AIV 14

## Npro deletion mutants as efficient and safe Bovine viral diarrhea virus (BVDV) vaccine candidates

*Patricia König (1), Ilona Reimann (2), °Martin Beer (1)

(1) Institute of Diagnostic Virology, Friedrich-Loeffler-Institut, 17493 Greifswald-Insel Riems, Germany; (2) Institute of Molecular Biology, Friedrich-Loeffler-Institut, 17493 Greifswald-Insel Riems, Germany

Bovine viral diarrhea (BVD), a worldwide distributed Pestivirus infection of cattle, causes major economic losses due to reduced fertility, abortions, and the generation of persistently infected calves, which may develop fatal "Mucosal Disease". According to their cell culture properties, BVDV isolates are divided into two biotypes, referred to as cytopathogenic (cp) or non-cytopathogenic (ncp). Vaccination is an important tool for BVDV-control, claiming not only protection against disease, but also prevention from fetal infection. However, the safety of modified live vaccines relating to fetal infection is under discussion. The viral N-terminal autoproteinase Npro counteracts IFN-alpha/-beta induction and mediates evasion of the interferon response in infected cells. We constructed Npro deletion mutants based on full-length cDNA clones of an ncp and the homologous cp BVDV type 1 strain. Vaccine safety, immunogenicity, and efficacy were evaluated in vaccination-challenge experiments in calves. Furthermore, both mutants were delivered to pregnant heifers in the first trimester of the gravidity. Four months later, the animals were sacrificed and the fetuses were analyzed for persistent infection. Both recombinants were shown to be highly attenuated and efficacious vaccine candidates. The Npro mutants mediated complete protection from a virulent BVDV-I challenge infection in calves. After application to pregnant heifers, no infectious virus could be recovered from the fetuses, which was in clear contrast to the infection with the parental wild-type ncp-virus. In conclusion, the Npro deletion mutants are modified live vaccines with the potential to induce sterile immunity without the risk of establishing persistent infections of the fetuses.

Corresponding author:
**Beer, Martin**
martin.beer@fli.bund.de
Phone: ++4938351-7-200
Fax: ++4938351-7-151