

## Vaccines 2017-Ebolavirus GP stalk-specific antibodies from survivors effectively target multiple steps of viral infection- Alexander Bukreyev - University of Texas

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### Abstract

Research suggests that few glycoprotein specific monoclonal antibodies can prevent experimental animals against the filovirus Ebola virus. Different mAbs are isolated previously from blood samples of human survivors of natural Bundibugyoebolavirus (BDBV) infection (Flyak A. et al., Cell 2016). A panel of mAbs from four individual donors has been selected to review 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 ready to traffic to endosomal compartments alongside 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 only non-neutralizing BDBV52 mAb. BDBV223 MPER mAb resulted in better antiviral activity in vitro at each step of viral replication analyzed. In course of time taking experiments, only MPER mAbs inhibited virus replication is observed when added post-infection. The activation and degranulation of natural killer cells and monocyte phagocytosis relied totally on IgG subclass, with the very best levels demonstrated by IgG3 mAbs. Finally, MPER mAbs conferred full protection against EBOV infection in mice. All the factors and results suggest usage of mAbs with different epitope accuracy could complement inhibition of multiple steps of filovirus infection through Fab- and Fc-mediated mechanisms.

There are 2 types of antibodies that specialize in different kinds of the Ebola virus synergize their antiviral effects by inhibiting different steps of infection, according to a study published August 23 within the open-access journal PLOS Pathogens by Philipp Ilinykh and colleagues from the University of Texas Medical Branch, Vanderbilt University, and Ragon Institute. These new insights into how the human system protects against Ebola infections could lead on to the event of effective antibody-based therapies. The unprecedented Ebola virus epidemic in West Africa from 2013 to 2016 resulted in additional than 11,000 human fatalities, demonstrating the urgent need for treatments against this virus and related highly pathogenic filoviruses.

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To address this gap in knowledge, Ilinykh and colleagues evaluated the mechanisms underlying the antiviral effects of a various panel of monoclonal antibodies obtained from several survivors of natural Ebola virus infections. Monoclonal antibodies that targeted either the glycan cap or stem region of the viral glycoprotein interfered with and targeted different steps of filovirus infection. For instance, glycan cap-specific antibodies inhibited viral attachment to the cell surface, cell-to-cell transmission and virion budding. Against this, stem-specific antibodies triggered the activation of natural killer cells and therefore the destruction of infected cells by monocytes and neutrophils.

Taken together, the findings suggest that differing types of antibodies exert cooperative effects by blocking distinct steps of filovirus infection. Consistent with the authors, antibody cocktails that combine complementary antiviral effects should be tested in future studies.

The current development for treatment of filovirus infections are tested with antibody cocktails in animal models utilizes the method of targeting the non-overlapping epitopes. The research suggests that possible synergistic effects of antibodies those that block different steps of viral replication must be also involved."

These new insights into how the human system protects against Ebola infections could lead on to the event of effective antibody-based therapies. The unprecedented Ebola virus epidemic in West Africa from 2013 to 2016 resulted in additional than 11,000 human fatalities, demonstrating the urgent need for treatments against this virus and related highly pathogenic filoviruses. Despite intense international collaborative efforts, there's still no licensed therapeutic available again stalk-specific BDBV259, BDBV317 and BDBV223 mAbs were ready to traffic to endosomal compartments alongside 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.

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