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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 e ective adjunct therapy to RYGB surgery. However, the mechanisms by which exercise or weight loss improve peripheral SI a er 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 pro ling 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.

Ninety-four (94) miRNAs implicated in metabolism were pro led in plasma samples from 22 severely obese subjects who were recruited 1-3 months a er 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. e subjects were selected, considering a priori sample size calculations, among the participants in the parent study. Mixed-e ect modeling for repeated measures and partial correlation analysis was implemented in the R environment for statistical analysis.

Mirroring results in the parent trial, both groups experienced signi cant weight loss and improvements in cardiometabolic risk. In the CON group, weight loss signi cantly 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 signi cantly associated with improvements in acute insulin response, SI and other cardiometabolic risk factors.

ese ndings present novel insights into the RYGB surgery-induced molecular changes and the e ects of mild exercise to facilitate and/or maintain the bene ts 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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