Ebola, Nipah, and ???: ‘Plug-and-Play’ for the rapid production of protective antibodies

Epidemics caused by dangerous pathogens such as Ebola virus can occur without warning. The administration of protective antibodies against a pathogen is one approach to save lives and reduce the number of victims. How can they be produced quickly and in large quantities in the event of outbreaks? Researchers at the Paul-Ehrlich-Institut with scientists at DZIF (German Center for Infection Research) have shown that adjuvanted virus-like particles (VLPs) could be used as a plug-and-play system to rapidly generate functional antibodies in animals that could then be used to treat infected individuals. The results are reported in the online edition of npj Vaccines on 05.10.2018.

Outbreaks of infectious diseases can sometimes reach epidemic proportions, such as the large Ebola virus outbreak in Western Africa in 2014, which resulted in more than 28,500 infections and 11,000 deaths. A new Ebola outbreak in the Democratic Republic of the Congo is currently being fought. Nipah and Hendra viruses are examples of other dangerous pathogens, which have thus far caused only minor outbreaks, such as the Nipah outbreak ongoing in India.

Effective vaccines against known pathogens have been available for many years. However, in the event of an outbreak with new life-threatening pathogens, therapeutics are needed that can be produced very quickly for many people and provide protection until a vaccine becomes available. Passive immunisation, the administration of convalescent plasma containing specific functional antibodies, provides a straightforward way to treat infected individuals. Here one makes use of the fact that during an infection, antibodies are produced by the immune system and then circulate in the blood of the convalescent patient. The convalescents’ blood plasma, which contains sufficient levels of neutralising antibodies against the specific pathogen, can then be administered to newly infected patients and protect them from disease, or at least prevent severe outcomes. However, convalescent plasma is often scarce, since only individuals who have already recovered from the disease can serve as donors. Here the production of hyperimmune sera in animals constitutes an attractive alternative. Researchers at Paul Ehrlich Institute led by Prof. Veronika von Messling, Director of the Division of Veterinary Medicine, have collaborated with researchers from the Universities of Marburg and Munich as part of the German Center for Infection Research (DZIF) using Ebola and Nipah viruses as models to investigate how the production of functional antibodies in rabbits can be induced as effectively as possible.

The researchers found that adjuvanted virus-like particles (VLPs) efficiently stimulated the production of functional antibodies at high titers in animals. VLP-based vaccines are particularly interesting because the immune system recognises them as virus particles, but VLPs do not multiply in target cells. The high antibody titres observed here indicate that de novo antigen expression is less important for the production of functional antibodies than the presentation of the antigen in its natural form. With an optimised purification process, concentrated polyclonal antibodies were obtained that were stable in vivo. Such polyclonal antibody concentrates have the advantage to be directed against different sites (epitopes) of the pathogen, so there is less risk of loss of function due to mutations in the virus compared to monoclonal antibodies which are directed against only one epitope. Nipah VLPs were also able to induce the production of high-titre functional antibodies. VLPs can be produced in sufficient quantities for the immunisation of animals within one to two weeks, and can be produced for different pathogens, so that they could
potentially be used as a convenient plug-and-play system for antibody production. “We consider the production of polyclonal antibodies using pathogen-adapted adjuvanted VLPs a promising approach for the rapid delivery of protective immune sera in the event of outbreaks of new dangerous viruses”, says Dr. Veronika von Messling in explaining the research team’s results.

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Immediate Immunity provided by passive antibody transfer as a first line defence in outbreak of emerging infections

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