

Fred Hutchinson Cancer Center 1100 Fairview Ave. N. Seattle, WA 98109 FredHutch.org

Dear Dr. Narasimhan,

Thank you for your support and continued interest in our paper "Early underdetected dissemination across countries followed by extensive local transmission propelled the 2022 mpox epidemic" This is the resubmission of manuscript CELL-D-23-02872.

Attached you will find our point-by-point response letter. Editorial and reviewer comments are shown in black, and our responses in blue.

The majority of the revisions have been textual in nature surrounding clarification of the data and limitations of our work. At the suggestion of the reviewers, we have included a flowchart of our inclusion and exclusion criteria that resulted in our final datasets (Figure S1A), a sensitivity analysis of how the time lag for the development of vaccine-derived immunity impacts our conclusions about US vaccination campaigns (Figure S6C-D), and a expansion of Table S2 in order to help compare and contrast the various models used in our study in order to make it more accessible to a non-specialist audience. We have also slightly adjusted the format of our Methods section to adhere to the STAR Methods guidelines and consolidated our supplementary figures down to seven in order to adhere to the Cell guidelines for supplemental information.

Again, thank you very much for your consideration.

Yours sincerely,

Miguel Paredes and Trevor Bedford, on behalf of all co-authors