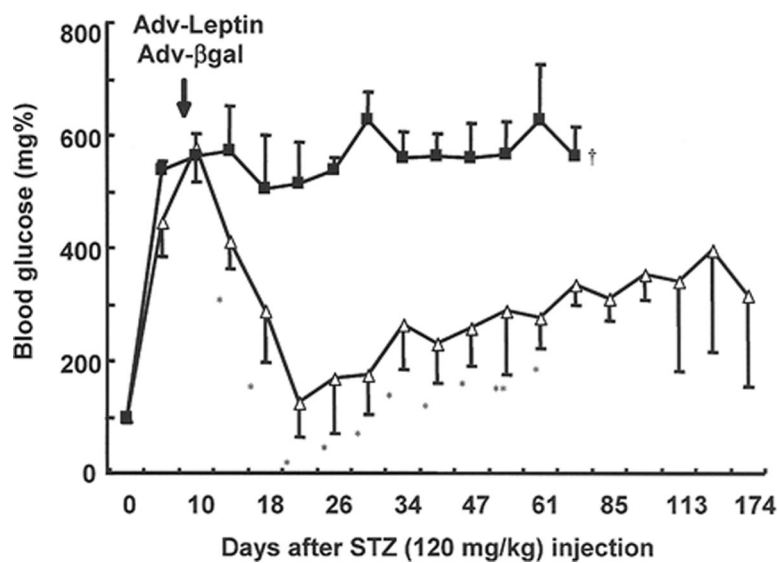
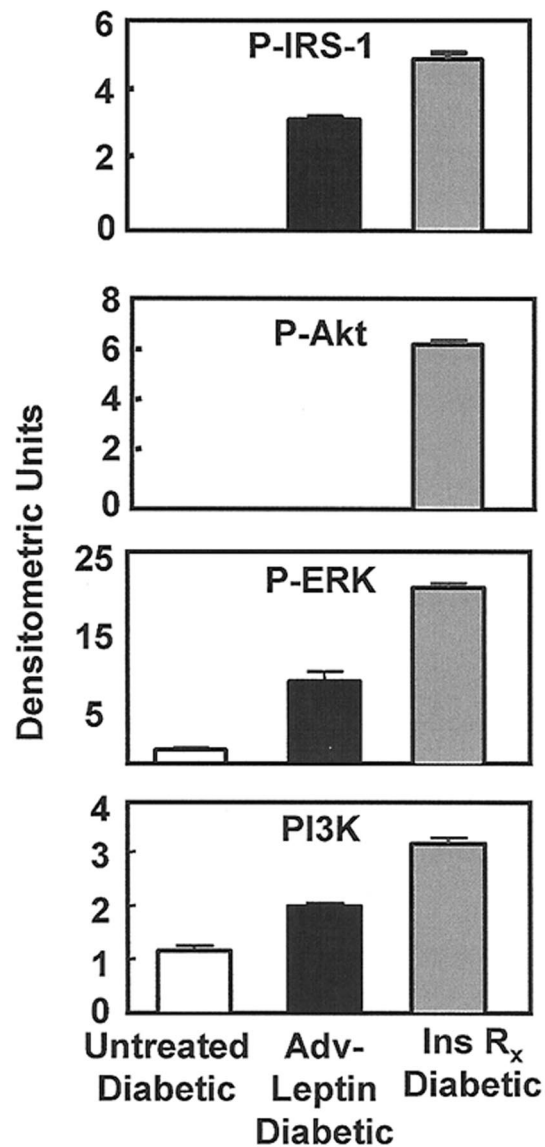


# Supporting Information

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**Fig. S1.** A long-term study showing a gradual return of hyperglycemia that nevertheless remains below pretreatment levels. The animals retained body weight and appeared to be in normal health. (■ = Adv-leptin; △ = Adv-βgal; \*,  $P < 0.01$ ; \*\*,  $P < 0.05$ ).



**Fig. S2.** Hyperleptinemia increases activation of certain components of the insulin signaling pathway in skeletal muscle. Immunoblotting for phosphoproteins of the insulin signaling transduction pathway in skeletal muscle of double-dose STZ-diabetic rats. Rats were untreated ( $\square$ ) ( $n = 4$ ), or they received Adv-leptin 3 days earlier ( $\blacksquare$ ) ( $n = 5$ ) or insulin 3 h earlier ( $\blacksquare$ ) ( $n = 3$ ). Results are expressed as densitometric units.

**Table S1. Metabolic profiles of untreated STZ and Adv-leptin-treated STZ rats, and nondiabetic (nd) controls 30 days after time of treatment ( $n = 6$ )**

Measurement	Untreated	Adv-leptin	nd	<i>P</i> value (untreated vs. Adv-leptin)	<i>P</i> value (Adv-leptin vs. lean)
Blood glucose, mg/dl	678 ± 17	99 ± 57.4	74 ± 6	0.001	0.18
Urine glucose, mg/dl	1,000–2,000	negative	negative		
Insulin, ng/ml	0	0	1.4 ± 0.1		
Leptin, ng/ml	0.02 ± 0.02	20.4 ± 5.9	1.7 ± 0.5	0.006	0.008
TAG, mg/dl	1,062 ± 236	9 ± 2	50 ± 12	0.011	0.02
FFA, mEq/ml	2.2 ± 1.2	0.19 ± 0.1	0.3 ± 0.2	0.04	0.42
Liver TAG, mg/g	1.1 ± 0.5	4.7 ± 0.8	6.8 ± 0.8	0.003	0.02
Muscle TAG, mg/g	0.3 ± 0.1	1.6 ± 0.3	3.4 ± 1.1	0.02	0.04

**Table S2. Primer sequences used for real-time RT-PCR**

Gene	Forward	Reverse
Rat AKT-1	GGCCACTGGCCGCTATT	GCGACTTCATCCTTTGCAATG
Rat IGF-1	ATTCATTTGCGTTTGAAAA	CAGACCCAGCACGAAAGAA
Rat PEPCK	GCCTGTGGAAAACCAACCT	CACCCACACATTCAACTTCCA
Rat PGC-1	CAGCCAGTACAGCCCTGATGA	TGGTAAGCGCAGCCAAGAG
Rat preproinsulin	TTTGTCAAACAGCACCTTTGTG	GGGTGTGTAGAAGAAACCACGTT
Mouse preproinsulin	GGGGAGCGTGGCTTCTTA	GGGACAGAATTCAGTGGCA