

Reviewer Report

Title: A hybrid pipeline for reconstruction and analysis of viral genomes at multi-organ level

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Reviewer name: Brett E. Pickett, Ph.D.

Reviewer Comments to Author:

The manuscript entitled "A hybrid pipeline for reconstruction and analysis of viral genomes at multi-organ level", by Pratas et al. describes their development of a novel bioinformatics pipeline named TRACESPipe. Overall this software specializes in assembling and analyzing viral genomes from multiple organ sites. As such, it will enable the rapid analysis of various types of datasets that explore intra-host viral diversity. The workflow is very logical and expresses an impressive knowledge of the tools involved as well as the file formats that are produced.

The described methods are appropriate for this study and the authors do an excellent job to ensure that multiple approaches are used to facilitate performing the necessary controls on the data being analyzed. The authors do a good job with ensuring that the conclusions drawn are supported by the data and results reported elsewhere in the manuscript.

The manuscript could be improved by including additional text to describe:

- 1) Why 40 was selected as the optimal number of genes with high similarity scores? Can the authors provide additional justification and/or data to reinforce this decision?
- 2) The abbreviations used in the caption for Table 2. Although these abbreviations are defined in the List of Abbreviations at the end of the manuscript, readability could be improved by including the relevant abbreviations in the Table caption.

Although not required for the current publication, it may be helpful for the authors to consider the below recommendations as part of future development plans:

- 1) Enable the analysis of mitochondrial sequence from non-human primates. These animals are often used as model organisms for a variety of viruses. As such, the userbase of the TRACESPipe software could be expanded by providing this capability.
- 2) Adapt the installation process such that TRACESPipe can be installed into an auto-generated Conda environment (i.e. "conda install -c bioconda TRACESPipe")?

Level of Interest

Please indicate how interesting you found the manuscript: Choose an item.

Quality of Written English

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