Online Supplemental Materials

Supplemental figure 1: Adipocyte differentiation capacity of the Chub-S7 human pre-adipocyte cell line. Chub-s7 pre-adipocytes were seeded in 6-well plates and grown to complete confluence, then treated with differentiation media (as described in methods) for 14-21 days. (**A**) Cells were imaged using light microscopy before the start and after 21 days of differentiation. (**B**) Oil-red-O (ORO) staining was used to visualize lipid droplets, and quantified using absorbance measurements after cell monolayers were dissolved in DMSO. (**C**) Differentiated adipocytes were stained for neutral lipids with Bodipy (green), and nuclei were visualized with DAPI (blue). Shown are representative confocal microscopy images. (**D**) mRNA expression of lipogenic genes was quantified in cells before and after differentiation (presented as ddCT of endogenous controls: PPIA, PGK1). Results are from two independent experiments, each performed with two biological duplicates.

Supplemental figure 2: Validation of *TRAIL* and *DR3* results from the RNA-seq analyses using an independent set of E2F1-discordant, age, sex and BMI-matched, pairs. For validation purposes of the differential expression of *TRAIL* and *DR3* between E2F1-low and high patients in the RNA-seq analysis (sub-cohort 1, **Table 1B**), we matched 11 pairs of participants from sub-cohort 2 (see **Table 1B**) who were $E2F1^{low}$ or $E2F1^{high}$: (**A**) for BMI; (**B**) age; (**C**), and sex. mRNA expression (presented as ddCT of endogenous controls: PPIA, PGK1) of TRAIL (**D**) and DR3 (**E**) among the matched pairs. Lines between individual participants depict each of the $E2F1^{low/high}$ pairs.

Supplemental figure 3: TRAIL expression in HEK-293 cells is E2F1-dependent, and TRAIL-induced TL1A in human macrophages differentiated in human adipose tissue media. HEK-293 cells were grown to 80% confluence in 6 well plates. (**A**) Cells were transfected with plasmids encoding either "empty" pCMV plasmid or a pCMV-hE2F1 plasmid, incubated for 24h, then snap-frozen and processed for mRNA isolation. mRNA expression of *E2F1* and *TRAIL* by q-rtPCR. Presented are results of two independent experiments, each with two biological replicates and two technical replicates. (**B**) Cells were transfected with either non-coding siRNA (si_NS) or anti-E2F1 siRNA (si_E2F1). mRNA expression of *E2F1* and *TRAIL* was quantified as above (presented are results of two independent experiments, each with three biological replicates and two technical replicates). (**C**) promoter analysis was conducted using JASPAR©. The minimal TRAIL promoter was defined at -1000-+500 BP of the transcription start site (TSS), and was screened for putative E2F1-binding site. The three highest-scored (out of seven) possible site are presented (relative predictive score is presented in percentage). (**D**) Human monocyte-derived macrophages were differentiated as detailed in Methods in the presence of human visceral adipose tissue conditioned medium, to better represent adipose tissue macrophages. Cells were stimulated with hTRAIL for 24 h at the indicated concentrations, after which *TL1A* mRNA was assessed by q-rtPCR. Shown are results of 2 independent experiments performed in technical duplicates.

Supplemental figure 4: TRAIL-induced *DR4* and *DR5* (TRAIL-receptors) in human primary T-lymphocytes. CD14-negative cells were isolated from peripheral human blood samples and T-lymphocytes were isolated using antiCD3-Abs coated culture plates. Cultured cells were stimulated with hTRAIL at the indicated concentrations for 24h, and the expression of TRAIL-receptors *DR4&DR5*-mRNA was measured by qRT-PCR (results are ddCT mean±SD of two experiments, each with three biological replicates and two technical replicates). Green=*DR4* mRNA, Blue=*DR5* mRNA.