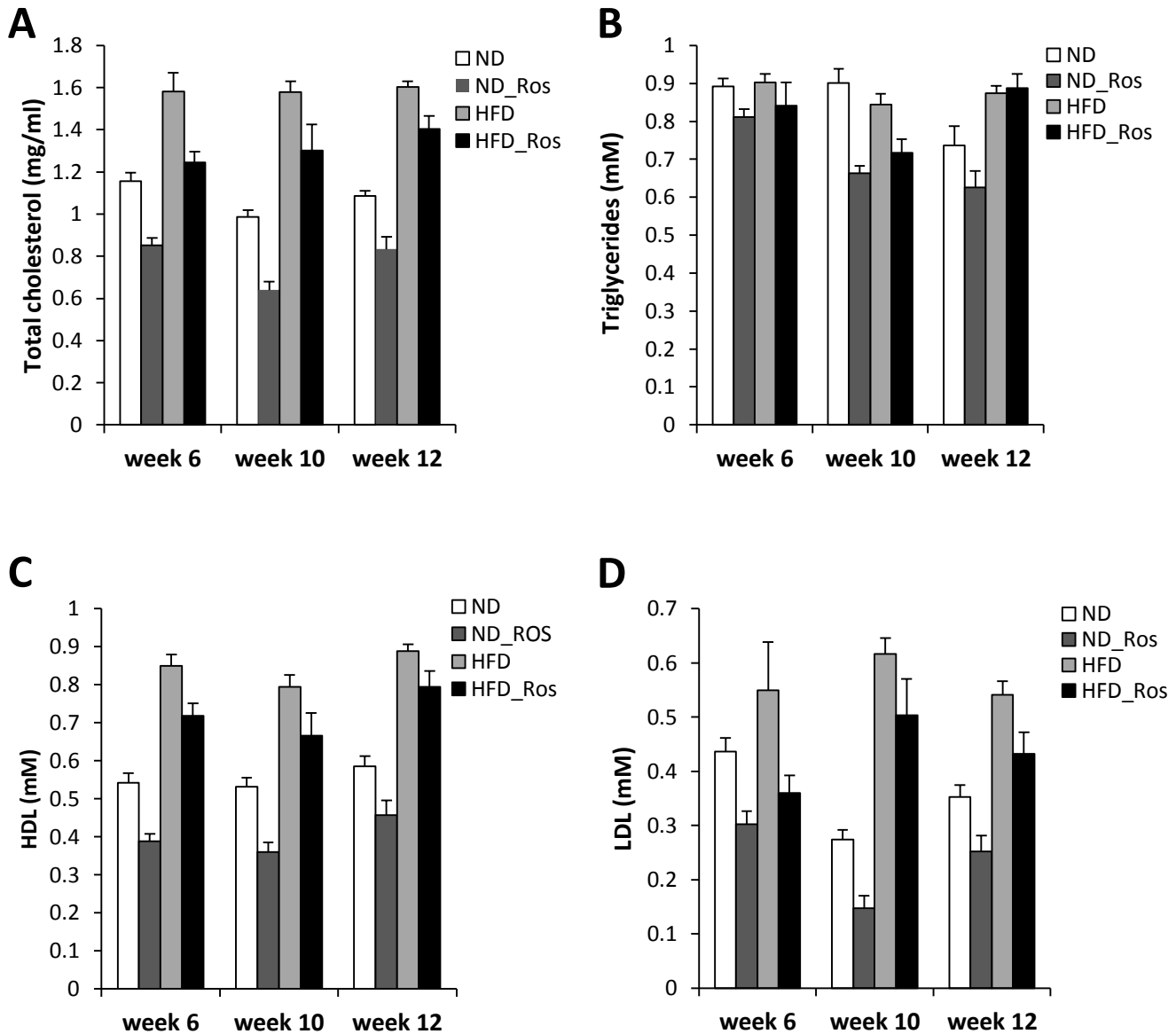
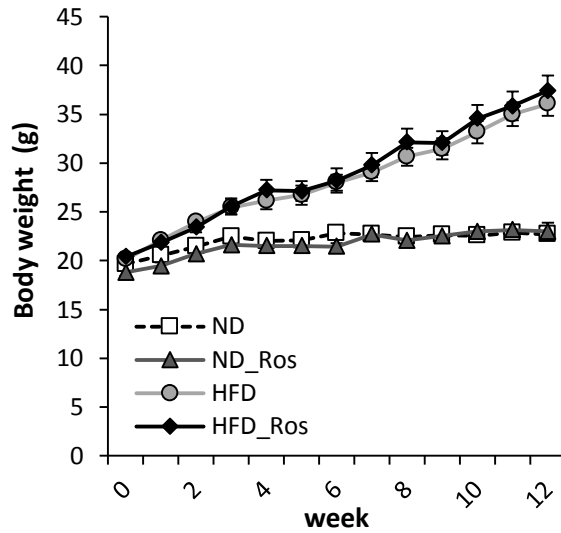
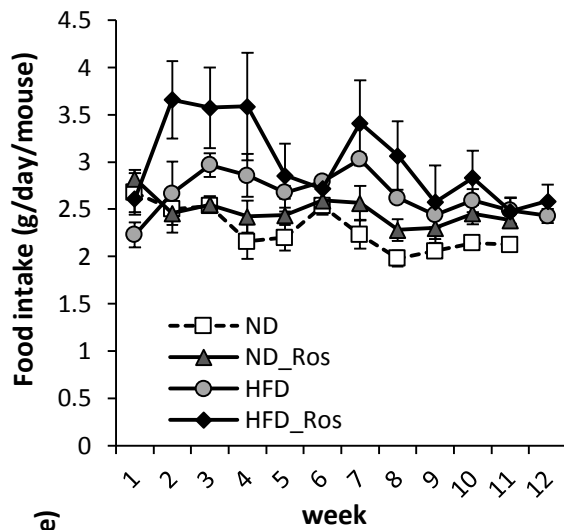
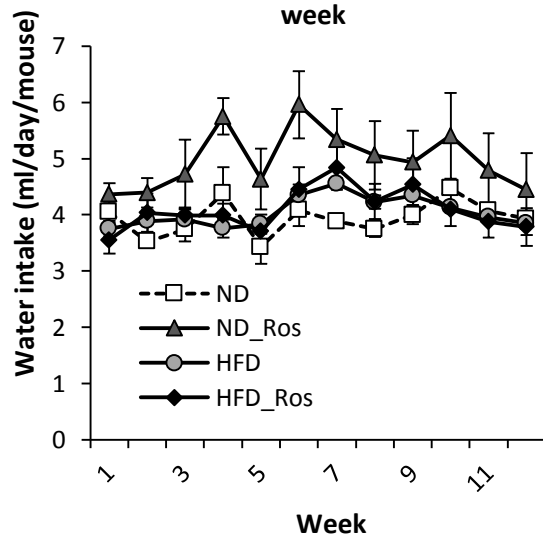


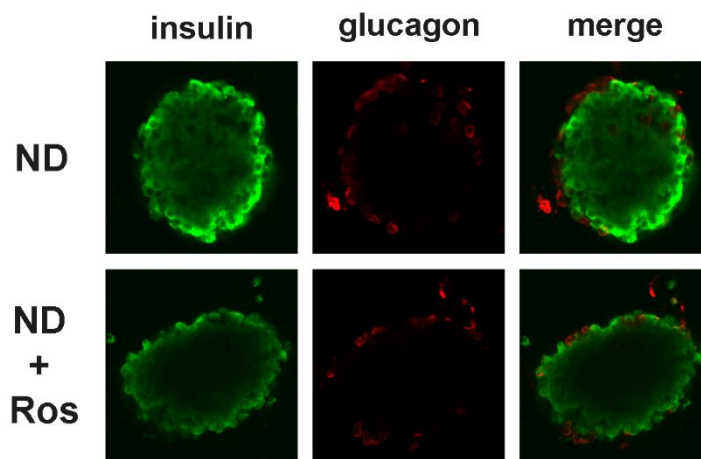
**Figure S1. Description of the Study design.** Yellow arrows – measurement of weight and food and water intake. Black arrow – indicate start of diet and treatment as indicated as well as time for OGTT (oral glucose tolerance test) and termination of the in vivo study. Red arrows- blood samples to measure lipids. ND-normal diet, ND\_Ros-normal diet with rosuvastatin, HFD-high fat diet, HFD\_Ros- high fat diet with rosuvastatin.



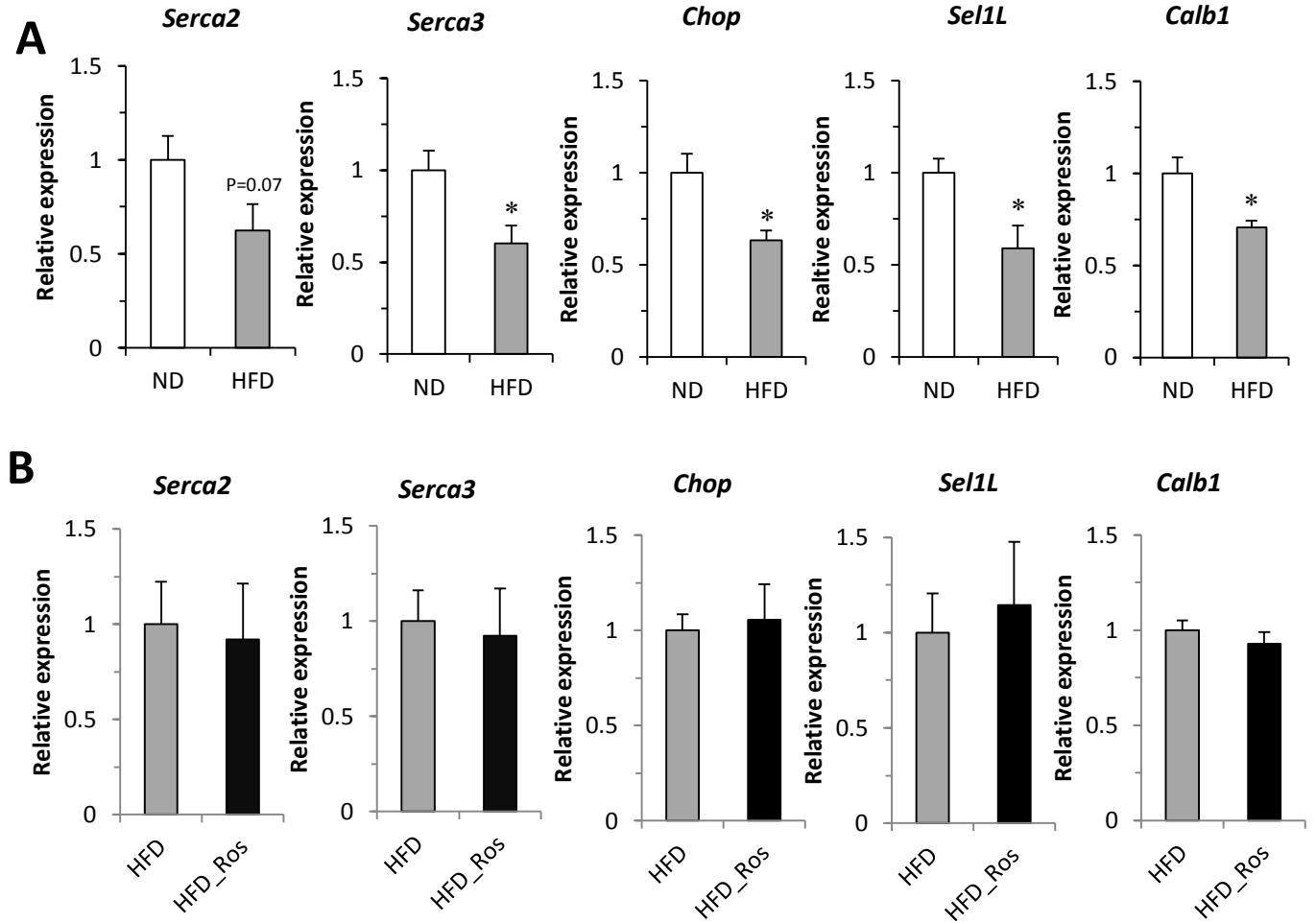
**Figure S2. Measurements of total cholesterol, triglycerides and HDL and estimates of LDL.** (A) Total cholesterol measured in blood from ND, ND\_Ros, HFD and HFD\_Ros mice as indicated. All values HFD vs ND, ND\_Ros vs ND and HFD\_Ros vs HFD has  $p < 0.001$  except 6 week HFD\_Ros vs HFD where  $p < 0.02$ . (B) As in A but triglycerides were. N:S HFD vs ND;  $p < 0.01$  ND\_Ros vs ND and HFD\_Ros vs HFD except 12 week ND\_Ros vs ND where  $p = 0.06$ . (C) As in A, but HDL was measured.  $P < 0.05$  HFD vs ND,  $p < 0.01$  ND\_Ros vs ND and  $p < 0.05$  HFD\_Ros vs HFD. N=13-15 mice.

**A****B****C****Figure S3. Effect of rosuvastatin on body weight, food and water intake**

Mice were fed normal diet or HFD for 4 week and then continued on respective diets with or without rosuvastatin in the drinking water for 8 week. A) Weight gain, B) food intake and C) water intake were measured every week throughout the study. N=13-15 mice.



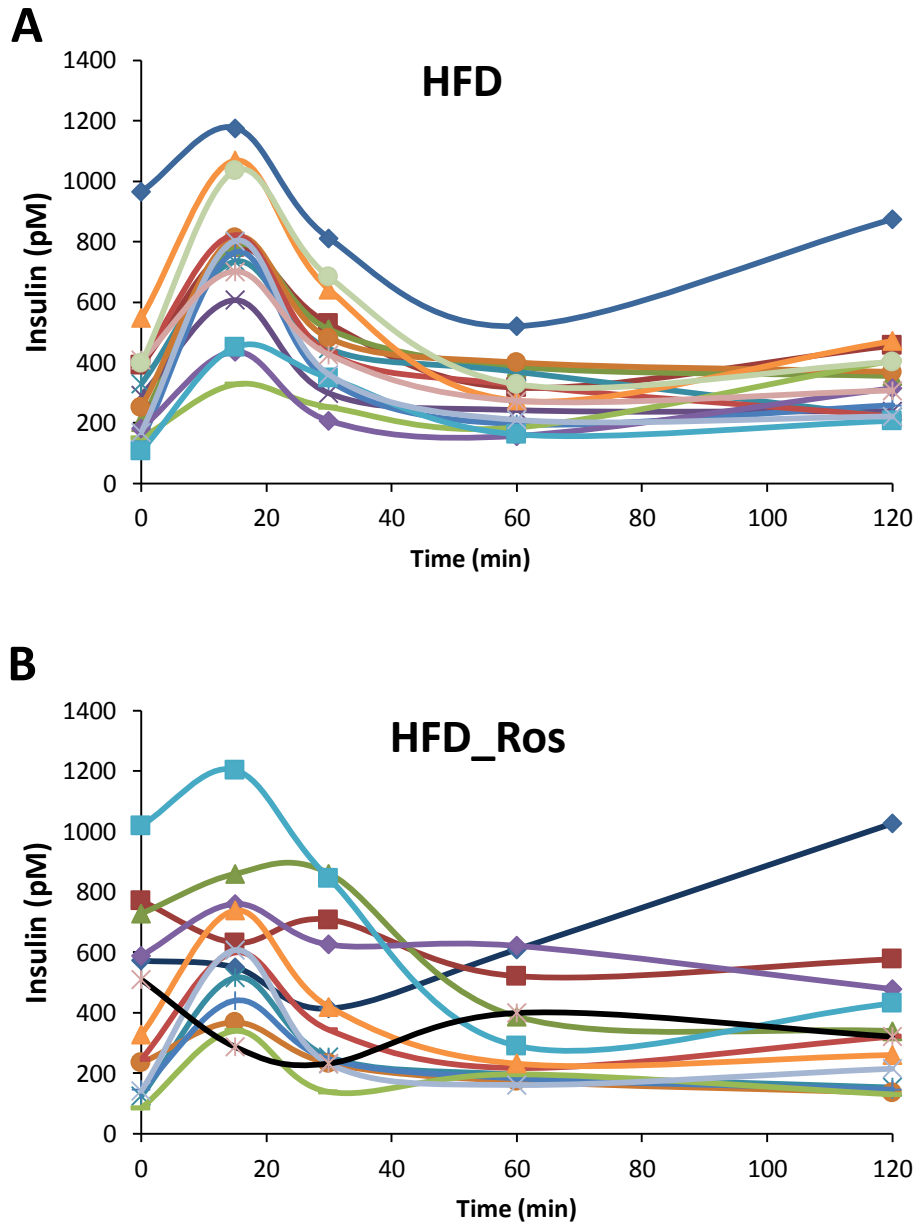
**Figure S4. Confocal images of insulin and glucagon staining in islet from ND mice.** Insulin (green) and glucagon (red) staining in an islet from a mice on ND in the absence (top) and presence (bottom) of rosuvastatin treatment. Representative image of N=12-14 islets in each group.



**Figure S5. Expression of ER and Ca<sup>2+</sup> associated proteins in islets of ND and HFD mice.**

(A) Expression of SERCA2, SERCA3, Sel1L, CHOP and Calb1 in islet from mice on HFD vs ND.

\*p<0.05 HFD vs ND. (B) As in A, but comparing the expression in islets from HFD mice with and without Rosuvastatin. \*p<0.05 HFD\_Ros vs HFD.



**Figure S6. Insulin response during OGTT in HFD mice with or without rosuvastatin treatment.** (A) All individual insulin responses during OGTT in HFD mice. (B) All individual insulin responses during OGTT in HFD rosuvastatin mice. Notice the variable responses in the HFD\_Ros group.

Parameter	$A_d$ Initial dip area (AU)		$A_t$ Total area under graph (AU)		Frequency of 2nd phase oscillations (peaks/min)		$C_0$ Fura2 (340/380)		$D_0$ - Delay response to 16.7mM glucose (min)		$D_1$ - Delay response to 2.8mM glucose (min)	
	Control	RS	Control	RS	Control	RS	Control	RS	Control	RS	Control	RS
Mean	3938	2386	18707 3	23914 6	1.05	1.07	0.030	0.024	4.11	6.43	1.61	2.25
SEM	234	229	9211	21426	0.31	0.20	0.001	0.001	0.19	0.34	0.12	0.21
p-value	2.30E-05		0.018		0.96		7.74E-04		8.90E-08		7.86E-03	

Parameter	$C_1$ - Fura2 (340/380)		$C_2$ - Fura2 (340/380)		$C_3$ - Fura2 (340/380)		$C_4$ - Fura2 (340/380)		$C_1/C_4$	
	Control	RS	Control	RS	Control	RS	Control	RS	Control	RS
Mean	0.47	0.52	0.44	0.24	0.08	0.16	0.39	0.36	1.21	1.45
SEM	0.03	0.04	0.04	0.02	0.01	0.02	0.03	0.03	0.04	0.05
p-value	0.32		2.03E-04		2.01E-04		0.42		7.64E-04	

**Supplementary Table 1 - Calcium Imaging of islets from C57BL/6 mice fed normal Chow diet and treated with Rosuvastatin for 8 weeks**

**Summary Statistics :**  $A_d$  – Area of initial dip in calcium before the first calcium peak (below baseline);  $A_t$  – Total area under the graph;  $C_0$  – height of dip in calcium before the first calcium peak;  $D_0$  - delay response to 16.7 mM glucose;  $D_1$  – delay response to 2.8 mM glucose;  $C_1$  – height of first calcium peak (from baseline) ;  $C_2$  - measure of  $Ca^{2+}$  exit between 1<sup>st</sup> and 2<sup>nd</sup> Phase (difference between top of first peak and the following trough);  $C_3$  – difference between the top of the first peak and the midpoint of 2<sup>nd</sup> phase oscillations;  $C_4$  – mean height of 2<sup>nd</sup> phase oscillation (from baseline).