Effects of Intermittent Fasting on Naïve T Cells and Cellular Senescence in Aged Mice

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Introduction

As humans age, our immune function starts to decline, characterized by a reduction in Naive T Cells and an increase in senescent cells, which are associated with age-related health issues. At the same time, the gut microbiome undergoes significant shifts that impact immune regulation. Intermittent fasting (IF) is a non-pharmaceutical intervention shown to delay age-associated decline in metabolic and immune function. Understanding how IF impacts immune aging could help identify health-based strategies to improve immune responses in older individuals. This study investigates how IF affects immune aging in aged mice, focusing on naive T cells, senescence, and gut microbiome composition.

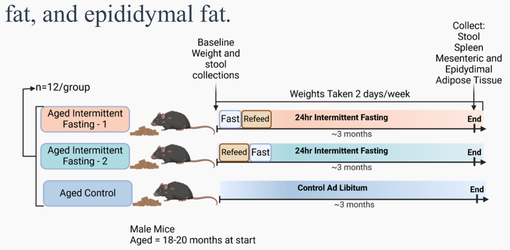
Hypothesis

We hypothesize that intermittent fasting in aged mice increases the production of naïve T cells and reduces senescent cell markers and is also associated with shifts in gut microbiome composition.

These changes may reflect a delay in immune aging and contribute to a more youthful immune profile.

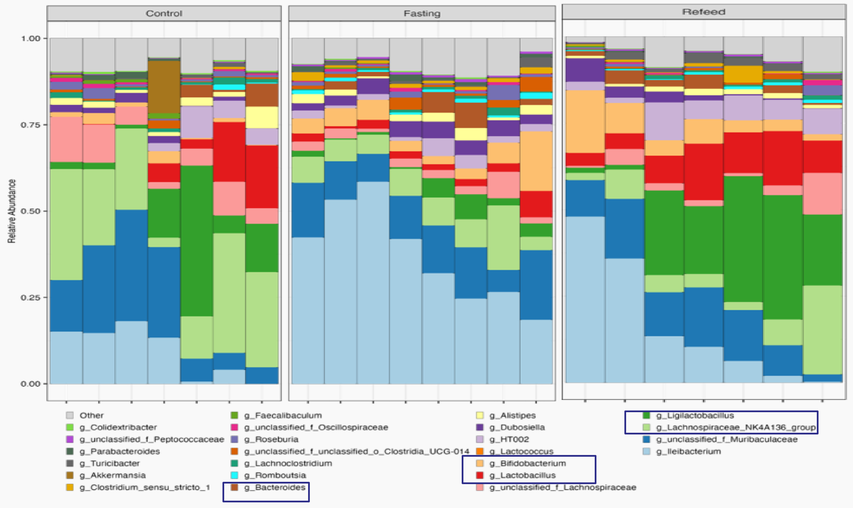
Methods

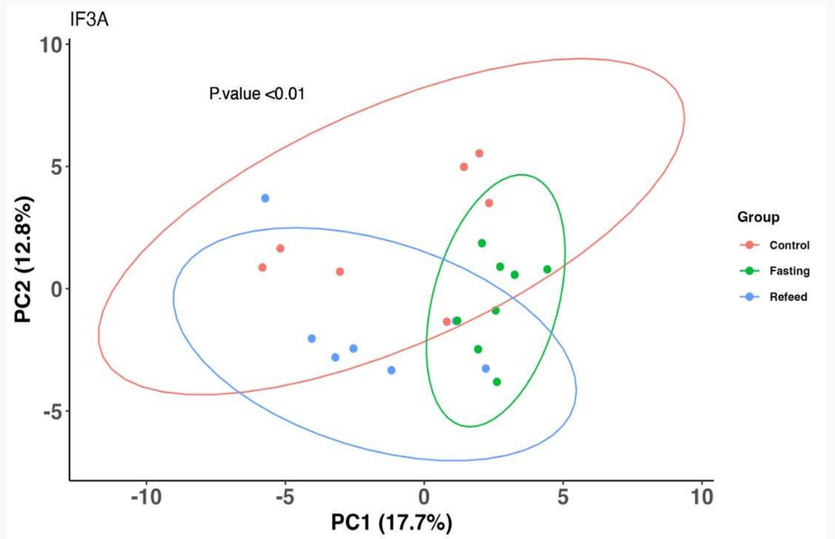
- Aged mice (18-21 month) were placed on either ad libitum feeding or an every-other-day intermittent fasting regimen for 3 months. At the end of the study, mice were dissected, and samples were collected from stool, spleen, mesenteric fat, and epididymal fat.



- Fecal samples were analyzed by 16S rRNA sequencing to assess microbial diversity and community composition.
- Naive and memory T cells ($CD4^+$ and $CD8^+$) were quantified using the Bio Legend LEGENDplex™ T Cell Panel on spleen and lymph node samples.
- Senescent cells were assessed by flow cytometry using γH2AX and SA-beta-gal expression

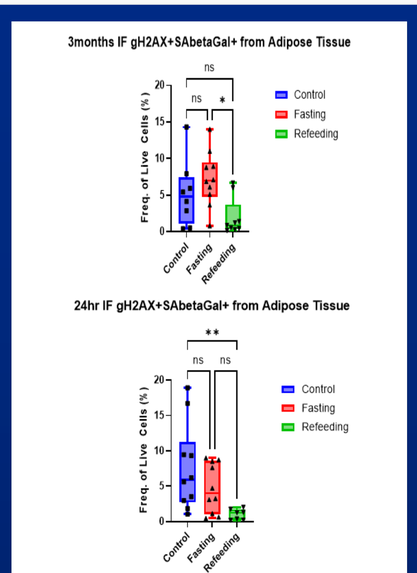
Results

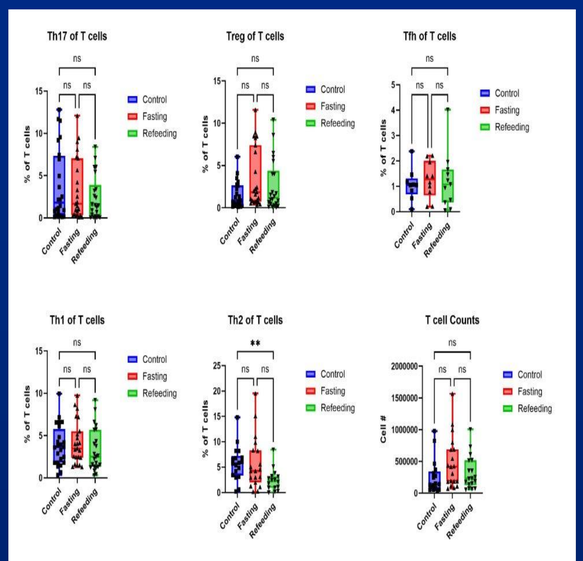


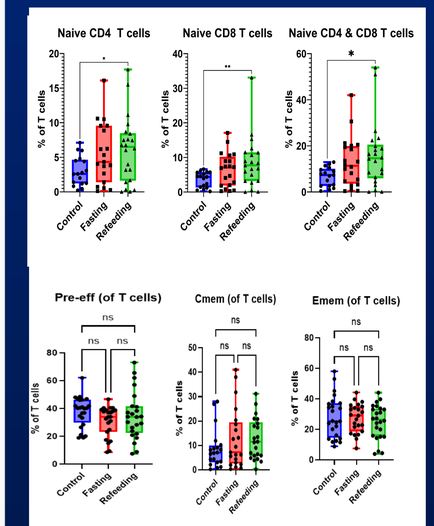


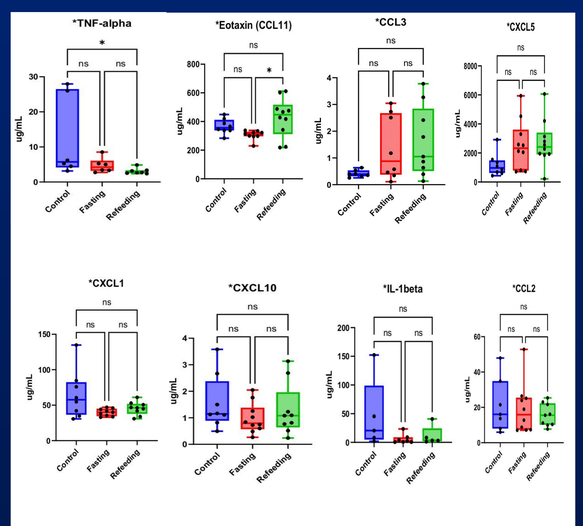
Findings

- IF altered gut microbial composition and increased microbial diversity (bifidobacteria, Bacteroides, lactobacillus) compared to AL-fed aged mice.
- IF preserved a greater proportion of naive T cells, suggesting a delay in immune aging.
- Mice under IF showed reduced cellular senescence markers, indicating improved cellular health.
- IF reduced pro-inflammatory cytokines and increased chemokines associated with immune cell trafficking, suggesting enhanced immune readiness.
- Mice in the intermittent fasting group showed lower expression of senescence markers, including γH2AX and SA-β-gal, as well as reduced levels of inflammatory cytokines such as CXCL1 and TNF-α. In contrast, chemokines CCL3 and CXCL5, which promote immune cell recruitment, were increased.









Conclusion

Intermittent fasting in aged mice increases naive T cell frequency, enhances gut microbiome diversity, and reduces senescent cells in adipose tissue. These changes suggest IF may help delay immune and tissue aging.

Future Directions

We observed an increase in Bifidobacteria and microbial diversity in IF mice. Moving forward, the lab aims to investigate how Bifidobacteria influences the immune response to viral infections such as influenza. Given the observed increase in naive T cells and reduction in senescence, future studies will explore how these changes affect the ability of IF mice to combat viral infections and how Bifidobacteria may contribute to this enhanced immune response.

Acknowledgments

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