Will we have and why do we need an Ebola vaccine?

A DNA vaccine protects macaques against Ebola virus infection. Is a human vaccine finally on the way?

HANS-DIETER KLENK

Over the past month there have been numerous news reports regarding the Ugandan outbreak of Ebola virus hemorrhagic fever. As of 8 November, the Ugandan ministry of health reported 286 cases, including 94 deaths, in the Gulu district and the epidemic had spread to other parts of the country. Furthermore, a hemorrhagic fever outbreak with even higher case-fatality rates occurred in the Durba-Watsa region of the Democratic Republic of Congo. This epidemic was caused by Marburg virus, which together with Ebola virus forms the filovirus group. The outbreak began in 1999 and has not yet been contained. Both epidemics should serve to remind us that these dangerous viruses are not as rare as we used to think they were, and that we are still unable to cure or prevent them.

In the 30 November issue of *Nature*, however, Sullivan *et al.*[1] report that a vaccine may soon become available. These researchers demonstrated that DNA vaccination, followed by an adenoviral boost, protected cynomolgus macaques against the lethal effects of Ebola virus infection. The DNA immunogen consisted of a plasmid encoding the Ebola virus membrane glycoprotein and internal nucleocapsid protein. Macaques receiving the DNA boost, a recombinant adenovirus encoding the same Ebola virus proteins, had a 10–20-fold increase in antibody titer in comparison with control animals. Lymphocyte proliferation assays also revealed a strong cellular immune response against the antigen in vaccinated animals.

To determine the protective efficacy of this vaccination strategy, Sullivan *et al.*[1] infected four immunized monkeys with a highly pathogenic strain of Ebola virus. All of these animals survived without showing clinical symptoms of disease. Sterilizing immunity was achieved in three individuals, whereas one showed a transient rise in viral antigen. In contrast, the four non-immunized control animals died or were killed in moribund condition within seven days after infection.

Associated Press

People suspected of being infected with the Ebola virus at a ward in Lacor hospital, Gulu, northern Uganda

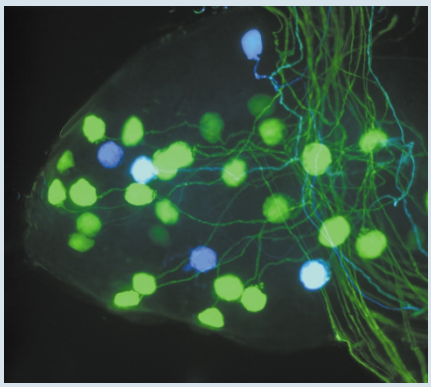
Since there are at last three different Ebola subtypes that are known to be human pathogens, a multivalent vaccine is needed. The authors therefore addressed the question of whether there would be interference between the different vaccine components, reducing the protective effect. When guinea pigs were immunized with plasmids encoding the glycoprotein of three different viral strains, protection was obtained after viral challenge, indicating that multivalent vaccines can be effective.

The Ebola virus study is not the first report to show that a filovirus vaccine can have protective effects in primates. A study performed two years ago reported that cynomolgus macaques could be completely protected against infection with Marburg virus. This vaccine was composed of Venezuelan equine encephalitis virus-based replicons expressing the glycoprotein and the nucleocapsid protein of Marburg virus[2].

Although the ability of an immuniza-

In living color

Jellyfish green fluorescent protein (GFP) can used to label living cells or proteins without exogenous cofactors or substrates, and has been a boon to neuroscientists who study neuronal development and plasticity. In addition to GFP, four other spectral variants—yellow (YFP), cyan (CFP) and red (RFP) fluorescent proteins have been developed and shown to label neurons *in vivo*. In the October issue of *Neuron*, Feng *et al*. report the generation of transgenic mice expressing CFP, YFP, GFP, or RFP under the control of neuron-specific elements from the *thy1* gene. Fluorescent neurons were found in many parts of the peripheral nervous system, including sympathetic and sensory ganglia, retina, forebrain, midbrain, cerebellum and spinal cord. Non-neuronal cells, such as muscle cells, were not labeled. The authors also showed that repeated imaging of YFP did not have toxic effects, and that this approach can be used to image neurons in living animals over long periods of time. Furthermore, fluorescently-labeled axons can survive,



grow, and even form synapses during illumination. "We plan to exploit this potential to follow synapse formation over time in wild-type animals and in mutants known to have synapse formation defects", says Joshua Sanes, senior author of the study.

Feng *et al*. also crossed *thy-1-CFP* transgenic mice with *thy1-YFP* transgenic mice to create a *CRP+YFP* double transgenic. The picture shows peripherhal ganglia of these mice, in which CFP- (dark blue), YFP- (green) and CFP + YFP double labeled (light blue) neurons are readily distinguishable. This technology will allow researchers to specifically label distinct neuronal subsets, such as motor or sensory neurons, and study their development, interaction, or response to different agents. "Now we can also easily identify and isolate specific neuronal cell types for gene expression profiling", says Sanes.

KRISTINE NOVAK