



***Clostridium perfringens* Vaccines**

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Dstl technologies

Dstl (the Defence Science and Technology Laboratory) is an agency of the UK Ministry of Defence with a research budget exceeding £180 million per annum and is the UK's centre of excellence for research into prophylactics and therapeutics against potential Biological Warfare agents. Dstl owns patents on inventions providing recombinant peptides for use as vaccines against both *Clostridium perfringens* alpha and epsilon toxins, thereby providing prophylaxis or therapy against infections caused by either toxin. *C. perfringens* is found in soil, dust, faeces, feed and litter. It has been associated with gas gangrene and food poisoning in man, necrotic enteritis (NE) in poultry and various forms of acute enteritis and fatal enterotoxemias in other livestock.

Vaccine against Alpha toxin

Alpha-toxin is haemolytic, necrotic and frequently lethal in animals as a consequence of its enzymatic activity which disrupts cell membranes. Its toxic effect is thought to primarily result from its rapid action; destroying membranes more quickly than they can be replaced by biosynthetic pathways.

The Dstl patent covers peptides encoding a portion of the alpha-toxin (preferably comprising residues 247-370) but which lack the epitopes for phospholipase C and/or sphingomyelin hydrolyzing activity and which provide a protective immune response against alpha-toxin when administered to humans or animals. The patent also covers DNA encoding the peptides, fusion proteins and vaccines comprising the peptide together with a pharmaceutically acceptable carrier. In an example given, 100% of vaccinated mice survived both intraperitoneal challenge with ~ 50 LD₅₀ alpha-toxin and intramuscular challenge with 10¹⁰ viable *C. perfringens* cells.

WO 1993/023543 – Patent status:

Granted in: Australia, China, Europe (Austria, Belgium, Denmark, France, GB, Germany, Ireland, Italy, Lichtenstein, Luxembourg, Monaco, Netherlands, Portugal, Spain, Sweden and Switzerland), Japan, Mexico, New Zealand, South Africa and USA.

Pending in: Canada and Israel.

Vaccine against Epsilon toxin

Epsilon-toxin is a potent, 32kDa peptide produced by *C. perfringens*. Of the five *C. perfringens* biotypes, Type B and D produce epsilon-toxin. They are responsible for producing a very severe and often fatal form of enterotoxaemia, usually in sheep and lambs, though also in goats and cattle.

The Dstl patent covers purified polypeptides for use in vaccines which produce protective antibodies directed against the *C. perfringens* epsilon-toxin when administered to animals or man and thereby providing prophylaxis or therapy against infection by *C. perfringens* epsilon-toxin. The polypeptides are mature epsilon-toxin which is altered such that residue 106 is mutated to proline rather than the histidine present in wild-type toxin (the effect of which is termed "genetic toxioding"). The patent also claims polypeptides in fusion with glutathione-S-transferase. In an example given, 100% of mice immunised intraperitoneally with the polypeptide were protected against intravenous challenge with 1000 LD₅₀ epsilon-toxin.

Ploughshare Innovations Limited
Case References: P1102 and P1171

26th October 2007

WO 1997/034001 – Patent status:

Granted in: Australia, Europe (Belgium, Denmark, France, Germany, GB, Netherlands, Spain) and USA

Pending in: Canada, Japan and New Zealand

Technology status

In addition to the R&D and challenge studies referred to in the patents, Dstl has developed *E. coli* cell lines stably expressing the antigens together with monoclonal antibody-producing hybridomas, having utility for QA and QC purposes.

Licensing

No recombinant vaccines have as yet been approved for use against *C. perfringens*. Ploughshare is able to licence the above patents with related know-how on a non-exclusive basis for animal health applications. Support from within the Dstl organisation in technology transfer and further development may be available.

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