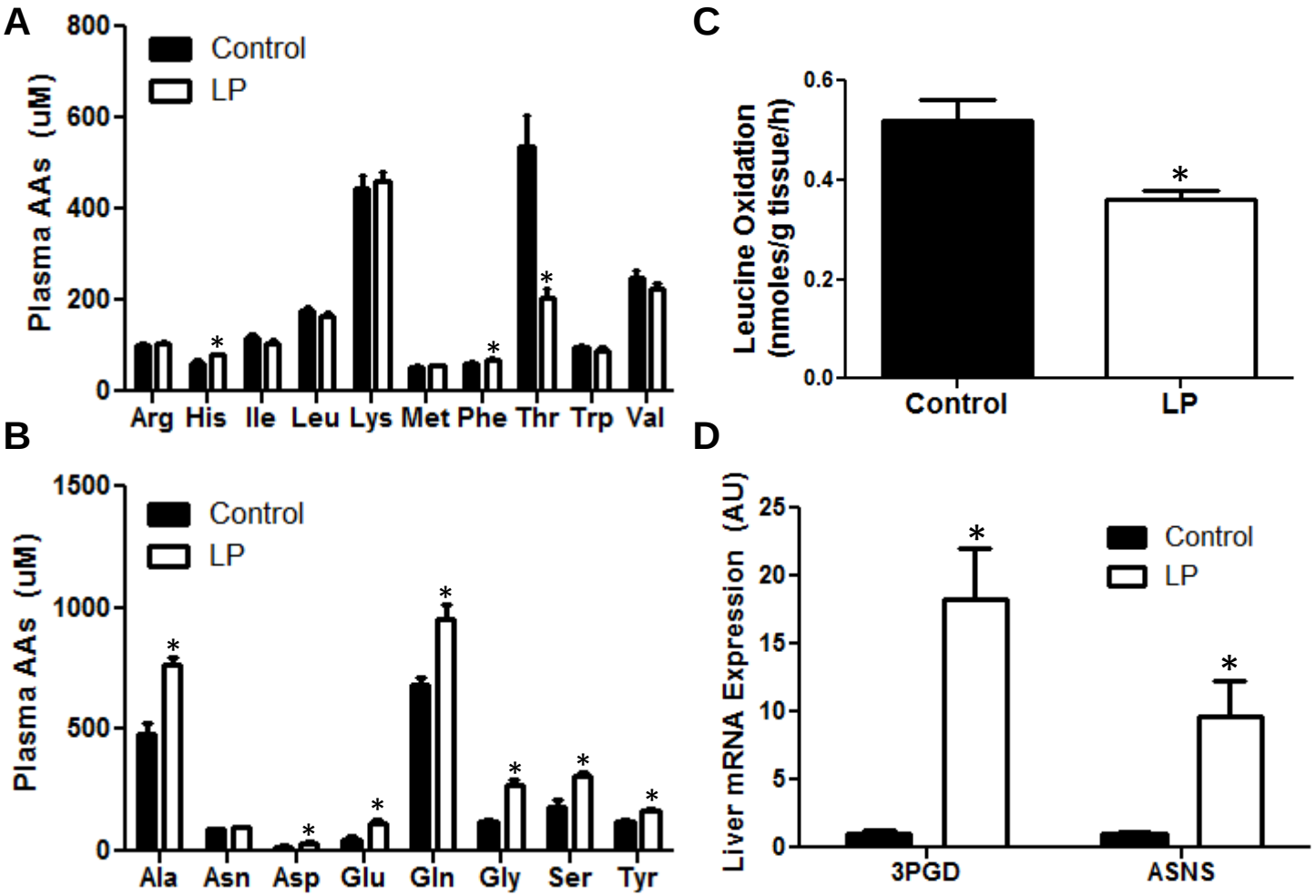

Figure S1. Effect of dietary protein restriction on hepatic amino acid metabolism in rats. Exposure to the LP diet for 14 days altered plasma concentrations of essential (**A**) and nonessential (**B**) amino acids, while also reducing hepatic leucine oxidation (**C**) and increasing hepatic mRNA expression of the amino acid biosynthetic enzymes 3-phosphoglycerate dehydrogenase (3PGD) and asparagine synthetase (ASNS, **D**). n=8/group. *P< 0.05 vs. Control.

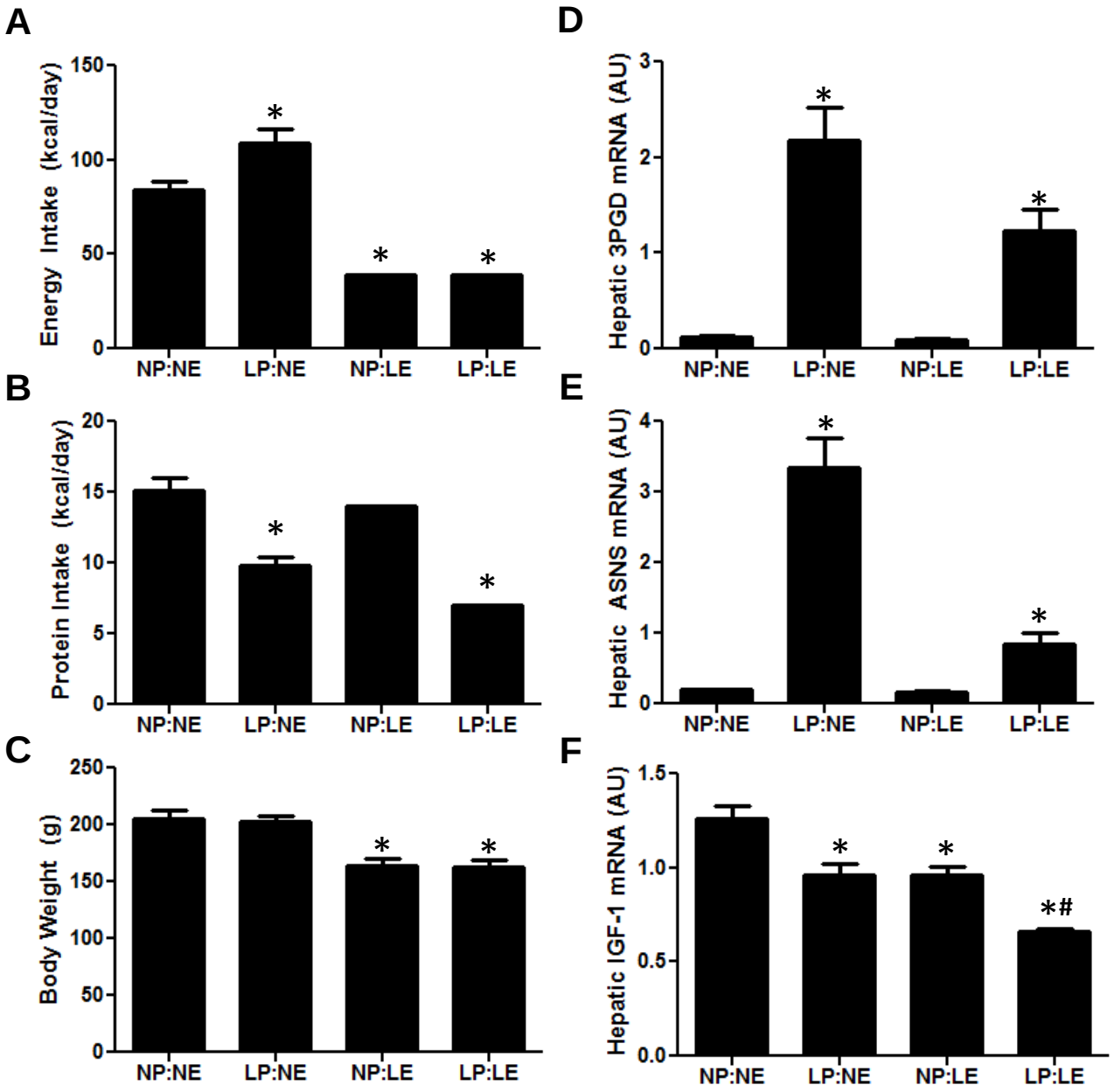

Figure S2. Differential effect of energy vs. protein restriction in rats. Energy Intake (**A**), protein intake (**B**) and body weight (**C**) in rats restricted for either energy or protein intake for 4 days. Expression of the hepatic amino acid biosynthetic enzymes 3-phosphoglycerate dehydrogenase (3PGD, **D**), and asparagine synthetase (ASNS, **E**), as well as hepatic IGF-1 mRNA (**F**) in these rats. n=5/group. *P< 0.05 vs. Control.

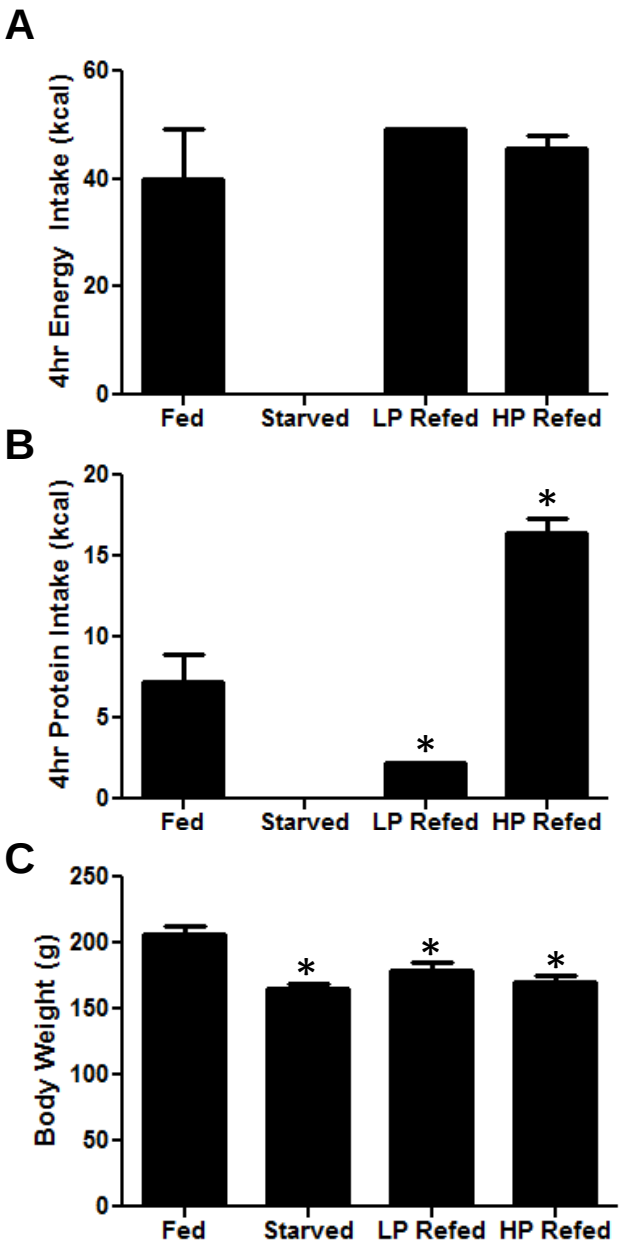

Figure S3. Food intake and body weight in starved and refed rats. Energy intake (**A**) and protein intake (**B**) over the 4hrs of LP or HP refeeding in rats following 48hrs of food deprivation. Final body weight at sacrifice (**C**). n=5/group. *P< 0.05 vs. Control.

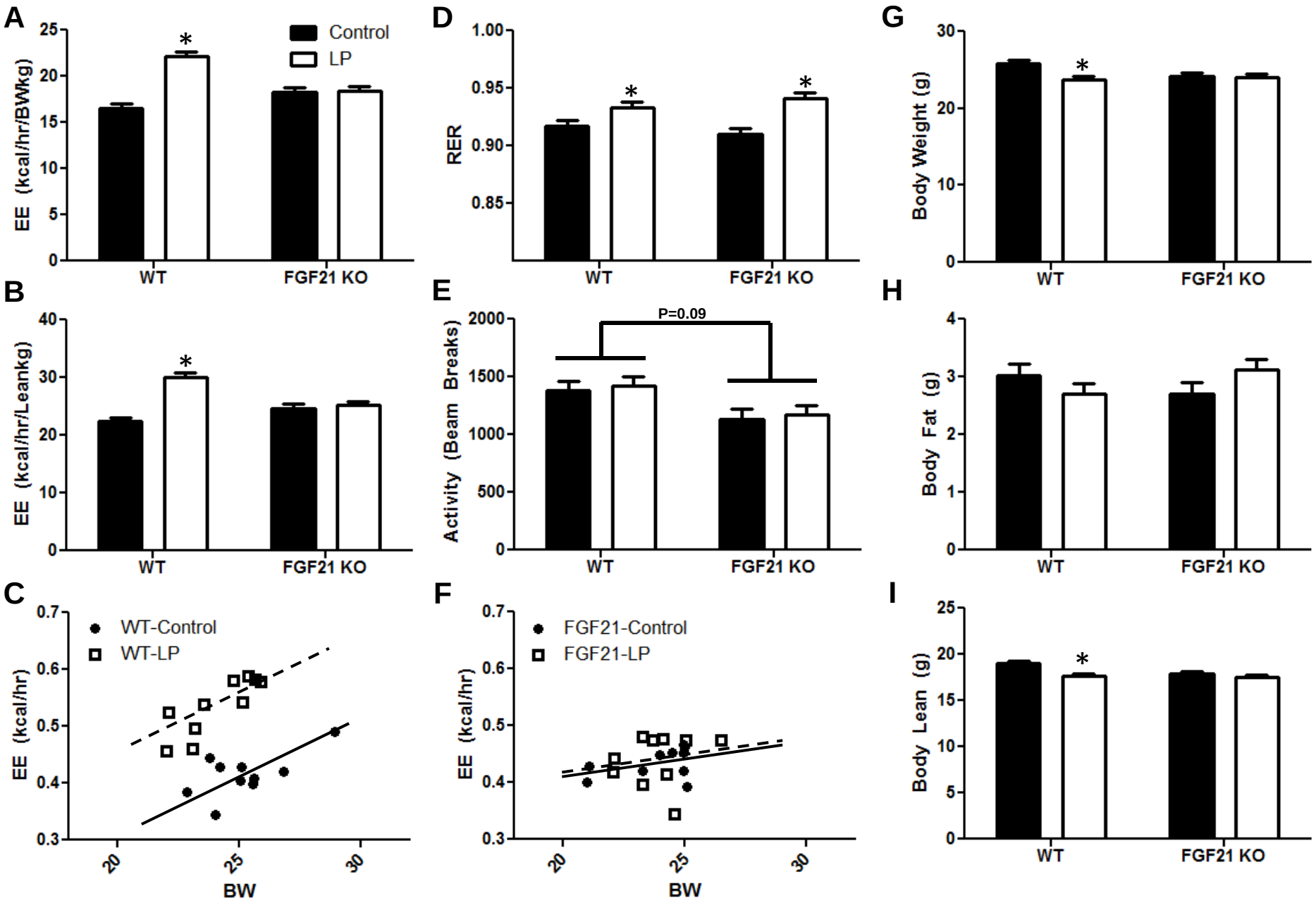

Figure S4. Energy expenditure, RER, physical activity and final body weight and composition in wild-type and FGF21 KO mice on LP. Energy expenditure normalized to body weight (**A**), energy expenditure normalized to lean mass (**B**), respiratory exchange ratio (RER, **D**) activity (**E**) in wild-type and FGF21 mice consuming control or LP diet. Scatter plots illustrating the relationship between body weight and EE, based on ANCOVA, in wildtype (**C**) and FGF21 KO (**F**) mice. Final body weight (**G**), body fat (**H**) and body lean mass (**I**). n=10/group. *P<0.05 vs. Control.

Table S1: Composition of diets

Ingredient (g)	Mouse LP 5% Casein	Rat LP 10% Casein	Control 20% Casein	HP 40% Casein	KD BioServ:#F3666
Casein	51	101	200	400	95
L-Cystine	0.8	1.5	3.0	6	
Corn Starch	492	445	375	232	
Maltodextrin 10	152	152	125	73	7.6
Sucrose	109	108	107	104	
Cellulose	51	51	50	49	50
Soybean Oil	25	25	25	24	114*
Lard	76	76	75	73	475/199.5**
Mineral Mix S10022C	3.6	3.5	3.5	3.4	38
Calcium Carbonate	8.8	10.1	12.5	11.9	
Calcium Phosphate Dibasic	5.4	3.5	0.0	0.0	
Potassium Citrate	2.5	2.5	2.5	7.8	
Potassium Phosphate, Monobasic	7.0	6.9	6.9	0.0	
Sodium Chloride	2.6	2.6	2.6	2.5	
Vitamin Mix V10037	10.2	10.1	10.0	9.8	20.9
Choline Bitrartrate	2.5	2.5	2.5	2.4	
FD&C Yellow Die #5	0.00	0.00	0.05	0.00	
FD&C Red Dye #40	0.05	0.05	0.00	0.00	
FD&C Blue Dye #1	0.00	0.00	0.00	0.05	
Kcals/gram	4.1	4.1	4.1	4.1	7.24
Protein (gm%)	5	9	18	36	9
Carbohydrate (gm%)	76	71	62	42	3
Fat (gm%)	10	10	10	10	75
Protein (kcal%)	4	9	18	36	5
Carbohydrate (kcal%)	74	69	60	42	2
Fat (kcal%)	22	22	22	22	93

*KD uses Corn Oil instead of Soybean Oil

**KD uses both Lard and Butter