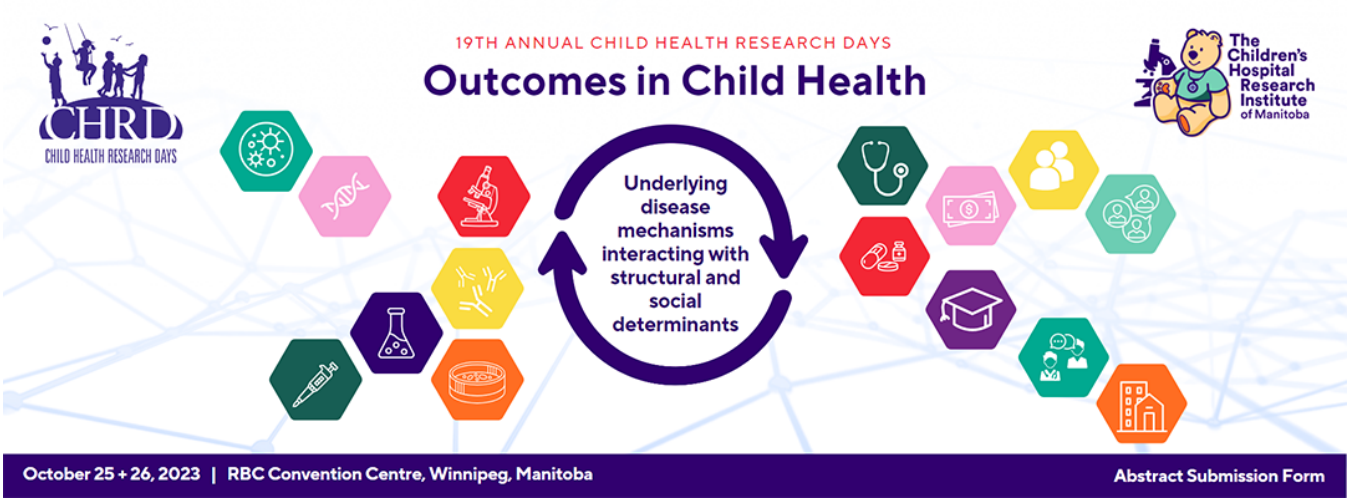

CHRD 2023: Abstract Submission Form

Submitter Name
Doris Goubran

Presenter Name
Doris Goubran

Presenter Status
Undergraduate Students

Research Category
Basic Science

Role in the project
Perform Experiments
Analyze Data
Write Abstract

Title
Does the HNF1G319S variant and diet interact to influence kidney structure and function?

Background
Manitoba has one of the highest incidences of youth Type 2 Diabetes (T2D) worldwide at over 12.5 cases/100,000 children/year. Approximately 90% of these youth are Indigenous with over one third from the Anishiniwuk community. Youth with T2D have worse renal survival than youth with Type 1 Diabetes. A private variant in the HNF1 gene (G319S) has been found in 40% of youth with T2D in Manitoba. Experiments demonstrated this variant has protective metabolic effects in mice fed a diet resembling a traditional Anishininew diet (high fat/low carbohydrate; HF/LC); however, mice with the same variant on a high fat/high carbohydrate (HF/HC) modern diet display greater metabolic dysfunction.

Objective
Since diet and the variant can interact to have detrimental or protective effects on metabolism, we hypothesized that HNF1G319S and diet interact to influence kidney structure and function.

Methods
Male and female GG, GS, and SS mice were fed either a low fat/high carbohydrate (chow), HF/LC, or HF/HC diet. Kidneys were paraffin embedded stained with Periodic Acid–Schiff. Twenty glomeruli were imagined per sample. The cross-sectional glomerular and mesangial area were measured. Ordinary one-way ANOVAs Dunnett's Multiple Comparisons Tests were used to compare groups.

Results
The HF/HC diet drove hypertrophy in all genotypes but to a lesser degree in S-allele mice. The HF/LC diet

also drove hypertrophy in all genotypes but mice with the S-allele had a greater hypertrophy compared to the wild type. Glomerular hypertrophy can be a compensatory mechanism during metabolic stress. Our results suggest that S-allele-expressing mice have reduced compensatory response to the HF/HC modern diet while S-allele-expressing mice on the HF/LC diet maintain the ability to adapt.

Conclusion
This supports our hypothesis that the variant may have protective effects and promote metabolic resiliency on a traditional high fat diet.

Table/Figure File
Doris Goubran Figure 1 HNF1a and diet interact to influence kidney structure.pdf

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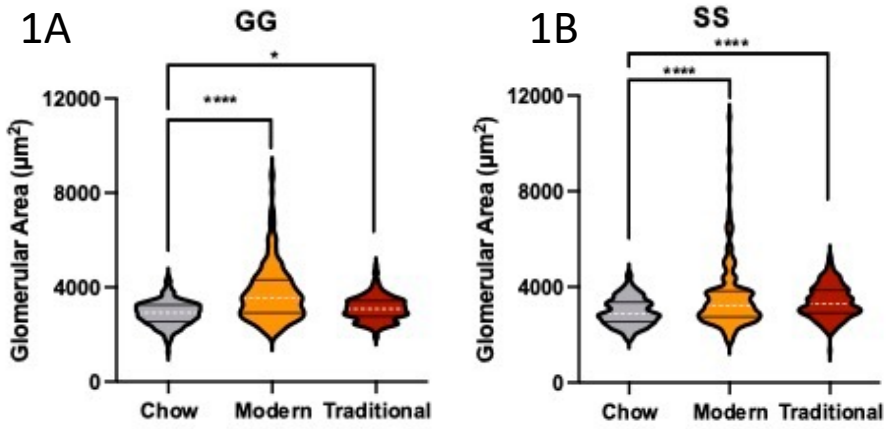

Figure 1 A) Glomerular area in mice with the GG genotype on different diets. Both the modern and traditional diets show glomerular hypertrophy compared to the chow diet.
B) Glomerular area in mice with the SS genotype on different diets. Again, both diets show hypertrophy compared to the chow diet, but those on the modern diet have a lesser degree of hypertrophy than GG mice on the modern diet in figure 1A. However, SS mice on the traditional diet maintain this ability to adapt via hypertrophy.