Vaccine

Plant-produced Bluetongue chimaeric VLP vaccine candidates elicit serotype-specific immunity in sheep

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https://pubmed.ncbi.nlm.nih.gov/31471154/

Abstract

Bluetongue (BT) is a hemorrhagic non-contagious, biting midge-transmitted disease of wild and domestic ruminants that is caused by bluetongue virus (BTV). Annual vaccination plays a pivotal role in BT disease control in endemic regions. Due to safety concerns of the current BTV multivalent live attenuated vaccine (LAV), a safe efficacious new generation subunit vaccine such as a plant-produced BT virus-like particle (VLP) vaccine is imperative. Previously, homogenous BTV serotype 8 (BTV-8) VLPs were successfully produced in Nicotiana benthamiana plants and provided protective immunity in sheep. In this study, combinations of BTV capsid proteins from more than one serotype were expressed and assembled to form chimaeric BTV-3 and BTV-4 VLPs in N. benthamiana plants. The assembled homogenous BTV-8, as well as chimaeric BTV-3 and chimaeric BTV-4 VLP serotypes, were confirmed by SDS-PAGE, Transmission Electron microscopy (TEM) and protein confirmation using liquid chromatography-mass spectrometry (LC-MS/MS) based peptide sequencing. As VP2 is the major determinant eliciting protective immunity, the percentage coverage and number of unique VP2 peptides detected in assembled chimaeric BT VLPs were used as a guide to assemble the most appropriate chimaeric combinations. Both plant-produced chimaeric BTV-3 and BTV-4 VLPs were able to induce long-lasting serotype-specific neutralizing antibodies equivalent to the monovalent LAV controls. Antibody levels remained high to the end of the trial. Combinations of homogenous and chimaeric BT VLPs have great potential as a safe, effective multivalent vaccine with the ability to distinguish between vaccinated and infected individuals (DIVA) due to the absence of non-structural proteins.