

P018 Targeted delivery of clostridial endopeptidase
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Clostridial neurotoxins (CNTs) are di-chain proteins consisting of a heavy chain containing binding, translocation domains and a light chain (LC) endopeptidase domain. Following binding, CNT internalises to an endosomal compartment from where LC enters the cytosol, cleaves its SNARE protein substrate and so inhibits secretion.

We have produced modified CNT molecules by replacing the natural binding domain with different cell-binding ligands. This delivers the neurotoxin endopeptidase into a target cell defined by the presence of the relevant ligand receptor on its surface. This approach allows us to develop a family of recombinant proteins able to inhibit secretion from defined target cells. Secretion can contribute to the pathology of certain medical conditions or diseases and so such proteins have therapeutic potential. This approach has been investigated using different ligands and CNTs. A conjugate of *Erythrina cristagalli* lectin (ECL) with a fragment of BoNT/A (ECL-LH_N/A) targets cleaving the SNARE protein SNAP-25 and inhibiting substance P release. A fusion of epidermal growth factor (EGF) and a fragment of BoNT/C (EGF-LH_N/C) binds to airway epithelial cells and inhibits mucin secretion. These novel proteins will be described together with their therapeutic potential