CLAIMS

1. A polypeptide comprising a modified receptor binding domain of *Clostridial botulinum* serotype B (B-H_c) comprising a substitution mutation at a position corresponding to position E1191 in serotype B, strain 1, in which the substitution mutation produces enhanced binding of the modified B-H_c to human Syt II as compared to an identical molecule lacking the substitution mutation.

2. A botulinum neurotoxin (BoNT) polypeptide comprising:

(a) a protease domain;

(b) a protease cleavage site;

(c) a translocation domain; and

(d) a modified receptor binding domain of *Clostridial botulinum* serotype B (B-H_c), comprising a substitution mutation at a position corresponding to position E1191 in serotype B, strain 1, in which the substitution mutation produces enhanced binding of the modified B-H_c to human Syt II as compared to an identical molecule lacking the substitution mutation.

3. A polypeptide or BoNT polypeptide according to Claim 1 or 2, in which the modified (B-H_c) is of strain 1.

4. A BoNT polypeptide according to Claim 2 or 3, in which the protease domain, translocation domain, and protease cleavage site are from a serotype selected from the group consisting of A, B, C, D, E, F, G, and combinations thereof, such as in which the protease domain, translocation domain, and protease cleavage site are from serotype B, strain 1 or serotype A, strain 1.

5. A polypeptide or BoNT polypeptide according to any preceding claim, in which the modified (B-Hc) comprises a substitution mutation selected from the group consisting of: E1191M, E1191I, E1191T, E1191Q, E1191L, E1191N and E1191S.

6. A polypeptide or BoNT polypeptide according to any preceding claim, in which the modified (B-Hc) comprises two substitution mutations.

7. A polypeptide or BoNT polypeptide according to Claim 6, in which the two substitution mutations are selected from the group consisting of:

E1191M and S1199Y,

E1191M and S1199L,

E1191M and S1199F,

E1191M and V1118M,

E1191M and S1201V,

E1191M and Y1183M,

E1191Q and S1199Y,

E1191Q and S1199L, and

E1191Q and S1199F.

8. A polypeptide or BoNT polypeptide according to any preceding claim that is a chimeric molecule, comprising a first portion that is the modified receptor binding domain of *Clostridial botulinum* serotype B (B-H_c) linked to a second portion.

9. A polypeptide or BoNT polypeptide according to Claim 8, in which the first portion and the second portion are linked covalently or are linked non-covalently; in which the second portion is selected from the group consisting of a small molecule, a nucleic acid, a short polypeptide and a protein; in which the second portion is a bioactive molecule; or in which the second portion is a therapeutic polypeptide or non-polypeptide drug.

10. A nucleic acid such as a vector comprising a nucleotide sequence that encodes a polypeptide or BoNT polypeptide according to any preceding claim.

11. A cell expressing a polypeptide or BoNT polypeptide according to any of Claims 1 to 9 or comprising a nucleic acid or vector according to Claim 10.

12. A pharmaceutical composition comprising a polypeptide or BoNT polypeptide according to any of Claims 1 to 9, a nucleic acid or vector according to Claim 10 or a cell according to Claim 11, and optionally comprising a pharmaceutically acceptable excipient.

13. A kit comprising a pharmaceutical composition according to Claim 12, and directions for therapeutic administration of the pharmaceutical composition.

14. A method of producing a polypeptide or botulinum neurotoxin (BoNT) polypeptide, the method comprising the steps of culturing a cell according to Claim 11 under conditions in which the polypeptide or BoNT polypeptide is produced, and optionally recovering the polypeptide or BoNT polypeptide from the culture.

15. A polypeptide or botulinum neurotoxin (BoNT) polypeptide according to any of Claims 1 to 9, a nucleic acid according to Claim 10, a cell according to Claim 11, or a pharmaceutical composition according to Claim 12, for use in therapy.

16. A polypeptide or botulinum neurotoxin (BoNT) polypeptide according to any of Claims 1 to 9, a nucleic acid according to Claim 10 or a cell according to Claim 11, or a pharmaceutical composition according to Claim 12, for use in treating a condition associated with unwanted neuronal activity.

17. A polypeptide, botulinum neurotoxin (BoNT) polypeptide, nucleic acid, cell, or pharmaceutical composition according to Claim 15 or 16, for a use as specified therein, in which the use comprises administering a therapeutically effective amount of the polypeptide, BoNT polypeptide, nucleic acid, cell or pharmaceutical composition to a subject to thereby contact one or more neurons exhibiting unwanted neuronal activity.

18. A polypeptide, botulinum neurotoxin (BoNT) polypeptide, nucleic acid, cell, or pharmaceutical composition according to Claim 15, 16, or 17, for use as specified therein, in which the use comprises treating a condition selected from the group consisting of spasmodic dysphonia, spasmodic torticollis, laryngeal dystonia, oromandibular dysphonia, lingual dystonia, cervical dystonia, focal hand dystonia, blepharospasm, strabismus, hemifacial spasm, eyelid disorder, cerebral palsy, focal spasticity and other voice disorders, spasmodic colitis, neurogenic bladder, anismus, limb spasticity, tics, tremors, bruxism, anal fissure, achalasia, dysphagia and other muscle tone disorders and other disorders characterized by involuntary movements of muscle groups, lacrimation, hyperhydrosis, excessive salivation, excessive gastrointestinal secretions, secretory disorders, pain from muscle spasms, headache pain, and dermatological or aesthetic/cosmetic conditions.

19. Use of a polypeptide or botulinum neurotoxin (BoNT) polypeptide according to any of Claims 1 to 9, a nucleic acid according to Claim 10 or a cell according to Claim 11 in the preparation of a medicament for the treatment or prevention of a condition associated with unwanted neuronal activity, such as a condition selected from the group consisting of:

spasmodic dysphonia, spasmodic torticollis, laryngeal dystonia, oromandibular dysphonia, lingual dystonia, cervical dystonia, focal hand dystonia, blepharospasm, strabismus, hemifacial spasm, eyelid disorder, cerebral palsy, focal spasticity and other voice disorders, spasmodic colitis, neurogenic bladder, anismus, limb spasticity, tics, tremors, bruxism, anal fissure, achalasia, dysphagia and other muscle tone disorders and other disorders characterized by involuntary movements of muscle groups, lacrimation, hyperhydrosis, excessive salivation, excessive gastrointestinal secretions, secretory disorders, pain from muscle spasms, headache pain, and dermatological or aesthetic/cosmetic conditions.