Diurnal Immune Cell Migration Patterns Characterized in the Spaceflight Environment

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Abstract

Daily diurnal immune rhythm shapes biological pathways of organisms and closely aligns with optimizing energy usage in response to environmental light-dark cycles. Immune mobilization depends on diurnal signals to regulate immunity. In spaceflight, disrupted circadian rhythms and immune systems are noted. However, crosstalk between these systems has not been fully characterized. This work expands our understanding of diurnal immunity which is important to consider for personalized medicine directives for astronauts.

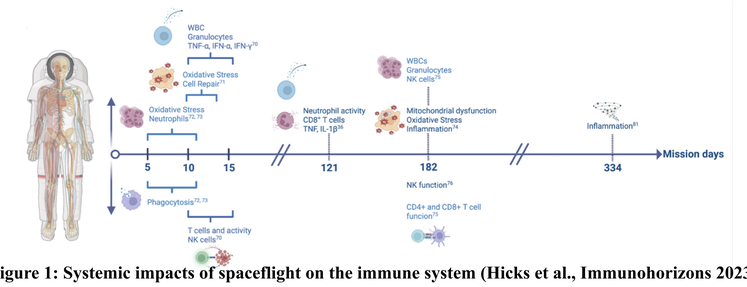

Figure 1: Systemic impacts of spaceflight on the immune system (Hicks et al., Immunohorizons 2023)

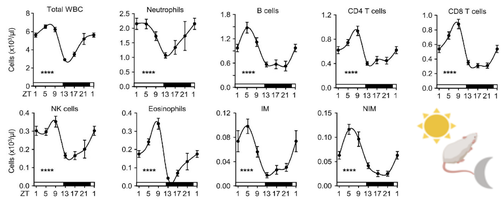

Figure 2: Diurnal immune rhythms under non-spaceflight conditions (He et al., Immunity 2018)

Methodology

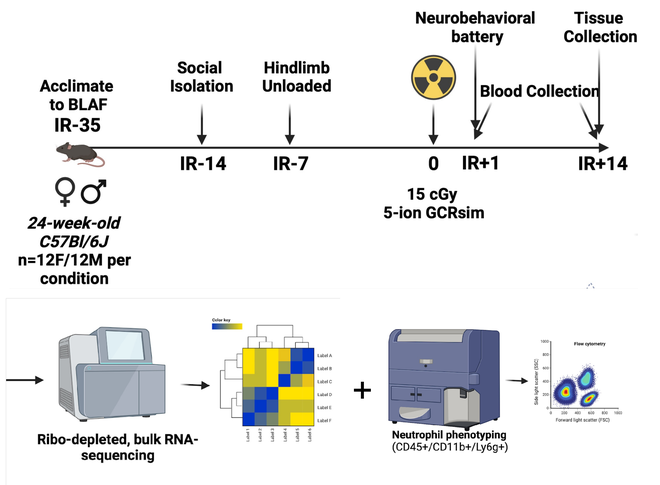

Figure 3: Methodology schematic demonstrating animal procedures and analytical approaches

Results

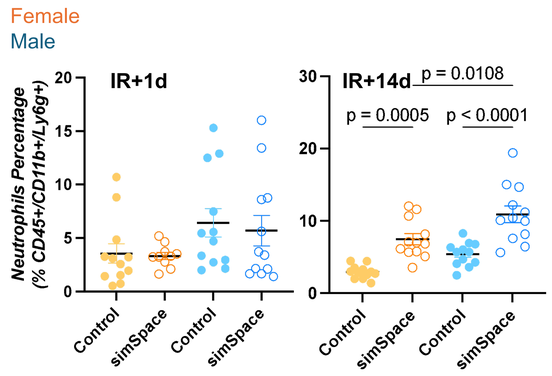

Figure 3: Neutrophil proportion at 1 day and 14 days post IR+HU

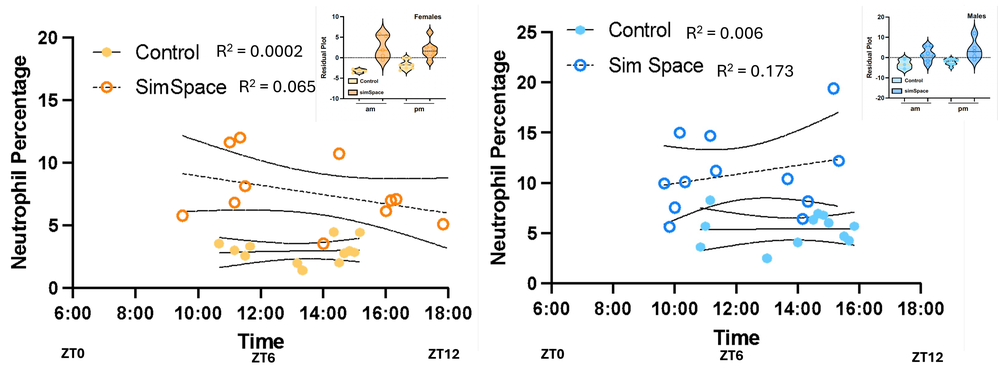

Figure 4: Neutrophil proportion over time at 14 days post IR+HU

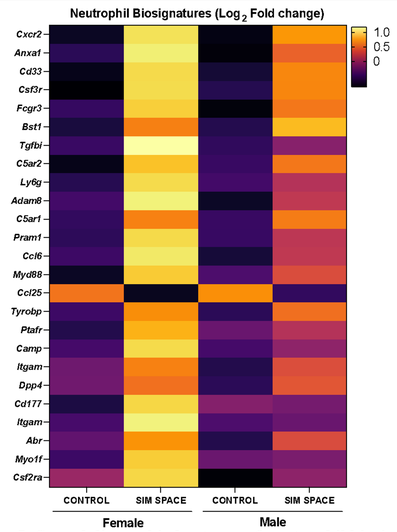

Figure 5: Sexual dimorphic heatmap of neutrophil biosignatures

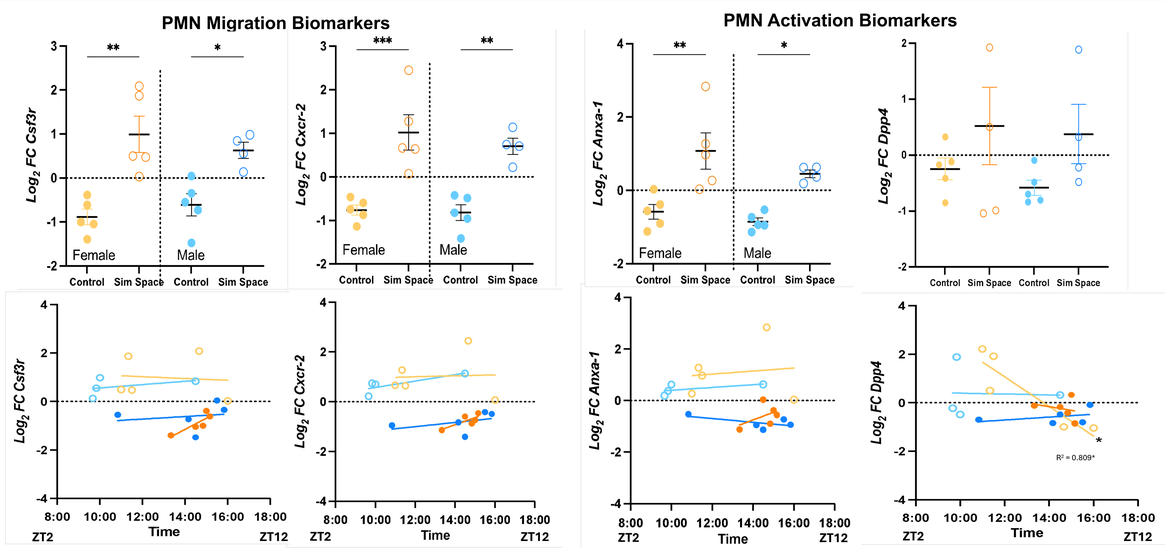

Figure 8: Polymorphonuclear neutrophils migration and activation gene expression Log_2 fold change

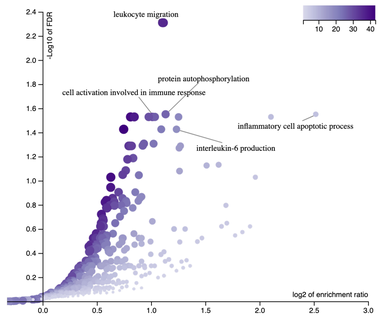

Figure 6: Overrepresentation analysis of neutrophil biosignatures

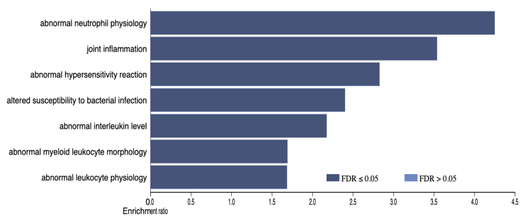

Figure 7: Enrichment analysis of overrepresented genes

Discussion

- **Sexual dimorphic differences in immune populations are noted**
- **SimSpace has a profound effect on number of neutrophils in blood**
  - Significantly elevated % of circulatory neutrophils
  - Males elevated slightly more than females
  - Females show reduced PMN percentage in evening where males are elevated
- **Gene expression in neutrophils also impacted by SimSpace**
  - All mice express elevated levels of activation, migration, and adhesion genes
  - Females more so than males
  - Neutrophil physiology is impacted in SimSpace
  - *Dpp4* – circadian regulated neutrophil activation gene, inhibition causes reduced adhesion to endothelium
- **Statistical variance is not a technical problem but a result of diurnal differences**

References

He, W., Holtkamp, S., Hergenhan, S. M., Kraus, K., de Juan, A., Weber, J., Bradfield, P., Grenier, J. M. P., Pelletier, J., Druzd, D., Chen, C.-S., Ince, L. M., Bierschenk, S., Pick, R., Sperandio, M., Aurrand-Lions, M., & Scheiermann, C. (2018). Circadian Expression of Migratory Factors Establishes Lineage-Specific Signatures that Guide the Homing of Leukocyte Subsets to Tissues. *Immunity*, *49*(6), 1175-1190.e7. https://doi.org/10.1016/j.immuni.2018.10.007

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