

## Peer Review File

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Single-cell multi-ome and immune profiles of the Inspiration4 crew reveal conserved, cell-type, and sex-specific responses to spaceflight



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**Editorial Note:** This manuscript has been previously reviewed at another journal. This document only contains reviewer comments and rebuttal letters for versions considered at *Nature Communications*.

#### REVIEWERS' COMMENTS

Reviewer #1 (Remarks to the Author):

I have carefully considered the manuscript and the response to the reviewers document, with a particular focus on reviewer number 4 requests and authors responses to these comment. In my opinion I think the authors comprehensively addressed the requests of reviewer 4, particularly around the issues of statistics and data analysis. The authors have integrated their dataset with almost every available datasets (including other resources from the same initiative), correctly performed statistical analyses and more importantly, acknowledged the limitations of the current study. Overall, I do not think the authors have left any stone unturned and the findings are as robust as possibly can considering the experimental design (which is not trivial considering the inherent constraints in these types of experiments).