

Supplementary Table S1. Pearson's correlations of betatrophin with laboratory parameters in enrolled study groups.

| Variable                             | T2D           |                  | NDO           |              | Controls      |              |
|--------------------------------------|---------------|------------------|---------------|--------------|---------------|--------------|
|                                      | r             | p                | r             | p            | r             | p            |
| Age (yrs)                            | -0.110        | 0.447            | -0.226        | 0.060        | 0.039         | 0.789        |
| Body mass index (kg/m <sup>2</sup> ) | <b>0.346</b>  | <b>0.017</b>     | 0.195         | 0.114        | 0.092         | 0.567        |
| Waist circumference (cm)             | <b>0.366</b>  | <b>0.024</b>     | <b>0.262</b>  | <b>0.049</b> | 0.275         | 0.105        |
| log10 fasting glucose (mmol/L)       | 0.116         | 0.442            | 0.229         | 0.079        | -0.155        | 0.289        |
| HbA1C (%)                            | 0.044         | 0.781            | 0.042         | 0.773        | 0.279         | 0.070        |
| log10 insulin (mU/L)                 | <b>0.797</b>  | <b>&lt;0.001</b> | 0.233         | 0.076        | 0.454         | 0.078        |
| log10 hsCRP (mg/L)                   | 0.387         | 0.051            | 0.093         | 0.499        | 0.074         | 0.687        |
| log10 triglyceride (mmol/L)          | <b>0.400</b>  | <b>0.039</b>     | 0.130         | 0.341        | <b>0.408</b>  | <b>0.020</b> |
| Total cholesterol (mmol/L)           | 0.149         | 0.317            | 0.227         | 0.076        | 0.214         | 0.140        |
| Apolipoprotein-AI (g/L)              | -0.081        | 0.677            | -0.125        | 0.324        | -0.057        | 0.724        |
| LDL subfraction test                 |               |                  |               |              |               |              |
| VLDL (%)                             | 0.199         | 0.164            | 0.140         | 0.247        | <b>0.308</b>  | <b>0.031</b> |
| IDL (%)                              | <b>-0.307</b> | <b>0.030</b>     | -0.150        | 0.216        | <b>-0.395</b> | <b>0.005</b> |
| Large LDL (%)                        | 0.118         | 0.415            | 0.100         | 0.412        | <b>0.367</b>  | <b>0.010</b> |
| Small LDL (%)                        | 0.200         | 0.164            | <b>0.324</b>  | <b>0.006</b> | <b>0.341</b>  | <b>0.017</b> |
| Mean LDL size (nm)                   | -0.249        | 0.081            | <b>-0.317</b> | <b>0.008</b> | <b>-0.411</b> | <b>0.003</b> |
| HDL subfraction test                 |               |                  |               |              |               |              |
| HDL-1 (%)                            | -0.102        | 0.490            | <b>-0.252</b> | <b>0.036</b> | -0.143        | 0.328        |
| HDL-2 (%)                            | <b>-0.308</b> | <b>0.033</b>     | <b>-0.354</b> | <b>0.003</b> | <b>-0.295</b> | <b>0.040</b> |
| HDL-3 (%)                            | <b>-0.356</b> | <b>0.016</b>     | <b>-0.261</b> | <b>0.029</b> | <b>-0.300</b> | <b>0.036</b> |
| HDL-4 (%)                            | -0.271        | 0.062            | -0.156        | 0.198        | <b>-0.346</b> | <b>0.015</b> |
| HDL-5 (%)                            | -0.164        | 0.267            | -0.046        | 0.704        | 0.002         | 0.987        |
| HDL-6 (%)                            | 0.185         | 0.208            | 0.155         | 0.200        | 0.211         | 0.146        |
| HDL-7 (%)                            | <b>0.379</b>  | <b>0.008</b>     | <b>0.276</b>  | <b>0.021</b> | <b>0.286</b>  | <b>0.047</b> |
| HDL-8 (%)                            | <b>0.333</b>  | <b>0.021</b>     | <b>0.303</b>  | <b>0.011</b> | <b>0.304</b>  | <b>0.034</b> |
| HDL-9 (%)                            | 0.269         | 0.064            | <b>0.273</b>  | <b>0.022</b> | <b>0.317</b>  | <b>0.027</b> |
| HDL-10 (%)                           | 0.169         | 0.252            | 0.221         | 0.067        | <b>0.355</b>  | <b>0.012</b> |
| Large HDL (%)                        | <b>-0.327</b> | <b>0.020</b>     | <b>-0.339</b> | <b>0.004</b> | <b>-0.297</b> | <b>0.039</b> |
| Intermediate HDL (%)                 | 0.058         | 0.690            | 0.118         | 0.330        | 0.078         | 0.596        |
| Small HDL (%)                        | 0.240         | 0.093            | <b>0.288</b>  | <b>0.016</b> | <b>0.351</b>  | <b>0.013</b> |

Abbreviations: HbA1C, hemoglobin A1C; HDL, high-density lipoprotein; hsCRP, high-sensitivity C-reactive protein; IDL, intermediate-density lipoprotein; LDL, low-density lipoprotein; NDO, nondiabetic obese patients; T2D, patients with type 2 diabetes; VLDL, very low-density lipoprotein.

Notes: Serum betatrophin concentrations were measured by ELISA and lipoprotein subfractions were detected by Lipoprint® acrylamide gel electrophoresis. Nonnormally distributed data were transformed logarithmically before Pearson's correlation analysis. Significant data ( $p < 0.05$ ) are bolded.

Supplementary Table S2. Pearson's correlations of conventional cardiovascular risk factors with lipoprotein subfractions in all subjects.

| Variable                    | Age<br>(yrs)  |              | BMI<br>(kg/m <sup>2</sup> ) |                  | log10 hsCRP<br>(mg/L) |                  | log10 insulin<br>(mU/L) |                  | HOMA-IR       |              |
|-----------------------------|---------------|--------------|-----------------------------|------------------|-----------------------|------------------|-------------------------|------------------|---------------|--------------|
|                             | r             | p            | r                           | p                | r                     | p                | r                       | p                | r             | p            |
| <b>LDL subfraction test</b> |               |              |                             |                  |                       |                  |                         |                  |               |              |
| VLDL (%)                    | 0.005         | 0.940        | <b>0.171</b>                | <b>0.015</b>     | 0.126                 | 0.127            | 0.127                   | 0.162            | -0.015        | 0.887        |
| IDL (%)                     | -0.091        | 0.183        | -0.065                      | 0.356            | <b>-0.308</b>         | <b>&lt;0.001</b> | -0.004                  | 0.966            | -0.162        | 0.126        |
| Large LDL (%)               | 0.050         | 0.461        | <b>0.244</b>                | <b>&lt;0.001</b> | <b>0.419</b>          | <b>&lt;0.001</b> | 0.021                   | 0.822            | 0.111         | 0.295        |
| Small LDL (%)               | <b>0.139</b>  | <b>0.041</b> | -0.024                      | 0.737            | 0.121                 | 0.143            | 0.069                   | 0.448            | <b>0.240</b>  | <b>0.022</b> |
| Mean LDL size (nm)          | -0.167        | 0.014        | -0.081                      | 0.251            | <b>-0.221</b>         | <b>0.007</b>     | -0.138                  | 0.128            | <b>-0.244</b> | <b>0.020</b> |
| <b>HDL subfraction test</b> |               |              |                             |                  |                       |                  |                         |                  |               |              |
| HDL-1 (%)                   | -0.002        | 0.983        | <b>0.278</b>                | <b>&lt;0.001</b> | <b>-0.181</b>         | <b>0.027</b>     | -0.146                  | 0.110            | -0.136        | 0.198        |
| HDL-2 (%)                   | 0.033         | 0.635        | <b>-0.352</b>               | <b>&lt;0.001</b> | -0.143                | 0.083            | <b>-0.308</b>           | <b>&lt;0.001</b> | <b>-0.243</b> | <b>0.020</b> |
| HDL-3 (%)                   | 0.015         | 0.833        | <b>-0.249</b>               | <b>&lt;0.001</b> | -0.135                | 0.099            | <b>-0.289</b>           | <b>0.001</b>     | <b>-0.248</b> | <b>0.018</b> |
| HDL-4 (%)                   | -0.089        | 0.194        | <b>-0.181</b>               | <b>0.010</b>     | -0.147                | 0.073            | <b>-0.289</b>           | <b>0.001</b>     | <b>-0.288</b> | <b>0.006</b> |
| HDL-5 (%)                   | <b>-0.199</b> | <b>0.003</b> | -0.028                      | 0.696            | -0.060                | 0.470            | <b>-0.204</b>           | <b>0.025</b>     | <b>-0.238</b> | <b>0.023</b> |
| HDL-6 (%)                   | -0.105        | 0.125        | <b>0.256</b>                | <b>&lt;0.001</b> | 0.153                 | 0.063            | 0.116                   | 0.204            | 0.150         | 0.156        |
| HDL-7 (%)                   | -0.020        | 0.773        | <b>0.319</b>                | <b>&lt;0.001</b> | 0.109                 | 0.187            | <b>0.254</b>            | <b>0.050</b>     | <b>0.260</b>  | <b>0.013</b> |
| HDL-8 (%)                   | 0.016         | 0.821        | <b>0.159</b>                | <b>0.024</b>     | 0.017                 | 0.835            | <b>0.139</b>            | <b>0.011</b>     | 0.087         | 0.412        |
| HDL-9 (%)                   | 0.022         | 0.750        | 0.091                       | 0.197            | -0.035                | 0.671            | <b>0.230</b>            | <b>0.011</b>     | 0.168         | 0.113        |
| HDL-10 (%)                  | 0.112         | 0.103        | <b>0.279</b>                | <b>&lt;0.001</b> | <b>0.244</b>          | <b>0.003</b>     | <b>0.379</b>            | <b>&lt;0.001</b> | <b>0.326</b>  | <b>0.002</b> |
| Large HDL (%)               | 0.018         | 0.788        | <b>-0.350</b>               | <b>&lt;0.001</b> | <b>-0.183</b>         | <b>0.026</b>     | <b>-0.308</b>           | <b>&lt;0.001</b> | <b>-0.247</b> | <b>0.019</b> |
| Intermediate HDL (%)        | <b>-0.211</b> | <b>0.002</b> | <b>0.181</b>                | <b>0.010</b>     | 0.044                 | 0.596            | -0.060                  | 0.509            | -0.055        | 0.605        |
| Small HDL (%)               | 0.089         | 0.120        | <b>0.255</b>                | <b>&lt;0.001</b> | <b>0.178</b>          | <b>0.030</b>     | <b>0.361</b>            | <b>&lt;0.001</b> | <b>0.297</b>  | <b>0.004</b> |

Abbreviations: BMI, body mass index; HDL, high-density lipoprotein; hsCRP, high-sensitivity C-reactive protein; HOMA-IR, homeostasis model assessment insulin resistance; IDL, intermediate-density lipoprotein; LDL, low-density lipoprotein; VLDL, very low-density lipoprotein.

Notes: Nonnormally distributed data were transformed logarithmically before Pearson's correlation analysis.

Significant data ( $p < 0.05$ ) are marked in bold.