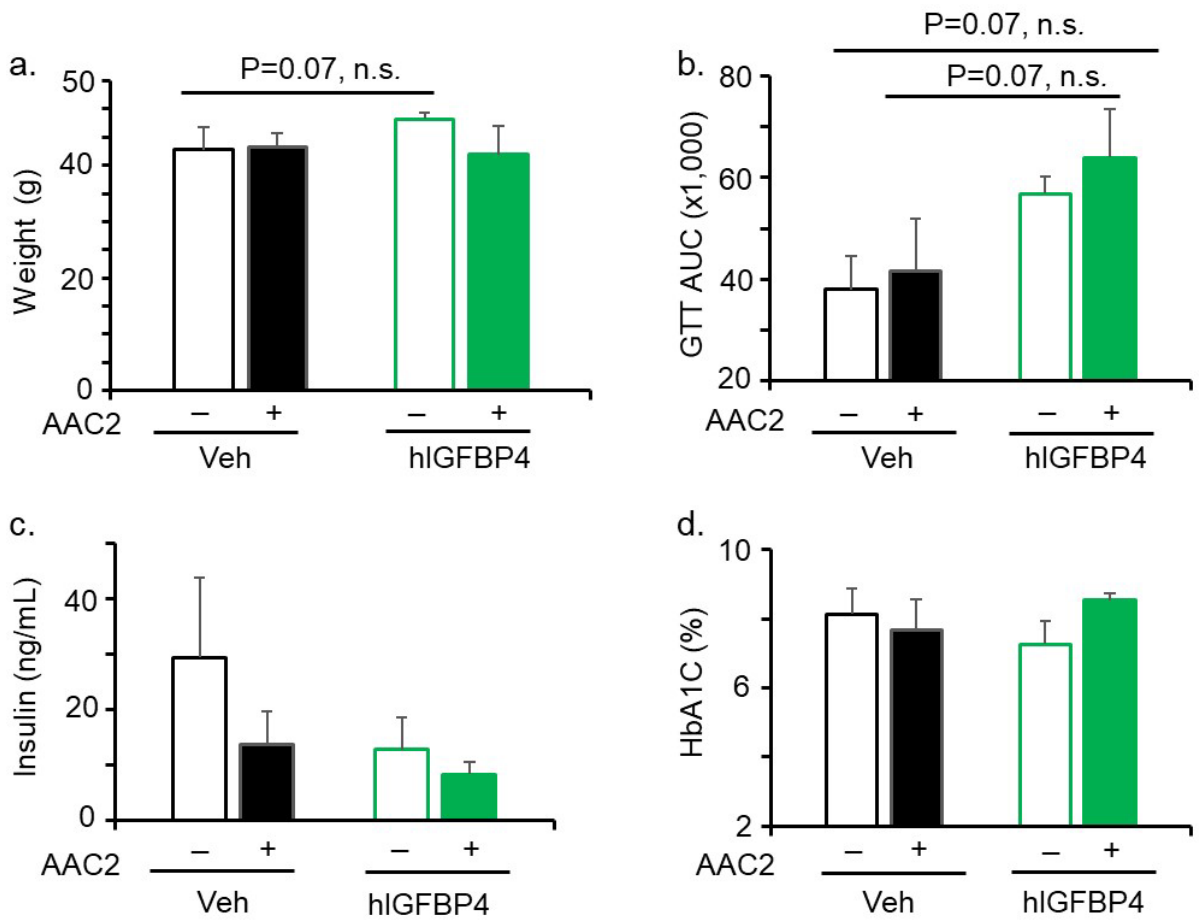
Supplementary Materials:

Table S1. Characteristics of patient donors providing subcutaneous tissue for isolation of primary stromal vascular fraction (SVF) cells

ID	Sex	Age	Race	BMI	HbA1c	Medication
AVO 185 (SF p4)	Male	49	Caucasian	41.5	5.3	No medication
AVO 195 (SF p2)	Female	34	Caucasian	43.3	5.2	No medication
AVO 190 (SF p3)	Male	38	Other race	52.2	6.1	Metformin, glipizide, Victoza
AVO 192 (SF p3)	Female	53	Caucasian	58	5.5	No medication
AVO 179 (SF p4)	Female	32	African-American	55.9	7.0	Metformin
AVO 202 (SF p5)	Female	51	Caucasian	51.5	None	Metformin

Figure S1.

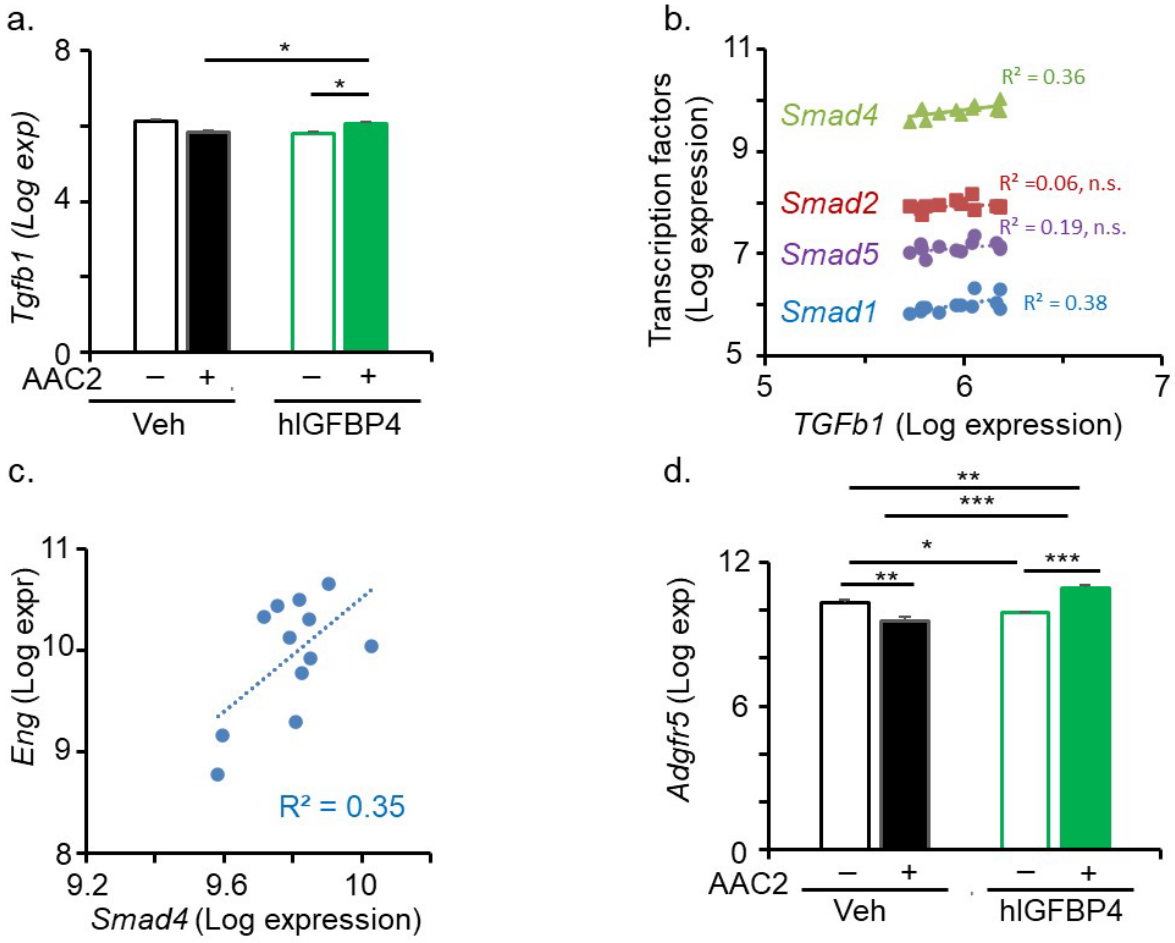


FigureS1. Similar effects of treatments with AAC2-hIGFBP4 complex or its individual components on weight, glucose tolerance, and insulin and HbA1c levels in blood in *db*/*db* mice.(a–d) Five-week-old male leptin receptor–deficient mice (*db*/*db*; homozygous for Lepr^db, JAX stock number 000642) were purchased from The Jackson Laboratory (Bar Harbor, ME). Mice were housed under a 12 h:12 h light–dark cycle and fed a standard chow diet (Teklad LM-485 mouse/rat diet, irradiated; Envigo, Somerset, NJ). After a one-week acclimation period, mice were randomly assigned to four treatment groups and received subcutaneous injections (20 μL/g BW) every 48 h for 51 days. Control group (n = 4): PBS (10 μL/g BW); AAC2 group (n = 3): AAC2 at 0.1 nmol/g BW; hIGFBP4 group (n = 3): human IGFBP4 at 50 ng/g BW (1.79 nmol/g BW); AAC2-hIGFBP4 complex group (n = 3): AAC2 (0.1 nmol/g BW) combined with hIGFBP4 (50 ng/g BW) and incubated at room temperature for 30 minutes prior to injection. All injections were administered subcutaneously into the scapular region of non-fasted mice.

(a) body weight at baseline (day 0) and at the end of the study. (b) glucose tolerance test (GTT) performed on day 49.

(c) area under the curve (AUC) analysis of GTT response. (d) endogenous mouse insulin levels in plasma measured by ELISA at the end of the study. (e) HbA1c levels in blood measured by enzymatic colorimetric assay.Statistical significance was determined by one-way ANOVA and unpaired t-test.

Figure S2.



FigureS2. Similar effects of treatments with AAC2-hIGFBP4 complex or its individual components on expression of genes involved in TGFb pathways and insuling clearance in *ob*/*ob* mice.(a–d) gene expression in livers from *ob*/*ob* mice treated with Veh, AAC2, hIGFBP4, or the AAC2-hIGFBP4 complex (n=3 per group). Transcriptomic profiling was performed using Affymetrix microarrays, and genes with significant changes ($P < 0.005$) are shown. *Tgfb1* expresttion in all groups of *ob*/*ob* mice (a). Pearson correlation between expression of *Tgfb1* and *Smad* transcription factorss, n.s. non significant (b). Pearson correlation betweenexpression of *Smad4* and *Eng*, $P<0.05$ (c). Expression of Adgfr5 in all groups of *ob*/*ob* mice (d).