

Low-cost Tularaemia vaccine

Summary

Novel, versatile glycoconjugate vaccine technology generates a safe and effective low-cost Tularaemia vaccine, countering the threat of bioterrorism.

Efficacious vaccines are a critical countermeasure to protect against the use of pathogens as bioweapons. *Francisella tularensis*, the causative agent of Tularaemia, is classed as one of the most concerning bioterrorism agents, yet no vaccines are available. A Tularaemia vaccine has been generated applying transformative glycoconjugate vaccine technology, ushering in a new era in glycoconjugate vaccine production for this pathogen and other pathogens that pose a threat to mankind.

Background

F. tularensis is one of the most infectious pathogens known to man and can cause epidemics. It is found in North America, Europe and Asia. Tularaemia is caused by contact with infected animals or vectors such as ticks and deer flies. It may also spread by inhalation or ingestion of contaminated food or water. *F. tularensis* is highly infectious: just 10-50 organisms are sufficient to infect and kill victims. Natural disasters or other humanitarian crises, which lead to poor sanitary conditions, are associated with higher rates of Tularaemia. Tularaemia has a mortality rate of up to 30%. Symptoms may include fever, chills, weakness, skin ulcers, diarrhoea, headaches, joint pain and enlarged lymph nodes. A form that results in pneumonia is often lethal.

Due to its extremely low infectious dose, ease of spread by aerosol, and high virulence, *F. tularensis* is a potential bioweapon. The bacterium has been a part of several biological warfare programs and is currently classified as a Class A bioterrorism agent. The WHO has estimated that 50kg of *F. tularensis* dispersed over a city of 5 million people would result in about 250,000 cases of severe disease and 19,000 deaths.

Antibiotics are currently used to treat Tularaemia with variable success, but antibiotic resistance remains a concern. Therefore, a vaccine is a current imperative.

This *F. tularensis* glycoconjugate vaccine produced using PGCT will be critical in protecting vulnerable populations from bioterrorism.

Technology and its advantages

Live attenuated vaccines carry a risk of reversion to the disease-causing form and inactivated vaccines require multiple vaccinations. Glycoconjugates vaccines provide long-lasting immunity with fewer side effects. They are tried and trusted with over a billion doses given to humans worldwide. However, the

Applications

- A Tularaemia vaccine for military, and general population applications

Benefits

- Low-cost - bringing potential Tularaemia vaccine faster to market
- Improved safety and efficacy - flexibility in design enables tailor-made vaccine
- Higher versatility - the glycoconjugate Tularaemia vaccine can protect against other diseases

traditional production process using chemical conjugation is time-consuming and costly and suffers from low yield and purity and significant batch variation.

Scientists at the London School of Hygiene and Tropical Medicine have developed a technology to produce a highly effective *F. tularensis* glycoconjugate vaccine in bacterial cell culture.

The benefits of the proposed technology for the production of *F. tularensis* vaccine include:

- A simple and safe purification process in the widely used *E. coli*
- High yields
- Reproducible purity
- Proven efficacy in murine and rat *F. tularensis* models and superior to unconjugated vaccines
- Versatility: Potential to target other pathogens using different protein/glycan combinations

The double-hit approach (immunogenic protein and glycan) provides significant protection in both murine and rat *F. tularensis* infection models when compared to LPS-alone vaccines and was associated with significantly reduced levels of inflammatory cytokines and a greater IgG immune response.

Market Opportunity

According to Persistence Market Research, rising prevalence of Tularemia in northern hemisphere and increased number of outbreaks in various countries will drive the market of Tularemia treatment in the future. The two major markets are North America and Europe. The US market holds the largest revenue share potential due to increasing incidence of Tularemia and increasing awareness of the disease. The US also has favorable reimbursement scenario. Europe is estimated to be the second large revenue share in the global market, due to increasing prevalence of infection and increasing number of reported cases.

Team

Prof. Brendan Wren's research interests predominantly involve determining the genetic basis by which bacterial pathogens cause disease. His research group exploits a range of post genome research strategies to gain a comprehensive understanding of how these pathogens function, how they evolve and how they interact with their respective hosts.

Dr. Jon Cuccui interests revolve around the biological characterisation and subsequent exploitation of bacterial glycosylation systems. He was the first Royal Society of Edinburgh / BBSRC Enterprise Fellow to emanate from the LSHTM.

Intellectual Property

The technology is protected by two families of patents (PCT/GB2014/050159 and PCT/GB2017/052653)

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