ARVO 2012
Translational Research: Seeing the Possibilities

| | |
|---|---|
| **Program#/Poster#:** | 6016/D837 |
| **Abstract Title:** | **System to High-Throughput Drug Screening with Corneal Endothelial Survival Effect against ER and Oxidative Stress** |
| **Presentation Start/End Time:** | Thursday, May 10, 2012, 8:30 AM -10:15 AM |
| **Session Number:** | 523 |
| **Session Title:** | Corneal Endothelium |
| **Location:** | Hall B/C |
| **Reviewing Code:** | 150 corneal cell and molecular biology - CO |

**Author Block:** *Eun Chul Kim, Huan Meng, Mario Matthaei, Gustavo Bonfadini, Albert S. Jun.* Ophthalmology, Wilmer Eye Institute, Baltimore, MD.

**Keywords:** 481 cornea: endothelium, 424 antioxidants, 426 apoptosis/cell death

**Abstract Body:**

**Purpose:** To screen an FDA approved drug library to identify drugs which have a survival effect for corneal endothelial cells against ER and oxidative stress. Positive drugs will be confirmed in cultured corneal endothelial cells and an in vivo mouse model of FECD.

**Methods:** The bovine corneal endothelial cells was cultured into 96 wells plates in Dulbecco's modified Eagle's minimum essential medium (DMEM). An FDA-approved drug library (Enzo Life Science, Farmingdale, NY) consisting of 640 biologically active drugs at 10 mM starting concentration was treated at both a 1:100 dilution (100 μM) and a 1:500 dilution (20 μM) for 2 days. Duplicate cultures then were treated with thapsigargin (25μM) for one day or $H_2O_2$ (0.4mM) for 4 hours. At the end of incubation, cell viability will be determined using CellTiter-Glo® luminescent reagent (Promega, Madison, WI) and a scanning spectrophotometer. Compounds resulting in increased cell viability in both cell stress conditions and at both concentrations were compared to untreated controls.

**Results:** 55 drugs treated in 100 μM medium and 41 in 20 μM increased cell survival in H2O2 conditioning, and 2 in 100 μM and 8 in 20 μM in thapsigargin compared to untreated control. Nicergoline (20 μM $H_2O_2$ & 20 μM Thapsigargin), nimesulide (100 and 20 μM $H_2O_2$ & 20 μM Thapsigargin), and ergothioneine(20 μM $H_2O_2$ & 100 μM Thapsigargin) increased light intensities in both H2O2 and thapsigargin conditioning compared to untreated control.

**Conclusions:** Nicergoline, nimesulide, and ergothioneine have protective effects against both oxidative and ER stress in bovine corneal endothelial cells. These agents may have potential as survival factors for endothelial cells under oxidative and ER stress.