

Supplementary figures:

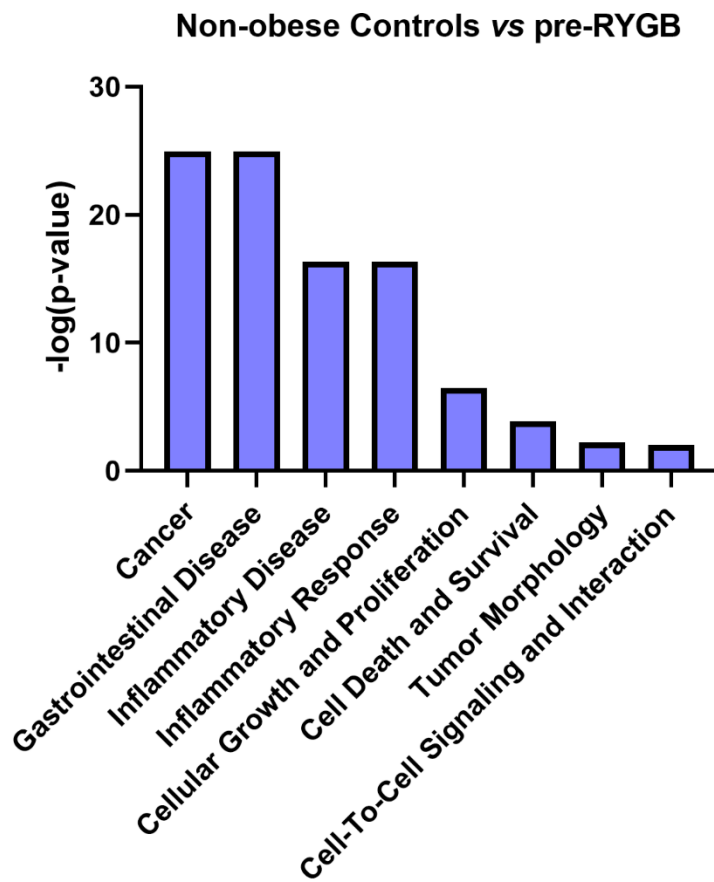


Figure S1: Significant IPA predicted interplay in diseases between miRNAs and molecules occurring in network number 1 (Figure 1D) when comparing non-obese Controls with obese individuals before RYGB.

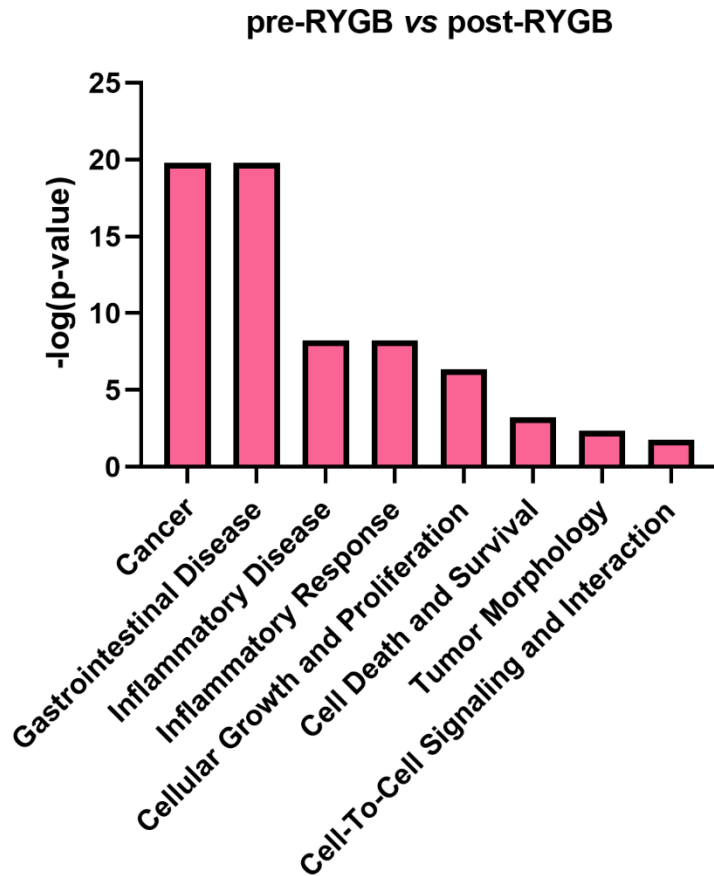
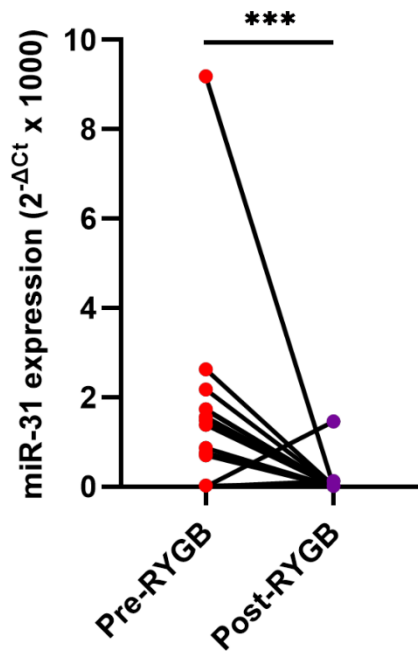


Figure S2: Significant IPA predicted interplay in diseases between miRNAs and molecules occurring in network number 2 (Figure 2D) when comparing obese patients pre- vs post-RYGB.

A)



B)

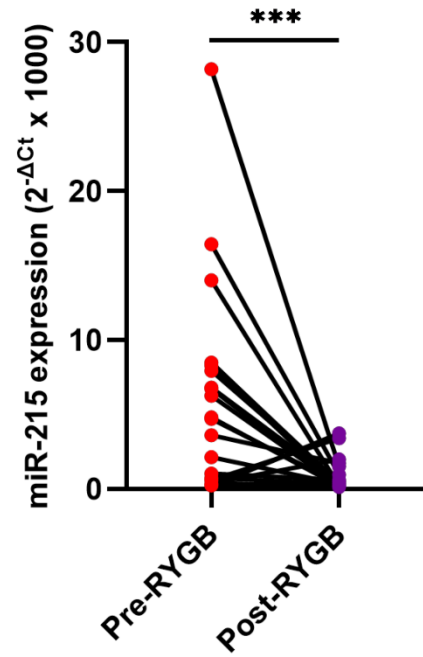


Figure S3: Inter-individual change in miRNA expression in the rectal mucosa of participants pre- and post-RYGB A) miR-31 B) miR-215.

Supplementary tables:

Table S3: Mean raw and normalised miRNA counts for pre- and post-RYGB patients and non-obese Controls.

| | Pre-RYGB patients | Post-RYGB patients | Non-obese Controls |
|--------------------------|--------------------------|---------------------------|---------------------------|
| Raw counts | 206515.5 | 195584.6923 | 124993.0909 |
| Normalised counts | 150204.25 | 149292.9989 | 158932.0198 |

Table S7: Significant IPA predicted interplay in diseases between miRNAs and molecules occurring in network number 2 (Figure 2D) when comparing obese patients pre- vs post-RYGB.

| Disease | p-value | minus log pvalue | Molecules |
|--|----------|------------------|---|
| Cancer | 1.54E-20 | -19.8125 | let-7a-3p, let-7a-5p, miR-125b-5p, miR-126a-3p, miR-126a-5p, miR-129-5p, miR-132-3p, miR-148a-3p, miR-15b-3p, miR-16-5p, miR-181a-1-3p, miR-185-5p, miR-191-5p, miR-192-5p, miR-194-5p, miR-196a-5p, miR-200a-5p, miR-200b-3p, miR-203a-3p, miR-204-5p, miR-210-3p, miR-223-3p, miR-29b-3p, miR-30a-3p, miR-30c-5p, miR-31-5p, miR-335-3p, miR-338-3p, miR-342-3p, miR-421-3p, miR-450a-5p, miR-452-5p, miR-455-3p, miR-652-3p, miR-671-5p, miR-7a-5p, miR-874-3p, miR-9-5p |
| Gastrointestinal Disease | 1.54E-20 | -19.8125 | let-7a-5p, miR-125b-5p, miR-126a-3p, miR-126a-5p, miR-129-5p, miR-148a-3p, miR-16-5p, miR-181a-1-3p, miR-185-5p, miR-191-5p, miR-192-5p, miR-196a-5p, miR-200a-5p, miR-200b-3p, miR-203a-3p, miR-204-5p, miR-210-3p, miR-223-3p, miR-28-3p, miR-29b-3p, miR-30a-3p, miR-30c-5p, miR-31-5p, miR-421-3p, miR-450a-5p, miR-452-5p, miR-455-3p, miR-652-3p, miR-671-5p, miR-7a-5p, miR-874-3p, miR-9-5p |
| Inflammatory Disease | 5.98E-09 | -8.2233 | let-7a-5p, miR-125b-5p, miR-126a-3p, miR-129-5p, miR-148a-3p, miR-16-5p, miR-181a-1-3p, miR-185-5p, miR-192-5p, miR-196a-5p, miR-200b-3p, miR-203a-3p, miR-210-3p, miR-223-3p, miR-29b-3p, miR-30a-3p, miR-30c-5p, miR-342-3p, miR-671-5p |
| Inflammatory Response | 5.98E-09 | -8.2233 | let-7a-5p, miR-125b-5p, miR-148a-3p, miR-16-5p, miR-185-5p, miR-192-5p, miR-200b-3p, miR-210-3p, miR-223-3p, miR-30c-5p, miR-342-3p, miR-671-5p |
| Cellular Growth and Proliferation | 4.23E-07 | -6.37366 | let-7a-5p, miR-125b-5p, miR-126a-5p, miR-129-5p, miR-132-3p, miR-148a-3p, miR-16-5p, miR-185-5p, miR-192-5p, miR-194-5p, miR-200a-5p, miR-200b-3p, miR-203a-3p, miR-204-5p, miR-223-3p, miR-29b-3p, miR-30a-3p, miR-31-5p, miR-342-3p, miR-7a-5p, miR-874-3p |
| Cell Death and Survival | 0.000569 | -3.24489 | let-7a-5p, miR-125b-5p, miR-129-5p, miR-148a-3p, miR-16-5p, miR-185-5p, miR-194-5p, miR-200b-3p, miR-203a-3p, miR-204-5p, miR-210-3p, miR-223-3p, miR-29b-3p, miR-455-3p, miR-7a-5p |
| Tumor Morphology | 0.00433 | -2.36351 | miR-125b-5p, miR-16-5p, miR-200b-3p |
| Cell-To-Cell Signaling and Interaction | 0.0172 | -1.76447 | miR-16-5p |

Table S8: Overlapping molecules between the pre- vs post-RYGB network and the pre-RYBG vs non-obese Controls network from which the overlapping miRNAs were used to generate an additional network

| Molecules |
|--------------|
| miR-126a-3p |
| miR-16-5p |
| miR-196a-5p |
| miR-203a-3p |
| miR-204-5p |
| miR-210-3p |
| miR-3150b-3p |
| miR-455-3p |
| miR-7a-5p |
| mir-9 |
| miR-9-5p |

Table S10: MiRNA expression ($2^{-\Delta Ct} \times 1,000$) determined by qPCR in the rectal mucosa of initially obese individuals pre- and post-RYGB and in non-obese Controls (NS: not significant; *: p-value ≤ 0.05 ; **: p-value ≤ 0.01)

| miRNA | Obese pre-RYGB | Obese post-RYGB | Non-obese Controls | P-value; pre-RYGB vs Controls | P-value; pre- vs post-RYGB |
|----------|----------------|-----------------|--------------------|-------------------------------|----------------------------|
| miR-204 | 3.251229 | 2.037882 | 1.796871 | NS | NS |
| miR-671 | 1.785026 | 1.556161 | 0.535563 | NS | NS |
| miR-892 | 20.18802 | 11.68318 | 17.32017 | NS | NS |
| miR-1247 | 1.806269 | 0.388467 | 0.289823 | NS | NS |
| miR-3196 | 6.882955 | 5.672692 | 2.657616 | * | * |
| miR-4516 | 680.5764 | 683.1289 | 257.739 | ** | NS |