Supplemental Figure 1.
The transgene construct for human ENPP1 includes aP2 promoter and c-myc-tag. This is a representative western blot with antibodies against c-myc recombinant ENPP1 protein in various tissues of a*diposeENPP1-TG* mice. The recombinant protein is present in both white adipose tissue (WAT) and brown adipose tissue (BAT) but not in other tissues, including spleen and liver which contain significant number of macrophages.

Supplemental Figure 2.
Panel A is a representative Western blot using antibodies against murine (endogenous) ENPP1 protein at 110 KDa in **muscle** of *adiposeENPP1-TG* mice and wild-type littermate exposed to 12 weeks 60% fat diet with pair-feeding protocol. The optical density is expressed in arbitrary units (AU) as mean and SD for each study group.
Panel B is a representative Western blot for total and phospho-insulin receptor$_{\text{Tyr 1361}}$ (95 KDa) of liver and **panel C** is a representative Western blot for total and phospho-Akt$_{\text{Ser 473}}$ (60 KDa). Tissue was collected after food withheld for 5 hours. Fasting plasma insulin concentrations, at the time of adipose tissue collection, are also shown in panels B and C.

Supplemental Figure 3.
RT-PCR was performed in epididymal adipose tissue samples from 8 *adiposeENPP1-TG* and 7 wild-type littermate exposed to 12 weeks 60% fat diet with pair-feeding protocol. Results are reported as delta ct using cyclophilin as reference gene.

Supplemental Table 1. *AdiposeENPP1-TG* and wild-type littermate mice were given either regular chow diet or diet containing 60% fat without food quantity restrictions ("**ad lib**"). Each animal (n=5 for each group) was weighed at different intervals. The results are reported as group means and SD for each dietary period. Week indicate the number of weeks from diet initiation. All mice were 10 weeks old when started on specific diet. Student t-test was used for comparison within each diet group.

	Regular chow diet ("ad lib")		
	Wild-type	***AdiposeENPP1-TG***	p-value
Weight at week 8 (g)	26.6 ± 1.6	25.9 ± 0.6	0.3
Weight at week 16 (g)	31.4 ± 2.8	27.2 ± 2.3	0.08
Weight at week 24 (g)	37.3 ± 2.9	33.9 ± 2.5	0.2
Food intake at week 8 (g)	3.9 ± 0.1	3.8 ± 0.08	0.8
Food intake at week 16 (g)	4.0 ± 0.2	3.9 ± 0.1	0.6
Food intake at week 24 (g)	3.8 ± 0.1	3.6 ± 0.2	0.3
	60% fat diet ("ad lib")		
	Wild-type	***AdiposeENPP1-TG***	p-value
Weight at week 8 (g)	26.9 ± 0.7	27.1 ± 1.4	0.7
Weight at week 16 (g)	41.4 ± 6.8	36.5 ± 3.6	0.09
Weight at week 24 (g)	48.4 ± 5.8	42.2 ± 5.2	0.02
Food intake at week 8 (g)	2.8 ± 0.5	2.0 ± 0.2	0.0007
Food intake at week 16 (g)	2.8 ± 0.3	2.2 ± 0.4	0.002
Food intake at week 24 (g)	2.5 ± 0.07	1.9 ± 2.5	<0.0001

Supplemental Table 2. A group of *AdiposeENPP1-TG* (n=5) and a group of wild-type littermate mice (n=5) underwent metabolic cage studies during last week of 14 weeks feeding with 60% fat diet using **pair-feeding** protocol. Body fat was measured using MRI after 5 hours fasting and soon before dissection for measurements of other organs at age 24 weeks.

AdiposeENPP1-TG	**Wild-type mice**	**p-value**	
Body Weight at age20th week (g)	32.3±2.4	32.0±2.4	NS
Total Body Fat at age 20th week (% body weight)	26.5±3.3	26.2±6.3	NS
Epididymal Fat Weight (g)	1.4±0.3	1.6±0.5	NS
Liver Weight (g)	1.09±0.10	1.09±0.13	NS
Heart Weight (g)	0.17±0.02	0.17±0.02	NS
Kidney Weight(g)	0.33±0.03	0.35±0.02	NS
Food intake (g/body weight)	0.18±0.02	0.17±0.02	NS
Oxygen consumption (ml/hr/kg)	1363±105	1445±306	NS
Respiratory exchange rate (RER)	0.95±0.00	0.96±0.01	NS
Total locomotion (ambulatory and rearing)	5364±1716	4933±1343	NS