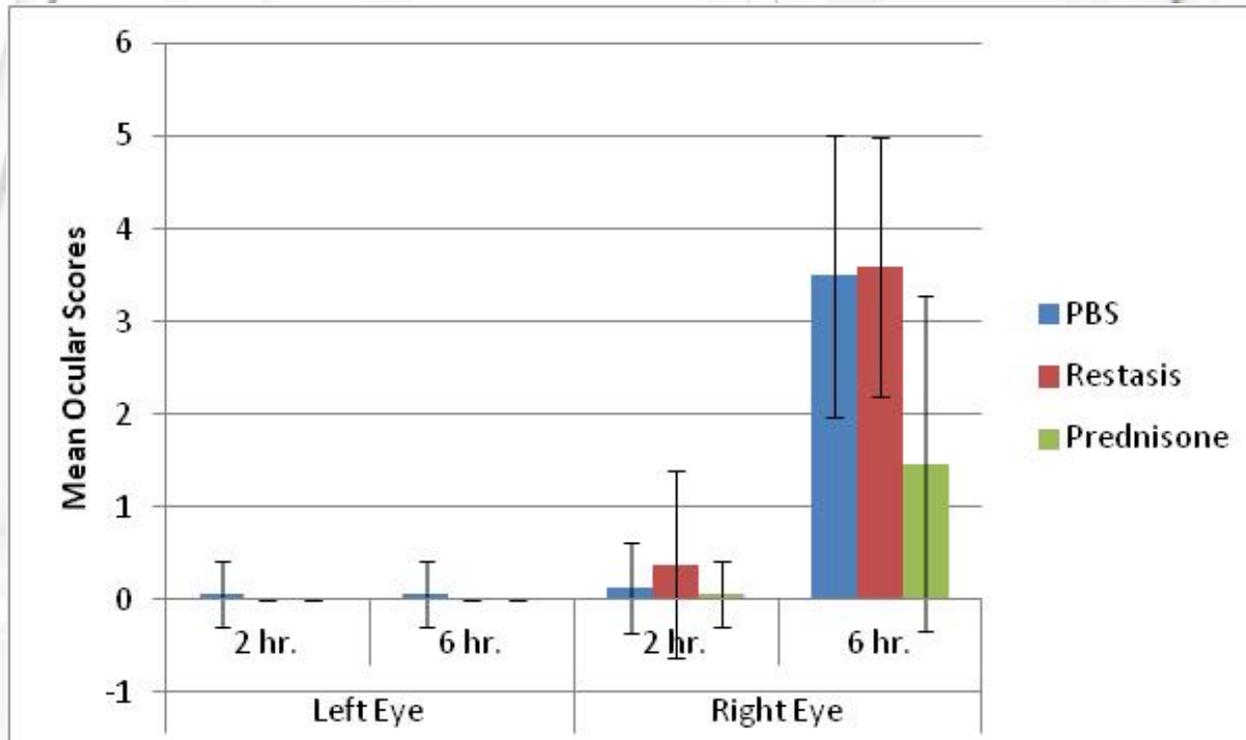
White blood cell counts in AH 24 hr after LPS administration in rabbits



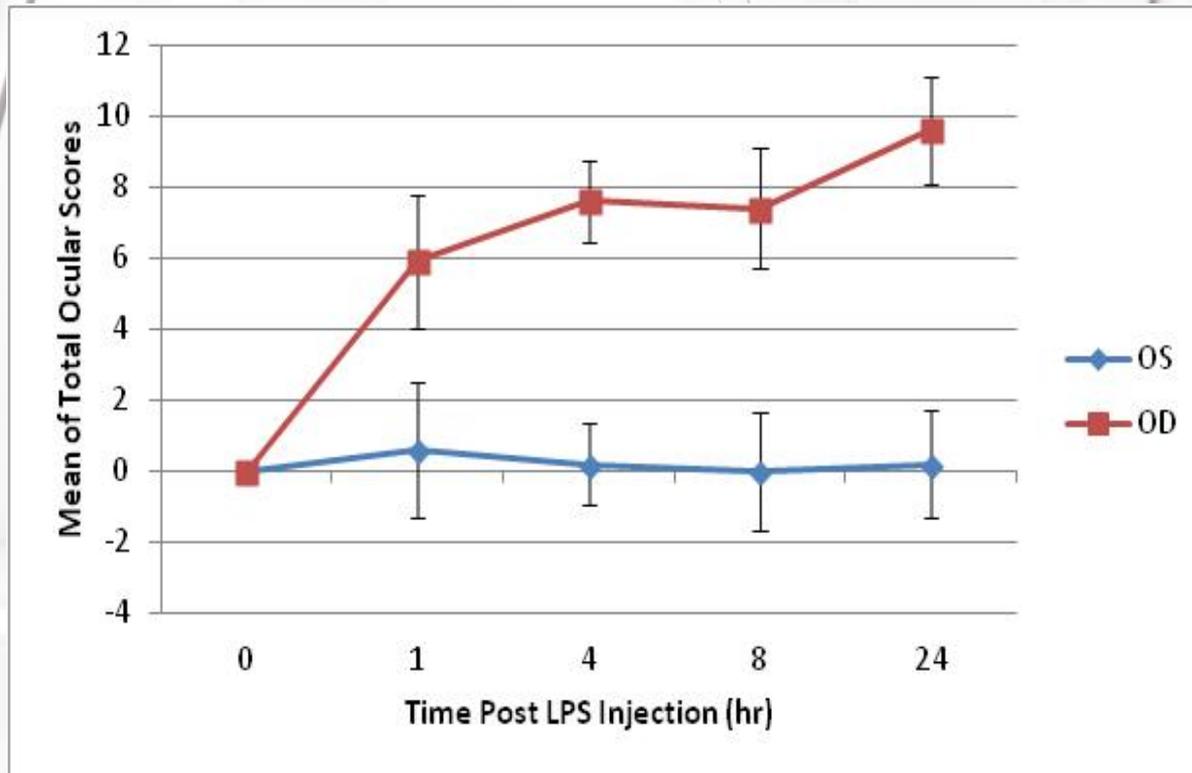
Severe inflammation of the anterior segment of rabbit eye administered LPS



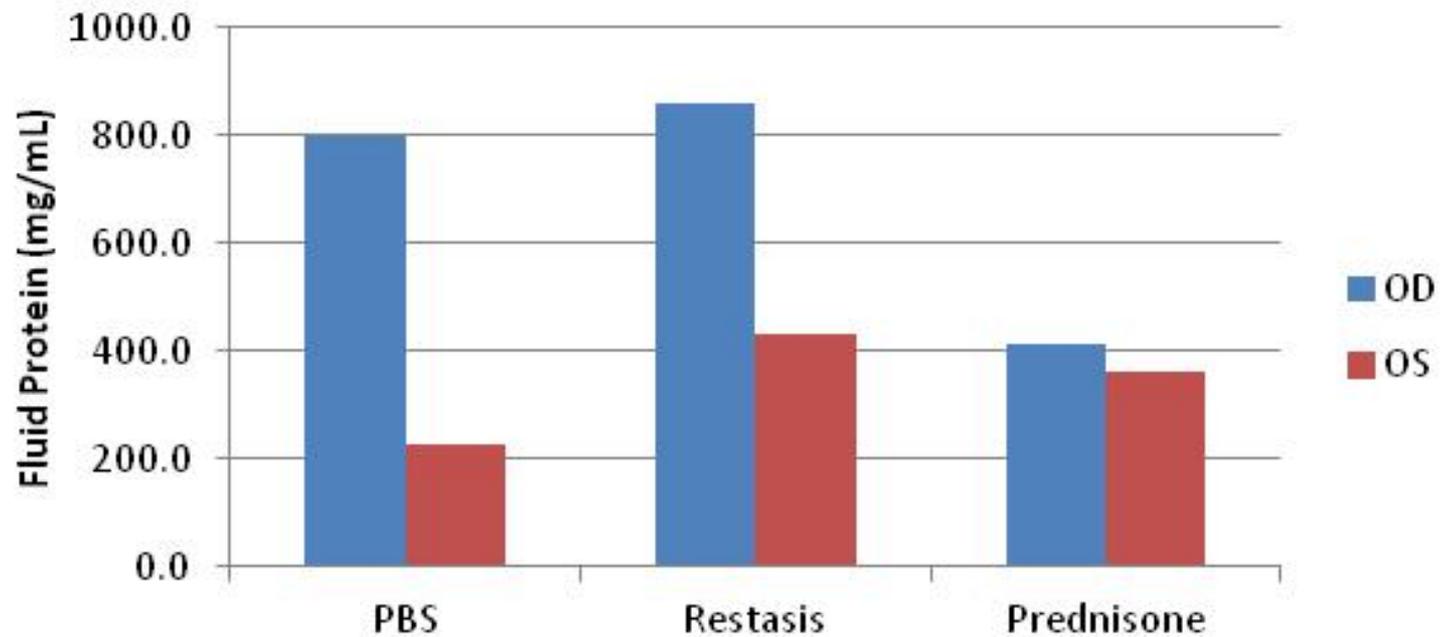
Mean McDonald-Shadduck ocular scores at 2 and 6 hr post intravitreal administration of LPS in mice



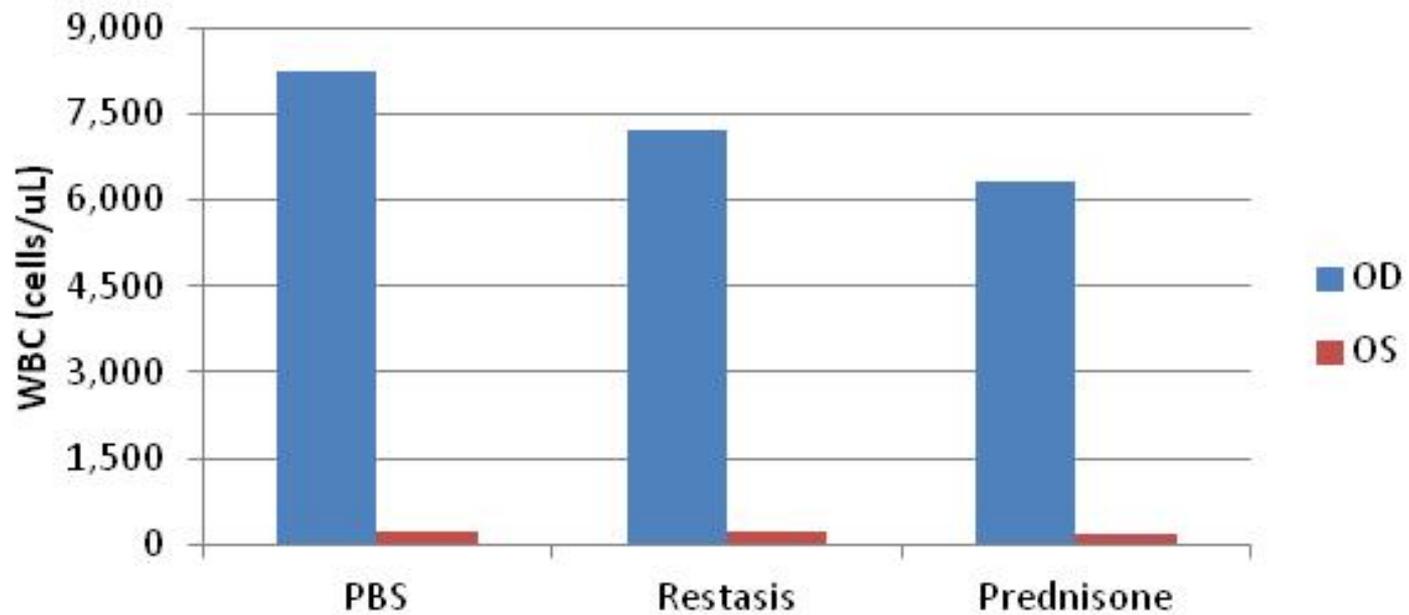
Mean McDonald-Shadduck scoring 0-24 hr post LPS administration in mice



AH Protein 6 hr. Post Intravitreal Injection of 1ng LPS



WBC in AH 6 hr. Post Intravitreal Injection of 1 ng LPS



Summary

- A single dose of intravitreal LPS induced a consistent brisk, 1-3 day ocular inflammation in mice and rabbits.
- Treatment with corticosteroids and Restasis produces significant inhibition of inflammation.
- This is a suitable model to assess acute neutrophilic ocular inflammation and to assess the effects of anti-inflammatory compounds in the eye.

