Abstract

Title: Determination of the Role of the Distal Outflow Pathway Tissue in Glucocorticoid-induced Ocular Hypertension

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Introduction
Prolonged application of glucocorticoids (GCs) induces ocular hypertension (OHT) and glaucoma. This increased intraocular pressure (IOP) is due to pathological changes in the trabecular meshwork (TM) outflow pathway tissues including impaired cell functions and extracellular matrix deposition. The changes and role of the TM in GC-induced OHT have been well studied. However, the role of the tissues distal to the TM (distal outflow tissues) is unclear. This study aims to further uncover the role of distal outflow tissue in GC-induced OHT using a novel perfusion organ culture (POC) model.

Methods
Huma corneal rims tissues were attached to 3D printed transparent perfusion plates using a combination of thin and thick glues. The artificial anterior chamber was perfused with DMEM-low glucose medium at 2ul/min to mimic aqueous humor production, and IOP was recorded using pressure transducers and a computerized system. To determine the role of distal tissue in GC-induced IOP changes, the TM tissue was carefully removed from both eyes, and one eye was treated with ethanol (EtOH) and the fellow eye with dexamethasone (DEX).

Results
The model was validated through a comparison of the IOP and TM stiffness of glue contaminated to non-contaminated corneal rims. The glue contaminated rim showed highly increased IOP and TM stiffness while the non-contaminated rim showed normal values. After validation, the TM was removed from paired corneal rims. One rim was treated with 100nM DEX and the fellow rim with 0.1% EtOH. The DEX treated rim showed increase in IOP while the EtOH control showed little change.

Conclusion
We created a novel corneal rim perfusion culture model for the study of GC-induced OHT. This model showed promising results of distal outflow involvement in glucocorticoid induced ocular hypertension. Further studies are needed to elucidate the role of distal outflow tissues in GC responsiveness in the eye.