Claims

1. A chimeric neurotoxin comprising a LH_N domain from a first neurotoxin covalently linked to a H_C domain from a second neurotoxin, wherein:

   (a) the C-terminal amino acid residue of said LH_N domain corresponds to the first amino acid residue of the 3_{10} helix separating the LH_N and H_C domains in said first neurotoxin;

   (b) the N-terminal amino acid residue of said H_C domain corresponds to the second amino acid residue of the 3_{10} helix separating the LH_N and H_C domains in said second neurotoxin; and

   (c) said first and second neurotoxins are different and (i) said first neurotoxin is a Botulinum Neurotoxin (BoNT) serotype A, serotype B, serotype C, serotype D, serotype E, serotype F or serotype G or a Tetanus Neurotoxin (TeNT); and (ii) said second neurotoxin is a Botulinum Neurotoxin (BoNT) serotype A, serotype B, serotype C, serotype D, serotype E, serotype F or serotype G or a Tetanus Neurotoxin (TeNT).

2. A chimeric neurotoxin according to claim 1, wherein:

   said LH_N domain from a first neurotoxin corresponds to:

   - amino acid residues 1 to 872 of BoNT/A1,
   - amino acid residues 1 to 859 of BoNT/B1,
   - amino acid residues 1 to 867 of BoNT/C1,
   - amino acid residues 1 to 863 of BoNT/D,
   - amino acid residues 1 to 846 of BoNT/E1,
   - amino acid residues 1 to 865 of BoNT/F1,
   - amino acid residues 1 to 864 of BoNT/G, or
   - amino acid residues 1 to 880 of TeNT.

   and wherein said H_C domain from a second neurotoxin corresponds to:

- amino acid residues 873 to 1296 of BoNT/A1,
- amino acid residues 860 to 1291 of BoNT/B1,
- amino acid residues 868 to 1291 of BoNT/C1,
- amino acid residues 864 to 1276 of BoNT/D,
- amino acid residues 847 to 1251 of BoNT/E1,
- amino acid residues 866 to 1275 of BoNT/F1,
- amino acid residues 865 to 1297 of BoNT/G, or
- amino acid residues 881 to 1315 of TeNT.

3. A chimeric neurotoxin according to claim 1 or 2, wherein said first neurotoxin is a BoNT/A and wherein said second neurotoxin is a BoNT/B.

4. A chimeric neurotoxin according to claim 3, wherein said first neurotoxin is a BoNT/A1 and wherein said second neurotoxin is a BoNT/B1, wherein optionally said LH_N domain from a first neurotoxin corresponds to amino acid residues 1 to 872 of BoNT/A1 and wherein said H_C domain from a second neurotoxin corresponds to amino acid residues 860 to 1291 of BoNT/B1.

5. A chimeric neurotoxin according to claim 3 or 4, wherein said H_C domain from a BoNT/B neurotoxin comprises at least one amino acid residue substitution, addition or deletion in the H_{CC} subdomain which has the effect of increasing the binding affinity of the BoNT/B neurotoxin for the human Syt II receptor as compared to the natural BoNT/B sequence.

6. A chimeric neurotoxin according to claim 5, wherein said at least one amino acid residue substitution, addition or deletion in the H_{CC} subdomain comprises:

   i) a substitution mutation selected from the group consisting of: V1118M; Y1183M; E1191M; E1191I; E1191Q; E1191T; S1199Y; S1199F; S1199L; S1201V*;* E1191C, E1191V, E1191L, E1191Y, S1199W, S1199E, S1199H, W1178Y, W1178Q, W1178A, W1178S, Y1183C, Y1183P and combinations thereof; or

ii) two substitution mutations selected from the group consisting of: E1191M and S1199L, E1191M and S1199Y, E1191M and S1199F, E1191Q and S1199L, E1191Q and S1199Y, E1191Q and S1199F, E1191M and S1199W, E1191M and W1178Q, E1191C and S1199W, E1191C and S1199Y, E1191C and W1178Q, E1191Q and S1199W, E1191V and S1199W, E1191V and S1199Y, or E1191V and W1178Q, wherein optionally said two substitution mutations are E1191M and S1199Y; or

iii) three substitution mutations which are E1191M, S1199W and W1178Q.

7. A chimeric neurotoxin according to claim 1 or 2, wherein said first neurotoxin is a BoNT/B and wherein said second neurotoxin is a BoNT/C.

8. A chimeric neurotoxin according to claim 7, wherein said first neurotoxin is a BoNT/B1 and wherein said second neurotoxin is a BoNT/C1, wherein optionally said LH_N domain from a first neurotoxin corresponds to amino acid residues 1 to 859 of BoNT/B1 and wherein said H_C domain from a second neurotoxin corresponds to amino acid residues 868 to 1291 of BoNT/C1.

9. A nucleotide sequence encoding a chimeric neurotoxin according to any one of claims 1 to 8, or a vector comprising said nucleotide sequence.

10. A cell comprising a nucleotide sequence or a vector according to claim 9.

11. A pharmaceutical composition comprising a chimeric neurotoxin according to any one of claims 1 to 8.

12. A kit comprising a pharmaceutical composition of claim 11 and instructions for therapeutic or cosmetic administration of said composition to a subject in need thereof.

13. A method for producing a chimeric neurotoxin as defined in any one of claims 1 to 8, said method comprising the step of culturing a cell of claim 10, under conditions wherein said chimeric neurotoxin is produced.

14. A chimeric neurotoxin according to any one of claims 1 to 8 or pharmaceutical composition according to claim 11 for use in therapy, wherein optionally said use is in

the treatment of a condition associated with unwanted neuronal activity, for example 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, hyperhidrosis, excessive salivation, excessive gastrointestinal secretions, secretory disorders, pain from muscle spasms, headache pain, migraine and dermatological conditions.

15. Non therapeutic use of a chimeric neurotoxin according to any one of claims 1 to 8 or of a pharmaceutical composition according to claim 11, for treating an aesthetic or cosmetic condition.