CLAIMS

1. 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 one or more substitution mutations corresponding to a Y1183M substitution mutation in serotype B, strain 1.

2. A BoNT polypeptide according to Claim 1, in which the modified (B-H_c) comprises two substitution mutations.

3. A 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 1, 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.

5. A BoNT polypeptide according to Claim 4, in which the protease domain, translocation domain, and protease cleavage site are from serotype B, strain 1.

6. A BoNT polypeptide according to Claim 4, in which the protease domain, translocation domain, and protease cleavage site are from serotype A, strain 1.

7. A polypeptide comprising a modified receptor binding domain of *Clostridial botulinum* serotype B (B-H_c) comprising one or more substitution mutations corresponding to a Y1183M substitution mutation in serotype B, strain 1.

8. A polypeptide according to Claim 7, in which the modified (B-H_c) comprises two substitution mutations.

9. A polypeptide according to Claim 7 or 8, in which the modified B-H_c is of strain 1.

10. A chimeric molecule comprising a first portion that is a modified receptor binding domain of *Clostridial botulinum* serotype B (B-H_c) linked to a second portion, in which the modified B-H_c comprises a substitution mutation Y1183M in serotype B, strain.

11. A chimeric molecule according to Claim 10, in which the modified B-H_c comprises two substitution mutations.

12. A chimeric molecule according to Claim 10 or 11, in which the first portion and the second portion are linked covalently.

13. A chimeric molecule according to Claim 10 or 11, in which the first portion and the second portion are linked non-covalently.

14. A chimeric molecule according to any of Claims 10 to 13 in which the second portion is selected from the group consisting of a small molecule, a nucleic acid, a short polypeptide and a protein.

15. A chimeric molecule according to Claim 14, in which the second portion is a bioactive molecule.

16. A chimeric molecule according to Claim 14 or 15, in which the second portion is a therapeutic polypeptide or non-polypeptide drug.

17. A nucleic acid comprising a nucleotide sequence that encodes a polypeptide or chimeric molecule according to any preceding claim.

18. A nucleic acid vector comprising a nucleic acid according to Claim 17.

19. A cell comprising a nucleic acid vector according to Claim 18 or a nucleic acid according to Claim 17.

20. A cell expressing a polypeptide or chimeric molecule according to any of Claims 1 to 16.

21. A pharmaceutical composition comprising a botulinum neurotoxin (BoNT) polypeptide according to any of Claims 1 to 6, a chimeric molecule according to any of Claims 10 to 16, a nucleic acid vector according to Claim 18 or a nucleic acid according to Claim 17.

22. A pharmaceutical composition according to Claim 21, further comprising a pharmaceutically acceptable excipient.

23. A kit comprising a pharmaceutical composition according to Claim 21 or 22 and directions for therapeutic administration of the pharmaceutical composition.

24. A method of producing a botulinum neurotoxin (BoNT) polypeptide, the method comprising the steps of culturing a host cell according to Claim 20 under conditions in which the BoNT polypeptide is produced.

25. A method according to Claim 24, further comprising recovering the BoNT polypeptide from the culture.

26. A botulinum neurotoxin (BoNT) polypeptide according to any of Claims 1 to 6, a pharmaceutical composition according to Claim 21 or 22, a chimeric molecule according to any of Claims 10 to 16, or a polypeptide according to any of Claims 7 to 9, for use in medicine.

27. A botulinum neurotoxin (BoNT) polypeptide according to any of Claims 1 to 6, a pharmaceutical composition according to Claim 21 or 22, a chimeric molecule according to any of Claims 10 to 16, or a polypeptide according to any of Claims 7 to 9, for use in treating a condition associated with unwanted neuronal activity.

28. A botulinum neurotoxin (BoNT) polypeptide, pharmaceutical composition, chimeric molecule, or a polypeptide according to Claim 26 or 27 for a use as specified therein, in which the method comprises administering a therapeutically effective amount of the BoNT polypeptide to a subject to thereby contact one or more neurons exhibiting unwanted neuronal activity, to thereby treat the condition.

29. A botulinum neurotoxin (BoNT) polypeptide, pharmaceutical composition, chimeric molecule, or a polypeptide according to Claim 26, 27 or 28 for a use as specified therein, in which the condition is 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.

30. Use of a botulinum neurotoxin (BoNT) polypeptide according to any of Claims 1 to 6, a chimeric molecule according to any of Claims 10 to 16, or a polypeptide according to any of Claims 7 to 9, in the preparation of a medicament for the treatment of a condition associated with unwanted neuronal activity, preferably a condition set out in Claim 29.

CLAIMS

1. 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 ($B\text{-}H_c$), comprising one or more substitution mutations corresponding to a Y1183M substitution mutation in serotype B, strain 1 of SEQ ID NO: 4.

2. A BoNT polypeptide according to Claim 1, in which the modified ($B\text{-}H_c$) comprises two substitution mutations.

3. A BoNT polypeptide according to Claim 1 or 2, in which the modified $B\text{-}H_c$ is of strain 1.

4. A BoNT polypeptide according to Claim 1, 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.

5. A BoNT polypeptide according to Claim 4, in which the protease domain, translocation domain, and protease cleavage site are from serotype B, strain 1.

6. A BoNT polypeptide according to Claim 4, in which the protease domain, translocation domain, and protease cleavage site are from serotype A, strain 1.

7. A polypeptide comprising a modified receptor binding domain of *Clostridial botulinum* serotype B ($B\text{-}H_c$) comprising one or more substitution mutations corresponding to a Y1183M substitution mutation in serotype B, strain 1.

8. A polypeptide according to Claim 7, in which the modified ($B\text{-}H_c$) comprises two substitution mutations.

9. A polypeptide according to Claim 7 or 8, in which the modified $B\text{-}H_c$ is of strain 1.

10. A chimeric molecule comprising a first portion that is a modified receptor binding domain of *Clostridial botulinum* serotype B ($B\text{-}H_c$) linked to a second portion, in which the

modified B-H_c comprises a Y to M substitution mutation at a position corresponding to Y1183 in serotype B, strain 1 of SEQ ID NO: 4.

11. A chimeric molecule according to Claim 10, in which the modified B-H_c comprises two substitution mutations.

12. A chimeric molecule according to Claim 10 or 11, in which the first portion and the second portion are linked covalently.

13. A chimeric molecule according to Claim 10 or 11, in which the first portion and the second portion are linked non-covalently.

14. A chimeric molecule according to any of Claims 10 to 13 in which the second portion is selected from the group consisting of a small molecule, a nucleic acid, a short polypeptide and a protein.

15. A chimeric molecule according to Claim 14, in which the second portion is a bioactive molecule.

16. A chimeric molecule according to Claim 14 or 15, in which the second portion is a therapeutic polypeptide or non-polypeptide drug.

17. A nucleic acid comprising a nucleotide sequence that encodes a polypeptide or chimeric molecule according to any preceding claim.

18. A nucleic acid vector comprising a nucleic acid according to Claim 17.

19. A cell comprising a nucleic acid vector according to Claim 18 or a nucleic acid according to Claim 17.

20. A cell expressing a polypeptide or chimeric molecule according to any of Claims 1 to 16.

21. A pharmaceutical composition comprising a botulinum neurotoxin (BoNT) polypeptide according to any of Claims 1 to 6, a chimeric molecule according to any of Claims 10 to 16, a nucleic acid vector according to Claim 18 or a nucleic acid according to Claim 17.

22. A pharmaceutical composition according to Claim 21, further comprising a pharmaceutically acceptable excipient.

23. A kit comprising a pharmaceutical composition according to Claim 21 or 22 and directions for therapeutic administration of the pharmaceutical composition.

24. A method of producing a botulinum neurotoxin (BoNT) polypeptide, the method comprising the steps of culturing a host cell according to Claim 20 under conditions in which the BoNT polypeptide is produced.

25. A method according to Claim 24, further comprising recovering the BoNT polypeptide from the culture.

26. A botulinum neurotoxin (BoNT) polypeptide according to any of Claims 1 to 6, a pharmaceutical composition according to Claim 21 or 22, a chimeric molecule according to any of Claims 10 to 16, or a polypeptide according to any of Claims 7 to 9, for use in medicine.

27. A botulinum neurotoxin (BoNT) polypeptide according to any of Claims 1 to 6, a pharmaceutical composition according to Claim 21 or 22, a chimeric molecule according to any of Claims 10 to 16, or a polypeptide according to any of Claims 7 to 9, for use in treating a condition associated with unwanted neuronal activity.

28. A botulinum neurotoxin (BoNT) polypeptide, pharmaceutical composition, chimeric molecule, or a polypeptide according to Claim 26 or 27 for a use as specified therein, in which the method comprises administering a therapeutically effective amount of the BoNT polypeptide to a subject to thereby contact one or more neurons exhibiting unwanted neuronal activity, to thereby treat the condition.

29. A botulinum neurotoxin (BoNT) polypeptide, pharmaceutical composition, chimeric molecule, or a polypeptide according to Claim 26, 27 or 28 for a use as specified therein, in which the condition is 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.

30. Use of a botulinum neurotoxin (BoNT) polypeptide according to any of Claims 1 to 6, a chimeric molecule according to any of Claims 10 to 16, or a polypeptide according to any of Claims 7 to 9, in the preparation of a medicament for the treatment of a condition associated with unwanted neuronal activity, preferably a condition set out in Claim 29.