Decision Letter (JCQ-2025-0039)

From: [redacted]
To:
CC:
BCC:

Subject: Journal of Clinical Question - Decision on Manuscript ID JCQ-2025-0039

Body: 17-Dec-2025

Dear Dr Li:

Manuscript ID JCQ-2025-0039 entitled "RSV-Induced Epigenetic Reprogramming: Mechanisms and Therapeutic Opportunities" which you submitted to the Journal of Clinical Question, has been reviewed. The comments of the reviewer(s) are included at the bottom of this letter.

The reviewer(s) have recommended publication, but also suggest some minor revisions to your manuscript. Therefore, I invite you to respond to the reviewer(s)' comments and revise your manuscript.

To submit your revised manuscript, follow the below steps.
1. Access to https://mc.manuscriptcentral.com/jcq and log into the site.
2. Click "Author" at the top left of the screen at "Home" page.
3. Click "Manuscripts with Decisions" on Author Dashboard page.
4. Click "create a revision" on the manuscript you are going to revise.
5. The system creates your revision manuscript form. Provide your comments about the revised points at the response field, fill in on each field step by step as same as you did for the original submission, and submit your revised manuscript.
IMPORTANT: Your original files are available to you when you upload your revised manuscript. Please delete any redundant files before completing the submission.
Your manuscript number has been appended to denote a revision.

You will be unable to make your revisions on the originally submitted version of the manuscript. Instead, revise your manuscript using a word processing program and save it on your computer. Please also highlight the changes to your manuscript within the document by using the track changes mode in MS Word or by using bold or colored text.

Once the revised manuscript is prepared, you can upload it and submit it through your Author Center.

When submitting your revised manuscript, you will be able to respond to the comments made by the reviewer(s) in the space provided. You can use this space to document any changes you make to the original manuscript. In order to expedite the processing of the revised manuscript, please be as specific as possible in your response to the reviewer(s).

IMPORTANT: Your original files are available to you when you upload your revised manuscript. Please delete any redundant files before completing the submission.

Because we are trying to facilitate timely publication of manuscripts submitted to the Journal of Clinical Question, your revised manuscript should be uploaded as soon as possible. If it is not possible for you to submit your revision in a reasonable amount of time, we may have to consider your paper as a new submission.

Once again, thank you for submitting your manuscript to the Journal of Clinical Question and I look forward to receiving your revision.

Sincerely,
Richard S. Isaacs
Editor in Chief
Journal of Clinical Question

[Editor's Comments]
Associate Editor
Comments to the Author:
1. Check grammar and flow for minor errors.
2. Ensure all abbreviations are defined on first use in both abstract and main text.
3. Add ORCID IDs for authors if available

[Reviewer(s)' Comments]
Reviewer: 1

Comments to the Author
This is a comprehensive and timely review entitled “RSV-Induced Epigenetic Reprogramming: Mechanisms and Therapeutic Opportunities.” The manuscript provides a thorough synthesis of current knowledge on how RSV modulates host epigenetic mechanisms across epithelial, innate, and adaptive immune compartments and clearly links these molecular changes to disease severity and long-term respiratory outcomes. The topic is relevant to infectious diseases, immunology, and pediatric medicine, and the review has strong translational potential. The manuscript is well-structured and logically organized, progressing from clinical features to mechanistic insights and translational implications. The discussion of multiple epigenetic layers, including DNA methylation, histone modifications, non-coding RNAs, and chromatin remodeling, is comprehensive and well integrated. The inclusion of emerging concepts such as histone lactylation, m^{6}A modification, and multi-omics approaches adds novelty. The translational sections on biomarkers and epigenetic therapeutics are particularly strong and clinically relevant.

Major Suggestions
1. The manuscript would benefit from a clearer distinction between findings derived from human studies and those from in vitro studies, which would strengthen translational interpretation.
2. The therapeutic section could be improved by briefly discussing safety considerations relevant to pediatric populations when targeting epigenetic regulators.

Minor Comments
1. Use abbreviations consistently by defining them the first time, then use the abbreviated form throughout
2. In the reference section, duplicate entries are present (e.g., references 43 and 113) along with formatting inconsistencies. I kindly request the authors to revise the reference list carefully.
3. In Section 4.4 (Future Avenues: Multi-Omics Integration and Organoid Models), the authors are encouraged to cite recent primary studies rather than relying mainly on review articles. For example, recent single-cell analyses of RSV-infected pediatric and adult human nasal organoids have demonstrated age-dependent cellular responses, proliferative diversity, and previously unrecognized cellular tropism, highlighting the value of organoid-based single-cell approaches in RSV research.

Once these minor issues are addressed, I recommend that the manuscript be accepted.

Reviewer: 2

Comments to the Author
This manuscript presents a comprehensive, timely, and well-organized review of RSV-induced epigenetic reprogramming, encompassing epithelial, innate, and adaptive immune compartments and extending to important translational considerations. The topic is highly relevant to pediatric infectious diseases and immunology, and the authors effectively integrate recent literature, including studies published in 2024–2025. The manuscript is generally well written, the figures are conceptually informative, and the clinical framing broadens its appeal to both basic and translational audiences.
Only minor revisions are necessary to further improve clarity, consistency, and balance between mechanistic depth and evidentiary support.
1. Please ensure consistent use of gene and protein nomenclature throughout the manuscript (e.g., IFN-β vs. interferon-β; CD8$^+$ vs. CD8+).
2. The discussions of HDAC inhibitors and CRISPR-based approaches are informative but somewhat optimistic. The authors are encouraged to briefly expand on: Safety considerations, particularly in infants and pregnant populations. Regulatory and ethical challenges associated with epigenetic editing.

Date Sent: 17-Dec-2025

Author's Response to Decision Letter for (JCQ-2025-0039)

RSV-Induced Epigenetic Reprogramming: Mechanisms and Therapeutic Opportunities

Response Letter

Dear Editor,
Thank you for the opportunity to revise our manuscript entitled "RSV-Induced Epigenetic Reprogramming: Mechanisms and Therapeutic Opportunities." We sincerely appreciate the time and effort invested by you and the reviewers in evaluating our work. The constructive comments and insightful suggestions have been invaluable in improving the clarity, rigor, and overall quality of this review.
We have carefully addressed all concerns raised during the review process. The major revisions include:
1. Addition of a dedicated section addressing safety, ethical, and regulatory considerations for epigenetic therapies in pediatric populations.
2. Clear differentiation between in vitro, in vivo, and human clinical findings throughout the manuscript.
3. Updating the "Future Avenues" section with recent primary studies utilizing organoid models and single-cell omics approaches.
4. Thorough standardization of abbreviations, gene/protein nomenclature, and references, and correction of minor grammatical and stylistic issues.
A detailed, point-by-point response to each comment is provided below.

Editor's Comments
Comment 1: Check grammar and flow for minor errors.
Response: The manuscript has been carefully proofread to improve grammar, clarity, and overall flow. Minor typographical and stylistic issues have been corrected throughout.
Comment 2: Ensure all abbreviations are defined on first use in both the abstract and main text.
Response: All abbreviations are now defined upon first appearance in the Abstract and again, where appropriate, in the main text, and are used consistently thereafter.
Comment 3: Add ORCID IDs for authors if available.
Response: ORCID IDs have been added for all authors where available.

Reviewer 1
Major Comment 1: The manuscript would benefit from a clearer distinction between findings derived from human studies and those from in vitro studies.
Response: We agree with this important point. The manuscript has been systematically revised to explicitly state the experimental context of each major finding. We now use precise terminology such as "in bronchial epithelial cell models," "in murine models," and "in clinical nasal swab specimens" to clearly distinguish mechanistic in vitro studies from in vivo and human observations, thereby strengthening translational interpretation.

Major Comment 2: The therapeutic section should discuss safety considerations relevant to pediatric populations.
Response: A new section entitled "4.3 Safety, Ethical, and Regulatory Considerations in Pediatric Populations" has been added. This section discusses:
Developmental toxicity, including potential effects of HDAC inhibitors on skeletal growth and neurodevelopment. Genomic stability concerns, particularly off-target effects and oncogenic risks associated with CRISPR-based approaches.Ethical and regulatory challenges, such as informed consent and stringent risk–benefit assessments required for pediatric clinical trials.

Minor Comment 1: Use abbreviations consistently.
Response: All abbreviations have been standardized and are used consistently throughout the manuscript.

Minor Comment 2: Duplicate references and formatting inconsistencies are present.
Response: Duplicate references (e.g., previous references 43 and 113) have been removed, and the entire reference list has been reformatted to strictly comply with the journal's guidelines.

Minor Comment 3: Cite recent primary studies in Section 4.4 rather than relying on reviews.
Response: Section 4.4 has been revised to include recent primary research. We now cite studies by Rajan et al. (2025) and Aloisio et al. (2024), which employ human nasal organoids and single-cell RNA sequencing to demonstrate age-dependent RSV pathogenesis. These studies replace prior general review citations and better reflect current advances in the field.

Reviewer 2
Comment 1: Please ensure consistent use of gene and protein nomenclature throughout the manuscript (e.g., IFN-β vs. interferon-β; $CD8^+$ vs. CD8+).
Response: Gene names are now italicized (e.g., IFNB1), protein names are presented in standard text (e.g., IFN-β), and cell surface markers are consistently formatted (e.g., $CD8^+$) throughout the manuscript.

Comment 2: The discussions of HDAC inhibitors and CRISPR-based approaches are informative but somewhat optimistic. The authors are encouraged to briefly expand on: Safety considerations, particularly in infants and pregnant populations. Regulatory and ethical challenges associated with epigenetic editing.

Response: As noted above, these points are now comprehensively addressed in the newly added Section 4.3, providing a balanced and cautious discussion of translational potential, particularly in infants and pediatric populations.

We once again thank the editor and reviewers for their thoughtful and constructive feedback. We believe that these revisions have substantially strengthened the manuscript and hope it is now suitable for publication.

Sincerely,
Zi Lv
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The First Affiliated Hospital of Chongqing Medical University, Chongqing, China
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