

**Table S1.** Enriched pathways based on predicted and validated targets of dysregulated miRNAs identified in T2DM patients.

| Pathway Description                 | Suppressed Pathway<br>(increased miRNA concentration)  |       |        |       |      |        |       | Enhanced Pathway<br>(decreased miRNA concentration) |       |        |       |      |        |          |          |          |          |          |          |
|-------------------------------------|--------------------------------------------------------|-------|--------|-------|------|--------|-------|-----------------------------------------------------|-------|--------|-------|------|--------|----------|----------|----------|----------|----------|----------|
|                                     | Adipose                                                | Islet | Muscle | Blood | PBMC | Plasma | Serum | Adipose                                             | Islet | Muscle | Blood | PBMC | Plasma | Serum    |          |          |          |          |          |
| Carbohydrate metabolism             | Amino sugar and nucleotide sugar metabolism            |       |        |       |      |        |       |                                                     |       |        |       |      |        | 2.08E-02 |          |          |          |          |          |
|                                     | Citrate cycle (TCA cycle)                              |       |        |       |      |        |       |                                                     |       |        |       |      |        | 8.59E-02 |          |          |          |          |          |
|                                     | Fructose and mannose metabolism                        |       |        |       |      |        |       |                                                     |       |        |       |      |        | 9.83E-02 |          |          |          |          |          |
|                                     | Galactose metabolism                                   |       |        |       |      |        |       |                                                     |       |        |       |      |        | 6.56E-02 |          |          |          |          |          |
|                                     | Glycolysis gluconeogenesis                             |       |        |       |      |        |       |                                                     |       |        |       |      |        | 8.77E-02 |          |          |          |          |          |
|                                     | Pentose and glucuronate interconversions               |       |        |       |      |        |       |                                                     |       |        |       |      |        | 1.23E-02 |          |          |          |          |          |
|                                     | Pentose phosphate pathway                              |       |        |       |      |        |       |                                                     |       |        |       |      |        | 6.56E-02 |          |          |          |          |          |
|                                     | Propanoate metabolism                                  |       |        |       |      |        |       |                                                     |       |        |       |      |        | 6.98E-02 |          |          |          |          |          |
|                                     | Pyruvate metabolism                                    |       |        |       |      |        |       |                                                     |       |        |       |      |        | 7.26E-02 |          |          |          |          |          |
|                                     | Starch and sucrose metabolism                          |       |        |       |      |        |       |                                                     |       |        |       |      |        | 4.24E-02 |          |          |          |          |          |
| Xenobiotics metabolism              | Metabolism of xenobiotics by cyp450                    |       |        |       |      |        |       |                                                     |       |        |       |      |        | 3.22E-02 | 1.14E-02 |          |          |          |          |
| Energy metabolism                   | Oxidative phosphorylation                              |       |        |       |      |        |       |                                                     |       |        |       |      |        | 7.63E-02 | 1.44E-02 |          |          |          |          |
| Lipid metabolism                    | Sphingolipid metabolism                                |       |        |       |      |        |       |                                                     |       |        |       |      |        | 8.78E-02 | 8.78E-02 |          |          |          |          |
|                                     | Steroid hormone biosynthesis                           |       |        |       |      |        |       |                                                     |       |        |       |      |        | 3.53E-03 |          |          |          |          |          |
| Amino acid metabolism               | Arginine and proline metabolism                        |       |        |       |      |        |       |                                                     |       |        |       |      |        | 9.34E-02 |          |          |          |          |          |
|                                     | Cysteine and methionine metabolism                     |       |        |       |      |        |       |                                                     |       |        |       |      |        | 6.44E-02 |          |          |          |          |          |
|                                     | Lysine degradation                                     |       |        |       |      |        |       |                                                     |       |        |       |      |        | 1.42E-02 |          |          |          |          |          |
| Glycan biosynthesis and metabolism  | Glycosylphosphatidylinositol (gpi)-anchor biosynthesis |       |        |       |      |        |       |                                                     |       |        |       |      |        | 4.56E-02 |          |          |          |          |          |
|                                     | N-glycan biosynthesis                                  |       |        |       |      |        |       |                                                     |       |        |       |      |        | 2.81E-02 |          |          |          |          |          |
|                                     | O-glycan biosynthesis                                  |       |        |       |      |        |       |                                                     |       |        |       |      |        | 6.75E-02 | 6.75E-02 |          |          |          |          |
| Transcription                       | Basal transcription factors                            |       |        |       |      |        |       |                                                     |       |        |       |      |        | 2.64E-02 | 2.01E-02 | 7.78E-02 | 9.82E-03 |          |          |
| Folding, sorting and degradation    | Protein processing in ER                               |       |        |       |      |        |       |                                                     |       |        |       |      |        | 3.03E-04 | 1.85E-02 | 3.69E-02 | 1.31E-03 |          |          |
|                                     | Ubiquitin mediated proteolysis                         |       |        |       |      |        |       |                                                     |       |        |       |      |        | 2.95E-02 | 9.07E-02 | 4.49E-02 | 7.06E-03 |          |          |
| Signal transduction                 | ERBB signaling pathway                                 |       |        |       |      |        |       |                                                     |       |        |       |      |        | 7.25E-02 | 1.44E-02 |          |          |          |          |
|                                     | ErbB signaling pathway                                 |       |        |       |      |        |       |                                                     |       |        |       |      |        | 7.25E-02 |          |          |          |          |          |
|                                     | JAK-stat signaling pathway                             |       |        |       |      |        |       |                                                     |       |        |       |      |        | 4.04E-02 | 5.33E-02 | 9.47E-02 |          |          |          |
|                                     | MAPK signaling pathway                                 |       |        |       |      |        |       |                                                     |       |        |       |      |        | 1.60E-03 | 5.39E-02 | 1.01E-02 | 1.37E-02 | 9.95E-02 | 1.82E-02 |
|                                     | TGF-beta signaling pathway                             |       |        |       |      |        |       |                                                     |       |        |       |      |        | 1.04E-02 | 4.99E-03 | 4.45E-02 | 1.09E-04 |          |          |
| Signaling molecules and interaction | Wnt signaling pathway                                  |       |        |       |      |        |       |                                                     |       |        |       |      |        | 4.19E-02 | 8.87E-02 |          |          |          |          |
|                                     | Cytokine-cytokine receptor interaction                 |       |        |       |      |        |       |                                                     |       |        |       |      |        | 2.87E-03 | 7.50E-03 | 8.32E-02 |          |          |          |
|                                     | ECM-receptor interaction                               |       |        |       |      |        |       |                                                     |       |        |       |      |        | 9.88E-05 | 5.59E-02 |          |          |          |          |
| Transport and catabolism            | Neuroactive ligand-receptor interaction                |       |        |       |      |        |       |                                                     |       |        |       |      |        | 1.33E-02 | 3.40E-02 | 5.73E-02 | 3.07E-02 |          |          |
|                                     | Peroxisome                                             |       |        |       |      |        |       |                                                     |       |        |       |      |        | 1.47E-02 | 5.45E-02 |          |          |          |          |
| Cell growth and death               | Regulation of autophagy                                |       |        |       |      |        |       |                                                     |       |        |       |      |        | 7.57E-02 |          |          |          |          |          |
|                                     | Apoptosis                                              |       |        |       |      |        |       |                                                     |       |        |       |      |        | 6.83E-02 | 4.82E-02 |          |          |          |          |
|                                     | Cell cycle                                             |       |        |       |      |        |       |                                                     |       |        |       |      |        | 5.79E-02 | 7.59E-02 |          |          |          |          |
| Cell communication                  | P53 signaling pathway                                  |       |        |       |      |        |       |                                                     |       |        |       |      |        | 9.36E-02 | 4.51E-02 | 2.89E-03 |          |          |          |
|                                     | Adherens junction                                      |       |        |       |      |        |       |                                                     |       |        |       |      |        | 5.65E-02 | 5.80E-02 |          |          |          |          |
|                                     | Focal adhesion                                         |       |        |       |      |        |       |                                                     |       |        |       |      |        | 4.18E-07 | 7.54E-02 |          |          |          |          |
|                                     | Gap junction                                           |       |        |       |      |        |       |                                                     |       |        |       |      |        | 8.64E-04 | 5.97E-02 | 8.52E-02 |          |          |          |
|                                     | Tight junction                                         |       |        |       |      |        |       |                                                     |       |        |       |      |        | 7.63E-02 | 2.05E-02 | 1.44E-02 |          |          |          |

Table S1. Cont.

| Pathway Description               |                                                 | Suppressed Pathway<br>(increased miRNA concentration) |          |          |          |      |          | Enhanced Pathway<br>(decreased miRNA concentration) |          |          |        |          |          |          |          |  |
|-----------------------------------|-------------------------------------------------|-------------------------------------------------------|----------|----------|----------|------|----------|-----------------------------------------------------|----------|----------|--------|----------|----------|----------|----------|--|
|                                   |                                                 | Adipose                                               | Islet    | Muscle   | Blood    | PBMC | Plasma   | Serum                                               | Adipose  | Islet    | Muscle | Blood    | PBMC     | Plasma   | Serum    |  |
| Immune system                     | Antigen processing and presentation             | 5.87E-02                                              |          |          |          |      |          | 3.40E-02                                            |          |          |        |          |          |          |          |  |
|                                   | B cell receptor signaling pathway               | 5.74E-02                                              |          |          |          |      |          |                                                     |          |          |        |          |          |          |          |  |
|                                   | Chemokine signaling pathway                     |                                                       |          |          |          |      | 1.50E-02 | 8.78E-02                                            | 1.07E-02 |          |        |          | 2.70E-02 |          |          |  |
|                                   | Complement and coagulation cascades             |                                                       |          |          |          |      |          |                                                     |          |          |        | 6.25E-02 |          | 3.20E-02 |          |  |
|                                   | Fc epsilon ri signaling pathway                 |                                                       |          |          |          |      |          |                                                     |          |          |        |          | 6.64E-02 | 4.03E-02 | 4.03E-02 |  |
|                                   | Leukocyte transendothelial migration            |                                                       |          |          |          |      |          | 6.51E-02                                            |          |          |        |          |          |          |          |  |
|                                   | Nod-like receptor signaling pathway             | 4.21E-02                                              |          |          |          |      |          |                                                     |          |          |        |          |          |          |          |  |
| T cell receptor signaling pathway | 1.96E-02                                        |                                                       |          |          |          |      | 8.09E-02 |                                                     |          |          |        |          | 4.08E-02 |          |          |  |
| Endocrine system                  | Adipocytokine signaling pathway                 |                                                       | 9.00E-02 |          |          |      |          |                                                     |          |          |        |          |          |          |          |  |
|                                   | Insulin signaling pathway                       |                                                       |          |          |          |      |          |                                                     |          |          |        | 4.63E-02 |          |          | 1.81E-02 |  |
|                                   | PPAR signaling pathway                          |                                                       |          | 5.14E-02 |          |      |          |                                                     |          |          |        |          |          | 5.17E-02 |          |  |
| Circulatory system                | Vascular smooth muscle contraction              |                                                       |          |          | 6.97E-02 |      |          |                                                     | 9.91E-02 |          |        |          |          | 1.95E-02 |          |  |
| Digestive system                  | Pancreatic secretion                            |                                                       |          |          |          |      | 8.12E-02 | 7.29E-02                                            | 7.37E-02 |          |        | 8.23E-02 |          |          |          |  |
|                                   | Protein digestion and absorption                |                                                       |          |          |          |      |          | 1.23E-06                                            |          |          |        |          |          |          |          |  |
| Excretory system                  | Aldosterone-regulated sodium reabsorption       |                                                       |          |          |          |      |          |                                                     |          |          |        |          |          |          | 9.18E-02 |  |
|                                   | Vasopressin-regulated water reabsorption        | 1.80E-03                                              |          |          |          |      |          |                                                     |          | 1.75E-02 |        |          |          | 9.45E-02 |          |  |
| Cancers                           | Pathways in cancer                              |                                                       |          |          |          |      | 5.91E-02 | 3.26E-03                                            |          |          |        | 6.03E-02 | 7.29E-02 |          |          |  |
| Cardiovascular diseases           | Arrhythmogenic right ventricular cardiomyopathy |                                                       |          |          |          |      | 3.16E-02 |                                                     |          |          |        |          |          |          |          |  |
|                                   | Dilated cardiomyopathy                          |                                                       |          |          |          |      |          | 5.30E-02                                            |          |          |        |          | 8.52E-02 |          |          |  |
|                                   | Hypertrophic cardiomyopathy                     |                                                       |          |          |          |      |          | 4.87E-02                                            |          |          |        |          |          |          |          |  |
| Endocrine and metabolic diseases  | Maturity onset diabetes of the young            |                                                       |          |          |          |      |          |                                                     |          | 5.69E-02 |        |          |          |          | 9.18E-02 |  |
|                                   | Type I diabetes mellitus                        |                                                       |          |          |          |      |          | 3.29E-02                                            |          |          |        |          | 9.15E-02 |          |          |  |
|                                   | Type II diabetes mellitus                       |                                                       |          |          |          |      |          |                                                     |          |          |        |          | 9.15E-02 |          |          |  |