

Evolutionary origin of the proteins involved in the entry of and defense to the Ebola virus in the host cell

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The Ebola virus (EBOV) belongs to Filoviridae family and is the causative of a devastating disease, with a mortality rate of about 50-90%, known as Ebola hemorrhagic fever. The first symptoms developed by infected patient are fever, malaise and muscle pain, and can be followed by bleeding and organ failure. The known virus hosts are humans as well as non-human hosts, like other primates and fruit bats. The Ebola mechanism of infection is complex, which makes it versatile. In this work, we revised the scientific literature that unravels the infection mechanism of EBOV and collected the host proteins known to mediate infection by their interaction with the viral proteins. We also analyzed the homologous of each collected human proteins along the taxonomic tree using the software SeedServer and Genesis to infer their clade/epoch of origin. Several researches indicate the relevance of Ebola glycoproteins GP1 and GP2 as targets for evolutionary researches and therapeutics, since they participate in virus infection mechanism on host cells and they are conserved throughout EBOV strains. The glycoproteins GP1 and GP2 interact with some main proteins on host cell: CLEC4M, CD209, EGFR, NPC1, NPC2, CLEC10A, TYRO3, FOLR1, CTSB, CTSL, which participate directly or indirectly of the infection mechanism. Conversely, the defense capability of the host to the Ebola virus is much debilitated because of the genomic diversity of the five known EBOV strains and the virus interaction with the host immune system proteins responsible for signaling an invader agent. They are: MHCI, EGFR, TETHERIN, ITGA1, ITGA2, ITGA3, ITGA4, ITGA5, ITGA6, ITGAV, ITGB1, ITGB3 and ADAM17. This interaction of the virus with proteins causes a delay leading to low expression of the immune response. The result of the evolutionary origin analysis of these proteins showed that the virus could infect even vertebrates, suggesting that animals such as fish and amphibians could be infected and retransmit the virus to other hosts such as man. Regarding the immune response, the evolutionary analysis suggests that it began to be developed in Eukaryota but the full response was achieved more recently, only in Eutheria (placental animals like dog, elephant, primates, among others). The origin and the Ebola virus cycle in hosts is still uncertain, therefore these results bring questions about new reservoirs and suggest that defense against it is more recent than the possibility of infection.

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