

JOINT EVENT

10th International Conference on **Childhood Obesity and Nutrition**
&
2nd International Conference on **Metabolic and Bariatric Surgery**

June 12-13, 2017 Rome, Italy

Gastric bypass surgery with exercise alters plasma microRNAs that predict improvements in cardiometabolic riskAttila A Seyhan^{1,2,3}, Yury O Nunez Lopez¹, Paul M Coen^{1,2} and Bret Goodpaster^{1,2}¹Florida Hospital, USA²Sanford Burnham Prebys Medical Discovery Institute, USA³Massachusetts Institute of Technology, USA

Statement of the Problem: Roux-en-Y gastric bypass (RYGB) surgery improves insulin sensitivity (SI) and β -cell function in obese non-diabetic subjects. Exercise also improves SI and may be an effective adjunct therapy to RYGB surgery. However, the mechanisms by which exercise or weight loss improve peripheral SI after RYGB surgery are unclear. We hypothesized that microRNAs (miRNAs) mediate at least some of the regulatory processes driving such mechanisms. Consequently, this work aimed at profiling plasma miRNAs in participants of the Physical Activity Following Surgery Induced Weight Loss study (NCT00692367), to assess whether miRNA levels track with improvements in SI and cardiometabolic risk factors.

Methodology & Theoretical Orientation: Ninety-four (94) miRNAs implicated in metabolism were profiled in plasma samples from 22 severely obese subjects who were recruited 1-3 months after RYGB surgery and followed for 6 months of RYGB surgery-induced weight loss with (exercise program (EX), N=11) or without (CON, N=11) an exercise training intervention. The subjects were selected, considering a priori sample size calculations, among the participants in the parent study. Mixed-effect modeling for repeated measures and partial correlation analysis was implemented in the R environment for statistical analysis.

Results: Mirroring results in the parent trial, both groups experienced significant weight loss and improvements in cardiometabolic risk. In the CON group, weight loss significantly altered the pattern of circulating miR-7, miR-15a, miR-34a, miR-106a, miR-122 and miR-221. In the EX group, a distinct miRNA signature was altered: miR-15a, miR-34a, miR-122, miR-135b, miR-144, miR-149 and miR-206. Several miRNAs were significantly associated with improvements in acute insulin response, SI and other cardiometabolic risk factors.

Conclusion & Significance: These findings present novel insights into the RYGB surgery-induced molecular changes and the effects of mild exercise to facilitate and/or maintain the benefits of a comprehensive weight-loss intervention with concomitant improvements in cardiometabolic functions. Notably, we show a predictive value for miR-7, miR-15a, miR-106b and miR-135b.

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