**2016 WOMEN’S HEALTH RESEARCH DAY**

**Title of Poster:** Estrogen Receptor α Protects Pancreatic β cells from Apoptosis by Maintaining Autophagy and Suppressing Endoplasmic Reticulum Stress
**Presenter:** Zhenqi Zhou **Institution:** Select an institution

[ ]  Faculty [ ]  Fellow [ ]  Resident [x]  Post-doc Research Fellow [ ]  Graduate Student [ ]  Medical Student [ ] Other

**Principal Investigator/Mentor:** Andrea Hevener   **Co-Investigators:**

**Thematic Poster Category:**  Select a Category

**Abstract**

**Estrogen Receptor α Protects Pancreatic β cells from Apoptosis by Maintaining Autophagy and Suppressing Endoplasmic Reticulum Stress**

Zhenqi Zhou, Vicent Ribas,Brian G. Drew, Timothy M. Moore, Amy H. Fluitt, Senta Georgia,

Sushil K. Mahata, Anil Bhushan, Andrea Hevener

David Geffen School of Medicine, Division of Endocrinology, Diabetes and Hypertension, University of California, Los Angeles, CA USA

**Abstract:**

17β-estradiol (E2) and estrogen receptor alpha (ERα) play an important role to protect pancreatic β-cell survival. However, the mechanisms underlying this protection remain unclear. Endoplasmic reticulum (ER) stress due to impaired autophagic flux can result in increased apoptosis causing β-cell depletion and impaired insulin secretion. We therefore hypothesized that ERα acts to preserve β-cell survival by regulating autophagy pathways and limiting ER stress. We found that ERα is critical for maintaining autophagy in isolated pancreatic islets and Min6 β-cells. ERα knockdown (KD) impaired autopahgic flux and elevated reactive oxygen species (ROS) production in Min6 β-cells. Imbalanced mitochondrial fission-fusion-mitophagy dynamics were also observed in KD cells and we hypothesize that this impairment in organelle remodeling contributed to chronic enlargement and a hyperfusion phenotype of the mitochondria. In addition, we observed marked endoplasmic reticulum stress signaling and dilation in Min6 β-cells with ERα KD, and this was accompanied by enhanced apoptosis susceptibility compared with ERα replete cells. We found that ERα activation by overexpression or agonist treatment (PPT) prevented endoplasmic reticulum stress induced by H2O2. Moreover, we found that ERα represses the expression of the stress marker Chop by direct promoter binding. Our findings suggest that ERα action is critical for the repression of endoplasmic reticulum stress and the maintenance of mitochondrial fission-fusion-mitophagy dynamics to preserve β-cell function and integrity.