Cell Entry and Antibody Response to Ebola

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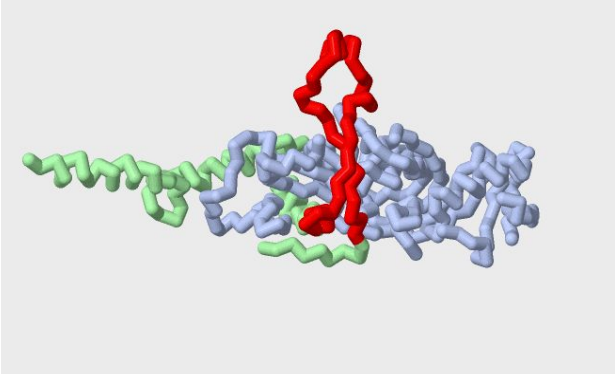
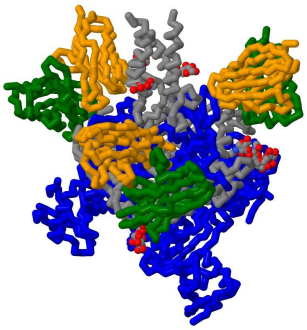
Cell entry



Cell entry for Ebola occurs through macropinocytosis with Glycoproteins(GP) GP1 and GP2. How Ebola initiates macropinocytosis is not fully understood, however; a group of Hydrophobic residues in GP2 referred to as the internal fusion loop(IFL) shown in red is key in this process, and governs fusion of GP. It has been proposed that IFL disrupts lipids at the contact point between virus and host cell to initiate fusion. Once the GP complex attaches to the Nieman Pic receptor in a low pH solution, the GP2 changes shape, pulling the Virus membrane and cell membranes closer together to initiate fusion. This is very similar to other common viruses such as influenza.



Antibody Response

Antibodies are the body's natural defence against viruses. Antibodies operate by interrupting an active process in an invading cell. In a human survivor of a 1995 outbreak in Kikwit this antibody response is directed at a vulnerable non-glycosylated epitope located near the bottom of the glycoprotein chalice. This antibody was named KZ52. Most of the GP smothered by the KZ52 is GP2; however, the presence GP1 is necessary for GP2 to be in the proper perfusion stated for KZ52 to bind. It is suspected that KZ52 operates by Interfering with the IFL which blocks GP2 from rearranging.

Sources

Ehrhardt, Stefanie A., et al. “Polyclonal and Convergent Antibody Response to Ebola Virus Vaccine RVSV-ZEBOV.” Nature News, Nature Publishing Group, 7 Oct. 2019, www.nature.com/articles/s41591-019-0602-4.

Gregory, Sonia M, et al. “Structure and Function of the Complete Internal Fusion Loop from Ebolavirus Glycoprotein 2.” Proceedings of the National Academy of Sciences of the United States of America, National Academy of Sciences, 5 July 2011, www.ncbi.nlm.nih.gov/pubmed/21690393.

Lee, et al. “Structure of the Ebola Virus Glycoprotein Bound to an Antibody from a Human Survivor.” Nature, www.rcsb.org/structure/3csy.

Lee, Jeffrey E, et al. “Structure of the Ebola Virus Glycoprotein Bound to an Antibody from a Human Survivor.” Nature, U.S. National Library of Medicine, 10 July 2008, www.ncbi.nlm.nih.gov/pmc/articles/PMC2700032/#!po=22.9167.