Development of a novel marker vaccine platform for protection against African horse sickness and other orbiviruses

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Key words
Orbivirus, bluetongue virus, sheep, DIVA vaccine, RNA replicon particle, VP2 antigen, VP5 antigen, vesicular stomatitis virus (VSV)

Aim of the study
The goal of this study was to generate and evaluate recombinant RNA replicon particles as generic vaccine platform for protection against orbiviruses. The new vaccine was expected to allow discrimination of infected from vaccinated animals (DIVA).

Material and methods
A propagation-incompetent vesicular stomatitis virus (VSV) lacking the envelope glycoprotein G was engineered to express one or two different antigens of bluetongue virus serotype 8 (BTV-8). The replicon particles were propagated on helper cells providing the VSV G glycoprotein *in trans* and used to immunize sheep via the intramuscular route. Immune sera were tested for neutralizing antibodies against BTV-8, BTV-1 and VSV. Following challenge infection of the immunized animals with a virulent BTV-8 strain, clinical symptoms were recorded, viral loads in blood determined by quantitative RT-PCR, and seroconversion analyzed using a commercially available VP7-specific ELISA.

Results and significance
Immunization of sheep with infectious VSV replicon particles expressing the outer capsid VP2 protein of BTV-8 resulted in induction of BTV-8 serotype-specific neutralizing antibodies. After challenge with a virulent BTV-8 strain, the vaccinated animals neither developed signs of disease nor showed viremia. In contrast, immunization of sheep with recombinant VP5 - the second outer capsid protein of BTV - did not confer protection. Discrimination of infected from vaccinated animals was readily achieved using an ELISA for detection of antibodies against the VP7 antigen. These data indicate that VSV replicon particles potentially represent a safe and efficacious vaccine platform with which to control future outbreaks by BTV-8 or other serotypes, especially in previously non-endemic regions where discrimination between vaccinated and infected animals is crucial.

Publications, posters and presentations
Kochinger, S.; Renevey, N.; Hofmann, M.A.; Zimmer, G. (2014) Vesicular stomatitis virus replicon expressing the VP2 outer capsid protein of bluetongue virus serotype 8 induces complete protection of sheep against challenge infection. Vet. Res. 45:64.
Kochinger, S. (2014) Development of a novel marker vaccine platform for protection against Bluetongue Virus (BTV). PhD Thesis, Graduate School for Cellular and Biomedical Sciences, University of Bern.
Kochinger, S. (2013) Poster presentation, 23rd Annual Meeting of the Society for Virology (GfV), Kiel, Germany, 6-9 March 2013
Kochinger, S. (2013) Poster presentation: 7th EPIZONE Annual Meeting, Brussels, Belgium, 1-4 October 2013
Kochinger, S. (2013) Oral presentation: Münchenwiler Meeting, Münchenwiler Castle, Switzerland, 30-31 November 2013

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