P-0463 – Fecal Transplant From Resveratrol-fed Mice to Obese Mice Improves Glucose Homeostasis and Lowers Intestinal Inflammation

Ty T. Kim¹, Miranda M. Sung¹, Carrie-Lynn M. Soltys¹, Karen Madsen², and Jason R. B. Dyck¹

¹Cardiovascular Research Centre, Department of Pediatrics, Alberta Diabetes Institute, Faculty of Medicine and Dentistry, University of Alberta, Edmonton, AB, Canada. ²Division of Gastroenterology, Department of Medicine, University of Alberta, Edmonton, AB, Canada.

Background

Oral administration of resveratrol (resv) is able to improve glucose homeostasis in obese individuals. Herein we show that fecal microbiome transplants (FMT) from resv-fed donor mice to obese mice is able to improve glucose homeostasis within 11 days of the first transplant. Moreover, we show that an intact bacterial population is not necessary to impart the beneficial effects of a resv-FMT. Our findings demonstrate that non-living bacterial, metabolites, or other components within the feces of resv-fed mice is sufficient to reduce intestinal inflammation and these anti-inflammatory effects of FMTs may be an integral mechanism by which resv improves glucose homeostasis in obesity.

Aims

1. Determine if oral supplementation of resv is sufficient to rescue impaired glucose tolerance in obese mice
2. Determine whether live bacteria are required for the beneficial effects of fecal microbiome transplants (FMTs)
3. Elucidate the mechanisms by which FMTs improves glucose homeostasis.

Models & Methods

Fecal samples from mice fed a Chow ($\pm 0.4\%$ resveratrol) diet for 8 weeks were used for fecal microbiota transfer (FMT) in mice subjected to a HFHS diet for 6 weeks.

Results

Result 1. 2-week oral resv supplementation does not improve glucose homeostasis in obese mice.

Result 2. FMTs from resv-fed donor mice are sufficient to improve glucose homeostasis in obese mice.

Result 3. FMTs from resv-fed donor mice lower inflammatory cytokine levels in colon of obese mice.

Result 4. Resv-FMTs using heat-killed slurry is sufficient to improve glucose homeostasis in obese mice.

Result 5. Heat-killed Resv-FMTs indicate similar levels of inflammatory cytokine in the colon of obese mice in comparison to recipients of Resv-FMTs.

Conclusion

- Transplantation of fecal material from resveratrol-fed donor mice to obese mice is sufficient to improve glucose homeostasis during obesity-induced insulin resistance.
- Resveratrol-mediated changes in the gut microbiota play an important role in the beneficial effects of resveratrol.
- Heat-killed resveratrol FMTs improve glucose homeostasis in obese mice, demonstrating that non-living bacterial, metabolites, or other components within the feces of resveratrol-fed mice is responsible for the beneficial actions of resveratrol FMTs.
- Anti-inflammatory effects of resveratrol-FMTs may be an integral mechanism by which resveratrol improves glucose homeostasis in obesity.