Preventing Mitochondrial Dysfunction and Cell Death in the Lipid Exposed Cardiomyocyte

Amy Fernando, Matthew Martens, Dr. Joseph Gordon

Background

- Diabetic cardiomyopathy is a form of heart disease that occurs independently of other cardiac risk factors
- Lipotoxicity, an intracellular stressor caused by lipid accumulation, ultimately leads to diabetic cardiomyopathy and pathological remodelling of the heart.

Hypothesis

Roflumilast Prevents Mitochondrial Dysfunction and Cell Death in the Lipid Exposed Cardiomyocyte

Results

Roflumilast Prevents Lipid-Induced Mitochondrial Dysfunction and Cell Death

Fig 1. Lipotoxicity leads to diabetic cardiomyopathy and pathological remodelling of the heart

Fig 2. Assays for mitochondrial function and cell death. Quantification and epifluorescence of mitochondrial membrane potential in PVNC’s. Data are Mean ± SEM. (A) and (B) and quantification and epifluorescence of mitochondrial permeability transition pore opening in PVNC’s. Data are Mean ± SEM. (C) and (D). Data are Mean ± SEM. (A) and (B) indicate p<0.05 compared to control (CTL). (**) indicate p<0.05 compared to palmitate (PALM).

Fig 3. Assay for Nix Protein Expression. Quantification and immunofluorescence of Nix protein expression in PVNC’s. Data are Mean ± SEM. (*) indicate p<0.05 compared to control (CTL).

Fig 4. Assays for calcium homeostasis and mitochondrial permeability transition. Quantification and epifluorescence of mitochondrial calcium in PVNC’s. Data are Mean ± SEM. (A) and (B). Data are Mean ± SEM. (C) and (D). Data are Mean ± SEM. (C) and (D) indicate p<0.05 compared to control (CTL). (**) indicate p<0.05 compared to palmitate (PALM).

Fig 5. Assay for mitochondrial superoxide production. Quantification and epifluorescence of mitochondrial superoxide in PVNC’s. Data are Mean ± SEM. (*) indicate p<0.05 compared to control (CTL). (**) indicate p<0.05 compared to palmitate (PALM).

Proposed Mechanism

1. Roflumilast prevents lipid-induced mitochondrial dysfunction and cell death in cultured cardiomyocytes
2. Roflumilast likely follows a specific molecular mechanism

Conclusions

Roflumilast could treat and/or prevent lipid-induced mitochondrial dysfunction and cell death in the heart

Contact Information/Acknowledgements

Amy Fernando
BS (Hons) Student
Faculty of Science, University of Manitoba
fernando4@myumanitoba.ca

Acknowledging the University of Manitoba Undergraduate Research Award (URA), The Diabetes Research Envisioned and Accomplished in Manitoba (DREAM) Theme of the Children’s Hospital Research Institute of Manitoba, and the tremendous assistance and mentorship of the Gordon Laboratory.