

108454P502PC\_SeqListing\_ST25.txt  
SEQUENCE LISTING

<110> Merz Pharma GmbH & Co. KGaA  
<120> NOVEL METHOD FOR THE MANUFACTURING OF RECOMBINANT PROTEINS  
HARBOURING AN N-TERMINAL LYSINE  
<130> 108454P502PC  
<150> EP12005953.0  
<151> 2012-08-20  
<150> US61/684,948  
<151> 2012-08-20  
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<170> PatentIn version 3.5  
<210> 1  
<211> 1284  
<212> PRT  
<213> Artificial Sequence  
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<223> clostridial neurotoxin precursor  
<400> 1

Met Ala Tyr Pro Tyr Asp Val Pro Asp Tyr Ala Val Arg Gly Ile Ile  
1 5 10 15

Thr Ser Lys Thr Lys Gly Gly Pro Lys Ile Asn Ser Phe Asn Tyr Asn  
20 25 30

Asp Pro Val Asn Asp Arg Thr Ile Leu Tyr Ile Lys Pro Gly Gly Cys  
35 40 45

Gln Glu Phe Tyr Lys Ser Phe Asn Ile Met Lys Asn Ile Trp Ile Ile  
50 55 60

Pro Glu Arg Asn Val Ile Gly Thr Thr Pro Gln Asp Phe His Pro Pro  
65 70 75 80

Thr Ser Leu Lys Asn Gly Asp Ser Ser Tyr Tyr Asp Pro Asn Tyr Leu  
85 90 95

Gln Ser Asp Glu Glu Lys Asp Arg Phe Leu Lys Ile Val Thr Lys Ile  
100 105 110

Phe Asn Arg Ile Asn Asn Asn Leu Ser Gly Gly Ile Leu Leu Glu Glu  
115 120 125

Leu Ser Lys Ala Asn Pro Tyr Leu Gly Asn Asp Asn Thr Pro Asp Asn  
130 135 140

Gln Phe His Ile Gly Asp Ala Ser Ala Val Glu Ile Lys Phe Ser Asn  
145 150 155 160

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Gly Ser Gln Asp Ile Leu Leu Pro Asn Val Ile Ile Met Gly Ala Glu  
165 170 175

Pro Asp Leu Phe Glu Thr Asn Ser Ser Asn Ile Ser Leu Arg Asn Asn  
180 185 190

Tyr Met Pro Ser Asn His Gly Phe Gly Ser Ile Ala Ile Val Thr Phe  
195 200 205

Ser Pro Glu Tyr Ser Phe Arg Phe Asn Asp Asn Ser Met Asn Glu Phe  
210 215 220

Ile Gln Asp Pro Ala Leu Thr Leu Met His Glu Leu Ile His Ser Leu  
225 230 235 240

His Gly Leu Tyr Gly Ala Lys Gly Ile Thr Thr Lys Tyr Thr Ile Thr  
245 250 255

Gln Lys Gln Asn Pro Leu Ile Thr Asn Ile Arg Gly Thr Asn Ile Glu  
260 265 270

Glu Phe Leu Thr Phe Gly Gly Thr Asp Leu Asn Ile Ile Thr Ser Ala  
275 280 285

Gln Ser Asn Asp Ile Tyr Thr Asn Leu Leu Ala Asp Tyr Lys Lys Ile  
290 295 300

Ala Ser Lys Leu Ser Lys Val Gln Val Ser Asn Pro Leu Leu Asn Pro  
305 310 315 320

Tyr Lys Asp Val Phe Glu Ala Lys Tyr Gly Leu Asp Lys Asp Ala Ser  
325 330 335

Gly Ile Tyr Ser Val Asn Ile Asn Lys Phe Asn Asp Ile Phe Lys Lys  
340 345 350

Leu Tyr Ser Phe Thr Glu Phe Asp Leu Ala Thr Lys Phe Gln Val Lys  
355 360 365

Cys Arg Gln Thr Tyr Ile Gly Gln Tyr Lys Tyr Phe Lys Leu Ser Asn  
370 375 380

Leu Leu Asn Asp Ser Ile Tyr Asn Ile Ser Glu Gly Tyr Asn Ile Asn  
385 390 395 400

Asn Leu Lys Val Asn Phe Arg Gly Gln Asn Ala Asn Leu Asn Pro Arg  
405 410 415

Ile Ile Thr Pro Ile Thr Gly Arg Gly Leu Val Lys Lys Ile Ile Arg  
420 425 430

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Phe Cys Val Arg Gly Ile Ile Thr Ser Lys Thr Lys Ser Leu Val Pro  
 435 440 445  
 Arg Gly Ser Lys Ala Leu Asn Asp Leu Cys Ile Glu Ile Asn Asn Gly  
 450 455 460  
 Glu Leu Phe Phe Val Ala Ser Glu Asn Ser Tyr Asn Asp Asp Asn Ile  
 465 470 475 480  
 Asn Thr Pro Lys Glu Ile Asp Asp Thr Val Thr Ser Asn Asn Asn Tyr  
 485 490 495  
 Glu Asn Asp Leu Asp Gln Val Ile Leu Asn Phe Asn Ser Glu Ser Ala  
 500 505 510  
 Pro Gly Leu Ser Asp Glu Lys Leu Asn Leu Thr Ile Gln Asn Asp Ala  
 515 520 525  
 Tyr Ile Pro Lys Tyr Asp Ser Asn Gly Thr Ser Asp Ile Glu Gln His  
 530 535 540  
 Asp Val Asn Glu Leu Asn Val Phe Phe Tyr Leu Asp Ala Gln Lys Val  
 545 550 555 560  
 Pro Glu Gly Glu Asn Asn Val Asn Leu Thr Ser Ser Ile Asp Thr Ala  
 565 570 575  
 Leu Leu Glu Gln Pro Lys Ile Tyr Thr Phe Phe Ser Ser Glu Phe Ile  
 580 585 590  
 Asn Asn Val Asn Lys Pro Val Gln Ala Ala Leu Phe Val Ser Trp Ile  
 595 600 605  
 Gln Gln Val Leu Val Asp Phe Thr Thr Glu Ala Asn Gln Lys Ser Thr  
 610 615 620  
 Val Asp Lys Ile Ala Asp Ile Ser Ile Val Val Pro Tyr Ile Gly Leu  
 625 630 635 640  
 Ala Leu Asn Ile Gly Asn Glu Ala Gln Lys Gly Asn Phe Lys Asp Ala  
 645 650 655  
 Leu Glu Leu Leu Gly Ala Gly Ile Leu Leu Glu Phe Glu Pro Glu Leu  
 660 665 670  
 Leu Ile Pro Thr Ile Leu Val Phe Thr Ile Lys Ser Phe Leu Gly Ser  
 675 680 685  
 Ser Asp Asn Lys Asn Lys Val Ile Lys Ala Ile Asn Asn Ala Leu Lys  
 690 695 700

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Glu Arg Asp Glu Lys Trp Lys Glu Val Tyr Ser Phe Ile Val Ser Asn  
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 Trp Met Thr Lys Ile Asn Thr Gln Phe Asn Lys Arg Lys Glu Gln Met  
 725 730 735  
 Tyr Gln Ala Leu Gln Asn Gln Val Asn Ala Ile Lys Thr Ile Ile Glu  
 740 745 750  
 Ser Lys Tyr Asn Ser Tyr Thr Leu Glu Glu Lys Asn Glu Leu Thr Asn  
 755 760 765  
 Lys Tyr Asp Ile Lys Gln Ile Glu Asn Glu Leu Asn Gln Lys Val Ser  
 770 775 780  
 Ile Ala Met Asn Asn Ile Asp Arg Phe Leu Thr Glu Ser Ser Ile Ser  
 785 790 795 800  
 Tyr Leu Met Lys Leu Ile Asn Glu Val Lys Ile Asn Lys Leu Arg Glu  
 805 810 815  
 Tyr Asp Glu Asn Val Lys Thr Tyr Leu Leu Asn Tyr Ile Ile Gln His  
 820 825 830  
 Gly Ser Ile Leu Gly Glu Ser Gln Gln Glu Leu Asn Ser Met Val Thr  
 835 840 845  
 Asp Thr Leu Asn Asn Ser Ile Pro Phe Lys Leu Ser Ser Tyr Thr Asp  
 850 855 860  
 Asp Lys Ile Leu Ile Ser Tyr Phe Asn Lys Phe Phe Lys Arg Ile Lys  
 865 870 875 880  
 Ser Ser Ser Val Leu Asn Met Arg Tyr Lys Asn Asp Lys Tyr Val Asp  
 885 890 895  
 Thr Ser Gly Tyr Asp Ser Asn Ile Asn Ile Asn Gly Asp Val Tyr Lys  
 900 905 910  
 Tyr Pro Thr Asn Lys Asn Gln Phe Gly Ile Tyr Asn Asp Lys Leu Ser  
 915 920 925  
 Glu Val Asn Ile Ser Gln Asn Asp Tyr Ile Ile Tyr Asp Asn Lys Tyr  
 930 935 940  
 Lys Asn Phe Ser Ile Ser Phe Trp Val Arg Ile Pro Asn Tyr Asp Asn  
 945 950 955 960  
 Lys Ile Val Asn Val Asn Asn Glu Tyr Thr Ile Ile Asn Cys Met Arg  
 965 970 975

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Asp Asn Asn Ser Gly Trp Lys Val Ser Leu Asn His Asn Glu Ile Ile  
980 985 990

Trp Thr Leu Gln Asp Asn Ala Gly Ile Asn Gln Lys Leu Ala Phe Asn  
995 1000 1005

Tyr Gly Asn Ala Asn Gly Ile Ser Asp Tyr Ile Asn Lys Trp Ile  
1010 1015 1020

Phe Val Thr Ile Thr Asn Asp Arg Leu Gly Asp Ser Lys Leu Tyr  
1025 1030 1035

Ile Asn Gly Asn Leu Ile Asp Gln Lys Ser Ile Leu Asn Leu Gly  
1040 1045 1050

Asn Ile His Val Ser Asp Asn Ile Leu Phe Lys Ile Val Asn Cys  
1055 1060 1065

Ser Tyr Thr Arg Tyr Ile Gly Ile Arg Tyr Phe Asn Ile Phe Asp  
1070 1075 1080

Lys Glu Leu Asp Glu Thr Glu Ile Gln Thr Leu Tyr Ser Asn Glu  
1085 1090 1095

Pro Asn Thr Asn Ile Leu Lys Asp Phe Trp Gly Asn Tyr Leu Leu  
1100 1105 1110

Tyr Asp Lys Glu Tyr Tyr Leu Leu Asn Val Leu Lys Pro Asn Asn  
1115 1120 1125

Phe Ile Asp Arg Arg Lys Asp Ser Thr Leu Ser Ile Asn Asn Ile  
1130 1135 1140

Arg Ser Thr Ile Leu Leu Ala Asn Arg Leu Tyr Ser Gly Ile Lys  
1145 1150 1155

Val Lys Ile Gln Arg Val Asn Asn Ser Ser Thr Asn Asp Asn Leu  
1160 1165 1170

Val Arg Lys Asn Asp Gln Val Tyr Ile Asn Phe Val Ala Ser Lys  
1175 1180 1185

Thr His Leu Phe Pro Leu Tyr Ala Asp Thr Ala Thr Thr Asn Lys  
1190 1195 1200

Glu Lys Thr Ile Lys Ile Ser Ser Ser Gly Asn Arg Phe Asn Gln  
1205 1210 1215

Val Val Val Met Asn Ser Val Gly Asn Asn Cys Thr Met Asn Phe  
1220 1225 1230

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Lys Asn Asn Asn Gly Asn Asn Ile Gly Leu Leu Gly Phe Lys Ala  
1235 1240 1245

Asp Thr Val Val Ala Ser Thr Trp Tyr Tyr Thr His Met Arg Asp  
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His Thr Asn Ser Asn Gly Cys Phe Trp Asn Phe Ile Ser Glu Glu  
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His Gly Trp Gln Glu Lys  
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<212> PRT  
<213> Artificial Sequence

<220>  
<223> clostridial neurotoxin precursor

<400> 2

Met Ala Tyr Pro Tyr Asp Val Pro Asp Tyr Ala Val Arg Gly Ile Ile  
1 5 10 15

Thr Ser Lys Thr Lys Gly Gly Gly Gly Pro Lys Ile Asn Ser Phe Asn  
20 25 30

Tyr Asn Asp Pro Val Asn Asp Arg Thr Ile Leu Tyr Ile Lys Pro Gly  
35 40 45

Gly Cys Gln Glu Phe Tyr Lys Ser Phe Asn Ile Met Lys Asn Ile Trp  
50 55 60

Ile Ile Pro Glu Arg Asn Val Ile Gly Thr Thr Pro Gln Asp Phe His  
65 70 75 80

Pro Pro Thr Ser Leu Lys Asn Gly Asp Ser Ser Tyr Tyr Asp Pro Asn  
85 90 95

Tyr Leu Gln Ser Asp Glu Glu Lys Asp Arg Phe Leu Lys Ile Val Thr  
100 105 110

Lys Ile Phe Asn Arg Ile Asn Asn Asn Leu Ser Gly Gly Ile Leu Leu  
115 120 125

Glu Glu Leu Ser Lys Ala Asn Pro Tyr Leu Gly Asn Asp Asn Thr Pro  
130 135 140

Asp Asn Gln Phe His Ile Gly Asp Ala Ser Ala Val Glu Ile Lys Phe  
145 150 155 160

Ser Asn Gly Ser Gln Asp Ile Leu Leu Pro Asn Val Ile Ile Met Gly  
Seite 6

165

170

175

Ala Glu Pro Asp Leu Phe Glu Thr Asn Ser Ser Asn Ile Ser Leu Arg  
180 185 190

Asn Asn Tyr Met Pro Ser Asn His Gly Phe Gly Ser Ile Ala Ile Val  
195 200 205

Thr Phe Ser Pro Glu Tyr Ser Phe Arg Phe Asn Asp Asn Ser Met Asn  
210 215 220

Glu Phe Ile Gln Asp Pro Ala Leu Thr Leu Met His Glu Leu Ile His  
225 230 235 240

Ser Leu His Gly Leu Tyr Gly Ala Lys Gly Ile Thr Thr Lys Tyr Thr  
245 250 255

Ile Thr Gln Lys Gln Asn Pro Leu Ile Thr Asn Ile Arg Gly Thr Asn  
260 265 270

Ile Glu Glu Phe Leu Thr Phe Gly Gly Thr Asp Leu Asn Ile Ile Thr  
275 280 285

Ser Ala Gln Ser Asn Asp Ile Tyr Thr Asn Leu Leu Ala Asp Tyr Lys  
290 295 300

Lys Ile Ala Ser Lys Leu Ser Lys Val Gln Val Ser Asn Pro Leu Leu  
305 310 315 320

Asn Pro Tyr Lys Asp Val Phe Glu Ala Lys Tyr Gly Leu Asp Lys Asp  
325 330 335

Ala Ser Gly Ile Tyr Ser Val Asn Ile Asn Lys Phe Asn Asp Ile Phe  
340 345 350

Lys Lys Leu Tyr Ser Phe Thr Glu Phe Asp Leu Ala Thr Lys Phe Gln  
355 360 365

Val Lys Cys Arg Gln Thr Tyr Ile Gly Gln Tyr Lys Tyr Phe Lys Leu  
370 375 380

Ser Asn Leu Leu Asn Asp Ser Ile Tyr Asn Ile Ser Glu Gly Tyr Asn  
385 390 395 400

Ile Asn Asn Leu Lys Val Asn Phe Arg Gly Gln Asn Ala Asn Leu Asn  
405 410 415

Pro Arg Ile Ile Thr Pro Ile Thr Gly Arg Gly Leu Val Lys Lys Ile  
420 425 430

Ile Arg Phe Cys Val Arg Gly Ile Ile Thr Ser Lys Thr Lys Ser Leu  
Seite 7

435

440

445

Val Pro Arg Gly Ser Lys Ala Leu Asn Asp Leu Cys Ile Glu Ile Asn  
450 455 460

Asn Gly Glu Leu Phe Phe Val Ala Ser Glu Asn Ser Tyr Asn Asp Asp  
465 470 475 480

Asn Ile Asn Thr Pro Lys Glu Ile Asp Asp Thr Val Thr Ser Asn Asn  
485 490 495

Asn Tyr Glu Asn Asp Leu Asp Gln Val Ile Leu Asn Phe Asn Ser Glu  
500 505 510

Ser Ala Pro Gly Leu Ser Asp Glu Lys Leu Asn Leu Thr Ile Gln Asn  
515 520 525

Asp Ala Tyr Ile Pro Lys Tyr Asp Ser Asn Gly Thr Ser Asp Ile Glu  
530 535 540

Gln His Asp Val Asn Glu Leu Asn Val Phe Phe Tyr Leu Asp Ala Gln  
545 550 555 560

Lys Val Pro Glu Gly Glu Asn Asn Val Asn Leu Thr Ser Ser Ile Asp  
565 570 575

Thr Ala Leu Leu Glu Gln Pro Lys Ile Tyr Thr Phe Phe Ser Ser Glu  
580 585 590

Phe Ile Asn Asn Val Asn Lys Pro Val Gln Ala Ala Leu Phe Val Ser  
595 600 605

Trp Ile Gln Gln Val Leu Val Asp Phe Thr Thr Glu Ala Asn Gln Lys  
610 615 620

Ser Thr Val Asp Lys Ile Ala Asp Ile Ser Ile Val Val Pro Tyr Ile  
625 630 635 640

Gly Leu Ala Leu Asn Ile Gly Asn Glu Ala Gln Lys Gly Asn Phe Lys  
645 650 655

Asp Ala Leu Glu Leu Leu Gly Ala Gly Ile Leu Leu Glu Phe Glu Pro  
660 665 670

Glu Leu Leu Ile Pro Thr Ile Leu Val Phe Thr Ile Lys Ser Phe Leu  
675 680 685

Gly Ser Ser Asp Asn Lys Asn Lys Val Ile Lys Ala Ile Asn Asn Ala  
690 695 700

Leu Lys Glu Arg Asp Glu Lys Trp Lys Glu Val Tyr Ser Phe Ile Val  
Seite 8



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705                               710                               715                               720
Ser Asn Trp Met Thr Lys Ile Asn Thr Gln Phe Asn Lys Arg Lys Glu
      725                               730
Gln Met Tyr Gln Ala Leu Gln Asn Gln Val Asn Ala Ile Lys Thr Ile
      740                               745                               750
Ile Glu Ser Lys Tyr Asn Ser Tyr Thr Leu Glu Glu Lys Asn Glu Leu
      755                               760                               765
Thr Asn Lys Tyr Asp Ile Lys Gln Ile Glu Asn Glu Leu Asn Gln Lys
      770                               775                               780
Val Ser Ile Ala Met Asn Asn Ile Asp Arg Phe Leu Thr Glu Ser Ser
      785                               790                               795                               800
Ile Ser Tyr Leu Met Lys Leu Ile Asn Glu Val Lys Ile Asn Lys Leu
      805                               810                               815
Arg Glu Tyr Asp Glu Asn Val Lys Thr Tyr Leu Leu Asn Tyr Ile Ile
      820                               825                               830
Gln His Gly Ser Ile Leu Gly Glu Ser Gln Gln Glu Leu Asn Ser Met
      835                               840                               845
Val Thr Asp Thr Leu Asn Asn Ser Ile Pro Phe Lys Leu Ser Ser Tyr
      850                               855                               860
Thr Asp Asp Lys Ile Leu Ile Ser Tyr Phe Asn Lys Phe Phe Lys Arg
      865                               870                               875                               880
Ile Lys Ser Ser Ser Val Leu Asn Met Arg Tyr Lys Asn Asp Lys Tyr
      885                               890                               895
Val Asp Thr Ser Gly Tyr Asp Ser Asn Ile Asn Ile Asn Gly Asp Val
      900                               905                               910
Tyr Lys Tyr Pro Thr Asn Lys Asn Gln Phe Gly Ile Tyr Asn Asp Lys
      915                               920                               925
Leu Ser Glu Val Asn Ile Ser Gln Asn Asp Tyr Ile Ile Tyr Asp Asn
      930                               935                               940
Lys Tyr Lys Asn Phe Ser Ile Ser Phe Trp Val Arg Ile Pro Asn Tyr
      945                               950                               955                               960
Asp Asn Lys Ile Val Asn Val Asn Asn Glu Tyr Thr Ile Ile Asn Cys
      965                               970                               975
Met Arg Asp Asn Asn Ser Gly Trp Lys Val Ser Leu Asn His Asn Glu

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Ile Ile Trp Thr Leu Gln Asp Asn Ala Gly Ile Asn Gln Lys Leu Ala  
 995 1000 1005

Phe Asn Tyr Gly Asn Ala Asn Gly Ile Ser Asp Tyr Ile Asn Lys  
 1010 1015 1020

Trp Ile Phe Val Thr Ile Thr Asn Asp Arg Leu Gly Asp Ser Lys  
 1025 1030 1035

Leu Tyr Ile Asn Gly Asn Leu Ile Asp Gln Lys Ser Ile Leu Asn  
 1040 1045 1050

Leu Gly Asn Ile His Val Ser Asp Asn Ile Leu Phe Lys Ile Val  
 1055 1060 1065

Asn Cys Ser Tyr Thr Arg Tyr Ile Gly Ile Arg Tyr Phe Asn Ile  
 1070 1075 1080

Phe Asp Lys Glu Leu Asp Glu Thr Glu Ile Gln Thr Leu Tyr Ser  
 1085 1090 1095

Asn Glu Pro Asn Thr Asn Ile Leu Lys Asp Phe Trp Gly Asn Tyr  
 1100 1105 1110

Leu Leu Tyr Asp Lys Glu Tyr Tyr Leu Leu Asn Val Leu Lys Pro  
 1115 1120 1125

Asn Asn Phe Ile Asp Arg Arg Lys Asp Ser Thr Leu Ser Ile Asn  
 1130 1135 1140

Asn Ile Arg Ser Thr Ile Leu Leu Ala Asn Arg Leu Tyr Ser Gly  
 1145 1150 1155

Ile Lys Val Lys Ile Gln Arg Val Asn Asn Ser Ser Thr Asn Asp  
 1160 1165 1170

Asn Leu Val Arg Lys Asn Asp Gln Val Tyr Ile Asn Phe Val Ala  
 1175 1180 1185

Ser Lys Thr His Leu Phe Pro Leu Tyr Ala Asp Thr Ala Thr Thr  
 1190 1195 1200

Asn Lys Glu Lys Thr Ile Lys Ile Ser Ser Ser Gly Asn Arg Phe  
 1205 1210 1215

Asn Gln Val Val Val Met Asn Ser Val Gly Asn Asn Cys Thr Met  
 1220 1225 1230

Asn Phe Lys Asn Asn Asn Gly Asn Asn Ile Gly Leu Leu Gly Phe  
 Seite 10

1235

Lys Ala Asp Thr Val Val Ala Ser Thr Trp Tyr Tyr Thr His Met  
1250 1255 1260

Arg Asp His Thr Asn Ser Asn Gly Cys Phe Trp Asn Phe Ile Ser  
1265 1270 1275

Glu Glu His Gly Trp Gln Glu Lys  
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<213> Artificial Sequence

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<223> clostridial neurotoxin precursor  
<400> 3

Met Ala Tyr Pro Tyr Asp Val Pro Asp Tyr Ala Val Arg Gly Ile Ile  
1 5 10 15

Thr Ser Lys Thr Lys Gly Gly Gly Gly Gly Gly Gly Gly Pro Lys Ile  
20 25 30

Asn Ser Phe Asn Tyr Asn Asp Pro Val Asn Asp Arg Thr Ile Leu Tyr  
35 40 45

Ile Lys Pro Gly Gly Cys Gln Glu Phe Tyr Lys Ser Phe Asn Ile Met  
50 55 60

Lys Asn Ile Trp Ile Ile Pro Glu Arg Asn Val Ile Gly Thr Thr Pro  
65 70 75 80

Gln Asp Phe His Pro Pro Thr Ser Leu Lys Asn Gly Asp Ser Ser Tyr  
85 90 95

Tyr Asp Pro Asn Tyr Leu Gln Ser Asp Glu Glu Lys Asp Arg Phe Leu  
100 105 110

Lys Ile Val Thr Lys Ile Phe Asn Arg Ile Asn Asn Asn Leu Ser Gly  
115 120 125

Gly Ile Leu Leu Glu Glu Leu Ser Lys Ala Asn Pro Tyr Leu Gly Asn  
130 135 140

Asp Asn Thr Pro Asp Asn Gln Phe His Ile Gly Asp Ala Ser Ala Val  
145 150 155 160

Glu Ile Lys Phe Ser Asn Gly Ser Gln Asp Ile Leu Leu Pro Asn Val  
165 170 175

## 108454P502PC\_SeqListing\_ST25.txt

Ile Ile Met Gly Ala Glu Pro Asp Leu Phe Glu Thr Asn Ser Ser Asn  
 180 185 190  
 Ile Ser Leu Arg Asn Asn Tyr Met Pro Ser Asn His Gly Phe Gly Ser  
 195 200 205  
 Ile Ala Ile Val Thr Phe Ser Pro Glu Tyr Ser Phe Arg Phe Asn Asp  
 210 215 220  
 Asn Ser Met Asn Glu Phe Ile Gln Asp Pro Ala Leu Thr Leu Met His  
 225 230 235 240  
 Glu Leu Ile His Ser Leu His Gly Leu Tyr Gly Ala Lys Gly Ile Thr  
 245 250 255  
 Thr Lys Tyr Thr Ile Thr Gln Lys Gln Asn Pro Leu Ile Thr Asn Ile  
 260 265 270  
 Arg Gly Thr Asn Ile Glu Glu Phe Leu Thr Phe Gly Gly Thr Asp Leu  
 275 280 285  
 Asn Ile Ile Thr Ser Ala Gln Ser Asn Asp Ile Tyr Thr Asn Leu Leu  
 290 295 300  
 Ala Asp Tyr Lys Lys Ile Ala Ser Lys Leu Ser Lys Val Gln Val Ser  
 305 310 315 320  
 Asn Pro Leu Leu Asn Pro Tyr Lys Asp Val Phe Glu Ala Lys Tyr Gly  
 325 330 335  
 Leu Asp Lys Asp Ala Ser Gly Ile Tyr Ser Val Asn Ile Asn Lys Phe  
 340 345 350  
 Asn Asp Ile Phe Lys Lys Leu Tyr Ser Phe Thr Glu Phe Asp Leu Ala  
 355 360 365  
 Thr Lys Phe Gln Val Lys Cys Arg Gln Thr Tyr Ile Gly Gln Tyr Lys  
 370 375 380  
 Tyr Phe Lys Leu Ser Asn Leu Leu Asn Asp Ser Ile Tyr Asn Ile Ser  
 385 390 395 400  
 Glu Gly Tyr Asn Ile Asn Asn Leu Lys Val Asn Phe Arg Gly Gln Asn  
 405 410 415  
 Ala Asn Leu Asn Pro Arg Ile Ile Thr Pro Ile Thr Gly Arg Gly Leu  
 420 425 430  
 Val Lys Lys Ile Ile Arg Phe Cys Val Arg Gly Ile Ile Thr Ser Lys  
 435 440 445

108454P502PC\_SeqListing\_ST25.txt

Thr Lys Ser Leu Val Pro Arg Gly Ser Lys Ala Leu Asn Asp Leu Cys  
 450 455 460  
 Ile Glu Ile Asn Asn Gly Glu Leu Phe Phe Val Ala Ser Glu Asn Ser  
 465 470 475 480  
 Tyr Asn Asp Asp Asn Ile Asn Thr Pro Lys Glu Ile Asp Asp Thr Val  
 485 490 495  
 Thr Ser Asn Asn Asn Tyr Glu Asn Asp Leu Asp Gln Val Ile Leu Asn  
 500 505 510  
 Phe Asn Ser Glu Ser Ala Pro Gly Leu Ser Asp Glu Lys Leu Asn Leu  
 515 520 525  
 Thr Ile Gln Asn Asp Ala Tyr Ile Pro Lys Tyr Asp Ser Asn Gly Thr  
 530 535 540  
 Ser Asp Ile Glu Gln His Asp Val Asn Glu Leu Asn Val Phe Phe Tyr  
 545 550 555 560  
 Leu Asp Ala Gln Lys Val Pro Glu Gly Glu Asn Asn Val Asn Leu Thr  
 565 570 575  
 Ser Ser Ile Asp Thr Ala Leu Leu Glu Gln Pro Lys Ile Tyr Thr Phe  
 580 585 590  
 Phe Ser Ser Glu Phe Ile Asn Asn Val Asn Lys Pro Val Gln Ala Ala  
 595 600 605  
 Leu Phe Val Ser Trp Ile Gln Gln Val Leu Val Asp Phe Thr Thr Glu  
 610 615 620  
 Ala Asn Gln Lys Ser Thr Val Asp Lys Ile Ala Asp Ile Ser Ile Val  
 625 630 635 640  
 Val Pro Tyr Ile Gly Leu Ala Leu Asn Ile Gly Asn Glu Ala Gln Lys  
 645 650 655  
 Gly Asn Phe Lys Asp Ala Leu Glu Leu Leu Gly Ala Gly Ile Leu Leu  
 660 665 670  
 Glu Phe Glu Pro Glu Leu Leu Ile Pro Thr Ile Leu Val Phe Thr Ile  
 675 680 685  
 Lys Ser Phe Leu Gly Ser Ser Asp Asn Lys Asn Lys Val Ile Lys Ala  
 690 695 700  
 Ile Asn Asn Ala Leu Lys Glu Arg Asp Glu Lys Trp Lys Glu Val Tyr  
 705 710 715 720

108454P502PC\_SeqListing\_ST25.txt

Ser Phe Ile Val Ser Asn Trp Met Thr Lys Ile Asn Thr Gln Phe Asn  
725 730 735

Lys Arg Lys Glu Gln Met Tyr Gln Ala Leu Gln Asn Gln Val Asn Ala  
740 745 750

Ile Lys Thr Ile Ile Glu Ser Lys Tyr Asn Ser Tyr Thr Leu Glu Glu  
755 760 765

Lys Asn Glu Leu Thr Asn Lys Tyr Asp Ile Lys Gln Ile Glu Asn Glu  
770 775 780

Leu Asn Gln Lys Val Ser Ile Ala Met Asn Asn Ile Asp Arg Phe Leu  
785 790 795 800

Thr Glu Ser Ser Ile Ser Tyr Leu Met Lys Leu Ile Asn Glu Val Lys  
805 810 815

Ile Asn Lys Leu Arg Glu Tyr Asp Glu Asn Val Lys Thr Tyr Leu Leu  
820 825 830

Asn Tyr Ile Ile Gln His Gly Ser Ile Leu Gly Glu Ser Gln Gln Glu  
835 840 845

Leu Asn Ser Met Val Thr Asp Thr Leu Asn Asn Ser Ile Pro Phe Lys  
850 855 860

Leu Ser Ser Tyr Thr Asp Asp Lys Ile Leu Ile Ser Tyr Phe Asn Lys  
865 870 875 880

Phe Phe Lys Arg Ile Lys Ser Ser Ser Val Leu Asn Met Arg Tyr Lys  
885 890 895

Asn Asp Lys Tyr Val Asp Thr Ser Gly Tyr Asp Ser Asn Ile Asn Ile  
900 905 910

Asn Gly Asp Val Tyr Lys Tyr Pro Thr Asn Lys Asn Gln Phe Gly Ile  
915 920 925

Tyr Asn Asp Lys Leu Ser Glu Val Asn Ile Ser Gln Asn Asp Tyr Ile  
930 935 940

Ile Tyr Asp Asn Lys Tyr Lys Asn Phe Ser Ile Ser Phe Trp Val Arg  
945 950 955 960

Ile Pro Asn Tyr Asp Asn Lys Ile Val Asn Val Asn Asn Glu Tyr Thr  
965 970 975

Ile Ile Asn Cys Met Arg Asp Asn Asn Ser Gly Trp Lys Val Ser Leu  
980 985 990

## 108454P502PC\_SeqListing\_ST25.txt

Asn His Asn Glu Ile Ile Trp Thr Leu Gln Asp Asn Ala Gly Ile Asn  
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 Gln Lys Leu Ala Phe Asn Tyr Gly Asn Ala Asn Gly Ile Ser Asp  
 1010 1015 1020  
  
 Tyr Ile Asn Lys Trp Ile Phe Val Thr Ile Thr Asn Asp Arg Leu  
 1025 1030 1035  
  
 Gly Asp Ser Lys Leu Tyr Ile Asn Gly Asn Leu Ile Asp Gln Lys  
 1040 1045 1050  
  
 Ser Ile Leu Asn Leu Gly Asn Ile His Val Ser Asp Asn Ile Leu  
 1055 1060 1065  
  
 Phe Lys Ile Val Asn Cys Ser Tyr Thr Arg Tyr Ile Gly Ile Arg  
 1070 1075 1080  
  
 Tyr Phe Asn Ile Phe Asp Lys Glu Leu Asp Glu Thr Glu Ile Gln  
 1085 1090 1095  
  
 Thr Leu Tyr Ser Asn Glu Pro Asn Thr Asn Ile Leu Lys Asp Phe  
 1100 1105 1110  
  
 Trp Gly Asn Tyr Leu Leu Tyr Asp Lys Glu Tyr Tyr Leu Leu Asn  
 1115 1120 1125  
  
 Val Leu Lys Pro Asn Asn Phe Ile Asp Arg Arg Lys Asp Ser Thr  
 1130 1135 1140  
  
 Leu Ser Ile Asn Asn Ile Arg Ser Thr Ile Leu Leu Ala Asn Arg  
 1145 1150 1155  
  
 Leu Tyr Ser Gly Ile Lys Val Lys Ile Gln Arg Val Asn Asn Ser  
 1160 1165 1170  
  
 Ser Thr Asn Asp Asn Leu Val Arg Lys Asn Asp Gln Val Tyr Ile  
 1175 1180 1185  
  
 Asn Phe Val Ala Ser Lys Thr His Leu Phe Pro Leu Tyr Ala Asp  
 1190 1195 1200  
  
 Thr Ala Thr Thr Asn Lys Glu Lys Thr Ile Lys Ile Ser Ser Ser  
 1205 1210 1215  
  
 Gly Asn Arg Phe Asn Gln Val Val Val Met Asn Ser Val Gly Asn  
 1220 1225 1230  
  
 Asn Cys Thr Met Asn Phe Lys Asn Asn Asn Gly Asn Asn Ile Gly  
 1235 1240 1245

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Leu Leu Gly Phe Lys Ala Asp Thr Val Val Ala Ser Thr Trp Tyr  
1250 1255 1260

Tyr Thr His Met Arg Asp His Thr Asn Ser Asn Gly Cys Phe Trp  
1265 1270 1275

Asn Phe Ile Ser Glu Glu His Gly Trp Gln Glu Lys  
1280 1285 1290

<210> 4  
<211> 1266  
<212> PRT  
<213> Artificial sequence

<220>  
<223> clostridial neurotoxin with N-terminal lysine

<400> 4

Lys Thr Lys Gly Gly Pro Lys Ile Asn Ser Phe Asn Tyr Asn Asp Pro  
1 5 10 15

Val Asn Asp Arg Thr Ile Leu Tyr Ile Lys Pro Gly Gly Cys Gln Glu  
20 25 30

Phe Tyr Lys Ser Phe Asn Ile Met Lys Asn Ile Trp Ile Ile Pro Glu  
35 40 45

Arg Asn Val Ile Gly Thr Thr Pro Gln Asp Phe His Pro Pro Thr Ser  
50 55 60

Leu Lys Asn Gly Asp Ser Ser Tyr Tyr Asp Pro Asn Tyr Leu Gln Ser  
65 70 75 80

Asp Glu Glu Lys Asp Arg Phe Leu Lys Ile Val Thr Lys Ile Phe Asn  
85 90 95

Arg Ile Asn Asn Asn Leu Ser Gly Gly Ile Leu Leu Glu Glu Leu Ser  
100 105 110

Lys Ala Asn Pro Tyr Leu Gly Asn Asp Asn Thr Pro Asp Asn Gln Phe  
115 120 125

His Ile Gly Asp Ala Ser Ala Val Glu Ile Lys Phe Ser Asn Gly Ser  
130 135 140

Gln Asp Ile Leu Leu Pro Asn Val Ile Ile Met Gly Ala Glu Pro Asp  
145 150 155 160

Leu Phe Glu Thr Asn Ser Ser Asn Ile Ser Leu Arg Asn Asn Tyr Met  
165 170 175

Pro Ser Asn His Gly Phe Gly Ser Ile Ala Ile Val Thr Phe Ser Pro  
Seite 16



180

185

190

Glu Tyr Ser Phe Arg Phe Asn Asp Asn Ser Met Asn Glu Phe Ile Gln  
 195 200 205

Asp Pro Ala Leu Thr Leu Met His Glu Leu Ile His Ser Leu His Gly  
 210 215 220

Leu Tyr Gly Ala Lys Gly Ile Thr Thr Lys Tyr Thr Ile Thr Gln Lys  
 225 230 235 240

Gln Asn Pro Leu Ile Thr Asn Ile Arg Gly Thr Asn Ile Glu Glu Phe  
 245 250 255

Leu Thr Phe Gly Gly Thr Asp Leu Asn Ile Ile Thr Ser Ala Gln Ser  
 260 265 270

Asn Asp Ile Tyr Thr Asn Leu Leu Ala Asp Tyr Lys Lys Ile Ala Ser  
 275 280 285

Lys Leu Ser Lys Val Gln Val Ser Asn Pro Leu Leu Asn Pro Tyr Lys  
 290 295 300

Asp Val Phe Glu Ala Lys Tyr Gly Leu Asp Lys Asp Ala Ser Gly Ile  
 305 310 315 320

Tyr Ser Val Asn Ile Asn Lys Phe Asn Asp Ile Phe Lys Lys Leu Tyr  
 325 330 335

Ser Phe Thr Glu Phe Asp Leu Ala Thr Lys Phe Gln Val Lys Cys Arg  
 340 345 350

Gln Thr Tyr Ile Gly Gln Tyr Lys Tyr Phe Lys Leu Ser Asn Leu Leu  
 355 360 365

Asn Asp Ser Ile Tyr Asn Ile Ser Glu Gly Tyr Asn Ile Asn Asn Leu  
 370 375 380

Lys Val Asn Phe Arg Gly Gln Asn Ala Asn Leu Asn Pro Arg Ile Ile  
 385 390 395 400

Thr Pro Ile Thr Gly Arg Gly Leu Val Lys Lys Ile Ile Arg Phe Cys  
 405 410 415

Val Arg Gly Ile Ile Thr Ser Lys Thr Lys Ser Leu Val Pro Arg Gly  
 420 425 430

Ser Lys Ala Leu Asn Asp Leu Cys Ile Glu Ile Asn Asn Gly Glu Leu  
 435 440 445

Phe Phe Val Ala Ser Glu Asn Ser Tyr Asn Asp Asp Asn Ile Asn Thr  
 Seite 17

450

455

460

Pro Lys Glu Ile Asp Asp Thr Val Thr Ser Asn Asn Asn Tyr Glu Asn  
465 470 475 480

Asp Leu Asp Gln Val Ile Leu Asn Phe Asn Ser Glu Ser Ala Pro Gly  
485 490 495

Leu Ser Asp Glu Lys Leu Asn Leu Thr Ile Gln Asn Asp Ala Tyr Ile  
500 505 510

Pro Lys Tyr Asp Ser Asn Gly Thr Ser Asp Ile Glu Gln His Asp Val  
515 520 525

Asn Glu Leu Asn Val Phe Phe Tyr Leu Asp Ala Gln Lys Val Pro Glu  
530 535 540

Gly Glu Asn Asn Val Asn Leu Thr Ser Ser Ile Asp Thr Ala Leu Leu  
545 550 555 560

Glu Gln Pro Lys Ile Tyr Thr Phe Phe Ser Ser Glu Phe Ile Asn Asn  
565 570 575

Val Asn Lys Pro Val Gln Ala Ala Leu Phe Val Ser Trp Ile Gln Gln  
580 585 590

Val Leu Val Asp Phe Thr Thr Glu Ala Asn Gln Lys Ser Thr Val Asp  
595 600 605

Lys Ile Ala Asp Ile Ser Ile Val Val Pro Tyr Ile Gly Leu Ala Leu  
610 615 620

Asn Ile Gly Asn Glu Ala Gln Lys Gly Asn Phe Lys Asp Ala Leu Glu  
625 630 635 640

Leu Leu Gly Ala Gly Ile Leu Leu Glu Phe Glu Pro Glu Leu Leu Ile  
645 650 655

Pro Thr Ile Leu Val Phe Thr Ile Lys Ser Phe Leu Gly Ser Ser Asp  
660 665 670

Asn Lys Asn Lys Val Ile Lys Ala Ile Asn Asn Ala Leu Lys Glu Arg  
675 680 685

Asp Glu Lys Trp Lys Glu Val Tyr Ser Phe Ile Val Ser Asn Trp Met  
690 695 700

Thr Lys Ile Asn Thr Gln Phe Asn Lys Arg Lys Glu Gln Met Tyr Gln  
705 710 715 720

Ala Leu Gln Asn Gln Val Asn Ala Ile Lys Thr Ile Ile Glu Ser Lys

725

730

735

Tyr Asn Ser Tyr Thr Leu Glu Glu Lys Asn Glu Leu Thr Asn Lys Tyr  
740 745 750

Asp Ile Lys Gln Ile Glu Asn Glu Leu Asn Gln Lys Val Ser Ile Ala  
755 760 765

Met Asn Asn Ile Asp Arg Phe Leu Thr Glu Ser Ser Ile Ser Tyr Leu  
770 775 780

Met Lys Leu Ile Asn Glu Val Lys Ile Asn Lys Leu Arg Glu Tyr Asp  
785 790 795 800

Glu Asn Val Lys Thr Tyr Leu Leu Asn Tyr Ile Ile Gln His Gly Ser  
805 810 815

Ile Leu Gly Glu Ser Gln Gln Glu Leu Asn Ser Met Val Thr Asp Thr  
820 825 830

Leu Asn Asn Ser Ile Pro Phe Lys Leu Ser Ser Tyr Thr Asp Asp Lys  
835 840 845

Ile Leu Ile Ser Tyr Phe Asn Lys Phe Phe Lys Arg Ile Lys Ser Ser  
850 855 860

Ser Val Leu Asn Met Arg Tyr Lys Asn Asp Lys Tyr Val Asp Thr Ser  
865 870 875 880

Gly Tyr Asp Ser Asn Ile Asn Ile Asn Gly Asp Val Tyr Lys Tyr Pro  
885 890 895

Thr Asn Lys Asn Gln Phe Gly Ile Tyr Asn Asp Lys Leu Ser Glu Val  
900 905 910

Asn Ile Ser Gln Asn Asp Tyr Ile Ile Tyr Asp Asn Lys Tyr Lys Asn  
915 920 925

Phe Ser Ile Ser Phe Trp Val Arg Ile Pro Asn Tyr Asp Asn Lys Ile  
930 935 940

Val Asn Val Asn Asn Glu Tyr Thr Ile Ile Asn Cys Met Arg Asp Asn  
945 950 955 960

Asn Ser Gly Trp Lys Val Ser Leu Asn His Asn Glu Ile Ile Trp Thr  
965 970 975

Leu Gln Asp Asn Ala Gly Ile Asn Gln Lys Leu Ala Phe Asn Tyr Gly  
980 985 990

Asn Ala Asn Gly Ile Ser Asp Tyr Ile Asn Lys Trp Ile Phe Val Thr  
Seite 19

Ile	Thr	Asn	Asp	Arg	Leu	Gly	Asp	Ser	Lys	Leu	Tyr	Ile	Asn	Gly
	1010					1015					1020			
Asn	Leu	Ile	Asp	Gln	Lys	Ser	Ile	Leu	Asn	Leu	Gly	Asn	Ile	His
	1025					1030					1035			
Val	Ser	Asp	Asn	Ile	Leu	Phe	Lys	Ile	Val	Asn	Cys	Ser	Tyr	Thr
	1040					1045					1050			
Arg	Tyr	Ile	Gly	Ile	Arg	Tyr	Phe	Asn	Ile	Phe	Asp	Lys	Glu	Leu
	1055					1060					1065			
Asp	Glu	Thr	Glu	Ile	Gln	Thr	Leu	Tyr	Ser	Asn	Glu	Pro	Asn	Thr
	1070					1075					1080			
Asn	Ile	Leu	Lys	Asp	Phe	Trp	Gly	Asn	Tyr	Leu	Leu	Tyr	Asp	Lys
	1085					1090					1095			
Glu	Tyr	Tyr	Leu	Leu	Asn	Val	Leu	Lys	Pro	Asn	Asn	Phe	Ile	Asp
	1100					1105					1110			
Arg	Arg	Lys	Asp	Ser	Thr	Leu	Ser	Ile	Asn	Asn	Ile	Arg	Ser	Thr
	1115					1120					1125			
Ile	Leu	Leu	Ala	Asn	Arg	Leu	Tyr	Ser	Gly	Ile	Lys	Val	Lys	Ile
	1130					1135					1140			
Gln	Arg	Val	Asn	Asn	Ser	Ser	Thr	Asn	Asp	Asn	Leu	Val	Arg	Lys
	1145					1150					1155			
Asn	Asp	Gln	Val	Tyr	Ile	Asn	Phe	Val	Ala	Ser	Lys	Thr	His	Leu
	1160					1165					1170			
Phe	Pro	Leu	Tyr	Ala	Asp	Thr	Ala	Thr	Thr	Asn	Lys	Glu	Lys	Thr
	1175					1180					1185			
Ile	Lys	Ile	Ser	Ser	Ser	Gly	Asn	Arg	Phe	Asn	Gln	Val	Val	Val
	1190					1195					1200			
Met	Asn	Ser	Val	Gly	Asn	Asn	Cys	Thr	Met	Asn	Phe	Lys	Asn	Asn
	1205					1210					1215			
Asn	Gly	Asn	Asn	Ile	Gly	Leu	Leu	Gly	Phe	Lys	Ala	Asp	Thr	Val
	1220					1225					1230			
Val	Ala	Ser	Thr	Trp	Tyr	Tyr	Thr	His	Met	Arg	Asp	His	Thr	Asn
	1235					1240					1245			
Ser	Asn	Gly	Cys	Phe	Trp	Asn	Phe	Ile	Ser	Glu	Glu	His	Gly	Trp

1250

Gln Glu Lys  
1265

<210> 5  
<211> 1268  
<212> PRT  
<213> Artificial sequence

<220>  
<223> clostridial neurotoxin with N-terminal lysine

<400> 5

Lys Thr Lys Gly Gly Gly Gly Pro Lys Ile Asn Ser Phe Asn Tyr Asn  
1 5 10 15

Asp Pro Val Asn Asp Arg Thr Ile Leu Tyr Ile Lys Pro Gly Gly Cys  
20 25 30

Gln Glu Phe Tyr Lys Ser Phe Asn Ile Met Lys Asn Ile Trp Ile Ile  
35 40 45

Pro Glu Arg Asn Val Ile Gly Thr Thr Pro Gln Asp Phe His Pro Pro  
50 55 60

Thr Ser Leu Lys Asn Gly Asp Ser Ser Tyr Tyr Asp Pro Asn Tyr Leu  
65 70 75 80

Gln Ser Asp Glu Glu Lys Asp Arg Phe Leu Lys Ile Val Thr Lys Ile  
85 90 95

Phe Asn Arg Ile Asn Asn Asn Leu Ser Gly Gly Ile Leu Leu Glu Glu  
100 105 110

Leu Ser Lys Ala Asn Pro Tyr Leu Gly Asn Asp Asn Thr Pro Asp Asn  
115 120 125

Gln Phe His Ile Gly Asp Ala Ser Ala Val Glu Ile Lys Phe Ser Asn  
130 135 140

Gly Ser Gln Asp Ile Leu Leu Pro Asn Val Ile Ile Met Gly Ala Glu  
145 150 155 160

Pro Asp Leu Phe Glu Thr Asn Ser Ser Asn Ile Ser Leu Arg Asn Asn  
165 170 175

Tyr Met Pro Ser Asn His Gly Phe Gly Ser Ile Ala Ile Val Thr Phe  
180 185 190

Ser Pro Glu Tyr Ser Phe Arg Phe Asn Asp Asn Ser Met Asn Glu Phe  
195 200 205

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Ile Gln Asp Pro Ala Leu Thr Leu Met His Glu Leu Ile His Ser Leu  
210 215 220

His Gly Leu Tyr Gly Ala Lys Gly Ile Thr Thr Lys Tyr Thr Ile Thr  
225 230 235 240

Gln Lys Gln Asn Pro Leu Ile Thr Asn Ile Arg Gly Thr Asn Ile Glu  
245 250 255

Glu Phe Leu Thr Phe Gly Gly Thr Asp Leu Asn Ile Ile Thr Ser Ala  
260 265 270

Gln Ser Asn Asp Ile Tyr Thr Asn Leu Leu Ala Asp Tyr Lys Lys Ile  
275 280 285

Ala Ser Lys Leu Ser Lys Val Gln Val Ser Asn Pro Leu Leu Asn Pro  
290 295 300

Tyr Lys Asp Val Phe Glu Ala Lys Tyr Gly Leu Asp Lys Asp Ala Ser  
305 310 315 320

Gly Ile Tyr Ser Val Asn Ile Asn Lys Phe Asn Asp Ile Phe Lys Lys  
325 330 335

Leu Tyr Ser Phe Thr Glu Phe Asp Leu Ala Thr Lys Phe Gln Val Lys  
340 345 350

Cys Arg Gln Thr Tyr Ile Gly Gln Tyr Lys Tyr Phe Lys Leu Ser Asn  
355 360 365

Leu Leu Asn Asp Ser Ile Tyr Asn Ile Ser Glu Gly Tyr Asn Ile Asn  
370 375 380

Asn Leu Lys Val Asn Phe Arg Gly Gln Asn Ala Asn Leu Asn Pro Arg  
385 390 395 400

Ile Ile Thr Pro Ile Thr Gly Arg Gly Leu Val Lys Lys Ile Ile Arg  
405 410 415

Phe Cys Val Arg Gly Ile Ile Thr Ser Lys Thr Lys Ser Leu Val Pro  
420 425 430

Arg Gly Ser Lys Ala Leu Asn Asp Leu Cys Ile Glu Ile Asn Asn Gly  
435 440 445

Glu Leu Phe Phe Val Ala Ser Glu Asn Ser Tyr Asn Asp Asp Asn Ile  
450 455 460

Asn Thr Pro Lys Glu Ile Asp Asp Thr Val Thr Ser Asn Asn Asn Tyr  
465 470 475 480

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Glu Asn Asp Leu Asp Gln Val Ile Leu Asn Phe Asn Ser Glu Ser Ala  
485 490 495

Pro Gly Leu Ser Asp Glu Lys Leu Asn Leu Thr Ile Gln Asn Asp Ala  
500 505 510

Tyr Ile Pro Lys Tyr Asp Ser Asn Gly Thr Ser Asp Ile Glu Gln His  
515 520 525

Asp Val Asn Glu Leu Asn Val Phe Phe Tyr Leu Asp Ala Gln Lys Val  
530 535 540

Pro Glu Gly Glu Asn Asn Val Asn Leu Thr Ser Ser Ile Asp Thr Ala  
545 550 555 560

Leu Leu Glu Gln Pro Lys Ile Tyr Thr Phe Phe Ser Ser Glu Phe Ile  
565 570 575

Asn Asn Val Asn Lys Pro Val Gln Ala Ala Leu Phe Val Ser Trp Ile  
580 585 590

Gln Gln Val Leu Val Asp Phe Thr Thr Glu Ala Asn Gln Lys Ser Thr  
595 600 605

Val Asp Lys Ile Ala Asp Ile Ser Ile Val Val Pro Tyr Ile Gly Leu  
610 615 620

Ala Leu Asn Ile Gly Asn Glu Ala Gln Lys Gly Asn Phe Lys Asp Ala  
625 630 635 640

Leu Glu Leu Leu Gly Ala Gly Ile Leu Leu Glu Phe Glu Pro Glu Leu  
645 650 655

Leu Ile Pro Thr Ile Leu Val Phe Thr Ile Lys Ser Phe Leu Gly Ser  
660 665 670

Ser Asp Asn Lys Asn Lys Val Ile Lys Ala Ile Asn Asn Ala Leu Lys  
675 680 685

Glu Arg Asp Glu Lys Trp Lys Glu Val Tyr Ser Phe Ile Val Ser Asn  
690 695 700

Trp Met Thr Lys Ile Asn Thr Gln Phe Asn Lys Arg Lys Glu Gln Met  
705 710 715 720

Tyr Gln Ala Leu Gln Asn Gln Val Asn Ala Ile Lys Thr Ile Ile Glu  
725 730 735

Ser Lys Tyr Asn Ser Tyr Thr Leu Glu Glu Lys Asn Glu Leu Thr Asn  
740 745 750

108454P502PC\_SeqListing\_ST25.txt

Lys Tyr Asp Ile Lys Gln Ile Glu Asn Glu Leu Asn Gln Lys Val Ser  
 755 760 765  
 Ile Ala Met Asn Asn Ile Asp Arg Phe Leu Thr Glu Ser Ser Ile Ser  
 770 775 780  
 Tyr Leu Met Lys Leu Ile Asn Glu Val Lys Ile Asn Lys Leu Arg Glu  
 785 790 795 800  
 Tyr Asp Glu Asn Val Lys Thr Tyr Leu Leu Asn Tyr Ile Ile Gln His  
 805 810 815  
 Gly Ser Ile Leu Gly Glu Ser Gln Gln Glu Leu Asn Ser Met Val Thr  
 820 825 830  
 Asp Thr Leu Asn Asn Ser Ile Pro Phe Lys Leu Ser Ser Tyr Thr Asp  
 835 840 845  
 Asp Lys Ile Leu Ile Ser Tyr Phe Asn Lys Phe Phe Lys Arg Ile Lys  
 850 855 860  
 Ser Ser Ser Val Leu Asn Met Arg Tyr Lys Asn Asp Lys Tyr Val Asp  
 865 870 875 880  
 Thr Ser Gly Tyr Asp Ser Asn Ile Asn Ile Asn Gly Asp Val Tyr Lys  
 885 890 895  
 Tyr Pro Thr Asn Lys Asn Gln Phe Gly Ile Tyr Asn Asp Lys Leu Ser  
 900 905 910  
 Glu Val Asn Ile Ser Gln Asn Asp Tyr Ile Ile Tyr Asp Asn Lys Tyr  
 915 920 925  
 Lys Asn Phe Ser Ile Ser Phe Trp Val Arg Ile Pro Asn Tyr Asp Asn  
 930 935 940  
 Lys Ile Val Asn Val Asn Asn Glu Tyr Thr Ile Ile Asn Cys Met Arg  
 945 950 955 960  
 Asp Asn Asn Ser Gly Trp Lys Val Ser Leu Asn His Asn Glu Ile Ile  
 965 970 975  
 Trp Thr Leu Gln Asp Asn Ala Gly Ile Asn Gln Lys Leu Ala Phe Asn  
 980 985 990  
 Tyr Gly Asn Ala Asn Gly Ile Ser Asp Tyr Ile Asn Lys Trp Ile Phe  
 995 1000 1005  
 Val Thr Ile Thr Asn Asp Arg Leu Gly Asp Ser Lys Leu Tyr Ile  
 1010 1015 1020



108454P502PC\_SeqListing\_ST25.txt

Asn	Gly	Asn	Leu	Ile	Asp	Gln	Lys	Ser	Ile	Leu	Asn	Leu	Gly	Asn
	1025					1030					1035			
Ile	His	Val	Ser	Asp	Asn	Ile	Leu	Phe	Lys	Ile	Val	Asn	Cys	Ser
	1040					1045					1050			
Tyr	Thr	Arg	Tyr	Ile	Gly	Ile	Arg	Tyr	Phe	Asn	Ile	Phe	Asp	Lys
	1055					1060					1065			
Glu	Leu	Asp	Glu	Thr	Glu	Ile	Gln	Thr	Leu	Tyr	Ser	Asn	Glu	Pro
	1070					1075					1080			
Asn	Thr	Asn	Ile	Leu	Lys	Asp	Phe	Trp	Gly	Asn	Tyr	Leu	Leu	Tyr
	1085					1090					1095			
Asp	Lys	Glu	Tyr	Tyr	Leu	Leu	Asn	Val	Leu	Lys	Pro	Asn	Asn	Phe
	1100					1105					1110			
Ile	Asp	Arg	Arg	Lys	Asp	Ser	Thr	Leu	Ser	Ile	Asn	Asn	Ile	Arg
	1115					1120					1125			
Ser	Thr	Ile	Leu	Leu	Ala	Asn	Arg	Leu	Tyr	Ser	Gly	Ile	Lys	Val
	1130					1135					1140			
Lys	Ile	Gln	Arg	Val	Asn	Asn	Ser	Ser	Thr	Asn	Asp	Asn	Leu	Val
	1145					1150					1155			
Arg	Lys	Asn	Asp	Gln	Val	Tyr	Ile	Asn	Phe	Val	Ala	Ser	Lys	Thr
	1160					1165					1170			
His	Leu	Phe	Pro	Leu	Tyr	Ala	Asp	Thr	Ala	Thr	Thr	Asn	Lys	Glu
	1175					1180					1185			
Lys	Thr	Ile	Lys	Ile	Ser	Ser	Ser	Gly	Asn	Arg	Phe	Asn	Gln	Val
	1190					1195					1200			
Val	Val	Met	Asn	Ser	Val	Gly	Asn	Asn	Cys	Thr	Met	Asn	Phe	Lys
	1205					1210					1215			
Asn	Asn	Asn	Gly	Asn	Asn	Ile	Gly	Leu	Leu	Gly	Phe	Lys	Ala	Asp
	1220					1225					1230			
Thr	Val	Val	Ala	Ser	Thr	Trp	Tyr	Tyr	Thr	His	Met	Arg	Asp	His
	1235					1240					1245			
Thr	Asn	Ser	Asn	Gly	Cys	Phe	Trp	Asn	Phe	Ile	Ser	Glu	Glu	His
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Gly	Trp	Gln	Glu	Lys										
	1265													

<210> 6  
 <211> 1272  
 <212> PRT  
 <213> Artificial Sequence

<220>  
 <223> clostridial neurotoxin with N-terminal lysine

<400> 6

Lys Thr Lys Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Pro Lys Ile Asn Ser  
 1 5 10 15

Phe Asn Tyr Asn Asp Pro Val Asn Asp Arg Thr Ile Leu Tyr Ile Lys  
 20 25 30

Pro Gly Gly Cys Gln Glu Phe Tyr Lys Ser Phe Asn Ile Met Lys Asn  
 35 40 45

Ile Trp Ile Ile Pro Glu Arg Asn Val Ile Gly Thr Thr Pro Gln Asp  
 50 55 60

Phe His Pro Pro Thr Ser Leu Lys Asn Gly Asp Ser Ser Tyr Tyr Asp  
 65 70 75 80

Pro Asn Tyr Leu Gln Ser Asp Glu Glu Lys Asp Arg Phe Leu Lys Ile  
 85 90 95

Val Thr Lys Ile Phe Asn Arg Ile Asn Asn Asn Leu Ser Gly Gly Ile  
 100 105 110

Leu Leu Glu Glu Leu Ser Lys Ala Asn Pro Tyr Leu Gly Asn Asp Asn  
 115 120 125

Thr Pro Asp Asn Gln Phe His Ile Gly Asp Ala Ser Ala Val Glu Ile  
 130 135 140

Lys Phe Ser Asn Gly Ser Gln Asp Ile Leu Leu Pro Asn Val Ile Ile  
 145 150 155 160

Met Gly Ala Glu Pro Asp Leu Phe Glu Thr Asn Ser Ser Asn Ile Ser  
 165 170 175

Leu Arg Asn Asn Tyr Met Pro Ser Asn His Gly Phe Gly Ser Ile Ala  
 180 185 190

Ile Val Thr Phe Ser Pro Glu Tyr Ser Phe Arg Phe Asn Asp Asn Ser  
 195 200 205

Met Asn Glu Phe Ile Gln Asp Pro Ala Leu Thr Leu Met His Glu Leu  
 210 215 220

Ile His Ser Leu His Gly Leu Tyr Gly Ala Lys Gly Ile Thr Thr Lys  
 Seite 26

225                      230                      235                      240  
 Tyr Thr Ile Thr Gln Lys Gln Asn Pro Leu Ile Thr Asn Ile Arg Gly  
                          245                                      250                                      255  
 Thr Asn Ile Glu Glu Phe Leu Thr Phe Gly Gly Thr Asp Leu Asn Ile  
                          260                                      265                                      270  
 Ile Thr Ser Ala Gln Ser Asn Asp Ile Tyr Thr Asn Leu Leu Ala Asp  
                          275                                      280                                      285  
 Tyr Lys Lys Ile Ala Ser Lys Leu Ser Lys Val Gln Val Ser Asn Pro  
                          290                                      295                                      300  
 Leu Leu Asn Pro Tyr Lys Asp Val Phe Glu Ala Lys Tyr Gly Leu Asp  
                          305                                      310                                      315                                      320  
 Lys Asp Ala Ser Gly Ile Tyr Ser Val Asn Ile Asn Lys Phe Asn Asp  
                          325                                      330                                      335  
 Ile Phe Lys Lys Leu Tyr Ser Phe Thr Glu Phe Asp Leu Ala Thr Lys  
                          340                                      345                                      350  
 Phe Gln Val Lys Cys Arg Gln Thr Tyr Ile Gly Gln Tyr Lys Tyr Phe  
                          355                                      360                                      365  
 Lys Leu Ser Asn Leu Leu Asn Asp Ser Ile Tyr Asn Ile Ser Glu Gly  
                          370                                      375                                      380  
 Tyr Asn Ile Asn Asn Leu Lys Val Asn Phe Arg Gly Gln Asn Ala Asn  
                          385                                      390                                      395                                      400  
 Leu Asn Pro Arg Ile Ile Thr Pro Ile Thr Gly Arg Gly Leu Val Lys  
                          405                                      410                                      415  
 Lys Ile Ile Arg Phe Cys Val Arg Gly Ile Ile Thr Ser Lys Thr Lys  
                          420                                      425                                      430  
 Ser Leu Val Pro Arg Gly Ser Lys Ala Leu Asn Asp Leu Cys Ile Glu  
                          435                                      440                                      445  
 Ile Asn Asn Gly Glu Leu Phe Phe Val Ala Ser Glu Asn Ser Tyr Asn  
                          450                                      455                                      460  
 Asp Asp Asn Ile Asn Thr Pro Lys Glu Ile Asp Asp Thr Val Thr Ser  
                          465                                      470                                      475                                      480  
 Asn Asn Asn Tyr Glu Asn Asp Leu Asp Gln Val Ile Leu Asn Phe Asn  
                          485                                      490                                      495  
 Ser Glu Ser Ala Pro Gly Leu Ser Asp Glu Lys Leu Asn Leu Thr Ile

500

505

510

Gln Asn Asp Ala Tyr Ile Pro Lys Tyr Asp Ser Asn Gly Thr Ser Asp  
515 520 525

Ile Glu Gln His Asp Val Asn Glu Leu Asn Val Phe Phe Tyr Leu Asp  
530 535 540

Ala Gln Lys Val Pro Glu Gly Glu Asn Asn Val Asn Leu Thr Ser Ser  
545 550 555 560

Ile Asp Thr Ala Leu Leu Glu Gln Pro Lys Ile Tyr Thr Phe Phe Ser  
565 570 575

Ser Glu Phe Ile Asn Asn Val Asn Lys Pro Val Gln Ala Ala Leu Phe  
580 585 590

Val Ser Trp Ile Gln Gln Val Leu Val Asp Phe Thr Thr Glu Ala Asn  
595 600 605

Gln Lys Ser Thr Val Asp Lys Ile Ala Asp Ile Ser Ile Val Val Pro  
610 615 620

Tyr Ile Gly Leu Ala Leu Asn Ile Gly Asn Glu Ala Gln Lys Gly Asn  
625 630 635 640

Phe Lys Asp Ala Leu Glu Leu Leu Gly Ala Gly Ile Leu Leu Glu Phe  
645 650 655

Glu Pro Glu Leu Leu Ile Pro Thr Ile Leu Val Phe Thr Ile Lys Ser  
660 665 670

Phe Leu Gly Ser Ser Asp Asn Lys Asn Lys Val Ile Lys Ala Ile Asn  
675 680 685

Asn Ala Leu Lys Glu Arg Asp Glu Lys Trp Lys Glu Val Tyr Ser Phe  
690 695 700

Ile Val Ser Asn Trp Met Thr Lys Ile Asn Thr Gln Phe Asn Lys Arg  
705 710 715 720

Lys Glu Gln Met Tyr Gln Ala Leu Gln Asn Gln Val Asn Ala Ile Lys  
725 730 735

Thr Ile Ile Glu Ser Lys Tyr Asn Ser Tyr Thr Leu Glu Glu Lys Asn  
740 745 750

Glu Leu Thr Asn Lys Tyr Asp Ile Lys Gln Ile Glu Asn Glu Leu Asn  
755 760 765

Gln Lys Val Ser Ile Ala Met Asn Asn Ile Asp Arg Phe Leu Thr Glu

770

Ser Ser Ile Ser Tyr Leu Met Lys Leu Ile Asn Glu Val Lys Ile Asn  
785 790 795 800

Lys Leu Arg Glu Tyr Asp Glu Asn Val Lys Thr Tyr Leu Leu Asn Tyr  
805 810 815

Ile Ile Gln His Gly Ser Ile Leu Gly Glu Ser Gln Gln Glu Leu Asn  
820 825 830

Ser Met Val Thr Asp Thr Leu Asn Asn Ser Ile Pro Phe Lys Leu Ser  
835 840 845

Ser Tyr Thr Asp Asp Lys Ile Leu Ile Ser Tyr Phe Asn Lys Phe Phe  
850 855 860

Lys Arg Ile Lys Ser Ser Ser Val Leu Asn Met Arg Tyr Lys Asn Asp  
865 870 875 880

Lys Tyr Val Asp Thr Ser Gly Tyr Asp Ser Asn Ile Asn Ile Asn Gly  
885 890 895

Asp Val Tyr Lys Tyr Pro Thr Asn Lys Asn Gln Phe Gly Ile Tyr Asn  
900 905 910

Asp Lys Leu Ser Glu Val Asn Ile Ser Gln Asn Asp Tyr Ile Ile Tyr  
915 920 925

Asp Asn Lys Tyr Lys Asn Phe Ser Ile Ser Phe Trp Val Arg Ile Pro  
930 935 940

Asn Tyr Asp Asn Lys Ile Val Asn Val Asn Asn Glu Tyr Thr Ile Ile  
945 950 955 960

Asn Cys Met Arg Asp Asn Asn Ser Gly Trp Lys Val Ser Leu Asn His  
965 970 975

Asn Glu Ile Ile Trp Thr Leu Gln Asp Asn Ala Gly Ile Asn Gln Lys  
980 985 990

Leu Ala Phe Asn Tyr Gly Asn Ala Asn Gly Ile Ser Asp Tyr Ile Asn  
995 1000 1005

Lys Trp Ile Phe Val Thr Ile Thr Asn Asp Arg Leu Gly Asp Ser  
1010 1015 1020

Lys Leu Tyr Ile Asn Gly Asn Leu Ile Asp Gln Lys Ser Ile Leu  
1025 1030 1035

Asn Leu Gly Asn Ile His Val Ser Asp Asn Ile Leu Phe Lys Ile  
Seite 29

1040

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Ser	Asn	Glu	Pro	Asn	Thr	Asn	Ile	Leu	Lys	Asp	Phe	Trp	Gly	Asn
	1085					1090					1095			
Tyr	Leu	Leu	Tyr	Asp	Lys	Glu	Tyr	Tyr	Leu	Leu	Asn	Val	Leu	Lys
	1100					1105					1110			
Pro	Asn	Asn	Phe	Ile	Asp	Arg	Arg	Lys	Asp	Ser	Thr	Leu	Ser	Ile
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	1160					1165					1170			
Ala	Ser	Lys	Thr	His	Leu	Phe	Pro	Leu	Tyr	Ala	Asp	Thr	Ala	Thr
	1175					1180					1185			
Thr	Asn	Lys	Glu	Lys	Thr	Ile	Lys	Ile	Ser	Ser	Ser	Gly	Asn	Arg
	1190					1195					1200			
Phe	Asn	Gln	Val	Val	Val	Met	Asn	Ser	Val	Gly	Asn	Asn	Cys	Thr
	1205					1210					1215			
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	1220					1225					1230			
Phe	Lys	Ala	Asp	Thr	Val	Val	Ala	Ser	Thr	Trp	Tyr	Tyr	Thr	His
	1235					1240					1245			
Met	Arg	Asp	His	Thr	Asn	Ser	Asn	Gly	Cys	Phe	Trp	Asn	Phe	Ile
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Ser	Glu	Glu	His	Gly	Trp	Gln	Glu	Lys						
	1265					1270								

<210> 7  
<211> 3855  
<212> DNA  
<213> Artificial sequence

&lt;220&gt;

&lt;223&gt; DNA encoding clostridial neurotoxin precursor

&lt;400&gt; 7

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&lt;211&gt; 3861

&lt;212&gt; DNA

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; DNA encoding clostridial neurotoxin precursor 2

&lt;400&gt; 8

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3861

&lt;210&gt; 9

&lt;211&gt; 3873

&lt;212&gt; DNA

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; DNA encoding clostridial neurotoxin precursor 3

&lt;400&gt; 9

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