SUPPLEMENTARY DATA

Supplementary Table 1. Clinical characteristics of study subjects for DNA chip analyses.

	Non-obese diabetes	Obese diabetes
No. (M:F)	11 (8:3)	10 (7:3)
Age (yr)	56±5	50±13
BMI (kg/m2)	21.7±1.4	27.4±3.8*
FPG (mg/dl)	153±60	132±32
HbA1c (%)	8.1±1.8	7.3±1.3
HOMA-R	1.75±0.69	3.78±2.94
MCR (mg/kg/min)	6.76±5.6	4.51±2.11
TC (mg/dl)	200±41	199±20
Triglyceride (mg/dl)	118±95	144±60
HDL-C (mg/dl)	48±14	45±9
AST (IU/L)	21±4	30±14
ALT (IU/L)	23±6	47±32 **

Supplementary Table 2. Clinical characteristics of the subjects (N=24) for realtime RT-PCR analyses.

Male : Female	14:10
Age (yr)	50±3
BMI (kg/m^2)	27.1±1.2
FPG (mg/dl)	132±8
HbA1c (%)	7.8±1.6
HOMA-R	3.42±2.54

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SUPPLEMENTARY DATA

Supplementary Table 3. mRNA expression of genes involved in protein degradation in the livers of mice fed the high fat diet.

Gene name		Alilent ID	*HFD vs. STD*
Psme1	proteasome 28 subunit, alpha	NM_011189.1	1.04
Psme2	proteasome 28 subunit, beta	NM_011190.3	*1.24
Psme3	proteaseome 28 subunit, 3	NM_011192.3	1.05
Psma1	proteasome subunit, alpha type 1	NM_011965.1	1.04
Psma3	proteasome subunit, alpha type 3	NM_011184.2	1.01
Psma5	proteasome subunit, alpha type 5	NM_011967.2	0.99
Psmb1	proteasome subunit, beta type 1	NM_011185.2	1.11
Psmb2	proteasome subunit, beta type 2	NM_011970.2	1.09
Psmb5	proteasome subunit, beta type 5	NM_011186.1	1.19
Psmd1	proteasome 26S subunit, non-ATPase, 1	NM_027357.1	1.06
Psmd2	proteasome 26S subunit, non-ATPase, 2	NM_134101.1	1.22
Psmd14	proteasome 26S subunit, non-ATPase, 14	NM_021526.1	1.07
Dscr2	proteasome assembling protein 1 (PAC1)	NM_019537.1	1.02
Tnfsf5ip1	proteasome assembling protein 1 (PAC2)	NM_134138.1	1.12
Ubc	ubiquitin	NM_019639.3	1.14

Transcript levels for genes involved in protein degradation were determined using custom-made, high-precision DNA chips (Ando et al., 2009). Data represent the mean ±SEM of four mice and are expressed relative to the mice fed a standard diet for each gene (n=4-5). STD, standard chow diet, HFD, high-fat diet. *P<0.05.

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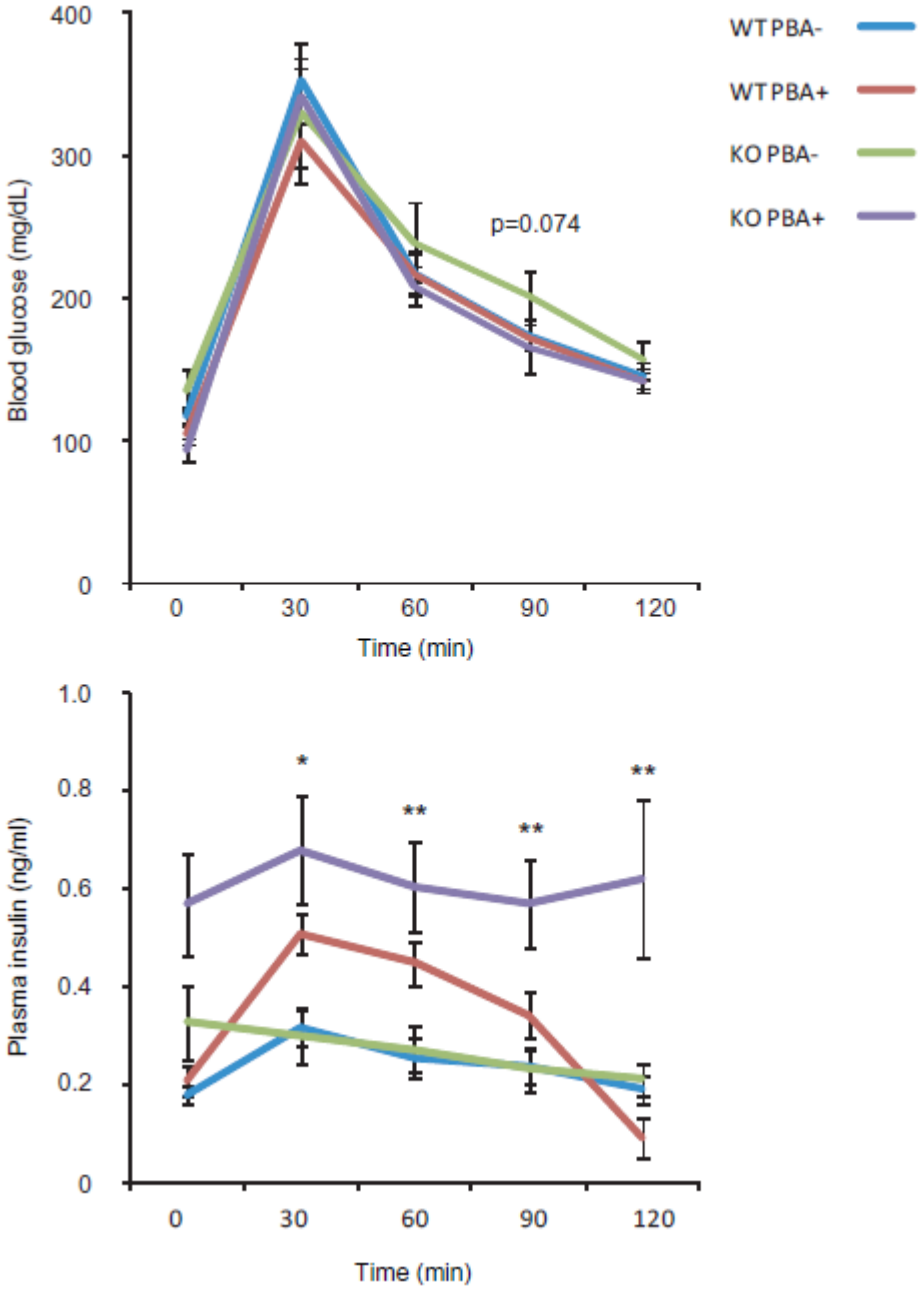
SUPPLEMENTARY DATA

Supplementary Figure 1. Blood levels of glucose and plasma levels of insulin during intraperitoneal glucose tolerant test (n = 6–10). Mice were fasted for 12 h, followed by a glucoseinjection (1.5 g/kg i.p.). Blood levels of glucose and plasma levels of insulin were measured before and after glucose infusion. *P < 0.05 and **P < 0.01 vs. PBA-untreated PA28 KO mice by ANOVA.



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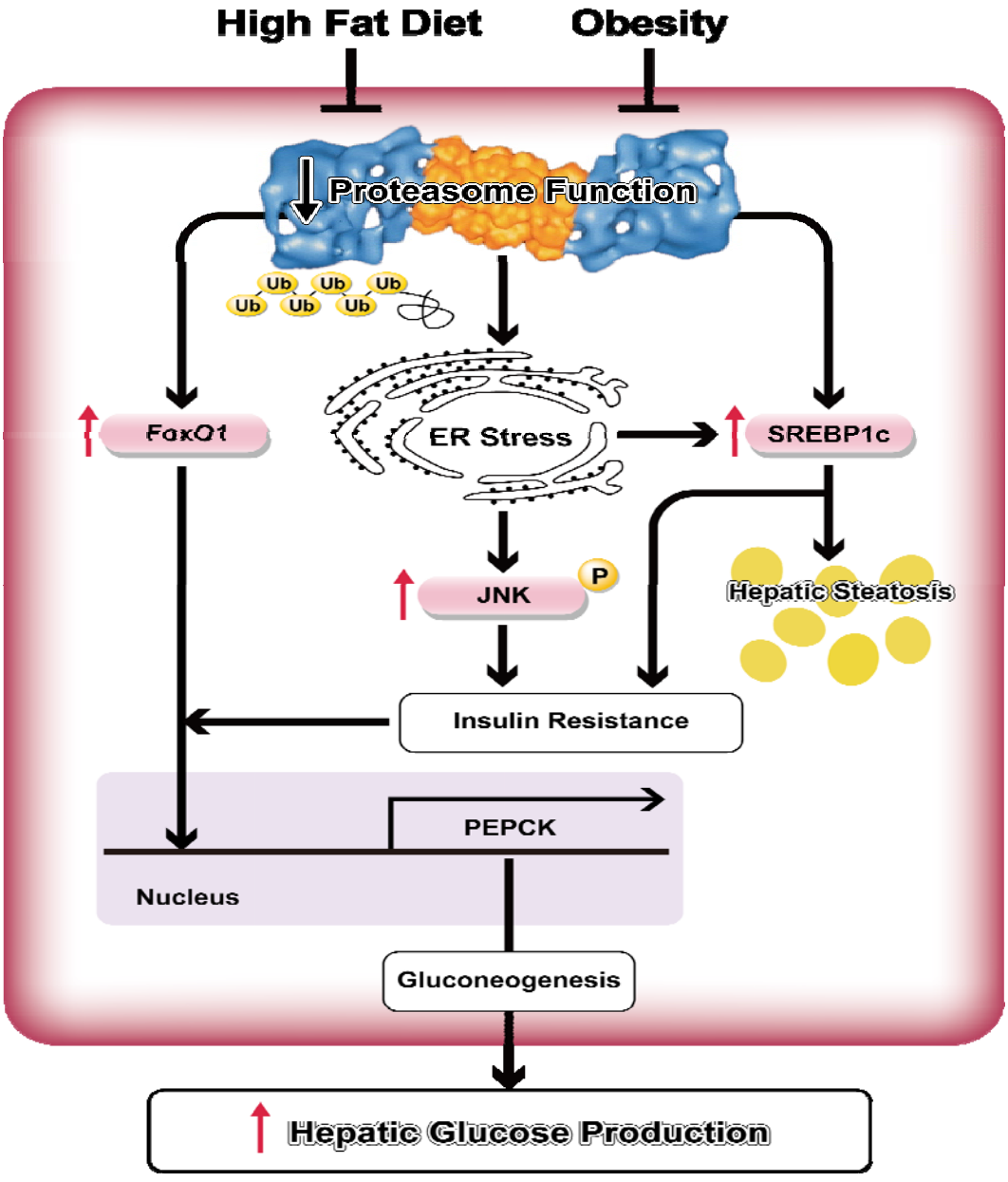
SUPPLEMENTARY DATA

Supplementary Figure 2. Model highlighting the metabolic pathways to hepatic glucose overproduction caused by proteasome dysfunction in the liver. Obesity and ingestion of a high-fat diet cause proteasome dysfunction that accumulates ubiquitinated proteins and causes ER stress, JNK activation, and insulin resistance in the liver. ER stress and proteasome dysfunction contributes to the development of hepatic steatosis via activating SREBP-1c. Proteasome dysfunction, directly and via insulin resistance, increases total and nuclear FoxO1 that enhances hepatic gluconeogenesis.



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