Abstract

Neutralizing Antibodies against Crimean–Congo Hemorrhagic Fever Virus Derived from a Human Survivor [†]

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Abstract: Crimean–Congo hemorrhagic fever virus (CCHFV) is an arbovirus belonging to the *Nairoviridae* family. The virus, as well as ticks of the *Hyalomma* genus, which serve as its reservoir host, are found in parts of Africa, western Asia, and southern Europe. Following sporadic zoonotic or human-to-human transmission, infection is characterized by fever, fatigue, vomiting, diarrhea, and in fatal cases, often hemorrhagic symptoms. There are currently no vaccines or targeted treatments available against CCHFV, leading the WHO to declare it a Blueprint priority pathogen in 2017. Here, we report the isolation and characterization of a panel of human monoclonal antibodies (mAbs) against CCHFV. Using a novel soluble Gn/Gc sorting antigen, we were able to isolate memory B cells specific for CCHFV from four convalescent donors. From each patient sample, we were able to derive several potentially neutralizing antibodies with IC₅₀ in the nanomolar range as determined by neutralization of CCHFV virus-like particles. Neutralization by candidate hits was also confirmed using authentic CCHFV. We further show that several of the most potentially neutralizing mAbs possess a breadth of neutralization spanning three clades of CCHFV strains. These broadly neutralizing mAbs are currently being tested in a mouse model of CCHFV infection, with preliminary results indicating that they have protective potential.

Keywords: CCHFV; antibody; B cell

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