Bluetongue Vaccine

A plant-expressed virus-like particle vaccine against Bluetongue Virus (BTV) serotype 8 with supporting animal data

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Background

Bluetongue virus (BTV) is a viral disease infecting sheep, cattle, deer, goats and camelids. Sheep are most severely affected whereas cattle are the main mammalian virus reservoir and are key in the epidemiology of the disease.

There are 24 classical serotypes with varying degrees of virulence and severity. Infections in susceptible sheep are considered to have the most impact, resulting in weight loss, a disruption in wool growth, and death.

BTV has historically been confined to tropical and subtropical areas (Central Africa, South East Asia) but climate change and trade patterns have seen increasing outbreaks in temperate regions (including Northern Europe) in recent years with outbreaks of up to 9 different serotypes occurring in Europe. The most significant of was the BTV-8 outbreak in Northern Europe in 2006-2008.

Climate change, changing weather patterns, and the animal trade have been attributed to aiding the spread of the virus and migration of the transmitter, *Culicoides* midges. BTV 8 is the most prolific serotype which has spread across Europe; while serotypes 1, 2, 4, 9 and 16 are prevalent in Northern Africa, the Middle East and Asia.

Commercially-available BTV vaccines generally comprise modified live viruses or inactivated viruses. Modified live vaccines (MLVs) run the risk of reversion to virulence, transmission by the *Culicoides* sp. vectors and can have undesirable side-effects. Inactivated vaccines usually require multiple doses as a result of short-lived immunity. In addition, cold-chain requirements for for transport and storage reduce accessibility to areas in most need of the vaccines..

The University of Cape Town's Biopharming Research Unit[1] has developed a plant-expressed vaccine against BTV 8[2] an supporting animal experiment results demonstrating that this candidate vaccine is safe and immunogenic.

1 https://science.uct.ac.za/department-mcb/ed-rybicki-biopharming-research-unit

2 https://doi.org/10.1111/pbi.12076

Technology Overview

The University of Cape Town's Biopharming Research Unit designed a plant expressed BTV virus- like particle vaccine against serotype 8.

The safety and efficacy of the candidate vaccine was confirmed in sheep trials, which confirmed that the plant-produced vaccine has the same protective efficacy as the live, attenuated monovalent BTV8 vaccine strain. The animals showed no clinical symptoms of the Bluetongue disease.

The plant expressed BTV VLPs formed protein bodies, confirming that the virus-like particles are in their native state and resembled BTV. (See Figure 1.)

It is possible that the vaccines candidates against serotypes 1 and 2; which could then be combined into a polyvalent vaccine with all the benefits associated with plant-expressed VLPs.

figure 1.

Benefits

The benefits of the University of Cape Town candidate BTV vaccines include:

- **Non-replicating vaccine.** VLPs are expressed proteins and don't contain nucleic acids that could potentially recombine from wild or vaccinated horses. This reduces the risk of virus escape and recombine with wild equine populations. It also reduces the risk of *Culicoides* midges to transmit the virus.
- **Safe and Immunogenic.** We have data demonstrating that the candidate vaccine is safe, immunogenic and efficacious in sheep challenge trial experiments. Animal trial experiments were compliant with the animal ethics standards.
- **Polyvalent vaccine with cross-reactivity**. In addition to the production of homologous BTV 8, the Biopharming Research Lab's vaccine design and plant expression capabilities could yield a combination vaccine against serotypes 1 and 2. A candidate vaccine combining serotypes 1,2, and 8 has the potential to provide cross-reactivity against serotypes; which could provide a broader protective range of protection against the disease.
- **Cost-effective scalability.** Plant-produced VLPs have demonstrated cost-effective and scalable uses as diagnostic reagents and vaccine candidates.

Applications

The prophylactic vaccination of sheep and cattle against BTV with a non-replicating, VLP-based vaccine across Europe could serve as a proactive risk management regime to reduce the chances of transmission and further evolution of the virus.

The cost-effectiveness of plant-produced vaccines presents an opportunity to distribute the candidate vaccine to more farmers, especially among subsistence farmers in developing and developed countries.

The scalability of plant-produced animal vaccines could enable pharmaceutical and aid agencies to sell and distribute the candidate vaccine at a suitable price point that ensures access, equity and an opportunity for protection.

Opportunity

The University of Cape Town seeks partnerships with the relevant players to bring the BTV candidate vaccine to market. We would like to license the manufacture, sales and distribution of the vaccine. The UCT Biopharming Research Unit will collaborate with the collaboration partners to complete the development of additional serotypes and facilitate the technology transfer.

The key roles and partnerships needed include:

- a clinical trial partner with access to compliant animal facilities and resources to complete the requisite horse challenge trials to demonstrate efficacy;
- a manufacturer capable of expressing plant-derived protein at scale, compliant with GMP standards for the supply of the candidate vaccines for trials and later for supply to Pharma;
- access to funders who could invest in the opportunity to complete the planned activities; and
- a sales, marketing and distribution partner or network that the partner could access.

It is a possibility to license the candidate vaccine to a single partner who could co-ordinate the activities needed to bring this vaccine to market.

Patents

- "PLANT-PRODUCED CHIMAERIC ORBIVIRUS VLPS." South African patent (2018/07464)
- "PLANT-PRODUCED CHIMAERIC ORBIVIRUS VLPS" United States patent (16095264) granted
- "PLANT-PRODUCED CHIMAERIC ORBIVIRUS VLPS" European patent application (2017720886)
- PLANT-PRODUCED CHIMAERIC ORBIVIRUS VLPS Namibian Patent application (2018/0034)
- PLANT-PRODUCED CHIMAERIC ORBIVIRUS VLPS ARIPO patent application (AP/P/2021/013697)

IP Status

- Patented
- Patent application submitted
- Know-how based

Seeking

- Development partner
- Commercial partner
- Licensing
- Seeking investment