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Ebolavirus GP stalk-specific antibodies from survivors effectively target multiple steps of viral infection

Recent studies suggest that some glycoprotein (GP) specific monoclonal antibodies (mAbs) can protect experimental animals against the filovirus Ebola virus (EBOV). Multiple mAbs have been isolated previously from blood samples of human survivors of natural Bundibugyo ebolavirus (BDBV) infection (Flyak A. et al., Cell 2016). A panel of mAbs from four individual donors has been selected to study the mechanisms of infection inhibition. BDBV41 and BDBV289 mAbs specific to GP glycan cap (GC) inhibited virus attachment to the cells, whereas stalk-specific BDBV259, BDBV317 and BDBV223 mAbs were able to traffic to endosomal compartments together with virions and block the late steps of entry. BDBV270 and BDBV289 GC mAbs and BDBV317 mAb targeting membrane proximal external region (MPER) dose-dependently inhibited cell-to-cell viral transmission, which corresponded to the observed differences in mAb efficiency against high multiplicity of infection. The egress of virus from infected cells was suppressed by all glycan cap-specific mAbs, with strongest inhibition observed for the single non-neutralizing BDBV52 mAb. BDBV223 MPER mAb showed superior antiviral activity in vitro at each step of viral replication analyzed. In time course experiments, only MPER mAbs inhibited virus replication when added post-infection. The activation and degranulation of natural killer cells and monocyte phagocytosis relied mostly on IgG subclass, with the highest levels demonstrated by IgG3 mAbs. Finally, MPER mAbs conferred full protection against EBOV infection in mice. Altogether, these results suggest usage of mAbs with different epitope specificity could complement inhibition of multiple steps of filovirus infection through Fab- and Fc-mediated mechanisms.

Biography

Prof. Bukreyev has completed his PhD in 1993 and completed his postdoctoral studies at the National Institute of Allergy and Infectious Diseases, NIH. He is professor at the University of Texas Medical Branch at Galveston. His laboratory focuses on development of vaccines against highly pathogenic viruses filoviruses Ebola and Marburg and on investigation of mechanisms of their high pathogenicity. He has published more about 90 papers in reputed journals including *Science, Cell, Journal of Clinical Investigation, PNAS, PLOS Pathogens, The Lancet, Journal of Virology, Vaccine* and others. He is a member of NIH Vaccines Against Microbial Diseases Study Section.

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