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Using the power of *in vitro* selection by phage display to identify recombinant antibodies with optimised properties to various life threatening viruses

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Using *in vitro* selections via phage display from both a human universal library or from libraries generated after immunisation, we were able to isolate a panel of recombinant antibodies to various viruses considered to be a bioterrorist threat agent. In particular, antibodies to Venezuelan equine encephalitis virus (VEEV), influenza H5N1, western equine encephalitis virus (WEEV), as well as other bioterrorist threat reagents like anthrax and ricin, were succesfully generated.

A major advantage of *in vitro* antibody selection is the ability to carefully control the biochemical conditions during the very moment of selection, for example, by presentation of specific conformations of the target antigen, or by including competitors to direct selection towards specific targets or epitopes of interest. Sequential use of different antigens facilitates the selection of shared epitopes. Here, we describe several cases where these strategies were crucial for the selection of novel antibodies with enhanced properties. The identification of specific human antibodies to VEEV benefited from the possibility to add soluble competitors during the *in vitro* selection process. In particular, the addition of host cell extract allowed to select for epitopes specific for the virus even allowing to use a virus preparation containing a substantial fraction of host cell proteins. In case of the neutralizing antibodies to a novel epitope in influenza (bird flu), a very broad specificity range was obtained by a sequential panning strategy on evolutionary distant virus strains, to identify the common epitope. These examples illustrate *in vitro* selection strategies which are be broadly applicable to other problems in virology.

Biography

Stefan Dübel is Full Professor of Biotechnology and Director of the Biotechnology department. He pioneered *in vitro* antibody selection technologies, resulting in several key inventions including antibody phage display (e.g. US-Patent 5849500) and human antibody libraries with randomised CDRs (e.g. US-Patent 5840479). His lab continued to contribute to multiple topics related to human antibody engineering and phage display, e.g. Hyperphage technology (2001) or targeted human RNases for cancer therapy (2008). He is initiator of the "Antibody factory" of the German National Gemome Research Network and editor of the three volume "Handbook of Therapeutic Antibodies" and other antibody engineering books.