The Effects of Palmitate and Milrinone on Cardiomyocytes
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Background
• Diabetes affected approximately 460 million people globally in 2019, with 90% of these cases being attributed to Type 2 Diabetes (T2D).
• T2D is a type of diabetes that results from insulin resistance in target tissues.
• Lipotoxicity is a form of cellular stress involving lipid metabolite accumulation and is implicated with the development of insulin resistance and mitochondrial dysfunction.
• Lipid metabolite accumulation has also been implicated with the expression of certain cellular proteins in the cell.
• Previous projects in our lab have demonstrated an increase in the cell death protein Nix during a high-fat diet (HFD) and that a Nix-dependent pathway was involved with mitochondrial dysfunction and subsequent cardiac dysfunction.

Hypothesis: Milrinone can inhibit the effects of lipotoxicity on cardiomyocytes.

Materials and Methods
Models:
• H9C2 rat cardiomyocytes were the cell lines used for all experiments.

Treatments:
• 200 µM Palmitate – treatment overnight to induce lipotoxicity.
• 10 µM Milrinone – treatment overnight to alleviate effects of palmitate.

Live Cell Imaging:
• Following treatments, cells were stained with MitoTracker, LysoTracker, Rhodamine-AM, and Ethidium homodimer to evaluate the physiological activities in the cardiomyocyte.

Results

Conclusions
• Lipid exposure is concurrent with mitochondrial dysfunction in the cardiomyocytes.
• Minimal rescuing capacity was observed after a 24-hour exposure co-treatment of a lipid metabolite and milrinone.
• Milrinone demonstrated minimal toxicity to the cardiomyocytes over a 24-hour exposure period at 10 µM.
• Mitochondrial morphological change is observed in lipid-exposed cardiomyocytes.

Future Directions
• Western blot to evaluate Nix expression.
• Evaluate the effects of a ppretreatment with milrinone followed by the addition palmitate.
• Observe the time-dependent effects of Milrinone on cardiomyocytes.
• Comparison of Roflumilast vs Milrinone effects.
• Conduct similar experiments on primary rat or human cardiomyocytes.
• Rhod-2 experiment to determine the presence of calcium release.

Acknowledgements