

(19) 日本国特許庁(JP)

(12) 公表特許公報(A)

(11) 特許出願公表番号

特表2005-537809

(P2005-537809A)

(43) 公表日 平成17年12月15日(2005. 12. 15)

(51) Int. Cl.⁷

C 1 2 N 15/09

A 6 1 K 39/00

A 6 1 K 39/08

A 6 1 P 31/04

C 1 2 N 9/52

F I

C 1 2 N 15/00

A 6 1 K 39/00

A 6 1 K 39/08

A 6 1 P 31/04

C 1 2 N 9/52

テーマコード (参考)

4 B O 2 4

4 B O 5 O

4 C O 8 5

審査請求 未請求 予備審査請求 未請求 (全 548 頁) 最終頁に続く

(21) 出願番号 特願2004-535633 (P2004-535633)
 (86) (22) 出願日 平成15年9月12日 (2003. 9. 12)
 (85) 翻訳文提出日 平成17年4月14日 (2005. 4. 14)
 (86) 国際出願番号 PCT/GB2003/003824
 (87) 国際公開番号 W02004/024909
 (87) 国際公開日 平成16年3月25日 (2004. 3. 25)
 (31) 優先権主張番号 10/241, 596
 (32) 優先日 平成14年9月12日 (2002. 9. 12)
 (33) 優先権主張国 米国 (US)

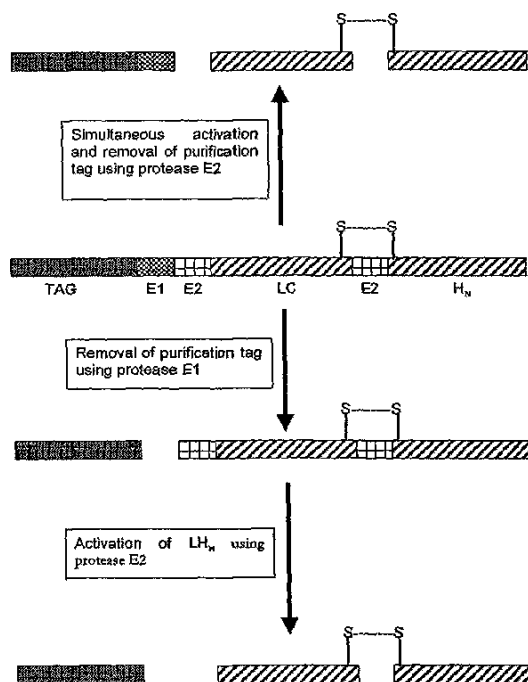
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(54) 【発明の名称】 組換え毒素フラグメント

(57) 【要約】

第1および第2ドメインを含む一本鎖ポリペプチドが提供される。第1ドメインは、このポリペプチドが、エキソサイトーシスに必須の1以上の小胞または形質膜結合タンパク質を切断することを可能にし、そして第2ドメインは、このポリペプチドが、標的細胞にトランスロケートされることを可能にするかまたはこのポリペプチドの溶解性を増加させるか、またはその両方である。したがって、このポリペプチドは、天然分子に関連する毒性なしに、ボツリヌス菌または破傷風菌毒素のようなクロストリジウム菌毒素の有用な特性を組み合わせる。このポリペプチドはまた、特異的細胞にターゲティングする第3ドメインを含み得、このポリペプチドは、標的細胞におけるエキソサイトーシスの阻害に有用になる。このポリペプチドを含む融合タンパク質、このポリペプチドをコードする核酸、およびこのポリペプチドの製造方法も提供される。ポリペプチドの制御された活性化が可能であり、そしてこのポリペプチドは、ワクチンおよび毒素アッセイに組み込まれ得る。



【特許請求の範囲】

【請求項 1】

第 1 および第 2 ドメインを含む一本鎖ポリペプチドであって：

該第 1 ドメインが、クロストリジウム菌神経毒素軽鎖またはそのフラグメントもしくは改変体であり、該第 1 ドメインが、エキソサイトーシスに必須の 1 以上の小胞または形質膜結合タンパク質を切断することが可能であり；そして

該第 2 ドメインが、クロストリジウム菌神経毒素重鎖 H_N 部分またはそのフラグメントもしくは改変体であり、該第 2 ドメインが、(i) 該ポリペプチドを細胞にトランスロケートし、または (ii) 該第 1 ドメイン自体の溶解性と比較して該ポリペプチドの溶解性を増加させ、または (iii) 該ポリペプチドを細胞にトランスロケートしそして該第 1 ドメイン自体の溶解性と比較して該ポリペプチドの溶解性を増加させる両方が可能であり；そして該第 2 ドメインが、 H_C と命名されたクロストリジウム菌神経毒素重鎖の機能的 C 末端部分を欠き、それによって該ポリペプチドが、天然のクロストリジウム菌神経毒素が結合する天然の細胞表面レセプターである細胞表面レセプターに結合できなくなり；そして該一本鎖ポリペプチドが、以下からなる群より選択される配列を含む、ポリペプチド：

(I) 配列番号 30、32、34、36、38、40、42、44、46、48、50、52、54、56、58、60、62、64、66、68、70、72、74、76、78、80、82、84、86、88、90、92、94、96、98、100、102、104、106、108、110、112、114、116、118、120、122、124、126、128、130、132、139、143、145、147、149、151、153、155、157、159、161、163、165、167、169、171、173、および 175；または

(II) エキソサイトーシスに必須の 1 以上の小胞または形質膜結合タンパク質を切断し得る第 1 ドメインを有する (I) のフラグメントまたは改変体。

【請求項 2】

前記クロストリジウム菌毒素重鎖が、ボツリヌス菌神経毒素重鎖である、請求項 1 に記載のポリペプチド。

【請求項 3】

前記クロストリジウム菌毒素重鎖が、破傷風菌神経毒素重鎖である、請求項 1 に記載のポリペプチド。

【請求項 4】

前記第 1 ドメインが、SNAP-25、シナプトブレビン/VAMP、およびシンタキシンの 1 以上から選択される基質に特異的なエンドペプチダーゼ活性を示す、請求項 1 から 3 のいずれかに記載のポリペプチド。

【請求項 5】

前記第 2 ドメインが、クロストリジウム菌毒素重鎖 H_N 部分である、請求項 1 から 4 のいずれかに記載のポリペプチド。

【請求項 6】

前記クロストリジウム菌神経毒素重鎖が、ボツリヌス菌神経毒素 A 型鎖である、請求項 1 に記載のポリペプチド。

【請求項 7】

前記第 2 ドメインが、ボツリヌス菌毒素 A 型重鎖の 423 個の N 末端アミノ酸を含む、請求項 1 に記載のポリペプチド。

【請求項 8】

前記クロストリジウム菌神経毒素重鎖が、ボツリヌス菌神経毒素 B 型鎖である、請求項 1 に記載のポリペプチド。

【請求項 9】

前記第 2 ドメインが、ボツリヌス菌毒素 B 型重鎖の 107 個の N 末端アミノ酸を含む、請求項 1 に記載のポリペプチド。

【請求項 10】

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前記第2ドメインが、ボツリヌス菌毒素B型重鎖の417個のN末端アミノ酸を含む、請求項1に記載のポリペプチド。

【請求項11】

前記第2ドメインが、破傷風菌重鎖の422個のN末端アミノ酸を含む、請求項1に記載のポリペプチド。

【請求項12】

前記第2ドメインが、クロストリジウム菌神経毒素重鎖の100個のN末端アミノ酸を含む、請求項1に記載のポリペプチド。

【請求項13】

タンパク質分解酵素によって切断される部位を含む、請求項1に記載のポリペプチド。 10

【請求項14】

前記切断部位が、天然のクロストリジウム菌神経毒素に存在しない、請求項13に記載のポリペプチド。

【請求項15】

前記切断部位が、前記第1および第2ドメインのタンパク質分解切断を可能にする、請求項13または14に記載のポリペプチド。

【請求項16】

前記切断部位が、前記第1および第2ドメインのタンパク質分解切断を可能にし、そしてそのように切断される場合、該第1ドメインが、該タンパク質分解切断前の前記ポリペプチドが示す1以上の小胞または形質膜結合タンパク質を切断する酵素活性よりも大きい酵素活性を示す、請求項13から15のいずれかに記載のポリペプチド。 20

【請求項17】

請求項1に記載のペプチドをコードする第2の核酸配列内に、前記切断部位をコードする第1の核酸配列を提供することによって得られ得る、請求項13から16のいずれかに記載のポリペプチド。

【請求項18】

前記第2ドメインが、H_Cと命名されたクロストリジウム菌神経毒素重鎖のC末端部分を欠く、請求項1から17のいずれかに記載のポリペプチド。

【請求項19】

前記ポリペプチドを細胞に結合する第3ドメインをさらに含む、請求項1から18のいずれかに記載のポリペプチドであって、該結合が、第3ドメインの細胞への直接的な結合によって、あるいは細胞に結合する1または複数のリガンドへの第3ドメインの結合によって行われる、ポリペプチド。 30

【請求項20】

前記第3ドメインが、前記ポリペプチドを免疫グロブリンに結合するためのものである、請求項19に記載のポリペプチド。

【請求項21】

前記第3ドメインが、ブドウ球菌のプロテインAのドメインbに由来するタンデムリピート合成IgG結合ドメインである、請求項20に記載のポリペプチド。

【請求項22】

前記第3ドメインが、細胞表面レセプターに結合するアミノ酸配列を含む、請求項19に記載のポリペプチド。 40

【請求項23】

前記第3ドメインが、インスリン様増殖因子1 (IGF-1) である、請求項22に記載のポリペプチド。

【請求項24】

前記第1ドメインと前記第2ドメインとの間にスペーサー分子を含む、請求項1から23のいずれかに記載のポリペプチド。

【請求項25】

前記第2ドメインと前記第3ドメインとの間にスペーサー分子を含む、請求項19から 50

2 3 のいずれかに記載のポリペプチド。

【請求項 2 6】

アフィニティーマトリクスに結合する精製タグをさらに含み、それによって該マトリクスを用いる前記ポリペプチドの精製を容易にする、請求項 1 から 2 5 のいずれかに記載のポリペプチド。

【請求項 2 7】

前記精製タグと前記ポリペプチドとの間にスペーサー分子を含む、請求項 2 6 に記載のポリペプチド。

【請求項 2 8】

前記精製タグが、グルタチオンセファロースのアフィニティーマトリクスに結合する、請求項 2 6 または 2 7 に記載のポリペプチド。 10

【請求項 2 9】

第 1 のプロテアーゼ切断部位が、請求項 1 から 2 3 のいずれかに記載のポリペプチドと前記精製タグとの間に組み込まれ、該プロテアーゼ切断部位が、該精製タグからの該ポリペプチドのタンパク質分解分離を可能にする、請求項 2 6 から 2 8 のいずれかに記載のポリペプチド。

【請求項 3 0】

第 2 のプロテアーゼ切断部位が、請求項 1 から 2 3 のいずれかに記載のポリペプチドの前記第 1 ドメインと前記第 2 ドメインとの間に組み込まれ、該プロテアーゼ切断部位が、該第 1 ドメインと該第 2 ドメインとのタンパク質分解切断を可能にする、請求項 2 6 から 2 9 のいずれかに記載のポリペプチド。 20

【請求項 3 1】

請求項 1 から 3 0 のいずれかに記載のポリペプチドをコードする、核酸。

【請求項 3 2】

前記核酸が、クロストリジウム菌神経毒素の H_C と命名された部分をコードするヌクレオチドを欠く、請求項 3 1 に記載の核酸。

【請求項 3 3】

ボツリヌス菌毒素 A 型重鎖 H_N ドメインの残基 1 から 4 2 3 をコードするヌクレオチドを含む、請求項 3 1 または 3 2 に記載の核酸。

【請求項 3 4】

ボツリヌス菌毒素 B 型重鎖 H_N ドメインの残基 1 から 4 1 7 をコードするヌクレオチドを含む、請求項 3 1 または 3 2 に記載の核酸。 30

【請求項 3 5】

タンパク質分解切断部位をコードするヌクレオチドを含む、請求項 3 1 から 3 4 のいずれかに記載の核酸。

【請求項 3 6】

前記タンパク質分解切断部位が、天然のクロストリジウム菌神経毒素に存在しない、請求項 3 5 に記載の核酸。

【請求項 3 7】

前記タンパク質分解切断部位が、前記ポリペプチドの前記第 1 ドメインと前記第 2 ドメインとの間に位置する、請求項 3 6 に記載の核酸。 40

【請求項 3 8】

請求項 2 9 に記載の核酸配列内に前記切断部位をコードする核酸配列を提供することによって得られ得る、請求項 3 6 または 3 7 に記載の核酸。

【請求項 3 9】

配列番号 6 9、7 1、7 3、7 5、7 7、1 1 3、1 3 4、またはそれらのフラグメントもしくは改変体からなる群より選択される、核酸配列。

【請求項 4 0】

配列番号 7 0、7 2、7 4、7 6、7 8、1 1 4、またはそれらのフラグメントもしくは改変体からなる群より選択される、一本鎖ポリペプチド。 50

【発明の詳細な説明】

【技術分野】

【0001】

本発明は、組換え毒素フラグメント、これらのフラグメントをコードするDNA、ならびにワクチンにおけるおよびインビトロおよびインビボ目的でのそれらの使用に関する。

【背景技術】

【0002】

クロストリジウム菌神経毒素は、神経細胞におけるカルシウム依存的神経伝達物質分泌の強力なインヒビターである。これらは、現在、神経伝達物質分泌の小胞ドッキングおよび膜融合事象の中心にある、VAMP、シンタキシン、またはSNAP-25の3つの小胞または前シナプス膜結合タンパク質うちの少なくとも1つの特異的なタンパク質内分解切断によってこの活性を媒介すると考えられている。破傷風菌神経毒素およびボツリヌス菌神経毒素の神経細胞ターゲティングは、レセプター媒介事象であると考えられ、その後、毒素は、インターナライズされ、そして続いて適切な細胞内コンパートメントに移り、そこでエンドペプチダーゼ活性を発揮する。

【0003】

クロストリジウム菌神経毒素は、レセプター結合およびトランスロケーションH鎖（HC、約100kDa）にジスルフィド結合した触媒L鎖（LC、約50kDa）の共通の構成物を有する。HCポリペプチドは、2つの異なる機能的ドメインのすべてまたは一部を含むと考えられる。HCドメインと命名したHCのカルボキシ末端半分（約50kDa）は、標的ニューロンにおける細胞表面レセプターへの神経毒素の高親和性の神経特異的結合に関連し、一方、HNドメインと命名したアミノ末端半分（約50kDa）は、神経毒素の少なくともいくつかの部分の細胞膜を横切るトランスロケーションを媒介すると考えられ、そのためLCの機能的活性が標的細胞内で発現される。HNドメインはまた、低pH条件下で、脂質膜においてイオン透過性チャンネルを形成する特性を有し、そしてこれは、いくつかの様式で、そのトランスロケーション機能に関連し得る。

【0004】

ボツリヌス菌神経毒素A型（BoNT/A）については、HCについてはアミノ酸残基872～1296、HNについてはアミノ酸残基449～871、およびLCについては残基1～448内に、これらのドメインがあると考えられる。トリプシンでの消化は、BoNT/AのHCドメインを効果的に分解して、LHNと命名された非毒性フラグメントを生成し、これはもはやニューロンに結合および侵入し得ない（図1）。このように生成されたLHNフラグメントもまた、親のホロ毒素および単離されたLCの両方と比較して増強された溶解性の特性を有する。

【0005】

したがって、神経毒素分子内のドメインの機能的定義を、以下のように提供することができる：

（A）クロストリジウム菌神経毒素軽鎖：

エキソサイトーシス過程に関連する小胞および／または形質膜結合タンパク質に高い基質特異性を示す、メタロプロテアーゼ。特に、これは、SNAP-25、VAMP（シナプトブレビン／セルブレビン）、およびシンタキシンの1つ以上を切断する。

【0006】

（B）クロストリジウム菌神経毒素重鎖HNドメイン：

重鎖の一部であって、これは、軽鎖活性の機能的発現が標的細胞内で起きるように、神経毒素分子のこの一部のトランスロケーションを可能にする。

【0007】

結合ドメインを介して神経毒素がその特異的細胞表面レセプターへ結合した後、標的細胞へのエンドペプチダーゼ活性のトランスロケーションの原因となるドメイン。

【0008】

低pH条件下で脂質膜においてイオン透過性孔の形成の原因となるドメイン。

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【0009】

軽鎖単独の溶解性と比較して、ポリペプチド全体の溶解性を増加させる原因となるドメイン。

【0010】

(C) クロストリジウム菌神経毒素重鎖H_Cドメイン：

細胞への毒素のインターナリゼーションの前の、クロストリジウム菌毒素の中毒作用に関連する細胞表面レセプターへの天然のホロ毒素の結合の原因である重鎖の一部。

【0011】

これらの毒素に対する細胞認識マーカーの同一性は、現在理解されておらず、そして特異的レセプター種は未だ同定されていないが、Kozakiらは、シナプトタグミンがボツリヌス菌神経毒素B型に対するレセプターであり得ることを報告している。神経毒素のそれぞれが異なるレセプターを有するようである。 10

【発明の開示】

【発明が解決しようとする課題】

【0012】

毒素アッセイのための陽性コントロールを有すること、クロストリジウム菌毒素ワクチンを開発すること、およびクロストリジウム菌毒素の所望の特性を組み込む治療剤を開発することが所望される。

【0013】

しかし、その極端な毒性のため、天然の毒素の取り扱いには危険である。 20

【0014】

本発明は、クロストリジウム菌毒素の生成および取り扱いに関連する問題を克服または少なくとも改善するために探求される。

【発明を実施するための最良の形態】

【0015】

したがって、本発明は、第1および第2ドメインを含むポリペプチドを提供し、該第1ドメインは、神経エキソサイトーシスに必須の1以上の小胞または形質膜結合タンパク質を切断するように適合され、そして該第2ドメインは、(i) 該ポリペプチドを細胞にトランスロケートするように、または(ii) 該第1ドメイン自体の溶解性と比較して該ポリペプチドの溶解性を増加させるように、または(iii) 該ポリペプチドを細胞にトランスロケートしそして該第1ドメイン自体の溶解性と比較して該ポリペプチドの溶解性を増加させる両方に適合され、該ポリペプチドは、クロストリジウム菌神経毒素を含まず、そしてタンパク質分解作用によって毒素に変換され得るあらゆるクロストリジウム菌神経毒素前駆体を含まない。したがって、本発明は、クロストリジウム菌毒素軽鎖に等価なドメインおよびクロストリジウム菌毒素重鎖のH_Nの機能的局面を提供するドメインを含むが、クロストリジウム菌毒素H_Cドメインの機能的局面を欠く、一本鎖ポリペプチドを提供し得る。 30

【0016】

好適な実施態様では、本発明は、第1および第2ドメインを含む一本鎖ポリペプチドを提供し、 40

該第1ドメインは、クロストリジウム菌神経毒素軽鎖またはそのフラグメントもしくは改変体であり、ここで該第1ドメインは、エキソサイトーシスに必須の1以上の小胞または形質膜結合タンパク質を切断し得；そして

該第2ドメインは、クロストリジウム菌神経毒素重鎖H_N部分またはそのフラグメントもしくは改変体であり、ここで該第2ドメインは、(i) 該ポリペプチドを細胞にトランスロケートし、または(ii) 該第1ドメイン自体の溶解性と比較して該ポリペプチドの溶解性を増加させ、または(iii) 該ポリペプチドを細胞にトランスロケートしそして該第1ドメイン自体の溶解性と比較して該ポリペプチドの溶解性を増加させる両方が可能であり；そして該第2ドメインは、H_Cと命名されたクロストリジウム菌神経毒素重鎖の機能的C末端部分を欠き、それによって該ポリペプチドが、天然のクロストリジウム菌神経毒 50

素が結合する天然の細胞表面レセプターである細胞表面レセプターに結合できなくなる。

【0017】

上記の好適な実施態様では、第1ドメインは、特定の切断機能の存在の必要条件によって認定される。この切断機能は、軽鎖（L鎖）成分が一本鎖ポリペプチド分子自体の一部である場合に存在し得る。あるいは、切断機能は、一本鎖ポリペプチド分子に実質的に潜在し得、そして第1ドメインと第2ドメインとの間の一本鎖ポリペプチドのタンパク質分解切断によって活性化されて、例えば、一緒にジスルフィド結合した第1および第2ドメインを含む二本鎖ポリペプチド分子を形成し得る。

【0018】

第1ドメインは、クロストリジウム菌神経毒素軽鎖（L鎖）に基づき、そしてこれらの成分が必要な切断機能を有する限り、該L鎖のフラグメントおよび改変体の両方を包含する。改変体の例は、1以上のアミノ酸残基が天然のクロストリジウム菌L鎖配列に関して変更されているL鎖（またはそのフラグメント）である。1つの実施態様では、改変は、1以上の保存的アミノ酸置換を包含し得る。他の改変は、天然のクロストリジウム菌L鎖配列に関して1以上のアミノ酸残基の除去または付加を包含し得る。しかし、あらゆるこのようなフラグメントまたは改変体は、前述の切断機能を保持しなければならない。

【0019】

クロストリジウム菌神経毒素の構造は、本発明の前に周知である—例えば、Kurazonoら(1992) J. Biol. Chem., 267, 21, 14721-14729頁を参照のこと。特に、Kurazonoの文献は、クロストリジウム菌神経毒素L鎖の切断活性（例えば、タンパク質分解酵素活性）に必要とされる最小ドメインを記載している。同様の議論は、Poulainら(1989) Eur. J. Biochem., 185, 197-203頁、Zhouら(1995), 34, 15175-15181頁、およびBlausteinら(1987), 226, 1号, 115-120頁により提供されている。

【0020】

例として、Kurazonoら(1992)の14726頁の表IIは、多くのL鎖欠失変異体を例示している（アミノ末端およびカルボキシ末端の両方のL鎖欠失変異体が例示されている）。問題のL鎖成分が必要な切断活性を有するならば、このような変異体は、例えば、類似アミノ酸欠失または保存的アミノ酸置換を含む他のL鎖変異体とともに、本発明の第1ドメインの定義に包含される。

【0021】

本出願の前に、多くの従来の簡単なアッセイが利用可能であり、所定のL鎖（または等価のL鎖成分）が必要な切断活性を有するかどうかを、当業者が日常的に確認できた。これらのアッセイは、機能的L鎖が、神経エキソサイトーシスに関連する特異的な小胞または形質膜結合タンパク質（例えば、シナプロブレピン、シンタキシン、SNAP-25）のペプチド切断を行う本来の能力に基づき、そしてこのタンパク質分解反応の切断された産物の存在についての簡単なテストである。

【0022】

例えば、間に合わせのアッセイでは、SNAP-25（またはシナプトブレピン、またはシンタキシン）は、テストするL鎖（または等価のL鎖成分）とともにチャレンジされ、次いでSDS-PAGEペプチド分離技法によって分析され得る。SNAP-25（または神経分泌機構の他の成分）の切断された産物に対応する分子量を有するペプチドの（例えば、銀染色による）その後の検出は、必要な切断活性を有するL鎖（または等価のL鎖成分）の存在を示す。

【0023】

代替のアッセイでは、SNAP-25（または異なる神経エキソサイトーシス分子）は、テストするL鎖（または等価のL鎖成分）とともにチャレンジされ、そして切断産物は、本願の出願人であるMicrobiological Research Authorityの名義でPCT/GB95/01279（すなわち、W095/33850）に記載されるように、抗体検出に供される。より詳細には、SNAP-25の切断を検出するための特異的抗体が用いられ、この抗体は、切断されたSNAP-25を認識するが切断されていないSNAP-25を認識しない。抗体によって切断された産物の同定は、必要

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な切断活性を有するL鎖（または等価のL鎖成分）の存在を確認する。例として、このような方法は、これもまたMicrobiological Research Authorityの名義のPCT/GB96/00916（すなわち、W096/33273）の実施例2および3に記載されている。

【0024】

本発明の好適な実施態様では、第2ドメインは、2つの機能、すなわち（i）トランスロケーションおよび／または（ii）第1ドメインの増加した溶解性、の1つまたは両方を提供する能力によって認定される。

【0025】

第2ドメインは、クロストリジウム菌神経毒素のH_N部分に基づき、この部分は、文献に広く記載されそして特徴付けられている。特定の記載がKurazonoら(1992)になされており、そこでは、クロストリジウム菌神経毒素重鎖の構造が、そのH_NおよびH_C部分と関連する機能とともに議論されている〔例えば、Kurazonoら(1992)の14722頁の図1の下
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の図を参照のこと〕。より詳細には、H_Nドメインは、小胞のエンドソーム膜を横切ってクロストリジウム菌L鎖をトランスロケートするように機能するクロストリジウム菌神経毒素のドメインであり、そしてクロストリジウム菌神経毒素のH₂ドメインと同義である〔Poulain, B.ら(1989)の197頁の左下欄および脚部；Blaustein, R.ら(1987)の図1；およびShone, C.ら(1987), Eur. J. Biochem., 167, 175-180頁の178～179頁にまたがる文を参照のこと〕。

【0026】

本発明の第2ドメインの定義は、これらの成分が必要な（i）トランスロケーションおよび／または（ii）改善された溶解性機能を提供する限り、クロストリジウム菌神経毒素のH_N部分のフラグメントおよび改変体を包含する。改変体の例は、1以上のアミノ酸残基が天然のクロストリジウム菌H_Nドメイン配列に関して変更されているH_N部分（またはそのフラグメント）である。1つの実施態様では、改変は、1以上の保存的アミノ酸置換を包含し得る。他の改変は、天然のクロストリジウム菌H_N配列に関する1以上のアミノ酸残基の除去または付加を包含し得る。しかし、あらゆるこのようなフラグメントまたは改変体は、上述の（i）トランスロケーションおよび／または（ii）改善された溶解性機能を提供しなければならない。
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【0027】

（i）トランスロケーションおよび（ii）改善された溶解性機能を、ここでより詳細に説明する。
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【0028】

本出願の前に、多くの従来の簡単なアッセイが利用可能であり、特定のクロストリジウム菌神経毒素H_N部分（または等価のH_N成分）が必要なトランスロケーション機能を有するかどうかを、当業者が日常的に確認できた。これに関して、Shoneら(1987)およびBlausteinら(1987)に記載されるアッセイに対して特定の記載がなされており、ここで議論する。

【0029】

これらの文献は、クロストリジウム菌神経毒素のトランスロケーション機能の研究を記載し、そしてこの神経毒素がチャネルを形成する能力が、トランスロケーション機能の存在に関連することを証明している。
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【0030】

Shoneら(1987)は、リン酸カリウム緩衝液（pH7.2）および放射標識したNADを充填した人工リボソームを用いるアッセイを記載している。したがって、クロストリジウム菌神経毒素のテストするH_N部分（または等価のH鎖成分）が必要なトランスロケーション機能を有するかどうかを確認するために、人工リボソームは、テストするH_N部分とともにチャレンジされる。リボソームからのK⁺およびNADの放出は、チャネル形成活性、したがって、トランスロケーション機能の存在の指標である。

【0031】

代替のアッセイが、Blausteinら(1987)に記載されており、ここでは、平面のリン脂質
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二層膜を用いてチャネル形成活性についてテストされている。膜のいずれかの側の塩溶液は、シス側はpH4.7または5.5およびトランス側はpH7.4の異なるpHに緩衝化されている。したがって、クロストリジウム菌神経毒素のH_N部分（または等価のH鎖成分）が必要なトランスロケーション機能を有するかどうかを確認するために、テストするH_N部分は、膜のシス側に添加されて、膜を横切る電流をモニターするために、電位固定条件下で電気測定が行われる（116～118頁の2.2段落を参照のこと）。所望のトランスロケーション活性の存在は、チャネルターンオンの定常速度によって確認される（118頁の3段落を参照のこと）。

【0032】

ここで第2の重鎖機能、すなわち(ii)第1ドメインの増加した溶解性に話を変える。クロストリジウム菌神経毒素L鎖分子の調製に関連する従来の問題は、このL鎖分子が、一般的に溶解性に乏しい特徴を有することである。したがって、本発明の1つの実施態様では、第2ドメイン（クロストリジウム菌神経毒素のH_N部分に基づく）のL鎖への融合は、L鎖の溶解性を増加させる。同様に、第2ドメインのL鎖等価分子（例えば、L鎖のフラグメントまたは改変体）への付加は、L鎖等価分子の溶解性を増加させる。

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【0033】

本出願の前に、多くの従来の簡単なアッセイが利用可能であり、特定のクロストリジウム菌神経毒素H_N部分（または等価のH_N成分）がL鎖（または等価のL鎖成分）の溶解性を増加させるために必要な能力を有するかどうかを、当業者が日常的に確認できた。溶解性を評価するための最も普通の方法は、遠心分離の使用、次いで一連のタンパク質決定方法による。例えば、発現したクロストリジウム菌エンドペプチダーゼを含む溶解した大腸菌細胞を、25,000×gで15分間遠心分離して細胞破砕物をペレットにし、そしてタンパク質材料を凝集させる。上清（可溶性タンパク質を含む）の除去後、細胞破砕物は、（乏しい溶解性のタンパク質を可溶化するために）SDS含有試料緩衝液中で再構成されて、SDS-PAGEによって2つの画分が分析され得る。電気泳動したタンパク質のクーマシーブルー染色、次いで関連のタンパク質バンドのデンストメトリー分析は、発現したタンパク質の溶解性の半定量分析を容易にする。

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【0034】

本発明の好適な実施態様によれば、一本鎖ポリペプチド分子のさらなる必要条件是、第2ドメインがH_Cと命名されたクロストリジウム菌神経毒素重鎖の機能的C末端部分を欠くことであり、それによって、このポリペプチドが、天然のクロストリジウム菌神経毒素が結合する天然の細胞表面レセプターである細胞表面レセプターに結合できなくなる。この必要条件是、ここでより詳細に議論され、そして本明細書を通して結合できないというときは、天然のクロストリジウム菌神経毒素と比較した場合に、実質的に結合できないまたは結合能力が減少していると解釈されるべきである。

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【0035】

例えば、上記の文献およびその他には、天然のクロストリジウム菌神経毒素が、毒素重鎖のH_Cドメインおよび標的細胞上の特異的レセプターに関連する結合相互作用によって、特異的標的細胞に結合することが十分に論じられている。

【0036】

しかし、天然の神経毒素とは逆に、本発明の好適な実施態様の一本鎖ポリペプチド分子は、天然のクロストリジウム菌神経毒素の機能的H_Cドメインを欠く。したがって、本発明の好適な一本鎖ポリペプチド分子は、天然のクロストリジウム菌神経毒素によってターゲットされる特異的レセプターに結合できない。

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【0037】

本出願の前に、多くの従来の簡単なアッセイが利用可能であり、特定のクロストリジウム菌神経毒素H_N部分（または等価のH_N成分）が天然のクロストリジウム菌神経毒素の結合能力を欠くかどうかを、当業者が日常的に確認できた。これに関して、Shoneら(1985) Eur. J. Biochem., 151(1), 75-82頁、ならびにBlackおよびDolly(1986) J. Cell. Biol., 103, 521-534頁に記載されるアッセイに対して特定の記載がなされている。基本的な

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Shoneら(1985)の方法は、破傷風菌毒素の結合能力を評価するために、近年、Suttonら(2001), 493, 45-49頁に報告されている。

【0038】

これらの文献は、クロストリジウム菌神経毒素のH鎖のその標的細胞である運動ニューロンへの結合を評価するための簡単な方法を記載している。したがって、これらの方法は、H鎖に対する改変により運動ニューロンに対するH鎖の天然の結合親和性がなくなるかまたは減少するかどうかを日常的に決定するための手段を提供する。この方法は、ここでもより詳細に議論される。

【0039】

Shoneら(1985)の方法は、競合結合アッセイに基づき、そこでは、テストする神経毒素H鎖フラグメントが、精製ラット大脳皮質シナプトソーム（すなわち、天然の毒素標的細胞）に結合する能力において、放射標識した天然の神経毒素と比較される。H_C機能（すなわち、結合能力）の減少は、テストするH鎖フラグメントが、シナプトソームへの結合に対して、標識された未処理の毒素と競合する能力が減少することによって証明される（76頁1欄51行目～2欄5行目を参照のこと）。

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【0040】

Suttonら(2001)は、放射標識した未処理の破傷風菌神経毒素（TeNT）および非標識の部位特異的（TeNT）変異体を用いる類似の競合結合実験を行った。上記のように、アッセイにおける陽性の結果は、変異体フラグメントが、シナプトソームへの結合に対して、標識されたTeNTと競合する能力がないことによって証明される。

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【0041】

代替のアプローチは、BlackおよびDolly(1986)によって記載され、この方法は、電子顕微鏡オートラジオグラフィーを用いて、インビボおよびインビトロの両方で、脊椎動物神経筋接合部での放射標識されたクロストリジウム菌神経毒素の結合を可視的に評価する。したがって、このアッセイは、テストするH_Nドメイン（または等価のH_N成分）が機能的H_Cドメインを欠くかどうかを確認するための簡単な可視方法を示す。

【0042】

機能的H_Cドメインを欠く第2ドメインが調製され得る多くの方法がある。これに関して、H_Cドメインの不活性化は、アミノ酸レベルで（例えば、誘導体化用化学品、またはタンパク質分解酵素の使用によって）、または核酸レベルで（例えば、部位特異的変異誘発、ヌクレオチド挿入または欠失または改変の使用によって、あるいは短縮型核酸の使用によって）達成され得る。

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【0043】

例えば、H_Cドメインの除去または改変に適切な従来の誘導体化用化学品またはタンパク質分解剤を選択することは、当業者には日常的である。標準的な誘導体化用化学品またはタンパク質分解剤は当該技術分野で容易に利用可能であり、そしてこの化学／薬剤が、上記のような多くの簡単なテストのいずれか1つを行うことによって、天然の結合親和性が減少または除去されたH_Nドメインを提供することを確認することは、当業者には日常的である。

【0044】

従来の誘導体化用化学品としては、以下のいずれか1つが挙げられ得、これは、非網羅的な例のリストを形成する：

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（1）無水物、より詳細にはマレイン酸無水物のような、チロシン誘導体化用化学品；

（2）ビス-ジアゾ化o-トリジン、およびジアゾ化p-アミノベンゾイルビオシチンのような、ジアゾニウムに基づく誘導体化用化学品；

（3）EDC（1-エチル1-3-(3-ジメチルアミノプロピル)カルボジイミド塩酸）；

（4）テトラニトロメタン続いて亜ジチオン酸ナトリウムでの二重の処理のような、イソシアネートに基づく誘導体化用化学品；および

（5）クロラミン-T（N-クロロトルエンスルホンアミド）またはIOD0-GEN（1,3,4,6-テトラクロロ-3a,ba-ジフェニルグリコウリル）のような、ヨウ素化誘導体化用化学品。

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【0045】

従来のタンパク質分解剤としては、以下のいずれか1つが挙げられ得、これは、非網羅的な例のリストを形成する：

- (1) トリプシン [Shoneら(1985)に示される]；
- (2) プロリンエンドペプチダーゼ；
- (3) lysCプロテイナーゼ；
- (4) キモトリプシン；
- (5) サーモリシン；および
- (6) argCプロテイナーゼ。

【0046】

あるいは、従来の核酸変異誘発方法が用いられて、機能的H_Cドメインを欠く第2ドメインをコードする改変された核酸配列を生成し得る。例えば、Kurazonoら(1992)に記載されるような変異誘発方法が用いられ得る。DNAの変異誘発のための一連のシステムが利用可能であり、これは、Kunkel T.(1985) Proc. Natl. Acad. Sci. USA, 82, 488-492頁；Taylor, J. W.ら(1985) Nucleic Acids Res. 13, 8749-8764頁 (1995)；ならびに、Deng G.およびNickeloff J. A.(1992) Anal. Biochem., 200, 81-88頁に記載のDNA操作技法に基づく。

【0047】

本発明のすべての一般的な局面によれば、本発明のポリペプチドは、可溶性であり得るが、天然の毒素のトランスロケーション機能を欠く—これは、毒素によるチャレンジに対して個体をワクチン接種するまたはワクチン接種を補助するための免疫源を提供することに使用される。以下の実施例に記載される本発明の特定の実施態様では、LH₄₂₃/Aと命名されたポリペプチドは、神経毒素A型に対する中和抗体を惹起した。したがって、本発明のポリペプチドは、同様に、比較的不溶性であり得るが、天然の毒素のトランスロケーション機能を保持する—これは、溶解性が、1以上の他の成分によって、ポリペプチドと1以上の他の成分とからなる組成物に付与される場合に使用される。

【0048】

本発明のポリペプチドの第1ドメインは、エキソサイトーシスの特異的な細胞プロセスに必須の1以上の小胞または形質膜結合タンパク質を切断し、そしてこれらのタンパク質の切断により、代表的には、非細胞傷害様式で、エキソサイトーシスが阻害される。影響を受けた1または複数の細胞は、特定のタイプまたはサブグループに制限されないが、神経および非神経の両方の細胞を包含し得る。クロストリジウム菌神経毒素がエキソサイトーシスを阻害する活性は、実際、Aplysia (アメフラシ)、Drosophila (ショウジョウバエ)、および哺乳動物の神経細胞のような多様な細胞を包含する、関連の細胞表面レセプターを発現する真核生物細胞に、ほとんど普遍的に観察されており、そして第1ドメインの活性は、対応する範囲の細胞を含むように理解されるべきである。

【0049】

本発明のポリペプチドは、組換え核酸、好ましくはDNAの発現によって得られ得、そして一本鎖ポリペプチドであり、言い換えると、別々の軽鎖および重鎖ドメインに切断されていない。したがって、ポリペプチドは、組換え技法を用いて便利におよび大量に入手可能である。

【0050】

本発明のポリペプチドにおいて、この第1ドメインは、好ましくは、クロストリジウム菌毒素軽鎖またはクロストリジウム菌毒素軽鎖のフラグメントもしくは改変体を含む。フラグメントは、エキソサイトーシスに必須の小胞または形質膜結合タンパク質を切断する能力を実質的に保持する限り、必要に応じて、軽鎖のN末端またはC末端フラグメントであり、あるいは内部フラグメントである。クロストリジウム菌毒素の軽鎖の活性に必要な最小ドメインは、J. Biol. Chem., 267巻, 21号, 1992年7月, 14721-14729頁に記載されている。改変体は、軽鎖またはフラグメントとは異なるペプチド配列を有するが、これもまた小胞または形質膜結合タンパク質を切断し得る。便利には、軽鎖またはそのフラグメ

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ントの挿入、欠失、および／または置換によって得られる。以下の記載の本発明の実施態様では、改変体配列は、(i) クロストリジウム菌毒素軽鎖またはフラグメントに対するN末端伸長、(ii) 少なくとも1つのアミノ酸の変更によって改変されたクロストリジウム菌毒素軽鎖またはフラグメント、(iii) クロストリジウム菌毒素軽鎖またはフラグメントに対するC末端伸長、または(iv) (i) ~ (iii) の2以上の組み合わせを含む。

【0051】

第1ドメインは、好適には、SNAP-25、シナプトブレビン/VAMP、およびシンタキシンの1以上から選択される基質に特異的なエンドペプチダーゼ活性を示す。クロストリジウム菌毒素は、好適には、ボツリヌス菌毒素または破傷風菌毒素である。

【0052】

以下の実施例に記載の本発明の1つの実施態様では、毒素軽鎖および毒素重鎖の部分は、ボツリヌス菌毒素A型由来である。以下の実施例に記載の本発明のさらなる実施態様では、毒素軽鎖および毒素重鎖の部分は、ボツリヌス菌毒素B型由来である。ポリペプチドは、必要に応じて、1つの毒素型の軽鎖またはフラグメントまたは改変体および他の毒素型の重鎖またはフラグメントまたは改変体を含む。

【0053】

本発明のポリペプチドでは、第2ドメインは、好適には、クロストリジウム菌毒素重鎖H_N部分またはクロストリジウム菌毒素重鎖H_N部分のフラグメントもしくは改変体を含む。フラグメントは、H_Nドメインの機能を保持する限り、必要に応じて、N末端またはC末端または内部フラグメントである。その機能の原因であるH_N内の領域の教示は、例えば、Biochemistry 1995, 34, 15175-15181頁およびEur. J. Biochem, 1989, 185, 197-203頁に提供される。改変体は、H_Nドメインまたはフラグメントとは異なる配列を有するが、これもまたH_Nドメインの機能を保持する。便利には、H_Nドメインまたはそのフラグメントの挿入、欠失、および／または置換によって得られる。以下に記載の本発明の実施態様では、これは、(i) H_Nドメインまたはフラグメントに対するN末端伸長、(ii) H_Nドメインまたはフラグメントに対するC末端伸長、(iii) 少なくとも1つのアミノ酸の変更によるH_Nドメインまたはフラグメントへの改変、または(iv) (i) ~ (iii) の2以上の組み合わせを含む。クロストリジウム菌毒素は、好適には、ボツリヌス菌毒素または破傷風菌毒素である。

【0054】

本発明はまた、クロストリジウム菌神経毒素軽鎖およびクロストリジウム菌神経毒素重鎖のN末端フラグメントを含むポリペプチドを提供し、このフラグメントは、好適には、ボツリヌス菌毒素A型の重鎖のN末端アミノ酸の少なくとも423個、ボツリヌス菌毒素B型の重鎖のN末端アミノ酸の少なくとも417個、または他の型のクロストリジウム菌毒素の重鎖のN末端アミノ酸の等価の数を含み、そのため、このフラグメントは、相同アミノ酸残基の等価のアラインメントを有する。

【0055】

したがって、本発明のこれらのポリペプチドは、例えば、ジスルフィド架橋によって複合分子に連結された、2以上のポリペプチドから構成されない。代わりに、これらのポリペプチドは一本鎖であり、そして活性がないか、またはそれらの活性が神経毒素エンドペプチダーゼ活性のインビトロアッセイで顕著に減少している。

【0056】

さらに、ポリペプチドは、トリプシンのようなタンパク質分解剤の作用によってエンドペプチダーゼ活性を示す形態に変換されやすくてよい。このように、毒素軽鎖のエンドペプチダーゼ活性を制御することが可能である。

【0057】

本発明のさらなる実施態様では、ポリペプチドは、改変されたアミノ酸配列を含み、そのため、(a) ポリペプチドのLC成分とH_N成分との間にプロテアーゼ感受性領域がない、または(b) プロテアーゼ感受性領域が特定のプロテアーゼに特異的である。この後者の実施態様は、特定の環境または細胞において軽鎖のエンドペプチダーゼ活性を活性化

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することが所望される場合に使用される。しかし、一般的には、本発明のポリペプチドは、投与前に活性化される。

【0058】

より一般的には、タンパク質分解切断部位は、一本鎖ポリペプチド分子の任意の2つのドメイン間に導入され得る。

【0059】

例えば、切断部位は、第1ドメインと第2ドメインとの間に導入され得、そのため、その切断は、一本鎖ポリペプチド分子を二本鎖ポリペプチド構造に変換し、ここで、第1および第2ドメインは、ジスルフィド結合によって一緒に連結される。このような分子の特定の実施例は、本出願の配列番号11～18に提供され、そこでは、第Xa因子切断部位が、第1ドメイン(L鎖)と第2ドメイン(H_N)との間に導入されている。 10

【0060】

固有の切断部位を有する一連のペプチド配列は、本発明のポリペプチドの1以上のドメイン間の接合部への挿入に利用可能である。例えば、第1ドメイン(L鎖)と第2ドメイン(H_N)との間の切断部位の挿入により、タンパク質分解切断可能である一本鎖ポリペプチド鎖分子が二本鎖ポリペプチドを形成し得、ここで第1および第2ドメインは、第1および第2ドメイン間のジスルフィド結合によって一緒に保持される。タンパク質分解切断は、インビトロでは使用前に、またはインビボでは細胞内タンパク質分解作用による細胞特異的活性化によって行われ得る。

【0061】

あるいは(またはさらに)、切断部位は、第2ドメインと第3ドメインとの間、または精製タグと本発明のポリペプチドとの間に導入され得る。本発明の第3ドメインおよび精製タグ局面は、以下でより詳細に論ずる。 20

【0062】

L_CドメインとH_Nドメインとの間の接合部への一連の切断部位の便利な挿入を容易にするために、将来のクローン開発のためのテンプレートとして用いられ得る発現クローンを調製することが好ましい。このようなテンプレートは、配列番号103に示され、ここでLH_N/BをコードするDNAは、独特の制限酵素部位を組み込むように標準的な変異誘発技法によって改変されている。接合部に新しい切断部位を導入することは、新しい切断部位をコードする新規なオリゴヌクレオチドの簡単な挿入を必要とする。 30

【0063】

適切な切断部位としては、表1に記載のものが挙げられるが、これらに限定されない。

【0064】

【表 1】

切断部位(例えば、 LH_N 活性化のための第1ドメインと第2ドメインとの間)

プロテアーゼ	認識部位のアミノ酸配列	配列番号の例示
第Xa因子	I-E/D-G-R ↓	71/72, 33/34, 55/56, 57/58, 115/116, 117/118, 119/120, 121/122
エンテロキナーゼ	D-D-D-D-K ↓	69/70, 31/32, 29/30, 43/44, 45/46, 113/114, 111/112, 59/60, 61/62, 63/64, 65/66, 79/80, 81/82, 83-98, 105/106, 107/108
プレシジョン	L-E-V-L-F-Q ↓ G-P	75/76, 35/36, 51/52, 53/54
トロンビン	L-V-P-R ↓ G-S	77/78, 37/38, 47/48, 49/50, 99/100
ジェネナーゼ	H-Y ↓ または Y ↓ -H	
TEV	E-N-L-Y-F-Q ↓ G	101/102
フリソ	R-X-X-R ↓, 好ましくは R-X-K/R-R ↓	

(ここで、X = 任意のアミノ酸)

【0065】

いくつかの場合、ある切断部位および対応するタンパク質分解酵素(例えば、プレシジョン、トロンビン)の使用は、ポリペプチド上の短いN末端伸長を切断部位のC末端位置に残す(表1で例示のプロテアーゼについて下向き矢印の切断パターンを参照のこと)。

【0066】

ペプチド配列は、任意の2つのドメイン間に導入されて、より後の段階でのドメインの特異的切断を容易にし得る。このアプローチは、精製タグを含む融合タンパク質からの精製タグ(例えば、マルトース結合タンパク質(MBP)、グルタチオンS-トランスフェラーゼ(GST)、ポリヒスチジン域(His6))の切断および遊離のための独特の発現系に通常用いられる。これに関して、精製タグは、好適には、問題のポリペプチドのNまたはC末端に融合される。

【0067】

切断部位の選択は、遊離されたポリペプチドのN末端(またはC末端)の正確な性質との関係を有し得る。これを示すために、このような独特の系で産生された同一の LH_N /Bフラグメントを、配列番号88、94、96、および98に記載し、ここで、 LH_N /B配列へのN末端伸長は、それぞれISEFGS、GS、SPGARGS、およびAMADIGSである。 LH_N /Cフラグメントの場合、配列番号126、128、および130は、N末端配列VPEFGSSRVDH、ISEFGSSRVDH、およびVPEFGSSRVDHに記載し、それに続いて、それぞれエンテロキナーゼ、ジェネナーゼ、およ

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び第 X a 因子による融合タグからの LH_N / C フラグメントを遊離する。これらの伸長ペプチド配列のそれぞれは、本発明の改変体 L 鎖配列の一例である。同様に、精製タグが第 2 ドメインの C 末端に融合されるべき場合、得られる切断されたポリペプチド（すなわち、融合タンパク質マイナス精製タグ）は、C 末端伸長アミノ酸を含む。これらの伸長ペプチドのそれぞれは、本発明の改変体 H_N 部分の一例を提供する。

【0068】

いくつかの場合、例えば、精製タグと本発明のポリペプチドとの間の特異的部位での切断は、所望よりも低い効率であり得る。この潜在的な問題に対して、本出願人は、2つの特定の方法で独特のベクターを改変し、この改変は、独立してまたは互いに組み合わせて用いられ得る。この改変は本発明のポリペプチドまたは融合タンパク質における任意の2つのドメイン間の切断部位に適用され得るが、以下の議論は、精製タグー第1ドメイン切断事象を簡単に説明する。

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【0069】

第1に、DNAは、さらなるペプチドスペーサー配列を含むように改変され、これは、必要に応じて、精製タグとポリペプチドとの接合部に1以上の追加の切断部位を示し得る。このアプローチからの全長の発現したポリペプチドの例は、配列番号86、90、および92に示される。このようなアプローチにより、目的のポリペプチドが効率的に切断および遊離している。任意のポリペプチド内切断部位（例えば、第1ドメインと第2ドメインとの間）の存在および性質に依存して、融合タンパク質からの精製タグの切断は、第1ドメインと第2ドメインとの間のタンパク質分解切断と同時に起こり得る。あるいは、精製タグの遊離は、第1ドメインと第2ドメインとの間でのタンパク質分解切断を生じることなく起こり得る。これらの2つの切断スキームを、図14に示す。

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【0070】

選択した切断酵素に依存して、この方策により、ポリペプチドのN末端（またはC末端）への短いアミノ酸伸長が生じ得る。例えば、配列番号92の場合、発現した産物のエンテロキナーゼでの切断により、第1ドメインー第2ドメイン接合部（すなわち、 LH_N 接合部）での単一のジスルフィド結合によってカップリングした2つのポリペプチドを生じ、これは、未処理の第 X a 因子部位に類似の短いN末端ペプチド伸長およびポリリンカー配列（IEGRISEFGS）による短いN末端伸長を有する。

【0071】

第2に、自己スプライシングするインテイン配列をコードするDNAが用いられ得、このインテインは、pHおよび/または温度制御下で自己スプライシングするように誘導され得る。インテイン配列（配列番号110に、ポリペプチド配列 ISEFRESGAISGDSLISLASTGKRVS IKDLLDEKDFE IWAINEQTMKLESAKVS RVFC T GK KLVY I L K TRLGR T I K A T A N H R F L T I D G W K R L D E L S L K E H I A L P R K L E S S S L Q L S P E I E K L S Q S D I Y W D S I V S I T E T G V E E V F D L T V P G P H N F V A N D I I V H N と示される）は、示されたポリペプチド（例えば、精製タグー LH_N / B ）の自己切断を容易にして、精製タグを含まない一本鎖ポリペプチド分子を得る。したがって、このプロセスは、最初の発現産物のプロテアーゼでの処理を必要とせず、そして得られたポリペプチド（すなわち、 LH_N ー第 X a 因子活性化部位ー H_N ）は、このアプローチが適用され得る方法を簡単に例示する。

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【0072】

以下の実施例に記載される本発明のさらなる実施態様によれば、クロストリジウム菌毒素重鎖の H_C と命名された部分を欠くポリペプチドが提供される。天然に産生される毒素で見られるこの部分は、毒素のインターナリゼーションの前の細胞表面レセプターへの毒素の結合の原因である。したがって、この特定の実施態様は、例えば、タンパク質分解酵素の作用によって活性な毒素に変換され得ないように適合される。したがって、本発明はまた、クロストリジウム菌毒素軽鎖およびクロストリジウム菌毒素重鎖のフラグメントを含むポリペプチドを提供し、このフラグメントは、クロストリジウム菌毒素の中毒作用に

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関連する細胞表面レセプターに結合できず、そしてこのようなポリペプチドが、クロストリジウム菌毒素重鎖の H_C と命名された未処理部分を欠くことが好ましい。

【0073】

本発明のさらなる実施態様では、クロストリジウム菌毒素軽鎖およびクロストリジウム菌毒素重鎖の H_N と命名された部分を含むポリペプチドを含む組成物が提供され、ここで、この組成物は、クロストリジウム菌毒素を含まず、そしてタンパク質分解酵素の作用によってクロストリジウム菌毒素に変換され得るあらゆるクロストリジウム菌毒素前駆体を含まない。これらの組成物の例としては、ボツリヌス菌毒素A、B、 C_1 、D、E、F、およびG型の毒素軽鎖配列および H_N 配列を含む組成物が挙げられる。

【0074】

本発明のポリペプチドは、第3ドメイン（例えば、所望の細胞にターゲティングするためのリガンド）に結合またはこれを含むように便利に適合される。ポリペプチドは、必要に応じて、例えば、免疫グロブリンに結合する配列を含む。適切な配列は、ブドウ球菌のプロテインAのドメインBに由来するタンデムリピートの合成IgG結合ドメインである。次いで、免疫グロブリン特異性の選択は、ポリペプチド-免疫グロブリン複合体に対する標的を決定する。あるいは、ポリペプチドは、細胞表面レセプターに結合する非クロストリジウム菌配列、特定の細胞タイプ上の特異的レセプターに結合するインスリン様増殖因子1（IGF-1）を含む適切な配列、およびコレラトキシンBサブユニットに結合してGM1ガングリオシドに結合し得るコレラトキシンAサブユニットのカルボキシ末端由来の14アミノ酸残基配列を含む。したがって、本発明のポリペプチドは、必要に応じて、ポリペプチドの細胞への結合のために適合された第3ドメインをさらに含む。

【0075】

好適な実施態様では、第3ドメインは、標的細胞上のレセプターに結合し、このレセプターは、エンドソームプロセッシングを受けやすい。

【0076】

本発明の第2の局面によれば、（a）上記のような本発明のポリペプチドと（b）クロマトグラフィーマトリクスへの結合のために適合された第2のポリペプチド（精製タグとしても公知である）との融合物を含む融合タンパク質が提供され、そのため、このクロマトグラフィーマトリクスを用いて融合タンパク質の精製が可能である。第2のポリペプチドがグルタチオンSepharoseのようなアフィニティマトリクスに結合するように適合されることは便利であり、細胞抽出物または上清のような不純なソースから融合タンパク質を迅速に分離および精製することが可能である。

【0077】

1つの可能性のある第2の精製ポリペプチドは、グルタチオン-S-トランスフェラーゼ（GST）であり、そして他は、当業者に明らかであり、従来の技法に従ってクロマトグラフィーカラムでの精製を可能にするように選択される。

【0078】

本発明の他の実施態様によれば、スペーサー配列が、一本鎖ポリペプチド分子の2以上のドメイン間に導入され得る。例えば、スペーサー配列は、本発明のポリペプチド分子の第2ドメインと第3ドメインとの間に導入され得る。あるいは（またはさらに）、スペーサー配列は、精製タグと本発明のポリペプチドとの間に、あるいは第1ドメインと第2ドメインとの間に導入され得る。スペーサー配列は、タンパク質分解切断部位を含み得る。

【0079】

より詳細には、第2ドメイン-第3ドメイン接合部への特異的ペプチド配列の挿入は、第3ドメイン（例えば、リガンド）と第2ドメイン（例えば、 H_N ）との間隔をあける目的で行われ得る。このアプローチは、第3ドメインと特異的結合標的との効率的な相互作用を容易にし、および／またはポリペプチドのフォールディング特徴を改善し得る。スペーサーペプチドの例を、表2に提供する。

【0080】

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【表 2】

スパーサー配列

配列

配列番号の例示

(GGGGS)₃

39/40, 43/44, 49/50, 53/54, 57/58

RNA分解酵素 A ループ

138/139

ヘリカル

41/42, 45/46, 47/48, 51/52, 55/56

A β 部位 (TSLYKKAGFGSまたはDPAFLYKV) 133

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【0081】

好適な実施態様では、スパーサー配列は、第1ドメインと第2ドメインとの間に導入され得る。例えば、新規な一本鎖ポリペプチドハイブリッド第1ドメイン-第2ドメイン融合物の調製に有利である特徴を組み込む種々の第1ドメイン（例えば、L鎖）発現構築物が調製されている。このような発現カセットを、配列番号69、71、73、75、77、および113に例示する。

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【0082】

上記のカセットは、天然のクロストリジウム菌神経毒素のL鎖のC末端とH_NドメインのN末端との間の領域に存在する天然のリンカー配列を利用する。より詳細には、L鎖およびH_Nドメインを一緒にカップリングするために用いる天然のリンカー配列の各末端にシステインがあり、次いで一本鎖ポリペプチド分子をタンパク質分解切断して、二本鎖カウンターパートとする。これらのシステイン基は、上記のカセット中に保存される。したがって、リンカー配列のいずれかの末端にシステインアミノ酸を維持することによって、および必要に応じて特異的タンパク質分解部位を組み込んで天然の配列を置換することによって、第1ドメインと第2ドメインとの間で特異的に切断可能な特性を有する種々の構築物が調製されている。

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【0083】

例えば、H_N/Bのような目的の配列を配列番号69に記載の配列に融合することによって、ジスルフィド結合形成を容易にする特異的リンカー領域によって連結されるL鎖/A-H_N/B新規ハイブリッドを日常的に調製することが可能である。したがって、発現された融合タンパク質は、第1ドメイン（L鎖）と第2ドメイン（H_N）との間のタンパク質分解切断に適切である。必要に応じてこの切断部位を含む同じリンカーは、本発明のポリペプチドまたは融合タンパク質の他のドメインと一緒に連結するために使用され得る。

【0084】

本発明のさらなる実施態様では、分子クランプは、本発明のポリペプチドまたは融合タンパク質の2以上のドメインとともにクランピングするために用いられ得る。分子クランプは、上記のスパーサー配列の特定のサブセットとみなされ得る。

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【0085】

より詳細には、分子クランピング（指示カップリングとしても公知である）は、非共有タンパク質-タンパク質相互作用を容易にする特異的相補ペプチド配列の使用によって2以上のポリペプチドドメインと一緒に連結する方法である。

【0086】

このようなペプチド配列の例としては、ロイシンジッパー（junおよびfos）、多イオン性ペプチド（例えば、ポリグルタミン酸およびそのポリアルギニン対）、およびブドウ球

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菌のプロテイン A の合成 I g G 結合ドメインが挙げられる。

【0087】

第1および第2ドメイン（例えば、 LH_N ）を含むポリペプチドが調製され、分子クランピング配列が2つの方法によって第2（例えば、 H_N ）ドメインのC末端に融合されている。

【0088】

第1に、分子クランプをコードするDNAは、 LH_N コード配列に存在する停止コドン除去した後、 LH_N ポリペプチドをコードするDNAに直接ライゲートされている。 LH_N 配列の3'へのクランプ配列をコードする重複オリゴヌクレオチドおよび3'停止コドンの挿入によって、発現カセットが生成されている。このような配列の例を、配列番号63に示し、ここでfos(LTDTLQAETDQLEDEKSA LQT E I A N L L K E K E K L E F I L A A H)として公知の分子クランプをコードするDNA配列は、 LH_N/A ポリペプチドをコードする核酸分子の3'に導入されており、この分子はまた、第1ドメイン(L鎖)と第2ドメイン(H_N)とのコード領域間にエンテロキナーゼ切断部位をコードする核酸配列を有する。

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【0089】

第2に、部位特異的組換えを利用して、短いペプチドGly-Glyによって H_N ドメインから離れた LH_N ポリペプチドの3'にクランプ配列を組み込んでいる（例えば、以下に記載のGATEWAYシステムを参照のこと）。 H_N のC末端からクランプ配列を離すためのこのペプチドの使用を、配列番号117/118に示す。

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【0090】

いくつかの実施態様では、システイン側鎖をクランプペプチドに組み込んで、クランプに渡したジスルフィド結合の形成を容易にすることが好ましいことであり得、そしてこうして、例えば、第2ドメイン(H_N)と第3ドメイン（例えば、リガンド）との間に共有結合を作成する。システインコドンのクランプ配列への組み込みは、標準的技法によって行われ、配列番号59/60、61/62、117/118、および119/120に示すタイプの配列が得られている。

【0091】

適切な LH_N ポリペプチドの調製への分子クランピングの応用についての模式図を図15に示す。

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【0092】

第3ドメイン（例えば、リガンド）への部位特異的カップリングに適切な第1および第2ドメインを含む全長ポリペプチドの発現のためのさらなる代替法は、第2ドメイン（例えば、 H_N ）の3'にインテインの自己切断配列を組み込むことである。配列番号67/68は、このような1つの構築物を示し、第1ドメイン（例えば、L鎖）と第2ドメイン（例えば、 H_N ）との間にエンテロキナーゼ切断部位を有する LH_N/A は、C末端にCys残基、次いでインテイン配列を有するように発現される。自己切断後、次いで、例えば、Bruickら, Chem. Biol. (1996), 49-56頁に記載のように、第3ドメインへの特異的カップリング反応に関与し得る反応性チオエステルが形成される。このようなポリペプチドは、他に異種最終産物を生じ得るランダム誘導体化およびランダムカップリングに関する問題を生じることなく、第3ドメイン（例えば、目的のリガンド）への部位特異的カップリングを容易にする。

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【0093】

本出願の全体の開示から当業者に明らかなように、第1および第2ドメインは、任意のクロストリジウム菌神経毒素ソース由来のL鎖およびH鎖成分を用い得る。ボツリヌス菌ソースが好適であり得るが、破傷風菌ソースは等しい適用可能性を有する。これに関して、Eisel, U.ら(1986) EMBO J. 5 (10), 2495-2502頁および受入図書番号X04436によって本出願前に公開されているように、破傷風菌神経毒素(TeNT)の全配列は、参照が容易なように、配列番号140/141として本出願に含まれている。

【0094】

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この点の説明を補助するために、いくつかのT e N Tに基づくポリペプチドが本発明に従って調製されており、そして配列番号143を参照すると、これはE E D I D V₈₇₉のC末端配列を有するL H_Nポリペプチドである。配列番号147も参照すると、これはE E D I D V I L K K S T I L₈₈₇のC末端配列を有するL H_Nポリペプチドである。これらのL H_N配列の両方とも「天然の」T e N T L H_N配列を代表し、これらはL鎖とH_Nドメインとの間に特異的切断部位が導入されていない。したがって、配列番号145は、本発明のT e N Tポリペプチドを示し、ここではL鎖とH_Nドメインとの間の天然のT e N Tリンカー領域が、特異的エンテロキナーゼ切断配列を含むポリペプチドで置換されている。

【0095】

任意の2つのドメイン（例えば、L鎖とH_Nドメイン、またはL鎖と精製タグ）間に特異的切断部位およびスパーサー／クランピング配列を導入するための本明細書に記載の一般的なアプローチが、本発明のT e N T含有ポリペプチド分子の調製に日常的に適用可能であることもまた理解される。

【0096】

本発明の第3の局面は、クロストリジウム菌毒素の誘導体を含む組成物を提供し、この誘導体は、クロストリジウム菌毒素のエンドペプチダーゼ活性の少なくとも10%を保持し、この誘導体は、さらに、細胞表面レセプターに結合する能力がないためインビボで非毒性であり、そしてこの組成物は、毒素またはさらなる毒素誘導体のようなインビボで毒性であるあらゆる成分を含まない。誘導体の活性は、好適には、天然の毒素の活性に近づき、したがって、好適には少なくとも30%および最も好適には天然の毒素の少なくとも60%である。組成物の全体のエンドペプチダーゼ活性はまた、当然、存在する誘導体の量によって決定される。

【0097】

天然に産生されるクロストリジウム菌毒素を処理してH_Cドメインを除去することは公知であるが、この処理は調製物の毒性を全体的に除去せず、代わりにいくつかの残存毒素活性が残ったままである。したがって、この方法で処理された天然の毒素は、未だ完全に安全ではない。ポリペプチドの純粋なソースの処理によって誘導体化された本発明の組成物は、有利には、毒性がなく、そして毒素アッセイにおける陽性コントロールとして、クロストリジウム菌毒素に対するワクチンとして、または組成物中に残存毒性がないことが

【0098】

本発明は、組換え手段によって本発明のポリペプチドおよび融合タンパク質の産生を可能にする。

【0099】

本発明の第4の局面は、上記の本発明のいずれかの局面のポリペプチドまたは融合タンパク質をコードする核酸を提供する。

【0100】

本発明のこの局面の1つの実施態様では、ポリペプチドまたは融合タンパク質をコードするために提供されるDNA配列は、天然のクロストリジウム菌配列に由来しないが、天然に予め存在しない人工的に誘導体化した配列である。

【0101】

以下で詳細に記載する特異的DNA（配列番号1）は、ボツリヌス菌毒素A型の残基1～871をコードするヌクレオチドを含むポリペプチドまたは融合タンパク質をコードする。このポリペプチドは、軽鎖ドメインおよびボツリヌス菌毒素A型重鎖のアミノ末端部分の最初の423アミノ酸残基を含む。この組換え産物は、L H₄₂₃／Aと命名されている（配列番号2）。

【0102】

本発明のこの局面の第2の実施態様では、ポリペプチドまたは融合タンパク質をコードするDNA配列は、天然のクロストリジウム菌配列に由来するが、天然には見られないポ

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リペプチドまたは融合タンパク質をコードする。

【0103】

以下で詳細に記載する特異的DNA（配列番号19）は、ポリペプチドまたは融合タンパク質をコードし、そしてボツリヌス菌毒素B型の残基1～1171をコードするヌクレオチドを含む。このポリペプチドは、軽鎖ドメインおよびボツリヌス菌B型重鎖のアミノ末端タンパク質の最初の728アミノ酸残基を含む。この組換え産物は、LH₇₂₈/Bと命名されている（配列番号20）。

【0104】

したがって、本発明はまた、本発明の第3の局面のDNAを宿主細胞中で発現させる工程を含む、ポリペプチドの製造方法を提供する。宿主細胞は、適切には、軽毒素鎖と重毒素鎖とを分離するように本発明のポリペプチドまたは融合タンパク質を切断できず；例えば、非クロストリジウム菌宿主である。 10

【0105】

本発明はさらに、ポリペプチドの製造方法を提供し、この方法は、上記の融合タンパク質をコードするDNAを宿主細胞中で発現させる工程、該融合タンパク質を保持するように適合したクロマトグラフィーカラムを通して溶出する工程、該融合タンパク質を置換するように適合したリガンドを該クロマトグラフィーカラムを通して溶出させる工程、および該融合タンパク質を回収する工程によって該融合タンパク質を精製することを含む。したがって、実質的に純粋な融合タンパク質の生成が可能になる。同様に、第2のポリペプチドは、同じタイプのクロマトグラフィーカラムを用いて便利に除去され得るので、融合タンパク質は、容易に切断されて、これもまた実質的に純粋な形態で、本発明のポリペプチドを得る。 20

【0106】

二本鎖の天然の毒素に由来するLH_N/Aは、重鎖のC末端の1/2であるH_Cドメインを除去するために、トリプシンでの広範囲の消化を必要とする。このドメインの喪失により、宿主標的細胞との相互作用を抑制することによって、インビボで毒素が効果的に不活性化される。しかし、残存毒性活性があり、これは、A型神経毒素の夾雑しているトリプシン非感受性形態を示し得る。

【0107】

逆に、本発明の組換え調製物は、慎重に定義された遺伝子コード配列の産物であり、そして全長毒素タンパク質によって夾雑され得ない。さらに、大腸菌からおよび他の組換え発現宿主から回収された産物は、不活性な一本鎖ペプチドであり、あるいは発現宿主がプロセッシングされた活性なポリペプチドを産生するならば、これは毒素ではない。現在のインビトロペプチド切断アッセイによって評価されるようなLH₄₂₃/Aのエンドペプチダーゼ活性は、トリプシンによる残基430と454との間の組換え分子の活性化に全体的に依存的である。これらの2つの残基間を切断する他のタンパク質分解酵素はまた、一般的に、組換え分子の活性化に適切である。トリプシンは、アルギニンのC末端側またはリジンのC末端側のペプチド結合を切断し、そしてこれらの残基は430～454領域で見出されそして露出しているので適切である（図12を参照のこと）。 30

【0108】

本発明の組換えポリペプチドは、関連の基質を発現する細胞にターゲティングするための可能性のある治療剤であるが、ボツリヌス中毒を起こすことに関連しない。神経伝達物質の分泌が不適切であるかまたは所望でない場合、あるいは神経細胞が神経伝達物質以外の物質の調節された分泌に関して活動過多である場合が、その例であり得る。このような例において、天然の毒素のH_Cドメインの機能は、例えば、細胞レセプターリガンドおよび/またはトランスロケーションドメインを提供する代替のターゲティング配列に置換され得る。 40

【0109】

本発明の組換えポリペプチドの1つの適用は、W0-A-94/21300に開示されるような、治療分子の合成のための試薬成分である。組換え産物はまた、例えば、EP-A-0763131に開示 50

されるような食料品または環境のいずれかにおける機能的ボツリヌス菌または破傷風菌神経毒素の検出のためのインビトロアッセイの評価および開発のための非毒性標準としての適用が見出される。

【0110】

さらなる選択肢は、本発明のポリペプチドのC末端への、タンパク質および非タンパク質の両方の起源のターゲティングリガンドへの特異的化学結合を可能にするペプチド配列の付加である。

【0111】

なおさらなる実施態様では、代わりのターゲティングリガンドが、本発明のポリペプチドのN末端に付加される。組換えLH_N誘導体は、推定トリプシン感受性領域のLCのC末端端および完全タンパク質産物の最もC末端でもまた、操作された特異的プロテアーゼ切断部位を有するように指定されている。これらの部位は、組換え産物の活性化特異性を増強し、そのため、二本鎖種は、トリプシンの使用よりも予測可能な性質のタンパク質分解切断によってのみ活性され得る。

【0112】

天然のBoNT/Aから酵素的に生成されたLH_Nは、効率的な免疫源であり、したがってあらゆる全長神経毒素と全体的に分離した組換え形態は、ワクチン成分を示す。組換え産物は、上記の領域のいずれかを支持する所定のタンパク質改変を生成するための基本的な試薬として用いられ得る。

【0113】

組換え構築物は、これらが公表されたドメイン中の翻訳されたDNA配列にまたは詳細には配列番号2および配列番号20に関連するので、それらのアミノ酸配列長および軽鎖(L鎖、L)および重鎖(H鎖、H)内容に基づいて区別される呼称が割り当てられている。「LH」の名称は「/X」が続き、ここで「X」は、対応するクロストリジウム菌毒素血清型またはクラス、例えば、ボツリヌス菌神経毒素A型については「A」あるいは破傷風菌毒素については「Tex」を示す。天然の毒素ポリペプチドに由来する配列改変体は、標準形式では括弧で示され、すなわち、残基の位置の番号は、天然の配列の残基が前に付きそして改変体の残基が終わりに付けられる。

【0114】

下付きの数字の接頭辞は、翻訳された配列に対するアミノ末端(N末端)伸張、あるいは負の場合は欠失を示す。同様に、下付きの数字の接尾辞は、カルボキシ末端(C末端)伸張あるいは負の数字が用いられる場合は欠失を示す。プロテアーゼ切断部位のような特異的な配列インサートは、略語を用いて示され、例えば、第Xa因子はFXaに略されている。L鎖C末端接尾辞およびH鎖N末端接頭辞は、「/」によって分離されて、L鎖とH鎖との間の予測接合部を示す。操作されたリガンド配列についての略語は、翻訳産物における位置に対応するクロストリジウム菌L鎖またはH鎖の前または後に付けられる。

【0115】

この用法を以下に示す、

LH_{423}/A = 配列番号2、L鎖全体およびボツリヌス菌神経毒素A型のH鎖の423アミノ酸を含む；

${}_2LH_{423}/A$ = この分子の改変体、L鎖のN末端への2アミノ酸伸長を含む；

${}_2L/{}_2H_{423}/A$ = さらに改変体、この分子は、L鎖およびH鎖の両方のN末端における2アミノ酸伸長を含む；

${}_2L_{FXa}/{}_2H_{423}/A$ = さらに改変体、L鎖のN末端への2アミノ酸伸長、L鎖のC末端での第Xa因子切断配列を含み、第Xa因子での分子の切断後に、H鎖成分に2アミノ酸N末端伸長が残る；および

${}_2L_{FXa}/{}_2H_{423}/A-IGF-1$ = この分子の改変体、H鎖へのさらなるC末端伸長を有し、この例では、インスリン様増殖因子1(IGF-1)配列である。

【0116】

本発明を実施するために必要とされる基本的分子生物学技法は、本出願の優先日以前に

当該技術分野で容易に利用可能であり、そしてこのように、当業者には日常的である。

【0117】

本出願の実施例1は、本発明のポリペプチドをコードする核酸配列を調製するための従来の制限エンドヌクレアーゼ依存的切断およびライゲーション方法論を説明する。

【0118】

実施例4以降は、DNAの制限エンドヌクレアーゼ依存的切断およびライゲーションの伝統的方法を必要としない組換えDNA分子を操作するための、多くの代替の従来の方法を説明する。1つのこのような方法は、Invitrogen, Inc.の部位特異的組換えGATEWAY（登録商標）クローニングシステムであり、これは、λファージベースの部位特異的組換えを用いる[Landy, A. (1989) Ann. Rev. Biochem. 58, 913-949頁]。この方法は、ここ

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【0119】

標準的制限エンドヌクレアーゼ消化、またはポリメラーゼ連鎖反応技法を用いて、第1および第2ドメイン（例えば、BONT LHN 分子）をコードするDNA配列は、侵入ベクター中にクローニングされ得る。GATEWAY（登録商標）マニュアルに記載のように、必要なatt部位組換え配列に隣接する正確なコード配列の生成については多くの選択肢がある。

【0120】

例えば、1つの経路は、一般的なポリリンカーを侵入ベクター中に挿入することであり、ここで、挿入されたDNAは、ポリリンカー配列によって分離された2つのatt部位を含む。このアプローチは、使用者が定義した制限エンドヌクレアーゼ部位で、種々のフラグメントを侵入ベクター中に挿入することを容易にする。

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【0121】

第2の経路は、目的のDNAの増幅のために使用されるプライマーにatt部位を挿入することである。このアプローチでは、増幅されたフラグメントのDNA配列は、5'および3'末端で適切なatt部位を含むように改変される。

【0122】

LHN / C（配列番号135）、停止コドンを含まずにリガンドへの直接融合を容易にするLHN / C（配列番号136）、および適切な第2または第3ドメインとの組み合わせを容易にし得るL鎖 / C配列（配列番号134）についての侵入ベクターの例が提供される。

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【0123】

改変された侵入ベクター（目的のDNAを含む）と選択した仕向ベクターとの組み合わせによって、発現クローンが生成される。仕向ベクターは、代表的には、目的の挿入されたDNAの転写を容易にし、そして適切な宿主細胞に導入される場合にタンパク質の発現を容易にするための必要な情報を提供する。

【0124】

仕向ベクターは、N末端および／またはC末端融合タグおよび／または追加のタンパク質ドメインの発現を確実にするように調製され得る。非伝達性ベクター骨格においてMBPタグ付けしたタンパク質の発現のための新規の操作された仕向ベクターの例を、配列番号137に示す。この特定の実施態様では、配列番号137で同定される仕向ベクターとともに目的の配列を有する侵入ベクターの組換えにより、大腸菌発現のための発現ベクターが得られる。

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【0125】

発現クローンを調製するための侵入ベクターと仕向ベクターとの組み合わせにより、改変された配列を有する発現されたタンパク質が得られる。配列番号30および124に示す実施例では、TSLYKKAGFのペプチド配列が、精製タグを除去するための切断後に、エンドペプチダーゼのN末端で見られるべきである。このペプチド配列は、att部位を形成しそしてこのように構築および発現されるすべてのクローンの特徴であるDNAによってコードされる。

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【0126】

att部位配列が、特異的プロテアーゼ切断部位をコードするDNA（例えば、表1から）を侵入クロンのatt部位の3'に挿入するように改変され得ることが理解される。

【0127】

任意のポリペプチド（例えば、LH_Nフラグメント）の正確なN末端が、エンドペプチダーゼDNAが侵入ベクターおよびその関連の5' att部位に導入される方法に依存して変化することも理解される。配列番号29/30および123/124は、適切な場合である。配列番号30のN末端伸長はTSLYKKAGFGSであるが、配列番号124のN末端伸長はITSLYKKAGFGSLDHである。これらのアミノ酸伸長含有ドメインは、本発明の第1/第2ドメイン改変体のさらなる例を提供する。

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【0128】

本発明の文脈内で、以下の定義を留意すべきである。

【0129】

用語ポリペプチド「フラグメント」とは、問題のポリペプチド「フラグメント」が、好適には参照の配列番号のポリペプチド配列の少なくとも50%の長さであることを意味する。したがって、参照の配列番号のポリペプチドが、例えば500アミノ酸残基を有するアミノ酸配列であるならば、対応する「フラグメント」は、少なくとも250アミノ酸残基を有するアミノ酸配列である。より好適な実施態様では、「フラグメント」は、参照の配列番号のポリペプチドの、少なくとも70%、より好ましくは少なくとも85%、特に好ましくは少なくとも90%、および最も好ましくは少なくとも95%の長さである。

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【0130】

ポリペプチド「フラグメント」は、好適には、参照の配列番号のポリペプチド配列のエピトープを含み、これは、抗体交差反応性によって確認され得る。ポリペプチド「フラグメント」は、好適には、エキソサイトーシスに必須の1以上の小胞または形質膜結合タンパク質を切断し得る第1ドメインを含む。

【0131】

用語「改変体」とは、参照の配列番号のポリペプチドと、少なくとも70%、好ましくは少なくとも80%、より好ましくは少なくとも90%パーセントのアミノ酸配列相同性を有するポリペプチドまたはポリペプチド「フラグメント」を意味する。「改変体」の例は、アミノ酸の1以上のアナログ（例えば、非天然アミノ酸）または置換された連結を含むポリペプチドまたはポリペプチドフラグメントである。用語「相同性」および「同一性」は、本明細書では同義とみなされる。

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【0132】

配列比較については、代表的には、1つの配列（例えば、参照の配列番号ポリペプチド）が参照配列として用いられ、これに対して「改変体」配列が比較され得る。配列比較アルゴリズムを用いる場合、「改変体」および参照配列はコンピュータに入力され、次の座標が指定され、そして必要ならば、配列アルゴリズムプログラムパラメータが指定される。次いで、配列比較アルゴリズムは、指定されたプログラムパラメータに基づいて、参照の配列番号のポリペプチド配列に対する「改変体」配列についての配列同一性の割合を算出する。

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【0133】

比較のための配列の最適アラインメントは、例えば、SmithおよびWaterman [Adv. Appl. Math. 2: 484 (1981)] の局所相同性アラインメントアルゴリズムによって、NeedlemanおよびWunsch [J. Mol. Biol. 48: 443 (1970)] のアルゴリズムによって、PearsonおよびLipman [Proc. Nat'l. Acad. Sci. USA 85: 2444 (1988)] の類似性方法についての検索によって、これらのアルゴリズム（GAP、BESTFIT、FASTA、およびTFASTA - Sequence Analysis Software Package of the Genetics Computer Group, University of Wisconsin Biotechnology Center, 1710 University Avenue, Madison, Wis. 53705）のコンピュータ実行によって、または目視検査によって行われ得る [Current Protocols; Molecular Biology, F.M. Ausbelら編, Current Protocols, a joint venture between Greene Publi

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shing Associates, Inc.およびJohn Wiley & Sons, Inc. (1995 Supplement) Ausubelを参照のこと】。

【0134】

配列類似性のパーセントを決定するために適切なアルゴリズムの例は、BLASTおよびBLAST 2.0アルゴリズム [Altschul (1990) J. Mol. Biol. 215: 403-410頁；およびthe National Center for Biotechnology Informationの「<http://www.ncbi.nlm.nih.gov/>」を参照のこと] である。

【0135】

好ましい相同性比較において、同一性は、少なくとも50アミノ酸残基長、より好ましくは少なくとも100アミノ酸残基長、特に好ましくは少なくとも150アミノ酸残基長、および最も好ましくは少なくとも200アミノ酸残基長である配列の領域にわたり存在する。あるいは、同一性は、例えば、「改変体」ポリペプチドの配列全体にわたって存在する。

【0136】

本発明で使用される場合、用語DNA「フラグメント」は、用語ポリペプチド「フラグメント」（上述）と一致して解釈されるべきであり、そして問題のDNA「フラグメント」が、好ましくは参照の配列番号のDNA配列の少なくとも50%の長さであることを意味する。したがって、参照の配列番号のDNA配列が、例えば、500ヌクレオチド残基を有する核酸配列であるならば、対応する「フラグメント」は、少なくとも250ヌクレオチド残基を有する核酸配列である。より好適な実施態様では、「フラグメント」は、参照の配列番号のDNA配列の、少なくとも70%、より好ましくは少なくとも85%、特に好ましくは少なくとも90%、および最も好ましくは少なくとも95%の長さである。

【0137】

用語DNA「改変体」とは、参照のDNA配列（またはそのフラグメント）と実質的な相同性または実質的な類似性を有するDNA配列を意味する。核酸またはそのフラグメントは、他の核酸（またはその相補鎖）と（適切なヌクレオチド挿入または欠失とともに）最適にアラインされる場合に、ヌクレオチド塩基の少なくとも約60%、通常は少なくとも約70%、より通常には少なくとも約80%、好ましくは少なくとも約90%、およびより好ましくはヌクレオチド塩基の少なくとも約95%～98%でヌクレオチド配列同一性があるならば、他に対して「実質的に相同」（または「実質的に類似」）である。相同性決定は、ペプチドについて上述のように行われる。

【0138】

あるいは、DNA「改変体」は、選択的ハイブリダイゼーション条件下でハイブリダイズし得る場合、参照の配列番号のDNA配列のコード配列（またはそのフラグメント）と実質的に相同（または実質的に類似）である。ハイブリダイゼーションの選択性は、ハイブリダイゼーションが生じる場合に存在し、全体的に特異性がない場合よりも実質的により選択的である。代表的には、少なくとも約50ヌクレオチドの長さによって少なくとも約65%、好ましくは少なくとも約70%、より好ましくは少なくとも約75%、および最も好ましくは少なくとも約90%の相同性がある場合に、選択的ハイブリダイゼーションが生じる。Kanehisa (1984) Nuc. Acids Res. 12: 203-213を参照のこと。上記のように、相同性比較の長さは、より長い長さにわたるものであり得、そしてある実施態様では、しばしば、少なくとも約100ヌクレオチド、通常は少なくとも約150ヌクレオチド、より通常には少なくとも約200ヌクレオチド、代表的には少なくとも約250ヌクレオチド、より代表的には少なくとも約300ヌクレオチド、および好ましくは少なくとも約350以上のヌクレオチドの長さにわたる。あるいは、同一性は、例えば、「改変体」DNA配列の配列全体にわたって存在する。

【0139】

核酸ハイブリダイゼーションが、塩基組成、相補鎖の長さ、およびハイブリダイズしている核酸間のヌクレオチド塩基ミスマッチの数に加えて、塩濃度（例えば、NaCl）、温度、または有機溶媒のような条件によって影響を受けることは、当業者には容易に理解され

る。好ましくは、ストリンジェントな温度条件が用いられ、そして一般的には30℃を超える、代表的には37℃を超える、および好ましくは45℃を超える温度を含む。ストリンジェントな塩条件は、普通には1000mM未満、代表的には500mM未満、および好ましくは200mM未満である。pHは、代表的には7.0～8.3である。しかし、パラメータの組み合わせは、任意の単一のパラメータの基準よりも非常に重要である。例えば、WetmurおよびDavidson (1968) J. Mol. Biol. 31: 349-370を参照のこと。

【0140】

上記の用語DNA「フラグメント」および「改変体」は、互いに共通して、得られるペプチド産物が、好ましくは、対応する参照の配列番号のポリペプチドと実質的に同じである交差反応性抗原性特性を有する。好ましくは、本発明の上記DNA「フラグメント」および「改変体」実施態様のポリペプチド産物のすべては、参照の配列番号のポリペプチドにも結合する抗体と結合する。

【0141】

以下は、本発明の特定の実施態様の説明であり、図面によって説明される。

【0142】

本出願に付随する配列表は、以下の配列を含む。

【0143】

配列番号	配列
1	LH _{4 2 3} / AをコードするDNA。

【0144】

2	LH _{4 2 3} / A。

【0145】

3	_{2 3} LH _{4 2 3} / A (Q ₂ E, N _{2 6} K, A _{2 7} Y)をコードするDNA、そのN末端部分を図4に示す。

【0146】

4	_{2 3} LH _{4 2 3} / A (Q ₂ E, N _{2 6} K, A _{2 7} Y)。

【0147】

5	₂ LH _{4 2 3} / A (Q ₂ E, N _{2 6} K, A _{2 7} Y)をコードするDNA、そのN末端部分を図4に示す。

【0148】

6	₂ LH _{4 2 3} / A (Q ₂ E, N _{2 6} K, A _{2 7} Y)。

【0149】

7	Binzらの天然のBoNT / AをコードするDNA。

【0150】

8	Binzらの天然のBoNT / A。

【0151】

9	L / ₄ H _{4 2 3} / AをコードするDNA。

【0152】

10	L / ₄ H _{4 2 3} / A。

【0153】

11	L _{F X a} / ₃ H _{4 2 3} / AをコードするDNA。

【0154】

12	L _{F X a} / ₃ H _{4 2 3} / A。

【0155】

13	L _{F X a} / ₃ H _{4 2 3} / A - IGF - 1をコードするDNA。

【0156】

14	L _{F X a} / ₃ H _{4 2 3} / A - IGF - 1。

【0157】

15	L _{F X a} / ₃ H _{4 2 3} / A - CtxA14をコードするDNA。

【0158】

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- 1 6 $L_{F X a} / 3 H_{4 2 3} / A - C t x A 1 4$ 。
- 【0 1 5 9】
- 1 7 $L_{F X a} / 3 H_{4 2 3} / A - Z Z$ をコードするDNA。
- 【0 1 6 0】
- 1 8 $L_{F X a} / 3 H_{4 2 3} / A - Z Z$ 。
- 【0 1 6 1】
- 1 9 $L H_{7 2 8} / B$ をコードするDNA。
- 【0 1 6 2】
- 2 0 $L H_{7 2 8} / B$ 。
- 【0 1 6 3】 10
- 2 1 $L H_{4 1 7} / B$ をコードするDNA。
- 【0 1 6 4】
- 2 2 $L H_{4 1 7} / B$ 。
- 【0 1 6 5】
- 2 3 $L H_{1 0 7} / B$ をコードするDNA。
- 【0 1 6 6】
- 2 4 $L H_{1 0 7} / B$ 。
- 【0 1 6 7】
- 2 5 $L H_{4 2 3} / A (Q_2 E, N_{2 6} K, A_{2 7} Y)$ をコードするDNA。
- 【0 1 6 8】 20
- 2 6 $L H_{4 2 3} / A (Q_2 E, N_{2 6} K, A_{2 7} Y)$ 。
- 【0 1 6 9】
- 2 7 $L H_{4 1 7} / B$ をコードするDNA、ここで、最初の2 7 4塩基は大腸菌コドンバイアスを有するように改変される。
- 【0 1 7 0】
- 2 8 $L H_{4 1 7} / B$ をコードするDNA、ここで、天然のB o N T / B配列の塩基6 9 1～1 6 4 1は、天然のB o N T / Bポリペプチドのアミノ酸残基2 3 1～5 4 7をコードする縮重DNAによって置換されている。
- 【0 1 7 1】
- 2 9 Gateway適合仕向ベクターから発現される $L H_N / A$ をコードするDNA 30
。 $L H_N / A$ は、 $L C - H_N$ 接合部にエンテロキナーゼ活性化部位、および $L H_N / A$ 配列の5'末端に1 1アミノ酸のatt部位ペプチド伸長を組み込む。
- 【0 1 7 2】
- 3 0 配列番号2 9の発現によって産生される $L H_N / A$ 、このポリペプチドは、 $L C - H_N$ 接合部にエンテロキナーゼ活性化部位、および $L H_N / A$ 配列の5'末端に1 1アミノ酸のatt部位ペプチド伸長を組み込んでいる。
- 【0 1 7 3】
- 3 1 $L C - H_N$ 接合部にエンテロキナーゼ活性化部位を有する $L H_N / A$ をコードするDNA。
- 【0 1 7 4】 40
- 3 2 配列番号3 1の発現によって産生される $L H_N / A$ 、このポリペプチドは、 $L C - H_N$ 接合部にエンテロキナーゼ活性化部位を有する。
- 【0 1 7 5】
- 3 3 $L C - H_N$ 接合部に第X a因子プロテアーゼ活性化部位を有する $L H_N / A$ をコードするDNA。
- 【0 1 7 6】
- 3 4 配列番号3 3の発現によって産生される $L H_N / A$ 、このポリペプチドは、 $L C - H_N$ 接合部に第X a因子プロテアーゼ活性化部位を有する。
- 【0 1 7 7】
- 3 5 $L C - H_N$ 接合部にプレシジョンプロテアーゼ活性化部位を有する $L H_N$ 50

／AをコードするDNA。

【0178】

36 配列番号35の発現によって産生される LH_N ／A、このポリペプチドは、 $LC-H_N$ 接合部にプレシヨンプロテアーゼ活性化部位を有する。

【0179】

37 $LC-H_N$ 接合部にトロンビンプロテアーゼ活性化部位を有する LH_N ／AをコードするDNA。

【0180】

38 配列番号37の発現によって産生される LH_N ／A、このポリペプチドは、 $LC-H_N$ 接合部にトロンビンプロテアーゼ活性化部位を有する。

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【0181】

39 LH_N ／Aーリガンド（*Erythrina cristagalli*レクチン）融合物をコードするDNA、ここで、 $LC-H_N$ 接合部は、特異的プロテアーゼ切断部位を組み込まず、そしてリガンドは、 $(GGGS)_3$ スパーサーによって H_N ドメインから離れている。

【0182】

40 配列番号39の発現によって産生される LH_N ／Aーリガンド（*Erythrina cristagalli*レクチン）融合物、ここで、 $LC-H_N$ 接合部は、特異的プロテアーゼ切断部位を組み込まず、そしてリガンドは、 $(GGGS)_3$ スパーサーによって H_N ドメインから離れている。

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【0183】

41 LH_N ／Aーリガンド（*Erythrina cristagalli*レクチン）融合物をコードするDNA、ここで、 $LC-H_N$ 接合部は、特異的プロテアーゼ切断部位を組み込まず、そしてリガンドは、ヘリカルスパーサーによって H_N ドメインから離れている。

【0184】

42 配列番号41の発現によって産生される LH_N ／Aーリガンド（*Erythrina cristagalli*レクチン）融合物、ここで、 $LC-H_N$ 接合部は、特異的プロテアーゼ切断部位を組み込まず、そしてリガンドは、ヘリカルスパーサーによって H_N ドメインから離れている。

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【0185】

43 LH_N ／Aーリガンド（*Erythrina cristagalli*レクチン）融合物をコードするDNA、ここで、 $LC-H_N$ 接合部は、特異的エンテロキナーゼプロテアーゼ活性化部位を組み込み、そしてリガンドは、 $(GGGS)_3$ スパーサーによって H_N ドメインから離れている。

【0186】

44 配列番号43の発現によって産生される LH_N ／Aーリガンド（*Erythrina cristagalli*レクチン）融合物、ここで、 $LC-H_N$ 接合部は、特異的エンテロキナーゼプロテアーゼ活性化部位を組み込み、そしてリガンドは、 $(GGGS)_3$ スパーサーによって H_N ドメインから離れている。

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【0187】

45 LH_N ／Aーリガンド（*Erythrina cristagalli*レクチン）融合物をコードするDNA、ここで、 $LC-H_N$ 接合部は、特異的エンテロキナーゼプロテアーゼ活性化部位を組み込み、そしてリガンドは、ヘリカルスパーサーによって H_N ドメインから離れている。

【0188】

46 配列番号45の発現によって産生される LH_N ／Aーリガンド（*Erythrina cristagalli*レクチン）融合物、ここで、 $LC-H_N$ 接合部は、特異的エンテロキナーゼプロテアーゼ活性化部位を組み込み、そしてリガンドは、ヘリカルスパーサーによって H_N ドメインから離れている。

【0189】

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47 LH_N / A-リガンド (Erythrina cristagalliレクチン) 融合物をコードする DNA、ここで、 $LC-H_N$ 接合部は、特異的トロンビンプロテアーゼ活性化部位を組み込み、そしてリガンドは、ヘリカルスパーサーによって H_N ドメインから離れている。

【0190】

48 配列番号 47 の発現によって産生される LH_N / A-リガンド (Erythrina cristagalliレクチン) 融合物、ここで、 $LC-H_N$ 接合部は、特異的トロンビンプロテアーゼ活性化部位を組み込み、そしてリガンドは、ヘリカルスパーサーによって H_N ドメインから離れている。

【0191】

49 LH_N / A-リガンド (Erythrina cristagalliレクチン) 融合物をコードする DNA、ここで、 $LC-H_N$ 接合部は、特異的トロンビンプロテアーゼ活性化部位を組み込み、そしてリガンドは、(GGGGS)₃ スパーサーによって H_N ドメインから離れている。

【0192】

50 配列番号 49 の発現によって産生される LH_N / A-リガンド (Erythrina cristagalliレクチン) 融合物、ここで、 $LC-H_N$ 接合部は、特異的トロンビンプロテアーゼ活性化部位を組み込み、そしてリガンドは、(GGGGS)₃ スパーサーによって H_N ドメインから離れている。

【0193】

51 LH_N / A-リガンド (Erythrina cristagalliレクチン) 融合物をコードする DNA、ここで、 $LC-H_N$ 接合部は、特異的プレシジョンプロテアーゼ活性化部位を組み込み、そしてリガンドは、ヘリカルスパーサーによって H_N ドメインから離れている。

【0194】

52 配列番号 51 の発現によって産生される LH_N / A-リガンド (Erythrina cristagalliレクチン) 融合物、ここで、 $LC-H_N$ 接合部は、特異的プレシジョンプロテアーゼ活性化部位を組み込み、そしてリガンドは、ヘリカルスパーサーによって H_N ドメインから離れている。

【0195】

53 LH_N / A-リガンド (Erythrina cristagalliレクチン) 融合物をコードする DNA、ここで、 $LC-H_N$ 接合部は、特異的プレシジョンプロテアーゼ活性化部位を組み込み、そしてリガンドは、(GGGGS)₃ スパーサーによって H_N ドメインから離れている。

【0196】

54 配列番号 53 の発現によって産生される LH_N / A-リガンド (Erythrina cristagalliレクチン) 融合物、ここで、 $LC-H_N$ 接合部は、特異的プレシジョンプロテアーゼ活性化部位を組み込み、そしてリガンドは、(GGGGS)₃ スパーサーによって H_N ドメインから離れている。

【0197】

55 LH_N / A-リガンド (Erythrina cristagalliレクチン) 融合物をコードする DNA、ここで、 $LC-H_N$ 接合部は、特異的第 Xa 因子プロテアーゼ活性化部位を組み込み、そしてリガンドは、ヘリカルスパーサーによって H_N ドメインから離れている。

【0198】

56 配列番号 55 の発現によって産生される LH_N / A-リガンド (Erythrina cristagalliレクチン) 融合物、ここで、 $LC-H_N$ 接合部は、特異的第 Xa 因子プロテアーゼ活性化部位を組み込み、そしてリガンドは、ヘリカルスパーサーによって H_N ドメインから離れている。

【0199】

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57 LH_N / A -リガンド (Erythrina cristagalliレクチン) 融合物をコードするDNA、ここで、 $LC-H_N$ 接合部は、特異的第Xa因子プロテアーゼ活性化部位を組み込み、そしてリガンドは、 $(GGGGS)_3$ スペーサーによって H_N ドメインから離れている。

【0200】

58 配列番号57の発現によって産生される LH_N / A -リガンド (Erythrina cristagalliレクチン) 融合物、ここで、 $LC-H_N$ 接合部は、特異的第Xa因子プロテアーゼ活性化部位を組み込み、そしてリガンドは、 $(GGGGS)_3$ スペーサーによって H_N ドメインから離れている。

【0201】

59 $LC-H_N$ 接合部にエンテロキナーゼプロテアーゼ活性化部位、および1対のCys残基によって結合したC末端fosリガンドを組み込んでいる LH_N / A をコードするDNA。

【0202】

60 配列番号59の発現によって産生される LH_N / A 、このポリペプチドは、 $LC-H_N$ 接合部にエンテロキナーゼプロテアーゼ活性化部位、および1対のCys残基によって結合したC末端fosリガンドを組み込んでいる。

【0203】

61 $LC-H_N$ 接合部にエンテロキナーゼプロテアーゼ活性化部位、および1対のCys残基によって結合したC末端 $(Glu)_8$ ペプチドを組み込んでいる LH_N / A をコードするDNA。

【0204】

62 配列番号61の発現によって産生される LH_N / A 、このポリペプチドは、 $LC-H_N$ 接合部にエンテロキナーゼプロテアーゼ活性化部位、および1対のCys残基によって結合したC末端 $(Glu)_8$ ペプチドを組み込んでいる。

【0205】

63 $LC-H_N$ 接合部にエンテロキナーゼプロテアーゼ活性化部位、およびC末端fosリガンドを組み込んでいる LH_N / A をコードするDNA。

【0206】

64 配列番号63の発現によって産生される LH_N / A 、このポリペプチドは、 $LC-H_N$ 接合部にエンテロキナーゼプロテアーゼ活性化部位、およびC末端fosリガンドを組み込んでいる。

【0207】

65 $LC-H_N$ 接合部にエンテロキナーゼプロテアーゼ活性化部位、およびC末端 $(Glu)_8$ ペプチドを組み込んでいる LH_N / A をコードするDNA。

【0208】

66 配列番号65の発現によって産生される LH_N / A 、このポリペプチドは、 $LC-H_N$ 接合部にエンテロキナーゼプロテアーゼ活性化部位、およびC末端 $(Glu)_8$ ペプチドを組み込んでいる。

【0209】

67 $LC-H_N$ 接合部にエンテロキナーゼプロテアーゼ活性化部位、および化学的指示カップリングにおける使用のためのチオエステル形成を容易にするためにC末端自己切断可能なインテインポリペプチドを組み込んでいる LH_N / A をコードするDNA。

【0210】

68 配列番号67の発現によって産生される LH_N / A 、このポリペプチドは、 $LC-H_N$ 接合部にエンテロキナーゼプロテアーゼ活性化部位、および化学的指示カップリングにおける使用のためのチオエステル形成を容易にするためにC末端自己切断可能なインテインポリペプチドを組み込んでいる。

【0211】

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69 停止コドンがなく、 H_N ドメインの最初の6アミノ酸を組み込むリンカーペプチド、およびエンテロキナーゼ切断部位を有するLC/AをコードするDNA。

【0212】

70 配列番号69の発現によって産生されるLC/A、このポリペプチドは、停止コドンがなく、 H_N ドメインの最初の6アミノ酸を組み込むリンカーペプチド、およびエンテロキナーゼ切断部位を有する。

【0213】

71 停止コドンを含まず、 H_N ドメインの最初の6アミノ酸を組み込むリンカーペプチド、および第Xa因子切断部位を有するLC/AをコードするDNA。

【0214】

72 配列番号71の発現によって産生されるLC/A、このポリペプチドは、停止コドンを含まず、 H_N ドメインの最初の6アミノ酸を組み込むリンカーペプチド、および第Xa因子切断部位を有する。

【0215】

73 停止コドンを含まず、 H_N ドメインの最初の6アミノ酸を組み込む天然のLC- H_N 配列を示すリンカーペプチドを有するLC/AをコードするDNA。

【0216】

74 配列番号73の発現によって産生されるLC/A、このポリペプチドは、停止コドンを含まず、 H_N ドメインの最初の6アミノ酸を組み込む天然のLC- H_N 配列を示すリンカーペプチドを有する。

【0217】

75 停止コドンを含まず、 H_N ドメインの最初の6アミノ酸を組み込むリンカーペプチド、およびプレシジョン切断部位を有するLC/AをコードするDNA。

【0218】

76 配列番号75の発現によって産生されるLC/A、このポリペプチドは、停止コドンを含まず、 H_N ドメインの最初の6アミノ酸を組み込むリンカーペプチド、およびプレシジョン切断部位を有する。

【0219】

77 停止コドンを含まず、 H_N ドメインの最初の6アミノ酸を組み込むリンカーペプチド、およびトロンピン切断部位を有するLC/AをコードするDNA。

【0220】

78 配列番号77の発現によって産生されるLC/A、このポリペプチドは、停止コドンを含まず、 H_N ドメインの最初の6アミノ酸を組み込むリンカーペプチド、およびトロンピン切断部位を有する。

【0221】

79 LC- H_N 接合部(LCおよび H_N ドメインのCys残基間に11アミノ酸がある)にエンテロキナーゼプロテアーゼ活性化部位、および6アミノ酸N末端伸長を組み込んでいるLH_N/BをコードするDNA。

【0222】

80 配列番号79の発現によって産生されるLH_N/B、このポリペプチドは、LC- H_N 接合部(LCおよび H_N ドメインのCys残基間に11アミノ酸がある)にエンテロキナーゼプロテアーゼ活性化部位、および6アミノ酸N末端伸長を組み込んでいる。

【0223】

81 LC- H_N 接合部(LCおよび H_N ドメインのCys残基間に20アミノ酸がある)にエンテロキナーゼプロテアーゼ活性化部位、および6アミノ酸N末端伸長を組み込んでいるLH_N/BをコードするDNA。

【0224】

82 配列番号81の発現によって産生されるLH_N/B、このポリペプチドは、LC- H_N 接合部(LCおよび H_N ドメインのCys残基間に20アミノ酸がある)に

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エンテロキナーゼプロテアーゼ活性化部位、および6アミノ酸N末端伸長を組み込んでいる。

【0225】

83 LC-H_N 接合部に第Xa因子プロテアーゼ活性化部位、およびインティン自己切断ポリペプチドに切断から生じる11アミノ酸N末端伸長を組み込んでいるLH_N/BをコードするDNA。

【0226】

84 配列番号83の発現によって産生されるLH_N/B、このポリペプチドは、LC-H_N 接合部に第Xa因子プロテアーゼ活性化部位、およびインティン自己切断ポリペプチドに切断から生じる11アミノ酸N末端伸長を組み込んでいる。

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【0227】

85 LC-H_N 接合部に第Xa因子プロテアーゼ活性化部位、およびTEVプロテアーゼ切断部位に切断（精製タグからLH_N/Bを遊離することを含む）から生じる11アミノ酸N末端伸長（第Xa因子プロテアーゼ切断部位を保持する）を組み込んでいるLH_N/BをコードするDNA。

【0228】

86 配列番号85の発現によって産生されるLH_N/B、このポリペプチドは、LC-H_N 接合部に第Xa因子プロテアーゼ活性化部位、およびTEVプロテアーゼ切断部位に切断（精製タグからLH_N/Bを遊離することを含む）から生じる11アミノ酸N末端伸長（第Xa因子プロテアーゼ切断部位を保持する）を組み込んでいる。

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【0229】

87 LC-H_N 接合部に第Xa因子プロテアーゼ活性化部位、および6アミノ酸N末端伸長を組み込んでいるLH_N/BをコードするDNA。

【0230】

88 配列番号87の発現によって産生されるLH_N/B、このポリペプチドは、LC-H_N 接合部に第Xa因子プロテアーゼ活性化部位、および6アミノ酸N末端伸長を組み込んでいる。

【0231】

89 LC-H_N 接合部に第Xa因子プロテアーゼ活性化部位、および第Xa因子プロテアーゼ切断部位に切断（精製タグからLH_N/Bを遊離することを含む）から生じる11アミノ酸N末端伸長（エンテロキナーゼプロテアーゼ切断部位を保持する）を組み込んでいるLH_N/BをコードするDNA。

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【0232】

90 配列番号89の発現によって産生されるLH_N/B、このポリペプチドは、LC-H_N 接合部に第Xa因子プロテアーゼ活性化部位、および第Xa因子プロテアーゼ切断部位に切断（精製タグからLH_N/Bを遊離することを含む）から生じる11アミノ酸N末端伸長（エンテロキナーゼプロテアーゼ切断部位を保持する）を組み込んでいる。

【0233】

91 LC-H_N 接合部に第Xa因子プロテアーゼ活性化部位、およびエンテロキナーゼプロテアーゼ切断部位に切断（精製タグからLH_N/Bを遊離することを含む）から生じる10アミノ酸N末端伸長（第Xa因子プロテアーゼ切断部位を保持する）を組み込んでいるLH_N/BをコードするDNA。

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【0234】

92 配列番号91の発現によって産生されるLH_N/B、このポリペプチドは、LC-H_N 接合部に第Xa因子プロテアーゼ活性化部位、およびエンテロキナーゼプロテアーゼ切断部位に切断（精製タグからLH_N/Bを遊離することを含む）から生じる10アミノ酸N末端伸長（第Xa因子プロテアーゼ切断部位を保持する）を組み込んでいる。

【0235】

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9 3 LC-H_N 接合部に第 X a 因子プロテアーゼ活性化部位、および 2 アミノ酸 (Gly-Ser) N 末端伸長を組み込んでいる LH_N / B をコードする DNA であり、pGEX-4T-2 で発現される。

【0 2 3 6】

9 4 配列番号 9 3 の発現によって産生される LH_N / B、このポリペプチドは、LC-H_N 接合部に第 X a 因子プロテアーゼ活性化部位、および 2 アミノ酸 (Gly-Ser) N 末端伸長を組み込んでおり、pGEX-4T-2 で発現される。

【0 2 3 7】

9 5 LC-H_N 接合部に第 X a 因子プロテアーゼ活性化部位、および 7 アミノ酸 (Ser-Pro-Gly-Ala-Arg-Gly-Ser) N 末端伸長を組み込んでいる LH_N / B をコードする DNA であり、pET-43a で発現される。 10

【0 2 3 8】

9 6 配列番号 9 5 の発現によって産生される LH_N / B、このポリペプチドは、LC-H_N 接合部に第 X a 因子プロテアーゼ活性化部位、および 7 アミノ酸 (Ser-Pro-Gly-Ala-Arg-Gly-Ser) N 末端伸長を組み込んでおり、pET-43a で発現される。

【0 2 3 9】

9 7 LC-H_N 接合部に第 X a 因子プロテアーゼ活性化部位、および 7 アミノ酸 (Ala-Met-Ala-Glu-Ile-Gly-Ser) N 末端伸長を組み込んでいる LH_N / B をコードする DNA であり、pET-32a で発現される。

【0 2 4 0】

9 8 配列番号 9 7 の発現によって産生される LH_N / B、このポリペプチドは、LC-H_N 接合部に第 X a 因子プロテアーゼ活性化部位、および 7 アミノ酸 (Ala-Met-Ala-Asp-Ile-Gly-Ser) N 末端伸長を組み込んでおり、pET-32a で発現される。 20

【0 2 4 1】

9 9 LC-H_N 接合部にトロンビンプロテアーゼ活性化部位、および 6 アミノ酸 (Ile-Ser-Glu-Phe-Gly-Ser) N 末端伸長を組み込んでいる LH_N / B をコードする DNA であり、pMAL-c2 で発現される。

【0 2 4 2】

1 0 0 配列番号 9 9 の発現によって産生される LH_N / B、このポリペプチドは、LC-H_N 接合部にトロンビンプロテアーゼ活性化部位、および 6 アミノ酸 (Ile-Ser-Glu-Phe-Gly-Ser) N 末端伸長を組み込んでおり、pMAL-c2 で発現される。 30

【0 2 4 3】

1 0 1 LC-H_N 接合部に T E V プロテアーゼ活性化部位、および 6 アミノ酸 (Ile-Ser-Glu-Phe-Gly-Ser) N 末端伸長を組み込んでいる LH_N / B をコードする DNA であり、pMAL-c2 で発現される。

【0 2 4 4】

1 0 2 配列番号 1 0 1 の発現によって産生される LH_N / B、このポリペプチドは、LC-H_N 接合部に T E V プロテアーゼ活性化部位、および 6 アミノ酸 (Ile-Ser-Glu-Phe-Gly-Ser) N 末端伸長を組み込んでおり、pMAL-c2 で発現される。

【0 2 4 5】

1 0 3 LC-H_N 接合部に第 X a 因子プロテアーゼ活性化部位、および 6 アミノ酸 (Ile-Ser-Glu-Phe-Gly-Ser) N 末端伸長を組み込んでいる LH_N / B をコードする DNA であり、pMAL-c2 で発現される。DNA は、LC-H_N 接合部に新規のリンカー配列の組み込みのための MfeI および AvrII 制限酵素部位を組み込む。 40

【0 2 4 6】

1 0 4 配列番号 1 0 3 の発現によって産生される LH_N / B、このポリペプチドは、LC-H_N 接合部に第 X a 因子プロテアーゼ活性化部位、および 6 アミノ酸 (Ile-Ser-Glu-Phe-Gly-Ser) N 末端伸長を組み込んでおり、pMAL-c2 で発現される。

【0 2 4 7】

1 0 5 LC-H_N 接合部 (LC および H_N ドメインの C y s 残基間に 2 0 アミノ 50

酸がある) にエンテロキナーゼプロテアーゼ活性化部位、および6アミノ酸 (Ile-Ser-Glu-Phe-Gly-Ser) N末端伸長を組み込んでいる LH_N / B をコードするDNA。ArvII制限部位は欠失されている。

【0248】

106 配列番号105の発現によって産生される LH_N / B 、このポリペプチドは、 $LC-H_N$ 接合部 (LC および H_N ドメインの Cys 残基間に20アミノ酸がある) にエンテロキナーゼプロテアーゼ活性化部位、および6アミノ酸 (Ile-Ser-Glu-Phe-Gly-Ser) N末端伸長を組み込んでいる。

【0249】

107 $LC-H_N$ 接合部 (LC および H_N ドメインの Cys 残基間に20アミノ酸がある) にエンテロキナーゼプロテアーゼ活性化部位、および6アミノ酸 (Ile-Ser-Glu-Phe-Gly-Ser) N末端伸長を組み込んでいる LH_N / B をコードするDNA。 10

【0250】

108 配列番号107の発現によって産生される LH_N / B 、このポリペプチドは、 $LC-H_N$ 接合部 (LC および H_N ドメインの Cys 残基間に20アミノ酸がある) にエンテロキナーゼプロテアーゼ活性化部位、および6アミノ酸 (Ile-Ser-Glu-Phe-Gly-Ser) N末端伸長を組み込んでいる。

【0251】

109 マルトース結合タンパク質-第Xa因子-インティン- LC / B -第Xa因子- H_N 発現構築物をコードするDNA。 20

【0252】

110 配列番号109の発現によって産生される $MBP-LH_N / B$ 、このポリペプチドは、 MBP 精製タグの除去を容易にするための自己切断可能なインティン配列、および $LC-H_N$ 接合部に第Xa因子プロテアーゼ活性化部位を組み込んでいる。

【0253】

111 $LC-H_N$ 接合部 (LC および H_N ドメインの Cys 残基間に11アミノ酸がある) にエンテロキナーゼプロテアーゼ活性化部位、およびベクターのatt部位適合に由来する11アミノ酸 (Thr-Ser-Leu-Tyr-Lys-Lys-Ala-Gly-Phe-Gly-Ser) N末端伸長を組み込んでいる LH_N / B をコードするDNA。この構築物は、フラグメントトリガン 30
ドとの直接融合を容易にするためにC末端停止コドンが除去されている。

【0254】

112 配列番号111の発現によって産生される LH_N / B 、このポリペプチドは、 $LC-H_N$ 接合部 (LC および H_N ドメインの Cys 残基間に11アミノ酸がある) にエンテロキナーゼプロテアーゼ活性化部位、およびベクターのatt部位適合に由来する11アミノ酸 (Thr-Ser-Leu-Tyr-Lys-Lys-Ala-Gly-Phe-Gly-Ser) N末端伸長を組み込んでいる。

【0255】

113 停止コドンを含まず、 H_N ドメインの最初の6アミノ酸を組み込むリンカーペプチド、および Cys 残基によって結合したエンテロキナーゼプロテアーゼ切断部位を有する LC / B をコードするDNA。 40

【0256】

114 配列番号113の発現によって産生される LC / B 、このポリペプチドは、停止コドンを含まず、 H_N ドメインの最初の6アミノ酸を組み込むリンカーペプチド、および Cys 残基によって結合したエンテロキナーゼプロテアーゼ切断部位を有する。

【0257】

115 $LC-H_N$ 接合部に第Xa因子切断部位、ベクターのatt部位適合に由来する11アミノ酸 (Thr-Ser-Leu-Tyr-Lys-Lys-Ala-Gly-Phe-Gly-Ser) N末端伸長、および分子クランピングを容易にするためのC末端 (Glu)₈ ペプチドを組み込んでいる LH_N / C をコードするDNA。

【0258】

1 1 6 配列番号 1 1 5 の発現によって產生される LH_N / C 、このポリペプチドは、 $LC - H_N$ 接合部に第 X a 因子切断部位、ベクターの att 部位適合に由来する 1 1 アミノ酸 (Thr-Ser-Leu-Tyr-Lys-Lys-Ala-Gly-Phe-Gly-Ser) N 末端伸長、および分子クラッピングを容易にするための C 末端 (Glu)₈ ペプチドを組み込んでいる。

【0 2 5 9】

1 1 7 $LC - H_N$ 接合部に第 X a 因子切断部位、ベクターの att 部位適合に由来する 1 1 アミノ酸 (Thr-Ser-Leu-Tyr-Lys-Lys-Ala-Gly-Phe-Gly-Ser) N 末端伸長、および分子クラッピングを容易にするために 1 対の Cys 残基によって結合された C 末端 fos リガンドを組み込んでいる LH_N / C をコードする DNA。

【0 2 6 0】

1 1 8 配列番号 1 1 7 の発現によって產生される LH_N / C 、このポリペプチドは、 $LC - H_N$ 接合部に第 X a 因子切断部位、ベクターの att 部位適合に由来する 1 1 アミノ酸 (Thr-Ser-Leu-Tyr-Lys-Lys-Ala-Gly-Phe-Gly-Ser) N 末端伸長、および分子クラッピングを容易にするために 1 対の Cys 残基によって結合された C 末端 fos リガンドを組み込んでいる。

【0 2 6 1】

1 1 9 $LC - H_N$ 接合部に第 X a 因子切断部位、ベクターの att 部位適合に由来する 1 1 アミノ酸 (Thr-Ser-Leu-Tyr-Lys-Lys-Ala-Gly-Phe-Gly-Ser) N 末端伸長、および分子クラッピングを容易にするために 1 対の Cys 残基によって結合された C 末端 (Glu)₈ ペプチドを組み込んでいる LH_N / C をコードする DNA。

【0 2 6 2】

1 2 0 配列番号 1 1 9 の発現によって產生される LH_N / C 、このポリペプチドは、 $LC - H_N$ 接合部に第 X a 因子切断部位、ベクターの att 部位適合に由来する 1 1 アミノ酸 (Thr-Ser-Leu-Tyr-Lys-Lys-Ala-Gly-Phe-Gly-Ser) N 末端伸長、および分子クラッピングを容易にするために 1 対の Cys 残基によって結合された C 末端 (Glu)₈ ペプチドを組み込んでいる。

【0 2 6 3】

1 2 1 $LC - H_N$ 接合部に第 X a 因子切断部位、ベクターの att 部位適合に由来する 1 1 アミノ酸 (Thr-Ser-Leu-Tyr-Lys-Lys-Ala-Gly-Phe-Gly-Ser) N 末端伸長、および分子クラッピングを容易にするための C 末端 fos リガンドを組み込んでいる LH_N / C をコードする DNA。

【0 2 6 4】

1 2 2 配列番号 1 2 1 の発現によって產生される LH_N / C 、このポリペプチドは、 $LC - H_N$ 接合部に第 X a 因子切断部位、ベクターの att 部位適合に由来する 1 1 アミノ酸 (Thr-Ser-Leu-Tyr-Lys-Lys-Ala-Gly-Phe-Gly-Ser) N 末端伸長、および分子クラッピングを容易にするための C 末端 fos リガンドを組み込んでいる。

【0 2 6 5】

1 2 3 $LC - H_N$ 接合部に第 X a 因子切断部位、およびベクターの att 部位適合に由来する 1 5 アミノ酸 (Ile-Thr-Ser-Leu-Tyr-Lys-Lys-Ala-Gly-Phe-Gly-Ser-Leu-Asp-His) N 末端伸長を組み込んでいる LH_N / C をコードする DNA。

【0 2 6 6】

1 2 4 配列番号 1 2 3 の発現によって產生される LH_N / C 、このポリペプチドは、 $LC - H_N$ 接合部に第 X a 因子切断部位、およびベクターの att 部位適合に由来する 1 5 アミノ酸 (Ile-Thr-Ser-Leu-Tyr-Lys-Lys-Ala-Gly-Phe-Gly-Ser-Leu-Asp-His) N 末端伸長を組み込んでいる。

【0 2 6 7】

1 2 5 $LC - H_N$ 接合部に第 X a 因子切断部位、およびエンテロキナーゼでのタンパク質の切断後に誘導される 1 1 アミノ酸 (Val-Pro-Glu-Phe-Gly-Ser-Ser-Arg-Val-Asp-His) N 末端伸長を組み込んでいる LH_N / C をコードする DNA。

【0 2 6 8】

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1 2 6 配列番号 1 2 5 の発現によって産生される LH_N / C 、このポリペプチドは、 $LC - H_N$ 接合部に第 X a 因子切断部位、および N 末端 MBP 精製タグを遊離させるためにエンテロキナーゼでのタンパク質の切断後に誘導される 1 1 アミノ酸 (Val-Pro-Glu-Phe-Gly-Ser-Ser-Arg-Val-Asp-His) N 末端伸長を組み込んでいる。

【0 2 6 9】

1 2 7 $LC - H_N$ 接合部に第 X a 因子切断部位、およびジェネナーゼでのタンパク質の切断後に誘導される 1 0 アミノ酸 (Val-Glu-Phe-Gly-Ser-Ser-Arg-Val-Asp-His) N 末端伸長を組み込んでいる LH_N / C をコードする DNA。

【0 2 7 0】

1 2 8 配列番号 1 2 7 の発現によって産生される LH_N / C 、このポリペプチドは、 $LC - H_N$ 接合部に第 X a 因子切断部位、および N 末端 MBP 精製タグを遊離させるためにジェネナーゼでのタンパク質の切断後に誘導される 1 0 アミノ酸 (Val-Glu-Phe-Gly-Ser-Ser-Arg-Val-Asp-His) N 末端伸長を組み込んでいる。 10

【0 2 7 1】

1 2 9 $LC - H_N$ 接合部に第 X a 因子切断部位、および第 X a 因子でのタンパク質の切断後に誘導される 1 1 アミノ酸 (Ile-Ser-Glu-Phe-Gly-Ser-Ser-Arg-Val-Asp-His) N 末端伸長を組み込んでいる LH_N / C をコードする DNA。

【0 2 7 2】

1 3 0 配列番号 1 2 9 の発現によって産生される LH_N / C 、このポリペプチドは、 $LC - H_N$ 接合部に第 X a 因子切断部位、および第 X a 因子でのタンパク質の切断後に誘導される 1 1 アミノ酸 (Ile-Ser-Glu-Phe-Gly-Ser-Ser-Arg-Val-Asp-His) N 末端伸長を組み込んでいる。 20

【0 2 7 3】

1 3 1 $LC - H_N$ 接合部に第 X a 因子切断部位、ベクターの att 部位適合に由来する 1 5 アミノ酸 (Ile-Thr-Ser-Leu-Tyr-Lys-Lys-Ala-Gly-Phe-Gly-Ser-Leu-Asp-His) N 末端伸長および 2 1 アミノ酸 (Leu-Gln-Thr-Leu-Asp-Asp-Pro-Ala-Phe-Leu-Tyr-Lys-Val-Val-Ile-Phe-Gln-Asn-Ser-Asp-Pro) C 末端伸長を組み込んでいる LH_N / C をコードする DNA。クロンは、 H_N ドメインの C 末端上へのリガンドの融合を容易にするために停止コドンを含さない。

【0 2 7 4】

1 3 2 配列番号 1 3 1 の発現によって産生される LH_N / C 、このポリペプチドは、 $LC - H_N$ 接合部に第 X a 因子切断部位、ベクターの att 部位適合に由来する 1 5 アミノ酸 (Ile-Thr-Ser-Leu-Tyr-Lys-Lys-Ala-Gly-Phe-Gly-Ser-Leu-Asp-His) N 末端伸長および 2 1 アミノ酸 (Leu-Gln-Thr-Leu-Asp-Asp-Pro-Ala-Phe-Leu-Tyr-Lys-Val-Val-Ile-Phe-Gln-Asn-Ser-Asp-Pro) C 末端伸長を組み込んでいる。クロンは、 H_N ドメインの C 末端上へのリガンドの融合を容易にするために停止コドンを含さない。 30

【0 2 7 5】

1 3 3 $LC - H_N$ 接合部に第 X a 因子切断部位、ベクターの att 部位適合に由来する N 末端伸長および C 末端伸長を組み込んでいる LH_N / C をコードする DNA。クロンは、 H_N ドメインの C 末端上へのリガンドの融合を容易にするために停止コドンを含さない。 40

【0 2 7 6】

1 3 4 Gateway 部位特異的組換えクローニングシステムにおける使用のための pENTRY2 で調製される場合の LC / C をコードする DNA。 LC / C は、組換えによる $LC - H_N$ 融合物の生成を容易にするために停止コドンを含さない。

【0 2 7 7】

1 3 5 Gateway 部位特異的組換えクローニングシステムにおける使用のための pENTRY2 で調製される場合の LH_N / C をコードする DNA。 LH_N / C は、停止コドンを含し、したがって適切な仕向ベクターへの組み込みのための正確な形式である。

【0 2 7 8】

1 3 6 Gateway部位特異的組換えクローニングシステムにおける使用のためのpEN TRY2で調製される場合の LH_N / C をコードするDNA。 LH_N / C は、組換えによる LH_N / C -リガンド融合物の生成を容易にするために停止コドンを含さない。

【0279】

1 3 7 侵入ベクター由来のエンドペプチダーゼフラグメントを挿入するために適切な仕向ベクターであるように改変されたpMTLベクターのDNA配列。ベクターは、pMAL-c2XへのGatewayベクター変換カセットリーディングフレームAの挿入によって構築された。発現カセット（ptacプロモーター、雄遺伝子、Gatewayカセット、およびポリリンカー）は、続いてpMTLにクローニングされた。

【0280】

1 3 8 LH_N / A -リガンド（Erythrina cristagalliレクチン）融合物をコードするDNA、ここで、 $LC-H_N$ 接合部は、特異的エンテロキナーゼプロテアーゼ活性化部位を組み込み、そしてリガンドは、RNアーゼAループ由来のペプチド配列によって H_N ドメインから離れている。

【0281】

1 3 9 配列番号138の発現によって産生される LH_N / A -リガンド（Erythrina cristagalliレクチン）融合物、ここで、 $LC-H_N$ 接合部は、特異的エンテロキナーゼプロテアーゼ活性化部位を組み込み、そしてリガンドは、RNアーゼAループ由来のペプチド配列によって H_N ドメインから離れている。

【0282】

1 4 0 破傷風菌毒素をコードするDNA。

【0283】

1 4 1 配列番号140の発現によって産生される破傷風菌毒素、このポリペプチドは、 LC 、 H_N 、および H_C ドメインを組み込んでいる。

【0284】

1 4 2 破傷風菌毒素の LH_N をコードするDNA、ここで、クローンの3'末端は、配列....Glu-Glu-Asp-Ile-Asp-Val-停止コドンを含し、残基Val879で終わる。

【0285】

1 4 3 配列番号142の発現によって産生される破傷風菌毒素の LH_N 、このポリペプチドは、配列....Glu-Glu-Asp-Ile-Asp-Val-停止コドンで終わり、残基Val879で終わる。

【0286】

1 4 4 破傷風菌毒素の LH_N をコードするDNA、ここで、クローンの3'末端は、配列番号142のような配列....Glu-Glu-Asp-Ile-Asp-Val-停止コドンを含する。クローンはまた、 LC および H_N ドメインの接合部に特異的エンテロキナーゼプロテアーゼ活性化部位を組み込む。

【0287】

1 4 5 配列番号144の発現によって産生される破傷風菌毒素の LH_N 、このポリペプチドは、配列番号143のような配列....Glu-Glu-Asp-Ile-Asp-Val-停止コドンで終わる。タンパク質はまた、 LC および H_N ドメインの接合部に特異的エンテロキナーゼプロテアーゼ活性化部位を組み込む。

【0288】

1 4 6 破傷風菌毒素の LH_N をコードするDNA、ここで、クローンの3'末端は、配列....Glu-Glu-Asp-Ile-Asp-Val-Ile-Leu-Lys-Lys-Ser-Thr-Ile-Leu-停止コドンを含し、残基Leu887で終わる。

【0289】

1 4 7 配列番号146の発現によって産生される破傷風菌毒素の LH_N 、このポリペプチドは、配列....Glu-Glu-Asp-Ile-Asp-Val-Ile-Leu-Lys-Lys-Ser-Thr-Ile-Leu-停止コドンで終わり、残基Leu887で終わる。

【0290】

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1 4 8 ₂ L H_{4 2 3} / A (Q₂ E) をコードする D N A。

【0 2 9 1】

1 4 9 ₂ L H_{4 2 3} / A (Q₂ E)、これは、B o N T / A の L 鎖、および B o N T / A の H 鎖の N 末端の 4 2 3 アミノ酸残基を含む一本鎖ポリペプチドである。このポリペプチドは、G S T 精製タグからの切断により生成し、そして精製タグからの L 鎖のタンパク質分解切断から生じる L 鎖の N 末端における 2 アミノ酸伸長 (G S) を有する。このポリペプチドは、天然の血清型 A の L 鎖における Q と比較して 2 位に改変アミノ酸残基 E を有する。

【0 2 9 2】

1 5 0 ₂ L H_{4 2 3} / A (Q₂ E) をコードする D N A、ここで、D N A は大腸菌コドンバイアスを有する。 10

【0 2 9 3】

1 5 1 ₂ L H_{4 2 3} / A (Q₂ E)、これは、配列番号 1 4 9 と等価である。

【0 2 9 4】

1 5 2 L H_{4 2 3} / A (Q₂ E) をコードする D N A、ここで、D N A は大腸菌コドンバイアスを有する。

【0 2 9 5】

1 5 3 L H_{4 2 3} / A (Q₂ E)、これは、配列番号 1 5 1 と等価であるが、L 鎖へのいずれの N 末端伸長も含まない。

【0 2 9 6】

1 5 4 L H_{4 2 3} / A (Q₂ E) をコードする D N A。 20

【0 2 9 7】

1 5 5 L H_{4 2 3} / A (Q₂ E)、これは、配列番号 1 4 9 と等価であるが、L 鎖へのいずれの N 末端伸長も含まない。

【0 2 9 8】

1 5 6 ₂ L_{F X a} / ₃ H_{4 2 3} / A (Q₂ E) をコードする D N A。

【0 2 9 9】

1 5 7 ₂ L_{F X a} / ₃ H_{4 2 3} / A (Q₂ E)、これは、配列番号 1 5 1 と等価であり、そして第 X a 因子切断部位がポリペプチドの L 鎖成分と H 鎖成分との間に導入されている。 30

【0 3 0 0】

1 5 8 L H_{4 2 3} / A (Q₂ E) - 6 H i s をコードする D N A。

【0 3 0 1】

1 5 9 L H_{4 2 3} / A (Q₂ E) - 6 H i s、これは、天然の L H_N 分子であり、そして C 末端ポリ H i s 精製タグを含む。

【0 3 0 2】

1 6 0 ₂ L_{F X a} / ₃ H_{4 2 3} / A (Q₂ E)_{F X a} - 6 H i s をコードする D N A。

【0 3 0 3】

1 6 1 ₂ L_{F X a} / ₃ H_{4 2 3} / A (Q₂ E)_{F X a} - 6 H i s、これは、配列番号 1 5 7 と等価であり、そしてポリ H i s 精製タグの除去を容易にするために第 X a 因子切断部位を含む。 40

【0 3 0 4】

1 6 2 ₂ L H_{4 2 3} / A (Q₂ E, H_{2 2 7} Y) をコードする D N A。

【0 3 0 5】

1 6 3 ₂ L H_{4 2 3} / A (Q₂ E, H_{2 2 7} Y)、これは、配列番号 1 4 9 と等価であり、そしてポリペプチドは、天然の血清型 A の L 鎖における H と比較して 2 2 7 位に改変アミノ酸残基 Y を有する。

【0 3 0 6】

1 6 4 ₂ L H_{4 2 3} / A (Q₂ E, H_{2 2 7} Y) をコードする D N A、ここで、 50

DNAは大腸菌コドンバイアスを有する。

【0307】

165 2 L H 4 2 3 / A (Q 2 E, H 2 2 7 Y)、これは、配列番号163と等価である。

【0308】

166 2 L H 4 2 3 / A (Q 2 E, E 2 2 4 Q)をコードするDNA、ここで、DNAは大腸菌コドンバイアスを有する。

【0309】

167 2 L H 4 2 3 / A (Q 2 E, E 2 2 4 Q)、これは、配列番号151と等価であり、そしてポリペプチドは、天然の血清型AのL鎖におけるEと比較して224位に改変アミノ酸残基Qを有する。 10

【0310】

168 2 L H 4 2 3 / A (Q 2 E, E 2 2 4 Q, H 2 2 7 Y)をコードするDNA、ここで、DNAは大腸菌コドンバイアスを有する。

【0311】

169 2 L H 4 2 3 / A (Q 2 E, E 2 2 4 Q, H 2 2 7 Y)、これは、配列番号167と等価であり、そしてポリペプチドは、天然の血清型AのL鎖におけるHと比較して227位に改変アミノ酸残基Yを有する。

【0312】

170 L F X a / H 4 1 7 / BをコードするDNA。 20

【0313】

171 L F X a / H 4 1 7 / B、これは、B o N T / BのL鎖、およびB o N T / BのH鎖のN末端の417アミノ酸残基を含む一本鎖ポリペプチドであり、第X a因子切断部位がL鎖とH鎖との間に存在する。

【0314】

172 L F X a / H 4 1 7 / BをコードするDNA。

【0315】

173 L F X a / H 4 1 7 / B、これは、B o N T / BのL鎖、およびB o N T / BのH鎖のN末端の417アミノ酸残基を含む一本鎖ポリペプチドであり、第X a因子切断部位がL鎖とH鎖との間に存在する。 30

【0316】

174 L F X a / H 4 1 7 / BをコードするDNA。

【0317】

175 L F X a / H 4 1 7 / B、これは、配列番号173と等価であり、改変されたリンカー配列が、配列番号173に対してL鎖とH鎖との間に存在する。

【実施例】

【0318】

実施例1

2616塩基対の二本鎖遺伝子配列（配列番号1）を、合成DNA、染色体DNA、およびポリメラーゼ連鎖反応で生成したDNAの組み合わせから組み立てた（図2）。この遺伝子は、軽鎖全体（LC、448アミノ酸）およびボツリヌス菌神経毒素A型の重鎖（H_C）のアミノ末端の423残基に対応する871アミノ酸残基のポリペプチドをコードする。この組換え産物を、L H 4 2 3 / Aフラグメントと命名する（配列番号2）。 40

【0319】

組換え産物の構築

最初の918塩基対の組換え遺伝子を、短いオリゴヌクレオチドの連結によって合成して、大腸菌コドンバイアスを有するコード配列を生成した。この領域における両方のDNA鎖を、短い重複オリゴヌクレオチドとして完全合成し、リン酸化し、アニールし、そしてライゲートして、独特のKpnI制限部位を有する完全合成領域末端を生成した。L H 4 2 3 / Aコード配列の残りを、Clostridium botulinum由来のトータル染色体DNAからP 50

C R 増幅し、そして遺伝子の合成部分にアニールした。

【0320】

次いで、内部PCR増幅産物配列を欠失させ、そして*C. botulinum*染色体起源のクローン由来の天然の完全に配列決定された領域と置換して、最終遺伝子構築物を生成した。最終組成は、合成DNA（塩基1～913）、ポリメラーゼ増幅したDNA（塩基914～1138および1976～2616）、および*C. botulinum*染色体起源である残り（塩基1139～1975）である。次いで、組み立てた遺伝子を完全に配列決定し、そして発現分析用の種々の大腸菌プラスミドベクターにクローニングした。

【0321】

組換え遺伝子の発現およびタンパク質産物の回収

DNAを、99,951ダルトンの推定分子量の可溶性一本鎖ポリペプチドを産生する単一の核酸転写物として、大腸菌で発現させる。遺伝子は、現在は、*Schistosoma japonicum*のグルタチオンS-トランスフェラーゼ（GST）の市販の利用可能なコード配列への融合物として大腸菌で発現されるが、pEZZ18、pTrc99、pFLAG、またはpMALシリーズのような広い範囲の組換え遺伝子発現ベクターのいずれも、グラム陽性桿菌、酵母*P. pastoris*のような他の真核生物または原核生物宿主において、あるいは昆虫または哺乳動物細胞において、適切な条件下での発現と等しく効果的であり得る。

【0322】

現在は、発現構築物を有する大腸菌を、細胞密度（バイオマス）が600nmで0.4～0.6の吸光度を有し、そして細胞が対数増殖中期になるまで、Luria-Bertaniブロス（LBブロス、pH7.0、10g/lのバクトトリプトン、5g/lのバクトイーストエキストラクト、および10g/lの塩化ナトリウムを含む）中で37℃にて増殖させる。次いで、遺伝子の発現を、0.5mMの最終濃度のイソプロピルチオ-β-ガラクトシダーゼ（IPTG）の添加によって誘導する。組換え遺伝子発現は、25℃の低い温度にて90分間行う。次いで、細胞を遠心分離によって回収し、10 mM Na₂HPO₄、0.5 M NaCl、10 mM EGTA、0.25% Tween、pH 7.0を含む緩衝液に再懸濁し、次いで-20℃で凍結する。組換えタンパク質の抽出については、細胞を超音波処理によって破碎する。次いで、細胞抽出物を、遠心分離によって破碎物を取り除き、そして可溶性組換え融合タンパク質（GST-LH₄₂₃/A）を含む澄清になった上清液を、精製するまで-20℃で保存する。組換え体物質の割合は、超音波処理によって放出されることがなく、これはおそらく不溶性または封入体形成を反映する。現在、発明者らは、分析のためにこの物質を抽出しないが、所望であれば、これは、当業者に公知の方法を用いて容易に達成され得る。

【0323】

組換えGST-LH₄₂₃/Aを、市販の調製されたアフィニティマトリクスであるグルタチオンSepharose上への吸着、次いで還元型グルタチオンでの溶出によって精製する。次いで、GSTアフィニティ精製マーカーをタンパク質分解切断およびグルタチオンSepharoseへの再吸着によって除去し；組換えLH₄₂₃/Aを非吸着材料中に回収する。

【0324】

構築物改変体

この分子の改変体であるLH₄₂₃/A（Q₂E, N₂₆K, A₂₇Y）（配列番号26）を、産生した。ここでは、LH₄₂₃/Aの軽鎖内で3つのアミノ酸残基が改変されており、BonT/Aの軽鎖の公表されたアミノ酸配列とは異なる軽鎖配列を含むポリペプチドを産生する。

【0325】

発現させた遺伝子配列および精製した対応する産物のさらに2つの改変体は、BonT/Aの推定の天然のL鎖と比較して23アミノ酸N末端伸長を有する₂₃LH₄₂₃/A（Q₂E, N₂₆K, A₂₇Y）（配列番号4）、および2アミノ酸N末端伸長を有する₂LH₄₂₃/A（Q₂E, N₂₆K, A₂₇Y）（配列番号6）である（図4）。

【0326】

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さらに他の改変体では、配列番号 1 に記載の遺伝子配列のヌクレオチド 1 3 4 4 と 1 3 4 5 との間に Eco 47 III 制限部位を含む遺伝子が産生されている。この改変は、天然の神経毒素において重鎖と軽鎖との界面を示す遺伝子中の位置に制限部位を提供し、そして当業者に公知の標準的な制限酵素方法論を用いてこの点に挿入する能力を提供する。多くの制限部位のいずれか 1 つがこのように用いられ得、そして Eco 47 III 挿入が単にこのアプローチの例示であることはまた、当業者に自明である。同様に、記載の方法での制限部位の挿入が本発明のいずれの遺伝子においても行われ得ることは、当業者に自明である。記載された遺伝子は、発現された場合、ポリペプチド L_{423}/A (配列番号 10) をコードし、これは、天然の BONT/A の重鎖のアミノ末端に等価の位置で LH_{423}/A のアミノ酸 448 と 449 との間に追加の 4 アミノ酸を含む。

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【0327】

遺伝子の改変体を発現させた $L_{FXa}/3H_{423}/A$ (配列番号 12) では、特異的タンパク質分解切断部位を、軽鎖ドメインのカルボキシ末端に、詳細には L_{423}/A の残基 448 の後に組み込んだ。組み込まれた切断部位は、第 Xa 因子プロテアーゼ用であり、そして配列番号 1 の改変によってコードされた。他の特定のプロテアーゼについての切断部位が同様に組み込まれ、そして必要とされる切断部位をコードするあらゆる遺伝子配列が用いられ得ることは、当業者に明らかである。所定のプロテアーゼ部位をコードするためのこの方法での遺伝子配列の改変は、本発明のあらゆる遺伝子において行われ得る。

【0328】

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$L_{FXa}/3H_{423}/A$ の改変体を構築し、ここでは、第 3 ドメインがポリペプチドのカルボキシ末端に存在し、これはポリペプチドに特異的結合活性を組み込む。

【0329】

記載した特定の例は以下のとおりである：

(1) $L_{FXa}/3H_{423}/A-IGF-1$ (配列番号 14)、ここでは、カルボキシ末端ドメインは、インスリン様増殖因子 1 (IGF-1) と等価の配列を有し、そして高い親和性でインスリン様増殖因子レセプターと結合し得る；

(2) $L_{FXa}/3H_{423}/A-CtxA14$ (配列番号 16)、ここでは、カルボキシ末端ドメインは、コレラトキシンの A サブユニット (CtxA) のカルボキシ末端由来の 14 アミノ酸と等価の配列を有し、そしてそれによってコレラトキシン B サブユニットペンタマーと相互作用し得る；および

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(3) $L_{FXa}/3H_{423}/A-ZZ$ (配列番号 18)、ここでは、カルボキシ末端ドメインは、タンデム繰り返し合成 IgG 結合ドメインである。この改変体もまた、本発明に適用可能な他の改変を例示し、すなわち、クロストリジウム菌重鎖配列の末端と結合リガンドをコードする配列との間に位置するプロテアーゼ切断部位をコードする配列の遺伝子に包含される。詳細には、この例では、ジェネラーゼ切断部位をコードするヌクレオチド 2650 ~ 2666 に配列が挿入される。この遺伝子の発現は、 H_N 機能を提供するドメインと結合ドメインとの間の界面に所望のプロテアーゼ感受性を有するポリペプチドを産生する。このような改変は、関連のプロテアーゼでのポリペプチドの処理による C 末端結合ドメインの選択的除去を可能にする。

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【0330】

このような多くの結合ドメインのいずれか 1 つが、本発明のポリペプチド配列に組み込まれ得、そして上記の例がこの概念を単に例示するだけであることは明らかである。同様に、このような結合ドメインは、本発明の基礎であるポリペプチド配列のいずれにも組み込まれ得る。さらに、このような結合ドメインが、本発明のポリペプチド分子内の任意の適切な位置に組み込まれ得ることに留意すべきである。

【0331】

したがって、本発明のさらなる実施態様を、所望の位置に所望の制限エンドヌクレアーゼ部位をさらに含む本発明の DNA によって、および所望の位置に所望のプロテアーゼ切断部位をさらに含む本発明のポリペプチドによって説明する。

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【0332】

制限エンドヌクレアーゼ部位は、本発明のポリペプチドを発現させるための発現ベクターの製造におけるDNAのさらなる操作を容易にするように導入され得；これは、DNAの製造における先の工程の結果として導入され得；これは、公知配列の挿入、置換、または欠失による改変によって導入され得る。DNAの改変の結果、アミノ酸配列は変化しなくてもよく、またはアミノ酸配列が変化して、例えば、所望のプロテアーゼ切断部位の導入を生じててもよく、いずれにせよ、ポリペプチドは、本発明に必要とされる特性を有する第1および第2ドメインを保持する。

【0333】

図10は、発現産物の模式図であり、本実施例に記載の特徴を例示する。詳細には、ボツリヌス菌神経毒素A型の軽鎖に等価のドメインおよびボツリヌス菌神経毒素A型の重鎖のH_Nドメインに等価のドメインを組み込んでいる一本鎖ポリペプチドを示し、N末端伸長は、アフィニティー精製ドメイン、すなわちGSTを提供し、そしてC末端伸長は、リガンド結合ドメイン、すなわちIgG結合ドメインを提供している。ポリペプチドのドメインは、図面に例示するようにドメインの選択的酵素分離を可能にする特異的プロテアーゼ切断部位によって空間的に離されている。この概念は、図11により詳細に記載され、ここでは、種々のプロテアーゼ感受性が例示の目的で定義されている。

【0334】

産物活性のアッセイ

ボツリヌス菌神経毒素A型のLCは、シナプス小胞結合タンパク質SNAP-25に対して亜鉛依存的エンドペプチダーゼ活性を発揮し、これは、特異的な様式で1つのペプチド結合を切断する。₂LH₄₂₃/A(Q₂E, N₂₆K, A₂₇Y)(配列番号6)は、天然の毒素と同じ条件下でインビトロで合成SNAP-25基質を切断する(図3)。したがって、天然の配列に対する₂LH₄₂₃/A(Q₂E, N₂₆K, A₂₇Y)のポリペプチド配列のおよび最小の機能的LCドメイン内での改変は、LCドメインの機能的活性を抑制しない。

【0335】

この活性は、一本鎖ポリペプチド産物をジスルフィド結合した二本鎖種に変換するための組換えGST-₂LH₄₂₃/A(Q₂E, N₂₆K, A₂₇Y)のタンパク質分解改変に依存的である。これは、現在は、タンパク質分解酵素のトリプシンを用いて行われる。組換え産物(100~600μg/ml)を、140 mM NaCl、2.7 mM KCl、10 mM Na₂HPO₄、1.8 mM KH₂PO₄、pH 7.3を含む溶液中で、トリプシン(10μg/ml)とともに37℃にて10~50分間インキュベートする。反応を、100倍モル過剰のトリプシンインヒビターの添加によって停止する。トリプシンによる活性化は、ジスルフィド結合した二本鎖種を生成し、ポリアクリルアミドゲル電気泳動およびポリクロナル抗ボツリヌス菌神経毒素A型抗血清を用いるイムノブロッティング分析によって決定される。

【0336】

₂LH₄₂₃/Aは、トリプシンの存在下でより安定であり、そして₂₃LH₄₂₃/Aよりもインビトロペプチド切断アッセイにおいてより活性である。しかし、両方の改変体とも、インビトロペプチド切断アッセイにおいては完全に機能的である。これは、組換え体分子が、N末端アミノ酸伸長に耐性があり、そしてこれは、当業者に明らかなように、他の化学または有機部分へ広げられ得ることを示す。

【0337】

実施例2

本発明のさらなる例示として、ボツリヌス菌神経毒素B型の軽鎖全体に対応し、そして重鎖のアミノ末端由来の残基の数を変化させているポリペプチドをコードする多くの遺伝子配列が組み立てられている。この開示の例示において、組み立てられた遺伝子配列は、染色体DNAおよびポリメラーゼ連鎖反応で生成したDNAの組み合わせから得られ、したがって天然の遺伝子の等価の領域のヌクレオチド配列を有し、そのためこの開示の物質が天然ならびに合成の遺伝子配列に基づき得るという原理を例示する。

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【0338】

本実施例に関連する遺伝子配列を、Sambrook J、Fritsch E F、およびManiatis T (1989) Molecular Cloning: A Laboratory Manual (第2版)、Ford N、Nolan C、Ferguson M、およびOckler M (編)、Cold Spring Harbor Laboratory Press、New Yorkに詳述されるおよび当業者に公知の方法論を用いて、すべて組み立てて発現させた。

【0339】

神経毒素B型の軽鎖全体(443アミノ酸)および重鎖のアミノ末端由来の728残基に対応する1171アミノ酸のポリペプチドをコードする遺伝子を構築した。この遺伝子の発現は、ポリペプチドLH₇₂₈/B(配列番号20)を産生し、これは、全長BONT/Bの特異的神経結合活性がない。

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【0340】

改変体ポリペプチドLH₄₁₇/B(配列番号22)をコードする遺伝子も組み立てた。これは、天然のLH_N/Aにおける重鎖フラグメントのC末端の配列とのアミノ酸相同性によって等価なアミノ酸配列をそのカルボキシ末端に有する。

【0341】

改変体ポリペプチドLH₁₀₇/B(配列番号24)をコードする遺伝子も組み立てた。これは、発現したポリペプチドの溶解性を維持するために十分なBONT/Bの重鎖のアミノ末端由来の短い配列をそのカルボキシ末端に発現する。

【0342】

構築物改変体

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配列番号21に示す遺伝子の最初の274塩基のコード配列の改変体を産生した。これは、非天然ヌクレオチド配列であるが、天然のポリペプチドをコードする。

【0343】

2つの二本鎖、すなわち268塩基対および951塩基対の遺伝子配列を、重複プライマーPCR方策を用いて生成した。大腸菌コドン使用バイアスを有するように、これらの配列のヌクレオチドバイアスを設計した。

【0344】

第1の配列については、ボツリヌス菌毒素B型についての天然の配列の最初の(5')268ヌクレオチドを示す6個のオリゴヌクレオチドを合成した。第2の配列については、ボツリヌス菌毒素B型についての天然の配列の内部配列のヌクレオチド691~1641を示す23個のオリゴヌクレオチドを合成した。これらのオリゴヌクレオチドは、57~73ヌクレオチドの長さの範囲であった。重複領域である17~20ヌクレオチドを設計して、52~56℃の範囲の融点を得た。さらに、合成産物の末端制限エンドヌクレアーゼ部位を構築して、天然の配列の正確な対応領域へのこれらの産物の挿入を容易にした。268bpの5'合成配列は、元の最初の268塩基の代わりに、配列番号21に示す遺伝子に組み込まれている(そして配列番号27に示される)。同様に、配列は、実施例の他の遺伝子に挿入され得る。

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【0345】

配列番号21のヌクレオチド691~1641に等価であり、そして非天然のコドン使用を用いるが天然のポリペプチド配列をコードする他の改変体配列が、内部合成配列を用いて構築されている。この配列(配列番号28)は、実施例の遺伝子のいずれかにおける等価のコード配列の代わりに、単独でまたは他の改変体配列と組み合わせて組み込まれ得る。

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【0346】

実施例3

本発明の有用性の例は、非毒性かつ有効な免疫源としてである。組換え体である一本鎖物質の非毒性の性質を、GST-LH₄₂₃/Aのマウスへの腹腔内投与によって証明した。ポリペプチドを、上記のように調製しそして精製した。最終調製物中の免疫反応性物質の量を、天然のLH_N/A上のコンホメーション依存的エピトープに対して反応性であるモノクローナル抗体(BA11)を用いる酵素結合免疫吸着アッセイ(ELISA)

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によって決定した。組換え体物質を、リン酸緩衝化生理食塩液（PBS；NaCl 8 g/l、KCl 0.2 g/l、Na₂HPO₄ 1.15 g/l、KH₂PO₄ 0.2 g/l、pH 7.4）中で連続希釈し、0.5ml容量を1群4匹からなる3群のマウスに注射し、各群のマウスは、それぞれ10、5、および1マイクログラムの物質を投与された。マウスを4日間観察し、そして死亡は見られなかった。

【0347】

免疫接種については、フロイント完全アジュバント（初回注射のみ）またはフロイント不完全アジュバントを用いる1.0ml容量の油中水型エマルジョン（1：1 容量：容量）中の20μgのGST-₂LH₄₂₃/Aを、モルモットに2箇所背部皮下注射によって投与した。10日間隔で3回注射し（1日目、10日目、および20日目）、そして30日目に抗血清を採取した。抗血清は、天然のボツリヌス菌神経毒素A型およびその誘導体であるLH_N/Aに対して免疫反応性であることが、ELISAによって示された。1：2000希釈でボツリヌス菌神経毒素反応性である抗血清を、マウスでの中和効率の評価に用いた。中和アッセイについては、0.1mlの抗血清を、2.5mlのゼラチンリン酸緩衝液（GPB；Na₂HPO₄無水物 10 g/l、ゼラチン(Difco) 2 g/l、pH 6.5～6.6）に希釈し、これは0.5μg（5×10⁻⁶g）～5ピコグラム（5×10⁻¹²g）の希釈範囲を含んでいた。0.5mlアリコートのマウスに腹腔内注射し、そして4日間にわたって死亡を記録した。結果を表3および表4に示す。0.5mlの1：40希釈した抗GST-₂LH₄₂₃/A抗血清が、5pg～50ngの範囲のボツリヌス菌神経毒素での腹腔内チャレンジに対してマウスを防御し得ることが明らかに示され得る（1～10,000マウスLD50；1マウスLD50=5pg）。

【0348】

【表3】

モルモット抗GST-₂LH₄₂₃/A抗血清によるマウスにおけるボツリヌス菌神経毒素の中和

ボツリヌス菌毒素/マウス

生存数	0.5μg	0.005μg	0.0005μg	0.5ng	0.005ng	5pg	コントロール (毒素なし)
日数							
1	0	4	4	4	4	4	4
2	-	4	4	4	4	4	4
3	-	4	4	4	4	4	4
4	-	4	4	4	4	4	4

【0349】

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【表 4】

非免疫モルモット抗血清によるマウスにおけるボツリヌス菌神経毒素の中和

ボツリヌス菌毒素/マウス

生存数	0.5 μ g	0.005 μ g	0.0005 μ g	0.5ng	0.005ng	5pg	コントロール (毒素なし)
日数							
1	0	0	0	0	0	2	4
2	-	-	-	-	-	0	4
3	-	-	-	-	-	-	4
4	-	-	-	-	-	-	4

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【0350】

実施例 4—大腸菌における組換え体 LH_{107}/B の発現

ボツリヌス菌神経毒素 A 型以外の血清型のクロストリジウム菌神経毒素の LH_N をコードする核酸の発現の例示として、ポリペプチド LH_{107}/B (配列番号 24) をコードする核酸配列 (配列番号 23) を、市販の入手可能なプラスミド pET28a (Novogen, Madison, WI, USA) に挿入した。この核酸を、N 末端 T7 融合ペプチドとの融合タンパク質として、1 mM の IPTG 誘導下で 37°C にて 90 分間、E. coli BL21 (DE3) (New England BioLabs, Beverly, MA, USA) 中で発現させた。培養物を回収し、そして組換えタンパク質を、 LH_{423}/A についての既述のように抽出した。

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【0351】

組換えタンパク質を回収し、そして T7 タグ精製キット (New England BioLabs, Beverly, MA, USA) を用いる固定化抗 T7 ペプチドモノクローナル抗体への免疫アフィニティー吸着によって細菌ペーストライセートから精製した。精製した組換えタンパク質をグラジエント (4~20%) 変性 SDS ポリアクリルアミドゲル電気泳動 (Novex, San Diego, CA, USA) およびポリクローナル抗ボツリヌス菌神経毒素型抗血清または抗 T7 抗血清を用いるウエスタンブロッティングによって分析した。ウエスタンブロッティング試薬は Novex から購入し、免疫染色したタンパク質を、Amersham から購入した増強化学発光システム (ECL) を用いて可視化した。抗 T7 抗体および抗ボツリヌス菌神経毒素 B 型抗血清に反応性の組換え産物の発現を、図 13 に示す。

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【0352】

組換え体産物は可溶性であり、そしてエンドペプチダーゼ活性の原因である軽鎖の一部を保持していた。

【0353】

したがって、本発明は、特に、免疫源として、酵素標準として、および W0-A-94/21300 に記載される分子の合成のための成分として有用な、組換えポリペプチドを提供する。

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【0354】

実施例 5： $LH_N C$ の発現および精製

天然のクロストリジウム菌神経毒素遺伝子由来の $LH_N C$ DNA フラグメントを、SalI-PstI フラグメントとして、発現ベクター pMal-c2x (New England Biolabs) 中にサブクローニングした。遺伝子フラグメントおよび MBP 融合タンパク質からタンパク質分解プロセッシング後に生成されるタンパク質産物を、配列番号 129/130 に定義する。pET ベクター (Novagen)、pGEX ベクター (Pharmacia)、または pQE ベクター (Qiagen) のような他の市販の入手可能な発現系も、遺伝子フラグメントの発現に適切である。

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【0355】

発現クローンを、コドンATA、AGA、およびCTAについてのtRNA遺伝子を有するpACYCプラスミドを含む宿主株AD494 (Novagen) にトランスファーした (例えば、NovagenからのRosetta株として市販で入手可能)。これらのコドンは大腸菌でめったに使用されないが、神経毒素をコードするクロストリジウム菌遺伝子では頻繁に使用されるので、これらのtRNA遺伝子の含有は、発現レベルを顕著に上昇させる。当業者は、この効果が、LH_N/Cに限定されず、すべての天然のクロストリジウム菌LH_Nフラグメントに広く適用可能であることを認識する。同様の効果を、HMS174 (Novagen) およびTB1 (NEB) を含む他の宿主株で観察し、そして広範な他の宿主がこれらのフラグメントの発現に適切であった。

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【0356】

AD494 (pACYC tRNA) pMalc2x LH_N/Cの発現培養物を、35 μg/ml クロラムフェニコール、100 μg/ml アンピシリン、1 μM ZnCl₂、および0.5% (w/v) グルコースを含むTerrific Broth中で増殖し、一晚培養物を、新鮮な培地で1:100に希釈し、0.6~1のOD₆₀₀になるまで37℃にて約3時間増殖させた。培養物を、1 mM IPTGで誘導し、そして30℃にて3~4時間増殖させた。他の発現系は、抗生物質をカナマイシンに変更したこと以外は同様の条件を用いた。細胞を、カラム緩衝液 (20 mM Hepes 125 mM NaCl 1 mM ZnCl₂ pH 7.2) 中での超音波処理または適切なデタージェント処理 (例えば、Bugduster試薬; Novagen) のいずれかによって溶解し、そして細胞破砕物を遠心分離によってペレットにした。上清タンパク質をカラム緩衝液で平衡化したアミロース樹脂カラムにロードし、そしてタンパク質を、10mMマルトースを含むカラム緩衝液を用いる1段階溶出によって溶出した。

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【0357】

本実施例に用いたMBP-LH_N/C構築物は、MBPとLH_Nドメインとの間に位置する第Xa因子部位を有し、そしてLドメインとH_Nドメインの間にも第Xa因子部位を有して、二本鎖LH_N形態の形成を可能にする。融合タグを除去するためにおよびこの場合にはLH_Nフラグメントを活性化するために、アミロースカラムから溶出したタンパク質を、50 μgの精製した融合タンパク質当たり1ユニットのプロテアーゼ活性の濃度の (製造業者、例えば、NEBによって概説されるように) 第Xa因子で、25℃にて約20時間処理する。次いで、タンパク質を20 mM Hepes pH 7.2で1:5希釈し、そしてQ-sepharose fast flowカラムにロードし、このカラムを洗浄し、そしてタンパク質を20 mM Hepes緩衝液中の25~500mM NaClの直線グラジエントを用いて溶出する。遊離のLH_Nフラグメントを、約50mM NaClで溶出し、そして非切断融合タンパク質および遊離のMBPを、より高濃度のNaClで溶出する。

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【0358】

当業者は、MBPタグの除去のための部位がジェネナーゼであるpMal-c2gのような別の発現ベクターについて、2つのその後のプロテアーゼ切断反応が、融合パートナーの除去 (ジェネナーゼ切断) およびその後のLH_Nの活性化 (第Xa因子消化) に必要とされることを認識する。これらの切断反応は、同時に、あるいは夾雑タンパク質を除去するための中間イオン交換精製とともに行われ得る。精製/活性化のこのモデルの例は、以下で同定される。これらの考察は、配列情報に詳述した天然または合成の活性化部位について、およびすべての血清型のLH_Nフラグメントについて、等しく有効である。

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【0359】

実施例6 LH_N/Fの発現および精製

天然のBoNT/F遺伝子由来のLH_NフラグメントをPCRによって改変して、BamHIおよびHindIII、または他の適切な部位を、5'および3'末端にそれぞれ組み込んだ。遺伝子フラグメントを、pET28にクローニングして、N末端His₆精製タグを有するリーディングフレームを維持した。発現クローンを、実施例5に概説するようなpACYC tRNAプラスミドと、T7ポリメラーゼ遺伝子を有するDE3リゾゲンとを有する宿主株にトランスファーした。適切な宿主株としては、適切な遺伝子エレメントを有するJM109、AD4

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94、HMS174、TB1 TG1、またはBL21が挙げられる。例えば、HMS174 (DE3) pACYC tRNA pET 28a LH_N/Fを、発現および精製に用いた。

【0360】

HMS174 (DE3) pACYC tRNA pET28a LH_N/Fの発現培養物を、35 μg/ml クロラムフェニコール、35 μg/mlカナマイシン、1 μM ZnCl₂、および0.5% (w/v)グルコースを含むTerrific Broth中で、OD₆₀₀が2.0になるまで30℃にて増殖し、そして培養物を500 μM IPTGで誘導し、25℃にて2時間増殖して、遠心分離によって回収した。細胞を、超音波処理またはデタージェント溶解によって20 mM Hepes 500 mM NaCl pH 7.4中で溶解し、そして可溶性タンパク質画分を、CuSO₄をロードした金属キレートカラム（例えば、IMAC HiTrap カラム Amersham-Pharmacia）上にロードした。タンパク質を、イミダゾールの直線グラジエントを用いて溶出し、His₆ LH_N/Fを50~250mMのイミダゾールで溶出した。

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【0361】

His₆ タグを、本質的に実施例5に記載のようにトロンピンでの処理によって除去した。遊離したLH_N フラグメントを、実施例5に記載のQ-sepharoseカラムでのイオン交換を用いて精製した。

【0362】

実施例7 LH_N TeNTの発現および精製

天然のLH_N TeNT遺伝子フラグメントを改変して、天然のリンカー領域を配列番号144/145に示すようにエンテロキナーゼ切断可能リンカーと置換しそして5'末端 (BamHI) および3'末端 (HindIII) にクローニング部位を組み込んだ。このフラグメントを、pMAL c2xにサブクローニングし、そして実施例5に記載のようにHMS174 (pACYC tRNA)中で発現させた。溶出ピークの位置が、遊離のMBPが遊離のLH_Nのピークの前に溶出するように逆転したこと以外は、アミロース樹脂カラムでの最初の精製、融合タグを除去するための第Xa因子での切断、およびイオン交換精製もまた、実施例5に記載のように行った。

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【0363】

実施例8 Gateway適合した発現ベクターからのLH_N/Cの発現

LH_N Cフラグメントを、SalI-PstIとしてGateway侵入ベクターにクローニングした。2つのバージョンを作成し、3' PstI部位内に停止コドンをもつこの位置でタンパク質を停止させた (LH_N C STOP; 配列番号123/124) か、あるいは停止コドンがなくC末端融合パートナーを有するフラグメントの発現を可能にした (LH_N C NS; 配列番号131/132)。侵入ベクターを、仕向ベクターと組換えて、N末端MBPタグを有するフラグメントの発現を可能にした。組換えは、標準的プロトコルに従って行った (Invitrogen Gateway発現マニュアル)。

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【0364】

AD494 (pACYC tRNA) pMTL-malE-GW LH_N C STOP株からの融合タンパク質の発現、およびその精製を、実施例5に記載のように行った。追加のN末端配列の付加は、全体の発現および精製に顕著な変化を起こさなかった。第Xa因子切断後の最終産物は、上記のようにジスルフィド結合した二本鎖フラグメントであった。

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【0365】

追加のC末端ドメインを有するフラグメントの発現のために、LH_N C NS侵入ベクターを付加部位の後かつ適切なフレーム内に付加配列を有する仕向ベクターと組換えた。完全融合物を生成するための組換えを容易にするために必要な特性を有するatt部位に隣接するLH_N/CフラグメントをコードするDNAの配列を、配列番号133に記載する。例えば、仕向ベクターpMTL-malE-GW-att-IGFを、ヒトIGFのコード配列をXbaI-HindIIIフラグメントとして適切な部位にサブクローニングすることによって生成した。このベクターへのLH_N/C NSフラグメントの組換えにより、pMTL-malE-GW-LH_N C-att-IGFを得た。

【0366】

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このクローンを、上記のように発現しそして精製した。C末端 I G F ドメインの結合特性を利用するさらなる精製方法も、所望であれば使用され得る。

【0367】

当業者は、同様のアプローチが B o N T / C または他の血清型のいずれかに由来する他の L H_N フラグメントに使用され得ることを認識する。同様に、他の C 末端精製タグまたはリガンドが、上記の I G F についてと同様に仕向ベクターに組み込まれ得る。

【0368】

実施例 9 Gateway 適合した発現ベクター由来の L H_N T e N T の発現

実施例 7 に記載の L H_N T e N T BamHI-HindIII フラグメントを、適切なリーディングフレームを維持するために侵入ベクターにサブクローニングした。侵入ベクターを、BamHI 10 I 部位に直接隣接する第 X a 因子部位を組み込むように設計し、そのため切断によって、BamHI 部位によってコードされる GlySer 残基で始まるタンパク質を得た。侵入ベクターを、N 末端 6-H i s タグを有する市販の入手可能な仕向ベクター（例えば、pDEST17; Invitrogen）と組換えた。得られたクローン pDEST17 L H_N T e N T を、実施例 6 に記載のように、宿主 HMS174 (pACYC tRNA) 株中で発現させた。融合タンパク質の精製も、実施例 5 に記載のとおりであり、N 末端 H i s タグを第 X a 因子処理で除去し、次いで第 X a 因子を Q-sepharose カラムで除去した。

【0369】

実施例 10 fos/jun または Glu/Arg 分子クランプによる L H_N / B フラグメントとリガンドとの指示カップリング 20

配列番号 115 / 116、117 / 118、119 / 120、および 121 / 122 に記載の型の L H_N / C クローンを、実施例 5 に既述のように発現および精製した。次いで、精製した活性化 L H_N / C タンパク質を、相補クランプパートナー（配列番号 117 / 118 および 121 / 122 については jun タグ付けリガンド；配列番号 115 / 116 および 119 / 120 については ポリアルギニン タグ付けリガンド）でタグ付けした当モル量のリガンドと混合した。タンパク質を穏やかに混合して結合を促進し、次いで精製して、結合したリガンドーエンドペプチダーゼフラグメントを単離した。

【0370】

実施例 11 酸 / 塩基分子クランプによる L H_N T e N T フラグメントとリガンドとの指示カップリング 30

配列番号 142 / 143、144 / 145、および 146 / 147 に記載の型の L H_N T e N T クローンを改変して、酸 / 塩基ロイシンジッパークランプシステムの一部を組み込んだ。実施例 5 に既述のようにタグ付けしたタンパク質の発現および精製後、タグ付けしたリガンドとの結合を、本質的に実施例 10 に記載のように行った。

【0371】

実施例 12 二本鎖フラグメントを得るための、トロンビンプロテアーゼプロセッシング部位を有する L H_N / B の活性化

配列番号 99 / 100 のように、L ドメインと H_N ドメインとの間のリンカーにトロンビン部位を有する L H_N / B を、本質的に実施例 5 に記載のよう pMAL c2x から発現させた。精製した L H_N / B フラグメントを、1 mg タンパク質あたり 1 ユニットのトロンビン 40 とともに 25°C にて 20 時間インキュベートした。実施例 5 に記載のよう Q-sepharose カラムでのさらなる精製によって、二本鎖 L H_N をトロンビンと分離した。

【0372】

実施例 13 二本鎖フラグメントを得るための、エンテロキナーゼプロセッシング部位を有する L H_N T e N T の活性化

活性化した二本鎖 L H_N を調製するために、精製したタンパク質（例えば、配列番号 144 / 145 から得られる）を、50 μg の精製タンパク質あたり 1 酵素ユニットの濃度のエンテロキナーゼで、25°C にて 20 時間処理した。次いで、活性化した二本鎖 L H_N を、（実施例 5 に記載のよう）第 X a 因子切断後の精製に用いたのと同条件下で Q-sepharose カラムでのイオン交換によって、あるいは、エンテロキナーゼに特異的に結合して除去 50

するための20 mM Hepes 100 mM NaCl pH 7.2中で平衡化したベンズアミジンセファロースカラムを用いて、エンテロキナーゼから精製した。

【図面の簡単な説明】

【0373】

【図1】ボツリヌス菌神経毒素A型（BoNT/A）のドメイン構造の模式図を示す。

【図2】 LH_{423}/A と命名した本発明の実施態様についての遺伝子のアセンブリの模式図を示す。

【図3】インビトロペプチド切断アッセイにおいて、天然の毒素、トリプシンで生成した「天然の」 LH_N/A 、および ${}_2LH_{423}/A$ （ Q_2E ， $N_{26}K$ ， $A_{27}Y$ ）と命名した本発明の実施態様の活性を比較するグラフである。

【図4】天然の毒素の公表された配列の最初の33アミノ酸と本発明の実施態様との比較である。

【図5】 $L/{}_4H_{423}/A$ と命名された本発明の実施態様の転位領域を示し、 H_N 配列のN末端の4つのアミノ酸の挿入を示す；Eco 47 III制限エンドヌクレアーゼ切断部位によってコードされるアミノ酸に印をつけ、そして H_N 配列は $ALN...$ で始まる。

【図6】 $L_{FXa}/{}_3H_{423}/A$ と命名された本発明の実施態様の転位領域を示し、L鎖のC末端の第Xa因子切断部位の挿入、およびH配列のN末端にコードされる3つの付加アミノ酸を示す；切断活性化した H_N のN末端アミノ酸はシステインである。

【図7】融合タンパク質である $L_{FXa}/{}_3H_{423}/A-IGF-1$ と命名された本発明の実施態様のアミノ酸配列のC末端部分を示す；IGF-1配列は G_{882} 位で始まる。

【図8】融合タンパク質である $L_{FXa}/{}_3H_{423}/A-CtxA14$ と命名された本発明の実施態様のアミノ酸配列のC末端部分を示す；C末端CtxA配列は Q_{882} 位で始まる。

【図9】融合タンパク質である $L_{FXa}/{}_3H_{423}/A-ZZ$ と命名された本発明の実施態様のアミノ酸配列のC末端部分を示す；C末端ZZ配列は、ジェネナーゼ認識部位（下線）のすぐ後の A_{890} 位で始まる。

【図10】本発明のポリペプチドの操作の模式図を示す；アフィニティー精製ペプチド（この場合はGST）のN末端付加およびIg結合ドメインのC末端付加を有する LH_{423}/A を示す；プロテアーゼ切断部位R1、R2、およびR3は、ドメインの選択的酵素分離を可能にする。

【図11】本発明のポリペプチドの操作の模式図を示す；プロテアーゼ切断部位R1、R2、およびR3ならびにC末端融合ペプチド配列の特定の例を示す。

【図12】本発明のポリペプチドのトリプシン感受性活性化領域を示す。

【図13】大腸菌から発現した組換え LH_{107}/B のウェスタンブロット分析を示す；パネルAは、抗BoNT/B抗血清でプローブした；レーン1、分子量標準；レーン2および3、天然のBoNT/B；レーン4、免疫精製した LH_{107}/B ；パネルBは、抗T7ペプチドタグ抗血清でプローブした；レーン1、分子量標準；レーン2および3、陽性コントロールの大腸菌T7発現；レーン4、免疫精製した LH_{107}/B 。

【図14】本発明の融合タンパク質を示し、この融合タンパク質は、精製タグ（TAG）と第1ドメイン（L鎖）との間に2つの異なるタンパク質分解切断部位（E1およびE2）を含み、そして第1ドメイン（L鎖）と第2ドメイン（ H_N ）との間に二重のタンパク質分解切断部位（E2）を含む。E2プロテアーゼの使用により、2つの所定のE2切断部位での同時切断が生じて、第1および第2ドメインを含む二本鎖ポリペプチド分子を残すが、E1プロテアーゼの使用により、単一の所定のE1切断部位での切断が生じて、第1および第2ドメインを含む単一のポリペプチド鎖分子が残る。

【図15】第1および第2ドメイン（例えば、 LH_N ）を含むポリペプチドと、第3ドメイン（例えば、リガンド）を含む第2分子とを一緒に融合するための分子クランピング技術の使用を示す。

【配列表】

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SEQUENCE LISTING

<110> Health Protection Agency
 Shone, Clifford
 Quinn, Conrad
 Foster, Keith
 Chaddock, John
 Marks, Philip
 Sutton, Mark
 Stancombe, Patrick
 Wayne, Jonathan

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Leu Asp Lys Tyr Thr Met Phe His Tyr Leu Arg Ala Gln Glu Phe Glu
 545 550 555 560
 His Gly Lys Ser Arg Ile Ala Leu Thr Asn Ser Val Asn Glu Ala Leu
 565 570 575
 Leu Asn Pro Ser Arg Val Tyr Thr Phe Phe Ser Ser Asp Tyr Val Lys
 580 585 590
 Lys Val Asn Lys Ala Thr Glu Ala Ala Met Phe Leu Gly Trp Val Glu
 595 600 605
 Gln Leu Val Tyr Asp Phe Thr Asp Glu Thr Ser Glu Val Ser Thr Thr
 610 615 620
 Asp Lys Ile Ala Asp Ile Thr Ile Ile Ile Pro Tyr Ile Gly Pro Ala
 625 630 635 640
 Leu Asn Ile Gly Asn Met Leu Tyr Lys Asp Asp Phe Val Gly Ala Leu
 645 650 655
 Ile Phe Ser Gly Ala Val Ile Leu Leu Glu Phe Ile Pro Glu Ile Ala
 660 665 670
 Ile Pro Val Leu Gly Thr Phe Ala Leu Val Ser Tyr Ile Ala Asn Lys
 675 680 685
 Val Leu Thr Val Gln Thr Ile Asp Asn Ala Leu Ser Lys Arg Asn Glu
 690 695 700
 Lys Trp Asp Glu Val Tyr Lys Tyr Ile Val Thr Asn Trp Leu Ala Lys
 705 710 715 720
 Val Asn Thr Gln Ile Asp Leu Ile Arg Lys Lys Met Lys Glu Ala Leu
 725 730 735
 Glu Asn Gln Ala Glu Ala Thr Lys Ala Ile Ile Asn Tyr Gln Tyr Asn
 740 745 750
 Gln Tyr Thr Glu Glu Glu Lys Asn Asn Ile Asn Phe Asn Ile Asp Asp
 755 760 765
 Leu Ser Ser Lys Leu Asn Glu Ser Ile Asn Lys Ala Met Ile Asn Ile
 770 775 780
 Asn Lys Phe Leu Asn Gln Cys Ser Val Ser Tyr Leu Met Asn Ser Met
 785 790 795 800
 Ile Pro Tyr Gly Val Lys Arg Leu Glu Asp Phe Asp Ala Ser Leu Lys
 805 810 815

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Asp Ala Leu Leu Lys Tyr Ile Tyr Asp Asn Arg Gly Thr Leu Ile Gly
820 825 830

Gln Val Asp Arg Leu Lys Asp Lys Val Asn Asn Thr Leu Ser Thr Asp
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Thr Phe Thr Glu Tyr Ile Lys
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<213> Clostridium botulinum

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gaa ttc gag ctc ccg ggt acc atg gag ttc gtg aac aag cag ttc aac 96
Glu Phe Glu Leu Pro Gly Thr Met Glu Phe Val Asn Lys Gln Phe Asn
20 25 30
tat aag gac cct gta aac ggt gtt gac att gcc tac atc aaa att cca 144
Tyr Lys Asp Pro Val Asn Gly Val Asp Ile Ala Tyr Ile Lys Ile Pro
35 40 45
aag tac ggc cag atg cag ccg gtg aag gct ttc aag att cat aac aaa 192
Lys Tyr Gly Gln Met Gln Pro Val Lys Ala Phe Lys Ile His Asn Lys
50 55 60
atc tgg gtt att ccg gaa cgc gat aca ttt acg aac ccg gaa gaa gga 240
Ile Trp Val Ile Pro Glu Arg Asp Thr Phe Thr Asn Pro Glu Glu Gly
65 70 75 80
gac ttg aac ccg ccg ccg gaa gca aag cag gtg cca gtt tca tac tac 288
Asp Leu Asn Pro Pro Pro Glu Ala Lys Gln Val Pro Val Ser Tyr Tyr
85 90 95
gat tca acc tat ctg agc aca gac aac gag aag gat aac tac ctg aag 336
Asp Ser Thr Tyr Leu Ser Thr Asp Asn Glu Lys Asp Asn Tyr Leu Lys
100 105 110
gga gtg acc aaa tta ttc gag cgt att tat tcc act gac ctg ggc cgt 384
Gly Val Thr Lys Leu Phe Glu Arg Ile Tyr Ser Thr Asp Leu Gly Arg
115 120 125
atg ctg ctg acc tca atc gtc cgc gga atc cca ttt tgg ggt ggc agt 432
Met Leu Leu Thr Ser Ile Val Arg Gly Ile Pro Phe Trp Gly Gly Ser
130 135 140
acc att gac acg gag ttg aag gtt att gac act aac tgc att aac gtg 480
Thr Ile Asp Thr Glu Leu Lys Val Ile Asp Thr Asn Cys Ile Asn Val

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145	150	155	160	
atc caa cca gac ggt agc tac aga tct gaa gaa ctt aac ctc gta atc Ile Gln Pro Asp Gly Ser Tyr Arg Ser Glu Glu Leu Asn Leu Val Ile	165	170	175	528
atc ggg ccc tcc gcg gac att atc cag ttt gag tgc aag agc ttt ggc Ile Gly Pro Ser Ala Asp Ile Ile Gln Phe Glu Cys Lys Ser Phe Gly	180	185	190	576
cac gaa gtg ttg aac ctg acg cgt aac ggt tac ggc tct act cag tac His Glu Val Leu Asn Leu Thr Arg Asn Gly Tyr Gly Ser Thr Gln Tyr	195	200	205	624
att cgt ttc agc cca gac ttc acg ttc ggt ttc gag gag agc ctg gag Ile Arg Phe Ser Pro Asp Phe Thr Phe Gly Phe Glu Glu Ser Leu Glu	210	215	220	672
gtt gat acc aac ccg ctg ttg ggt gca ggc aag ttc gca act gat cca Val Asp Thr Asn Pro Leu Leu Gly Ala Gly Lys Phe Ala Thr Asp Pro	225	230	235	720
gcg gtg acc ctg gca cac gag ctg atc cac gcc ggt cat cgt ctg tat Ala Val Thr Leu Ala His Glu Leu Ile His Ala Gly His Arg Leu Tyr	245	250	255	768
ggc att gcg att aac ccg aac cgc gtg ttc aag gtt aac acc aac gcc Gly Ile Ala Ile Asn Pro Asn Arg Val Phe Lys Val Asn Thr Asn Ala	260	265	270	816
tac tac gag atg agt ggt tta gaa gta agc ttc gag gaa ctg cgc acg Tyr Tyr Glu Met Ser Gly Leu Glu Val Ser Phe Glu Glu Leu Arg Thr	275	280	285	864
ttc ggt ggc cat gat gcg aag ttt atc gac agc ttg cag gag aac gag Phe Gly Gly His Asp Ala Lys Phe Ile Asp Ser Leu Gln Glu Asn Glu	290	295	300	912
ttc cgt ctg tac tac tac aac aag ttt aaa gat att gca agt aca ctg Phe Arg Leu Tyr Tyr Tyr Asn Lys Phe Lys Asp Ile Ala Ser Thr Leu	305	310	315	960
aac aag gct aag tcc att gtg ggt acc act gct tca tta cag tat atg Asn Lys Ala Lys Ser Ile Val Gly Thr Thr Ala Ser Leu Gln Tyr Met	325	330	335	1008
aaa aat gtt ttt aaa gag aaa tat ctc cta tct gaa gat aca tct gga Lys Asn Val Phe Lys Glu Lys Tyr Leu Leu Ser Glu Asp Thr Ser Gly	340	345	350	1056
aaa ttt tcc gta gat aaa tta aaa ttt gat aag tta tac aaa atg tta Lys Phe Ser Val Asp Lys Leu Lys Phe Asp Lys Leu Tyr Lys Met Leu	355	360	365	1104
aca gag att tac aca gag gat aat ttt gtt aag ttt ttt aaa gta ctt Thr Glu Ile Tyr Thr Glu Asp Asn Phe Val Lys Phe Phe Lys Val Leu	370	375	380	1152
aac aga aaa aca tat ttg aat ttt gat aaa gcc gta ttt aag ata aat Asn Arg Lys Thr Tyr Leu Asn Phe Asp Lys Ala Val Phe Lys Ile Asn	385	390	395	1200
ata gta cct aag gta aat tac aca ata tat gat gga ttt aat tta aga Ile Val Pro Lys Val Asn Tyr Thr Ile Tyr Asp Gly Phe Asn Leu Arg	405	410	415	1248

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aat aca aat tta gca gca aac ttt aat ggt caa aat aca gaa att aat Asn Thr Asn Leu Ala Ala Asn Phe Asn Gly Gln Asn Thr Glu Ile Asn 420 425 430	1296
aat atg aat ttt act aaa cta aaa aat ttt act gga ttg ttt gaa ttt Asn Met Asn Phe Thr Lys Leu Lys Asn Phe Thr Gly Leu Phe Glu Phe 435 440 445	1344
tat aag ttg cta tgt gta aga ggg ata ata act tct aaa act aaa tca Tyr Lys Leu Leu Cys Val Arg Gly Ile Ile Thr Ser Lys Thr Lys Ser 450 455 460	1392
tta gat aaa gga tac aat aag gca tta aat gat tta tgt atc aaa gtt Leu Asp Lys Gly Tyr Asn Lys Ala Leu Asn Asp Leu Cys Ile Lys Val 465 470 475 480	1440
aat aat tgg gac ttg ttt ttt agt cct tca gaa gat aat ttt act aat Asn Asn Trp Asp Leu Phe Phe Ser Pro Ser Glu Asp Asn Phe Thr Asn 485 490 495	1488
gat cta aat aaa gga gaa gaa att aca tct gat act aat ata gaa gca Asp Leu Asn Lys Gly Glu Glu Ile Thr Ser Asp Thr Asn Ile Glu Ala 500 505 510	1536
gca gaa gaa aat att agt tta gat tta ata caa caa tat tat tta acc Ala Glu Glu Asn Ile Ser Leu Asp Leu Ile Gln Gln Tyr Tyr Leu Thr 515 520 525	1584
ttt aat ttt gat aat gaa cct gaa aat att tca ata gaa aat ctt tca Phe Asn Phe Asp Asn Glu Pro Glu Asn Ile Ser Ile Glu Asn Leu Ser 530 535 540	1632
agt gac att ata ggc caa tta gaa ctt atg cct aat ata gaa aga ttt Ser Asp Ile Ile Gly Gln Leu Glu Leu Met Pro Asn Ile Glu Arg Phe 545 550 555 560	1680
cct aat gga aaa aag tat gag tta gat aaa tat act atg ttc cat tat Pro Asn Gly Lys Lys Tyr Glu Leu Asp Lys Tyr Thr Met Phe His Tyr 565 570 575	1728
ctt cgt gct caa gaa ttt gaa cat ggt aaa tct agg att gct tta aca Leu Arg Ala Gln Glu Phe Glu His Gly Lys Ser Arg Ile Ala Leu Thr 580 585 590	1776
aat tct gtt aac gaa gca tta tta aat cct agt cgt gtt tat aca ttt Asn Ser Val Asn Glu Ala Leu Leu Asn Pro Ser Arg Val Tyr Thr Phe 595 600 605	1824
ttt tct tca gac tat gta aag aaa gtt aat aaa gct acg gag gca gct Phe Ser Ser Asp Tyr Val Lys Lys Val Asn Lys Ala Thr Glu Ala Ala 610 615 620	1872
atg ttt tta ggc tgg gta gaa caa tta gta tat gat ttt acc gat gaa Met Phe Leu Gly Trp Val Glu Gln Leu Val Tyr Asp Phe Thr Asp Glu 625 630 635 640	1920
act agc gaa gta agt act acg gat aaa att gcg gat ata act ata att Thr Ser Glu Val Ser Thr Thr Asp Lys Ile Ala Asp Ile Thr Ile Ile 645 650 655	1968
att cca tat ata gga cct gct tta aat ata ggt aat atg tta tat aaa Ile Pro Tyr Ile Gly Pro Ala Leu Asn Ile Gly Asn Met Leu Tyr Lys 660 665 670	2016
gat gat ttt gta ggt gct tta ata ttt tca gga gct gtt att ctg tta Asp Asp Phe Val Gly Ala Leu Ile Phe Ser Gly Ala Val Ile Leu Leu 675 680 685 690	2064

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675	680	685	
gaa ttt ata cca gag att gca ata cct gta tta ggt act ttt gca ctt Glu Phe Ile Pro Glu Ile Ala Ile Pro Val Leu Gly Thr Phe Ala Leu 690 695 700			2112
gta tca tat att gcg aat aag gtt cta acc gtt caa aca ata gat aat Val Ser Tyr Ile Ala Asn Lys Val Leu Thr Val Gln Thr Ile Asp Asn 705 710 715 720			2160
gct tta agt aaa aga aat gaa aaa tgg gat gag gtc tat aaa tat ata Ala Leu Ser Lys Arg Asn Glu Lys Trp Asp Glu Val Tyr Lys Tyr Ile 725 730 735			2208
gta aca aat tgg tta gca aag gtt aat aca cag att gat cta ata aga Val Thr Asn Trp Leu Ala Lys Val Asn Thr Gln Ile Asp Leu Ile Arg 740 745 750			2256
aaa aaa atg aaa gaa gct tta gaa aat caa gca gaa gca aca aag gct Lys Lys Met Lys Glu Ala Leu Glu Asn Gln Ala Glu Ala Thr Lys Ala 755 760 765			2304
ata ata aac tat cag tat aat caa tat act gag gaa gag aaa aat aat Ile Ile Asn Tyr Gln Tyr Asn Gln Tyr Thr Glu Glu Glu Lys Asn Asn 770 775 780			2352
att aat ttt aat att gat gat tta agt tcg aaa ctt aat gag tct ata Ile Asn Phe Asn Ile Asp Asp Leu Ser Ser Lys Leu Asn Glu Ser Ile 785 790 795 800			2400
aat aaa gct atg att aat ata aat aaa ttt ttg aat caa tgc tct gtt Asn Lys Ala Met Ile Asn Ile Asn Lys Phe Leu Asn Gln Cys Ser Val 805 810 815			2448
tca tat tta atg aat tct atg atc cct tat ggt gtt aaa cgg tta gaa Ser Tyr Leu Met Asn Ser Met Ile Pro Tyr Gly Val Lys Arg Leu Glu 820 825 830			2496
gat ttt gat gct agt ctt aaa gat gca tta tta aag tat ata tat gat Asp Phe Asp Ala Ser Leu Lys Asp Ala Leu Leu Lys Tyr Ile Tyr Asp 835 840 845			2544
aat aga gga act tta att ggt caa gta gat aga tta aaa gat aaa gtt Asn Arg Gly Thr Leu Ile Gly Gln Val Asp Arg Leu Lys Asp Lys Val 850 855 860			2592
aat aat aca ctt agt aca gat ata cct ttt cag ctt tcc aaa tac gta Asn Asn Thr Leu Ser Thr Asp Ile Pro Phe Gln Leu Ser Lys Tyr Val 865 870 875 880			2640
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 Tyr Lys Asp Pro Val Asn Gly Val Asp Ile Ala Tyr Ile Lys Ile Pro
 35 40 45
 Lys Tyr Gly Gln Met Gln Pro Val Lys Ala Phe Lys Ile His Asn Lys
 50 55 60
 Ile Trp Val Ile Pro Glu Arg Asp Thr Phe Thr Asn Pro Glu Glu Gly
 65 70 75 80
 Asp Leu Asn Pro Pro Pro Glu Ala Lys Gln Val Pro Val Ser Tyr Tyr
 85 90 95
 Asp Ser Thr Tyr Leu Ser Thr Asp Asn Glu Lys Asp Asn Tyr Leu Lys
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 Gly Val Thr Lys Leu Phe Glu Arg Ile Tyr Ser Thr Asp Leu Gly Arg
 115 120 125
 Met Leu Leu Thr Ser Ile Val Arg Gly Ile Pro Phe Trp Gly Gly Ser
 130 135 140
 Thr Ile Asp Thr Glu Leu Lys Val Ile Asp Thr Asn Cys Ile Asn Val
 145 150 155 160
 Ile Gln Pro Asp Gly Ser Tyr Arg Ser Glu Glu Leu Asn Leu Val Ile
 165 170 175
 Ile Gly Pro Ser Ala Asp Ile Ile Gln Phe Glu Cys Lys Ser Phe Gly
 180 185 190
 His Glu Val Leu Asn Leu Thr Arg Asn Gly Tyr Gly Ser Thr Gln Tyr
 195 200 205
 Ile Arg Phe Ser Pro Asp Phe Thr Phe Gly Phe Glu Glu Ser Leu Glu
 210 215 220
 Val Asp Thr Asn Pro Leu Leu Gly Ala Gly Lys Phe Ala Thr Asp Pro
 225 230 235 240
 Ala Val Thr Leu Ala His Glu Leu Ile His Ala Gly His Arg Leu Tyr
 245 250 255
 Gly Ile Ala Ile Asn Pro Asn Arg Val Phe Lys Val Asn Thr Asn Ala
 260 265 270
 Tyr Tyr Glu Met Ser Gly Leu Glu Val Ser Phe Glu Glu Leu Arg Thr
 275 280 285

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Phe Gly Gly His Asp Ala Lys Phe Ile Asp Ser Leu Gln Glu Asn Glu
 290 295 300
 Phe Arg Leu Tyr Tyr Tyr Asn Lys Phe Lys Asp Ile Ala Ser Thr Leu
 305 310 315 320
 Asn Lys Ala Lys Ser Ile Val Gly Thr Thr Ala Ser Leu Gln Tyr Met
 325 330 335
 Lys Asn Val Phe Lys Glu Lys Tyr Leu Leu Ser Glu Asp Thr Ser Gly
 340 345 350
 Lys Phe Ser Val Asp Lys Leu Lys Phe Asp Lys Leu Tyr Lys Met Leu
 355 360 365
 Thr Glu Ile Tyr Thr Glu Asp Asn Phe Val Lys Phe Phe Lys Val Leu
 370 375 380
 Asn Arg Lys Thr Tyr Leu Asn Phe Asp Lys Ala Val Phe Lys Ile Asn
 385 390 395 400
 Ile Val Pro Lys Val Asn Tyr Thr Ile Tyr Asp Gly Phe Asn Leu Arg
 405 410 415
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 Asn Met Asn Phe Thr Lys Leu Lys Asn Phe Thr Gly Leu Phe Glu Phe
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 Tyr Lys Leu Leu Cys Val Arg Gly Ile Ile Thr Ser Lys Thr Lys Ser
 450 455 460
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 465 470 475 480
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 485 490 495
 Asp Leu Asn Lys Gly Glu Glu Ile Thr Ser Asp Thr Asn Ile Glu Ala
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 Ala Glu Glu Asn Ile Ser Leu Asp Leu Ile Gln Gln Tyr Tyr Leu Thr
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 Ser Asp Ile Ile Gly Gln Leu Glu Leu Met Pro Asn Ile Glu Arg Phe

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545 550 555 560
 Pro Asn Gly Lys Lys Tyr Glu Leu Asp Lys Tyr Thr Met Phe His Tyr
 565 570 575
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 580 585 590
 Asn Ser Val Asn Glu Ala Leu Leu Asn Pro Ser Arg Val Tyr Thr Phe
 595 600 605
 Phe Ser Ser Asp Tyr Val Lys Lys Val Asn Lys Ala Thr Glu Ala Ala
 610 615 620
 Met Phe Leu Gly Trp Val Glu Gln Leu Val Tyr Asp Phe Thr Asp Glu
 625 630 635 640
 Thr Ser Glu Val Ser Thr Thr Asp Lys Ile Ala Asp Ile Thr Ile Ile
 645 650 655
 Ile Pro Tyr Ile Gly Pro Ala Leu Asn Ile Gly Asn Met Leu Tyr Lys
 660 665 670
 Asp Asp Phe Val Gly Ala Leu Ile Phe Ser Gly Ala Val Ile Leu Leu
 675 680 685
 Glu Phe Ile Pro Glu Ile Ala Ile Pro Val Leu Gly Thr Phe Ala Leu
 690 695 700
 Val Ser Tyr Ile Ala Asn Lys Val Leu Thr Val Gln Thr Ile Asp Asn
 705 710 715 720
 Ala Leu Ser Lys Arg Asn Glu Lys Trp Asp Glu Val Tyr Lys Tyr Ile
 725 730 735
 Val Thr Asn Trp Leu Ala Lys Val Asn Thr Gln Ile Asp Leu Ile Arg
 740 745 750
 Lys Lys Met Lys Glu Ala Leu Glu Asn Gln Ala Glu Ala Thr Lys Ala
 755 760 765
 Ile Ile Asn Tyr Gln Tyr Asn Gln Tyr Thr Glu Glu Glu Lys Asn Asn
 770 775 780
 Ile Asn Phe Asn Ile Asp Asp Leu Ser Ser Lys Leu Asn Glu Ser Ile
 785 790 795 800
 Asn Lys Ala Met Ile Asn Ile Asn Lys Phe Leu Asn Gln Cys Ser Val
 805 810 815

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Ser Tyr Leu Met Asn Ser Met Ile Pro Tyr Gly Val Lys Arg Leu Glu
820 825 830

Asp Phe Asp Ala Ser Leu Lys Asp Ala Leu Leu Lys Tyr Ile Tyr Asp
835 840 845

Asn Arg Gly Thr Leu Ile Gly Gln Val Asp Arg Leu Lys Asp Lys Val
850 855 860

Asn Asn Thr Leu Ser Thr Asp Ile Pro Phe Gln Leu Ser Lys Tyr Val
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aac ggt gtt gac att gcc tac atc aaa att cca aag tac ggc cag atg 96
Asn Gly Val Asp Ile Ala Tyr Ile Lys Ile Pro Lys Tyr Gly Gln Met
20 25 30
cag ccg gtg aag gct ttc aag att cat aac aaa atc tgg gtt att ccg 144
Gln Pro Val Lys Ala Phe Lys Ile His Asn Lys Ile Trp Val Ile Pro
35 40 45
gaa cgc gat aca ttt acg aac ccg gaa gaa gga gac ttg aac ccg ccg 192
Glu Arg Asp Thr Phe Thr Asn Pro Glu Glu Gly Asp Leu Asn Pro Pro
50 55 60
ccg gaa gca aag cag gtg cca gtt tca tac tac gat tca acc tat ctg 240
Pro Glu Ala Lys Gln Val Pro Val Ser Tyr Tyr Asp Ser Thr Tyr Leu
65 70 75 80
agc aca gac aac gag aag gat aac tac ctg aag gga gtg acc aaa tta 288
Ser Thr Asp Asn Glu Lys Asp Asn Tyr Leu Lys Gly Val Thr Lys Leu
85 90 95
ttc gag cgt att tat tcc act gac ctg ggc cgt atg ctg ctg acc tca 336
Phe Glu Arg Ile Tyr Ser Thr Asp Leu Gly Arg Met Leu Leu Thr Ser
100 105 110
atc gtc cgc gga atc cca ttt tgg ggt ggc agt acc att gac acg gag 384
Ile Val Arg Gly Ile Pro Phe Trp Gly Gly Ser Thr Ile Asp Thr Glu
115 120 125
ttg aag gtt att gac act aac tgc att aac gtg atc caa cca gac ggt 432
Leu Lys Val Ile Asp Thr Asn Cys Ile Asn Val Ile Gln Pro Asp Gly
130 135 140

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gac att atc cag ttt gag tgc aag agc ttt ggc cac gaa gtg ttg aac Asp Ile Ile Gln Phe Glu Cys Lys Ser Phe Gly His Glu Val Leu Asn 165 170 175	528	
ctg acg cgt aac ggt tac ggc tct act cag tac att cgt ttc agc cca Leu Thr Arg Asn Gly Tyr Gly Ser Thr Gln Tyr Ile Arg Phe Ser Pro 180 185 190	576	
gac ttc acg ttc ggt ttc gag gag agc ctg gag gtt gat acc aac ccg Asp Phe Thr Phe Gly Phe Glu Glu Ser Leu Glu Val Asp Thr Asn Pro 195 200 205	624	10
ctg ttg ggt gca ggc aag ttc gca act gat cca gcg gtg acc ctg gca Leu Leu Gly Ala Gly Lys Phe Ala Thr Asp Pro Ala Val Thr Leu Ala 210 215 220	672	
cac gag ctg atc cac gcc ggt cat cgt ctg tat ggc att gcg att aac His Glu Leu Ile His Ala Gly His Arg Leu Tyr Gly Ile Ala Ile Asn 225 230 235 240	720	
ccg aac cgc gtg ttc aag gtt aac acc aac gcc tac tac gag atg agt Pro Asn Arg Val Phe Lys Val Asn Thr Asn Ala Tyr Tyr Glu Met Ser 245 250 255	768	
ggt tta gaa gta agc ttc gag gaa ctg cgc acg ttc ggt ggc cat gat Gly Leu Glu Val Ser Phe Glu Glu Leu Arg Thr Phe Gly Gly His Asp 260 265 270	816	20
gcg aag ttt atc gac agc ttg cag gag aac gag ttc cgt ctg tac tac Ala Lys Phe Ile Asp Ser Leu Gln Glu Asn Glu Phe Arg Leu Tyr Tyr 275 280 285	864	
tac aac aag ttt aaa gat att gca agt aca ctg aac aag gct aag tcc Tyr Asn Lys Phe Lys Asp Ile Ala Ser Thr Leu Asn Lys Ala Lys Ser 290 295 300	912	
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gag aaa tat ctc cta tct gaa gat aca tct gga aaa ttt tcg gta gat Glu Lys Tyr Leu Leu Ser Glu Asp Thr Ser Gly Lys Phe Ser Val Asp 325 330 335	1008	
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gca aac ttt aat ggt caa aat aca gaa att aat aat atg aat ttt act Ala Asn Phe Asn Gly Gln Asn Thr Glu Ile Asn Asn Met Asn Phe Thr 1248	1248	40

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Lys Leu Lys Asn Phe Thr Gly Leu Phe Glu Phe Tyr Lys Leu Leu Cys			
420	425	430	
gta aga ggg ata ata act tct aaa act aaa tca tta gat aaa gga tac			1344
Val Arg Gly Ile Ile Thr Ser Lys Thr Lys Ser Leu Asp Lys Gly Tyr			
435	440	445	
aat aag gca tta aat gat tta tgt atc aaa gtt aat aat tgg gac ttg			1392
Asn Lys Ala Leu Asn Asp Leu Cys Ile Lys Val Asn Asn Trp Asp Leu			
450	455	460	
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Phe Phe Ser Pro Ser Glu Asp Asn Phe Thr Asn Asp Leu Asn Lys Gly			
465	470	475	480
gaa gaa att aca tct gat act aat ata gaa gca gca gaa gaa aat att			1488
Glu Glu Ile Thr Ser Asp Thr Asn Ile Glu Ala Ala Glu Glu Asn Ile			
485	490	495	
agt tta gat tta ata caa caa tat tat tta acc ttt aat ttt gat aat			1536
Ser Leu Asp Leu Ile Gln Gln Tyr Tyr Leu Thr Phe Asn Phe Asp Asn			
500	505	510	
gaa cct gaa aat att tca ata gaa aat ctt tca agt gac att ata ggc			1584
Glu Pro Glu Asn Ile Ser Ile Glu Asn Leu Ser Ser Asp Ile Ile Gly			
515	520	525	
caa tta gaa ctt atg cct aat ata gaa aga ttt cct aat gga aaa aag			1632
Gln Leu Glu Leu Met Pro Asn Ile Glu Arg Phe Pro Asn Gly Lys Lys			
530	535	540	
tat gag tta gat aaa tat act atg ttc cat tat ctt cgt gct caa gaa			1680
Tyr Glu Leu Asp Lys Tyr Thr Met Phe His Tyr Leu Arg Ala Gln Glu			
545	550	555	560
ttt gaa cat ggt aaa tct agg att gct tta aca aat tct gtt aac gaa			1728
Phe Glu His Gly Lys Ser Arg Ile Ala Leu Thr Asn Ser Val Asn Glu			
565	570	575	
gca tta tta aat cct agt cgt gtt tat aca ttt ttt tct tca gac tat			1776
Ala Leu Leu Asn Pro Ser Arg Val Tyr Thr Phe Phe Ser Ser Asp Tyr			
580	585	590	
gta aag aaa gtt aat aaa gct acg gag gca gct atg ttt tta ggc tgg			1824
Val Lys Lys Val Asn Lys Ala Thr Glu Ala Ala Met Phe Leu Gly Trp			
595	600	605	
gta gaa caa tta gta tat gat ttt acc gat gaa act agc gaa gta agt			1872
Val Glu Gln Leu Val Tyr Asp Phe Thr Asp Glu Thr Ser Glu Val Ser			
610	615	620	
act acg gat aaa att gcg gat ata act ata att att cca tat ata gga			1920
Thr Thr Asp Lys Ile Ala Asp Ile Thr Ile Ile Ile Pro Tyr Ile Gly			
625	630	635	640
cct gct tta aat ata ggt aat atg tta tat aaa gat gat ttt gta ggt			1968
Pro Ala Leu Asn Ile Gly Asn Met Leu Tyr Lys Asp Asp Phe Val Gly			
645	650	655	
gct tta ata ttt tca gga gct gtt att ctg tta gaa ttt ata cca gag			2016
Ala Leu Ile Phe Ser Gly Ala Val Ile Leu Leu Glu Phe Ile Pro Glu			
660	665	670	

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att gca ata cct gta tta ggt act ttt gca ctt gta tca tat att gcg 2064
 Ile Ala Ile Pro Val Leu Gly Thr Phe Ala Leu Val Ser Tyr Ile Ala
 675 680 685

aat aag gtt cta acc gtt caa aca ata gat aat gct tta agt aaa aga 2112
 Asn Lys Val Leu Thr Val Gln Thr Ile Asp Asn Ala Leu Ser Lys Arg
 690 695 700

aat gaa aaa tgg gat gag gtc tat aaa tat ata gta aca aat tgg tta 2160
 Asn Glu Lys Trp Asp Glu Val Tyr Lys Tyr Ile Val Thr Asn Trp Leu
 705 710 715 720

gca aag gtt aat aca cag att gat cta ata aga aaa aaa atg aaa gaa 2208
 Ala Lys Val Asn Thr Gln Ile Asp Leu Ile Arg Lys Lys Met Lys Glu
 725 730 735

gct tta gaa aat caa gca gaa gca aca aag gct ata ata aac tat cag 2256
 Ala Leu Glu Asn Gln Ala Glu Ala Thr Lys Ala Ile Ile Asn Tyr Gln
 740 745 750

tat aat caa tat act gag gaa gag aaa aat aat att aat ttt aat att 2304
 Tyr Asn Gln Tyr Thr Glu Glu Glu Lys Asn Asn Ile Asn Phe Asn Ile
 755 760 765

gat gat tta agt tcg aaa ctt aat gag tct ata aat aaa gct atg att 2352
 Asp Asp Leu Ser Ser Lys Leu Asn Glu Ser Ile Asn Lys Ala Met Ile
 770 775 780

aat ata aat aaa ttt ttg aat caa tgc tct gtt tca tat tta atg aat 2400
 Asn Ile Asn Lys Phe Leu Asn Gln Cys Ser Val Ser Tyr Leu Met Asn
 785 790 795 800

tct atg atc cct tat ggt gtt aaa cgg tta gaa gat ttt gat gct agt 2448
 Ser Met Ile Pro Tyr Gly Val Lys Arg Leu Glu Asp Phe Asp Ala Ser
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ctt aaa gat gca tta tta aag tat ata tat gat aat aga gga act tta 2496
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 820 825 830

att ggt caa gta gat aga tta aaa gat aaa gtt aat aat aca ctt agt 2544
 Ile Gly Gln Val Asp Arg Leu Lys Asp Lys Val Asn Asn Thr Leu Ser
 835 840 845

aca gat ata cct ttt cag ctt tcc aaa tac gta gat aat caa aga tta 2592
 Thr Asp Ile Pro Phe Gln Leu Ser Lys Tyr Val Asp Asn Gln Arg Leu
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Gln Pro Val Lys Ala Phe Lys Ile His Asn Lys Ile Trp Val Ile Pro
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 Glu Arg Asp Thr Phe Thr Asn Pro Glu Glu Gly Asp Leu Asn Pro Pro
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 Pro Glu Ala Lys Gln Val Pro Val Ser Tyr Tyr Asp Ser Thr Tyr Leu
 65 70 75 80
 Ser Thr Asp Asn Glu Lys Asp Asn Tyr Leu Lys Gly Val Thr Lys Leu
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 Phe Glu Arg Ile Tyr Ser Thr Asp Leu Gly Arg Met Leu Leu Thr Ser
 100 105 110
 Ile Val Arg Gly Ile Pro Phe Trp Gly Gly Ser Thr Ile Asp Thr Glu
 115 120 125
 Leu Lys Val Ile Asp Thr Asn Cys Ile Asn Val Ile Gln Pro Asp Gly
 130 135 140
 Ser Tyr Arg Ser Glu Glu Leu Asn Leu Val Ile Ile Gly Pro Ser Ala
 145 150 155 160
 Asp Ile Ile Gln Phe Glu Cys Lys Ser Phe Gly His Glu Val Leu Asn
 165 170 175
 Leu Thr Arg Asn Gly Tyr Gly Ser Thr Gln Tyr Ile Arg Phe Ser Pro
 180 185 190
 Asp Phe Thr Phe Gly Phe Glu Glu Ser Leu Glu Val Asp Thr Asn Pro
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 Leu Leu Gly Ala Gly Lys Phe Ala Thr Asp Pro Ala Val Thr Leu Ala
 210 215 220
 His Glu Leu Ile His Ala Gly His Arg Leu Tyr Gly Ile Ala Ile Asn
 225 230 235 240
 Pro Asn Arg Val Phe Lys Val Asn Thr Asn Ala Tyr Tyr Glu Met Ser
 245 250 255
 Gly Leu Glu Val Ser Phe Glu Glu Leu Arg Thr Phe Gly Gly His Asp
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 Ala Lys Phe Ile Asp Ser Leu Gln Glu Asn Glu Phe Arg Leu Tyr Tyr
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 Tyr Asn Lys Phe Lys Asp Ile Ala Ser Thr Leu Asn Lys Ala Lys Ser

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290 295 300
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 Glu Lys Tyr Leu Leu Ser Glu Asp Thr Ser Gly Lys Phe Ser Val Asp
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 Lys Leu Lys Phe Asp Lys Leu Tyr Lys Met Leu Thr Glu Ile Tyr Thr
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 Glu Asp Asn Phe Val Lys Phe Phe Lys Val Leu Asn Arg Lys Thr Tyr
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 Leu Asn Phe Asp Lys Ala Val Phe Lys Ile Asn Ile Val Pro Lys Val
 370 375 380
 Asn Tyr Thr Ile Tyr Asp Gly Phe Asn Leu Arg Asn Thr Asn Leu Ala
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 420 425 430
 Val Arg Gly Ile Ile Thr Ser Lys Thr Lys Ser Leu Asp Lys Gly Tyr
 435 440 445
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 450 455 460
 Phe Phe Ser Pro Ser Glu Asp Asn Phe Thr Asn Asp Leu Asn Lys Gly
 465 470 475 480
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 485 490 495
 Ser Leu Asp Leu Ile Gln Gln Tyr Tyr Leu Thr Phe Asn Phe Asp Asn
 500 505 510
 Glu Pro Glu Asn Ile Ser Ile Glu Asn Leu Ser Ser Asp Ile Ile Gly
 515 520 525
 Gln Leu Glu Leu Met Pro Asn Ile Glu Arg Phe Pro Asn Gly Lys Lys
 530 535 540
 Tyr Glu Leu Asp Lys Tyr Thr Met Phe His Tyr Leu Arg Ala Gln Glu
 545 550 555 560

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Phe Glu His Gly Lys Ser Arg Ile Ala Leu Thr Asn Ser Val Asn Glu
 565 570 575
 Ala Leu Leu Asn Pro Ser Arg Val Tyr Thr Phe Phe Ser Ser Asp Tyr
 580 585 590
 Val Lys Lys Val Asn Lys Ala Thr Glu Ala Ala Met Phe Leu Gly Trp
 595 600 605
 Val Glu Gln Leu Val Tyr Asp Phe Thr Asp Glu Thr Ser Glu Val Ser
 610 615 620
 Thr Thr Asp Lys Ile Ala Asp Ile Thr Ile Ile Ile Pro Tyr Ile Gly
 625 630 635 640
 Pro Ala Leu Asn Ile Gly Asn Met Leu Tyr Lys Asp Asp Phe Val Gly
 645 650 655
 Ala Leu Ile Phe Ser Gly Ala Val Ile Leu Leu Glu Phe Ile Pro Glu
 660 665 670
 Ile Ala Ile Pro Val Leu Gly Thr Phe Ala Leu Val Ser Tyr Ile Ala
 675 680 685
 Asn Lys Val Leu Thr Val Gln Thr Ile Asp Asn Ala Leu Ser Lys Arg
 690 695 700
 Asn Glu Lys Trp Asp Glu Val Tyr Lys Tyr Ile Val Thr Asn Trp Leu
 705 710 715 720
 Ala Lys Val Asn Thr Gln Ile Asp Leu Ile Arg Lys Lys Met Lys Glu
 725 730 735
 Ala Leu Glu Asn Gln Ala Glu Ala Thr Lys Ala Ile Ile Asn Tyr Gln
 740 745 750
 Tyr Asn Gln Tyr Thr Glu Glu Glu Lys Asn Asn Ile Asn Phe Asn Ile
 755 760 765
 Asp Asp Leu Ser Ser Lys Leu Asn Glu Ser Ile Asn Lys Ala Met Ile
 770 775 780
 Asn Ile Asn Lys Phe Leu Asn Gln Cys Ser Val Ser Tyr Leu Met Asn
 785 790 795 800
 Ser Met Ile Pro Tyr Gly Val Lys Arg Leu Glu Asp Phe Asp Ala Ser
 805 810 815
 Leu Lys Asp Ala Leu Leu Lys Tyr Ile Tyr Asp Asn Arg Gly Thr Leu
 820 825 830

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Ile Gly Gln Val Asp Arg Leu Lys Asp Lys Val Asn Asn Thr Leu Ser
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Thr Asp Ile Pro Phe Gln Leu Ser Lys Tyr Val Asp Asn Gln Arg Leu
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gtt gat att gct tat ata aaa att cca aat gca gga caa atg caa cca 96
Val Asp Ile Ala Phe Tyr Ile Lys Ile Pro Asn Ala Gly Gln Met Gln Pro
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gta aaa gct ttt aaa att cat aat aaa ata tgg gtt att cca gaa aga 144
Val Lys Ala Phe Lys Ile His Asn Lys Ile Trp Val Ile Pro Glu Arg
35 40 45
gat aca ttt aca aat cct gaa gaa gga gat tta aat cca cca cca gaa 192
Asp Thr Phe Thr Asn Pro Glu Glu Gly Asp Leu Asn Pro Pro Pro Glu
50 55 60
gca aaa caa gtt cca gtt tca tat tat gat tca aca tat tta agt aca 240
Ala Lys Gln Val Pro Val Ser Tyr Tyr Asp Ser Thr Tyr Leu Ser Thr
65 70 75 80
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Asp Asn Glu Lys Asp Asn Tyr Leu Lys Gly Val Thr Lys Leu Phe Glu
85 90 95
aga att tat tca act gat ctt gga aga atg ttg tta aca tca ata gta 336
Arg Ile Tyr Ser Thr Asp Leu Gly Arg Met Leu Leu Thr Ser Ile Val
100 105 110
agg gga ata cca ttt tgg ggt gga agt aca ata gat aca gaa tta aaa 384
Arg Gly Ile Pro Phe Trp Gly Gly Ser Thr Ile Asp Thr Glu Leu Lys
115 120 125
gtt att gat act aat tgt att aat gtg ata caa cca gat ggt agt tat 432
Val Ile Asp Thr Asn Cys Ile Asn Val Ile Gln Pro Asp Gly Ser Tyr
130 135 140
aga tca gaa gaa ctt aat cta gta ata ata gga ccc tca gct gat att 480
Arg Ser Glu Glu Leu Asn Leu Val Ile Ile Gly Pro Ser Ala Asp Ile
145 150 155 160
ata cag ttt gaa tgt aaa agc ttt gga cat gaa gtt ttg aat ctt acg 528
Ile Gln Phe Glu Cys Lys Ser Phe Gly His Glu Val Leu Asn Leu Thr

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165	170	175	
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ggt gca ggc aaa ttt gct aca gat cca gca gta aca tta gca cat gaa Gly Ala Gly Lys Phe Ala Thr Asp Pro Ala Val Thr Leu Ala His Glu 210 215 220			672
ctt ata cat gct gga cat aga tta tat gga ata gca att aat cca aat Leu Ile His Ala Gly His Arg Leu Tyr Gly Ile Ala Ile Asn Pro Asn 225 230 235 240			720
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 Ala Leu Asn Asp Leu Cys Ile Lys Val Asn Asn Trp Asp Leu Phe Phe
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 Ser Pro Ser Glu Asp Asn Phe Thr Asn Asp Leu Asn Lys Gly Glu Glu
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 545 550 555 560
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 His Gly Lys Ser Arg Ile Ala Leu Thr Asn Ser Val Asn Glu Ala Leu
 565 570 575
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 580 585 590
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 595 600 605
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 675 680 685
 gtt cta acc gtt caa aca ata gat aat gct tta agt aaa aga aat gaa 2112
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	725 730 735		
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Glu Asn Gln Ala Glu Ala	Thr Lys Ala Ile Ile Asn Tyr Gln Tyr Asn		
	740 745 750		
caa tat act gag gaa gag	aaa aat aat att aat ttt aat att gat gat	2304	
Gln Tyr Thr Glu Glu Glu	Lys Asn Ile Asn Phe Asn Ile Asp Asp		
	755 760 765		
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	770 775 780		
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Asn Lys Phe Leu Asn Gln	Cys Ser Val Ser Tyr Leu Met Asn Ser Met		
	785 790 795 800		
atc cct tat ggt gtt aaa	cgg tta gaa gat ttt gat gct agt ctt aaa	2448	
Ile Pro Tyr Gly Val Lys	Arg Leu Glu Asp Phe Asp Ala Ser Leu Lys		
	805 810 815		
gat gca tta tta aag tat	ata tat gat aat aga gga act tta att ggt	2496	
Asp Ala Leu Leu Lys Tyr	Ile Tyr Asp Asn Arg Gly Thr Leu Ile Gly		
	820 825 830		
caa gta gat aga tta aaa	gat aaa gtt aat aat aca ctt agt aca gat	2544	
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Ile Pro Phe Gln Leu Ser	Lys Tyr Val Asp Asn Gln Arg Leu Leu Ser		
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Val Lys Ala Phe Lys Ile	His Asn Lys Ile Trp Val Ile Pro Glu Arg		
	35 40 45		

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Ala Lys Gln Val Pro Val Ser Tyr Tyr Asp Ser Thr Tyr Leu Ser Thr
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 85 90 95

Arg Ile Tyr Ser Thr Asp Leu Gly Arg Met Leu Leu Thr Ser Ile Val
 100 105 110

Arg Gly Ile Pro Phe Trp Gly Gly Ser Thr Ile Asp Thr Glu Leu Lys
 115 120 125

Val Ile Asp Thr Asn Cys Ile Asn Val Ile Gln Pro Asp Gly Ser Tyr
 130 135 140

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

Ile Gln Phe Glu Cys Lys Ser Phe Gly His Glu Val Leu Asn Leu Thr
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Arg Asn Gly Tyr Gly Ser Thr Gln Tyr Ile Arg Phe Ser Pro Asp Phe
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Thr Phe Gly Phe Glu Glu Ser Leu Glu Val Asp Thr Asn Pro Leu Leu
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Gly Ala Gly Lys Phe Ala Thr Asp Pro Ala Val Thr Leu Ala His Glu
 210 215 220

Leu Ile His Ala Gly His Arg Leu Tyr Gly Ile Ala Ile Asn Pro Asn
 225 230 235 240

Arg Val Phe Lys Val Asn Thr Asn Ala Tyr Tyr Glu Met Ser Gly Leu
 245 250 255

Glu Val Ser Phe Glu Glu Leu Arg Thr Phe Gly Gly His Asp Ala Lys
 260 265 270

Phe Ile Asp Ser Leu Gln Glu Asn Glu Phe Arg Leu Tyr Tyr Tyr Asn
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Lys Phe Lys Asp Ile Ala Ser Thr Leu Asn Lys Ala Lys Ser Ile Val
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Gly Thr Thr Ala Ser Leu Gln Tyr Met Lys Asn Val Phe Lys Glu Lys
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 Phe Asp Lys Ala Val Phe Lys Ile Asn Ile Val Pro Lys Val Asn Tyr
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 Thr Ile Tyr Asp Gly Phe Asn Leu Arg Asn Thr Asn Leu Ala Ala Asn
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 Gly Ile Ile Thr Ser Lys Thr Lys Ser Leu Asp Lys Gly Tyr Asn Lys
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 465 470 475 480
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 530 535 540
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 565 570 575
 Leu Asn Pro Ser Arg Val Tyr Thr Phe Phe Ser Ser Asp Tyr Val Lys

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580 585 590
 Lys Val Asn Lys Ala Thr Glu Ala Ala Met Phe Leu Gly Trp Val Glu
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 Asp Lys Ile Ala Asp Ile Thr Ile Ile Ile Pro Tyr Ile Gly Pro Ala
 625 630 635 640
 Leu Asn Ile Gly Asn Met Leu Tyr Lys Asp Asp Phe Val Gly Ala Leu
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 Ile Phe Ser Gly Ala Val Ile Leu Leu Glu Phe Ile Pro Glu Ile Ala
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 Val Leu Thr Val Gln Thr Ile Asp Asn Ala Leu Ser Lys Arg Asn Glu
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 Val Asn Thr Gln Ile Asp Leu Ile Arg Lys Lys Met Lys Glu Ala Leu
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 740 745 750
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 770 775 780
 Asn Lys Phe Leu Asn Gln Cys Ser Val Ser Tyr Leu Met Asn Ser Met
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 Ile Pro Tyr Gly Val Lys Arg Leu Glu Asp Phe Asp Ala Ser Leu Lys
 805 810 815
 Asp Ala Leu Leu Lys Tyr Ile Tyr Asp Asn Arg Gly Thr Leu Ile Gly
 820 825 830
 Gln Val Asp Arg Leu Lys Asp Lys Val Asn Asn Thr Leu Ser Thr Asp
 835 840 845

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gtt gac att gcc tac atc aaa att cca aac gcc ggc cag atg cag ccg 96
Val Asp Ile Ala Tyr Ile Lys Ile Pro Asn Ala Gly Gln Met Gln Pro
20 25 30
gtg aag gct ttc aag att cat aac aaa atc tgg gtt att ccg gaa cgc 144
Val Lys Ala Phe Lys Ile His Asn Lys Ile Trp Val Ile Pro Glu Arg
35 40 45
gat aca ttt acg aac ccg gaa gaa gga gac ttg aac ccg ccg ccg gaa 192
Asp Thr Phe Thr Asn Pro Glu Glu Gly Asp Leu Asn Pro Pro Pro Glu
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gca aag cag gtg cca gtt tca tac tac gat tca acc tat ctg agc aca 240
Ala Lys Gln Val Pro Val Ser Tyr Tyr Asp Ser Thr Tyr Leu Ser Thr
65 70 75 80
gac aac gag aag gat aac tac ctg aag gga gtg acc aaa tta ttc gag 288
Asp Asn Glu Lys Asp Asn Tyr Leu Lys Gly Val Thr Lys Leu Phe Glu
85 90 95
cgt att tat tcc act gac ctg ggc cgt atg ctg ctg acc tca atc gtc 336
Arg Ile Tyr Ser Thr Asp Leu Gly Arg Met Leu Leu Thr Ser Ile Val
100 105 110
cgc gga atc cca ttt tgg ggt ggc agt acc att gac acg gag ttg aag 384
Arg Gly Ile Pro Phe Trp Gly Gly Ser Thr Ile Asp Thr Glu Leu Lys
115 120 125
gtt att gac act aac tgc att aac gtg atc caa cca gac ggt agc tac 432
Val Ile Asp Thr Asn Cys Ile Asn Val Ile Gln Pro Asp Gly Ser Tyr
130 135 140
aga tct gaa gaa ctt aac ctc gta atc atc ggg ccc tcc gcg gac att 480
Arg Ser Glu Glu Leu Asn Leu Val Ile Ile Gly Pro Ser Ala Asp Ile
145 150 155 160
atc cag ttt gag tgc aag agc ttt ggc cac gaa gtg ttg aac ctg acg 528
Ile Gln Phe Glu Cys Lys Ser Phe Gly His Glu Val Leu Asn Leu Thr
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cgt aac ggt tac ggc tct act cag tac att cgt ttc agc cca gac ttc 576
Arg Asn Gly Tyr Gly Ser Thr Gln Tyr Ile Arg Phe Ser Pro Asp Phe
180 185 190

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ctg atc cac gcc ggt cat cgt ctg tat ggc att gcg att aac ccg aac Leu Ile His Ala Gly His Arg Leu Tyr Gly Ile Ala Ile Asn Pro Asn 225 230 235 240	720	
cgc gtg ttc aag gtt aac acc aac gcc tac tac gag atg agt ggt tta Arg Val Phe Lys Val Asn Thr Asn Ala Tyr Tyr Glu Met Ser Gly Leu 245 250 255	768	10
gaa gta agc ttc gag gaa ctg cgc acg ttc ggt ggc cat gat gcg aag Glu Val Ser Phe Glu Glu Leu Arg Thr Phe Gly Gly His Asp Ala Lys 260 265 270	816	
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ggt acc act gct tca tta cag tat atg aaa aat gtt ttt aaa gag aaa Gly Thr Thr Ala Ser Leu Gln Tyr Met Lys Asn Val Phe Lys Glu Lys 305 310 315 320	960	20
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aat att agt tta gat tta ata caa caa tat tat tta acc ttt aat ttt Asn Ile Ser Leu Asp Leu Ile Gln Gln Tyr Tyr Leu Thr Phe Asn Phe 500 505 510			1536
gat aat gaa cct gaa aat att tca ata gaa aat ctt tca agt gac att Asp Asn Glu Pro Glu Asn Ile Ser Ile Glu Asn Leu Ser Ser Asp Ile 515 520 525			1584
ata ggc caa tta gaa ctt atg cct aat ata gaa aga ttt cct aat gga Ile Gly Gln Leu Glu Leu Met Pro Asn Ile Glu Arg Phe Pro Asn Gly 530 535 540			1632
aaa aag tat gag tta gat aaa tat act atg ttc cat tat ctt cgt gct Lys Lys Tyr Glu Leu Asp Lys Tyr Thr Met Phe His Tyr Leu Arg Ala 545 550 555 560			1680
caa gaa ttt gaa cat ggt aaa tct agg att gct tta aca aat tct gtt Gln Glu Phe Glu His Gly Lys Ser Arg Ile Ala Leu Thr Asn Ser Val 565 570 575			1728
aac gaa gca tta tta aat cct agt cgt gtt tat aca ttt ttt tct tca Asn Glu Ala Leu Leu Asn Pro Ser Arg Val Tyr Thr Phe Phe Ser Ser 580 585 590			1776
gac tat gta aag aaa gtt aat aaa gct acg gag gca gct atg ttt tta Asp Tyr Val Lys Lys Val Asn Lys Ala Thr Glu Ala Ala Met Phe Leu 595 600 605			1824
ggc tgg gta gaa caa tta gta tat gat ttt acc gat gaa act agc gaa Gly Trp Val Glu Gln Leu Val Tyr Asp Phe Thr Asp Glu Thr Ser Glu 610 615 620			1872
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ata gga cct gct tta aat ata ggt aat atg tta tat aaa gat gat ttt Ile Gly Pro Ala Leu Asn Ile Gly Asn Met Leu Tyr Lys Asp Asp Phe 645 650 655			1968
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 aaa gaa gct tta gaa aat caa gca gaa gca aca aag gct ata ata aac 2256
 Lys Glu Ala Leu Glu Asn Gln Ala Glu Ala Thr Lys Ala Ile Ile Asn
 740 745 750
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 Tyr Gln Tyr Asn Gln Tyr Thr Glu Glu Lys Asn Asn Ile Asn Phe
 755 760 765
 aat att gat gat tta agt tcg aaa ctt aat gag tct ata aat aaa gct 2352
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 770 775 780
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 Met Ile Asn Ile Asn Lys Phe Leu Asn Gln Cys Ser Val Ser Tyr Leu
 785 790 795 800
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 Ala Ser Leu Lys Asp Ala Leu Leu Lys Tyr Ile Tyr Asp Asn Arg Gly
 820 825 830
 act tta att ggt caa gta gat aga tta aaa gat aaa gtt aat aat aca 2544
 Thr Leu Ile Gly Gln Val Asp Arg Leu Lys Asp Lys Val Asn Asn Thr
 835 840 845
 ctt agt aca gat ata cct ttt cag ctt tcc aaa tac gta gat aat caa 2592
 Leu Ser Thr Asp Ile Pro Phe Gln Leu Ser Lys Tyr Val Asp Asn Gln
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Val Lys Ala Phe Lys Ile His Asn Lys Ile Trp Val Ile Pro Glu Arg
35 40 45

Asp Thr Phe Thr Asn Pro Glu Glu Gly Asp Leu Asn Pro Pro Pro Glu
50 55 60

Ala Lys Gln Val Pro Val Ser Tyr Tyr Asp Ser Thr Tyr Leu Ser Thr
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Asp Asn Glu Lys Asp Asn Tyr Leu Lys Gly Val Thr Lys Leu Phe Glu
 85 90 95
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 115 120 125
 Val Ile Asp Thr Asn Cys Ile Asn Val Ile Gln Pro Asp Gly Ser Tyr
 130 135 140
 Arg Ser Glu Glu Leu Asn Leu Val Ile Ile Gly Pro Ser Ala Asp Ile
 145 150 155 160
 Ile Gln Phe Glu Cys Lys Ser Phe Gly His Glu Val Leu Asn Leu Thr
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 Arg Asn Gly Tyr Gly Ser Thr Gln Tyr Ile Arg Phe Ser Pro Asp Phe
 180 185 190
 Thr Phe Gly Phe Glu Glu Ser Leu Glu Val Asp Thr Asn Pro Leu Leu
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 Gly Ala Gly Lys Phe Ala Thr Asp Pro Ala Val Thr Leu Ala His Glu
 210 215 220
 Leu Ile His Ala Gly His Arg Leu Tyr Gly Ile Ala Ile Asn Pro Asn
 225 230 235 240
 Arg Val Phe Lys Val Asn Thr Asn Ala Tyr Tyr Glu Met Ser Gly Leu
 245 250 255
 Glu Val Ser Phe Glu Glu Leu Arg Thr Phe Gly Gly His Asp Ala Lys
 260 265 270
 Phe Ile Asp Ser Leu Gln Glu Asn Glu Phe Arg Leu Tyr Tyr Tyr Asn
 275 280 285
 Lys Phe Lys Asp Ile Ala Ser Thr Leu Asn Lys Ala Lys Ser Ile Val
 290 295 300
 Gly Thr Thr Ala Ser Leu Gln Tyr Met Lys Asn Val Phe Lys Glu Lys
 305 310 315 320
 Tyr Leu Leu Ser Glu Asp Thr Ser Gly Lys Phe Ser Val Asp Lys Leu
 325 330 335
 Lys Phe Asp Lys Leu Tyr Lys Met Leu Thr Glu Ile Tyr Thr Glu Asp

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 Phe Asp Lys Ala Val Phe Lys Ile Asn Ile Val Pro Lys Val Asn Tyr
 370 375 380
 Thr Ile Tyr Asp Gly Phe Asn Leu Arg Asn Thr Asn Leu Ala Ala Asn
 385 390 395 400
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 405 410 415
 Lys Asn Phe Thr Gly Leu Phe Glu Phe Tyr Lys Leu Leu Cys Val Arg
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 Gly Ile Ile Thr Ser Lys Thr Lys Ser Leu Asp Lys Gly Tyr Asn Lys
 435 440 445
 Ser Ala Asp Gly Ala Leu Asn Asp Leu Cys Ile Lys Val Asn Asn Trp
 450 455 460
 Asp Leu Phe Phe Ser Pro Ser Glu Asp Asn Phe Thr Asn Asp Leu Asn
 465 470 475 480
 Lys Gly Glu Glu Ile Thr Ser Asp Thr Asn Ile Glu Ala Ala Glu Glu
 485 490 495
 Asn Ile Ser Leu Asp Leu Ile Gln Gln Tyr Tyr Leu Thr Phe Asn Phe
 500 505 510
 Asp Asn Glu Pro Glu Asn Ile Ser Ile Glu Asn Leu Ser Ser Asp Ile
 515 520 525
 Ile Gly Gln Leu Glu Leu Met Pro Asn Ile Glu Arg Phe Pro Asn Gly
 530 535 540
 Lys Lys Tyr Glu Leu Asp Lys Tyr Thr Met Phe His Tyr Leu Arg Ala
 545 550 555 560
 Gln Glu Phe Glu His Gly Lys Ser Arg Ile Ala Leu Thr Asn Ser Val
 565 570 575
 Asn Glu Ala Leu Leu Asn Pro Ser Arg Val Tyr Thr Phe Phe Ser Ser
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 Asp Tyr Val Lys Lys Val Asn Lys Ala Thr Glu Ala Ala Met Phe Leu
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Gly Trp Val Glu Gln Leu Val Tyr Asp Phe Thr Asp Glu Thr Ser Glu
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625 630 635 640

Ile Gly Pro Ala Leu Asn Ile Gly Asn Met Leu Tyr Lys Asp Asp Phe
645 650 655

Val Gly Ala Leu Ile Phe Ser Gly Ala Val Ile Leu Leu Glu Phe Ile
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Pro Glu Ile Ala Ile Pro Val Leu Gly Thr Phe Ala Leu Val Ser Tyr
675 680 685

Ile Ala Asn Lys Val Leu Thr Val Gln Thr Ile Asp Asn Ala Leu Ser
690 695 700

Lys Arg Asn Glu Lys Trp Asp Glu Val Tyr Lys Tyr Ile Val Thr Asn
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Trp Leu Ala Lys Val Asn Thr Gln Ile Asp Leu Ile Arg Lys Lys Met
725 730 735

Lys Glu Ala Leu Glu Asn Gln Ala Glu Ala Thr Lys Ala Ile Ile Asn
740 745 750

Tyr Gln Tyr Asn Gln Tyr Thr Glu Glu Glu Lys Asn Asn Ile Asn Phe
755 760 765

Asn Ile Asp Asp Leu Ser Ser Lys Leu Asn Glu Ser Ile Asn Lys Ala
770 775 780

Met Ile Asn Ile Asn Lys Phe Leu Asn Gln Cys Ser Val Ser Tyr Leu
785 790 795 800

Met Asn Ser Met Ile Pro Tyr Gly Val Lys Arg Leu Glu Asp Phe Asp
805 810 815

Ala Ser Leu Lys Asp Ala Leu Leu Lys Tyr Ile Tyr Asp Asn Arg Gly
820 825 830

Thr Leu Ile Gly Gln Val Asp Arg Leu Lys Asp Lys Val Asn Asn Thr
835 840 845

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

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 Val Lys Ala Phe Lys Ile His Asn Lys Ile Trp Val Ile Pro Glu Arg 35 40 45
 gat aca ttt acg aac ccg gaa gaa gga gac ttg aac ccg ccg ccg gaa 192
 Asp Thr Phe Thr Asn Pro Val Glu Gly Asp Leu Asn Pro Pro Pro Glu 50 55 60
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 Ala Lys Gln Val Pro Val Ser Tyr Tyr Asp Ser Thr Tyr Leu Ser Thr 65 70 75 80
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 Asp Asn Glu Lys Asp Asn Tyr Leu Lys Gly Val Thr Lys Leu Phe Glu 85 90 95
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 Arg Ile Tyr Ser Thr Asp Leu Gly Arg Met Leu Leu Thr Ser Ile Val 100 105 110
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 Arg Gly Ile Pro Phe Trp Gly Gly Ser Thr Ile Asp Thr Glu Leu Lys 115 120 125
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 Ile Gln Phe Glu Cys Lys Ser Phe Gly His Glu Val Leu Asn Leu Thr 165 170 175
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 Arg Asn Gly Tyr Gly Ser Thr Gln Tyr Ile Arg Phe Ser Pro Asp Phe 180 185 190
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 Thr Phe Gly Phe Glu Glu Ser Leu Glu Val Asp Thr Asn Pro Leu Leu 195 200 205
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 Gly Ala Gly Lys Phe Ala Thr Asp Pro Ala Val Thr Leu Ala His Glu

210	215	220	
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gaa ttt ata cca gag att gca ata cct gta tta ggt act ttt gca ctt Glu Phe Ile Pro Glu Ile Ala Ile Pro Val Leu Gly Thr Phe Ala Leu 675 680 685	2064
gta tca tat att gcg aat aag gtt cta acc gtt caa aca ata gat aat Val Ser Tyr Ile Ala Asn Lys Val Leu Thr Val Gln Thr Ile Asp Asn 690 695 700	2112
gct tta agt aaa aga aat gaa aaa tgg gat gag gtc tat aaa tat ata Ala Leu Ser Lys Arg Asn Glu Lys Trp Asp Glu Val Tyr Lys Tyr Ile 705 710 715 720	2160
gta aca aat tgg tta gca aag gtt aat aca cag att gat cta ata aga Val Thr Asn Trp Leu Ala Lys Val Asn Thr Gln Ile Asp Leu Ile Arg 725 730 735	2208
aaa aaa atg aaa gaa gct tta gaa aat caa gca gaa gca aca aag gct Lys Lys Met Lys Glu Ala Leu Glu Asn Gln Ala Glu Ala Thr Lys Ala	2256

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740	745	750	
ata ata aac tat cag tat aat caa tat act gag gaa gag aaa aat aat Ile Ile Asn Tyr Gln Tyr Asn Gln Tyr Thr Glu Glu Glu Lys Asn Asn 755 760 765			2304
att aat ttt aat att gat gat tta agt tcg aaa ctt aat gag tct ata Ile Asn Phe Asn Ile Asp Asp Leu Ser Ser Lys Leu Asn Glu Ser Ile 770 775 780			2352
aat aaa gct atg att aat ata aat aaa ttt ttg aat caa tgc tct gtt Asn Lys Ala Met Ile Asn Ile Asn Lys Phe Leu Asn Gln Cys Ser Val 785 790 795 800			2400
tca tat tta atg aat tct atg atc cct tat ggt gtt aaa cgg tta gaa Ser Tyr Leu Met Asn Ser Met Ile Pro Tyr Gly Val Lys Arg Leu Glu 805 810 815			2448
gat ttt gat gct agt ctt aaa gat gca tta tta aag tat ata tat gat Asp Phe Asp Ala Ser Leu Lys Asp Ala Leu Leu Lys Tyr Ile Tyr Asp 820 825 830			2496
aat aga gga act tta att ggt caa gta gat aga tta aaa gat aaa gtt Asn Arg Gly Thr Leu Ile Gly Gln Val Asp Arg Leu Lys Asp Lys Val 835 840 845			2544
aat aat aca ctt agt aca gat ata cct ttt cag ctt tcc aaa tac gta Asn Asn Thr Leu Ser Thr Asp Ile Pro Phe Gln Leu Ser Lys Tyr Val 850 855 860			2592
gat aat caa aga tta tta tct aca ttt act gaa tat att aag taa Asp Asn Gln Arg Leu Leu Ser Thr Phe Thr Glu Tyr Ile Lys 865 870 875			2637

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		20						25					30		

Val	Lys	Ala	Phe	Lys	Ile	His	Asn	Lys	Ile	Trp	Val	Ile	Pro	Glu	Arg
		35					40					45			

Asp	Thr	Phe	Thr	Asn	Pro	Glu	Glu	Gly	Asp	Leu	Asn	Pro	Pro	Pro	Glu
	50					55					60				

Ala	Lys	Gln	Val	Pro	Val	Ser	Tyr	Tyr	Asp	Ser	Thr	Tyr	Leu	Ser	Thr
65					70				75					80	

Asp	Asn	Glu	Lys	Asp	Asn	Tyr	Leu	Lys	Gly	Val	Thr	Lys	Leu	Phe	Glu
			85						90					95	

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Arg Ile Tyr Ser Thr Asp Leu Gly Arg Met Leu Leu Thr Ser Ile Val
100 105 110

Arg Gly Ile Pro Phe Trp Gly Gly Ser Thr Ile Asp Thr Glu Leu Lys
115 120 125

Val Ile Asp Thr Asn Cys Ile Asn Val Ile Gln Pro Asp Gly Ser Tyr
130 135 140

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

Ile Gln Phe Glu Cys Lys Ser Phe Gly His Glu Val Leu Asn Leu Thr
165 170 175

Arg Asn Gly Tyr Gly Ser Thr Gln Tyr Ile Arg Phe Ser Pro Asp Phe
180 185 190

Thr Phe Gly Phe Glu Glu Ser Leu Glu Val Asp Thr Asn Pro Leu Leu
195 200 205

Gly Ala Gly Lys Phe Ala Thr Asp Pro Ala Val Thr Leu Ala His Glu
210 215 220

Leu Ile His Ala Gly His Arg Leu Tyr Gly Ile Ala Ile Asn Pro Asn
225 230 235 240

Arg Val Phe Lys Val Asn Thr Asn Ala Tyr Tyr Glu Met Ser Gly Leu
245 250 255

Glu Val Ser Phe Glu Glu Leu Arg Thr Phe Gly Gly His Asp Ala Lys
260 265 270

Phe Ile Asp Ser Leu Gln Glu Asn Glu Phe Arg Leu Tyr Tyr Tyr Asn
275 280 285

Lys Phe Lys Asp Ile Ala Ser Thr Leu Asn Lys Ala Lys Ser Ile Val
290 295 300

Gly Thr Thr Ala Ser Leu Gln Tyr Met Lys Asn Val Phe Lys Glu Lys
305 310 315 320

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

Lys Phe Asp Lys Leu Tyr Lys Met Leu Thr Glu Ile Tyr Thr Glu Asp
340 345 350

Asn Phe Val Lys Phe Phe Lys Val Leu Asn Arg Lys Thr Tyr Leu Asn
355 360 365

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Phe Asp Lys Ala Val Phe Lys Ile Asn Ile Val Pro Lys Val Asn Tyr
 370 375 380

Thr Ile Tyr Asp Gly Phe Asn Leu Arg Asn Thr Asn Leu Ala Ala Asn
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Phe Asn Gly Gln Asn Thr Glu Ile Asn Asn Met Asn Phe Thr Lys Leu
 405 410 415

Lys Asn Phe Thr Gly Leu Phe Glu Phe Tyr Lys Leu Leu Cys Val Arg
 420 425 430

Gly Ile Ile Thr Ser Lys Thr Lys Ser Leu Asp Lys Gly Tyr Asn Lys
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Ile Glu Gly Arg Cys Asp Gly Ala Leu Asn Asp Leu Cys Ile Lys Val
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Asn Asn Trp Asp Leu Phe Phe Ser Pro Ser Glu Asp Asn Phe Thr Asn
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Asp Leu Asn Lys Gly Glu Glu Ile Thr Ser Asp Thr Asn Ile Glu Ala
 485 490 495

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

Phe Asn Phe Asp Asn Glu Pro Glu Asn Ile Ser Ile Glu Asn Leu Ser
 515 520 525

Ser Asp Ile Ile Gly Gln Leu Glu Leu Met Pro Asn Ile Glu Arg Phe
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Pro Asn Gly Lys Lys Tyr Glu Leu Asp Lys Tyr Thr Met Phe His Tyr
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Leu Arg Ala Gln Glu Phe Glu His Gly Lys Ser Arg Ile Ala Leu Thr
 565 570 575

Asn Ser Val Asn Glu Ala Leu Leu Asn Pro Ser Arg Val Tyr Thr Phe
 580 585 590

Phe Ser Ser Asp Tyr Val Lys Lys Val Asn Lys Ala Thr Glu Ala Ala
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Met Phe Leu Gly Trp Val Glu Gln Leu Val Tyr Asp Phe Thr Asp Glu
 610 615 620

Thr Ser Glu Val Ser Thr Thr Asp Lys Ile Ala Asp Ile Thr Ile Ile

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625 630 635 640
 Ile Pro Tyr Ile Gly Pro Ala Leu Asn Ile Gly Asn Met Leu Tyr Lys
 645 650 655
 Asp Asp Phe Val Gly Ala Leu Ile Phe Ser Gly Ala Val Ile Leu Leu
 660 665 670
 Glu Phe Ile Pro Glu Ile Ala Ile Pro Val Leu Gly Thr Phe Ala Leu
 675 680 685
 Val Ser Tyr Ile Ala Asn Lys Val Leu Thr Val Gln Thr Ile Asp Asn
 690 695 700
 Ala Leu Ser Lys Arg Asn Glu Lys Trp Asp Glu Val Tyr Lys Tyr Ile
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 Val Thr Asn Trp Leu Ala Lys Val Asn Thr Gln Ile Asp Leu Ile Arg
 725 730 735
 Lys Lys Met Lys Glu Ala Leu Glu Asn Gln Ala Glu Ala Thr Lys Ala
 740 745 750
 Ile Ile Asn Tyr Gln Tyr Asn Gln Tyr Thr Glu Glu Glu Lys Asn Asn
 755 760 765
 Ile Asn Phe Asn Ile Asp Asp Leu Ser Ser Lys Leu Asn Glu Ser Ile
 770 775 780
 Asn Lys Ala Met Ile Asn Ile Asn Lys Phe Leu Asn Gln Cys Ser Val
 785 790 795 800
 Ser Tyr Leu Met Asn Ser Met Ile Pro Tyr Gly Val Lys Arg Leu Glu
 805 810 815
 Asp Phe Asp Ala Ser Leu Lys Asp Ala Leu Leu Lys Tyr Ile Tyr Asp
 820 825 830
 Asn Arg Gly Thr Leu Ile Gly Gln Val Asp Arg Leu Lys Asp Lys Val
 835 840 845
 Asn Asn Thr Leu Ser Thr Asp Ile Pro Phe Gln Leu Ser Lys Tyr Val
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<213> Clostridium botulinum

<220>

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1 5 10 15		
gtt gac att gcc tac atc aaa att cca aac gcc ggc cag atg cag ccg	96	
Val Asp Ile Ala Tyr Ile Lys Ile Pro Asn Ala Gly Gln Met Gln Pro		10
20 25 30		
gtg aag gct ttc aag att cat aac aaa atc tgg gtt att ccg gaa cgc	144	
Val Lys Ala Phe Lys Ile His Asn Lys Ile Trp Val Ile Pro Glu Arg		
35 40 45		
gat aca ttt acg aac ccg gaa gaa gga gac ttg aac ccg ccg ccg gaa	192	
Asp Thr Phe Thr Asn Pro Glu Glu Gly Asp Leu Asn Pro Pro Pro Glu		
50 55 60		
gca aag cag gtg cca gtt tca tac tac gat tca acc tat ctg agc aca	240	
Ala Lys Gln Val Pro Val Ser Tyr Tyr Asp Ser Thr Tyr Leu Ser Thr		
65 70 75 80		
gac aac gag aag gat aac tac ctg aag gga gtg acc aaa tta ttc gag	288	
Asp Asn Glu Lys Asp Asn Tyr Leu Lys Gly Val Thr Lys Leu Phe Glu		20
85 90 95		
cgt att tat tcc act gac ctg ggc cgt atg ctg ctg acc tca atc gtc	336	
Arg Ile Tyr Ser Thr Asp Leu Gly Arg Met Leu Leu Thr Ser Ile Val		
100 105 110		
cgc gga atc cca ttt tgg ggt ggc agt acc att gac acg gag ttg aag	384	
Arg Gly Ile Pro Phe Trp Gly Gly Ser Thr Ile Asp Thr Glu Leu Lys		
115 120 125		
gtt att gac act aac tgc att aac gtg atc caa cca gac ggt agc tac	432	
Val Ile Asp Thr Asn Cys Ile Asn Val Ile Gln Pro Asp Gly Ser Tyr		
130 135 140		
aga tct gaa gaa ctt aac ctc gta atc atc ggg ccc tcc gcg gac att	480	
Arg Ser Glu Glu Leu Asn Leu Val Ile Ile Gly Pro Ser Ala Asp Ile		
145 150 155 160		
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Ile Gln Phe Glu Cys Lys Ser Phe Gly His Glu Val Leu Asn Leu Thr		
165 170 175		
cgt aac ggt tac ggc tct act cag tac att cgt ttc agc cca gac ttc	576	
Arg Asn Gly Tyr Gly Ser Thr Gln Tyr Ile Arg Phe Ser Pro Asp Phe		
180 185 190		
acg ttc ggt ttc gag gag agc ctg gag gtt gat acc aac ccg ctg ttg	624	
Thr Phe Gly Phe Glu Glu Ser Leu Glu Val Asp Thr Asn Pro Leu Leu		
195 200 205		
ggt gca ggc aag ttc gca act gat cca gcg gtg acc ctg gca cac gag	672	
Gly Ala Gly Lys Phe Ala Thr Asp Pro Ala Val Thr Leu Ala His Glu		
210 215 220		
ctg atc cac gcc ggt cat cgt ctg tat ggc att gcg att aac ccg aac	720	40
Leu Ile His Ala Gly His Arg Leu Tyr Gly Ile Ala Ile Asn Pro Asn		

225	230	235	240	
cgc gtg ttc aag gtt aac acc aac gcc tac tac gag atg agt ggt tta				768
Arg Val Phe Lys Val Asn Thr Asn Ala Tyr Tyr Glu Met Ser Gly Leu	245	250	255	
gaa gta agc ttc gag gaa ctg cgc acg ttc ggt ggc cat gat gcg aag				816
Glu Val Ser Phe Glu Glu Leu Arg Thr Phe Gly Gly His Asp Ala Lys	260	265	270	
ttt atc gac agc ttg cag gag aac gag ttc cgt ctg tac tac tac aac				864
Phe Ile Asp Ser Leu Gln Glu Asn Glu Phe Arg Leu Tyr Tyr Tyr Asn	275	280	285	
aag ttt aaa gat att gca agt aca ctg aac aag gct aag tcc att gtg				912
Lys Phe Lys Lys Asp Ile Ala Ser Thr Leu Asn Lys Ala Lys Ser Ile Val	290	295	300	
ggt acc act gct tca tta cag tat atg aaa aat gtt ttt aaa gag aaa				960
Gly Thr Thr Ala Ser Leu Gln Tyr Met Lys Asn Val Phe Lys Glu Lys	305	310	315	320
tat ctg cta tct gaa gat aca tct gga aaa ttt tgg gta gat aaa tta				1008
Tyr Leu Leu Ser Glu Asp Thr Ser Gly Lys Phe Ser Val Asp Lys Leu	325	330	335	
aaa ttt gat aag tta tac aaa atg tta aca gag att tac aca gag gat				1056
Lys Phe Asp Lys Leu Tyr Lys Met Leu Thr Glu Ile Tyr Thr Glu Asp	340	345	350	
aat ttt gtt aag ttt ttt aaa gta ctt aac aga aaa aca tat ttg aat				1104
Asn Phe Val Lys Phe Phe Lys Val Leu Asn Arg Lys Thr Tyr Leu Asn	355	360	365	
ttt gat aaa gcc gta ttt aag ata aat ata gta cct aag gta aat tac				1152
Phe Asp Lys Ala Val Phe Lys Ile Asn Ile Val Pro Lys Val Asn Tyr	370	375	380	
aca ata tat gat gga ttt aat tta aga aat aca aat tta gca gca aac				1200
Thr Ile Tyr Asp Gly Phe Asn Leu Arg Asn Thr Asn Leu Ala Ala Asn	385	390	395	400
ttt aat ggt caa aat aca gaa att aat aat atg aat ttt act aaa cta				1248
Phe Asn Gly Gln Asn Thr Glu Ile Asn Asn Met Asn Phe Thr Lys Leu	405	410	415	
aaa aat ttt act gga ttg ttt gaa ttt tat aag ttg cta tgt gta aga				1296
Lys Asn Phe Thr Gly Leu Phe Glu Phe Tyr Lys Leu Leu Cys Val Arg	420	425	430	
ggg ata ata act tct aaa act aaa tca tta gat aaa gga tac aat aag				1344
Gly Ile Ile Thr Ser Lys Thr Lys Ser Leu Asp Lys Gly Tyr Asn Lys	435	440	445	
atc gaa ggt cgt tgc gat ggg gca tta aat gat tta tgt atc aaa gtt				1392
Ile Glu Gly Arg Cys Asp Gly Ala Leu Asn Asp Leu Cys Ile Lys Val	450	455	460	
aat aat tgg gac ttg ttt ttt agt cct tca gaa gat aat ttt act aat				1440
Asn Asn Trp Asp Leu Phe Phe Ser Pro Ser Glu Asp Asn Phe Thr Asn	465	470	475	480
gat cta aat aaa gga gaa gaa att aca tct gat act aat ata gaa gca				1488
Asp Leu Asn Lys Gly Glu Glu Ile Thr Ser Asp Thr Asn Ile Glu Ala	485	490	495	

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gca gaa gaa aat att agt tta gat tta ata caa caa tat tat tta acc 1536
Ala Glu Glu Asn Ile Ser Leu Asp Leu Ile Gln Gln Tyr Tyr Leu Thr
500 505 510

ttt aat ttt gat aat gaa cct gaa aat att tca ata gaa aat ctt tca 1584
Phe Asn Phe Asp Asn Glu Pro Glu Asn Ile Ser Ile Glu Asn Leu Ser
515 520 525

agt gac att ata ggc caa tta gaa ctt atg cct aat ata gaa aga ttt 1632
Ser Asp Ile Ile Gly Gln Leu Glu Leu Met Pro Asn Ile Glu Arg Phe
530 535 540

cct aat gga aaa aag tat gag tta gat aaa tat act atg ttc cat tat 1680
Pro Asn Gly Lys Lys Tyr Glu Leu Asp Lys Tyr Thr Met Phe His Tyr
545 550 555 560

ctt cgt gct caa gaa ttt gaa cat ggt aaa tct agg att gct tta aca 1728
Leu Arg Ala Gln Glu Phe Glu His Gly Lys Ser Arg Ile Ala Leu Thr
565 570 575

aat tct gtt aac gaa gca tta tta aat cct agt cgt gtt tat aca ttt 1776
Asn Ser Val Asn Glu Ala Leu Leu Asn Pro Ser Arg Val Tyr Thr Phe
580 585 590

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

atg ttt tta ggc tgg gta gaa caa tta gta tat gat ttt acc gat gaa 1872
Met Phe Leu Gly Trp Val Glu Gln Leu Val Tyr Asp Phe Thr Asp Glu
610 615 620

act agc gaa gta agt act acg gat aaa att gcg gat ata act ata att 1920
Thr Ser Glu Val Ser Thr Thr Asp Lys Ile Ala Asp Ile Thr Ile Ile
625 630 635 640

att cca tat ata gga cct gct tta aat ata ggt aat atg tta tat aaa 1968
Ile Pro Tyr Ile Gly Pro Ala Leu Asn Ile Gly Asn Met Leu Tyr Lys
645 650 655

gat gat ttt gta ggt gct tta ata ttt tca gga gct gtt att ctg tta 2016
Asp Asp Phe Val Gly Ala Leu Ile Phe Ser Gly Ala Val Ile Leu Leu
660 665 670

gaa ttt ata cca gag att gca ata cct gta tta ggt act ttt gca ctt 2064
Glu Phe Ile Pro Glu Ile Ala Ile Pro Val Leu Gly Thr Phe Ala Leu
675 680 685

gta tca tat att gcg aat aag gtt cta acc gtt caa aca ata gat aat 2112
Val Ser Tyr Ile Ala Asn Lys Val Leu Thr Val Gln Thr Ile Asp Asn
690 695 700

gct tta agt aaa aga aat gaa aaa tgg gat gag gtc tat aaa tat ata 2160
Ala Leu Ser Lys Arg Asn Glu Lys Trp Asp Glu Val Tyr Lys Tyr Ile
705 710 715 720

gta aca aat tgg tta gca aag gtt aat aca cag att gat cta ata aga 2208
Val Thr Asn Trp Leu Ala Lys Val Asn Thr Gln Ile Asp Leu Ile Arg
725 730 735

aaa aaa atg aaa gaa gct tta gaa aat caa gca gaa gca aca aag gct 2256
Lys Lys Met Lys Glu Ala Leu Glu Asn Gln Ala Glu Ala Thr Lys Ala
740 745 750

ata ata aac tat cag tat aat caa tat act gag gaa gag aaa aat aat 2304
Ile Ile Asn Tyr Gln Tyr Asn Gln Tyr Thr Glu Glu Glu Lys Asn Asn

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755	760	765	
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Ile Asn Phe Asn Ile Asp Asp Leu Ser Ser Lys Leu Asn Glu Ser Ile			
770	775	780	
aat aaa gct atg att aat ata aat aaa ttt ttg aat caa tgc tct gtt			2400
Asn Lys Ala Met Ile Asn Ile Asn Lys Phe Leu Asn Gln Cys Ser Val			
785	790	795	800
tca tat tta atg aat tct atg atc cct tat ggt gtt aaa cgg tta gaa			2448
Ser Tyr Leu Met Asn Ser Met Ile Pro Tyr Gly Val Lys Arg Leu Glu			
805	810	815	
gat ttt gat gct agt ctt aaa gat gca tta tta aag tat ata tat gat			2496
Asp Phe Asp Ala Ser Leu Lys Asp Ala Leu Leu Lys Tyr Ile Tyr Asp			
820	825	830	
aat aga gga act tta att ggt caa gta gat aga tta aaa gat aaa gtt			2544
Asn Arg Gly Thr Leu Ile Gly Gln Val Asp Arg Leu Lys Asp Lys Val			
835	840	845	
aat aat aca ctt agt aca gat ata cct ttt cag ctt tcc aaa tac gta			2592
Asn Asn Thr Leu Ser Thr Asp Ile Pro Phe Gln Leu Ser Lys Tyr Val			
850	855	860	
gat aat caa aga tta tta tct aca ttt act gaa tat att aag tct agg			2640
Asp Asn Gln Arg Leu Leu Ser Thr Phe Thr Glu Tyr Ile Lys Ser Arg			
865	870	875	880
cct gga ccg gag acg ctc tgc ggg gct gag ctg gtg gat gct ctt cag			2688
Pro Gly Pro Glu Thr Leu Cys Gly Ala Glu Leu Val Asp Ala Leu Gln			
885	890	895	
ttc gtg tgt gga gac agg ggc ttt tat ttc aac aag ccc aca ggg tat			2736
Phe Val Cys Gly Asp Arg Gly Phe Tyr Phe Asn Lys Pro Thr Gly Tyr			
900	905	910	
ggc tcc agc agt cgg agg gcg cct cag aca ggt atc gtg gat gag tgc			2784
Gly Ser Ser Ser Arg Arg Ala Pro Gln Thr Gly Ile Val Asp Glu Cys			
915	920	925	
tgc ttc cgg agc tgt gat cta agg agg ctg gag atg tat tgc gca ccc			2832
Cys Phe Arg Ser Cys Asp Leu Arg Arg Leu Glu Met Tyr Cys Ala Pro			
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ctc aag cct gcc aag tca gct gaa gct tag			2862
Leu Lys Pro Ala Lys Ser Ala Glu Ala			
945	950		

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<400> 14

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Val Lys Ala Phe Lys Ile His Asn Lys Ile Trp Val Ile Pro Glu Arg
 35 40 45
 Asp Thr Phe Thr Asn Pro Glu Gly Asp Leu Asn Pro Pro Pro Glu
 50 55 60
 Ala Lys Gln Val Pro Val Ser Tyr Tyr Asp Ser Thr Tyr Leu Ser Thr
 65 70 75 80
 Asp Asn Glu Lys Asp Asn Tyr Leu Lys Gly Val Thr Lys Leu Phe Glu
 85 90 95
 Arg Ile Tyr Ser Thr Asp Leu Gly Arg Met Leu Leu Thr Ser Ile Val
 100 105 110
 Arg Gly Ile Pro Phe Trp Gly Gly Ser Thr Ile Asp Thr Glu Leu Lys
 115 120 125
 Val Ile Asp Thr Asn Cys Ile Asn Val Ile Gln Pro Asp Gly Ser Tyr
 130 135 140
 Arg Ser Glu Glu Leu Asn Leu Val Ile Ile Gly Pro Ser Ala Asp Ile
 145 150 155 160
 Ile Gln Phe Glu Cys Lys Ser Phe Gly His Glu Val Leu Asn Leu Thr
 165 170 175
 Arg Asn Gly Tyr Gly Ser Thr Gln Tyr Ile Arg Phe Ser Pro Asp Phe
 180 185 190
 Thr Phe Gly Phe Glu Glu Ser Leu Glu Val Asp Thr Asn Pro Leu Leu
 195 200 205
 Gly Ala Gly Lys Phe Ala Thr Asp Pro Ala Val Thr Leu Ala His Glu
 210 215 220
 Leu Ile His Ala Gly His Arg Leu Tyr Gly Ile Ala Ile Asn Pro Asn
 225 230 235 240
 Arg Val Phe Lys Val Asn Thr Asn Ala Tyr Tyr Glu Met Ser Gly Leu
 245 250 255
 Glu Val Ser Phe Glu Glu Leu Arg Thr Phe Gly Gly His Asp Ala Lys
 260 265 270
 Phe Ile Asp Ser Leu Gln Glu Asn Glu Phe Arg Leu Tyr Tyr Tyr Asn
 275 280 285
 Lys Phe Lys Asp Ile Ala Ser Thr Leu Asn Lys Ala Lys Ser Ile Val
 290 295 300

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Gly Thr Thr Ala Ser Leu Gln Tyr Met Lys Asn Val Phe Lys Glu Lys
305 310 315 320

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

Lys Phe Asp Lys Leu Tyr Lys Met Leu Thr Glu Ile Tyr Thr Glu Asp
340 345 350

Asn Phe Val Lys Phe Phe Lys Val Leu Asn Arg Lys Thr Tyr Leu Asn
355 360 365

Phe Asp Lys Ala Val Phe Lys Ile Asn Ile Val Pro Lys Val Asn Tyr
370 375 380

Thr Ile Tyr Asp Gly Phe Asn Leu Arg Asn Thr Asn Leu Ala Ala Asn
385 390 395 400

Phe Asn Gly Gln Asn Thr Glu Ile Asn Asn Met Asn Phe Thr Lys Leu
405 410 415

Lys Asn Phe Thr Gly Leu Phe Glu Phe Tyr Lys Leu Leu Cys Val Arg
420 425 430

Gly Ile Ile Thr Ser Lys Thr Lys Ser Leu Asp Lys Gly Tyr Asn Lys
435 440 445

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

Asn Asn Trp Asp Leu Phe Phe Ser Pro Ser Glu Asp Asn Phe Thr Asn
465 470 475 480

Asp Leu Asn Lys Gly Glu Glu Ile Thr Ser Asp Thr Asn Ile Glu Ala
485 490 495

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

Phe Asn Phe Asp Asn Glu Pro Glu Asn Ile Ser Ile Glu Asn Leu Ser
515 520 525

Ser Asp Ile Ile Gly Gln Leu Glu Leu Met Pro Asn Ile Glu Arg Phe
530 535 540

Pro Asn Gly Lys Lys Tyr Glu Leu Asp Lys Tyr Thr Met Phe His Tyr
545 550 555 560

Leu Arg Ala Gln Glu Phe Glu His Gly Lys Ser Arg Ile Ala Leu Thr

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565 570 575
 Asn Ser Val Asn Glu Ala Leu Leu Asn Pro Ser Arg Val Tyr Thr Phe
 580 585 590
 Phe Ser Ser Asp Tyr Val Lys Lys Val Asn Lys Ala Thr Glu Ala Ala
 595 600 605
 Met Phe Leu Gly Trp Val Glu Gln Leu Val Tyr Asp Phe Thr Asp Glu
 610 615 620
 Thr Ser Glu Val Ser Thr Thr Asp Lys Ile Ala Asp Ile Thr Ile Ile
 625 630 635 640
 Ile Pro Tyr Ile Gly Pro Ala Leu Asn Ile Gly Asn Met Leu Tyr Lys
 645 650 655
 Asp Asp Phe Val Gly Ala Leu Ile Phe Ser Gly Ala Val Ile Leu Leu
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 Glu Phe Ile Pro Glu Ile Ala Ile Pro Val Leu Gly Thr Phe Ala Leu
 675 680 685
 Val Ser Tyr Ile Ala Asn Lys Val Leu Thr Val Gln Thr Ile Asp Asn
 690 695 700
 Ala Leu Ser Lys Arg Asn Glu Lys Trp Asp Glu Val Tyr Lys Tyr Ile
 705 710 715 720
 Val Thr Asn Trp Leu Ala Lys Val Asn Thr Gln Ile Asp Leu Ile Arg
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 Lys Lys Met Lys Glu Ala Leu Glu Asn Gln Ala Glu Ala Thr Lys Ala
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 Ile Ile Asn Tyr Gln Tyr Asn Gln Tyr Thr Glu Glu Glu Lys Asn Asn
 755 760 765
 Ile Asn Phe Asn Ile Asp Asp Leu Ser Ser Lys Leu Asn Glu Ser Ile
 770 775 780
 Asn Lys Ala Met Ile Asn Ile Asn Lys Phe Leu Asn Gln Cys Ser Val
 785 790 795 800
 Ser Tyr Leu Met Asn Ser Met Ile Pro Tyr Gly Val Lys Arg Leu Glu
 805 810 815
 Asp Phe Asp Ala Ser Leu Lys Asp Ala Leu Leu Lys Tyr Ile Tyr Asp
 820 825 830

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Asn Arg Gly Thr Leu Ile Gly Gln Val Asp Arg Leu Lys Asp Lys Val
835 840 845

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

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

Pro Gly Pro Glu Thr Leu Cys Gly Ala Glu Leu Val Asp Ala Leu Gln
885 890 895

Phe Val Cys Gly Asp Arg Gly Phe Tyr Phe Asn Lys Pro Thr Gly Tyr
900 905 910

Gly Ser Ser Ser Arg Arg Ala Pro Gln Thr Gly Ile Val Asp Glu Cys
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gtt gac att gcc tac atc aaa att cca aac gcc gcc cag atg cag ccg 96
Val Asp Ile Ala Tyr Ile Lys Ile Pro Asn Ala Gly Gln Met Gln Pro
20 25 30
gtg aag gct ttc aag att cat aac aaa atc tgg gtt att ccg gaa cgc 144
Val Lys Ala Phe Lys Ile His Asn Lys Ile Trp Val Ile Pro Glu Arg
35 40 45
gat aca ttt acg aac ccg gaa gaa gga gac ttg aac ccg ccg ccg gaa 192
Asp Thr Phe Thr Asn Pro Glu Glu Gly Asp Leu Asn Pro Pro Pro Glu
50 55 60
gca aag cag gtg cca gtt tca tac tac gat tca acc tat ctg agc aca 240
Ala Lys Gln Val Pro Val Ser Tyr Tyr Asp Ser Thr Tyr Leu Ser Thr
65 70 75 80
gac aac gag aag gat aac tac ctg aag gga gtg acc aaa tta ttc gag 288
Asp Asn Glu Lys Asp Asn Tyr Leu Lys Gly Val Thr Lys Leu Phe Glu
85 90 95

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cgt att tat tcc act gac ctg ggc cgt atg ctg ctg acc tca atc gtc Arg Ile Tyr Ser Thr Asp Leu Gly Arg Met Leu Leu Thr Ser Ile Val 100 105 110	336
cgc gga atc cca ttt tgg ggt ggc agt acc att gac acg gag ttg aag Arg Gly Ile Pro Phe Trp Gly Gly Ser Thr Ile Asp Thr Glu Leu Lys 115 120 125	384
gtt att gac act aac tgc att aac gtg atc caa cca gac ggt agc tac Val Ile Asp Thr Asn Cys Ile Asn Val Ile Gln Pro Asp Gly Ser Tyr 130 135 140	432
aga tct gaa gaa ctt aac ctg gta atc atc ggg ccc tcc gcg gac att Arg Ser Glu Glu Leu Asn Leu Val Ile Ile Gly Pro Ser Ala Asp Ile 145 150 155 160	480
atc cag ttt gag tgc aag agc ttt ggc cac gaa gtg ttg aac ctg acg Ile Gln Phe Glu Cys Lys Ser Phe Gly His Glu Val Leu Asn Leu Thr 165 170 175	528
cgt aac ggt tac ggc tct act cag tac att cgt ttc agc cca gac ttc Arg Asn Gly Tyr Gly Ser Thr Gln Tyr Ile Arg Phe Ser Pro Asp Phe 180 185 190	576
acg ttc ggt ttc gag gag agc ctg gag gtt gat acc aac ccg ctg ttg Thr Phe Gly Phe Glu Glu Ser Leu Glu Val Asp Thr Asn Pro Leu Leu 195 200 205	624
ggt gca ggc aag ttc gca act gat cca gcg gtg acc ctg gca cac gag Gly Ala Gly Lys Phe Ala Thr Asp Pro Ala Val Thr Leu Ala His Glu 210 215 220	672
ctg atc cac gcc ggt cat cgt ctg tat ggc att gcg att aac ccg aac Leu Ile His Ala Gly His Arg Leu Tyr Gly Ile Ala Ile Asn Pro Asn 225 230 235 240	720
cgc gtg ttc aag gtt aac acc aac gcc tac tac gag atg agt ggt tta Arg Val Phe Lys Val Asn Thr Asn Ala Tyr Tyr Glu Met Ser Gly Leu 245 250 255	768
gaa gta agc ttc gag gaa ctg cgc acg ttc ggt ggc cat gat gcg aag Glu Val Ser Phe Glu Glu Leu Arg Thr Phe Gly Gly His Asp Ala Lys 260 265 270	816
ttt atc gac agc ttg cag gag aac gag ttc cgt ctg tac tac tac aac Phe Ile Asp Ser Leu Gln Glu Asn Glu Phe Arg Leu Tyr Tyr Tyr Asn 275 280 285	864
aag ttt aaa gat att gca agt aca ctg aac aag gct aag tcc att gtg Lys Phe Lys Asp Ile Ala Ser Thr Leu Asn Lys Ala Lys Ser Ile Val 290 295 300	912
ggt acc act gct tca tta cag tat atg aaa aat gtt ttt aaa gag aaa Gly Thr Thr Ala Ser Leu Gln Tyr Met Lys Asn Val Phe Lys Glu Lys 305 310 315 320	960
tat ctg cta tct gaa gat aca tct gga aaa ttt tgc gta gat aaa tta Tyr Leu Leu Ser Glu Asp Thr Ser Gly Lys Phe Ser Val Asp Lys Leu 325 330 335	1008
aaa ttt gat aag tta tac aaa atg tta aca gag att tac aca gag gat Lys Phe Asp Lys Leu Tyr Lys Met Leu Thr Glu Ile Tyr Thr Glu Asp 340 345 350	1056
aat ttt gtt aag ttt ttt aaa gta ctt aac aga aaa aca tat ttg aat Asn Phe Val Lys Phe Phe Lys Val Leu Asn Arg Lys Thr Tyr Leu Asn 355 360 365 370	1104

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355	360	365	
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aca ata tat gat gga ttt aat tta aga aat aca aat tta gca gca aac Thr Ile Tyr Asp Gly Phe Asn Leu Arg Asn Thr Asn Leu Ala Ala Asn 385 390 395 400			1200
ttt aat ggt caa aat aca gaa att aat aat atg aat ttt act aaa cta Phe Asn Gly Gln Asn Thr Glu Ile Asn Met Asn Phe Thr Lys Leu 405 410 415			1248
aaa aat ttt act gga ttg ttt gaa ttt tat aag ttg cta tgt gta aga Lys Asn Phe Thr Gly Leu Phe Glu Phe Tyr Lys Leu Leu Cys Val Arg 420 425 430			1296
ggg ata ata act tct aaa act aaa tca tta gat aaa gga tac aat aag Gly Ile Ile Thr Ser Lys Thr Lys Ser Leu Asp Lys Gly Tyr Asn Lys 435 440 445			1344
atc gaa ggt cgt tgc gat ggg gca tta aat gat tta tgt atc aaa gtt Ile Glu Gly Arg Cys Asp Gly Ala Leu Asn Asp Leu Cys Ile Lys Val 450 455 460			1392
aat aat tgg gac ttg ttt ttt agt cct tca gaa gat aat ttt act aat Asn Asn Trp Asp Leu Phe Phe Ser Pro Ser Glu Asp Asn Phe Thr Asn 465 470 475 480			1440
gat cta aat aaa gga gaa gaa att aca tct gat act aat ata gaa gca Asp Leu Asn Lys Gly Glu Glu Ile Thr Ser Asp Thr Asn Ile Glu Ala 485 490 495			1488
gca gaa gaa aat att agt tta gat tta ata caa caa tat tat tta acc Ala Glu Glu Asn Ile Ser Leu Asp Leu Ile Gln Gln Tyr Tyr Leu Thr 500 505 510			1536
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agt gac att ata ggc caa tta gaa ctt atg cct aat ata gaa aga ttt Ser Asp Ile Ile Gly Gln Leu Glu Leu Met Pro Asn Ile Glu Arg Phe 530 535 540			1632
cct aat gga aaa aag tat gag tta gat aaa tat act atg ttc cat tat Pro Asn Gly Lys Lys Tyr Glu Leu Asp Lys Tyr Thr Met Phe His Tyr 545 550 555 560			1680
ctt cgt gct caa gaa ttt gaa cat ggt aaa tct agg att gct tta aca Leu Arg Ala Gln Glu Phe Glu His Gly Lys Ser Arg Ile Ala Leu Thr 565 570 575			1728
aat tct gtt aac gaa gca tta tta aat cct agt cgt gtt tat aca ttt Asn Ser Val Asn Glu Ala Leu Leu Asn Pro Ser Arg Val Tyr Thr Phe 580 585 590			1776
ttt tct tca gac tat gta aag aaa gtt aat aaa gct acg gag gca gct Phe Ser Ser Asp Tyr Val Lys Lys Val Asn Lys Ala Thr Glu Ala Ala 595 600 605			1824
atg ttt tta ggc tgg gta gaa caa tta gta tat gat ttt acc gat gaa Met Phe Leu Gly Trp Val Glu Gln Leu Val Tyr Asp Phe Thr Asp Glu 610 615 620			1872

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act agc gaa gta agt act acg gat aaa att gcg gat ata act ata att Thr Ser Glu Val Ser Thr Thr Asp Lys Ile Ala Asp Ile Thr Ile Ile 625 630 635 640	1920
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gat gat ttt gta ggt gct tta ata ttt tca gga gct gtt att ctg tta Asp Asp Phe Val Gly Ala Leu Ile Phe Ser Gly Ala Val Ile Leu Leu 660 665 670	2016
gaa ttt ata cca gag att gca ata cct gta tta ggt act ttt gca ctt Glu Phe Ile Pro Glu Ile Ala Ile Pro Val Leu Gly Thr Phe Ala Leu 675 680 685	2064
gta tca tat att gcg aat aag gtt cta acc gtt caa aca ata gat aat Val Ser Tyr Ile Ala Asn Lys Val Leu Thr Val Gln Thr Ile Asp Asn 690 695 700	2112
gct tta agt aaa aga aat gaa aaa tgg gat gag gtc tat aaa tat ata Ala Leu Ser Lys Arg Asn Glu Lys Trp Asp Glu Val Tyr Lys Tyr Ile 705 710 715 720	2160
gta aca aat tgg tta gca aag gtt aat aca cag att gat cta ata aga Val Thr Asn Trp Lys Ala Lys Val Asn Thr Gln Ile Asp Leu Ile Arg 725 730 735	2208
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ata ata aac tat cag tat aat caa tat act gag gaa gag aaa aat aat Ile Ile Asn Tyr Gln Tyr Asn Gln Tyr Thr Glu Glu Glu Lys Asn Asn 755 760 765	2304
att aat ttt aat att gat gat tta agt tcg aaa ctt aat gag tct ata Ile Asn Phe Asn Ile Asp Asp Leu Ser Ser Lys Leu Asn Glu Ser Ile 770 775 780	2352
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gat ttt gat gct agt ctt aaa gat gca tta tta aag tat ata tat gat Asp Phe Asp Ala Ser Leu Lys Asp Ala Leu Leu Lys Tyr Ile Tyr Asp 820 825 830	2496
aat aga gga act tta att ggt caa gta gat aga tta aaa gat aaa gtt Asn Arg Gly Thr Leu Ile Gly Gln Val Asp Arg Leu Lys Asp Lys Val 835 840 845	2544
aat aat aca ctt agt aca gat ata cct ttt cag ctt tcc aaa tac gta Asn Asn Thr Leu Ser Thr Asp Ile Pro Phe Gln Leu Ser Lys Tyr Val 850 855 860	2592
gat aat caa aga tta tta tct aca ttt act gaa tat att aag tct agg Asp Asn Gln Arg Leu Leu Ser Thr Phe Thr Glu Tyr Ile Lys Ser Arg 865 870 875 880	2640
cct caa tct aaa gtt aaa aga caa ata ttt tca ggc tat caa tct gat Pro Gln Ser Lys Val Lys Arg Gln Ile Phe Ser Gly Tyr Gln Ser Asp 885 890 895 900	2688

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 900 905

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Val Lys Ala Phe Lys Ile His Asn Lys Ile Trp Val Ile Pro Glu Arg
 35 40 45

Asp Thr Phe Thr Asn Pro Glu Glu Gly Asp Leu Asn Pro Pro Pro Glu
 50 55 60

Ala Lys Gln Val Pro Val Ser Tyr Tyr Asp Ser Thr Tyr Leu Ser Thr
 65 70 75 80

Asp Asn Glu Lys Asp Asn Tyr Leu Lys Gly Val Thr Lys Leu Phe Glu
 85 90 95

Arg Ile Tyr Ser Thr Asp Leu Gly Arg Met Leu Leu Thr Ser Ile Val
 100 105 110

Arg Gly Ile Pro Phe Trp Gly Gly Ser Thr Ile Asp Thr Glu Leu Lys
 115 120 125

Val Ile Asp Thr Asn Cys Ile Asn Val Ile Gln Pro Asp Gly Ser Tyr
 130 135 140

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

Ile Gln Phe Glu Cys Lys Ser Phe Gly His Glu Val Leu Asn Leu Thr
 165 170 175

Arg Asn Gly Tyr Gly Ser Thr Gln Tyr Ile Arg Phe Ser Pro Asp Phe
 180 185 190

Thr Phe Gly Phe Glu Glu Ser Leu Glu Val Asp Thr Asn Pro Leu Leu
 195 200 205

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Gly Ala Gly Lys Phe Ala Thr Asp Pro Ala Val Thr Leu Ala His Glu
 210 215 220
 Leu Ile His Ala Gly His Arg Leu Tyr Gly Ile Ala Ile Asn Pro Asn
 225 230 235 240
 Arg Val Phe Lys Val Asn Thr Asn Ala Tyr Tyr Glu Met Ser Gly Leu
 245 250 255
 Glu Val Ser Phe Glu Glu Leu Arg Thr Phe Gly Gly His Asp Ala Lys
 260 265 270
 Phe Ile Asp Ser Leu Gln Glu Asn Glu Phe Arg Leu Tyr Tyr Tyr Asn
 275 280 285
 Lys Phe Lys Asp Ile Ala Ser Thr Leu Asn Lys Ala Lys Ser Ile Val
 290 295 300
 Gly Thr Thr Ala Ser Leu Gln Tyr Met Lys Asn Val Phe Lys Glu Lys
 305 310 315 320
 Tyr Leu Leu Ser Glu Asp Thr Ser Gly Lys Phe Ser Val Asp Lys Leu
 325 330 335
 Lys Phe Asp Lys Leu Tyr Lys Met Leu Thr Glu Ile Tyr Thr Glu Asp
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 Asn Phe Val Lys Phe Phe Lys Val Leu Asn Arg Lys Thr Tyr Leu Asn
 355 360 365
 Phe Asp Lys Ala Val Phe Lys Ile Asn Ile Val Pro Lys Val Asn Tyr
 370 375 380
 Thr Ile Tyr Asp Gly Phe Asn Leu Arg Asn Thr Asn Leu Ala Ala Asn
 385 390 395 400
 Phe Asn Gly Gln Asn Thr Glu Ile Asn Asn Met Asn Phe Thr Lys Leu
 405 410 415
 Lys Asn Phe Thr Gly Leu Phe Glu Phe Tyr Lys Leu Leu Cys Val Arg
 420 425 430
 Gly Ile Ile Thr Ser Lys Thr Lys Ser Leu Asp Lys Gly Tyr Asn Lys
 435 440 445
 Ile Glu Gly Arg Cys Asp Gly Ala Leu Asn Asp Leu Cys Ile Lys Val
 450 455 460
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Asp Leu Asn Lys Gly Glu Glu Ile Thr Ser Asp Thr Asn Ile Glu Ala
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 Ser Asp Ile Ile Gly Gln Leu Glu Leu Met Pro Asn Ile Glu Arg Phe
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 Pro Asn Gly Lys Lys Tyr Glu Leu Asp Lys Tyr Thr Met Phe His Tyr
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 565 570 575
 Asn Ser Val Asn Glu Ala Leu Leu Asn Pro Ser Arg Val Tyr Thr Phe
 580 585 590
 Phe Ser Ser Asp Tyr Val Lys Lys Val Asn Lys Ala Thr Glu Ala Ala
 595 600 605
 Met Phe Leu Gly Trp Val Glu Gln Leu Val Tyr Asp Phe Thr Asp Glu
 610 615 620
 Thr Ser Glu Val Ser Thr Thr Asp Lys Ile Ala Asp Ile Thr Ile Ile
 625 630 635 640
 Ile Pro Tyr Ile Gly Pro Ala Leu Asn Ile Gly Asn Met Leu Tyr Lys
 645 650 655
 Asp Asp Phe Val Gly Ala Leu Ile Phe Ser Gly Ala Val Ile Leu Leu
 660 665 670
 Glu Phe Ile Pro Glu Ile Ala Ile Pro Val Leu Gly Thr Phe Ala Leu
 675 680 685
 Val Ser Tyr Ile Ala Asn Lys Val Leu Thr Val Gln Thr Ile Asp Asn
 690 695 700
 Ala Leu Ser Lys Arg Asn Glu Lys Trp Asp Glu Val Tyr Lys Tyr Ile
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 Val Thr Asn Trp Leu Ala Lys Val Asn Thr Gln Ile Asp Leu Ile Arg
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 Lys Lys Met Lys Glu Ala Leu Glu Asn Gln Ala Glu Ala Thr Lys Ala

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 Ile Asn Phe Asn Ile Asp Asp Leu Ser Ser Lys Leu Asn Glu Ser Ile
 770 775 780
 Asn Lys Ala Met Ile Asn Ile Asn Lys Phe Leu Asn Gln Cys Ser Val
 785 790 795 800
 Ser Tyr Leu Met Asn Ser Met Ile Pro Tyr Gly Val Lys Arg Leu Glu
 805 810 815
 Asp Phe Asp Ala Ser Leu Lys Asp Ala Leu Leu Lys Tyr Ile Tyr Asp
 820 825 830
 Asn Arg Gly Thr Leu Ile Gly Gln Val Asp Arg Leu Lys Asp Lys Val
 835 840 845
 Asn Asn Thr Leu Ser Thr Asp Ile Pro Phe Gln Leu Ser Lys Tyr Val
 850 855 860
 Asp Asn Gln Arg Leu Leu Ser Thr Phe Thr Glu Tyr Ile Lys Ser Arg
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 gtt gac att gcc tac atc aaa att cca aac gcc gcc cag atg cag ccg 96
 Val Asp Ile Ala Tyr Ile Lys Ile Pro Asn Ala Gly Gln Met Gln Pro
 20 25 30
 gtg aag gct ttc aag att cat aac aaa atc tgg gtt att ccg gaa cgc 144
 Val Lys Ala Phe Lys Ile His Asn Lys Ile Trp Val Ile Pro Glu Arg
 35 40 45

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gat aca ttt acg aac ccg gaa gaa gga gac ttg aac ccg ccg ccg gaa 192
Asp Thr Phe Thr Asn Pro Glu Glu Gly Asp Leu Asn Pro Pro Pro Glu
50 55 60
gca aag cag gtg cca gtt tca tac tac gat tca acc tat ctg agc aca 240
Ala Lys Gln Val Pro Val Ser Tyr Tyr Asp Ser Thr Tyr Leu Ser Thr
65 70 75 80
gac aac gag aag gat aac tac ctg aag gga gtg acc aaa tta ttc gag 288
Asp Asn Glu Lys Asp Asn Tyr Leu Lys Gly Val Thr Lys Leu Phe Glu
85 90 95
cgt att tat tcc act gac ctg ggc cgt atg ctg ctg acc tca atc gtc 336
Arg Ile Tyr Ser Thr Asp Leu Gly Arg Met Leu Leu Thr Ser Ile Val
100 105 110
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Arg Gly Ile Pro Phe Trp Gly Gly Ser Thr Ile Asp Thr Glu Leu Lys
115 120 125
gtt att gac act aac tgc att aac gtg atc caa cca gac ggt agc tac 432
Val Ile Asp Thr Asn Cys Ile Asn Val Ile Gln Pro Asp Gly Ser Tyr
130 135 140
aga tct gaa gaa ctt aac ctc gta atc atc ggg ccc tcc gcg gac att 480
Arg Ser Glu Glu Leu Asn Leu Val Ile Ile Gly Pro Ser Ala Asp Ile
145 150 155 160
atc cag ttt gag tgc aag agc ttt ggc cac gaa gtg ttg aac ctg acg 528
Ile Gln Phe Glu Cys Lys Ser Phe Gly His Glu Val Leu Asn Leu Thr
165 170 175
cgt aac ggt tac ggc tct act cag tac att cgt ttc agc cca gac ttc 576
Arg Asn Gly Tyr Gly Ser Thr Gln Tyr Ile Arg Phe Ser Pro Asp Phe
180 185 190
acg ttc ggt ttc gag gag agc ctg gag gtt gat acc aac ccg ctg ttg 624
Thr Phe Gly Phe Glu Glu Ser Leu Glu Val Asp Thr Asn Pro Leu Leu
195 200 205
ggt gca ggc aag ttc gca act gat cca gcg gtg acc ctg gca cac gag 672
Gly Ala Gly Lys Phe Ala Thr Asp Pro Ala Val Thr Leu Ala His Glu
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Leu Ile His Ala Gly His Arg Leu Tyr Gly Ile Ala Ile Asn Pro Asn
225 230 235 240
cgc gtg ttc aag gtt aac acc aac gcc tac tac gag atg agt ggt tta 768
Arg Val Phe Lys Val Asn Thr Asn Ala Tyr Tyr Glu Met Ser Gly Leu
245 250 255
gaa gta agc ttc gag gaa ctg cgc acg ttc ggt ggc cat gat gcg aag 816
Glu Val Ser Phe Glu Glu Leu Arg Thr Phe Gly Gly His Asp Ala Lys
260 265 270
ttt atc gac agc ttg cag gag aac gag ttc cgt ctg tac tac tac aac 864
Phe Ile Asp Ser Leu Gln Glu Asn Glu Phe Arg Leu Tyr Tyr Tyr Asn
275 280 285
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290 295 300
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	325	330	335	
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Lys Phe Asp Lys Leu Tyr Lys Met Leu Thr Glu Ile Tyr Thr Glu Asp				
	340	345	350	
aat ttt gtt aag ttt ttt aaa gta ctt aac aga aaa aca tat ttg aat				1104
Asn Phe Val Lys Phe Phe Lys Val Leu Asn Arg Lys Thr Tyr Leu Asn				
	355	360	365	
ttt gat aaa gcc gta ttt aag ata aat ata gta cct aag gta aat tac				1152
Phe Asp Lys Ala Val Phe Lys Ile Asn Ile Val Pro Lys Val Asn Tyr				
	370	375	380	
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Thr Ile Tyr Asp Gly Phe Asn Leu Arg Asn Thr Asn Leu Ala Ala Asn				
	385	390	400	
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	405	410	415	
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Lys Asn Phe Thr Gly Leu Phe Glu Phe Tyr Lys Leu Leu Cys Val Arg				
	420	425	430	
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	435	440	445	
atc gaa ggt cgt tgc gat ggg gca tta aat gat tta tgt atc aaa gtt				1392
Ile Glu Gly Arg Cys Asp Gly Ala Leu Asn Asp Leu Cys Ile Lys Val				
	450	455	460	
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Asn Asn Trp Asp Leu Phe Phe Ser Pro Ser Glu Asp Asn Phe Thr Asn				
	465	470	475	480
gat cta aat aaa gga gaa gaa att aca tct gat act aat ata gaa gca				1488
Asp Leu Asn Lys Gly Glu Glu Ile Thr Ser Asp Thr Asn Ile Glu Ala				
	485	490	495	
gca gaa gaa aat att agt tta gat tta ata caa caa tat tat tta acc				1536
Ala Glu Glu Asn Ile Ser Leu Asp Leu Ile Gln Gln Tyr Tyr Leu Thr				
	500	505	510	
ttt aat ttt gat aat gaa cct gaa aat att tca ata gaa aat ctt tca				1584
Phe Asn Phe Asp Asn Glu Pro Glu Asn Ile Ser Ile Glu Asn Leu Ser				
	515	520	525	
agt gac att ata ggc caa tta gaa ctt atg cct aat ata gaa aga ttt				1632
Ser Asp Ile Ile Gly Gln Leu Glu Leu Met Pro Asn Ile Glu Arg Phe				
	530	535	540	
cct aat gga aaa aag tat gag tta gat aaa tat act atg ttc cat tat				1680
Pro Asn Gly Lys Lys Tyr Glu Leu Asp Lys Tyr Thr Met Phe His Tyr				
	545	550	555	560
ctt cgt gct caa gaa ttt gaa cat ggt aaa tct agg att gct tta aca				1728
Leu Arg Ala Gln Glu Phe Glu His Gly Lys Ser Arg Ile Ala Leu Thr				
	565	570	575	

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aat tct gtt aac gaa gca tta tta aat cct agt cgt gtt tat aca ttt 1776
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 580 585 590

ttt tct tca gac tat gta aag aaa gtt aat aaa gct acg gag gca gct 1824
 Phe Ser Ser Asp Tyr Val Lys Lys Val Asn Lys Ala Thr Glu Ala Ala
 595 600 605

atg ttt tta ggc tgg gta gaa caa tta gta tat gat ttt acc gat gaa 1872
 Met Phe Leu Gly Trp Val Glu Gln Leu Val Tyr Asp Phe Thr Asp Glu
 610 615 620

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gta tca tat att gcg aat aag gtt cta acc gtt caa aca ata gat aat 2112
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 Glu Val Ser Phe Glu Glu Leu Arg Thr Phe Gly Gly His Asp Ala Lys
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 Phe Ile Asp Ser Leu Gln Glu Asn Glu Phe Arg Leu Tyr Tyr Tyr Asn
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Lys Asn Phe Thr Gly Leu Phe Glu Phe Tyr Lys Leu Leu Cys Val Arg
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Pro Asn Gly Lys Lys Tyr Glu Leu Asp Lys Tyr Thr Met Phe His Tyr
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His Leu Pro Asn Leu Asn Glu Glu Gln Arg Asn Ala Phe Ile Gln Ser
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Asn Asn Ile Ile Met Met Glu Pro Pro Phe Ala Arg Gly Thr Gly Arg
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Tyr Tyr Lys Ala Phe Lys Ile Thr Asp Arg Ile Trp Ile Ile Pro Glu
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 Ile Phe Asn Arg Asp Val Cys Glu Tyr Tyr Asp Pro Asp Tyr Leu Asn
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 Asn Arg Ile Lys Ser Lys Pro Leu Gly Glu Lys Leu Leu Glu Met Ile
 100 105 110

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 Ile Gln Asn His Phe Ala Ser Arg Glu Gly Phe Gly Gly Ile Met Gln
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 Gln Asn Ser Lys Tyr Ile Asn Tyr Arg Asp Leu Tyr Ile Gly Glu
 1130 1135 1140

aaa ttt att ata aga aga aag tca aat tct caa tct ata aat gat 3474
 Lys Phe Ile Ile Arg Arg Lys Ser Asn Ser Gln Ser Ile Asn Asp
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gat ata gtt aga aaa gaa gat tat ata tat cta ga 3509
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Tyr Tyr Lys Ala Phe Lys Ile Thr Asp Arg Ile Trp Ile Ile Pro Glu
 35 40 45

Arg Tyr Thr Phe Gly Tyr Lys Pro Glu Asp Phe Asn Lys Ser Ser Gly
 50 55 60

Ile Phe Asn Arg Asp Val Cys Glu Tyr Tyr Asp Pro Asp Tyr Leu Asn
 65 70 75 80

Thr Asn Asp Lys Lys Asn Ile Phe Leu Gln Thr Met Ile Lys Leu Phe
 85 90 95

Asn Arg Ile Lys Ser Lys Pro Leu Gly Glu Lys Leu Leu Glu Met Ile
 100 105 110

Ile Asn Gly Ile Pro Tyr Leu Gly Asp Arg Arg Val Pro Leu Glu Glu
 115 120 125

Phe Asn Thr Asn Ile Ala Ser Val Thr Val Asn Lys Leu Ile Ser Asn
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Pro Gly Glu Val Glu Arg Lys Lys Gly Ile Phe Ala Asn Leu Ile Ile
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Phe Gly Pro Gly Pro Val Leu Asn Glu Asn Glu Thr Ile Asp Ile Gly
165 170 175

Ile Gln Asn His Phe Ala Ser Arg Glu Gly Phe Gly Gly Ile Met Gln
180 185 190

Met Lys Phe Cys Pro Glu Tyr Val Ser Val Phe Asn Asn Val Gln Glu
195 200 205

Asn Lys Gly Ala Ser Ile Phe Asn Arg Arg Gly Tyr Phe Ser Asp Pro
210 215 220

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Ala Leu Ile Leu Met His Glu Leu Ile His Val Leu His Gly Leu Tyr
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Gly Ile Lys Val Asp Asp Leu Pro Ile Val Pro Asn Glu Lys Lys Phe
245 250 255

Phe Met Gln Ser Thr Asp Ala Ile Gln Ala Glu Glu Leu Tyr Thr Phe
260 265 270

Gly Gly Gln Asp Pro Ser Ile Ile Thr Pro Ser Thr Asp Lys Ser Ile
275 280 285

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Tyr Asp Lys Val Leu Gln Asn Phe Arg Gly Ile Val Asp Arg Leu Asn
290 295 300

Lys Val Leu Val Cys Ile Ser Asp Pro Asn Ile Asn Ile Asn Ile Tyr
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Lys Asn Lys Phe Lys Asp Lys Tyr Lys Phe Val Glu Asp Ser Glu Gly
325 330 335

Lys Tyr Ser Ile Asp Val Glu Ser Phe Asp Lys Leu Tyr Lys Ser Leu
340 345 350

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Met Phe Gly Phe Thr Glu Thr Asn Ile Ala Glu Asn Tyr Lys Ile Lys
355 360 365

Thr Arg Ala Ser Tyr Phe Ser Asp Ser Leu Pro Pro Val Lys Ile Lys
370 375 380

Asn Leu Leu Asp Asn Glu Ile Tyr Thr Ile Glu Glu Gly Phe Asn Ile
385 390 395 400

Ser Asp Lys Asp Met Glu Lys Glu Tyr Arg Gly Gln Asn Lys Ala Ile
405 410 415

Asn Lys Gln Ala Tyr Glu Glu Ile Ser Lys Glu His Leu Ala Val Tyr

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Arg Asn Glu Lys Trp Ser Asp Met Tyr Gly Leu Ile Val Ala Gln Trp
 690 695 700
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 Lys Ala Leu Asn Tyr Gln Ala Gln Ala Leu Glu Glu Ile Ile Lys Tyr
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 Arg Tyr Asn Ile Tyr Ser Glu Lys Glu Lys Ser Asn Ile Asn Ile Asp
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 Phe Asn Asp Ile Asn Ser Lys Leu Asn Glu Gly Ile Asn Gln Ala Ile
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 Asp Asn Ile Asn Asn Phe Ile Asn Gly Cys Ser Val Ser Tyr Leu Met
 770 775 780
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 Lys Thr Ile Met Pro Phe Asp Leu Ser Ile Tyr Thr Asn Asp Thr Ile
 835 840 845
 Leu Ile Glu Met Phe Asn Lys Tyr Asn Ser Glu Ile Leu Asn Asn Ile
 850 855 860
 Ile Leu Asn Leu Arg Tyr Lys Asp Asn Asn Leu Ile Asp Leu Ser Gly
 865 870 875 880
 Tyr Gly Ala Lys Val Glu Val Tyr Asp Gly Val Glu Leu Asn Asp Lys
 885 890 895
 Asn Gln Phe Lys Leu Thr Ser Ser Ala Asn Ser Lys Ile Arg Val Thr
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 Gln Asn Gln Asn Ile Ile Phe Asn Ser Val Phe Leu Asp Phe Ser Val
 915 920 925
 Ser Phe Trp Ile Arg Ile Pro Lys Tyr Lys Asn Asp Gly Ile Gln Asn
 930 935 940
 Tyr Ile His Asn Glu Tyr Thr Ile Ile Asn Cys Met Lys Asn Asn Ser
 945 950 955 960

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Gly Trp Lys Ile Ser Ile Arg Gly Asn Arg Ile Ile Trp Thr Leu Ile
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Asp Ile Asn Gly Lys Thr Lys Ser Val Phe Phe Glu Tyr Asn Ile Arg
 980 985 990

Glu Asp Ile Ser Glu Tyr Ile Asn Arg Trp Phe Phe Val Thr Ile Thr
 995 1000 1005

Asn Asn Leu Asn Asn Ala Lys Ile Tyr Ile Asn Gly Lys Leu Glu
 1010 1015 1020

Ser Asn Thr Asp Ile Lys Asp Ile Arg Glu Val Ile Ala Asn Gly
 1025 1030 1035

Glu Ile Ile Phe Lys Leu Asp Gly Asp Ile Asp Arg Thr Gln Phe
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Ile Trp Met Lys Tyr Phe Ser Ile Phe Asn Thr Glu Leu Ser Gln
 1055 1060 1065

Ser Asn Ile Glu Glu Arg Tyr Lys Ile Gln Ser Tyr Ser Glu Tyr
 1070 1075 1080

Leu Lys Asp Phe Trp Gly Asn Pro Leu Met Tyr Asn Lys Glu Tyr
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Tyr Met Phe Asn Ala Gly Asn Lys Asn Ser Tyr Ile Lys Leu Lys
 1100 1105 1110

Lys Asp Ser Pro Val Gly Glu Ile Leu Thr Arg Ser Lys Tyr Asn
 1115 1120 1125

Gln Asn Ser Lys Tyr Ile Asn Tyr Arg Asp Leu Tyr Ile Gly Glu
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Lys Phe Ile Ile Arg Arg Lys Ser Asn Ser Gln Ser Ile Asn Asp
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Asp Ile Val Arg Lys Glu Asp Tyr Ile Tyr Leu
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 aat aat att att atg atg gag cct cca ttt gcg aga ggt acg ggg aga 96
 Asn Asn Ile Ile Met Met Glu Pro Pro Phe Ala Arg Gly Thr Gly Arg
 20 25 30
 tat tat aaa gct ttt aaa atc aca gat cgt att tgg ata ata ccg gaa 144
 Tyr Tyr Lys Ala Phe Lys Ile Thr Asp Arg Ile Trp Ile Ile Pro Glu
 35 40 45
 aga tat act ttt gga tat aaa cct gag gat ttt aat aaa agt tcc ggt 192
 Arg Tyr Thr Phe Gly Tyr Lys Pro Glu Asp Phe Asn Lys Ser Ser Gly
 50 55 60
 att ttt aat aga gat gtt tgt gaa tat tat gat cca gat tac tta aat 240
 Ile Phe Asn Arg Asp Val Cys Glu Tyr Tyr Asp Pro Asp Tyr Leu Asn
 65 70 75 80
 act aat gat aaa aag aat ata ttt tta caa aca atg atc aag tta ttt 288
 Thr Asn Asp Lys Lys Asn Ile Phe Leu Gln Thr Met Ile Lys Leu Phe
 85 90 95
 aat aga atc aaa tca aaa cca ttg ggt gaa aag tta tta gag atg att 336
 Asn Arg Ile Lys Ser Lys Pro Leu Gly Glu Lys Leu Leu Glu Met Ile
 100 105 110
 ata aat ggt ata cct tat ctt gga gat aga cgt gtt cca ctc gaa gag 384
 Ile Asn Gly Ile Pro Tyr Leu Gly Asp Arg Arg Val Pro Leu Glu Glu
 115 120 125
 ttt aac aca aac att gct agt gta act gtt aat aaa tta atc agt aat 432
 Phe Asn Thr Asn Ile Ala Ser Val Thr Val Asn Lys Leu Ile Ser Asn
 130 135 140
 cca gga gaa gtg gag cga aaa aaa ggt att ttc gca aat tta ata ata 480
 Pro Gly Glu Val Glu Arg Lys Lys Gly Ile Phe Ala Asn Leu Ile Ile
 145 150 155 160
 ttt gga cct ggg cca gtt tta aat gaa aat gag act ata gat ata ggt 528
 Phe Gly Pro Gly Val Leu Asn Glu Glu Thr Ile Asp Ile Gly
 165 170 175
 ata caa aat cat ttt gca tca agg gaa ggc ttc ggg ggt ata atg caa 576
 Ile Gln Asn His Phe Ala Ser Arg Glu Gly Phe Gly Gly Ile Met Gln
 180 185 190
 atg aag ttt tgc cca gaa tat gta agc gta ttt aat aat gtt caa gaa 624
 Met Lys Phe Cys Pro Glu Tyr Val Ser Val Phe Asn Asn Val Gln Glu
 195 200 205
 aac aaa ggc gca agt ata ttt aat aga cgt gga tat ttt tca gat cca 672
 Asn Lys Gly Ala Ser Ile Phe Asn Arg Arg Gly Tyr Phe Ser Asp Pro
 210 215 220
 gcc ttg ata tta atg cat gaa ctt ata cat gtt tta cat gga tta tat 720
 Ala Leu Ile Leu Met His Glu Leu Ile His Val Leu His Gly Leu Tyr
 225 230 235 240
 ggc att aaa gta gat gat tta cca att gta cca aat gaa aaa aaa ttt 768
 Gly Ile Lys Val Asp Asp Leu Pro Ile Val Pro Asn Glu Lys Lys Phe
 245 250 255
 ttt atg caa tct aca gat gct ata cag gca gaa gaa cta tat aca ttt 816

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Phe Met Gln Ser Thr Asp Ala Ile Gln Ala Glu Glu Leu Tyr Thr Phe	
260 265 270	
gga gga caa gat ccc agc atc ata act cct tct acg gat aaa agt atc	864
Gly Gly Gln Asp Pro Ser Ile Ile Thr Pro Ser Thr Asp Lys Ser Ile	
275 280 285	
tat gat aaa gtt ttg caa aat ttt aga ggg ata gtt gat aga ctt aac	912
Tyr Asp Lys Val Leu Gln Asn Phe Arg Gly Ile Val Asp Arg Leu Asn	
290 295 300	
aag gtt tta gtt tgc ata tca gat cct aac att aat att aat ata tat	960
Lys Val Leu Val Cys Ile Ser Asp Pro Asn Ile Asn Ile Asn Ile Tyr	
305 310 315 320	
aaa aat aaa ttt aaa gat aaa tat aaa ttc gtt gaa gat tct gag gga	1008
Lys Asn Lys Phe Lys Asp Lys Tyr Lys Phe Val Glu Asp Ser Glu Gly	
325 330 335	
aaa tat agt ata gat gta gaa agt ttt gat aaa tta tat aaa agc tta	1056
Lys Tyr Ser Ile Asp Val Glu Ser Phe Asp Lys Leu Tyr Lys Ser Leu	
340 345 350	
atg ttt ggt ttt aca gaa act aat ata gca gaa aat tat aaa ata aaa	1104
Met Phe Gly Phe Thr Glu Thr Asn Ile Ala Glu Asn Tyr Lys Ile Lys	
355 360 365	
act aga gct tct tat ttt agt gat tcc tta cca cca gta aaa ata aaa	1152
Thr Arg Ala Ser Tyr Phe Ser Asp Ser Leu Pro Val Lys Ile Lys	
370 375 380	
aat tta tta gat aat gaa atc tat act ata gag gaa ggg ttt aat ata	1200
Asn Leu Leu Asp Asn Glu Ile Tyr Thr Ile Glu Glu Gly Phe Asn Ile	
385 390 395 400	
tct gat aaa gat atg gaa aaa gaa tat aga ggt cag aat aaa gct ata	1248
Ser Asp Lys Asp Met Glu Lys Glu Tyr Arg Gly Gln Asn Lys Ala Ile	
405 410 415	
aat aaa caa gct tat gaa gaa att agc aag gag cat ttg gct gta tat	1296
Asn Lys Gln Ala Tyr Glu Glu Ile Ser Lys Glu His Leu Ala Val Tyr	
420 425 430	
aag ata caa atg tgt aaa agt gtt aaa gct cca gga ata tgt att gat	1344
Lys Ile Gln Met Cys Lys Ser Val Lys Ala Pro Gly Ile Cys Ile Asp	
435 440 445	
gtt gat aat gaa gat ttg ttc ttt ata gct gat aaa aat agt ttt tca	1392
Val Asp Asn Glu Asp Leu Phe Phe Ile Ala Asp Lys Asn Ser Phe Ser	
450 455 460	
gat gat tta tct aaa aac gaa aga ata gaa tat aat aca cag agt aat	1440
Asp Asp Leu Ser Lys Asn Glu Arg Ile Glu Tyr Asn Thr Gln Ser Asn	
465 470 475 480	
tat ata gaa aat gac ttc cct ata aat gaa tta att tta gat act gat	1488
Tyr Ile Glu Asn Asp Phe Pro Ile Asn Glu Leu Ile Leu Asp Thr Asp	
485 490 495	
tta ata agt aaa ata gaa tta cca agt gaa aat aca gaa tca ctt act	1536
Leu Ile Ser Lys Ile Glu Leu Pro Ser Glu Asn Thr Glu Ser Leu Thr	
500 505 510	
gat ttt aat gta gat gtt cca gta tat gaa aaa caa ccc gct ata aaa	1584
Asp Phe Asn Val Asp Val Pro Val Tyr Glu Lys Gln Pro Ala Ile Lys	
515 520 525	

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aaa att ttt aca gat gaa aat acc atc ttt caa tat tta tac tct cag 1632
 Lys Ile Phe Thr Asp Glu Asn Thr Ile Phe Gln Tyr Leu Tyr Ser Gln
 530 535 540

aca ttt cct cta gat ata aga gat ata agt tta aca tct tca ttt gat 1680
 Thr Phe Pro Leu Asp Ile Arg Asp Ile Ser Leu Thr Ser Ser Phe Asp
 545 550 555 560

gat gca tta tta ttt tct aac aaa gtt tat tca ttt ttt tct atg gat 1728
 Asp Ala Leu Leu Phe Ser Asn Lys Val Tyr Ser Phe Phe Ser Met Asp
 565 570 575

tat att aaa act gct aat aaa gtg gta gaa gca gga tta ttt gca ggt 1776
 Tyr Ile Lys Thr Ala Asn Lys Val Val Glu Ala Gly Leu Phe Ala Gly
 580 585 590

tgg gtg aaa cag ata gta aat gat ttt gta atc gaa gct aat aaa agc 1824
 Trp Val Lys Gln Ile Val Asn Asp Phe Val Ile Glu Ala Asn Lys Ser
 595 600 605

aat thr atg gat aaa att gca gat ata tct cta att gtt cct tat ata 1872
 Asn Thr Met Asp Lys Ile Ala Asp Ile Ser Leu Ile Val Pro Tyr Ile
 610 615 620

gga tta gct tta aat gta gga aat gaa aca gct aaa gga aat ttt gaa 1920
 Gly Leu Ala Leu Asn Val Gly Asn Glu Thr Ala Lys Gly Asn Phe Glu
 625 630 635 640

aat gct ttt gag att gca gga gcc agt att cta cta gaa ttt ata cca 1968
 Asn Ala Phe Glu Ile Ala Gly Ala Ser Ile Leu Leu Glu Phe Ile Pro
 645 650 655

gaa ctt tta ata cct gta gtt gga gcc ttt tta tta gaa tca tat att 2016
 Glu Leu Leu Ile Pro Val Val Gly Ala Phe Leu Leu Glu Ser Tyr Ile
 660 665 670

gac aat aaa aat aaa att att aaa aca ata gat aat gct tta act aaa 2064
 Asp Asn Lys Asn Lys Ile Ile Lys Thr Ile Asp Asn Ala Leu Thr Lys
 675 680 685

aga aat gaa aaa tgg agt gat atg tac gga tta ata gta gcg caa tgg 2112
 Arg Asn Glu Lys Trp Ser Asp Met Tyr Gly Leu Ile Val Ala Gln Trp
 690 695 700

ctc tca aca gtt aat act caa ttt tat aca ata aaa gag gga atg tat 2160
 Leu Ser Thr Val Asn Thr Gln Phe Tyr Thr Ile Lys Glu Gly Met Tyr
 705 710 715 720

aag gct tta aat tat caa gca caa gca ttg gaa gaa ata ata aaa tac 2208
 Lys Ala Leu Asn Tyr Gln Ala Gln Ala Leu Glu Glu Ile Ile Lys Tyr
 725 730 735

aga tat aat ata tat tct gaa aaa gaa aag tca aat att aac atc gat 2256
 Arg Tyr Asn Ile Tyr Ser Glu Lys Glu Lys Ser Asn Ile Asn Ile Asp
 740 745 750

ttt aat gat ata aat tct aaa ctt aat gag ggt att aac caa gct ata 2304
 Phe Asn Asp Ile Asn Ser Lys Leu Asn Glu Gly Ile Asn Gln Ala Ile
 755 760 765

gat aat ata aat aat ttt ata aat gga tgt tct gta tca tat tta atg 2352
 Asp Asn Ile Asn Asn Phe Ile Asn Gly Cys Ser Val Ser Tyr Leu Met
 770 775 780

aaa aaa atg att cca tta gct gta gaa aaa tta cta gac ttt gat aat 2400
 Lys Lys Met Ile Pro Leu Ala Val Glu Lys Leu Leu Asp Phe Asp Asn

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785 790 795 800
 act ctc aaa aaa aat ttg tta aat tat ata gat gaa aat aaa tta tat 2448
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 805 810 815
 ttg att gga agt gca gaa tat gaa aaa tca aaa gta aat aaa tac ttg 2496
 Leu Ile Gly Ser Ala Glu Tyr Glu Lys Ser Lys Val Asn Lys Tyr Leu
 820 825 830
 aaa acc att atg ccg ttt gat ctt tca ata tat acc aat gat aca ata 2544
 Lys Thr Ile Met Pro Phe Asp Leu Ser Ile Tyr Thr Asn Asp Thr Ile
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 cta ata gaa atg ttt aat aaa tat aat agc 2574
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 <212> PRT
 <213> Clostridium botulinum

<400> 22

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Tyr Tyr Lys Ala Phe Lys Ile Thr Asp Arg Ile Trp Ile Ile Pro Glu
 35 40 45

Arg Tyr Thr Phe Gly Tyr Lys Pro Glu Asp Phe Asn Lys Ser Ser Gly
 50 55 60

Ile Phe Asn Arg Asp Val Cys Glu Tyr Tyr Asp Pro Asp Tyr Leu Asn
 65 70 75 80

Thr Asn Asp Lys Lys Asn Ile Phe Leu Gln Thr Met Ile Lys Leu Phe
 85 90 95

Asn Arg Ile Lys Ser Lys Pro Leu Gly Glu Lys Leu Leu Glu Met Ile
 100 105 110

Ile Asn Gly Ile Pro Tyr Leu Gly Asp Arg Arg Val Pro Leu Glu Glu
 115 120 125

Phe Asn Thr Asn Ile Ala Ser Val Thr Val Asn Lys Leu Ile Ser Asn
 130 135 140

Pro Gly Glu Val Glu Arg Lys Lys Gly Ile Phe Ala Asn Leu Ile Ile
 145 150 155 160

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Phe Gly Pro Gly Pro Val Leu Asn Glu Asn Glu Thr Ile Asp Ile Gly
 165 170 175
 Ile Gln Asn His Phe Ala Ser Arg Glu Gly Phe Gly Gly Ile Met Gln
 180 185 190
 Met Lys Phe Cys Pro Glu Tyr Val Ser Val Phe Asn Asn Val Gln Glu
 195 200 205
 Asn Lys Gly Ala Ser Ile Phe Asn Arg Arg Gly Tyr Phe Ser Asp Pro
 210 215 220
 Ala Leu Ile Leu Met His Glu Leu Ile His Val Leu His Gly Leu Tyr
 225 230 235 240
 Gly Ile Lys Val Asp Asp Leu Pro Ile Val Pro Asn Glu Lys Lys Phe
 245 250 255
 Phe Met Gln Ser Thr Asp Ala Ile Gln Ala Glu Glu Leu Tyr Thr Phe
 260 265 270
 Gly Gly Gln Asp Pro Ser Ile Ile Thr Pro Ser Thr Asp Lys Ser Ile
 275 280 285
 Tyr Asp Lys Val Leu Gln Asn Phe Arg Gly Ile Val Asp Arg Leu Asn
 290 295 300
 Lys Val Leu Val Cys Ile Ser Asp Pro Asn Ile Asn Ile Asn Ile Tyr
 305 310 315 320
 Lys Asn Lys Phe Lys Asp Lys Tyr Lys Phe Val Glu Asp Ser Glu Gly
 325 330 335
 Lys Tyr Ser Ile Asp Val Glu Ser Phe Asp Lys Leu Tyr Lys Ser Leu
 340 345 350
 Met Phe Gly Phe Thr Glu Thr Asn Ile Ala Glu Asn Tyr Lys Ile Lys
 355 360 365
 Thr Arg Ala Ser Tyr Phe Ser Asp Ser Leu Pro Pro Val Lys Ile Lys
 370 375 380
 Asn Leu Leu Asp Asn Glu Ile Tyr Thr Ile Glu Glu Gly Phe Asn Ile
 385 390 395 400
 Ser Asp Lys Asp Met Glu Lys Glu Tyr Arg Gly Gln Asn Lys Ala Ile
 405 410 415
 Asn Lys Gln Ala Tyr Glu Glu Ile Ser Lys Glu His Leu Ala Val Tyr
 420 425 430

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Lys Ile Gln Met Cys Lys Ser Val Lys Ala Pro Gly Ile Cys Ile Asp
435 440 445

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

Asp Asp Leu Ser Lys Asn Glu Arg Ile Glu Tyr Asn Thr Gln Ser Asn
465 470 475 480

Tyr Ile Glu Asn Asp Phe Pro Ile Asn Glu Leu Ile Leu Asp Thr Asp
485 490 495

Leu Ile Ser Lys Ile Glu Leu Pro Ser Glu Asn Thr Glu Ser Leu Thr
500 505 510

Asp Phe Asn Val Asp Val Pro Val Tyr Glu Lys Gln Pro Ala Ile Lys
515 520 525

Lys Ile Phe Thr Asp Glu Asn Thr Ile Phe Gln Tyr Leu Tyr Ser Gln
530 535 540

Thr Phe Pro Leu Asp Ile Arg Asp Ile Ser Leu Thr Ser Ser Phe Asp
545 550 555 560

Asp Ala Leu Leu Phe Ser Asn Lys Val Tyr Ser Phe Phe Ser Met Asp
565 570 575

Tyr Ile Lys Thr Ala Asn Lys Val Val Glu Ala Gly Leu Phe Ala Gly
580 585 590

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

Asn Thr Met Asp Lys Ile Ala Asp Ile Ser Leu Ile Val Pro Tyr Ile
610 615 620

Gly Leu Ala Leu Asn Val Gly Asn Glu Thr Ala Lys Gly Asn Phe Glu
625 630 635 640

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

Glu Leu Leu Ile Pro Val Val Gly Ala Phe Leu Leu Glu Ser Tyr Ile
660 665 670

Asp Asn Lys Asn Lys Ile Ile Lys Thr Ile Asp Asn Ala Leu Thr Lys
675 680 685

Arg Asn Glu Lys Trp Ser Asp Met Tyr Gly Leu Ile Val Ala Gln Trp

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690 695 700
 Leu Ser Thr Val Asn Thr Gln Phe Tyr Thr Ile Lys Glu Gly Met Tyr
 705 710 715 720
 Lys Ala Leu Asn Tyr Gln Ala Gln Ala Leu Glu Glu Ile Ile Lys Tyr
 725 730 735
 Arg Tyr Asn Ile Tyr Ser Glu Lys Glu Lys Ser Asn Ile Asn Ile Asp
 740 745 750
 Phe Asn Asp Ile Asn Ser Lys Leu Asn Glu Gly Ile Asn Gln Ala Ile
 755 760 765
 Asp Asn Ile Asn Asn Phe Ile Asn Gly Cys Ser Val Ser Tyr Leu Met
 770 775 780
 Lys Lys Met Ile Pro Leu Ala Val Glu Lys Leu Leu Asp Phe Asp Asn
 785 790 795 800
 Thr Leu Lys Lys Asn Leu Leu Asn Tyr Ile Asp Glu Asn Lys Leu Tyr
 805 810 815
 Leu Ile Gly Ser Ala Glu Tyr Glu Lys Ser Lys Val Asn Lys Tyr Leu
 820 825 830
 Lys Thr Ile Met Pro Phe Asp Leu Ser Ile Tyr Thr Asn Asp Thr Ile
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 Leu Ile Glu Met Phe Asn Lys Tyr Asn Ser
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 aat aat att att atg atg gag cct cca ttt gcg aga ggt acg ggg aga 96
 Asn Asn Ile Ile Met Met Glu Pro Pro Phe Ala Arg Gly Thr Gly Arg
 20 25 30
 tat tat aaa gct ttt aaa atc aca gat cgt att tgg ata ata ccg gaa 144
 Tyr Tyr Lys Ala Phe Lys Ile Thr Asp Arg Ile Trp Ile Ile Pro Glu
 35 40 45

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aga tat act ttt gga tat aaa cct gag gat ttt aat aaa agt tcc ggt Arg Tyr Thr Phe Gly Tyr Lys Pro Glu Asp Phe Asn Lys Ser Ser Gly 50 55 60	192
att ttt aat aga gat gtt tgt gaa tat tat gat cca gat tac tta aat Ile Phe Asn Arg Asp Val Cys Glu Tyr Tyr Asp Pro Asp Tyr Leu Asn 65 70 75 80	240
act aat gat aaa aag aat ata ttt tta caa aca atg atc aag tta ttt Thr Asn Asp Lys Lys Asn Ile Phe Leu Gln Thr Met Ile Lys Leu Phe 85 90 95	288
aat aga atc aaa tca aaa cca ttg ggt gaa aag tta tta gag atg att Asn Arg Ile Lys Ser Lys Pro Leu Gly Glu Lys Leu Leu Glu Met Ile 100 105 110	336
ata aat ggt ata cct tat ctt gga gat aga cgt gtt cca ctc gaa gag Ile Asn Gly Ile Pro Tyr Leu Gly Asp Arg Arg Val Pro Leu Glu Glu 115 120 125	384
ttt aac aca aac att gct agt gta act gtt aat aaa tta atc agt aat Phe Asn Thr Asn Ile Ala Ser Val Thr Val Asn Lys Leu Ile Ser Asn 130 135 140	432
cca gga gaa gtg gag cga aaa aaa ggt att ttc gca aat tta ata ata Pro Gly Glu Val Glu Arg Lys Lys Gly Ile Phe Ala Asn Leu Ile Ile 145 150 155 160	480
ttt gga cct ggg cca gtt tta aat gaa aat gag act ata gat ata ggt Phe Gly Pro Gly Pro Val Leu Asn Glu Thr Ile Asp Ile Gly 165 170 175	528
ata caa aat cat ttt gca tca agg gaa ggc ttc ggg ggt ata atg caa Ile Gln Asn His Phe Ala Ser Arg Glu Gly Phe Gly Gly Ile Met Gln 180 185 190	576
atg aag ttt tgc cca gaa tat gta agc gta ttt aat aat gtt caa gaa Met Lys Phe Cys Pro Glu Tyr Val Ser Val Phe Asn Asn Val Gln Glu 195 200 205	624
aac aaa ggc gca agt ata ttt aat aga cgt gga tat ttt tca gat cca Asn Lys Gly Ala Ser Ile Phe Asn Arg Arg Gly Tyr Phe Ser Asp Pro 210 215 220	672
gcc ttg ata tta atg cat gaa ctt ata cat gtt tta cat gga tta tat Ala Leu Ile Leu Met His Glu Leu Ile His Val Leu His Gly Leu Tyr 225 230 235 240	720
ggc att aaa gta gat gat tta cca att gta cca aat gaa aaa aaa ttt Gly Ile Lys Val Asp Asp Leu Pro Ile Val Pro Asn Glu Lys Lys Phe 245 250 255	768
ttt atg caa tct aca gat gct ata cag gca gaa gaa cta tat aca ttt Phe Met Gln Ser Thr Asp Ala Ile Gln Ala Glu Glu Leu Tyr Thr Phe 260 265 270	816
gga gga caa gat ccc agc atc ata act cct tct acg gat aaa agt atc Gly Gly Gln Asp Pro Ser Ile Ile Thr Pro Ser Thr Asp Lys Ser Ile 275 280 285	864
tat gat aaa gtt ttg caa aat ttt aga ggg ata gtt gat aga ctt aac Tyr Asp Lys Val Leu Gln Asn Phe Arg Gly Ile Val Asp Arg Leu Asn 290 295 300	912
aag gtt tta gtt tgc ata tca gat cct aac att aat att aat ata tat Lys Val Leu Val Cys Ile Ser Asp Pro Asn Ile Asn Ile Asn Ile Tyr 305 310 315 320 325 330 335 340	960

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305	310	315	320	
aaa aat aaa ttt aaa gat aaa tat aaa ttc gtt gaa gat tct gag gga				1008
Lys Asn Lys Phe Lys Asp Lys Tyr Lys Phe Val Glu Asp Ser Glu Gly				
	325	330	335	
aaa tat agt ata gat gta gaa agt ttt gat aaa tta tat aaa agc tta				1056
Lys Tyr Ser Ile Asp Val Glu Ser Phe Asp Lys Leu Tyr Lys Ser Leu				
	340	345	350	
atg ttt ggt ttt aca gaa act aat ata gca gaa aat tat aaa ata aaa				1104
Met Phe Gly Phe Thr Glu Thr Asn Ile Ala Glu Asn Tyr Lys Ile Lys				
	355	360	365	
act aga gct tct tat ttt agt gat tcc tta cca cca gta aaa ata aaa				1152
Thr Arg Ala Ser Tyr Phe Ser Asp Ser Leu Pro Pro Val Lys Ile Lys				
	370	375	380	
aat tta tta gat aat gaa atc tat act ata gag gaa ggg ttt aat ata				1200
Asn Leu Leu Asp Asn Glu Ile Tyr Thr Ile Glu Glu Gly Phe Asn Ile				
	385	390	395	400
tct gat aaa gat atg gaa aaa gaa tat aga ggt cag aat aaa gct ata				1248
Ser Asp Lys Asp Met Glu Lys Glu Tyr Arg Gly Gln Asn Lys Ala Ile				
	405	410	415	
aat aaa caa gct tat gaa gaa att agc aag gag cat ttg gct gta tat				1296
Asn Lys Gln Ala Tyr Glu Glu Ile Ser Lys Glu His Leu Ala Val Tyr				
	420	425	430	
aag ata caa atg tgt aaa agt gtt aaa gct cca gga ata tgt att gat				1344
Lys Ile Gln Met Cys Lys Ser Val Lys Ala Pro Gly Ile Cys Ile Asp				
	435	440	445	
gtt gat aat gaa gat ttg ttc ttt ata gct gat aaa aat agt ttt tca				1392
Val Asp Asn Glu Asp Leu Phe Phe Ile Ala Asp Lys Asn Ser Phe Ser				
	450	455	460	
gat gat tta tct aaa aac gaa aga ata gaa tat aat aca cag agt aat				1440
Asp Asp Leu Ser Lys Asn Glu Arg Ile Glu Tyr Asn Thr Gln Ser Asn				
	465	470	475	480
tat ata gaa aat gac ttc cct ata aat gaa tta att tta gat act gat				1488
Tyr Ile Glu Asn Asp Phe Pro Ile Asn Glu Leu Ile Leu Asp Thr Asp				
	485	490	495	
tta ata agt aaa ata gaa tta cca agt gaa aat aca gaa tca ctt act				1536
Leu Ile Ser Lys Ile Glu Leu Pro Ser Glu Asn Thr Glu Ser Leu Thr				
	500	505	510	
gat ttt aat gta gat gtt cca gta tat gaa aaa caa ccc gct ata aaa				1584
Asp Phe Asn Val Asp Val Pro Val Tyr Glu Lys Gln Pro Ala Ile Lys				
	515	520	525	
aaa att ttt aca gat gaa aat acc atc ttt caa tat tta tac tct cag				1632
Lys Ile Phe Thr Asp Glu Asn Thr Ile Phe Gln Tyr Leu Tyr Ser Gln				
	530	535	540	
aca ttt cct cta				1644
Thr Phe Pro Leu				
545				
<210> 24				
<211> 548				
<212> PRT				

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<213> Clostridium botulinum

<400> 24

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Asn Asn Ile Ile Met Met Glu Pro Pro Phe Ala Arg Gly Thr Gly Arg
20 25 30

Tyr Tyr Lys Ala Phe Lys Ile Thr Asp Arg Ile Trp Ile Ile Pro Glu
35 40 45

Arg Tyr Thr Phe Gly Tyr Lys Pro Glu Asp Phe Asn Lys Ser Ser Gly
50 55 60

Ile Phe Asn Arg Asp Val Cys Glu Tyr Tyr Asp Pro Asp Tyr Leu Asn
65 70 75 80

Thr Asn Asp Lys Lys Asn Ile Phe Leu Gln Thr Met Ile Lys Leu Phe
85 90 95

Asn Arg Ile Lys Ser Lys Pro Leu Gly Glu Lys Leu Leu Glu Met Ile
100 105 110

Ile Asn Gly Ile Pro Tyr Leu Gly Asp Arg Arg Val Pro Leu Glu Glu
115 120 125

Phe Asn Thr Asn Ile Ala Ser Val Thr Val Asn Lys Leu Ile Ser Asn
130 135 140

Pro Gly Glu Val Glu Arg Lys Lys Gly Ile Phe Ala Asn Leu Ile Ile
145 150 155 160

Phe Gly Pro Gly Pro Val Leu Asn Glu Asn Glu Thr Ile Asp Ile Gly
165 170 175

Ile Gln Asn His Phe Ala Ser Arg Glu Gly Phe Gly Gly Ile Met Gln
180 185 190

Met Lys Phe Cys Pro Glu Tyr Val Ser Val Phe Asn Asn Val Gln Glu
195 200 205

Asn Lys Gly Ala Ser Ile Phe Asn Arg Arg Gly Tyr Phe Ser Asp Pro
210 215 220

Ala Leu Ile Leu Met His Glu Leu Ile His Val Leu His Gly Leu Tyr
225 230 235 240

Gly Ile Lys Val Asp Asp Leu Pro Ile Val Pro Asn Glu Lys Lys Phe
245 250 255

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Phe Met Gln Ser Thr Asp Ala Ile Gln Ala Glu Glu Leu Tyr Thr Phe
 260 265 270
 Gly Gly Gln Asp Pro Ser Ile Ile Thr Pro Ser Thr Asp Lys Ser Ile
 275 280 285
 Tyr Asp Lys Val Leu Gln Asn Phe Arg Gly Ile Val Asp Arg Leu Asn
 290 295 300
 Lys Val Leu Val Cys Ile Ser Asp Pro Asn Ile Asn Ile Asn Ile Tyr
 305 310 315 320
 Lys Asn Lys Phe Lys Asp Lys Tyr Lys Phe Val Glu Asp Ser Glu Gly
 325 330 335
 Lys Tyr Ser Ile Asp Val Glu Ser Phe Asp Lys Leu Tyr Lys Ser Leu
 340 345 350
 Met Phe Gly Phe Thr Glu Thr Asn Ile Ala Glu Asn Tyr Lys Ile Lys
 355 360 365
 Thr Arg Ala Ser Tyr Phe Ser Asp Ser Leu Pro Pro Val Lys Ile Lys
 370 375 380
 Asn Leu Leu Asp Asn Glu Ile Tyr Thr Ile Glu Glu Gly Phe Asn Ile
 385 390 395 400
 Ser Asp Lys Asp Met Glu Lys Glu Tyr Arg Gly Gln Asn Lys Ala Ile
 405 410 415
 Asn Lys Gln Ala Tyr Glu Glu Ile Ser Lys Glu His Leu Ala Val Tyr
 420 425 430
 Lys Ile Gln Met Cys Lys Ser Val Lys Ala Pro Gly Ile Cys Ile Asp
 435 440 445
 Val Asp Asn Glu Asp Leu Phe Phe Ile Ala Asp Lys Asn Ser Phe Ser
 450 455 460
 Asp Asp Leu Ser Lys Asn Glu Arg Ile Glu Tyr Asn Thr Gln Ser Asn
 465 470 475 480
 Tyr Ile Glu Asn Asp Phe Pro Ile Asn Glu Leu Ile Leu Asp Thr Asp
 485 490 495
 Leu Ile Ser Lys Ile Glu Leu Pro Ser Glu Asn Thr Glu Ser Leu Thr
 500 505 510
 Asp Phe Asn Val Asp Val Pro Val Tyr Glu Lys Gln Pro Ala Ile Lys

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515 520 525

Lys Ile Phe Thr Asp Glu Asn Thr Ile Phe Gln Tyr Leu Tyr Ser Gln
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Thr Phe Pro Leu
 545

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 <213> Clostridium botulinum

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gtt gac att gcc tac atc aaa att cca aac gcc ggc cag atg cag ccg 96
 Val Asp Ile Ala Tyr Ile Lys Ile Pro Asn Ala Gly Gln Met Gln Pro
 20 25 30

gtg aag gct ttc aag att cat aac aaa atc tgg gtt att ccg gaa cgc 144
 Val Lys Ala Phe Lys Ile His Asn Lys Ile Trp Val Ile Pro Glu Arg
 35 40 45

gat aca ttt acg aac ccg gaa gaa gga gac ttg aac ccg ccg ccg gaa 192
 Asp Thr Phe Thr Asn Pro Glu Glu Gly Asp Leu Asn Pro Pro Pro Glu
 50 55 60

gca aag cag gtg cca gtt tca tac tac gat tca acc tat ctg agc aca 240
 Ala Lys Gln Val Pro Val Ser Tyr Tyr Asp Ser Thr Tyr Leu Ser Thr
 65 70 75 80

gac aac gag aag gat aac tac ctg aag gga gtg acc aaa tta ttc gag 288
 Asp Asn Glu Lys Asp Asn Tyr Leu Lys Gly Val Thr Lys Leu Phe Glu
 85 90 95

cgt att tat tcc act gac ctg ggc cgt atg ctg ctg acc tca atc gtc 336
 Arg Ile Tyr Ser Thr Asp Leu Gly Arg Met Leu Leu Thr Ser Ile Val
 100 105 110

cgc gga atc cca ttt tgg ggt ggc agt acc att gac acg gag ttg aag 384
 Arg Gly Ile Pro Phe Trp Gly Gly Ser Thr Ile Asp Thr Glu Leu Lys
 115 120 125

gtt att gac act aac tgc att aac gtg atc caa cca gac ggt agc tac 432
 Val Ile Asp Thr Asn Cys Ile Asn Val Ile Gln Pro Asp Gly Ser Tyr
 130 135 140

aga tct gaa gaa ctt aac ctc gta atc atc ggg ccc tcc gcg gac att 480
 Arg Ser Glu Glu Leu Asn Leu Val Ile Ile Gly Pro Ser Ala Asp Ile
 145 150 155 160

atc cag ttt gag tgc aag agc ttt ggc cac gaa gtg ttg aac ctg acg 528
 Ile Gln Phe Glu Cys Lys Ser Phe Gly His Glu Val Leu Asn Leu Thr
 165 170 175

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cgt aac ggt tac ggc tct act cag tac att cgt ttc agc cca gac ttc Arg Asn Gly Tyr Gly Ser Thr Gln Tyr Ile Arg Phe Ser Pro Asp Phe 180 185 190	576
acg ttc ggt ttc gag gag agc ctg gag gtt gat acc aac ccg ctg ttg Thr Phe Gly Phe Glu Glu Ser Leu Glu Val Asp Thr Asn Pro Leu Leu 195 200 205	624
ggg gca ggc aag ttc gca act gat cca gcg gtg acc ctg gca cac gag Gly Ala Gly Lys Phe Ala Thr Asp Pro Ala Val Thr Leu Ala His Glu 210 215 220	672
ctg atc cac gcc ggt cat cgt ctg tat ggc att gcg att aac ccg aac Leu Ile His Ala Gly His Arg Leu Tyr Gly Ile Ala Ile Asn Pro Asn 225 230 235 240	720
cgc gtg ttc aag gtt aac acc aac gcc tac tac gag atg agt ggt tta Arg Val Phe Lys Val Asn Thr Asn Ala Tyr Tyr Glu Met Ser Gly Leu 245 250 255	768
gaa gta agc ttc gag gaa ctg cgc acg ttc ggt ggc cat gat gcg aag Glu Val Ser Phe Glu Glu Leu Arg Thr Phe Gly Gly His Asp Ala Lys 260 265 270	816
ttt atc gac agc ttg cag gag aac gag ttc cgt ctg tac tac tac aac Phe Ile Asp Ser Leu Gln Glu Asn Glu Phe Arg Leu Tyr Tyr Tyr Asn 275 280 285	864
aag ttt aaa gat att gca agt aca ctg aac aag gct aag tcc att gtg Lys Phe Lys Asp Ile Ala Ser Thr Leu Asn Lys Ala Lys Ser Ile Val 290 295 300	912
ggg acc act gct tca tta cag tat atg aaa aat gtt ttt aaa gag aaa Gly Thr Thr Ala Ser Leu Gln Tyr Met Lys Asn Val Phe Lys Glu Lys 305 310 315 320	960
tat ctg cta tct gaa gat aca tct gga aaa ttt tcg gta gat aaa tta Tyr Leu Leu Ser Glu Asp Thr Ser Gly Lys Phe Ser Val Asp Lys Leu 325 330 335	1008
aaa ttt gat aag tta tac aaa atg tta aca gag att tac aca gag gat Lys Phe Asp Lys Leu Tyr Lys Met Leu Thr Glu Ile Tyr Thr Glu Asp 340 345 350	1056
aat ttt gtt aag ttt ttt aaa gta ctt aac aga aaa aca tat ttg aat Asn Phe Val Lys Phe Phe Lys Val Leu Asn Arg Lys Thr Tyr Leu Asn 355 360 365	1104
ttt gat aaa gcc gta ttt aag ata aat ata gta cct aag gta aat tac Phe Asp Lys Ala Val Phe Lys Ile Asn Ile Val Pro Lys Val Asn Tyr 370 375 380	1152
aca ata tat gat gga ttt aat tta aga aat aca aat tta gca gca aac Thr Ile Tyr Asp Gly Phe Asn Leu Arg Asn Thr Asn Leu Ala Ala Asn 385 390 395 400	1200
ttt aat ggt caa aat aca gaa att aat aat atg aat ttt act aaa cta Phe Asn Gly Gln Asn Thr Glu Ile Asn Asn Met Asn Phe Thr Lys Leu 405 410 415	1248
aaa aat ttt act gga ttg ttt gaa ttt tat aag ttg cta tgt gta aga Lys Asn Phe Thr Gly Leu Phe Glu Phe Tyr Lys Leu Leu Cys Val Arg 420 425 430	1296
ggg ata ata act tct aaa act aaa tca tta gat aaa gga tac aat aag Gly Ile Ile Thr Ser Lys Thr Lys Ser Leu Asp Lys Gly Tyr Asn Lys 435 440 445	1344

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435	440	445	
gca tta aat gat tta tgt atc aaa gtt aat aat tgg gac ttg ttt ttt Ala Leu Asn Asp Leu Cys Ile Lys Val Asn Asn Trp Asp Leu Phe Phe 450 455 460			1392
agt cct tca gaa gat aat ttt act aat gat cta aat aaa gga gaa gaa Ser Pro Ser Glu Asp Asn Phe Thr Asn Asp Leu Asn Lys Gly Glu Glu 465 470 475 480			1440
att aca tct gat act aat ata gaa gca gca gaa gaa aat att agt tta Ile Thr Ser Asp Thr Asn Ile Glu Ala Glu Glu Asn Ile Ser Leu 485 490 495			1488
gat tta ata caa caa tat tat tta acc ttt aat ttt gat aat gaa cct Asp Leu Ile Gln Tyr Tyr Leu Thr Phe Asn Phe Asp Asn Glu Pro 500 505 510			1536
gaa aat att tca ata gaa aat ctt tca agt gac att ata ggc caa tta Glu Asn Ile Ser Ile Glu Asn Leu Ser Ser Asp Ile Ile Gly Gln Leu 515 520 525			1584
gaa ctt atg cct aat ata gaa aga ttt cct aat gga aaa aag tat gag Glu Leu Met Pro Asn Ile Glu Arg Phe Pro Asn Gly Lys Lys Tyr Glu 530 535 540			1632
tta gat aaa tat act atg ttc cat tat ctt cgt gct caa gaa ttt gaa Leu Asp Lys Tyr Thr Met Phe His Tyr Leu Arg Ala Gln Glu Phe Glu 545 550 555 560			1680
cat ggt aaa tct agg att gct tta aca aat tct gtt aac gaa gca tta His Gly Lys Ser Arg Ile Ala Leu Thr Asn Ser Val Asn Glu Ala Leu 565 570 575			1728
tta aat cct agt cgt gtt tat aca ttt ttt tct tca gac tat gta aag Leu Asn Pro Ser Arg Val Tyr Thr Phe Phe Ser Ser Asp Tyr Val Lys 580 585 590			1776
aaa gtt aat aaa gct acg gag gca gct atg ttt tta ggc tgg gta gaa Lys Val Asn Lys Ala Thr Glu Ala Ala Met Phe Leu Gly Trp Val Glu 595 600 605			1824
caa tta gta tat gat ttt acc gat gaa act agc gaa gta agt act acg Gln Leu Val Tyr Asp Phe Thr Asp Glu Thr Ser Glu Val Ser Thr Thr 610 615 620			1872
gat aaa att gcg gat ata act ata att att cca tat ata gga cct gct Asp Lys Ile Ala Asp Ile Thr Ile Ile Ile Pro Tyr Ile Gly Pro Ala 625 630 635 640			1920
tta aat ata ggt aat atg tta tat aaa gat gat ttt gta ggt gct tta Leu Asn Ile Gly Asn Met Leu Tyr Lys Asp Asp Phe Val Gly Ala Leu 645 650 655			1968
ata ttt tca gga gct gtt att ctg tta gaa ttt ata cca gag att gca Ile Phe Ser Gly Ala Val Ile Leu Leu Glu Phe Ile Pro Glu Ile Ala 660 665 670			2016
ata cct gta tta ggt act ttt gca ctt gta tca tat att gcg aat aag Ile Pro Val Leu Gly Thr Phe Ala Leu Val Ser Tyr Ile Ala Asn Lys 675 680 685			2064
gtt cta acc gtt caa aca ata gat aat gct tta agt aaa aga aat gaa Val Leu Thr Val Gln Thr Ile Asp Asn Ala Leu Ser Lys Arg Asn Glu 690 695 700			2112

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aaa tgg gat gag gtc tat aaa tat ata gta aca aat tgg tta gca aag 2160
 Lys Trp Asp Glu Val Tyr Lys Tyr Ile Val Thr Asn Trp Leu Ala Lys
 705 710 715 720

 gtt aat aca cag att gat cta ata aga aaa aaa atg aaa gaa gct tta 2208
 Val Asn Thr Gln Ile Asp Leu Ile Arg Lys Lys Met Lys Glu Ala Leu
 725 730 735

 gaa aat caa gca gaa gca aca aag gct ata ata aac tat cag tat aat 2256
 Glu Asn Gln Ala Glu Ala Thr Lys Ala Ile Ile Asn Tyr Gln Tyr Asn
 740 745 750

 caa tat act gag gaa gag aaa aat aat att aat ttt aat att gat gat 2304
 Gln Tyr Thr Glu Glu Glu Lys Asn Asn Ile Asn Phe Asn Ile Asp Asp
 755 760 765

 tta agt tcg aaa ctt aat gag tct ata aat aaa gct atg att aat ata 2352
 Leu Ser Ser Lys Leu Asn Glu Ser Ile Asn Lys Ala Met Ile Asn Ile
 770 775 780

 aat aaa ttt ttg aat caa tgc tct gtt tca tat tta atg aat tct atg 2400
 Asn Lys Phe Leu Asn Gln Cys Ser Val Ser Tyr Leu Met Asn Ser Met
 785 790 795 800

 atc cct tat ggt gtt aaa cgg tta gaa gat ttt gat gct agt ctt aaa 2448
 Ile Pro Tyr Gly Val Lys Arg Leu Glu Asp Phe Asp Ala Ser Leu Lys
 805 810 815

 gat gca tta tta aag tat ata tat gat aat aga gga act tta att ggt 2496
 Asp Ala Leu Leu Lys Tyr Ile Tyr Asp Asn Arg Gly Thr Leu Ile Gly
 820 825 830

 caa gta gat aga tta aaa gat aaa gtt aat aat aca ctt agt aca gat 2544
 Gln Val Asp Arg Leu Lys Asp Lys Val Asn Asn Thr Leu Ser Thr Asp
 835 840 845

 ata cct ttt cag ctt tcc aaa tac gta gat aat caa aga tta tta tct 2592
 Ile Pro Phe Gln Leu Ser Lys Tyr Val Asp Asn Gln Arg Leu Leu Ser
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 aca ttt act gaa tat att aag taa 2616
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 865 870

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Val Lys Ala Phe Lys Ile His Asn Lys Ile Trp Val Ile Pro Glu Arg
35 40 45

Asp Thr Phe Thr Asn Pro Glu Glu Gly Asp Leu Asn Pro Pro Pro Glu
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Ala Lys Gln Val Pro Val Ser Tyr Tyr Asp Ser Thr Tyr Leu Ser Thr
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Asp Asn Glu Lys Asp Asn Tyr Leu Lys Gly Val Thr Lys Leu Phe Glu
85 90 95

Arg Ile Tyr Ser Thr Asp Leu Gly Arg Met Leu Leu Thr Ser Ile Val
100 105 110

Arg Gly Ile Pro Phe Trp Gly Gly Ser Thr Ile Asp Thr Glu Leu Lys
115 120 125

Val Ile Asp Thr Asn Cys Ile Asn Val Ile Gln Pro Asp Gly Ser Tyr
130 135 140

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

Ile Gln Phe Glu Cys Lys Ser Phe Gly His Glu Val Leu Asn Leu Thr
165 170 175

Arg Asn Gly Tyr Gly Ser Thr Gln Tyr Ile Arg Phe Ser Pro Asp Phe
180 185 190

Thr Phe Gly Phe Glu Glu Ser Leu Glu Val Asp Thr Asn Pro Leu Leu
195 200 205

Gly Ala Gly Lys Phe Ala Thr Asp Pro Ala Val Thr Leu Ala His Glu
210 215 220

Leu Ile His Ala Gly His Arg Leu Tyr Gly Ile Ala Ile Asn Pro Asn
225 230 235 240

Arg Val Phe Lys Val Asn Thr Asn Ala Tyr Tyr Glu Met Ser Gly Leu
245 250 255

Glu Val Ser Phe Glu Glu Leu Arg Thr Phe Gly Gly His Asp Ala Lys
260 265 270

Phe Ile Asp Ser Leu Gln Glu Asn Glu Phe Arg Leu Tyr Tyr Tyr Asn
275 280 285

Lys Phe Lys Asp Ile Ala Ser Thr Leu Asn Lys Ala Lys Ser Ile Val
290 295 300

Gly Thr Thr Ala Ser Leu Gln Tyr Met Lys Asn Val Phe Lys Glu Lys
305 310 315 320

Tyr Leu Leu Ser Glu Asp Thr Ser Gly Lys Phe Ser Val Asp Lys Leu

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325 330 335
 Lys Phe Asp Lys Leu Tyr Lys Met Leu Thr Glu Ile Tyr Thr Glu Asp
 340 345 350
 Asn Phe Val Lys Phe Phe Lys Val Leu Asn Arg Lys Thr Tyr Leu Asn
 355 360 365
 Phe Asp Lys Ala Val Phe Lys Ile Asn Ile Val Pro Lys Val Asn Tyr
 370 375 380
 Thr Ile Tyr Asp Gly Phe Asn Leu Arg Asn Thr Asn Leu Ala Ala Asn
 385 390 395 400
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 420 425 430
 Gly Ile Ile Thr Ser Lys Thr Lys Ser Leu Asp Lys Gly Tyr Asn Lys
 435 440 445
 Ala Leu Asn Asp Leu Cys Ile Lys Val Asn Asn Trp Asp Leu Phe Phe
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 Ser Pro Ser Glu Asp Asn Phe Thr Asn Asp Leu Asn Lys Gly Glu Glu
 465 470 475 480
 Ile Thr Ser Asp Thr Asn Ile Glu Ala Ala Glu Glu Asn Ile Ser Leu
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 Asp Leu Ile Gln Gln Tyr Tyr Leu Thr Phe Asn Phe Asp Asn Glu Pro
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 Glu Asn Ile Ser Ile Glu Asn Leu Ser Ser Asp Ile Ile Gly Gln Leu
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 Glu Leu Met Pro Asn Ile Glu Arg Phe Pro Asn Gly Lys Lys Tyr Glu
 530 535 540
 Leu Asp Lys Tyr Thr Met Phe His Tyr Leu Arg Ala Gln Glu Phe Glu
 545 550 555 560
 His Gly Lys Ser Arg Ile Ala Leu Thr Asn Ser Val Asn Glu Ala Leu
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 Leu Asn Pro Ser Arg Val Tyr Thr Phe Phe Ser Ser Asp Tyr Val Lys
 580 585 590

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Lys Val Asn Lys Ala Thr Glu Ala Ala Met Phe Leu Gly Trp Val Glu
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Gln Leu Val Tyr Asp Phe Thr Asp Glu Thr Ser Glu Val Ser Thr Thr
610 615 620

Asp Lys Ile Ala Asp Ile Thr Ile Ile Ile Pro Tyr Ile Gly Pro Ala
625 630 635 640

Leu Asn Ile Gly Asn Met Leu Tyr Lys Asp Asp Phe Val Gly Ala Leu
645 650 655

Ile Phe Ser Gly Ala Val Ile Leu Leu Glu Phe Ile Pro Glu Ile Ala
660 665 670

Ile Pro Val Leu Gly Thr Phe Ala Leu Val Ser Tyr Ile Ala Asn Lys
675 680 685

Val Leu Thr Val Gln Thr Ile Asp Asn Ala Leu Ser Lys Arg Asn Glu
690 695 700

Lys Trp Asp Glu Val Tyr Lys Tyr Ile Val Thr Asn Trp Leu Ala Lys
705 710 715 720

Val Asn Thr Gln Ile Asp Leu Ile Arg Lys Lys Met Lys Glu Ala Leu
725 730 735

Glu Asn Gln Ala Glu Ala Thr Lys Ala Ile Ile Asn Tyr Gln Tyr Asn
740 745 750

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

Leu Ser Ser Lys Leu Asn Glu Ser Ile Asn Lys Ala Met Ile Asn Ile
770 775 780

Asn Lys Phe Leu Asn Gln Cys Ser Val Ser Tyr Leu Met Asn Ser Met
785 790 795 800

Ile Pro Tyr Gly Val Lys Arg Leu Glu Asp Phe Asp Ala Ser Leu Lys
805 810 815

Asp Ala Leu Leu Lys Tyr Ile Tyr Asp Asn Arg Gly Thr Leu Ile Gly
820 825 830

Gln Val Asp Arg Leu Lys Asp Lys Val Asn Asn Thr Leu Ser Thr Asp
835 840 845

Ile Pro Phe Gln Leu Ser Lys Tyr Val Asp Asn Gln Arg Leu Leu Ser
850 855 860

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Thr Phe Thr Glu Tyr Ile Lys
865 870

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gaccgtatct ggatcatccc ggaacgttac accttcgggtt acaaacctga ggacttcaac 180
aagagtagcg ggattttcaa tcgtgacgtc tgcgagtact atgatccaga ttatctgaat 240
accaacgata agaagaacat attccttcag actatgatca agttatttaa tagaatcaaa 300
tcaaaacat tgggtgaaaa gttatttag atgattataa atgggtatacc ttatottgga 360
gatagacgtg ttccactcga agagttaa acaaacattg ctagtgtaac tgtaataaa 420
ttaatcagta atccaggaga agtgagcga aaaaaggta ttttcgcaa ttaataata 480
tttgacctg ggccagtttt aaatgaaaat gagactatag atatagggtat acaaatcat 540
tttgcacaa gggaaggctt cggggtata atgcaaata agttttgcc agaataatgta 600
agcgtattta ataagtcca agaaaacaaa ggcgcaagta tatttaatat agctggatat 660
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gatgcattat ttttttctaa caaagtttat tcattttttt ctatggatta tattaataact 1740
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 <213> Clostridium botulinum

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 <211> 2640
 <212> DNA
 <213> Clostridium botulinum

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atgcagccgg taaaggcatt caaaatccac aacaaaatct gggttatccc ggaacgtgat 180
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 aacctgggtga tcatcgcccc gtctgctgat atcatccagt tcgagtgtaa gagctttggg 540
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<210> 30
<211> 879
<212> PRT
<213> Clostridium botulinum

<400> 30

Thr Ser Leu Tyr Lys Lys Ala Gly Phe Gly Ser Met Glu Phe Val Asn
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Lys Gln Phe Asn Tyr Lys Asp Pro Val Asn Gly Val Asp Ile Ala Tyr
20 25 30

Ile Lys Ile Pro Asn Ala Gly Gln Met Gln Pro Val Lys Ala Phe Lys
35 40 45

Ile His Asn Lys Ile Trp Val Ile Pro Glu Arg Asp Thr Phe Thr Asn
50 55 60

Pro Glu Glu Gly Asp Leu Asn Pro Pro Pro Glu Ala Lys Gln Val Pro
65 70 75 80

Val Ser Tyr Tyr Asp Ser Thr Tyr Leu Ser Thr Asp Asn Glu Lys Asp
85 90 95

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

Asp Leu Gly Arg Met Leu Leu Thr Ser Ile Val Arg Gly Ile Pro Phe
115 120 125

Trp Gly Gly Ser Thr Ile Asp Thr Glu Leu Lys Val Ile Asp Thr Asn
130 135 140

Cys Ile Asn Val Ile Gln Pro Asp Gly Ser Tyr Arg Ser Glu Glu Leu
145 150 155 160

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Asn Leu Val Ile Ile Gly Pro Ser Ala Asp Ile Ile Gln Phe Glu Cys
 165 170 175
 Lys Ser Phe Gly His Glu Val Leu Asn Leu Thr Arg Asn Gly Tyr Gly
 180 185 190
 Ser Thr Gln Tyr Ile Arg Phe Ser Pro Asp Phe Thr Phe Gly Phe Glu
 195 200 205
 Glu Ser Leu Glu Val Asp Thr Asn Pro Leu Leu Gly Ala Gly Lys Phe
 210 215 220
 Ala Thr Asp Pro Ala Val Thr Leu Ala His Glu Leu Ile His Ala Gly
 225 230 235 240
 His Arg Leu Tyr Gly Ile Ala Ile Asn Pro Asn Arg Val Phe Lys Val
 245 250 255
 Asn Thr Asn Ala Tyr Tyr Glu Met Ser Gly Leu Glu Val Ser Phe Glu
 260 265 270
 Glu Leu Arg Thr Phe Gly Gly His Asp Ala Lys Phe Ile Asp Ser Leu
 275 280 285
 Gln Glu Asn Glu Phe Arg Leu Tyr Tyr Tyr Asn Lys Phe Lys Asp Ile
 290 295 300
 Ala Ser Thr Leu Asn Lys Ala Lys Ser Ile Val Gly Thr Thr Ala Ser
 305 310 315 320
 Leu Gln Tyr Met Lys Asn Val Phe Lys Glu Lys Tyr Leu Leu Ser Glu
 325 330 335
 Asp Thr Ser Gly Lys Phe Ser Val Asp Lys Leu Lys Phe Asp Lys Leu
 340 345 350
 Tyr Lys Met Leu Thr Glu Ile Tyr Thr Glu Asp Asn Phe Val Lys Phe
 355 360 365
 Phe Lys Val Leu Asn Arg Lys Thr Tyr Leu Asn Phe Asp Lys Ala Val
 370 375 380
 Phe Lys Ile Asn Ile Val Pro Lys Val Asn Tyr Thr Ile Tyr Asp Gly
 385 390 395 400
 Phe Asn Leu Arg Asn Thr Asn Leu Ala Ala Asn Phe Asn Gly Gln Asn
 405 410 415
 Thr Glu Ile Asn Asn Met Asn Phe Thr Lys Leu Lys Asn Phe Thr Gly
 420 425 430

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Leu Phe Glu Phe Tyr Lys Leu Leu Cys Val Arg Gly Ile Ile Thr Ser
435 440 445

Lys Thr Lys Ser Leu Asp Asp Asp Asp Lys Gly Tyr Asn Lys Ala Leu
450 455 460

Asn Asp Leu Cys Ile Lys Val Asn Asn Trp Asp Leu Phe Phe Ser Pro
465 470 475 480

Ser Glu Asp Asn Phe Thr Asn Asp Leu Asn Lys Gly Glu Glu Ile Thr
485 490 495

Ser Asp Thr Asn Ile Glu Ala Ala Glu Glu Asn Ile Ser Leu Asp Leu
500 505 510

Ile Gln Gln Tyr Tyr Leu Thr Phe Asn Phe Asp Asn Glu Pro Glu Asn
515 520 525

Ile Ser Ile Glu Asn Leu Ser Ser Asp Ile Ile Gly Gln Leu Glu Leu
530 535 540

Met Pro Asn Ile Glu Arg Phe Pro Asn Gly Lys Lys Tyr Glu Leu Asp
545 550 555 560

Lys Tyr Thr Met Phe His Tyr Leu Arg Ala Gln Glu Phe Glu His Gly
565 570 575

Lys Ser Arg Ile Ala Leu Thr Asn Ser Val Asn Glu Ala Leu Leu Asn
580 585 590

Pro Ser Arg Val Tyr Thr Phe Phe Ser Ser Asp Tyr Val Lys Lys Val
595 600 605

Asn Lys Ala Thr Glu Ala Ala Met Phe Leu Gly Trp Val Glu Gln Leu
610 615 620

Val Tyr Asp Phe Thr Asp Glu Thr Ser Glu Val Ser Thr Thr Asp Lys
625 630 635 640

Ile Ala Asp Ile Thr Ile Ile Ile Pro Tyr Ile Gly Pro Ala Leu Asn
645 650 655

Ile Gly Asn Met Leu Tyr Lys Asp Asp Phe Val Gly Ala Leu Ile Phe
660 665 670

Ser Gly Ala Val Ile Leu Leu Glu Phe Ile Pro Glu Ile Ala Ile Pro
675 680 685

Val Leu Gly Thr Phe Ala Leu Val Ser Tyr Ile Ala Asn Lys Val Leu

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690 695 700
 Thr Val Gln Thr Ile Asp Asn Ala Leu Ser Lys Arg Asn Glu Lys Trp
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 Asp Glu Val Tyr Lys Tyr Ile Val Thr Asn Trp Leu Ala Lys Val Asn
 725 730 735
 Thr Gln Ile Asp Leu Ile Arg Lys Lys Met Lys Glu Ala Leu Glu Asn
 740 745 750
 Gln Ala Glu Ala Thr Lys Ala Ile Ile Asn Tyr Gln Tyr Asn Gln Tyr
 755 760 765
 Thr Glu Glu Glu Lys Asn Asn Ile Asn Phe Asn Ile Asp Asp Leu Ser
 770 775 780
 Ser Lys Leu Asn Glu Ser Ile Asn Lys Ala Met Ile Asn Ile Asn Lys
 785 790 795 800
 Phe Leu Asn Gln Cys Ser Val Ser Tyr Leu Met Asn Ser Met Ile Pro
 805 810 815
 Tyr Gly Val Lys Arg Leu Glu Asp Phe Asp Ala Ser Leu Lys Asp Ala
 820 825 830
 Leu Leu Lys Tyr Ile Tyr Asp Asn Arg Gly Thr Leu Ile Gly Gln Val
 835 840 845
 Asp Arg Leu Lys Asp Lys Val Asn Asn Thr Leu Ser Thr Asp Ile Pro
 850 855 860
 Phe Gln Leu Ser Lys Tyr Val Asp Asn Gln Arg Leu Leu Ser Thr
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 <212> DNA
 <213> Clostridium botulinum

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ctgatgaact ccatgatccc gtacggtggt aaacgtctgg aggacttcga tgcgtctctg 2460
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<210> 32
 <211> 866
 <212> PRT
 <213> Clostridium botulinum

<400> 32

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Val Asp Ile Ala Tyr Ile Lys Ile Pro Asn Ala Gly Gln Met Gln Pro
 20 25 30

Val Lys Ala Phe Lys Ile His Asn Lys Ile Trp Val Ile Pro Glu Arg
 35 40 45

Asp Thr Phe Thr Asn Pro Glu Glu Gly Asp Leu Asn Pro Pro Pro Glu
 50 55 60

Ala Lys Gln Val Pro Val Ser Tyr Tyr Asp Ser Thr Tyr Leu Ser Thr
 65 70 75 80

Asp Asn Glu Lys Asp Asn Tyr Leu Lys Gly Val Thr Lys Leu Phe Glu
 85 90 95

Arg Ile Tyr Ser Thr Asp Leu Gly Arg Met Leu Leu Thr Ser Ile Val
 100 105 110

Arg Gly Ile Pro Phe Trp Gly Gly Ser Thr Ile Asp Thr Glu Leu Lys
 115 120 125

Val Ile Asp Thr Asn Cys Ile Asn Val Ile Gln Pro Asp Gly Ser Tyr
 130 135 140

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

Ile Gln Phe Glu Cys Lys Ser Phe Gly His Glu Val Leu Asn Leu Thr
 165 170 175

Arg Asn Gly Tyr Gly Ser Thr Gln Tyr Ile Arg Phe Ser Pro Asp Phe
 180 185 190

Thr Phe Gly Phe Glu Glu Ser Leu Glu Val Asp Thr Asn Pro Leu Leu
 195 200 205

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Gly Ala Gly Lys Phe Ala Thr Asp Pro Ala Val Thr Leu Ala His Glu
210 215 220

Leu Ile His Ala Gly His Arg Leu Tyr Gly Ile Ala Ile Asn Pro Asn
225 230 235 240

Arg Val Phe Lys Val Asn Thr Asn Ala Tyr Tyr Glu Met Ser Gly Leu
245 250 255

Glu Val Ser Phe Glu Glu Leu Arg Thr Phe Gly Gly His Asp Ala Lys
260 265 270

Phe Ile Asp Ser Leu Gln Glu Asn Glu Phe Arg Leu Tyr Tyr Tyr Asn
275 280 285

Lys Phe Lys Asp Ile Ala Ser Thr Leu Asn Lys Ala Lys Ser Ile Val
290 295 300

Gly Thr Thr Ala Ser Leu Gln Tyr Met Lys Asn Val Phe Lys Glu Lys
305 310 315 320

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

Lys Phe Asp Lys Leu Tyr Lys Met Leu Thr Glu Ile Tyr Thr Glu Asp
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Asn Phe Val Lys Phe Phe Lys Val Leu Asn Arg Lys Thr Tyr Leu Asn
355 360 365

Phe Asp Lys Ala Val Phe Lys Ile Asn Ile Val Pro Lys Val Asn Tyr
370 375 380

Thr Ile Tyr Asp Gly Phe Asn Leu Arg Asn Thr Asn Leu Ala Ala Asn
385 390 395 400

Phe Asn Gly Gln Asn Thr Glu Ile Asn Asn Met Asn Phe Thr Lys Leu
405 410 415

Lys Asn Phe Thr Gly Leu Phe Glu Phe Tyr Lys Leu Leu Cys Val Arg
420 425 430

Gly Ile Ile Thr Ser Lys Thr Lys Ser Leu Asp Asp Asp Asp Lys Gly
435 440 445

Tyr Asn Lys Ala Leu Asn Asp Leu Cys Ile Lys Val Asn Asn Trp Asp
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Leu Phe Phe Ser Pro Ser Glu Asp Asn Phe Thr Asn Asp Leu Asn Lys

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 Gly Gln Leu Glu Leu Met Pro Asn Ile Glu Arg Phe Pro Asn Gly Lys
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 Lys Tyr Glu Leu Asp Lys Tyr Thr Met Phe His Tyr Leu Arg Ala Gln
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 Glu Phe Glu His Gly Lys Ser Arg Ile Ala Leu Thr Asn Ser Val Asn
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 Glu Ala Leu Leu Asn Pro Ser Arg Val Tyr Thr Phe Phe Ser Ser Asp
 580 585 590
 Tyr Val Lys Lys Val Asn Lys Ala Thr Glu Ala Ala Met Phe Leu Gly
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 Trp Val Glu Gln Leu Val Tyr Asp Phe Thr Asp Glu Thr Ser Glu Val
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 Ser Thr Thr Asp Lys Ile Ala Asp Ile Thr Ile Ile Ile Pro Tyr Ile
 625 630 635 640
 Gly Pro Ala Leu Asn Ile Gly Asn Met Leu Tyr Lys Asp Asp Phe Val
 645 650 655
 Gly Ala Leu Ile Phe Ser Gly Ala Val Ile Leu Leu Glu Phe Ile Pro
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 Ala Asn Lys Val Leu Thr Val Gln Thr Ile Asp Asn Ala Leu Ser Lys
 690 695 700
 Arg Asn Glu Lys Trp Asp Glu Val Tyr Lys Tyr Ile Val Thr Asn Trp
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 Leu Ala Lys Val Asn Thr Gln Ile Asp Leu Ile Arg Lys Lys Met Lys
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Glu Ala Leu Glu Asn Gln Ala Glu Ala Thr Lys Ala Ile Ile Asn Tyr
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Gln Tyr Asn Gln Tyr Thr Glu Glu Lys Asn Asn Ile Asn Phe Asn
755 760 765

Ile Asp Asp Leu Ser Ser Lys Leu Asn Glu Ser Ile Asn Lys Ala Met
770 775 780

Ile Asn Ile Asn Lys Phe Leu Asn Gln Cys Ser Val Ser Tyr Leu Met
785 790 795 800

Asn Ser Met Ile Pro Tyr Gly Val Lys Arg Leu Glu Asp Phe Asp Ala
805 810 815

Ser Leu Lys Asp Ala Leu Leu Lys Tyr Ile Tyr Asp Asn Arg Gly Thr
820 825 830

Leu Ile Gly Gln Val Asp Arg Leu Lys Asp Lys Val Asn Asn Thr Leu
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Leu Leu
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 <213> Clostridium botulinum

<400> 34

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 35 40 45

Asp Thr Phe Thr Asn Pro Glu Glu Gly Asp Leu Asn Pro Pro Pro Glu
 50 55 60

Ala Lys Gln Val Pro Val Ser Tyr Tyr Asp Ser Thr Tyr Leu Ser Thr
 65 70 75 80

Asp Asn Glu Lys Asp Asn Tyr Leu Lys Gly Val Thr Lys Leu Phe Glu
 85 90 95

Arg Ile Tyr Ser Thr Asp Leu Gly Arg Met Leu Leu Thr Ser Ile Val
 100 105 110

Arg Gly Ile Pro Phe Trp Gly Gly Ser Thr Ile Asp Thr Glu Leu Lys
 115 120 125

Val Ile Asp Thr Asn Cys Ile Asn Val Ile Gln Pro Asp Gly Ser Tyr
 130 135 140

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

Ile Gln Phe Glu Cys Lys Ser Phe Gly His Glu Val Leu Asn Leu Thr
 165 170 175

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

Gly Ala Gly Lys Phe Ala Thr Asp Pro Ala Val Thr Leu Ala His Glu
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Leu Ile His Ala Gly His Arg Leu Tyr Gly Ile Ala Ile Asn Pro Asn
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Arg Val Phe Lys Val Asn Thr Asn Ala Tyr Tyr Glu Met Ser Gly Leu
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Glu Val Ser Phe Glu Glu Leu Arg Thr Phe Gly Gly His Asp Ala Lys
260 265 270

Phe Ile Asp Ser Leu Gln Glu Asn Glu Phe Arg Leu Tyr Tyr Tyr Asn
275 280 285

Lys Phe Lys Asp Ile Ala Ser Thr Leu Asn Lys Ala Lys Ser Ile Val
290 295 300

Gly Thr Thr Ala Ser Leu Gln Tyr Met Lys Asn Val Phe Lys Glu Lys
305 310 315 320

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

Lys Phe Asp Lys Leu Tyr Lys Met Leu Thr Glu Ile Tyr Thr Glu Asp
340 345 350

Asn Phe Val Lys Phe Phe Lys Val Leu Asn Arg Lys Thr Tyr Leu Asn
355 360 365

Phe Asp Lys Ala Val Phe Lys Ile Asn Ile Val Pro Lys Val Asn Tyr
370 375 380

Thr Ile Tyr Asp Gly Phe Asn Leu Arg Asn Thr Asn Leu Ala Ala Asn
385 390 395 400

Phe Asn Gly Gln Asn Thr Glu Ile Asn Asn Met Asn Phe Thr Lys Leu
405 410 415

Lys Asn Phe Thr Gly Leu Phe Glu Phe Tyr Lys Leu Leu Cys Val Arg
420 425 430

Gly Ile Ile Thr Ser Lys Thr Lys Ser Leu Ile Glu Gly Arg Asn Lys
435 440 445

Ala Leu Asn Asp Leu Cys Ile Lys Val Asn Asn Trp Asp Leu Phe Phe
450 455 460

Ser Pro Ser Glu Asp Asn Phe Thr Asn Asp Leu Asn Lys Gly Glu Glu
465 470 475 480

Ile Thr Ser Asp Thr Asn Ile Glu Ala Ala Glu Glu Asn Ile Ser Leu
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Asp Leu Ile Gln Gln Tyr Tyr Leu Thr Phe Asn Phe Asp Asn Glu Pro
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 Gln Leu Val Tyr Asp Phe Thr Asp Glu Thr Ser Glu Val Ser Thr Thr
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 Leu Asn Ile Gly Asn Met Leu Tyr Lys Asp Asp Phe Val Gly Ala Leu
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 Ile Phe Ser Gly Ala Val Ile Leu Leu Glu Phe Ile Pro Glu Ile Ala
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 Ile Pro Val Leu Gly Thr Phe Ala Leu Val Ser Tyr Ile Ala Asn Lys
 675 680 685
 Val Leu Thr Val Gln Thr Ile Asp Asn Ala Leu Ser Lys Arg Asn Glu
 690 695 700
 Lys Trp Asp Glu Val Tyr Lys Tyr Ile Val Thr Asn Trp Leu Ala Lys
 705 710 715 720
 Val Asn Thr Gln Ile Asp Leu Ile Arg Lys Lys Met Lys Glu Ala Leu
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 Glu Asn Gln Ala Glu Ala Thr Lys Ala Ile Ile Asn Tyr Gln Tyr Asn
 740 745 750
 Gln Tyr Thr Glu Glu Glu Lys Asn Asn Ile Asn Phe Asn Ile Asp Asp
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770 775 780

Asn Lys Phe Leu Asn Gln Cys Ser Val Ser Tyr Leu Met Asn Ser Met
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Ile Pro Tyr Gly Val Lys Arg Leu Glu Asp Phe Asp Ala Ser Leu Lys
 805 810 815

Asp Ala Leu Leu Lys Tyr Ile Tyr Asp Asn Arg Gly Thr Leu Ile Gly
 820 825 830

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<400> 36

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 Leu Ile His Ala Gly His Arg Leu Tyr Gly Ile Ala Ile Asn Pro Asn
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 Arg Val Phe Lys Val Asn Thr Asn Ala Tyr Tyr Glu Met Ser Gly Leu
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 Glu Val Ser Phe Glu Glu Leu Arg Thr Phe Gly Gly His Asp Ala Lys
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 Phe Ile Asp Ser Leu Gln Glu Asn Glu Phe Arg Leu Tyr Tyr Tyr Asn
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 Lys Phe Lys Asp Ile Ala Ser Thr Leu Asn Lys Ala Lys Ser Ile Val
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 35 40 45

Asp Thr Phe Thr Asn Pro Glu Glu Gly Asp Leu Asn Pro Pro Pro Glu
 50 55 60

Ala Lys Gln Val Pro Val Ser Tyr Tyr Asp Ser Thr Tyr Leu Ser Thr
 65 70 75 80

Asp Asn Glu Lys Asp Asn Tyr Leu Lys Gly Val Thr Lys Leu Phe Glu
 85 90 95

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Arg Ile Tyr Ser Thr Asp Leu Gly Arg Met Leu Leu Thr Ser Ile Val
100 105 110

Arg Gly Ile Pro Phe Trp Gly Gly Ser Thr Ile Asp Thr Glu Leu Lys
115 120 125

Val Ile Asp Thr Asn Cys Ile Asn Val Ile Gln Pro Asp Gly Ser Tyr
130 135 140

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

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Ile Gln Phe Glu Cys Lys Ser Phe Gly His Glu Val Leu Asn Leu Thr
165 170 175

Arg Asn Gly Tyr Gly Ser Thr Gln Tyr Ile Arg Phe Ser Pro Asp Phe
180 185 190

Thr Phe Gly Phe Glu Glu Ser Leu Glu Val Asp Thr Asn Pro Leu Leu
195 200 205

Gly Ala Gly Lys Phe Ala Thr Asp Pro Ala Val Thr Leu Ala His Glu
210 215 220

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Leu Ile His Ala Gly His Arg Leu Tyr Gly Ile Ala Ile Asn Pro Asn
225 230 235 240

Arg Val Phe Lys Val Asn Thr Asn Ala Tyr Tyr Glu Met Ser Gly Leu
245 250 255

Glu Val Ser Phe Glu Glu Leu Arg Thr Phe Gly Gly His Asp Ala Lys
260 265 270

Phe Ile Asp Ser Leu Gln Glu Asn Glu Phe Arg Leu Tyr Tyr Tyr Asn
275 280 285

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Lys Phe Lys Asp Ile Ala Ser Thr Leu Asn Lys Ala Lys Ser Ile Val
290 295 300

Gly Thr Thr Ala Ser Leu Gln Tyr Met Lys Asn Val Phe Lys Glu Lys
305 310 315 320

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

Lys Phe Asp Lys Leu Tyr Lys Met Leu Thr Glu Ile Tyr Thr Glu Asp
340 345 350

Asn Phe Val Lys Phe Phe Lys Val Leu Asn Arg Lys Thr Tyr Leu Asn

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355 360 365
 Phe Asp Lys Ala Val Phe Lys Ile Asn Ile Val Pro Lys Val Asn Tyr
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 Thr Ile Tyr Asp Gly Phe Asn Leu Arg Asn Thr Asn Leu Ala Ala Asn
 385 390 395 400
 Phe Asn Gly Gln Asn Thr Glu Ile Asn Asn Met Asn Phe Thr Lys Leu
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 Lys Asn Phe Thr Gly Leu Phe Glu Phe Tyr Lys Leu Leu Cys Val Arg
 420 425 430
 Gly Ile Ile Thr Ser Lys Thr Lys Leu Val Pro Arg Gly Ser Asn Lys
 435 440 445
 Ala Leu Asn Asp Leu Cys Ile Lys Val Asn Asn Trp Asp Leu Phe Phe
 450 455 460
 Ser Pro Ser Glu Asp Asn Phe Thr Asn Asp Leu Asn Lys Gly Glu Glu
 465 470 475 480
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 Asp Leu Ile Gln Gln Tyr Tyr Leu Thr Phe Asn Phe Asp Asn Glu Pro
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 Glu Leu Met Pro Asn Ile Glu Arg Phe Pro Asn Gly Lys Lys Tyr Glu
 530 535 540
 Leu Asp Lys Tyr Thr Met Phe His Tyr Leu Arg Ala Gln Glu Phe Glu
 545 550 555 560
 His Gly Lys Ser Arg Ile Ala Leu Thr Asn Ser Val Asn Glu Ala Leu
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 Leu Asn Pro Ser Arg Val Tyr Thr Phe Phe Ser Ser Asp Tyr Val Lys
 580 585 590
 Lys Val Asn Lys Ala Thr Glu Ala Ala Met Phe Leu Gly Trp Val Glu
 595 600 605
 Gln Leu Val Tyr Asp Phe Thr Asp Glu Thr Ser Glu Val Ser Thr Thr
 610 615 620

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Asp Lys Ile Ala Asp Ile Thr Ile Ile Ile Pro Tyr Ile Gly Pro Ala
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Leu Asn Ile Gly Asn Met Leu Tyr Lys Asp Asp Phe Val Gly Ala Leu
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Ile Phe Ser Gly Ala Val Ile Leu Leu Glu Phe Ile Pro Glu Ile Ala
660 665 670

Ile Pro Val Leu Gly Thr Phe Ala Leu Val Ser Tyr Ile Ala Asn Lys
675 680 685

Val Leu Thr Val Gln Thr Ile Asp Asn Ala Leu Ser Lys Arg Asn Glu
690 695 700

Lys Trp Asp Glu Val Tyr Lys Tyr Ile Val Thr Asn Trp Leu Ala Lys
705 710 715 720

Val Asn Thr Gln Ile Asp Leu Ile Arg Lys Lys Met Lys Glu Ala Leu
725 730 735

Glu Asn Gln Ala Glu Ala Thr Lys Ala Ile Ile Asn Tyr Gln Tyr Asn
740 745 750

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

Leu Ser Ser Lys Leu Asn Glu Ser Ile Asn Lys Ala Met Ile Asn Ile
770 775 780

Asn Lys Phe Leu Asn Gln Cys Ser Val Ser Tyr Leu Met Asn Ser Met
785 790 795 800

Ile Pro Tyr Gly Val Lys Arg Leu Glu Asp Phe Asp Ala Ser Leu Lys
805 810 815

Asp Ala Leu Leu Lys Tyr Ile Tyr Asp Asn Arg Gly Thr Leu Ile Gly
820 825 830

Gln Val Asp Arg Leu Lys Asp Lys Val Asn Asn Thr Leu Ser Thr Asp
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Ile Pro Phe Gln Leu Ser Lys Tyr Val Asp Asn Gln Arg Leu Leu
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Val Lys Ala Phe Lys Ile His Asn Lys Ile Trp Val Ile Pro Glu Arg
 35 40 45

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Asp Thr Phe Thr Asn Pro Glu Glu Gly Asp Leu Asn Pro Pro Pro Glu
 50 55 60
 Ala Lys Gln Val Pro Val Ser Tyr Tyr Asp Ser Thr Tyr Leu Ser Thr
 65 70 75 80
 Asp Asn Glu Lys Asp Asn Tyr Leu Lys Gly Val Thr Lys Leu Phe Glu
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 Arg Ile Tyr Ser Thr Asp Leu Gly Arg Met Leu Leu Thr Ser Ile Val
 100 105 110
 Arg Gly Ile Pro Phe Trp Gly Gly Ser Thr Ile Asp Thr Glu Leu Lys
 115 120 125
 Val Ile Asp Thr Asn Cys Ile Asn Val Ile Gln Pro Asp Gly Ser Tyr
 130 135 140
 Arg Ser Glu Glu Leu Asn Leu Val Ile Ile Gly Pro Ser Ala Asp Ile
 145 150 155 160
 Ile Gln Phe Glu Cys Lys Ser Phe Gly His Glu Val Leu Asn Leu Thr
 165 170 175
 Arg Asn Gly Tyr Gly Ser Thr Gln Tyr Ile Arg Phe Ser Pro Asp Phe
 180 185 190
 Thr Phe Gly Phe Glu Glu Ser Leu Glu Val Asp Thr Asn Pro Leu Leu
 195 200 205
 Gly Ala Gly Lys Phe Ala Thr Asp Pro Ala Val Thr Leu Ala His Glu
 210 215 220
 Leu Ile His Ala Gly His Arg Leu Tyr Gly Ile Ala Ile Asn Pro Asn
 225 230 235 240
 Arg Val Phe Lys Val Asn Thr Asn Ala Tyr Tyr Glu Met Ser Gly Leu
 245 250 255
 Glu Val Ser Phe Glu Glu Leu Arg Thr Phe Gly Gly His Asp Ala Lys
 260 265 270
 Phe Ile Asp Ser Leu Gln Glu Asn Glu Phe Arg Leu Tyr Tyr Tyr Asn
 275 280 285
 Lys Phe Lys Asp Ile Ala Ser Thr Leu Asn Lys Ala Lys Ser Ile Val
 290 295 300
 Gly Thr Thr Ala Ser Leu Gln Tyr Met Lys Asn Val Phe Lys Glu Lys

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305 310 315 320
 Tyr Leu Leu Ser Glu Asp Thr Ser Gly Lys Phe Ser Val Asp Lys Leu
 325 330 335
 Lys Phe Asp Lys Leu Tyr Lys Met Leu Thr Glu Ile Tyr Thr Glu Asp
 340 345 350
 Asn Phe Val Lys Phe Phe Lys Val Leu Asn Arg Lys Thr Tyr Leu Asn
 355 360 365
 Phe Asp Lys Ala Val Phe Lys Ile Asn Ile Val Pro Lys Val Asn Tyr
 370 375 380
 Thr Ile Tyr Asp Gly Phe Asn Leu Arg Asn Thr Asn Leu Ala Ala Asn
 385 390 395 400
 Phe Asn Gly Gln Asn Thr Glu Ile Asn Asn Met Asn Phe Thr Lys Leu
 405 410 415
 Lys Asn Phe Thr Gly Leu Phe Glu Phe Tyr Lys Leu Leu Cys Val Arg
 420 425 430
 Gly Ile Ile Thr Ser Lys Thr Lys Ser Leu Asp Lys Gly Tyr Asn Lys
 435 440 445
 Ala Leu Asn Asp Leu Cys Ile Lys Val Asn Asn Trp Asp Leu Phe Phe
 450 455 460
 Ser Pro Ser Glu Asp Asn Phe Thr Asn Asp Leu Asn Lys Gly Glu Glu
 465 470 475 480
 Ile Thr Ser Asp Thr Asn Ile Glu Ala Ala Glu Glu Asn Ile Ser Leu
 485 490 495
 Asp Leu Ile Gln Gln Tyr Tyr Leu Thr Phe Asn Phe Asp Asn Glu Pro
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 Glu Asn Ile Ser Ile Glu Asn Leu Ser Ser Asp Ile Ile Gly Gln Leu
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 Glu Leu Met Pro Asn Ile Glu Arg Phe Pro Asn Gly Lys Lys Tyr Glu
 530 535 540
 Leu Asp Lys Tyr Thr Met Phe His Tyr Leu Arg Ala Gln Glu Phe Glu
 545 550 555 560
 His Gly Lys Ser Arg Ile Ala Leu Thr Asn Ser Val Asn Glu Ala Leu
 565 570 575

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Leu Asn Pro Ser Arg Val Tyr Thr Phe Phe Ser Ser Asp Tyr Val Lys
580 585 590

Lys Val Asn Lys Ala Thr Glu Ala Ala Met Phe Leu Gly Trp Val Glu
595 600 605

Gln Leu Val Tyr Asp Phe Thr Asp Glu Thr Ser Glu Val Ser Thr Thr
610 615 620

Asp Lys Ile Ala Asp Ile Thr Ile Ile Ile Pro Tyr Ile Gly Pro Ala
625 630 635 640

Leu Asn Ile Gly Asn Met Leu Tyr Lys Asp Asp Phe Val Gly Ala Leu
645 650 655

Ile Phe Ser Gly Ala Val Ile Leu Leu Glu Phe Ile Pro Glu Ile Ala
660 665 670

Ile Pro Val Leu Gly Thr Phe Ala Leu Val Ser Tyr Ile Ala Asn Lys
675 680 685

Val Leu Thr Val Gln Thr Ile Asp Asn Ala Leu Ser Lys Arg Asn Glu
690 695 700

Lys Trp Asp Glu Val Tyr Lys Tyr Ile Val Thr Asn Trp Leu Ala Lys
705 710 715 720

Val Asn Thr Gln Ile Asp Leu Ile Arg Lys Lys Met Lys Glu Ala Leu
725 730 735

Glu Asn Gln Ala Glu Ala Thr Lys Ala Ile Ile Asn Tyr Gln Tyr Asn
740 745 750

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

Leu Ser Ser Lys Leu Asn Glu Ser Ile Asn Lys Ala Met Ile Asn Ile
770 775 780

Asn Lys Phe Leu Asn Gln Cys Ser Val Ser Tyr Leu Met Asn Ser Met
785 790 795 800

Ile Pro Tyr Gly Val Lys Arg Leu Glu Asp Phe Asp Ala Ser Leu Lys
805 810 815

Asp Ala Leu Leu Lys Tyr Ile Tyr Asp Asn Arg Gly Thr Leu Ile Gly
820 825 830

Gln Val Asp Arg Leu Lys Asp Lys Val Asn Asn Thr Leu Ser Thr Asp
835 840 845

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Ile Pro Phe Gln Leu Ser Lys Tyr Val Asp Asn Gln Arg Leu Leu Ser
850 855 860

Thr Phe Thr Glu Tyr Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly
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Ser Gly Gly Gly Gly Ser Val Glu Thr Ile Ser Phe Ser Phe Ser Glu
885 890 895

Phe Glu Pro Gly Asn Asn Asp Leu Thr Leu Gln Gly Ala Ala Ile Ile
900 905 910

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Thr Gln Ser Gly Val Leu Gln Leu Thr Lys Ile Asn Gln Asn Gly Met
915 920 925

Pro Ala Trp Asp Ser Thr Gly Arg Thr Leu Tyr Thr Lys Pro Val His
930 935 940

Ile Trp Asp Met Thr Thr Gly Thr Val Ala Ser Phe Glu Thr Arg Phe
945 950 955 960

Ser Phe Ser Ile Glu Gln Pro Tyr Thr Arg Pro Leu Pro Ala Asp Gly
965 970 975

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Leu Val Phe Phe Met Gly Pro Thr Lys Ser Lys Pro Ala Gln Gly Tyr
980 985 990

Gly Tyr Leu Gly Val Phe Asn Asn Ser Lys Gln Asp Asn Ser Tyr Gln
995 1000 1005

Thr Leu Ala Val Glu Phe Asp Thr Phe Ser Asn Pro Trp Asp Pro
1010 1015 1020

Pro Gln Val Pro His Ile Gly Ile Asp Val Asn Ser Ile Arg Ser
1025 1030 1035

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Ile Lys Thr Gln Pro Phe Gln Leu Asp Asn Gly Gln Val Ala Asn
1040 1045 1050

Val Val Ile Lys Tyr Asp Ala Ser Ser Lys Ile Leu Leu Ala Val
1055 1060 1065

Leu Val Tyr Pro Ser Ser Gly Ala Ile Tyr Thr Ile Ala Glu Ile
1070 1075 1080

Val Asp Val Lys Gln Val Leu Pro Glu Trp Val Asp Val Gly Leu
1085 1090 1095

Ser Gly Ala Thr Gly Ala Gln Arg Asp Ala Ala Glu Thr His Asp

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 ccgggtaaca acgatttgac cttgcaaggt gcagccatta ttacacaatc tggggtttta 2760
 caactcacca agattaatca aaatggcatg ccggcttggg actcaacggg ccgaactcta 2820
 tataactaac ctgtgcacat ttgggatatg accacaggca ctgtggccag ctttgaaact 2880
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<400> 42

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Val Lys Ala Phe Lys Ile His Asn Lys Ile Trp Val Ile Pro Glu Arg
35 40 45

Asp Thr Phe Thr Asn Pro Glu Glu Gly Asp Leu Asn Pro Pro Pro Glu
50 55 60

Ala Lys Gln Val Pro Val Ser Tyr Tyr Asp Ser Thr Tyr Leu Ser Thr
65 70 75 80

Asp Asn Glu Lys Asp Asn Tyr Leu Lys Gly Val Thr Lys Leu Phe Glu
85 90 95

Arg Ile Tyr Ser Thr Asp Leu Gly Arg Met Leu Leu Thr Ser Ile Val
100 105 110

Arg Gly Ile Pro Phe Trp Gly Gly Ser Thr Ile Asp Thr Glu Leu Lys
115 120 125

Val Ile Asp Thr Asn Cys Ile Asn Val Ile Gln Pro Asp Gly Ser Tyr
130 135 140

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

Ile Gln Phe Glu Cys Lys Ser Phe Gly His Glu Val Leu Asn Leu Thr
165 170 175

Arg Asn Gly Tyr Gly Ser Thr Gln Tyr Ile Arg Phe Ser Pro Asp Phe
180 185 190

Thr Phe Gly Phe Glu Glu Ser Leu Glu Val Asp Thr Asn Pro Leu Leu
195 200 205

Gly Ala Gly Lys Phe Ala Thr Asp Pro Ala Val Thr Leu Ala His Glu
210 215 220

Leu Ile His Ala Gly His Arg Leu Tyr Gly Ile Ala Ile Asn Pro Asn
225 230 235 240

Arg Val Phe Lys Val Asn Thr Asn Ala Tyr Tyr Glu Met Ser Gly Leu
245 250 255

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Glu Val Ser Phe Glu Glu Leu Arg Thr Phe Gly Gly His Asp Ala Lys
 260 265 270
 Phe Ile Asp Ser Leu Gln Glu Asn Glu Phe Arg Leu Tyr Tyr Tyr Asn
 275 280 285
 Lys Phe Lys Asp Ile Ala Ser Thr Leu Asn Lys Ala Lys Ser Ile Val
 290 295 300
 Gly Thr Thr Ala Ser Leu Gln Tyr Met Lys Asn Val Phe Lys Glu Lys
 305 310 315 320
 Tyr Leu Leu Ser Glu Asp Thr Ser Gly Lys Phe Ser Val Asp Lys Leu
 325 330 335
 Lys Phe Asp Lys Leu Tyr Lys Met Leu Thr Glu Ile Tyr Thr Glu Asp
 340 345 350
 Asn Phe Val Lys Phe Phe Lys Val Leu Asn Arg Lys Thr Tyr Leu Asn
 355 360 365
 Phe Asp Lys Ala Val Phe Lys Ile Asn Ile Val Pro Lys Val Asn Tyr
 370 375 380
 Thr Ile Tyr Asp Gly Phe Asn Leu Arg Asn Thr Asn Leu Ala Ala Asn
 385 390 395 400
 Phe Asn Gly Gln Asn Thr Glu Ile Asn Asn Met Asn Phe Thr Lys Leu
 405 410 415
 Lys Asn Phe Thr Gly Leu Phe Glu Phe Tyr Lys Leu Leu Cys Val Arg
 420 425 430
 Gly Ile Ile Thr Ser Lys Thr Lys Ser Leu Asp Lys Gly Tyr Asn Lys
 435 440 445
 Ala Leu Asn Asp Leu Cys Ile Lys Val Asn Asn Trp Asp Leu Phe Phe
 450 455 460
 Ser Pro Ser Glu Asp Asn Phe Thr Asn Asp Leu Asn Lys Gly Glu Glu
 465 470 475 480
 Ile Thr Ser Asp Thr Asn Ile Glu Ala Ala Glu Glu Asn Ile Ser Leu
 485 490 495
 Asp Leu Ile Gln Gln Tyr Tyr Leu Thr Phe Asn Phe Asp Asn Glu Pro
 500 505 510
 Glu Asn Ile Ser Ile Glu Asn Leu Ser Ser Asp Ile Ile Gly Gln Leu
 515 520 525

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Glu Leu Met Pro Asn Ile Glu Arg Phe Pro Asn Gly Lys Lys Tyr Glu
530 535 540

Leu Asp Lys Tyr Thr Met Phe His Tyr Leu Arg Ala Gln Glu Phe Glu
545 550 555 560

His Gly Lys Ser Arg Ile Ala Leu Thr Asn Ser Val Asn Glu Ala Leu
565 570 575

Leu Asn Pro Ser Arg Val Tyr Thr Phe Phe Ser Ser Asp Tyr Val Lys
580 585 590

Lys Val Asn Lys Ala Thr Glu Ala Ala Met Phe Leu Gly Trp Val Glu
595 600 605

Gln Leu Val Tyr Asp Phe Thr Asp Glu Thr Ser Glu Val Ser Thr Thr
610 615 620

Asp Lys Ile Ala Asp Ile Thr Ile Ile Ile Pro Tyr Ile Gly Pro Ala
625 630 635 640

Leu Asn Ile Gly Asn Met Leu Tyr Lys Asp Asp Phe Val Gly Ala Leu
645 650 655

Ile Phe Ser Gly Ala Val Ile Leu Leu Glu Phe Ile Pro Glu Ile Ala
660 665 670

Ile Pro Val Leu Gly Thr Phe Ala Leu Val Ser Tyr Ile Ala Asn Lys
675 680 685

Val Leu Thr Val Gln Thr Ile Asp Asn Ala Leu Ser Lys Arg Asn Glu
690 695 700

Lys Trp Asp Glu Val Tyr Lys Tyr Ile Val Thr Asn Trp Leu Ala Lys
705 710 715 720

Val Asn Thr Gln Ile Asp Leu Ile Arg Lys Lys Met Lys Glu Ala Leu
725 730 735

Glu Asn Gln Ala Glu Ala Thr Lys Ala Ile Ile Asn Tyr Gln Tyr Asn
740 745 750

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

Leu Ser Ser Lys Leu Asn Glu Ser Ile Asn Lys Ala Met Ile Asn Ile
770 775 780

Asn Lys Phe Leu Asn Gln Cys Ser Val Ser Tyr Leu Met Asn Ser Met

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 Ile Pro Tyr Gly Val Lys Arg Leu Glu Asp Phe Asp Ala Ser Leu Lys
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 Asp Ala Leu Leu Lys Tyr Ile Tyr Asp Asn Arg Gly Thr Leu Ile Gly
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 Gln Val Asp Arg Leu Lys Asp Lys Val Asn Asn Thr Leu Ser Thr Asp
 835 840 845
 Ile Pro Phe Gln Leu Ser Lys Tyr Val Asp Asn Gln Arg Leu Leu Ser
 850 855 860
 Thr Phe Thr Glu Tyr Ile Lys Ala Glu Ala Ala Ala Lys Glu Ala Ala
 865 870 875 880
 Ala Lys Glu Ala Ala Ala Lys Ala Val Glu Thr Ile Ser Phe Ser Phe
 885 890 895
 Ser Glu Phe Glu Pro Gly Asn Asn Asp Leu Thr Leu Gln Gly Ala Ala
 900 905 910
 Ile Ile Thr Gln Ser Gly Val Leu Gln Leu Thr Lys Ile Asn Gln Asn
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 Gly Met Pro Ala Trp Asp Ser Thr Gly Arg Thr Leu Tyr Thr Lys Pro
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 Val His Ile Trp Asp Met Thr Thr Gly Thr Val Ala Ser Phe Glu Thr
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 Arg Phe Ser Phe Ser Ile Glu Gln Pro Tyr Thr Arg Pro Leu Pro Ala
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 Asp Gly Leu Val Phe Phe Met Gly Pro Thr Lys Ser Lys Pro Ala Gln
 980 985 990
 Gly Tyr Gly Tyr Leu Gly Val Phe Asn Asn Ser Lys Gln Asp Asn Ser
 995 1000 1005
 Tyr Gln Thr Leu Ala Val Glu Phe Asp Thr Phe Ser Asn Pro Trp
 1010 1015 1020
 Asp Pro Pro Gln Val Pro His Ile Gly Ile Asp Val Asn Ser Ile
 1025 1030 1035
 Arg Ser Ile Lys Thr Gln Pro Phe Gln Leu Asp Asn Gly Gln Val
 1040 1045 1050

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Ala Asn Val Val Ile Lys Tyr Asp Ala Ser Ser Lys Ile Leu Leu
1055 1060 1065

Ala Val Leu Val Tyr Pro Ser Ser Gly Ala Ile Tyr Thr Ile Ala
1070 1075 1080

Glu Ile Val Asp Val Lys Gln Val Leu Pro Glu Trp Val Asp Val
1085 1090 1095

Gly Leu Ser Gly Ala Thr Gly Ala Gln Arg Asp Ala Ala Glu Thr
1100 1105 1110

His Asp Val Tyr Ser Trp Ser Phe His Ala Ser Leu Pro Glu Thr
1115 1120 1125

Asn

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<211> 3391
<212> DNA
<213> Clostridium botulinum

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gataacgaaa aggacaacta cctgaaaggt gttactaaac tgttcgagcg tatttactcc 300
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 <211> 1130
 <212> PRT
 <213> Clostridium botulinum

<400> 44

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Val Lys Ala Phe Lys Ile His Asn Lys Ile Trp Val Ile Pro Glu Arg
 35 40 45

Asp Thr Phe Thr Asn Pro Glu Glu Gly Asp Leu Asn Pro Pro Pro Glu
 50 55 60

Ala Lys Gln Val Pro Val Ser Tyr Tyr Asp Ser Thr Tyr Leu Ser Thr
 65 70 75 80

Asp Asn Glu Lys Asp Asn Tyr Leu Lys Gly Val Thr Lys Leu Phe Glu
 85 90 95

Arg Ile Tyr Ser Thr Asp Leu Gly Arg Met Leu Leu Thr Ser Ile Val
 100 105 110

Arg Gly Ile Pro Phe Trp Gly Gly Ser Thr Ile Asp Thr Glu Leu Lys
 115 120 125

Val Ile Asp Thr Asn Cys Ile Asn Val Ile Gln Pro Asp Gly Ser Tyr
 130 135 140

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

Ile Gln Phe Glu Cys Lys Ser Phe Gly His Glu Val Leu Asn Leu Thr
 165 170 175

Arg Asn Gly Tyr Gly Ser Thr Gln Tyr Ile Arg Phe Ser Pro Asp Phe
 180 185 190

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Thr Phe Gly Phe Glu Glu Ser Leu Glu Val Asp Thr Asn Pro Leu Leu
195 200 205

Gly Ala Gly Lys Phe Ala Thr Asp Pro Ala Val Thr Leu Ala His Glu
210 215 220

Leu Ile His Ala Gly His Arg Leu Tyr Gly Ile Ala Ile Asn Pro Asn
225 230 235 240

Arg Val Phe Lys Val Asn Thr Asn Ala Tyr Tyr Glu Met Ser Gly Leu
245 250 255

Glu Val Ser Phe Glu Glu Leu Arg Thr Phe Gly Gly His Asp Ala Lys
260 265 270

Phe Ile Asp Ser Leu Gln Glu Asn Glu Phe Arg Leu Tyr Tyr Tyr Asn
275 280 285

Lys Phe Lys Asp Ile Ala Ser Thr Leu Asn Lys Ala Lys Ser Ile Val
290 295 300

Gly Thr Thr Ala Ser Leu Gln Tyr Met Lys Asn Val Phe Lys Glu Lys
305 310 315 320

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

Lys Phe Asp Lys Leu Tyr Lys Met Leu Thr Glu Ile Tyr Thr Glu Asp
340 345 350

Asn Phe Val Lys Phe Phe Lys Val Leu Asn Arg Lys Thr Tyr Leu Asn
355 360 365

Phe Asp Lys Ala Val Phe Lys Ile Asn Ile Val Pro Lys Val Asn Tyr
370 375 380

Thr Ile Tyr Asp Gly Phe Asn Leu Arg Asn Thr Asn Leu Ala Ala Asn
385 390 395 400

Phe Asn Gly Gln Asn Thr Glu Ile Asn Asn Met Asn Phe Thr Lys Leu
405 410 415

Lys Asn Phe Thr Gly Leu Phe Glu Phe Tyr Lys Leu Leu Cys Val Arg
420 425 430

Gly Ile Ile Thr Ser Lys Thr Lys Ser Leu Asp Asp Asp Asp Lys Gly
435 440 445

Tyr Asn Lys Ala Leu Asn Asp Leu Cys Ile Lys Val Asn Asn Trp Asp

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

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Leu Ala Lys Val Asn Thr Gln Ile Asp Leu Ile Arg Lys Lys Met Lys
 725 730 735
 Glu Ala Leu Glu Asn Gln Ala Glu Ala Thr Lys Ala Ile Ile Asn Tyr
 740 745 750
 Gln Tyr Asn Gln Tyr Thr Glu Glu Glu Lys Asn Asn Ile Asn Phe Asn
 755 760 765
 Ile Asp Asp Leu Ser Ser Lys Leu Asn Glu Ser Ile Asn Lys Ala Met
 770 775 780
 Ile Asn Ile Asn Lys Phe Leu Asn Gln Cys Ser Val Ser Tyr Leu Met
 785 790 795 800
 Asn Ser Met Ile Pro Tyr Gly Val Lys Arg Leu Glu Asp Phe Asp Ala
 805 810 815
 Ser Leu Lys Asp Ala Leu Leu Lys Tyr Ile Tyr Asp Asn Arg Gly Thr
 820 825 830
 Leu Ile Gly Gln Val Asp Arg Leu Lys Asp Lys Val Asn Asn Thr Leu
 835 840 845
 Ser Thr Asp Ile Pro Phe Gln Leu Ser Lys Tyr Val Asp Asn Gln Arg
 850 855 860
 Leu Leu Ser Thr Phe Thr Glu Tyr Ile Lys Gly Gly Gly Gly Ser Gly
 865 870 875 880
 Gly Gly Gly Ser Gly Gly Gly Gly Ser Val Glu Thr Ile Ser Phe Ser
 885 890 895
 Phe Ser Glu Phe Glu Pro Gly Asn Asn Asp Leu Thr Leu Gln Gly Ala
 900 905 910
 Ala Ile Ile Thr Gln Ser Gly Val Leu Gln Leu Thr Lys Ile Asn Gln
 915 920 925
 Asn Gly Met Pro Ala Trp Asp Ser Thr Gly Arg Thr Leu Tyr Thr Lys
 930 935 940
 Pro Val His Ile Trp Asp Met Thr Thr Gly Thr Val Ala Ser Phe Glu
 945 950 955 960
 Thr Arg Phe Ser Phe Ser Ile Glu Gln Pro Tyr Thr Arg Pro Leu Pro
 965 970 975
 Ala Asp Gly Leu Val Phe Phe Met Gly Pro Thr Lys Ser Lys Pro Ala
 980 985 990

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Gln Gly Tyr Gly Tyr Leu Gly Val Phe Asn Asn Ser Lys Gln Asp Asn
995 1000 1005

Ser Tyr Gln Thr Leu Ala Val Glu Phe Asp Thr Phe Ser Asn Pro
1010 1015 1020

Trp Asp Pro Pro Gln Val Pro His Ile Gly Ile Asp Val Asn Ser
1025 1030 1035

Ile Arg Ser Ile Lys Thr Gln Pro Phe Gln Leu Asp Asn Gly Gln
1040 1045 1050

Val Ala Asn Val Val Ile Lys Tyr Asp Ala Ser Ser Lys Ile Leu
1055 1060 1065

Leu Ala Val Leu Val Tyr Pro Ser Ser Gly Ala Ile Tyr Thr Ile
1070 1075 1080

Ala Glu Ile Val Asp Val Lys Gln Val Leu Pro Glu Trp Val Asp
1085 1090 1095

Val Gly Leu Ser Gly Ala Thr Gly Ala Gln Arg Asp Ala Ala Glu
1100 1105 1110

Thr His Asp Val Tyr Ser Trp Ser Phe His Ala Ser Leu Pro Glu
1115 1120 1125

Thr Asn
1130

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<211> 3397
<212> DNA
<213> Clostridium botulinum

<400> 45
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Val Asp Ile Ala Tyr Ile Lys Ile Pro Asn Ala Gly Gln Met Gln Pro
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Val Lys Ala Phe Lys Ile His Asn Lys Ile Trp Val Ile Pro Glu Arg
 35 40 45

Asp Thr Phe Thr Asn Pro Glu Glu Gly Asp Leu Asn Pro Pro Pro Glu
 50 55 60

Ala Lys Gln Val Pro Val Ser Tyr Tyr Asp Ser Thr Tyr Leu Ser Thr
 65 70 75 80

Asp Asn Glu Lys Asp Asn Tyr Leu Lys Gly Val Thr Lys Leu Phe Glu
 85 90 95

Arg Ile Tyr Ser Thr Asp Leu Gly Arg Met Leu Leu Thr Ser Ile Val
 100 105 110

Arg Gly Ile Pro Phe Trp Gly Gly Ser Thr Ile Asp Thr Glu Leu Lys
 115 120 125

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Val Ile Asp Thr Asn Cys Ile Asn Val Ile Gln Pro Asp Gly Ser Tyr
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 Arg Ser Glu Glu Leu Asn Leu Val Ile Ile Gly Pro Ser Ala Asp Ile
 145 150 155 160
 Ile Gln Phe Glu Cys Lys Ser Phe Gly His Glu Val Leu Asn Leu Thr
 165 170 175
 Arg Asn Gly Tyr Gly Ser Thr Gln Tyr Ile Arg Phe Ser Pro Asp Phe
 180 185 190
 Thr Phe Gly Phe Glu Glu Ser Leu Glu Val Asp Thr Asn Pro Leu Leu
 195 200 205
 Gly Ala Gly Lys Phe Ala Thr Asp Pro Ala Val Thr Leu Ala His Glu
 210 215 220
 Leu Ile His Ala Gly His Arg Leu Tyr Gly Ile Ala Ile Asn Pro Asn
 225 230 235 240
 Arg Val Phe Lys Val Asn Thr Asn Ala Tyr Tyr Glu Met Ser Gly Leu
 245 250 255
 Glu Val Ser Phe Glu Glu Leu Arg Thr Phe Gly Gly His Asp Ala Lys
 260 265 270
 Phe Ile Asp Ser Leu Gln Glu Asn Glu Phe Arg Leu Tyr Tyr Tyr Asn
 275 280 285
 Lys Phe Lys Asp Ile Ala Ser Thr Leu Asn Lys Ala Lys Ser Ile Val
 290 295 300
 Gly Thr Thr Ala Ser Leu Gln Tyr Met Lys Asn Val Phe Lys Glu Lys
 305 310 315 320
 Tyr Leu Leu Ser Glu Asp Thr Ser Gly Lys Phe Ser Val Asp Lys Leu
 325 330 335
 Lys Phe Asp Lys Leu Tyr Lys Met Leu Thr Glu Ile Tyr Thr Glu Asp
 340 345 350
 Asn Phe Val Lys Phe Phe Lys Val Leu Asn Arg Lys Thr Tyr Leu Asn
 355 360 365
 Phe Asp Lys Ala Val Phe Lys Ile Asn Ile Val Pro Lys Val Asn Tyr
 370 375 380
 Thr Ile Tyr Asp Gly Phe Asn Leu Arg Asn Thr Asn Leu Ala Ala Asn

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385 390 395 400
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 Lys Asn Phe Thr Gly Leu Phe Glu Phe Tyr Lys Leu Leu Cys Val Arg
 420 425 430
 Gly Ile Ile Thr Ser Lys Thr Lys Ser Leu Asp Asp Asp Asp Lys Gly
 435 440 445
 Tyr Asn Lys Ala Leu Asn Asp Leu Cys Ile Lys Val Asn Asn Trp Asp
 450 455 460
 Leu Phe Phe Ser Pro Ser Glu Asp Asn Phe Thr Asn Asp Leu Asn Lys
 465 470 475 480
 Gly Glu Glu Ile Thr Ser Asp Thr Asn Ile Glu Ala Ala Glu Glu Asn
 485 490 495
 Ile Ser Leu Asp Leu Ile Gln Gln Tyr Tyr Leu Thr Phe Asn Phe Asp
 500 505 510
 Asn Glu Pro Glu Asn Ile Ser Ile Glu Asn Leu Ser Ser Asp Ile Ile
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 Gly Gln Leu Glu Leu Met Pro Asn Ile Glu Arg Phe Pro Asn Gly Lys
 530 535 540
 Lys Tyr Glu Leu Asp Lys Tyr Thr Met Phe His Tyr Leu Arg Ala Gln
 545 550 555 560
 Glu Phe Glu His Gly Lys Ser Arg Ile Ala Leu Thr Asn Ser Val Asn
 565 570 575
 Glu Ala Leu Leu Asn Pro Ser Arg Val Tyr Thr Phe Phe Ser Ser Asp
 580 585 590
 Tyr Val Lys Lys Val Asn Lys Ala Thr Glu Ala Ala Met Phe Leu Gly
 595 600 605
 Trp Val Glu Gln Leu Val Tyr Asp Phe Thr Asp Glu Thr Ser Glu Val
 610 615 620
 Ser Thr Thr Asp Lys Ile Ala Asp Ile Thr Ile Ile Ile Pro Tyr Ile
 625 630 635 640
 Gly Pro Ala Leu Asn Ile Gly Asn Met Leu Tyr Lys Asp Asp Phe Val
 645 650 655

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Gly Ala Leu Ile Phe Ser Gly Ala Val Ile Leu Leu Glu Phe Ile Pro
660 665 670

Glu Ile Ala Ile Pro Val Leu Gly Thr Phe Ala Leu Val Ser Tyr Ile
675 680 685

Ala Asn Lys Val Leu Thr Val Gln Thr Ile Asp Asn Ala Leu Ser Lys
690 695 700

Arg Asn Glu Lys Trp Asp Glu Val Tyr Lys Tyr Ile Val Thr Asn Trp
705 710 715 720

Leu Ala Lys Val Asn Thr Gln Ile Asp Leu Ile Arg Lys Lys Met Lys
725 730 735

Glu Ala Leu Glu Asn Gln Ala Glu Ala Thr Lys Ala Ile Ile Asn Tyr ...
740 745 750

Gln Tyr Asn Gln Tyr Thr Glu Glu Glu Lys Asn Asn Ile Asn Phe Asn
755 760 765

Ile Asp Asp Leu Ser Ser Lys Leu Asn Glu Ser Ile Asn Lys Ala Met
770 775 780

Ile Asn Ile Asn Lys Phe Leu Asn Gln Cys Ser Val Ser Tyr Leu Met
785 790 795 800

Asn Ser Met Ile Pro Tyr Gly Val Lys Arg Leu Glu Asp Phe Asp Ala
805 810 815

Ser Leu Lys Asp Ala Leu Leu Lys Tyr Ile Tyr Asp Asn Arg Gly Thr
820 825 830

Leu Ile Gly Gln Val Asp Arg Leu Lys Asp Lys Val Asn Asn Thr Leu
835 840 845

Ser Thr Asp Ile Pro Phe Gln Leu Ser Lys Tyr Val Asp Asn Gln Arg
850 855 860

Leu Leu Ser Thr Phe Thr Glu Tyr Ile Lys Ala Glu Ala Ala Ala Lys
865 870 875 880

Glu Ala Ala Ala Lys Glu Ala Ala Ala Lys Ala Val Glu Thr Ile Ser
885 890 895

Phe Ser Phe Ser Glu Phe Glu Pro Gly Asn Asn Asp Leu Thr Leu Gln
900 905 910

Gly Ala Ala Ile Ile Thr Gln Ser Gly Val Leu Gln Leu Thr Lys Ile
915 920 925

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Asn Gln Asn Gly Met Pro Ala Trp Asp Ser Thr Gly Arg Thr Leu Tyr
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Thr Lys Pro Val His Ile Trp Asp Met Thr Thr Gly Thr Val Ala Ser
 945 950 955 960

Phe Glu Thr Arg Phe Ser Phe Ser Ile Glu Gln Pro Tyr Thr Arg Pro
 965 970 975

Leu Pro Ala Asp Gly Leu Val Phe Phe Met Gly Pro Thr Lys Ser Lys
 980 985 990

Pro Ala Gln Gly Tyr Gly Tyr Leu Gly Val Phe Asn Asn Ser Lys Gln
 995 1000 1005

Asp Asn Ser Tyr Gln Thr Leu Ala Val Glu Phe Asp Thr Phe Ser
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Asn Pro Trp Asp Pro Pro Gln Val Pro His Ile Gly Ile Asp Val
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Asn Ser Ile Arg Ser Ile Lys Thr Gln Pro Phe Gln Leu Asp Asn
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Gly Gln Val Ala Asn Val Val Ile Lys Tyr Asp Ala Ser Ser Lys
 1055 1060 1065

Ile Leu Leu Ala Val Leu Val Tyr Pro Ser Ser Gly Ala Ile Tyr
 1070 1075 1080

Thr Ile Ala Glu Ile Val Asp Val Lys Gln Val Leu Pro Glu Trp
 1085 1090 1095

Val Asp Val Gly Leu Ser Gly Ala Thr Gly Ala Gln Arg Asp Ala
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Ala Glu Thr His Asp Val Tyr Ser Trp Ser Phe His Ala Ser Leu
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Pro Glu Thr Asn
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<400> 48

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Val Lys Ala Phe Lys Ile His Asn Lys Ile Trp Val Ile Pro Glu Arg
 35 40 45

Asp Thr Phe Thr Asn Pro Glu Glu Gly Asp Leu Asn Pro Pro Pro Glu
 50 55 60

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Ala Lys Gln Val Pro Val Ser Tyr Tyr Asp Ser Thr Tyr Leu Ser Thr
 65 70 75 80
 Asp Asn Glu Lys Asp Asn Tyr Leu Lys Gly Val Thr Lys Leu Phe Glu
 85 90 95
 Arg Ile Tyr Ser Thr Asp Leu Gly Arg Met Leu Leu Thr Ser Ile Val
 100 105 110
 Arg Gly Ile Pro Phe Trp Gly Gly Ser Thr Ile Asp Thr Glu Leu Lys
 115 120 125
 Val Ile Asp Thr Asn Cys Ile Asn Val Ile Gln Pro Asp Gly Ser Tyr
 130 135 140
 Arg Ser Glu Glu Leu Asn Leu Val Ile Ile Gly Pro Ser Ala Asp Ile
 145 150 155 160
 Ile Gln Phe Glu Cys Lys Ser Phe Gly His Glu Val Leu Asn Leu Thr
 165 170 175
 Arg Asn Gly Tyr Gly Ser Thr Gln Tyr Ile Arg Phe Ser Pro Asp Phe
 180 185 190
 Thr Phe Gly Phe Glu Glu Ser Leu Glu Val Asp Thr Asn Pro Leu Leu
 195 200 205
 Gly Ala Gly Lys Phe Ala Thr Asp Pro Ala Val Thr Leu Ala His Glu
 210 215 220
 Leu Ile His Ala Gly His Arg Leu Tyr Gly Ile Ala Ile Asn Pro Asn
 225 230 235 240
 Arg Val Phe Lys Val Asn Thr Asn Ala Tyr Tyr Glu Met Ser Gly Leu
 245 250 255
 Glu Val Ser Phe Glu Glu Leu Arg Thr Phe Gly Gly His Asp Ala Lys
 260 265 270
 Phe Ile Asp Ser Leu Gln Glu Asn Glu Phe Arg Leu Tyr Tyr Tyr Asn
 275 280 285
 Lys Phe Lys Asp Ile Ala Ser Thr Leu Asn Lys Ala Lys Ser Ile Val
 290 295 300
 Gly Thr Thr Ala Ser Leu Gln Tyr Met Lys Asn Val Phe Lys Glu Lys
 305 310 315 320
 Tyr Leu Leu Ser Glu Asp Thr Ser Gly Lys Phe Ser Val Asp Lys Leu

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325 330 335
 Lys Phe Asp Lys Leu Tyr Lys Met Leu Thr Glu Ile Tyr Thr Glu Asp
 340 345 350
 Asn Phe Val Lys Phe Phe Lys Val Leu Asn Arg Lys Thr Tyr Leu Asn
 355 360 365
 Phe Asp Lys Ala Val Phe Lys Ile Asn Ile Val Pro Lys Val Asn Tyr
 370 375 380
 Thr Ile Tyr Asp Gly Phe Asn Leu Arg Asn Thr Asn Leu Ala Ala Asn
 385 390 395 400
 Phe Asn Gly Gln Asn Thr Glu Ile Asn Asn Met Asn Phe Thr Lys Leu
 405 410 415
 Lys Asn Phe Thr Gly Leu Phe Glu Phe Tyr Lys Leu Leu Cys Val Arg
 420 425 430
 Gly Ile Ile Thr Ser Lys Thr Lys Leu Val Pro Arg Gly Ser Asn Lys
 435 440 445
 Ala Leu Asn Asp Leu Cys Ile Lys Val Asn Asn Trp Asp Leu Phe Phe
 450 455 460
 Ser Pro Ser Glu Asp Asn Phe Thr Asn Asp Leu Asn Lys Gly Glu Glu
 465 470 475 480
 Ile Thr Ser Asp Thr Asn Ile Glu Ala Ala Glu Glu Asn Ile Ser Leu
 485 490 495
 Asp Leu Ile Gln Gln Tyr Tyr Leu Thr Phe Asn Phe Asp Asn Glu Pro
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 Glu Asn Ile Ser Ile Glu Asn Leu Ser Ser Asp Ile Ile Gly Gln Leu
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 Glu Leu Met Pro Asn Ile Glu Arg Phe Pro Asn Gly Lys Lys Tyr Glu
 530 535 540
 Leu Asp Lys Tyr Thr Met Phe His Tyr Leu Arg Ala Gln Glu Phe Glu
 545 550 555 560
 His Gly Lys Ser Arg Ile Ala Leu Thr Asn Ser Val Asn Glu Ala Leu
 565 570 575
 Leu Asn Pro Ser Arg Val Tyr Thr Phe Phe Ser Ser Asp Tyr Val Lys
 580 585 590

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Lys Val Asn Lys Ala Thr Glu Ala Ala Met Phe Leu Gly Trp Val Glu
595 600 605

Gln Leu Val Tyr Asp Phe Thr Asp Glu Thr Ser Glu Val Ser Thr Thr
610 615 620

Asp Lys Ile Ala Asp Ile Thr Ile Ile Ile Pro Tyr Ile Gly Pro Ala
625 630 635 640

Leu Asn Ile Gly Asn Met Leu Tyr Lys Asp Asp Phe Val Gly Ala Leu
645 650 655

Ile Phe Ser Gly Ala Val Ile Leu Leu Glu Phe Ile Pro Glu Ile Ala
660 665 670

Ile Pro Val Leu Gly Thr Phe Ala Leu Val Ser Tyr Ile Ala Asn Lys
675 680 685

Val Leu Thr Val Gln Thr Ile Asp Asn Ala Leu Ser Lys Arg Asn Glu
690 695 700

Lys Trp Asp Glu Val Tyr Lys Tyr Ile Val Thr Asn Trp Leu Ala Lys
705 710 715 720

Val Asn Thr Gln Ile Asp Leu Ile Arg Lys Lys Met Lys Glu Ala Leu
725 730 735

Glu Asn Gln Ala Glu Ala Thr Lys Ala Ile Ile Asn Tyr Gln Tyr Asn
740 745 750

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

Leu Ser Ser Lys Leu Asn Glu Ser Ile Asn Lys Ala Met Ile Asn Ile
770 775 780

Asn Lys Phe Leu Asn Gln Cys Ser Val Ser Tyr Leu Met Asn Ser Met
785 790 795 800

Ile Pro Tyr Gly Val Lys Arg Leu Glu Asp Phe Asp Ala Ser Leu Lys
805 810 815

Asp Ala Leu Leu Lys Tyr Ile Tyr Asp Asn Arg Gly Thr Leu Ile Gly
820 825 830

Gln Val Asp Arg Leu Lys Asp Lys Val Asn Asn Thr Leu Ser Thr Asp
835 840 845

Ile Pro Phe Gln Leu Ser Lys Tyr Val Asp Asn Gln Arg Leu Leu Ser
850 855 860

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Thr Phe Thr Glu Tyr Ile Lys Ala Glu Ala Ala Lys Glu Ala Ala
865 870 875 880

Ala Lys Glu Ala Ala Ala Lys Ala Val Glu Thr Ile Ser Phe Ser Phe
885 890 895

Ser Glu Phe Glu Pro Gly Asn Asn Asp Leu Thr Leu Gln Gly Ala Ala
900 905 910

Ile Ile Thr Gln Ser Gly Val Leu Gln Leu Thr Lys Ile Asn Gln Asn
915 920 925

Gly Met Pro Ala Trp Asp Ser Thr Gly Arg Thr Leu Tyr Thr Lys Pro
930 935 940

Val His Ile Trp Asp Met Thr Thr Gly Thr Val Ala Ser Phe Glu Thr
945 950 955 960

Arg Phe Ser Phe Ser Ile Glu Gln Pro Tyr Thr Arg Pro Leu Pro Ala
965 970 975

Asp Gly Leu Val Phe Phe Met Gly Pro Thr Lys Ser Lys Pro Ala Gln
980 985 990

Gly Tyr Gly Tyr Leu Gly Val Phe Asn Asn Ser Lys Gln Asp Asn Ser
995 1000 1005

Tyr Gln Thr Leu Ala Val Glu Phe Asp Thr Phe Ser Asn Pro Trp
1010 1015 1020

Asp Pro Pro Gln Val Pro His Ile Gly Ile Asp Val Asn Ser Ile
1025 1030 1035

Arg Ser Ile Lys Thr Gln Pro Phe Gln Leu Asp Asn Gly Gln Val
1040 1045 1050

Ala Asn Val Val Ile Lys Tyr Asp Ala Ser Ser Lys Ile Leu Leu
1055 1060 1065

Ala Val Leu Val Tyr Pro Ser Ser Gly Ala Ile Tyr Thr Ile Ala
1070 1075 1080

Glu Ile Val Asp Val Lys Gln Val Leu Pro Glu Trp Val Asp Val
1085 1090 1095

Gly Leu Ser Gly Ala Thr Gly Ala Gln Arg Asp Ala Ala Glu Thr
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His Asp Val Tyr Ser Trp Ser Phe His Ala Ser Leu Pro Glu Thr

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Val Lys Ala Phe Lys Ile His Asn Lys Ile Trp Val Ile Pro Glu Arg
 35 40 45

Asp Thr Phe Thr Asn Pro Glu Glu Gly Asp Leu Asn Pro Pro Pro Glu
 50 55 60

Ala Lys Gln Val Pro Val Ser Tyr Tyr Asp Ser Thr Tyr Leu Ser Thr
 65 70 75 80

Asp Asn Glu Lys Asp Asn Tyr Leu Lys Gly Val Thr Lys Leu Phe Glu
 85 90 95

Arg Ile Tyr Ser Thr Asp Leu Gly Arg Met Leu Leu Thr Ser Ile Val
 100 105 110

Arg Gly Ile Pro Phe Trp Gly Gly Ser Thr Ile Asp Thr Glu Leu Lys
 115 120 125

Val Ile Asp Thr Asn Cys Ile Asn Val Ile Gln Pro Asp Gly Ser Tyr
 130 135 140

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

Ile Gln Phe Glu Cys Lys Ser Phe Gly His Glu Val Leu Asn Leu Thr
 165 170 175

Arg Asn Gly Tyr Gly Ser Thr Gln Tyr Ile Arg Phe Ser Pro Asp Phe
 180 185 190

Thr Phe Gly Phe Glu Glu Ser Leu Glu Val Asp Thr Asn Pro Leu Leu
 195 200 205

Gly Ala Gly Lys Phe Ala Thr Asp Pro Ala Val Thr Leu Ala His Glu
 210 215 220

Leu Ile His Ala Gly His Arg Leu Tyr Gly Ile Ala Ile Asn Pro Asn
 225 230 235 240

Arg Val Phe Lys Val Asn Thr Asn Ala Tyr Tyr Glu Met Ser Gly Leu
 245 250 255

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Glu Val Ser Phe Glu Glu Leu Arg Thr Phe Gly Gly His Asp Ala Lys
 260 265 270
 Phe Ile Asp Ser Leu Gln Glu Asn Glu Phe Arg Leu Tyr Tyr Tyr Asn
 275 280 285
 Lys Phe Lys Asp Ile Ala Ser Thr Leu Asn Lys Ala Lys Ser Ile Val
 290 295 300
 Gly Thr Thr Ala Ser Leu Gln Tyr Met Lys Asn Val Phe Lys Glu Lys
 305 310 315 320
 Tyr Leu Leu Ser Glu Asp Thr Ser Gly Lys Phe Ser Val Asp Lys Leu
 325 330 335
 Lys Phe Asp Lys Leu Tyr Lys Met Leu Thr Glu Ile Tyr Thr Glu Asp
 340 345 350
 Asn Phe Val Lys Phe Phe Lys Val Leu Asn Arg Lys Thr Tyr Leu Asn
 355 360 365
 Phe Asp Lys Ala Val Phe Lys Ile Asn Ile Val Pro Lys Val Asn Tyr
 370 375 380
 Thr Ile Tyr Asp Gly Phe Asn Leu Arg Asn Thr Asn Leu Ala Ala Asn
 385 390 395 400
 Phe Asn Gly Gln Asn Thr Glu Ile Asn Asn Met Asn Phe Thr Lys Leu
 405 410 415
 Lys Asn Phe Thr Gly Leu Phe Glu Phe Tyr Lys Leu Leu Cys Val Arg
 420 425 430
 Gly Ile Ile Thr Ser Lys Thr Lys Leu Val Pro Arg Gly Ser Asn Lys
 435 440 445
 Ala Leu Asn Asp Leu Cys Ile Lys Val Asn Asn Trp Asp Leu Phe Phe
 450 455 460
 Ser Pro Ser Glu Asp Asn Phe Thr Asn Asp Leu Asn Lys Gly Glu Glu
 465 470 475 480
 Ile Thr Ser Asp Thr Asn Ile Glu Ala Ala Glu Glu Asn Ile Ser Leu
 485 490 495
 Asp Leu Ile Gln Gln Tyr Tyr Leu Thr Phe Asn Phe Asp Asn Glu Pro
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 Glu Asn Ile Ser Ile Glu Asn Leu Ser Ser Asp Ile Ile Gly Gln Leu
 515 520 525

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Glu Leu Met Pro Asn Ile Glu Arg Phe Pro Asn Gly Lys Lys Tyr Glu
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 Leu Asp Lys Tyr Thr Met Phe His Tyr Leu Arg Ala Gln Glu Phe Glu
 545 550 555 560
 His Gly Lys Ser Arg Ile Ala Leu Thr Asn Ser Val Asn Glu Ala Leu
 565 570 575
 Leu Asn Pro Ser Arg Val Tyr Thr Phe Phe Ser Ser Asp Tyr Val Lys
 580 585 590
 Lys Val Asn Lys Ala Thr Glu Ala Ala Met Phe Leu Gly Trp Val Glu
 595 600 605
 Gln Leu Val Tyr Asp Phe Thr Asp Glu Thr Ser Glu Val Ser Thr Thr
 610 615 620
 Asp Lys Ile Ala Asp Ile Thr Ile Ile Ile Pro Tyr Ile Gly Pro Ala
 625 630 635 640
 Leu Asn Ile Gly Asn Met Leu Tyr Lys Asp Asp Phe Val Gly Ala Leu
 645 650 655
 Ile Phe Ser Gly Ala Val Ile Leu Leu Glu Phe Ile Pro Glu Ile Ala
 660 665 670
 Ile Pro Val Leu Gly Thr Phe Ala Leu Val Ser Tyr Ile Ala Asn Lys
 675 680 685
 Val Leu Thr Val Gln Thr Ile Asp Asn Ala Leu Ser Lys Arg Asn Glu
 690 695 700
 Lys Trp Asp Glu Val Tyr Lys Tyr Ile Val Thr Asn Trp Leu Ala Lys
 705 710 715 720
 Val Asn Thr Gln Ile Asp Leu Ile Arg Lys Lys Met Lys Glu Ala Leu
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 Glu Asn Gln Ala Glu Ala Thr Lys Ala Ile Ile Asn Tyr Gln Tyr Asn
 740 745 750
 Gln Tyr Thr Glu Glu Glu Lys Asn Asn Ile Asn Phe Asn Ile Asp Asp
 755 760 765
 Leu Ser Ser Lys Leu Asn Glu Ser Ile Asn Lys Ala Met Ile Asn Ile
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 Asn Lys Phe Leu Asn Gln Cys Ser Val Ser Tyr Leu Met Asn Ser Met

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785 790 795 800
 Ile Pro Tyr Gly Val Lys Arg Leu Glu Asp Phe Asp Ala Ser Leu Lys
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 Asp Ala Leu Leu Lys Tyr Ile Tyr Asp Asn Arg Gly Thr Leu Ile Gly
 820 825 830
 Gln Val Asp Arg Leu Lys Asp Lys Val Asn Asn Thr Leu Ser Thr Asp
 835 840 845
 Ile Pro Phe Gln Leu Ser Lys Tyr Val Asp Asn Gln Arg Leu Leu Ser
 850 855 860
 Thr Phe Thr Glu Tyr Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly
 865 870 875 880
 Ser Gly Gly Gly Gly Ser Val Glu Thr Ile Ser Phe Ser Phe Ser Glu
 885 890 895
 Phe Glu Pro Gly Asn Asn Asp Leu Thr Leu Gln Gly Ala Ala Ile Ile
 900 905 910
 Thr Gln Ser Gly Val Leu Gln Leu Thr Lys Ile Asn Gln Asn Gly Met
 915 920 925
 Pro Ala Trp Asp Ser Thr Gly Arg Thr Leu Tyr Thr Lys Pro Val His
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 Ile Trp Asp Met Thr Thr Gly Thr Val Ala Ser Phe Glu Thr Arg Phe
 945 950 955 960
 Ser Phe Ser Ile Glu Gln Pro Tyr Thr Arg Pro Leu Pro Ala Asp Gly
 965 970 975
 Leu Val Phe Phe Met Gly Pro Thr Lys Ser Lys Pro Ala Gln Gly Tyr
 980 985 990
 Gly Tyr Leu Gly Val Phe Asn Asn Ser Lys Gln Asp Asn Ser Tyr Gln
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 Thr Leu Ala Val Glu Phe Asp Thr Phe Ser Asn Pro Trp Asp Pro
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 Pro Gln Val Pro His Ile Gly Ile Asp Val Asn Ser Ile Arg Ser
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 Ile Lys Thr Gln Pro Phe Gln Leu Asp Asn Gly Gln Val Ala Asn
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Val Val Ile Lys Tyr Asp Ala Ser Ser Lys Ile Leu Leu Ala Val
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Leu Val Tyr Pro Ser Ser Gly Ala Ile Tyr Thr Ile Ala Glu Ile
1070 1075 1080

Val Asp Val Lys Gln Val Leu Pro Glu Trp Val Asp Val Gly Leu
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Ser Gly Ala Thr Gly Ala Gln Arg Asp Ala Ala Glu Thr His Asp
1100 1105 1110

Val Tyr Ser Trp Ser Phe His Ala Ser Leu Pro Glu Thr Asn
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<212> DNA
<213> Clostridium botulinum

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 <212> PRT
 <213> Clostridium botulinum

<400> 52

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 35 40 45

Asp Thr Phe Thr Asn Pro Glu Glu Gly Asp Leu Asn Pro Pro Pro Glu
 50 55 60

Ala Lys Gln Val Pro Val Ser Tyr Tyr Asp Ser Thr Tyr Leu Ser Thr
 65 70 75 80

Asp Asn Glu Lys Asp Asn Tyr Leu Lys Gly Val Thr Lys Leu Phe Glu
 85 90 95

Arg Ile Tyr Ser Thr Asp Leu Gly Arg Met Leu Leu Thr Ser Ile Val
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Arg Gly Ile Pro Phe Trp Gly Gly Ser Thr Ile Asp Thr Glu Leu Lys
 115 120 125

Val Ile Asp Thr Asn Cys Ile Asn Val Ile Gln Pro Asp Gly Ser Tyr
 130 135 140

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

Ile Gln Phe Glu Cys Lys Ser Phe Gly His Glu Val Leu Asn Leu Thr
 165 170 175

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

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

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465 470 475 480
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 485 490 495
 Asp Leu Ile Gln Gln Tyr Tyr Leu Thr Phe Asn Phe Asp Asn Glu Pro
 500 505 510
 Glu Asn Ile Ser Ile Glu Asn Leu Ser Ser Asp Ile Ile Gly Gln Leu
 515 520 525
 Glu Leu Met Pro Asn Ile Glu Arg Phe Pro Asn Gly Lys Lys Tyr Glu
 530 535 540
 Leu Asp Lys Tyr Thr Met Phe His Tyr Leu Arg Ala Gln Glu Phe Glu
 545 550 555 560
 His Gly Lys Ser Arg Ile Ala Leu Thr Asn Ser Val Asn Glu Ala Leu
 565 570 575
 Leu Asn Pro Ser Arg Val Tyr Thr Phe Phe Ser Ser Asp Tyr Val Lys
 580 585 590
 Lys Val Asn Lys Ala Thr Glu Ala Ala Met Phe Leu Gly Trp Val Glu
 595 600 605
 Gln Leu Val Tyr Asp Phe Thr Asp Glu Thr Ser Glu Val Ser Thr Thr
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 Asp Lys Ile Ala Asp Ile Thr Ile Ile Ile Pro Tyr Ile Gly Pro Ala
 625 630 635 640
 Leu Asn Ile Gly Asn Met Leu Tyr Lys Asp Asp Phe Val Gly Ala Leu
 645 650 655
 Ile Phe Ser Gly Ala Val Ile Leu Leu Glu Phe Ile Pro Glu Ile Ala
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 Ile Pro Val Leu Gly Thr Phe Ala Leu Val Ser Tyr Ile Ala Asn Lys
 675 680 685
 Val Leu Thr Val Gln Thr Ile Asp Asn Ala Leu Ser Lys Arg Asn Glu
 690 695 700
 Lys Trp Asp Glu Val Tyr Lys Tyr Ile Val Thr Asn Trp Leu Ala Lys
 705 710 715 720
 Val Asn Thr Gln Ile Asp Leu Ile Arg Lys Lys Met Lys Glu Ala Leu
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Glu Asn Gln Ala Glu Ala Thr Lys Ala Ile Ile Asn Tyr Gln Tyr Asn
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Gln Tyr Thr Glu Glu Glu Lys Asn Asn Ile Asn Phe Asn Ile Asp Asp
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Leu Ser Ser Lys Leu Asn Glu Ser Ile Asn Lys Ala Met Ile Asn Ile
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Asn Lys Phe Leu Asn Gln Cys Ser Val Ser Tyr Leu Met Asn Ser Met
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Ile Pro Tyr Gly Val Lys Arg Leu Glu Asp Phe Asp Ala Ser Leu Lys
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Asp Ala Leu Leu Lys Tyr Ile Tyr Asp Asn Arg Gly Thr Leu Ile Gly
 820 825 830

Gln Val Asp Arg Leu Lys Asp Lys Val Asn Asn Thr Leu Ser Thr Asp
 835 840 845

Ile Pro Phe Gln Leu Ser Lys Tyr Val Asp Asn Gln Arg Leu Leu Ser
 850 855 860

Thr Phe Thr Glu Tyr Ile Lys Ala Glu Ala Ala Ala Lys Glu Ala Ala
 865 870 875 880

Ala Lys Glu Ala Ala Ala Lys Ala Val Glu Thr Ile Ser Phe Ser Phe
 885 890 895

Ser Glu Phe Glu Pro Gly Asn Asn Asp Leu Thr Leu Gln Gly Ala Ala
 900 905 910

Ile Ile Thr Gln Ser Gly Val Leu Gln Leu Thr Lys Ile Asn Gln Asn
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Gly Met Pro Ala Trp Asp Ser Thr Gly Arg Thr Leu Tyr Thr Lys Pro
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Val His Ile Trp Asp Met Thr Thr Gly Thr Val Ala Ser Phe Glu Thr
 945 950 955 960

Arg Phe Ser Phe Ser Ile Glu Gln Pro Tyr Thr Arg Pro Leu Pro Ala
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Asp Gly Leu Val Phe Phe Met Gly Pro Thr Lys Ser Lys Pro Ala Gln
 980 985 990

Gly Tyr Gly Tyr Leu Gly Val Phe Asn Asn Ser Lys Gln Asp Asn Ser
 995 1000 1005

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Tyr Gln Thr Leu Ala Val Glu Phe Asp Thr Phe Ser Asn Pro Trp
1010 1015 1020

Asp Pro Pro Gln Val Pro His Ile Gly Ile Asp Val Asn Ser Ile
1025 1030 1035

Arg Ser Ile Lys Thr Gln Pro Phe Gln Leu Asp Asn Gly Gln Val
1040 1045 1050

Ala Asn Val Val Ile Lys Tyr Asp Ala Ser Ser Lys Ile Leu Leu
1055 1060 1065

Ala Val Leu Val Tyr Pro Ser Ser Gly Ala Ile Tyr Thr Ile Ala
1070 1075 1080

Glu Ile Val Asp Val Lys Gln Val Leu Pro Glu Trp Val Asp Val
1085 1090 1095

Gly Leu Ser Gly Ala Thr Gly Ala Gln Arg Asp Ala Ala Glu Thr
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His Asp Val Tyr Ser Trp Ser Phe His Ala Ser Leu Pro Glu Thr
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Asn

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<211> 3382
<212> DNA
<213> Clostridium botulinum

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<213> Clostridium botulinum

<400> 54

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35 40 45

Asp Thr Phe Thr Asn Pro Glu Gly Asp Leu Asn Pro Pro Pro Glu
50 55 60

Ala Lys Gln Val Pro Val Ser Tyr Tyr Asp Ser Thr Tyr Leu Ser Thr
65 70 75 80

Asp Asn Glu Lys Asp Asn Tyr Leu Lys Gly Val Thr Lys Leu Phe Glu
85 90 95

Arg Ile Tyr Ser Thr Asp Leu Gly Arg Met Leu Leu Thr Ser Ile Val
100 105 110

Arg Gly Ile Pro Phe Trp Gly Gly Ser Thr Ile Asp Thr Glu Leu Lys
115 120 125

Val Ile Asp Thr Asn Cys Ile Asn Val Ile Gln Pro Asp Gly Ser Tyr
130 135 140

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Arg Ser Glu Glu Leu Asn Leu Val Ile Ile Gly Pro Ser Ala Asp Ile
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 Ile Gln Phe Glu Cys Lys Ser Phe Gly His Glu Val Leu Asn Leu Thr
 165 170 175
 Arg Asn Gly Tyr Gly Ser Thr Gln Tyr Ile Arg Phe Ser Pro Asp Phe
 180 185 190
 Thr Phe Gly Phe Glu Glu Ser Leu Glu Val Asp Thr Asn Pro Leu Leu
 195 200 205
 Gly Ala Gly Lys Phe Ala Thr Asp Pro Ala Val Thr Leu Ala His Glu
 210 215 220
 Leu Ile His Ala Gly His Arg Leu Tyr Gly Ile Ala Ile Asn Pro Asn
 225 230 235 240
 Arg Val Phe Lys Val Asn Thr Asn Ala Tyr Tyr Glu Met Ser Gly Leu
 245 250 255
 Glu Val Ser Phe Glu Glu Leu Arg Thr Phe Gly Gly His Asp Ala Lys
 260 265 270
 Phe Ile Asp Ser Leu Gln Glu Asn Glu Phe Arg Leu Tyr Tyr Tyr Asn
 275 280 285
 Lys Phe Lys Asp Ile Ala Ser Thr Leu Asn Lys Ala Lys Ser Ile Val
 290 295 300
 Gly Thr Thr Ala Ser Leu Gln Tyr Met Lys Asn Val Phe Lys Glu Lys
 305 310 315 320
 Tyr Leu Leu Ser Glu Asp Thr Ser Gly Lys Phe Ser Val Asp Lys Leu
 325 330 335
 Lys Phe Asp Lys Leu Tyr Lys Met Leu Thr Glu Ile Tyr Thr Glu Asp
 340 345 350
 Asn Phe Val Lys Phe Phe Lys Val Leu Asn Arg Lys Thr Tyr Leu Asn
 355 360 365
 Phe Asp Lys Ala Val Phe Lys Ile Asn Ile Val Pro Lys Val Asn Tyr
 370 375 380
 Thr Ile Tyr Asp Gly Phe Asn Leu Arg Asn Thr Asn Leu Ala Ala Asn
 385 390 395 400
 Phe Asn Gly Gln Asn Thr Glu Ile Asn Asn Met Asn Phe Thr Lys Leu

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405 410 415
 Lys Asn Phe Thr Gly Leu Phe Glu Phe Tyr Lys Leu Leu Cys Val Arg
 420 425 430
 Gly Ile Ile Thr Ser Lys Leu Glu Val Leu Phe Gln Gly Pro Asn Lys
 435 440 445
 Ala Leu Asn Asp Leu Cys Ile Lys Val Asn Asn Trp Asp Leu Phe Phe
 450 455 460
 Ser Pro Ser Glu Asp Asn Phe Thr Asn Asp Leu Asn Lys Gly Glu Glu
 465 470 475 480
 Ile Thr Ser Asp Thr Asn Ile Glu Ala Ala Glu Glu Asn Ile Ser Leu
 485 490 495
 Asp Leu Ile Gln Gln Tyr Tyr Leu Thr Phe Asn Phe Asp Asn Glu Pro
 500 505 510
 Glu Asn Ile Ser Ile Glu Asn Leu Ser Ser Asp Ile Ile Gly Gln Leu
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 Glu Leu Met Pro Asn Ile Glu Arg Phe Pro Asn Gly Lys Lys Tyr Glu
 530 535 540
 Leu Asp Lys Tyr Thr Met Phe His Tyr Leu Arg Ala Gln Glu Phe Glu
 545 550 555 560
 His Gly Lys Ser Arg Ile Ala Leu Thr Asn Ser Val Asn Glu Ala Leu
 565 570 575
 Leu Asn Pro Ser Arg Val Tyr Thr Phe Phe Ser Ser Asp Tyr Val Lys
 580 585 590
 Lys Val Asn Lys Ala Thr Glu Ala Ala Met Phe Leu Gly Trp Val Glu
 595 600 605
 Gln Leu Val Tyr Asp Phe Thr Asp Glu Thr Ser Glu Val Ser Thr Thr
 610 615 620
 Asp Lys Ile Ala Asp Ile Thr Ile Ile Ile Pro Tyr Ile Gly Pro Ala
 625 630 635 640
 Leu Asn Ile Gly Asn Met Leu Tyr Lys Asp Asp Phe Val Gly Ala Leu
 645 650 655
 Ile Phe Ser Gly Ala Val Ile Leu Leu Glu Phe Ile Pro Glu Ile Ala
 660 665 670

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Ile Pro Val Leu Gly Thr Phe Ala Leu Val Ser Tyr Ile Ala Asn Lys
 675 680 685
 Val Leu Thr Val Gln Thr Ile Asp Asn Ala Leu Ser Lys Arg Asn Glu
 690 695 700
 Lys Trp Asp Glu Val Tyr Lys Tyr Ile Val Thr Asn Trp Leu Ala Lys
 705 710 715 720
 Val Asn Thr Gln Ile Asp Leu Ile Arg Lys Lys Met Lys Glu Ala Leu
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 Glu Asn Gln Ala Glu Ala Thr Lys Ala Ile Ile Asn Tyr Gln Tyr Asn
 740 745 750
 Gln Tyr Thr Glu Glu Glu Lys Asn Asn Ile Asn Phe Asn Ile Asp Asp
 755 760 765
 Leu Ser Ser Lys Leu Asn Glu Ser Ile Asn Lys Ala Met Ile Asn Ile
 770 775 780
 Asn Lys Phe Leu Asn Gln Cys Ser Val Ser Tyr Leu Met Asn Ser Met
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 Ile Pro Tyr Gly Val Lys Arg Leu Glu Asp Phe Asp Ala Ser Leu Lys
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 Asp Ala Leu Leu Lys Tyr Ile Tyr Asp Asn Arg Gly Thr Leu Ile Gly
 820 825 830
 Gln Val Asp Arg Leu Lys Asp Lys Val Asn Asn Thr Leu Ser Thr Asp
 835 840 845
 Ile Pro Phe Gln Leu Ser Lys Tyr Val Asp Asn Gln Arg Leu Leu Ser
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 Thr Phe Thr Glu Tyr Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly
 865 870 875 880
 Ser Gly Gly Gly Gly Ser Val Glu Thr Ile Ser Phe Ser Phe Ser Glu
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 Phe Glu Pro Gly Asn Asn Asp Leu Thr Leu Gln Gly Ala Ala Ile Ile
 900 905 910
 Thr Gln Ser Gly Val Leu Gln Leu Thr Lys Ile Asn Gln Asn Gly Met
 915 920 925
 Pro Ala Trp Asp Ser Thr Gly Arg Thr Leu Tyr Thr Lys Pro Val His
 930 935 940

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Ile Trp Asp Met Thr Thr Gly Thr Val Ala Ser Phe Glu Thr Arg Phe
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Ser Phe Ser Ile Glu Gln Pro Tyr Thr Arg Pro Leu Pro Ala Asp Gly
 965 970 975

Leu Val Phe Phe Met Gly Pro Thr Lys Ser Lys Pro Ala Gln Gly Tyr
 980 985 990

Gly Tyr Leu Gly Val Phe Asn Asn Ser Lys Gln Asp Asn Ser Tyr Gln
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Thr Leu Ala Val Glu Phe Asp Thr Phe Ser Asn Pro Trp Asp Pro
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Pro Gln Val Pro His Ile Gly Ile Asp Val Asn Ser Ile Arg Ser
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Ile Lys Thr Gln Pro Phe Gln Leu Asp Asn Gly Gln Val Ala Asn
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Val Val Ile Lys Tyr Asp Ala Ser Ser Lys Ile Leu Leu Ala Val
 1055 1060 1065

Leu Val Tyr Pro Ser Ser Gly Ala Ile Tyr Thr Ile Ala Glu Ile
 1070 1075 1080

Val Asp Val Lys Gln Val Leu Pro Glu Trp Val Asp Val Gly Leu
 1085 1090 1095

Ser Gly Ala Thr Gly Ala Gln Arg Asp Ala Ala Glu Thr His Asp
 1100 1105 1110

Val Tyr Ser Trp Ser Phe His Ala Ser Leu Pro Glu Thr Asn
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 <213> Clostridium botulinum

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<400> 56

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 35 40 45

Asp Thr Phe Thr Asn Pro Glu Glu Gly Asp Leu Asn Pro Pro Pro Glu
 50 55 60

Ala Lys Gln Val Pro Val Ser Tyr Tyr Asp Ser Thr Tyr Leu Ser Thr
 65 70 75 80

Asp Asn Glu Lys Asp Asn Tyr Leu Lys Gly Val Thr Lys Leu Phe Glu
 85 90 95

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Arg Ile Tyr Ser Thr Asp Leu Gly Arg Met Leu Leu Thr Ser Ile Val
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 Arg Gly Ile Pro Phe Trp Gly Gly Ser Thr Ile Asp Thr Glu Leu Lys
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 Val Ile Asp Thr Asn Cys Ile Asn Val Ile Gln Pro Asp Gly Ser Tyr
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 Arg Ser Glu Glu Leu Asn Leu Val Ile Ile Gly Pro Ser Ala Asp Ile
 145 150 155 160
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 165 170 175
 Arg Asn Gly Tyr Gly Ser Thr Gln Tyr Ile Arg Phe Ser Pro Asp Phe
 180 185 190
 Thr Phe Gly Phe Glu Glu Ser Leu Glu Val Asp Thr Asn Pro Leu Leu
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 210 215 220
 Leu Ile His Ala Gly His Arg Leu Tyr Gly Ile Ala Ile Asn Pro Asn
 225 230 235 240
 Arg Val Phe Lys Val Asn Thr Asn Ala Tyr Tyr Glu Met Ser Gly Leu
 245 250 255
 Glu Val Ser Phe Glu Glu Leu Arg Thr Phe Gly Gly His Asp Ala Lys
 260 265 270
 Phe Ile Asp Ser Leu Gln Glu Asn Glu Phe Arg Leu Tyr Tyr Tyr Asn
 275 280 285
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 290 295 300
 Gly Thr Thr Ala Ser Leu Gln Tyr Met Lys Asn Val Phe Lys Glu Lys
 305 310 315 320
 Tyr Leu Leu Ser Glu Asp Thr Ser Gly Lys Phe Ser Val Asp Lys Leu
 325 330 335
 Lys Phe Asp Lys Leu Tyr Lys Met Leu Thr Glu Ile Tyr Thr Glu Asp
 340 345 350
 Asn Phe Val Lys Phe Phe Lys Val Leu Asn Arg Lys Thr Tyr Leu Asn

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355 360 365
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 Thr Ile Tyr Asp Gly Phe Asn Leu Arg Asn Thr Asn Leu Ala Ala Asn
 385 390 395 400
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 405 410 415
 Lys Asn Phe Thr Gly Leu Phe Glu Phe Tyr Lys Leu Leu Cys Val Arg
 420 425 430
 Gly Ile Ile Thr Ser Lys Thr Lys Ser Leu Ile Glu Gly Arg Asn Lys
 435 440 445
 Ala Leu Asn Asp Leu Cys Ile Lys Val Asn Asn Trp Asp Leu Phe Phe
 450 455 460
 Ser Pro Ser Glu Asp Asn Phe Thr Asn Asp Leu Asn Lys Gly Glu Glu
 465 470 475 480
 Ile Thr Ser Asp Thr Asn Ile Glu Ala Ala Glu Glu Asn Ile Ser Leu
 485 490 495
 Asp Leu Ile Gln Gln Tyr Tyr Leu Thr Phe Asn Phe Asp Asn Glu Pro
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 Glu Asn Ile Ser Ile Glu Asn Leu Ser Ser Asp Ile Ile Gly Gln Leu
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 Glu Leu Met Pro Asn Ile Glu Arg Phe Pro Asn Gly Lys Lys Tyr Glu
 530 535 540
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 545 550 555 560
 His Gly Lys Ser Arg Ile Ala Leu Thr Asn Ser Val Asn Glu Ala Leu
 565 570 575
 Leu Asn Pro Ser Arg Val Tyr Thr Phe Phe Ser Ser Asp Tyr Val Lys
 580 585 590
 Lys Val Asn Lys Ala Thr Glu Ala Ala Met Phe Leu Gly Trp Val Glu
 595 600 605
 Gln Leu Val Tyr Asp Phe Thr Asp Glu Thr Ser Glu Val Ser Thr Thr
 610 615 620

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Asp Lys Ile Ala Asp Ile Thr Ile Ile Ile Pro Tyr Ile Gly Pro Ala
 625 630 635 640
 Leu Asn Ile Gly Asn Met Leu Tyr Lys Asp Asp Phe Val Gly Ala Leu
 645 650 655
 Ile Phe Ser Gly Ala Val Ile Leu Leu Glu Phe Ile Pro Glu Ile Ala
 660 665 670
 Ile Pro Val Leu Gly Thr Phe Ala Leu Val Ser Tyr Ile Ala Asn Lys
 675 680 685
 Val Leu Thr Val Gln Thr Ile Asp Asn Ala Leu Ser Lys Arg Asn Glu
 690 695 700
 Lys Trp Asp Glu Val Tyr Lys Tyr Ile Val Thr Asn Trp Leu Ala Lys
 705 710 715 720
 Val Asn Thr Gln Ile Asp Leu Ile Arg Lys Lys Met Lys Glu Ala Leu
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 755 760 765
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 Asn Lys Phe Leu Asn Gln Cys Ser Val Ser Tyr Leu Met Asn Ser Met
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 Ile Pro Phe Gln Leu Ser Lys Tyr Val Asp Asn Gln Arg Leu Leu Ser
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 865 870 875 880
 Ala Lys Glu Ala Ala Ala Lys Ala Val Glu Thr Ile Ser Phe Ser Phe
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Ser Glu Phe Glu Pro Gly Asn Asn Asp Leu Thr Leu Gln Gly Ala Ala
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Ile Ile Thr Gln Ser Gly Val Leu Gln Leu Thr Lys Ile Asn Gln Asn
915 920 925

Gly Met Pro Ala Trp Asp Ser Thr Gly Arg Thr Leu Tyr Thr Lys Pro
930 935 940

Val His Ile Trp Asp Met Thr Thr Gly Thr Val Ala Ser Phe Glu Thr
945 950 955 960

Arg Phe Ser Phe Ser Ile Glu Gln Pro Tyr Thr Arg Pro Leu Pro Ala
965 970 975

Asp Gly Leu Val Phe Phe Met Gly Pro Thr Lys Ser Lys Pro Ala Gln
980 985 990

Gly Tyr Gly Tyr Leu Gly Val Phe Asn Asn Ser Lys Gln Asp Asn Ser
995 1000 1005

Tyr Gln Thr Leu Ala Val Glu Phe Asp Thr Phe Ser Asn Pro Trp
1010 1015 1020

Asp Pro Pro Gln Val Pro His Ile Gly Ile Asp Val Asn Ser Ile
1025 1030 1035

Arg Ser Ile Lys Thr Gln Pro Phe Gln Leu Asp Asn Gly Gln Val
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Ala Asn Val Val Ile Lys Tyr Asp Ala Ser Ser Lys Ile Leu Leu
1055 1060 1065

Ala Val Leu Val Tyr Pro Ser Ser Gly Ala Ile Tyr Thr Ile Ala
1070 1075 1080

Glu Ile Val Asp Val Lys Gln Val Leu Pro Glu Trp Val Asp Val
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Gly Leu Ser Gly Ala Thr Gly Ala Gln Arg Asp Ala Ala Glu Thr
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His Asp Val Tyr Ser Trp Ser Phe His Ala Ser Leu Pro Glu Thr
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Val Lys Ala Phe Lys Ile His Asn Lys Ile Trp Val Ile Pro Glu Arg
 35 40 45
 Asp Thr Phe Thr Asn Pro Glu Glu Gly Asp Leu Asn Pro Pro Pro Glu
 50 55 60
 Ala Lys Gln Val Pro Val Ser Tyr Tyr Asp Ser Thr Tyr Leu Ser Thr
 65 70 75 80
 Asp Asn Glu Lys Asp Asn Tyr Leu Lys Gly Val Thr Lys Leu Phe Glu
 85 90 95
 Arg Ile Tyr Ser Thr Asp Leu Gly Arg Met Leu Leu Thr Ser Ile Val
 100 105 110
 Arg Gly Ile Pro Phe Trp Gly Gly Ser Thr Ile Asp Thr Glu Leu Lys
 115 120 125
 Val Ile Asp Thr Asn Cys Ile Asn Val Ile Gln Pro Asp Gly Ser Tyr
 130 135 140
 Arg Ser Glu Glu Leu Asn Leu Val Ile Ile Gly Pro Ser Ala Asp Ile
 145 150 155 160
 Ile Gln Phe Glu Cys Lys Ser Phe Gly His Glu Val Leu Asn Leu Thr
 165 170 175
 Arg Asn Gly Tyr Gly Ser Thr Gln Tyr Ile Arg Phe Ser Pro Asp Phe
 180 185 190
 Thr Phe Gly Phe Glu Glu Ser Leu Glu Val Asp Thr Asn Pro Leu Leu
 195 200 205
 Gly Ala Gly Lys Phe Ala Thr Asp Pro Ala Val Thr Leu Ala His Glu
 210 215 220
 Leu Ile His Ala Gly His Arg Leu Tyr Gly Ile Ala Ile Asn Pro Asn
 225 230 235 240
 Arg Val Phe Lys Val Asn Thr Asn Ala Tyr Tyr Glu Met Ser Gly Leu
 245 250 255
 Glu Val Ser Phe Glu Glu Leu Arg Thr Phe Gly Gly His Asp Ala Lys
 260 265 270
 Phe Ile Asp Ser Leu Gln Glu Asn Glu Phe Arg Leu Tyr Tyr Tyr Asn
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 Lys Phe Lys Asp Ile Ala Ser Thr Leu Asn Lys Ala Lys Ser Ile Val

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290 295 300
 Gly Thr Thr Ala Ser Leu Gln Tyr Met Lys Asn Val Phe Lys Glu Lys
 305 310 315 320
 Tyr Leu Leu Ser Glu Asp Thr Ser Gly Lys Phe Ser Val Asp Lys Leu
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 Lys Phe Asp Lys Leu Tyr Lys Met Leu Thr Glu Ile Tyr Thr Glu Asp
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 Asn Phe Val Lys Phe Phe Lys Val Leu Asn Arg Lys Thr Tyr Leu Asn
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 Phe Asp Lys Ala Val Phe Lys Ile Asn Ile Val Pro Lys Val Asn Tyr
 370 375 380
 Thr Ile Tyr Asp Gly Phe Asn Leu Arg Asn Thr Asn Leu Ala Ala Asn
 385 390 395 400
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 405 410 415
 Lys Asn Phe Thr Gly Leu Phe Glu Phe Tyr Lys Leu Leu Cys Val Arg
 420 425 430
 Gly Ile Ile Thr Ser Lys Thr Lys Ser Leu Ile Glu Gly Arg Asn Lys
 435 440 445
 Ala Leu Asn Asp Leu Cys Ile Lys Val Asn Asn Trp Asp Leu Phe Phe
 450 455 460
 Ser Pro Ser Glu Asp Asn Phe Thr Asn Asp Leu Asn Lys Gly Glu Glu
 465 470 475 480
 Ile Thr Ser Asp Thr Asn Ile Glu Ala Ala Glu Glu Asn Ile Ser Leu
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 Asp Leu Ile Gln Gln Tyr Tyr Leu Thr Phe Asn Phe Asp Asn Glu Pro
 500 505 510
 Glu Asn Ile Ser Ile Glu Asn Leu Ser Ser Asp Ile Ile Gly Gln Leu
 515 520 525
 Glu Leu Met Pro Asn Ile Glu Arg Phe Pro Asn Gly Lys Lys Tyr Glu
 530 535 540
 Leu Asp Lys Tyr Thr Met Phe His Tyr Leu Arg Ala Gln Glu Phe Glu
 545 550 555 560

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His Gly Lys Ser Arg Ile Ala Leu Thr Asn Ser Val Asn Glu Ala Leu
 565 570 575
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 580 585 590
 Lys Val Asn Lys Ala Thr Glu Ala Ala Met Phe Leu Gly Trp Val Glu
 595 600 605
 Gln Leu Val Tyr Asp Phe Thr Asp Glu Thr Ser Glu Val Ser Thr Thr
 610 615 620
 Asp Lys Ile Ala Asp Ile Thr Ile Ile Ile Pro Tyr Ile Gly Pro Ala
 625 630 635 640
 Leu Asn Ile Gly Asn Met Leu Tyr Lys Asp Asp Phe Val Gly Ala Leu
 645 650 655
 Ile Phe Ser Gly Ala Val Ile Leu Leu Glu Phe Ile Pro Glu Ile Ala
 660 665 670
 Ile Pro Val Leu Gly Thr Phe Ala Leu Val Ser Tyr Ile Ala Asn Lys
 675 680 685
 Val Leu Thr Val Gln Thr Ile Asp Asn Ala Leu Ser Lys Arg Asn Glu
 690 695 700
 Lys Trp Asp Glu Val Tyr Lys Tyr Ile Val Thr Asn Trp Leu Ala Lys
 705 710 715 720
 Val Asn Thr Gln Ile Asp Leu Ile Arg Lys Lys Met Lys Glu Ala Leu
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 Glu Asn Gln Ala Glu Ala Thr Lys Ala Ile Ile Asn Tyr Gln Tyr Asn
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 Gln Tyr Thr Glu Glu Glu Lys Asn Asn Ile Asn Phe Asn Ile Asp Asp
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 Asn Lys Phe Leu Asn Gln Cys Ser Val Ser Tyr Leu Met Asn Ser Met
 785 790 795 800
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 Asp Ala Leu Leu Lys Tyr Ile Tyr Asp Asn Arg Gly Thr Leu Ile Gly
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Gln Val Asp Arg Leu Lys Asp Lys Val Asn Asn Thr Leu Ser Thr Asp
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 Ile Pro Phe Gln Leu Ser Lys Tyr Val Asp Asn Gln Arg Leu Leu Ser
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 Thr Phe Thr Glu Tyr Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly
 865 870 875 880
 Ser Gly Gly Gly Gly Ser Val Glu Thr Ile Ser Phe Ser Phe Ser Glu
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 Phe Glu Pro Gly Asn Asn Asp Leu Thr Leu Gln Gly Ala Ala Ile Ile
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 Thr Gln Ser Gly Val Leu Gln Leu Thr Lys Ile Asn Gln Asn Gly Met
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 Pro Ala Trp Asp Ser Thr Gly Arg Thr Leu Tyr Thr Lys Pro Val His
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 Ile Trp Asp Met Thr Thr Gly Thr Val Ala Ser Phe Glu Thr Arg Phe
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 Ser Phe Ser Ile Glu Gln Pro Tyr Thr Arg Pro Leu Pro Ala Asp Gly
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 980 985 990
 Gly Tyr Leu Gly Val Phe Asn Asn Ser Lys Gln Asp Asn Ser Tyr Gln
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 Thr Leu Ala Val Glu Phe Asp Thr Phe Ser Asn Pro Trp Asp Pro
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 Pro Gln Val Pro His Ile Gly Ile Asp Val Asn Ser Ile Arg Ser
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 Val Val Ile Lys Tyr Asp Ala Ser Ser Lys Ile Leu Leu Ala Val
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 Val Asp Val Lys Gln Val Leu Pro Glu Trp Val Asp Val Gly Leu

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Val Tyr Ser Trp Ser Phe His Ala Ser Leu Pro Glu Thr Asn
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 <212> PRT
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<400> 60

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Val Lys Ala Phe Lys Ile His Asn Lys Ile Trp Val Ile Pro Glu Arg
 35 40 45

Asp Thr Phe Thr Asn Pro Glu Glu Gly Asp Leu Asn Pro Pro Pro Glu
 50 55 60

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Ala Lys Gln Val Pro Val Ser Tyr Tyr Asp Ser Thr Tyr Leu Ser Thr
 65 70 75 80
 Asp Asn Glu Lys Asp Asn Tyr Leu Lys Gly Val Thr Lys Leu Phe Glu
 85 90 95
 Arg Ile Tyr Ser Thr Asp Leu Gly Arg Met Leu Leu Thr Ser Ile Val
 100 105 110
 Arg Gly Ile Pro Phe Trp Gly Gly Ser Thr Ile Asp Thr Glu Leu Lys
 115 120 125
 Val Ile Asp Thr Asn Cys Ile Asn Val Ile Gln Pro Asp Gly Ser Tyr
 130 135 140
 Arg Ser Glu Glu Leu Asn Leu Val Ile Ile Gly Pro Ser Ala Asp Ile
 145 150 155 160
 Ile Gln Phe Glu Cys Lys Ser Phe Gly His Glu Val Leu Asn Leu Thr
 165 170 175
 Arg Asn Gly Tyr Gly Ser Thr Gln Tyr Ile Arg Phe Ser Pro Asp Phe
 180 185 190
 Thr Phe Gly Phe Glu Glu Ser Leu Glu Val Asp Thr Asn Pro Leu Leu
 195 200 205
 Gly Ala Gly Lys Phe Ala Thr Asp Pro Ala Val Thr Leu Ala His Glu
 210 215 220
 Leu Ile His Ala Gly His Arg Leu Tyr Gly Ile Ala Ile Asn Pro Asn
 225 230 235 240
 Arg Val Phe Lys Val Asn Thr Asn Ala Tyr Tyr Glu Met Ser Gly Leu
 245 250 255
 Glu Val Ser Phe Glu Glu Leu Arg Thr Phe Gly Gly His Asp Ala Lys
 260 265 270
 Phe Ile Asp Ser Leu Gln Glu Asn Glu Phe Arg Leu Tyr Tyr Tyr Asn
 275 280 285
 Lys Phe Lys Asp Ile Ala Ser Thr Leu Asn Lys Ala Lys Ser Ile Val
 290 295 300
 Gly Thr Thr Ala Ser Leu Gln Tyr Met Lys Asn Val Phe Lys Glu Lys
 305 310 315 320
 Tyr Leu Leu Ser Glu Asp Thr Ser Gly Lys Phe Ser Val Asp Lys Leu
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Lys Phe Asp Lys Leu Tyr Lys Met Leu Thr Glu Ile Tyr Thr Glu Asp
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Asn Phe Val Lys Phe Phe Lys Val Leu Asn Arg Lys Thr Tyr Leu Asn
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Phe Asp Lys Ala Val Phe Lys Ile Asn Ile Val Pro Lys Val Asn Tyr
370 375 380

Thr Ile Tyr Asp Gly Phe Asn Leu Arg Asn Thr Asn Leu Ala Ala Asn
385 390 395 400

Phe Asn Gly Gln Asn Thr Glu Ile Asn Asn Met Asn Phe Thr Lys Leu
405 410 415

Lys Asn Phe Thr Gly Leu Phe Glu Phe Tyr Lys Leu Leu Cys Val Arg
420 425 430

Gly Ile Ile Thr Ser Lys Thr Lys Ser Leu Asp Asp Asp Asp Lys Gly
435 440 445

Tyr Asn Lys Ala Leu Asn Asp Leu Cys Ile Lys Val Asn Asn Trp Asp
450 455 460

Leu Phe Phe Ser Pro Ser Glu Asp Asn Phe Thr Asn Asp Leu Asn Lys
465 470 475 480

Gly Glu Glu Ile Thr Ser Asp Thr Asn Ile Glu Ala Ala Glu Glu Asn
485 490 495

Ile Ser Leu Asp Leu Ile Gln Gln Tyr Tyr Leu Thr Phe Asn Phe Asp
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Asn Glu Pro Glu Asn Ile Ser Ile Glu Asn Leu Ser Ser Asp Ile Ile
515 520 525

Gly Gln Leu Glu Leu Met Pro Asn Ile Glu Arg Phe Pro Asn Gly Lys
530 535 540

Lys Tyr Glu Leu Asp Lys Tyr Thr Met Phe His Tyr Leu Arg Ala Gln
545 550 555 560

Glu Phe Glu His Gly Lys Ser Arg Ile Ala Leu Thr Asn Ser Val Asn
565 570 575

Glu Ala Leu Leu Asn Pro Ser Arg Val Tyr Thr Phe Phe Ser Ser Asp
580 585 590

Tyr Val Lys Lys Val Asn Lys Ala Thr Glu Ala Ala Met Phe Leu Gly

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595 600 605
 Trp Val Glu Gln Leu Val Tyr Asp Phe Thr Asp Glu Thr Ser Glu Val
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 625 630 635 640
 Gly Pro Ala Leu Asn Ile Gly Asn Met Leu Tyr Lys Asp Asp Phe Val
 645 650 655
 Gly Ala Leu Ile Phe Ser Gly Ala Val Ile Leu Leu Glu Phe Ile Pro
 660 665 670
 Glu Ile Ala Ile Pro Val Leu Gly Thr Phe Ala Leu Val Ser Tyr Ile
 675 680 685
 Ala Asn Lys Val Leu Thr Val Gln Thr Ile Asp Asn Ala Leu Ser Lys
 690 695 700
 Arg Asn Glu Lys Trp Asp Glu Val Tyr Lys Tyr Ile Val Thr Asn Trp
 705 710 715 720
 Leu Ala Lys Val Asn Thr Gln Ile Asp Leu Ile Arg Lys Lys Met Lys
 725 730 735
 Glu Ala Leu Glu Asn Gln Ala Glu Ala Thr Lys Ala Ile Ile Asn Tyr
 740 745 750
 Gln Tyr Asn Gln Tyr Thr Glu Glu Glu Lys Asn Asn Ile Asn Phe Asn
 755 760 765
 Ile Asp Asp Leu Ser Ser Lys Leu Asn Glu Ser Ile Asn Lys Ala Met
 770 775 780
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 Ser Leu Lys Asp Ala Leu Leu Lys Tyr Ile Tyr Asp Asn Arg Gly Thr
 820 825 830
 Leu Ile Gly Gln Val Asp Arg Leu Lys Asp Lys Val Asn Asn Thr Leu
 835 840 845
 Ser Thr Asp Ile Pro Phe Gln Leu Ser Lys Tyr Val Asp Asn Gln Arg
 850 855 860

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Leu Leu Ser Thr Cys Gly Gly Leu Thr Asp Thr Leu Gln Ala Glu Thr
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Asp Gln Leu Glu Asp Glu Lys Ser Ala Leu Gln Thr Glu Ile Ala Asn
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tga 2643

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<212> PRT
<213> Clostridium botulinum

<400> 62

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Val Lys Ala Phe Lys Ile His Asn Lys Ile Trp Val Ile Pro Glu Arg
35 40 45

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Asp Thr Phe Thr Asn Pro Glu Glu Gly Asp Leu Asn Pro Pro Pro Glu
50 55 60

Ala Lys Gln Val Pro Val Ser Tyr Tyr Asp Ser Thr Tyr Leu Ser Thr
65 70 75 80

Asp Asn Glu Lys Asp Asn Tyr Leu Lys Gly Val Thr Lys Leu Phe Glu
85 90 95

Arg Ile Tyr Ser Thr Asp Leu Gly Arg Met Leu Leu Thr Ser Ile Val
100 105 110

Arg Gly Ile Pro Phe Trp Gly Gly Ser Thr Ile Asp Thr Glu Leu Lys
115 120 125

Val Ile Asp Thr Asn Cys Ile Asn Val Ile Gln Pro Asp Gly Ser Tyr
130 135 140

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

Ile Gln Phe Glu Cys Lys Ser Phe Gly His Glu Val Leu Asn Leu Thr
165 170 175

Arg Asn Gly Tyr Gly Ser Thr Gln Tyr Ile Arg Phe Ser Pro Asp Phe
180 185 190

Thr Phe Gly Phe Glu Glu Ser Leu Glu Val Asp Thr Asn Pro Leu Leu
195 200 205

Gly Ala Gly Lys Phe Ala Thr Asp Pro Ala Val Thr Leu Ala His Glu
210 215 220

Leu Ile His Ala Gly His Arg Leu Tyr Gly Ile Ala Ile Asn Pro Asn
225 230 235 240

Arg Val Phe Lys Val Asn Thr Asn Ala Tyr Tyr Glu Met Ser Gly Leu
245 250 255

Glu Val Ser Phe Glu Glu Leu Arg Thr Phe Gly Gly His Asp Ala Lys
260 265 270

Phe Ile Asp Ser Leu Gln Glu Asn Glu Phe Arg Leu Tyr Tyr Tyr Asn
275 280 285

Lys Phe Lys Asp Ile Ala Ser Thr Leu Asn Lys Ala Lys Ser Ile Val
290 295 300

Gly Thr Thr Ala Ser Leu Gln Tyr Met Lys Asn Val Phe Lys Glu Lys
305 310 315 320

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Tyr Leu Leu Ser Glu Asp Thr Ser Gly Lys Phe Ser Val Asp Lys Leu
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 Lys Phe Asp Lys Leu Tyr Lys Met Leu Thr Glu Ile Tyr Thr Glu Asp
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 Asn Phe Val Lys Phe Phe Lys Val Leu Asn Arg Lys Thr Tyr Leu Asn
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 Phe Asp Lys Ala Val Phe Lys Ile Asn Ile Val Pro Lys Val Asn Tyr
 370 375 380
 Thr Ile Tyr Asp Gly Phe Asn Leu Arg Asn Thr Asn Leu Ala Ala Asn
 385 390 395 400
 Phe Asn Gly Gln Asn Thr Glu Ile Asn Asn Met Asn Phe Thr Lys Leu
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 Gly Ile Ile Thr Ser Lys Thr Lys Ser Leu Asp Asp Asp Asp Lys Gly
 435 440 445
 Tyr Asn Lys Ala Leu Asn Asp Leu Cys Ile Lys Val Asn Asn Trp Asp
 450 455 460
 Leu Phe Phe Ser Pro Ser Glu Asp Asn Phe Thr Asn Asp Leu Asn Lys
 465 470 475 480
 Gly Glu Glu Ile Thr Ser Asp Thr Asn Ile Glu Ala Ala Glu Glu Asn
 485 490 495
 Ile Ser Leu Asp Leu Ile Gln Gln Tyr Tyr Leu Thr Phe Asn Phe Asp
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 Gly Gln Leu Glu Leu Met Pro Asn Ile Glu Arg Phe Pro Asn Gly Lys
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 Lys Tyr Glu Leu Asp Lys Tyr Thr Met Phe His Tyr Leu Arg Ala Gln
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 Glu Phe Glu His Gly Lys Ser Arg Ile Ala Leu Thr Asn Ser Val Asn
 565 570 575
 Glu Ala Leu Leu Asn Pro Ser Arg Val Tyr Thr Phe Phe Ser Ser Asp

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580 585 590
 Tyr Val Lys Lys Val Asn Lys Ala Thr Glu Ala Ala Met Phe Leu Gly
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 Trp Val Glu Gln Leu Val Tyr Asp Phe Thr Asp Glu Thr Ser Glu Val
 610 615 620
 Ser Thr Thr Asp Lys Ile Ala Asp Ile Thr Ile Ile Ile Pro Tyr Ile
 625 630 635 640
 Gly Pro Ala Leu Asn Ile Gly Asn Met Leu Tyr Lys Asp Asp Phe Val
 645 650 655
 Gly Ala Leu Ile Phe Ser Gly Ala Val Ile Leu Leu Glu Phe Ile Pro
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 Glu Ile Ala Ile Pro Val Leu Gly Thr Phe Ala Leu Val Ser Tyr Ile
 675 680 685
 Ala Asn Lys Val Leu Thr Val Gln Thr Ile Asp Asn Ala Leu Ser Lys
 690 695 700
 Arg Asn Glu Lys Trp Asp Glu Val Tyr Lys Tyr Ile Val Thr Asn Trp
 705 710 715 720
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 Glu Ala Leu Glu Asn Gln Ala Glu Ala Thr Lys Ala Ile Ile Asn Tyr
 740 745 750
 Gln Tyr Asn Gln Tyr Thr Glu Glu Glu Lys Asn Asn Ile Asn Phe Asn
 755 760 765
 Ile Asp Asp Leu Ser Ser Lys Leu Asn Glu Ser Ile Asn Lys Ala Met
 770 775 780
 Ile Asn Ile Asn Lys Phe Leu Asn Gln Cys Ser Val Ser Tyr Leu Met
 785 790 795 800
 Asn Ser Met Ile Pro Tyr Gly Val Lys Arg Leu Glu Asp Phe Asp Ala
 805 810 815
 Ser Leu Lys Asp Ala Leu Leu Lys Tyr Ile Tyr Asp Asn Arg Gly Thr
 820 825 830
 Leu Ile Gly Gln Val Asp Arg Leu Lys Asp Lys Val Asn Asn Thr Leu
 835 840 845

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Ser Thr Asp Ile Pro Phe Gln Leu Ser Lys Tyr Val Asp Asn Gln Arg
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Leu Leu Ser Thr Cys Glu Glu Glu Glu Glu Glu Glu Cys
865 870 875

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<213> Clostridium botulinum

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 <212> PRT
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<400> 64

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Val Lys Ala Phe Lys Ile His Asn Lys Ile Trp Val Ile Pro Glu Arg
 35 40 45

Asp Thr Phe Thr Asn Pro Glu Glu Gly Asp Leu Asn Pro Pro Pro Glu
 50 55 60

Ala Lys Gln Val Pro Val Ser Tyr Tyr Asp Ser Thr Tyr Leu Ser Thr
 65 70 75 80

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Asp Asn Glu Lys Asp Asn Tyr Leu Lys Gly Val Thr Lys Leu Phe Glu
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 Arg Ile Tyr Ser Thr Asp Leu Gly Arg Met Leu Leu Thr Ser Ile Val
 100 105 110
 Arg Gly Ile Pro Phe Trp Gly Gly Ser Thr Ile Asp Thr Glu Leu Lys
 115 120 125
 Val Ile Asp Thr Asn Cys Ile Asn Val Ile Gln Pro Asp Gly Ser Tyr
 130 135 140
 Arg Ser Glu Glu Leu Asn Leu Val Ile Ile Gly Pro Ser Ala Asp Ile
 145 150 155 160
 Ile Gln Phe Glu Cys Lys Ser Phe Gly His Glu Val Leu Asn Leu Thr
 165 170 175
 Arg Asn Gly Tyr Gly Ser Thr Gln Tyr Ile Arg Phe Ser Pro Asp Phe
 180 185 190
 Thr Phe Gly Phe Glu Glu Ser Leu Glu Val Asp Thr Asn Pro Leu Leu
 195 200 205
 Gly Ala Gly Lys Phe Ala Thr Asp Pro Ala Val Thr Leu Ala His Glu
 210 215 220
 Leu Ile His Ala Gly His Arg Leu Tyr Gly Ile Ala Ile Asn Pro Asn
 225 230 235 240
 Arg Val Phe Lys Val Asn Thr Asn Ala Tyr Tyr Glu Met Ser Gly Leu
 245 250 255
 Glu Val Ser Phe Glu Glu Leu Arg Thr Phe Gly Gly His Asp Ala Lys
 260 265 270
 Phe Ile Asp Ser Leu Gln Glu Asn Glu Phe Arg Leu Tyr Tyr Tyr Asn
 275 280 285
 Lys Phe Lys Asp Ile Ala Ser Thr Leu Asn Lys Ala Lys Ser Ile Val
 290 295 300
 Gly Thr Thr Ala Ser Leu Gln Tyr Met Lys Asn Val Phe Lys Glu Lys
 305 310 315 320
 Tyr Leu Leu Ser Glu Asp Thr Ser Gly Lys Phe Ser Val Asp Lys Leu
 325 330 335
 Lys Phe Asp Lys Leu Tyr Lys Met Leu Thr Glu Ile Tyr Thr Glu Asp

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340 345 350
 Asn Phe Val Lys Phe Phe Lys Val Leu Asn Arg Lys Thr Tyr Leu Asn
 355 360 365
 Phe Asp Lys Ala Val Phe Lys Ile Asn Ile Val Pro Lys Val Asn Tyr
 370 375 380
 Thr Ile Tyr Asp Gly Phe Asn Leu Arg Asn Thr Asn Leu Ala Ala Asn
 385 390 395 400
 Phe Asn Gly Gln Asn Thr Glu Ile Asn Asn Met Asn Phe Thr Lys Leu
 405 410 415
 Lys Asn Phe Thr Gly Leu Phe Glu Phe Tyr Lys Leu Leu Cys Val Arg
 420 425 430
 Gly Ile Ile Thr Ser Lys Thr Lys Ser Leu Asp Asp Asp Asp Lys Gly
 435 440 445
 Tyr Asn Lys Ala Leu Asn Asp Leu Cys Ile Lys Val Asn Asn Trp Asp
 450 455 460
 Leu Phe Phe Ser Pro Ser Glu Asp Asn Phe Thr Asn Asp Leu Asn Lys
 465 470 475 480
 Gly Glu Glu Ile Thr Ser Asp Thr Asn Ile Glu Ala Ala Glu Glu Asn
 485 490 495
 Ile Ser Leu Asp Leu Ile Gln Gln Tyr Tyr Leu Thr Phe Asn Phe Asp
 500 505 510
 Asn Glu Pro Glu Asn Ile Ser Ile Glu Asn Leu Ser Ser Asp Ile Ile
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 Gly Gln Leu Glu Leu Met Pro Asn Ile Glu Arg Phe Pro Asn Gly Lys
 530 535 540
 Lys Tyr Glu Leu Asp Lys Tyr Thr Met Phe His Tyr Leu Arg Ala Gln
 545 550 555 560
 Glu Phe Glu His Gly Lys Ser Arg Ile Ala Leu Thr Asn Ser Val Asn
 565 570 575
 Glu Ala Leu Leu Asn Pro Ser Arg Val Tyr Thr Phe Phe Ser Ser Asp
 580 585 590
 Tyr Val Lys Lys Val Asn Lys Ala Thr Glu Ala Ala Met Phe Leu Gly
 595 600 605

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Trp Val Glu Gln Leu Val Tyr Asp Phe Thr Asp Glu Thr Ser Glu Val
 610 615 620
 Ser Thr Thr Asp Lys Ile Ala Asp Ile Thr Ile Ile Ile Pro Tyr Ile
 625 630 635 640
 Gly Pro Ala Leu Asn Ile Gly Asn Met Leu Tyr Lys Asp Asp Phe Val
 645 650 655
 Gly Ala Leu Ile Phe Ser Gly Ala Val Ile Leu Leu Glu Phe Ile Pro
 660 665 670
 Glu Ile Ala Ile Pro Val Leu Gly Thr Phe Ala Leu Val Ser Tyr Ile
 675 680 685
 Ala Asn Lys Val Leu Thr Val Gln Thr Ile Asp Asn Ala Leu Ser Lys
 690 695 700
 Arg Asn Glu Lys Trp Asp Glu Val Tyr Lys Tyr Ile Val Thr Asn Trp
 705 710 715 720
 Leu Ala Lys Val Asn Thr Gln Ile Asp Leu Ile Arg Lys Lys Met Lys
 725 730 735
 Glu Ala Leu Glu Asn Gln Ala Glu Ala Thr Lys Ala Ile Ile Asn Tyr
 740 745 750
 Gln Tyr Asn Gln Tyr Thr Glu Glu Glu Lys Asn Asn Ile Asn Phe Asn
 755 760 765
 Ile Asp Asp Leu Ser Ser Lys Leu Asn Glu Ser Ile Asn Lys Ala Met
 770 775 780
 Ile Asn Ile Asn Lys Phe Leu Asn Gln Cys Ser Val Ser Tyr Leu Met
 785 790 795 800
 Asn Ser Met Ile Pro Tyr Gly Val Lys Arg Leu Glu Asp Phe Asp Ala
 805 810 815
 Ser Leu Lys Asp Ala Leu Leu Lys Tyr Ile Tyr Asp Asn Arg Gly Thr
 820 825 830
 Leu Ile Gly Gln Val Asp Arg Leu Lys Asp Lys Val Asn Asn Thr Leu
 835 840 845
 Ser Thr Asp Ile Pro Phe Gln Leu Ser Lys Tyr Val Asp Asn Gln Arg
 850 855 860
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<210> 66
 <211> 876
 <212> PRT
 <213> Clostridium botulinum

<400> 66

Met Glu Phe Val Asn Lys Gln Phe Asn Tyr Lys Asp Pro Val Asn Gly
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Val Asp Ile Ala Tyr Ile Lys Ile Pro Asn Ala Gly Gln Met Gln Pro
 20 25 30

Val Lys Ala Phe Lys Ile His Asn Lys Ile Trp Val Ile Pro Glu Arg
 35 40 45

Asp Thr Phe Thr Asn Pro Glu Glu Gly Asp Leu Asn Pro Pro Pro Glu
 50 55 60

Ala Lys Gln Val Pro Val Ser Tyr Tyr Asp Ser Thr Tyr Leu Ser Thr
 65 70 75 80

Asp Asn Glu Lys Asp Asn Tyr Leu Lys Gly Val Thr Lys Leu Phe Glu
 85 90 95

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Arg Ile Tyr Ser Thr Asp Leu Gly Arg Met Leu Leu Thr Ser Ile Val
 100 105 110

Arg Gly Ile Pro Phe Trp Gly Gly Ser Thr Ile Asp Thr Glu Leu Lys
 115 120 125

Val Ile Asp Thr Asn Cys Ile Asn Val Ile Gln Pro Asp Gly Ser Tyr
 130 135 140

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

10

Ile Gln Phe Glu Cys Lys Ser Phe Gly His Glu Val Leu Asn Leu Thr
 165 170 175

Arg Asn Gly Tyr Gly Ser Thr Gln Tyr Ile Arg Phe Ser Pro Asp Phe
 180 185 190

Thr Phe Gly Phe Glu Glu Ser Leu Glu Val Asp Thr Asn Pro Leu Leu
 195 200 205

Gly Ala Gly Lys Phe Ala Thr Asp Pro Ala Val Thr Leu Ala His Glu
 210 215 220

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Leu Ile His Ala Gly His Arg Leu Tyr Gly Ile Ala Ile Asn Pro Asn
 225 230 235 240

Arg Val Phe Lys Val Asn Thr Asn Ala Tyr Tyr Glu Met Ser Gly Leu
 245 250 255

Glu Val Ser Phe Glu Glu Leu Arg Thr Phe Gly Gly His Asp Ala Lys
 260 265 270

Phe Ile Asp Ser Leu Gln Glu Asn Glu Phe Arg Leu Tyr Tyr Tyr Asn
 275 280 285

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Lys Phe Lys Asp Ile Ala Ser Thr Leu Asn Lys Ala Lys Ser Ile Val
 290 295 300

Gly Thr Thr Ala Ser Leu Gln Tyr Met Lys Asn Val Phe Lys Glu Lys
 305 310 315 320

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

Lys Phe Asp Lys Leu Tyr Lys Met Leu Thr Glu Ile Tyr Thr Glu Asp
 340 345 350

Asn Phe Val Lys Phe Phe Lys Val Leu Asn Arg Lys Thr Tyr Leu Asn

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355	360	365
Phe Asp Lys Ala Val	Phe Lys Ile Asn Ile Val	Pro Lys Val Asn Tyr
370	375	380
Thr Ile Tyr Asp Gly	Phe Asn Leu Arg Asn Thr	Asn Leu Ala Ala Asn
385	390	400
Phe Asn Gly Gln Asn Thr	Glu Ile Asn Asn Met Asn	Phe Thr Lys Leu
405	410	415
Lys Asn Phe Thr Gly	Leu Phe Glu Phe Tyr Lys	Leu Leu Cys Val Arg
420	425	430
Gly Ile Ile Thr Ser	Lys Thr Lys Ser Leu Asp	Asp Asp Lys Gly
435	440	445
Tyr Asn Lys Ala Leu	Asn Asp Leu Cys Ile Lys	Val Asn Asn Trp Asp
450	455	460
Leu Phe Phe Ser Pro	Ser Glu Asp Asn Phe Thr	Asn Asp Leu Asn Lys
465	470	475
Gly Glu Glu Ile Thr	Ser Asp Thr Asn Ile Glu	Ala Ala Glu Glu Asn
485	490	495
Ile Ser Leu Asp Leu	Ile Gln Gln Tyr Tyr	Leu Thr Phe Asn Phe Asp
500	505	510
Asn Glu Pro Glu Asn	Ile Ser Ile Glu Asn	Leu Ser Ser Asp Ile Ile
515	520	525
Gly Gln Leu Glu Leu	Met Pro Asn Ile Glu Arg	Phe Pro Asn Gly Lys
530	535	540
Lys Tyr Glu Leu Asp	Lys Tyr Thr Met Phe His	Tyr Leu Arg Ala Gln
545	550	555
Glu Phe Glu His Gly	Lys Ser Arg Ile Ala Leu	Thr Asn Ser Val Asn
565	570	575
Glu Ala Leu Leu Asn	Pro Ser Arg Val Tyr Thr	Phe Phe Ser Ser Asp
580	585	590
Tyr Val Lys Lys Val	Asn Lys Ala Thr Glu Ala	Ala Met Phe Leu Gly
595	600	605
Trp Val Glu Gln Leu	Val Tyr Asp Phe Thr Asp	Glu Thr Ser Glu Val
610	615	620

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

Gly Pro Ala Leu Asn Ile Gly Asn Met Leu Tyr Lys Asp Asp Phe Val
645 650 655

Gly Ala Leu Ile Phe Ser Gly Ala Val Ile Leu Leu Glu Phe Ile Pro
660 665 670

Glu Ile Ala Ile Pro Val Leu Gly Thr Phe Ala Leu Val Ser Tyr Ile
675 680 685

Ala Asn Lys Val Leu Thr Val Gln Thr Ile Asp Asn Ala Leu Ser Lys
690 695 700

Arg Asn Glu Lys Trp Asp Glu Val Tyr Lys Tyr Ile Val Thr Asn Trp
705 710 715 720

Leu Ala Lys Val Asn Thr Gln Ile Asp Leu Ile Arg Lys Lys Met Lys
725 730 735

Glu Ala Leu Glu Asn Gln Ala Glu Ala Thr Lys Ala Ile Ile Asn Tyr
740 745 750

Gln Tyr Asn Gln Tyr Thr Glu Glu Glu Lys Asn Asn Ile Asn Phe Asn
755 760 765

Ile Asp Asp Leu Ser Ser Lys Leu Asn Glu Ser Ile Asn Lys Ala Met
770 775 780

Ile Asn Ile Asn Lys Phe Leu Asn Gln Cys Ser Val Ser Tyr Leu Met
785 790 795 800

Asn Ser Met Ile Pro Tyr Gly Val Lys Arg Leu Glu Asp Phe Asp Ala
805 810 815

Ser Leu Lys Asp Ala Leu Leu Lys Tyr Ile Tyr Asp Asn Arg Gly Thr
820 825 830

Leu Ile Gly Gln Val Asp Arg Leu Lys Asp Lys Val Asn Asn Thr Leu
835 840 845

Ser Thr Asp Ile Pro Phe Gln Leu Ser Lys Tyr Val Asp Asn Gln Arg
850 855 860

Leu Leu Ser Thr Glu Glu Glu Glu Glu Glu Glu
865 870 875

<210> 67
<211> 2850

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<212> DNA

<213> Clostridium botulinum

<400> 67

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aaaatctggg ttatcccga acgtgacacc ttcaccaacc cggagaagg tgacctgaac	180
cgcgcgcggg aagctaaaca ggttcgggtt tcttactacg actctaccta cctgtctacc	240
gacaacgaaa aagacaacta cctgaaagg gttaccaaac tgttcgaacg tatctactct	300
accgacctgg gtctatgct gctgacctct atcgttcgtg gtatcccggt ctgggggtgg	360
tctaccatcg acaccgaact gaaagtatc gacaccaact gcatcaacgt tatccagccg	420
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ggttctaccc agtacatcg ttctctccg gacttcacct tgggttctga agaactctctg	600
gaagttgaca ccaaccgct gctgggtgct ggtaaattcg ctaccgacct ggctgttacc	660
ctgggtcacc aactgatcca cgctgggtc cgtctgtacg gtatcgctat caaccogaac	720
cgtgttttca aagttaacac caacgcttac tacgaaatgt ctgggtctgga agtttctttc	780
gaagaactgc gtacctcgg tggtcacgac gctaaattca tgcactctct gcaggaaaac	840
gaattccgtc tgtactacta caacaaattc aaagacatcg ctctaccct gaacaaagct	900
aatctatcgt ttgggtaccac cgcttctctg cagtacatga aaaacgtttt caaagaaaaa	960
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accgaagctg ctatgttcct ggggtgggtt gaacagctgg ttacgactt caccgacgaa	1860

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acctctgaag tttctaccac cgacaaaatc gctgacatca ccatcatcat cccgtacatc 1920
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 atcaacgaac agaccatgaa actggaatct gctaaagttt ctcgtgtttt ctgcaccggt 2760
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<210> 68
 <211> 949
 <212> PRT
 <213> Clostridium botulinum

<400> 68

Met Glu Phe Val Asn Lys Gln Phe Asn Tyr Lys Asp Pro Val Asn Gly
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Val Asp Ile Ala Tyr Ile Lys Ile Pro Asn Ala Gly Gln Met Gln Pro
 20 25 30

Val Lys Ala Phe Lys Ile His Asn Lys Ile Trp Val Ile Pro Glu Arg
 35 40 45

Asp Thr Phe Thr Asn Pro Glu Glu Gly Asp Leu Asn Pro Pro Pro Glu
 50 55 60

Ala Lys Gln Val Pro Val Ser Tyr Tyr Asp Ser Thr Tyr Leu Ser Thr
 65 70 75 80

Asp Asn Glu Lys Asp Asn Tyr Leu Lys Gly Val Thr Lys Leu Phe Glu
 85 90 95

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Arg Ile Tyr Ser Thr Asp Leu Gly Arg Met Leu Leu Thr Ser Ile Val
 100 105 110
 Arg Gly Ile Pro Phe Trp Gly Gly Ser Thr Ile Asp Thr Glu Leu Lys
 115 120 125
 Val Ile Asp Thr Asn Cys Ile Asn Val Ile Gln Pro Asp Gly Ser Tyr
 130 135 140
 Arg Ser Glu Glu Leu Asn Leu Val Ile Ile Gly Pro Ser Ala Asp Ile
 145 150 155 160
 Ile Gln Phe Glu Cys Lys Ser Phe Gly His Glu Val Leu Asn Leu Thr
 165 170 175
 Arg Asn Gly Tyr Gly Ser Thr Gln Tyr Ile Arg Phe Ser Pro Asp Phe
 180 185 190
 Thr Phe Gly Phe Glu Glu Ser Leu Glu Val Asp Thr Asn Pro Leu Leu
 195 200 205
 Gly Ala Gly Lys Phe Ala Thr Asp Pro Ala Val Thr Leu Ala His Glu
 210 215 220
 Leu Ile His Ala Gly His Arg Leu Tyr Gly Ile Ala Ile Asn Pro Asn
 225 230 235 240
 Arg Val Phe Lys Val Asn Thr Asn Ala Tyr Tyr Glu Met Ser Gly Leu
 245 250 255
 Glu Val Ser Phe Glu Glu Leu Arg Thr Phe Gly Gly His Asp Ala Lys
 260 265 270
 Phe Ile Asp Ser Leu Gln Glu Asn Glu Phe Arg Leu Tyr Tyr Tyr Asn
 275 280 285
 Lys Phe Lys Asp Ile Ala Ser Thr Leu Asn Lys Ala Lys Ser Ile Val
 290 295 300
 Gly Thr Thr Ala Ser Leu Gln Tyr Met Lys Asn Val Phe Lys Glu Lys
 305 310 315 320
 Tyr Leu Leu Ser Glu Asp Thr Ser Gly Lys Phe Ser Val Asp Lys Leu
 325 330 335
 Lys Phe Asp Lys Leu Tyr Lys Met Leu Thr Glu Ile Tyr Thr Glu Asp
 340 345 350
 Asn Phe Val Lys Phe Phe Lys Val Leu Asn Arg Lys Thr Tyr Leu Asn
 355 360 365

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Phe Asp Lys Ala Val Phe Lys Ile Asn Ile Val Pro Lys Val Asn Tyr
370 375 380

Thr Ile Tyr Asp Gly Phe Asn Leu Arg Asn Thr Asn Leu Ala Ala Asn
385 390 395 400

Phe Asn Gly Gln Asn Thr Glu Ile Asn Asn Met Asn Phe Thr Lys Leu
405 410 415

Lys Asn Phe Thr Gly Leu Phe Glu Phe Tyr Lys Leu Leu Cys Val Arg
420 425 430

Gly Ile Ile Thr Ser Lys Thr Lys Ser Leu Asp Asp Asp Asp Lys Gly
435 440 445

Tyr Asn Lys Ala Leu Asn Asp Leu Cys Ile Lys Val Asn Asn Trp Asp
450 455 460

Leu Phe Phe Ser Pro Ser Glu Asp Asn Phe Thr Asn Asp Leu Asn Lys
465 470 475 480

Gly Glu Glu Ile Thr Ser Asp Thr Asn Ile Glu Ala Ala Glu Glu Asn
485 490 495

Ile Ser Leu Asp Leu Ile Gln Gln Tyr Tyr Leu Thr Phe Asn Phe Asp
500 505 510

Asn Glu Pro Glu Asn Ile Ser Ile Glu Asn Leu Ser Ser Asp Ile Ile
515 520 525

Gly Gln Leu Glu Leu Met Pro Asn Ile Glu Arg Phe Pro Asn Gly Lys
530 535 540

Lys Tyr Glu Leu Asp Lys Tyr Thr Met Phe His Tyr Leu Arg Ala Gln
545 550 555 560

Glu Phe Glu His Gly Lys Ser Arg Ile Ala Leu Thr Asn Ser Val Asn
565 570 575

Glu Ala Leu Leu Asn Pro Ser Arg Val Tyr Thr Phe Phe Ser Ser Asp
580 585 590

Tyr Val Lys Lys Val Asn Lys Ala Thr Glu Ala Ala Met Phe Leu Gly
595 600 605

Trp Val Glu Gln Leu Val Tyr Asp Phe Thr Asp Glu Thr Ser Glu Val
610 615 620

Ser Thr Thr Asp Lys Ile Ala Asp Ile Thr Ile Ile Ile Pro Tyr Ile

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625 630 635 640
 Gly Pro Ala Leu Asn Ile Gly Asn Met Leu Tyr Lys Asp Asp Phe Val
 645 650 655
 Gly Ala Leu Ile Phe Ser Gly Ala Val Ile Leu Leu Glu Phe Ile Pro
 660 665 670
 Glu Ile Ala Ile Pro Val Leu Gly Thr Phe Ala Leu Val Ser Tyr Ile
 675 680 685
 Ala Asn Lys Val Leu Thr Val Gln Thr Ile Asp Asn Ala Leu Ser Lys
 690 695 700
 Arg Asn Glu Lys Trp Asp Glu Val Tyr Lys Tyr Ile Val Thr Asn Trp
 705 710 715 720
 Leu Ala Lys Val Asn Thr Gln Ile Asp Leu Ile Arg Lys Lys Met Lys
 725 730 735
 Glu Ala Leu Glu Asn Gln Ala Glu Ala Thr Lys Ala Ile Ile Asn Tyr
 740 745 750
 Gln Tyr Asn Gln Tyr Thr Glu Glu Glu Lys Asn Asn Ile Asn Phe Asn
 755 760 765
 Ile Asp Asp Leu Ser Ser Lys Leu Asn Glu Ser Ile Asn Lys Ala Met
 770 775 780
 Ile Asn Ile Asn Lys Phe Leu Asn Gln Cys Ser Val Ser Tyr Leu Met
 785 790 795 800
 Asn Ser Met Ile Pro Tyr Gly Val Lys Arg Leu Glu Asp Phe Asp Ala
 805 810 815
 Ser Leu Lys Asp Ala Leu Leu Lys Tyr Ile Tyr Asp Asn Arg Gly Thr
 820 825 830
 Leu Ile Gly Gln Val Asp Arg Leu Lys Asp Lys Val Asn Asn Thr Leu
 835 840 845
 Ser Thr Asp Ile Pro Phe Gln Leu Ser Lys Tyr Val Asp Asn Gln Arg
 850 855 860
 Leu Leu Ser Thr Cys Ile Ser Gly Asp Ser Leu Ile Ser Leu Ala Ser
 865 870 875 880
 Thr Gly Lys Arg Val Ser Ile Lys Asp Leu Leu Asp Glu Lys Asp Phe
 885 890 895

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Glu Ile Trp Ala Ile Asn Glu Gln Thr Met Lys Leu Glu Ser Ala Lys
 900 905 910

Val Ser Arg Val Phe Cys Thr Gly Lys Lys Leu Val Tyr Ile Leu Lys
 915 920 925

Thr Arg Leu Gly Arg Thr Ile Lys Ala Thr Ala Asn His Arg Phe Leu
 930 935 940

Thr Ile Asp Gly Trp
 945

<210> 69
 <211> 1385
 <212> DNA
 <213> Clostridium botulinum

<400> 69
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 cacaacaaaa tctgggttat ccggaacgt gataccttta ctaaccgga agaaggtgac 180
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 tctaccgata acgaaaagga caactacctg aaaggtgtta ctaaactggt cgagcgtatt 300
 tactccaccg acctgggccc tatgctgctg actagcatcg ttccgggtat ccggttctgg 360
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 cagccggagc gttcctatcg ttccgaagaa ctgaacctgg tgatcatcgg cccgtctgct 480
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 ggctacgggt ccaactcagta catccgttcc tctccggaact tcaccttcgg ttttgaagaa 600
 tccttggaag tagacacgaa cccactgctg ggcgctggta aattcgcaac tgatcctgcg 660
 gttaccctgg ctcaacgaact gattcatgca ggccaccgcc tgtacggtat cgccatcaat 720
 ccgaaccgtg tcttcaaagt taacaccaac gcgtattacg agatgtccgg tctggaagta 780
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 gctaatttta acggccagaa caccgaaatc aacaacatga acttcacaaa actgaaaaac 1260
 ttcactggtc tgttcgagtt ttacaagctg ctgtgcgtac gtggcatcat tacctccaaa 1320

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actaaatctc tggatgacga tgacaaaggt tataacaaag cgctgaacga cctctgtggg 1380

tcgac 1385

<210> 70

<211> 457

<212> PRT

<213> Clostridium botulinum

<400> 70

Met Glu Phe Val Asn Lys Gln Phe Asn Tyr Lys Asp Pro Val Asn Gly
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Val Asp Ile Ala Tyr Ile Lys Ile Pro Asn Ala Gly Gln Met Gln Pro
20 25 30

Val Lys Ala Phe Lys Ile His Asn Lys Ile Trp Val Ile Pro Glu Arg
35 40 45

Asp Thr Phe Thr Asn Pro Glu Glu Gly Asp Leu Asn Pro Pro Pro Glu
50 55 60

Ala Lys Gln Val Pro Val Ser Tyr Tyr Asp Ser Thr Tyr Leu Ser Thr
65 70 75 80

Asp Asn Glu Lys Asp Asn Tyr Leu Lys Gly Val Thr Lys Leu Phe Glu
85 90 95

Arg Ile Tyr Ser Thr Asp Leu Gly Arg Met Leu Leu Thr Ser Ile Val
100 105 110

Arg Gly Ile Pro Phe Trp Gly Gly Ser Thr Ile Asp Thr Glu Leu Lys
115 120 125

Val Ile Asp Thr Asn Cys Ile Asn Val Ile Gln Pro Asp Gly Ser Tyr
130 135 140

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

Ile Gln Phe Glu Cys Lys Ser Phe Gly His Glu Val Leu Asn Leu Thr
165 170 175

Arg Asn Gly Tyr Gly Ser Thr Gln Tyr Ile Arg Phe Ser Pro Asp Phe
180 185 190

Thr Phe Gly Phe Glu Glu Ser Leu Glu Val Asp Thr Asn Pro Leu Leu
195 200 205

Gly Ala Gly Lys Phe Ala Thr Asp Pro Ala Val Thr Leu Ala His Glu
210 215 220

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Leu Ile His Ala Gly His Arg Leu Tyr Gly Ile Ala Ile Asn Pro Asn
225 230 235 240

Arg Val Phe Lys Val Asn Thr Asn Ala Tyr Tyr Glu Met Ser Gly Leu
245 250 255

Glu Val Ser Phe Glu Glu Leu Arg Thr Phe Gly Gly His Asp Ala Lys
260 265 270

Phe Ile Asp Ser Leu Gln Glu Asn Glu Phe Arg Leu Tyr Tyr Tyr Asn
275 280 285

Lys Phe Lys Asp Ile Ala Ser Thr Leu Asn Lys Ala Lys Ser Ile Val
290 295 300

Gly Thr Thr Ala Ser Leu Gln Tyr Met Lys Asn Val Phe Lys Glu Lys
305 310 315 320

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

Lys Phe Asp Lys Leu Tyr Lys Met Leu Thr Glu Ile Tyr Thr Glu Asp
340 345 350

Asn Phe Val Lys Phe Phe Lys Val Leu Asn Arg Lys Thr Tyr Leu Asn
355 360 365

Phe Asp Lys Ala Val Phe Lys Ile Asn Ile Val Pro Lys Val Asn Tyr
370 375 380

Thr Ile Tyr Asp Gly Phe Asn Leu Arg Asn Thr Asn Leu Ala Ala Asn
385 390 395 400

Phe Asn Gly Gln Asn Thr Glu Ile Asn Asn Met Asn Phe Thr Lys Leu
405 410 415

Lys Asn Phe Thr Gly Leu Phe Glu Phe Tyr Lys Leu Leu Cys Val Arg
420 425 430

Gly Ile Ile Thr Ser Lys Thr Lys Ser Leu Asp Asp Asp Asp Lys Gly
435 440 445

Tyr Asn Lys Ala Leu Asn Asp Leu Cys
450 455

<210> 71

<211> 1376

<212> DNA

<213> Clostridium botulinum

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<400> 71
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 cagccggagc gttcctatcg ttccgaagaa ctgaacctgg tgatcatcgg cccgtctgct 480
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 gataaacttt acaaaatgct gactgaaatt tacaccgaag acaacttcgt taagttcttt 1080
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 ttcactggte tgttcgagtt ttacaagctg ctgtgcgtac gtggcatcat tacctccaaa 1320
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<210> 72
 <211> 454
 <212> PRT
 <213> Clostridium botulinum

<400> 72

Met Glu Phe Val Asn Lys Gln Phe Asn Tyr Lys Asp Pro Val Asn Gly
 1 5 10 15

Val Asp Ile Ala Tyr Ile Lys Ile Pro Asn Ala Gly Gln Met Gln Pro
 20 25 30

Val Lys Ala Phe Lys Ile His Asn Lys Ile Trp Val Ile Pro Glu Arg
 35 40 45

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Asp Thr Phe Thr Asn Pro Glu Glu Gly Asp Leu Asn Pro Pro Pro Glu
 50 55 60
 Ala Lys Gln Val Pro Val Ser Tyr Tyr Asp Ser Thr Tyr Leu Ser Thr
 65 70 75 80
 Asp Asn Glu Lys Asp Asn Tyr Leu Lys Gly Val Thr Lys Leu Phe Glu
 85 90 95
 Arg Ile Tyr Ser Thr Asp Leu Gly Arg Met Leu Leu Thr Ser Ile Val
 100 105 110
 Arg Gly Ile Pro Phe Trp Gly Gly Ser Thr Ile Asp Thr Glu Leu Lys
 115 120 125
 Val Ile Asp Thr Asn Cys Ile Asn Val Ile Gln Pro Asp Gly Ser Tyr
 130 135 140
 Arg Ser Glu Glu Leu Asn Leu Val Ile Ile Gly Pro Ser Ala Asp Ile
 145 150 155 160
 Ile Gln Phe Glu Cys Lys Ser Phe Gly His Glu Val Leu Asn Leu Thr
 165 170 175
 Arg Asn Gly Tyr Gly Ser Thr Gln Tyr Ile Arg Phe Ser Pro Asp Phe
 180 185 190
 Thr Phe Gly Phe Glu Glu Ser Leu Glu Val Asp Thr Asn Pro Leu Leu
 195 200 205
 Gly Ala Gly Lys Phe Ala Thr Asp Pro Ala Val Thr Leu Ala His Glu
 210 215 220
 Leu Ile His Ala Gly His Arg Leu Tyr Gly Ile Ala Ile Asn Pro Asn
 225 230 235 240
 Arg Val Phe Lys Val Asn Thr Asn Ala Tyr Tyr Glu Met Ser Gly Leu
 245 250 255
 Glu Val Ser Phe Glu Glu Leu Arg Thr Phe Gly Gly His Asp Ala Lys
 260 265 270
 Phe Ile Asp Ser Leu Gln Glu Asn Glu Phe Arg Leu Tyr Tyr Tyr Asn
 275 280 285
 Lys Phe Lys Asp Ile Ala Ser Thr Leu Asn Lys Ala Lys Ser Ile Val
 290 295 300
 Gly Thr Thr Ala Ser Leu Gln Tyr Met Lys Asn Val Phe Lys Glu Lys
 305 310 315 320

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

Lys Phe Asp Lys Leu Tyr Lys Met Leu Thr Glu Ile Tyr Thr Glu Asp
340 345 350

Asn Phe Val Lys Phe Phe Lys Val Leu Asn Arg Lys Thr Tyr Leu Asn
355 360 365

Phe Asp Lys Ala Val Phe Lys Ile Asn Ile Val Pro Lys Val Asn Tyr
370 375 380

Thr Ile Tyr Asp Gly Phe Asn Leu Arg Asn Thr Asn Leu Ala Ala Asn
385 390 395 400

Phe Asn Gly Gln Asn Thr Glu Ile Asn Asn Met Asn Phe Thr Lys Leu
405 410 415

Lys Asn Phe Thr Gly Leu Phe Glu Phe Tyr Lys Leu Leu Cys Val Arg
420 425 430

Gly Ile Ile Thr Ser Lys Thr Lys Ser Leu Ile Glu Gly Arg Asn Lys
435 440 445

Ala Leu Asn Asp Leu Cys
450

<210> 73
<211> 1376
<212> DNA
<213> Clostridium botulinum

<400> 73
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attgcttaca tcaaaatccc gaacgctggc cagatgcagc cggtaaaggc attcaaaatc 120
cacaacaaaa tctgggttat cccggaacgt gataccttta ctaacccgga agaagggtgac 180
ctgaacccgc caccggaagc gaaacaggtg cgggtatctt actatgactc cacctacctg 240
totaccgata acgaaaagga caactacctg aaaggtgtta ctaaactggt cgagcgtatt 300
tactccaccg acctgggccc tatgtctgtg actagcatcg ttccggttat cccgttctgg 360
ggcggttcta ccatcgatac cgaactgaaa gtaatcgaca ctaactgcat caacgttatt 420
cagccggacg gttcctatcg ttccgaagaa ctgaacctgg tgatcatcgg cccgtctgct 480
gatatcatcc agttcgagtg taagagcttt ggtcacgaag ttctgaacct caccgtaac 540
ggctacgggt ccaactcagta catccgtttc tctcggact tcaccttcgg ttttgaagaa 600
tccctggaag tagacacgaa cccactgctg ggcgctggta aattcgcaac tgatcctgcg 660
gttacccctgg ctcacgaact gattcatgca ggccaccgcc tgtaagggtat cgccatcaat 720

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ccgaaccgtg tcttcaaagt taacaccaac gcgtattacg agatgtccgg tctggaagta 780
 agcttcgaag aactgcgtac ttttgccggg caccgacgta aattcatoga ctctctgcaa 840
 gaaaacgagt tccgtctgta ctactataac aagttcaaag atatcgcatc caccctgaac 900
 aaagcgaaat ccatcgtagg taccactgct tctctgcagt acatgaagaa cgttttttaa 960
 gaaaaatacc tgcgcagcga agacacctcc ggcaaattct ctgtagacaa gttgaaatc 1020
 gataaacttt acaaaatgct gactgaaatt tacaccgaag acaacttcgt taagttcttt 1080
 aaagttctga accgcaaaac ctatctgaac ttcgacaagg cagtattcaa aatcaacatc 1140
 gtgccgaaag ttaactacac tatctacgat gggttcaacc tgcgtaacac caacctggct 1200
 gctaatttta acggccagaa caccgaaatc aacaacatga acttcacaaa actgaaaaac 1260
 ttcactggct tggtcgagtt ttacaagctg ctgtgcgtac gtggcatcat tacctccaaa 1320
 actaaatctc tggacaaagg ttataacaaa gcgctgaacg acctctgtgg gtcgac 1376

<210> 74
 <211> 454
 <212> PRT
 <213> Clostridium botulinum

<400> 74

Met Glu Phe Val Asn Lys Gln Phe Asn Tyr Lys Asp Pro Val Asn Gly
 1 5 10 15

Val Asp Ile Ala Tyr Ile Lys Ile Pro Asn Ala Gly Gln Met Gln Pro
 20 25 30

Val Lys Ala Phe Lys Ile His Asn Lys Ile Trp Val Ile Pro Glu Arg
 35 40 45

Asp Thr Phe Thr Asn Pro Glu Glu Gly Asp Leu Asn Pro Pro Pro Glu
 50 55 60

Ala Lys Gln Val Pro Val Ser Tyr Tyr Asp Ser Thr Tyr Leu Ser Thr
 65 70 75 80

Asp Asn Glu Lys Asp Asn Tyr Leu Lys Gly Val Thr Lys Leu Phe Glu
 85 90 95

Arg Ile Tyr Ser Thr Asp Leu Gly Arg Met Leu Leu Thr Ser Ile Val
 100 105 110

Arg Gly Ile Pro Phe Trp Gly Gly Ser Thr Ile Asp Thr Glu Leu Lys
 115 120 125

Val Ile Asp Thr Asn Cys Ile Asn Val Ile Gln Pro Asp Gly Ser Tyr
 130 135 140

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Arg Ser Glu Glu Leu Asn Leu Val Ile Ile Gly Pro Ser Ala Asp Ile
 145 150 155 160
 Ile Gln Phe Glu Cys Lys Ser Phe Gly His Glu Val Leu Asn Leu Thr
 165 170 175
 Arg Asn Gly Tyr Gly Ser Thr Gln Tyr Ile Arg Phe Ser Pro Asp Phe
 180 185 190
 Thr Phe Gly Phe Glu Glu Ser Leu Glu Val Asp Thr Asn Pro Leu Leu
 195 200 205
 Gly Ala Gly Lys Phe Ala Thr Asp Pro Ala Val Thr Leu Ala His Glu
 210 215 220
 Leu Ile His Ala Gly His Arg Leu Tyr Gly Ile Ala Ile Asn Pro Asn
 225 230 235 240
 Arg Val Phe Lys Val Asn Thr Asn Ala Tyr Tyr Glu Met Ser Gly Leu
 245 250 255
 Glu Val Ser Phe Glu Glu Leu Arg Thr Phe Gly Gly His Asp Ala Lys
 260 265 270
 Phe Ile Asp Ser Leu Gln Glu Asn Glu Phe Arg Leu Tyr Tyr Tyr Asn
 275 280 285
 Lys Phe Lys Asp Ile Ala Ser Thr Leu Asn Lys Ala Lys Ser Ile Val
 290 295 300
 Gly Thr Thr Ala Ser Leu Gln Tyr Met Lys Asn Val Phe Lys Glu Lys
 305 310 315 320
 Tyr Leu Leu Ser Glu Asp Thr Ser Gly Lys Phe Ser Val Asp Lys Leu
 325 330 335
 Lys Phe Asp Lys Leu Tyr Lys Met Leu Thr Glu Ile Tyr Thr Glu Asp
 340 345 350
 Asn Phe Val Lys Phe Phe Lys Val Leu Asn Arg Lys Thr Tyr Leu Asn
 355 360 365
 Phe Asp Lys Ala Val Phe Lys Ile Asn Ile Val Pro Lys Val Asn Tyr
 370 375 380
 Thr Ile Tyr Asp Gly Phe Asn Leu Arg Asn Thr Asn Leu Ala Ala Asn
 385 390 395 400
 Phe Asn Gly Gln Asn Thr Glu Ile Asn Asn Met Asn Phe Thr Lys Leu
 405 410 415

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Lys Asn Phe Thr Gly Leu Phe Glu Phe Tyr Lys Leu Leu Cys Val Arg
 420 425 430

Gly Ile Ile Thr Ser Lys Thr Lys Ser Leu Asp Lys Gly Tyr Asn Lys
 435 440 445

Ala Leu Asn Asp Leu Cys
 450

<210> 75
 <211> 1376
 <212> DNA
 <213> Clostridium botulinum

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<400> 75
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 attgcttaca tcaaaatccc gaacgctggc cagatgcagc cggtaaaggc attcaaaatc 120
 cacaacaaaa tctgggttat cccggaacgt gataccttta ctaaccggga agaagggtgac 180
 ctgaaccggc caccggaagc gaaacaggtg cgggtatctt actatgactc cacctacctg 240
 totaccgata acgaaaagga caactacctg aaaggtgtta ctaaactggt cgagcgtatt 300
 tactccaccg acctgggccc tatgctgctg actagcatcg ttccgggtat cccgttctgg 360
 ggcgggttcta ccatcgatac cgaactgaaa gtaatcgaca ctaactgcat caacgttatt 420
 cagccggacg gttcctatcg ttccgaagaa ctgaacctgg tgatcatcgg cccgtctgct 480
 gatatcatcc agttcagtg taagagcttt ggtcacgaag ttctgaacct caccgtaac 540
 ggctacgggt cactcagta catccgtttc tctccggact tcaccttogg ttttgaagaa 600
 tccctggaag tagacacgaa cccactgctg ggcgctggta aattcgcaac tgatcctgcg 660
 gttacctggt ctacgaact gattcatgca ggccaccggc tgtagcgtat cgccatcaat 720
 ccgaaccgtg tcttcaaagt taacaccaac gcgtattacg agatgtccgg tctggaagta 780
 agcttcgaag aactgcgtac ttttggcggc cagcagccta aattcatcga ctctctgcaa 840
 gaaaacgagt tccgtctgta ctactataac aagttcaaag atatcgcatc caccctgaac 900
 aaagcgaaat ccatcgtggg taccactgct tctctgcagt acatgaagaa cgtttttaaa 960
 gaaaaatacc tgctcagcga agacacctcc ggcaaattct ctgtagacaa gttgaaattc 1020
 gataaacttt acaaaatgct gactgaaatt tacaccgaag acaacttcgt taagttcttt 1080
 aaagttctga accgcaaaac ctatctgaac ttcgacaagg cagtattcaa aatcaacatc 1140
 gtgccgaaag ttaactacac tatctacgat gggttcaacc tgcgtaaac caacctggct 1200
 gctaatttta acggccagaa cacggaaatc aacaacatga acttcacaaa actgaaaaac 1260
 ttcactggtc tgttcgagtt ttacaagctg ctgtgcgtac gtggcatcat tacctocaaa 1320
 ttagaagttt tattccaagg acctaacaaa gcgctgaacg acctctgtgg gtcgac 1376

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<210> 76
 <211> 454
 <212> PRT
 <213> Clostridium botulinum

<400> 76

Met Glu Phe Val Asn Lys Gln Phe Asn Tyr Lys Asp Pro Val Asn Gly
 1 5 10 15

Val Asp Ile Ala Tyr Ile Lys Ile Pro Asn Ala Gly Gln Met Gln Pro
 20 25 30

Val Lys Ala Phe Lys Ile His Asn Lys Ile Trp Val Ile Pro Glu Arg
 35 40 45

Asp Thr Phe Thr Asn Pro Glu Glu Gly Asp Leu Asn Pro Pro Pro Glu
 50 55 60

Ala Lys Gln Val Pro Val Ser Tyr Tyr Asp Ser Thr Tyr Leu Ser Thr
 65 70 75 80

Asp Asn Glu Lys Asp Asn Tyr Leu Lys Gly Val Thr Lys Leu Phe Glu
 85 90 95

Arg Ile Tyr Ser Thr Asp Leu Gly Arg Met Leu Leu Thr Ser Ile Val
 100 105 110

Arg Gly Ile Pro Phe Trp Gly Gly Ser Thr Ile Asp Thr Glu Leu Lys
 115 120 125

Val Ile Asp Thr Asn Cys Ile Asn Val Ile Gln Pro Asp Gly Ser Tyr
 130 135 140

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

Ile Gln Phe Glu Cys Lys Ser Phe Gly His Glu Val Leu Asn Leu Thr
 165 170 175

Arg Asn Gly Tyr Gly Ser Thr Gln Tyr Ile Arg Phe Ser Pro Asp Phe
 180 185 190

Thr Phe Gly Phe Glu Glu Ser Leu Glu Val Asp Thr Asn Pro Leu Leu
 195 200 205

Gly Ala Gly Lys Phe Ala Thr Asp Pro Ala Val Thr Leu Ala His Glu
 210 215 220

Leu Ile His Ala Gly His Arg Leu Tyr Gly Ile Ala Ile Asn Pro Asn
 225 230 235 240

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Arg Val Phe Lys Val Asn Thr Asn Ala Tyr Tyr Glu Met Ser Gly Leu
245 250 255

Glu Val Ser Phe Glu Glu Leu Arg Thr Phe Gly Gly His Asp Ala Lys
260 265 270

Phe Ile Asp Ser Leu Gln Glu Asn Glu Phe Arg Leu Tyr Tyr Tyr Asn
275 280 285

Lys Phe Lys Asp Ile Ala Ser Thr Leu Asn Lys Ala Lys Ser Ile Val
290 295 300

Gly Thr Thr Ala Ser Leu Gln Tyr Met Lys Asn Val Phe Lys Glu Lys
305 310 315 320

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

Lys Phe Asp Lys Leu Tyr Lys Met Leu Thr Glu Ile Tyr Thr Glu Asp
340 345 350

Asn Phe Val Lys Phe Phe Lys Val Leu Asn Arg Lys Thr Tyr Leu Asn
355 360 365

Phe Asp Lys Ala Val Phe Lys Ile Asn Ile Val Pro Lys Val Asn Tyr
370 375 380

Thr Ile Tyr Asp Gly Phe Asn Leu Arg Asn Thr Asn Leu Ala Ala Asn
385 390 395 400

Phe Asn Gly Gln Asn Thr Glu Ile Asn Asn Met Asn Phe Thr Lys Leu
405 410 415

Lys Asn Phe Thr Gly Leu Phe Glu Phe Tyr Lys Leu Leu Cys Val Arg
420 425 430

Gly Ile Ile Thr Ser Lys Leu Glu Val Leu Phe Gln Gly Pro Asn Lys
435 440 445

Ala Leu Asn Asp Leu Cys
450

<210> 77
<211> 1376
<212> DNA
<213> Clostridium botulinum

<400> 77
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attgottaca tcaaaatccc gaacgctggc cagatgcagc cggtaaaggc attcaaaatc 120

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cacaacaaaa tctgggttat ccggaacgt gataccttta ctaaccgga agaaggtgac 180
 ctgaaccgc caccggaagc gaaacaggtg ccggtatctt actatgactc caccctacgt 240
 tctaccgata acgaaaagga caactacctg aaaggtgtta ctaaactgtt cgagcgtatt 300
 tactccaccg acctgggccc tatgctgctg actagcatcg ttccggttat ccggttctgg 360
 ggcggttcta ccatcgatag cgaactgaaa gtaatcgaca ctaactgcat caacgttatt 420
 cagccggacg gttcctatcg ttccgaagaa ctgaacctgg tgatcatcgg ccgctctgct 480
 gatatcatcc agttcgagtg taagagcttt ggtcacgaag ttctgaacct caccgtaac 540
 ggctacggtt ccaactcagta catccgtttc tctccggact tcaccttcgg ttttgaagaa 600
 tccctggaag tagacacgaa cccactgctg ggcgctggta aattcgcaac tgatcctgcg 660
 gttaccctgg ctacgaact gattcatgca ggccaccgcc tgtacggtat cgccatcaat 720
 ccgaaccgtg tcttcaaagt taacaccaac gcgtattcag agatgtccgg tctggaagta 780
 agcttcgaag aactgcgtac ttttggcggg cagcagccta aattcatcga ctctctgcaa 840
 gaaaacgagt tccgtctgta ctactataac aagttcaaag atatcgcatc caccctgaac 900
 aaagcgaaat ccatcggtgg taccactgct tctctgcagt acatgaagaa cgttttttaa 960
 gaaaaatacc tgctcagcga agacacctcc ggcaaattct ctgtagacaa gttgaaattc 1020
 gataaacttt acaaaatgct gactgaaatt tacaccgaag acaacttcgt taagttcttt 1080
 aaagttctga accgcaaac ctatctgaac ttcgacaagg cagtattcaa aatcaacatc 1140
 gtgccgaaag ttaactacac tatctacgat gggttcaacc tgcgtaacac caacctggct 1200
 gctaatttta acggccagaa caccgaaatc aacaacatga acttcacaaa actgaaaaac 1260
 ttcactggtc tgttcgagtt ttacaagctg ctgtgcgtac gtggcatcat tacctccaaa 1320
 actaaattag taccaagagg aagtaacaaa gcgctgaacg acctctgtgg gtcgac 1376

<210> 78
 <211> 454
 <212> PRT
 <213> Clostridium botulinum

<400> 78

Met Glu Phe Val Asn Lys Gln Phe Asn Tyr Lys Asp Pro Val Asn Gly
 1 5 10 15

Val Asp Ile Ala Tyr Ile Lys Ile Pro Asn Ala Gly Gln Met Gln Pro
 20 25 30

Val Lys Ala Phe Lys Ile His Asn Lys Ile Trp Val Ile Pro Glu Arg
 35 40 45

Asp Thr Phe Thr Asn Pro Glu Glu Gly Asp Leu Asn Pro Pro Pro Glu
 50 55 60

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Ala Lys Gln Val Pro Val Ser Tyr Tyr Asp Ser Thr Tyr Leu Ser Thr
65 70 75 80

Asp Asn Glu Lys Asp Asn Tyr Leu Lys Gly Val Thr Lys Leu Phe Glu
85 90 95

Arg Ile Tyr Ser Thr Asp Leu Gly Arg Met Leu Leu Thr Ser Ile Val
100 105 110

Arg Gly Ile Pro Phe Trp Gly Gly Ser Thr Ile Asp Thr Glu Leu Lys
115 120 125

Val Ile Asp Thr Asn Cys Ile Asn Val Ile Gln Pro Asp Gly Ser Tyr
130 135 140

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

Ile Gln Phe Glu Cys Lys Ser Phe Gly His Glu Val Leu Asn Leu Thr
165 170 175

Arg Asn Gly Tyr Gly Ser Thr Gln Tyr Ile Arg Phe Ser Pro Asp Phe
180 185 190

Thr Phe Gly Phe Glu Glu Ser Leu Glu Val Asp Thr Asn Pro Leu Leu
195 200 205

Gly Ala Gly Lys Phe Ala Thr Asp Pro Ala Val Thr Leu Ala His Glu
210 215 220

Leu Ile His Ala Gly His Arg Leu Tyr Gly Ile Ala Ile Asn Pro Asn
225 230 235 240

Arg Val Phe Lys Val Asn Thr Asn Ala Tyr Tyr Glu Met Ser Gly Leu
245 250 255

Glu Val Ser Phe Glu Glu Leu Arg Thr Phe Gly Gly His Asp Ala Lys
260 265 270

Phe Ile Asp Ser Leu Gln Glu Asn Glu Phe Arg Leu Tyr Tyr Tyr Asn
275 280 285

Lys Phe Lys Asp Ile Ala Ser Thr Leu Asn Lys Ala Lys Ser Ile Val
290 295 300

Gly Thr Thr Ala Ser Leu Gln Tyr Met Lys Asn Val Phe Lys Glu Lys
305 310 315 320

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

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Lys Phe Asp Lys Leu Tyr Lys Met Leu Thr Glu Ile Tyr Thr Glu Asp
 340 345 350

Asn Phe Val Lys Phe Phe Lys Val Leu Asn Arg Lys Thr Tyr Leu Asn
 355 360 365

Phe Asp Lys Ala Val Phe Lys Ile Asn Ile Val Pro Lys Val Asn Tyr
 370 375 380

Thr Ile Tyr Asp Gly Phe Asn Leu Arg Asn Thr Asn Leu Ala Ala Asn
 385 390 395 400

Phe Asn Gly Gln Asn Thr Glu Ile Asn Asn Met Asn Phe Thr Lys Leu
 405 410 415

Lys Asn Phe Thr Gly Leu Phe Glu Phe Tyr Lys Leu Leu Cys Val Arg
 420 425 430

Gly Ile Ile Thr Ser Lys Thr Lys Leu Val Pro Arg Gly Ser Asn Lys
 435 440 445

Ala Leu Asn Asp Leu Cys
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<210> 79
 <211> 2601
 <212> DNA
 <213> Clostridium botulinum

<400> 79
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 aaggctttta agatcaccga ccgtatctgg atcatcccg aacgttacac cttcggttac 180
 aaacctgagg acttcaacaa gagtagcggg attttcaatc gtgacgtctg cgagtactat 240
 gatccagatt atctgaatac caacgataag aagaacatat tccttcagac tatgattaaa 300
 ctcttcaacc gtatcaaaag caaacgcgc ggtgaaaaac tcttcgaaat gattatcaac 360
 ggtatcccg acctcggtga ccgtcgtgtc ccgcttgaag agttcaacac caacatcgca 420
 agcgtcaccg tcaacaaact catcagcaac ccagggtgaag tcgaacgtaa aaaagggtatc 480
 ttcgcaaacc tcatcatctt ccgtccgggt ccggtcctca acgaaaacga aaccatcgac 540
 atcggtatcc agaaccactt cgcaagccgt gaagggttcg gtggtatcat gcagatgaaa 600
 ttctgcccgg aatacgtcag tgtcttcaac aacgtccagg aaaacaaagg tgcaagcatc 660
 ttcaaccgtc gtggttactt cagcgaccgg gcaatcatcc tcatgcatga actcatccac 720
 gtcctccacg gtctctacgg tatcaaagtt gacgacctcc cgatcgctcc gaacgagaag 780
 aaattcttca tgcagagcac cgacgcaatc caggctgagg aactctacac cttcggtggc 840

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caagacccaa gtatcataac ccggtccacc gacaaaagca tctacgacaa agtcctccag 900
 aacttcaggg gtatcgtgga cagactcaac aaagtcctcg tctgcatcag cgacccgaac 960
 atcaatatca acatatacaa gaacaagttc aaagacaagt acaaattcgt cgaggacagc 1020
 gaaggcaaat acagcatoga cgtagaaagt ttogacaagc tctacaaaag cctcatgttc 1080
 ggtttcaccg aaaccaacat cgccgagaac tacaagatca agacaagggc aagttacttc 1140
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 gaagagggtc tcaacatcag tgacaaagac atggagaagg aatacagagg tcagaacaag 1260
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 gaagacctgt tcttcacgc tgacaaaaac agcttcagt acgacctgag caaaaacgaa 1440
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 gggtgggta aacagatcgt taacgacttc gttatcgaag ctaacaaaag caacactatg 1860
 gacaaaatcg ctgacatcag tctgatcgtt ccgtacatcg gtctggctct gaacgttggc 1920
 aacgaaaccg ctaaaaggtaa ctttgaaaac gctttcgaga tcgctggctc aagcatcctg 1980
 ctggagtcca tcccggaact gctgatcccg gttgttggcg ctttcctgct ggaaagttac 2040
 atcgacaaca aaaacaagat catcaaaacc atcgacaacg ctctgacca aagtaacgaa 2100
 aaatggagtg atatgtacgg tctgatcgtt gctcagtggtc tgagcaccgt caacaccag 2160
 ttctacacca tcaaagaagg tatgtacaaa gctctgaact accaggtca ggctctggaa 2220
 gagatcatca aataccgtta caacatctac agtgagaagg aaaagagtaa catcaacatc 2280
 gacttcaacg acatcaacag caaactgaac gaaggtatca accaggtat cgacaacatc 2340
 aacaacttca tcaacggttg cagtgttagc tacctgatga agaagatgat cccgctggct 2400
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 atgttcaaca aatacaacag c 2601

<210> 80
 <211> 867
 <212> PRT
 <213> Clostridium botulinum

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<400> 80

Ile Ser Glu Phe Gly Ser Met Pro Val Thr Ile Asn Asn Phe Asn Tyr
1 5 10 15

Asn Asp Pro Ile Asp Asn Asn Asn Ile Ile Met Met Glu Pro Pro Phe
20 25 30

Ala Arg Gly Thr Gly Arg Tyr Tyr Lys Ala Phe Lys Ile Thr Asp Arg
35 40 45

Ile Trp Ile Ile Pro Glu Arg Tyr Thr Phe Gly Tyr Lys Pro Glu Asp
50 55 60

Phe Asn Lys Ser Ser Gly Ile Phe Asn Arg Asp Val Cys Glu Tyr Tyr
65 70 75 80

Asp Pro Asp Tyr Leu Asn Thr Asn Asp Lys Lys Asn Ile Phe Leu Gln
85 90 95

Thr Met Ile Lys Leu Phe Asn Arg Ile Lys Ser Lys Pro Leu Gly Glu
100 105 110

Lys Leu Leu Glu Met Ile Ile Asn Gly Ile Pro Tyr Leu Gly Asp Arg
115 120 125

Arg Val Pro Leu Glu Glu Phe Asn Thr Asn Ile Ala Ser Val Thr Val
130 135 140

Asn Lys Leu Ile Ser Asn Pro Gly Glu Val Glu Arg Lys Lys Gly Ile
145 150 155 160

Phe Ala Asn Leu Ile Ile Phe Gly Pro Gly Pro Val Leu Asn Glu Asn
165 170 175

Glu Thr Ile Asp Ile Gly Ile Gln Asn His Phe Ala Ser Arg Glu Gly
180 185 190

Phe Gly Gly Ile Met Gln Met Lys Phe Cys Pro Glu Tyr Val Ser Val
195 200 205

Phe Asn Asn Val Gln Glu Asn Lys Gly Ala Ser Ile Phe Asn Arg Arg
210 215 220

Gly Tyr Phe Ser Asp Pro Ala Leu Ile Leu Met His Glu Leu Ile His
225 230 235 240

Val Leu His Gly Leu Tyr Gly Ile Lys Val Asp Asp Leu Pro Ile Val
245 250 255

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Pro Asn Glu Lys Lys Phe Phe Met Gln Ser Thr Asp Ala Ile Gln Ala
 260 265 270

Glu Glu Leu Tyr Thr Phe Gly Gly Gln Asp Pro Ser Ile Ile Thr Pro
 275 280 285

Ser Thr Asp Lys Ser Ile Tyr Asp Lys Val Leu Gln Asn Phe Arg Gly
 290 295 300

Ile Val Asp Arg Leu Asn Lys Val Leu Val Cys Ile Ser Asp Pro Asn
 305 310 315 320

Ile Asn Ile Asn Ile Tyr Lys Asn Lys Phe Lys Asp Lys Tyr Lys Phe
 325 330 335

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

Lys Leu Tyr Lys Ser Leu Met Phe Gly Phe Thr Glu Thr Asn Ile Ala
 355 360 365

Glu Asn Tyr Lys Ile Lys Thr Arg Ala Ser Tyr Phe Ser Asp Ser Leu
 370 375 380

Pro Pro Val Lys Ile Lys Asn Leu Leu Asp Asn Glu Ile Tyr Thr Ile
 385 390 395 400

Glu Glu Gly Phe Asn Ile Ser Asp Lys Asp Met Glu Lys Glu Tyr Arg
 405 410 415

Gly Gln Asn Lys Ala Ile Asn Lys Gln Ala Tyr Glu Glu Ile Ser Lys
 420 425 430

Glu His Leu Ala Val Tyr Lys Ile Gln Met Cys Lys Ser Asp Asp Asp
 435 440 445

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

Phe Ile Ala Asp Lys Asn Ser Phe Ser Asp Asp Leu Ser Lys Asn Glu
 465 470 475 480

Arg Ile Glu Tyr Asn Thr Gln Ser Asn Tyr Ile Glu Asn Asp Phe Pro
 485 490 495

Ile Asn Glu Leu Ile Leu Asp Thr Asp Leu Ile Ser Lys Ile Glu Leu
 500 505 510

Pro Arg Glu Asn Thr Glu Ser Leu Thr Asp Phe Asn Val Asp Val Pro
 515 520 525

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

Thr Ile Phe Gln Tyr Leu Tyr Ser Gln Thr Phe Pro Leu Asp Ile Arg
545 550 555 560

Asp Ile Ser Leu Thr Ser Ser Phe Asp Asp Ala Leu Leu Phe Ser Asn
565 570 575

Lys Val Tyr Ser Phe Phe Ser Met Asp Tyr Ile Lys Thr Ala Asn Lys
580 585 590

Val Val Glu Ala Gly Leu Phe Ala Gly Trp Val Lys Gln Ile Val Asn
595 600 605

Asp Phe Val Ile Glu Ala Asn Lys Ser Asn Thr Met Asp Lys Ile Ala
610 615 620

Asp Ile Ser Leu Ile Val Pro Tyr Ile Gly Leu Ala Leu Asn Val Gly
625 630 635 640

Asn Glu Thr Ala Lys Gly Asn Phe Glu Asn Ala Phe Glu Ile Ala Gly
645 650 655

Ala Ser Ile Leu Leu Glu Phe Ile Pro Glu Leu Leu Ile Pro Val Val
660 665 670

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

Lys Thr Ile Asp Asn Ala Leu Thr Lys Arg Asn Glu Lys Trp Ser Asp
690 695 700

Met Tyr Gly Leu Ile Val Ala Gln Trp Leu Ser Thr Val Asn Thr Gln
705 710 715 720

Phe Tyr Thr Ile Lys Glu Gly Met Tyr Lys Ala Leu Asn Tyr Gln Ala
725 730 735

Gln Ala Leu Glu Glu Ile Ile Lys Tyr Arg Tyr Asn Ile Tyr Ser Glu
740 745 750

Lys Glu Lys Ser Asn Ile Asn Ile Asp Phe Asn Asp Ile Asn Ser Lys
755 760 765

Leu Asn Glu Gly Ile Asn Gln Ala Ile Asp Asn Ile Asn Asn Phe Ile
770 775 780

Asn Gly Cys Ser Val Ser Tyr Leu Met Lys Lys Met Ile Pro Leu Ala

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785 790 795 800

Val Glu Lys Leu Leu Asp Phe Asp Asn Thr Leu Lys Lys Asn Leu Leu
 805 810 815

Asn Tyr Ile Asp Glu Asn Lys Leu Tyr Leu Ile Gly Ser Ala Glu Tyr
 820 825 830

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

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

Tyr Asn Ser
 865

<210> 81
 <211> 2628
 <212> DNA
 <213> Clostridium botulinum

<400> 81
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 aaggctttta agatcaccca ccgtatctgg atcatcccg aacgttacac cticgggttac 180
 aaacctgagg acttcaacaa gagtagcggg attttcaatc gtgacgtctg cgagtactat 240
 gatccagatt atotgaatac caacgataag aagaacatat tccttcagac tatgattaaa 300
 ctcttcaacc gtatcaaaaag caaacggctc ggtgaaaaac tcctcgaaat gattatcaac 360
 ggtatcccg acctcgggtga ccgtcgtgtc ccgcttgaag agttcaacac caacatcgca 420
 agcgtcaccg tcaacaaact catcagcaac ccagggtgaag tcgaacgtaa aaaagggtatc 480
 ttcgcaaac tcactcatctt cgggtccgggt ccggctcctca acgaaaaaga aaccatcgac 540
 atcggtatcc agaaccactt cgcaagccgt gaagggttcg gtggtatcat gcagatgaaa 600
 ttctgcccg aatacgtcag tgtcttcaac aacgtccagg aaaacaaagg tgcaagcatc 660
 ttcaaccgct gtggttactt cagcgacccg gcaactcatc tcatgcatga actcatccac 720
 gtctccacg gtctctacgg tatcaaagtt gacgacctcc cgatcgtccc gaacgagaag 780
 aaattcttca tgcagagcac cgacgcaatc cagggtgagg aactctacac cticgggtggc 840
 caagacccaa gtatcataac ccgtccacc gacaaaagca tctacgacaa agtcctccag 900
 aacttcaggg gtatcgtgga cagactcaac aaagtccctg tctgcatcag cgaccggaac 960
 atcaatatca acatatacaa gaacaagttc aaagacaagt acaaattcgt cgaggacagc 1020
 gaaggcaaat acagcatcga cgtagaaagt ttcgacaagc tctacaaaag cctcatgttc 1080
 ggtttcaccg aaaccaacat cgcgagaac tacaagatca agacaagggc aagttacttc 1140

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agcgacagcc tcccgctgt caaatcaag aacctcttag acaacgagat ttacacaatt 1200
 gaagagggct tcaacatcag tgacaaagac atggagaagg aatacagagg tcagaacaag 1260
 gctatcaaca aacaggcata cgaggagatc agcaaagaac acctcgagct ctacaagatc 1320
 cagatgtgca aatctgaaga aaagctttac gacgacgacg acaaagaccg ttgggggttct 1380
 tcggtatctt gcatcgagct tgacaacgaa gacctgttct tcatcgctga caaaaacagc 1440
 ttcagtgcag acctgagcaa aaacgaacgt atcgaatata acaccagag caactacatc 1500
 gaaaacgact tcccgatcaa cgaactgac ctggacaccg acctgataag taaaatcgaa 1560
 ctgcctaggg aaaacaccga aagtctgacc gacttcaacg ttgacgttcc ggtttacgaa 1620
 aaacagccgg ctatcaagaa aatcttcacc gacgaaaaca ccatcttcca gtacctgtac 1680
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 tacatcggtc tggtctgtaa cgtttgtaac gaaaccgcta aaggtaactt tgaaaacgct 1980
 ttcgagatcg ctggtgcaag catcctgctg gagttcatcc cggaactgct gatcccggtt 2040
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 gacaacgctc tgacaaaacg taacgaaaaa tggagtgata tgtacggtct gatcggtgct 2160
 cagtggctga gcaccgtcaa caccagttc tacaccatca aagaaggtat gtacaaagct 2220
 ctgaactacc aggtcagggc tctggaagag atcatcaaat accgttataa catctacagt 2280
 gagaaggaaa agagtaacat caacatcgac ttcaacgaca tcaacagcaa actgaacgaa 2340
 ggtatcaacc aggtatcga caacatcaac aacttcatca acggttgca tggttagctac 2400
 ctgatgaaga agatgatccc gctggctggt gaaaaactgc tggacttoga caacaccctg 2460
 aaaaagaacc tgctgaacta catcgacgaa aacaagctgt acctgatcgg tagtgctgaa 2520
 tacgaaaaaa gtaaaagtga caaatacctg aagaccatca tgccgttoga cctgagtatc 2580
 tacaccaacg acaccatcct gatcgaaatg ttcaacaaat acaacagc 2628

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<210> 82
 <211> 876
 <212> PRT
 <213> Clostridium botulinum

<400> 82

Ile Ser Glu Phe Gly Ser Met Pro Val Thr Ile Asn Asn Phe Asn Tyr
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Asn Asp Pro Ile Asp Asn Asn Asn Ile Ile Met Met Glu Pro Pro Phe
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40

Ala Arg Gly Thr Gly Arg Tyr Tyr Lys Ala Phe Lys Ile Thr Asp Arg
 35 40 45
 Ile Trp Ile Ile Pro Glu Arg Tyr Thr Phe Gly Tyr Lys Pro Glu Asp
 50 55 60
 Phe Asn Lys Ser Ser Gly Ile Phe Asn Arg Asp Val Cys Glu Tyr Tyr
 65 70 75 80
 Asp Pro Asp Tyr Leu Asn Thr Asn Asp Lys Lys Asn Ile Phe Leu Gln
 85 90 95
 Thr Met Ile Lys Leu Phe Asn Arg Ile Lys Ser Lys Pro Leu Gly Glu
 100 105 110
 Lys Leu Leu Glu Met Ile Ile Asn Gly Ile Pro Tyr Leu Gly Asp Arg
 115 120 125
 Arg Val Pro Leu Glu Glu Phe Asn Thr Asn Ile Ala Ser Val Thr Val
 130 135 140
 Asn Lys Leu Ile Ser Asn Pro Gly Glu Val Glu Arg Lys Lys Gly Ile
 145 150 155 160
 Phe Ala Asn Leu Ile Ile Phe Gly Pro Gly Pro Val Leu Asn Glu Asn
 165 170 175
 Glu Thr Ile Asp Ile Gly Ile Gln Asn His Phe Ala Ser Arg Glu Gly
 180 185 190
 Phe Gly Gly Ile Met Gln Met Lys Phe Cys Pro Glu Tyr Val Ser Val
 195 200 205
 Phe Asn Asn Val Gln Glu Asn Lys Gly Ala Ser Ile Phe Asn Arg Arg
 210 215 220
 Gly Tyr Phe Ser Asp Pro Ala Leu Ile Leu Met His Glu Leu Ile His
 225 230 235 240
 Val Leu His Gly Leu Tyr Gly Ile Lys Val Asp Asp Leu Pro Ile Val
 245 250 255
 Pro Asn Glu Lys Lys Phe Phe Met Gln Ser Thr Asp Ala Ile Gln Ala
 260 265 270
 Glu Glu Leu Tyr Thr Phe Gly Gly Gln Asp Pro Ser Ile Ile Thr Pro
 275 280 285
 Ser Thr Asp Lys Ser Ile Tyr Asp Lys Val Leu Gln Asn Phe Arg Gly
 290 295 300

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Ile Val Asp Arg Leu Asn Lys Val Leu Val Cys Ile Ser Asp Pro Asn
305 310 315 320

Ile Asn Ile Asn Ile Tyr Lys Asn Lys Phe Lys Asp Lys Tyr Lys Phe
325 330 335

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

Lys Leu Tyr Lys Ser Leu Met Phe Gly Phe Thr Glu Thr Asn Ile Ala
355 360 365

Glu Asn Tyr Lys Ile Lys Thr Arg Ala Ser Tyr Phe Ser Asp Ser Leu
370 375 380

Pro Pro Val Lys Ile Lys Asn Leu Leu Asp Asn Glu Ile Tyr Thr Ile
385 390 395 400

Glu Glu Gly Phe Asn Ile Ser Asp Lys Asp Met Glu Lys Glu Tyr Arg
405 410 415

Gly Gln Asn Lys Ala Ile Asn Lys Gln Ala Tyr Glu Glu Ile Ser Lys
420 425 430

Glu His Leu Ala Val Tyr Lys Ile Gln Met Cys Lys Ser Glu Glu Lys
435 440 445

Leu Tyr Asp Asp Asp Asp Lys Asp Arg Trp Gly Ser Ser Arg Ile Cys
450 455 460

Ile Asp Val Asp Asn Glu Asp Leu Phe Phe Ile Ala Asp Lys Asn Ser
465 470 475 480

Phe Ser Asp Asp Leu Ser Lys Asn Glu Arg Ile Glu Tyr Asn Thr Gln
485 490 495

Ser Asn Tyr Ile Glu Asn Asp Phe Pro Ile Asn Glu Leu Ile Leu Asp
500 505 510

Thr Asp Leu Ile Ser Lys Ile Glu Leu Pro Arg Glu Asn Thr Glu Ser
515 520 525

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

Ile Lys Lys Ile Phe Thr Asp Glu Asn Thr Ile Phe Gln Tyr Leu Tyr
545 550 555 560

Ser Gln Thr Phe Pro Leu Asp Ile Arg Asp Ile Ser Leu Thr Ser Ser

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565 570 575
 Phe Asp Asp Ala Leu Leu Phe Ser Asn Lys Val Tyr Ser Phe Phe Ser
 580 585 590
 Met Asp Tyr Ile Lys Thr Ala Asn Lys Val Val Glu Ala Gly Leu Phe
 595 600 605
 Ala Gly Trp Val Lys Gln Ile Val Asn Asp Phe Val Ile Glu Ala Asn
 610 615 620
 Lys Ser Asn Thr Met Asp Lys Ile Ala Asp Ile Ser Leu Ile Val Pro
 625 630 635 640
 Tyr Ile Gly Leu Ala Leu Asn Val Gly Asn Glu Thr Ala Lys Gly Asn
 645 650 655
 Phe Glu Asn Ala Phe Glu Ile Ala Gly Ala Ser Ile Leu Leu Glu Phe
 660 665 670
 Ile Pro Glu Leu Leu Ile Pro Val Val Gly Ala Phe Leu Leu Glu Ser
 675 680 685
 Tyr Ile Asp Asn Lys Asn Lys Ile Ile Lys Thr Ile Asp Asn Ala Leu
 690 695 700
 Thr Lys Arg Asn Glu Lys Trp Ser Asp Met Tyr Gly Leu Ile Val Ala
 705 710 715 720
 Gln Trp Leu Ser Thr Val Asn Thr Gln Phe Tyr Thr Ile Lys Glu Gly
 725 730 735
 Met Tyr Lys Ala Leu Asn Tyr Gln Ala Gln Ala Leu Glu Glu Ile Ile
 740 745 750
 Lys Tyr Arg Tyr Asn Ile Tyr Ser Glu Lys Glu Lys Ser Asn Ile Asn
 755 760 765
 Ile Asp Phe Asn Asp Ile Asn Ser Lys Leu Asn Glu Gly Ile Asn Gln
 770 775 780
 Ala Ile Asp Asn Ile Asn Asn Phe Ile Asn Gly Cys Ser Val Ser Tyr
 785 790 795 800
 Leu Met Lys Lys Met Ile Pro Leu Ala Val Glu Lys Leu Leu Asp Phe
 805 810 815
 Asp Asn Thr Leu Lys Lys Asn Leu Leu Asn Tyr Ile Asp Glu Asn Lys
 820 825 830

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Leu Tyr Leu Ile Gly Ser Ala Glu Tyr Glu Lys Ser Lys Val Asn Lys
 835 840 845

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

Thr Ile Leu Ile Glu Met Phe Asn Lys Tyr Asn Ser
 865 870 875

<210> 83
 <211> 2613
 <212> DNA
 <213> Clostridium botulinum

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<400> 83
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 accggacgtt actacaaggc ttttaagatc accgaccgta tctggatcat cccggaacgt 180
 tacaccttcg gttacaaacc tgaggacttc aacaagagta gcgggatttt caatcgtgac 240
 gtctgcgagt actatgatcc agattatctg aataccaacg ataagaagaa catattcctt 300
 cagactatga ttaaaactctt caaccgtatc aaaagcaaac cgctcgggtga aaaactcctc 360
 gaaatgatta tcaacgggtat cccgtacctc ggtgacogtc gtgtcccgtc tgaagagttc 420
 aacaccaaca tcgcaagcgt caccgtcaac aaactcatca gcaaccagc tgaagtcgaa 480
 cgtaaaaaag gtatcttcgc aaactcatc atcttcggtc cgggtccggc cctcaacgaa 540
 aacgaaacca tcgacatcgg tatccagaac cacttcgcaa gccgtgaagg tttcggtggt 600
 atcatgcaga tgaaattctg cccggaatac gtcagtgtct tcaacaacgt ccaggaaaac 660
 aaaggtgcaa gcatcttcaa ccgtcgtggt tacttcagcg acccggcact catcctcatg 720
 catgaactca tccacgtcct ccacgggtctc tacggtatca aagttgacga cctcccgatc 780
 gtcccgaacg agaagaaatt cttcatgcag agcaccgacg caatccaggc tgaggaactc 840
 tacaccttcg gtggccaaga cccaagtatc ataaccccggt ccaccgacaa aagcatctac 900
 gacaaagtcc tccagaactt caggggtatc gtggacagac tcaacaaagt cctcgtctgc 960
 atcagcgacc cgaacatcaa tatcaacata tacaagaaca agttcaaaga caagtacaaa 1020
 ttcgtcgagg acagcgaagg caaatacagc atcgacgtag aaagtcttga caagctctac 1080
 aaaagcctca tgttcgggtt caccgaaacc aacatcgccg agaactacaa gatcaagaca 1140
 agggcaagtt acttcagcga cagcctcccg cctgtcaaaa tcaagaacct cttagacaac 1200
 gagatttaca ctatagaaga gggcttcaac atcagtgaac aagacatgga gaaggaatac 1260
 agaggtcaga acaaggctat caacaacacg gcatacgagg agatcagcaa agaacacctc 1320
 gcagttcaca agatccagat gtgtagcgct atcgaaggcc gagctcccg gatctgcac 1380
 gacgttgaca acgaagacct gttcttcacg gctgacaaaa acagcttcag tgacgacctg 1440

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agcaaaaacg aacgtatcga atacaacacc cagagcaact acatcgaaaa cgacttcccg 1500
 atcaacgaac tgatcctgga caccgacctg ataagtaaaa tcgaactgcc gagcgaaaaac 1560
 accgaaagtc tgaccgactt caacgttgac gttccgggtt acgaaaaaca gccggctatc 1620
 aagaaaatct tcaccgacga aaacaccatc ttccagtacc tgtacagcca gaccttcccg 1680
 ctggacatcc gtgacatcag tctgaccagc agtttgcagc acgotctgct gttcagcaac 1740
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 gggctgttcg ctgggtgggt taaacagatc gttaacgact tcgttatcga agctaacaaa 1860
 agcaacacta tggacaaaat cgctgacatc agtctgatcg ttccgtacat cggctctggct 1920
 ctgaacgttg gtaacgaaac cgctaaaggt aactttgaaa acgctttcga gatcgctggg 1980
 gcaagcatcc tgctggagtt catcccgga ctgctgatcc cgggtgttg tgctttcctg 2040
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 gtcaacaccc agttctacac catcaaagaa ggtatgtaca aagctctgaa ctaccaggct 2220
 caggctctgg aagagatcat caaataccgt tacaacatct acagtggaa ggaaaagagt 2280
 aacatcaaca tcgacttcaa cgacatcaac agcaaactga acgaaggat caaccaggct 2340
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 atcccgctgg ctgttgaaaa actgctggac ttcgacaaca cctgaaaaa gaacctgctg 2460
 aactacatcg acgaaaacaa gctgtacctg atcggtagtg ctgaatacga aaaaagtaaa 2520
 gtgaacaaat acctgaagac catcatgccg ttcgacctga gtatctacac caacgacacc 2580
 atcctgatcg aaatgttcaa caaatacaac agc 2613

<210> 84
 <211> 871
 <212> PRT
 <213> Clostridium botulinum

<400> 84

Gly Arg Ala Met Gly Gly Arg Glu Phe Gly Ser Met Pro Val Thr Ile
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 20 25 30

Met Glu Pro Pro Phe Ala Arg Gly Thr Gly Arg Tyr Tyr Lys Ala Phe
 35 40 45

Lys Ile Thr Asp Arg Ile Trp Ile Ile Pro Glu Arg Tyr Thr Phe Gly
 50 55 60

Tyr Lys Pro Glu Asp Phe Asn Lys Ser Ser Gly Ile Phe Asn Arg Asp
 65 70 75 80

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Val Cys Glu Tyr Tyr Asp Pro Asp Tyr Leu Asn Thr Asn Asp Lys Lys
85 90 95

Asn Ile Phe Leu Gln Thr Met Ile Lys Leu Phe Asn Arg Ile Lys Ser
100 105 110

Lys Pro Leu Gly Glu Lys Leu Leu Glu Met Ile Ile Asn Gly Ile Pro
115 120 125

Tyr Leu Gly Asp Arg Arg Val Pro Leu Glu Glu Phe Asn Thr Asn Ile
130 135 140

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Ala Ser Val Thr Val Asn Lys Leu Ile Ser Asn Pro Gly Glu Val Glu
145 150 155 160

Arg Lys Lys Gly Ile Phe Ala Asn Leu Ile Ile Phe Gly Pro Gly Pro
165 170 175

Val Leu Asn Glu Asn Glu Thr Ile Asp Ile Gly Ile Gln Asn His Phe
180 185 190

Ala Ser Arg Glu Gly Phe Gly Gly Ile Met Gln Met Lys Phe Cys Pro
195 200 205

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Glu Tyr Val Ser Val Phe Asn Asn Val Gln Glu Asn Lys Gly Ala Ser
210 215 220

Ile Phe Asn Arg Arg Gly Tyr Phe Ser Asp Pro Ala Leu Ile Leu Met
225 230 235 240

His Glu Leu Ile His Val Leu His Gly Leu Tyr Gly Ile Lys Val Asp
245 250 255

Asp Leu Pro Ile Val Pro Asn Glu Lys Lys Phe Phe Met Gln Ser Thr
260 265 270

30

Asp Ala Ile Gln Ala Glu Glu Leu Tyr Thr Phe Gly Gly Gln Asp Pro
275 280 285

Ser Ile Ile Thr Pro Ser Thr Asp Lys Ser Ile Tyr Asp Lys Val Leu
290 295 300

Gln Asn Phe Arg Gly Ile Val Asp Arg Leu Asn Lys Val Leu Val Cys
305 310 315 320

Ile Ser Asp Pro Asn Ile Asn Ile Asn Ile Tyr Lys Asn Lys Phe Lys
325 330 335

Asp Lys Tyr Lys Phe Val Glu Asp Ser Glu Gly Lys Tyr Ser Ile Asp

40

340 345 350
 Val Glu Ser Phe Asp Lys Leu Tyr Lys Ser Leu Met Phe Gly Phe Thr
 355 360 365
 Glu Thr Asn Ile Ala Glu Asn Tyr Lys Ile Lys Thr Arg Ala Ser Tyr
 370 375 380
 Phe Ser Asp Ser Leu Pro Pro Val Lys Ile Lys Asn Leu Leu Asp Asn
 385 390 395 400
 Glu Ile Tyr Thr Ile Glu Glu Gly Phe Asn Ile Ser Asp Lys Asp Met
 405 410 415
 Glu Lys Glu Tyr Arg Gly Gln Asn Lys Ala Ile Asn Lys Gln Ala Tyr
 420 425 430
 Glu Glu Ile Ser Lys Glu His Leu Ala Val Tyr Lys Ile Gln Met Cys
 435 440 445
 Ser Ala Ile Glu Gly Arg Ala Pro Gly Ile Cys Ile Asp Val Asp Asn
 450 455 460
 Glu Asp Leu Phe Phe Ile Ala Asp Lys Asn Ser Phe Ser Asp Asp Leu
 465 470 475 480
 Ser Lys Asn Glu Arg Ile Glu Tyr Asn Thr Gln Ser Asn Tyr Ile Glu
 485 490 495
 Asn Asp Phe Pro Ile Asn Glu Leu Ile Leu Asp Thr Asp Leu Ile Ser
 500 505 510
 Lys Ile Glu Leu Pro Ser Glu Asn Thr Glu Ser Leu Thr Asp Phe Asn
 515 520 525
 Val Asp Val Pro Val Tyr Glu Lys Gln Pro Ala Ile Lys Lys Ile Phe
 530 535 540
 Thr Asp Glu Asn Thr Ile Phe Gln Tyr Leu Tyr Ser Gln Thr Phe Pro
 545 550 555 560
 Leu Asp Ile Arg Asp Ile Ser Leu Thr Ser Ser Phe Asp Asp Ala Leu
 565 570 575
 Leu Phe Ser Asn Lys Val Tyr Ser Phe Phe Ser Met Asp Tyr Ile Lys
 580 585 590
 Thr Ala Asn Lys Val Val Glu Ala Gly Leu Phe Ala Gly Trp Val Lys
 595 600 605

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Gln Ile Val Asn Asp Phe Val Ile Glu Ala Asn Lys Ser Asn Thr Met
 610 615 620
 Asp Lys Ile Ala Asp Ile Ser Leu Ile Val Pro Tyr Ile Gly Leu Ala
 625 630 635 640
 Leu Asn Val Gly Asn Glu Thr Ala Lys Gly Asn Phe Glu Asn Ala Phe
 645 650 655
 Glu Ile Ala Gly Ala Ser Ile Leu Leu Glu Phe Ile Pro Glu Leu Leu
 660 665 670
 Ile Pro Val Val Gly Ala Phe Leu Leu Glu Ser Tyr Ile Asp Asn Lys
 675 680 685
 Asn Lys Ile Ile Lys Thr Ile Asp Asn Ala Leu Thr Lys Arg Asn Glu
 690 695 700
 Lys Trp Ser Asp Met Tyr Gly Leu Ile Val Ala Gln Trp Leu Ser Thr
 705 710 715 720
 Val Asn Thr Gln Phe Tyr Thr Ile Lys Glu Gly Met Tyr Lys Ala Leu
 725 730 735
 Asn Tyr Gln Ala Gln Ala Leu Glu Glu Ile Ile Lys Tyr Arg Tyr Asn
 740 745 750
 Ile Tyr Ser Glu Lys Glu Lys Ser Asn Ile Asn Ile Asp Phe Asn Asp
 755 760 765
 Ile Asn Ser Lys Leu Asn Glu Gly Ile Asn Gln Ala Ile Asp Asn Ile
 770 775 780
 Asn Asn Phe Ile Asn Gly Cys Ser Val Ser Tyr Leu Met Lys Lys Met
 785 790 795 800
 Ile Pro Leu Ala Val Glu Lys Leu Leu Asp Phe Asp Asn Thr Leu Lys
 805 810 815
 Lys Asn Leu Leu Asn Tyr Ile Asp Glu Asn Lys Leu Tyr Leu Ile Gly
 820 825 830
 Ser Ala Glu Tyr Glu Lys Ser Lys Val Asn Lys Tyr Leu Lys Thr Ile
 835 840 845
 Met Pro Phe Asp Leu Ser Ile Tyr Thr Asn Asp Thr Ile Leu Ile Glu
 850 855 860
 Met Phe Asn Lys Tyr Asn Ser
 865 870

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<210> 85
 <211> 2613
 <212> DNA
 <213> Clostridium botulinum

<400> 85
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 accggacgtt actacaaggc ttttaagatc accgaccgta tctggatcat cccggaacgt 180
 tacaccttcg gttacaaacc tgaggacttc aacaagagta gcgggatttt caatcgtgac 240
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 cagactatga ttaaactctt caaccgatc aaaagcaaac cgctcgggta aaaactcctc 360
 gaaatgatta tcaacggtat cccgtacctc ggtgaccgtc gtgtcccgtc tgaagagttc 420
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 catgaactca tccacgtcct ccacggtctc tacggtatca aagttgacga cctcccgatc 780
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 <212> PRT
 <213> Clostridium botulinum

<400> 86

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Met Glu Pro Pro Phe Ala Arg Gly Thr Gly Arg Tyr Tyr Lys Ala Phe
 35 40 45

Lys Ile Thr Asp Arg Ile Trp Ile Ile Pro Glu Arg Tyr Thr Phe Gly
 50 55 60

Tyr Lys Pro Glu Asp Phe Asn Lys Ser Ser Gly Ile Phe Asn Arg Asp
 65 70 75 80

Val Cys Glu Tyr Tyr Asp Pro Asp Tyr Leu Asn Thr Asn Asp Lys Lys
 85 90 95

Asn Ile Phe Leu Gln Thr Met Ile Lys Leu Phe Asn Arg Ile Lys Ser
 100 105 110

Lys Pro Leu Gly Glu Lys Leu Leu Glu Met Ile Ile Asn Gly Ile Pro
 115 120 125

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Tyr Leu Gly Asp Arg Arg Val Pro Leu Glu Glu Phe Asn Thr Asn Ile
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 Ala Ser Val Thr Val Asn Lys Leu Ile Ser Asn Pro Gly Glu Val Glu
 145 150 155 160
 Arg Lys Lys Gly Ile Phe Ala Asn Leu Ile Ile Phe Gly Pro Gly Pro
 165 170 175
 Val Leu Asn Glu Asn Glu Thr Ile Asp Ile Gly Ile Gln Asn His Phe
 180 185 190
 Ala Ser Arg Glu Gly Phe Gly Gly Ile Met Gln Met Lys Phe Cys Pro
 195 200 205
 Glu Tyr Val Ser Val Phe Asn Asn Val Gln Glu Asn Lys Gly Ala Ser
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 Ile Phe Asn Arg Arg Gly Tyr Phe Ser Asp Pro Ala Leu Ile Leu Met
 225 230 235 240
 His Glu Leu Ile His Val Leu His Gly Leu Tyr Gly Ile Lys Val Asp
 245 250 255
 Asp Leu Pro Ile Val Pro Asn Glu Lys Lys Phe Phe Met Gln Ser Thr
 260 265 270
 Asp Ala Ile Gln Ala Glu Glu Leu Tyr Thr Phe Gly Gly Gln Asp Pro
 275 280 285
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 290 295 300
 Gln Asn Phe Arg Gly Ile Val Asp Arg Leu Asn Lys Val Leu Val Cys
 305 310 315 320
 Ile Ser Asp Pro Asn Ile Asn Ile Asn Ile Tyr Lys Asn Lys Phe Lys
 325 330 335
 Asp Lys Tyr Lys Phe Val Glu Asp Ser Glu Gly Lys Tyr Ser Ile Asp
 340 345 350
 Val Glu Ser Phe Asp Lys Leu Tyr Lys Ser Leu Met Phe Gly Phe Thr
 355 360 365
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 370 375 380
 Phe Ser Asp Ser Leu Pro Pro Val Lys Ile Lys Asn Leu Leu Asp Asn

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385 390 395 400
 Glu Ile Tyr Thr Ile Glu Glu Gly Phe Asn Ile Ser Asp Lys Asp Met
 405 410 415
 Glu Lys Glu Tyr Arg Gly Gln Asn Lys Ala Ile Asn Lys Gln Ala Tyr
 420 425 430
 Glu Glu Ile Ser Lys Glu His Leu Ala Val Tyr Lys Ile Gln Met Cys
 435 440 445
 Ser Ala Ile Glu Gly Arg Ala Pro Gly Ile Cys Ile Asp Val Asp Asn
 450 455 460
 Glu Asp Leu Phe Phe Ile Ala Asp Lys Asn Ser Phe Ser Asp Asp Leu
 465 470 475 480
 Ser Lys Asn Glu Arg Ile Glu Tyr Asn Thr Gln Ser Asn Tyr Ile Glu
 485 490 495
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 Lys Ile Glu Leu Pro Ser Glu Asn Thr Glu Ser Leu Thr Asp Phe Asn
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 Val Asp Val Pro Val Tyr Glu Lys Gln Pro Ala Ile Lys Lys Ile Phe
 530 535 540
 Thr Asp Glu Asn Thr Ile Phe Gln Tyr Leu Tyr Ser Gln Thr Phe Pro
 545 550 555 560
 Leu Asp Ile Arg Asp Ile Ser Leu Thr Ser Ser Phe Asp Asp Ala Leu
 565 570 575
 Leu Phe Ser Asn Lys Val Tyr Ser Phe Phe Ser Met Asp Tyr Ile Lys
 580 585 590
 Thr Ala Asn Lys Val Val Glu Ala Gly Leu Phe Ala Gly Trp Val Lys
 595 600 605
 Gln Ile Val Asn Asp Phe Val Ile Glu Ala Asn Lys Ser Asn Thr Met
 610 615 620
 Asp Lys Ile Ala Asp Ile Ser Leu Ile Val Pro Tyr Ile Gly Leu Ala
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 Leu Asn Val Gly Asn Glu Thr Ala Lys Gly Asn Phe Glu Asn Ala Phe
 645 650 655

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

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

Asn Lys Ile Ile Lys Thr Ile Asp Asn Ala Leu Thr Lys Arg Asn Glu
690 695 700

Lys Trp Ser Asp Met Tyr Gly Leu Ile Val Ala Gln Trp Leu Ser Thr
705 710 715 720

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

Asn Tyr Gln Ala Gln Ala Leu Glu Glu Ile Ile Lys Tyr Arg Tyr Asn
740 745 750

Ile Tyr Ser Glu Lys Glu Lys Ser Asn Ile Asn Ile Asp Phe Asn Asp
755 760 765

Ile Asn Ser Lys Leu Asn Glu Gly Ile Asn Gln Ala Ile Asp Asn Ile
770 775 780

Asn Asn Phe Ile Asn Gly Cys Ser Val Ser Tyr Leu Met Lys Lys Met
785 790 795 800

Ile Pro Leu Ala Val Glu Lys Leu Leu Asp Phe Asp Asn Thr Leu Lys
805 810 815

Lys Asn Leu Leu Asn Tyr Ile Asp Glu Asn Lys Leu Tyr Leu Ile Gly
820 825 830

Ser Ala Glu Tyr Glu Lys Ser Lys Val Asn Lys Tyr Leu Lys Thr Ile
835 840 845

Met Pro Phe Asp Leu Ser Ile Tyr Thr Asn Asp Thr Ile Leu Ile Glu
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Met Phe Asn Lys Tyr Asn Ser
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<212> DNA
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gagttcatcc cggaactgct gatcccggtt gttggtgctt tctgctgga aagttacatc 2040
gacaacaaaa acaagatcat caaaaccatc gacaacgctc tgaccaaacy taacgaaaaa 2100

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 <211> 866
 <212> PRT
 <213> Clostridium botulinum

<400> 88

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Asn Asp Pro Ile Asp Asn Asn Asn Ile Ile Met Met Glu Pro Pro Phe
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Ala Arg Gly Thr Gly Arg Tyr Tyr Lys Ala Phe Lys Ile Thr Asp Arg
35 40 45

Ile Trp Ile Ile Pro Glu Arg Tyr Thr Phe Gly Tyr Lys Pro Glu Asp
50 55 60

Phe Asn Lys Ser Ser Gly Ile Phe Asn Arg Asp Val Cys Glu Tyr Tyr
65 70 75 80

Asp Pro Asp Tyr Leu Asn Thr Asn Asp Lys Lys Asn Ile Phe Leu Gln
85 90 95

Thr Met Ile Lys Leu Phe Asn Arg Ile Lys Ser Lys Pro Leu Gly Glu
100 105 110

Lys Leu Leu Glu Met Ile Ile Asn Gly Ile Pro Tyr Leu Gly Asp Arg
115 120 125

Arg Val Pro Leu Glu Glu Phe Asn Thr Asn Ile Ala Ser Val Thr Val
130 135 140

Asn Lys Leu Ile Ser Asn Pro Gly Glu Val Glu Arg Lys Lys Gly Ile
145 150 155 160

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

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Glu His Leu Ala Val Tyr Lys Ile Gln Met Cys Ser Ala Ile Glu Gly
435 440 445

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

Ile Ala Asp Lys Asn Ser Phe Ser Asp Asp Leu Ser Lys Asn Glu Arg
465 470 475 480

Ile Glu Tyr Asn Thr Gln Ser Asn Tyr Ile Glu Asn Asp Phe Pro Ile
485 490 495

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

Ser Glu Asn Thr Glu Ser Leu Thr Asp Phe Asn Val Asp Val Pro Val
515 520 525

Tyr Glu Lys Gln Pro Ala Ile Lys Lys Ile Phe Thr Asp Glu Asn Thr
530 535 540

Ile Phe Gln Tyr Leu Tyr Ser Gln Thr Phe Pro Leu Asp Ile Arg Asp
545 550 555 560

Ile Ser Leu Thr Ser Ser Phe Asp Asp Ala Leu Leu Phe Ser Asn Lys
565 570 575

Val Tyr Ser Phe Phe Ser Met Asp Tyr Ile Lys Thr Ala Asn Lys Val
580 585 590

Val Glu Ala Gly Leu Phe Ala Gly Trp Val Lys Gln Ile Val Asn Asp
595 600 605

Phe Val Ile Glu Ala Asn Lys Ser Asn Thr Met Asp Lys Ile Ala Asp
610 615 620

Ile Ser Leu Ile Val Pro Tyr Ile Gly Leu Ala Leu Asn Val Gly Asn
625 630 635 640

Glu Thr Ala Lys Gly Asn Phe Glu Asn Ala Phe Glu Ile Ala Gly Ala
645 650 655

Ser Ile Leu Leu Glu Phe Ile Pro Glu Leu Leu Ile Pro Val Val Gly
660 665 670

Ala Phe Leu Leu Glu Ser Tyr Ile Asp Asn Lys Asn Lys Ile Ile Lys
675 680 685

Thr Ile Asp Asn Ala Leu Thr Lys Arg Asn Glu Lys Trp Ser Asp Met

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<210>      89
<211>     2613
<212>      DNA
<213>    Clostridium botulinum
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[illegible]

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<400> 90

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Met Glu Pro Pro Phe Ala Arg Gly Thr Gly Arg Tyr Tyr Lys Ala Phe
 35 40 45

Lys Ile Thr Asp Arg Ile Trp Ile Ile Pro Glu Arg Tyr Thr Phe Gly
 50 55 60

Tyr Lys Pro Glu Asp Phe Asn Lys Ser Ser Gly Ile Phe Asn Arg Asp
 65 70 75 80

Val Cys Glu Tyr Tyr Asp Pro Asp Tyr Leu Asn Thr Asn Asp Lys Lys
 85 90 95

Asn Ile Phe Leu Gln Thr Met Ile Lys Leu Phe Asn Arg Ile Lys Ser
 100 105 110

Lys Pro Leu Gly Glu Lys Leu Leu Glu Met Ile Ile Asn Gly Ile Pro
 115 120 125

Tyr Leu Gly Asp Arg Arg Val Pro Leu Glu Glu Phe Asn Thr Asn Ile
 130 135 140

Ala Ser Val Thr Val Asn Lys Leu Ile Ser Asn Pro Gly Glu Val Glu
 145 150 155 160

Arg Lys Lys Gly Ile Phe Ala Asn Leu Ile Ile Phe Gly Pro Gly Pro
 165 170 175

Val Leu Asn Glu Asn Glu Thr Ile Asp Ile Gly Ile Gln Asn His Phe
 180 185 190

Ala Ser Arg Glu Gly Phe Gly Gly Ile Met Gln Met Lys Phe Cys Pro
 195 200 205

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Glu Tyr Val Ser Val Phe Asn Asn Val Gln Glu Asn Lys Gly Ala Ser
210 215 220

Ile Phe Asn Arg Arg Gly Tyr Phe Ser Asp Pro Ala Leu Ile Leu Met
225 230 235 240

His Glu Leu Ile His Val Leu His Gly Leu Tyr Gly Ile Lys Val Asp
245 250 255

Asp Leu Pro Ile Val Pro Asn Glu Lys Lys Phe Phe Met Gln Ser Thr
260 265 270

Asp Ala Ile Gln Ala Glu Glu Leu Tyr Thr Phe Gly Gly Gln Asp Pro
275 280 285

Ser Ile Ile Thr Pro Ser Thr Asp Lys Ser Ile Tyr Asp Lys Val Leu
290 295 300

Gln Asn Phe Arg Gly Ile Val Asp Arg Leu Asn Lys Val Leu Val Cys
305 310 315 320

Ile Ser Asp Pro Asn Ile Asn Ile Asn Ile Tyr Lys Asn Lys Phe Lys
325 330 335

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

Val Glu Ser Phe Asp Lys Leu Tyr Lys Ser Leu Met Phe Gly Phe Thr
355 360 365

Glu Thr Asn Ile Ala Glu Asn Tyr Lys Ile Lys Thr Arg Ala Ser Tyr
370 375 380

Phe Ser Asp Ser Leu Pro Pro Val Lys Ile Lys Asn Leu Leu Asp Asn
385 390 395 400

Glu Ile Tyr Thr Ile Glu Glu Gly Phe Asn Ile Ser Asp Lys Asp Met
405 410 415

Glu Lys Glu Tyr Arg Gly Gln Asn Lys Ala Ile Asn Lys Gln Ala Tyr
420 425 430

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

Glu Asp Leu Phe Phe Ile Ala Asp Lys Asn Ser Phe Ser Asp Asp Leu

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465 470 475 480
 Ser Lys Asn Glu Arg Ile Glu Tyr Asn Thr Gln Ser Asn Tyr Ile Glu
 485 490 495
 Asn Asp Phe Pro Ile Asn Glu Leu Ile Leu Asp Thr Asp Leu Ile Ser
 500 505 510
 Lys Ile Glu Leu Pro Ser Glu Asn Thr Glu Ser Leu Thr Asp Phe Asn
 515 520 525
 Val Asp Val Pro Val Tyr Glu Lys Gln Pro Ala Ile Lys Lys Ile Phe
 530 535 540
 Thr Asp Glu Asn Thr Ile Phe Gln Tyr Leu Tyr Ser Gln Thr Phe Pro
 545 550 555 560
 Leu Asp Ile Arg Asp Ile Ser Leu Thr Ser Ser Phe Asp Asp Ala Leu
 565 570 575
 Leu Phe Ser Asn Lys Val Tyr Ser Phe Phe Ser Met Asp Tyr Ile Lys
 580 585 590
 Thr Ala Asn Lys Val Val Glu Ala Gly Leu Phe Ala Gly Trp Val Lys
 595 600 605
 Gln Ile Val Asn Asp Phe Val Ile Glu Ala Asn Lys Ser Asn Thr Met
 610 615 620
 Asp Lys Ile Ala Asp Ile Ser Leu Ile Val Pro Tyr Ile Gly Leu Ala
 625 630 635 640
 Leu Asn Val Gly Asn Glu Thr Ala Lys Gly Asn Phe Glu Asn Ala Phe
 645 650 655
 Glu Ile Ala Gly Ala Ser Ile Leu Leu Glu Phe Ile Pro Glu Leu Leu
 660 665 670
 Ile Pro Val Val Gly Ala Phe Leu Leu Glu Ser Tyr Ile Asp Asn Lys
 675 680 685
 Asn Lys Ile Ile Lys Thr Ile Asp Asn Ala Leu Thr Lys Arg Asn Glu
 690 695 700
 Lys Trp Ser Asp Met Tyr Gly Leu Ile Val Ala Gln Trp Leu Ser Thr
 705 710 715 720
 Val Asn Thr Gln Phe Tyr Thr Ile Lys Glu Gly Met Tyr Lys Ala Leu
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Asn Tyr Gln Ala Gln Ala Leu Glu Glu Ile Ile Lys Tyr Arg Tyr Asn
740 745 750

Ile Tyr Ser Glu Lys Glu Lys Ser Asn Ile Asn Ile Asp Phe Asn Asp
755 760 765

Ile Asn Ser Lys Leu Asn Glu Gly Ile Asn Gln Ala Ile Asp Asn Ile
770 775 780

Asn Asn Phe Ile Asn Gly Cys Ser Val Ser Tyr Leu Met Lys Lys Met
785 790 795 800

Ile Pro Leu Ala Val Glu Lys Leu Leu Asp Phe Asp Asn Thr Leu Lys
805 810 815

Lys Asn Leu Leu Asn Tyr Ile Asp Glu Asn Lys Leu Tyr Leu Ile Gly
820 825 830

Ser Ala Glu Tyr Glu Lys Ser Lys Val Asn Lys Tyr Leu Lys Thr Ile
835 840 845

Met Pro Phe Asp Leu Ser Ile Tyr Thr Asn Asp Thr Ile Leu Ile Glu
850 855 860

Met Phe Asn Lys Tyr Asn Ser
865 870

<210> 91
<211> 2610
<212> DNA
<213> Clostridium botulinum

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atgattatca acggatatcc gtacctcggt gaccgtcgtg tcccgttga agagttcaac 420
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atgcagatga aattctgccc ggaatacgtc agtgtcttca acaacgtcca ggaaaacaaa 660
ggtgcaagca tcttcaaccg tcgtggttac ttccagcgacc cggcactcat cctcatgcat 720

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gaactcatcc acgtcctcca cggctctctac ggtatcaaag ttgacgacct cccgatcgtc 780
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 aaagtctccc agaacttcag gggatctgtg gacagactca acaaagtcct cgtctgcata 960
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 gtcgaggaca gcgaaggcaa atacagcatc gacgtagaaa gtttcgacaa gctctacaaa 1080
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 atttacacta tagaagaggg cttcaacatc agtgacaaag acatggagaa ggaatacaga 1260
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<211> 870
 <212> PRT
 <213> Clostridium botulinum

<400> 92

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Asn Phe Asn Tyr Asn Asp Pro Ile Asp Asn Asn Asn Ile Ile Met Met
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Glu Pro Pro Phe Ala Arg Gly Thr Gly Arg Tyr Tyr Lys Ala Phe Lys
 35 40 45

Ile Thr Asp Arg Ile Trp Ile Ile Pro Glu Arg Tyr Thr Phe Gly Tyr
 50 55 60

Lys Pro Glu Asp Phe Asn Lys Ser Ser Gly Ile Phe Asn Arg Asp Val
 65 70 75 80

Cys Glu Tyr Tyr Asp Pro Asp Tyr Leu Asn Thr Asn Asp Lys Lys Asn
 85 90 95

Ile Phe Leu Gln Thr Met Ile Lys Leu Phe Asn Arg Ile Lys Ser Lys
 100 105 110

Pro Leu Gly Glu Lys Leu Leu Glu Met Ile Ile Asn Gly Ile Pro Tyr
 115 120 125

Leu Gly Asp Arg Arg Val Pro Leu Glu Glu Phe Asn Thr Asn Ile Ala
 130 135 140

Ser Val Thr Val Asn Lys Leu Ile Ser Asn Pro Gly Glu Val Glu Arg
 145 150 155 160

Lys Lys Gly Ile Phe Ala Asn Leu Ile Ile Phe Gly Pro Gly Pro Val
 165 170 175

Leu Asn Glu Asn Glu Thr Ile Asp Ile Gly Ile Gln Asn His Phe Ala
 180 185 190

Ser Arg Glu Gly Phe Gly Gly Ile Met Gln Met Lys Phe Cys Pro Glu
 195 200 205

Tyr Val Ser Val Phe Asn Asn Val Gln Glu Asn Lys Gly Ala Ser Ile
 210 215 220

Phe Asn Arg Arg Gly Tyr Phe Ser Asp Pro Ala Leu Ile Leu Met His
 225 230 235 240

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Glu Leu Ile His Val Leu His Gly Leu Tyr Gly Ile Lys Val Asp Asp
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 Leu Pro Ile Val Pro Asn Glu Lys Lys Phe Phe Met Gln Ser Thr Asp
 260 265 270
 Ala Ile Gln Ala Glu Glu Leu Tyr Thr Phe Gly Gly Gln Asp Pro Ser
 275 280 285
 Ile Ile Thr Pro Ser Thr Asp Lys Ser Ile Tyr Asp Lys Val Leu Gln
 290 295 300
 Asn Phe Arg Gly Ile Val Asp Arg Leu Asn Lys Val Leu Val Cys Ile
 305 310 315 320
 Ser Asp Pro Asn Ile Asn Ile Asn Ile Tyr Lys Asn Lys Phe Lys Asp
 325 330 335
 Lys Tyr Lys Phe Val Glu Asp Ser Glu Gly Lys Tyr Ser Ile Asp Val
 340 345 350
 Glu Ser Phe Asp Lys Leu Tyr Lys Ser Leu Met Phe Gly Phe Thr Glu
 355 360 365
 Thr Asn Ile Ala Glu Asn Tyr Lys Ile Lys Thr Arg Ala Ser Tyr Phe
 370 375 380
 Ser Asp Ser Leu Pro Pro Val Lys Ile Lys Asn Leu Leu Asp Asn Glu
 385 390 395 400
 Ile Tyr Thr Ile Glu Glu Gly Phe Asn Ile Ser Asp Lys Asp Met Glu
 405 410 415
 Lys Glu Tyr Arg Gly Gln Asn Lys Ala Ile Asn Lys Gln Ala Tyr Glu
 420 425 430
 Glu Ile Ser Lys Glu His Leu Ala Val Tyr Lys Ile Gln Met Cys Ser
 435 440 445
 Ala Ile Glu Gly Arg Ala Pro Gly Ile Cys Ile Asp Val Asp Asn Glu
 450 455 460
 Asp Leu Phe Phe Ile Ala Asp Lys Asn Ser Phe Ser Asp Asp Leu Ser
 465 470 475 480
 Lys Asn Glu Arg Ile Glu Tyr Asn Thr Gln Ser Asn Tyr Ile Glu Asn
 485 490 495
 Asp Phe Pro Ile Asn Glu Leu Ile Leu Asp Thr Asp Leu Ile Ser Lys
 500 505 510

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Ile Glu Leu Pro Ser Glu Asn Thr Glu Ser Leu Thr Asp Phe Asn Val
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 Asp Val Pro Val Tyr Glu Lys Gln Pro Ala Ile Lys Lys Ile Phe Thr
 530 535 540
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 545 550 555 560
 Asp Ile Arg Asp Ile Ser Leu Thr Ser Ser Phe Asp Asp Ala Leu Leu
 565 570 575
 Phe Ser Asn Lys Val Tyr Ser Phe Phe Ser Met Asp Tyr Ile Lys Thr
 580 585 590
 Ala Asn Lys Val Val Glu Ala Gly Leu Phe Ala Gly Trp Val Lys Gln
 595 600 605
 Ile Val Asn Asp Phe Val Ile Glu Ala Asn Lys Ser Asn Thr Met Asp
 610 615 620
 Lys Ile Ala Asp Ile Ser Leu Ile Val Pro Tyr Ile Gly Leu Ala Leu
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 Asn Val Gly Asn Glu Thr Ala Lys Gly Asn Phe Glu Asn Ala Phe Glu
 645 650 655
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 660 665 670
 Pro Val Val Gly Ala Phe Leu Leu Glu Ser Tyr Ile Asp Asn Lys Asn
 675 680 685
 Lys Ile Ile Lys Thr Ile Asp Asn Ala Leu Thr Lys Arg Asn Glu Lys
 690 695 700
 Trp Ser Asp Met Tyr Gly Leu Ile Val Ala Gln Trp Leu Ser Thr Val
 705 710 715 720
 Asn Thr Gln Phe Tyr Thr Ile Lys Glu Gly Met Tyr Lys Ala Leu Asn
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 Tyr Gln Ala Gln Ala Leu Glu Glu Ile Ile Lys Tyr Arg Tyr Asn Ile
 740 745 750
 Tyr Ser Glu Lys Glu Lys Ser Asn Ile Asn Ile Asp Phe Asn Asp Ile
 755 760 765
 Asn Ser Lys Leu Asn Glu Gly Ile Asn Gln Ala Ile Asp Asn Ile Asn

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770 775 780

Asn Phe Ile Asn Gly Cys Ser Val Ser Tyr Leu Met Lys Lys Met Ile
 785 790 795 800

Pro Leu Ala Val Glu Lys Leu Leu Asp Phe Asp Asn Thr Leu Lys Lys
 805 810 815

Asn Leu Leu Asn Tyr Ile Asp Glu Asn Lys Leu Tyr Leu Ile Gly Ser
 820 825 830

Ala Glu Tyr Glu Lys Ser Lys Val Asn Lys Tyr Leu Lys Thr Ile Met
 835 840 845

Pro Phe Asp Leu Ser Ile Tyr Thr Asn Asp Thr Ile Leu Ile Glu Met
 850 855 860

Phe Asn Lys Tyr Asn Ser
 865 870

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 atcgtggaca gactcaacaa agtcctcgtc tgcacagcg acccgaacat caatatcaac 960
 atatacaaga acaagttcaa agacaagtac aaattcgtcg aggacagcga aggcaaatat 1020

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 aacagc 2586

<210> 94
 <211> 862
 <212> PRT
 <213> Clostridium botulinum

<400> 94

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 35 40 45
 Pro Glu Arg Tyr Thr Phe Gly Tyr Lys Pro Glu Asp Phe Asn Lys Ser
 50 55 60
 Ser Gly Ile Phe Asn Arg Asp Val Cys Glu Tyr Tyr Asp Pro Asp Tyr
 65 70 75 80
 Leu Asn Thr Asn Asp Lys Lys Asn Ile Phe Leu Gln Thr Met Ile Lys
 85 90 95
 Leu Phe Asn Arg Ile Lys Ser Lys Pro Leu Gly Glu Lys Leu Leu Glu
 100 105 110
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 115 120 125
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 130 135 140
 Ser Asn Pro Gly Glu Val Glu Arg Lys Lys Gly Ile Phe Ala Asn Leu
 145 150 155 160
 Ile Ile Phe Gly Pro Gly Pro Val Leu Asn Glu Asn Glu Thr Ile Asp
 165 170 175
 Ile Gly Ile Gln Asn His Phe Ala Ser Arg Glu Gly Phe Gly Gly Ile
 180 185 190
 Met Gln Met Lys Phe Cys Pro Glu Tyr Val Ser Val Phe Asn Asn Val
 195 200 205
 Gln Glu Asn Lys Gly Ala Ser Ile Phe Asn Arg Arg Gly Tyr Phe Ser
 210 215 220
 Asp Pro Ala Leu Ile Leu Met His Glu Leu Ile His Val Leu His Gly
 225 230 235 240
 Leu Tyr Gly Ile Lys Val Asp Asp Leu Pro Ile Val Pro Asn Glu Lys
 245 250 255
 Lys Phe Phe Met Gln Ser Thr Asp Ala Ile Gln Ala Glu Glu Leu Tyr
 260 265 270
 Thr Phe Gly Gly Gln Asp Pro Ser Ile Ile Thr Pro Ser Thr Asp Lys
 275 280 285

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Ser Ile Tyr Asp Lys Val Leu Gln Asn Phe Arg Gly Ile Val Asp Arg
290 295 300

Leu Asn Lys Val Leu Val Cys Ile Ser Asp Pro Asn Ile Asn Ile Asn
305 310 315 320

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

Glu Gly Lys Tyr Ser Ile Asp Val Glu Ser Phe Asp Lys Leu Tyr Lys
340 345 350

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Ser Leu Met Phe Gly Phe Thr Glu Thr Asn Ile Ala Glu Asn Tyr Lys
355 360 365

Ile Lys Thr Arg Ala Ser Tyr Phe Ser Asp Ser Leu Pro Pro Val Lys
370 375 380

Ile Lys Asn Leu Leu Asp Asn Glu Ile Tyr Thr Ile Glu Glu Gly Phe
385 390 395 400

Asn Ile Ser Asp Lys Asp Met Glu Lys Glu Tyr Arg Gly Gln Asn Lys
405 410 415

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Ala Ile Asn Lys Gln Ala Tyr Glu Glu Ile Ser Lys Glu His Leu Ala
420 425 430

Val Tyr Lys Ile Gln Met Cys Ser Ala Ile Glu Gly Arg Ala Pro Gly
435 440 445

Ile Cys Ile Asp Val Asp Asn Glu Asp Leu Phe Phe Ile Ala Asp Lys
450 455 460

Asn Ser Phe Ser Asp Asp Leu Ser Lys Asn Glu Arg Ile Glu Tyr Asn
465 470 475 480

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Thr Gln Ser Asn Tyr Ile Glu Asn Asp Phe Pro Ile Asn Glu Leu Ile
485 490 495

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

Glu Ser Leu Thr Asp Phe Asn Val Asp Val Pro Val Tyr Glu Lys Gln
515 520 525

Pro Ala Ile Lys Lys Ile Phe Thr Asp Glu Asn Thr Ile Phe Gln Tyr
530 535 540

Leu Tyr Ser Gln Thr Phe Pro Leu Asp Ile Arg Asp Ile Ser Leu Thr

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545 550 555 560
 Ser Ser Phe Asp Asp Ala Leu Leu Phe Ser Asn Lys Val Tyr Ser Phe
 565 570 575
 Phe Ser Met Asp Tyr Ile Lys Thr Ala Asn Lys Val Val Glu Ala Gly
 580 585 590
 Leu Phe Ala Gly Trp Val Lys Gln Ile Val Asn Asp Phe Val Ile Glu
 595 600 605
 Ala Asn Lys Ser Asn Thr Met Asp Lys Ile Ala Asp Ile Ser Leu Ile
 610 615 620
 Val Pro Tyr Ile Gly Leu Ala Leu Asn Val Gly Asn Glu Thr Ala Lys
 625 630 635 640
 Gly Asn Phe Glu Asn Ala Phe Glu Ile Ala Gly Ala Ser Ile Leu Leu
 645 650 655
 Glu Phe Ile Pro Glu Leu Leu Ile Pro Val Val Gly Ala Phe Leu Leu
 660 665 670
 Glu Ser Tyr Ile Asp Asn Lys Asn Lys Ile Ile Lys Thr Ile Asp Asn
 675 680 685
 Ala Leu Thr Lys Arg Asn Glu Lys Trp Ser Asp Met Tyr Gly Leu Ile
 690 695 700
 Val Ala Gln Trp Leu Ser Thr Val Asn Thr Gln Phe Tyr Thr Ile Lys
 705 710 715 720
 Glu Gly Met Tyr Lys Ala Leu Asn Tyr Gln Ala Gln Ala Leu Glu Glu
 725 730 735
 Ile Ile Lys Tyr Arg Tyr Asn Ile Tyr Ser Glu Lys Glu Lys Ser Asn
 740 745 750
 Ile Asn Ile Asp Phe Asn Asp Ile Asn Ser Lys Leu Asn Glu Gly Ile
 755 760 765
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 770 775 780
 Ser Tyr Leu Met Lys Lys Met Ile Pro Leu Ala Val Glu Lys Leu Leu
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 Asp Phe Asp Asn Thr Leu Lys Lys Asn Leu Leu Asn Tyr Ile Asp Glu
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Asn Lys Leu Tyr Leu Ile Gly Ser Ala Glu Tyr Glu Lys Ser Lys Val
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Asn Lys Tyr Leu Lys Thr Ile Met Pro Phe Asp Leu Ser Ile Tyr Thr
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Asn Asp Thr Ile Leu Ile Glu Met Phe Asn Lys Tyr Asn Ser
 850 855 860

<210> 95

<211> 2601

<212> DNA

<213> Clostridium botulinum

<400> 95

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aaggctatca acaaacaggc atacgaggag atcagcaaag aacacctcgc agtctacaag     1320
atccagatgt gtagcgctat cgaaggccga gctcccgga tctgcatcga cgttgacaac     1380
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Arg Ile Trp Ile Ile Pro Glu Arg Tyr Thr Phe Gly Tyr Lys Pro Glu
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Asp Phe Asn Lys Ser Ser Gly Ile Phe Asn Arg Asp Val Cys Glu Tyr
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Tyr Asp Pro Asp Tyr Leu Asn Thr Asn Asp Lys Lys Asn Ile Phe Leu
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 Arg Arg Val Pro Leu Glu Glu Phe Asn Thr Asn Ile Ala Ser Val Thr
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 180 185 190
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 210 215 220
 Arg Gly Tyr Phe Ser Asp Pro Ala Leu Ile Leu Met His Glu Leu Ile
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 245 250 255
 Val Pro Asn Glu Lys Lys Phe Phe Met Gln Ser Thr Asp Ala Ile Gln
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 Ala Glu Glu Leu Tyr Thr Phe Gly Gly Gln Asp Pro Ser Ile Ile Thr
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 Pro Ser Thr Asp Lys Ser Ile Tyr Asp Lys Val Leu Gln Asn Phe Arg
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 Gly Ile Val Asp Arg Leu Asn Lys Val Leu Val Cys Ile Ser Asp Pro
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 405 410 415
 Arg Gly Gln Asn Lys Ala Ile Asn Lys Gln Ala Tyr Glu Glu Ile Ser
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 Lys Glu His Leu Ala Val Tyr Lys Ile Gln Met Cys Ser Ala Ile Glu
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 Gly Arg Ala Pro Gly Ile Cys Ile Asp Val Asp Asn Glu Asp Leu Phe
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 465 470 475 480
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 Val Tyr Glu Lys Gln Pro Ala Ile Lys Lys Ile Phe Thr Asp Glu Asn
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 Thr Ile Phe Gln Tyr Leu Tyr Ser Gln Thr Phe Pro Leu Asp Ile Arg
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 Asp Ile Ser Leu Thr Ser Ser Phe Asp Asp Ala Leu Leu Phe Ser Asn
 565 570 575
 Lys Val Tyr Ser Phe Phe Ser Met Asp Tyr Ile Lys Thr Ala Asn Lys
 580 585 590
 Val Val Glu Ala Gly Leu Phe Ala Gly Trp Val Lys Gln Ile Val Asn
 595 600 605

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Asp Phe Val Ile Glu Ala Asn Lys Ser Asn Thr Met Asp Lys Ile Ala
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Asp Ile Ser Leu Ile Val Pro Tyr Ile Gly Leu Ala Leu Asn Val Gly
625 630 635 640

Asn Glu Thr Ala Lys Gly Asn Phe Glu Asn Ala Phe Glu Ile Ala Gly
645 650 655

Ala Ser Ile Leu Leu Glu Phe Ile Pro Glu Leu Leu Ile Pro Val Val
660 665 670

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

Lys Thr Ile Asp Asn Ala Leu Thr Lys Arg Asn Glu Lys Trp Ser Asp
690 695 700

Met Tyr Gly Leu Ile Val Ala Gln Trp Leu Ser Thr Val Asn Thr Gln
705 710 715 720

Phe Tyr Thr Ile Lys Glu Gly Met Tyr Lys Ala Leu Asn Tyr Gln Ala
725 730 735

Gln Ala Leu Glu Glu Ile Ile Lys Tyr Arg Tyr Asn Ile Tyr Ser Glu
740 745 750

Lys Glu Lys Ser Asn Ile Asn Ile Asp Phe Asn Asp Ile Asn Ser Lys
755 760 765

Leu Asn Glu Gly Ile Asn Gln Ala Ile Asp Asn Ile Asn Asn Phe Ile
770 775 780

Asn Gly Cys Ser Val Ser Tyr Leu Met Lys Lys Met Ile Pro Leu Ala
785 790 795 800

Val Glu Lys Leu Leu Asp Phe Asp Asn Thr Leu Lys Lys Asn Leu Leu
805 810 815

Asn Tyr Ile Asp Glu Asn Lys Leu Tyr Leu Ile Gly Ser Ala Glu Tyr
820 825 830

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

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850 855 860

Tyr Asn Ser
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<400> 98

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Phe Ala Arg Gly Thr Gly Arg Tyr Tyr Lys Ala Phe Lys Ile Thr Asp
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Arg Ile Trp Ile Ile Pro Glu Arg Tyr Thr Phe Gly Tyr Lys Pro Glu
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Asp Phe Asn Lys Ser Ser Gly Ile Phe Asn Arg Asp Val Cys Glu Tyr
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Tyr Asp Pro Asp Tyr Leu Asn Thr Asn Asp Lys Lys Asn Ile Phe Leu
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Gln Thr Met Ile Lys Leu Phe Asn Arg Ile Lys Ser Lys Pro Leu Gly
100 105 110

Glu Lys Leu Leu Glu Met Ile Ile Asn Gly Ile Pro Tyr Leu Gly Asp
115 120 125

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Arg Arg Val Pro Leu Glu Glu Phe Asn Thr Asn Ile Ala Ser Val Thr
 130 135 140
 Val Asn Lys Leu Ile Ser Asn Pro Gly Glu Val Glu Arg Lys Lys Gly
 145 150 155 160
 Ile Phe Ala Asn Leu Ile Ile Phe Gly Pro Gly Pro Val Leu Asn Glu
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 Asn Glu Thr Ile Asp Ile Gly Ile Gln Asn His Phe Ala Ser Arg Glu
 180 185 190
 Gly Phe Gly Gly Ile Met Gln Met Lys Phe Cys Pro Glu Tyr Val Ser
 195 200 205
 Val Phe Asn Asn Val Gln Glu Asn Lys Gly Ala Ser Ile Phe Asn Arg
 210 215 220
 Arg Gly Tyr Phe Ser Asp Pro Ala Leu Ile Leu Met His Glu Leu Ile
 225 230 235 240
 His Val Leu His Gly Leu Tyr Gly Ile Lys Val Asp Asp Leu Pro Ile
 245 250 255
 Val Pro Asn Glu Lys Lys Phe Phe Met Gln Ser Thr Asp Ala Ile Gln
 260 265 270
 Ala Glu Glu Leu Tyr Thr Phe Gly Gly Gln Asp Pro Ser Ile Ile Thr
 275 280 285
 Pro Ser Thr Asp Lys Ser Ile Tyr Asp Lys Val Leu Gln Asn Phe Arg
 290 295 300
 Gly Ile Val Asp Arg Leu Asn Lys Val Leu Val Cys Ile Ser Asp Pro
 305 310 315 320
 Asn Ile Asn Ile Asn Ile Tyr Lys Asn Lys Phe Lys Asp Lys Tyr Lys
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 340 345 350
 Asp Lys Leu Tyr Lys Ser Leu Met Phe Gly Phe Thr Glu Thr Asn Ile
 355 360 365
 Ala Glu Asn Tyr Lys Ile Lys Thr Arg Ala Ser Tyr Phe Ser Asp Ser
 370 375 380
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385 390 395 400
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 420 425 430
 Lys Glu His Leu Ala Val Tyr Lys Ile Gln Met Cys Ser Ala Ile Glu
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 Gly Arg Ala Pro Gly Ile Cys Ile Asp Val Asp Asn Glu Asp Leu Phe
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 Arg Ile Glu Tyr Asn Thr Gln Ser Asn Tyr Ile Glu Asn Asp Phe Pro
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 Asp Ile Ser Leu Thr Ser Ser Phe Asp Asp Ala Leu Leu Phe Ser Asn
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 Lys Val Tyr Ser Phe Phe Ser Met Asp Tyr Ile Lys Thr Ala Asn Lys
 580 585 590
 Val Val Glu Ala Gly Leu Phe Ala Gly Trp Val Lys Gln Ile Val Asn
 595 600 605
 Asp Phe Val Ile Glu Ala Asn Lys Ser Asn Thr Met Asp Lys Ile Ala
 610 615 620
 Asp Ile Ser Leu Ile Val Pro Tyr Ile Gly Leu Ala Leu Asn Val Gly
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 Asn Glu Thr Ala Lys Gly Asn Phe Glu Asn Ala Phe Glu Ile Ala Gly
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Ala Ser Ile Leu Leu Glu Phe Ile Pro Glu Leu Leu Ile Pro Val Val
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Gly Ala Phe Leu Leu Glu Ser Tyr Ile Asp Asn Lys Asn Lys Ile Ile
675 680 685

Lys Thr Ile Asp Asn Ala Leu Thr Lys Arg Asn Glu Lys Trp Ser Asp
690 695 700

Met Tyr Gly Leu Ile Val Ala Gln Trp Leu Ser Thr Val Asn Thr Gln
705 710 715 720

Phe Tyr Thr Ile Lys Glu Gly Met Tyr Lys Ala Leu Asn Tyr Gln Ala
725 730 735

Gln Ala Leu Glu Glu Ile Ile Lys Tyr Arg Tyr Asn Ile Tyr Ser Glu
740 745 750

Lys Glu Lys Ser Asn Ile Asn Ile Asp Phe Asn Asp Ile Asn Ser Lys
755 760 765

Leu Asn Glu Gly Ile Asn Gln Ala Ile Asp Asn Ile Asn Asn Phe Ile
770 775 780

Asn Gly Cys Ser Val Ser Tyr Leu Met Lys Lys Met Ile Pro Leu Ala
785 790 795 800

Val Glu Lys Leu Leu Asp Phe Asp Asn Thr Leu Lys Lys Asn Leu Leu
805 810 815

Asn Tyr Ile Asp Glu Asn Lys Leu Tyr Leu Ile Gly Ser Ala Glu Tyr
820 825 830

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

Tyr Asn Ser
865

<210> 99

<211> 2595

<212> DNA

<213> Clostridium botulinum

<400> 99

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Ala Arg Gly Thr Gly Arg Tyr Tyr Lys Ala Phe Lys Ile Thr Asp Arg
 35 40 45

Ile Trp Ile Ile Pro Glu Arg Tyr Thr Phe Gly Tyr Lys Pro Glu Asp
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Phe Asn Lys Ser Ser Gly Ile Phe Asn Arg Asp Val Cys Glu Tyr Tyr
 65 70 75 80

Asp Pro Asp Tyr Leu Asn Thr Asn Asp Lys Lys Asn Ile Phe Leu Gln
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Thr Met Ile Lys Leu Phe Asn Arg Ile Lys Ser Lys Pro Leu Gly Glu
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Lys Leu Leu Glu Met Ile Ile Asn Gly Ile Pro Tyr Leu Gly Asp Arg
 115 120 125

Arg Val Pro Leu Glu Glu Phe Asn Thr Asn Ile Ala Ser Val Thr Val
 130 135 140

Asn Lys Leu Ile Ser Asn Pro Gly Glu Val Glu Arg Lys Lys Gly Ile
 145 150 155 160

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Phe Ala Asn Leu Ile Ile Phe Gly Pro Gly Pro Val Leu Asn Glu Asn
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 180 185 190
 Phe Gly Gly Ile Met Gln Met Lys Phe Cys Pro Glu Tyr Val Ser Val
 195 200 205
 Phe Asn Asn Val Gln Glu Asn Lys Gly Ala Ser Ile Phe Asn Arg Arg
 210 215 220
 Gly Tyr Phe Ser Asp Pro Ala Leu Ile Leu Met His Glu Leu Ile His
 225 230 235 240
 Val Leu His Gly Leu Tyr Gly Ile Lys Val Asp Asp Leu Pro Ile Val
 245 250 255
 Pro Asn Glu Lys Lys Phe Phe Met Gln Ser Thr Asp Ala Ile Gln Ala
 260 265 270
 Glu Glu Leu Tyr Thr Phe Gly Gly Gln Asp Pro Ser Ile Ile Thr Pro
 275 280 285
 Ser Thr Asp Lys Ser Ile Tyr Asp Lys Val Leu Gln Asn Phe Arg Gly
 290 295 300
 Ile Val Asp Arg Leu Asn Lys Val Leu Val Cys Ile Ser Asp Pro Asn
 305 310 315 320
 Ile Asn Ile Asn Ile Tyr Lys Asn Lys Phe Lys Asp Lys Tyr Lys Phe
 325 330 335
 Val Glu Asp Ser Glu Gly Lys Tyr Ser Ile Asp Val Glu Ser Phe Asp
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 Lys Leu Tyr Lys Ser Leu Met Phe Gly Phe Thr Glu Thr Asn Ile Ala
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 Glu Asn Tyr Lys Ile Lys Thr Arg Ala Ser Tyr Phe Ser Asp Ser Leu
 370 375 380
 Pro Pro Val Lys Ile Lys Asn Leu Leu Asp Asn Glu Ile Tyr Thr Ile
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 Glu Glu Gly Phe Asn Ile Ser Asp Lys Asp Met Glu Lys Glu Tyr Arg
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 Gly Gln Asn Lys Ala Ile Asn Lys Gln Ala Tyr Glu Glu Ile Ser Lys
 420 425 430

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Glu His Leu Ala Val Tyr Lys Ile Gln Met Cys Gly Leu Val Pro Arg
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Gly Ser Gly Pro Cys Ile Asp Val Asp Asn Glu Asp Leu Phe Phe Ile
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Ala Asp Lys Asn Ser Phe Ser Asp Asp Leu Ser Lys Asn Glu Arg Ile
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Glu Tyr Asn Thr Gln Ser Asn Tyr Ile Glu Asn Asp Phe Pro Ile Asn
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Glu Leu Ile Leu Asp Thr Asp Leu Ile Ser Lys Ile Glu Leu Pro Arg
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Glu Asn Thr Glu Ser Leu Thr Asp Phe Asn Val Asp Val Pro Val Tyr
 515 520 525

Glu Lys Gln Pro Ala Ile Lys Lys Ile Phe Thr Asp Glu Asn Thr Ile
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Phe Gln Tyr Leu Tyr Ser Gln Thr Phe Pro Leu Asp Ile Arg Asp Ile
 545 550 555 560

Ser Leu Thr Ser Ser Phe Asp Asp Ala Leu Leu Phe Ser Asn Lys Val
 565 570 575

Tyr Ser Phe Phe Ser Met Asp Tyr Ile Lys Thr Ala Asn Lys Val Val
 580 585 590

Glu Ala Gly Leu Phe Ala Gly Trp Val Lys Gln Ile Val Asn Asp Phe
 595 600 605

Val Ile Glu Ala Asn Lys Ser Asn Thr Met Asp Lys Ile Ala Asp Ile
 610 615 620

Ser Leu Ile Val Pro Tyr Ile Gly Leu Ala Leu Asn Val Gly Asn Glu
 625 630 635 640

Thr Ala Lys Gly Asn Phe Glu Asn Ala Phe Glu Ile Ala Gly Ala Ser
 645 650 655

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

Phe Leu Leu Glu Ser Tyr Ile Asp Asn Lys Asn Lys Ile Ile Lys Thr
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<212> DNA
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		gatccagatt	atctgaatac	caacgataag	aagaacatat	tccttcagac	tatgattaaa	300
		ctcttcaacc	gtatcaaaag	caaaccgctc	ggtgaaaaac	tcctcgaat	gattatcaac	360
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 <212> PRT
 <213> Clostridium botulinum

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Ala Arg Gly Thr Gly Arg Tyr Tyr Lys Ala Phe Lys Ile Thr Asp Arg
 35 40 45

Ile Trp Ile Ile Pro Glu Arg Tyr Thr Phe Gly Tyr Lys Pro Glu Asp
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Phe Asn Lys Ser Ser Gly Ile Phe Asn Arg Asp Val Cys Glu Tyr Tyr
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Asp Pro Asp Tyr Leu Asn Thr Asn Asp Lys Lys Asn Ile Phe Leu Gln
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Thr Met Ile Lys Leu Phe Asn Arg Ile Lys Ser Lys Pro Leu Gly Glu
 100 105 110

Lys Leu Leu Glu Met Ile Ile Asn Gly Ile Pro Tyr Leu Gly Asp Arg
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Arg Val Pro Leu Glu Glu Phe Asn Thr Asn Ile Ala Ser Val Thr Val
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Asn Lys Leu Ile Ser Asn Pro Gly Glu Val Glu Arg Lys Lys Gly Ile
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Phe Ala Asn Leu Ile Ile Phe Gly Pro Gly Pro Val Leu Asn Glu Asn
 165 170 175

Glu Thr Ile Asp Ile Gly Ile Gln Asn His Phe Ala Ser Arg Glu Gly
 180 185 190

Phe Gly Gly Ile Met Gln Met Lys Phe Cys Pro Glu Tyr Val Ser Val
 195 200 205

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Phe Asn Asn Val Gln Glu Asn Lys Gly Ala Ser Ile Phe Asn Arg Arg
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Gly Tyr Phe Ser Asp Pro Ala Leu Ile Leu Met His Glu Leu Ile His
225 230 235 240

Val Leu His Gly Leu Tyr Gly Ile Lys Val Asp Asp Leu Pro Ile Val
245 250 255

Pro Asn Glu Lys Lys Phe Phe Met Gln Ser Thr Asp Ala Ile Gln Ala
260 265 270

Glu Glu Leu Tyr Thr Phe Gly Gly Gln Asp Pro Ser Ile Ile Thr Pro
275 280 285

Ser Thr Asp Lys Ser Ile Tyr Asp Lys Val Leu Gln Asn Phe Arg Gly
290 295 300

Ile Val Asp Arg Leu Asn Lys Val Leu Val Cys Ile Ser Asp Pro Asn
305 310 315 320

Ile Asn Ile Asn Ile Tyr Lys Asn Lys Phe Lys Asp Lys Tyr Lys Phe
325 330 335

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

Lys Leu Tyr Lys Ser Leu Met Phe Gly Phe Thr Glu Thr Asn Ile Ala
355 360 365

Glu Asn Tyr Lys Ile Lys Thr Arg Ala Ser Tyr Phe Ser Asp Ser Leu
370 375 380

Pro Pro Val Lys Ile Lys Asn Leu Leu Asp Asn Glu Ile Tyr Thr Ile
385 390 395 400

Glu Glu Gly Phe Asn Ile Ser Asp Lys Asp Met Glu Lys Glu Tyr Arg
405 410 415

Gly Gln Asn Lys Ala Ile Asn Lys Gln Ala Tyr Glu Glu Ile Ser Lys
420 425 430

Glu His Leu Ala Val Tyr Lys Ile Gln Met Cys Glu Asn Leu Tyr Phe
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Gln Gly Ile Cys Ile Asp Val Asp Asn Glu Asp Leu Phe Phe Ile Ala
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Asp Lys Asn Ser Phe Ser Asp Asp Leu Ser Lys Asn Glu Arg Ile Glu

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 Asn Thr Glu Ser Leu Thr Asp Phe Asn Val Asp Val Pro Val Tyr Glu
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 Ile Lys Glu Gly Met Tyr Lys Ala Leu Asn Tyr Gln Ala Gln Ala Leu
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Glu Glu Ile Ile Lys Tyr Arg Tyr Asn Ile Tyr Ser Glu Lys Glu Lys
740 745 750

Ser Asn Ile Asn Ile Asp Phe Asn Asp Ile Asn Ser Lys Leu Asn Glu
755 760 765

Gly Ile Asn Gln Ala Ile Asp Asn Ile Asn Asn Phe Ile Asn Gly Cys
770 775 780

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

Leu Leu Asp Phe Asp Asn Thr Leu Lys Lys Asn Leu Leu Asn Tyr Ile
805 810 815

Asp Glu Asn Lys Leu Tyr Leu Ile Gly Ser Ala Glu Tyr Glu Lys Ser
820 825 830

Lys Val Asn Lys Tyr Leu Lys Thr Ile Met Pro Phe Asp Leu Ser Ile
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Tyr Thr Asn Asp Thr Ile Leu Ile Glu Met Phe Asn Lys Tyr Asn Ser
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 <212> PRT
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 Ile Trp Ile Ile Pro Glu Arg Tyr Thr Phe Gly Tyr Lys Pro Glu Asp
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 Phe Asn Lys Ser Ser Gly Ile Phe Asn Arg Asp Val Cys Glu Tyr Tyr
 65 70 75 80
 Asp Pro Asp Tyr Leu Asn Thr Asn Asp Lys Lys Asn Ile Phe Leu Gln
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 Thr Met Ile Lys Leu Phe Asn Arg Ile Lys Ser Lys Pro Leu Gly Glu
 100 105 110
 Lys Leu Leu Glu Met Ile Ile Asn Gly Ile Pro Tyr Leu Gly Asp Arg
 115 120 125
 Arg Val Pro Leu Glu Glu Phe Asn Thr Asn Ile Ala Ser Val Thr Val
 130 135 140
 Asn Lys Leu Ile Ser Asn Pro Gly Glu Val Glu Arg Lys Lys Gly Ile
 145 150 155 160
 Phe Ala Asn Leu Ile Ile Phe Gly Pro Gly Pro Val Leu Asn Glu Asn
 165 170 175
 Glu Thr Ile Asp Ile Gly Ile Gln Asn His Phe Ala Ser Arg Glu Gly
 180 185 190
 Phe Gly Gly Ile Met Gln Met Lys Phe Cys Pro Glu Tyr Val Ser Val
 195 200 205
 Phe Asn Asn Val Gln Glu Asn Lys Gly Ala Ser Ile Phe Asn Arg Arg
 210 215 220
 Gly Tyr Phe Ser Asp Pro Ala Leu Ile Leu Met His Glu Leu Ile His
 225 230 235 240
 Val Leu His Gly Leu Tyr Gly Ile Lys Val Asp Asp Leu Pro Ile Val
 245 250 255

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Pro Asn Glu Lys Lys Phe Phe Met Gln Ser Thr Asp Ala Ile Gln Ala
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 Glu Glu Leu Tyr Thr Phe Gly Gly Gln Asp Pro Ser Ile Ile Thr Pro
 275 280 285
 Ser Thr Asp Lys Ser Ile Tyr Asp Lys Val Leu Gln Asn Phe Arg Gly
 290 295 300
 Ile Val Asp Arg Leu Asn Lys Val Leu Val Cys Ile Ser Asp Pro Asn
 305 310 315 320
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 Val Glu Asp Ser Glu Gly Lys Tyr Ser Ile Asp Val Glu Ser Phe Asp
 340 345 350
 Lys Leu Tyr Lys Ser Leu Met Phe Gly Phe Thr Glu Thr Asn Ile Ala
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 Glu Asn Tyr Lys Ile Lys Thr Arg Ala Ser Tyr Phe Ser Asp Ser Leu
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 Pro Pro Val Lys Ile Lys Asn Leu Leu Asp Asn Glu Ile Tyr Thr Ile
 385 390 395 400
 Glu Glu Gly Phe Asn Ile Ser Asp Lys Asp Met Glu Lys Glu Tyr Arg
 405 410 415
 Gly Gln Asn Lys Ala Ile Asn Lys Gln Ala Tyr Glu Glu Ile Ser Lys
 420 425 430
 Glu His Leu Ala Val Tyr Lys Ile Gln Met Cys Ser Ala Ile Glu Gly
 435 440 445
 Arg Ala Pro Gly Ile Cys Ile Asp Val Asp Asn Glu Asp Leu Phe Phe
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 Ile Ala Asp Lys Asn Ser Phe Ser Asp Asp Leu Ser Lys Asn Glu Arg
 465 470 475 480
 Ile Glu Tyr Asn Thr Gln Ser Asn Tyr Ile Glu Asn Asp Phe Pro Ile
 485 490 495
 Asn Glu Leu Ile Leu Asp Thr Asp Leu Ile Ser Lys Ile Glu Leu Pro
 500 505 510
 Arg Glu Asn Thr Glu Ser Leu Thr Asp Phe Asn Val Asp Val Pro Val
 515 520 525

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 Phe Val Ile Glu Ala Asn Lys Ser Asn Thr Met Asp Lys Ile Ala Asp
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 Ser Ile Leu Leu Glu Phe Ile Pro Glu Leu Leu Ile Pro Val Val Gly
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 Ala Phe Leu Leu Glu Ser Tyr Ile Asp Asn Lys Asn Lys Ile Ile Lys
 675 680 685
 Thr Ile Asp Asn Ala Leu Thr Lys Arg Asn Glu Lys Trp Ser Asp Met
 690 695 700
 Tyr Gly Leu Ile Val Ala Gln Trp Leu Ser Thr Val Asn Thr Gln Phe
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 Ala Leu Glu Glu Ile Ile Lys Tyr Arg Tyr Asn Ile Tyr Ser Glu Lys
 740 745 750
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 755 760 765
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 Gly Cys Ser Val Ser Tyr Leu Met Lys Lys Met Ile Pro Leu Ala Val

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785 790 795 800

Glu Lys Leu Leu Asp Phe Asp Asn Thr Leu Lys Lys Asn Leu Leu Asn
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Tyr Ile Asp Glu Asn Lys Leu Tyr Leu Ile Gly Ser Ala Glu Tyr Glu
820 825 830

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

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

Asn Ser
865

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<211> 2628
<212> DNA
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 <212> PRT
 <213> Clostridium botulinum

<400> 106

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 Asp Pro Asp Tyr Leu Asn Thr Asn Asp Lys Lys Asn Ile Phe Leu Gln
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 Thr Met Ile Lys Leu Phe Asn Arg Ile Lys Ser Lys Pro Leu Gly Glu
 100 105 110
 Lys Leu Leu Glu Met Ile Ile Asn Gly Ile Pro Tyr Leu Gly Asp Arg
 115 120 125
 Arg Val Pro Leu Glu Glu Phe Asn Thr Asn Ile Ala Ser Val Thr Val
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 Asn Lys Leu Ile Ser Asn Pro Gly Glu Val Glu Arg Lys Lys Gly Ile
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 Phe Ala Asn Leu Ile Ile Phe Gly Pro Gly Pro Val Leu Asn Glu Asn
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 Glu Thr Ile Asp Ile Gly Ile Gln Asn His Phe Ala Ser Arg Glu Gly
 180 185 190
 Phe Gly Gly Ile Met Gln Met Lys Phe Cys Pro Glu Tyr Val Ser Val
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 Gly Tyr Phe Ser Asp Pro Ala Leu Ile Leu Met His Glu Leu Ile His
 225 230 235 240
 Val Leu His Gly Leu Tyr Gly Ile Lys Val Asp Asp Leu Pro Ile Val
 245 250 255
 Pro Asn Glu Lys Lys Phe Phe Met Gln Ser Thr Asp Ala Ile Gln Ala
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 Glu Glu Leu Tyr Thr Phe Gly Gly Gln Asp Pro Ser Ile Ile Thr Pro
 275 280 285
 Ser Thr Asp Lys Ser Ile Tyr Asp Lys Val Leu Gln Asn Phe Arg Gly
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Ile Val Asp Arg Leu Asn Lys Val Leu Val Cys Ile Ser Asp Pro Asn
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Ile Asn Ile Asn Ile Tyr Lys Asn Lys Phe Lys Asp Lys Tyr Lys Phe
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355 360 365

Glu Asn Tyr Lys Ile Lys Thr Arg Ala Ser Tyr Phe Ser Asp Ser Leu
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Pro Pro Val Lys Ile Lys Asn Leu Leu Asp Asn Glu Ile Tyr Thr Ile
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Gly Gln Asn Lys Ala Ile Asn Lys Gln Ala Tyr Glu Glu Ile Ser Lys
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Leu Tyr Asp Asp Asp Asp Lys Asp Arg Trp Gly Ser Ser Arg Ile Cys
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Thr Asp Leu Ile Ser Lys Ile Glu Leu Pro Ser Glu Asn Thr Glu Ser
515 520 525

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

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 Ile Pro Glu Leu Leu Ile Pro Val Val Gly Ala Phe Leu Leu Glu Ser
 675 680 685
 Tyr Ile Asp Asn Lys Asn Lys Ile Ile Lys Thr Ile Asp Asn Ala Leu
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 755 760 765
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 785 790 795 800
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 Asp Asn Thr Leu Lys Lys Asn Leu Leu Asn Tyr Ile Asp Glu Asn Lys
 820 825 830

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Leu Tyr Leu Ile Gly Ser Ala Glu Tyr Glu Lys Ser Lys Val Asn Lys
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<212> DNA

<213> Clostridium botulinum

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<400> 107

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<400> 108

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Ile Trp Ile Ile Pro Glu Arg Tyr Thr Phe Gly Tyr Lys Pro Glu Asp
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Phe Asn Lys Ser Ser Gly Ile Phe Asn Arg Asp Val Cys Glu Tyr Tyr
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 Arg Val Pro Leu Glu Glu Phe Asn Thr Asn Ile Ala Ser Val Thr Val
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 Phe Ala Asn Leu Ile Ile Phe Gly Pro Gly Pro Val Leu Asn Glu Asn
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 Glu Thr Ile Asp Ile Gly Ile Gln Asn His Phe Ala Ser Arg Glu Gly
 180 185 190
 Phe Gly Gly Ile Met Gln Met Lys Phe Cys Pro Glu Tyr Val Ser Val
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 Phe Asn Asn Val Gln Glu Asn Lys Gly Ala Ser Ile Phe Asn Arg Arg
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 Gly Tyr Phe Ser Asp Pro Ala Leu Ile Leu Met His Glu Leu Ile His
 225 230 235 240
 Val Leu His Gly Leu Tyr Gly Ile Lys Val Asp Asp Leu Pro Ile Val
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 Pro Asn Glu Lys Lys Phe Phe Met Gln Ser Thr Asp Ala Ile Gln Ala
 260 265 270
 Glu Glu Leu Tyr Thr Phe Gly Gly Gln Asp Pro Ser Ile Ile Thr Pro
 275 280 285
 Ser Thr Asp Lys Ser Ile Tyr Asp Lys Val Leu Gln Asn Phe Arg Gly
 290 295 300
 Ile Val Asp Arg Leu Asn Lys Val Leu Val Cys Ile Ser Asp Pro Asn
 305 310 315 320
 Ile Asn Ile Asn Ile Tyr Lys Asn Lys Phe Lys Asp Lys Tyr Lys Phe
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 Val Glu Asp Ser Glu Gly Lys Tyr Ser Ile Asp Val Glu Ser Phe Asp

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 Pro Pro Val Lys Ile Lys Asn Leu Leu Asp Asn Glu Ile Tyr Thr Ile
 385 390 395 400
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 405 410 415
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 Ser Gln Thr Phe Pro Leu Asp Ile Arg Asp Ile Ser Leu Thr Ser Ser
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 Met Asp Tyr Ile Lys Thr Ala Asn Lys Val Val Glu Ala Gly Leu Phe
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Tyr Ile Gly Leu Ala Leu Asn Val Gly Asn Glu Thr Ala Lys Gly Asn
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Phe Glu Asn Ala Phe Glu Ile Ala Gly Ala Ser Ile Leu Leu Glu Phe
660 665 670

Ile Pro Glu Leu Leu Ile Pro Val Val Gly Ala Phe Leu Leu Glu Ser
675 680 685

Tyr Ile Asp Asn Lys Asn Lys Ile Ile Lys Thr Ile Asp Asn Ala Leu
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Thr Lys Arg Asn Glu Lys Trp Ser Asp Met Tyr Gly Leu Ile Val Ala
705 710 715 720

Gln Trp Leu Ser Thr Val Asn Thr Gln Phe Tyr Thr Ile Lys Glu Gly
725 730 735

Met Tyr Lys Ala Leu Asn Tyr Gln Ala Gln Ala Leu Glu Glu Ile Ile
740 745 750

Lys Tyr Arg Tyr Asn Ile Tyr Ser Glu Lys Glu Lys Ser Asn Ile Asn
755 760 765

Ile Asp Phe Asn Asp Ile Asn Ser Lys Leu Asn Glu Gly Ile Asn Gln
770 775 780

Ala Ile Asp Asn Ile Asn Asn Phe Ile Asn Gly Cys Ser Val Ser Tyr
785 790 795 800

Leu Met Lys Lys Met Ile Pro Leu Ala Val Glu Lys Leu Leu Asp Phe
805 810 815

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

Leu Tyr Leu Ile Gly Ser Ala Glu Tyr Glu Lys Ser Lys Val Asn Lys
835 840 845

Tyr Leu Lys Thr Ile Met Pro Phe Asp Leu Ser Ile Tyr Thr Asn Asp
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 atcaaaacca tcgacaacgc tctgacaaa cgtaacgaaa aatggagtga tatgtacgg 3780

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ctgacgcttg ctcagtggt gagcacgctc aacacccagt tctacacat caaagaaggt 3840
 atgtacaaag ctctgaacta ccaggctcag gctctggaag agatcatcaa ataccgttac 3900
 aacatctaca gtgagaagga aaagagtaac atcaacatcg acttcaacga catcaacagc 3960
 aaactgaacg aaggtatcaa ccaggctatc gacaacatca acaacttcat caacgggttg 4020
 agtggttagct acctgatgaa gaagatgac ccgctggctg ttgaaaaact gctggacttc 4080
 gacaacaccc tgaaaaagaa cctgctgaac tacatcgacg aaaacaagct gtacctgac 4140
 ggtagtgctg aatacgaaaa aagtaaagtg aacaaatacc tgaagaccat catgccgttc 4200
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<210> 110
 <211> 1420
 <212> PRT
 <213> Clostridium botulinum

<400> 110

Met Lys Thr Glu Glu Gly Lys Leu Val Ile Trp Ile Asn Gly Asp Lys
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Gly Tyr Asn Gly Leu Ala Glu Val Gly Lys Lys Phe Glu Lys Asp Thr
 20 25 30

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Gly Ile Lys Val Thr Val Glu His Pro Asp Lys Leu Glu Glu Lys Phe
 35 40 45

Pro Gln Val Ala Ala Thr Gly Asp Gly Pro Asp Ile Ile Phe Trp Ala
 50 55 60

His Asp Arg Phe Gly Gly Tyr Ala Gln Ser Gly Leu Leu Ala Glu Ile
 65 70 75 80

Thr Pro Asp Lys Ala Phe Gln Asp Lys Leu Tyr Pro Phe Thr Trp Asp
 85 90 95

Ala Val Arg Tyr Asn Gly Lys Leu Ile Ala Tyr Pro Ile Ala Val Glu
 100 105 110

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Ala Leu Ser Leu Ile Tyr Asn Lys Asp Leu Leu Pro Asn Pro Pro Lys
 115 120 125

Thr Trp Glu Glu Ile Pro Ala Leu Asp Lys Glu Leu Lys Ala Lys Gly
 130 135 140

Lys Ser Ala Leu Met Phe Asn Leu Gln Glu Pro Tyr Phe Thr Trp Pro
 145 150 155 160

Leu Ile Ala Ala Asp Gly Gly Tyr Ala Phe Lys Tyr Glu Asn Gly Lys
 165 170 175

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Tyr Asp Ile Lys Asp Val Gly Val Asp Asn Ala Gly Ala Lys Ala Gly
180 185 190

Leu Thr Phe Leu Val Asp Leu Ile Lys Asn Lys His Met Asn Ala Asp
195 200 205

Thr Asp Tyr Ser Ile Ala Glu Ala Ala Phe Asn Lys Gly Glu Thr Ala
210 215 220

Met Thr Ile Asn Gly Pro Trp Ala Trp Ser Asn Ile Asp Thr Ser Lys
225 230 235 240

Val Asn Tyr Gly Val Thr Val Leu Pro Thr Phe Lys Gly Gln Pro Ser
245 250 255

Lys Pro Phe Val Gly Val Leu Ser Ala Gly Ile Asn Ala Ala Ser Pro
260 265 270

Asn Lys Glu Leu Ala Lys Glu Phe Leu Glu Asn Tyr Leu Leu Thr Asp
275 280 285

Glu Gly Leu Glu Ala Val Asn Lys Asp Lys Pro Leu Gly Ala Val Ala
290 295 300

Leu Lys Ser Tyr Glu Glu Glu Leu Ala Lys Asp Pro Arg Ile Ala Ala
305 310 315 320

Thr Met Glu Asn Ala Gln Lys Gly Glu Ile Met Pro Asn Ile Pro Gln
325 330 335

Met Ser Ala Phe Trp Tyr Ala Val Arg Thr Ala Val Ile Asn Ala Ala
340 345 350

Ser Gly Arg Gln Thr Val Asp Glu Ala Leu Lys Asp Ala Gln Thr Asn
355 360 365

Ser Ser Ser Asn Asn Asn Asn Asn Asn Asn Asn Asn Asn Leu Gly Ile
370 375 380

Glu Gly Arg Ile Ser Glu Phe Arg Glu Ser Gly Ala Ile Ser Gly Asp
385 390 395 400

Ser Leu Ile Ser Leu Ala Ser Thr Gly Lys Arg Val Ser Ile Lys Asp
405 410 415

Leu Leu Asp Glu Lys Asp Phe Glu Ile Trp Ala Ile Asn Glu Gln Thr
420 425 430

Met Lys Leu Glu Ser Ala Lys Val Ser Arg Val Phe Cys Thr Gly Lys

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

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Pro Gly Glu Val Glu Arg Lys Lys Gly Ile Phe Ala Asn Leu Ile Ile
705 710 715 720

Phe Gly Pro Gly Pro Val Leu Asn Glu Asn Glu Thr Ile Asp Ile Gly
725 730 735

Ile Gln Asn His Phe Ala Ser Arg Glu Gly Phe Gly Gly Ile Met Gln
740 745 750

Met Lys Phe Cys Pro Glu Tyr Val Ser Val Phe Asn Asn Val Gln Glu
755 760 765

Asn Lys Gly Ala Ser Ile Phe Asn Arg Arg Gly Tyr Phe Ser Asp Pro
770 775 780

Ala Leu Ile Leu Met His Glu Leu Ile His Val Leu His Gly Leu Tyr
785 790 795 800

Gly Ile Lys Val Asp Asp Leu Pro Ile Val Pro Asn Glu Lys Lys Phe
805 810 815

Phe Met Gln Ser Thr Asp Ala Ile Gln Ala Glu Glu Leu Tyr Thr Phe
820 825 830

Gly Gly Gln Asp Pro Ser Ile Ile Thr Pro Ser Thr Asp Lys Ser Ile
835 840 845

Tyr Asp Lys Val Leu Gln Asn Phe Arg Gly Ile Val Asp Arg Leu Asn
850 855 860

Lys Val Leu Val Cys Ile Ser Asp Pro Asn Ile Asn Ile Asn Ile Tyr
865 870 875 880

Lys Asn Lys Phe Lys Asp Lys Tyr Lys Phe Val Glu Asp Ser Glu Gly
885 890 895

Lys Tyr Ser Ile Asp Val Glu Ser Phe Asp Lys Leu Tyr Lys Ser Leu
900 905 910

Met Phe Gly Phe Thr Glu Thr Asn Ile Ala Glu Asn Tyr Lys Ile Lys
915 920 925

Thr Arg Ala Ser Tyr Phe Ser Asp Ser Leu Pro Pro Val Lys Ile Lys
930 935 940

Asn Leu Leu Asp Asn Glu Ile Tyr Thr Ile Glu Glu Gly Phe Asn Ile
945 950 955 960

Ser Asp Lys Asp Met Glu Lys Glu Tyr Arg Gly Gln Asn Lys Ala Ile
965 970 975

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Asn Lys Gln Ala Tyr Glu Glu Ile Ser Lys Glu His Leu Ala Val Tyr
 980 985 990

Lys Ile Gln Met Cys Ser Ala Ile Glu Gly Arg Ala Pro Gly Ile Cys
 995 1000 1005

Ile Asp Val Asp Asn Glu Asp Leu Phe Phe Ile Ala Asp Lys Asn
 1010 1015 1020

Ser Phe Ser Asp Asp Leu Ser Lys Asn Glu Arg Ile Glu Tyr Asn
 1025 1030 1035

Thr Gln Ser Asn Tyr Ile Glu Asn Asp Phe Pro Ile Asn Glu Leu
 1040 1045 1050

Ile Leu Asp Thr Asp Leu Ile Ser Lys Ile Glu Leu Pro Arg Glu
 1055 1060 1065

Asn Thr Glu Ser Leu Thr Asp Phe Asn Val Asp Val Pro Val Tyr
 1070 1075 1080

Glu Lys Gln Pro Ala Ile Lys Lys Ile Phe Thr Asp Glu Asn Thr
 1085 1090 1095

Ile Phe Gln Tyr Leu Tyr Ser Gln Thr Phe Pro Leu Asp Ile Arg
 1100 1105 1110

Asp Ile Ser Leu Thr Ser Ser Phe Asp Asp Ala Leu Leu Phe Ser
 1115 1120 1125

Asn Lys Val Tyr Ser Phe Phe Ser Met Asp Tyr Ile Lys Thr Ala
 1130 1135 1140

Asn Lys Val Val Glu Ala Gly Leu Phe Ala Gly Trp Val Lys Gln
 1145 1150 1155

Ile Val Asn Asp Phe Val Ile Glu Ala Asn Lys Ser Asn Thr Met
 1160 1165 1170

Asp Lys Ile Ala Asp Ile Ser Leu Ile Val Pro Tyr Ile Gly Leu
 1175 1180 1185

Ala Leu Asn Val Gly Asn Glu Thr Ala Lys Gly Asn Phe Glu Asn
 1190 1195 1200

Ala Phe Glu Ile Ala Gly Ala Ser Ile Leu Leu Glu Phe Ile Pro
 1205 1210 1215

Glu Leu Leu Ile Pro Val Val Gly Ala Phe Leu Leu Glu Ser Tyr

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1220 1225 1230
 Ile Asp Asn Lys Asn Lys Ile Ile Lys Thr Ile Asp Asn Ala Leu
 1235 1240 1245
 Thr Lys Arg Asn Glu Lys Trp Ser Asp Met Tyr Gly Leu Ile Val
 1250 1255 1260
 Ala Gln Trp Leu Ser Thr Val Asn Thr Gln Phe Tyr Thr Ile Lys
 1265 1270 1275
 Glu Gly Met Tyr Lys Ala Leu Asn Tyr Gln Ala Gln Ala Leu Glu
 1280 1285 1290
 Glu Ile Ile Lys Tyr Arg Tyr Asn Ile Tyr Ser Glu Lys Glu Lys
 1295 1300 1305
 Ser Asn Ile Asn Ile Asp Phe Asn Asp Ile Asn Ser Lys Leu Asn
 1310 1315 1320
 Glu Gly Ile Asn Gln Ala Ile Asp Asn Ile Asn Asn Phe Ile Asn
 1325 1330 1335
 Gly Cys Ser Val Ser Tyr Leu Met Lys Lys Met Ile Pro Leu Ala
 1340 1345 1350
 Val Glu Lys Leu Leu Asp Phe Asp Asn Thr Leu Lys Lys Asn Leu
 1355 1360 1365
 Leu Asn Tyr Ile Asp Glu Asn Lys Leu Tyr Leu Ile Gly Ser Ala
 1370 1375 1380
 Glu Tyr Glu Lys Ser Lys Val Asn Lys Tyr Leu Lys Thr Ile Met
 1385 1390 1395
 Pro Phe Asp Leu Ser Ile Tyr Thr Asn Asp Thr Ile Leu Ile Glu
 1400 1405 1410
 Met Phe Asn Lys Tyr Asn Ser
 1415 1420

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 <211> 2664
 <212> DNA
 <213> Clostridium botulinum

<400> 111
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 accggacggt actacaaggc ttttaagatc accgaccgta tctggatcat cccggaacgt 180

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tacaccttcg gttacaaacc tgaggacttc aacaagagta gcgggatttt caatcgtgac	240
gtctgcgagt actatgatcc agattatctg aataccaaacg ataagaagaa catattcctt	300
cagactatga ttaaaactctt caaccgtatc aaaagcaaac cgctcgggtga aaaactcctc	360
gaaatgatta ttaacggtat cccgtacctc ggtgaccgtc gtgtcccgtc cgaagagttc	420
aacaccaaca tcgcaagcgt caccgtcaac aaactcatca gcaacccagg tgaagtcgaa	480
cgtaaaaaag gtatcttcgc aaacctcatc atcttcggtc cgggtccggt cctcaacgaa	540
aacgaaacca tcgacatcgg tatccagaac cacttcgcaa gccgtgaagg ttctcgggtgt	600
atcatgcaga tgaaattctg cccggaatac gtcagcgtct tcaacaacgt ccaggaaaac	660
aaaggtgcaa gcatcttcaa ccgtcgtggt tacttcagcg acccggcact catcctcatg	720
catgaactca tccacgtcct ccacggtctc tacggtatca aagttgacga cctcccgatc	780
gtcccgaacg agaagaaatt ctatcatgcag agcaccgacg caatccaggc tgaggaaatc	840
tacaccttcg gtggccaaga cccaagtatc ataaccocgt ccaccgacaa aagcatctac	900
gacaaagtc cccagaactt caggggtatc gtggacagac tcaacaaagt cctcgtctgc	960
atcagcgacc cgaacatcaa tatcaacata tacaagaaca agttcaaaga caagtacaaa	1020
ttcgtcgagg acagcgaagg caaatacagc atcgacgtag aaagtttoga caagctctac	1080
aaaagcctca tgttcggttt caccgaaacc aacatcgccg agaactacaa gatcaagaca	1140
agggcaggtt acttcagcga cagcctcccg cctgtcaaaa tcaagaacct cttagacaac	1200
gagatttaca caattgaaga gggcttcaac atcagtgaca aagacatgga gaaggaatac	1260
agaggtcaga acaaggctat caacaaacag gcatacgagg agatcagcaa agaacacctc	1320
gcagcttaca agatccagat gtgtaaatct gacgacgacg acaaagctcc cgggatctgc	1380
atcgacgttg acaacgaaga cctgttcttc atcgctgaca aaaacagctt cagtgacgac	1440
ctgagcaaaa acgaacgtat cgaatacaac acccagagca actacatcga aaacgacttc	1500
ccgatcaacg aactgatcct ggacaccgac ctgataagta aaatcgaact gcctagggaa	1560
aacaccgaaa gtctgaccga cttcaacgtt gacgttcggg tttaacgaaa acagccggct	1620
atcaagaaaa tottcaccga cgaaaacacc atcttccagt acctgtacag ccagaccttc	1680
ccgtgggaca tccgtgacat cagtctgacc agcagtttcg acgacgctct gctgttcagc	1740
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gcagggctgt tcgctggttg ggttaaacag atcgtaaacg acttcgttat cgaagctaac	1860
aaaagcaaca ctatggacaa aatcgctgac atcagtotga tcgttcgta catcggctctg	1920
gctctgaacg ttggtaacga aaccgctaaa ggtaactttg aaaacgcttt cgagatcgct	1980
gggtcaagca tcctgctgga gttcatcccg gaactgctga tcccggttgt tgggtctttc	2040
ctgctggaaa gttacatcga caacaaaaac aagatcatca aaaccatcga caacgctctg	2100
accaaacgta acgaaaaatg gagtgatatg tacggtctga tcgttgctca gtggtgagc	2160

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accgtcaaca cccagttcta caccatcaaa gaaggtatgt acaaagctct gaactaccag 2220
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 agtaacatca acatcgactt caacgacatc aacagcaaac tgaacgaagg tatcaaccag 2340
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 atgatccgcg tggctgttga aaaactgctg gacttcgaca acaccctgaa aaagaacctg 2460
 ctgaactaca tcgacgaaaa caagctgtac ctgatcggta gtgctgaata cgaaaaaagt 2520
 aaagtgaaca aatacctgaa gaccatcatg ccgttcgacc tgagtatcta caccaacgac 2580
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 ccagctttct tgtacaaagt ggtc 2664

<210> 112
 <211> 888
 <212> PRT
 <213> Clostridium botulinum

<400> 112

Thr Ser Leu Tyr Lys Lys Ala Gly Phe Gly Ser Met Pro Val Thr Ile
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Asn Asn Phe Asn Tyr Asn Asp Pro Ile Asp Asn Asn Asn Ile Ile Met
 20 25 30

Met Glu Pro Pro Phe Ala Arg Gly Thr Gly Arg Tyr Tyr Lys Ala Phe
 35 40 45

Lys Ile Thr Asp Arg Ile Trp Ile Ile Pro Glu Arg Tyr Thr Phe Gly
 50 55 60

Tyr Lys Pro Glu Asp Phe Asn Lys Ser Ser Gly Ile Phe Asn Arg Asp
 65 70 75 80

Val Cys Glu Tyr Tyr Asp Pro Asp Tyr Leu Asn Thr Asn Asp Lys Lys
 85 90 95

Asn Ile Phe Leu Gln Thr Met Ile Lys Leu Phe Asn Arg Ile Lys Ser
 100 105 110

Lys Pro Leu Gly Glu Lys Leu Leu Glu Met Ile Ile Asn Gly Ile Pro
 115 120 125

Tyr Leu Gly Asp Arg Arg Val Pro Leu Glu Glu Phe Asn Thr Asn Ile
 130 135 140

Ala Ser Val Thr Val Asn Lys Leu Ile Ser Asn Pro Gly Glu Val Glu
 145 150 155 160

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Arg Lys Lys Gly Ile Phe Ala Asn Leu Ile Ile Phe Gly Pro Gly Pro
 165 170 175
 Val Leu Asn Glu Asn Glu Thr Ile Asp Ile Gly Ile Gln Asn His Phe
 180 185 190
 Ala Ser Arg Glu Gly Phe Gly Gly Ile Met Gln Met Lys Phe Cys Pro
 195 200 205
 Glu Tyr Val Ser Val Phe Asn Asn Val Gln Glu Asn Lys Gly Ala Ser
 210 215 220
 Ile Phe Asn Arg Arg Gly Tyr Phe Ser Asp Pro Ala Leu Ile Leu Met
 225 230 235 240
 His Glu Leu Ile His Val Leu His Gly Leu Tyr Gly Ile Lys Val Asp
 245 250 255
 Asp Leu Pro Ile Val Pro Asn Glu Lys Lys Phe Phe Met Gln Ser Thr
 260 265 270
 Asp Ala Ile Gln Ala Glu Glu Leu Tyr Thr Phe Gly Gly Gln Asp Pro
 275 280 285
 Ser Ile Ile Thr Pro Ser Thr Asp Lys Ser Ile Tyr Asp Lys Val Leu
 290 295 300
 Gln Asn Phe Arg Gly Ile Val Asp Arg Leu Asn Lys Val Leu Val Cys
 305 310 315 320
 Ile Ser Asp Pro Asn Ile Asn Ile Asn Ile Tyr Lys Asn Lys Phe Lys
 325 330 335
 Asp Lys Tyr Lys Phe Val Glu Asp Ser Glu Gly Lys Tyr Ser Ile Asp
 340 345 350
 Val Glu Ser Phe Asp Lys Leu Tyr Lys Ser Leu Met Phe Gly Phe Thr
 355 360 365
 Glu Thr Asn Ile Ala Glu Asn Tyr Lys Ile Lys Thr Arg Ala Ser Tyr
 370 375 380
 Phe Ser Asp Ser Leu Pro Pro Val Lys Ile Lys Asn Leu Leu Asp Asn
 385 390 395 400
 Glu Ile Tyr Thr Ile Glu Glu Gly Phe Asn Ile Ser Asp Lys Asp Met
 405 410 415
 Glu Lys Glu Tyr Arg Gly Gln Asn Lys Ala Ile Asn Lys Gln Ala Tyr
 420 425 430

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

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690 695 700

Glu Lys Trp Ser Asp Met Tyr Gly Leu Ile Val Ala Gln Trp Leu Ser
705 710 715 720

Thr Val Asn Thr Gln Phe Tyr Thr Ile Lys Glu Gly Met Tyr Lys Ala
725 730 735

Leu Asn Tyr Gln Ala Gln Ala Leu Glu Glu Ile Ile Lys Tyr Arg Tyr
740 745 750

Asn Ile Tyr Ser Glu Lys Glu Lys Ser Asn Ile Asn Ile Asp Phe Asn
755 760 765

Asp Ile Asn Ser Lys Leu Asn Glu Gly Ile Asn Gln Ala Ile Asp Asn
770 775 780

Ile Asn Asn Phe Ile Asn Gly Cys Ser Val Ser Tyr Leu Met Lys Lys
785 790 795 800

Met Ile Pro Leu Ala Val Glu Lys Leu Leu Asp Phe Asp Asn Thr Leu
805 810 815

Lys Lys Asn Leu Leu Asn Tyr Ile Asp Glu Asn Lys Leu Tyr Leu Ile
820 825 830

Gly Ser Ala Glu Tyr Glu Lys Ser Lys Val Asn Lys Tyr Leu Lys Thr
835 840 845

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

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

Pro Ala Phe Leu Tyr Lys Val Val
885

<210> 113
<211> 1375
<212> DNA
<213> Clostridium botulinum

<400> 113
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atcaccgacc gtatctggat catcccggaa cgttacacct tcggttacaa acctgaggac 180
ttcaacaaga gtagcgggat tttcaatcgt gacgtctgcg agtactatga tccagattat 240
ctgaataacca acgataagaa gaacatattc cttcagacta tgattaaact cttcaaccgt 300

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atcaaaagca aaccgctcgg tgaaaaactc ctcgaaatga ttatcaacgg tatcccgtag 360
 ctcggtgacc gtcgtgtccc gtcgaagag ttcaacacca acatcgcaag cgtcacccgac 420
 aacaaactca tcagcaaccc aggtgaagtc gaacgtaaaa aaggtatctt cgcaaacctc 480
 atcatcttcg gtcgggttcc gtcctcaac gaaaacgaaa ccatcgacat cggatccag 540
 aaccacttcg caagccgtga aggtttcggg ggtatcatgc agatgaaatt ctgcccgga 600
 tacgtcagcg tcttcaacaa cgtccaggaa aacaaagggt caagcatctt caaccgtcgt 660
 gggtacttca ggcacccggc actcatcctc atgcatgaac tcattccagc cctccacggt 720
 ctctacggta tcaaagtgta cgacctcccg atcgctccga acgagaagaa attcttcatg 780
 cagagcaccg acgcaatcca ggctgaggaa ctctacacct tcgggtggcca agacccaagt 840
 atcataaccc cgtccaccga caaaagcatc tacgacaaag tcctccagaa cttcaggggt 900
 atcgtggaca gactcaacaa agtcctcgtc tgcattcagc accggaacat caatatcaac 960
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 accaacatcg ccgagaacta caagatcaag acaagggcaa gttacttcag cgacagcctc 1140
 ccgcctgtca aaatcaagaa cctcttagac aacgagattt acacaattga agagggttc 1200
 aacatcagtg acaaagacat ggagaaggaa tacagaggtc agaacaaggc tatcaacaaa 1260
 caggcatacg aggagatcag caaagaacac ctgcagctct acaagatcca gatgtgtaaa 1320
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<210> 114
 <211> 458
 <212> PRT
 <213> Clostridium botulinum

<400> 114

Gly Ser Met Pro Val Thr Ile Asn Asn Phe Asn Tyr Asn Asp Pro Ile
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Asp Asn Asn Asn Ile Ile Met Met Glu Pro Pro Phe Ala Arg Gly Thr
 20 25 30

Gly Arg Tyr Tyr Lys Ala Phe Lys Ile Thr Asp Arg Ile Trp Ile Ile
 35 40 45

Pro Glu Arg Tyr Thr Phe Gly Tyr Lys Pro Glu Asp Phe Asn Lys Ser
 50 55 60

Ser Gly Ile Phe Asn Arg Asp Val Cys Glu Tyr Tyr Asp Pro Asp Tyr
 65 70 75 80

Leu Asn Thr Asn Asp Lys Lys Asn Ile Phe Leu Gln Thr Met Ile Lys
 85 90 95

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Leu Phe Asn Arg Ile Lys Ser Lys Pro Leu Gly Glu Lys Leu Leu Glu
 100 105 110
 Met Ile Ile Asn Gly Ile Pro Tyr Leu Gly Asp Arg Arg Val Pro Leu
 115 120 125
 Glu Glu Phe Asn Thr Asn Ile Ala Ser Val Thr Val Asn Lys Leu Ile
 130 135 140
 Ser Asn Pro Gly Glu Val Glu Arg Lys Lys Gly Ile Phe Ala Asn Leu
 145 150 155 160
 Ile Ile Phe Gly Pro Gly Pro Val Leu Asn Glu Asn Glu Thr Ile Asp
 165 170 175
 Ile Gly Ile Gln Asn His Phe Ala Ser Arg Glu Gly Phe Gly Gly Ile
 180 185 190
 Met Gln Met Lys Phe Cys Pro Glu Tyr Val Ser Val Phe Asn Asn Val
 195 200 205
 Gln Glu Asn Lys Gly Ala Ser Ile Phe Asn Arg Arg Gly Tyr Phe Ser
 210 215 220
 Asp Pro Ala Leu Ile Leu Met His Glu Leu Ile His Val Leu His Gly
 225 230 235 240
 Leu Tyr Gly Ile Lys Val Asp Asp Leu Pro Ile Val Pro Asn Glu Lys
 245 250 255
 Lys Phe Phe Met Gln Ser Thr Asp Ala Ile Gln Ala Glu Glu Leu Tyr
 260 265 270
 Thr Phe Gly Gly Gln Asp Pro Ser Ile Ile Thr Pro Ser Thr Asp Lys
 275 280 285
 Ser Ile Tyr Asp Lys Val Leu Gln Asn Phe Arg Gly Ile Val Asp Arg
 290 295 300
 Leu Asn Lys Val Leu Val Cys Ile Ser Asp Pro Asn Ile Asn Ile Asn
 305 310 315 320
 Ile Tyr Lys Asn Lys Phe Lys Asp Lys Tyr Lys Phe Val Glu Asp Ser
 325 330 335
 Glu Gly Lys Tyr Ser Ile Asp Val Glu Ser Phe Asp Lys Leu Tyr Lys
 340 345 350
 Ser Leu Met Phe Gly Phe Thr Glu Thr Asn Ile Ala Glu Asn Tyr Lys

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355 360 365
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 385 390 395 400
 Asn Ile Ser Asp Lys Asp Met Glu Lys Glu Tyr Arg Gly Gln Asn Lys
 405 410 415
 Ala Ile Asn Lys Gln Ala Tyr Glu Glu Ile Ser Lys Glu His Leu Ala
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<211> 912

<212> PRT

<213> Clostridium botulinum

<400> 116

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 35 40 45
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 65 70 75 80
 Ser Pro Lys Ser Gly Tyr Tyr Asp Pro Asn Tyr Leu Ser Thr Asp Ser
 85 90 95
 Asp Lys Asp Thr Phe Leu Lys Glu Ile Ile Lys Leu Phe Lys Arg Ile
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 Ile Ser Pro Arg Phe Met Leu Thr Tyr Ser Asn Ala Thr Asn Asp Val
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 Ala Ile Pro Asn Asp Gln Thr Ile Ser Ser Val Thr Ser Asn Ile Phe
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 Glu Glu Lys Ala Leu Asp Tyr Tyr Arg Ser Ile Ala Lys Arg Leu Asn
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 Ser Ile Thr Thr Ala Asn Pro Ser Ser Phe Asn Lys Tyr Ile Gly Glu
 325 330 335
 Tyr Lys Gln Lys Leu Ile Arg Lys Tyr Arg Phe Val Val Glu Ser Ser
 340 345 350
 Gly Glu Val Thr Val Asn Arg Asn Lys Phe Val Glu Leu Tyr Asn Glu
 355 360 365
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 370 375 380
 Gln Asn Arg Lys Ile Tyr Leu Ser Asn Val Tyr Thr Pro Val Thr Ala
 385 390 395 400
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 Pro Lys Ser Asn Leu Asn Val Leu Phe Met Gly Gln Asn Leu Ser Arg
 420 425 430
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 450 455 460
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 485 490 495
 Ile Asn Glu Glu Thr Glu Val Ile Tyr Tyr Pro Asp Asn Val Ser Val
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 Asp Gln Val Ile Leu Ser Lys Asn Thr Ser Glu His Gly Gln Leu Asp
 515 520 525
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 565 570 575
 Phe Thr Phe Thr Arg Ser Ile Glu Glu Ala Leu Asp Asn Ser Ala Lys
 580 585 590
 Val Tyr Thr Tyr Phe Pro Thr Leu Ala Asn Lys Val Asn Ala Gly Val
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 Gln Gly Gly Leu Phe Leu Met Trp Ala Asn Asp Val Val Glu Asp Phe
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 Ser Ala Ile Ile Pro Tyr Ile Gly Pro Ala Leu Asn Ile Ser Asn Ser
 645 650 655
 Val Arg Arg Gly Asn Phe Thr Glu Ala Phe Ala Val Thr Gly Val Thr
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 Ile Leu Leu Glu Ala Phe Pro Glu Phe Thr Ile Pro Ala Leu Gly Ala
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 Glu Trp Met Met Gly Thr Trp Leu Ser Arg Ile Ile Thr Gln Phe Asn
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 Asn Ile Ser Tyr Gln Met Tyr Asp Ser Leu Asn Tyr Gln Ala Gly Ala
 740 745 750
 Ile Lys Ala Lys Ile Asp Leu Glu Tyr Lys Lys Tyr Ser Gly Ser Asp
 755 760 765
 Lys Glu Asn Ile Lys Ser Gln Val Glu Asn Leu Lys Asn Ser Leu Asp
 770 775 780
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 785 790 795 800

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Cys Ser Val Thr Tyr Leu Phe Lys Asn Met Leu Pro Lys Val Ile Asp
805 810 815

Glu Leu Asn Glu Phe Asp Arg Asn Thr Lys Ala Lys Leu Ile Asn Leu
820 825 830

Ile Asp Ser His Asn Ile Ile Leu Val Gly Glu Val Asp Lys Leu Lys
835 840 845

Ala Lys Val Asn Asn Ser Phe Gln Asn Thr Ile Pro Phe Asn Ile Phe
850 855 860

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

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<211> 2853

<212> DNA

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<400> 117

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<400> 118

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Glu Lys Ala Phe Arg Ile Thr Gly Asn Ile Trp Val Ile Pro Asp Arg
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Phe Ser Arg Asn Ser Asn Pro Asn Leu Asn Lys Pro Pro Arg Val Thr
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Ser Pro Lys Ser Gly Tyr Tyr Asp Pro Asn Tyr Leu Ser Thr Asp Ser
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Asp Lys Asp Thr Phe Leu Lys Glu Ile Ile Lys Leu Phe Lys Arg Ile
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Asn Ser Arg Glu Ile Gly Glu Glu Leu Ile Tyr Arg Leu Ser Thr Asp
 115 120 125

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

Trp Val Lys Thr Gly Ser Ile Asn Pro Ser Val Ile Ile Thr Gly Pro
 165 170 175

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

Asn Thr Phe Ala Ala Gln Glu Gly Phe Gly Ala Leu Ser Ile Ile Ser
 195 200 205

Ile Ser Pro Arg Phe Met Leu Thr Tyr Ser Asn Ala Thr Asn Asp Val
 210 215 220

Gly Glu Gly Arg Phe Ser Lys Ser Glu Phe Cys Met Asp Pro Ile Leu
 225 230 235 240

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Ile Leu Met His Glu Leu Asn His Ala Met His Asn Leu Tyr Gly Ile
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 260 265 270
 Tyr Ser Gln Tyr Asn Val Lys Leu Glu Tyr Ala Glu Ile Tyr Ala Phe
 275 280 285
 Gly Gly Pro Thr Ile Asp Leu Ile Pro Lys Ser Ala Arg Lys Tyr Phe
 290 295 300
 Glu Glu Lys Ala Leu Asp Tyr Tyr Arg Ser Ile Ala Lys Arg Leu Asn
 305 310 315 320
 Ser Ile Thr Thr Ala Asn Pro Ser Ser Phe Asn Lys Tyr Ile Gly Glu
 325 330 335
 Tyr Lys Gln Lys Leu Ile Arg Lys Tyr Arg Phe Val Val Glu Ser Ser
 340 345 350
 Gly Glu Val Thr Val Asn Arg Asn Lys Phe Val Glu Leu Tyr Asn Glu
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 370 375 380
 Gln Asn Arg Lys Ile Tyr Leu Ser Asn Val Tyr Thr Pro Val Thr Ala
 385 390 395 400
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 Pro Lys Ser Asn Leu Asn Val Leu Phe Met Gly Gln Asn Leu Ser Arg
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 450 455 460
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 755 760 765
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770 775 780

Val Lys Ile Ser Glu Ala Met Asn Asn Ile Asn Lys Phe Ile Arg Glu
785 790 795 800

Cys Ser Val Thr Tyr Leu Phe Lys Asn Met Leu Pro Lys Val Ile Asp
805 810 815

Glu Leu Asn Glu Phe Asp Arg Asn Thr Lys Ala Lys Leu Ile Asn Leu
820 825 830

Ile Asp Ser His Asn Ile Ile Leu Val Gly Glu Val Asp Lys Leu Lys
835 840 845

Ala Lys Val Asn Asn Ser Phe Gln Asn Thr Ile Pro Phe Asn Ile Phe
850 855 860

Ser Tyr Thr Asn Asn Ser Leu Leu Lys Asp Ile Ile Asn Glu Tyr Phe
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Asn Leu Gln Thr Leu Asp Asp Pro Ala Phe Leu Tyr Lys Val Val Ile
885 890 895

Phe Gln Asn Ser Asp Pro Leu Asp Cys Gly Gly Leu Thr Asp Thr Leu
900 905 910

Gln Ala Glu Thr Asp Gln Leu Glu Asp Glu Lys Ser Ala Leu Gln Thr
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 35 40 45

Glu Lys Ala Phe Arg Ile Thr Gly Asn Ile Trp Val Ile Pro Asp Arg
 50 55 60

Phe Ser Arg Asn Ser Asn Pro Asn Leu Asn Lys Pro Pro Arg Val Thr
 65 70 75 80

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

Asp Lys Asp Thr Phe Leu Lys Glu Ile Ile Lys Leu Phe Lys Arg Ile
 100 105 110

Asn Ser Arg Glu Ile Gly Glu Glu Leu Ile Tyr Arg Leu Ser Thr Asp
 115 120 125

Ile Pro Phe Pro Gly Asn Asn Asn Thr Pro Ile Asn Thr Phe Asp Phe
 130 135 140

Asp Val Asp Phe Asn Ser Val Asp Val Lys Thr Arg Gln Gly Asn Asn
 145 150 155 160

Trp Val Lys Thr Gly Ser Ile Asn Pro Ser Val Ile Ile Thr Gly Pro
 165 170 175

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

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Asn Thr Phe Ala Ala Gln Glu Gly Phe Gly Ala Leu Ser Ile Ile Ser
195 200 205

Ile Ser Pro Arg Phe Met Leu Thr Tyr Ser Asn Ala Thr Asn Asp Val
210 215 220

Gly Glu Gly Arg Phe Ser Lys Ser Glu Phe Cys Met Asp Pro Ile Leu
225 230 235 240

Ile Leu Met His Glu Leu Asn His Ala Met His Asn Leu Tyr Gly Ile
245 250 255

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Ala Ile Pro Asn Asp Gln Thr Ile Ser Ser Val Thr Ser Asn Ile Phe
260 265 270

Tyr Ser Gln Tyr Asn Val Lys Leu Glu Tyr Ala Glu Ile Tyr Ala Phe
275 280 285

Gly Gly Pro Thr Ile Asp Leu Ile Pro Lys Ser Ala Arg Lys Tyr Phe
290 295 300

Glu Glu Lys Ala Leu Asp Tyr Tyr Arg Ser Ile Ala Lys Arg Leu Asn
305 310 315 320

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Ser Ile Thr Thr Ala Asn Pro Ser Ser Phe Asn Lys Tyr Ile Gly Glu
325 330 335

Tyr Lys Gln Lys Leu Ile Arg Lys Tyr Arg Phe Val Val Glu Ser Ser
340 345 350

Gly Glu Val Thr Val Asn Arg Asn Lys Phe Val Glu Leu Tyr Asn Glu
355 360 365

Leu Thr Gln Ile Phe Thr Glu Phe Asn Tyr Ala Lys Ile Tyr Asn Val
370 375 380

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Gln Asn Arg Lys Ile Tyr Leu Ser Asn Val Tyr Thr Pro Val Thr Ala
385 390 395 400

Asn Ile Leu Asp Asp Asn Val Tyr Asp Ile Gln Asn Gly Phe Asn Ile
405 410 415

Pro Lys Ser Asn Leu Asn Val Leu Phe Met Gly Gln Asn Leu Ser Arg
420 425 430

Asn Pro Ala Leu Arg Lys Val Asn Pro Glu Asn Met Leu Tyr Leu Phe
435 440 445

Thr Lys Phe Cys His Lys Ala Ile Asp Gly Arg Ser Leu Tyr Asn Lys

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450 455 460
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 Ile Gly Asp Ile Ser Asp Val Lys Thr Asp Ile Phe Leu Arg Lys Asp
 485 490 495
 Ile Asn Glu Glu Thr Glu Val Ile Tyr Tyr Pro Asp Asn Val Ser Val
 500 505 510
 Asp Gln Val Ile Leu Ser Lys Asn Thr Ser Glu His Gly Gln Leu Asp
 515 520 525
 Leu Leu Tyr Pro Ser Ile Asp Ser Glu Ser Glu Ile Leu Pro Gly Glu
 530 535 540
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 545 550 555 560
 Ser Tyr Tyr Tyr Leu Glu Ser Gln Lys Leu Ser Asp Asn Val Glu Asp
 565 570 575
 Phe Thr Phe Thr Arg Ser Ile Glu Glu Ala Leu Asp Asn Ser Ala Lys
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 Val Tyr Thr Tyr Phe Pro Thr Leu Ala Asn Lys Val Asn Ala Gly Val
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 625 630 635 640
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 645 650 655
 Val Arg Arg Gly Asn Phe Thr Glu Ala Phe Ala Val Thr Gly Val Thr
 660 665 670
 Ile Leu Leu Glu Ala Phe Pro Glu Phe Thr Ile Pro Ala Leu Gly Ala
 675 680 685
 Phe Val Ile Tyr Ser Lys Val Gln Glu Arg Asn Glu Ile Ile Lys Thr
 690 695 700
 Ile Asp Asn Cys Leu Glu Gln Arg Ile Lys Arg Trp Lys Asp Ser Tyr
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Glu Trp Met Met Gly Thr Trp Leu Ser Arg Ile Ile Thr Gln Phe Asn
725 730 735

Asn Ile Ser Tyr Gln Met Tyr Asp Ser Leu Asn Tyr Gln Ala Gly Ala
740 745 750

Ile Lys Ala Lys Ile Asp Leu Glu Tyr Lys Lys Tyr Ser Gly Ser Asp
755 760 765

Lys Glu Asn Ile Lys Ser Gln Val Glu Asn Leu Lys Asn Ser Leu Asp
770 775 780

Val Lys Ile Ser Glu Ala Met Asn Asn Ile Asn Lys Phe Ile Arg Glu
785 790 795 800

Cys Ser Val Thr Tyr Leu Phe Lys Asn Met Leu Pro Lys Val Ile Asp
805 810 815

Glu Leu Asn Glu Phe Asp Arg Asn Thr Lys Ala Lys Leu Ile Asn Leu
820 825 830

Ile Asp Ser His Asn Ile Ile Leu Val Gly Glu Val Asp Lys Leu Lys
835 840 845

Ala Lys Val Asn Asn Ser Phe Gln Asn Thr Ile Pro Phe Asn Ile Phe
850 855 860

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

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

Glu Cys

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<211> 2835

<212> DNA

<213> Clostridium botulinum

<400> 121

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ctgaacaccc tggctaacga accggaaaaa gctttccgta tcaccggtaa catctgggtt 180

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 <212> PRT
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<400> 122

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Asn Ile Leu Tyr Leu Asp Thr His Leu Asn Thr Leu Ala Asn Glu Pro
 35 40 45

Glu Lys Ala Phe Arg Ile Thr Gly Asn Ile Trp Val Ile Pro Asp Arg
 50 55 60

Phe Ser Arg Asn Ser Asn Pro Asn Leu Asn Lys Pro Pro Arg Val Thr
 65 70 75 80

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

Asp Lys Asp Thr Phe Leu Lys Glu Ile Ile Lys Leu Phe Lys Arg Ile
 100 105 110

Asn Ser Arg Glu Ile Gly Glu Glu Leu Ile Tyr Arg Leu Ser Thr Asp
 115 120 125

Ile Pro Phe Pro Gly Asn Asn Asn Thr Pro Ile Asn Thr Phe Asp Phe
 130 135 140

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Asp Val Asp Phe Asn Ser Val Asp Val Lys Thr Arg Gln Gly Asn Asn
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 Trp Val Lys Thr Gly Ser Ile Asn Pro Ser Val Ile Ile Thr Gly Pro
 165 170 175
 Arg Glu Asn Ile Ile Asp Pro Glu Thr Ser Thr Phe Lys Leu Thr Asn
 180 185 190
 Asn Thr Phe Ala Ala Gln Glu Gly Phe Gly Ala Leu Ser Ile Ile Ser
 195 200 205
 Ile Ser Pro Arg Phe Met Leu Thr Tyr Ser Asn Ala Thr Asn Asp Val
 210 215 220
 Gly Glu Gly Arg Phe Ser Lys Ser Glu Phe Cys Met Asp Pro Ile Leu
 225 230 235 240
 Ile Leu Met His Glu Leu Asn His Ala Met His Asn Leu Tyr Gly Ile
 245 250 255
 Ala Ile Pro Asn Asp Gln Thr Ile Ser Ser Val Thr Ser Asn Ile Phe
 260 265 270
 Tyr Ser Gln Tyr Asn Val Lys Leu Glu Tyr Ala Glu Ile Tyr Ala Phe
 275 280 285
 Gly Gly Pro Thr Ile Asp Leu Ile Pro Lys Ser Ala Arg Lys Tyr Phe
 290 295 300
 Glu Glu Lys Ala Leu Asp Tyr Tyr Arg Ser Ile Ala Lys Arg Leu Asn
 305 310 315 320
 Ser Ile Thr Thr Ala Asn Pro Ser Ser Phe Asn Lys Tyr Ile Gly Glu
 325 330 335
 Tyr Lys Gln Lys Leu Ile Arg Lys Tyr Arg Phe Val Val Glu Ser Ser
 340 345 350
 Gly Glu Val Thr Val Asn Arg Asn Lys Phe Val Glu Leu Tyr Asn Glu
 355 360 365
 Leu Thr Gln Ile Phe Thr Glu Phe Asn Tyr Ala Lys Ile Tyr Asn Val
 370 375 380
 Gln Asn Arg Lys Ile Tyr Leu Ser Asn Val Tyr Thr Pro Val Thr Ala
 385 390 395 400
 Asn Ile Leu Asp Asp Asn Val Tyr Asp Ile Gln Asn Gly Phe Asn Ile
 405 410 415

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Pro Lys Ser Asn Leu Asn Val Leu Phe Met Gly Gln Asn Leu Ser Arg
 420 425 430
 Asn Pro Ala Leu Arg Lys Val Asn Pro Glu Asn Met Leu Tyr Leu Phe
 435 440 445
 Thr Lys Phe Cys His Lys Ala Ile Asp Gly Arg Ser Leu Tyr Asn Lys
 450 455 460
 Thr Leu Asp Cys Arg Glu Leu Leu Val Lys Asn Thr Asp Leu Pro Phe
 465 470 475 480
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 485 490 495
 Ile Asn Glu Glu Thr Glu Val Ile Tyr Tyr Pro Asp Asn Val Ser Val
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 Asp Gln Val Ile Leu Ser Lys Asn Thr Ser Glu His Gly Gln Leu Asp
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 Ser Tyr Tyr Tyr Leu Glu Ser Gln Lys Leu Ser Asp Asn Val Glu Asp
 565 570 575
 Phe Thr Phe Thr Arg Ser Ile Glu Glu Ala Leu Asp Asn Ser Ala Lys
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 Val Tyr Thr Tyr Phe Pro Thr Leu Ala Asn Lys Val Asn Ala Gly Val
 595 600 605
 Gln Gly Gly Leu Phe Leu Met Trp Ala Asn Asp Val Val Glu Asp Phe
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 Thr Thr Asn Ile Leu Arg Lys Asp Thr Leu Asp Lys Ile Ser Asp Val
 625 630 635 640
 Ser Ala Ile Ile Pro Tyr Ile Gly Pro Ala Leu Asn Ile Ser Asn Ser
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 Val Arg Arg Gly Asn Phe Thr Glu Ala Phe Ala Val Thr Gly Val Thr
 660 665 670
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675 680 685
 Phe Val Ile Tyr Ser Lys Val Gln Glu Arg Asn Glu Ile Ile Lys Thr
 690 695 700
 Ile Asp Asn Cys Leu Glu Gln Arg Ile Lys Arg Trp Lys Asp Ser Tyr
 705 710 715 720
 Glu Trp Met Met Gly Thr Trp Leu Ser Arg Ile Ile Thr Gln Phe Asn
 725 730 735
 Asn Ile Ser Tyr Gln Met Tyr Asp Ser Leu Asn Tyr Gln Ala Gly Ala
 740 745 750
 Ile Lys Ala Lys Ile Asp Leu Glu Tyr Lys Lys Tyr Ser Gly Ser Asp
 755 760 765
 Lys Glu Asn Ile Lys Ser Gln Val Glu Asn Leu Lys Asn Ser Leu Asp
 770 775 780
 Val Lys Ile Ser Glu Ala Met Asn Asn Ile Asn Lys Phe Ile Arg Glu
 785 790 795 800
 Cys Ser Val Thr Tyr Leu Phe Lys Asn Met Leu Pro Lys Val Ile Asp
 805 810 815
 Glu Leu Asn Glu Phe Asp Arg Asn Thr Lys Ala Lys Leu Ile Asn Leu
 820 825 830
 Ile Asp Ser His Asn Ile Ile Leu Val Gly Glu Val Asp Lys Leu Lys
 835 840 845
 Ala Lys Val Asn Asn Ser Phe Gln Asn Thr Ile Pro Phe Asn Ile Phe
 850 855 860
 Ser Tyr Thr Asn Asn Ser Leu Leu Lys Asp Ile Ile Asn Glu Tyr Phe
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 Asn Leu Gln Thr Leu Asp Asp Pro Ala Phe Leu Tyr Lys Val Val Ile
 885 890 895
 Phe Gln Asn Ser Asp Pro Leu Asp Leu Thr Asp Thr Leu Gln Ala Glu
 900 905 910
 Thr Asp Gln Leu Glu Asp Glu Lys Ser Ala Leu Gln Thr Glu Ile Ala
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 aat 2643

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 <212> PRT
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Glu Lys Ala Phe Arg Ile Thr Gly Asn Ile Trp Val Ile Pro Asp Arg
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Phe Ser Arg Asn Ser Asn Pro Asn Leu Asn Lys Pro Pro Arg Val Thr
 65 70 75 80

Ser Pro Lys Ser Gly Tyr Tyr Asp Pro Asn Tyr Leu Ser Thr Asp Ser
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Asp Lys Asp Thr Phe Leu Lys Glu Ile Ile Lys Leu Phe Lys Arg Ile
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Asn Ser Arg Glu Ile Gly Glu Glu Leu Ile Tyr Arg Leu Ser Thr Asp
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 145 150 155 160
 Trp Val Lys Thr Gly Ser Ile Asn Pro Ser Val Ile Ile Thr Gly Pro
 165 170 175
 Arg Glu Asn Ile Ile Asp Pro Glu Thr Ser Thr Phe Lys Leu Thr Asn
 180 185 190
 Asn Thr Phe Ala Ala Gln Glu Gly Phe Gly Ala Leu Ser Ile Ile Ser
 195 200 205
 Ile Ser Pro Arg Phe Met Leu Thr Tyr Ser Asn Ala Thr Asn Asp Val
 210 215 220
 Gly Glu Gly Arg Phe Ser Lys Ser Glu Phe Cys Met Asp Pro Ile Leu
 225 230 235 240
 Ile Leu Met His Glu Leu Asn His Ala Met His Asn Leu Tyr Gly Ile
 245 250 255
 Ala Ile Pro Asn Asp Gln Thr Ile Ser Ser Val Thr Ser Asn Ile Phe
 260 265 270
 Tyr Ser Gln Tyr Asn Val Lys Leu Glu Tyr Ala Glu Ile Tyr Ala Phe
 275 280 285
 Gly Gly Pro Thr Ile Asp Leu Ile Pro Lys Ser Ala Arg Lys Tyr Phe
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 Glu Glu Lys Ala Leu Asp Tyr Tyr Arg Ser Ile Ala Lys Arg Leu Asn
 305 310 315 320
 Ser Ile Thr Thr Ala Asn Pro Ser Ser Phe Asn Lys Tyr Ile Gly Glu
 325 330 335
 Tyr Lys Gln Lys Leu Ile Arg Lys Tyr Arg Phe Val Val Glu Ser Ser
 340 345 350
 Gly Glu Val Thr Val Asn Arg Asn Lys Phe Val Glu Leu Tyr Asn Glu
 355 360 365
 Leu Thr Gln Ile Phe Thr Glu Phe Asn Tyr Ala Lys Ile Tyr Asn Val
 370 375 380

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Gln Asn Arg Lys Ile Tyr Leu Ser Asn Val Tyr Thr Pro Val Thr Ala
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 405 410 415
 Pro Lys Ser Asn Leu Asn Val Leu Phe Met Gly Gln Asn Leu Ser Arg
 420 425 430
 Asn Pro Ala Leu Arg Lys Val Asn Pro Glu Asn Met Leu Tyr Leu Phe
 435 440 445
 Thr Lys Phe Cys His Lys Ala Ile Asp Gly Arg Ser Leu Tyr Asn Lys
 450 455 460
 Thr Leu Asp Cys Arg Glu Leu Leu Val Lys Asn Thr Asp Leu Pro Phe
 465 470 475 480
 Ile Gly Asp Ile Ser Asp Val Lys Thr Asp Ile Phe Leu Arg Lys Asp
 485 490 495
 Ile Asn Glu Glu Thr Glu Val Ile Tyr Tyr Pro Asp Asn Val Ser Val
 500 505 510
 Asp Gln Val Ile Leu Ser Lys Asn Thr Ser Glu His Gly Gln Leu Asp
 515 520 525
 Leu Leu Tyr Pro Ser Ile Asp Ser Glu Ser Glu Ile Leu Pro Gly Glu
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 545 550 555 560
 Ser Tyr Tyr Tyr Leu Glu Ser Gln Lys Leu Ser Asp Asn Val Glu Asp
 565 570 575
 Phe Thr Phe Thr Arg Ser Ile Glu Glu Ala Leu Asp Asn Ser Ala Lys
 580 585 590
 Val Tyr Thr Tyr Phe Pro Thr Leu Ala Asn Lys Val Asn Ala Gly Val
 595 600 605
 Gln Gly Gly Leu Phe Leu Met Trp Ala Asn Asp Val Val Glu Asp Phe
 610 615 620
 Thr Thr Asn Ile Leu Arg Lys Asp Thr Leu Asp Lys Ile Ser Asp Val
 625 630 635 640
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645 650 655
 Val Arg Arg Gly Asn Phe Thr Glu Ala Phe Ala Val Thr Gly Val Thr
 660 665 670
 Ile Leu Leu Glu Ala Phe Pro Glu Phe Thr Ile Pro Ala Leu Gly Ala
 675 680 685
 Phe Val Ile Tyr Ser Lys Val Gln Glu Arg Asn Glu Ile Ile Lys Thr
 690 695 700
 Ile Asp Asn Cys Leu Glu Gln Arg Ile Lys Arg Trp Lys Asp Ser Tyr
 705 710 715 720
 Glu Trp Met Met Gly Thr Trp Leu Ser Arg Ile Ile Thr Gln Phe Asn
 725 730 735
 Asn Ile Ser Tyr Gln Met Tyr Asp Ser Leu Asn Tyr Gln Ala Gly Ala
 740 745 750
 Ile Lys Ala Lys Ile Asp Leu Glu Tyr Lys Lys Tyr Ser Gly Ser Asp
 755 760 765
 Lys Glu Asn Ile Lys Ser Gln Val Glu Asn Leu Lys Asn Ser Leu Asp
 770 775 780
 Val Lys Ile Ser Glu Ala Met Asn Asn Ile Asn Lys Phe Ile Arg Glu
 785 790 795 800
 Cys Ser Val Thr Tyr Leu Phe Lys Asn Met Leu Pro Lys Val Ile Asp
 805 810 815
 Glu Leu Asn Glu Phe Asp Arg Asn Thr Lys Ala Lys Leu Ile Asn Leu
 820 825 830
 Ile Asp Ser His Asn Ile Ile Leu Val Gly Glu Val Asp Lys Leu Lys
 835 840 845
 Ala Lys Val Asn Asn Ser Phe Gln Asn Thr Ile Pro Phe Asn Ile Phe
 850 855 860
 Ser Tyr Thr Asn Asn Ser Leu Leu Lys Asp Ile Ile Asn Glu Tyr Phe
 865 870 875 880

Asn

<210> 125
 <211> 2631
 <212> DNA

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<213> Clostridium botulinum

<400> 125

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ggttattatg atcctaatta tttgagtact gattctgaca aagatacatt tttaaaagaa    300
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ccctatatag gacccgcatt aaatataagt aattctgtaa gaagaggaaa ttttactgaa 1980
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gataaattaa aagcaaaaagt aaataatagc tttcaaaaata caataccctt taatattttt 2580
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<210> 126
<211> 877
<212> PRT
<213> Clostridium botulinum

<400> 126

Val Pro Glu Phe Gly Ser Ser Arg Val Asp His Met Pro Ile Thr Ile
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Asn Asn Phe Asn Tyr Ser Asp Pro Val Asp Asn Lys Asn Ile Leu Tyr
20 25 30

Leu Asp Thr His Leu Asn Thr Leu Ala Asn Glu Pro Glu Lys Ala Phe
35 40 45

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

Ser Asn Pro Asn Leu Asn Lys Pro Pro Arg Val Thr Ser Pro Lys Ser
65 70 75 80

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

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

Ile Gly Glu Glu Leu Ile Tyr Arg Leu Ser Thr Asp Ile Pro Phe Pro
115 120 125

Gly Asn Asn Asn Thr Pro Ile Asn Thr Phe Asp Phe Asp Val Asp Phe
130 135 140

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Asn Ser Val Asp Val Lys Thr Arg Gln Gly Asn Asn Trp Val Lys Thr
145 150 155 160

Gly Ser Ile Asn Pro Ser Val Ile Ile Thr Gly Pro Arg Glu Asn Ile
165 170 175

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

Ala Gln Glu Gly Phe Gly Ala Leu Ser Ile Ile Ser Ile Ser Pro Arg
195 200 205

Phe Met Leu Thr Tyr Ser Asn Ala Thr Asn Asp Val Gly Glu Gly Arg
210 215 220

Phe Ser Lys Ser Glu Phe Cys Met Asp Pro Ile Leu Ile Leu Met His
225 230 235 240

Glu Leu Asn His Ala Met His Asn Leu Tyr Gly Ile Ala Ile Pro Asn
245 250 255

Asp Gln Thr Ile Ser Ser Val Thr Ser Asn Ile Phe Tyr Ser Gln Tyr
260 265 270

Asn Val Lys Leu Glu Tyr Ala Glu Ile Tyr Ala Phe Gly Gly Pro Thr
275 280 285

Ile Asp Leu Ile Pro Lys Ser Ala Arg Lys Tyr Phe Glu Glu Lys Ala
290 295 300

Leu Asp Tyr Tyr Arg Ser Ile Ala Lys Arg Leu Asn Ser Ile Thr Thr
305 310 315 320

Ala Asn Pro Ser Ser Phe Asn Lys Tyr Ile Gly Glu Tyr Lys Gln Lys
325 330 335

Leu Ile Arg Lys Tyr Arg Phe Val Val Glu Ser Ser Gly Glu Val Thr
340 345 350

Val Asn Arg Asn Lys Phe Val Glu Leu Tyr Asn Glu Leu Thr Gln Ile
355 360 365

Phe Thr Glu Phe Asn Tyr Ala Lys Ile Tyr Asn Val Gln Asn Arg Lys
370 375 380

Ile Tyr Leu Ser Asn Val Tyr Thr Pro Val Thr Ala Asn Ile Leu Asp
385 390 395 400

Asp Asn Val Tyr Asp Ile Gln Asn Gly Phe Asn Ile Pro Lys Ser Asn

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Leu Asn Val 420	Leu Phe Met Gly Gln Asn Leu Ser Arg Asn Pro Ala Leu 425	
Arg Lys Val 435	Asn Pro Glu Asn Met Leu Tyr Leu Phe Thr Lys Phe Cys 440	
His Lys Ala 450	Ile Asp Gly Arg Ser Leu Tyr Asn Lys Thr Leu Asp Cys 455	
Arg Glu Leu 465	Leu Val Lys Asn Thr Asp Leu Pro Phe Ile Gly Asp Ile 470	
Ser Asp Val 485	Lys Thr Asp Ile Phe Leu Arg Lys Asp Ile Asn Glu Glu 490	
Thr Glu Val 500	Ile Tyr Tyr Pro Asp Asn Val Ser Val Asp Gln Val Ile 505	
Leu Ser Lys 515	Asn Thr Ser Glu His Gly Gln Leu Asp Leu Leu Tyr Pro 520	
Ser Ile Asp 530	Ser Glu Ser Glu Ile Leu Pro Gly Glu Asn Gln Val Phe 535	
Tyr Asp Asn 545	Arg Thr Gln Asn Val Asp Tyr Leu Asn Ser Tyr Tyr Tyr 550	
Leu Glu Ser 565	Gln Lys Leu Ser Asp Asn Val Glu Asp Phe Thr Phe Thr 570	
Arg Ser Ile 580	Glu Glu Ala Leu Asp Asn Ser Ala Lys Val Tyr Thr Tyr 585	
Phe Pro Thr 595	Leu Ala Asn Lys Val Asn Ala Gly Val Gln Gly Gly Leu 600	
Phe Leu Met 610	Trp Ala Asn Asp Val Val Glu Asp Phe Thr Thr Asn Ile 615	
Leu Arg Lys 625	Asp Thr Leu Asp Lys Ile Ser Asp Val Ser Ala Ile Ile 630	
Pro Tyr Ile 645	Gly Pro Ala Leu Asn Ile Ser Asn Ser Val Arg Arg Gly 650	
Asn Phe Thr 660	Glu Ala Phe Ala Val Thr Gly Val Thr Ile Leu Leu Glu 665	

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Ala Phe Pro Glu Phe Thr Ile Pro Ala Leu Gly Ala Phe Val Ile Tyr
675 680 685

Ser Lys Val Gln Glu Arg Asn Glu Ile Ile Lys Thr Ile Asp Asn Cys
690 695 700

Leu Glu Gln Arg Ile Lys Arg Trp Lys Asp Ser Tyr Glu Trp Met Met
705 710 715 720

Gly Thr Trp Leu Ser Arg Ile Ile Thr Gln Phe Asn Asn Ile Ser Tyr
725 730 735

Gln Met Tyr Asp Ser Leu Asn Tyr Gln Ala Gly Ala Ile Lys Ala Lys
740 745 750

Ile Asp Leu Glu Tyr Lys Lys Tyr Ser Gly Ser Asp Lys Glu Asn Ile
755 760 765

Lys Ser Gln Val Glu Asn Leu Lys Asn Ser Leu Asp Val Lys Ile Ser
770 775 780

Glu Ala Met Asn Asn Ile Asn Lys Phe Ile Arg Glu Cys Ser Val Thr
785 790 795 800

Tyr Leu Phe Lys Asn Met Leu Pro Lys Val Ile Asp Glu Leu Asn Glu
805 810 815

Phe Asp Arg Asn Thr Lys Ala Lys Leu Ile Asn Leu Ile Asp Ser His
820 825 830

Asn Ile Ile Leu Val Gly Glu Val Asp Lys Leu Lys Ala Lys Val Asn
835 840 845

Asn Ser Phe Gln Asn Thr Ile Pro Phe Asn Ile Phe Ser Tyr Thr Asn
850 855 860

Asn Ser Leu Leu Lys Asp Ile Ile Asn Glu Tyr Phe Asn
865 870 875

<210> 127

<211> 2628

<212> DNA

<213> Clostridium botulinum

<400> 127

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tcaagaaatt ctaatccaaa tttaaataaa cctcctcgag ttacaagccc taaaagtgg 240

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gataattggt tagaacaag gattaagaga tggaaagatt catatgaatg gatgatggga 2160
acgtggttat ccaggattat tactcaattt aataatataa gttatcaaat gtatgattct 2220

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<210> 128
 <211> 876
 <212> PRT
 <213> Clostridium botulinum.

<400> 128

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35 40 45

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

Asn Pro Asn Leu Asn Lys Pro Pro Arg Val Thr Ser Pro Lys Ser Gly
65 70 75 80

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

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

Gly Glu Glu Leu Ile Tyr Arg Leu Ser Thr Asp Ile Pro Phe Pro Gly
115 120 125

Asn Asn Asn Thr Pro Ile Asn Thr Phe Asp Phe Asp Val Asp Phe Asn
130 135 140

Ser Val Asp Val Lys Thr Arg Gln Gly Asn Asn Trp Val Lys Thr Gly
145 150 155 160

Ser Ile Asn Pro Ser Val Ile Ile Thr Gly Pro Arg Glu Asn Ile Ile
165 170 175

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

Gln Glu Gly Phe Gly Ala Leu Ser Ile Ile Ser Ile Ser Pro Arg Phe
 195 200 205

Met Leu Thr Tyr Ser Asn Ala Thr Asn Asp Val Gly Glu Gly Arg Phe
 210 215 220

Ser Lys Ser Glu Phe Cys Met Asp Pro Ile Leu Ile Leu Met His Glu
 225 230 235 240

Leu Asn His Ala Met His Asn Leu Tyr Gly Ile Ala Ile Pro Asn Asp
 245 250 255

Gln Thr Ile Ser Ser Val Thr Ser Asn Ile Phe Tyr Ser Gln Tyr Asn
 260 265 270

Val Lys Leu Glu Tyr Ala Glu Ile Tyr Ala Phe Gly Gly Pro Thr Ile
 275 280 285

Asp Leu Ile Pro Lys Ser Ala Arg Lys Tyr Phe Glu Glu Lys Ala Leu
 290 295 300

Asp Tyr Tyr Arg Ser Ile Ala Lys Arg Leu Asn Ser Ile Thr Thr Ala
 305 310 315 320

Asn Pro Ser Ser Phe Asn Lys Tyr Ile Gly Glu Tyr Lys Gln Lys Leu
 325 330 335

Ile Arg Lys Tyr Arg Phe Val Val Glu Ser Ser Gly Glu Val Thr Val
 340 345 350

Asn Arg Asn Lys Phe Val Glu Leu Tyr Asn Glu Leu Thr Gln Ile Phe
 355 360 365

Thr Glu Phe Asn Tyr Ala Lys Ile Tyr Asn Val Gln Asn Arg Lys Ile
 370 375 380

Tyr Leu Ser Asn Val Tyr Thr Pro Val Thr Ala Asn Ile Leu Asp Asp
 385 390 395 400

Asn Val Tyr Asp Ile Gln Asn Gly Phe Asn Ile Pro Lys Ser Asn Leu
 405 410 415

Asn Val Leu Phe Met Gly Gln Asn Leu Ser Arg Asn Pro Ala Leu Arg
 420 425 430

Lys Val Asn Pro Glu Asn Met Leu Tyr Leu Phe Thr Lys Phe Cys His
 435 440 445

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Lys Ala Ile Asp Gly Arg Ser Leu Tyr Asn Lys Thr Leu Asp Cys Arg
 450 455 460

Glu Leu Leu Val Lys Asn Thr Asp Leu Pro Phe Ile Gly Asp Ile Ser
 465 470 475 480

Asp Val Lys Thr Asp Ile Phe Leu Arg Lys Asp Ile Asn Glu Glu Thr
 485 490 495

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

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

Ile Asp Ser Glu Ser Glu Ile Leu Pro Gly Glu Asn Gln Val Phe Tyr
 530 535 540

Asp Asn Arg Thr Gln Asn Val Asp Tyr Leu Asn Ser Tyr Tyr Tyr Leu
 545 550 555 560

Glu Ser Gln Lys Leu Ser Asp Asn Val Glu Asp Phe Thr Phe Thr Arg
 565 570 575

Ser Ile Glu Glu Ala Leu Asp Asn Ser Ala Lys Val Tyr Thr Tyr Phe
 580 585 590

Pro Thr Leu Ala Asn Lys Val Asn Ala Gly Val Gln Gly Gly Leu Phe
 595 600 605

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

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

Tyr Ile Gly Pro Ala Leu Asn Ile Ser Asn Ser Val Arg Arg Gly Asn
 645 650 655

Phe Thr Glu Ala Phe Ala Val Thr Gly Val Thr Ile Leu Leu Glu Ala
 660 665 670

Phe Pro Glu Phe Thr Ile Pro Ala Leu Gly Ala Phe Val Ile Tyr Ser
 675 680 685

Lys Val Gln Glu Arg Asn Glu Ile Ile Lys Thr Ile Asp Asn Cys Leu
 690 695 700

Glu Gln Arg Ile Lys Arg Trp Lys Asp Ser Tyr Glu Trp Met Met Gly

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705 710 715 720

Thr Trp Leu Ser Arg Ile Ile Thr Gln Phe Asn Asn Ile Ser Tyr Gln
725 730 735

Met Tyr Asp Ser Leu Asn Tyr Gln Ala Gly Ala Ile Lys Ala Lys Ile
740 745 750

Asp Leu Glu Tyr Lys Lys Tyr Ser Gly Ser Asp Lys Glu Asn Ile Lys
755 760 765

Ser Gln Val Glu Asn Leu Lys Asn Ser Leu Asp Val Lys Ile Ser Glu
770 775 780

Ala Met Asn Asn Ile Asn Lys Phe Ile Arg Glu Cys Ser Val Thr Tyr
785 790 795 800

Leu Phe Lys Asn Met Leu Pro Lys Val Ile Asp Glu Leu Asn Glu Phe
805 810 815

Asp Arg Asn Thr Lys Ala Lys Leu Ile Asn Leu Ile Asp Ser His Asn
820 825 830

Ile Ile Leu Val Gly Glu Val Asp Lys Leu Lys Ala Lys Val Asn Asn
835 840 845

Ser Phe Gln Asn Thr Ile Pro Phe Asn Ile Phe Ser Tyr Thr Asn Asn
850 855 860

Ser Leu Leu Lys Asp Ile Ile Asn Glu Tyr Phe Asn
865 870 875

<210> 129
<211> 2631
<212> DNA
<213> Clostridium botulinum

<400> 129

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gctaattgagc ctgaaaaagc ctttcgcatt acaggaaata tatgggtaat acctgataga 180

ttttcaagaa attctaattc aaatttaaatt aaacctcctc gagttacaag ccctaaaagt 240

ggttattatg atcctaatta tttagagtact gattctgaca aagatacatt tttaaaagaa 300

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gatgtagatt ttaacagtgt tgatgttaaa actagacaag gtaacaactg gggtaaaact 480

ggtagcataa atcctagtgt tataataact ggacctagag aaaacattat agatccagaa 540

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 ggagagggta gattttctaa gtctgaattt tgcattggatc caataactaat tttaatgcat 720
 gaacttaatc atgcaatgca taatttatat ggaatagcta taccaaatga tcaaacaatt 780
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 gagggaaaagg cattggatta ttatagatct atagctaaaa gacttaatat tataactact 960
 gcaaaccctt caagcttta taaatatata ggggaatata aacagaaact tattagaaag 1020
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 ttatataatg aacttacaca aatatttaca gaatttaact acgctaaaat atataatgta 1140
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 gataatgttt atgatataca aaatggattt aatataccta aaagtaattt aaatgtacta 1260
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gataaattaa aagcaaaagt aaataatagc ttccaaaata caataccctt taatattttt 2580
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 <212> PRT
 <213> Clostridium botulinum

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 35 40 45

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

Ser Asn Pro Asn Leu Asn Lys Pro Pro Arg Val Thr Ser Pro Lys Ser
 65 70 75 80

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

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

Ile Gly Glu Glu Leu Ile Tyr Arg Leu Ser Thr Asp Ile Pro Phe Pro
 115 120 125

Gly Asn Asn Asn Thr Pro Ile Asn Thr Phe Asp Phe Asp Val Asp Phe
 130 135 140

Asn Ser Val Asp Val Lys Thr Arg Gln Gly Asn Asn Trp Val Lys Thr
 145 150 155 160

Gly Ser Ile Asn Pro Ser Val Ile Ile Thr Gly Pro Arg Glu Asn Ile
 165 170 175

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

Ala Gln Glu Gly Phe Gly Ala Leu Ser Ile Ile Ser Ile Ser Pro Arg
 195 200 205

Phe Met Leu Thr Tyr Ser Asn Ala Thr Asn Asp Val Gly Glu Gly Arg
 210 215 220

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

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485 490 495
 Thr Glu Val Ile Tyr Tyr Pro Asp Asn Val Ser Val Asp Gln Val Ile
 500 505 510
 Leu Ser Lys Asn Thr Ser Glu His Gly Gln Leu Asp Leu Leu Tyr Pro
 515 520 525
 Ser Ile Asp Ser Glu Ser Glu Ile Leu Pro Gly Glu Asn Gln Val Phe
 530 535 540
 Tyr Asp Asn Arg Thr Gln Asn Val Asp Tyr Leu Asn Ser Tyr Tyr Tyr
 545 550 555 560
 Leu Glu Ser Gln Lys Leu Ser Asp Asn Val Glu Asp Phe Thr Phe Thr
 565 570 575
 Arg Ser Ile Glu Glu Ala Leu Asp Asn Ser Ala Lys Val Tyr Thr Tyr
 580 585 590
 Phe Pro Thr Leu Ala Asn Lys Val Asn Ala Gly Val Gln Gly Gly Leu
 595 600 605
 Phe Leu Met Trp Ala Asn Asp Val Val Glu Asp Phe Thr Thr Asn Ile
 610 615 620
 Leu Arg Lys Asp Thr Leu Asp Lys Ile Ser Asp Val Ser Ala Ile Ile
 625 630 635 640
 Pro Tyr Ile Gly Pro Ala Leu Asn Ile Ser Asn Ser Val Arg Arg Gly
 645 650 655
 Asn Phe Thr Glu Ala Phe Ala Val Thr Gly Val Thr Ile Leu Leu Glu
 660 665 670
 Ala Phe Pro Glu Phe Thr Ile Pro Ala Leu Gly Ala Phe Val Ile Tyr
 675 680 685
 Ser Lys Val Gln Glu Arg Asn Glu Ile Ile Lys Thr Ile Asp Asn Cys
 690 695 700
 Leu Glu Gln Arg Ile Lys Arg Trp Lys Asp Ser Tyr Glu Trp Met Met
 705 710 715 720
 Gly Thr Trp Leu Ser Arg Ile Ile Thr Gln Phe Asn Asn Ile Ser Tyr
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 Gln Met Tyr Asp Ser Leu Asn Tyr Gln Ala Gly Ala Ile Lys Ala Lys
 740 745 750

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Ile Asp Leu Glu Tyr Lys Lys Tyr Ser Gly Ser Asp Lys Glu Asn Ile
755 760 765

Lys Ser Gln Val Glu Asn Leu Lys Asn Ser Leu Asp Val Lys Ile Ser
770 775 780

Glu Ala Met Asn Asn Ile Asn Lys Phe Ile Arg Glu Cys Ser Val Thr
785 790 795 800

Tyr Leu Phe Lys Asn Met Leu Pro Lys Val Ile Asp Glu Leu Asn Glu
805 810 815

Phe Asp Arg Asn Thr Lys Ala Lys Leu Ile Asn Leu Ile Asp Ser His
820 825 830

Asn Ile Ile Leu Val Gly Glu Val Asp Lys Leu Lys Ala Lys Val Asn
835 840 845

Asn Ser Phe Gln Asn Thr Ile Pro Phe Asn Ile Phe Ser Tyr Thr Asn
850 855 860

Asn Ser Leu Leu Lys Asp Ile Ile Asn Glu Tyr Phe Asn
865 870 875

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ttaaatacac tagctaata gacctgaaaa gcctttcgca ttacaggaaa tatatgggta 180
atacctgata gattttcaag aaattctaata ccaaatttaa ataaacctcc tcgagttaca 240
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tttttaaaag aaattataaa gttatttaaa agaattaatt ctagagaaat aggagaagaa 360
ttaatatata gactttcgac agatatacc tttcctggga ataacaatac tccaattaat 420
acctttgatt ttgatgtaga ttttaacagt gttgatgta aaactagaca aggtaacaac 480
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atagatccag aaacttctac gtttaaatta actaacaata cctttgoggc acaagaagga 600
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actaatgatg taggagaggg tagattttct aagtctgaat tttgcatgga tccaatacta 720
attttaatgc atgaacttaa tcatgcaatg cataatttat atggaatagc tataccaaat 780
gatcaaacia tttcatctgt aactagtaat attttttatt ctcaatataa tgtgaaatta 840

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 agtataacta ctgcaaatac ttcaagcttt aataaatata taggggaata taaacagaaa 1020
 cttattagaa agtatagatt cgtagtagaa tcttcagggt aagttacagt aaatcgtaat 1080
 aagtttgttg agttatataa tgaacttaca caaatattta cagaatttaa ctacgctaaa 1140
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 gatcctct 2708

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 <212> PRT
 <213> Clostridium botulinum

<400> 132

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Asn Ile Leu Tyr Leu Asp Thr His Leu Asn Thr Leu Ala Asn Glu Pro
 35 40 45

Glu Lys Ala Phe Arg Ile Thr Gly Asn Ile Trp Val Ile Pro Asp Arg
 50 55 60

Phe Ser Arg Asn Ser Asn Pro Asn Leu Asn Lys Pro Pro Arg Val Thr
 65 70 75 80

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

Asp Lys Asp Thr Phe Leu Lys Glu Ile Ile Lys Leu Phe Lys Arg Ile
 100 105 110

Asn Ser Arg Glu Ile Gly Glu Glu Leu Ile Tyr Arg Leu Ser Thr Asp
 115 120 125

Ile Pro Phe Pro Gly Asn Asn Asn Thr Pro Ile Asn Thr Phe Asp Phe
 130 135 140

Asp Val Asp Phe Asn Ser Val Asp Val Lys Thr Arg Gln Gly Asn Asn
 145 150 155 160

Trp Val Lys Thr Gly Ser Ile Asn Pro Ser Val Ile Ile Thr Gly Pro
 165 170 175

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

Asn Thr Phe Ala Ala Gln Glu Gly Phe Gly Ala Leu Ser Ile Ile Ser
 195 200 205

Ile Ser Pro Arg Phe Met Leu Thr Tyr Ser Asn Ala Thr Asn Asp Val
 210 215 220

Gly Glu Gly Arg Phe Ser Lys Ser Glu Phe Cys Met Asp Pro Ile Leu
 225 230 235 240

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Ile Leu Met His Glu Leu Asn His Ala Met His Asn Leu Tyr Gly Ile
 245 250 255
 Ala Ile Pro Asn Asp Gln Thr Ile Ser Ser Val Thr Ser Asn Ile Phe
 260 265 270
 Tyr Ser Gln Tyr Asn Val Lys Leu Glu Tyr Ala Glu Ile Tyr Ala Phe
 275 280 285
 Gly Gly Pro Thr Ile Asp Leu Ile Pro Lys Ser Ala Arg Lys Tyr Phe
 290 295 300
 Glu Glu Lys Ala Leu Asp Tyr Tyr Arg Ser Ile Ala Lys Arg Leu Asn
 305 310 315 320
 Ser Ile Thr Thr Ala Asn Pro Ser Ser Phe Asn Lys Tyr Ile Gly Glu
 325 330 335
 Tyr Lys Gln Lys Leu Ile Arg Lys Tyr Arg Phe Val Val Glu Ser Ser
 340 345 350
 Gly Glu Val Thr Val Asn Arg Asn Lys Phe Val Glu Leu Tyr Asn Glu
 355 360 365
 Leu Thr Gln Ile Phe Thr Glu Phe Asn Tyr Ala Lys Ile Tyr Asn Val
 370 375 380
 Gln Asn Arg Lys Ile Tyr Leu Ser Asn Val Tyr Thr Pro Val Thr Ala
 385 390 395 400
 Asn Ile Leu Asp Asp Asn Val Tyr Asp Ile Gln Asn Gly Phe Asn Ile
 405 410 415
 Pro Lys Ser Asn Leu Asn Val Leu Phe Met Gly Gln Asn Leu Ser Arg
 420 425 430
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 435 440 445
 Thr Lys Phe Cys His Lys Ala Ile Asp Gly Arg Ser Leu Tyr Asn Lys
 450 455 460
 Thr Leu Asp Cys Arg Glu Leu Leu Val Lys Asn Thr Asp Leu Pro Phe
 465 470 475 480
 Ile Gly Asp Ile Ser Asp Val Lys Thr Asp Ile Phe Leu Arg Lys Asp
 485 490 495
 Ile Asn Glu Glu Thr Glu Val Ile Tyr Tyr Pro Asp Asn Val Ser Val
 500 505 510

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Asp Gln Val Ile Leu Ser Lys Asn Thr Ser Glu His Gly Gln Leu Asp
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 545 550 555 560
 Ser Tyr Tyr Tyr Leu Glu Ser Gln Lys Leu Ser Asp Asn Val Glu Asp
 565 570 575
 Phe Thr Phe Thr Arg Ser Ile Glu Glu Ala Leu Asp Asn Ser Ala Lys
 580 585 590
 Val Tyr Thr Tyr Phe Pro Thr Leu Ala Asn Lys Val Asn Ala Gly Val
 595 600 605
 Gln Gly Gly Leu Phe Leu Met Trp Ala Asn Asp Val Val Glu Asp Phe
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 Thr Thr Asn Ile Leu Arg Lys Asp Thr Leu Asp Lys Ile Ser Asp Val
 625 630 635 640
 Ser Ala Ile Ile Pro Tyr Ile Gly Pro Ala Leu Asn Ile Ser Asn Ser
 645 650 655
 Val Arg Arg Gly Asn Phe Thr Glu Ala Phe Ala Val Thr Gly Val Thr
 660 665 670
 Ile Leu Leu Glu Ala Phe Pro Glu Phe Thr Ile Pro Ala Leu Gly Ala
 675 680 685
 Phe Val Ile Tyr Ser Lys Val Gln Glu Arg Asn Glu Ile Ile Lys Thr
 690 695 700
 Ile Asp Asn Cys Leu Glu Gln Arg Ile Lys Arg Trp Lys Asp Ser Tyr
 705 710 715 720
 Glu Trp Met Met Gly Thr Trp Leu Ser Arg Ile Ile Thr Gln Phe Asn
 725 730 735
 Asn Ile Ser Tyr Gln Met Tyr Asp Ser Leu Asn Tyr Gln Ala Gly Ala
 740 745 750
 Ile Lys Ala Lys Ile Asp Leu Glu Tyr Lys Lys Tyr Ser Gly Ser Asp
 755 760 765
 Lys Glu Asn Ile Lys Ser Gln Val Glu Asn Leu Lys Asn Ser Leu Asp

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770 775 780

Val Lys Ile Ser Glu Ala Met Asn Asn Ile Asn Lys Phe Ile Arg Glu
785 790 795 800

Cys Ser Val Thr Tyr Leu Phe Lys Asn Met Leu Pro Lys Val Ile Asp
 805 810 815

Glu Leu Asn Glu Phe Asp Arg Asn Thr Lys Ala Lys Leu Ile Asn Leu
 820 825 830

Ile Asp Ser His Asn Ile Ile Leu Val Gly Glu Val Asp Lys Leu Lys
 835 840 845

Ala Lys Val Asn Asn Ser Phe Gln Asn Thr Ile Pro Phe Asn Ile Phe
 850 855 860

Ser Tyr Thr Asn Asn Ser Leu Leu Lys Asp Ile Ile Asn Glu Tyr Phe
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Phe Gln Asn Ser Asp Pro
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<211> 2831
<212> DNA
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caaggtaaca actggggtta aactggtagc ataaatccta gtgttataat aactggacct 600
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aatgaatatt tcaatctgca gactctagac gaccagctt tcttgtaaa agttggcatt 2760

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atcattattt g 2831

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<212> DNA
<213> Clostridium botulinum

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 attgaatata atgatatggt taataatttt accgttagct tttgggtgag ggttcctaaa 2880
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<210> 141
<211> 1315
<212> PRT
<213> Clostridium tetani

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<400> 141

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Asp Thr Ile Ile Met Met Glu Pro Pro Tyr Cys Lys Gly Leu Asp Ile
20           25           30

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Tyr Tyr Lys Ala Phe Lys Ile Thr Asp Arg Ile Trp Ile Val Pro Glu
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Arg Tyr Glu Phe Gly Thr Lys Pro Glu Asp Phe Asn Pro Pro Ser Ser
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Leu Ile Glu Gly Ala Ser Glu Tyr Tyr Asp Pro Asn Tyr Leu Arg Thr
65           70           75           80

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Asp Ser Asp Lys Asp Arg Phe Leu Gln Thr Met Val Lys Leu Phe Asn
85           90           95

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Arg Ile Lys Asn Asn Val Ala Gly Glu Ala Leu Leu Asp Lys Ile Ile
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 Asn Ala Ile Pro Tyr Leu Gly Asn Ser Tyr Ser Leu Leu Asp Lys Phe
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 Asp Thr Asn Ser Asn Ser Val Ser Phe Asn Leu Leu Glu Gln Asp Pro
 130 135 140
 Ser Gly Ala Thr Thr Lys Ser Ala Met Leu Thr Asn Leu Ile Ile Phe
 145 150 155 160
 Gly Pro Gly Pro Val Leu Asn Lys Asn Glu Val Arg Gly Ile Val Leu
 165 170 175
 Arg Val Asp Asn Lys Asn Tyr Phe Pro Cys Arg Asp Gly Phe Gly Ser
 180 185 190
 Ile Met Gln Met Ala Phe Cys Pro Glu Tyr Val Pro Thr Phe Asp Asn
 195 200 205
 Val Ile Glu Asn Ile Thr Ser Leu Thr Ile Gly Lys Ser Lys Tyr Phe
 210 215 220
 Gln Asp Pro Ala Leu Leu Leu Met His Glu Leu Ile His Val Leu His
 225 230 235 240
 Gly Leu Tyr Gly Met Gln Val Ser Ser His Glu Ile Ile Pro Ser Lys
 245 250 255
 Gln Glu Ile Tyr Met Gln His Thr Tyr Pro Ile Ser Ala Glu Glu Leu
 260 265 270
 Phe Thr Phe Gly Gly Gln Asp Ala Asn Leu Ile Ser Ile Asp Ile Lys
 275 280 285
 Asn Asp Leu Tyr Glu Lys Thr Leu Asn Asp Tyr Lys Ala Ile Ala Asn
 290 295 300
 Lys Leu Ser Gln Val Thr Ser Cys Asn Asp Pro Asn Ile Asp Ile Asp
 305 310 315 320
 Ser Tyr Lys Gln Ile Tyr Gln Gln Lys Tyr Gln Phe Asp Lys Asp Ser
 325 330 335
 Asn Gly Gln Tyr Ile Val Asn Glu Asp Lys Phe Gln Ile Leu Tyr Asn
 340 345 350
 Ser Ile Met Tyr Gly Phe Thr Glu Ile Glu Leu Gly Lys Lys Phe Asn
 355 360 365

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Ile Lys Thr Arg Leu Ser Tyr Phe Ser Met Asn His Asp Pro Val Lys
370 375 380

Ile Pro Asn Leu Leu Asp Asp Thr Ile Tyr Asn Asp Thr Glu Gly Phe
385 390 395 400

Asn Ile Glu Ser Lys Asp Leu Lys Ser Glu Tyr Lys Gly Gln Asn Met
405 410 415

Arg Val Asn Thr Asn Ala Phe Arg Asn Val Asp Gly Ser Gly Leu Val
420 425 430

Ser Lys Leu Ile Gly Leu Cys Lys Lys Ile Ile Pro Pro Thr Asn Ile
435 440 445

Arg Glu Asn Leu Tyr Asn Arg Thr Ala Ser Leu Thr Asp Leu Gly Gly
450 455 460

Glu Leu Cys Ile Lys Ile Lys Asn Glu Asp Leu Thr Phe Ile Ala Glu
465 470 475 480

Lys Asn Ser Phe Ser Glu Glu Pro Phe Gln Asp Glu Ile Val Ser Tyr
485 490 495

Asn Thr Lys Asn Lys Pro Leu Asn Phe Asn Tyr Ser Leu Asp Lys Ile
500 505 510

Ile Val Asp Tyr Asn Leu Gln Ser Lys Ile Thr Leu Pro Asn Asp Arg
515 520 525

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

Asn Ala Ala Ser Thr Ile Glu Ile His Asn Ile Asp Asp Asn Thr Ile
545 550 555 560

Tyr Gln Tyr Leu Tyr Ala Gln Lys Ser Pro Thr Thr Leu Gln Arg Ile
565 570 575

Thr Met Thr Asn Ser Val Asp Asp Ala Leu Ile Asn Ser Thr Lys Ile
580 585 590

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

Gly Ile Leu Phe Leu Gln Trp Val Arg Asp Ile Ile Asp Asp Phe Thr
610 615 620

Asn Glu Ser Ser Gln Lys Thr Thr Ile Asp Lys Ile Ser Asp Val Ser

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625 630 635 640
 Thr Ile Val Pro Tyr Ile Gly Pro Ala Leu Asn Ile Val Lys Gln Gly
 645 650 655
 Tyr Glu Gly Asn Phe Ile Gly Ala Leu Glu Thr Thr Gly Val Val Leu
 660 665 670
 Leu Leu Glu Tyr Ile Pro Glu Ile Thr Leu Pro Val Ile Ala Ala Leu
 675 680 685
 Ser Ile Ala Glu Ser Ser Thr Gln Lys Glu Lys Ile Ile Lys Thr Ile
 690 695 700
 Asp Asn Phe Leu Glu Lys Arg Tyr Glu Lys Trp Ile Glu Val Tyr Lys
 705 710 715 720
 Leu Val Lys Ala Lys Trp Leu Gly Thr Val Asn Thr Gln Phe Gln Lys
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 Arg Ser Tyr Gln Met Tyr Arg Ser Leu Glu Tyr Gln Val Asp Ala Ile
 740 745 750
 Lys Lys Ile Ile Asp Tyr Glu Tyr Lys Ile Tyr Ser Gly Pro Asp Lys
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 Glu Gln Ile Ala Asp Glu Ile Asn Asn Leu Lys Asn Lys Leu Glu Glu
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 Lys Ala Asn Lys Ala Met Ile Asn Ile Asn Ile Phe Met Arg Glu Ser
 785 790 795 800
 Ser Arg Ser Phe Leu Val Asn Gln Met Ile Asn Glu Ala Lys Lys Gln
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 Lys Ala Asn Ser Lys Phe Ile Gly Ile Thr Glu Leu Lys Lys Leu Glu
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 Ser Lys Ile Asn Lys Val Phe Ser Thr Pro Ile Pro Phe Ser Tyr Ser
 850 855 860
 Lys Asn Leu Asp Cys Trp Val Asp Asn Glu Glu Asp Ile Asp Val Ile
 865 870 875 880
 Leu Lys Lys Ser Thr Ile Leu Asn Leu Asp Ile Asn Asn Asp Ile Ile
 885 890 895

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Ser Asp Ile Ser Gly Phe Asn Ser Ser Val Ile Thr Tyr Pro Asp Ala
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 Gln Leu Val Pro Gly Ile Asn Gly Lys Ala Ile His Leu Val Asn Asn
 915 920 925
 Glu Ser Ser Glu Val Ile Val His Lys Ala Met Asp Ile Glu Tyr Asn
 930 935 940
 Asp Met Phe Asn Asn Phe Thr Val Ser Phe Trp Leu Arg Val Pro Lys
 945 950 955 960
 Val Ser Ala Ser His Leu Glu Gln Tyr Gly Thr Asn Glu Tyr Ser Ile
 965 970 975
 Ile Ser Ser Met Lys Lys His Ser Leu Ser Ile Gly Ser Gly Trp Ser
 980 985 990
 Val Ser Leu Lys Gly Asn Asn Leu Ile Trp Thr Leu Lys Asp Ser Ala
 995 1000 1005
 Gly Glu Val Arg Gln Ile Thr Phe Arg Asp Leu Pro Asp Lys Phe
 1010 1015 1020
 Asn Ala Tyr Leu Ala Asn Lys Trp Val Phe Ile Thr Ile Thr Asn
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 Asp Arg Leu Ser Ser Ala Asn Leu Tyr Ile Asn Gly Val Leu Met
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 Gly Ser Ala Glu Ile Thr Gly Leu Gly Ala Ile Arg Glu Asp Asn
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 Asn Ile Thr Leu Lys Leu Asp Arg Cys Asn Asn Asn Asn Gln Tyr
 1070 1075 1080
 Val Ser Ile Asp Lys Phe Arg Ile Phe Cys Lys Ala Leu Asn Pro
 1085 1090 1095
 Lys Glu Ile Glu Lys Leu Tyr Thr Ser Tyr Leu Ser Ile Thr Phe
 1100 1105 1110
 Leu Arg Asp Phe Trp Gly Asn Pro Leu Arg Tyr Asp Thr Glu Tyr
 1115 1120 1125
 Tyr Leu Ile Pro Val Ala Ser Ser Ser Lys Asp Val Gln Leu Lys
 1130 1135 1140
 Asn Ile Thr Asp Tyr Met Tyr Leu Thr Asn Ala Pro Ser Tyr Thr
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Asn Gly Lys Leu Asn Ile Tyr Tyr Arg Arg Leu Tyr Asn Gly Leu
1160 1165 1170

Lys Phe Ile Ile Lys Arg Tyr Thr Pro Asn Asn Glu Ile Asp Ser
1175 1180 1185

Phe Val Lys Ser Gly Asp Phe Ile Lys Leu Tyr Val Ser Tyr Asn
1190 1195 1200

Asn Asn Glu His Ile Val Gly Tyr Pro Lys Asp Gly Asn Ala Phe
1205 1210 1215

Asn Asn Leu Asp Arg Ile Leu Arg Val Gly Tyr Asn Ala Pro Gly
1220 1225 1230

Ile Pro Leu Tyr Lys Lys Met Glu Ala Val Lys Leu Arg Asp Leu
1235 1240 1245

Lys Thr Tyr Ser Val Gln Leu Lys Leu Tyr Asp Asp Lys Asn Ala
1250 1255 1260

Ser Leu Gly Leu Val Gly Thr His Asn Gly Gln Ile Gly Asn Asp
1265 1270 1275

Pro Asn Arg Asp Ile Leu Ile Ala Ser Asn Trp Tyr Phe Asn His
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Asp Glu Gly Trp Thr Asn Asp
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<212> DNA
<213> Clostridium tetani

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ccaccatctt cattaataga aggtgcattc gagtattacg atccaaatta ttttaaggact 240
gattctgata aagatagatt ttacaaacc atggtaaaac tgtttaacag aattaaaaac 300
aatgtagcag gtgaagcctt attagataag ataataaatg ccatacctta ccttggaat 360
tcatattcct tactagacaa gtttgatata aactctaatt cagtattctt taatttatta 420
gaacaagacc ccagtggagc aactacaaaa tcagcaatgc tgacaaatatt aataatattt 480

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ggacctgggc ctgtttttaa taaaaatgag gttagaggta ttgtattgag ggtagataat 540
 aaaaattact tcccatgtag agatggtttt ggctcaataa tgcaaatggc attttgccca 600
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 <212> PRT
 <213> Clostridium tetani

<400> 143

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Tyr Tyr Lys Ala Phe Lys Ile Thr Asp Arg Ile Trp Ile Val Pro Glu
 35 40 45

Arg Tyr Glu Phe Gly Thr Lys Pro Glu Asp Phe Asn Pro Pro Ser Ser
 50 55 60

Leu Ile Glu Gly Ala Ser Glu Tyr Tyr Asp Pro Asn Tyr Leu Arg Thr
 65 70 75 80

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Asp Ser Asp Lys Asp Arg Phe Leu Gln Thr Met Val Lys Leu Phe Asn
 85 90 95

Arg Ile Lys Asn Asn Val Ala Gly Glu Ala Leu Leu Asp Lys Ile Ile
 100 105 110

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

Asp Thr Asn Ser Asn Ser Val Ser Phe Asn Leu Leu Glu Gln Asp Pro
 130 135 140

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Ser Gly Ala Thr Thr Lys Ser Ala Met Leu Thr Asn Leu Ile Ile Phe
 145 150 155 160

Gly Pro Gly Pro Val Leu Asn Lys Asn Glu Val Arg Gly Ile Val Leu
 165 170 175

Arg Val Asp Asn Lys Asn Tyr Phe Pro Cys Arg Asp Gly Phe Gly Ser
 180 185 190

Ile Met Gln Met Ala Phe Cys Pro Glu Tyr Val Pro Thr Phe Asp Asn
 195 200 205

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Val Ile Glu Asn Ile Thr Ser Leu Thr Ile Gly Lys Ser Lys Tyr Phe
 210 215 220
 Gln Asp Pro Ala Leu Leu Leu Met His Glu Leu Ile His Val Leu His
 225 230 235 240
 Gly Leu Tyr Gly Met Gln Val Ser Ser His Glu Ile Ile Pro Ser Lys
 245 250 255
 Gln Glu Ile Tyr Met Gln His Thr Tyr Pro Ile Ser Ala Glu Glu Leu
 260 265 270
 Phe Thr Phe Gly Gly Gln Asp Ala Asn Leu Ile Ser Ile Asp Ile Lys
 275 280 285
 Asn Asp Leu Tyr Glu Lys Thr Leu Asn Asp Tyr Lys Ala Ile Ala Asn
 290 295 300
 Lys Leu Ser Gln Val Thr Ser Cys Asn Asp Pro Asn Ile Asp Ile Asp
 305 310 315 320
 Ser Tyr Lys Gln Ile Tyr Gln Gln Lys Tyr Gln Phe Asp Lys Asp Ser
 325 330 335
 Asn Gly Gln Tyr Ile Val Asn Glu Asp Lys Phe Gln Ile Leu Tyr Asn
 340 345 350
 Ser Ile Met Tyr Gly Phe Thr Glu Ile Glu Leu Gly Lys Lys Phe Asn
 355 360 365
 Ile Lys Thr Arg Leu Ser Tyr Phe Ser Met Asn His Asp Pro Val Lys
 370 375 380
 Ile Pro Asn Leu Leu Asp Asp Thr Ile Tyr Asn Asp Thr Glu Gly Phe
 385 390 395 400
 Asn Ile Glu Ser Lys Asp Leu Lys Ser Glu Tyr Lys Gly Gln Asn Met
 405 410 415
 Arg Val Asn Thr Asn Ala Phe Arg Asn Val Asp Gly Ser Gly Leu Val
 420 425 430
 Ser Lys Leu Ile Gly Leu Cys Lys Lys Ile Ile Pro Pro Thr Asn Ile
 435 440 445
 Arg Glu Asn Leu Tyr Asn Arg Thr Ala Ser Leu Thr Asp Leu Gly Gly
 450 455 460
 Glu Leu Cys Ile Lys Ile Lys Asn Glu Asp Leu Thr Phe Ile Ala Glu
 465 470 475 480

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Lys Asn Ser Phe Ser Glu Glu Pro Phe Gln Asp Glu Ile Val Ser Tyr
485 490 495

Asn Thr Lys Asn Lys Pro Leu Asn Phe Asn Tyr Ser Leu Asp Lys Ile
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Ile Val Asp Tyr Asn Leu Gln Ser Lys Ile Thr Leu Pro Asn Asp Arg
515 520 525

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

Asn Ala Ala Ser Thr Ile Glu Ile His Asn Ile Asp Asp Asn Thr Ile
545 550 555 560

Tyr Gln Tyr Leu Tyr Ala Gln Lys Ser Pro Thr Thr Leu Gln Arg Ile
565 570 575

Thr Met Thr Asn Ser Val Asp Asp Ala Leu Ile Asn Ser Thr Lys Ile
580 585 590

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

Gly Ile Leu Phe Leu Gln Trp Val Arg Asp Ile Ile Asp Asp Phe Thr
610 615 620

Asn Glu Ser Ser Gln Lys Thr Thr Ile Asp Lys Ile Ser Asp Val Ser
625 630 635 640

Thr Ile Val Pro Tyr Ile Gly Pro Ala Leu Asn Ile Val Lys Gln Gly
645 650 655

Tyr Glu Gly Asn Phe Ile Gly Ala Leu Glu Thr Thr Gly Val Val Leu
660 665 670

Leu Leu Glu Tyr Ile Pro Glu Ile Thr Leu Pro Val Ile Ala Ala Leu
675 680 685

Ser Ile Ala Glu Ser Ser Thr Gln Lys Glu Lys Ile Ile Lys Thr Ile
690 695 700

Asp Asn Phe Leu Glu Lys Arg Tyr Glu Lys Trp Ile Glu Val Tyr Lys
705 710 715 720

Leu Val Lys Ala Lys Trp Leu Gly Thr Val Asn Thr Gln Phe Gln Lys
725 730 735

Arg Ser Tyr Gln Met Tyr Arg Ser Leu Glu Tyr Gln Val Asp Ala Ile

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740 745 750
 Lys Lys Ile Ile Asp Tyr Glu Tyr Lys Ile Tyr Ser Gly Pro Asp Lys
 755 760 765
 Glu Gln Ile Ala Asp Glu Ile Asn Asn Leu Lys Asn Lys Leu Glu Glu
 770 775 780
 Lys Ala Asn Lys Ala Met Ile Asn Ile Asn Ile Phe Met Arg Glu Ser
 785 790 795 800
 Ser Arg Ser Phe Leu Val Asn Gln Met Ile Asn Glu Ala Lys Lys Gln
 805 810 815
 Leu Leu Glu Phe Asp Thr Gln Ser Lys Asn Ile Leu Met Gln Tyr Ile
 820 825 830
 Lys Ala Asn Ser Lys Phe Ile Gly Ile Thr Glu Leu Lys Lys Leu Glu
 835 840 845
 Ser Lys Ile Asn Lys Val Phe Ser Thr Pro Ile Pro Phe Ser Tyr Ser
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 <212> DNA
 <213> Clostridium tetani

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 aaaaattact tcccatgtag agatggtttt ggctcaataa tgcaaatggc attttgcca 600
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atgcagcata catatccaat aagtgtgaa gaactattca cttttggcgg acaggatgct 840
 aatcttataa gtattgatat aaaaaacgat ttatatgaaa aaacttttaa tgattataaa 900
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 attgaattgg gaaaaaaatt taatataaaa actagacttt cttatttttag tatgaatcat 1140
 gaccctgtaa aaattccaaa tttattagat gatacaattt acaatgatac agaaggattt 1200
 aatatagaaa gcaaagatct gaaatctgaa tataaaggac aaaatatgag ggtaaataca 1260
 aatgctttta gaaatgttga tggatcaggc ctagtgtcaa aacttattgg cttatgtaaa 1320
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 ccatttcaag atgaaatagt tagttataat aaaaaaata aaccattaaa ttttaattat 1500
 tcgctagata aaattattgt agattataat ctacaaagta aaattacatt acctaattgat 1560
 aggacaacc cagttacaaa aggaattcca tatgtctccag aatataaaag taatgtctga 1620
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 aaatctccta caactctaca aagaataact atgactaatt ctgttgatga cgcattaata 1740
 aattccacca aaatatattc atattttcca tctgtaatca gtaaagttaa ccaagggtga 1800
 caaggaattt tattcttaca gtgggtgaga gatataattg atgattttac caatgaatct 1860
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 cccgcattaa acattgtaaa acaaggctat gagggaaact ttataggcgc tttagaaact 1980
 accggagtgg ttttattatt agaatatatt ccagaaatta ctttaccagt aattgcagct 2040
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 ttagaaaaaa gatatgaaaa atggattgaa gtatataaac tagtaaaagc aaaatgggta 2160
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 aaagcaatga taaacataaa tatatttatg agggaaagtt ctagatcatt tttagtta 2400
 caaatgatta acgaagctaa aaagcagtta ttagagtttg atactcaaag caaaaatatt 2460
 ttaatgcagt atataaaagc aaattctaaa tttataggta taactgaact aaaaaatta 2520
 gaatcaaaaa taaacaaagt tttttcaaca ccaattccat tttcttattc taaaaatctg 2580
 gattgttggg ttgataatga agaagatata gatgtt 2616

<210> 145
 <211> 872
 <212> PRT

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<213> Clostridium tetani

<400> 145

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Asp Thr Ile Ile Met Met Glu Pro Pro Tyr Cys Lys Gly Leu Asp Ile
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Tyr Tyr Lys Ala Phe Lys Ile Thr Asp Arg Ile Trp Ile Val Pro Glu
35 40 45

Arg Tyr Glu Phe Gly Thr Lys Pro Glu Asp Phe Asn Pro Pro Ser Ser
50 55 60

Leu Ile Glu Gly Ala Ser Glu Tyr Tyr Asp Pro Asn Tyr Leu Arg Thr
65 70 75 80

Asp Ser Asp Lys Asp Arg Phe Leu Gln Thr Met Val Lys Leu Phe Asn
85 90 95

Arg Ile Lys Asn Asn Val Ala Gly Glu Ala Leu Leu Asp Lys Ile Ile
100 105 110

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

Asp Thr Asn Ser Asn Ser Val Ser Phe Asn Leu Leu Glu Gln Asp Pro
130 135 140

Ser Gly Ala Thr Thr Lys Ser Ala Met Leu Thr Asn Leu Ile Ile Phe
145 150 155 160

Gly Pro Gly Pro Val Leu Asn Lys Asn Glu Val Arg Gly Ile Val Leu
165 170 175

Arg Val Asp Asn Lys Asn Tyr Phe Pro Cys Arg Asp Gly Phe Gly Ser
180 185 190

Ile Met Gln Met Ala Phe Cys Pro Glu Tyr Val Pro Thr Phe Asp Asn
195 200 205

Val Ile Glu Asn Ile Thr Ser Leu Thr Ile Gly Lys Ser Lys Tyr Phe
210 215 220

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

Gly Leu Tyr Gly Met Gln Val Ser Ser His Glu Ile Ile Pro Ser Lys
245 250 255

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Gln Glu Ile Tyr Met Gln His Thr Tyr Pro Ile Ser Ala Glu Glu Leu
260 265 270

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

Asn Asp Leu Tyr Glu Lys Thr Leu Asn Asp Tyr Lys Ala Ile Ala Asn
290 295 300

Lys Leu Ser Gln Val Thr Ser Cys Asn Asp Pro Asn Ile Asp Ile Asp
305 310 315 320

Ser Tyr Lys Gln Ile Tyr Gln Gln Lys Tyr Gln Phe Asp Lys Asp Ser
325 330 335

Asn Gly Gln Tyr Ile Val Asn Glu Asp Lys Phe Gln Ile Leu Tyr Asn
340 345 350

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

Ile Lys Thr Arg Leu Ser Tyr Phe Ser Met Asn His Asp Pro Val Lys
370 375 380

Ile Pro Asn Leu Leu Asp Asp Thr Ile Tyr Asn Asp Thr Glu Gly Phe
385 390 395 400

Asn Ile Glu Ser Lys Asp Leu Lys Ser Glu Tyr Lys Gly Gln Asn Met
405 410 415

Arg Val Asn Thr Asn Ala Phe Arg Asn Val Asp Gly Ser Gly Leu Val
420 425 430

Ser Lys Leu Ile Gly Leu Cys Lys Ser Glu Glu Lys Leu Tyr Asp Asp
435 440 445

Asp Asp Lys Asp Arg Trp Gly Ser Ser Arg Ile Cys Ile Lys Ile Lys
450 455 460

Asn Glu Asp Leu Thr Phe Ile Ala Glu Lys Asn Ser Phe Ser Glu Glu
465 470 475 480

Pro Phe Gln Asp Glu Ile Val Ser Tyr Asn Thr Lys Asn Lys Pro Leu
485 490 495

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

Ser Lys Ile Thr Leu Pro Asn Asp Arg Thr Thr Pro Val Thr Lys Gly

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515 520 525
 Ile Pro Tyr Ala Pro Glu Tyr Lys Ser Asn Ala Ala Ser Thr Ile Glu
 530 535 540
 Ile His Asn Ile Asp Asp Asn Thr Ile Tyr Gln Tyr Leu Tyr Ala Gln
 545 550 555 560
 Lys Ser Pro Thr Thr Leu Gln Arg Ile Thr Met Thr Asn Ser Val Asp
 565 570 575
 Asp Ala Leu Ile Asn Ser Thr Lys Ile Tyr Ser Tyr Phe Pro Ser Val
 580 585 590
 Ile Ser Lys Val Asn Gln Gly Ala Gln Gly Ile Leu Phe Leu Gln Trp
 595 600 605
 Val Arg Asp Ile Ile Asp Asp Phe Thr Asn Glu Ser Ser Gln Lys Thr
 610 615 620
 Thr Ile Asp Lys Ile Ser Asp Val Ser Thr Ile Val Pro Tyr Ile Gly
 625 630 635 640
 Pro Ala Leu Asn Ile Val Lys Gln Gly Tyr Glu Gly Asn Phe Ile Gly
 645 650 655
 Ala Leu Glu Thr Thr Gly Val Val Leu Leu Leu Glu Tyr Ile Pro Glu
 660 665 670
 Ile Thr Leu Pro Val Ile Ala Ala Leu Ser Ile Ala Glu Ser Ser Thr
 675 680 685
 Gln Lys Glu Lys Ile Ile Lys Thr Ile Asp Asn Phe Leu Glu Lys Arg
 690 695 700
 Tyr Glu Lys Trp Ile Glu Val Tyr Lys Leu Val Lys Ala Lys Trp Leu
 705 710 715 720
 Gly Thr Val Asn Thr Gln Phe Gln Lys Arg Ser Tyr Gln Met Tyr Arg
 725 730 735
 Ser Leu Glu Tyr Gln Val Asp Ala Ile Lys Lys Ile Ile Asp Tyr Glu
 740 745 750
 Tyr Lys Ile Tyr Ser Gly Pro Asp Lys Glu Gln Ile Ala Asp Glu Ile
 755 760 765
 Asn Asn Leu Lys Asn Lys Leu Glu Glu Lys Ala Asn Lys Ala Met Ile
 770 775 780

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Asn Ile Asn Ile Phe Met Arg Glu Ser Ser Arg Ser Phe Leu Val Asn
785 790 795 800

Gln Met Ile Asn Glu Ala Lys Lys Gln Leu Leu Glu Phe Asp Thr Gln
805 810 815

Ser Lys Asn Ile Leu Met Gln Tyr Ile Lys Ala Asn Ser Lys Phe Ile
820 825 830

Gly Ile Thr Glu Leu Lys Lys Leu Glu Ser Lys Ile Asn Lys Val Phe
835 840 845

Ser Thr Pro Ile Pro Phe Ser Tyr Ser Lys Asn Leu Asp Cys Trp Val
850 855 860

Asp Asn Glu Glu Asp Ile Asp Val
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<210> 146
<211> 2661
<212> DNA
<213> Clostridium tetani

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gatcgtatgtt ggatagtgcc ggaaagggtat gaatttggga caaaacctga agattttaac 180
ccaccatctt cattaataga aggtgcctct gagtattacg atccaaatta ttttaaggact 240
gattctgata aagatagatt ttacaaaacc atggtaaaac tgtttaacag aattaaaaac 300
aatgtagcag gtgaagcctt attagataag ataataaatg ccatacetta ccttggaaat 360
tcatattcct tactagacaa gtttgataca aactctaatt cagtattctt taatttatta 420
gaacaagacc ccagtggagc aactacaaaa tcagcaatgc tgacaaatgt aataatattt 480
ggacctgggc ctgtttttaa taaaaatgag gtttagagga ttgtattgag ggtagataat 540
aaaaattact tcccatgtag agatgggtttt ggctcaataa tgcaaatggc attttgccca 600
gaatatgtac ctacctttga taatgtaata gaaaatatta cgtcactcac tattggcaaa 660
agcaaatatt ttcaagatcc agcattacta ttaatgcacg aacttataca tgtactacat 720
ggtttatacg gaatgcaggt atcaagccat gaaattattc catccaaaca agaaatttat 780
atgcagcata catatccaat aagtgcctgaa gaactattca cttttggcgg acaggatgct 840
aatcttataa gtattgatat aaaaaacgat ttatatgaaa aaactttaaa tgattataaa 900
gctatagcta acaaaacttag tcaagtcact agctgcaatg atcccaacat tgatattgat 960
agctacaaac aaatatatca acaaaaatat caattcgata aagatagcaa tggacaatat 1020
attgtaaatg aggataaatt tcagatacta tataatagca taatgtatgg ttttacagag 1080

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attgaattgg gaaaaaaatt taatataaaa actagacttt cttatttttag tatgaatcat 1140
 gaccctgtaa aaattccaaa tttatttagat gatacaattt acaatgatac agaaggattt 1200
 aatatagaaa gcaaaagatct gaaatctgaa tataaaggac aaaatatgag ggtaaataca 1260
 aatgctttta gaaatgttga tggatcaggc ctagtittcaa aacttattgg cttatgtaaa 1320
 aaaattatac caccaacaaa tataagagaa aatttatata atagaactgc atcattaaca 1380
 gatttaggag gagaattatg tataaaaaatt aaaaatgaag atttaacttt tatagctgaa 1440
 aaaaatagct tttcagaaga accatttcaa gatgaaatag ttagttataa tacaaaaaat 1500
 aaaccattaa attttaatta ttogctagat aaaattattg tagattataa tctacaaagt 1560
 aaaattacat tacctaataa taggacaacc ccagttacaa aaggaattcc atagtctcca 1620
 gaatataaaa gtaatgctgc aagtacaata gaaatacata atattgatga caatacaata 1680
 tatcaatatt tgtatgctca aaaatctcct acaactctac aaagaataac tatgactaat 1740
 tctgttgatg acgcattaat aaattccacc aaaatatatt catattttcc atctgtaac 1800
 agtaaagtta accaagggtgc acaaggaatt ttattcttac agtgggtgag agatataatt 1860
 gatgatttta ccaatgaatc ttcacaaaaa actactattg ataaaatttc agatgtatcc 1920
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 tttataggcg ctttagaaac taccggagtg gttttattat tagaatatat tccagaaatt 2040
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 ataaaaacaa tagataactt tttagaaaaa agatatgaaa aatggattga agtatataaa 2160
 ctagtaaaag caaaatggtt aggcacagtt aatagcgaat tccaaaaaag aagttatcaa 2220
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 aaaatatatt caggacctga taaggaacaa attgcccagc aaattaataa tctgaaaaac 2340
 aaacttgaag aaaaggctaa taaagcaatg ataaacataa atatatttat gagggaaagt 2400
 tctagatcat ttttagttaa tcaaagtatt aacgaagcta aaaagcagtt attagagttt 2460
 gatactcaaa gcaaaaatat tttaatgcag tatataaaag caaattctaa atttataggt 2520
 ataactgaac taaaaaaatt agaatacaaa ataaacaaag ttttttcaac accaattcca 2580
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 ttaaaaaaga gtacaatttt a 2661

<210> 147
 <211> 887
 <212> PRT
 <213> Clostridium tetani
 <400> 147

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 Tyr Tyr Lys Ala Phe Lys Ile Thr Asp Arg Ile Trp Ile Val Pro Glu
 35 40 45
 Arg Tyr Glu Phe Gly Thr Lys Pro Glu Asp Phe Asn Pro Pro Ser Ser
 50 55 60
 Leu Ile Glu Gly Ala Ser Glu Tyr Tyr Asp Pro Asn Tyr Leu Arg Thr
 65 70 75 80
 Asp Ser Asp Lys Asp Arg Phe Leu Gln Thr Met Val Lys Leu Phe Asn
 85 90 95
 Arg Ile Lys Asn Asn Val Ala Gly Glu Ala Leu Leu Asp Lys Ile Ile
 100 105 110
 Asn Ala Ile Pro Tyr Leu Gly Asn Ser Tyr Ser Leu Leu Asp Lys Phe
 115 120 125
 Asp Thr Asn Ser Asn Ser Val Ser Phe Asn Leu Leu Glu Gln Asp Pro
 130 135 140
 Ser Gly Ala Thr Thr Lys Ser Ala Met Leu Thr Asn Leu Ile Ile Phe
 145 150 155 160
 Gly Pro Gly Pro Val Leu Asn Lys Asn Glu Val Arg Gly Ile Val Leu
 165 170 175
 Arg Val Asp Asn Lys Asn Tyr Phe Pro Cys Arg Asp Gly Phe Gly Ser
 180 185 190
 Ile Met Gln Met Ala Phe Cys Pro Glu Tyr Val Pro Thr Phe Asp Asn
 195 200 205
 Val Ile Glu Asn Ile Thr Ser Leu Thr Ile Gly Lys Ser Lys Tyr Phe
 210 215 220
 Gln Asp Pro Ala Leu Leu Leu Met His Glu Leu Ile His Val Leu His
 225 230 235 240
 Gly Leu Tyr Gly Met Gln Val Ser Ser His Glu Ile Ile Pro Ser Lys
 245 250 255
 Gln Glu Ile Tyr Met Gln His Thr Tyr Pro Ile Ser Ala Glu Glu Leu
 260 265 270
 Phe Thr Phe Gly Gly Gln Asp Ala Asn Leu Ile Ser Ile Asp Ile Lys
 275 280 285

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Asn Asp Leu Tyr Glu Lys Thr Leu Asn Asp Tyr Lys Ala Ile Ala Asn
 290 295 300
 Lys Leu Ser Gln Val Thr Ser Cys Asn Asp Pro Asn Ile Asp Ile Asp
 305 310 315 320
 Ser Tyr Lys Gln Ile Tyr Gln Gln Lys Tyr Gln Phe Asp Lys Asp Ser
 325 330 335
 Asn Gly Gln Tyr Ile Val Asn Glu Asp Lys Phe Gln Ile Leu Tyr Asn
 340 345 350
 Ser Ile Met Tyr Gly Phe Thr Glu Ile Glu Leu Gly Lys Lys Phe Asn
 355 360 365
 Ile Lys Thr Arg Leu Ser Tyr Phe Ser Met Asn His Asp Pro Val Lys
 370 375 380
 Ile Pro Asn Leu Leu Asp Asp Thr Ile Tyr Asn Asp Thr Glu Gly Phe
 385 390 395 400
 Asn Ile Glu Ser Lys Asp Leu Lys Ser Glu Tyr Lys Gly Gln Asn Met
 405 410 415
 Arg Val Asn Thr Asn Ala Phe Arg Asn Val Asp Gly Ser Gly Leu Val
 420 425 430
 Ser Lys Leu Ile Gly Leu Cys Lys Lys Ile Ile Pro Pro Thr Asn Ile
 435 440 445
 Arg Glu Asn Leu Tyr Asn Arg Thr Ala Ser Leu Thr Asp Leu Gly Gly
 450 455 460
 Glu Leu Cys Ile Lys Ile Lys Asn Glu Asp Leu Thr Phe Ile Ala Glu
 465 470 475 480
 Lys Asn Ser Phe Ser Glu Glu Pro Phe Gln Asp Glu Ile Val Ser Tyr
 485 490 495
 Asn Thr Lys Asn Lys Pro Leu Asn Phe Asn Tyr Ser Leu Asp Lys Ile
 500 505 510
 Ile Val Asp Tyr Asn Leu Gln Ser Lys Ile Thr Leu Pro Asn Asp Arg
 515 520 525
 Thr Thr Pro Val Thr Lys Gly Ile Pro Tyr Ala Pro Glu Tyr Lys Ser
 530 535 540
 Asn Ala Ala Ser Thr Ile Glu Ile His Asn Ile Asp Asp Asn Thr Ile

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545 550 555 560
 Tyr Gln Tyr Leu Tyr Ala Gln Lys Ser Pro Thr Thr Leu Gln Arg Ile
 565 570 575
 Thr Met Thr Asn Ser Val Asp Asp Ala Leu Ile Asn Ser Thr Lys Ile
 580 585 590
 Tyr Ser Tyr Phe Pro Ser Val Ile Ser Lys Val Asn Gln Gly Ala Gln
 595 600 605
 Gly Ile Leu Phe Leu Gln Trp Val Arg Asp Ile Ile Asp Asp Phe Thr
 610 615 620
 Asn Glu Ser Ser Gln Lys Thr Thr Ile Asp Lys Ile Ser Asp Val Ser
 625 630 635 640
 Thr Ile Val Pro Tyr Ile Gly Pro Ala Leu Asn Ile Val Lys Gln Gly
 645 650 655
 Tyr Glu Gly Asn Phe Ile Gly Ala Leu Glu Thr Thr Gly Val Val Leu
 660 665 670
 Leu Leu Glu Tyr Ile Pro Glu Ile Thr Leu Pro Val Ile Ala Ala Leu
 675 680 685
 Ser Ile Ala Glu Ser Ser Thr Gln Lys Glu Lys Ile Ile Lys Thr Ile
 690 695 700
 Asp Asn Phe Leu Glu Lys Arg Tyr Glu Lys Trp Ile Glu Val Tyr Lys
 705 710 715 720
 Leu Val Lys Ala Lys Trp Leu Gly Thr Val Asn Thr Gln Phe Gln Lys
 725 730 735
 Arg Ser Tyr Gln Met Tyr Arg Ser Leu Glu Tyr Gln Val Asp Ala Ile
 740 745 750
 Lys Lys Ile Ile Asp Tyr Glu Tyr Lys Ile Tyr Ser Gly Pro Asp Lys
 755 760 765
 Glu Gln Ile Ala Asp Glu Ile Asn Asn Leu Lys Asn Lys Leu Glu Glu
 770 775 780
 Lys Ala Asn Lys Ala Met Ile Asn Ile Asn Ile Phe Met Arg Glu Ser
 785 790 795 800
 Ser Arg Ser Phe Leu Val Asn Gln Met Ile Asn Glu Ala Lys Lys Gln
 805 810 815

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Leu Leu Glu Phe Asp Thr Gln Ser Lys Asn Ile Leu Met Gln Tyr Ile
820 825 830

Lys Ala Asn Ser Lys Phe Ile Gly Ile Thr Glu Leu Lys Lys Leu Glu
835 840 845

Ser Lys Ile Asn Lys Val Phe Ser Thr Pro Ile Pro Phe Ser Tyr Ser
850 855 860

Lys Asn Leu Asp Cys Trp Val Asp Asn Glu Glu Asp Ile Asp Val Ile
865 870 875 880

Leu Lys Lys Ser Thr Ile Leu
885

<210> 148
<211> 2619
<212> DNA
<213> Clostridium botulinum

<220>
<221> CDS
<222> (1)..(2619)

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Gly Ser Met Glu Phe Val Asn Lys Gln Phe Asn Tyr Lys Asp Pro Val
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aac ggt gtt gac att gcc tac atc aaa att cca aac gcc ggc cag atg 96
Asn Gly Val Asp Ile Ala Tyr Ile Lys Ile Pro Asn Ala Gly Gln Met
20 25 30

cag ccg gtg aag gct ttc aag att cat aac aaa atc tgg gtt att ccg 144
Gln Pro Val Lys Ala Phe Lys Ile His Asn Lys Ile Trp Val Ile Pro
35 40 45

gaa cgc gat aca ttt acg aac ccg gaa gaa gga gac ttg aac ccg ccg 192
Glu Arg Asp Thr Phe Thr Asn Pro Glu Glu Gly Asp Leu Asn Pro Pro
50 55 60

ccg gaa gca aag cag gtg cca gtt tca tac tac gat tca acc tat ctg 240
Pro Glu Ala Lys Gln Val Pro Val Ser Tyr Tyr Asp Ser Thr Tyr Leu
65 70 75 80

agc aca gac aac gag aag gat aac tac ctg aag gga gtg acc aaa tta 288
Ser Thr Asp Asn Glu Lys Asp Asn Tyr Leu Lys Gly Val Thr Lys Leu
85 90 95

ttc gag cgt att tat tcc act gac ctg ggc cgt atg ctg ctg acc tca 336
Phe Glu Arg Ile Tyr Ser Thr Asp Leu Gly Arg Met Leu Leu Thr Ser
100 105 110

atc gtc cgc gga atc cca ttt tgg ggt ggc agt acc att gac acg gag 384
Ile Val Arg Gly Ile Pro Phe Trp Gly Gly Ser Thr Ile Asp Thr Glu
115 120 125

ttg aag gtt att gac act aac tgc att aac gtg atc caa cca gac ggt 432
Leu Lys Val Ile Asp Thr Asn Cys Ile Asn Val Ile Gln Pro Asp Gly
130 135 140

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agc tac aga tct gaa gaa ctt aac ctc gta atc atc ggg ccc tcc gcg Ser Tyr Arg Ser Glu Glu Leu Asn Leu Val Ile Ile Gly Pro Ser Ala 145 150 155 160	480
gac att atc cag ttt gag tgc aag agc ttt ggc cac gaa gtg ttg aac Asp Ile Ile Gln Phe Glu Cys Lys Ser Phe Gly His Glu Val Leu Asn 165 170 175	528
ctg acg cgt aac ggt tac ggc tct act cag tac att cgt ttc agc cca Leu Thr Arg Asn Gly Tyr Gly Ser Thr Gln Tyr Ile Arg Phe Ser Pro 180 185 190	576
gac ttc acg ttc ggt ttc gag gag agc ctg gag gtt gat acc aac ccg Asp Phe Thr Phe Gly Phe Glu Glu Ser Leu Glu Val Asp Thr Asn Pro 195 200 205	624
ctg ttg ggt gca ggc aag ttc gca act gat cca gcg gtg acc ctg gca Leu Leu Gly Ala Gly Lys Phe Ala Thr Asp Pro Ala Val Thr Leu Ala 210 215 220	672
cac gag ctg atc cac gcc ggt cat cgt ctg tat ggc att gcg att aac His Glu Leu Ile His Ala Gly His Arg Leu Tyr Gly Ile Ala Ile Asn 225 230 235 240	720
ccg aac cgc gtg ttc aag gtt aac acc aac gcc tac tac gag atg agt Pro Asn Arg Val Phe Lys Val Asn Thr Asn Ala Tyr Tyr Glu Met Ser 245 250 255	768
ggt tta gaa gta agc ttc gag gaa ctg cgc acg ttc ggt ggc cat gat Gly Leu Glu Val Ser Phe Glu Glu Leu Arg Thr Phe Gly Gly His Asp 260 265 270	816
gcg aag ttt atc gac agc ttg cag gag aac gag ttc cgt ctg tac tac Ala Lys Phe Ile Asp Ser Leu Gln Glu Asn Glu Phe Arg Leu Tyr Tyr 275 280 285	864
tac aac aag ttt aaa gat att gca agt aca ctg aac aag gct aag tcc Tyr Asn Lys Phe Lys Asp Ile Ala Ser Thr Leu Asn Lys Ala Lys Ser 290 295 300	912
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aaa tta aaa ttt gat aag tta tac aaa atg tta aca gag att tac aca Lys Leu Lys Phe Asp Lys Leu Tyr Lys Met Leu Thr Glu Ile Tyr Thr 340 345 350	1056
gag gat aat ttt gtt aag ttt ttt aaa gta ctt aac aga aaa aca tat Glu Asp Asn Phe Val Lys Phe Phe Lys Val Leu Asn Arg Lys Thr Tyr 355 360 365	1104
ttg aat ttt gat aaa gcc gta ttt aag ata aat ata gta cct aag gta Leu Asn Phe Asp Lys Ala Val Phe Lys Ile Asn Ile Val Pro Lys Val 370 375 380	1152
aat tac aca ata tat gat gga ttt aat tta aga aat aca aat tta gca Asn Tyr Thr Ile Tyr Asp Gly Phe Asn Leu Arg Asn Thr Asn Leu Ala 385 390 395 400	1200
gca aac ttt aat ggt caa aat aca gaa att aat aat atg aat ttt act Ala Asn Phe Asn Gly Gln Asn Thr Glu Ile Asn Asn Met Asn Phe Thr	1248

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405	410	415	
aaa cta aaa aat ttt act gga ttg ttt gaa ttt tat aag ttg cta tgt Lys Leu Lys Asn Phe Thr Gly Leu Phe Glu Phe Tyr Lys Leu Leu Cys 420 425 430			1296
gta aga ggg ata ata act tct aaa act aaa tca tta gat aaa gga tac Val Arg Gly Ile Ile Thr Ser Lys Thr Lys Ser Leu Asp Lys Gly Tyr 435 440 445			1344
aat aag gca tta aat gat tta tgt atc aaa gtt aat aat tgg gac ttg Asn Lys Ala Leu Asn Asp Leu Cys Ile Lys Val Asn Asn Trp Asp Leu 450 455 460			1392
ttt ttt agt cct tca gaa gat aat ttt act aat gat cta aat aaa gga Phe Phe Ser Pro Ser Glu Asp Asn Phe Thr Asn Asp Leu Asn Lys Gly 465 470 475 480			1440
gaa gaa att aca tct gat act aat ata gaa gca gca gaa gaa aat att Glu Glu Ile Thr Ser Asp Thr Asn Ile Glu Ala Ala Glu Glu Asn Ile 485 490 495			1488
agt tta gat tta ata caa caa tat tat tta acc ttt aat ttt gat aat Ser Leu Asp Leu Ile Gln Gln Tyr Tyr Leu Thr Phe Asn Phe Asp Asn 500 505 510			1536
gaa cct gaa aat att tca ata gaa aat ctt tca agt gac att ata ggc Glu Pro Glu Asn Ile Ser Ile Glu Asn Leu Ser Ser Asp Ile Ile Gly 515 520 525			1584
caa tta gaa ctt atg cct aat ata gaa aga ttt cct aat gga aaa aag Gln Leu Glu Leu Met Pro Asn Ile Glu Arg Phe Pro Asn Gly Lys Lys 530 535 540			1632
tat gag tta gat aaa tat act atg ttc cat tat ctt cgt gct caa gaa Tyr Glu Leu Asp Lys Tyr Thr Met Phe His Tyr Leu Arg Ala Gln Glu 545 550 555 560			1680
ttt gaa cat ggt aaa tct agg att gct tta aca aat tct gtt aac gaa Phe Glu His Gly Lys Ser Arg Ile Ala Leu Thr Asn Ser Val Asn Glu 565 570 575			1728
gca tta tta aat cct agt cgt gtt tat aca ttt ttt tct tca gac tat Ala Leu Leu Asn Pro Ser Arg Val Tyr Thr Phe Phe Ser Ser Asp Tyr 580 585 590			1776
gta aag aaa gtt aat aaa gct acg gag gca gct atg ttt tta ggc tgg Val Lys Lys Val Asn Lys Ala Thr Glu Ala Ala Met Phe Leu Gly Trp 595 600 605			1824
gta gaa caa tta gta tat gat ttt acc gat gaa act agc gaa gta agt Val Glu Gln Leu Val Tyr Asp Phe Thr Asp Glu Thr Ser Glu Val Ser 610 615 620			1872
act acg gat aaa att gcg gat ata act ata att att cca tat ata gga Thr Thr Asp Lys Ile Ala Asp Ile Thr Ile Ile Ile Pro Tyr Ile Gly 625 630 635 640			1920
cct gct tta aat ata ggt aat atg tta tat aaa gat gat ttt gta ggt Pro Ala Leu Asn Ile Gly Asn Met Leu Tyr Lys Asp Asp Phe Val Gly 645 650 655			1968
gct tta ata ttt tca gga gct gtt att ctg tta gaa ttt ata cca gag Ala Leu Ile Phe Ser Gly Ala Val Ile Leu Leu Glu Phe Ile Pro Glu 660 665 670			2016

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att gca ata cct gta tta ggt act ttt gca ctt gta tca tat att gcg 2064
 Ile Ala Ile Pro Val Leu Gly Thr Phe Ala Leu Val Ser Tyr Ile Ala
 675 680 685

aat aag gtt cta acc gtt caa aca ata gat aat gct tta agt aaa aga 2112
 Asn Lys Val Leu Thr Val Gln Thr Ile Asp Asn Ala Leu Ser Lys Arg
 690 695 700

aat gaa aaa tgg gat gag gtc tat aaa tat ata gta aca aat tgg tta 2160
 Asn Glu Lys Trp Asp Glu Val Tyr Lys Tyr Ile Val Thr Asn Trp Leu
 705 710 715 720

gca aag gtt aat aca cag att gat cta ata aga aaa aaa atg aaa gaa 2208
 Ala Lys Val Asn Thr Gln Ile Asp Leu Ile Arg Lys Lys Met Lys Glu
 725 730 735

gct tta gaa aat caa gca gaa gca aca aag gct ata ata aac tat cag 2256
 Ala Leu Glu Asn Gln Ala Glu Ala Thr Lys Ala Ile Ile Asn Tyr Gln
 740 745 750

tat aat caa tat act gag gaa gag aaa aat aat att aat ttt aat att 2304
 Tyr Asn Gln Tyr Thr Glu Glu Lys Asn Asn Ile Asn Phe Asn Ile
 755 760 765

gat gat tta agt tcg aaa ctt aat gag tct ata aat aaa gct atg att 2352
 Asp Asp Leu Ser Ser Lys Leu Asn Glu Ser Ile Asn Lys Ala Met Ile
 770 775 780

aat ata aat aaa ttt ttg aat caa tgc tct gtt tca tat tta atg aat 2400
 Asn Ile Asn Lys Phe Leu Asn Gln Cys Ser Val Ser Tyr Leu Met Asn
 785 790 795 800

tct atg atc cct tat ggt gtt aaa cgg tta gaa gat ttt gat gct agt 2448
 Ser Met Ile Pro Tyr Gly Val Lys Arg Leu Glu Asp Phe Asp Ala Ser
 805 810 815

ctt aaa gat gca tta tta aag tat ata tat gat aat aga gga act tta 2496
 Leu Lys Asp Ala Leu Leu Lys Tyr Ile Tyr Asp Asn Arg Gly Thr Leu
 820 825 830

att ggt caa gta gat aga tta aaa gat aaa gtt aat aat aca ctt agt 2544
 Ile Gly Gln Val Asp Arg Leu Lys Asp Lys Val Asn Asn Thr Leu Ser
 835 840 845

aca gat ata cct ttt cag ctt tcc aaa tac gta gat aat caa aga tta 2592
 Thr Asp Ile Pro Phe Gln Leu Ser Lys Tyr Val Asp Asn Gln Arg Leu
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tta tct aca ttt act gaa tat att aag 2619
 Leu Ser Thr Phe Thr Glu Tyr Ile Lys
 865 870

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Gln Pro Val Lys Ala Phe Lys Ile His Asn Lys Ile Trp Val Ile Pro
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 Glu Arg Asp Thr Phe Thr Asn Pro Glu Glu Gly Asp Leu Asn Pro Pro
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 Pro Glu Ala Lys Gln Val Pro Val Ser Tyr Tyr Asp Ser Thr Tyr Leu
 65 70 75 80
 Ser Thr Asp Asn Glu Lys Asp Asn Tyr Leu Lys Gly Val Thr Lys Leu
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 Phe Glu Arg Ile Tyr Ser Thr Asp Leu Gly Arg Met Leu Leu Thr Ser
 100 105 110
 Ile Val Arg Gly Ile Pro Phe Trp Gly Gly Ser Thr Ile Asp Thr Glu
 115 120 125
 Leu Lys Val Ile Asp Thr Asn Cys Ile Asn Val Ile Gln Pro Asp Gly
 130 135 140
 Ser Tyr Arg Ser Glu Glu Leu Asn Leu Val Ile Ile Gly Pro Ser Ala
 145 150 155 160
 Asp Ile Ile Gln Phe Glu Cys Lys Ser Phe Gly His Glu Val Leu Asn
 165 170 175
 Leu Thr Arg Asn Gly Tyr Gly Ser Thr Gln Tyr Ile Arg Phe Ser Pro
 180 185 190
 Asp Phe Thr Phe Gly Phe Glu Glu Ser Leu Glu Val Asp Thr Asn Pro
 195 200 205
 Leu Leu Gly Ala Gly Lys Phe Ala Thr Asp Pro Ala Val Thr Leu Ala
 210 215 220
 His Glu Leu Ile His Ala Gly His Arg Leu Tyr Gly Ile Ala Ile Asn
 225 230 235 240
 Pro Asn Arg Val Phe Lys Val Asn Thr Asn Ala Tyr Tyr Glu Met Ser
 245 250 255
 Gly Leu Glu Val Ser Phe Glu Glu Leu Arg Thr Phe Gly Gly His Asp
 260 265 270
 Ala Lys Phe Ile Asp Ser Leu Gln Glu Asn Glu Phe Arg Leu Tyr Tyr
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 Tyr Asn Lys Phe Lys Asp Ile Ala Ser Thr Leu Asn Lys Ala Lys Ser

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290 295 300
 Ile Val Gly Thr Thr Ala Ser Leu Gln Tyr Met Lys Asn Val Phe Lys
 305 310 315 320
 Glu Lys Tyr Leu Leu Ser Glu Asp Thr Ser Gly Lys Phe Ser Val Asp
 325 330 335
 Lys Leu Lys Phe Asp Lys Leu Tyr Lys Met Leu Thr Glu Ile Tyr Thr
 340 345 350
 Glu Asp Asn Phe Val Lys Phe Phe Lys Val Leu Asn Arg Lys Thr Tyr
 355 360 365
 Leu Asn Phe Asp Lys Ala Val Phe Lys Ile Asn Ile Val Pro Lys Val
 370 375 380
 Asn Tyr Thr Ile Tyr Asp Gly Phe Asn Leu Arg Asn Thr Asn Leu Ala
 385 390 395 400
 Ala Asn Phe Asn Gly Gln Asn Thr Glu Ile Asn Asn Met Asn Phe Thr
 405 410 415
 Lys Leu Lys Asn Phe Thr Gly Leu Phe Glu Phe Tyr Lys Leu Leu Cys
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 Val Arg Gly Ile Ile Thr Ser Lys Thr Lys Ser Leu Asp Lys Gly Tyr
 435 440 445
 Asn Lys Ala Leu Asn Asp Leu Cys Ile Lys Val Asn Asn Trp Asp Leu
 450 455 460
 Phe Phe Ser Pro Ser Glu Asp Asn Phe Thr Asn Asp Leu Asn Lys Gly
 465 470 475 480
 Glu Glu Ile Thr Ser Asp Thr Asn Ile Glu Ala Ala Glu Glu Asn Ile
 485 490 495
 Ser Leu Asp Leu Ile Gln Gln Tyr Tyr Leu Thr Phe Asn Phe Asp Asn
 500 505 510
 Glu Pro Glu Asn Ile Ser Ile Glu Asn Leu Ser Ser Asp Ile Ile Gly
 515 520 525
 Gln Leu Glu Leu Met Pro Asn Ile Glu Arg Phe Pro Asn Gly Lys Lys
 530 535 540
 Tyr Glu Leu Asp Lys Tyr Thr Met Phe His Tyr Leu Arg Ala Gln Glu
 545 550 555 560

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Phe Glu His Gly Lys Ser Arg Ile Ala Leu Thr Asn Ser Val Asn Glu
 565 570 575
 Ala Leu Leu Asn Pro Ser Arg Val Tyr Thr Phe Phe Ser Ser Asp Tyr
 580 585 590
 Val Lys Lys Val Asn Lys Ala Thr Glu Ala Ala Met Phe Leu Gly Trp
 595 600 605
 Val Glu Gln Leu Val Tyr Asp Phe Thr Asp Glu Thr Ser Glu Val Ser
 610 615 620
 Thr Thr Asp Lys Ile Ala Asp Ile Thr Ile Ile Ile Pro Tyr Ile Gly
 625 630 635 640
 Pro Ala Leu Asn Ile Gly Asn Met Leu Tyr Lys Asp Asp Phe Val Gly
 645 650 655
 Ala Leu Ile Phe Ser Gly Ala Val Ile Leu Leu Glu Phe Ile Pro Glu
 660 665 670
 Ile Ala Ile Pro Val Leu Gly Thr Phe Ala Leu Val Ser Tyr Ile Ala
 675 680 685
 Asn Lys Val Leu Thr Val Gln Thr Ile Asp Asn Ala Leu Ser Lys Arg
 690 695 700
 Asn Glu Lys Trp Asp Glu Val Tyr Lys Tyr Ile Val Thr Asn Trp Leu
 705 710 715 720
 Ala Lys Val Asn Thr Gln Ile Asp Leu Ile Arg Lys Lys Met Lys Glu
 725 730 735
 Ala Leu Glu Asn Gln Ala Glu Ala Thr Lys Ala Ile Ile Asn Tyr Gln
 740 745 750
 Tyr Asn Gln Tyr Thr Glu Glu Glu Lys Asn Asn Ile Asn Phe Asn Ile
 755 760 765
 Asp Asp Leu Ser Ser Lys Leu Asn Glu Ser Ile Asn Lys Ala Met Ile
 770 775 780
 Asn Ile Asn Lys Phe Leu Asn Gln Cys Ser Val Ser Tyr Leu Met Asn
 785 790 795 800
 Ser Met Ile Pro Tyr Gly Val Lys Arg Leu Glu Asp Phe Asp Ala Ser
 805 810 815
 Leu Lys Asp Ala Leu Leu Lys Tyr Ile Tyr Asp Asn Arg Gly Thr Leu
 820 825 830

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Ile Gly Gln Val Asp Arg Leu Lys Asp Lys Val Asn Asn Thr Leu Ser
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Thr Asp Ile Pro Phe Gln Leu Ser Lys Tyr Val Asp Asn Gln Arg Leu
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aac ggt gtt gac att gct tac atc aaa atc ccg aac gct ggc cag atg 96
Asn Gly Val Asp Ile Ala Tyr Ile Lys Ile Pro Asn Ala Gly Gln Met
20 25 30
cag ccg gta aag gca ttc aaa atc cac aac aaa atc tgg gtt atc ccg 144
Gln Pro Val Lys Ala Phe Lys Ile His Asn Lys Ile Trp Val Ile Pro
35 40 45
gaa cgt gat acc ttt act aac ccg gaa gaa ggt gac ctg aac ccg cca 192
Glu Arg Asp Thr Phe Thr Asn Pro Glu Glu Gly Asp Leu Asn Pro Pro
50 55 60
ccg gaa gcg aaa cag gtg ccg gta tct tac tat gac tcc acc tac ctg 240
Pro Glu Ala Lys Gln Val Pro Val Ser Tyr Tyr Asp Ser Thr Tyr Leu
65 70 75 80
tct acc gat aac gaa aag gac aac tac ctg aaa ggt gtt act aaa ctg 288
Ser Thr Asp Asn Glu Lys Asp Asn Tyr Leu Lys Gly Val Thr Lys Leu
85 90 95
ttc gag cgt att tac tcc acc gac ctg ggc cgt atg ctg ctg act agc 336
Phe Glu Arg Ile Tyr Ser Thr Asp Leu Gly Arg Met Leu Leu Thr Ser
100 105 110
atc gtt cgc ggt atc ccg ttc tgg ggc ggt tct acc atc gat acc gaa 384
Ile Val Arg Gly Ile Pro Phe Trp Gly Gly Ser Thr Ile Asp Thr Glu
115 120 125
ctg aaa gta atc gac act aac tgc atc aac gtt att cag ccg gac ggt 432
Leu Lys Val Ile Asp Thr Asn Cys Ile Asn Val Ile Gln Pro Asp Gly
130 135 140
tcc tat cgt tcc gaa gaa ctg aac ctg gtg atc atc ggc ccg tct gct 480
Ser Tyr Arg Ser Glu Glu Leu Asn Leu Val Ile Ile Gly Pro Ser Ala
145 150 155 160
gat atc atc cag ttc gag tgt aag agc ttt ggt cac gaa gtt ctg aac 528
Asp Ile Ile Gln Phe Glu Cys Lys Ser Phe Gly His Glu Val Leu Asn

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165							170					175					
ctc	acc	cgt	aac	ggc	tac	ggc	tcc	act	cag	tac	atc	cgt	ttc	tct	ccg	576	
Leu	Thr	Arg	Asn	Gly	Tyr	Gly	Ser	Thr	Gln	Tyr	Ile	Arg	Phe	Ser	Pro		
			180					185					190				
gac	ttc	acc	ttc	ggc	ttt	gaa	gaa	tcc	ctg	gaa	gta	gac	acg	aac	cca	624	
Asp	Phe	Thr	Phe	Gly	Phe	Glu	Glu	Ser	Leu	Glu	Val	Asp	Thr	Asn	Pro		
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ctg	ctg	ggc	gct	ggc	aaa	ttc	gca	act	gat	cct	gcg	gtt	acc	ctg	gct	672	
Leu	Leu	Gly	Ala	Gly	Lys	Phe	Ala	Thr	Asp	Pro	Ala	Val	Thr	Leu	Ala		
	210					215					220						
cac	gaa	ctg	att	cat	gca	ggc	cac	cgc	ctg	tac	ggc	atc	gcc	atc	aat	720	
His	Glu	Leu	Ile	His	Ala	Gly	His	Arg	Leu	Tyr	Gly	Ile	Ala	Ile	Asn		
225					230					235					240		
ccg	aac	cgt	gtc	ttc	aaa	gtt	aac	acc	aac	gcg	tat	tac	gag	atg	tcc	768	
Pro	Asn	Arg	Val	Phe	Lys	Val	Asn	Thr	Asn	Ala	Tyr	Tyr	Glu	Met	Ser		
			245					250						255			
ggc	ctg	gaa	gta	agc	ttc	gaa	gaa	ctg	cgt	act	ttt	ggc	ggc	cac	gac	816	
Gly	Leu	Glu	Val	Ser	Phe	Glu	Glu	Leu	Arg	Thr	Phe	Gly	Gly	His	Asp		
		260					265					270					
gct	aaa	ttc	atc	gac	tct	ctg	caa	gaa	aac	gag	ttc	cgt	ctg	tac	tac	864	
Ala	Lys	Phe	Ile	Asp	Ser	Leu	Gln	Glu	Asn	Glu	Phe	Arg	Leu	Tyr	Tyr		
	275					280					285						
tat	aac	aag	ttc	aaa	gat	atc	gca	tcc	acc	ctg	aac	aaa	gcg	aaa	tcc	912	
Tyr	Asn	Lys	Phe	Lys	Asp	Ile	Ala	Ser	Thr	Leu	Asn	Lys	Ala	Lys	Ser		
	290					295					300						
atc	gtg	ggc	acc	act	gct	tct	ctg	cag	tac	atg	aag	aac	gtt	ttt	aaa	960	
Ile	Val	Gly	Thr	Thr	Ala	Ser	Leu	Gln	Tyr	Met	Lys	Asn	Val	Phe	Lys		
305				310					315					320			
gaa	aaa	tac	ctg	ctc	agc	gaa	gac	acc	tcc	ggc	aaa	ttc	tct	gta	gac	1008	
Glu	Lys	Tyr	Leu	Ser	Glu	Asp	Thr	Ser	Gly	Lys	Phe	Ser	Val	Asp			
			325				330						335				
aag	ttg	aaa	ttc	gat	aaa	ctt	tac	aaa	atg	ctg	act	gaa	att	tac	acc	1056	
Lys	Leu	Lys	Phe	Asp	Lys	Leu	Tyr	Lys	Met	Leu	Thr	Glu	Ile	Tyr	Thr		
		340					345					350					
gaa	gac	aac	ttc	gtt	aag	ttc	ttt	aaa	gtt	ctg	aac	cgc	aaa	acc	tat	1104	
Glu	Asp	Asn	Phe	Val	Lys	Phe	Phe	Lys	Val	Leu	Asn	Arg	Lys	Thr	Tyr		
	355					360					365						
ctg	aac	ttc	gac	aag	gca	gta	ttc	aaa	atc	aac	atc	gtg	ccg	aaa	gtt	1152	
Leu	Asn	Phe	Asp	Lys	Ala	Val	Phe	Lys	Ile	Asn	Ile	Val	Pro	Lys	Val		
	370					375					380						
aac	tac	act	atc	tac	gat	ggc	ttc	aac	ctg	cgt	aac	acc	aac	ctg	gct	1200	
Asn	Tyr	Thr	Ile	Tyr	Asp	Gly	Phe	Asn	Leu	Arg	Asn	Thr	Asn	Leu	Ala		
	385				390					395				400			
gct	aat	ttt	aac	ggc	cag	aac	acg	gaa	atc	aac	aac	atg	aac	ttc	aca	1248	
Ala	Asn	Phe	Asn	Gly	Gln	Asn	Thr	Glu	Ile	Asn	Asn	Met	Asn	Phe	Thr		
			405						410					415			
aaa	ctg	aaa	aac	ttc	act	ggc	ctg	ttc	gag	ttt	tac	aag	ctg	ctg	tgc	1296	
Lys	Leu	Lys	Asn	Phe	Thr	Gly	Leu	Phe	Glu	Phe	Tyr	Lys	Leu	Leu	Cys		
		420					425						430				

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gta cgt ggc atc att acc tcc aaa act aaa tct ctg gac aaa ggt tat	1344
Val Arg Gly Ile Ile Thr Ser Lys Thr Lys Ser Leu Asp Lys Gly Tyr	
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aac aaa gcg ctg aac gac ctc tgt atc aag gtt aac aac tgg gat tta	1392
Asn Lys Ala Leu Asn Asp Leu Cys Ile Lys Val Asn Asn Trp Asp Leu	
450 455 460	
ttc ttc agc ccg agt gaa gac aac ttc acc aac gac ctg aac aaa ggt	1440
Phe Phe Ser Pro Ser Glu Asp Asn Phe Thr Asn Asp Leu Asn Lys Gly	
465 470 475 480	
gaa gaa atc acc tca gat act aac atc gaa gca gcc gaa gaa aac atc	1488
Glu Glu Ile Thr Ser Asp Thr Asn Ile Glu Ala Ala Glu Glu Asn Ile	
485 490 495	
tcg ctg gac ctg atc cag cag tac tac ctg acc ttt aat ttc gac aac	1536
Ser Leu Asp Leu Ile Gln Gln Tyr Tyr Leu Thr Phe Asn Phe Asp Asn	
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515 520 525	
cag ctg gaa ctg atg ccg aac atc gaa cgt ttc cca aac ggt aaa aag	1632
Gln Leu Glu Leu Met Pro Asn Ile Glu Arg Phe Pro Asn Gly Lys Lys	
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Tyr Glu Leu Asp Lys Tyr Thr Met Phe His Tyr Leu Arg Ala Gln Glu	
545 550 555 560	
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Phe Glu His Gly Lys Ser Arg Ile Ala Leu Thr Asn Ser Val Asn Glu	
565 570 575	
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Ala Leu Leu Asn Pro Ser Arg Val Tyr Thr Phe Phe Ser Ser Asp Tyr	
580 585 590	
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Val Lys Lys Val Asn Lys Ala Thr Glu Ala Ala Met Phe Leu Gly Trp	
595 600 605	
gtt gaa cag ctt gtt tat gat ttt acc gac gag acg tcc gaa gta tct	1872
Val Glu Gln Leu Val Tyr Asp Phe Thr Asp Glu Thr Ser Glu Val Ser	
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Thr Thr Asp Lys Ile Ala Asp Ile Thr Ile Ile Ile Pro Tyr Ile Gly	
625 630 635 640	
ccg gct ctg aac att ggc aac atg ctg tac aaa gac gac ttc gtt ggt	1968
Pro Ala Leu Asn Ile Gly Asn Met Leu Tyr Lys Asp Asp Phe Val Gly	
645 650 655	
gca ctg atc ttc tcc ggt gcg gtg atc ctg ctg gag ttc atc ccg gaa	2016
Ala Leu Ile Phe Ser Gly Ala Val Ile Leu Leu Glu Phe Ile Pro Glu	
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atc gcc atc ccg gta ctg ggc acc ttt gct ctg gtt tct tac att gca	2064
Ile Ala Ile Pro Val Leu Gly Thr Phe Ala Leu Val Ser Tyr Ile Ala	
675 680 685	
aac aag gtt ctg act gta caa acc atc gac aac gcg ctg agc aaa cgt	2112
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690	695	700	
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Asn Glu Lys Trp Asp	Glu Val Tyr Lys Tyr	Ile Val Thr Asn Trp Leu	
705	710	715	720
gct aag gtt aat act	cag atc gac ctc atc	cgc aaa aaa atg aaa gaa	2208
Ala Lys Val Asn Thr	Gln Ile Asp Leu	Ile Arg Lys Lys Met Lys Glu	
	725	730	735
gca ctg gaa aac cag	gcg gaa gct acc aag	gca atc att aac tac cag	2256
Ala Leu Glu Asn Gln	Ala Glu Ala Thr	Lys Ala Ile Ile Asn Tyr Gln	
	740	745	750
tac aac cag tac acc	gag gaa gaa aaa aac	aac atc aac ttc aac atc	2304
Tyr Asn Gln Tyr Thr	Glu Glu Lys Asn Asn	Ile Asn Phe Asn Ile	
	755	760	765
gac gat ctg tcc tct	aaa ctg aac gaa tcc	atc aac aaa gct atg atc	2352
Asp Asp Leu Ser Ser	Lys Leu Asn Glu Ser	Ile Asn Lys Ala Met Ile	
	770	775	780
aac atc aac aag ttc	ctg aac cag tgc tct	gta agc tat ctg atg aac	2400
Asn Ile Asn Lys Phe	Leu Asn Gln Cys Ser	Val Ser Tyr Leu Met Asn	
	785	790	800
tcc atg atc ccg tac	ggg gtt aaa cgt ctg	gag gac ttc gat gcg tct	2448
Ser Met Ile Pro Tyr	Gly Val Lys Arg Leu	Glu Asp Phe Asp Ala Ser	
	805	810	815
ctg aaa gac gcc ctg	ctg aaa tac att tac	gac aac cgt ggc act ctg	2496
Leu Lys Asp Ala Leu	Leu Lys Tyr Ile Tyr	Asp Asn Arg Gly Thr Leu	
	820	825	830
atc ggt cag gtt gat	cgt ctg aag gac aaa	gtg aac aat acc tta tcg	2544
Ile Gly Gln Val Asp	Arg Leu Lys Asp Lys	Val Asn Asn Thr Leu Ser	
	835	840	845
acc gac atc cct ttt	cag ctc agt aaa tat	gtc gat aac caa cgc ctt	2592
Thr Asp Ile Pro Phe	Gln Leu Ser Lys Tyr	Val Asp Asn Gln Arg Leu	
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Leu Ser Thr Phe Thr	Glu Tyr Ile Lys		
	865	870	

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Glu Arg Asp Thr Phe Thr Asn Pro Glu Glu Gly Asp Leu Asn Pro Pro
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 Pro Glu Ala Lys Gln Val Pro Val Ser Tyr Tyr Asp Ser Thr Tyr Leu
 65 70 75 80
 Ser Thr Asp Asn Glu Lys Asp Asn Tyr Leu Lys Gly Val Thr Lys Leu
 85 90 95
 Phe Glu Arg Ile Tyr Ser Thr Asp Leu Gly Arg Met Leu Leu Thr Ser
 100 105 110
 Ile Val Arg Gly Ile Pro Phe Trp Gly Gly Ser Thr Ile Asp Thr Glu
 115 120 125
 Leu Lys Val Ile Asp Thr Asn Cys Ile Asn Val Ile Gln Pro Asp Gly
 130 135 140
 Ser Tyr Arg Ser Glu Glu Leu Asn Leu Val Ile Ile Gly Pro Ser Ala
 145 150 155 160
 Asp Ile Ile Gln Phe Glu Cys Lys Ser Phe Gly His Glu Val Leu Asn
 165 170 175
 Leu Thr Arg Asn Gly Tyr Gly Ser Thr Gln Tyr Ile Arg Phe Ser Pro
 180 185 190
 Asp Phe Thr Phe Gly Phe Glu Glu Ser Leu Glu Val Asp Thr Asn Pro
 195 200 205
 Leu Leu Gly Ala Gly Lys Phe Ala Thr Asp Pro Ala Val Thr Leu Ala
 210 215 220
 His Glu Leu Ile His Ala Gly His Arg Leu Tyr Gly Ile Ala Ile Asn
 225 230 235 240
 Pro Asn Arg Val Phe Lys Val Asn Thr Asn Ala Tyr Tyr Glu Met Ser
 245 250 255
 Gly Leu Glu Val Ser Phe Glu Glu Leu Arg Thr Phe Gly Gly His Asp
 260 265 270
 Ala Lys Phe Ile Asp Ser Leu Gln Glu Asn Glu Phe Arg Leu Tyr Tyr
 275 280 285
 Tyr Asn Lys Phe Lys Asp Ile Ala Ser Thr Leu Asn Lys Ala Lys Ser
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 Ile Val Gly Thr Thr Ala Ser Leu Gln Tyr Met Lys Asn Val Phe Lys
 305 310 315 320

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Glu Lys Tyr Leu Leu Ser Glu Asp Thr Ser Gly Lys Phe Ser Val Asp
 325 330 335
 Lys Leu Lys Phe Asp Lys Leu Tyr Lys Met Leu Thr Glu Ile Tyr Thr
 340 345 350
 Glu Asp Asn Phe Val Lys Phe Phe Lys Val Leu Asn Arg Lys Thr Tyr
 355 360 365
 Leu Asn Phe Asp Lys Ala Val Phe Lys Ile Asn Ile Val Pro Lys Val
 370 375 380
 Asn Tyr Thr Ile Tyr Asp Gly Phe Asn Leu Arg Asn Thr Asn Leu Ala
 385 390 395 400
 Ala Asn Phe Asn Gly Gln Asn Thr Glu Ile Asn Asn Met Asn Phe Thr
 405 410 415
 Lys Leu Lys Asn Phe Thr Gly Leu Phe Glu Phe Tyr Lys Leu Leu Cys
 420 425 430
 Val Arg Gly Ile Ile Thr Ser Lys Thr Lys Ser Leu Asp Lys Gly Tyr
 435 440 445
 Asn Lys Ala Leu Asn Asp Leu Cys Ile Lys Val Asn Asn Trp Asp Leu
 450 455 460
 Phe Phe Ser Pro Ser Glu Asp Asn Phe Thr Asn Asp Leu Asn Lys Gly
 465 470 475 480
 Glu Glu Ile Thr Ser Asp Thr Asn Ile Glu Ala Ala Glu Glu Asn Ile
 485 490 495
 Ser Leu Asp Leu Ile Gln Gln Tyr Tyr Leu Thr Phe Asn Phe Asp Asn
 500 505 510
 Glu Pro Glu Asn Ile Ser Ile Glu Asn Leu Ser Ser Asp Ile Ile Gly
 515 520 525
 Gln Leu Glu Leu Met Pro Asn Ile Glu Arg Phe Pro Asn Gly Lys Lys
 530 535 540
 Tyr Glu Leu Asp Lys Tyr Thr Met Phe His Tyr Leu Arg Ala Gln Glu
 545 550 555 560
 Phe Glu His Gly Lys Ser Arg Ile Ala Leu Thr Asn Ser Val Asn Glu
 565 570 575
 Ala Leu Leu Asn Pro Ser Arg Val Tyr Thr Phe Phe Ser Ser Asp Tyr

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Thr Asp Ile Pro Phe Gln Leu Ser Lys Tyr Val Asp Asn Gln Arg Leu
 850 855 860

Leu Ser Thr Phe Thr Glu Tyr Ile Lys
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 <211> 2619
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 <213> Clostridium botulinum

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 gtt gac att gct tac atc aaa atc ccg aac gct ggc cag atg cag ccg 96
 Val Asp Ile Ala Tyr Ile Lys Ile Pro Asn Ala Gly Gln Met Gln Pro
 20 25 30
 gta aag gca ttc aaa atc cac aac aaa atc tgg gtt atc ccg gaa cgt 144
 Val Lys Ala Phe Lys Ile His Asn Lys Ile Trp Val Ile Pro Glu Arg
 35 40 45
 gat acc ttt act aac ccg gaa gaa ggt gac ctg aac ccg cca ccg gaa 192
 Asp Thr Phe Thr Asn Pro Glu Glu Gly Asp Leu Asn Pro Pro Pro Glu
 50 55 60
 gcg aaa cag gtg ccg gta tct tac tat gac tcc acc tac ctg tct acc 240
 Ala Lys Gln Val Pro Val Ser Tyr Tyr Asp Ser Thr Tyr Leu Ser Thr
 65 70 75 80
 gat aac gaa aag gac aac tac ctg aaa ggt gtt act aaa ctg ttc gag 288
 Asp Asn Glu Lys Asp Asn Tyr Leu Lys Gly Val Thr Lys Leu Phe Glu
 85 90 95
 cgt att tac tcc acc gac ctg ggc cgt atg ctg ctg act agc atc gtt 336
 Arg Ile Tyr Ser Thr Asp Leu Gly Arg Met Leu Leu Thr Ser Ile Val
 100 105 110
 cgc ggt atc ccg ttc tgg ggc ggt tct acc atc gat acc gaa ctg aaa 384
 Arg Gly Ile Pro Phe Trp Gly Gly Ser Thr Ile Asp Thr Glu Leu Lys
 115 120 125
 gta atc gac act aac tgc atc aac gtt att cag ccg gac ggt tcc tat 432
 Val Ile Asp Thr Asn Cys Ile Asn Val Ile Gln Pro Asp Gly Ser Tyr
 130 135 140
 cgt tcc gaa gaa ctg aac ctg gtg atc atc ggc ccg tct gct gat atc 480
 Arg Ser Glu Glu Leu Asn Leu Val Ile Ile Gly Pro Ser Ala Asp Ile
 145 150 155 160
 atc cag ttc gag tgt aag agc ttt ggt cac gaa gtt ctg aac ctc acc 528
 Ile Gln Phe Glu Cys Lys Ser Phe Gly His Glu Val Leu Asn Leu Thr
 165 170 175
 cgt aac ggc tac ggt tcc act cag tac atc cgt ttc tct ccg gac ttc 576
 Arg Asn Gly Tyr Gly Ser Thr Gln Tyr Ile Arg Phe Ser Pro Asp Phe
 180 185 190

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acc ttc ggt ttt gaa gaa tcc ctg gaa gta gac acg aac cca ctg ctg 624
 Thr Phe Gly Phe Glu Glu Ser Leu Glu Val Asp Thr Asn Pro Leu Leu
 195 200 205

ggc gct ggt aaa ttc gca act gat cct gcg gtt acc ctg gct cac gaa 672
 Gly Ala Gly Lys Phe Ala Thr Asp Pro Ala Val Thr Leu Ala His Glu
 210 215 220

ctg att cat gca ggc cac cgc ctg tac ggt atc gcc atc aat ccg aac 720
 Leu Ile His Ala Gly His Arg Leu Tyr Gly Ile Ala Ile Asn Pro Asn
 225 230 235 240

cgt gtc ttc aaa gtt aac acc aac gcg tat tac gag atg tcc ggt ctg 768
 Arg Val Phe Lys Val Asn Thr Asn Ala Tyr Tyr Glu Met Ser Gly Leu
 245 250 255

gaa gta agc ttc gaa gaa ctg cgt act ttt ggc ggt cac gac gct aaa 816
 Glu Val Ser Phe Glu Glu Leu Arg Thr Phe Gly Gly His Asp Ala Lys
 260 265 270

ttc atc gac tct ctg caa gaa aac gag ttc cgt ctg tac tac tat aac 864
 Phe Ile Asp Ser Leu Gln Glu Asn Glu Phe Arg Leu Tyr Tyr Tyr Asn
 275 280 285

aag ttc aaa gat atc gca tcc acc ctg aac aaa gcg aaa tcc atc gtg 912
 Lys Phe Lys Asp Ile Ala Ser Thr Leu Asn Lys Ala Lys Ser Ile Val
 290 295 300

ggt acc act gct tct ctg cag tac atg aag aac gtt ttt aaa gaa aaa 960
 Gly Thr Thr Ala Ser Leu Gln Tyr Met Lys Asn Val Phe Lys Glu Lys
 305 310 315 320

tac ctg ctc agc gaa gac acc tcc gcg aaa ttc tct gta gac aag ttg 1008
 Tyr Leu Leu Ser Glu Asp Thr Ser Gly Lys Phe Ser Val Asp Lys Leu
 325 330 335

aaa ttc gat aaa ctt tac aaa atg ctg act gaa att tac acc gaa gac 1056
 Lys Phe Asp Lys Leu Tyr Lys Met Leu Thr Glu Ile Tyr Thr Glu Asp
 340 345 350

aac ttc gtt aag ttc ttt aaa gtt ctg aac gcg aaa acc tat ctg aac 1104
 Asn Phe Val Lys Phe Phe Lys Val Leu Asn Arg Lys Thr Tyr Leu Asn
 355 360 365

ttc gac aag gca gta ttc aaa atc aac atc gtg ccg aaa gtt aac tac 1152
 Phe Asp Lys Ala Val Phe Lys Ile Asn Ile Val Pro Lys Val Asn Tyr
 370 375 380

act atc tac gat ggt ttc aac ctg cgt aac acc aac ctg gct gct aat 1200
 Thr Ile Tyr Asp Gly Phe Asn Leu Arg Asn Thr Asn Leu Ala Ala Asn
 385 390 395 400

ttt aac ggc cag aac acg gaa atc aac aac atg aac ttc aca aaa ctg 1248
 Phe Asn Gly Gln Asn Thr Glu Ile Asn Asn Met Asn Phe Thr Lys Leu
 405 410 415

aaa aac ttc act ggt ctg ttc gag ttt tac aag ctg ctg tgc gta cgt 1296
 Lys Asn Phe Thr Gly Leu Phe Glu Phe Tyr Lys Leu Leu Cys Val Arg
 420 425 430

ggc atc att acc tcc aaa act aaa tct ctg gac aaa ggt tat aac aaa 1344
 Gly Ile Ile Thr Ser Lys Thr Lys Ser Leu Asp Lys Gly Tyr Asn Lys
 435 440 445

gcg ctg aac gac ctc tgt atc aag gtt aac aac tgg gat tta ttc ttc 1392
 Ala Leu Asn Asp Leu Cys Ile Lys Val Asn Asn Trp Asp Leu Phe Phe

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450	455	460	
agc ccg agt gaa gac aac ttc acc aac gac ctg aac aaa ggt gaa gaa Ser Pro Ser Glu Asp Asn Phe Thr Asn Asp Leu Asn Lys Gly Glu Glu 465 470 475 480			1440
atc acc tca gat act aac atc gaa gca gcc gaa gaa aac atc tgc ctg Ile Thr Ser Asp Thr Asn Ile Glu Ala Ala Glu Glu Asn Ile Ser Leu 485 490 495			1488
gac ctg atc cag cag tac tac ctg acc ttt aat ttc gac aac gag ccg Asp Leu Ile Gln Gln Tyr Tyr Leu Thr Phe Asn Phe Asp Asn Glu Pro 500 505 510			1536
gaa aac att tct atc gaa aac ctg agc tct gat atc atc ggc cag ctg Glu Asn Ile Ser Ile Glu Asn Leu Ser Ser Asp Ile Ile Gly Gln Leu 515 520 525			1584
gaa ctg atg ccg aac atc gaa cgt ttc cca aac ggt aaa aag tac gag Glu Leu Met Pro Asn Ile Glu Arg Phe Pro Asn Gly Lys Lys Tyr Glu 530 535 540			1632
ctg gac aaa tat acc atg ttc cac tac ctg cgc gcg cag gaa ttt gaa Leu Asp Lys Tyr Thr Met Phe His Tyr Leu Arg Ala Gln Glu Phe Glu 545 550 555 560			1680
cac ggc aaa tcc cgt atc gca ctg act aac tcc gtt aac gaa gct ctg His Gly Lys Ser Arg Ile Ala Leu Thr Asn Ser Val Asn Glu Ala Leu 565 570 575			1728
ctc aac ccg tcc cgt gta tac acc ttc ttc tct agc gac tac gtg aaa Leu Asn Pro Ser Arg Val Tyr Thr Phe Phe Ser Ser Asp Tyr Val Lys 580 585 590			1776
aag gtc aac aaa gcg act gaa gct gca atg ttc ttg ggt tgg gtt gaa Lys Val Asn Lys Ala Thr Glu Ala Ala Met Phe Leu Gly Trp Val Glu 595 600 605			1824
cag ctt gtt tat gat ttt acc gac gag acg tcc gaa gta tct act acc Gln Leu Val Tyr Asp Phe Thr Asp Glu Thr Ser Glu Val Ser Thr Thr 610 615 620			1872
gac aaa att gcg gat atc act atc atc atc ccg tac atc ggt ccg gct Asp Lys Ile Ala Asp Ile Thr Ile Ile Ile Pro Tyr Ile Gly Pro Ala 625 630 635 640			1920
ctg aac att ggc aac atg ctg tac aaa gac gac ttc gtt ggt gca ctg Leu Asn Ile Gly Asn Met Leu Tyr Lys Asp Asp Phe Val Gly Ala Leu 645 650 655			1968
atc ttc tcc ggt gcg gtg atc ctg ctg gag ttc atc ccg gaa atc gcc Ile Phe Ser Gly Ala Val Ile Leu Leu Glu Phe Ile Pro Glu Ile Ala 660 665 670			2016
atc ccg gta ctg ggc acc ttt gct ctg gtt tct tac att gca aac aag Ile Pro Val Leu Gly Thr Phe Ala Leu Val Ser Tyr Ile Ala Asn Lys 675 680 685			2064
gtt ctg act gta caa acc atc gac aac gcg ctg agc aaa cgt aac gaa Val Leu Thr Val Gln Thr Ile Asp Asn Ala Leu Ser Lys Arg Asn Glu 690 695 700			2112
aaa tgg gat gaa gtt tac aaa tat atc gtg acc aac tgg ctg gct aag Lys Trp Asp Glu Val Tyr Lys Tyr Ile Val Thr Asn Trp Leu Ala Lys 705 710 715 720			2160

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gtt aat act cag atc gac ctc atc cgc aaa aaa atg aaa gaa gca ctg 2208
 Val Asn Thr Gln Ile Asp Leu Ile Arg Lys Lys Met Lys Glu Ala Leu
 725 730 735

gaa aac cag gcg gaa gct acc aag gca atc att aac tac cag tac aac 2256
 Glu Asn Gln Ala Glu Ala Thr Lys Ala Ile Ile Asn Tyr Gln Tyr Asn
 740 745 750

cag tac acc gag gaa gaa aaa aac aac atc aac ttc aac atc gac gat 2304
 Gln Tyr Thr Glu Glu Glu Lys Asn Asn Ile Asn Phe Asn Ile Asp Asp
 755 760 765

ctg tcc tct aaa ctg aac gaa tcc atc aac aaa gct atg atc aac atc 2352
 Leu Ser Ser Lys Leu Asn Glu Ser Ile Asn Lys Ala Met Ile Asn Ile
 770 775 780

aac aag ttc ctg aac cag tgc tct gta agc tat ctg atg aac tcc atg 2400
 Asn Lys Phe Leu Asn Gln Cys Ser Val Ser Tyr Leu Met Asn Ser Met
 785 790 795 800

atc ccg tac ggt gtt aaa cgt ctg gag gac ttc gat gcg tct ctg aaa 2413
 Ile Pro Tyr Gly Val Lys Arg Leu Glu Asp Phe Asp Ala Ser Leu Lys
 805 810 815

gac gcc ctg ctg aaa tac att tac gac aac cgt gcc act ctg atc ggt 2496
 Asp Ala Leu Leu Lys Tyr Ile Tyr Asp Asn Arg Gly Thr Leu Ile Gly
 820 825 830

cag gtt gat cgt ctg aag gac aaa gtg aac aat acc tta tcg acc gac 2544
 Gln Val Asp Arg Leu Lys Asp Lys Val Asn Asn Thr Leu Ser Thr Asp
 835 840 845

atc cct ttt cag ctc agt aaa tat gtc gat aac caa cgc ctt ttg agc 2592
 Ile Pro Phe Gln Leu Ser Lys Tyr Val Asp Asn Gln Arg Leu Leu Ser
 850 855 860

acg ttc aca gag tac atc aag taa tga 2619
 Thr Phe Thr Glu Tyr Ile Lys
 865 870

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 <213> Clostridium botulinum

<400> 153

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Val Lys Ala Phe Lys Ile His Asn Lys Ile Trp Val Ile Pro Glu Arg
 35 40 45

Asp Thr Phe Thr Asn Pro Glu Glu Gly Asp Leu Asn Pro Pro Pro Glu
 50 55 60

Ala Lys Gln Val Pro Val Ser Tyr Tyr Asp Ser Thr Tyr Leu Ser Thr
 65 70 75 80

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Asp Asn Glu Lys Asp Asn Tyr Leu Lys Gly Val Thr Lys Leu Phe Glu
 85 90 95
 Arg Ile Tyr Ser Thr Asp Leu Gly Arg Met Leu Leu Thr Ser Ile Val
 100 105 110
 Arg Gly Ile Pro Phe Trp Gly Gly Ser Thr Ile Asp Thr Glu Leu Lys
 115 120 125
 Val Ile Asp Thr Asn Cys Ile Asn Val Ile Gln Pro Asp Gly Ser Tyr
 130 135 140
 Arg Ser Glu Glu Leu Asn Leu Val Ile Ile Gly Pro Ser Ala Asp Ile
 145 150 155 160
 Ile Gln Phe Glu Cys Lys Ser Phe Gly His Glu Val Leu Asn Leu Thr
 165 170 175
 Arg Asn Gly Tyr Gly Ser Thr Gln Tyr Ile Arg Phe Ser Pro Asp Phe
 180 185 190
 Thr Phe Gly Phe Glu Glu Ser Leu Glu Val Asp Thr Asn Pro Leu Leu
 195 200 205
 Gly Ala Gly Lys Phe Ala Thr Asp Pro Ala Val Thr Leu Ala His Glu
 210 215 220
 Leu Ile His Ala Gly His Arg Leu Tyr Gly Ile Ala Ile Asn Pro Asn
 225 230 235 240
 Arg Val Phe Lys Val Asn Thr Asn Ala Tyr Tyr Glu Met Ser Gly Leu
 245 250 255
 Glu Val Ser Phe Glu Glu Leu Arg Thr Phe Gly Gly His Asp Ala Lys
 260 265 270
 Phe Ile Asp Ser Leu Gln Glu Asn Glu Phe Arg Leu Tyr Tyr Tyr Asn
 275 280 285
 Lys Phe Lys Asp Ile Ala Ser Thr Leu Asn Lys Ala Lys Ser Ile Val
 290 295 300
 Gly Thr Thr Ala Ser Leu Gln Tyr Met Lys Asn Val Phe Lys Glu Lys
 305 310 315 320
 Tyr Leu Leu Ser Glu Asp Thr Ser Gly Lys Phe Ser Val Asp Lys Leu
 325 330 335
 Lys Phe Asp Lys Leu Tyr Lys Met Leu Thr Glu Ile Tyr Thr Glu Asp

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340 345 350
 Asn Phe Val Lys Phe Phe Lys Val Leu Asn Arg Lys Thr Tyr Leu Asn
 355 360 365
 Phe Asp Lys Ala Val Phe Lys Ile Asn Ile Val Pro Lys Val Asn Tyr
 370 375 380
 Thr Ile Tyr Asp Gly Phe Asn Leu Arg Asn Thr Asn Leu Ala Ala Asn
 385 390 395 400
 Phe Asn Gly Gln Asn Thr Glu Ile Asn Asn Met Asn Phe Thr Lys Leu
 405 410 415
 Lys Asn Phe Thr Gly Leu Phe Glu Phe Tyr Lys Leu Leu Cys Val Arg
 420 425 430
 Gly Ile Ile Thr Ser Lys Thr Lys Ser Leu Asp Lys Gly Tyr Asn Lys
 435 440 445
 Ala Leu Asn Asp Leu Cys Ile Lys Val Asn Asn Trp Asp Leu Phe Phe
 450 455 460
 Ser Pro Ser Glu Asp Asn Phe Thr Asn Asp Leu Asn Lys Gly Glu Glu
 465 470 475 480
 Ile Thr Ser Asp Thr Asn Ile Glu Ala Ala Glu Glu Asn Ile Ser Leu
 485 490 495
 Asp Leu Ile Gln Gln Tyr Tyr Leu Thr Phe Asn Phe Asp Asn Glu Pro
 500 505 510
 Glu Asn Ile Ser Ile Glu Asn Leu Ser Ser Asp Ile Ile Gly Gln Leu
 515 520 525
 Glu Leu Met Pro Asn Ile Glu Arg Phe Pro Asn Gly Lys Lys Tyr Glu
 530 535 540
 Leu Asp Lys Tyr Thr Met Phe His Tyr Leu Arg Ala Gln Glu Phe Glu
 545 550 555 560
 His Gly Lys Ser Arg Ile Ala Leu Thr Asn Ser Val Asn Glu Ala Leu
 565 570 575
 Leu Asn Pro Ser Arg Val Tyr Thr Phe Phe Ser Ser Asp Tyr Val Lys
 580 585 590
 Lys Val Asn Lys Ala Thr Glu Ala Ala Met Phe Leu Gly Trp Val Glu
 595 600 605

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Gln Leu Val Tyr Asp Phe Thr Asp Glu Thr Ser Glu Val Ser Thr Thr
 610 615 620
 Asp Lys Ile Ala Asp Ile Thr Ile Ile Ile Pro Tyr Ile Gly Pro Ala
 625 630 635 640
 Leu Asn Ile Gly Asn Met Leu Tyr Lys Asp Asp Phe Val Gly Ala Leu
 645 650 655
 Ile Phe Ser Gly Ala Val Ile Leu Leu Glu Phe Ile Pro Glu Ile Ala
 660 665 670
 Ile Pro Val Leu Gly Thr Phe Ala Leu Val Ser Tyr Ile Ala Asn Lys
 675 680 685
 Val Leu Thr Val Gln Thr Ile Asp Asn Ala Leu Ser Lys Arg Asn Glu
 690 695 700
 Lys Trp Asp Glu Val Tyr Lys Tyr Ile Val Thr Asn Trp Leu Ala Lys
 705 710 715 720
 Val Asn Thr Gln Ile Asp Leu Ile Arg Lys Lys Met Lys Glu Ala Leu
 725 730 735
 Glu Asn Gln Ala Glu Ala Thr Lys Ala Ile Ile Asn Tyr Gln Tyr Asn
 740 745 750
 Gln Tyr Thr Glu Glu Glu Lys Asn Asn Ile Asn Phe Asn Ile Asp Asp
 755 760 765
 Leu Ser Ser Lys Leu Asn Glu Ser Ile Asn Lys Ala Met Ile Asn Ile
 770 775 780
 Asn Lys Phe Leu Asn Gln Cys Ser Val Ser Tyr Leu Met Asn Ser Met
 785 790 795 800
 Ile Pro Tyr Gly Val Lys Arg Leu Glu Asp Phe Asp Ala Ser Leu Lys
 805 810 815
 Asp Ala Leu Leu Lys Tyr Ile Tyr Asp Asn Arg Gly Thr Leu Ile Gly
 820 825 830
 Gln Val Asp Arg Leu Lys Asp Lys Val Asn Asn Thr Leu Ser Thr Asp
 835 840 845
 Ile Pro Phe Gln Leu Ser Lys Tyr Val Asp Asn Gln Arg Leu Leu Ser
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 Thr Phe Thr Glu Tyr Ile Lys
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<220>
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 gtt gac att gcc tac atc aaa att cca aac gcc ggc cag atg cag ccg 96
 Val Asp Ile Ala Tyr Ile Lys Ile Pro Asn Ala Gly Gln Met Gln Pro
 20 25 30
 gtg aag gct ttc aag att cat aac aaa atc tgg gtt att ccg gaa cgc 144
 Val Lys Ala Phe Lys Ile His Asn Lys Ile Trp Val Ile Pro Glu Arg
 35 40 45
 gat aca ttt acg aac ccg gaa gaa gga gac ttg aac ccg ccg ccg gaa 192
 Asp Thr Phe Thr Asn Pro Glu Gly Asp Leu Asn Pro Pro Pro Glu
 50 55 60
 gca aag cag gtg cca gtt tca tac tac gat tca acc tat ctg agc aca 240
 Ala Lys Gln Val Pro Val Ser Tyr Tyr Asp Ser Thr Tyr Leu Ser Thr
 65 70 75 80 20
 gac aac gag aag gat aac tac ctg aag gga gtg acc aaa tta ttc gag 288
 Asp Asn Glu Lys Asp Asn Tyr Leu Lys Gly Val Thr Lys Leu Phe Glu
 85 90 95
 cgt att tat tcc act gac ctg ggc cgt atg ctg ctg acc tca atc gtc 336
 Arg Ile Tyr Ser Thr Asp Leu Gly Arg Met Leu Leu Thr Ser Ile Val
 100 105 110
 cgc gga atc cca ttt tgg ggt ggc agt acc att gac acg gag ttg aag 384
 Arg Gly Ile Pro Phe Trp Gly Gly Ser Thr Ile Asp Thr Glu Leu Lys
 115 120 125
 gtt att gac act aac tgc att aac gtg atc caa cca gac ggt agc tac 432
 Val Ile Asp Thr Asn Cys Ile Asn Val Ile Gln Pro Asp Gly Ser Tyr
 130 135 140
 aga tct gaa gaa ctt aac ctc gta atc atc ggg ccc tcc gcg gac att 480
 Arg Ser Glu Glu Leu Asn Leu Val Ile Ile Gly Pro Ser Ala Asp Ile
 145 150 155 160 30
 atc cag ttt gag tgc aag agc ttt ggc cac gaa gtg ttg aac ctg acg 528
 Ile Gln Phe Glu Cys Lys Ser Phe Gly His Glu Val Leu Asn Leu Thr
 165 170 175
 cgt aac ggt tac ggc tct act cag tac att cgt ttc agc cca gac ttc 576
 Arg Asn Gly Tyr Gly Ser Thr Gln Tyr Ile Arg Phe Ser Pro Asp Phe
 180 185 190
 acg ttc ggt ttc gag gag agc ctg gag gtt gat acc aac ccg ctg ttg 624
 Thr Phe Gly Phe Glu Glu Ser Leu Glu Val Asp Thr Asn Pro Leu Leu
 195 200 205
 ggt gca ggc aag ttc gca act gat cca gcg gtg acc ctg gca cac gag 672
 Gly Ala Gly Lys Phe Ala Thr Asp Pro Ala Val Thr Leu Ala His Glu 40

210	215	220	
ctc atc tac gcc ggt cat cgt ctg tat ggc att gcg att aac ccg aac Leu Ile Tyr Ala Gly His Arg Leu Tyr Gly Ile Ala Ile Asn Pro Asn 225 230 235 240			720
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ggg acc act gct tca tta cag tat atg aaa aat gtt ttt aaa gag aaa Gly Thr Thr Ala Ser Leu Gln Tyr Met Lys Asn Val Phe Lys Glu Lys 305 310 315 320			960
tat ctc cta tct gaa gat aca tct gga aaa ttt tcg gta gat aaa tta Tyr Leu Leu Ser Glu Asp Thr Ser Gly Lys Phe Ser Val Asp Lys Leu 325 330 335			1008
aaa ttt gat aag tta tac aaa atg tta aca gag att tac aca gag gat Lys Phe Asp Lys Leu Tyr Lys Met Leu Thr Glu Ile Tyr Thr Glu Asp 340 345 350			1056
aat ttt gtt aag ttt ttt aaa gta ctt aac aga aaa aca tat ttg aat Asn Phe Val Lys Phe Phe Lys Val Leu Asn Arg Lys Thr Tyr Leu Asn 355 360 365			1104
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aca ata tat gat gga ttt aat tta aga aat aca aat tta gca gca aac Thr Ile Tyr Asp Gly Phe Asn Leu Arg Asn Thr Asn Leu Ala Ala Asn 385 390 395 400			1200
ttt aat ggt caa aat aca gaa att aat aat atg aat ttt act aaa cta Phe Asn Gly Gln Asn Thr Glu Ile Asn Asn Met Asn Phe Thr Lys Leu 405 410 415			1248
aaa aat ttt act gga ttg ttt gaa ttt tat aag ttg cta tgt gta aga Lys Asn Phe Thr Gly Leu Phe Glu Phe Tyr Lys Leu Leu Cys Val Arg 420 425 430			1296
ggg ata ata act tct aaa act aaa tca tta gat aaa gga tac aat aag Gly Ile Ile Thr Ser Lys Thr Lys Ser Leu Asp Lys Gly Tyr Asn Lys 435 440 445			1344
gca tta aat gat tta tgt atc aaa gtt aat aat tgg gac ttg ttt ttt Ala Leu Asn Asp Leu Cys Ile Lys Val Asn Asn Trp Asp Leu Phe Phe 450 455 460			1392
agt cct tca gaa gat aat ttt act aat gat cta aat aaa gga gaa gaa Ser Pro Ser Glu Asp Asn Phe Thr Asn Asp Leu Asn Lys Gly Glu Glu 465 470 475 480			1440

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att aca tct gat act aat ata gaa gca gca gaa gaa aat att agt tta Ile Thr Ser Asp Thr Asn Ile Glu Ala Ala Glu Glu Asn Ile Ser Leu 485 490 495	1488	
gat tta ata caa caa tat tat tta acc ttt aat ttt gat aat gaa cct Asp Leu Ile Gln Gln Tyr Tyr Leu Thr Phe Asn Phe Asp Asn Glu Pro 500 505 510	1536	
gaa aat att tca ata gaa aat ctt tca agt gac att ata ggc caa tta Glu Asn Ile Ser Ile Glu Asn Leu Ser Ser Asp Ile Ile Gly Gln Leu 515 520 525	1584	
gaa ctt atg cct aat ata gaa aga ttt cct aat gga aaa aag tat gag Glu Leu Met Pro Asn Ile Glu Arg Phe Pro Asn Gly Lys Lys Tyr Glu 530 535 540	1632	10
tta gat aaa tat act atg ttc cat tat ctt cgt gct caa gaa ttt gaa Leu Asp Lys Tyr Thr Met Phe His Tyr Leu Arg Ala Gln Glu Phe Glu 545 550 555 560	1680	
cat ggt aaa tct agg att gct tta aca aat tct gtt aac gaa gca tta His Gly Lys Ser Arg Ile Ala Leu Thr Asn Ser Val Asn Glu Ala Leu 565 570 575	1728	
tta aat cct agt cgt gtt tat aca ttt ttt tct tca gac tat gta aag Leu Asn Pro Ser Arg Val Tyr Thr Phe Phe Ser Ser Asp Tyr Val Lys 580 585 590	1776	
aaa gtt aat aaa gct acg gag gca gct atg ttt tta ggc tgg gta gaa Lys Val Asn Lys Ala Thr Glu Ala Ala Met Phe Leu Gly Trp Val Glu 595 600 605	1824	20
caa tta gta tat gat ttt acc gat gaa act agc gaa gta agt act acg Gln Leu Val Tyr Asp Phe Thr Asp Glu Thr Ser Glu Val Ser Thr Thr 610 615 620	1872	
gat aaa att gcg gat ata act ata att att cca tat ata gga cct gct Asp Lys Ile Ala Asp Ile Thr Ile Ile Ile Pro Tyr Ile Gly Pro Ala 625 630 635 640	1920	
tta aat ata ggt aat atg tta tat aaa gat gat ttt gta ggt gct tta Leu Asn Ile Gly Asn Met Leu Tyr Lys Asp Asp Phe Val Gly Ala Leu 645 650 655	1968	
ata ttt tca gga gct gtt att ctg tta gaa ttt ata cca gag att gca Ile Phe Ser Gly Ala Val Ile Leu Leu Glu Phe Ile Pro Glu Ile Ala 660 665 670	2016	
ata cct gta tta ggt act ttt gca ctt gta tca tat att gcg aat aag Ile Pro Val Leu Gly Thr Phe Ala Leu Val Ser Tyr Ile Ala Asn Lys 675 680 685	2064	30
gtt cta acc gtt caa aca ata gat aat gct tta agt aaa aga aat gaa Val Leu Thr Val Gln Thr Ile Asp Asn Ala Leu Ser Lys Arg Asn Glu 690 695 700	2112	
aaa tgg gat gag gtc tat aaa tat ata gta aca aat tgg tta gca aag Lys Trp Asp Glu Val Tyr Lys Tyr Ile Val Thr Asn Trp Leu Ala Lys 705 710 715 720	2160	
gtt aat aca cag att gat cta ata aga aaa aaa atg aaa gaa gct tta Val Asn Thr Gln Ile Asp Leu Ile Arg Lys Lys Met Lys Glu Ala Leu 725 730 735	2208	
gaa aat caa gca gaa gca aca aag gct ata ata aac tat cag tat aat Glu Asn Gln Ala Glu Ala Thr Lys Ala Ile Ile Asn Tyr Gln Tyr Asn 740 745 750	2256	40

740 745 750
 caa tat act gag gaa gag aaa aat aat att aat ttt aat att gat gat 2304
 Gln Tyr Thr Glu Glu Glu Lys Asn Asn Ile Asn Phe Asn Ile Asp Asp
 755 760 765
 tta agt tcg aaa ctt aat gag tct ata aat aaa gct atg att aat ata 2352
 Leu Ser Ser Lys Leu Asn Glu Ser Ile Asn Lys Ala Met Ile Asn Ile
 770 775 780
 aat aaa ttt ttg aat caa tgc tct gtt tca tat tta atg aat tct atg 2400
 Asn Lys Phe Leu Asn Gln Cys Ser Val Ser Tyr Leu Met Asn Ser Met
 785 790 795 800
 atc cct tat ggt gtt aaa cgg tta gaa gat ttt gat gct agt ctt aaa 2448
 Ile Pro Tyr Gly Val Lys Arg Leu Glu Asp Phe Asp Ala Ser Leu Lys
 805 810 815
 gat gca tta tta aag tat ata tat gat aat aga gga act tta att ggt 2496
 Asp Ala Leu Leu Lys Tyr Ile Tyr Asp Asn Arg Gly Thr Leu Ile Gly
 820 825 830
 caa gta gat aga tta aaa gat aaa gtt aat aat aca ctt agt aca gat 2544
 Gln Val Asp Arg Leu Lys Asp Lys Val Asn Asn Thr Leu Ser Thr Asp
 835 840 845
 ata cct ttt cag ctt tcc aaa tac gta gat aat caa aga tta tta tct 2592
 Ile Pro Phe Gln Leu Ser Lys Tyr Val Asp Asn Gln Arg Leu Leu Ser
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 aca ttt act gaa tat att aag 2613
 Thr Phe Thr Glu Tyr Ile Lys
 865 870

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 <212> PRT
 <213> Clostridium botulinum

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 Val Lys Ala Phe Lys Ile His Asn Lys Ile Trp Val Ile Pro Glu Arg
 35 40 45

 Asp Thr Phe Thr Asn Pro Glu Glu Gly Asp Leu Asn Pro Pro Pro Glu
 50 55 60

 Ala Lys Gln Val Pro Val Ser Tyr Tyr Asp Ser Thr Tyr Leu Ser Thr
 65 70 75 80

 Asp Asn Glu Lys Asp Asn Tyr Leu Lys Gly Val Thr Lys Leu Phe Glu
 85 90 95

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Arg Ile Tyr Ser Thr Asp Leu Gly Arg Met Leu Leu Thr Ser Ile Val
 100 105 110

Arg Gly Ile Pro Phe Trp Gly Gly Ser Thr Ile Asp Thr Glu Leu Lys
 115 120 125

Val Ile Asp Thr Asn Cys Ile Asn Val Ile Gln Pro Asp Gly Ser Tyr
 130 135 140

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

Ile Gln Phe Glu Cys Lys Ser Phe Gly His Glu Val Leu Asn Leu Thr
 165 170 175

Arg Asn Gly Tyr Gly Ser Thr Gln Tyr Ile Arg Phe Ser Pro Asp Phe
 180 185 190

Thr Phe Gly Phe Glu Glu Ser Leu Glu Val Asp Thr Asn Pro Leu Leu
 195 200 205

Gly Ala Gly Lys Phe Ala Thr Asp Pro Ala Val Thr Leu Ala His Glu
 210 215 220

Leu Ile Tyr Ala Gly His Arg Leu Tyr Gly Ile Ala Ile Asn Pro Asn
 225 230 235 240

Arg Val Phe Lys Val Asn Thr Asn Ala Tyr Tyr Glu Met Ser Gly Leu
 245 250 255

Glu Val Ser Phe Glu Glu Leu Arg Thr Phe Gly Gly His Asp Ala Lys
 260 265 270

Phe Ile Asp Ser Leu Gln Glu Asn Glu Phe Arg Leu Tyr Tyr Tyr Asn
 275 280 285

Lys Phe Lys Asp Ile Ala Ser Thr Leu Asn Lys Ala Lys Ser Ile Val
 290 295 300

Gly Thr Thr Ala Ser Leu Gln Tyr Met Lys Asn Val Phe Lys Glu Lys
 305 310 315 320

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

Lys Phe Asp Lys Leu Tyr Lys Met Leu Thr Glu Ile Tyr Thr Glu Asp
 340 345 350

Asn Phe Val Lys Phe Phe Lys Val Leu Asn Arg Lys Thr Tyr Leu Asn
 355 360 365

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Phe Asp Lys Ala Val Phe Lys Ile Asn Ile Val Pro Lys Val Asn Tyr
 370 375 380
 Thr Ile Tyr Asp Gly Phe Asn Leu Arg Asn Thr Asn Leu Ala Ala Asn
 385 390 395 400
 Phe Asn Gly Gln Asn Thr Glu Ile Asn Asn Met Asn Phe Thr Lys Leu
 405 410 415
 Lys Asn Phe Thr Gly Leu Phe Glu Phe Tyr Lys Leu Leu Cys Val Arg
 420 425 430
 Gly Ile Ile Thr Ser Lys Thr Lys Ser Leu Asp Lys Gly Tyr Asn Lys
 435 440 445
 Ala Leu Asn Asp Leu Cys Ile Lys Val Asn Asn Trp Asp Leu Phe Phe
 450 455 460
 Ser Pro Ser Glu Asp Asn Phe Thr Asn Asp Leu Asn Lys Gly Glu Glu
 465 470 475 480
 Ile Thr Ser Asp Thr Asn Ile Glu Ala Ala Glu Glu Asn Ile Ser Leu
 485 490 495
 Asp Leu Ile Gln Gln Tyr Tyr Leu Thr Phe Asn Phe Asp Asn Glu Pro
 500 505 510
 Glu Asn Ile Ser Ile Glu Asn Leu Ser Ser Asp Ile Ile Gly Gln Leu
 515 520 525
 Glu Leu Met Pro Asn Ile Glu Arg Phe Pro Asn Gly Lys Lys Tyr Glu
 530 535 540
 Leu Asp Lys Tyr Thr Met Phe His Tyr Leu Arg Ala Gln Glu Phe Glu
 545 550 555 560
 His Gly Lys Ser Arg Ile Ala Leu Thr Asn Ser Val Asn Glu Ala Leu
 565 570 575
 Leu Asn Pro Ser Arg Val Tyr Thr Phe Phe Ser Ser Asp Tyr Val Lys
 580 585 590
 Lys Val Asn Lys Ala Thr Glu Ala Ala Met Phe Leu Gly Trp Val Glu
 595 600 605
 Gln Leu Val Tyr Asp Phe Thr Asp Glu Thr Ser Glu Val Ser Thr Thr
 610 615 620
 Asp Lys Ile Ala Asp Ile Thr Ile Ile Ile Pro Tyr Ile Gly Pro Ala

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625 630 635 640
 Leu Asn Ile Gly Asn Met Leu Tyr Lys Asp Asp Phe Val Gly Ala Leu
 645 650 655
 Ile Phe Ser Gly Ala Val Ile Leu Leu Glu Phe Ile Pro Glu Ile Ala
 660 665 670
 Ile Pro Val Leu Gly Thr Phe Ala Leu Val Ser Tyr Ile Ala Asn Lys
 675 680 685
 Val Leu Thr Val Gln Thr Ile Asp Asn Ala Leu Ser Lys Arg Asn Glu
 690 695 700
 Lys Trp Asp Glu Val Tyr Lys Tyr Ile Val Thr Asn Trp Leu Ala Lys
 705 710 715 720
 Val Asn Thr Gln Ile Asp Leu Ile Arg Lys Lys Met Lys Glu Ala Leu
 725 730 735
 Glu Asn Gln Ala Glu Ala Thr Lys Ala Ile Ile Asn Tyr Gln Tyr Asn
 740 745 750
 Gln Tyr Thr Glu Glu Glu Lys Asn Asn Ile Asn Phe Asn Ile Asp Asp
 755 760 765
 Leu Ser Ser Lys Leu Asn Glu Ser Ile Asn Lys Ala Met Ile Asn Ile
 770 775 780
 Asn Lys Phe Leu Asn Gln Cys Ser Val Ser Tyr Leu Met Asn Ser Met
 785 790 795 800
 Ile Pro Tyr Gly Val Lys Arg Leu Glu Asp Phe Asp Ala Ser Leu Lys
 805 810 815
 Asp Ala Leu Leu Lys Tyr Ile Tyr Asp Asn Arg Gly Thr Leu Ile Gly
 820 825 830
 Gln Val Asp Arg Leu Lys Asp Lys Val Asn Asn Thr Leu Ser Thr Asp
 835 840 845
 Ile Pro Phe Gln Leu Ser Lys Tyr Val Asp Asn Gln Arg Leu Leu Ser
 850 855 860
 Thr Phe Thr Glu Tyr Ile Lys
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 <210> 156
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 <212> DNA

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<213> Clostridium botulinum

<220>

<221> CDS

<222> (1)..(2637)

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Gly Ser Met Glu Phe Val Asn Lys Gln Phe Asn Tyr Lys Asp Pro Val	
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aac ggt gtt gac att gct tac atc aaa atc ccg aac gct ggc cag atg	96
Asn Gly Val Asp Ile Ala Tyr Ile Lys Ile Pro Asn Ala Gly Gln Met	
20 25 30	
cag ccg gta aag gca ttc aaa atc cac aac aaa atc tgg gtt atc ccg	144
Gln Pro Val Lys Ala Phe Lys Ile His Asn Lys Ile Trp Val Ile Pro	
35 40 45	
gaa cgt gat acc ttt act aac ccg gaa gaa ggt gac ctg aac ccg cca	192
Glu Arg Asp Thr Phe Thr Asn Pro Glu Glu Gly Asp Leu Asn Pro Pro	
50 55 60	
ccg gaa gcg aaa cag gtg ccg gta tct tac tat gac tcc acc tac ctg	240
Pro Glu Ala Lys Gln Val Pro Val Ser Tyr Tyr Asp Ser Thr Tyr Leu	
65 70 75 80	
tct acc gat aac gaa aag gac aac tac ctg aaa ggt gtt act aaa ctg	288
Ser Thr Asp Asn Glu Lys Asp Asn Tyr Leu Lys Gly Val Thr Lys Leu	
85 90 95	
ttc gag cgt att tac tcc acc gac ctg ggc cgt atg ctg ctg act agc	336
Phe Glu Arg Ile Tyr Ser Thr Asp Leu Gly Arg Met Leu Leu Thr Ser	
100 105 110	
atc gtt cgc ggt atc ccg ttc tgg ggc ggt tct acc atc gat acc gaa	384
Ile Val Arg Gly Ile Pro Phe Trp Gly Gly Ser Thr Ile Asp Thr Glu	
115 120 125	
ctg aaa gta atc gac act aac tgc atc aac gtt att cag ccg gac ggt	432
Leu Lys Val Ile Asp Thr Asn Cys Ile Asn Val Ile Gln Pro Asp Gly	
130 135 140	
tcc tat cgt tcc gaa gaa ctg aac ctg gtg atc atc ggc ccg tct gct	480
Ser Tyr Arg Ser Glu Glu Leu Asn Leu Val Ile Ile Gly Pro Ser Ala	
145 150 155 160	
gat atc atc cag ttc gag tgt aag agc ttt ggt cac gaa gtt ctg aac	528
Asp Ile Ile Gln Phe Glu Cys Lys Ser Phe Gly His Glu Val Leu Asn	
165 170 175	
ctc acc cgt aac ggc tac ggt tcc act cag tac atc cgt ttc tct ccg	576
Leu Thr Arg Asn Gly Tyr Gly Ser Thr Gln Tyr Ile Arg Phe Ser Pro	
180 185 190	
gac ttc acc ttc ggt ttt gaa gaa tcc ctg gaa gta gac acg aac cca	624
Asp Phe Thr Phe Gly Phe Glu Glu Ser Leu Glu Val Asp Thr Asn Pro	
195 200 205	
ctg ctg ggc gct ggt aaa ttc gca act gat cct gcg gtt acc ctg gct	672
Leu Leu Gly Ala Gly Lys Phe Ala Thr Asp Pro Ala Val Thr Leu Ala	
210 215 220	
cac gaa ctg att cat gca ggc cac cgc ctg tac ggt atc gcc atc aat	720
His Glu Leu Ile His Ala Gly His Arg Leu Tyr Gly Ile Ala Ile Asn	

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225	230	235	240	
cgc aac cgt gtc ttc aaa gtt aac acc aac gcg tat tac gag atg tcc				768
Pro Asn Arg Val Phe Lys Val Asn Thr Asn Ala Tyr Tyr Glu Met Ser				
	245	250	255	
ggc ctg gaa gta agc ttc gaa gaa ctg cgt act ttt ggc ggt cac gac				816
Gly Leu Glu Val Ser Phe Glu Glu Leu Arg Thr Phe Gly Gly His Asp				
	260	265	270	
gct aaa ttc atc gac tct ctg caa gaa aac gag ttc cgt ctg tac tac				864
Ala Lys Phe Ile Asp Ser Leu Gln Glu Asn Glu Phe Arg Leu Tyr Tyr				
	275	280	285	
tat aac aag ttc aaa gat atc gca tcc acc ctg aac aaa gcg aaa tcc				912
Tyr Asn Lys Phe Lys Asp Ile Ala Ser Thr Leu Asn Lys Ala Lys Ser				
	290	295	300	
atc gtg ggt acc act gct tct ctg cag tac atg aag aac gtt ttt aaa				960
Ile Val Gly Thr Thr Ala Ser Leu Gln Tyr Met Lys Asn Val Phe Lys				
	305	310	315	320
gaa aaa tac ctg ctc agc gaa gac acc tcc ggc aaa ttc tct gta gac				1008
Glu Lys Tyr Leu Leu Ser Glu Asp Thr Ser Gly Lys Phe Ser Val Asp				
	325	330	335	
aag ttg aaa ttc gat aaa ctt tac aaa atg ctg act gaa att tac acc				1056
Lys Leu Lys Phe Asp Lys Leu Tyr Lys Met Leu Thr Glu Ile Tyr Thr				
	340	345	350	
gaa gac aac ttc gtt aag ttc ttt aaa gtt ctg aac cgc aaa acc tat				1104
Glu Asp Asn Phe Val Lys Phe Phe Lys Val Leu Asn Arg Lys Thr Tyr				
	355	360	365	
ctg aac ttc gac aag gca gta ttc aaa atc aac atc gtg cgc aaa gtt				1152
Leu Asn Phe Asp Lys Ala Val Phe Lys Ile Asn Ile Val Pro Lys Val				
	370	375	380	
aac tac act atc tac gat ggt ttc aac ctg cgt aac acc aac ctg gct				1200
Asn Tyr Thr Ile Tyr Asp Gly Phe Asn Leu Arg Asn Thr Asn Leu Ala				
	385	390	395	400
gct aat ttt aac ggc cag aac acg gaa atc aac aac atg aac ttc aca				1248
Ala Asn Phe Asn Gly Gln Asn Thr Glu Ile Asn Asn Met Asn Phe Thr				
	405	410	415	
aaa ctg aaa aac ttc act ggt ctg ttc gag ttt tac aag ctg ctg tgc				1296
Lys Leu Lys Asn Phe Thr Gly Leu Phe Glu Phe Tyr Lys Leu Leu Cys				
	420	425	430	
gta cgt ggc atc att acc tcc aaa act aaa tct ctg gac aaa ggt tat				1344
Val Arg Gly Ile Ile Thr Ser Lys Thr Lys Ser Leu Asp Lys Gly Tyr				
	435	440	445	
aac aaa atc gaa ggt cgt gcg ctg aac gac ctc tgt atc aag gtt aac				1392
Asn Lys Ile Glu Gly Arg Ala Leu Asn Asp Leu Cys Ile Lys Val Asn				
	450	455	460	
aac tgg gat tta ttc ttc agc ccg agt gaa gac aac ttc acc aac gac				1440
Asn Trp Asp Leu Phe Phe Ser Pro Ser Glu Asp Asn Phe Thr Asn Asp				
	465	470	475	480
ctg aac aaa ggt gaa gaa atc acc tca gat act aac atc gaa gca gcc				1488
Leu Asn Lys Gly Glu Glu Ile Thr Ser Asp Thr Asn Ile Glu Ala Ala				
	485	490	495	

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gaa gaa aac atc tcg ctg gac ctg atc cag cag tac tac ctg acc ttt 1536
 Glu Glu Asn Ile Ser Leu Asp Leu Ile Gln Gln Tyr Tyr Leu Thr Phe
 500 505 510
 aat ttc gac aac gag ccg gaa aac att tct atc gaa aac ctg agc tct 1584
 Asn Phe Asp Asn Glu Pro Glu Asn Ile Ser Ile Glu Asn Leu Ser Ser
 515 520 525
 gat atc atc ggc cag ctg gaa ctg atg ccg aac atc gaa cgt ttc cca 1632
 Asp Ile Ile Gly Gln Leu Glu Leu Met Pro Asn Ile Glu Arg Phe Pro
 530 535 540
 aac ggt aaa aag tac gag ctg gac aaa tat acc atg ttc cac tac ctg 1680
 Asn Gly Lys Lys Tyr Glu Leu Asp Lys Tyr Thr Met Phe His Tyr Leu
 545 550 555 560
 cgc gcg cag gaa ttt gaa cac ggc aaa tcc cgt atc gca ctg act aac 1728
 Arg Ala Gln Glu Phe Glu His Gly Lys Ser Arg Ile Ala Leu Thr Asn
 565 570 575
 tcc gtt aac gaa gct ctg ctc aac ccg tcc cgt gta tac acc ttc ttc 1776
 Ser Val Asn Glu Ala Leu Leu Asn Pro Ser Arg Val Tyr Thr Phe Phe
 580 585 590
 tct agc gac tac gtg aaa aag gtc aac aaa gcg act gaa gct gca atg 1824
 Ser Ser Asp Tyr Val Lys Lys Val Asn Lys Ala Thr Glu Ala Ala Met
 595 600 605
 ttc ttg ggt tgg gtt gaa cag ctt gtt tat gat ttt acc gac gag acg 1872
 Phe Leu Gly Trp Val Glu Gln Leu Val Tyr Asp Phe Thr Asp Glu Thr
 610 615 620
 tcc gaa gta tct act acc gac aaa att gcg gat atc act atc atc atc 1920
 Ser Glu Val Ser Thr Thr Asp Lys Ile Ala Asp Ile Thr Ile Ile Ile
 625 630 635 640
 ccg tac atc ggt ccg gct ctg aac att ggc aac atg ctg tac aaa gac 1968
 Pro Tyr Ile Gly Pro Ala Leu Asn Ile Gly Asn Met Leu Tyr Lys Asp
 645 650 655
 gac ttc gtt ggt gca ctg atc ttc tcc ggt gcg gtg atc ctg ctg gag 2016
 Asp Phe Val Gly Ala Leu Ile Phe Ser Gly Ala Val Ile Leu Leu Glu
 660 665 670
 ttc atc ccg gaa atc gcc atc ccg gta ctg ggc acc ttt gct ctg gtt 2064
 Phe Ile Pro Glu Ile Ala Ile Pro Val Leu Gly Thr Phe Ala Leu Val
 675 680 685
 tct tac att gca aac aag gtt ctg act gta caa acc atc gac aac gcg 2112
 Ser Tyr Ile Ala Asn Lys Val Leu Thr Val Gln Thr Ile Asp Asn Ala
 690 695 700
 ctg agc aaa cgt aac gaa aaa tgg gat gaa gtt tac aaa tat atc gtg 2160
 Leu Ser Lys Arg Asn Glu Lys Trp Asp Glu Val Tyr Lys Tyr Ile Val
 705 710 715 720
 acc aac tgg ctg gct aag gtt aat act cag atc gac ctc atc cgc aaa 2208
 Thr Asn Trp Leu Ala Lys Val Asn Thr Gln Ile Asp Leu Ile Arg Lys
 725 730 735
 aaa atg aaa gaa gca ctg gaa aac cag gcg gaa gct acc aag gca atc 2256
 Lys Met Lys Glu Ala Leu Glu Asn Gln Ala Glu Ala Thr Lys Ala Ile
 740 745 750
 att aac tac cag tac aac cag tac acc gag gaa gaa aaa aac aac atc 2304
 Ile Asn Tyr Gln Tyr Asn Gln Tyr Thr Glu Glu Glu Lys Asn Asn Ile

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755	760	765	
aac ttc aac atc gac gat ctg tcc tct aaa ctg aac gaa tcc atc aac Asn Phe Asn Ile Asp Asp Leu Ser Ser Lys Leu Asn Glu Ser Ile Asn 770 775 780			2352
aaa gct atg atc aac atc aac aag ttc ctg aac cag tgc tot gta agc Lys Ala Met Ile Asn Ile Asn Lys Phe Leu Asn Gln Cys Ser Val Ser 785 790 795 800			2400
tat ctg atg aac tcc atg atc ccg tac ggt gtt aaa cgt ctg gag gac Tyr Leu Met Asn Ser Met Ile Pro Tyr Gly Val Lys Arg Leu Glu Asp 805 810 815			2448
ttc gat gcg tct ctg aaa gac gcc ctg ctg aaa tac att tac gac aac Phe Asp Ala Ser Leu Lys Asp Ala Leu Leu Lys Tyr Ile Tyr Asp Asn 820 825 830			2496
cgt gcc act ctg atc ggt cag gtt gat cgt ctg aag gac aaa gtg aac Arg Gly Thr Leu Ile Gly Gln Val Asp Arg Leu Lys Asp Lys Val Asn 835 840 845			2544
aat acc tta tcg acc gac atc cct ttt cag ctg agt aaa tat gtc gat Asn Thr Leu Ser Thr Asp Ile Pro Phe Gln Leu Ser Lys Tyr Val Asp 850 855 860			2592
aac caa cgc ctt ttg agc acg ttc aca gag tac atc aag taa tga Asn Gln Arg Leu Leu Ser Thr Phe Thr Glu Tyr Ile Lys 865 870 875			2637

<210> 157
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 <212> PRT
 <213> Clostridium botulinum

<400> 157

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Asn Gly Val Asp Ile Ala Tyr Ile Lys Ile Pro Asn Ala Gly Gln Met
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Gln Pro Val Lys Ala Phe Lys Ile His Asn Lys Ile Trp Val Ile Pro
 35 40 45

Glu Arg Asp Thr Phe Thr Asn Pro Glu Glu Gly Asp Leu Asn Pro Pro
 50 55 60

Pro Glu Ala Lys Gln Val Pro Val Ser Tyr Tyr Asp Ser Thr Tyr Leu
 65 70 75 80

Ser Thr Asp Asn Glu Lys Asp Asn Tyr Leu Lys Gly Val Thr Lys Leu
 85 90 95

Phe Glu Arg Ile Tyr Ser Thr Asp Leu Gly Arg Met Leu Leu Thr Ser
 100 105 110

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Ile Val Arg Gly Ile Pro Phe Trp Gly Gly Ser Thr Ile Asp Thr Glu
 115 120 125
 Leu Lys Val Ile Asp Thr Asn Cys Ile Asn Val Ile Gln Pro Asp Gly
 130 135 140
 Ser Tyr Arg Ser Glu Glu Leu Asn Leu Val Ile Ile Gly Pro Ser Ala
 145 150 155 160
 Asp Ile Ile Gln Phe Glu Cys Lys Ser Phe Gly His Glu Val Leu Asn
 165 170 175
 Leu Thr Arg Asn Gly Tyr Gly Ser Thr Gln Tyr Ile Arg Phe Ser Pro
 180 185 190
 Asp Phe Thr Phe Gly Phe Glu Glu Ser Leu Gln Val Asp Thr Asn Pro
 195 200 205
 Leu Leu Gly Ala Gly Lys Phe Ala Thr Asp Pro Ala Val Thr Leu Ala
 210 215 220
 His Glu Leu Ile His Ala Gly His Arg Leu Tyr Gly Ile Ala Ile Asn
 225 230 235 240
 Pro Asn Arg Val Phe Lys Val Asn Thr Asn Ala Tyr Tyr Glu Met Ser
 245 250 255
 Gly Leu Glu Val Ser Phe Glu Glu Leu Arg Thr Phe Gly Gly His Asp
 260 265 270
 Ala Lys Phe Ile Asp Ser Leu Gln Glu Asn Glu Phe Arg Leu Tyr Tyr
 275 280 285
 Tyr Asn Lys Phe Lys Asp Ile Ala Ser Thr Leu Asn Lys Ala Lys Ser
 290 295 300
 Ile Val Gly Thr Thr Ala Ser Leu Gln Tyr Met Lys Asn Val Phe Lys
 305 310 315 320
 Glu Lys Tyr Leu Leu Ser Glu Asp Thr Ser Gly Lys Phe Ser Val Asp
 325 330 335
 Lys Leu Lys Phe Asp Lys Leu Tyr Lys Met Leu Thr Glu Ile Tyr Thr
 340 345 350
 Glu Asp Asn Phe Val Lys Phe Phe Lys Val Leu Asn Arg Lys Thr Tyr
 355 360 365
 Leu Asn Phe Asp Lys Ala Val Phe Lys Ile Asn Ile Val Pro Lys Val
 370 375 380

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Asn Tyr Thr Ile Tyr Asp Gly Phe Asn Leu Arg Asn Thr Asn Leu Ala
385 390 395 400

Ala Asn Phe Asn Gly Gln Asn Thr Glu Ile Asn Asn Met Asn Phe Thr
405 410 415

Lys Leu Lys Asn Phe Thr Gly Leu Phe Glu Phe Tyr Lys Leu Leu Cys
420 425 430

Val Arg Gly Ile Ile Thr Ser Lys Thr Lys Ser Leu Asp Lys Gly Tyr
435 440 445

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

Asn Trp Asp Leu Phe Phe Ser Pro Ser Glu Asp Asn Phe Thr Asn Asp
465 470 475 480

Leu Asn Lys Gly Glu Glu Ile Thr Ser Asp Thr Asn Ile Glu Ala Ala
485 490 495

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

Asn Phe Asp Asn Glu Pro Glu Asn Ile Ser Ile Glu Asn Leu Ser Ser
515 520 525

Asp Ile Ile Gly Gln Leu Glu Leu Met Pro Asn Ile Glu Arg Phe Pro
530 535 540

Asn Gly Lys Lys Tyr Glu Leu Asp Lys Tyr Thr Met Phe His Tyr Leu
545 550 555 560

Arg Ala Gln Glu Phe Glu His Gly Lys Ser Arg Ile Ala Leu Thr Asn
565 570 575

Ser Val Asn Glu Ala Leu Leu Asn Pro Ser Arg Val Tyr Thr Phe Phe
580 585 590

Ser Ser Asp Tyr Val Lys Lys Val Asn Lys Ala Thr Glu Ala Ala Met
595 600 605

Phe Leu Gly Trp Val Glu Gln Leu Val Tyr Asp Phe Thr Asp Glu Thr
610 615 620

Ser Glu Val Ser Thr Thr Asp Lys Ile Ala Asp Ile Thr Ile Ile Ile
625 630 635 640

Pro Tyr Ile Gly Pro Ala Leu Asn Ile Gly Asn Met Leu Tyr Lys Asp

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645 650 655
 Asp Phe Val Gly Ala Leu Ile Phe Ser Gly Ala Val Ile Leu Leu Glu
 660 665 670
 Phe Ile Pro Glu Ile Ala Ile Pro Val Leu Gly Thr Phe Ala Leu Val
 675 680 685
 Ser Tyr Ile Ala Asn Lys Val Leu Thr Val Gln Thr Ile Asp Asn Ala
 690 695 700
 Leu Ser Lys Arg Asn Glu Lys Trp Asp Glu Val Tyr Lys Tyr Ile Val
 705 710 715 720
 Thr Asn Trp Leu Ala Lys Val Asn Thr Gln Ile Asp Leu Ile Arg Lys
 725 730 735
 Lys Met Lys Glu Ala Leu Glu Asn Gln Ala Glu Ala Thr Lys Ala Ile
 740 745 750
 Ile Asn Tyr Gln Tyr Asn Gln Tyr Thr Glu Glu Glu Lys Asn Asn Ile
 755 760 765
 Asn Phe Asn Ile Asp Asp Leu Ser Ser Lys Leu Asn Glu Ser Ile Asn
 770 775 780
 Lys Ala Met Ile Asn Ile Asn Lys Phe Leu Asn Gln Cys Ser Val Ser
 785 790 795 800
 Tyr Leu Met Asn Ser Met Ile Pro Tyr Gly Val Lys Arg Leu Glu Asp
 805 810 815
 Phe Asp Ala Ser Leu Lys Asp Ala Leu Leu Lys Tyr Ile Tyr Asp Asn
 820 825 830
 Arg Gly Thr Leu Ile Gly Gln Val Asp Arg Leu Lys Asp Lys Val Asn
 835 840 845
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 850 855 860
 Asn Gln Arg Leu Leu Ser Thr Phe Thr Glu Tyr Ile Lys
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 <212> DNA
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<220>

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<221> CDS
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<400> 158

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ggt gac att gct tac atc aaa atc ccg aac gct ggc cag atg cag ccg	96
Val Asp Ile Ala Tyr Ile Lys Ile Pro Asn Ala Gly Gln Met Gln Pro	
20 25 30	
gta aag gca ttc aaa atc cac aac aaa atc tgg gtt atc ccg gaa cgt	144
Val Lys Ala Phe Lys Ile His Asn Lys Ile Trp Val Ile Pro Glu Arg	
35 40 45	
gat acc ttt act aac ccg gaa gaa ggt gac ctg aac ccg cca ccg gaa	192
Asp Thr Phe Thr Asn Pro Glu Glu Gly Asp Leu Asn Pro Pro Pro Glu	
50 55 60	
gcg aaa cag gtg ccg gta tct tac tat gac tcc acc tac ctg tct acc	240
Ala Lys Gln Val Pro Val Ser Tyr Tyr Asp Ser Thr Tyr Leu Ser Thr	
65 70 75 80	
gat aac gaa aag gac aac tac ctg aaa ggt gtt act aaa ctg ttc gag	288
Asp Asn Glu Lys Asp Asn Tyr Leu Lys Gly Val Thr Lys Leu Phe Glu	
85 90 95	
cgt att tac tcc acc gac ctg ggc cgt atg ctg ctg act agc atc gtt	336
Arg Ile Tyr Ser Thr Asp Leu Gly Arg Met Leu Leu Thr Ser Ile Val	
100 105 110	
cgc ggt atc ccg ttc tgg ggc ggt tct acc atc gat acc gaa ctg aaa	384
Arg Gly Ile Pro Phe Trp Gly Gly Ser Thr Ile Asp Thr Glu Leu Lys	
115 120 125	
gta atc gac act aac tgc atc aac gtt att cag ccg gac ggt tcc tat	432
Val Ile Asp Thr Asn Cys Ile Asn Val Ile Gln Pro Asp Gly Ser Tyr	
130 135 140	
cgt tcc gaa gaa ctg aac ctg gtg atc atc ggc ccg tct gct gat atc	480
Arg Ser Glu Glu Leu Asn Leu Val Ile Ile Gly Pro Ser Ala Asp Ile	
145 150 155 160	
atc cag ttc gag tgt aag agc ttt ggt cac gaa gtt ctg aac ctc acc	528
Ile Gln Phe Glu Cys Lys Ser Phe Gly His Glu Val Leu Asn Leu Thr	
165 170 175	
cgt aac ggc tac ggt tcc act cag tac atc cgt ttc tct ccg gac ttc	576
Arg Asn Gly Tyr Gly Ser Thr Gln Tyr Ile Arg Phe Ser Pro Asp Phe	
180 185 190	
acc ttc ggt ttt gaa gaa tcc ctg gaa gta gac acg aac cca ctg ctg	624
Thr Phe Gly Phe Glu Glu Ser Leu Glu Val Asp Thr Asn Pro Leu Leu	
195 200 205	
ggc gct ggt aaa ttc gca act gat cct gcg gtt acc ctg gct cac gaa	672
Gly Ala Gly Lys Phe Ala Thr Asp Pro Ala Val Thr Leu Ala His Glu	
210 215 220	
ctg att cat gca ggc cac cgc ctg tac ggt atc gcc atc aat ccg aac	720
Leu Ile His Ala Gly His Arg Leu Tyr Gly Ile Ala Ile Asn Pro Asn	
225 230 235 240	
cgt gtc ttc aaa gtt aac acc aac gcg tat tac gag atg tcc ggt ctg	768
Arg Val Phe Lys Val Asn Thr Asn Ala Tyr Tyr Glu Met Ser Gly Leu	

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245	250	255	
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ggg acc act gct tct ctg cag tac atg aag aac gtt ttt aaa gaa aaa Gly Thr Thr Ala Ser Leu Gln Tyr Met Lys Asn Val Phe Lys Glu Lys 305 310 315 320			960
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aac ttc gtt aag ttc ttt aaa gtt ctg aac cgc aaa acc tat ctg aac Asn Phe Val Lys Phe Phe Lys Val Leu Asn Arg Lys Thr Tyr Leu Asn 355 360 365			1104
ttc gac aag gca gta ttc aaa atc aac atc gtg ccg aaa gtt aac tac Phe Asp Lys Ala Val Phe Lys Ile Asn Ile Val Pro Lys Val Asn Tyr 370 375 380			1152
act atc tac gat ggt ttc aac ctg cgt aac acc aac ctg gct gct aat Thr Ile Tyr Asp Gly Phe Asn Leu Arg Asn Thr Asn Leu Ala Ala Asn 385 390 395 400			1200
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aaa aac ttc act ggt ctg ttc gag ttt tac aag ctg ctg tgc gta cgt Lys Asn Phe Thr Gly Leu Phe Glu Phe Tyr Lys Leu Leu Cys Val Arg 420 425 430			1296
ggc atc att acc tcc aaa act aaa tct ctg gac aaa ggt tat aac aaa Gly Ile Ile Thr Ser Lys Thr Lys Ser Leu Asp Lys Gly Tyr Asn Lys 435 440 445			1344
gcg ctg aac gac ctc tgt atc aag gtt aac aac tgg gat tta ttc ttc Ala Leu Asn Asp Leu Cys Ile Lys Val Asn Asn Trp Asp Leu Phe Phe 450 455 460			1392
agc ccg agt gaa gac aac ttc acc aac gac ctg aac aaa ggt gaa gaa Ser Pro Ser Glu Asp Asn Phe Thr Asn Asp Leu Asn Lys Gly Glu Glu 465 470 475 480			1440
atc acc tca gat act aac atc gaa gca gcc gaa gaa aac atc tgc ctg Ile Thr Ser Asp Thr Asn Ile Glu Ala Ala Glu Glu Asn Ile Ser Leu 485 490 495			1488
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 gaa ctg atg ccg aac atc gaa cgt ttc cca aac ggt aaa aag tac gag 1632
 Glu Leu Met Pro Asn Ile Glu Arg Phe Pro Asn Gly Lys Lys Tyr Glu
 530 535 540
 ctg gac aaa tat acc atg ttc cac tac ctg cgc gcg cag gaa ttt gaa 1680
 Leu Asp Lys Tyr Thr Met Phe His Tyr Leu Arg Ala Gln Glu Phe Glu
 545 550 555 560
 cac ggc aaa tcc cgt atc gca ctg act aac tcc gtt aac gaa gct ctg 1728
 His Gly Lys Ser Arg Ile Ala Leu Thr Asn Ser Val Asn Glu Ala Leu
 565 570 575
 ctc aac ccg tcc cgt gta tac acc ttc ttc tct agc gac tac gtg aaa 1776
 Leu Asn Pro Ser Arg Val Tyr Thr Phe Phe Ser Ser Asp Tyr Val Lys
 580 585 590
 aag gtc aac aaa gcg act gaa gct gca atg ttc ttg ggt tgg gtt gaa 1824
 Lys Val Asn Lys Ala Thr Glu Ala Ala Met Phe Leu Gly Trp Val Glu
 595 600 605
 cag ctt gtt tat gat ttt acc gac gag acg tcc gaa gta tct act acc 1872
 Gln Leu Val Tyr Asp Phe Thr Asp Glu Thr Ser Glu Val Ser Thr Thr
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 gac aaa att gcg gat atc act atc atc atc ccg tac atc ggt ccg gct 1920
 Asp Lys Ile Ala Asp Ile Thr Ile Ile Ile ccg Tyr Ile Gly Pro Ala
 625 630 635 640
 ctg aac att ggc aac atg ctg tac aaa gac gac ttc gtt ggt gca ctg 1968
 Leu Asn Ile Gly Asn Met Leu Tyr Lys Asp Asp Phe Val Gly Ala Leu
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 atc ttc tcc ggt gcg gtg atc ctg ctg gag ttc atc ccg gaa atc gcc 2016
 Ile Phe Ser Gly Ala Val Ile Leu Leu Glu Phe Ile Pro Glu Ile Ala
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 Ile Pro Val Leu Gly Thr Phe Ala Leu Val Ser Tyr Ile Ala Asn Lys
 675 680 685
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 Val Leu Thr Val Gln Thr Ile Asp Asn Ala Leu Ser Lys Arg Asn Glu
 690 695 700
 aaa tgg gat gaa gtt tac aaa tat atc gtg acc aac tgg ctg gct aag 2160
 Lys Trp Asp Glu Val Tyr Lys Tyr Ile Val Thr Asn Trp Leu Ala Lys
 705 710 715 720
 gtt aat act cag atc gac ctc atc cgc aaa aaa atg aaa gaa gca ctg 2208
 Val Asn Thr Gln Ile Asp Leu Ile Arg Lys Lys Met Lys Glu Ala Leu
 725 730 735
 gaa aac cag gcg gaa gct acc aag gca atc att aac tac cag tac aac 2256
 Glu Asn Gln Ala Glu Ala Thr Lys Ala Ile Ile Asn Tyr Gln Tyr Asn
 740 745 750
 cag tac acc gag gaa gaa aaa aac aac atc aac ttc aac atc gac gat 2304
 Gln Tyr Thr Glu Glu Glu Lys Asn Asn Ile Asn Phe Asn Ile Asp Asp
 755 760 765
 ctg tcc tct aaa ctg aac gaa tcc atc aac aaa gct atg atc aac atc 2352
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Val Ile Asp Thr Asn Cys Ile Asn Val Ile Gln Pro Asp Gly Ser Tyr
130 135 140

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

Ile Gln Phe Glu Cys Lys Ser Phe Gly His Glu Val Leu Asn Leu Thr
165 170 175

Arg Asn Gly Tyr Gly Ser Thr Gln Tyr Ile Arg Phe Ser Pro Asp Phe
180 185 190

Thr Phe Gly Phe Glu Glu Ser Leu Glu Val Asp Thr Asn Pro Leu Leu
195 200 205

Gly Ala Gly Lys Phe Ala Thr Asp Pro Ala Val Thr Leu Ala His Glu
210 215 220

Leu Ile His Ala Gly His Arg Leu Tyr Gly Ile Ala Ile Asn Pro Asn
225 230 235 240

Arg Val Phe Lys Val Asn Thr Asn Ala Tyr Tyr Glu Met Ser Gly Leu
245 250 255

Glu Val Ser Phe Glu Glu Leu Arg Thr Phe Gly Gly His Asp Ala Lys
260 265 270

Phe Ile Asp Ser Leu Gln Glu Asn Glu Phe Arg Leu Tyr Tyr Tyr Asn
275 280 285

Lys Phe Lys Asp Ile Ala Ser Thr Leu Asn Lys Ala Lys Ser Ile Val
290 295 300

Gly Thr Thr Ala Ser Leu Gln Tyr Met Lys Asn Val Phe Lys Glu Lys
305 310 315 320

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

Lys Phe Asp Lys Leu Tyr Lys Met Leu Thr Glu Ile Tyr Thr Glu Asp
340 345 350

Asn Phe Val Lys Phe Phe Lys Val Leu Asn Arg Lys Thr Tyr Leu Asn
355 360 365

Phe Asp Lys Ala Val Phe Lys Ile Asn Ile Val Pro Lys Val Asn Tyr
370 375 380

Thr Ile Tyr Asp Gly Phe Asn Leu Arg Asn Thr Asn Leu Ala Ala Asn

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385 390 395 400
 Phe Asn Gly Gln Asn Thr Glu Ile Asn Asn Met Asn Phe Thr Lys Leu
 405 410 415
 Lys Asn Phe Thr Gly Leu Phe Glu Phe Tyr Lys Leu Leu Cys Val Arg
 420 425 430
 Gly Ile Ile Thr Ser Lys Thr Lys Ser Leu Asp Lys Gly Tyr Asn Lys
 435 440 445
 Ala Leu Asn Asp Leu Cys Ile Lys Val Asn Asn Trp Asp Leu Phe Phe
 450 455 460
 Ser Pro Ser Glu Asp Asn Phe Thr Asn Asp Leu Asn Lys Gly Glu Glu
 465 470 475 480
 Ile Thr Ser Asp Thr Asn Ile Glu Ala Ala Glu Glu Asn Ile Ser Leu
 485 490 495
 Asp Leu Ile Gln Gln Tyr Tyr Leu Thr Phe Asn Phe Asp Asn Glu Pro
 500 505 510
 Glu Asn Ile Ser Ile Glu Asn Leu Ser Ser Asp Ile Ile Gly Gln Leu
 515 520 525
 Glu Leu Met Pro Asn Ile Glu Arg Phe Pro Asn Gly Lys Lys Tyr Glu
 530 535 540
 Leu Asp Lys Tyr Thr Met Phe His Tyr Leu Arg Ala Gln Glu Phe Glu
 545 550 555 560
 His Gly Lys Ser Arg Ile Ala Leu Thr Asn Ser Val Asn Glu Ala Leu
 565 570 575
 Leu Asn Pro Ser Arg Val Tyr Thr Phe Phe Ser Ser Asp Tyr Val Lys
 580 585 590
 Lys Val Asn Lys Ala Thr Glu Ala Ala Met Phe Leu Gly Trp Val Glu
 595 600 605
 Gln Leu Val Tyr Asp Phe Thr Asp Glu Thr Ser Glu Val Ser Thr Thr
 610 615 620
 Asp Lys Ile Ala Asp Ile Thr Ile Ile Ile Pro Tyr Ile Gly Pro Ala
 625 630 635 640
 Leu Asn Ile Gly Asn Met Leu Tyr Lys Asp Asp Phe Val Gly Ala Leu
 645 650 655

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Ile Phe Ser Gly Ala Val Ile Leu Leu Glu Phe Ile Pro Glu Ile Ala
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Ile Pro Val Leu Gly Thr Phe Ala Leu Val Ser Tyr Ile Ala Asn Lys
675 680 685

Val Leu Thr Val Gln Thr Ile Asp Asn Ala Leu Ser Lys Arg Asn Glu
690 695 700

Lys Trp Asp Glu Val Tyr Lys Tyr Ile Val Thr Asn Trp Leu Ala Lys
705 710 715 720

Val Asn Thr Gln Ile Asp Leu Ile Arg Lys Lys Met Lys Glu Ala Leu
725 730 735

Glu Asn Gln Ala Glu Ala Thr Lys Ala Ile Ile Asn Tyr Gln Tyr Asp
740 745 750

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

Leu Ser Ser Lys Leu Asn Glu Ser Ile Asn Lys Ala Met Ile Asn Ile
770 775 780

Asn Lys Phe Leu Asn Gln Cys Ser Val Ser Tyr Leu Met Asn Ser Met
785 790 795 800

Ile Pro Tyr Gly Val Lys Arg Leu Glu Asp Phe Asp Ala Ser Leu Lys
805 810 815

Asp Ala Leu Leu Lys Tyr Ile Tyr Asp Asn Arg Gly Thr Leu Ile Gly
820 825 830

Gln Val Asp Arg Leu Lys Asp Lys Val Asn Asn Thr Leu Ser Thr Asp
835 840 845

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Thr Phe Thr Glu Tyr Ile Lys Leu Glu His His His His His
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<212> DNA
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Ala Lys Phe Ile Asp Ser Leu Gln Glu Asn Glu Phe Arg Leu Tyr Tyr	
275 280 285	
tat aac aag ttc aaa gat atc gca tcc acc ctg aac aaa gcg aaa tcc	912
Tyr Asn Lys Phe Lys Asp Ile Ala Ser Thr Leu Asn Lys Ala Lys Ser	
290 295 300	
atc gtg ggt acc act gct tct ctg cag tac atg aag aac gtt ttt aaa	960
Ile Val Gly Thr Thr Ala Ser Leu Gln Tyr Met Lys Asn Val Phe Lys	
305 310 315 320	
gaa aaa tac ctg ctc agc gaa gac acc tcc ggc aaa ttc tct gta gac	1008
Glu Lys Tyr Leu Leu Ser Glu Asp Thr Ser Gly Lys Phe Ser Val Asp	
325 330 335	
aag ttg aaa ttc gat aaa ctt tac aaa atg ctg act gaa att tac acc	1056
Lys Leu Lys Phe Asp Lys Leu Tyr Lys Met Leu Thr Glu Ile Tyr Thr	
340 345 350	
gaa gac aac ttc gtt aag ttc ttt aaa gtt ctg aac cgc aaa acc tat	1104
Glu Asp Asn Phe Val Lys Phe Phe Lys Val Leu Asn Arg Lys Thr Tyr	
355 360 365	
ctg aac ttc gac aag gca gta ttc aaa atc aac atc gtg ccg aaa gtt	1152
Leu Asn Phe Asp Lys Ala Val Phe Lys Ile Asn Ile Val Pro Lys Val	
370 375 380	
aac tac act atc tac gat ggt ttc aac ctg cgt aac acc aac ctg gct	1200
Asn Tyr Thr Ile Tyr Asp Gly Phe Asn Leu Arg Asn Thr Asn Leu Ala	
385 390 395 400	
gct aat ttt aac ggc cag aac acg gaa atc aac aac atg aac ttc aca	1248
Ala Asn Phe Asn Gly Gln Asn Thr Glu Ile Asn Asn Met Asn Phe Thr	
405 410 415	
aaa ctg aaa aac ttc act ggt ctg ttc gag ttt tac aag ctg ctg tgc	1296
Lys Leu Lys Asn Phe Thr Gly Leu Phe Glu Phe Tyr Lys Leu Leu Cys	
420 425 430	
gta cgt ggc atc att acc tcc aaa act aaa tct ctg gac aaa ggt tat	1344
Val Arg Gly Ile Ile Thr Ser Lys Thr Lys Ser Leu Asp Lys Gly Tyr	
435 440 445	
aac aaa gca tcg aag gtc gtg ctg aac gac ctc tgt atc aag gtt aac	1392
Asn Lys Ala Ser Lys Val Val Leu Asn Asp Leu Cys Ile Lys Val Asn	
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aac tgg gat tta ttc ttc agc ccg agt gaa gac aac ttc acc aac gac	1440
Asn Trp Asp Leu Phe Phe Ser Pro Ser Glu Asp Asn Phe Thr Asn Asp	
465 470 475 480	
ctg aac aaa ggt gaa gaa atc acc tca gat act aac atc gaa gca gcc	1488
Leu Asn Lys Gly Glu Glu Ile Thr Ser Asp Thr Asn Ile Glu Ala Ala	
485 490 495	
gaa gaa aac atc tcg ctg gac ctg atc cag cag tac tac ctg acc ttt	1536
Glu Glu Asn Ile Ser Leu Asp Leu Ile Gln Gln Tyr Tyr Leu Thr Phe	
500 505 510	
aat ttc gac aac gag ccg gaa aac att tct atc gaa aac ctg agc tct	1584
Asn Phe Asp Asn Glu Pro Glu Asn Ile Ser Ile Glu Asn Leu Ser Ser	
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tcc gtt aac gaa gct ctg ctc aac ccg tcc cgt gta tac acc ttc ttc Ser Val Asn Glu Ala Leu Leu Asn Pro Ser Arg Val Tyr Thr Phe Phe 580 585 590	1776
tct agc gac tac gtg aaa aag gtc aac aaa gcg act gaa gct gca atg Ser Ser Asp Tyr Val Lys Lys Val Asn Lys Ala Thr Glu Ala Ala Met 595 600 605	1824
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ccg tac atc ggt ccg gct ctg aac att ggc aac atg ctg tac aaa gac Pro Tyr Ile Gly Pro Ala Leu Asn Ile Gly Asn Met Leu Tyr Lys Asp 645 650 655	1968
gac ttc gtt ggt gca ctg atc ttc tcc ggt gcg gtg atc ctg ctg gag Asp Phe Val Gly Ala Leu Ile Phe Ser Gly Ala Val Ile Leu Leu Glu 660 665 670	2016
ttc atc ccg gaa atc gcc atc ccg gta ctg ggc acc ttt gct ctg gtt Phe Ile Pro Glu Ile Ala Ile Pro Val Leu Gly Thr Phe Ala Leu Val 675 680 685	2064
tct tac att gca aac aag gtt ctg act gta caa acc atc gac aac gcg Ser Tyr Ile Ala Asn Lys Val Leu Thr Val Gln Thr Ile Asp Asn Ala 690 695 700	2112
ctg agc aaa cgt aac gaa aaa tgg gat gaa gtt tac aaa tat atc gtg Leu Ser Lys Arg Asn Glu Lys Trp Asp Glu Val Tyr Lys Tyr Ile Val 705 710 715 720	2160
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att aac tac cag tac aac cag tac acc gag gaa gaa aaa aac aac atc Ile Asn Tyr Gln Tyr Asn Gln Tyr Thr Glu Glu Glu Lys Asn Asn Ile 755 760 765	2304
aac ttc aac atc gac gat ctg tcc tct aaa ctg aac gaa tcc atc aac Asn Phe Asn Ile Asp Asp Leu Ser Ser Lys Leu Asn Glu Ser Ile Asn 770 775 780	2352
aaa gct atg atc aac atc aac aag ttc ctg aac cag tgc tct gta agc Lys Ala Met Ile Asn Ile Asn Lys Phe Leu Asn Gln Cys Ser Val Ser	2400

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785		790		795		800	
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Tyr Leu Met Asn Ser Met Ile Pro Tyr Gly Val Lys Arg Leu Glu Asp							
		805		810		815	
ttc gat gcg tct ctg aaa gac gcc ctg ctg aaa tac att tac gac aac	2496						
Phe Asp Ala Ser Leu Lys Asp Ala Leu Leu Lys Tyr Ile Tyr Asp Asn							
		820		825		830	
cgt ggc act ctg atc ggt cag gtt gat cgt ctg aag gac aaa gtg aac	2544						
Arg Gly Thr Leu Ile Gly Gln Val Asp Arg Leu Lys Asp Lys Val Asn							
		835		840		845	
aat acc tta tcg acc gac atc cct ttt cag ctc agt aaa tat gtc gat	2592						
Asn Thr Leu Ser Thr Asp Ile Pro Phe Gln Leu Ser Lys Tyr Val Asp							
		850		855		860	
aac caa cgc ctt ttg agc acg ttc aca gag tac atc aag atc gaa ggt	2640						
Asn Gln Arg Leu Leu Ser Thr Phe Thr Glu Tyr Ile Lys Ile Glu Gly							
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cgt cac cac cac cac cac cac taa tga	2667						
Arg His His His His His His							
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35 40 45

Glu Arg Asp Thr Phe Thr Asn Pro Glu Glu Gly Asp Leu Asn Pro Pro
50 55 60

Pro Glu Ala Lys Gln Val Pro Val Ser Tyr Tyr Asp Ser Thr Tyr Leu
65 70 75 80

Ser Thr Asp Asn Glu Lys Asp Asn Tyr Leu Lys Gly Val Thr Lys Leu
85 90 95

Phe Glu Arg Ile Tyr Ser Thr Asp Leu Gly Arg Met Leu Leu Thr Ser
100 105 110

Ile Val Arg Gly Ile Pro Phe Trp Gly Gly Ser Thr Ile Asp Thr Glu
115 120 125

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Leu Lys Val Ile Asp Thr Asn Cys Ile Asn Val Ile Gln Pro Asp Gly
 130 135 140
 Ser Tyr Arg Ser Glu Glu Leu Asn Leu Val Ile Ile Gly Pro Ser Ala
 145 150 155 160
 Asp Ile Ile Gln Phe Glu Cys Lys Ser Phe Gly His Glu Val Leu Asn
 165 170 175
 Leu Thr Arg Asn Gly Tyr Gly Ser Thr Gln Tyr Ile Arg Phe Ser Pro
 180 185 190
 Asp Phe Thr Phe Gly Phe Glu Glu Ser Leu Glu Val Asp Thr Asn Pro
 195 200 205
 Leu Leu Gly Ala Gly Lys Phe Ala Thr Asp Pro Ala Val Thr Leu Ala
 210 215 220
 His Glu Leu Ile His Ala Gly His Arg Leu Tyr Gly Ile Ala Ile Asn
 225 230 235 240
 Pro Asn Arg Val Phe Lys Val Asn Thr Asn Ala Tyr Tyr Glu Met Ser
 245 250 255
 Gly Leu Glu Val Ser Phe Glu Glu Leu Arg Thr Phe Gly Gly His Asp
 260 265 270
 Ala Lys Phe Ile Asp Ser Leu Gln Glu Asn Glu Phe Arg Leu Tyr Tyr
 275 280 285
 Tyr Asn Lys Phe Lys Asp Ile Ala Ser Thr Leu Asn Lys Ala Lys Ser
 290 295 300
 Ile Val Gly Thr Thr Ala Ser Leu Gln Tyr Met Lys Asn Val Phe Lys
 305 310 315 320
 Glu Lys Tyr Leu Leu Ser Glu Asp Thr Ser Gly Lys Phe Ser Val Asp
 325 330 335
 Lys Leu Lys Phe Asp Lys Leu Tyr Lys Met Leu Thr Glu Ile Tyr Thr
 340 345 350
 Glu Asp Asn Phe Val Lys Phe Phe Lys Val Leu Asn Arg Lys Thr Tyr
 355 360 365
 Leu Asn Phe Asp Lys Ala Val Phe Lys Ile Asn Ile Val Pro Lys Val
 370 375 380
 Asn Tyr Thr Ile Tyr Asp Gly Phe Asn Leu Arg Asn Thr Asn Leu Ala
 385 390 395 400

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Ala Asn Phe Asn Gly Gln Asn Thr Glu Ile Asn Asn Met Asn Phe Thr
405 410 415

Lys Leu Lys Asn Phe Thr Gly Leu Phe Glu Phe Tyr Lys Leu Leu Cys
420 425 430

Val Arg Gly Ile Ile Thr Ser Lys Thr Lys Ser Leu Asp Lys Gly Tyr
435 440 445

Asn Lys Ala Ser Lys Val Val Leu Asn Asp Leu Cys Ile Lys Val Asn
450 455 460

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Asn Trp Asp Leu Phe Phe Ser Pro Ser Glu Asp Asn Phe Thr Asn Asp
465 470 475 480

Leu Asn Lys Gly Glu Glu Ile Thr Ser Asp Thr Asn Ile Glu Ala Ala
485 490 495

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

Asn Phe Asp Asn Glu Pro Glu Asn Ile Ser Ile Glu Asn Leu Ser Ser
515 520 525

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Asp Ile Ile Gly Gln Leu Glu Leu Met Pro Asn Ile Glu Arg Phe Pro
530 535 540

Asn Gly Lys Lys Tyr Glu Leu Asp Lys Tyr Thr Met Phe His Tyr Leu
545 550 555 560

Arg Ala Gln Glu Phe Glu His Gly Lys Ser Arg Ile Ala Leu Thr Asn
565 570 575

Ser Val Asn Glu Ala Leu Leu Asn Pro Ser Arg Val Tyr Thr Phe Phe
580 585 590

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Ser Ser Asp Tyr Val Lys Lys Val Asn Lys Ala Thr Glu Ala Ala Met
595 600 605

Phe Leu Gly Trp Val Glu Gln Leu Val Tyr Asp Phe Thr Asp Glu Thr
610 615 620

Ser Glu Val Ser Thr Thr Asp Lys Ile Ala Asp Ile Thr Ile Ile Ile
625 630 635 640

Pro Tyr Ile Gly Pro Ala Leu Asn Ile Gly Asn Met Leu Tyr Lys Asp
645 650 655

Asp Phe Val Gly Ala Leu Ile Phe Ser Gly Ala Val Ile Leu Leu Glu

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660 665 670
 Phe Ile Pro Glu Ile Ala Ile Pro Val Leu Gly Thr Phe Ala Leu Val
 675 680 685
 Ser Tyr Ile Ala Asn Lys Val Leu Thr Val Gln Thr Ile Asp Asn Ala
 690 695 700
 Leu Ser Lys Arg Asn Glu Lys Trp Asp Glu Val Tyr Lys Tyr Ile Val
 705 710 715 720
 Thr Asn Trp Leu Ala Lys Val Asn Thr Gln Ile Asp Leu Ile Arg Lys
 725 730 735
 Lys Met Lys Glu Ala Leu Glu Asn Gln Ala Glu Ala Thr Lys Ala Ile
 740 745 750
 Ile Asn Tyr Gln Tyr Asn Gln Tyr Thr Glu Glu Glu Lys Asn Asn Ile
 755 760 765
 Asn Phe Asn Ile Asp Asp Leu Ser Ser Lys Leu Asn Glu Ser Ile Asn
 770 775 780
 Lys Ala Met Ile Asn Ile Asn Lys Phe Leu Asn Gln Cys Ser Val Ser
 785 790 795 800
 Tyr Leu Met Asn Ser Met Ile Pro Tyr Gly Val Lys Arg Leu Glu Asp
 805 810 815
 Phe Asp Ala Ser Leu Lys Asp Ala Leu Leu Lys Tyr Ile Tyr Asp Asn
 820 825 830
 Arg Gly Thr Leu Ile Gly Gln Val Asp Arg Leu Lys Asp Lys Val Asn
 835 840 845
 Asn Thr Leu Ser Thr Asp Ile Pro Phe Gln Leu Ser Lys Tyr Val Asp
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<210> 162
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 <213> Clostridium botulinum

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aac ggt gtt gac att gcc tac atc aaa att cca aac gcc ggc cag atg	96
Asn Gly Val Asp Ile Ala Tyr Ile Lys Ile Pro Asn Ala Gly Gln Met	
20 25 30	
cag ccg gtg aag gct ttc aag att cat aac aaa atc tgg gtt att ccg	144
Gln Pro Val Lys Ala Phe Lys Ile His Asn Lys Ile Trp Val Ile Pro	
35 40 45	
gaa cgc gat aca ttt acg aac ccg gaa gaa gga gac ttg aac ccg ccg	192
Glu Arg Asp Thr Phe Thr Asn Pro Glu Glu Gly Asp Leu Asn Pro Pro	
50 55 60	
ccg gaa gca aag cag gtg cca gtt tca tac tac gat tca acc tat ctg	240
Pro Glu Ala Lys Gln Val Pro Val Ser Tyr Tyr Asp Ser Thr Tyr Leu	
65 70 75 80	
agc aca gac aac gag aag gat aac tac ctg aag gga gtg acc aaa tta	288
Ser Thr Asp Asn Gln Lys Asp Asn Tyr Leu Lys Gly Val Thr Lys Leu	
85 90 95	
ttc gag cgt att tat tcc act gac ctg ggc cgt atg ctg ctg acc tca	336
Phe Glu Arg Ile Tyr Ser Thr Asp Leu Gly Arg Met Leu Leu Thr Ser	
100 105 110	
atc gtc cgc gga atc cca ttt tgg ggt ggc agt acc att gac acg gag	384
Ile Val Arg Gly Ile Pro Phe Trp Gly Gly Ser Thr Ile Asp Thr Glu	
115 120 125	
ttg aag gtt att gac act aac tgc att aac gtg atc caa cca gac ggt	432
Leu Lys Val Ile Asp Thr Asn Cys Ile Asn Val Ile Gln Pro Asp Gly	
130 135 140	
agc tac aga tot gaa gaa ctt aac ctc gta atc atc ggg ccc tcc gcg	480
Ser Tyr Arg Ser Glu Glu Leu Asn Leu Val Ile Ile Gly Pro Ser Ala	
145 150 155 160	
gac att atc cag ttt gag tgc aag agc ttt ggc cac gaa gtg ttg aac	528
Asp Ile Ile Gln Phe Glu Cys Lys Ser Phe Gly His Glu Val Leu Asn	
165 170 175	
ctg acg cgt aac ggt tac ggc tct act cag tac att cgt ttc agc cca	576
Leu Thr Arg Asn Gly Tyr Gly Ser Thr Gln Tyr Ile Arg Phe Ser Pro	
180 185 190	
gac ttc acg ttc ggt ttc gag gag agc ctg gag gtt gat acc aac ccg	624
Asp Phe Thr Phe Gly Phe Glu Glu Ser Leu Glu Val Asp Thr Asn Pro	
195 200 205	
ctg ttg ggt gca ggc aag ttc gca act gat cca gcg gtg acc ctg gca	672
Leu Leu Gly Ala Gly Lys Phe Ala Thr Asp Pro Ala Val Thr Leu Ala	
210 215 220	
cac gag ctc atc tac gcc ggt cat cgt ctg tat ggc att gcg att aac	720
His Glu Leu Ile Tyr Ala Gly His Arg Leu Tyr Gly Ile Ala Ile Asn	
225 230 235 240	
ccg aac cgc gtg ttc aag gtt aac acc aac gcc tac tac gag atg agt	768
Pro Asn Arg Val Phe Lys Val Asn Thr Asn Ala Tyr Tyr Glu Met Ser	

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245	250	255	
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gcg aag ttt atc gac agc ttg cag gag aac gag ttc cgt ctg tac tac Ala Lys Phe Ile Asp Ser Leu Gln Glu Asn Glu Phe Arg Leu Tyr Tyr 275 280 285			864
tac aac aag ttt aaa gat att gca agt aca ctg aac aag gct aag tcc Tyr Asn Lys Phe Lys Asp Ile Ala Ser Thr Leu Asn Lys Ala Lys Ser 290 295 300			912
att gtg ggt acc act gct tca tta cag tat atg aaa aat gtt ttt aaa Ile Val Gly Thr Thr Ala Ser Leu Gln Tyr Met Lys Asn Val Phe Lys 305 310 315 320			960
gag aaa tat ctc cta tct gaa gat aca tct gga aaa ttt tcg gta gat Glu Lys Tyr Leu Leu Ser Glu Asp Thr Ser Gly Lys Phe Ser Val Asp 325 330 335			1008
aaa tta aaa ttt gat aag tta tac aaa atg tta aca gag att tac aca Lys Leu Lys Phe Asp Lys Leu Tyr Lys Met Leu Thr Glu Ile Tyr Thr 340 345 350			1056
gag gat aat ttt gtt aag ttt ttt aaa gta ott aac aga aaa aca tat Glu Asp Asn Phe Val Lys Phe Phe Lys Val Leu Asn Arg Lys Thr Tyr 355 360 365			1104
ttg aat ttt gat aaa gcc gta ttt aag ata aat ata gta cct aag gta Leu Asn Phe Asp Lys Ala Val Phe Lys Ile Asn Ile Val Pro Lys Val 370 375 380			1152
aat tac aca ata tat gat gga ttt aat tta aga aat aca aat tta gca Asn Tyr Thr Ile Tyr Asp Gly Phe Asn Leu Arg Asn Thr Asn Leu Ala 385 390 395 400			1200
gca aac ttt aat ggt caa aat aca gaa att aat aat atg aat ttt act Ala Asn Phe Asn Gly Gln Asn Thr Glu Ile Asn Asn Met Asn Phe Thr 405 410 415			1248
aaa cta aaa aat ttt act gga ttg ttt gaa ttt tat aag ttg cta tgt Lys Leu Lys Asn Phe Thr Gly Leu Phe Glu Phe Tyr Lys Leu Leu Cys 420 425 430			1296
gta aga ggg ata ata act tct aaa act aaa tca tta gat aaa gga tac Val Arg Gly Ile Ile Thr Ser Lys Thr Lys Ser Leu Asp Lys Gly Tyr 435 440 445			1344
aat aag gca tta aat gat tta tgt atc aaa gtt aat aat tgg gac ttg Asn Lys Ala Leu Asn Asp Leu Cys Ile Lys Val Asn Asn Trp Asp Leu 450 455 460			1392
ttt ttt agt cct tca gaa gat aat ttt act aat gat cta aat aaa gga Phe Phe Ser Pro Ser Glu Asp Asn Phe Thr Asn Asp Leu Asn Lys Gly 465 470 475 480			1440
gaa gaa att aca tct gat act aat ata gaa gca gca gaa gaa aat att Glu Glu Ile Thr Ser Asp Thr Asn Ile Glu Ala Ala Glu Glu Asn Ile 485 490 495			1488
agt tta gat tta ata caa caa tat tat tta acc ttt aat ttt gat aat Ser Leu Asp Leu Ile Gln Gln Tyr Tyr Leu Thr Phe Asn Phe Asp Asn 500 505 510			1536

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gaa cct gaa aat att tca ata gaa aat ctt tca agt gac att ata ggc Glu Pro Glu Asn Ile Ser Ile Glu Asn Leu Ser Ser Asp Ile Ile Gly 515 520 525	1584
caa tta gaa ctt atg cct aat ata gaa aga ttt cct aat gga aaa aag Gln Leu Glu Leu Met Pro Asn Ile Glu Arg Phe Pro Asn Gly Lys Lys 530 535 540	1632
tat gag tta gat aaa tat act atg ttc cat tat ctt cgt gct caa gaa Tyr Glu Leu Asp Lys Tyr Thr Met Phe His Tyr Leu Arg Ala Gln Glu 545 550 555 560	1680
ttt gaa cat ggt aaa tct agg att gct tta aca aat tct gtt aac gaa Phe Glu His Gly Lys Ser Arg Ile Ala Leu Thr Asn Ser Val Asn Glu 565 570 575	1728
gca tta tta aat cct agt cgt gtt tat aca ttt ttt tct tca gac tat Ala Leu Leu Asn Pro Ser Arg Val Tyr Thr Phe Phe Ser Ser Asp Tyr 580 585 590	1776
gta aag aaa gtt aat aaa gct acg gag gca gct atg ttt tta ggc tgg Val Lys Lys Val Asn Lys Ala Thr Glu Ala Ala Met Phe Leu Gly Trp 595 600 605	1824
gta gaa caa tta gta tat gat ttt acc gat gaa act agc gaa gta agt Val Glu Gln Leu Val Tyr Asp Phe Thr Asp Glu Thr Ser Glu Val Ser 610 615 620	1872
act acg gat aaa att gcg gat ata act ata att att cca tat ata gga Thr Thr Asp Lys Ile Ala Asp Ile Thr Ile Ile Ile Pro Tyr Ile Gly 625 630 635 640	1920
cct gct tta aat ata ggt aat atg tta tat aaa gat gat ttt gta ggt Pro Ala Leu Asn Ile Gly Asn Met Leu Tyr Lys Asp Asp Phe Val Gly 645 650 655	1968
gct tta ata ttt tca gga gct gtt att ctg tta gaa ttt ata cca gag Ala Leu Ile Phe Ser Gly Ala Val Ile Leu Leu Glu Phe Ile Pro Glu 660 665 670	2016
att gca ata cct gta tta ggt act ttt gca ctt gta tca tat att gcg Ile Ala Ile Pro Val Leu Gly Thr Phe Ala Leu Val Ser Tyr Ile Ala 675 680 685	2064
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aat gaa aaa tgg gat gag gtc tat aaa tat ata gta aca aat tgg tta Asn Glu Lys Trp Asp Glu Val Tyr Lys Tyr Ile Val Thr Asn Trp Leu 705 710 715 720	2160
gca aag gtt aat aca cag att gat cta ata aga aaa aaa atg aaa gaa Ala Lys Val Asn Thr Gln Ile Asp Leu Ile Arg Lys Lys Met Lys Glu 725 730 735	2208
gct tta gaa aat caa gca gaa gca aca aag gct ata ata aac tat cag Ala Leu Glu Asn Gln Ala Glu Ala Thr Lys Ala Ile Ile Asn Tyr Gln 740 745 750	2256
tat aat caa tat act gag gaa gag aaa aat aat att aat ttt aat att Tyr Asn Gln Tyr Thr Glu Glu Glu Lys Asn Asn Ile Asn Phe Asn Ile 755 760 765	2304
gat gat tta agt tcg aaa ctt aat gag tct ata aat aaa gct atg att Asp Asp Leu Ser Ser Lys Leu Asn Glu Ser Ile Asn Lys Ala Met Ile 770 775 780	2352

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770 775 780
 aat ata aat aaa ttt ttg aat caa tgc tct gtt tca tat tta atg aat 2400
 Asn Ile Asn Lys Phe Leu Asn Gln Cys Ser Val Ser Tyr Leu Met Asn
 785 790 795 800
 tct atg atc cct tat ggt gtt aaa cgg tta gaa gat ttt gat gct agt 2448
 Ser Met Ile Pro Tyr Gly Val Lys Arg Leu Glu Asp Phe Asp Ala Ser
 805 810 815
 ctt aaa gat gca tta tta aag tat ata tat gat aat aga gga act tta 2496
 Leu Lys Asp Ala Leu Leu Lys Tyr Ile Tyr Asp Asn Arg Gly Thr Leu
 820 825 830
 att ggt caa gta gat aga tta aaa gat aaa gtt aat aat aca ctt agt 2544
 Ile Gly Gln Val Asp Arg Leu Lys Asp Lys Val Asn Asn Thr Leu Ser
 835 840 845
 aca gat ata cct ttt cag ctt tcc aaa tac gta gat aat caa aga tta 2592
 Thr Asp Ile Pro Phe Gln Leu Ser Lys Tyr Val Asp Asn Gln Arg Leu
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 tta tct aca ttt act gaa tat att aag taa tga 2625
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 35 40 45
 Glu Arg Asp Thr Phe Thr Asn Pro Glu Glu Gly Asp Leu Asn Pro Pro
 50 55 60
 Pro Glu Ala Lys Gln Val Pro Val Ser Tyr Tyr Asp Ser Thr Tyr Leu
 65 70 75 80
 Ser Thr Asp Asn Glu Lys Asp Asn Tyr Leu Lys Gly Val Thr Lys Leu
 85 90 95
 Phe Glu Arg Ile Tyr Ser Thr Asp Leu Gly Arg Met Leu Leu Thr Ser
 100 105 110
 Ile Val Arg Gly Ile Pro Phe Trp Gly Gly Ser Thr Ile Asp Thr Glu
 115 120 125

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Leu Lys Val Ile Asp Thr Asn Cys Ile Asn Val Ile Gln Pro Asp Gly
 130 135 140
 Ser Tyr Arg Ser Glu Glu Leu Asn Leu Val Ile Ile Gly Pro Ser Ala
 145 150 155 160
 Asp Ile Ile Gln Phe Glu Cys Lys Ser Phe Gly His Glu Val Leu Asn
 165 170 175
 Leu Thr Arg Asn Gly Tyr Gly Ser Thr Gln Tyr Ile Arg Phe Ser Pro
 180 185 190
 Asp Phe Thr Phe Gly Phe Glu Glu Ser Leu Glu Val Asp Thr Asn Pro
 195 200 205
 Leu Leu Gly Ala Gly Lys Phe Ala Thr Asp Pro Ala Val Thr Leu Ala
 210 215 220
 His Glu Leu Ile Tyr Ala Gly His Arg Leu Tyr Gly Ile Ala Ile Asn
 225 230 235 240
 Pro Asn Arg Val Phe Lys Val Asn Thr Asn Ala Tyr Tyr Glu Met Ser
 245 250 255
 Gly Leu Glu Val Ser Phe Glu Glu Leu Arg Thr Phe Gly Gly His Asp
 260 265 270
 Ala Lys Phe Ile Asp Ser Leu Gln Glu Asn Glu Phe Arg Leu Tyr Tyr
 275 280 285
 Tyr Asn Lys Phe Lys Asp Ile Ala Ser Thr Leu Asn Lys Ala Lys Ser
 290 295 300
 Ile Val Gly Thr Thr Ala Ser Leu Gln Tyr Met Lys Asn Val Phe Lys
 305 310 315 320
 Glu Lys Tyr Leu Leu Ser Glu Asp Thr Ser Gly Lys Phe Ser Val Asp
 325 330 335
 Lys Leu Lys Phe Asp Lys Leu Tyr Lys Met Leu Thr Glu Ile Tyr Thr
 340 345 350
 Glu Asp Asn Phe Val Lys Phe Phe Lys Val Leu Asn Arg Lys Thr Tyr
 355 360 365
 Leu Asn Phe Asp Lys Ala Val Phe Lys Ile Asn Ile Val Pro Lys Val
 370 375 380
 Asn Tyr Thr Ile Tyr Asp Gly Phe Asn Leu Arg Asn Thr Asn Leu Ala
 385 390 395 400

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Ala Asn Phe Asn Gly Gln Asn Thr Glu Ile Asn Asn Met Asn Phe Thr
405 410 415

Lys Leu Lys Asn Phe Thr Gly Leu Phe Glu Phe Tyr Lys Leu Leu Cys
420 425 430

Val Arg Gly Ile Ile Thr Ser Lys Thr Lys Ser Leu Asp Lys Gly Tyr
435 440 445

Asn Lys Ala Leu Asn Asp Leu Cys Ile Lys Val Asn Asn Trp Asp Leu
450 455 460

Phe Phe Ser Pro Ser Glu Asp Asn Phe Thr Asn Asp Leu Asn Lys Gly
465 470 475 480

Glu Glu Ile Thr Ser Asp Thr Asn Ile Glu Ala Ala Glu Glu Asn Ile
485 490 495

Ser Leu Asp Leu Ile Gln Gln Tyr Tyr Leu Thr Phe Asn Phe Asp Asn
500 505 510

Glu Pro Glu Asn Ile Ser Ile Glu Asn Leu Ser Ser Asp Ile Ile Gly
515 520 525

Gln Leu Glu Leu Met Pro Asn Ile Glu Arg Phe Pro Asn Gly Lys Lys
530 535 540

Tyr Glu Leu Asp Lys Tyr Thr Met Phe His Tyr Leu Arg Ala Gln Glu
545 550 555 560

Phe Glu His Gly Lys Ser Arg Ile Ala Leu Thr Asn Ser Val Asn Glu
565 570 575

Ala Leu Leu Asn Pro Ser Arg Val Tyr Thr Phe Phe Ser Ser Asp Tyr
580 585 590

Val Lys Lys Val Asn Lys Ala Thr Glu Ala Ala Met Phe Leu Gly Trp
595 600 605

Val Glu Gln Leu Val Tyr Asp Phe Thr Asp Glu Thr Ser Glu Val Ser
610 615 620

Thr Thr Asp Lys Ile Ala Asp Ile Thr Ile Ile Ile Pro Tyr Ile Gly
625 630 635 640

Pro Ala Leu Asn Ile Gly Asn Met Leu Tyr Lys Asp Asp Phe Val Gly
645 650 655

Ala Leu Ile Phe Ser Gly Ala Val Ile Leu Leu Glu Phe Ile Pro Glu

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660 665 670
 Ile Ala Ile Pro Val Leu Gly Thr Phe Ala Leu Val Ser Tyr Ile Ala
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 Asn Lys Val Leu Thr Val Gln Thr Ile Asp Asn Ala Leu Ser Lys Arg
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 Asn Glu Lys Trp Asp Glu Val Tyr Lys Tyr Ile Val Thr Asn Trp Leu
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 Ala Lys Val Asn Thr Gln Ile Asp Leu Ile Arg Lys Lys Met Lys Glu
 725 730 735
 Ala Leu Glu Asn Gln Ala Glu Ala Thr Lys Ala Ile Ile Asn Tyr Gln
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 Tyr Asn Gln Tyr Thr Glu Glu Glu Lys Asn Asn Ile Asn Phe Asn Ile
 755 760 765
 Asp Asp Leu Ser Ser Lys Leu Asn Glu Ser Ile Asn Lys Ala Met Ile
 770 775 780
 Asn Ile Asn Lys Phe Leu Asn Gln Cys Ser Val Ser Tyr Leu Met Asn
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 Ser Met Ile Pro Tyr Gly Val Lys Arg Leu Glu Asp Phe Asp Ala Ser
 805 810 815
 Leu Lys Asp Ala Leu Leu Lys Tyr Ile Tyr Asp Asn Arg Gly Thr Leu
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 Ile Gly Gln Val Asp Arg Leu Lys Asp Lys Val Asn Asn Thr Leu Ser
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<400> 164

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cag ccg gta aag gca ttc aaa atc cac aac aaa atc tgg gtt atc ccg Gln Pro Val Lys Ala Phe Lys Ile His Asn Lys Ile Trp Val Ile Pro 35 40 45	144
gaa cgt gat acc ttt act aac ccg gaa gaa ggt gac ctg aac ccg cca Glu Arg Asp Thr Phe Thr Asn Pro Glu Glu Gly Asp Leu Asn Pro Pro 50 55 60	192
ccg gaa gcg aaa cag gtg ccg gta tct tac tat gac tcc acc tac ctg Pro Glu Ala Lys Gln Val Pro Val Ser Tyr Tyr Asp Ser Thr Tyr Leu 65 70 75 80	240
tct acc gat aac gaa aag gac aac tac ctg aaa ggt gtt act aaa ctg Ser Thr Asp Asn Glu Lys Asp Asn Tyr Leu Lys Gly Val Thr Lys Leu 85 90 95	288
ttc gag cgt att tac tcc acc gac ctg ggc cgt atg ctg ctg act agc Phe Glu Arg Ile Tyr Ser Thr Asp Leu Gly Arg Met Leu Leu Thr Ser 100 105 110	336
atc gtt cgc ggt atc ccg ttc tgg ggc ggt tct acc atc gat acc gaa Ile Val Arg Gly Ile Pro Phe Trp Gly Gly Ser Thr Ile Asp Thr Glu 115 120 125	384
ctg aaa gta atc gac act aac tgc atc aac gtt att cag ccg gac ggt Leu Lys Val Ile Asp Thr Asn Cys Ile Asn Val Ile Gln Pro Asp Gly 130 135 140	432
tcc tat cgt tcc gaa gaa ctg aac ctg gtg atc atc ggc ccg tct gct Ser Tyr Arg Ser Glu Glu Leu Asn Leu Val Ile Ile Gly Pro Ser Ala 145 150 155 160	480
gat atc atc cag ttc gag tgt aag agc ttt ggt cac gaa gtt ctg aac Asp Ile Ile Gln Phe Glu Cys Lys Ser Phe Gly His Glu Val Leu Asn 165 170 175	528
ctc acc cgt aac ggc tac ggt tcc act cag tac atc cgt ttc tct ccg Leu Thr Arg Asn Gly Tyr Gly Ser Thr Gln Tyr Ile Arg Phe Ser Pro 180 185 190	576
gac ttc acc ttc ggt ttt gaa gaa tcc ctg gaa gta gac acg aac cca Asp Phe Thr Phe Gly Phe Glu Glu Ser Leu Glu Val Asp Thr Asn Pro 195 200 205	624
ctg ctg ggc gct ggt aaa ttc gca act gat cct gcg gtt acc ctg gct Leu Leu Gly Ala Gly Lys Phe Ala Thr Asp Pro Ala Val Thr Leu Ala 210 215 220	672
cac gaa ctg att tat gca ggc cac cgc ctg tac ggt atc gcc atc aat His Glu Leu Ile Tyr Ala Gly His Arg Leu Tyr Gly Ile Ala Ile Asn 225 230 235 240	720
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tat aac aag ttc aaa gat atc gca tcc acc ctg aac aaa gcg aaa tcc Tyr Asn Lys Phe Lys Asp Ile Ala Ser Thr Leu Asn Lys Ala Lys Ser 290 295 300			912
atc gtg ggt acc act gct tct ctg cag tac atg aag aac gtt ttt aaa Ile Val Gly Thr Thr Ala Ser Leu Gln Tyr Met Lys Asn Val Phe Lys 305 310 315 320			960
gaa aaa tac ctg ctc agc gaa gac acc tcc ggc aaa ttc tct gta gac Glu Lys Tyr Leu Leu Ser Glu Asp Thr Ser Gly Lys Phe Ser Val Asp 325 330 335			1008
aag ttg aaa ttc gat aaa ctt tac aaa atg ctg act gaa att tac acc Lys Leu Lys Phe Asp Lys Leu Tyr Lys Met Leu Thr Glu Ile Tyr Thr 340 345 350			1056
gaa gac aac ttc gtt aag ttc ttt aaa gtt ctg aac cgc aaa acc tat Glu Asp Asn Phe Val Lys Phe Phe Lys Val Leu Asn Arg Lys Thr Tyr 355 360 365			1104
ctg aac ttc gac aag gca gta ttc aaa atc aac atc gtg ccg aaa gtt Leu Asn Phe Asp Lys Ala Val Phe Lys Ile Asn Ile Val Pro Lys Val 370 375 380			1152
aac tac act atc tac gat ggt ttc aac ctg cgt aac acc aac ctg gct Asn Tyr Thr Ile Tyr Asp Gly Phe Asn Leu Arg Asn Thr Asn Leu Ala 385 390 395 400			1200
gct aat ttt aac ggc cag aac acg gaa atc aac aac atg aac ttc aca Ala Asn Phe Asn Gly Gln Asn Thr Glu Ile Asn Asn Met Asn Phe Thr 405 410 415			1248
aaa ctg aaa aac ttc act ggt ctg ttc gag ttt tac aag ctg ctg tgc Lys Leu Lys Asn Phe Thr Gly Leu Phe Glu Phe Tyr Lys Leu Leu Cys 420 425 430			1296
gta cgt ggc atc att acc tcc aaa act aaa tct ctg gac aaa ggt tat Val Arg Gly Ile Ile Thr Ser Lys Thr Lys Ser Leu Asp Lys Gly Tyr 435 440 445			1344
aac aaa gcg ctg aac gac ctc tgt atc aag gtt aac aac tgg gat tta Asn Lys Ala Leu Asn Asp Leu Cys Ile Lys Val Asn Asn Trp Asp Leu 450 455 460			1392
ttc ttc agc ccg agt gaa gac aac ttc acc aac gac ctg aac aaa ggt Phe Phe Ser Pro Ser Glu Asp Asn Phe Thr Asn Asp Leu Asn Lys Gly 465 470 475 480			1440
gaa gaa atc acc tca gat act aac atc gaa gca gcc gaa gaa aac atc Glu Glu Ile Thr Ser Asp Thr Asn Ile Glu Ala Ala Glu Glu Asn Ile 485 490 495			1488
tcg ctg gac ctg atc cag cag tac tac ctg acc ttt aat ttc gac aac Ser Leu Asp Leu Ile Gln Gln Tyr Tyr Leu Thr Phe Asn Phe Asp Asn 500 505 510			1536
gag ccg gaa aac att tct atc gaa aac ctg agc tct gat atc atc ggc Glu Pro Glu Asn Ile Ser Ile Glu Asn Leu Ser Ser Asp Ile Ile Gly 515 520 525			1584

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cag ctg gaa ctg atg ccg aac atc gaa cgt ttc cca aac ggt aaa aag Gln Leu Glu Leu Met Pro Asn Ile Glu Arg Phe Pro Asn Gly Lys Lys 530 535 540	1632
tac gag ctg gac aaa tat acc atg ttc cac tac ctg cgc gcg cag gaa Tyr Glu Leu Asp Lys Tyr Thr Met Phe His Tyr Leu Arg Ala Gln Glu 545 550 555 560	1680
ttt gaa cac ggc aaa tcc cgt atc gca ctg act aac tcc gtt aac gaa Phe Glu His Gly Lys Ser Arg Ile Ala Leu Thr Asn Ser Val Asn Glu 565 570 575	1728
gct ctg ctc aac ccg tcc cgt gta tac acc ttc ttc tct agc gac tac Ala Leu Leu Asn Pro Ser Arg Val Tyr Thr Phe Phe Ser Ser Asp Tyr 580 585 590	1776
gtg aaa aag gtc aac aaa gcg act gaa gct gca atg ttc ttg ggt tgg Val Lys Lys Val Asn Lys Ala Thr Glu Ala Ala Met Phe Leu Gly Trp 595 600 605	1824
gtt gaa cag ctt gtt tat gat ttt acc gac gag acg tcc gaa gta tct Val Glu Gln Leu Val Tyr Asp Phe Thr Asp Glu Thr Ser Glu Val Ser 610 615 620	1872
act acc gac aaa att gcg gat atc act atc atc atc ccg tac atc ggt Thr Thr Asp Lys Ile Ala Asp Ile Thr Ile Ile Ile Pro Tyr Ile Gly 625 630 635 640	1920
ccg gct ctg aac att gcg aac atg ctg tac aaa gac gac ttc gtt ggt Pro Ala Leu Asn Ile Gly Asn Met Leu Tyr Lys Asp Asp Phe Val Gly 645 650 655	1968
gca ctg atc ttc tcc ggt gcg gtg atc ctg ctg gag ttc atc ccg gaa Ala Leu Ile Phe Ser Gly Ala Val Ile Leu Leu Glu Phe Ile Pro Glu 660 665 670	2016
atc gcc atc ccg gta ctg gcc acc ttt gct ctg gtt tct tac att gca Ile Ala Ile Pro Val Leu Gly Thr Phe Ala Leu Val Ser Tyr Ile Ala 675 680 685	2064
aac aag gtt ctg act gta caa acc atc gac aac gcg ctg agc aaa cgt Asn Lys Val Leu Thr Val Gln Thr Ile Asp Asn Ala Leu Ser Lys Arg 690 695 700	2112
aac gaa aaa tgg gat gaa gtt tac aaa tat atc gtg acc aac tgg ctg Asn Glu Lys Trp Asp Glu Val Tyr Lys Tyr Ile Val Thr Asn Trp Leu 705 710 715 720	2160
gct aag gtt aat act cag atc gac ctc atc cgc aaa aaa atg aaa gaa Ala Lys Val Asn Thr Gln Ile Asp Leu Ile Arg Lys Lys Met Lys Glu 725 730 735	2208
gca ctg gaa aac cag gcg gaa gct acc aag gca atc att aac tac cag Ala Leu Glu Asn Gln Ala Glu Ala Thr Lys Ala Ile Ile Asn Tyr Gln 740 745 750	2256
tac aac cag tac acc gag gaa gaa aaa aac aac atc aac ttc aac atc Tyr Asn Gln Tyr Thr Glu Glu Glu Lys Asn Asn Ile Asn Phe Asn Ile 755 760 765	2304
gac gat ctg tcc tct aaa ctg aac gaa tcc atc aac aaa gct atg atc Asp Asp Leu Ser Ser Lys Leu Asn Glu Ser Ile Asn Lys Ala Met Ile 770 775 780	2352
aac atc aac aag ttc ctg aac cag tgc tct gta agc tat ctg atg aac Asn Ile Asn Lys Phe Leu Asn Gln Cys Ser Val Ser Tyr Leu Met Asn 785 790 795	2400

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Leu Lys Val Ile Asp Thr Asn Cys Ile Asn Val Ile Gln Pro Asp Gly
130 135 140

Ser Tyr Arg Ser Glu Glu Leu Asn Leu Val Ile Ile Gly Pro Ser Ala
 145 150 155 160
 Asp Ile Ile Gln Phe Glu Cys Lys Ser Phe Gly His Glu Val Leu Asn
 165 170 175
 Leu Thr Arg Asn Gly Tyr Gly Ser Thr Gln Tyr Ile Arg Phe Ser Pro
 180 185 190
 Asp Phe Thr Phe Gly Phe Glu Glu Ser Leu Glu Val Asp Thr Asn Pro
 195 200 205
 Leu Leu Gly Ala Gly Lys Phe Ala Thr Asp Pro Ala Val Thr Leu Ala
 210 215 220
 His Glu Leu Ile Tyr Ala Gly His Arg Leu Tyr Gly Ile Ala Ile Asn
 225 230 235 240
 Pro Asn Arg Val Phe Lys Val Asn Thr Asn Ala Tyr Tyr Glu Met Ser
 245 250 255
 Gly Leu Glu Val Ser Phe Glu Glu Leu Arg Thr Phe Gly Gly His Asp
 260 265 270
 Ala Lys Phe Ile Asp Ser Leu Gln Glu Asn Glu Phe Arg Leu Tyr Tyr
 275 280 285
 Tyr Asn Lys Phe Lys Asp Ile Ala Ser Thr Leu Asn Lys Ala Lys Ser
 290 295 300
 Ile Val Gly Thr Thr Ala Ser Leu Gln Tyr Met Lys Asn Val Phe Lys
 305 310 315 320
 Glu Lys Tyr Leu Leu Ser Glu Asp Thr Ser Gly Lys Phe Ser Val Asp
 325 330 335
 Lys Leu Lys Phe Asp Lys Leu Tyr Lys Met Leu Thr Glu Ile Tyr Thr
 340 345 350
 Glu Asp Asn Phe Val Lys Phe Phe Lys Val Leu Asn Arg Lys Thr Tyr
 355 360 365
 Leu Asn Phe Asp Lys Ala Val Phe Lys Ile Asn Ile Val Pro Lys Val
 370 375 380
 Asn Tyr Thr Ile Tyr Asp Gly Phe Asn Leu Arg Asn Thr Asn Leu Ala
 385 390 395 400
 Ala Asn Phe Asn Gly Gln Asn Thr Glu Ile Asn Asn Met Asn Phe Thr
 405 410 415

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Lys Leu Lys Asn Phe Thr Gly Leu Phe Glu Phe Tyr Lys Leu Leu Cys
 420 425 430
 Val Arg Gly Ile Ile Thr Ser Lys Thr Lys Ser Leu Asp Lys Gly Tyr
 435 440 445
 Asn Lys Ala Leu Asn Asp Leu Cys Ile Lys Val Asn Asn Trp Asp Leu
 450 455 460
 Phe Phe Ser Pro Ser Glu Asp Asn Phe Thr Asn Asp Leu Asn Lys Gly
 465 470 475 480
 Glu Glu Ile Thr Ser Asp Thr Asn Ile Glu Ala Ala Glu Glu Asn Ile
 485 490 495
 Ser Leu Asp Leu Ile Gln Gln Tyr Tyr Leu Thr Phe Asn Phe Asp Asn
 500 505 510
 Glu Pro Glu Asn Ile Ser Ile Glu Asn Leu Ser Ser Asp Ile Ile Gly
 515 520 525
 Gln Leu Glu Leu Met Pro Asn Ile Glu Arg Phe Pro Asn Gly Lys Lys
 530 535 540
 Tyr Glu Leu Asp Lys Tyr Thr Met Phe His Tyr Leu Arg Ala Gln Glu
 545 550 555 560
 Phe Glu His Gly Lys Ser Arg Ile Ala Leu Thr Asn Ser Val Asn Glu
 565 570 575
 Ala Leu Leu Asn Pro Ser Arg Val Tyr Thr Phe Phe Ser Ser Asp Tyr
 580 585 590
 Val Lys Lys Val Asn Lys Ala Thr Glu Ala Ala Met Phe Leu Gly Trp
 595 600 605
 Val Glu Gln Leu Val Tyr Asp Phe Thr Asp Glu Thr Ser Glu Val Ser
 610 615 620
 Thr Thr Asp Lys Ile Ala Asp Ile Thr Ile Ile Ile Pro Tyr Ile Gly
 625 630 635 640
 Pro Ala Leu Asn Ile Gly Asn Met Leu Tyr Lys Asp Asp Phe Val Gly
 645 650 655
 Ala Leu Ile Phe Ser Gly Ala Val Ile Leu Leu Glu Phe Ile Pro Glu
 660 665 670
 Ile Ala Ile Pro Val Leu Gly Thr Phe Ala Leu Val Ser Tyr Ile Ala

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675 680 685
 Asn Lys Val Leu Thr Val Gln Thr Ile Asp Asn Ala Leu Ser Lys Arg
 690 695 700
 Asn Glu Lys Trp Asp Glu Val Tyr Lys Tyr Ile Val Thr Asn Trp Leu
 705 710 715 720
 Ala Lys Val Asn Thr Gln Ile Asp Leu Ile Arg Lys Lys Met Lys Glu
 725 730 735
 Ala Leu Glu Asn Gln Ala Glu Ala Thr Lys Ala Ile Ile Asn Tyr Gln
 740 745 750
 Tyr Asn Gln Tyr Thr Glu Glu Glu Lys Asn Asn Ile Asn Phe Asn Ile
 755 760 765
 Asp Asp Leu Ser Ser Lys Leu Asn Glu Ser Ile Asn Lys Ala Met Ile
 770 775 780
 Asn Ile Asn Lys Phe Leu Asn Gln Cys Ser Val Ser Tyr Leu Met Asn
 785 790 795 800
 Ser Met Ile Pro Tyr Gly Val Lys Arg Leu Glu Asp Phe Asp Ala Ser
 805 810 815
 Leu Lys Asp Ala Leu Leu Lys Tyr Ile Tyr Asp Asn Arg Gly Thr Leu
 820 825 830
 Ile Gly Gln Val Asp Arg Leu Lys Asp Lys Val Asn Asn Thr Leu Ser
 835 840 845
 Thr Asp Ile Pro Phe Gln Leu Ser Lys Tyr Val Asp Asn Gln Arg Leu
 850 855 860
 Leu Ser Thr Phe Thr Glu Tyr Ile Lys
 865 870

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 <212> DNA
 <213> Clostridium botulinum

<220>
 <221> CDS
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 Gly Ser Met Glu Phe Val Asn Lys Gln Phe Asn Tyr Lys Asp Pro Val
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aac ggt gtt gac att gct tac atc aaa atc ccg aac gct ggc cag atg 96
 Asn Gly Val Asp Ile Ala Tyr Ile Lys Ile Pro Asn Ala Gly Gln Met
 20 25 30

cag ccg gta aag gca ttc aaa atc cac aac aaa atc tgg gtt atc ccg 144
 Gln Pro Val Lys Ala Phe Lys Ile His Asn Lys Ile Trp Val Ile Pro
 35 40 45

gaa cgt gat acc ttt act aac ccg gaa gaa ggt gac ctg aac ccg cca 192
 Glu Arg Asp Thr Phe Thr Asn Pro Glu Glu Gly Asp Leu Asn Pro Pro
 50 55 60

ccg gaa gcg aaa cag gtg ccg gta tct tac tat gac tcc acc tac ctg 240
 Pro Glu Ala Lys Gln Val Pro Val Ser Tyr Tyr Asp Ser Thr Tyr Leu
 65 70 75 80

tct acc gat aac gaa aag gac aac tac ctg leu aaa ggt gtt act aaa ctg 288
 Ser Thr Asp Asn Glu Lys Asp Asn Tyr Leu Lys Gly Val Thr Lys Leu
 85 90 95

ttc gag cgt att tac tcc acc gac ctg ggc cgt atg ctg ctg act agc 336
 Phe Glu Arg Ile Tyr Ser Thr Asp Leu Gly Arg Met Leu Thr Ser
 100 105 110

atc gtt cgc ggt atc ccg ttc tgg ggc ggt tct acc atc gat acc gaa 384
 Ile Val Arg Gly Ile Pro Phe Trp Gly Gly Ser Thr Ile Asp Thr Glu
 115 120 125

ctg aaa gta atc gac act aac tgc atc aac gtt att cag ccg gac ggt 432
 Leu Lys Val Ile Asp Thr Asn Cys Ile Asn Val Ile Gln Pro Asp Gly
 130 135 140

tcc tat cgt tcc gaa gaa ctg aac ctg gtg atc atc ggc ccg tct gct 480
 Ser Tyr Arg Ser Glu Glu Leu Asn Leu Val Ile Ile Gly Pro Ser Ala
 145 150 155 160

gat atc atc cag ttc gag tgt aag agc ttt ggt cac gaa gtt ctg aac 528
 Asp Ile Ile Gln Phe-Glu Cys Lys Ser Phe Gly His Glu Val Leu Asn
 165 170 175

ctc acc cgt aac ggc tac ggt tcc act cag tac atc cgt ttc tct ccg 576
 Leu Thr Arg Asn Gly Tyr Gly Ser Thr Gln Tyr Ile Arg Phe Ser Pro
 180 185 190

gac ttc acc ttc ggt ttt gaa gaa tcc ctg gaa gta gac acg aac cca 624
 Asp Phe Thr Phe Gly Phe Glu Glu Ser Leu Glu Val Asp Thr Asn Pro
 195 200 205

ctg ctg ggc gct ggt aaa ttc gca act gat cct gcg gtt acc ctg gct 672
 Leu Leu Gly Ala Gly Lys Phe Ala Thr Asp Pro Ala Val Thr Leu Ala
 210 215 220

cac cag ctg att cat gca ggc cac cgc ctg tac ggt atc gcc atc aat 720
 His Gln Leu Ile His Ala Gly His Arg Leu Tyr Gly Ile Ala Ile Asn
 225 230 235 240

ccg aac cgt gtc ttc aaa gtt aac acc aac gcg tat tac gag atg tcc 768
 Pro Asn Arg Val Phe Lys Val Asn Thr Asn Ala Tyr Tyr Glu Met Ser
 245 250 255

ggt ctg gaa gta agc ttc gaa gaa ctg cgt act ttt ggc ggt cac gac 816
 Gly Leu Glu Val Ser Phe Glu Glu Leu Arg Thr Phe Gly Gly His Asp
 260 265 270

gct aaa ttc atc gac tct ctg caa gaa aac gag ttc cgt ctg tac tac 864
 Ala Lys Phe Ile Asp Ser Leu Gln Glu Asn Glu Phe Arg Leu Tyr Tyr

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275	280	285	
tat aac aag ttc aaa gat atc gca tcc acc ctg aac aaa gcg aaa tcc Tyr Asn Lys Phe Lys Asp Ile Ala Ser Thr Leu Asn Lys Ala Lys Ser 290 295 300			912
atc gtg ggt acc act gct tct ctg cag tac atg aag aac gtt ttt aaa Ile Val Gly Thr Thr Ala Ser Leu Gln Tyr Met Lys Asn Val Phe Lys 305 310 315 320			960
gaa aaa tac ctg ctc agc gaa gac acc tcc ggc aaa ttc tct gta gac Glu Lys Tyr Leu Leu Ser Glu Asp Thr Ser Gly Lys Phe Ser Val Asp 325 330 335			1008
aag ttg aaa ttc gat aaa ctt tac aaa atg ctg act gaa att tac acc Lys Leu Lys Phe Asp Lys Leu Tyr Lys Met Leu Thr Glu Ile Tyr Thr 340 345 350			1056
gaa gac aac ttc gtt aag ttc ttt aaa gtt ctg aac cgc aaa acc tat Glu Asp Asn Phe Val Lys Phe Phe Lys Val Leu Asn Arg Lys Thr Tyr 355 360 365			1104
ctg aac ttc gac aag gca gta ttc aaa atc aac atc gtg ccg aaa gtt Leu Asn Phe Asp Lys Ala Val Phe Lys Ile Asn Ile Val Pro Lys Val 370 375 380			1152
aac tac act atc tac gat ggt ttc aac ctg cgt aac acc aac ctg gct Asn Tyr Thr Ile Tyr Asp Gly Phe Asn Leu Arg Asn Thr Asn Leu Ala 385 390 395 400			1200
gct aat ttt aac ggc cag aac acg gaa atc aac aac atg aac ttc aca Ala Asn Phe Asn Gly Gln Asn Thr Glu Ile Asn Asn Met Asn Phe Thr 405 410 415			1248
aaa ctg aaa aac ttc act ggt ctg ttc gag ttt tac aag ctg ctg tgc Lys Leu Lys Asn Phe Thr Gly Leu Phe Glu Phe Tyr Lys Leu Leu Cys 420 425 430			1296
gta cgt ggc atc att acc tcc aaa act aaa tct ctg gac aaa ggt tat Val Arg Gly Ile Ile Thr Ser Lys Thr Lys Ser Leu Asp Lys Gly Tyr 435 440 445			1344
aac aaa gcg ctg aac gac ctc tgt atc aag gtt aac aac tgg gat tta Asn Lys Ala Leu Asn Asp Leu Cys Ile Lys Val Asn Asn Trp Asp Leu 450 455 460			1392
ttc ttc agc ccg agt gaa gac aac ttc acc aac gac ctg aac aaa ggt Phe Phe Ser Pro Ser Glu Asp Asn Phe Thr Asn Asp Leu Asn Lys Gly 465 470 475 480			1440
gaa gaa atc acc tca gat act aac atc gaa gca gcc gaa gaa aac atc Glu Glu Ile Thr Ser Asp Thr Asn Ile Glu Ala Ala Glu Glu Asn Ile 485 490 495			1488
tcg ctg gac ctg atc cag cag tac tac ctg acc ttt aat ttc gac aac Ser Leu Asp Leu Ile Gln Gln Tyr Tyr Leu Thr Phe Asn Phe Asp Asn 500 505 510			1536
gag ccg gaa aac att tct atc gaa aac ctg agc tct gat atc atc ggc Glu Pro Glu Asn Ile Ser Ile Glu Asn Leu Ser Ser Asp Ile Ile Gly 515 520 525			1584
cag ctg gaa ctg atg ccg aac atc gaa cgt ttc cca aac ggt aaa aag Gln Leu Glu Leu Met Pro Asn Ile Glu Arg Phe Pro Asn Gly Lys Lys 530 535 540			1632

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tac gag ctg gac aaa tat acc atg ttc cac tac ctg cgc gcg cag gaa Tyr Glu Leu Asp Lys Tyr Thr Met Phe His Tyr Leu Arg Ala Gln Glu 545 550 555 560	1680
ttt gaa cac ggc aaa tcc cgt atc gca ctg act aac tcc gtt aac gaa Phe Glu His Gly Lys Ser Arg Ile Ala Leu Thr Asn Ser Val Asn Glu 565 570 575	1728
gct ctg ctc aac ccg tcc cgt gta tac acc ttc ttc tct agc gac tac Ala Leu Leu Asn Pro Ser Arg Val Tyr Thr Phe Phe Ser Ser Asp Tyr 580 585 590	1776
gtg aaa aag gtc aac aaa gcg act gaa gct gca atg ttc ttg ggt tgg Val Lys Lys Val Asn Lys Ala Thr Glu Ala Ala Met Phe Leu Gly Trp 595 600 605	1824
gtt gaa cag ctt gtt tat gat ttt acc gac gag acg tcc gaa gta tct Val Glu Gln Leu Val Tyr Asp Phe Thr Asp Glu Thr Ser Glu Val Ser 610 615 620	1872
act acc gac aaa att gcg gat atc act atc atc atc ccg tac atc ggt Thr Thr Asp Lys Ile Ala Asp Ile Thr Ile Ile Ile Pro Tyr Ile Gly 625 630 635 640	1920
ccg gct ctg aac att ggc aac atg ctg tac aaa gac gac ttc gtt ggt Pro Ala Leu Asn Ile Gly Asn Met Leu Tyr Lys Asp Asp Phe Val Gly 645 650 655	1968
gca ctg atc ttc tcc ggt gcg gtg atc ctg ctg gag ttc atc ccg gaa Ala Leu Ile Phe Ser Gly Ala Val Ile Leu Leu Glu Phe Ile Pro Glu 660 665 670	2016
atc gcc atc ccg gta ctg ggc acc ttt gct ctg gtt tct tac att gca Ile Ala Ile Pro Val Leu Gly Thr Phe Ala Leu Val Ser Tyr Ile Ala 675 680 685	2064
aac aag gtt ctg act gta caa acc atc gac aac gcg ctg agc aaa cgt Asn Lys Val Leu Thr Val Gln Thr Ile Asp Asn Ala Leu Ser Lys Arg 690 695 700	2112
aac gaa aaa tgg gat gaa gtt tac aaa tat atc gtg acc aac tgg ctg Asn Glu Lys Trp Asp Glu Val Tyr Lys Tyr Ile Val Thr Asn Trp Leu 705 710 715 720	2160
gct aag gtt aat act cag atc gac ctc atc cgc aaa aaa atg aaa gaa Ala Lys Val Asn Thr Gln Ile Asp Leu Ile Arg Lys Lys Met Lys Glu 725 730 735	2208
gca ctg gaa aac cag gcg gaa gct acc aag gca atc att aac tac cag Ala Leu Glu Asn Gln Ala Glu Ala Thr Lys Ala Ile Ile Asn Tyr Gln 740 745 750	2256
tac aac cag tac acc gag gaa gaa aaa aac aac atc aac ttc aac atc Tyr Asn Gln Tyr Thr Glu Glu Glu Lys Asn Asn Ile Asn Phe Asn Ile 755 760 765	2304
gac gat ctg tcc tct aaa ctg aac gaa tcc atc aac aaa gct atg atc Asp Asp Leu Ser Ser Lys Leu Asn Glu Ser Ile Asn Lys Ala Met Ile 770 775 780	2352
aac atc aac aag ttc ctg aac cag tgc tct gta agc tat ctg atg aac Asn Ile Asn Lys Phe Leu Asn Gln Cys Ser Val Ser Tyr Leu Met Asn 785 790 795 800	2400
tcc atg atc ccg tac ggt gtt aaa cgt ctg gag gac ttc gat gcg tct Ser Met Ile Pro Tyr Gly Val Lys Arg Leu Glu Asp Phe Asp Ala Ser	2448

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805 810 815
 ctg aaa gac gcc ctg ctg aaa tac att tac gac aac cgt ggc act ctg 2496
 Leu Lys Asp Ala Leu Leu Lys Tyr Ile Tyr Asp Asn Arg Gly Thr Leu
 820 825 830
 atc ggt cag gtt gat cgt ctg aag gac aaa gtg aac aat acc tta tcg 2544
 Ile Gly Gln Val Asp Arg Leu Lys Asp Lys Val Asn Asn Thr Leu Ser
 835 840 845
 acc gac atc cct ttt cag ctc agt aaa tat gtc gat aac caa cgc ctt 2592
 Thr Asp Ile Pro Phe Gln Leu Ser Lys Tyr Val Asp Asn Gln Arg Leu
 850 855 860
 ttg agc acg ttc aca gag tac atc aag taa tga 2625
 Leu Ser Thr Phe Thr Glu Tyr Ile Lys
 865 870

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<210> 167
 <211> 873
 <212> PRT
 <213> Clostridium botulinum

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Asn Gly Val Asp Ile Ala Tyr Ile Lys Ile Pro Asn Ala Gly Gln Met
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Gln Pro Val Lys Ala Phe Lys Ile His Asn Lys Ile Trp Val Ile Pro
 35 40 45

Glu Arg Asp Thr Phe Thr Asn Pro Glu Glu Gly Asp Leu Asn Pro Pro
 50 55 60

Pro Glu Ala Lys Gln Val Pro Val Ser Tyr Tyr Asp Ser Thr Tyr Leu
 65 70 75 80

Ser Thr Asp Asn Glu Lys Asp Asn Tyr Leu Lys Gly Val Thr Lys Leu
 85 90 95

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Phe Glu Arg Ile Tyr Ser Thr Asp Leu Gly Arg Met Leu Leu Thr Ser
 100 105 110

Ile Val Arg Gly Ile Pro Phe Trp Gly Gly Ser Thr Ile Asp Thr Glu
 115 120 125

Leu Lys Val Ile Asp Thr Asn Cys Ile Asn Val Ile Gln Pro Asp Gly
 130 135 140

Ser Tyr Arg Ser Glu Glu Leu Asn Leu Val Ile Ile Gly Pro Ser Ala
 145 150 155 160

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Asp Ile Ile Gln Phe Glu Cys Lys Ser Phe Gly His Glu Val Leu Asn
 165 170 175
 Leu Thr Arg Asn Gly Tyr Gly Ser Thr Gln Tyr Ile Arg Phe Ser Pro
 180 185 190
 Asp Phe Thr Phe Gly Phe Glu Glu Ser Leu Glu Val Asp Thr Asn Pro
 195 200 205
 Leu Leu Gly Ala Gly Lys Phe Ala Thr Asp Pro Ala Val Thr Leu Ala
 210 215 220
 His Gln Leu Ile His Ala Gly His Arg Leu Tyr Gly Ile Ala Ile Asn
 225 230 235 240
 Pro Asn Arg Val Phe Lys Val Asn Thr Asn Ala Tyr Tyr Glu Met Ser
 245 250 255
 Gly Leu Glu Val Ser Phe Glu Glu Leu Arg Thr Phe Gly Gly His Asp
 260 265 270
 Ala Lys Phe Ile Asp Ser Leu Gln Glu Asn Glu Phe Arg Leu Tyr Tyr
 275 280 285
 Tyr Asn Lys Phe Lys Asp Ile Ala Ser Thr Leu Asn Lys Ala Lys Ser
 290 295 300
 Ile Val Gly Thr Thr Ala Ser Leu Gln Tyr Met Lys Asn Val Phe Lys
 305 310 315 320
 Glu Lys Tyr Leu Leu Ser Glu Asp Thr Ser Gly Lys Phe Ser Val Asp
 325 330 335
 Lys Leu Lys Phe Asp Lys Leu Tyr Lys Met Leu Thr Glu Ile Tyr Thr
 340 345 350
 Glu Asp Asn Phe Val Lys Phe Phe Lys Val Leu Asn Arg Lys Thr Tyr
 355 360 365
 Leu Asn Phe Asp Lys Ala Val Phe Lys Ile Asn Ile Val Pro Lys Val
 370 375 380
 Asn Tyr Thr Ile Tyr Asp Gly Phe Asn Leu Arg Asn Thr Asn Leu Ala
 385 390 395 400
 Ala Asn Phe Asn Gly Gln Asn Thr Glu Ile Asn Asn Met Asn Phe Thr
 405 410 415
 Lys Leu Lys Asn Phe Thr Gly Leu Phe Glu Phe Tyr Lys Leu Leu Cys
 420 425 430

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

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690 695 700
 Asn Glu Lys Trp Asp Glu Val Tyr Lys Tyr Ile Val Thr Asn Trp Leu
 705 710 715 720
 Ala Lys Val Asn Thr Gln Ile Asp Leu Ile Arg Lys Lys Met Lys Glu
 725 730 735
 Ala Leu Glu Asn Gln Ala Glu Ala Thr Lys Ala Ile Ile Asn Tyr Gln
 740 745 750
 Tyr Asn Gln Tyr Thr Glu Glu Glu Lys Asn Asn Ile Asn Phe Asn Ile
 755 760 765
 Asp Asp Leu Ser Ser Lys Leu Asn Glu Ser Ile Asn Lys Ala Met Ile
 770 775 780
 Asn Ile Asn Lys Phe Leu Asn Gln Cys Ser Val Ser Tyr Leu Met Asn
 785 790 795 800
 Ser Met Ile Pro Tyr Gly Val Lys Arg Leu Glu Asp Phe Asp Ala Ser
 805 810 815
 Leu Lys Asp Ala Leu Leu Lys Tyr Ile Tyr Asp Asn Arg Gly Thr Leu
 820 825 830
 Ile Gly Gln Val Asp Arg Leu Lys Asp Lys Val Asn Asn Thr Leu Ser
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 Thr Asp Ile Pro Phe Gln Leu Ser Lys Tyr Val Asp Asn Gln Arg Leu
 850 855 860
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<220>
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 aac ggt gtt gac att gct tac atc aaa atc ccg aac gct ggc cag atg 96
 Asn Gly Val Asp Ile Ala Tyr Ile Lys Ile Pro Asn Ala Gly Gln Met
 20 25 30

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cag ccg gta aag gca ttc aaa atc cac aac aaa atc tgg gtt atc ccg Gln Pro Val Lys Ala Phe Lys Ile His Asn Lys Ile Trp Val Ile Pro 35 40 45	144
gaa cgt gat acc ttt act aac ccg gaa gaa ggt gac ctg aac ccg cca Glu Arg Asp Thr Phe Thr Asn Pro Glu Glu Gly Asp Leu Asn Pro Pro 50 55 60	192
ccg gaa gcg aaa cag gtg ccg gta tct tac tat gac tcc acc tac ctg Pro Glu Ala Lys Gln Val Pro Val Ser Tyr Tyr Asp Ser Thr Tyr Leu 65 70 75 80	240
tct acc gat aac gaa aag gac aac tac ctg aaa ggt gtt act aaa ctg Ser Thr Asp Asn Glu Lys Asp Asn Tyr Leu Lys Gly Val Thr Lys Leu 85 90 95	288
ttc gag cgt att tac tcc acc gac ctg ggc cgt atg ctg ctg act agc Phe Glu Arg Ile Tyr Ser Thr Asp Leu Gly Arg Met Leu Leu Thr Ser 100 105 110	336
atc gtt cgc ggt atc ccg ttc tgg ggc ggt tct acc atc gat acc gaa Ile Val Arg Gly Ile Pro Phe Trp Gly Gly Ser Thr Ile Asp Thr Glu 115 120 125	384
ctg aaa gta atc gac act aac tgc atc aac gtt att cag ccg gac ggt Leu Lys Val Ile Asp Thr Asn Cys Ile Asn Val Ile Gln Pro Asp Gly 130 135 140	432
tcc tat cgt tcc gaa gaa ctg aac ctg gtg atc atc ggc ccg tct gct Ser Tyr Arg Ser Glu Glu Leu Asn Leu Val Ile Ile Gly Pro Ser Ala 145 150 155 160	480
gat atc atc cag ttc gag tgt aag agc ttt ggt cac gaa gtt ctg aac Asp Ile Ile Gln Phe Glu Cys Lys Ser Phe Gly His Glu Val Leu Asn 165 170 175	528
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cac cag ctg att tat gca ggc cac cgc ctg tac ggt atc gcc atc aat His Gln Leu Ile Tyr Ala Gly His Arg Leu Tyr Gly Ile Ala Ile Asn 225 230 235 240	720
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ggt ctg gaa gta agc ttc gaa gaa ctg cgt act ttt ggc ggt cac gac Gly Leu Glu Val Ser Phe Glu Glu Leu Arg Thr Phe Gly Gly His Asp 260 265 270	816
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290	295	300	
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gag ccg gaa aac att tct atc gaa aac ctg agc tct gat atc atc ggc Glu Pro Glu Asn Ile Ser Ile Glu Asn Leu Ser Ser Asp Ile Ile Gly 515 520 525			1584
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tac gag ctg gac aaa tat acc atg ttc cac tac ctg cgc gcg cag gaa Tyr Glu Leu Asp Lys Tyr Thr Met Phe His Tyr Leu Arg Ala Gln Glu 545 550 555 560			1680

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 Val Glu Gln Leu Val Tyr Asp Phe Thr Asp Glu Thr Ser Glu Val Ser
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 Tyr Asn Gln Tyr Thr Glu Glu Glu Lys Asn Asn Ile Asn Phe Asn Ile
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 Thr Asp Ile Pro Phe Gln Leu Ser Lys Tyr Val Asp Asn Gln Arg Leu
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Glu Arg Asp Thr Phe Thr Asn Pro Glu Glu Gly Asp Leu Asn Pro Pro
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Ser Thr Asp Asn Glu Lys Asp Asn Tyr Leu Lys Gly Val Thr Lys Leu
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Phe Glu Arg Ile Tyr Ser Thr Asp Leu Gly Arg Met Leu Leu Thr Ser
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Ile Val Arg Gly Ile Pro Phe Trp Gly Gly Ser Thr Ile Asp Thr Glu
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Leu Lys Val Ile Asp Thr Asn Cys Ile Asn Val Ile Gln Pro Asp Gly
 130 135 140

Ser Tyr Arg Ser Glu Glu Leu Asn Leu Val Ile Ile Gly Pro Ser Ala
 145 150 155 160

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

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 Asp Phe Thr Phe Gly Phe Glu Glu Ser Leu Glu Val Asp Thr Asn Pro
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 Leu Leu Gly Ala Gly Lys Phe Ala Thr Asp Pro Ala Val Thr Leu Ala
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 His Gln Leu Ile Tyr Ala Gly His Arg Leu Tyr Gly Ile Ala Ile Asn
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 Pro Asn Arg Val Phe Lys Val Asn Thr Asn Ala Tyr Tyr Glu Met Ser
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 Gly Leu Glu Val Ser Phe Glu Glu Leu Arg Thr Phe Gly Gly His Asp
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 Ile Val Gly Thr Thr Ala Ser Leu Gln Tyr Met Lys Asn Val Phe Lys
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 Glu Lys Tyr Leu Leu Ser Glu Asp Thr Ser Gly Lys Phe Ser Val Asp
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 Glu Asp Asn Phe Val Lys Phe Phe Lys Val Leu Asn Arg Lys Thr Tyr
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 Leu Asn Phe Asp Lys Ala Val Phe Lys Ile Asn Ile Val Pro Lys Val
 370 375 380
 Asn Tyr Thr Ile Tyr Asp Gly Phe Asn Leu Arg Asn Thr Asn Leu Ala
 385 390 395 400
 Ala Asn Phe Asn Gly Gln Asn Thr Glu Ile Asn Asn Met Asn Phe Thr
 405 410 415
 Lys Leu Lys Asn Phe Thr Gly Leu Phe Glu Phe Tyr Lys Leu Leu Cys
 420 425 430
 Val Arg Gly Ile Ile Thr Ser Lys Thr Lys Ser Leu Asp Lys Gly Tyr
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 Glu Glu Ile Thr Ser Asp Thr Asn Ile Glu Ala Ala Glu Glu Asn Ile
 485 490 495
 Ser Leu Asp Leu Ile Gln Gln Tyr Tyr Leu Thr Phe Asn Phe Asp Asn
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 Glu Pro Glu Asn Ile Ser Ile Glu Asn Leu Ser Ser Asp Ile Ile Gly
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 Gln Leu Glu Leu Met Pro Asn Ile Glu Arg Phe Pro Asn Gly Lys Lys
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 Tyr Glu Leu Asp Lys Tyr Thr Met Phe His Tyr Leu Arg Ala Gln Glu
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 Phe Glu His Gly Lys Ser Arg Ile Ala Leu Thr Asn Ser Val Asn Glu
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 Ala Leu Leu Asn Pro Ser Arg Val Tyr Thr Phe Phe Ser Ser Asp Tyr
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 Val Lys Lys Val Asn Lys Ala Thr Glu Ala Ala Met Phe Leu Gly Trp
 595 600 605
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 Thr Thr Asp Lys Ile Ala Asp Ile Thr Ile Ile Ile Pro Tyr Ile Gly
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 Pro Ala Leu Asn Ile Gly Asn Met Leu Tyr Lys Asp Asp Phe Val Gly
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 Ala Leu Ile Phe Ser Gly Ala Val Ile Leu Leu Glu Phe Ile Pro Glu
 660 665 670
 Ile Ala Ile Pro Val Leu Gly Thr Phe Ala Leu Val Ser Tyr Ile Ala
 675 680 685
 Asn Lys Val Leu Thr Val Gln Thr Ile Asp Asn Ala Leu Ser Lys Arg
 690 695 700
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Tyr Asn Gln Tyr Thr Glu Glu Glu Lys Asn Asn Ile Asn Phe Asn Ile
755 760 765

Asp Asp Leu Ser Ser Lys Leu Asn Glu Ser Ile Asn Lys Ala Met Ile
770 775 780

Asn Ile Asn Lys Phe Leu Asn Gln Cys Ser Val Ser Tyr Leu Met Asn
785 790 795 800

Ser Met Ile Pro Tyr Gly Val Lys Arg Leu Glu Asp Phe Asp Ala Ser
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Leu Lys Asp Ala Leu Leu Lys Tyr Ile Tyr Asp Asn Arg Gly Thr Leu
820 825 830

Ile Gly Gln Val Asp Arg Leu Lys Asp Lys Val Asn Asn Thr Leu Ser
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Asn Asn Ile Ile Met Met Glu Pro Pro Phe Ala Arg Gly Thr Gly Arg
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Tyr Tyr Lys Ala Phe Lys Ile Thr Asp Arg Ile Trp Ile Ile Pro Glu
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 Ile Phe Asn Arg Asp Val Cys Glu Tyr Tyr Asp Pro Asp Tyr Leu Asn
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 Thr Asn Asp Lys Lys Asn Ile Phe Leu Gln Thr Met Ile Lys Leu Phe
 85 90 95
 aac cgt atc aaa agc aaa ccg ctc ggt gaa aaa ctc ctc gaa atg att 336
 Asn Arg Ile Lys Ser Lys Pro Leu Gly Glu Lys Leu Leu Glu Met Ile
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 atc aac ggt atc ccg tac ctc ggt gac cgt cgt gtc ccg ctc gaa gag 384
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 Phe Gly Pro Gly Pro Val Leu Asn Glu Asn Glu Thr Ile Asp Ile Gly
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 Ile Gln Asn His Phe Ala Ser Arg Glu Gly Phe Gly Gly Ile Met Gln
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Glu Ser Leu Thr	Asp Phe Asn Val	Asp Val Pro Val	Tyr Glu Lys Gln	
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agc tac ctg atg aag aag atg atc ccg ctg gct gtt gaa aaa ctg ctg Ser Tyr Leu Met Lys Lys Met Ile Pro Leu Ala Val Glu Lys Leu Leu 785 790 795 800	2400
gac ttc gac aac acc ctg aaa aag aac ctg ctg aac tac atc gac gaa Asp Phe Asp Asn Thr Leu Lys Lys Asn Leu Leu Asn Tyr Ile Asp Glu 805 810 815	2448
aac aag ctg tac ctg atc ggt agt gct gaa tac gaa aaa agt aaa gtg Asn Lys Leu Tyr Leu Ile Gly Ser Ala Glu Tyr Glu Lys Ser Lys Val 820 825 830	2496
aac aaa tac ctg aag acc atc atg ccg ttc gac ctg agt atc tac acc Asn Lys Tyr Leu Lys Thr Ile Met Pro Phe Asp Leu Ser Ile Tyr Thr	2544

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835 840 845
 aac gac acc atc ctg atc gaa atg ttc aac aaa tac aac agc taa tag 2592
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 850 855 860

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 <212> PRT
 <213> Clostridium botulinum

<400> 171

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Tyr Tyr Lys Ala Phe Lys Ile Thr Asp Arg Ile Trp Ile Ile Pro Glu
 35 40 45

Arg Tyr Thr Phe Gly Tyr Lys Pro Glu Asp Phe Asn Lys Ser Ser Gly
 50 55 60

Ile Phe Asn Arg Asp Val Cys Glu Tyr Tyr Asp Pro Asp Tyr Leu Asn
 65 70 75 80

Thr Asn Asp Lys Lys Asn Ile Phe Leu Gln Thr Met Ile Lys Leu Phe
 85 90 95

Asn Arg Ile Lys Ser Lys Pro Leu Gly Glu Lys Leu Leu Glu Met Ile
 100 105 110

Ile Asn Gly Ile Pro Tyr Leu Gly Asp Arg Arg Val Pro Leu Glu Glu
 115 120 125

Phe Asn Thr Asn Ile Ala Ser Val Thr Val Asn Lys Leu Ile Ser Asn
 130 135 140

Pro Gly Glu Val Glu Arg Lys Lys Gly Ile Phe Ala Asn Leu Ile Ile
 145 150 155 160

Phe Gly Pro Gly Pro Val Leu Asn Glu Asn Glu Thr Ile Asp Ile Gly
 165 170 175

Ile Gln Asn His Phe Ala Ser Arg Glu Gly Phe Gly Gly Ile Met Gln
 180 185 190

Met Lys Phe Cys Pro Glu Tyr Val Ser Val Phe Asn Asn Val Gln Glu
 195 200 205

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Asn Lys Gly Ala Ser Ile Phe Asn Arg Arg Gly Tyr Phe Ser Asp Pro
 210 215 220
 Ala Leu Ile Leu Met His Glu Leu Ile His Val Leu His Gly Leu Tyr
 225 230 235 240
 Gly Ile Lys Val Asp Asp Leu Pro Ile Val Pro Asn Glu Lys Lys Phe
 245 250 255
 Phe Met Gln Ser Thr Asp Ala Ile Gln Ala Glu Glu Leu Tyr Thr Phe
 260 265 270
 Gly Gly Gln Asp Pro Ser Ile Ile Thr Pro Ser Thr Asp Lys Ser Ile
 275 280 285
 Tyr Asp Lys Val Leu Gln Asn Phe Arg Gly Ile Val Asp Arg Leu Asn
 290 295 300
 Lys Val Leu Val Cys Ile Ser Asp Pro Asn Ile Asn Ile Asn Ile Tyr
 305 310 315 320
 Lys Asn Lys Phe Lys Asp Lys Tyr Lys Phe Val Glu Asp Ser Glu Gly
 325 330 335
 Lys Tyr Ser Ile Asp Val Glu Ser Phe Asp Lys Leu Tyr Lys Ser Leu
 340 345 350
 Met Phe Gly Phe Thr Glu Thr Asn Ile Ala Glu Asn Tyr Lys Ile Lys
 355 360 365
 Thr Arg Ala Ser Tyr Phe Ser Asp Ser Leu Pro Pro Val Lys Ile Lys
 370 375 380
 Asn Leu Leu Asp Asn Glu Ile Tyr Thr Ile Glu Glu Gly Phe Asn Ile
 385 390 395 400
 Ser Asp Lys Asp Met Glu Lys Glu Tyr Arg Gly Gln Asn Lys Ala Ile
 405 410 415
 Asn Lys Gln Ala Tyr Glu Glu Ile Ser Lys Glu His Leu Ala Val Tyr
 420 425 430
 Lys Ile Gln Met Cys Ser Ala Ile Glu Gly Arg Cys Ser Ala Pro Gly
 435 440 445
 Ile Cys Ile Asp Val Asp Asn Glu Asp Leu Phe Phe Ile Ala Asp Lys
 450 455 460
 Asn Ser Phe Ser Asp Asp Leu Ser Lys Asn Glu Arg Ile Glu Tyr Asn
 465 470 475 480

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Thr Gln Ser Asn Tyr Ile Glu Asn Asp Phe Pro Ile Asn Glu Leu Ile
485 490 495

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

Glu Ser Leu Thr Asp Phe Asn Val Asp Val Pro Val Tyr Glu Lys Gln
515 520 525

Pro Ala Ile Lys Lys Ile Phe Thr Asp Glu Asn Thr Ile Phe Gln Tyr
530 535 540

Leu Tyr Ser Gln Thr Phe Pro Leu Asp Ile Arg Asp Ile Ser Leu Thr
545 550 555 560

Ser Ser Phe Asp Asp Ala Leu Leu Phe Ser Asn Lys Val Tyr Ser Phe
565 570 575

Phe Ser Met Asp Tyr Ile Lys Thr Ala Asn Lys Val Val Glu Ala Gly
580 585 590

Leu Phe Ala Gly Trp Val Lys Gln Ile Val Asn Asp Phe Val Ile Glu
595 600 605

Ala Asn Lys Ser Asn Thr Met Asp Lys Ile Ala Asp Ile Ser Leu Ile
610 615 620

Val Pro Tyr Ile Gly Leu Ala Leu Asn Val Gly Asn Glu Thr Ala Lys
625 630 635 640

Gly Asn Phe Glu Asn Ala Phe Glu Ile Ala Gly Ala Ser Ile Leu Leu
645 650 655

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

Glu Ser Tyr Ile Asp Asn Lys Asn Lys Ile Ile Lys Thr Ile Asp Asn
675 680 685

Ala Leu Thr Lys Arg Asn Glu Lys Trp Ser Asp Met Tyr Gly Leu Ile
690 695 700

Val Ala Gln Trp Leu Ser Thr Val Asn Thr Gln Phe Tyr Thr Ile Lys
705 710 715 720

Glu Gly Met Tyr Lys Ala Leu Asn Tyr Gln Ala Gln Ala Leu Glu Glu
725 730 735

Ile Ile Lys Tyr Arg Tyr Asn Ile Tyr Ser Glu Lys Glu Lys Ser Asn

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740 745 750

Ile Asn Ile Asp Phe Asn Asp Ile Asn Ser Lys Leu Asn Glu Gly Ile
755 760 765

Asn Gln Ala Ile Asp Asn Ile Asn Asn Phe Ile Asn Gly Cys Ser Val
770 775 780

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

Asp Phe Asp Asn Thr Leu Lys Lys Asn Leu Leu Asn Tyr Ile Asp Glu
805 810 815

Asn Lys Leu Tyr Leu Ile Gly Ser Ala Glu Tyr Glu Lys Ser Lys Val
820 825 830

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

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

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<400> 172

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1 5 10 15	
aac aac atc att atg atg gaa ccg ccg ttc gca cgt ggt acc ggt cgt	96
Asn Asn Ile Ile Met Met Glu Pro Pro Phe Ala Arg Gly Thr Gly Arg	
20 25 30	
tac tgc aag gct ttc aag atc acc gac cgt atc tgg atc atc ccg gaa	144
Tyr Cys Lys Ala Phe Lys Ile Thr Asp Arg Ile Trp Ile Ile Pro Glu	
35 40 45	
cgt tac acc ttc ggt tac aaa cct gag gac ttc aac aag agt agc ggg	192
Arg Tyr Thr Phe Gly Tyr Lys Pro Glu Asp Phe Asn Lys Ser Ser Gly	
50 55 60	
att ttc aat cgt gac gtc tgc gag tac tat gat cca gat tat ctg aat	240
Ile Phe Asn Arg Asp Val Cys Glu Tyr Tyr Asp Pro Asp Tyr Leu Asn	
65 70 75 80	
acc aac gat aag aag aac ata ttc ttt cag act atg atc aaa ctc ttc	288
Thr Asn Asp Lys Lys Asn Ile Phe Phe Gln Thr Met Ile Lys Leu Phe	
85 90 95	

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aac cgt atc aaa agc aaa ccg ctc ggt gaa aaa ctc ctc gaa atg att 336
 Asn Arg Ile Lys Ser Lys Pro Leu Gly Glu Lys Leu Leu Glu Met Ile
 100 105 110

atc aac ggt atc ccg tac ctc ggt gac cgt cgt gtc ccg ctt gaa gag 384
 Ile Asn Gly Ile Pro Tyr Leu Gly Asp Arg Arg Val Pro Leu Glu Glu
 115 120 125

ttc aac acc aac atc gca agc gtc acc gtc aac aaa ctc atc agc aac 432
 Phe Asn Thr Asn Ile Ala Ser Val Thr Val Asn Lys Leu Ile Ser Asn
 130 135 140

cca ggt gaa gtc gaa cgt aaa aaa ggt atc ttc gca aac ctc atc atc 480
 Pro Gly Glu Val Glu Arg Lys Lys Gly Ile Phe Ala Asn Leu Ile Ile
 145 150 155 160

ttc ggt ccg ggt ccg gtc ctc aac gaa aac gaa acc atc gac atc ggt 528
 Phe Gly Pro Gly Pro Val Leu Asn Glu Asn Glu Thr Ile Asp Ile Gly
 165 170 175

atc cag aac cac ttc gca agc cgt gaa ggt ttc ggt ggt atc atg cag 576
 Ile Gln Asn His Phe Ala Ser Arg Glu Gly Phe Gly Gly Ile Met Gln
 180 185 190

atg aaa ttc tgc ccg gaa tac gtc agt gtc ttc aac aac gtc cag gaa 624
 Met Lys Phe Cys Pro Glu Tyr Val Ser Val Phe Asn Asn Val Gln Glu
 195 200 205

aac aaa ggt gca agc atc ttc aac cgt cgt ggt tac ttc agc gac ccg 672
 Asn Lys Gly Ala Ser Ile Phe Asn Arg Arg Gly Tyr Phe Ser Asp Pro
 210 215 220

gca ctc atc ctc atg cat gaa ctc atc cac gtc ctc cac ggt ctc tac 720
 Ala Leu Ile Leu Met His Glu Leu Ile His Val Leu His Gly Leu Tyr
 225 230 235 240

ggt atc aaa gtt gac gac ctc ccg atc gtc ccg aac gag aag aaa ttc 768
 Gly Ile Lys Val Asp Asp Leu Pro Ile Val Pro Asn Glu Lys Lys Phe
 245 250 255

ttc atg cag agc acc gac gca atc cag gct gag gaa ctc tac acc ttc 816
 Phe Met Gln Ser Thr Asp Ala Ile Gln Ala Glu Glu Leu Tyr Thr Phe
 260 265 270

ggt ggc caa gac cca agt atc ata acc ccg tcc acc gac aaa agc atc 864
 Gly Gly Gln Asp Pro Ser Ile Ile Thr Pro Ser Thr Asp Lys Ser Ile
 275 280 285

tac gac aaa gtc ctc cag aac ttc agg ggt atc gtg gac aga ctc aac 912
 Tyr Asp Lys Val Leu Gln Asn Phe Arg Gly Ile Val Asp Arg Leu Asn
 290 295 300

aaa gtc ctc gtc tgc atc agc gac ccg aac atc aat atc aac ata tac 960
 Lys Val Leu Val Cys Ile Ser Asp Pro Asn Ile Asn Ile Asn Ile Tyr
 305 310 315 320

aag aac aag ttc aaa gac aag tac aaa ttc gtc gag gac agc gaa ggc 1008
 Lys Asn Lys Phe Lys Asp Lys Tyr Lys Phe Val Glu Asp Ser Glu Gly
 325 330 335

aaa tac agc atc gac gta gaa agt ttc gac aag ctc tac aaa agc ctc 1056
 Lys Tyr Ser Ile Asp Val Glu Ser Phe Asp Lys Leu Tyr Lys Ser Leu
 340 345 350

atg ttc ggt ttc acc gaa acc aac atc gcc gag aac tac aag atc aag 1104
 Met Phe Gly Phe Thr Glu Thr Asn Ile Ala Glu Asn Tyr Lys Ile Lys

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355	360	365	
aca agg gca agt tac ttc agc gac agc ctc ccg cct gtc aaa atc aag Thr Arg Ala Ser Tyr Phe Ser Asp Ser Leu Pro Pro Val Lys Ile Lys 370 375 380			1152
aac ctc tta gac aac gag att tac act ata gaa gag ggc ttc aac atc Asn Leu Leu Asp Asn Glu Ile Tyr Thr Ile Glu Gly Phe Asn Ile 385 390 395 400			1200
agt gac aaa gac atg gag aag gaa tac aga ggt cag aac aag gct atc Ser Asp Lys Asp Met Glu Lys Glu Tyr Arg Gly Gln Asn Lys Ala Ile 405 410 415			1248
aac aaa cag gca tac gag gag atc agc aaa gaa cac ctc gca gtc tac Asn Lys Gln Ala Tyr Glu Glu Ile Ser Lys Glu His Leu Ala Val Tyr 420 425 430			1296
aag atc cag atg tgt agc gct atc gaa ggc cga tgc agc gct ccg ggt Lys Ile Gln Met Cys Ser Ala Ile Glu Gly Arg Cys Ser Ala Pro Gly 435 440 445			1344
atc tgc atc gac gtt gac aac gaa gac ctg ttc ttc atc gct gac aaa Ile Cys Ile Asp Val Asp Asn Glu Asp Leu Phe Phe Ile Ala Asp Lys 450 455 460			1392
aac agc ttc agt gac gac ctg agc aaa aac gaa cgt atc gaa tac aac Asn Ser Phe Ser Asp Asp Leu Ser Lys Asn Glu Arg Ile Glu Tyr Asn 465 470 475 480			1440
acc cag agc aac tac atc gaa aac gac ttc ccg atc aac gaa ctg atc Thr Gln Ser Asn Tyr Ile Glu Asn Asp Phe Pro Ile Asn Glu Leu Ile 485 490 495			1488
ctg gac acc gac ctg gaa agt aaa atc gaa ctg ccg agc gaa aac acc Leu Asp Thr Asp Leu Ile Ser Lys Ile Glu Leu Pro Ser Glu Asn Thr 500 505 510			1536
gaa agt ctg acc gac ttc aac gtt gac gtt ccg gtt tac gaa aaa cag Glu Ser Leu Thr Asp Phe Asn Val Asp Val Pro Val Tyr Glu Lys Gln 515 520 525			1584
ccg gct atc aag aaa atc ttc acc gac gaa aac acc atc ttc cag tac Pro Ala Ile Lys Lys Ile Phe Thr Asp Glu Asn Thr Ile Phe Gln Tyr 530 535 540			1632
ctg tac agc cag acc ttc ccg ctg gac atc cgt gac atc agt ctg acc Leu Tyr Ser Gln Thr Phe Pro Leu Asp Ile Arg Asp Ile Ser Leu Thr 545 550 555 560			1680
agc agt ttc gac gac gct ctg ctg ttc agc aac aaa gtt tac agt ttc Ser Ser Phe Asp Asp Ala Leu Leu Phe Ser Asn Lys Val Tyr Ser Phe 565 570 575			1728
ttc agc atg gac tac atc aaa acc gct aac aaa gtt gtt gaa gca ggg Phe Ser Met Asp Tyr Ile Lys Thr Ala Asn Lys Val Val Glu Ala Gly 580 585 590			1776
ctg ttc gct ggt tgg gtt aaa cag atc gtt aac gac ttc gtt atc gaa Leu Phe Ala Gly Trp Val Lys Gln Ile Val Asn Asp Phe Val Ile Glu 595 600 605			1824
gct aac aaa agc aac act atg gac aaa atc gct gac atc agt ctg atc Ala Asn Lys Ser Asn Thr Met Asp Lys Ile Ala Asp Ile Ser Leu Ile 610 615 620			1872

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gtt ccg tac atc ggt ctg gct ctg aac gtt ggt aac gaa acc gct aaa 1920
 Val Pro Tyr Ile Gly Leu Ala Leu Asn Val Gly Asn Glu Thr Ala Lys
 625 630 635 640
 ggt aac ttt gaa aac gct ttc gag atc gct ggt gca agc atc ctg ctg 1968
 Gly Asn Phe Glu Asn Ala Phe Glu Ile Ala Gly Ala Ser Ile Leu Leu
 645 650 655
 gag ttc atc ccg gaa ctg ctg atc ccg gtt gtt ggt gct ttc ctg ctg 2016
 Glu Phe Ile Pro Glu Leu Leu Ile Pro Val Val Gly Ala Phe Leu Leu
 660 665 670
 gaa agt tac atc gac aac aaa aac aag atc atc aaa acc atc gac aac 2064
 Glu Ser Tyr Ile Asp Asn Lys Asn Lys Ile Ile Lys Thr Ile Asp Asn
 675 680 685
 gct ctg acc aaa cgt aac gaa aaa tgg agt gat atg tac ggt ctg atc 2112
 Ala Leu Thr Lys Arg Asn Glu Lys Trp Ser Asp Met Tyr Gly Leu Ile
 690 695 700
 gtt gct cag tgg ctg agc acc gtc aac acc cag ttc tac acc atc aaa 2160
 Val Ala Gln Trp Leu Ser Thr Val Asn Thr Gln Phe Tyr Thr Ile Lys
 705 710 715 720
 gaa ggt atg tac aaa gct ctg aac tac cag gct cag gct ctg gaa gag 2208
 Glu Gly Met Tyr Lys Ala Leu Asn Tyr Gln Ala Gln Ala Leu Glu Glu
 725 730 735
 atc atc aaa tac cgt tac aac atc tac agt gag aag gaa aag agt aac 2256
 Ile Ile Lys Tyr Arg Tyr Asn Ile Tyr Ser Glu Lys Glu Lys Ser Asn
 740 745 750
 atc aac atc gac ttc aac gac atc aac agc aaa ctg aac gaa ggt atc 2304
 Ile Asn Ile Asp Phe Asn Asp Ile Asn Ser Lys Leu Asn Glu Gly Ile
 755 760 765
 aac cag gct atc gac aac atc aac aac ttc atc aac ggt tgc agt gtt 2352
 Asn Gln Ala Ile Asp Asn Ile Asn Asn Phe Ile Asn Gly Cys Ser Val
 770 775 780
 agc tac ctg atg aag aag atg atc ccg ctg gct gtt gaa aaa ctg ctg 2400
 Ser Tyr Leu Met Lys Lys Met Ile Pro Leu Ala Val Glu Lys Leu Leu
 785 790 795 800
 gac ttc gac aac acc ctg aaa aag aac ctg ctg aac tac atc gac gaa 2448
 Asp Phe Asp Asn Thr Leu Lys Lys Asn Leu Leu Asn Tyr Ile Asp Glu
 805 810 815
 aac aag ctg tac ctg atc ggt agt gct gaa tac gaa aaa agt aaa gtg 2496
 Asn Lys Leu Tyr Leu Ile Gly Ser Ala Glu Tyr Glu Lys Ser Lys Val
 820 825 830
 aac aaa tac ctg aag acc atc atg ccg ttc gac ctg agt atc tac acc 2544
 Asn Lys Tyr Leu Lys Thr Ile Met Pro Phe Asp Leu Ser Ile Tyr Thr
 835 840 845
 aac gac acc atc ctg atc gaa atg ttc aac aaa tac aac agc taa tag 2592
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Tyr Cys Lys Ala Phe Lys Ile Thr Asp Arg Ile Trp Ile Ile Pro Glu
35 40 45

Arg Tyr Thr Phe Gly Tyr Lys Pro Glu Asp Phe Asn Lys Ser Ser Gly
50 55 60

Ile Phe Asn Arg Asp Val Cys Glu Tyr Tyr Asp Pro Asp Tyr Leu Asn
65 70 75 80

Thr Asn Asp Lys Lys Asn Ile Phe Phe Gln Thr Met Ile Lys Leu Phe
85 90 95

Asn Arg Ile Lys Ser Lys Pro Leu Gly Glu Lys Leu Leu Glu Met Ile
100 105 110

Ile Asn Gly Ile Pro Tyr Leu Gly Asp Arg Arg Val Pro Leu Glu Glu
115 120 125

Phe Asn Thr Asn Ile Ala Ser Val Thr Val Asn Lys Leu Ile Ser Asn
130 135 140

Pro Gly Glu Val Glu Arg Lys Lys Gly Ile Phe Ala Asn Leu Ile Ile
145 150 155 160

Phe Gly Pro Gly Pro Val Leu Asn Glu Asn Glu Thr Ile Asp Ile Gly
165 170 175

Ile Gln Asn His Phe Ala Ser Arg Glu Gly Phe Gly Gly Ile Met Gln
180 185 190

Met Lys Phe Cys Pro Glu Tyr Val Ser Val Phe Asn Asn Val Gln Glu
195 200 205

Asn Lys Gly Ala Ser Ile Phe Asn Arg Arg Gly Tyr Phe Ser Asp Pro
210 215 220

Ala Leu Ile Leu Met His Glu Leu Ile His Val Leu His Gly Leu Tyr
225 230 235 240

Gly Ile Lys Val Asp Asp Leu Pro Ile Val Pro Asn Glu Lys Lys Phe
245 250 255

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Phe Met Gln Ser Thr Asp Ala Ile Gln Ala Glu Glu Leu Tyr Thr Phe
 260 265 270
 Gly Gly Gln Asp Pro Ser Ile Ile Thr Pro Ser Thr Asp Lys Ser Ile
 275 280 285
 Tyr Asp Lys Val Leu Gln Asn Phe Arg Gly Ile Val Asp Arg Leu Asn
 290 295 300
 Lys Val Leu Val Cys Ile Ser Asp Pro Asn Ile Asn Ile Asn Ile Tyr
 305 310 315 320
 Lys Asn Lys Phe Lys Asp Lys Tyr Lys Phe Val Glu Asp Ser Glu Gly
 325 330 335
 Lys Tyr Ser Ile Asp Val Glu Ser Phe Asp Lys Leu Tyr Lys Ser Leu
 340 345 350
 Met Phe Gly Phe Thr Glu Thr Asn Ile Ala Glu Asn Tyr Lys Ile Lys
 355 360 365
 Thr Arg Ala Ser Tyr Phe Ser Asp Ser Leu Pro Pro Val Lys Ile Lys
 370 375 380
 Asn Leu Leu Asp Asn Glu Ile Tyr Thr Ile Glu Glu Gly Phe Asn Ile
 385 390 395 400
 Ser Asp Lys Asp Met Glu Lys Glu Tyr Arg Gly Gln Asn Lys Ala Ile
 405 410 415
 Asn Lys Gln Ala Tyr Glu Glu Ile Ser Lys Glu His Leu Ala Val Tyr
 420 425 430
 Lys Ile Gln Met Cys Ser Ala Ile Glu Gly Arg Cys Ser Ala Pro Gly
 435 440 445
 Ile Cys Ile Asp Val Asp Asn Glu Asp Leu Phe Phe Ile Ala Asp Lys
 450 455 460
 Asn Ser Phe Ser Asp Asp Leu Ser Lys Asn Glu Arg Ile Glu Tyr Asn
 465 470 475 480
 Thr Gln Ser Asn Tyr Ile Glu Asn Asp Phe Pro Ile Asn Glu Leu Ile
 485 490 495
 Leu Asp Thr Asp Leu Ile Ser Lys Ile Glu Leu Pro Ser Glu Asn Thr
 500 505 510
 Glu Ser Leu Thr Asp Phe Asn Val Asp Val Pro Val Tyr Glu Lys Gln
 515 520 525

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Pro Ala Ile Lys Lys Ile Phe Thr Asp Glu Asn Thr Ile Phe Gln Tyr
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 Leu Tyr Ser Gln Thr Phe Pro Leu Asp Ile Arg Asp Ile Ser Leu Thr
 545 550 555 560
 Ser Ser Phe Asp Asp Ala Leu Leu Phe Ser Asn Lys Val Tyr Ser Phe
 565 570 575
 Phe Ser Met Asp Tyr Ile Lys Thr Ala Asn Lys Val Val Glu Ala Gly
 580 585 590
 Leu Phe Ala Gly Trp Val Lys Gln Ile Val Asn Asp Phe Val Ile Glu
 595 600 605
 Ala Asn Lys Ser Asn Thr Met Asp Lys Ile Ala Asp Ile Ser Leu Ile
 610 615 620
 Val Pro Tyr Ile Gly Leu Ala Leu Asn Val Gly Asn Glu Thr Ala Lys
 625 630 635 640
 Gly Asn Phe Glu Asn Ala Phe Glu Ile Ala Gly Ala Ser Ile Leu Leu
 645 650 655
 Glu Phe Ile Pro Glu Leu Leu Ile Pro Val Val Gly Ala Phe Leu Leu
 660 665 670
 Glu Ser Tyr Ile Asp-Asn Lys Asn Lys Ile Ile Lys Thr Ile Asp Asn
 675 680 685
 Ala Leu Thr Lys Arg Asn Glu Lys Trp Ser Asp Met Tyr Gly Leu Ile
 690 695 700
 Val Ala Gln Trp Leu Ser Thr Val Asn Thr Gln Phe Tyr Thr Ile Lys
 705 710 715 720
 Glu Gly Met Tyr Lys Ala Leu Asn Tyr Gln Ala Gln Ala Leu Glu Glu
 725 730 735
 Ile Ile Lys Tyr Arg Tyr Asn Ile Tyr Ser Glu Lys Glu Lys Ser Asn
 740 745 750
 Ile Asn Ile Asp Phe Asn Asp Ile Asn Ser Lys Leu Asn Glu Gly Ile
 755 760 765
 Asn Gln Ala Ile Asp Asn Ile Asn Asn Phe Ile Asn Gly Cys Ser Val
 770 775 780
 Ser Tyr Leu Met Lys Lys Met Ile Pro Leu Ala Val Glu Lys Leu Leu

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cca ggt gaa gtc gaa cgt aaa aaa ggt atc ttc gca aac ctc atc atc 480
Pro Gly Glu Val Glu Arg Lys Lys Gly Ile Phe Ala Asn Leu Ile Ile
145 150 155 160

ttc ggt ccg ggt ccg gtc ctc aac gaa aac gaa acc atc gac atc ggt 528
Phe Gly Pro Gly Pro Val Leu Asn Glu Asn Glu Thr Ile Asp Ile Gly
165 170 175

atc cag aac cac ttc gca agc cgt gaa ggt ttc ggt ggt atc atg cag 576
Ile Gln Asn His Phe Ala Ser Arg Glu Gly Phe Gly Gly Ile Met Gln
180 185 190

atg aaa ttc tgc ccg gaa tac gtc agt gtc ttc aac aac gtc cag gaa 624
Met Lys Phe Cys Pro Glu Tyr Val Ser Val Phe Asn Asn Val Gln Glu
195 200 205

aac aaa ggt gca agc atc ttc aac cgt cgt ggt tac ttc agc gac ccg 672
Asn Lys Gly Ala Ser Ile Phe Asn Arg Arg Gly Tyr Phe Ser Asp Pro
210 215 220

gca ctc atc ctc atg cat gaa ctc atc cac gtc ctc cac ggt ctc tac 720
Ala Leu Ile Leu Met His Glu Leu Ile His Val Leu His Gly Leu Tyr
225 230 235 240

ggt atc aaa gtt gac gac ctc ccg atc gtc ccg aac gag aag aaa ttc 768
Gly Ile Lys Val Asp Asp Leu Pro Ile Val Pro Asn Glu Lys Lys Phe
245 250 255

ttc atg cag agc acc gac gca atc cag gct gag gaa ctc tac acc ttc 816
Phe Met Gln Ser Thr Asp Ala Ile Gln Ala Glu Glu Leu Tyr Thr Phe
260 265 270

ggt ggc caa gac cca agt atc ata acc ccg tcc acc gac aaa agc atc 864
Gly Gly Gln Asp Pro Ser Ile Ile Thr Pro Ser Thr Asp Lys Ser Ile
275 280 285

tac gac aaa gtc ctc cag aac ttc agg ggt atc gtg gac aga ctc aac 912
Tyr Asp Lys Val Leu Gln Asn Phe Arg Gly Ile Val Asp Arg Leu Asn
290 295 300

aaa gtc ctc gtc tgc atc agc gac ccg aac atc aat atc aac ata tac 960
Lys Val Leu Val Cys Ile Ser Asp Pro Asn Ile Asn Ile Asn Ile Tyr
305 310 315 320

aag aac aag ttc aaa gac aag tac aaa ttc gtc gag gac agc gaa ggc 1008
Lys Asn Lys Phe Lys Asp Lys Tyr Lys Phe Val Glu Asp Ser Glu Gly
325 330 335

aaa tac agc atc gac gta gaa agt ttc gac aag ctc tac aaa agc ctc 1056
Lys Tyr Ser Ile Asp Val Glu Ser Phe Asp Lys Leu Tyr Lys Ser Leu
340 345 350

atg ttc ggt ttc acc gaa acc aac atc gcc gag aac tac aag atc aag 1104
Met Phe Gly Phe Thr Glu Thr Asn Ile Ala Glu Asn Tyr Lys Ile Lys
355 360 365

aca agg gca agt tac ttc agc gac agc ctc ccg cct gtc aaa atc aag 1152
Thr Arg Ala Ser Tyr Phe Ser Asp Ser Leu Pro Pro Val Lys Ile Lys
370 375 380

aac ctc tta gac aac gag att tac act ata gaa gag ggc ttc aac atc 1200
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385 390 395 400

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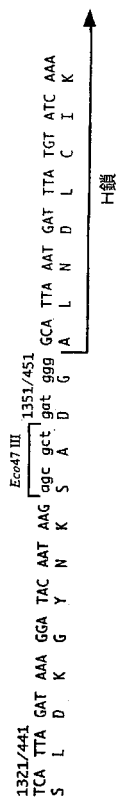
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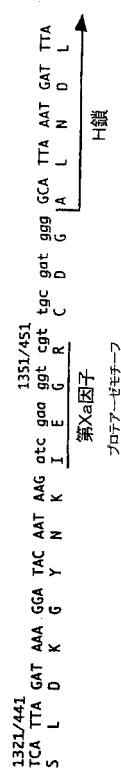
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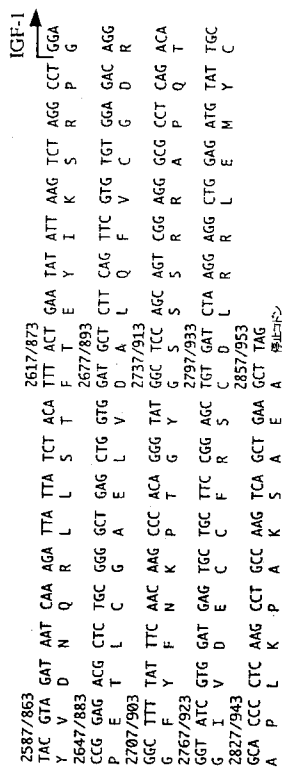
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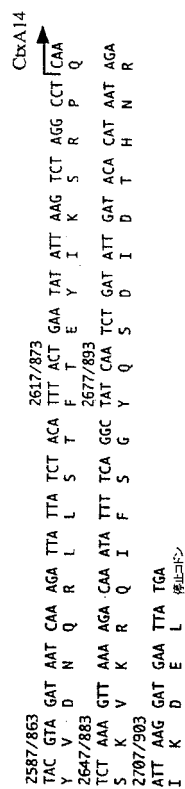
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【図 7】



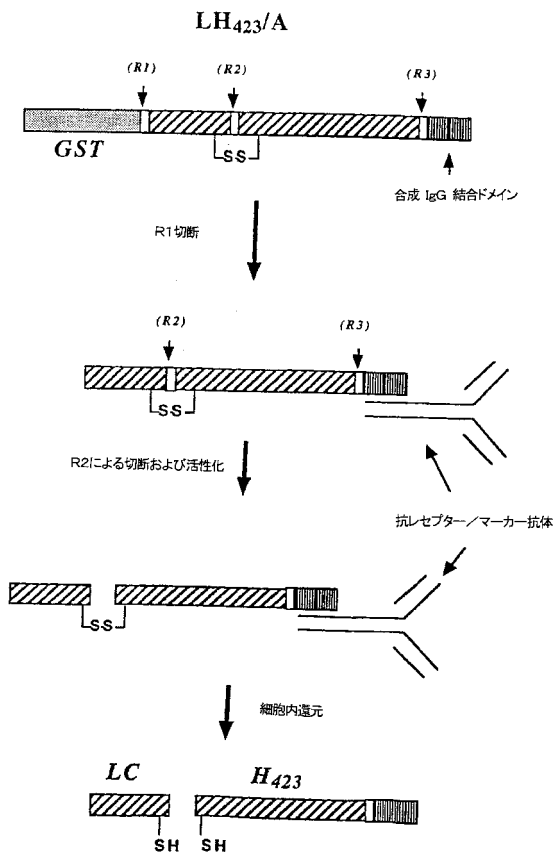
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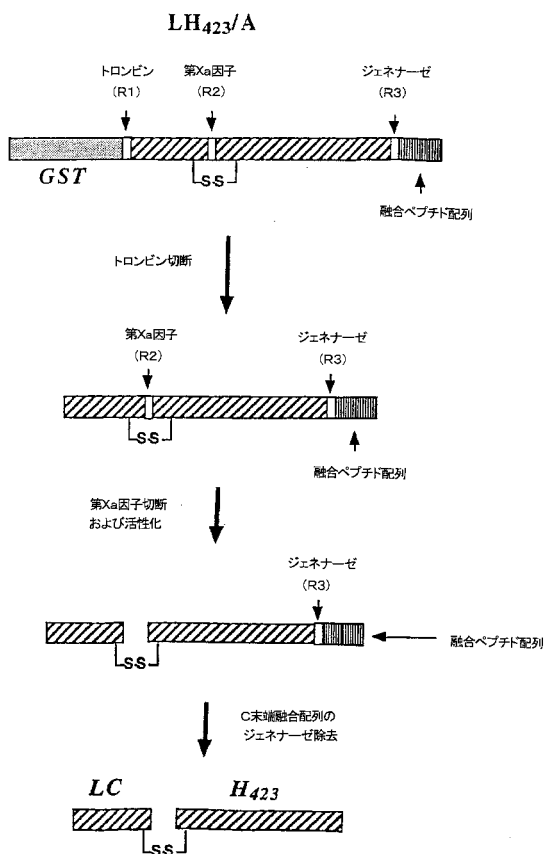
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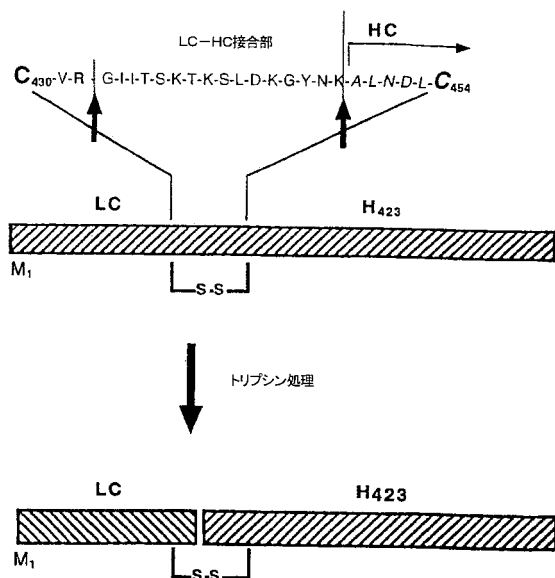
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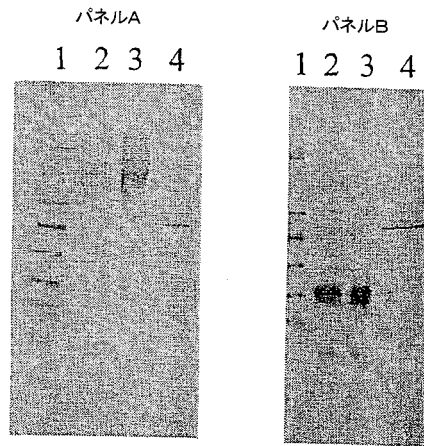
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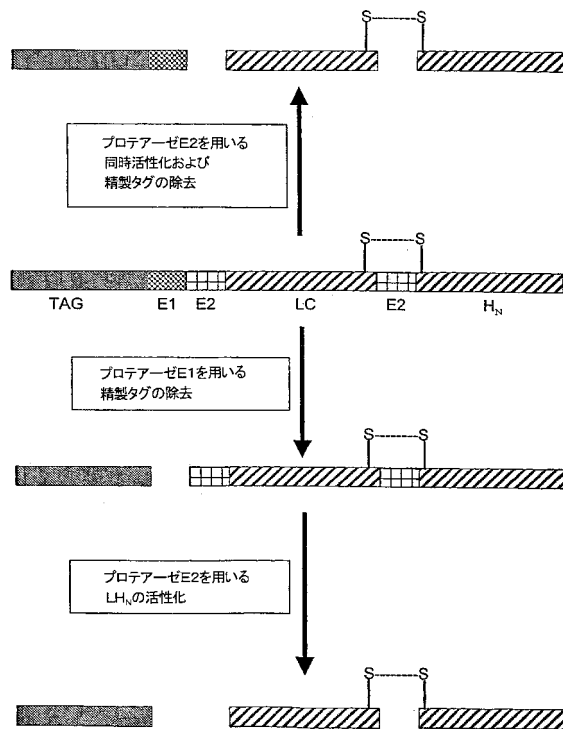
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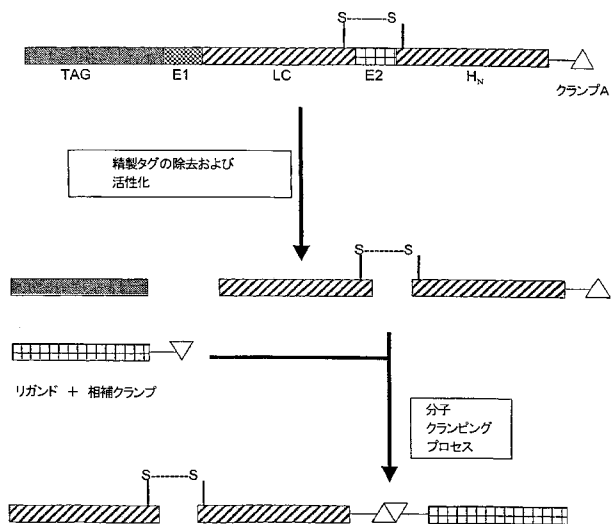
【図 13】



【図 14】



【図 15】



【国際調査報告】

INTERNATIONAL SEARCH REPORT		International Application No. PCT/GB 03/03824
A. CLASSIFICATION OF SUBJECT MATTER IPC 7 C12N9/52		
According to International Patent Classification (IPC) or to both national classification and IPC		
B. FIELDS SEARCHED Minimum documentation searched (classification system followed by classification symbols) IPC 7 C12N		
Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched		
Electronic data base consulted during the international search (name of data base and, where practical, search terms used) EPO-Internal, BIOSIS, WPI Data, PAJ, SEQUENCE SEARCH		
C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 98 07864 A (FOSTER KEITH ALAN ; MICROBIOLOGICAL RES AUTHORITY (GB); QUINN CONRA) 26 February 1998 (1998-02-26) page 3 -page 8 page 19-21; figures 10,11	1-38
Y	WO 01 14570 A (CHAN KUO CHION ; DOLLY J OLIVER (GB); LI YAN (GB); ALLERGAN SALES I) 1 March 2001 (2001-03-01) claims 1,12; figure 1	1-38
Y	WO 02 44199 A (ALLERGAN SALES INC) 6 June 2002 (2002-06-06) page 8 -page 10; tables 1,2	1-38
-/-		
☒ Further documents are listed in the continuation of box C. ☒ Patent family members are listed in annex.		
* Special categories of cited documents : "A" document defining the general state of the art which is not considered to be of particular relevance "E" earlier document but published on or after the international filing date "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "O" document referring to an oral disclosure, use, exhibition or other means "P" document published prior to the international filing date but later than the priority date claimed "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art. "Z" document member of the same patent family		
Date of the actual completion of the international search		Date of mailing of the international search report
5 April 2004		28.04.2004
Name and mailing address of the ISA European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016		Authorized officer Steffen, P

INTERNATIONAL SEARCH REPORT

Int. Application No.
PCT/GB 03/03824

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	DUGGAN MICHAEL J ET AL: "Inhibition of release of neurotransmitters from rat dorsal root ganglia by a novel conjugate of a Clostridium botulinum toxin A endopeptidase fragment and Erythrina cristagalli lectin" JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 277, no. 38, 20 September 2002 (2002-09-20), pages 34846-34852, XP002266555 ISSN: 0021-9258 Published online 08 July 2002 (2002-07-08) the whole document ---	
A	CHADDOCK JOHN A ET AL: "Expression and purification of catalytically active, non-toxic endopeptidase derivatives of Clostridium botulinum toxin type A" PROTEIN EXPRESSION AND PURIFICATION, vol. 25, no. 2, July 2002 (2002-07), pages 219-228, XP002266556 ISSN: 1046-5928 the whole document -----	

INTERNATIONAL SEARCH REPORT

national application No.
PCT/GB 03/03824

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this International application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☒ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
1-38 (all partly; SEQ ID NO's 30, 32 and 34)
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
☒ No protest accompanied the payment of additional search fees.

International Application No. PCT/ GB 03 /03824

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

Invention 1: claims 1-38 (all partly)

A single chain polypeptide comprising a first and second domain as described in the introductory part of claim 1 and wherein the single chain polypeptide comprises a sequence which is of SEQ ID NO: 30. Furthermore variants and fragments as well as further embodiments thereof and nucleic acids encoding the said polypeptide.

Inventions 2-64: claims 1-38 (all partly)

A single chain polypeptide comprising a first and second domain as described in the introductory part of claim 1 and wherein the single chain polypeptide comprises a sequence selected each respectively from the sequences SEQ ID NO's: 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 116, 118, 120, 122, 124, 126, 128, 130, 132, 139, 143, 145, 147, 149, 151, 153, 155, 157, 159, 161, 163, 165, 167, 169, 171, 173, 175. Furthermore variants and fragments as well as further embodiments thereof and nucleic acids encoding the respectively each said polypeptide.

Inventions 65-70: claims 1-40 (all partly)

A single chain polypeptide comprising a first and second domain as described in the introductory part of claim 1 and wherein the single chain polypeptide comprises a sequence selected each respectively from the sequences SEQ ID NO's: 70, 72, 74, 76, 78, 114. Furthermore variants and fragments as well as further embodiments thereof and nucleic acids of respectively SEQ ID NO's: 69, 71, 73, 75, 77, 113 encoding the each said polypeptide.

Invention 71: claim 39 (partly)

A nucleic acid of SEQ ID 134 or a fragment or variant thereof.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No.

PCT/GB 03/03824

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 9807864	A	26-02-1998	AU 723397 B2	24-08-2000
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			CA 2430365 A1	06-06-2002
			EP 1381677 A2	21-01-2004
			WO 0244199 A2	06-06-2002

フロントページの続き

(51)Int.Cl. ⁷	F I	テーマコード (参考)
//(C 1 2 N 9/52	C 1 2 N 9/52	
C 1 2 R 1:145)	C 1 2 R 1:145	

(81)指定国 AP(GH,GM,KE,LS,MW,MZ,SD,SL,SZ,TZ,UG,ZM,ZW),EA(AM,AZ,BY,KG,KZ,MD,RU,TJ,TM),EP(AT, BE,BG,CH,CY,CZ,DE,DK,EE,ES,FI,FR,GB,GR,HU,IE,IT,LU,MC,NL,PT,RO,SE,SI,SK,TR),OA(BF,BJ,CF,CG,CI,CM,GA, GN,GQ,GW,ML,MR,NE,SN,TD,TG),AE,AG,AL,AM,AT,AU,AZ,BA,BB,BG,BR,BY,BZ,CA,CH,CN,CO,CR,CU,CZ,DE,DK,DM,DZ, EC,EE,EG,ES,FI,GB,GD,GE,GH,GM,HR,HU,ID,IL,IN,IS,JP,KE,KG,KP,KR,KZ,LC,LK,LR,LS,LT,LU,LV,MA,MD,MG,MK,M N,MW,MX,MZ,NI,NO,NZ,OM,PG,PH,PL,PT,RO,RU,SC,SD,SE,SG,SK,SL,SY,TJ,TM,TN,TR,TT,TZ,UA,UG,US,UZ,VC,VN,YU ,ZA,ZM,ZW

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Fターム(参考) 4B024 AA01 BA14 BA31 BA38 CA04 CA07 DA06 GA11 HA01 HA03
4B050 CC01 CC04 DD02 GG06 LL01
4C085 AA03 BA12 BB11 CC07 DD62