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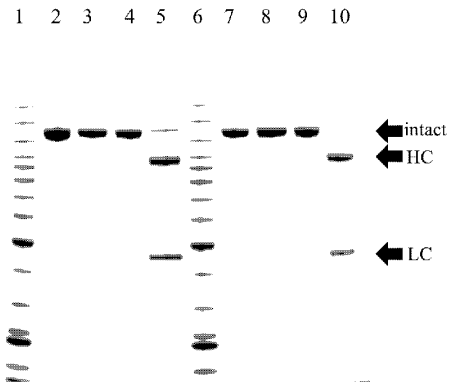
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(54) Title: CLOSTRIDIAL NEUROTOXINS COMPRISING AN EXOGENOUS ACTIVATION LOOP

FIGURE 6



(57) Abstract: The present invention relates to a method for proteolytically processing a single-chain clostridial neurotoxin into a corresponding di-chain clostridial neurotoxin, the method comprising: providing a single-chain clostridial neurotoxin; and contacting the single-chain clostridial neurotoxin with enterokinase or factor Xa; wherein the single-chain clostridial neurotoxin has an activation loop comprising the polypeptide sequence Cys-$(Xaa)_a$ -Ile- Asp/Glu-Gly-Arg-$(Yaa)_b$ -Cys (SEQ ID NO: 1), wherein a = 1-10 and b = 4-15; and wherein enterokinase or factor Xa hydrolyses a peptide bond of the activation loop thereby producing a di-chain clostridial neurotoxin. The invention also relates to engineered clostridial neurotoxins and methods for manufacturing the same, as well as related pharmaceutical compositions, nucleotide sequences, and therapeutic uses.

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