

Bispecific single-domain antibody based complexes protect against bunyavirus infections

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Facts & Figures

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Challenge

Zoonotic diseases have a profound impact on human and animal health. To combat these diseases, a “One Health approach”, uniting the human medical and veterinary fields, is required. The ZAPI project aims to develop universal pipelines for the design and surge production of vaccines and protective antibodies. Here we describe the development of neutralizing antibodies targeting two important bunyaviruses; Rift Valley fever virus (RVFV) and Schmallenberg virus (SBV).

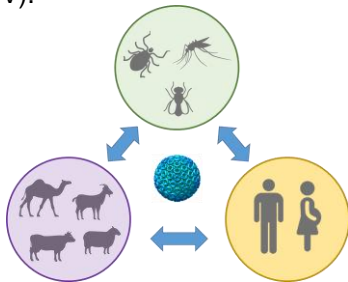


Figure 1. Bunyaviruses are arthropod-borne viruses that cause disease in humans and animals

Approach & Methodology

Single-domain antibodies targeting key immunogens were used as building blocks to design RVFV and SBV-specific neutralizing antibodies.

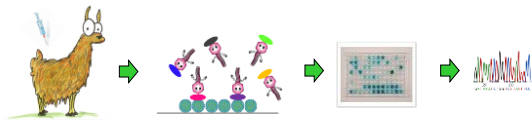


Figure 2. Illustration of single-domain antibody selection procedure

Results

Two panels of single-domain antibodies targeting RVFV-Gn and SBV-Gc were identified and characterized.

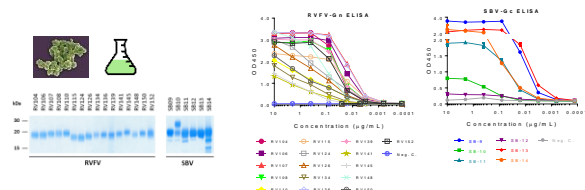


Figure 3. RVFV and SBV-specific single-domain antibodies were produced in yeast and confirmed to bind to the key immunogens used for selection.

Although individual single-domain antibodies hardly showed neutralization, combinations of two antibodies targeting distinct antigenic sites revealed efficient neutralization.

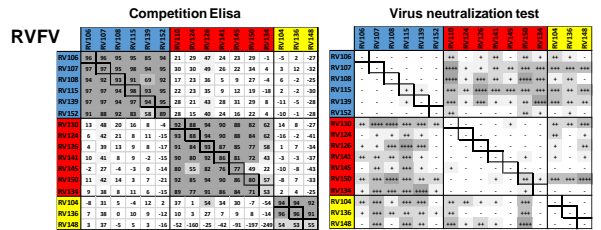


Figure 4. Mapping of single-domain antibody binding sites and *in vitro* virus neutralization

Single-domain antibody complex formation using bacterial superglue considerably improved neutralization activity

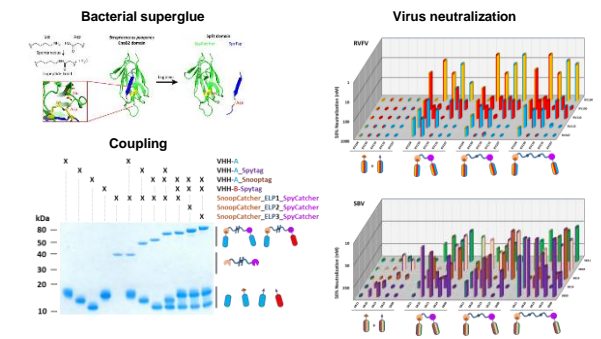


Figure 5. Formatting of single-domain antibodies with the use of bacterial superglue and evaluation of neutralization activity

Single-domain antibody complexes are effective *in vivo*

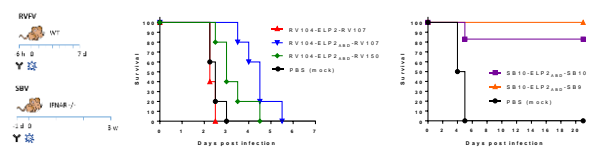


Figure 6. ELP scaffold based *in vivo* neutralization of single-domain antibody complexes

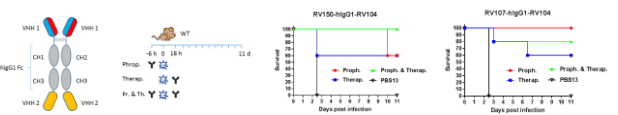


Figure 7. Human IgG1 based *in vivo* neutralization of single domain antibodies

Value of IMI collaboration

The interplay between EFPIA and academic partners facilitated product development.

Impact & take home message

Single-domain antibodies provide a valuable platform for the development of bunyavirus protective antibodies.