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The Effect of High Fat Diet on Marrow Adipocytes from C57BL/6J (B6) Mice

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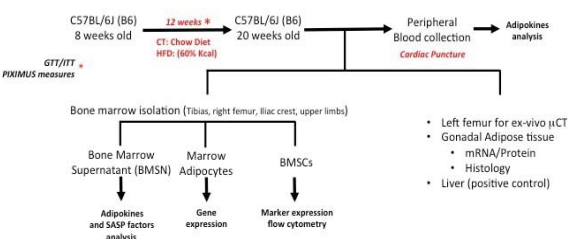
Background

- In mice models, the administration of a high fat diet (HFD) is an accelerating factor for metabolic syndrome, impaired glucose tolerance, and early type 2 diabetes mellitus (T2DM) (1)
- Bone marrow adiposity and bone loss are characteristic features of aging as well as diet-induced obesity (DIO), but little is known about whether adipocyte expansion is associated with macrophage activation in the marrow.
- The present study aimed to assess the impact of a HFD (60 kcal% fat) on marrow adipocytes from C57BL/6J (B6) male vs. female mice.

Materials and Methods

To determine the effect of HFD on adipokines, marrow adipose tissue, marrow/peripheral blood serum, and marrow adipocytes from B6 mice after 12 weeks of HFD were collected according to published protocols. (2,3). To analyze the expression of Resistin, TNF α , Sema3E/PlexinD1 and F4/80 on marrow adipocyte, qRT-PCR was performed. Glucose and insulin tolerance tests (GTT/ITT) and PIXImus measures were performed at the end of the HFD treatment. Cell surface marker expression of MHCII, CD8, CD48, CD150, Ly6C, CD11b, and F4/80 were performed by flow cytometry.

Study Timeline



Hypothesis

We have approached this study by testing the hypothesis that HFD induce expansion of adipocytes that drives the recruitment of activated macrophages and/or the inflammasome to accentuate bone loss.

Results

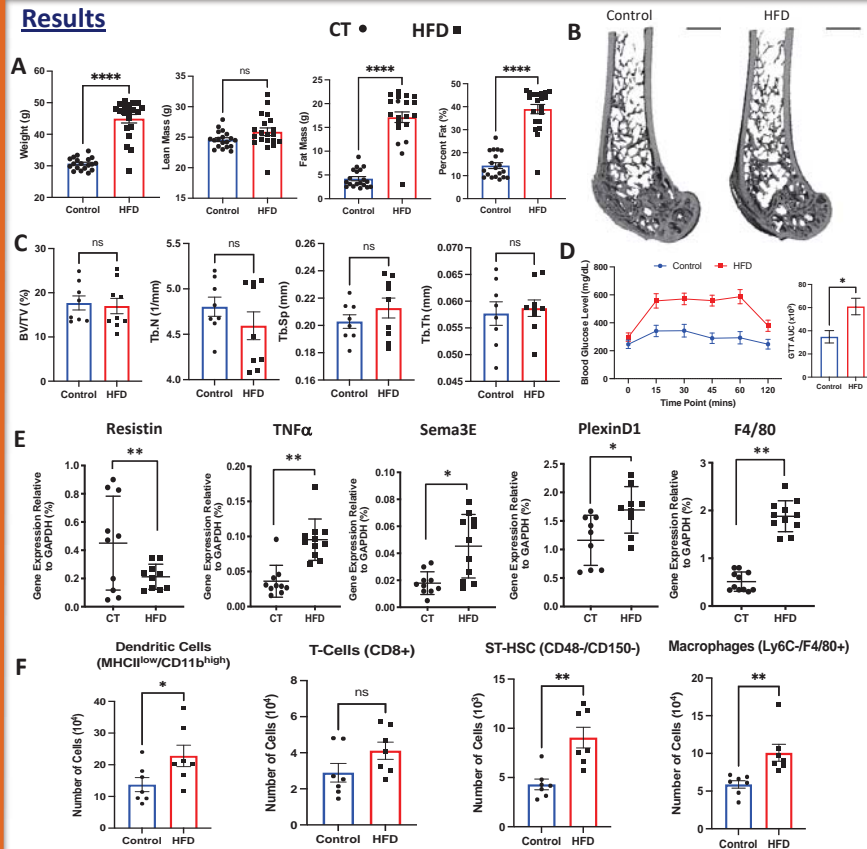
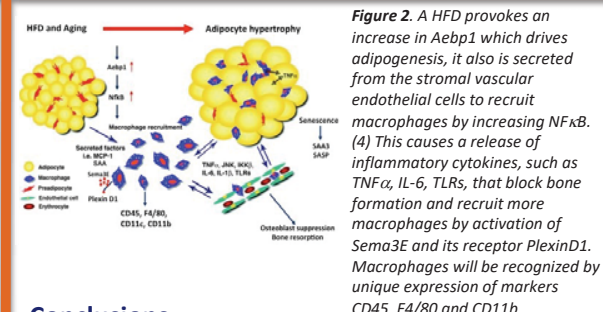


Figure 1. (A): PIXImus body composition data; blue bars (CT), red bars (HFD) (B): Sagittal representative femoral μ CT images from male B6 mice (C): μ CT analysis of the distal femoral metaphysis in male B6 mice (D): GTT in male B6 mice (E): Gene expression of Resistin, TNF α , Sema3E, PlexinD1 and F4/80 in marrow adipocytes from male B6 mice (F): Cell surface marker expression by flow cytometry; blue bars (CT), red bars (HFD). All analyses were performed as T-tests within Prism. Significance was defined as: *p<0.05, **p<0.01, ***p<0.001, and ****p<0.0001.



Conclusions

- There was a significant increase in body weight, fat mass, and percentage of fat in male and female mice after HFD.
- Femoral μ CT results proved unremarkable in the males, while HFD in the females showed significant changes in trabecular parameters (trabecular number, thickness, and spacing), but not in the cortical parameters.
- Interestingly, TNF α and IL-6 decreased markedly with HFD, without significant changes in resistin levels.
- The expression of Sema3E/PlexinD1 and TNF α were increased on marrow adipocytes from males and females under HFD.
- We identified up-regulation of the macrophage gene F4/80 as well as CD11c; suggestive of an inflammatory response in the marrow of B6 mice under HFD.
- Further analysis is needed to understand the immune response in the context of marrow adiposity in mouse models.

Acknowledgements

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