Editorial

Rainer Ulrich^a George P. Lomonosoff^b Detlev H. Krüger^a

^aInstitute of Virology, Charité Medical School, Humboldt University, Berlin, Germany;

^bDepartment of Metabolic Biology, John Innes Centre, Norwich, UK

The development of efficient vaccines requires an interdisciplinary collaboration between physicians, epidemiologists, researchers in basic virology and immunology and experts in vaccine development. In addition, this cooperation should include not only research groups but also representatives of the World Health Organization, admittance authorities and pharmaceutical companies. The need to develop such a wide-ranging collaboration formed the background for the organisation of the latest International Workshop 'Virus-Like Particles as Vaccines', held for the third time at the Charité Medical School in Berlin in September 2001.

In contrast to the previous two workshops held in 1995 and 1998 [1, 2], which mainly focussed on the development of different virus-like particle carriers as potential sources of novel vaccines, the recent workshop was specifically dedicated to the creation and evaluation of vaccines against important viral pathogens such as hepatitis B virus (HBV), human immunodeficiency virus (HIV), human papilloma virus (HPV) and hantaviruses. These pathogens were selected not only because of their importance but also because of the fact that virus-like particles (VLPs) represent plausible vaccine candidates to combat infections by these viruses. This is confirmed by the fact that the first clinical trials for VLP-based vaccines against HIV, HPV, Norwalk virus and parvovirus infections have been completed (see Lechner et al.). However, in addition to VLPs (see contributions of Lechner et al., Menne et al., Wakabayashi et al., Sasnauskas et al., Kazaks et al., Sällberg et al. and Brown et al.), other vaccination strategies

such as those based on the use of inactivated viruses (see Norley et al. and Cho et al.), live attenuated viruses (see Norley et al.), recombinant viruses (see Chatterji et al.), recombinant proteins (see Khattak et al.), synthetic peptides (see Norley et al.) and naked DNA vaccines (see El Kholy et al., Bojak et al., Norley et al. and Michel et al.) are covered by this issue, since the comparative evaluation of different approaches will be extremely important in the development of effective vaccines.

As an advance on the previous meetings, the recent workshop enabled the generation of a more complex and complete picture of the nature of the viral infections mentioned above and the basic knowledge which will be necessary for vaccine development. Consequently, in this issue of *Intervirology*, original papers specifically about development of vaccines against HBV, HIV, HPV and hantaviruses are introduced by reviews summarizing recent knowledge regarding the molecular biology, pathogenicity, epidemiology and immunology of these virus infections (see Pumpens et al., Marcus et al., Streeck and Ulrich et al.).

This issue covers selected presentations, most of which were delivered at the workshop in Berlin. The first two papers consist of general overviews of the history and perspectives of vaccine development (Hilleman) and the value of VLPs in vaccine development and treatment of allergy (Lechner et al.). The latter contribution also describes a unique principle of modular VLPs based on specific attachment sites (lysine) on the carrier and (engineered) single free cysteines on the antigen.

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Prof. Detlev H. Krüger
Institute of Virology
Humboldt University, School of Medicine Charité
D-10098 Berlin (Germany)
Tel. +49 30 450 525092, Fax +49 30 450 525907, E-Mail detlev.kruger@charite.de

Contributions dealing with new insights into HBV vaccine development are introduced by an update of recent knowledge regarding the molecular epidemiology and immunology of HBV infections (Pumpens et al.). A new approach to establishing an *in vivo* model for HBV infection based on recombinant HBV genomes containing substitutions of the preS1 of HBV by the corresponding segments of woodchuck hepatitis virus is described by Hourieux et al. The use of the woodchuck model also demonstrated the feasibility of a combination therapy of antiviral treatment with 1-(2-fluoro-5-methyl- β -*L*-arabinofuranosyl)-uracil and therapeutic vaccination with woodchuck hepatitis virus surface antigen for the control of chronic HBV infections in humans (Menne et al.). El Kholy et al. investigated the B cell immunogenicity of two HBV epitopes, namely the linear 'e2' epitope and the conformational 'a' epitope, fused to hsp73-binding or non-hsp-binding simian virus 40-T-antigen sequences when delivered as DNA vaccines. Because of the differences in immunogenicity, the authors concluded that the prerequisites that have to be fulfilled for optimal immunogenicity differ strikingly between individual epitopes. This is an important observation, since it might be true not only for HBV but for all other epitope-based vaccines.

Besides HBV, HIV represents one of the major targets for vaccine development. The epidemiology of HIV infections as well as strategies for therapy and vaccination are reviewed by Marcus et al. A number of HIV vaccine trials are summarized by Norley et al., which suggest that the 'traditional' types of vaccine are either ineffective or inappropriate for use in humans. An attractive alternative is the naked DNA vaccine approach, which can be improved in its efficiency by codon usage modification to induce a strong and long-lasting humoral and cellular immunity (Bojak et al.).

Cervical carcinoma represents one of the most frequent cancers in women worldwide. The biology of papillomaviruses, including viral structure, tropism, function of viral proteins, analysis of the immune response and search for the viral receptor, is covered by Streeck. To analyse the T cell responses to the HPV-16 E7 protein, a variety of different assays such as chromium release, ELISPOT, tetramer staining and intracellular IFN- γ assay were compared (Michel et al.). Wakabayashi et al. compared the vaccine efficacy of two types of chimeric HPV VLPs (L1-E7 or L1/L2-E7). Whereas L1-E7 VLPs are more efficient in tumor prevention than L1/L2-E7 VLPs, the L1-E7 VLPs are more limited with respect to their insertion capacity and yield in insect cells. The exciting properties of a yeast expression system allowing the for-

mation of VLPs derived from the major capsid protein of various human and non-human polyomaviruses are described by Sasnauskas et al.

Hantaviruses have attracted more interest in the public and scientific community since the discovery of the hantavirus pulmonary syndrome, with a case fatality index of up to 60%, in the USA in 1993. The review of Ulrich et al. briefly summarizes the state of the art in hantavirus research and raises selected questions which it will be necessary to address in the future. Cho et al. tested two different inactivated hantavirus vaccines, Hantavax and a bivalent Hantaan-Puumala virus vaccine, in human volunteers, demonstrating them to be immunogenic and well tolerated. Nevertheless, the authors state that these vaccines need further improvements for the induction of a long-lasting immunity. To develop an edible potential hantavirus vaccine, Khattak et al. generated transgenic tobacco and potato plants expressing a Puumala virus nucleocapsid protein which induced humoral and mucosal immune responses in rabbits and mice. Kazaks et al. highlight the advantages of using HBV core mosaic particles to accommodate larger pieces of foreign proteins.

Sällberg et al. presented promising data about a potential malaria vaccine based on chimeric HBV core particles. A new approach to coupling foreign epitopes on the surface of cowpea mosaic virus has been developed by Chatterji et al., extending the potential use of VLPs. In a similar vein, Brown et al. report that VLPs are useful not only for the presentation of foreign epitopes, but also for the encapsidation of nucleic acids and antiviral drugs.

Knowledge of the intimate interplay between a virus and the immune system of the infected host is not only necessary to understand its pathogenicity but also forms a vital background for rational vaccine development. From the aspect of the virus, genetic events like mutation, genetic drift and recombination lead to the emergence of virus variants and eventually quasispecies populations in infected humans. Consequently, the understanding of the evolution of viruses and their underlying mechanisms might have an impact on the development of vaccines and antiviral drugs. This idea should be further explored at a next workshop.

References

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