

Supplementary Table I. Characteristics of the experimental groups before and during the pancreatic clamp studies

	SCR ASO SC	SCR ASO OF	SCD1 ASO OF
Basal			
Body weight (g)	296±4	300±2	295±5
Food Intake (Kcal/day)‡	69±3	134±6	138±4
Glucose (mM)	8.1±0.2	7.8±0.3	8.1±0.2
Insulin (ng/ml)	1.1±0.1	1.3±0.3	1.1±0.1
Leptin (ng/ml)	1.5±0.2	1.6±0.2	1.5±0.3
FFA (mM)	1.0±0.2	0.9±0.1	1.0±0.1
Clamp			
Glucose (mM)	7.6±0.1	7.6±0.1	7.2±0.4
Insulin (ng/ml)	2.6±0.1	3.1±0.2	2.6±0.2
Leptin (ng/ml)	1.2±0.2	1.5±0.2	1.5±0.3
FFA (mM)	0.8±0.1	0.8±0.1	0.6±0.1*
Adiponectin (ng/ml)	1.7±0.0	1.8±0.4	1.4±0.2
Glucagon (pg/ml)	35±1	35±3	30±5

Values during the clamp represent the steady-state levels obtained by averaging the results of at least four samples during the experimental period. FFA, free fatty acids. ‡ Average food intake over last 3-days before the clamp study. SC=standard chow; OF=over-feeding *p<0.05 vs SCR ASO OF.

Supplementary Table 2. Specific activities of hepatic substrates used to calculate the “direct pathway” and the “indirect pathway” at the end of the [3-³H]glucose-[U-¹⁴C]lactate infusions

Group	[¹⁴ C]-PEP	[¹⁴ C]UDPGlc	Indirect	[³ H]Glc	[³ H]UDPGlc	Direct
	dpm/mmol		%	dpm/mmol		%
SCR ASO SC	23.2±1.9	11.0±1.3	23.7±2.6	36.6±3.1	12.5±1.3	34.7±3.3
SCR ASO OF	7.2±2.6	2.4±0.7	20.8±8.4	26.4±1.9	7.5±1.3	33.0±5.3
SCD1 ASO OF	27.8±13.6	6.2±1.3	38.0±18.9	24.9±3.5	5.9±1.1	23.9±2.1

Abbreviations: PEP, phosphoenolpyruvate; UDPGlc, uridinediphosphoglucose; Indirect, percent of the hepatic Glc-6-P pool derived from PEP-gluconeogenesis; Glc, glucose; Direct, percent of the hepatic Glc-6-P pool derived from plasma glucose.

Supplementary Table 3. Diet Composition

Calories provided	Standard Chow Diet (SC)	SC Diet with 10% Lard* (High Fat Diet)
Carbohydrate (%)	60	45
Protein (%)	28	22
Fat (%)	12	33
Saturated	3.1	9.4
Monounsaturated	4.7	11.2
Polyunsaturated	5.0	4.9
Total Calorie Provided by Digestible Nutrients (Kcal/g)	3.00	5.14
*Lard composition:2% myristic acid, 24% palmitic acid, 13% stearic acid, 46% oleic acid, 12% linoleic acid.		