Maternal RESV Supplementation and the Effects on Mitochondrial Metabolism and Calcium Transport

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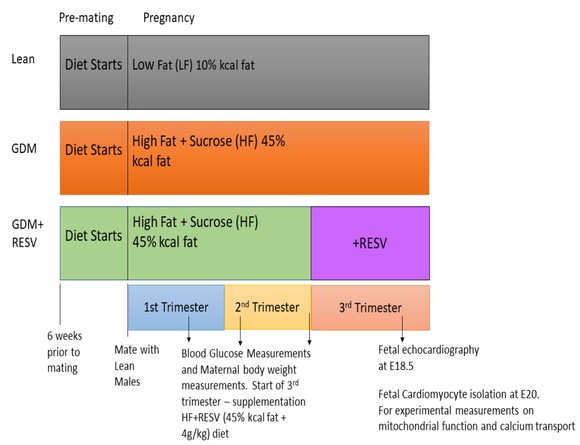
Introduction

- Gestational Diabetes Mellitus (GDM) is a metabolic condition observed in the second and third trimester of pregnancy.
- GDM is characterized by excess gestation weight gain, insulin resistance, hyperglycemia, and glucose intolerance.
- GDM exposure has a higher risk of cardiovascular disease in offspring
- Common treatments include dietary intervention and insulin therapy.
- Glucose-lowering medications such as metformin and glyburide can have negative impact on maternal and child health
- Resveratrol (RESV) is a natural health product from fruits and vegetables that shows promise in potential GDM treatment

Hypothesis

- Maternal RESV supplementation will attenuate GDM-induced mitochondrial dysfunction in fetal cardiomyocytes

Experimental Design



Animal Model:

- A subgroup of GDM dams was switched with a diet supplemented with RESV (45% fat + 4g/kg RESV)

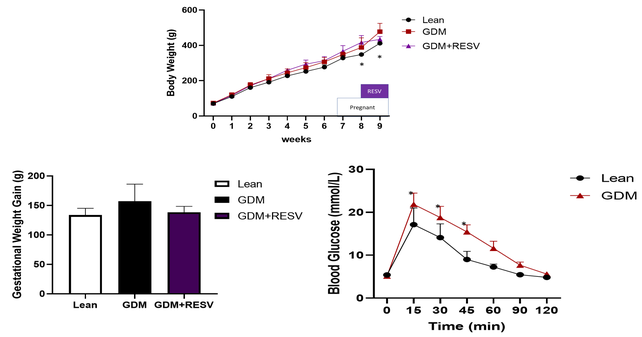
Cardiomyocyte Isolations

- Fetal cardiomyocytes were isolated at e.20 for experimental measurements of mitochondrial function.

Echocardiography

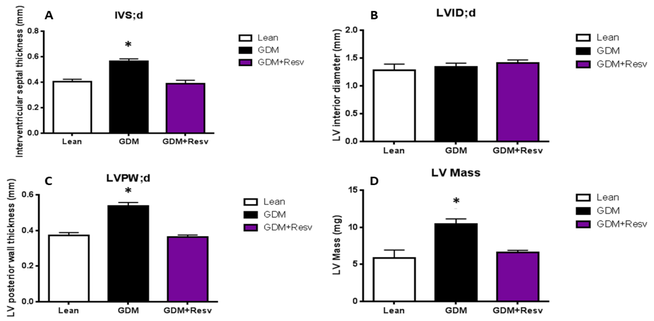
- Fetal echocardiography scans were taken at e.18.5 to measure cardiac structure and function

Maternal RESV Supplementation Improved Maternal Glucose Tolerance



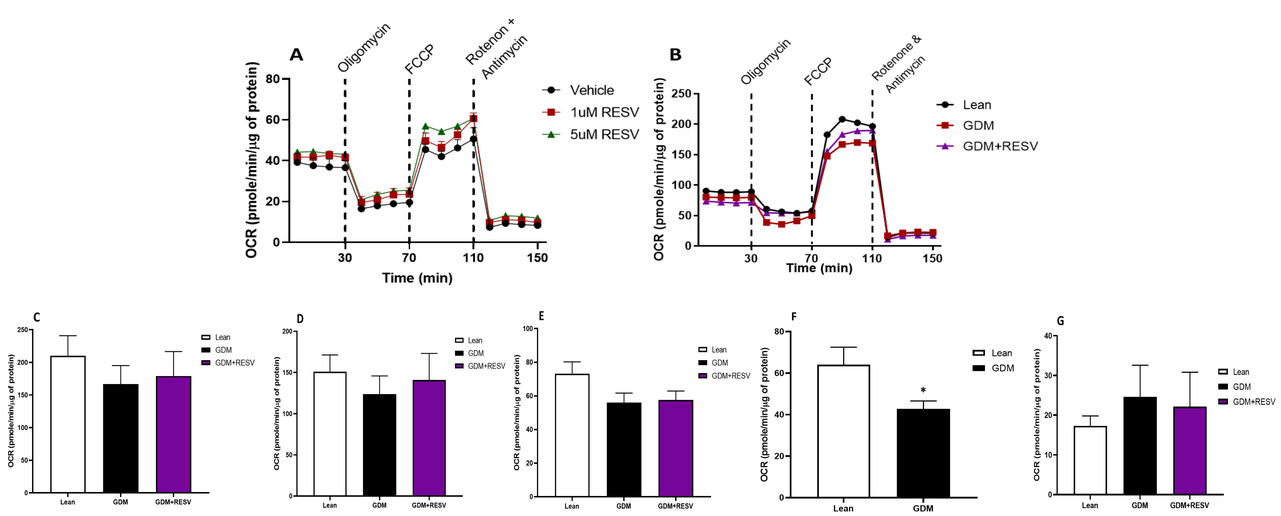
- A) Maternal body weight gain during pre-pregnancy and gestational pregnancy, B) Gestational weight gain in lean, GDM, and GDM + RESV dams, C) pre-pregnancy maternal glucose tolerance test in lean and GDM dams. P-values, where applicable, represent significance (<0.05) after Two-Way ANOVA, Mixed-effect analysis, or Welch's T-test. *p<0.05 vs Lean. Data present as means +/- S.E.M.

RESV Attenuated Cardiac Hypertrophy in GDM-Induced Fetal Offspring



- Echocardiography data of fetal hearts (n=5). A) Intraventricular septal thickness (IVS). B) Left ventricular interior diameter (LVID). C) Left Ventricular posterior wall thickness. D) Left Ventricular (LV) mass. p- values represent significance after One-Way ANOVA with Bonferroni post-hoc test. *p<0.05 vs Lean. Data presented as mean +/- S.E.M.

Maternal RESV Supplementation Improved Mitochondrial Function in Primary Fetal Cardiomyocytes



- A) Mitochondrial Stress test performed on isolated primary (e.20) cardiomyocytes under 6-hour RESV treatment. B) mitochondrial Stress on isolated neonatal cardiomyocytes (e.20) of Lean, GDM, and GDM + RESV dams, C) Mitochondrial maximal respiratory capacity, D) mitochondrial spare respiratory capacity, E) Mitochondrial Basal Respiration F) ATP production. G) Proton leak. Readings normalized to protein concentration (µg). p-values represent significance (<0.05) after One-Way ANOVA with multiple comparisons or Welsh's two-tailed t-test were applicable. *p<0.05 vs Lean. Data represented as mean +/- S.E.M. (n=1 litter, n=4 technical replicates)

Conclusion

- When RESV was applied to the maternal diet, Gestation weight gain was attenuated among Maternal GDM parents.
- RESV attenuated cardiac hypertrophy induced by GDM in neonatal offspring's
- RESV improved mitochondrial oxygen consumption in GDM-exposed offspring
- RESV supplementation attenuated overall mitochondrial function in GDM-induced neonatal offsprings

Future Directions

- Explore potential molecular targets and pathways involved in improving mitochondrial function in GDM + RESV offsprings
- Highlight potential molecular pathways involved in protecting against GDM-induced cardiac hypertrophy
- Further explore the role of RESV on cardiac function through pathways involved in calcium transport necessary for cardiac contraction
- Explore other mitochondrial pathways involved in energy metabolism that may be affected by RESV supplementation

Significance

- Increase the understanding of how RESV affects the cardiac health in offspring exposed to GDM
- Characterize the effects of RESV supplementation on offspring mitochondrial function
- Highlight the potential of RESV as a novel GDM treatment

Acknowledgments

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