CLAIMS

1. A clostridial neurotoxin for use in the treatment of an autonomic disorder in a human patient, wherein the clostridial neurotoxin comprises an H_{CC} domain from a BoNT/B, BoNT/F, BoNT/D, BoNT/D-C, or BoNT/G, and wherein the dose of said clostridial neurotoxin to be administered to the patient is lower than or equivalent to the dose of BoNT/A treating said autonomic disorder.

2. Use of a clostridial neurotoxin in the manufacture of a medicament for treating an autonomic disorder in a human patient, wherein the clostridial neurotoxin comprises an H_{CC} domain from a BoNT/B, BoNT/F, BoNT/D, BoNT/D-C, or BoNT/G, and wherein the dose of said clostridial neurotoxin to be administered to the patient is lower than or equivalent to the dose of BoNT/A treating said autonomic disorder.

3. The clostridial neurotoxin for use according to claim 1, or the use according to claim 2, wherein the dose of said clostridial neurotoxin is ~~about~~ 1.1 times to ~~about~~ 100 times lower than the dose of BoNT/A treating said autonomic disorder, said dose being preferably quantified in nanograms.

4. The clostridial neurotoxin for use according to claim 1 or claim 3, or the use according to claim 2 or claim 3, wherein the dose of said clostridial neurotoxin is ranging from ~~about~~ 0.00025 ng to ~~about~~ 3 ng.

5. The clostridial neurotoxin for use according to any one of claim 1 or claims 3 to 4, or the use according to any one of claims 2 to 4, wherein said autonomic disorder is selected from smooth muscle disorders, ~~hypersecretary~~hypersecretory disorders, respiratory disorders, inflammatory disorders with an autonomic component, neuroendocrine disorders and other autonomic disorders directly associated with a central neurological disorder.

6. The clostridial neurotoxin for use according to any one of claim 1 or claims 3 to 5, or the use according to any one of claims 2 to 5, wherein said H_{CC} domain is a BoNT/B H_{CC} domain or a BoNT/F H_{CC} domain.

7. The clostridial neurotoxin for use according to any one of claim 1 or claims 3 to 6, or the use according to any one of claims 2 to 6, wherein said BoNT/B H_{CC} domain

comprises at least one amino acid residue mutation increasing its binding affinity for the human Syt II receptor by at least 50 % as compared to the natural BoNT/B H_{CC} domain.

~~8. The clostridial neurotoxin for use, or the use according to claim 7, wherein said at least one amino acid residue mutation is selected from the group consisting of 1118M, 1183M, 1191M, 1191I, 1191Q, 1191T, 1199Y, 1199F, 1199L, 1201V, 1191C, 1191V, 1191L, 1191Y, 1199W, 1199E, 1199H, 1178Y, 1178Q, 1178A, 1178S, 1183C, 1183P and any combinations thereof.~~

~~9.~~8. The clostridial neurotoxin for use, or the use according to claim 7~~ or 8~~, wherein said at least one amino acid residue mutation consists of the two amino acid mutations 1191M and 1199Y.

~~10.~~9. The clostridial neurotoxin for use according to any one of claim 1 or claims 3 to 6, or the use according to any one of claims 2-6, wherein said BoNT/F H_{CC} domain comprises at least one amino acid residue mutation increasing its binding affinity for one or more gangliosides as compared to the natural BoNT/F Hcc domain.

~~11.~~10. The clostridial neurotoxin for use, or the use according to claim ~~10~~9, wherein said gangliosides are selected from GD1a and/or GM1a, and/or said amino acid residue mutation is 1241K.

~~12.~~11. The clostridial neurotoxin for use according to any one of claim 1 or claims 3 to ~~9~~8, or the use according to any one of claims 2-~~9~~8, wherein said clostridial neurotoxin is a BoNT/B neurotoxin.

~~13.~~12. The clostridial neurotoxin for use according to any one of claims 1, ~~2~~3-6, ~~10~~ 9 or ~~11~~10, or the use according to any one of claims 2-6, ~~10~~ 9 or ~~11~~10, wherein said clostridial neurotoxin is a BoNT/F neurotoxin.

~~14.~~13. The clostridial neurotoxin for use according to any one of claim 1 or claims 3 to ~~13~~10, or the use according to any one of claims 2 to ~~13~~10, wherein said clostridial neurotoxin is a chimeric neurotoxin.

~~15.~~14. The clostridial neurotoxin for use according to any one of claims 1 or 3-8, or the use according to any one of claim~~s 14~~2-8, wherein said clostridial neurotoxin is a

chimeric neurotoxin ~~comprises~~ comprising a BoNT/B H_C domain and a BoNT/A LH_N domain.

~~16.~~15. The clostridial neurotoxin for use according to any one of claims 1, 3-6, 9 or 10, or the use according to any one of claims ~~14~~2-6, 9 or 10, wherein said clostridial neurotoxin is a chimeric neurotoxin ~~comprises~~ comprising an LH_N domain from a first BoNT/F subtype and an activation loop from a second BoNT/F subtype, and wherein said second BoNT/F subtype differs from said first BoNT/F subtype.

~~17.~~16. The clostridial neurotoxin for use, or the use according to claim ~~16~~15, wherein said LH_N domain is a BoNT/F7 LH_N domain and/or said activation loop is a BoNT/F1 activation loop.

~~18.~~17. The clostridial neurotoxin for use according to any one of claim 1 or claims 3 to ~~17~~16, or the use according to any one of claims 2 to ~~17~~16, wherein the clostridial neurotoxin comprises an amino acid sequence selected from any one of SEQ ID NOs: 2-13 or an amino acid sequence having at least 70% sequence identity thereto, preferably at least 90% or 95% sequence identity thereto.

~~19.~~18. The clostridial neurotoxin for use according to any one of claim 1 or claims 3 to ~~18~~17, or the use according to any one of claims 2 to ~~18~~17, wherein the clostridial neurotoxin comprises:

a. an amino acid sequence SEQ ID NO: 13 or an amino acid sequence having at least 70% sequence identity thereto, preferably at least 90% or 95% sequence identity thereto; or
b. an amino acid sequence SEQ ID NO: 9 or an amino acid sequence having at least 70% sequence identity thereto, preferably at least 90% or 95% sequence identity thereto; or
c. an amino acid sequence SEQ ID NO: 12 or an amino acid sequence having at least 70% sequence identity thereto, preferably at least 90% or 95% sequence identity thereto; or
d. an amino acid sequence SEQ ID NO: 10 or an amino acid sequence having at least 70% sequence identity thereto, preferably at least 90% or 95% sequence identity thereto; or

e. an amino acid sequence SEQ ID NO: 6 or an amino acid sequence having at least 70% sequence identity thereto, preferably at least 90% or 95% sequence identity thereto.