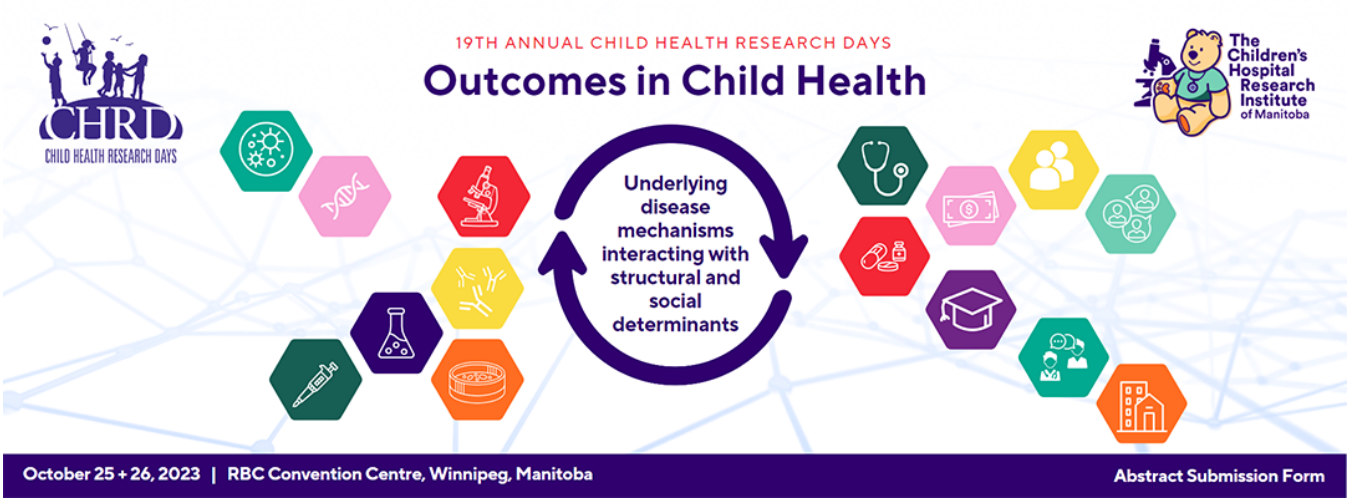

CHRD 2023: Abstract Submission Form

Submitter Name
Michael Byun

Presenter Name
Michael Byun

Presenter Status
Masters Student

Research Category
Basic Science

Role in the project
Design
Perform Experiments
Analyze Data
Write Abstract

Title
Omega-3 fatty acids modify monocyte glucose metabolism through mitochondrial bioenergetic rewiring

Background
Background: Chronic inflammation is a driving factor in diseases like obesity and type 2 diabetes. Enhanced glucose metabolism, including via oxidative phosphorylation, may contribute to heightened immune activation. A recent clinical trial showed that supplementation with the omega-3 fatty acid α-linolenic acid (ALA) reduced oxidative phosphorylation rates in circulating monocytes. However, the mechanism remains unknown.

Objective
Therefore, our objective was to replicate the findings in a cell culture model to explore the molecular mechanism.

Methods
Methods: THP-1 monocytes were treated for 48h with 10-40 μM of fatty acid. The Seahorse XFe24 system was used to approximate catabolic rates (including oxidative phosphorylation and glycolysis) in the presence of either glucose or palmitic acid as metabolic substrate. We also examined mitochondrial reactive oxygen species (ROS) levels using the fluorescent indicator mitoSOX measured by flow cytometry. Finally, gene expression was assessed by reverse-transcription quantitative polymerase chain reaction (RT-qPCR).

Results

Results: ALA significantly reduced mitochondrial ATP production by ~26% and increased glycolytic ATP production by ~50% in the presence of glucose. Unexpectedly, another omega-3 fatty acid, docosahexaenoic acid (DHA) had similar effects. There was no apparent change in fatty acid catabolism. ALA had no effect on ROS while DHA enhanced ROS by ~30%. We identified pyruvate dehydrogenase kinase 4 (PDK4), an enzyme that inhibits the conversion of pyruvate to acetyl-CoA, as a possible mechanistic candidate. It was significantly upregulated by ALA and DHA by 4- and 13-fold, respectively.

Conclusion
Conclusion: Overall, ALA and DHA both upregulated PDK4 and dampened oxidative phosphorylation rates in our cell culture model. This was accompanied by enhanced ROS in the case of DHA, a sign of mitochondrial stress. This is an important step towards understanding how omega-3 fatty acids may be useful as part of an intervention strategy to prevent or treat chronic metabolic diseases relevant to children and youth.

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