

HIV-1 nuclear import is selective and depends on both capsid elasticity and nuclear pore adaptability

Corresponding Author: Professor Peijun Zhang

Version 0:

Reviewer comments:

Reviewer #1

(Remarks to the Author)

This is a very important study on nuclear import of HIV-1 cores.

It has been established that HIV-1 cores pass the NPC in a self-translocating manner, but a structural understanding of the process is lacking. Here, the authors devised an innovative approach, using permeabilized cells in conjunction with cryoCLEM, FIB-milling, and cryo-ET analysis to visualize HIV-1 cores during their passage through NPCs. We learn that NPCs apparently select for smaller HIV-1 cores, that the E45A and N74D mutants largely reduce NPC passage, and that NPCs do not have to open laterally for core passage. The latter a particularly important finding in light of a recent publication to suggest otherwise.

I am in full support of publication of the manuscript in its current form. It is well written, highly accessible to a broad audience, and a major advance in the field.

Reviewer #2

(Remarks to the Author)

This revised study addresses all of the concerns I provided in the prior review, and also appears to similarly address the concerns of the other reviewers. While I have not reviewed the prior manuscript again, this manuscript has clearly been expanded significantly and with great effort and the numbers and quantification of events are now quite strong, much stronger than I recall in the previous version. I agree with the other reviewer that the manuscript felt a bit rushed. However, In my opinion, the current manuscript is strong and worthy of publication in its current state.

Decision Letter:

Our ref: NMICROBIOL-25031043-T

30th April 2025

Dear Dr. Zhang,

Thank you for submitting your revised manuscript "Correlative In Situ Cryo-ET Reveals Cellular and Viral Remodeling for Selective Nuclear Import of HIV-1 Cores" (NMICROBIOL-25031043-T). It has now been seen by the original referees and their comments are below. The reviewers find that the paper has improved in revision, and therefore we'll be happy in principle to publish it in Nature Microbiology, pending minor revisions to comply with our editorial and formatting guidelines.

If the current version of your manuscript is in a PDF format, please email us a copy of the file in an editable format (Microsoft Word or LaTeX)-- we can not proceed with PDFs at this stage.

We are now performing detailed checks on your paper and will send you a checklist detailing our editorial and formatting requirements in about a week. Please do not upload the final materials and make any revisions until you receive this additional information from us.

Thank you again for your interest in Nature Microbiology Please do not hesitate to contact me if you have any questions.

Sincerely,

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Version 1:

Decision Letter:

3rd June 2025

Dear Peijun,

I am delighted to accept your Article "HIV-1 nuclear import is selective and depends on both capsid elasticity and nuclear pore adaptability" for publication in Nature Microbiology. Thank you for having chosen to submit your work to us and many congratulations.

Over the next few weeks, your paper will be copyedited to ensure that it conforms to Nature Microbiology style. We look particularly carefully at the titles of all papers to ensure that they are relatively brief and understandable.

Once your paper is typeset, you will receive an email with a link to choose the appropriate publishing options for your paper and our Author Services team will be in touch regarding any additional information that may be required. Once your paper has been scheduled for online publication, the Nature press office will be in touch to confirm the details.

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With kind regards,

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Point-by-point responses to reviewers' comments

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