Capturing structural variants of herpes simplex virus genome in full length by Oxford Nanopore sequencing

William Jacobs, Saranathan Rajagopalan, Emmanuel Asare, Lawrence Leung, Anna de Oliveira, Katherine Kaugars, Claire Mulholland, Regy Lukose, and Michael Berney

Corresponding Author(s): William Jacobs, Albert Einstein college of Medicine

Review Timeline:

Submission Date: June 17, 2022
Editorial Decision: August 3, 2022
Revision Received: August 5, 2022
Accepted: August 10, 2022

Editor: JJ Miranda

Reviewer(s): The reviewers have opted to remain anonymous.

Transaction Report:

(Note: With the exception of the correction of typographical or spelling errors that could be a source of ambiguity, letters and reports are not edited. The original formatting of letters and referee reports may not be reflected in this compilation.)

DOI: https://doi.org/10.1128/spectrum.02285-22
August 3, 2022

Dr. William R Jacobs  
Albert Einstein college of Medicine  
Department of Microbiology and Immunology  
1300 Morris park Ave  
Price 569  
Bronx, New York 10461

Re: Spectrum02285-22 (Capturing structural variants of herpes simplex virus genome in full length by Oxford Nanopore sequencing)

Dear Dr. William R Jacobs:

I thank you for your contribution to those interested in herpesviruses sequencing. Two experts in the field have reviewed this manuscript, and the comments were split on the novelty and significance of the findings. I’ve also examined the submission and concluded that the work is technically sound and within the scope of Spectrum’s mission to publish Observations that are rigorous without consideration of potential impact.

I look forward to a thoughtful revision that includes data sharing depositions and a more thorough review of similar previously published methods.

Thank you for submitting your manuscript to Microbiology Spectrum. When submitting the revised version of your paper, please provide (1) point-by-point responses to the issues raised by the reviewers as file type "Response to Reviewers," not in your cover letter, and (2) a PDF file that indicates the changes from the original submission (by highlighting or underlining the changes) as file type "Marked Up Manuscript - For Review Only". Please use this link to submit your revised manuscript - we strongly recommend that you submit your paper within the next 60 days or reach out to me. Detailed instructions on submitting your revised paper are below.

Link Not Available

Below you will find instructions from the Microbiology Spectrum editorial office and comments generated during the review.

ASM policy requires that data be available to the public upon online posting of the article, so please verify all links to sequence records, if present, and make sure that each number retrieves the full record of the data. If a new accession number is not linked or a link is broken, provide production staff with the correct URL for the record. If the accession numbers for new data are not publicly accessible before the expected online posting of the article, publication of your article may be delayed; please contact the ASM production staff immediately with the expected release date.

The ASM Journals program strives for constant improvement in our submission and publication process. Please tell us how we can improve your experience by taking this quick Author Survey.

Sincerely,

JJ Miranda  
Editor, Microbiology Spectrum

Journals Department  
American Society for Microbiology  
1752 N St., NW  
Washington, DC 20036  
E-mail: spectrum@asmusa.org

Reviewer comments:

Reviewer #1 (Public repository details (Required)):
The raw sequencing data need to be deposited to the Sequencing Read Archive.

Reviewer #1 (Comments for the Author):

This is a very interesting study, the full-genome sequences of the virus are extremely important. The manuscript could gain by citing and commenting on a previous study performed by Karamitros et al. where Nanopore and short read sequenced were combined. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4910999/

Reviewer #2 (Public repository details (Required)):

ONT sequencing data and Illumina sequencing data need to be deposited to NCBI SRA database

Reviewer #2 (Comments for the Author):

In "Capturing structural variants of herpes simplex virus genome in full length by Oxford Nanopore sequencing", authors improved HSV-1 improved viral genome DNA, observed 15 full-length genome of four types isomers and obtained the composition of four isomers based on reads containing IRL, IRS and flanking regions.

Both the viral DNA prep method improvement and virology discovery aren't significant enough for publication.

Staff Comments:

Preparing Revision Guidelines

To submit your modified manuscript, log onto the eJP submission site at https://spectrum.msubmit.net/cgi-bin/main.plex. Go to Author Tasks and click the appropriate manuscript title to begin the revision process. The information that you entered when you first submitted the paper will be displayed. Please update the information as necessary. Here are a few examples of required updates that authors must address:

• Point-by-point responses to the issues raised by the reviewers in a file named "Response to Reviewers," NOT IN YOUR COVER LETTER.
• Upload a compare copy of the manuscript (without figures) as a "Marked-Up Manuscript" file.
• Each figure must be uploaded as a separate file, and any multipanel figures must be assembled into one file.
• Manuscript: A .DOC version of the revised manuscript
• Figures: Editable, high-resolution, individual figure files are required at revision, TIFF or EPS files are preferred

For complete guidelines on revision requirements, please see the journal Submission and Review Process requirements at https://journals.asm.org/journal/Spectrum/submission-review-process. Submissions of a paper that does not conform to Microbiology Spectrum guidelines will delay acceptance of your manuscript.

Please return the manuscript within 60 days; if you cannot complete the modification within this time period, please contact me. If you do not wish to modify the manuscript and prefer to submit it to another journal, please notify me of your decision immediately so that the manuscript may be formally withdrawn from consideration by Microbiology Spectrum.

If your manuscript is accepted for publication, you will be contacted separately about payment when the proofs are issued; please follow the instructions in that e-mail. Arrangements for payment must be made before your article is published. For a complete list of Publication Fees, including supplemental material costs, please visit our website.

Corresponding authors may join or renew ASM membership to obtain discounts on publication fees. Need to upgrade your membership level? Please contact Customer Service at Service@asmusa.org.

Thank you for submitting your paper to Microbiology Spectrum.
In "Capturing structural variants of herpes simplex virus genome in full length by Oxford Nanopore sequencing", authors improved HSV-1 improved viral genome DNA, observed 15 full-length genomes of four types of isomers and obtained the composition of four isomers based on reads containing IRL, IRS and flanking regions.

Both the viral DNA prep method improvement and virology discovery aren't significant enough for publication.
Dear Dr. Miranda

We thank you and the two reviewers for taking the time to review our submission and their comments. Please find below the pointwise response in bold letters. The manuscript has been revised and we have highlighted all changes in the manuscript.

Reviewer #1

The raw sequencing data need to be deposited to the Sequencing Read Archive.

We submitted both ONT and Illumina Miseq raw data to NCBI-SRA database and included the SRA number in the revised manuscript

This is a very interesting study, the full-genome sequences of the virus are extremely important. The manuscript could gain by citing and commenting on a previous study performed by Karamitros et al. where Nanopore and short read sequenced were combined.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4910999/

We thank the reviewer for pointing out this important study. We discussed the findings of this publication and included in the revised manuscript

Reviewer #2

ONT sequencing data and Illumina sequencing data need to be deposited to NCBI SRA database

We submitted both ONT and Illumina Miseq raw data to NCBI-SRA database and included the SRA number in the revised manuscript

In "Capturing structural variants of herpes simplex virus genome in full length by Oxford Nanopore sequencing", authors improved HSV-1 improved viral genome DNA, observed 15 full-length genome of four types isomers and obtained the composition of four isomers based on reads containing IRL, IRS and flanking regions.

Both the viral DNA prep method improvement and virology discovery aren't significant enough for publication.

To our knowledge, this would be first report on capturing full-length sequences of the four isomers as single read from a herpesvirus DNA preparation. This is important as mutations are often found among the genes in inverted repeat elements, which are present in two copies and hard to capture
with shotgun sequencing approaches. Causality of mutation-induced phenotypes could only be concluded with full-length genome sequences. We believe that future work will improve using this DNA isolation method and ONT would be the assay for studying HSV. B3x1.1 is a highly virulent recent clinical isolate that is a valuable strain for future vaccine works and genetic studies.

We thank the reviewers for the opportunity to improve our manuscript,

William R. Jacobs Jr, PhD
August 10, 2022

Dr. William R Jacobs
Albert Einstein college of Medicine
Department of Microbiology and Immunology
1300 Morris park Ave
Price 569
Bronx, New York 10461

Re: Spectrum02285-22R1 (Capturing structural variants of herpes simplex virus genome in full length by Oxford Nanopore sequencing)

Dear Dr. William R Jacobs:

Thank you for your contribution of methods that may further the study of herpesvirus genomics.

Your manuscript has been accepted, and I am forwarding it to the ASM Journals Department for publication. You will be notified when your proofs are ready to be viewed.

The ASM Journals program strives for constant improvement in our submission and publication process. Please tell us how we can improve your experience by taking this quick Author Survey.

As an open-access publication, Spectrum receives no financial support from paid subscriptions and depends on authors’ prompt payment of publication fees as soon as their articles are accepted. You will be contacted separately about payment when the proofs are issued; please follow the instructions in that e-mail. Arrangements for payment must be made before your article is published. For a complete list of Publication Fees, including supplemental material costs, please visit our website.

ASM policy requires that data be available to the public upon online posting of the article, so please verify all links to sequence records, if present, and make sure that each number retrieves the full record of the data. If a new accession number is not linked or a link is broken, provide production staff with the correct URL for the record. If the accession numbers for new data are not publicly accessible before the expected online posting of the article, publication of your article may be delayed; please contact the ASM production staff immediately with the expected release date.

Corresponding authors may join or renew ASM membership to obtain discounts on publication fees. Need to upgrade your membership level? Please contact Customer Service at Service@asmusa.org.

Thank you for submitting your paper to Spectrum.

Sincerely,

JJ Miranda
Editor, Microbiology Spectrum

Journals Department
American Society for Microbiology
1752 N St., NW
Washington, DC 20036
E-mail: spectrum@asmusa.org

Supplemental Material: Accept