Supplemental Figure 1. Body weight changes in individual mice. Changes in body weight in individual mice fed the HFD group and treated with (A) BSA treated, (B) 2 μg/kg IL-25 administered 3 times per week for 21 days, and (C) 5 μg/kg IL-25 administered 3 times per week for 21 days. The numbers indicate the Mean±SEM before and after treatment.

Supplemental Figure 2. **Changes in tissue weights in response to IL-25 therapy.** At euthanasia organs were harvested and weighed. (A) liver weight (g), and (B) epididymal fat weight expressed as percent of body weight, (C) subcutaneous fat weight expressed as percent of body weight, (D) spleen weight expressed as percent of body weight. *p<0.05 and ** p<0.01 vs NCD, ф p<0.05 and ф ф p<0.01 vs BSA treated HFD, n=7-8.

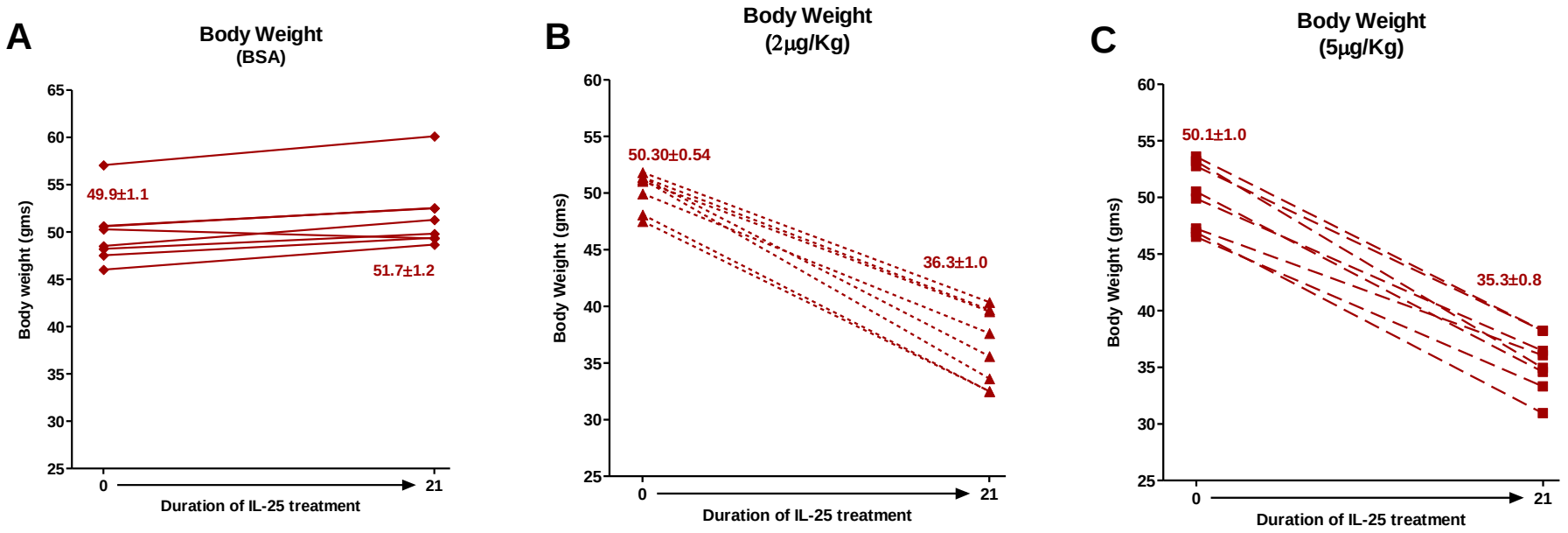
Supplemental Figure 3. Changes in fasting blood glucose levels in individual mice. HFD fed mice were treated with (A) BSA, (B) 2 μg/kg IL-25 administered 3 times per week for 21 days, or (C) 5 μg/kg IL-25 administered 3 times per week for 21 days. The numbers indicate the Mean±SEM before and after treatment.

Supplemental Figure 4. Effect of IL-25 treatment on SGLT1 and GLUT 2 expression in the small intestine from WT and ob/ob mice. WT or ob/ob mice were treated with BSA or IL-25 (5 ug/kg) for 21 days and the expression of SGLT1 and GLUT2 in the small intestine measured. Mean±SEM, *p<0.05, n=5.

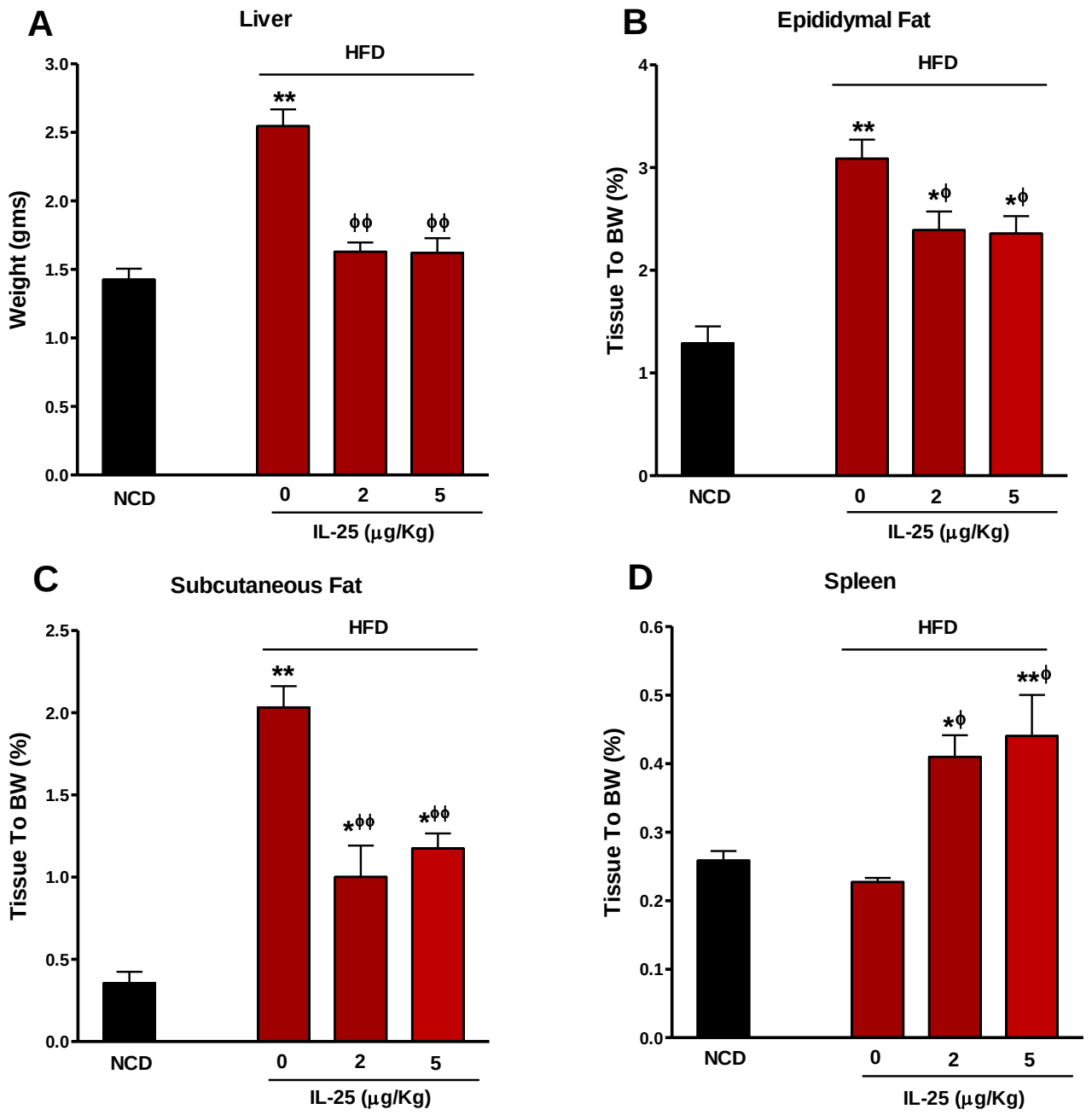
Supplemental Figure 5. Effects of IL-25 on transepithelial resistance (TEER) in HFD-induced obesity and ob/ob mice. Muscle-free sections of small intestinal mucosae were taken from mice fed the NCD, the HFD and treated with IL-25, panel A, or ob/ob mice treated with IL-25, panel B and mounted in modified microsnapwells to determine changes transepithelial electrical resistance (TEER), Mean±SEM, n=5, **p<0.01 vs NCD panel A and BSA treated, panel B.

Supplemental Figure 6. Schematic summarizing the effect of IL-25 therapy on obesity-induced type 2 diabetes. High fat diet (HFD) or genetically (Ob/Ob) induced obesity is associated with development of Type 2 diabetes (T2D) and the metabolic syndrome that is characterized by hyperglycemia, hepatic steatosis, enteropathy, and the presence of proinflammatory macrophages (M1) and CD4+ T cells (Th1/Th17). Therapeutic administration of the anti-inflammatory cytokine IL-25 has beneficial effects on glucose metabolism leading to attenuation or normalization of the T2D metabolic syndrome. Importantly, the effects of IL-25 are independent of weight loss and are maintained for a period of time after cessation of therapy.

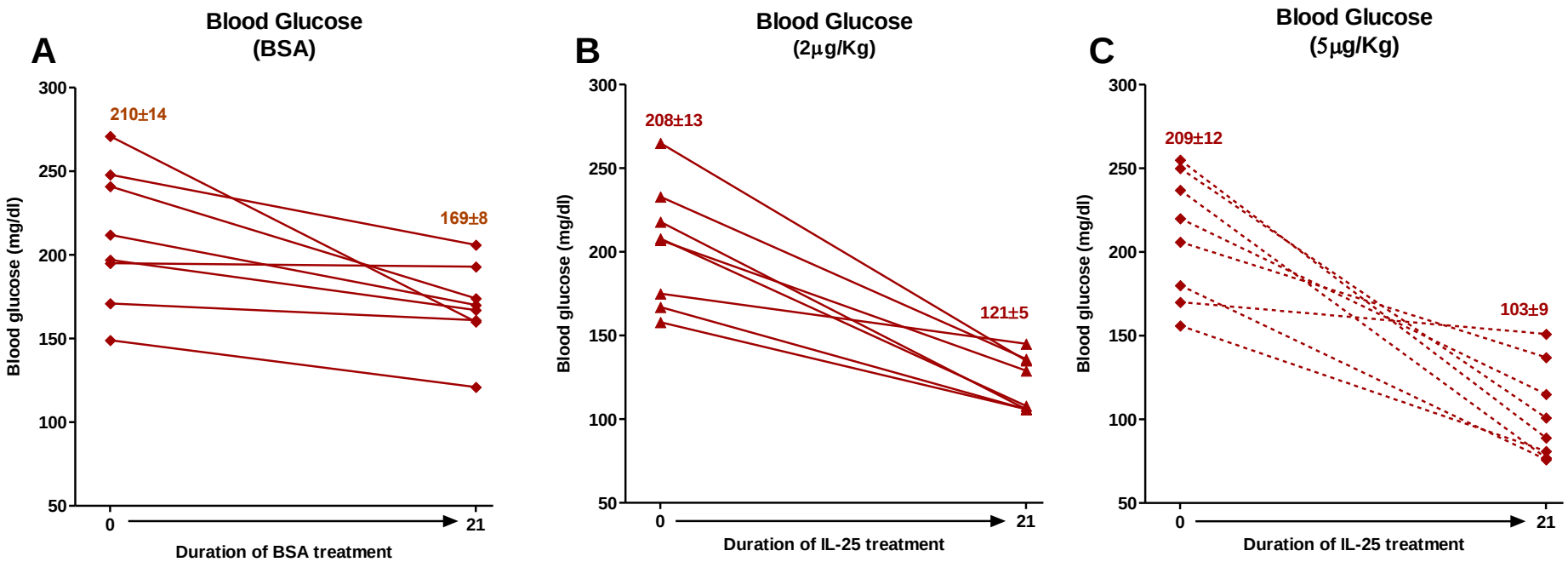
Supplemental Figure 1.



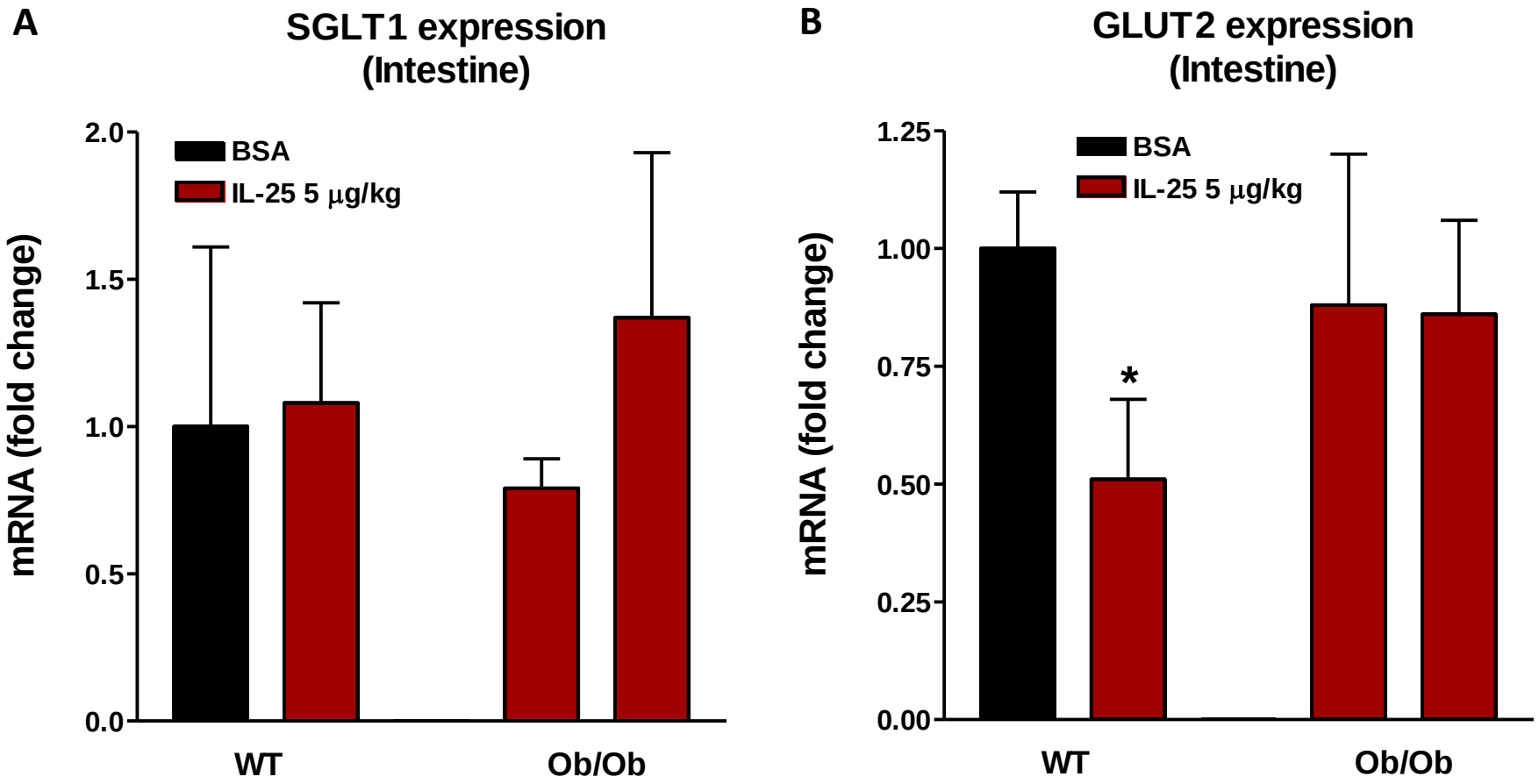
Supplemental Figure 2.



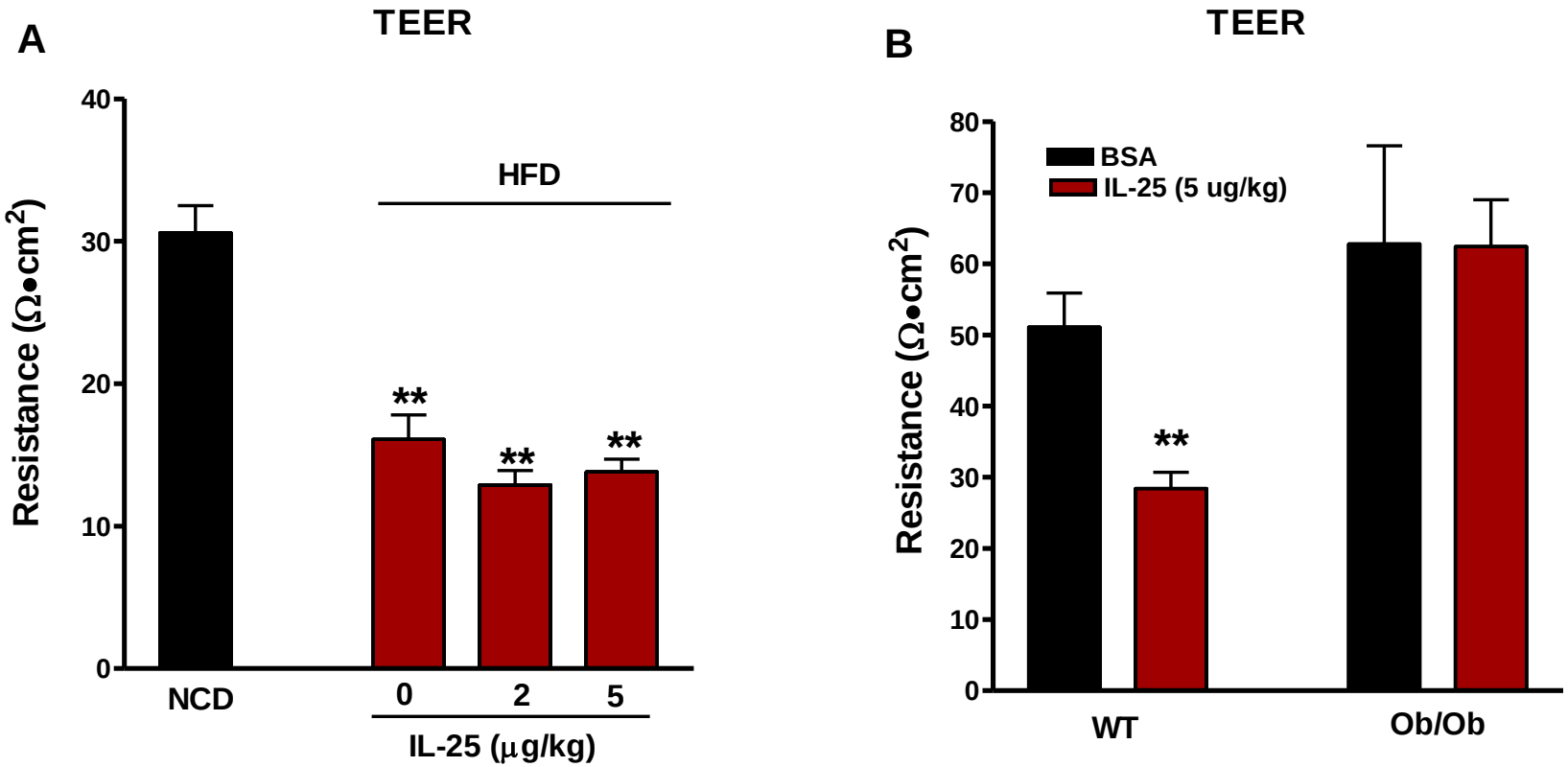
Supplemental Figure 3.



Supplemental Figure 4.



Supplemental Figure 5.



Supplemental Figure 6.