Peer Review: Sex biases in ILC1 phenotypes do not alter immune control of cytomegalovirus

Remi Marrocco[1*], Meghan Nguyen[1], Andrea Balcan[1], Kaia Robinson[1] & Chris A. Benedict[1*]

Collaborators: Susan Kovats + 2 other reviewers

[1] Center for Vaccine Innovation and Center for Autoimmunity and Inflammation, La Jolla Institute for Immunology, La Jolla, CA, USA

Transparent Peer Review

- View reviewer summaries
- View resubmission with reviewer comments and author responses
- View initial submission with reviewer comments and author responses

Recommended Citation

Marrocco, R., M. Nguyen, A. Balcan, K. Robinson, and C. A. Benedict. 2026. Sex biases in ILC1 phenotypes do not alter immune control of cytomegalovirus. Stacks Journal: 26004. https://doi.org/10.60102/stacks-26004.

Accepted by 3 of 3 reviewers

Conflicts of Interest

The authors declare no conflicts of interest.

Publishing History

Submitted August 20 2025
Accepted February 9 2026
Published March 31 2026

Corresponding Author

Remi Marrocco
rmarrocco@lji.org

Chris A. Benedict
benedict@lji.org

Open Access
Peer-Reviewed
Creative Commons

Reviewer Summaries

Susan Kovats

Initial Submission

Do you have any conflicts of interest that could bias your ability to provide an independent review?

no

What did the authors do a good job with?

Rigorous work; well written manuscript; I especially liked the use of different mutant MCMVs to increase the potential impact of ILC1s in the response

How do you think this research will contribute to the field?

Sex differences in NK cells have been reported. Given the potential overlap between ILC1 and NK functional responses, it is important to know about sex differences in ILC1s as well.

Regarding the study design and methods, what do the authors need to fix or improve upon to be fit for publication?

there were some issues of reproducibility - for example sex differences shown in Fig. 1 were less apparent in Fig. 4 (time 0 data). This may be due to the low n reported in some figures.

Regarding the analysis and interpretation of their findings, what do the authors need to fix or improve upon to be fit for publication?

Fig. 4 experiment would benefit from showing representative flow plots, and from increasing the number of mice through an additional experiment (may have been only 1 experiment involving 5 mice). A titration of the virus may yield more sex differences in viral load. An earlier time point than day 4 pi may show a greater response of the ILC1s.

Is there anything else you think the authors need to fix in their article to be fit for publication?

Discuss (ref 21) showing strong sex differences in NK cells (given the presented finding of no sex differences).

Do you have any concerns about the ethics of this research?

no

Do you believe the article, in its current form, is fit for publication?

This paper requires minor revisions but does not need further peer review

Would you like to be listed as a Collaborator on the final publication?

Yes, please list me as a Collaborator

Revised Submission

Do you have any conflicts of interest that could bias your ability to provide an independent review?

no

How well did the authors respond to your comments?

5/5

What - if any - feedback do you feel the authors did not adequately respond to?

N/A

Based on your review, what should happen next?
This paper is ready for publication
Would you like to be listed as a Collaborator on the final publication?
Yes, please list me as a Collaborator

Katarina Pinjusic

Initial Submission
Do you have any conflicts of interest that could bias your ability to provide an independent review?
No
What did the authors do a good job with?
The authors are addressing an important question by investigating sex differences in ILC1 biology using commonly employed mouse models. The author's efforts to examine these differences are commendable.
How do you think this research will contribute to the field?
By investigating the sex differences and characterizing the immune responses in widely used mouse models, this research will help inform a more accurate interpretation of immune responses in experimental settings. This work may also guide future studies that account for sex differences, ultimately contributing to a better understanding of immune regulation and sex-specific differences in humans.
Regarding the study design and methods, what do the authors need to fix or improve upon to be fit for publication?
Inconsistent data reporting:
The use of MFI versus % positive cells varies across panels, even for the same marker.
Additionally, given that the authors state they normalize data between groups, it is unclear why normalization is applied selectively. A consistent and transparent approach to data reporting would improve interpretability.
Inclusion criteria for animals and experiment replication:
It remains unclear why not all animals from replicated experiments are included in each analysis. Clear inclusion/exclusion criteria and justification for data selection are needed to assess the robustness and reproducibility of the findings.
Regarding the analysis and interpretation of their findings, what do the authors need to fix or improve upon to be fit for publication?
Some of the statistical differences reported in the manuscript appear to lack clear biological relevance but are nonetheless emphasized. It would strengthen the manuscript if the authors more carefully distinguished between statistically significant findings and those that are biologically meaningful.
Given the inconsistency and variability of the data, as well as concerns about reproducibility, some conclusions appear to be overstated.
Is there anything else you think the authors need to fix in their article to be fit for publication?
The manuscript would benefit from addressing the translational relevance of the findings, particularly since notable differences were observed between the two mouse strains studied. Currently, it is unclear how these mouse data relate to human ILC1 biology. To strengthen the impact and broader applicability of the study, the authors should consider incorporating an analysis of publicly available human ILC1

datasets, if feasible. This could help validate whether the observed sex differences and phenotypic characteristics extend to humans, thereby enhancing the significance of the work.
Do you have any concerns about the ethics of this research?
No, this study was approved by the Institutional Animal Care and Use Committee (IACUC)
Do you believe the article, in its current form, is fit for publication?
This paper needs major revisions and another round of peer review

Revised Submission
Do you have any conflicts of interest that could bias your ability to provide an independent review?
no
How well did the authors respond to your comments?
4/5
What - if any - feedback do you feel the authors did not adequately respond to?
No further comments
Based on your review, what should happen next?
This paper is ready for publication
Would you like to be listed as a Collaborator on the final publication?
No, I do not want to be listed as a Collaborator

Keri Smith

Initial Submission
Do you have any conflicts of interest that could bias your ability to provide an independent review?
no
What did the authors do a good job with?
Justifying the reasons for this study. Nicely comparing responses in two strains of mice. Using targeted knockouts of MCMV proteins to attempt to define the mechanisms by which viral control might be compromised.
How do you think this research will contribute to the field?
This is nice supporting evidence for a slight sex bias in iLC responses. Understanding of iLC is still pretty limited, so any sort of observational data like this is welcome.
Regarding the study design and methods, what do the authors need to fix or improve upon to be fit for publication?
The presentation of the flow cytometry data in figure 1 is not ideal - it is tough to compare a "representative" plot with a standardized plot.
Regarding the analysis and interpretation of their findings, what do the authors need to fix or improve upon to be fit for publication?
The authors overstate the significance of some of their findings. It is interesting that there wasn't a huge difference in response to the virus in male vs. female mice, but I think they need to be careful in assuming the minor differences in iLC response would add up to major effects on anti-viral response.
Is there anything else you think the authors need to fix in their article to be fit for publication?
There are some typos and clunky phrases that might benefit from proofreading by a professional english-speaking writer.

Do you have any concerns about the ethics of this research?
no
Do you believe the article, in its current form, is fit for publication?
This paper requires minor revisions but does not need further peer review
Would you like to be listed as a Collaborator on the final publication?
No, I do not want to be listed as a Collaborator

Revised Submission
Do you have any conflicts of interest that could bias your ability to provide an independent review?
no
How well did the authors respond to your comments?
5/5
What - if any - feedback do you feel the authors did not adequately respond to?
none that I saw
Based on your review, what should happen next?
This paper is ready for publication
Would you like to be listed as a Collaborator on the final publication?
No, I do not want to be listed as a Collaborator