Protection against Pseudomonas exotoxin A and diphtheria toxin

Technology

Pseudomonas aeruginosa infection is very common worldwide. Pseudomonas exotoxin A is the most virulent factor involved in the pathogenesis of this bacteria. It acts by inactivating the elongation factor-2 (EF-2), therefore blocking protein synthesis and leading to cell death. Diphthamide formation on EF-2 is a prerequisite step in the inactivation of EF-2 by this toxin. The blockade of diphthamide formation in cells would counterract the toxic effect of this toxin.

Dph2(C-) is a C-terminal deletion mutant of Dph2 that can confer resistance to diphtheria toxin and Pseudomonas exotoxin A. Dph2(C-) expression is nontoxic to cells, and it blocks the first step of diphthamide formation, the target of diphtheria toxin and Pseudomonas exotoxin A.

Dph2(C-) can block the activity diphtheria toxin, the virulence factor of Corynebacterium. diphtheria, and exotoxin A, the most virulence factors of Pseudomonas aeruginosa, by preventing the formation of their target, diphthamide.

Applications

A strategy that would block diphthamide formation could be used for the treatment of diphtheria and Pseudomonas infections. It could be used to alleviate the side effects of diphtheria toxin and Pseudomonas exotoxin A-based immunotoxin treatments. It could also be used in gene therapy to select genetically corrected cells containing a resistant gene with toxins before reimplanting them into patients.

Competitive advantages

1) The targeting of a cellular component should reduce the risk of *Pseudomonas* resistance commonly seen with antibiotic treatments.
2) The selection of gene-modified cells with diphtheria toxin or exotoxin A will be fast, and the gene product (Dph2(C-)) should be less immunogenic than bacterial-derived resistance genes that can trigeer an immune response that lead to the disappearance of the gene-modified cells.

State of development

Early stage

Business opportunity

Université Laval is seeking partners to develop and commercialize this technology.

Intellectual Property

M.Caruso, V.Roy
DPH2 gene deletion mutant and uses thereof
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