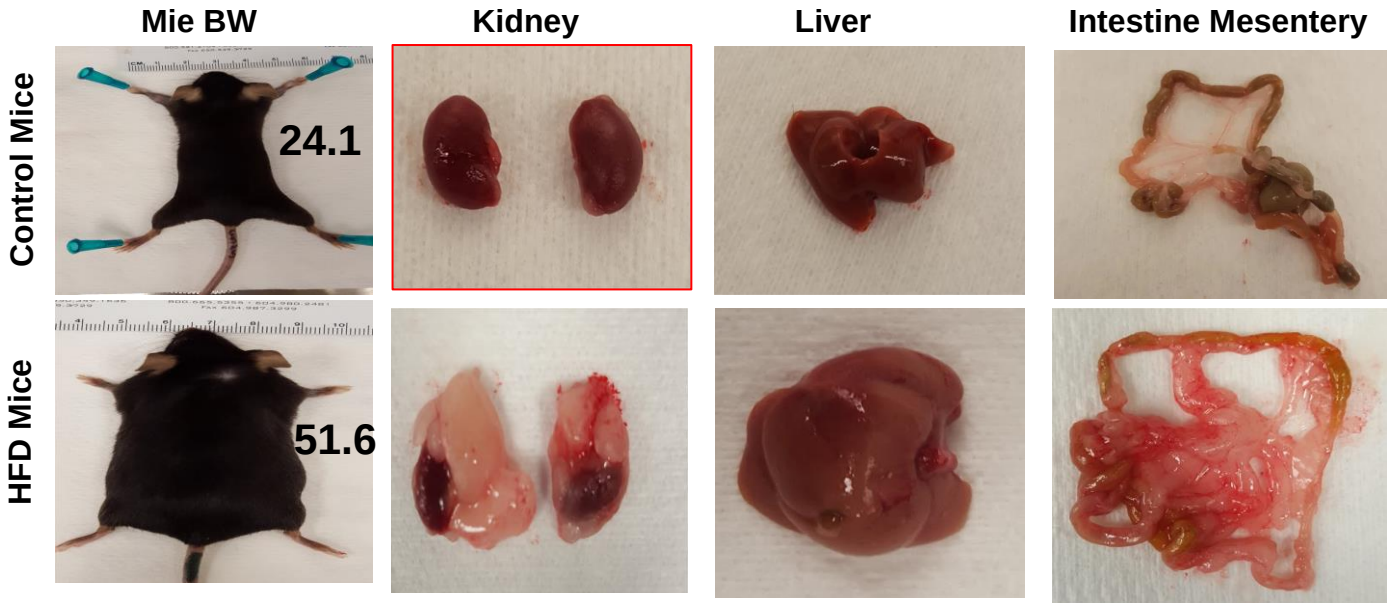
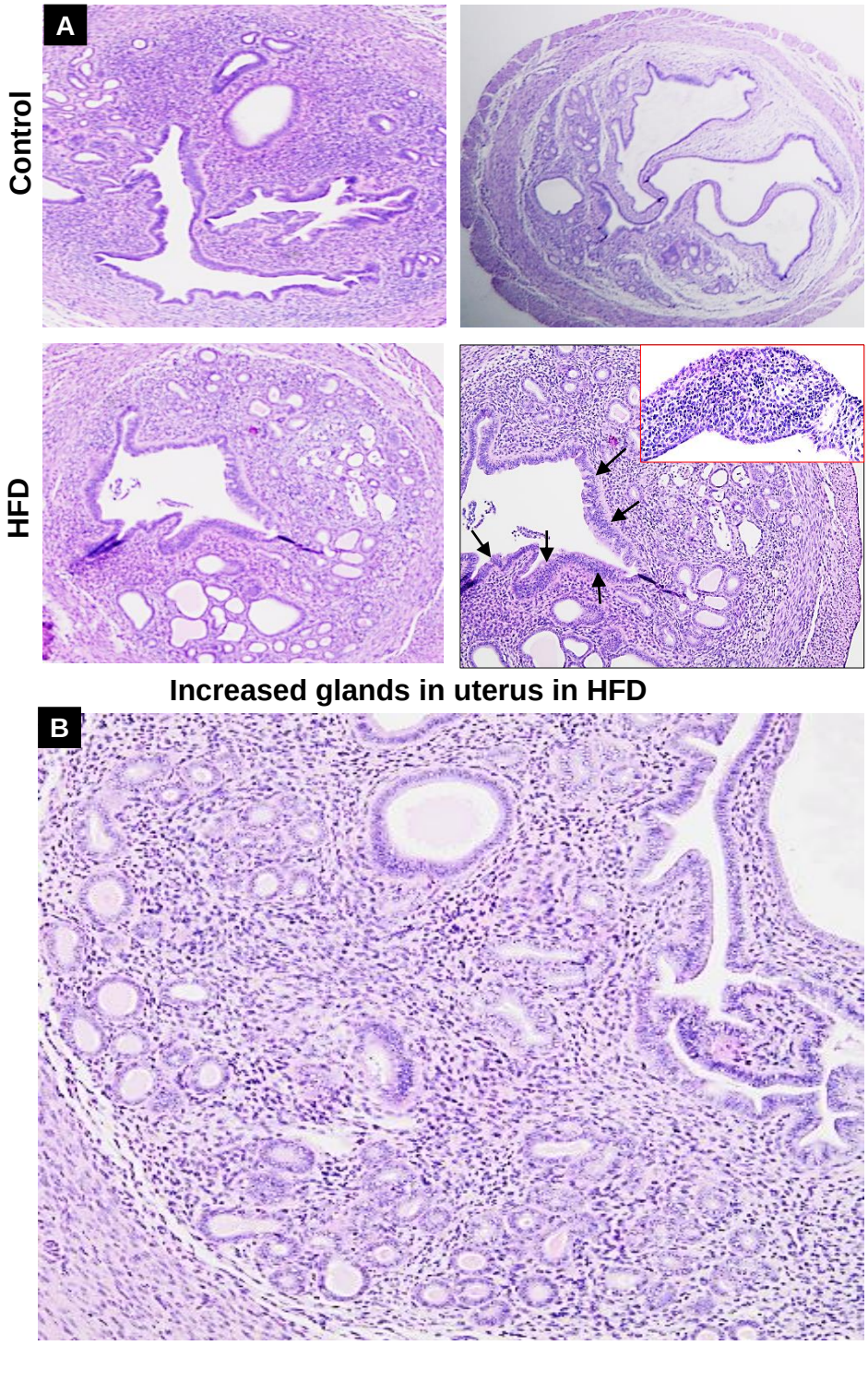
Sup Figure 1



Sup. Fig.1. Immunocompetent mice were treated with a high-fat diet (HFD, 45% protein calorie) for 24 weeks. Changes in body weight were assessed at the end (24 weeks) of the HFD treatment (n = 10/group, $p<0.05$). Representative images depict accumulated levels of adipose tissue in kidney, liver and intestine, which is enlarged in mice fed a HFD for 24 weeks.

Sup Figure 2

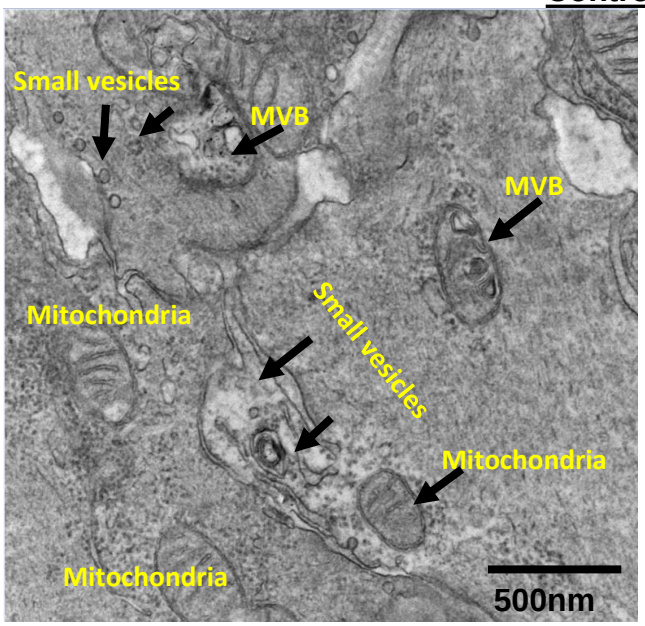


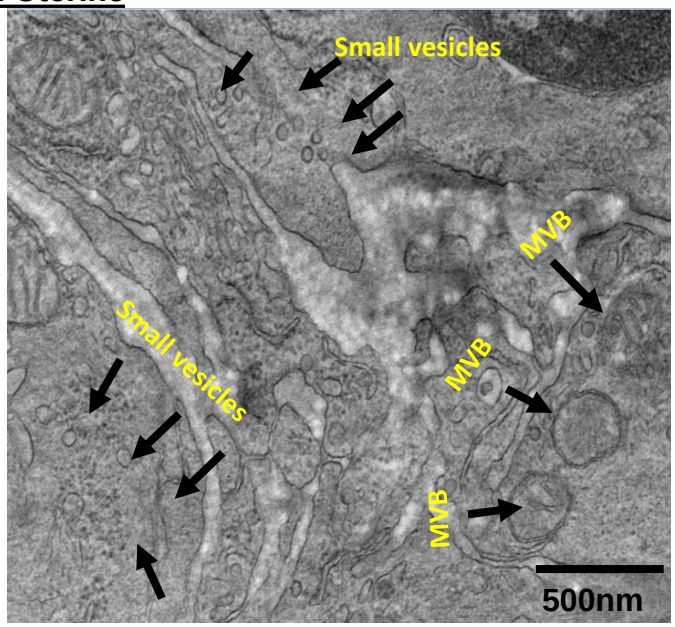
Sup. Fig. 2. A & B. Morphological changes in the uterus, which is enlarged in mice fed a HFD for 24 weeks.

Sup Figure 3

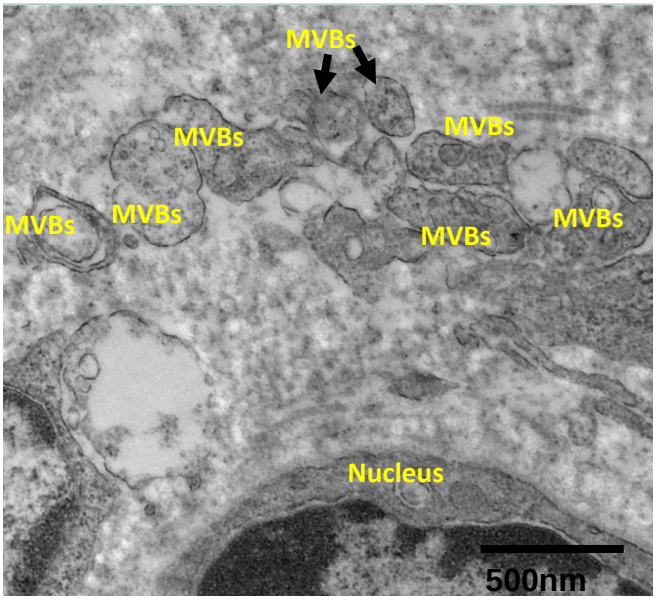
TEM Analysis of vesicles in Obese Mice Control and HFD Uterine tissues

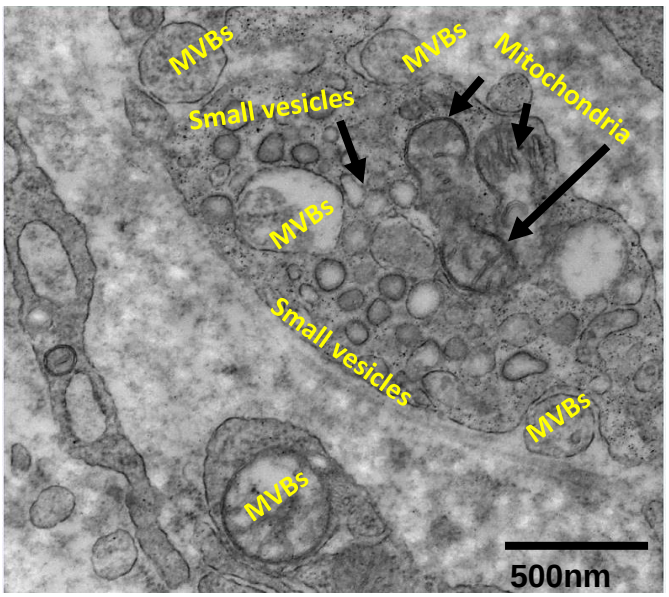
Control Uterine





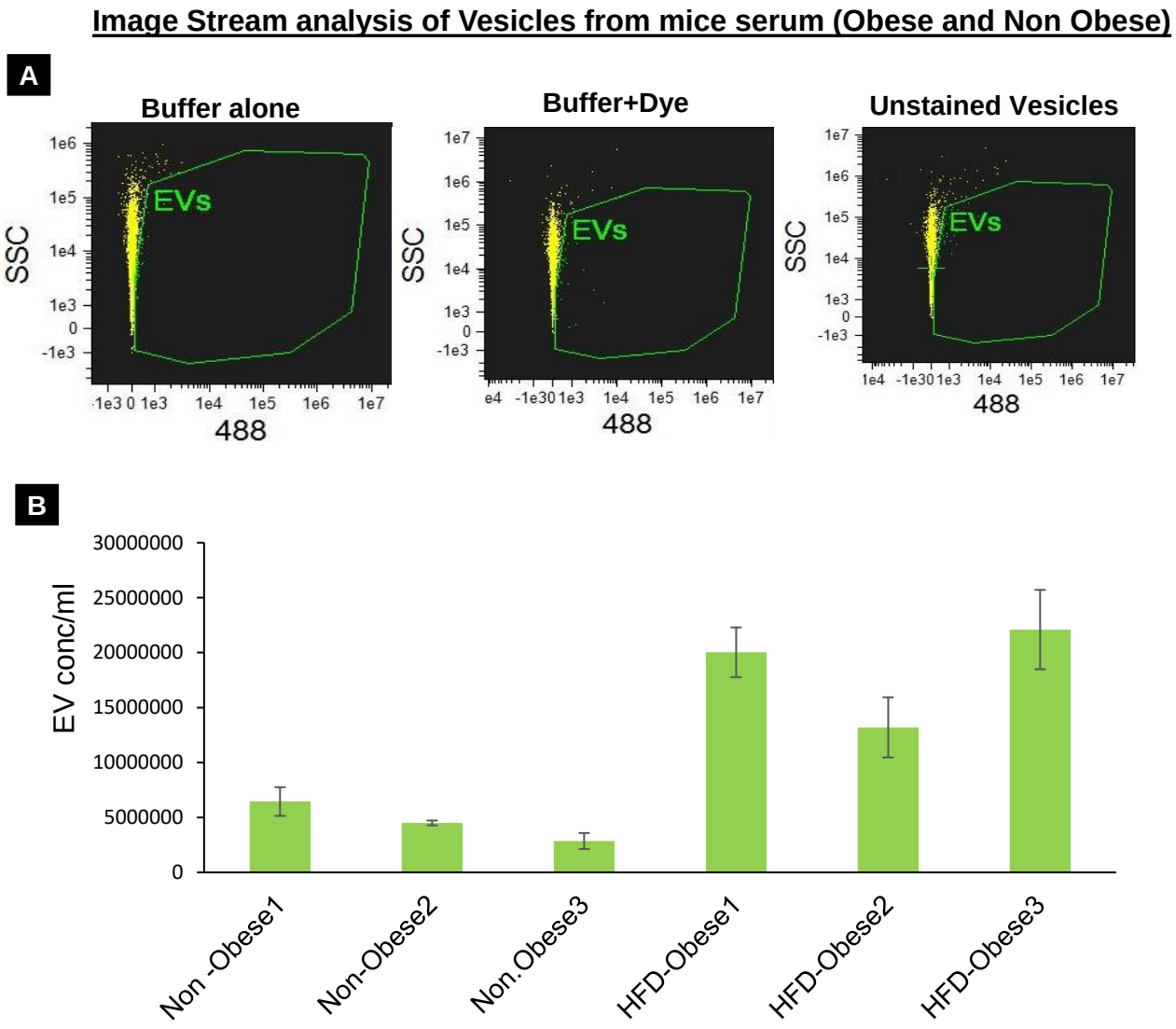
HFD Uterine





Sup. Fig. 3. Transmission Electron Microscopy (TEM) reveals increased formation of EVs in uterine tissues of high-fat diet (HFD) treated and control diet mice.

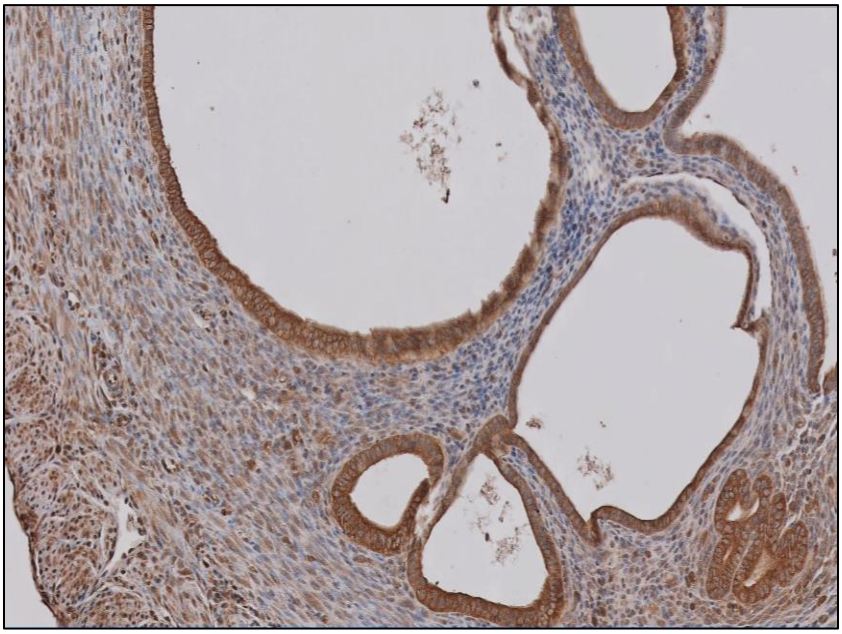
Sup Figure 4



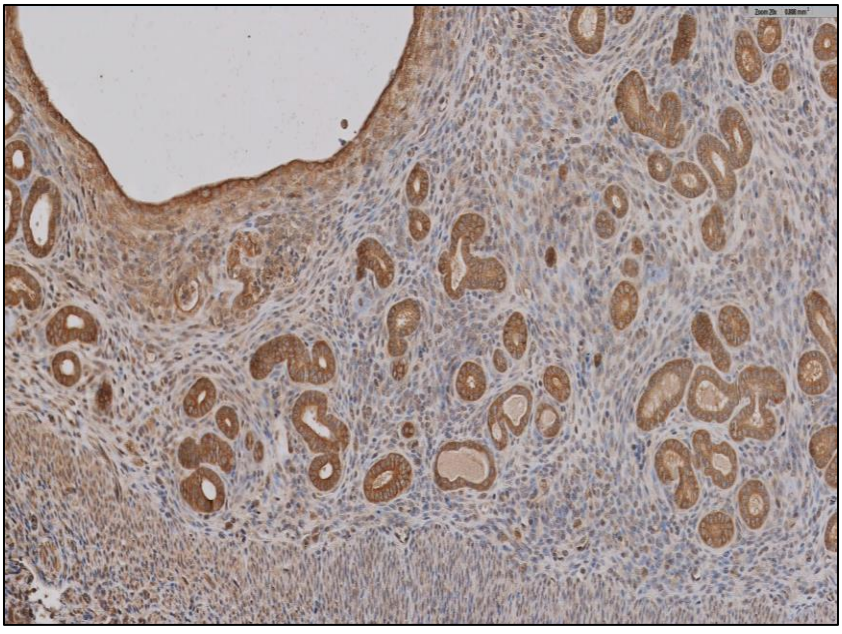
Sup. Fig. 4. A & B. EVs staining process and observed an increased formation of EVs in uterine tissues of high-fat diet (HFD) treated and control diet mice serum samples.

Sup Figure 5

Control UT PIAS3



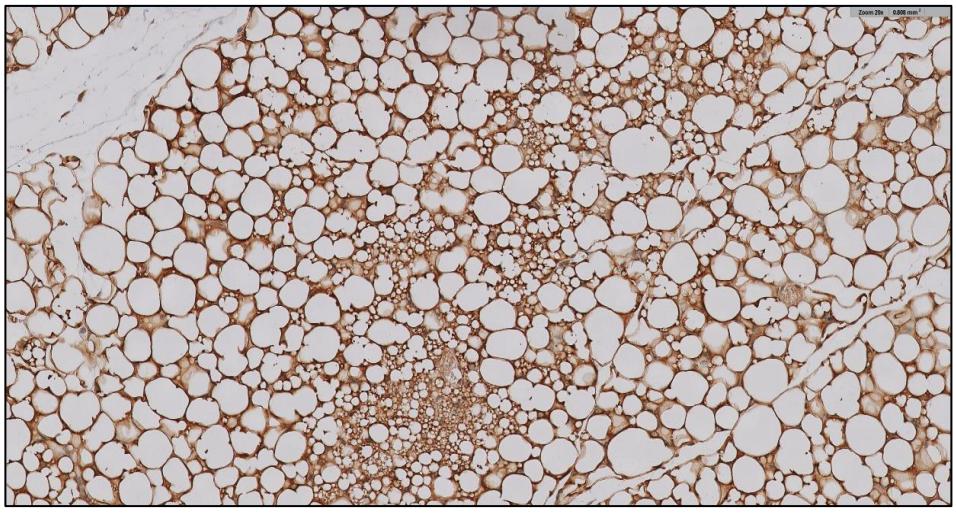
HFD UT PIAS3



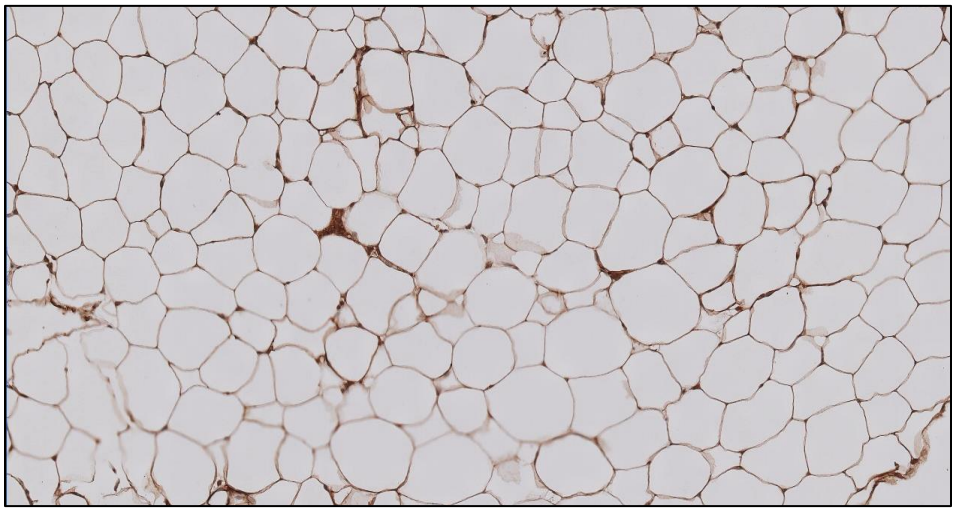
Sup. Fig. 5. PIAS3 expression alteration in HFD treated uterine tissues compared with control diet-treated mice.

Sup Figure 6

Control AT PIAS3

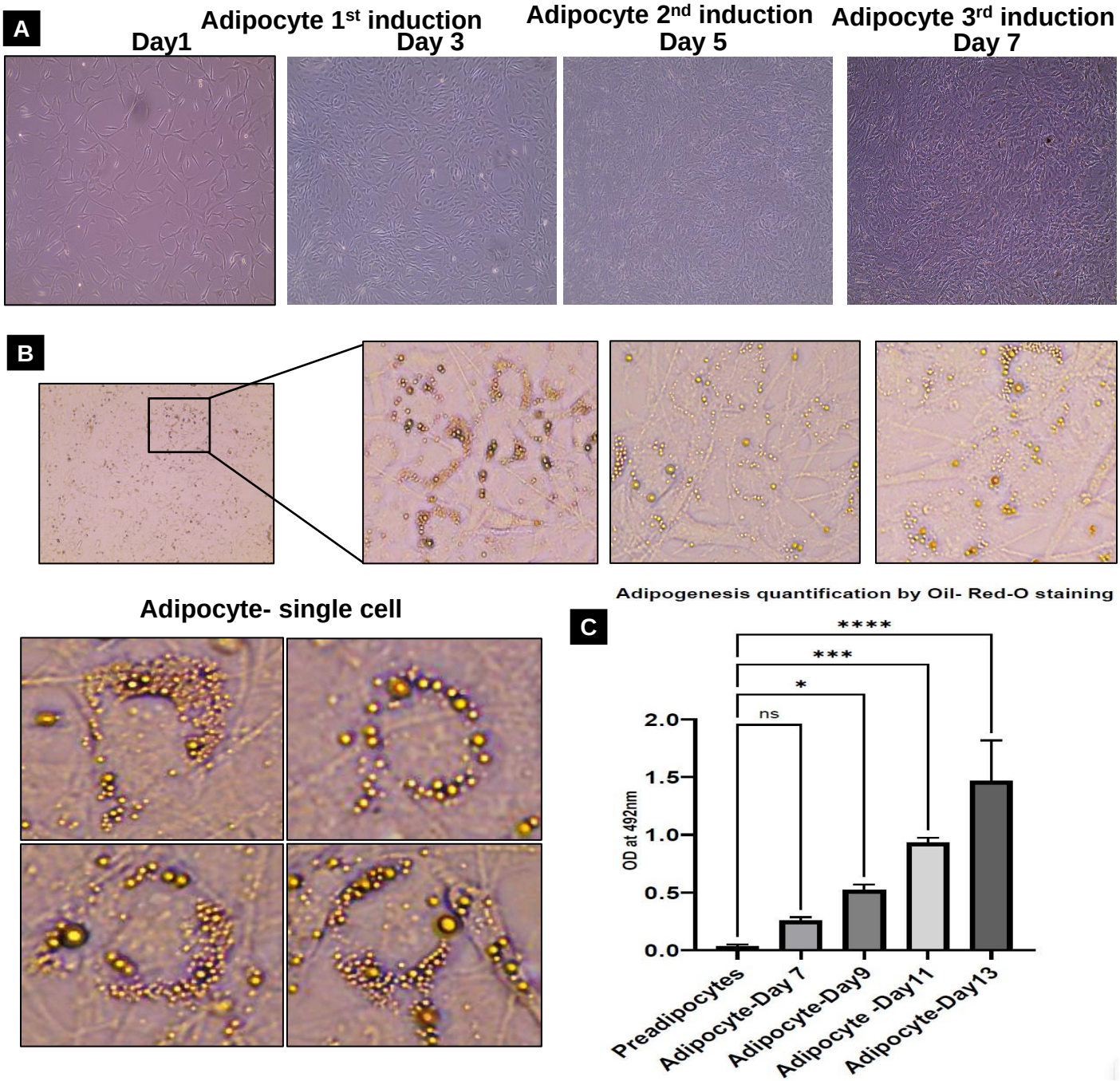


HFD AT PIAS3



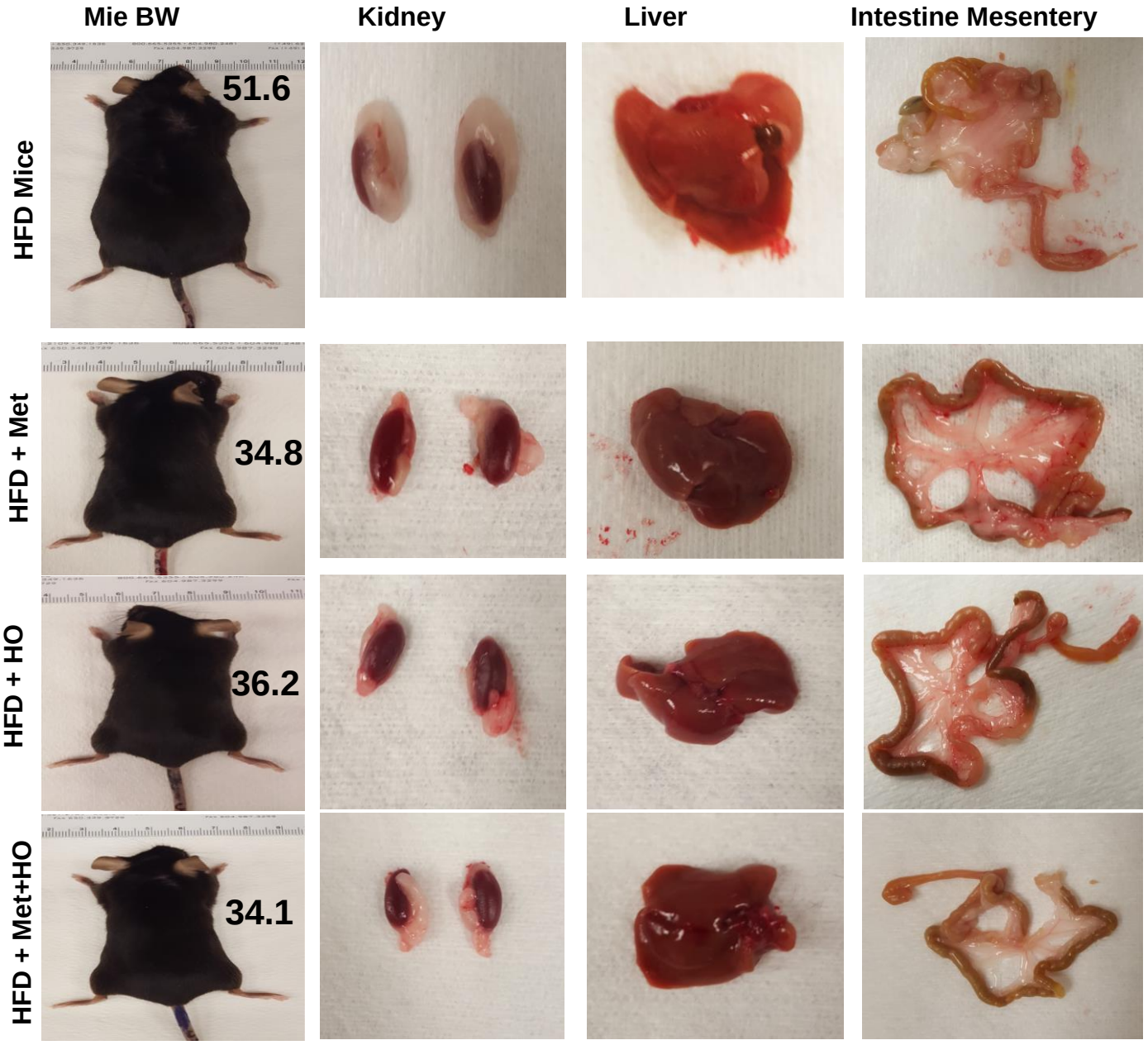
Sup. Fig. 6. PIAS3 expression alteration in HFD treated adipose tissues compared with control diet-treated mice.

Sup Figure 7



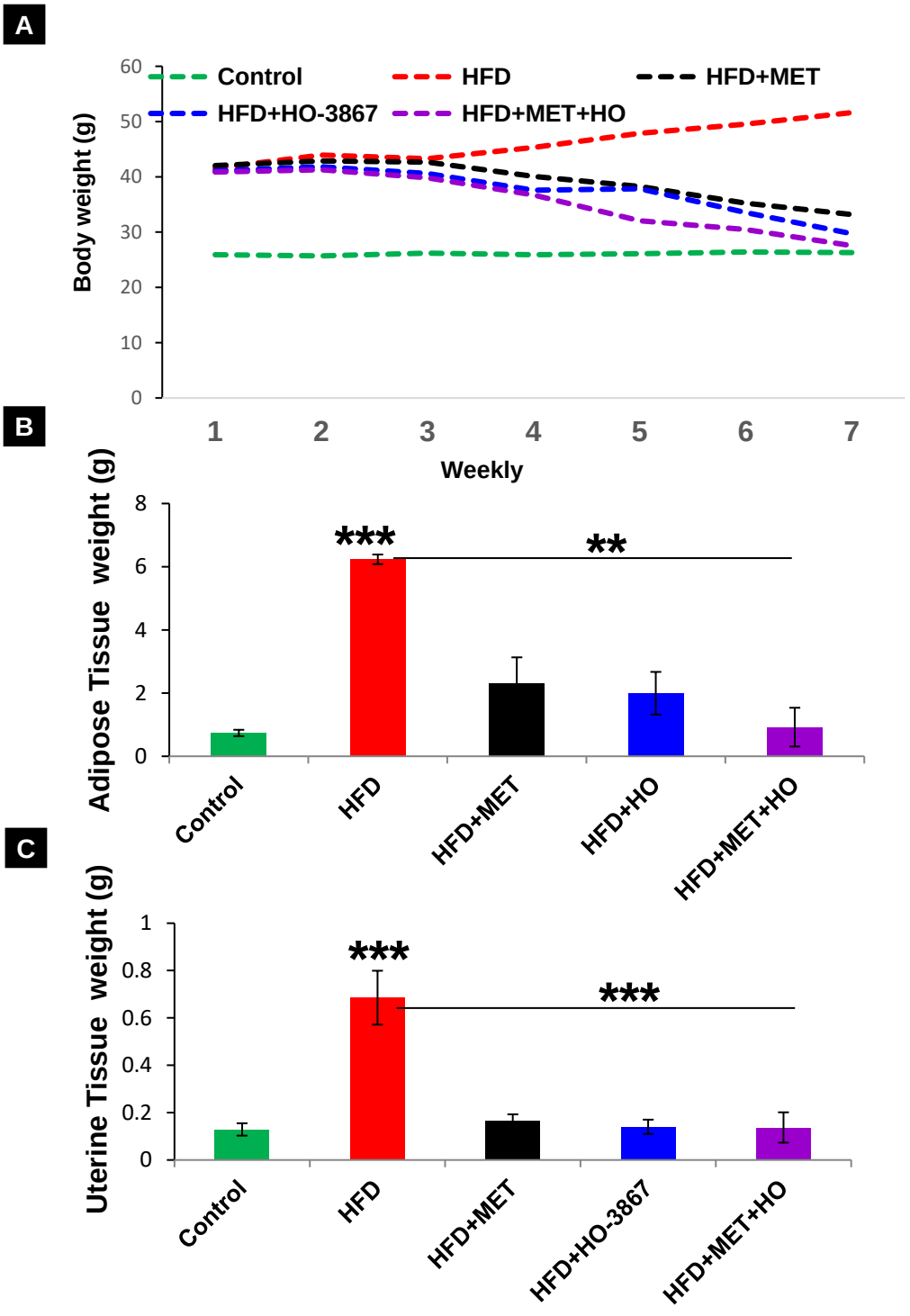
Sup. Fig. 7. Differentiation of adipose derived mesenchymal stem cells to adipocytes :
A. Adipose derived mesenchymal stem cells were cultured till confluency and then were initiated to differentiate into adipocytes 72hrs post confluency on Day3, 5&7 and then continued to be cultured in adipocyte maintenance medium for further differentiation and maturation till day 15. Light (10x)and phase contrast (40x) microscope pictures of cells at different time points of adipocyte differentiation showing increased lipid accumulation.
B & C. Confirmation and Quantification of Adipocyte formation: Cells were grown on a 12 well plate and then fixed and stained with 0.2% oil red O in 2-propanol for 10 min at room temperature at different time points to measure the adipogenesis. After washing, plates were dried, and dye was eluted with 100% 2-propanol, and were transferred to a microtiter plate for reading the extracted dye at 492nm for correlation of adipogenesis.

Sup Figure 8



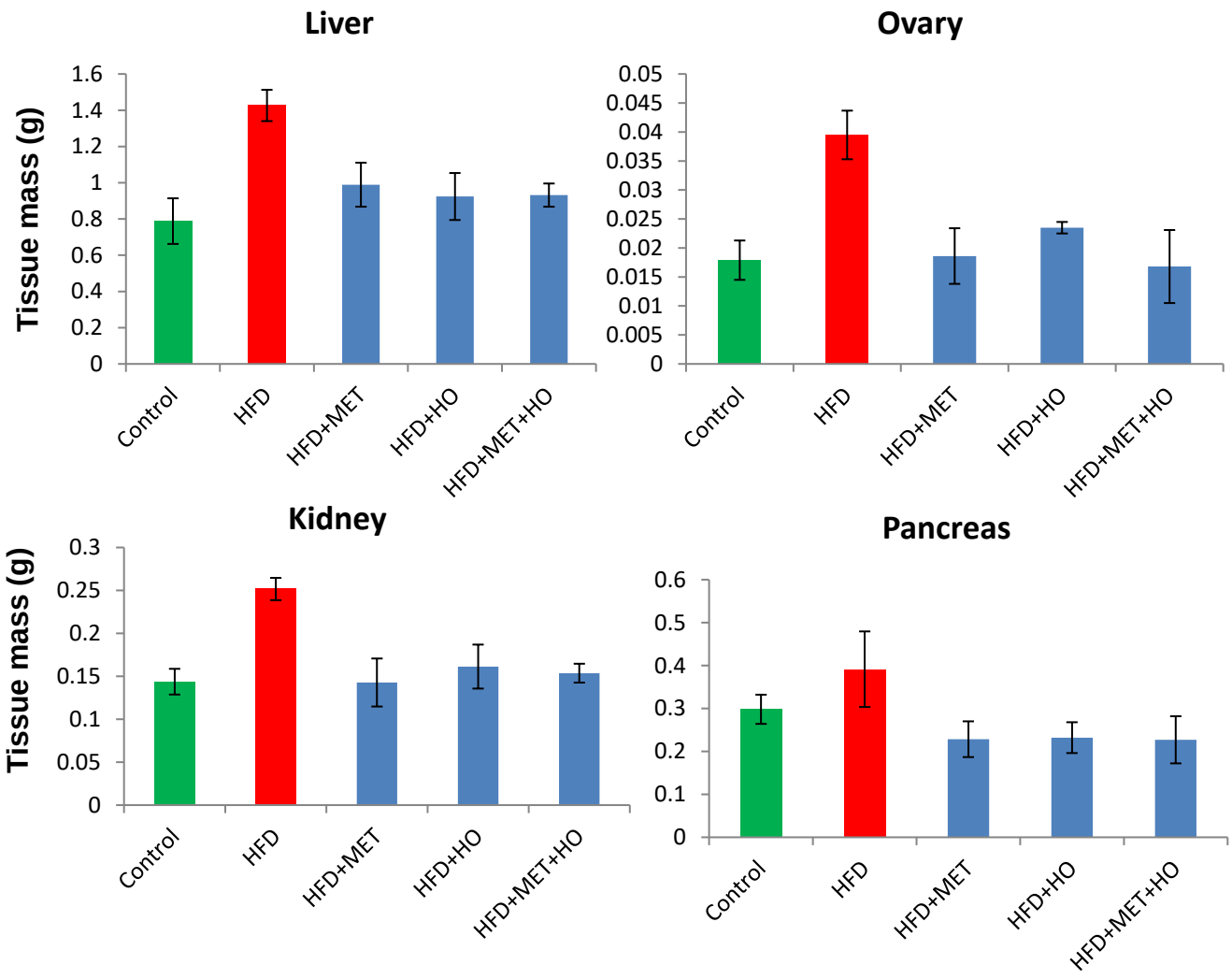
Sup. Fig.8. Immunocompetent mice were treated with a high-fat diet (HFD, 45% protein calorie) for 24 weeks. Changes in body weight were assessed at the end (24 weeks) of the HFD treatment with small molecule inhibitor HO-3867 (5mg/kg, weekly twice) and Metformin (10mg/kg, daily in water). Representative images depict accumulated levels of adipose tissue in kidney, liver and intestine, which is enlarged in mice fed a HFD for 24 or treatment groups 8 weeks.

Sup Figure 9



Sup. Fig. 9. A-C. Changes in body, adipose and uterine weight were assessed at the beginning of first weeks) and end (24 weeks) of the HFD treatment, HO-3867 and Metformin treatment mice (n = 10/group, $p<0.05$).

Sup Figure 10



Sup. Fig. 10. Changes in internal organs liver, kidney, ovary and pancreas weight were assessed at the beginning of first weeks) and end (24 weeks) of the HFD treatment, HO-3867 and Metformin treatment mice (n = 10/group, $p<0.05$).