

**Supplementary Table S1: Animals, Drugs and treatment**

| <b>Material</b>   | <b>manufacturer</b>                    |
|-------------------|--|
| empagliflozin     | Boehringer Ingelheim, Germany          |
| exendin 9-39      | Abcam, Cambridge, UK                   |
| high fat diet     | #D12451 HF, Ssniff, Germany            |
| JNJ-31020028      | Janssen, New Jersey, USA               |
| low fat diet      | #D12450J LF, Ssniff, Germany           |
| NNC0165-0020      | Novo Nordisk, Denmark                  |
| NNC0165-1273      | Novo Nordisk, Denmark                  |
| Osmotic minipumps | pump model 2006, ALZET, Cupertino, USA |
| PYY3-36           | Cayman Chemical, Ann Arbor, USA        |
| semaglutide       | Novo Nordisk, Denmark                  |

**Supplementary Table S2: Enzyme-Linked Immunosorbent Assay and serum measurements**

| <b>Target</b> | <b>manufacturer</b>                                      |
|---------------|--|
| adiponectin   | #80570; Crystal Chem, Elk Grove Village, IL, USA         |
| fructosamine  | #RTEB1805; AssayGenie, Dublin, Ireland                   |
| insulin       | #90010; Crystal Chem, Elk Grove Village, IL, USA         |
| leptin        | #EK-003-17; Phoenix Pharmaceuticals, Burlingame, CA, USA |

**Supplementary Table S3: Gene expression analysis, Instruments**

| <b>Instrument</b>                     | <b>manufacturer</b>                            |
|---------------------------------------|--|
| QIAGEN Tissue Lyser II                | #85300; QIAGEN, Venlo, The Netherlands         |
| Maxwell® RSC Instrument               | #AS4500; Promega, Fitchburg, WI, USA           |
| NanoDrop 2000c spectrophotometer      | Thermo Fisher Scientific, Santa Clara, CA, USA |
| QIAxcel Connect                       | QIAGEN, Venlo, the Netherlands                 |
| Mastercycler Gradient Instrument      | Eppendorf SE, Hamburg, Germany                 |
| CFX96™ Real-Time PCR Detection System | Bio-Rad, Hercules, CA, United States           |

**Supplementary Table S4: Gene expression analysis, Chemicals**

| <b>Chemical</b>   | <b>manufacturer</b>                                      |
|---|--|
| Proteinase K Solution   | #MC5005; Promega, Fitchburg, WI, USA                     |
| Maxwell® RSC simplyRNA Tissue Kit                                 | #AS1340; Promega, Fitchburg, WI, USA                     |
| QIAGEN RNeasy Plus Universal Mini Kit                             | #73404, QIAGEN, Venlo, The Netherlands                   |
| High-Capacity cDNA Reverse Transcription Kit with RNase Inhibitor | #4374966; Thermo Fisher Scientific, Santa Clara, CA, USA |
| QuantiTect Reverse Transcription Kit                              | #205314; QIAGEN, Venlo, The Netherlands                  |

**Supplementary Table S5: Gene expression analysis, TaqMan Probes (Thermo Fisher Scientific, Santa Clara, CA, USA)**

| <b>Gene</b> | <b>ID</b>     | <b>GenBankSeq</b> |
|-------------|---------------|-------------------|
| TNF         | Rn99999017_m1 | NM_012675.3       |
| IL1B        | Rn00580432_m1 | NM_031512.2       |
| FGF21       | Rn00590706_m1 | NM_130752.1       |

|                      |               |                |
|----------------------|---------------|----------------|
| SLC2A4               | Rn00562597_m1 | NM_012751.1    |
| SREBP1               | Rn01495769_m1 | NM_001276707.1 |
| MLXIPL               | Rn00591943_m1 | NM_133552.1    |
| GAPDH                | Rn01775763_g1 | NM_017008.4    |
| UBC                  | Rn01499642_m1 | BC103477.1     |
| beta-2 microglobulin | Rn03928990_g1 | FQ219455.1     |