Subject: Submission of Revised Manuscript - Manuscript ID: 88612

Dear Editor,

I trust this email finds you well. We have diligently addressed the feedback provided and made substantial improvements to our manuscript Manuscript Number: 88612

- 1. Introduction Enhancement: Based on your valuable suggestions, we have revised the global epidemiological information on colorectal cancer in the introduction, incorporating additional details on potential causes of cancer.
- 2. Supplementary notes in the introduction: We have made additional clarifications based on your comments that the introductory section should include information on potential causes of cancer, including cancer and colorectal cancer
- 3. Rationale for Tool Selection: Regarding the choice of R language, Seurat package, and Blueprint Encode dataset, we are well aware of the widespread application and effectiveness of these tools in the analysis of single-cell RNA sequencing data, especially the outstanding performance of R language in the fields of bioinformatics and genomics.

Seurat package, designed specifically for single-cell RNA sequencing, is renowned for its robust functionality in data analysis and visualization. The Blueprint Encode dataset serves as a valuable resource, providing epigenomic data for various cell types and robustly supporting the inference of cell type identities in our research. We acknowledge the critical importance of these choices in ensuring the robustness and broad applicability of our study. If necessary, we are willing to provide further clarification on the rationale and necessity of these choices in the manuscript.

- 4. Quality Enhancement of Figures: We have carefully re-examined and improved the quality of all figures in the manuscript to ensure optimal clarity and visibility. This modification is vital to facilitating a better understanding of the presented data.
- 5. Language Refinement Report: We have diligently addressed language issues throughout the manuscript and have submitted a language refinement report as per your requirements. We yellow-highlighted the manuscript based on the revisions made to it, but we were unsuccessful in uploading our own manuscript because the journal does not support uploading it. If necessary, please teach us how to upload manuscript files in your journal.

We appreciate the thorough review and constructive feedback provided by

the reviewers. Our revisions are aimed at improving the overall quality and

clarity of the manuscript. We believe these enhancements contribute

significantly to the scientific merit of our work.

Thank you for your continued consideration of our manuscript. We look

forward to any further guidance or feedback you may provide.

Sincerely,

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