VP40: Transformer Extraordinaire

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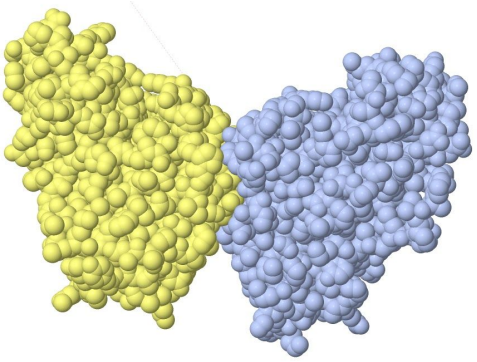
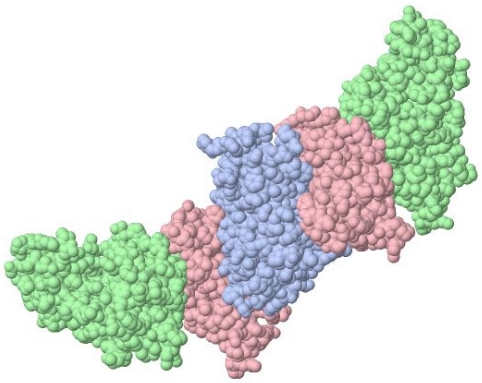
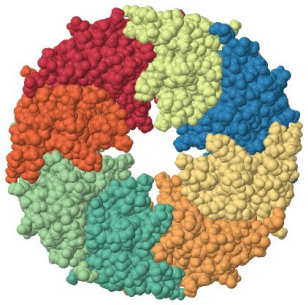


EBOV Matrix Protein VP40 is responsible for multiple roles throughout the infection process, mainly in part due to its multiple different forms as a dimer, hexamer, and octamer. The VP40 dimer as shown to the right is responsible for cell invasion, primarily through cellular trafficking. The VP40 dimer is then responsible for viral budding and transcription, but much is unknown about the nature of viral budding in the dimer state. Furthermore, the use of dimers is necessary for the formation of the hexamer and octamer, and is initiated through the CTD (carboxyl terminal domain).



Following oligomerization of VP40, three VP40 dimers combine together to form the hexamer. The hexamer is the second stage and the second 'role' of VP40, responsible for viral budding similar to the dimer. VP40 as a hexamer is almost identical to tomographic images of authentic virions, accentuating the key role of VP40 and its transformations. The importance of the hexamer phase of VP40 is heavily reliant on its ability to interact with both the infected cell membrane, as well as the nucleocapsid. By being able to interact with both sides, VP40 is capable of mechanics beyond solely immune evasion and viral budding. Access to both the cell membrane and nucleocapsid encourages cellular bridging between the two points, allowing for viral budding and the structure of VP40.

Finally, VP40 is capable of forming a perfectly symmetrical structure in the shape of a ring as an octamer. The ring shaped is formed via the binding of eight VP40 NTDs with RNA trinucleotides, which in turn allow the CTD to bind to one another. The octamer is responsible for RNA-binding, and does not take place in the process of budding or assembly. VP40 as an octamer is responsible for a more regulatory function rather than the building of a structural one, responsible for the advancement of infection. The role of octameric VP40 lies in viral transcription of RNA and as a result viral replication. Much is still unknown about the nature and function of the octamer, and information is still being gathered on the function that VP40 as an octamer provides.



Sources

Bornholdt, Z A, et al. "Structural Rearrangement of Ebola Virus VP40 Begets Multiple Functions in the Virus Life Cycle." *Cell.*, U.S. National Library of Medicine, 15 Aug. 2013, www.ncbi.nlm.nih.gov/pubmed/?term=23953110.

Brandt, Janine, et al. "Structure and Functions of the Ebola Virus Matrix Protein VP40." *Future Virology*, vol. 14, no. 1, 18 Dec. 2018, pp. 21–30., doi:10.2217/fvl-2018-0162.

Hoenen, Thomas, et al. "VP40 Octamers Are Essential for Ebola Virus Replication." *Journal of Virology*, American Society for Microbiology, Feb. 2005, www.ncbi.nlm.nih.gov/pubmed/15650213.

Noda, Takeshi, et al. "Assembly and Budding of Ebolavirus." *PLoS Pathogens*, Public Library of Science, Sept. 2006, www.ncbi.nlm.nih.gov/pmc/articles/PMC1579243/#idm140443680147936title.

"PDB101: Molecule of the Month: Ebola Virus Proteins." Edited by David Goodsell, *RCSB*, Oct. 2014, pdb101.rcsb.org/motm/178.