Online-Only Supplemental Material

Figure S1. Study design. The insulin response in subcutaneous abdominal white adipose tissue before (fasting) and two hours into a hyperinsulinemic euglycemic clamp (hyperinsulinemia) was determined in needle biopsies taking advantage of the paired design for individuals (fasting vs hyperinsulinemia) in each of the three groups. These included 23 women with obesity (OB) scheduled for bariatric surgery which were reinvestigated two years later when they had attained a body mass index below 30 kg/m^2 (termed post-obese, POB). The latter were matched for age, BMI and M-value (an insulin sensitivity measure obtained from during clamp) with 23 never-obese women (NO). We did not perform direct comparisons of the fasting or the hyperinsulinemic states between the three groups, which would have to take into consideration that the OBs and POBs are the same individuals.

Figure S2. Comparison of insulin responses. A-F. The expression fold-change (FC) in tag cluster (TC) expression (given as the ratio between the expression level under hyperinsulinaemic over fasting state, hi/f) in each of the three groups (NO, OB and POB) compared with the other two groups. Symbols denote the *common* (orange circles), *obesity-attenuated* (yellow squares) and *POB-enriched* (green diamonds) TCs detailed in Figure 3A. Tag clusters on or close to the diagonal line display similar FC in the two compared groups. Note that *common* and *obesity-attenuated* TCs in NO and POB subjects tend to be above the diagonal line when compared to the OB group (panels B-C) suggesting that the overall induction in TC expression is more pronounced in the non-obese state. Furthermore, both the induced and attenuated *POB-enriched* genes display a significant deviation from the diagonal line compared with the NO and OB group (panels D and F). P-values for paired (OB vs POB) or unpaired (NO vs OB and NO vs POB) t-test are shown. NO: never-obese, OB: obese, POB: post-obese.

Figure S3. Expression of transcription factors with altered motif activity. A-C. Fold changes (hyperinsulinemia/fasting) of tag clusters (left y-axis) of the corresponding transcription factors (x-axis) detailed in Figure 4. Results are subdivided according to *common* (A), *obesity-attenuated* (B) and *POB-enriched* (C) for NO, OB and POB. NO: never-obese, OB: obese, POB: post-obese.

Figure S4. Mapping of genes and transcription factor targets in lipid biosynthesis. Lipid biosynthesis pathways were subdivided according to **A.** *de novo* lipogenesis, **B.** triglyceride and **C.** cholesterol synthesis. S-score (see Methods) for significantly insulin-regulated genes in OB, POB and NO are shown. Detected but not regulated genes are highlighted in green while not detected genes are presented in grey. Analyses of published ChIP-sequencing or microarray data (see Methods) allowed identification of target genes for SREBP1/2, LXRα/β, PPARγ and ChREBP as indicated. NO: never-obese, OB: obese, POB: post-obese.

Figure S5. Predicted TFs regulating RNP genes.

The graph provides the Fisher exact test p-values (x-axis) and odds ratio (y-axis) for the enrichment of TF binding sites (TFBS) sets from UniBind Motif activities enriched among RNP genes. The most significant TF binding sites indicated.

Table S1. Numbers and type of detected tag clusters. Tag clusters identified in the entire data set were annotated to Gencode V19 and FANTOM5 as described in Methods. The total number of genes according to biotype is shown.

Table S2. Clinical cohort characterization. Values are mean ± SD or numbers and compared by paired (OB vs POB) or unpaired (NO vs POB and NO vs OB) t-test. BMI, body mass index; fP, fasting plasma; fS, fasting insulin; WHR, waist-to-hip ratio.

Table S3. Differentially expressed insulin-regulated tag clusters, corresponding genes and biotypes.

Table S4. Enriched transcription factor binding sites for the groups OB, POB and NO.

Table S5. Gene set enrichment analysis. GSEA on gene transcripts constituting the *common*, *obesity-attenuated* and *POB-enriched* gene sets. Similar pathways were grouped in order to avoid redundancy.

Table S6. Enriched transcription factor binding sites for tag clusters related to ribosomal proteins.