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一、發明名稱：(中文/英文)

抑制骨再吸收的方法

METHOD OF INHIBITING BONE RESORPTION

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1. 美國 U.S.A.
2. 美國 U.S.A.

四、聲明事項：

☐ 主張專利法第二十二條第二項 ☐ 第一款或 ☐ 第二款規定之事實，其事實發生日期為： 年 月 日。

☒ 申請前已向下列國家（地區）申請專利：

【格式請依：受理國家（地區）、申請日、申請案號 順序註記】

☒ 有主張專利法第二十七條第一項國際優先權：

1. 美國；2007年09月17日；60/973,024

2.

☐ 無主張專利法第二十七條第一項國際優先權：

1.

2.

☐ 主張專利法第二十九條第一項國內優先權：

【格式請依：申請日、申請案號 順序註記】

☒ 主張專利法第三十條生物材料：

☐ 須寄存生物材料者：

國內生物材料 【格式請依：寄存機構、日期、號碼 順序註記】

國外生物材料 【格式請依：寄存國家、機構、日期、號碼 順序註記】

☒ 不須寄存生物材料者：

所屬技術領域中具有通常知識者易於獲得時，不須寄存。

九、發明說明：

【發明所屬之技術領域】

本發明大體而言係關於使用骨硬化素結合劑調節骨密度之方法。

本申請案主張2008年9月17日申請之美國臨時專利申請案第60/973,024號之優先權。

以下申請案全文係以引用之方式併入本文中：2006年4月25日申請之美國專利申請案第11/410,540號，其主張以下申請案之優先權：2006年4月17日申請之美國臨時專利申請案第60/792,645號、2006年3月13日申請之美國臨時專利申請案第60/782,244號、2006年2月24日申請之美國臨時專利申請案第60/776,847號及2005年5月3日申請之美國臨時專利申請案第60/677,583號；及2006年4月25日申請之美國專利申請案第11/411,003號，其主張以下申請案之優先權：2006年4月17日申請之美國臨時專利申請案第60/792,645號、2006年3月13日申請之美國臨時專利申請案第60/782,244號及2006年2月24日申請之美國臨時專利申請案第60/776,847號。

【先前技術】

骨礦物質含量之損失可由多種病狀所引起且可能導致嚴重的醫學問題。舉例而言，骨質疏鬆症為人類之衰弱性疾病且其特徵在於患病個體之骨骼骨量及礦物質密度顯著減小、骨結構損壞(包括骨微結構退化及骨脆性相應增加(亦即，骨強度減小))及易骨折。人類之骨質疏鬆症之前通常

出現臨床骨質減少，即一種可見於美國約2500萬人之病狀。在美國亦已診斷出有700-800萬患者患有臨床骨質疏鬆症。人群中骨質疏鬆症之頻率隨年齡而增加。對於白種人，骨質疏鬆症在女性中佔優勢，在美國女性佔骨質疏鬆症患者群之80%。老年人骨骼骨之脆性增加及易於骨折因該群體偶然摔倒之風險較高而加劇。髖部、腕及椎骨骨折為與骨質疏鬆症相關的最常見損傷。對患者而言，髖部骨折尤其不舒服且治療費用高，且對於女性，此與高死亡率及發病率相關。

【發明內容】

本發明係針對使用骨硬化素抑制劑抑制人類骨再吸收之方法。該方法包含向人類投與有效減少骨再吸收標記之含量且視情況增加骨形成標記之含量之量的骨硬化素抑制劑。在一些實施例中，抑制骨再吸收且增加骨形成達至少約7天、2週、3週、4週、1個月、5週、6週、7週、8週、2個月、3個月或更久。在相關實施例中，本發明提供一種增加骨礦物質密度或治療骨相關病症之方法。本發明進一步提供一種改善蝕骨細胞相關病症之影響之方法。該方法包含向人類投與使骨再吸收標記之含量與未治療之骨標記含量相比減少的骨硬化素抑制劑。此外，骨硬化素抑制劑使骨形成標記之含量與未治療之骨標記含量相比增加至少約10%。骨硬化素抑制劑可經由單次劑量或多次劑量投與。舉例而言，骨硬化素抑制劑可以短期療法方案投與以(例如)增加骨形成，及/或可以維持治療方案長期投與以阻

止骨礦物質密度損失。

在本文中所揭示之任何方法中，一或多種骨再吸收標記之含量與該患者群體之治療前含量或正常含量相比減少至少約5%、10%、15%、20%、30%、40%、50%或以上，歷時至少2週、3週、30天、1個月、6週、2個月或更久。作為非限制性實例，治療後3週骨再吸收標記之含量與該患者群體之治療前含量或正常含量相比減少(例如)至少約20%。在任何前述方法中，骨形成標記之含量與該患者群體之治療前含量或正常含量相比增加至少約10%、約20%、約30%、約40%、約50%、約60%、約70%、約80%、約90%、約100%或更多，歷時至少約2週、3週、30天、1個月、6週、2個月或更久。作為非限制性實例，治療後3週骨形成標記之含量與該患者群體之治療前含量或正常含量相比增加(例如)至少約20%。在一例示性實施例中，骨再吸收之標記為I型膠原之C端肽(CTX)之血清含量。在其他例示性實施例中，骨形成標記為骨特異性鹼性磷酸酶(BSAP)、骨鈣素(OstCa)及/或I型原膠原之N末端延長(P1NP)。

本發明亦提供一種治療骨相關病症之方法，其中該方法包含向人類投與一或多次有效使整個身體(例如，頭、軀幹、臂及腿)或髖部(例如，整個髖部及/或股骨頸骨)、脊骨(例如，脊椎)、腕、手指、脛骨及/或足跟的骨礦物質密度增加約1%、約2%、約3%、約4%、約5%、約6%、約8%、約10%、約12%、約15%、約18%、約20%、約25%或

30%或以上之量的骨硬化素抑制劑。在一些實施例中，治療之前人類之骨礦物質密度表現為骨質疏鬆或骨質減少，且以有效改進骨礦物質密度以使骨礦物質密度不再表現為骨質疏鬆及/或骨質減少之量及時間投與一或多劑骨硬化素抑制劑。舉例而言，對於年輕人，在最初之時間段可投與一或多劑以使骨礦物質密度增加至正常密度之2.5或1個標準偏差以內(亦即，如以下所定義，T分數 ≥ -2.5 或T分數 ≥ -1)的劑量。在例示性實施例中，最始之時間段為約3個月或更短、6個月或更短、9個月或更短、1年或更短、18個月或更短，或更長時間。該方法可進一步包含接著投與一或多種有效維持骨礦物質密度之量之骨硬化素抑制劑視情況歷時至少約6個月、1年、2年或更久(例如，個體之一生)之維持時間。

本發明進一步提供藉由投與一或多次劑量來治療人類之骨相關病症之方法，該一或多次劑量介於約0.1至約20 mg/kg、或約0.1至約12 mg/kg、或約0.5至約12 mg/kg、或約1至約10 mg/kg、或約1至約8 mg/kg、或約2至約8 mg/kg、或約3至約8 mg/kg之間。在一些實施例中，可以約每2週或更久1次、每月或更久一次、或每2個月或更久一次、或每3個月或更久一次、或每4個月或更久一次、或每5個月或更久一次、或每6個月或更久一次、或每9個月或更久一次、或每年或更久一次之間隔投與該等劑量。骨硬化素抑制劑可用於製備使用本文中所述之任何給藥及計時方案投與之藥物。視情況，骨硬化素抑制劑係諸如以含

有供投與之一定劑量之骨硬化素抑制劑(例如，約70 mg至約450 mg骨硬化素抑制劑)的單次劑量或多次劑量小瓶形式存在於容器中。在一例示性實施例中，小瓶可含有約70 mg或75 mg骨硬化素抑制劑(例如抗骨硬化素抗體)且將適於投與約1 mg/kg之單次劑量。在其他實施例中，小瓶可含有約140 mg或150 mg；或約210 mg或220 mg或250 mg；或約280 mg或290 mg或300 mg；或約350 mg或360 mg；或約420 mg或430 mg或440 mg或450 mg骨硬化素抑制劑(例如抗骨硬化素抗體)。

另外，本發明提供一種治療患有低鈣血症或高鈣血症或處於患低鈣血症或高鈣血症風險中之人類、忌用副甲狀腺素或其類似物治療之人類或忌用雙膦酸鹽治療之人類之骨相關病症的方法。該方法包含向人類投與有效增加骨形成標記之含量及/或減少骨再吸收標記之含量而不導致低鈣血症或高鈣血症(例如臨床上明顯的低鈣血症或高鈣血症)之量的骨硬化素抑制劑。

本發明亦提供一種監測抗骨硬化素療法(亦即，對骨硬化素抑制劑之生理反應)之方法。該方法包含投與一或多劑骨硬化素抑制劑及偵測一或多種骨再吸收標記之含量的步驟，其中骨再吸收標記之含量與該患者群體之治療前含量或正常含量相比減少至少約5%、約10%、約15%、約20%、約30%、約40%、約50%或更多表明治療有效。該方法視情況進一步包含偵測一或多種骨形成標記之含量的步驟，其中骨形成標記之含量與該患者群體之治療前含量或

正常含量相比增加至少約10%、約20%、約30%、約40%、約50%、約60%、約70%、約80%、約90%或約100%表明治療有效。在某些實施例中，骨形成標記含量之增加為約20%。該方法可進一步包含將骨硬化素抑制劑之劑量調節為不同量之步驟，例如若骨再吸收及/或骨形成之變化小於想要的，則調節為較高量，或若骨再吸收及/或骨形成之變化大於想要的，則調節為較小量。

在一不同態樣中，本發明提供使骨再吸收標記之含量減少至少約5%、約10%、約15%、約20%、約30%、約40%、約50%或更多且使骨形成標記之含量增加至少約10%、約20%、約30%、約40%、約50%、約60%、約70%、約80%、約90%、約100%或更多達至少約1週、約2週、約1個月、約6週、約2個月、約10週或約3個月的選定骨硬化素抑制劑。在一相關態樣中，本發明提供一種選擇該等骨硬化素抑制劑之方法，該方法係藉由向動物投與候選骨硬化素抑制劑及選擇改變骨再吸收及/或骨形成標記之含量達想要之程度的候選骨硬化素抑制劑。

在本發明之任何前述方法或實施例中，骨硬化素抑制劑可為骨硬化素結合劑。尤其涵蓋美國專利公開案第20070110747號中所揭示之骨硬化素結合劑在(例如)本文中所示之任何方法中或供製備根據本文中所揭示之任何方法投與之藥物的用途。就此而論，本發明包括骨硬化素結合劑於製備以約1 mg/kg至約10 mg/kg之量抑制骨再吸收之藥物的用途，其中該量到治療開始後3週時即有效使I型膠

原C端肽(CTX)之血清含量與治療前或正常含量相比減少至少20%。本發明亦包括骨硬化素結合劑於製備以約1 mg/kg至約10 mg/kg之量增加骨礦物質密度之藥物的用途，其中該量有效(a)使治療開始後3週時CTX之血清含量與治療前或正常含量相比減少至少20%及(b)使治療開始後3週時選自由骨特異性鹼性磷酸酶(BSAP)血清含量、I型膠原之胺基末端延長肽(PINP)之血清含量及骨鈣素(OstCa)之血清含量組成之群的骨形成標記之血清含量與治療前或正常含量相比增加至少20%。

本發明進一步包括骨硬化素結合劑於製備治療骨相關病症之藥物的用途，其中將該藥物以約1 mg/kg至約10 mg/kg之量治療第一段時間，其中該量有效使髌部、脊骨、腕、手指、脛骨及/或足跟之骨礦物質密度增加至少約3%，接著以約1 mg/kg至約10 mg/kg之量治療第二段時間以有效維持骨礦物質密度。亦涵蓋骨硬化素結合劑於製備以約1 mg/kg至約10 mg/kg之量治療患有低鈣血症或高鈣血症或處於患低鈣血症或高鈣血症之風險中的人類之骨相關病症之藥物的用途，以及骨硬化素結合劑於製備治療(a)忌用副甲狀腺素或其類似物治療之人類或(b)忌用雙膦酸鹽治療之人類的骨相關病症之藥物的用途。

本發明亦包括容器，其包含抗骨硬化素抗體或其片段。在一實施例中，該容器包含抗骨硬化素抗體或其片段，及有關以有效(a)使治療開始後3週時I型膠原C端肽(CTX)之血清含量與治療前或正常含量相比減少至少20%及(b)使治

療開始後3週時骨特异性鹼性磷酸酶(BSAP)之血清含量、I型原膠原之胺基末端延長肽(PINP)之血清含量或骨鈣素(OstCa)之血清含量與治療前或正常含量相比增加至少20%之量投與該抗體或其片段的說明書。其他或另外，容器包含約70 mg至約450 mg之量的抗骨硬化素抗體。本發明進一步提供一種容器，其包含抗骨硬化素抗體或其片段及有關每兩週或每四週以約1 mg/kg至約10 mg/kg之量投與該抗體或其片段來治療骨相關病症之說明書。另外，本發明提供一種容器，其包含抗骨硬化素抗體或其片段及有關歷時約3個月之時間以約1 mg/kg至約10 mg/kg之量投與該抗體或其片段來治療骨相關病症之說明書。

【實施方式】

本發明至少部分係基於阻斷或抑制人類骨硬化素之生物活性會引發多種與骨礦物質密度(BMD)增加相關聯之生理學反應(包括顯著抑制骨再吸收)之令人驚訝的發現。大多數現用療法僅抑制骨再吸收而不增加骨形成。針對與BMD降低相關之病症的一些現用療法僅增加骨形成而不顯著減少骨再吸收。舉例而言，當由一些當前藥物引發骨形成時，骨再吸收亦可能增加(即使潛在地以比先前療法低之速率)。相比之下，干擾骨硬化素活性之藥劑增強骨形成且減少骨再吸收。換言之，骨硬化素抑制劑"解除"骨形成與骨再吸收之間的聯繫，從而更有效地建骨。本發明之材料及方法優於治療功效受限且伴隨有潛在地嚴重不良副作用之現有療法。

就此而論，本發明提供一種抑制骨再吸收、例如由蝕骨細胞、溶解骨礦物質基質之骨細胞介導之骨再吸收之方法。本發明進一步提供一種改善蝕骨細胞相關病症(亦即，由在一些實施例中表現為異常高之骨再吸收的蝕骨細胞活性之異常增加引起的病症)之影響之方法。本發明方法包含向人類投與減少骨再吸收標記之含量且視情況增加骨形成標記之含量之量的骨硬化素結合劑。

骨硬化素抑制劑(例如骨硬化素結合劑)之活性(下文進一步描述)可以多種方法量測。骨硬化素結合劑介導之骨礦物質含量或骨密度增加可使用單能及雙能X射線吸收測定法、超音波法、電腦斷層攝影、放射線照相術及磁共振成像量測。骨量之量亦可由體重或使用其他方法計算(參見 Guinness-Hey, *Metab. Bone Dis. Relat. Res.*, 5:177-181 (1984))。在此項技術中使用模擬諸如骨質疏鬆及骨質減少之人類疾病之病狀的動物及特定動物模型測試醫藥組合物及方法對(例如)骨流失、骨再吸收、骨形成、骨強度或骨礦化之參數的影響。該等模型之實例包括切除卵巢大鼠模型(Kalu, *Bone and Mineral*, 15:175-192 (1991); Frost及 Jee, *Bone and Mineral*, 18:221-236 (1992); 及 Jee及 Yao, *J. Musculoskel. Neuron. Interact.*, 1:193-207 (2001))。本文中所述之量測骨硬化素結合劑活性之方法亦可用於測定其他骨硬化素抑制劑之功效。

對於人類，可在臨床上使用(例如)髖部及脊骨之雙能X射線吸光測定法(DXA)測定骨礦物質密度。其他技術包括

定量電腦斷層攝影(QCT)、超音波掃描術、單能x射線吸光測定法(SXA)及放射線照相吸光測定法。用於量測之常見中央骨骼部位包括脊椎及髖部；周邊部位包括前臂、手指、腕及足跟。除超音波掃描術以外，美國醫藥協會(American Medical Association)提出BMD技術通常包括使用x射線且基於放射衰減視放射路徑中組織之厚度及組成而定的原理。所有技術均包括結果與標準資料庫之比較。

或者，可藉由監測骨標記含量計量對一或多種骨硬化素結合劑之生理反應。骨標記為骨再成型過程期間所產生之產物且由骨、成骨細胞及/或蝕骨細胞釋放。骨再吸收及/或骨形成"標記"含量之波動暗示骨再成型/成型之變化。國際骨質疏鬆基金會(International Osteoporosis Foundation, IOF)推薦使用骨標記來監測骨密度療法(參見，例如 Delmas等人，*Osteoporos Int.*，增刊6:S2-17 (2000)，其以引用之方式併入本文中)。指示骨再吸收(或蝕骨細胞活性)之標記包括(例如)C端肽(1型膠原C末端端肽(CTX)或血清交聯C端肽)、N端肽(1型膠原N末端端肽(NTX))、脫氧吡啶啉(deoxypyridinoline, DPD)、吡啶啉、尿羥基脯胺酸、半乳糖羥基離胺酸及抗酒石酸酸性磷酸酶(例如，血清抗酒石酸酸性磷酸酶同功異型物5b)。骨形成/礦化標記包括(但不限於)骨特異性鹼性磷酸酶(BSAP)、I型原膠原N末端及C末端延長(P1NP, PICP)釋放之肽及骨鈣素(OstCa)。可購得數種套組來偵測及量化臨床樣品(諸如尿及血液)中之標記。

當投藥時，骨硬化素結合劑較佳係減少一或多種骨再吸收標記之含量，諸如I型膠原C端肽(CTX)之血清含量。因此，本發明進一步提供一種監測抗骨硬化素療法(亦即對骨硬化素結合劑或其他骨硬化素抑制劑之生理反應)之方法。該方法包含投與骨硬化素結合劑，隨後量測一或多種骨再吸收標記之含量。另外，該方法可包含在投與骨硬化素結合劑之前先量測一或多種骨形成標記之含量。可將骨硬化素結合劑治療期間及/或之後之骨再吸收標記之含量與治療前含量比較，或者可與該患者群體之典型標準範圍比較。一般熟習此項技術者很容易藉由測試代表性數量之具有相似年齡、性別、疾病程度及/或其他特徵的患者之患者族群體確定合適的標準範圍。單次劑量之骨硬化素結合劑可使骨再吸收標記之含量減少至少約5%(例如，約10%、約20%或約30%)。在一些實施例中，骨硬化素結合劑之劑量使骨再吸收標記之含量比投與骨硬化素結合劑之前骨再吸收標記之含量減少至少約40%(例如約50%、約60%或約70%)。另外，在投與單次劑量之骨硬化素結合劑後，骨再吸收標記之含量可減少達至少約3天(例如，約7天、約2週、約3週、約1個月、約5週、約6週、約7週、約2個月、約9週、約10週、約11週或約3個月)

除減少骨再吸收標記之含量外，向患者投與之骨硬化素結合劑之量亦可增加一或多種骨形成標記之含量，諸如BSAP血清含量、PINP血清含量及/或OstCa血清含量。骨硬化素結合劑之單次劑量可使骨形成標記之含量增加例如

至少約5%(例如,約10%、約20%或約30%)。在一些實施例中,骨硬化素結合劑之劑量使骨形成標記之含量升高至少約40%(例如,約50%、約60%或約70%)。在其他實施例中,骨硬化素結合劑之劑量使一或多種骨形成標記之含量增加至少約75%(例如約80%、約90%、約100%或約110%)。在其他實施例中,骨硬化素結合劑之劑量使骨形成標記之含量增加至少約120%(例如約130%、約140%、約150%、約160%或約170%)。在替代性實施例中,骨硬化素結合劑使骨形成標記之含量增加至少約180%(例如約190%或約200%)。在投與單次劑量之骨硬化素結合劑後,骨形成標記之含量理想地保持升高(與治療前骨形成標記之含量或該患者群體之典型標準範圍相比)達至少約3天(例如,約7天、約2週、約3週、約1個月、約5週、約6週、約7週、約2個月、約9週、約10週、約11週或約3個月)。

本發明亦提供一種增加骨礦物質密度(BMD)之方法,其中向人類投與(a)減少骨再吸收標記之含量及(b)增加骨形成標記之含量之量的骨硬化素結合劑。BMD通常與骨骼脆性及骨質疏鬆相關。BMD通常可以"全身"(例如,頭、軀幹、臂及腿)或髖部(例如,整個髖部及/或股骨頸骨)、脊椎(例如,脊椎)、腕、手指、脛骨及/或足跟量測。在骨質疏鬆之診斷中,將患者之BMD與30歲健康成人(亦即,"年輕人")之峰值密度相比較,產生所謂的"T分數"。亦可將患者之BMD與"年齡匹配"之骨密度相比較(參見,例如 World Health Organization Scientific Group on the Prevention and

Management of Osteoporosis, "Prevention and management of osteoporosis: report of a WHO scientific group." *WHO Technical Report Series*; 921, Geneva, Switzerland (2000))。患者之BMD與健康年輕人之BMD之間的差異通常以"標準偏差"之倍數表示，"標準偏差"通常相當於骨密度之約10%至約12%之減少。世界衛生組織(World Health Organization)基於BMD T分數提出四個診斷級別。在年輕人參考平均值之1個標準偏差內的BMD值(T分數 ≥ -1)為"正常"。低骨量(骨質減少)係由比年輕人平均值低超過1個標準偏差但小於2個標準偏差(T分數 < -1 且 > -2.5)之BMD值指示。比正常值低超過2.5個標準偏差之T分數支持骨質疏鬆症之診斷。若患者另外患有一或多種脆性骨折，則認為該患者患有重度骨質疏鬆症。

不考慮患者之T分數，可向患者投與骨硬化素抑制劑(例如骨硬化素結合劑)以改進骨礦物質密度。骨硬化素結合劑可以有效使患者之BMD增加至少約1%(約2%、約3%、約4%、約5%或約6%)之劑量及時間投與。在一些實施例中，BMD增加至少約8%(例如，至少約10%、約12%、約15%或約18%)。在其他實施例中，骨硬化素結合劑使髖部、脊骨、腕、手指、脛骨及/或足跟之BMD增加至少約20%(例如，至少約22%、約25%或約28%)。在其他實施例中，BMD增加至少約30%(例如，至少約32%、約35%、約38%或約40%)。換言之，BMD可增加至健康年輕人之正常BMD以下約1個至約2.5個標準偏差之範圍內(較佳在約0至

約1個標準偏差之範圍內)。

骨再成型之變化可導致整個身體礦物質濃度之波動。骨為血流中鈣含量之一個主要調控物。蝕骨細胞介導之骨再吸收將所儲存之鈣釋放至全身循環中，而成骨細胞介導之骨形成將鈣自循環中移出而併入骨組織中。在正常骨再成型過程中，該等過程循環以維持健康強健的骨且將游離鈣含量維持在約8.5 mg/dL至約10.5 mg/dL(例如約2.2 mmol/L至約2.6 mmol/L)。骨病症、其他疾病及甚至某些療法可破壞全身鈣含量，產生可怕的後果。高鈣血症與血液中鈣含量高(例如，超過12 mg/dL或3 mmol/L)相關。極高之鈣含量導致(例如)疲勞、意識模糊、便秘、食慾減退、尿頻、心臟問題及骨痛。低鈣血症為由血液中異常低之鈣含量(例如，小於約9 mg/dL或2.2 mmol/L)指示之電解質不平衡。小於7.5 mg/dL(小於1.87 mmol/L)或更小之鈣含量被視為重度低鈣血症且可能伴隨臨床症狀。

低鈣血症之共同症狀包括神經及肌肉痙攣及痛性痙攣、麻木、四肢刺痛、意識模糊及心律不齊。全身鈣之急劇變化可能導致昏迷及死亡。

數種疾病及醫藥療法可改變全身鈣含量。高鈣血症及低鈣血症可由以下疾病引起：例如慢性腎病、腎衰竭、原發性或繼發性副甲狀腺功能亢進、假副甲狀腺功能減退、副甲狀腺功能減退、假副甲狀腺功能減退、鎂耗盡、酒精中毒、雙膦酸鹽療法、重度高鎂血症、維生素D缺乏、高磷酸鹽血症、急性胰炎、骨饑餓症候群、螯合作用、成骨細

胞轉移、膿毒病、手術、化學療法、瘤形成症候群、家族性低尿鈣高鈣血症、肉狀瘤病、肺結核、鉍中毒症、組織漿菌病、念珠菌病 (Candidiasis)、球黴菌病 (Coccidioidomycosis)、組織細胞增多病 X、霍奇金氏或非霍奇金氏淋巴瘤 (Hodgkin's or Non-Hodgkin's lymphoma)、克羅恩氏病 (Crohn's disease)、韋格納肉牙腫病 (Wegener's granulomatosis)、白血病、肺炎、聚矽氧誘發肉芽瘤、行動不便，或藥物療法，諸如投與噻嗪 (thiazide) 利尿劑、鋰、雌激素、氟化物、葡萄糖及胰島素。另外，血清鈣波動為許多現有骨相關療法 (諸如雙膦酸鹽及副甲狀腺素療法) 之副作用。由於鈣不平衡之潛在危急生命的結果，因此易患低鈣血症或高鈣血症之患者可能需要前述某些療法選擇。

已展示骨硬化素抑制劑 (例如骨硬化素結合劑) 顯著促進骨形成且抑制 (或減緩) 骨再吸收，而全身性鈣含量波動極小 (例如，鈣含量自基線血清鈣含量波動 10% 或更小)。因此，本發明材料及方法尤其有利於治療易受不穩定鈣含量影響或對不穩定鈣含量敏感之患者。在本發明該態樣之情況下，向人類投與之骨硬化素結合劑之量為不導致低鈣血症或高鈣血症 (例如，臨床上顯著的低鈣血症或高鈣血症) 之量。另外，本發明提供一種治療患有低鈣血症或高鈣血症或處於患低鈣血症或高鈣血症風險中之人類或者忌用雙膦酸鹽、副甲狀腺素或副甲狀腺素類似物治療之人類之骨相關病症的方法。該方法包含向人類投與有效增加骨形成

標記之含量(諸如 BSAP、PINP 及 / 或 OstCa 之血清含量)及 / 或減少骨再吸收標記(諸如 CTX)之含量之量的骨硬化素結合劑。

本發明方法適用於治療或預防骨相關病症，諸如與異常成骨細胞或蝕骨細胞活性相關之骨相關病症。實際上，可將骨硬化素抑制劑(例如，骨硬化素結合劑)投與患有選自由以下疾病組成之群的骨相關病症之人類：軟骨發育不全、鎖骨顱骨發育不全、內生性軟骨瘤、纖維結構不良、高雪氏病(Gaucher's Disease)、低磷酸鹽性佝僂病、馬凡氏症候群(Marfan's syndrome)、多發性遺傳性外生骨疣(multiple hereditary exostose)、神經纖維瘤、成骨不全症、骨硬化病、脆弱性骨硬化、硬化病變、假關節、化膿性骨髓炎、牙周病、抗癲癇藥物誘發之骨流失、原發性和繼發性副甲狀腺功能亢進、家族性副甲狀腺功能亢進症候群、體重減輕誘發之骨流失、男性之骨質疏鬆症、絕經後骨流失、骨關節炎、腎性骨營養不良、浸潤性骨病症、口腔骨流失、頷骨壞死、青少年佩吉特氏病(juvenile Paget's disease)、肢骨紋狀肥大、代謝性骨病、肥大細胞增多症、鐮刀型細胞貧血/疾病、器官移植相關骨流失、腎移植相關骨流失、全身性紅斑狼瘡、強直性脊椎炎、癲癇症、青少年關節炎皮疹、地中海貧血、黏多醣病、法布瑞疾病(Fabry Disease)、特納症候群(Turner Syndrome)、唐氏症候群(Down Syndrome)、克林費特症候群(Klinefelter Syndrome)、麻瘋病、佩特茲病(Perthe's Disease)、青少年

特發性脊柱側凸、嬰兒發作之多系統發炎性疾病、韋徹斯特症候群 (Winchester Syndrome)、曼克斯疾病 (Menkes Disease)、威爾遜氏病 (Wilson's Disease)、缺血性骨病 (諸如股骨頭缺血性壞死 (Legg-Calve-Perthes disease) 及區域遷移性骨質疏鬆症)、貧血狀態、由類固醇引起之病狀、糖皮質激素誘發之骨流失、肝素誘發之骨流失、骨髓病症、壞血病、營養不良、鈣缺乏症、骨質疏鬆症、骨質減少、酒精中毒、慢性肝病、絕經後狀態、慢性發炎性病狀、類風濕性關節炎、發炎性腸病、潰瘍性結腸炎、發炎性結腸炎、克羅恩氏病、月經過少、閉經、妊娠、糖尿病、甲狀腺功能亢進、甲狀腺病症、副甲狀腺病症、庫欣氏病 (Cushing's disease)、肢端肥大症、性腺功能減退、行動不便 (immobilization) 或失能、反射性交感神經營養不良症候群、區域性骨質疏鬆症、骨軟化、與關節置換相關之骨流失、HIV 相關骨流失、與生長激素損失相關之骨流失、與囊性纖維化相關之骨流失、化學療法相關骨流失、腫瘤誘發之骨流失、癌症相關骨流失、激素去除之骨流失、多發性骨髓瘤、藥物誘發之骨流失、神經性厭食、疾病相關面骨流失、疾病相關顱骨流失、疾病相關頷骨流失、疾病相關顱骨流失、與老化相關之骨流失、與老化相關之面骨流失、與老化相關之顱骨流失、與老化相關之頷骨流失、與老化相關之顱骨流失及與空間飛行相關之骨流失。

本發明方法不需治癒患有病症的患者或完全防止骨相關病症發作來達成有益生物反應。該方法可預防性使用，意

謂完全或部分防止骨相關病症或其症狀。該方法亦可治療性使用以完全或部分改善骨相關病症或其症狀或者完全或部分防止骨相關病症或其症狀進一步進展。實際上，本發明材料及方法尤其適用於增加骨礦物質密度及維持BMD增加一段時間。就此而論，本發明提供一種治療骨相關病症之方法，該方法包含(a)投與一或多次有效使全身(例如，頭、軀幹、臂及腿)或髖部(例如，整個髖部及/或股骨頸骨)、脊骨(例如，脊椎)、腕、手指、脛骨及/或足跟處所量測之BMD增加約1%、約2%、約3%、約6%、約8%、約10%、約12%、約15%、約18%、約20%、約25%或30%或更多之量的骨硬化素結合劑。可在例如約1個月至約12個月(例如，約2個月、約3個月、約4個月、約5個月、約6個月、約7個月、約8個月、約9個月、約10個月或約11個月)之治療期內進行一或多次包含骨硬化素結合劑之醫藥組合物的投與。該方法進一步包括(b)接著投與一或多次有效維持骨礦物質密度之量之骨硬化素結合劑。"維持骨礦物質密度"意謂在步驟(b)之過程中(例如，約6個月、約9個月、約1年、約18個月、約2年或歷經患者一生之過程)，由步驟(a)引起之BMD增加不會下降超過約1%至約5%。應瞭解，患者可需要增加骨密度與維持骨密度之交替治療階段。

骨硬化素結合劑較佳係以生理學上可接受之(例如，醫藥)組合物形式向患者投與，該組合物可包括載劑、賦形劑或稀釋劑。應瞭解，本文中所述之骨硬化素結合劑可用

於製備使用本文中所揭示之任何劑量及計時方案投與之藥物。醫藥組合物及治療方法揭示於美國專利公開案第20050106683號中，其以引用之方式併入本文中。"生理學上可接受"係指分子實體及組合物當向人類投與時不產生過敏性反應或類似不良反應。另外，向個體投與之組合物可含有一種以上骨硬化素抑制劑(例如，骨硬化素結合劑及合成化學骨硬化素抑制劑)或與一或多種具有不同作用機制之治療劑組合之骨硬化素抑制劑。

在多種治療方案中使用本文中所述之特定組合物之合適給藥及治療方案(包括例如皮下、經口、非經腸、靜脈內、鼻內及肌肉內投藥及調配)的開發為此項技術所熟知且論述於美國專利公開案第20070110747號中。舉例而言，在某些境況下，將希望經皮下、非經腸、靜脈內、肌肉內或甚至腹膜內傳遞包含骨硬化素結合劑之醫藥組合物。該等方法為熟習此項技術者所熟知，其中有一些進一步描述於(例如)美國專利第5,543,158號、第5,641,515號及第5,399,363號中。適於注射使用之說明性醫藥形式包括無菌水溶液或分散液及臨時製備無菌可注射溶液或分散液之無菌散劑(例如，參見美國專利第5,466,468號)。在所有情況下，該形式必須為無菌的且必須為流動的達出現易於注射性之程度。

在一實施例中，對於以水溶液形式非經腸投藥，該溶液必要時應經適當緩衝且首先用足夠生理食鹽水或葡萄糖使液體稀釋劑等張。該等特定水溶液尤其適於靜脈內、肌肉

內、皮下及腹膜內投藥。舉例而言，可將一劑溶解於1 ml等張NaCl溶液中，且將其添加至1000 ml皮下灌注流體中或注射於所建議之輸注部位處(參見，例如Remington's Pharmaceutical Sciences，第15版，Mack Pub. Co., Easton, PA，第1035-1038及1570-1580頁)。視所治療之個體之病狀；患者之年齡、身高、體重及總體健康狀況及任何副作用之存在而定，投藥劑量及頻率可發生一定變化。另外，可將包含骨硬化素結合劑之醫藥組合物與提供關於使用該等醫藥組合物之說明書的包裝材料一起置放於容器(例如，小瓶)中。該等說明書通常將包括描述試劑濃度之明確表達，以及在某些實施例中，描述復水醫藥組合物所必需之賦形劑成分或稀釋劑(例如水、生理食鹽水或PBS)之相對量。

骨硬化素結合劑係以減少骨再吸收標記之含量及/或增加骨形成標記之含量及/或增加骨密度之量投與。所投與之骨硬化素結合劑之劑量可在每公斤體重約0.5 mg至約20 mg(例如，12 mg)之範圍內。舉例而言，骨硬化素結合劑之劑量可在約1 mg/kg至約10 mg/kg(例如，約2 mg/kg或約9 mg/kg)、約1 mg/kg至約3 mg/kg或約3 mg/kg至約8 mg/kg(例如，約4 mg/kg、5 mg/kg、6 mg/kg或7 mg/kg)之範圍內。

另外，視關於特定患者所選擇之治療方案而定，可有利地投與多劑骨硬化素結合劑或分開投與多劑。骨硬化素結合劑可在1年或更短之時間(例如，9個月或更短、6個月或

更短或3個月或更短)內週期性投與。就此而論，可每約7天、或2週、或3週、或1個月、或5週、或6週、或7週、或2個月、或9週、或10週、或11週、或3個月、或13週、或14週、或15週、或4個月、或17週、或18週、或19週、或5個月、或21週、或22週、或23週、或6個月、或12個月一次向人類投與骨硬化素結合劑。

本發明方法包含投與一定量之"骨硬化素抑制劑"。如本文中所使用，術語"骨硬化素抑制劑"意謂如由骨礦化、骨密度、對成骨細胞及/或蝕骨細胞之影響、骨形成標記、骨再吸收標記、成骨細胞活性標記及/或蝕骨細胞活性標記之變化所量測，抑制骨硬化素對骨之生物活性的任何分子。該等抑制劑可藉由與骨硬化素或其受體或結合搭配物結合起作用。該類抑制劑包括"骨硬化素結合劑"，諸如抗體或肽基分子。"骨硬化素抑制劑"亦指結合骨硬化素且抑制其活性之視情況分子量小於約1000道爾頓(Dalton)的小有機化學化合物。抑制劑或者可藉由抑制骨硬化素之表現起作用。該類抑制劑包括與骨硬化素DNA或mRNA結合且抑制骨硬化素表現之聚核苷酸或寡核苷酸，包括反義寡核苷酸、抑制性RNA、DNA酶、核糖酶、適體或抑制骨硬化素表現之其醫藥學上可接受之鹽。

"骨硬化素結合劑"與骨硬化素或其部分特異性結合以阻斷或減弱人類骨硬化素與一或多個配位體之結合。在骨硬化症(一種以骨過度生長及強緻密骨為特徵之骨骼疾病)中無骨硬化素(SOST基因之產物)(Brunkow等人，*Am. J. Hum.*

Genet., 68:577-589 (2001) ; Balemans 等人 , *Hum. Mol. Genet.*, 10:537-543 (2001))。人類骨硬化素之胺基酸序列經 Brunkow 等人報導且在美國專利公開案第 20070110747 號中以 SEQ ID NO: 1 揭示(該專利公開案中關於骨硬化素結合劑及序列表之描述係全文併入本文中)。重組人類骨硬化素 /SOST 可購自 R&D Systems(Minneapolis, Minn., USA ; 2006 目錄號 1406-ST-025)。另外，重組小鼠骨硬化素 /SOST 可購自 R&D Systems(Minneapolis, Minn., USA ; 2006 目錄號 1589-ST-025)。研究級骨硬化素結合單株抗體可購自 R&D Systems(Minneapolis, Minn., USA ; 小鼠單株 : 2006 目錄號 MAB1406 ; 大鼠單株 : 2006 目錄號 MAB1589)。美國專利第 6,395,511 號及第 6,803,453 號以及美國專利公開案第 20040009535 號及第 20050106683 號大致提及抗骨硬化素抗體。適於在本發明之情況下使用之骨硬化素結合劑的實例亦描述於美國專利公開案第 20070110747 號及第 20070072797 號中，其以引用之方式併入本文中。關於產生骨硬化素結合劑之材料及方法之其他資訊可見於美國專利公開案第 20040158045 號中。

本發明之骨硬化素結合劑較佳為抗體。術語"抗體"係指完整抗體或其結合片段。抗體可包含完整抗體分子(包括具有全長重鏈及/或輕鏈之多株、單株、嵌合、人化或人類形式)或包含其抗原結合片段。抗體片段包括 F(ab')₂、Fab、Fab'、Fv、Fc 及 Fd 片段，且其可併入單結構域抗體、單鏈抗體、巨型抗體(maxibody)、微型抗體

(minibody)、胞內抗體(intrabody)、雙功能抗體、三功能抗體、四功能抗體、v-NAR及bis-scFv中(參見, 例如 Hollinger及Hudson, *Nature Biotechnology*, 23(9): 1126-1136 (2005))。包括纖維結合蛋白多肽單功能抗體之抗體多肽亦揭示於美國專利第6,703,199號中。其他抗體多肽揭示於美國專利公開案第20050238646號中。抗骨硬化素抗體可以小於或等於 1×10^{-7} M、小於或等於 1×10^{-8} M、小於或等於 1×10^{-9} M、小於或等於 1×10^{-10} M、小於或等於 1×10^{-11} M或小於或等於 1×10^{-12} M之親和力與SEQ ID NO: 1之骨硬化素或其天然存在之變體結合。親和力可由親和力ELISA檢定測定。在某些實施例中, 親和力可由BIAcore檢定測定。在某些實施例中, 親和力可由動力學方法測定。在某些實施例中, 親和力可由平衡/溶液法測定。

抗體片段可為任何合成或基因工程改造之蛋白質。舉例而言, 抗體片段包括由輕鏈可變區組成之經分離片段、由重鏈及輕鏈之可變區組成之"Fv"片段、輕鏈及重鏈可變區經由肽連接子連接之重組單鏈多肽分子(scFv蛋白)。

抗體片段之另一形式為包含一或多個抗體互補決定區(CDR)之肽。CDR(亦稱為"最小識別單元"或"高變區")可藉由構築編碼所關注之CDR之聚核苷酸獲得。該等聚核苷酸係(例如)藉由使用以產生抗體之細胞之mRNA作為模板之聚合酶鏈反應合成可變區來製備(參見, 例如, Larrick等人, *Methods: A Companion to Methods in Enzymology*, 2:106 (1991); Courtenay-Luck, "Genetic Manipulation of

Monoclonal Antibodies", *Monoclonal Antibodies Production, Engineering and Clinical Application*, Ritter等人(編), 第166頁, Cambridge University Press (1995); 及Ward等人, "Genetic Manipulation and Expression of Antibodies", *Monoclonal Antibodies: Principles and Applications*, Birch等人(編), 第137頁, Wiley-Liss, Inc. (1995))。

在本發明之一實施例中, 骨硬化素結合劑交叉阻斷以下抗體中之至少一種與骨硬化素之結合: Ab-A、Ab-B、Ab-C、Ab-D、Ab-1、Ab-2、Ab-3、Ab-4、Ab-5、Ab-6、Ab-7、Ab-8、Ab-9、Ab-10、Ab-11、Ab-12、Ab-13、Ab-14、Ab-15、Ab-16、Ab-17、Ab-18、Ab-19、Ab-20、Ab-21、Ab-22、Ab-23及Ab-24(所有該等抗體均描述於美國專利公開案第20070110747號中)。其他或另外, 以下抗體中之至少一種交叉阻斷骨硬化素結合劑與骨硬化素結合: Ab-A、Ab-B、Ab-C、Ab-D、Ab-1、Ab-2、Ab-3、Ab-4、Ab-5、Ab-6、Ab-7、Ab-8、Ab-9、Ab-10、Ab-11、Ab-12、Ab-13、Ab-14、Ab-15、Ab-16、Ab-17、Ab-18、Ab-19、Ab-20、Ab-21、Ab-22、Ab-23及Ab-24(所有該等抗體均描述於美國專利公開案第20070110747號中)。術語"交叉阻斷"在本文中可互換使用以意謂抗體或其他結合劑干擾其他抗體或結合劑與骨硬化素之結合的能力。抗體或其他結合劑能夠干擾另一抗體與骨硬化素之結合的程度且因此其是否能認為是交叉阻斷可使用競爭結合檢定確定。在本發明之一些態樣中, 交叉阻斷抗體或其片段使骨硬化素

與參考抗體之結合降低介於約40%與約100%之間，諸如約60%與約100%、尤其70%與100%之間且更尤其80%與100%之間。尤其適於偵測交叉阻斷之定量檢定使用Biacore機器，其使用表面電漿共振技術量測相互作用之程度。另一合適的定量交叉阻斷檢定使用基於ELISA之方法量測抗體或其他結合劑關於與骨硬化素結合的競爭。

合適之骨硬化素結合劑包括美國專利公開案第20070110747號中所述之抗體及其部分，諸如其中特別揭示之CDR-H1、CDR-H2、CDR-H3、CDR-L1、CDR-L2及CDR-L3中之一或多者。CDR-H1、CDR-H2、CDR-H3、CDR-L1、CDR-L2及CDR-L3之區域中至少一個可具有至少一個胺基酸取代，其限制條件為結合劑保留未經取代之CDR之結合特異性。結合劑之非CDR部分可為非蛋白質分子，其中結合劑交叉阻斷本文中所揭示之抗體與骨硬化素之結合及/或中和骨硬化素。結合劑之非CDR部分可為非蛋白質分子，其中結合劑在人類骨硬化素肽抗原決定基競爭結合檢定中展現與以下抗體中之至少一個所展現之結合模式類似的與人類骨硬化素肽之結合模式：Ab-A、Ab-B、Ab-C、Ab-D、Ab-1、Ab-2、Ab-3、Ab-4、Ab-5、Ab-6、Ab-7、Ab-8、Ab-9、Ab-10、Ab-11、Ab-12、Ab-13、Ab-14、Ab-15、Ab-16、Ab-17、Ab-18、Ab-19、Ab-20、Ab-21、Ab-22、Ab-23及Ab-24(所有該等抗體均描述於美國專利公開案第20070110747號中)及/或中和骨硬化素。結合劑之非CDR部分可由胺基酸構成，其中該結合劑為重組

結合蛋白或合成肽，且重組結合蛋白交叉阻斷抗體與骨硬化素之結合及/或中和骨硬化素。結合劑之非CDR部分可由胺基酸構成，其中該結合劑為重組結合蛋白，且該重組結合蛋白在人類骨硬化素肽抗原決定基競爭結合檢定(描述於美國專利公開案第20070110747號中)中展現與以下抗體中之至少一個所展現之結合模式類似的與人類骨硬化素肽之結合模式：Ab-A、Ab-B、Ab-C、Ab-D、Ab-1、Ab-2、Ab-3、Ab-4、Ab-5、Ab-6、Ab-7、Ab-8、Ab-9、Ab-10、Ab-11、Ab-12、Ab-13、Ab-14、Ab-15、Ab-16、Ab-17、Ab-18、Ab-19、Ab-20、Ab-21、Ab-22、Ab-23及Ab-24(均描述於美國專利公開案第20070110747號中)，及/或中和骨硬化素。骨硬化素結合劑較佳為美國專利公開案第20070110747號之Ab-A、Ab-B、Ab-C、Ab-D、Ab-1、Ab-2、Ab-3、Ab-4、Ab-5、Ab-6、Ab-7、Ab-8、Ab-9、Ab-10、Ab-11、Ab-12、Ab-13、Ab-14、Ab-15、Ab-16、Ab-17、Ab-18、Ab-19、Ab-20、Ab-21、Ab-22、Ab-23或Ab-24。

另外，骨硬化素結合劑可包含至少一個與選自以下序列之CDR具有至少75%一致性(例如，100%一致性)的CDR序列：美國專利公開案第20070110747號中所揭示之SEQ ID NO: 39、40、41、42、43、44、45、46、47、48、49、50、51、52、53、54、55、56、57、58、59、60、61、62、78、79、80、81、99、100、101、102、103、104、105、106、107、108、109、110、111、112、113、114、

115、116、237、238、239、240、241、242、243、244、
245、246、247、248、249、250、251、252、253、254、
255、256、257、258、259、260、261、262、263、264、
265、266、267、268、269、270、271、272、273、274、
275、276、277、278、279、280、281、282、283、284、
285、286、287、288、289、290、291、292、293、294、
295、296、297、298、351、352、353、358、359及360。

骨硬化素結合劑較佳包含至少一個與選自以下序列之CDR
具有至少75%一致性的CDR序列：SEQ ID NO: 245、246、
247、78、79、80、269、270、271、239、240及24，所有
該等序列均描述於美國專利公開案第20070110747號中。
如美國專利公開案第20070110747號中所述，骨硬化素結
合劑可包含：a)SEQ ID NO: 54、55及56之CDR序列及SEQ
ID NO: 51、52及53之CDR序列；b)SEQ ID NO: 60、61及
62之CDR序列及SEQ ID NO: 57、58及59之CDR序列；
c)SEQ ID NO: 48、49及50之CDR序列及SEQ ID NO: 45、
46及47之CDR序列；d)SEQ ID NO: 42、43及44之CDR序列
及SEQ ID NO: 39、40及41之CDR序列；e)SEQ ID NO:
275、276及277之CDR序列及SEQ ID NO: 287、288及289
之CDR序列；f)SEQ ID NO: 278、279及280之CDR序列及
SEQ ID NO: 290、291及292之CDR序列；g)SEQ ID NO:
78、79及80之CDR序列及SEQ ID NO: 245、246及247之
CDR序列；h)SEQ ID NO: 81、99及100之CDR序列及SEQ
ID NO: 248、249及250之CDR序列；i)SEQ ID NO: 101、

102及103之CDR序列及SEQ ID NO: 251、252及253之CDR序列；j)SEQ ID NO: 104、105及106之CDR序列及SEQ ID NO: 254、255及256之CDR序列；k)SEQ ID NO: 107、108及109之CDR序列及SEQ ID NO: 257、258及259之CDR序列；l)SEQ ID NO: 110、111及112之CDR序列及SEQ ID NO: 260、261及262之CDR序列；m)SEQ ID NO: 281、282及283之CDR序列及SEQ ID NO: 293、294及295之CDR序列；n)SEQ ID NO: 113、114及115之CDR序列及SEQ ID NO: 263、264及265之CDR序列；o)SEQ ID NO: 284、285及286之CDR序列及SEQ ID NO: 296、297及298之CDR序列；p)SEQ ID NO: 116、237及238之CDR序列及SEQ ID NO: 266、267及268之CDR序列；q)SEQ ID NO: 239、240及241之CDR序列及SEQ ID NO: 269、270及271之CDR序列；r)SEQ ID NO: 242、243及244之CDR序列及SEQ ID NO: 272、273及274之CDR序列；或s)SEQ ID NO: 351、352及353之CDR序列及SEQ ID NO: 358、359及360之CDR序列。

骨硬化素結合劑亦可包含至少一個與選自CDR-H1、CDR-H2、CDR-H3、CDR-L1、CDR-L2及CDR-L3之CDR具有至少75%一致性的CDR序列，其中CDR-H1具有SEQ ID NO: 245或SEQ ID NO: 269中給出之序列，CDR-H2具有SEQ ID NO: 246或SEQ ID NO: 270中給出之序列，CDR-H3具有SEQ ID NO: 247或SEQ ID NO: 271中給出之序列，CDR-L1具有SEQ ID NO: 78或SEQ ID NO: 239中給出之序

列，CDR-L2具有SEQ ID NO: 79或SEQ ID NO: 240中給出之序列，且CDR-L3具有SEQ ID NO: 80或SEQ ID NO 241中給出之序列，所有該等序列均描述於美國專利公開案第20070110747號中。

另外，骨硬化素結合劑可具有重鏈，其包含CDR H1、H2及H3且包含具有SEQ ID NO: 137中提供之序列之多肽或其變體，其中該CDR H1、H2及H3分別與SEQ ID NO: 245、246及247至少75%一致；及輕鏈，其包含CDR L1、L2及L3且包含具有SEQ ID NO: 133中提供之序列的多肽或其變體，其中該CDR L1、L2及L3分別與SEQ ID NO: 78、79及80至少75%一致(如美國專利公開案第20070110747號中所述)。

骨硬化素結合劑可具有重鏈，其包含CDR H1、H2及H3且包含具有SEQ ID NO: 145或392中提供之序列之多肽或其變體，其中該CDR H1、H2及H3分別與SEQ ID NO: 245、246及247至少75%一致；及輕鏈，其包含CDR之L1、L2及L3且包含具有SEQ ID NO: 141中提供之序列的多肽或其變體，其中該CDR L1、L2及L3分別與SEQ ID NO: 78、79及80至少75%一致(如美國專利公開案第20070110747號中所述)。

骨硬化素結合劑可具有重鏈，其包含CDR H1、H2及H3且包含具有SEQ ID NO: 335中提供之序列之多肽或其變體，其中該CDR H1、H2及H3分別與SEQ ID NO: 269、270及271至少75%一致；及輕鏈，其包含CDR L1、L2及L3且

包含具有SEQ ID NO: 334中提供之序列的多肽或其變體，其中該CDR L1、L2及L3分別與SEQ ID NO: 239、240及241至少75%一致(如美國專利公開案第20070110747號中所述)。

或者，骨硬化素結合劑可具有重鏈，其包含CDR H1、H2及H3且包含具有SEQ ID NO: 331中提供之序列之多肽或其變體，其中該CDR H1、H2及H3分別與SEQ ID NO: 269、270及271至少75%一致；及輕鏈，其包含CDR L1、L2及L3且包含具有SEQ ID NO: 330中提供之序列的多肽或其變體，其中該CDR L1、L2及L3分別與SEQ ID NO: 239、240及241至少75%一致(如美國專利公開案第20070110747號中所述)。

骨硬化素結合劑可具有重鏈，其包含CDR H1、H2及H3且包含具有SEQ ID NO: 345或396中提供之序列之多肽或其變體，其中該CDR H1、H2及H3分別與SEQ ID NO: 269、270及271至少75%一致；及輕鏈，其包含CDR L1、L2及L3且包含具有SEQ ID NO: 341中提供之序列的多肽或其變體，其中該CDR L1、L2及L3分別與SEQ ID NO: 239、240及241至少75%一致(如美國專利公開案第20070110747號中所述)。

或者，骨硬化素結合劑具有包含具有SEQ ID NO: 137中提供之序列之多肽的重鏈及包含具有SEQ ID NO: 133中提供之序列之多肽的輕鏈；或包含具有SEQ ID NO: 145或392中提供之序列之多肽的重鏈及包含具有SEQ ID NO:

141中提供之序列之多肽的輕鏈；或包含具有SEQ ID NO: 335中提供之序列之多肽的重鏈及包含具有SEQ ID NO: 334中提供之序列之多肽的輕鏈；或包含具有SEQ ID NO: 331中提供之序列之多肽的重鏈及包含具有SEQ ID NO: 330中提供之序列之多肽的輕鏈；或包含具有SEQ ID NO: 345或396中提供之序列之多肽的重鏈及包含具有SEQ ID NO: 341中提供之序列之多肽的輕鏈(如美國專利公開案第20070110747號中所述)。

● 用於本發明方法中之骨硬化素結合劑較佳在美國專利公開案第20070110747號中所述之基於細胞之檢定中及/或美國專利公開案第20070110747號中所述之活體內檢定中調節骨硬化素功能，及/或結合美國專利公開案第20070110747號中所述之一或多個抗原決定基，及/或交叉阻斷美國專利公開案第20070110747號中所述之抗體中之一種的結合，及/或與骨硬化素之結合經美國專利公開案第20070110747號中所述之抗體中之一種交叉阻斷。

● 此外，本發明方法可包含投與除本文中所述之骨硬化素結合劑以外的骨硬化素抑制劑。該等藥劑可直接或間接作用於SOST或骨硬化素。預期用於本發明方法中之骨硬化素抑制劑包括美國專利公開案第20030229041號(其全部揭示內容以引用之方式併入本文中，尤其著重於骨硬化素抑制劑之描述)中所述之骨硬化素抑制劑。舉例而言，適用於調節SOST表現及骨硬化素活性之藥劑包括(但不限於)類固醇(諸如對應於美國專利公開案第20030229041號中之式

1之類固醇)、生物鹼、類萜、類肽(peptoid)及合成化學物質。在一些實施例中，SOST拮抗劑或激動劑可結合糖皮質激素受體。舉例而言，地塞米松(dexamethasone)傾向於消除BMP-4及BMP-6對SOST表現之刺激效應。包括糖皮質激素類似物、膽汁鹽(諸如對應於美國專利公開案第20030229041號中之式3之膽汁鹽)及前列腺素(諸如對應於美國專利公開案第20030229041號中之式2之前列腺素)之其他化學實體亦調節骨形態發生蛋白對SOST表現之效應且預期其可用於本發明方法中。

骨硬化素抑制劑亦可為直接或間接作用於SOST或骨硬化素以在活體內降低至少一種骨再吸收標記之含量及/或增加至少一種骨形成標記之含量的其他小分子治療劑。術語"小分子"包括合成、天然來源或部分合成且較佳分子量小於5,000道爾頓(例如，介於約100與1,500道爾頓之間)之化合物或分子複合物。藥劑可使用此項技術已知之組合文庫方法中之許多方法中之任一種獲得，包括空間可定位平行固相或溶液相文庫、需要重疊合(deconvolution)之合成文庫方法、"一珠粒一化合物(one-bead one-compound)"文庫方法及使用親和力層析選擇之合成文庫方法(參見，例如Lam, *Anticancer Drug Des.*, 12:145(1997)及美國專利第5,738,996號、第5,807,683號及第7,261,892號)。開發及篩選骨硬化素抑制劑之方法進一步描述於美國專利公開案第20030229041號中，其論述以引用之方式併入本文中。

可根據本發明之方法使用之骨硬化素表現抑制劑包括抑

制劑寡核苷酸或聚核苷酸，包括其醫藥學上可接受之鹽，例如鈉鹽。非限制性實例包括：反義寡核苷酸(Eckstein, *Antisense Nucleic Acid Drug Dev.*, 10: 117-121 (2000)；Crooke, *Methods Enzymol*, 313: 3-45 (2000)；Guvakova等人，*J. Biol. Chem.*, 270: 2620-2627 (1995)；Manoharan, *Biochim. Biophys. Acta*, 1489: 117-130 (1999)；Baker等人，*J. Biol. Chem.*, 272: 11994-12000 (1997)；Kurreck, *Eur. J. Biochem.*, 270: 1628-1644 (2003)；Sierakowska等人，*Proc. Natl. Acad. Sci. USA*, 93: 12840-12844 (1996)；Marwick, *J. Am. Med. Assoc*, 280: 871 (1998)；Tomita及Morishita, *Curr. Pharm. Des.*, 10: 797-803 (2004)；Gleave及Monia, *Nat. Rev. Cancer*, 5: 468-479(2005)及Patil, *AAPS J.*, 7: E61-E77 (2005))、三螺旋寡核苷酸(Francois等人，*Nucleic Acids Res.*, 16: 11431-11440 (1988)；及Moser及Dervan, *Science*, 238: 645-650 (1987))、核糖酶/脫氧核糖酶(DNA酶)(Kruger等人，*Tetrahymena. Cell*, 31: 147-157 (1982)；Uhlenbeck, *Nature*, 328: 596-600 (1987)；Sigurdsson及Eckstein, *Trends Biotechnol*, 13: 286-289 (1995)；Kumar等人，*Gene Ther.*, 12: 1486-1493 (2005)；Breaker及Joyce, *Chem. Biol.*, 1: 223-229 (1994)；Khachigian, *Curr. Pharm. Biotechnol.*, 5: 337-339 (2004)；Khachigian, *Biochem. Pharmacol*, 68: 1023-1025 (2004)；及Trulzsch及Wood, *J. Neurochem.*, 88: 257-265 (2004))、小干擾RNA/RNAi(Fire等人，*Nature*, 391: 806-811 (1998)；

Montgomery 等人，*Proc. Natl. Acad. Sci. U.S.A.*, 95: 15502-15507 (1998)；Cullen, *Nat. Immunol*, 3: 597-599 (2002)；Hannon, *Nature*, 418: 244-251 (2002)；Bernstein 等人，*Nature*, 409: 363-366 (2001)；Nykanen 等人，*Cell*, 107: 309-321 (2001)；Gilmore 等人，*J. Drug Target.*, 12: 315-340 (2004)；Reynolds 等人，*Nat. Biotechnol*, 22: 326-330 (2004)；Soutschek 等人，*Nature*, 432: 173-178 (2004)；Ralph 等人，*Nat. Med.*, 11: 429-433 (2005)；Xia 等人，*Nat. Med.*, 10: 816-820 (2004)；及 Miller 等人，*Nucleic Acids Res.*, 32: 661-668 (2004))、適體(Ellington及Szostak, *Nature*, 346: 818-822 (1990)；Doudna 等人，*Proc. Natl. Acad. Sci. U.S.A.*, 92: 2355-2359 (1995)；Tuerk及Gold, *Science*, 249: 505-510 (1990)；White 等人，*Mol Ther.*, 4: 567-573 (2001)；Rusconi 等人，*Nature*, 419: 90-94 (2002)；Nimjee 等人，*Mol. Ther.*, 14: 408-415 (2006)；Gragoudas 等人，*N. Engl J. Med.*, 351: 2805-2816 (2004)；Vinores, *Curr. Opin. Mol. Ther.*, 5: 673-679 (2003)；及 Kourlas及Schiller 等人，*Clin. Ther.*, 28: 36-44 (2006))，或誘騙寡核苷酸(decoy oligonucleotide)(Morishita 等人，*Proc. Natl. Acad. Sci. U.S.A.*, 92: 5855-5859 (1995)；Alexander 等人，*J. Am. Med. Assoc*, 294: 2446-2454 (2005)；Mann及Dzau, *J. Clin. Invest.*, 106: 1071-1075 (2000)；及 Nimjee 等人，*Annu. Rev. Med.*, 56: 555-583 (2005))。前述文獻全文係以引用之方式併入本文中，尤其

著重於文獻中與設計、製備及使用抑制性寡核苷酸之方法相關之部分。諸如 Ambion Inc.(Austin, TX)、Dharmacon Inc.(Lafayette, CO)、InvivoGen(San Diego, CA) 及 Molecular Research Laboratories, LLC(Herndon, VA)之供應商產生常規siRNA分子。另外，可使用商業套組製造常規siRNA分子，諸如 SILENCER™ siRNA構築套組 (siRNA Construction Kit)(Ambion Inc., Austin, TX)或psiRNA系統 (psiRNA System)(InvivoGen, San Diego, CA)。

預期穩定、具有高核酸酶抗性、具有合適之藥物動力學以使其在無毒劑量下運輸至靶組織部位且具有穿過質膜之能力的抑制性寡核苷酸可用作治療劑。抑制性寡核苷酸可與靶基因之編碼部分、3'或5'非轉譯區或基因中之內含子序列或靶mRNA中之編碼或內含子序列互補。內含子序列通常不太保守且因此可提供較高特異性。在一實施例中，抑制性寡核苷酸抑制基因產物於一個物種中之表現但不抑制其同源物於另一物種中之表現；在其他實施例中，抑制性寡核苷酸抑制基因於兩個物種(例如人類及靈長類動物，或人類及鼠類)中之表現。

已展示細胞中反義寡核苷酸之組成性表現會經由阻斷轉譯或阻止剪接來抑制基因表現。在某些實施例中，抑制性寡核苷酸能夠在中等或高度嚴格條件下與骨硬化素基因或mRNA之至少8、9、10、11或12個連續鹼基(或其反向鏈)雜交。合適的抑制性寡核苷酸可為單鏈且含有足以與mRNA或DNA分子互補且對mRNA或DNA分子具有特異性

以致其可與該 mRNA 或 DNA 分子雜交且抑制轉錄、剪接或轉譯的(例如)至少 12、15 或 18 個鹼基長之區段。小於 30 個鹼基之長度之互補性通常足夠。

嚴格條件通常將為以下條件：在 pH 7.0 至 8.3 下鹽濃度小於約 1.5 M 鈉離子、通常約 0.01 至 1.0 M 鈉離子濃度(或其他鹽)，且對於短核酸(例如，10 至 50 個核苷酸)，溫度為至少約 30°C；且對於較長核酸(例如，超過 50 個核苷酸)，溫度至少約 60°C。嚴格條件亦可藉由添加諸如甲醯胺之去穩定劑達成。例示性低嚴格度條件包括在 37°C 下在 30% 至 35% 甲醯胺、1 M NaCl、1% SDS(十二基硫酸鈉)之緩衝溶液中雜交且在 50°C 至 55°C 下於 1×SSC 至 2×SSC(20×SSC=3.0 M NaCl/0.3 M 檸檬酸三鈉)中洗滌。例示性中等嚴格度條件包括在 37°C 下在 40% 至 45% 甲醯胺、1.0 M NaCl、1% SDS 中雜交，且在 55°C 至 60°C 下於 0.5×SSC 至 1×SSC 中洗滌。例示性高嚴格度條件包括在 37°C 下在 50% 甲醯胺、1 M NaCl、1% SDS 中雜交且在 60°C 至 65°C 下於 0.1×SSC 中洗滌。雜交持續時間通常小於約 24 小時，通常為約 4 小時至約 12 小時。

在一些情況下，視互補區之長度而定，可容許 1 個、2 個或 2 個以上錯配而不影響抑制功能。在某些實施例中，抑制性寡核苷酸為反義寡核苷酸、抑制性 RNA(包括 siRNA 或 RNAi 或 shRNA)、DNA 酶、核糖酶(視情況錘頭狀核糖酶(hammerhead ribozyme))、適體或其醫藥學上可接受之鹽。在一實施例中，寡核苷酸與編碼美國專利公開案第

20040158045號之SEQ ID NO: 1之核苷酸序列的至少10個鹼基互補。在一實施例中，寡核苷酸靶向位於骨硬化素mRNA之3'非轉譯區附近之核苷酸。

用於設計寡核苷酸之特定序列可為該靶之經表現基因信息內所含之核苷酸的任何相鄰序列。控制抑制性寡核苷酸序列之靶位點之因素包括寡核苷酸之長度、結合親和力及靶序列可接近性。可藉由量測靶蛋白質轉譯及靶相關表型之抑制(例如，培養物中細胞之細胞增殖的抑制)針對抑制活性之能力活體外篩選序列。通常已知可使用反義寡核苷酸靶向RNA之大多數區域(5'及3'非轉譯區、AUG起始、編碼、剪接接頭及內含子)。可使用此項技術已知之程式及算法選擇適當靶序列。另外，可利用經設計以預測指定單鏈核酸序列之二級結構之程式選擇最佳序列，且使該等序列之選擇很可能發生於摺疊mRNA之經暴露單鏈區中。用於設計適當寡核苷酸之方法及組合物可見於(例如)美國專利第6,251,588號中，其內容全文係以引用之方式併入本文中。

可使用硫代磷酸酯反義寡核苷酸。磷酸二酯鍵聯以及雜環或糖之修飾可使效率增加。使用硫代磷酸酯修飾磷酸二酯鍵聯。N3'-P5'胺基磷酸酯鍵聯已描述為使寡核苷酸對核酸酶穩定且增加與RNA之結合。肽核酸(PNA)鍵聯為核糖及磷酸二酯主鏈之完全替換且其對核酸酶穩定，增加與RNA之結合親和力且不允許RNase H裂解。其基本結構亦可經受可使其最佳化為反義組分之修飾。關於雜環之修

飾，已證明某些雜環修飾可增大反義效應而不干擾RNAse H之活性。該等修飾之一實例為C-5噻唑修飾。最後，亦可考慮糖之修飾。2'-O-丙基及2'-甲氧基乙氧基核糖修飾使寡核苷酸在細胞培養物及活體內對核酸酶穩定。

已展示大多數mRNA含有多種二級及三級結構。RNA中之二級結構元件基本上係由同一RNA分子之不同區域之間的沃森-克里克(Watson-Crick)型相互作用形成。重要的二級結構元件包括分子內雙鏈區、髮夾環、雙螺旋RNA中之凸出及內部環。當二級結構元件彼此接觸或與單鏈區接觸產生更為複雜之三維結構時，形成三級結構元件。許多研究員已量測大量RNA雙螺旋結構之結合能量且已推導出一組可用於預測RNA二級結構之規則(參見，例如Jaeger等人，*Proc. Natl. Acad. Sci. USA*, 86:7706 (1989)；及Turner等人，*Annu. Rev. Biophys. Biophys. Chem.* 17:167 (1988))。該等規則適用於鑑別RNA結構元件且尤其適用於鑑別可代表靶向siRNA、核糖酶或反義技術之mRNA區段的單鏈RNA區。

短干擾(si)RNA技術(亦稱為RNAi)通常包括由與特定序列同源之雙鏈RNA(dsRNA)誘導之具有該特定序列之mRNA降解，從而"干擾"相應基因之表現。可藉由引入對應於該基因之整個mRNA或其實質性部分的dsRNA來阻遏任何選定基因。看起來，當表現長dsRNA時，其最初經核糖核酸酶III加工成少至21至22個鹼基對長之較短dsRNA寡核苷酸。因此，siRNA可受相對較短之同源dsRNA之引入

或表現影響。例示性 siRNA 具有具約 21 個核苷酸之有義鏈及反義鏈，其形成雙鏈 RNA 之約 19 個核苷酸且在各 3' 端處具有 2 個核苷酸之突出。實際上，使用相對較短之同源 dsRNA 可具有某些優點。

哺乳動物細胞具有至少兩個受雙鏈 RNA(dsRNA) 影響之路徑。在序列特異性 siRNA 路徑中，如上所述，首先使起始 dsRNA 分解為短干擾 RNA。認為短干擾 RNA 提供靶向特定信使 RNA 以使之降解的序列資訊。相反，非特異性路徑係由具有任何序列之 dsRNA 引發，只要其長度為至少約 30 個鹼基對即可。

非特異性效應因 dsRNA 激活兩種酶而發生：PKR，其活性形式使轉譯起始因子 eIF2 磷酸化以停止所有蛋白質合成；及 2',5' 寡腺苷酸合成酶 (2',5'-AS)，其合成激活 RNase L (一種靶向所有 mRNA 之非特異性酶) 之分子。非特異性路徑可代表宿主對應力或病毒感染之反應，且通常，非特異性路徑之效應較佳經最小化。顯然，誘導非特異性路徑似乎需要較長 dsRNA，且因此預期短於約 30 個鹼基對之 dsRNA 藉由 RNAi 實現基因阻遏 (參見，Hunter 等人，*J. Biol. Chem.*, 250: 409-17 (1975)；Manche 等人，*Mol. Cell. Biol.* 12: 5239-48 (1992)；Minks 等人，*J. Biol. Chem.*, 254: 10180-3 (1979)；及 Elbashir 等人，*Nature*, 411: 494-8 (2001))。

已證明 siRNA 為降低多種細胞類型中之基因表現之有效方式。siRNA 通常使基因之表現降低至低於使用反義技術

所達成之程度且時常完全清除表現(參見Bass, *Nature*, 411:428-9 (2001))。在哺乳動物細胞中，siRNA在比反義實驗中通常使用之濃度低數個數量級之濃度下有效(Elbashir等人，*Nature*, 411:494-8 (2001))。

用於實現RNAi之雙鏈寡核苷酸之長度較佳小於30個鹼基對，例如為約25、24、23、22、21、20、19、18或17個鹼基對長或更短長度，且含有足以與靶mRNA互補以允許與靶mRNA雜交之區段。dsRNA寡核苷酸視情況可包括3'突出端。例示性2-核苷酸3'突出可由任何類型之核糖核苷酸殘基構成且甚至可由2'-脫氧胸苷殘基構成，其降低RNA合成之成本且可增強細胞培養基中及轉染細胞內siRNA之核酸酶抗性(參見Elbashi等人，同上)。例示性dsRNA可經化學方式合成或使用適當表現載體於活體外或活體內產生(參見，例如Elbashir等人，*Genes Dev.*, 15:188-200 (2001))。較長RNA可由此項技術已知之啟動子(諸如T7 RNA聚合酶啟動子)轉錄。

在本發明之某些實施例中，亦可利用具有50、75、100或甚至500個鹼基對或更長之較長dsRNA。實現RNAi之dsRNA之例示性濃度為約0.05 nM、0.1 nM、0.5 nM、1.0 nM、1.5 nM、25 nM或100 nM，但視所治療之細胞之性質、基因靶及熟習此項技術者可容易地辨別之其他因素而定，可利用其他濃度。

siRNA技術之其他組合物、方法及應用提供於美國專利第6,278,039號、第5,723,750號及第5,244,805號中，其全

文係以引用之方式併入本文中。

與 siRNA 相比，shRNA 在沉默壽命及傳遞選擇方面提供優勢。關於綜述，參見例如 Hannon 等人，*Nature*, 431:371-378 (2004)。已報導產生 shRNA 之載體，shRNA 在細胞內經加工成具有類似 siRNA 之性質之短雙螺旋 RNA (Brummelkamp 等人，*Science*, 296: 550-553 (2000)；Paddison 等人，*Genes Dev.*, 16: 948-958 (2002))。該等載體提供在將載體穩定整合至宿主細胞基因組中之後可介導持久基因沉默之基因沉默試劑的可再生源。此外，可容易地將核心沉默"髮夾"盒插入反轉錄病毒、豆狀病毒或腺病毒載體中，從而有助於以經設計以傳遞允許異位 mRNA 表現之 DNA 構築體的無數種方式中之任一種將 shRNA 傳遞至多種細胞類型中 (Brummelkamp 等人，*Cancer Cell*, 2:243-247 (2002)；Dirac 等人，*J. Biol. Chem.*, 278:11731-11734 (2003)；Michiels 等人，*Nat. Biotechnol.*, 20:1154-1157 (2002)；Stegmeie 等人，*Proc. Natl. Acad. Sci. USA*, 102:13212-13217 (2005)；Khvorova 等人，*Cell*, 115:209-216 (2003))。

髮夾可組織為左手髮夾(亦即，5'-反義-環-有義-3')或右手髮夾(亦即，5'-有義-環-反義-3')。視髮夾之組織而定，siRNA 亦可在有義鏈或反義鏈之 5' 或 3' 端處含有突出。較佳地，若存在任何突出，則其在髮夾的 3' 端且包含 1 至 6 個之間個數的鹼基。突出可未經修飾，或可含有一或多個特異性或穩定修飾，諸如 2' 位之鹵素或 O-烷基修飾，或核苷酸

間修飾，諸如硫代磷酸酯、二硫代磷酸酯或膦酸甲酯修飾。突出可為核糖核酸、脫氧核糖核酸或核糖核酸與脫氧核糖核酸之組合。

另外，髮夾可進一步在5'最末端核苷酸處包含磷酸基。5'最末端核苷酸之磷酸化係指存在一或多個連接至5'末端核苷酸之糖部分之5'碳的磷酸基。較佳在Dicer加工後將形成反義鏈之區域之5'端處僅存在一個磷酸基。在一例示性實施例中，右手髮夾可包括不具有5'磷酸基之5'端(亦即，有義區之游離5'端)，或可具有以阻止磷酸化之方式修飾之有義區的游離5'最末端核苷酸之5'碳。此可以多種方法達成，該等方法包括(但不限於)添加磷酸化阻斷基(例如，5'-O-烷基)，或消除5'-OH官能基(例如，5'最末端核苷酸為5'-脫氧核苷酸)。在髮夾為左手髮夾的情況下，較佳5'最末端核苷酸之5'碳位置經磷酸化。

莖長大於26個鹼基對的髮夾可經Dicer加工以使某些部分不為有助於mRNA降解之所得siRNA的部分。因此，可包含有義核苷酸之第一區及可包含反義核苷酸之第二區亦可含有互補(或至少大體上彼此互補)但與或不與靶mRNA相同或互補之核苷酸伸長。雖然shRNA之莖可由除突出外互補或部分互補之反義及有義鏈構成，但shRNA亦可包括以下：(1)位於最終Dicer切割位點遠端之分子部分，其含有與靶mRNA大體上互補/同源之區域；及(2)鄰近Dicer切割位點之莖區(亦即，鄰近環之區域)，其與靶mRNA無關或僅與靶mRNA部分相關(例如，互補/同源)。該第二區之

核苷酸含量可基於若干參數(包括(但不限於)熱力學特性或分布)選擇。

經修飾 shRNA 可保留 Dicer 加工後雙螺旋中之修飾。在例示性實施例中，在髮夾為在分子 3' 端含有 2-6 個核苷酸突出之右手髮夾(例如，5'-S-環-AS-3')的情況下，可將 2'-O-甲基修飾添加至髮夾 5' 端之 2 位、1 位及 2 位或 1 位、2 位及 3 位處之核苷酸。具有該構型的髮夾的 Dicer 加工亦可保留完整的有義鏈 5' 端，因此保持 Dicer 加工後雙螺旋之化學修飾模式。該構型中 3' 突出之存在可尤其有利，因為含有指定修飾模式之鈍端分子可由 Dicer 以移除攜帶 2' 修飾之核苷酸之方式進一步加工。在存在/保留 3' 突出之情況下，所得攜帶有義修飾核苷酸之雙螺旋在沉默特異性及功能性方面可具有高度有利的特性。例示性修飾模式之實例詳細描述於美國專利公開案第 20050223427 號及國際專利公開案第 WO 2004/090105 及 WO 2005/078094 號中，其各自揭示內容之全文係以引用之方式併入本文中。

shRNA 可包含隨機或根據任何合理設計選擇程序選擇的序列。舉例而言，合理的設計算法描述於國際專利公開案第 WO 2004/045543 號及美國專利公開案第 20050255487 號中，其揭示內容之全文係以引用的方式併入本文中。另外，可能希望完全或部分基於平均內部穩定性分布("AISP")或區域內部穩定性分布("RISP")選擇可有助於由細胞機器接取或加工的序列。

核糖酶為能夠催化 mRNA 特異性裂解從而阻止轉譯之酶

促RNA分子(關於綜述，參見Rossi, *Current Biology*, 4:469-411 (1994))。核糖酶作用的機制包括核糖酶分子與互補靶RNA之序列特異性雜交，繼之以內切核苷酸裂解事件。核糖酶分子較佳包括(1)一或多個與靶mRNA互補的序列及(2)負責mRNA裂解之熟知催化序列或功能相當之序列(參見，例如美國專利第5,093,246號，其全文係以引用之方式併入本文中)。

雖然可使用在位點特異性識別序列處裂解mRNA之核糖酶破壞靶mRNA，但另外可使用錘頭狀核糖酶。錘頭狀核糖酶在與靶mRNA形成互補鹼基對之側接區指定之位置處裂解mRNA。靶mRNA較佳具有以下具有兩個鹼基的序列：5'-UG-3'。錘頭狀核糖酶之構築及產生在此項技術中為熟知的且較為完整地描述於Haseloff及Gerlach, *Nature*, 334:585-591(1988)及國際專利公開案第WO 89/05852號中，其內容全文係以引用之方式併入本文中。

靶向核糖酶之基因可含有與靶mRNA之兩個區互補之雜交區，該兩個區各自為至少5、6、7、8、9、10、11、12、13、14、15、16、17、18、19或20個相鄰核苷酸(但兩者之長度不需要相同)。

可將錘頭狀核糖酶序列嵌入諸如轉移核糖核酸(tRNA)之穩定RNA中以增加活體內裂解效率(Perriman等人, *Proc. Natl. Acad. Sci. USA*, 92:6175-79 (1995); de Feyter及Gaudron, *Methods in Molecular Biology*, 第74卷，第43章，"Expressing Ribozymes in Plants," Turner, P. C.(編),

Humana Press Inc., Totowa, N.J.)。此項技術中尤其熟知RNA聚合酶III介導之tRNA融合核糖酶之表現(參見Kawasaki等人, *Nature*, 393:284-9 (1998); Kuwabara等人, *Nature Biotechnol*, 16:961-5 (1998); 及 Kuwabara等人, *Mol. Cell*, 2:617-27 (1998); Koseki等人, *J. Virol.*, 73:1868-77 (1999); Kuwabara等人, *Proc. Natl. Acad. Sci. USA*, 96:1886-91 (1999); Tanabe等人, *Nature*, 406:473-4 (2000))。給定靶cDNA序列中通常存在若干潛在錘頭狀核糖酶裂解位點。核糖酶較佳經工程改造以使裂解識別位點位於靶mRNA之5'端附近,從而增加效率且最小化非功能性mRNA轉錄物之細胞內積聚。此外,使用位於編碼靶mRNA之不同部分之靶序列中的任何裂解識別位點將允許選擇性靶向一個或另一個靶基因。

本發明方法中使用之核糖酶亦包括RNA內切核糖核酸酶("Cech型核糖酶"),諸如嗜熱四膜蟲(*Tetrahymena thermophila*)中天然存在之內切核糖核酸酶(稱為IVS或L-19 IVS RNA)且其廣泛描述於以下文獻中:Zaug等人, *Science*, 224:574-578 (1984); Zaug, 等人, *Science*, 231:470-475 (1986); Zaug等人, *Nature*, 324:429-433 (1986); 國際專利公開案第WO 88/04300號;及 Been等人, *Cell*, 47:207-216 (1986)。Cech型核糖酶具有與靶RNA序列雜交且之後發生靶RNA裂解之8鹼基對活性位點。在一實施例中,本發明方法採用彼等靶向存在於靶基因或核酸序列中之8鹼基對活性位點序列之Cech型核糖酶。

核糖酶可由經修飾寡核苷酸(例如，供改進穩定性、靶向等)構成且可經化學方式合成或經由表現載體產生。因為不同於反義分子，核糖酶具有催化性，所以效率需要較低細胞內濃度。另外，在某些實施例中，可首先藉由鑑別足以引起RNAi有效敲除之序列部分來設計核糖酶。隨後可向核糖酶中併入具有相同序列之部分。

另外，可藉由靶向與基因之調控區(亦即，啟動子及/或強化子)互補之脫氧核糖核苷酸序列以形成阻止體內靶細胞中基因轉錄之三螺旋結構來降低靶基因表現。(大體而言，參見 Helene, C, *Anticancer Drug Des.*, 6:569-84 (1991); Helene 等人, *Ann. N.Y. Acad. Sci.*, 660:27-36 (1992); 及 Maher, L. J, *Bioassays*, 14:807-15(1992))。

用於三螺旋形成以抑制轉錄之核酸分子較佳為單鏈且由脫氧核糖核苷酸構成。該等寡核苷酸之鹼基組成應經由霍氏鹼基配對規則(Hoogsteen base pairing rule)促進三螺旋形成，該等規則通常需要相當大的嘌呤或嘧啶伸長存在於雙螺旋之一條鏈上。核苷酸序列可為基於嘧啶的，其將產生橫跨所得三螺旋之三個締合鏈之TAT及CGC三聯體(triplet)。富集嘧啶之分子與雙螺旋之單鏈之富集嘌呤的區域在與該鏈平行之方向上鹼基互補。另外，可選擇富集嘌呤(例如含有G殘基伸長)之核酸分子。該等分子將與富含GC對之DNA雙螺旋形成三螺旋，其中大部分嘌呤殘基位於靶雙螺旋之單鏈上，產生橫跨三螺旋中之三個鏈之CGC三聯體。

或者，可藉由產生所謂的"之字形(switchback)"核酸分子增加可靶向三螺旋形成之靶序列。之字形分子係以交替5'-3、3'-5'方式合成，以致其與雙螺旋之第一鏈鹼基配對，隨後與另一鏈鹼基配對，從而消除相當大的嘌呤或嘧啶伸長存在於雙螺旋之一條鏈上的必要性。

此外，可使用DNA酶抑制諸如骨硬化素基因之靶基因之表現。DNA酶併有反義與核糖酶技術之某些機械特徵。設計DNA酶以使其識別極類似反義寡核苷酸之特定靶核酸序列。然而，其亦具催化性且特異性裂解靶核酸。

DNA酶包括兩種由桑托羅(Santoro)及喬伊斯(Joyce)鑑別之基本類型(參見，例如美國專利第6,110,462號)。10-23 DNA酶包含連接兩個臂之環結構。該兩個臂藉由識別特定靶核酸序列提供特異性，而環結構在生理條件下提供催化功能。

唯一或大體上唯一的序列較佳為具有約18至22個核苷酸之富G/C區段。高G/C含量有助於確保DNA酶與靶序列之間的較強相互作用。將使酶靶向信使之特異性反義識別序列可在DNA酶之兩個臂之間分配。

製備且投與DNA酶之方法可見於(例如)美國專利第6,110,462號。另外，熟習此項技術者應認識到，與反義寡核苷酸類似，DNA酶可視情況經修飾以改進穩定性且改進抗降解性。

抑制性寡核苷酸可直接投與細胞或經由載體(包括病毒載體或質體)轉型或轉染傳遞至細胞中，該載體中已置放

具有適當調控序列(包括啟動子)之編碼抑制性寡核苷酸之DNA以使抑制性寡核苷酸於想要之細胞中表現。已知方法包括標準瞬時轉染、穩定轉染及使用反轉錄病毒至腺病毒範圍內之病毒傳遞。涵蓋藉由複製或複製缺陷型載體傳遞核酸抑制劑。表現也可由組成性或可誘導性啟動子系統驅動(Paddison 等人, *Methods Mol. Biol.*, 265:85-100 (2004))。在其他實施例中,表現可受組織或發育特異性啟動子控制。

● 舉例而言,可藉由使用諸如Lipofectamine 2000(Life Technologies)或Oligofectamine(Life Technologies)之載劑組合物轉染引入載體。hGFP編碼pAD3共轉染後,可使用螢光顯微鏡術檢查哺乳動物細胞株之轉染效率(Kehlenback 等人, *J. Cell Biol.*, 141:863-74(1998))。

傳遞途徑應為如根據上述標準所量測提供最佳抑制效應之途徑。陽離子脂質體介導之傳遞、反轉錄病毒載體之傳遞及直接傳遞為有效的。

● 抑制性寡核苷酸之效力可在阻遏新蛋白質合成後轉換內源池(endogenous pool)足夠時間後用多種檢定中之任一種評定,該等檢定包括逆轉錄酶聚合酶鏈反應,或測定現有人類骨硬化素mRNA之含量之北方墨點分析(Northern blot analysis),或使用識別人類骨硬化素蛋白質之抗體之西方墨點分析(Western blot analysis)。

本發明進一步描述於下文實例中。該等實例僅用於說明本發明且不意欲以任何方式限制本發明之範疇。

實例

該實例描述骨硬化素結合劑降低骨再吸收標記之含量且增加一或多個骨形成標記之含量的活體內研究。

對健康男性及絕經後女性進行單中心隨機雙盲安慰劑對照之遞增單劑量研究。將約72位個體編入六個劑量組中的一個中。對於組1、2、3a、4、5及6a，使8位健康絕經後女性隨機接收3:1之比率之經由皮下注射的骨硬化素結合劑或安慰劑，劑量含量分別為0.1 mg/kg、0.3 mg/kg、1 mg/kg、3 mg/kg、5 mg/kg或10 mg/kg。在組3b及6b中，使8位健康男性以3:3:1:1之比率(骨硬化素結合劑靜脈內:骨硬化素結合劑皮下:安慰劑靜脈內:安慰劑皮下)經靜脈內及皮下接收骨硬化素結合劑或安慰劑，劑量含量分別為1 mg/kg或10 mg/kg(降低至5 mg/kg)。對於組3c及6c，使4位健康絕經後女性以3:1比率隨機經靜脈內接收骨硬化素結合劑或安慰劑，劑量含量分別為1 mg/kg或10 mg/kg(降低至5 mg/kg)。

藉由在投藥之前、隨後在投藥後12週內至少每週量測骨再吸收標記及骨形成標記之含量來監測抗骨硬化素療法。監測在向健康絕經後女性單劑量皮下投與骨硬化素結合劑後P1NP及BSAP之含量(參見圖1及2)。給予0.1 mg/kg及0.3 mg/kg之個體享有P1NP或BSAP含量之最小升高(例如，含量增加小於20%)。

給予1 mg/kg之個體之P1NP含量到第10天時增加約20%且在約第56天時漸漸減少至基線，而BSAP含量在第14天

時達到峰值，達基線以上約30%。給予3 mg/kg之個體之P1NP及BSAP含量在第21天時達到峰值，自基線增加約100%(P1NP)及60%(BSAP)，且在約第56天時回至基線。在投與5 mg/kg之個體中，P1NP之含量在投藥後第14天上升至基線以上約140%且在第77天時保持升高。換言之，到治療後兩週時，P1NP之含量增加約140%。BSAP上升至基線以上約115%且在第84天時保持升高。類似地，投與10 mg/kg在約第28天時引發P1NP含量之180%增加。P1NP含量在整個監測期間保持升高。投與10 mg/kg之個體在第21天時顯現BSAP含量之峰值增加(投藥後3週達基線之125%)，其在第84天時亦保持升高。該研究之結果於圖1及2中說明。

亦在向健康絕經後女性單劑量皮下投與骨硬化素結合劑後監測骨鈣素(參見圖3)。給予小於1 mg/kg之個體經歷骨鈣素之少許升高。在投與1 mg/kg之患者中，骨鈣素含量波動，在第21天及第35天時達到峰值，達基線以上約30%。在投與3 mg/kg之個體中，骨鈣素含量在第21天時達到峰值，達基線以上約100%，且直至約第56天含量仍保持升高。同樣地，投與5 mg/kg骨硬化素結合劑導致在第28天時骨鈣素含量增加140%，該等含量在第84天時仍保持。給予10 mg/kg之個體在第35天時顯現達到基線以上約180%之峰值骨鈣素含量。直至至少約第77天時，骨鈣素含量仍保持高於基線。

亦監測骨再吸收標記sCTx之含量(參見圖4)。投與安慰

劑及 0.1 mg/kg 之個體顯現 sCTX 含量之適度降低(例如，小於 20%)。到第 21 天時，投與 0.3 mg/kg 骨硬化素結合劑使 sCTX 含量降低約 20%(亦即，到治療後兩週時，sCTX 含量降低約 20%)。在給予 1 mg/kg 之個體中，含量波動，但在第 10 天、第 28 天及第 49 天時達到基線以下約 30%。在投與 3 mg/kg、5 mg/kg 及 10 mg/kg 之個體中，含量在第 14 天時降至最低，分別達至基線以下約 35%、55% 及 55%，且當此後監測時，含量仍保持在基線以下。所有所監測之生物標記之含量的比較提供於圖 5 中。

在向健康絕經後女性皮下給予單劑量骨硬化素結合劑後，監測血清離子鈣含量(參見圖 6)。值得注意地是，離子鈣含量在任何劑量下均不顯著波動。實際上，所有個體(包括接收安慰劑之個體)在監測期間均經歷約 5% 之血清離子鈣之瞬時適度降低。

最後，量測接收 1 mg/kg、3 mg/kg、5 mg/kg 或 10 mg/kg 骨硬化素結合劑之健康絕經後女性之脊骨及髖部的骨礦物質密度(參見圖 7)。例如在第 28 天、第 56 天及第 84 天時，尤其在接收 5 mg/kg 及 10 mg/kg 之患者之脊骨中觀察到 BMD 之顯著增加。髖部 BMD 增加小於脊骨 BMD 之增加，但 BMD 在第 56 天時於投與 3 mg/kg、5 mg/kg 及 10 mg/kg 之患者中升高。BMD 在第 84 天時於給予 5 mg/kg 及 10 mg/kg 之患者中進一步升高。

該實例說明本發明方法減少骨再吸收標記之含量、提昇骨形成標記之含量及增加骨礦物質密度而不顯著改變血清

鈣的能力。單劑量骨硬化素結合劑之治療作用歷時長久，且在治療後第84天(12週)時繼續觀察到骨形成標記含量之增加及骨再吸收標記含量之減少。此外，本文中所述之資料提出本發明之治療功效與其他治療相比具有顯著優點："解除"骨形成與骨再吸收之間的聯繫從而使活體內骨形成及礦化最大化。

本文中所引用之所有文獻(包括專利、專利申請案、文獻公開案及其類似物)之全文係以引用之方式併入本文中。

雖然本發明已著重於較佳實施例加以描述，但一般熟習此項技術者將顯而易見，可使用較佳化合物及方法之變更，且預期可以除本文特定描述以外之方式實施本發明。因此，本發明包括涵蓋於如下文申請專利範圍所界定之本發明之精神及範疇內的所有修改。

【圖式簡單說明】

圖1為投與各種單次劑量之骨硬化素結合劑後健康絕經後女性的1型原膠原N-末端延長(P1NP)含量與基線及安慰劑P1NP含量相比之變化百分率與時間(天)之關係的曲線圖。

圖2為投與各種單次劑量之骨硬化素結合劑後健康絕經後女性的骨特異性鹼性磷酸酶(BSAP)含量與基線及安慰劑BSAP含量相比之變化百分率與時間(天)之關係的曲線圖。

圖3為投與各種單次劑量之骨硬化素結合劑後健康絕經後女性的骨鈣素含量與基線及安慰劑骨鈣素含量相比之變

化百分率與時間(天)之關係的曲線圖。

圖4為投與各種單次劑量之骨硬化素結合劑後健康絕經後女性的1型膠原血清C末端端肽(CTX)含量與基線及安慰劑血清CTX含量相比之變化百分率與時間(天)之關係的曲線圖。

圖5為投與5 mg/kg或10 mg/kg之單次劑量的骨硬化素結合劑後健康絕經後女性的骨鈣素、BSAP、P1NP及CTX含量與基線及安慰劑含量相比之變化百分率與時間(天)之關係的曲線圖。

圖6為投與各種單次劑量之骨硬化素結合劑後健康絕經後女性的血清鈣含量與基線及安慰劑血清鈣含量相比之變化百分率與時間(天)之關係的曲線圖。

圖7為投與各種單次劑量之骨硬化素結合劑後健康絕經後女性的骨礦物質密度與基線及安慰劑相比之變化百分率與時間(天)之關係的曲線圖。

序列表

<110> 美商安美基公司

<120> 抑制骨再吸收的方法

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35 40 45

Thr Lys Asp Val Ser Glu Tyr Ser Cys Arg Glu Leu His Phe Thr Arg
50 55 60

Tyr Val Thr Asp Gly Pro Cys Arg Ser Ala Lys Pro Val Thr Glu Leu
65 70 75 80

Val Cys Ser Gly Gln Cys Gly Pro Ala Arg Leu Leu Pro Asn Ala Ile
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Gly Arg Gly Lys Trp Trp Arg Pro Ser Gly Pro Asp Phe Arg Cys Ile
100 105 110

Pro Asp Arg Tyr Arg Ala Gln Arg Val Gln Leu Leu Cys Pro Gly Gly
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Glu Ala Pro Arg Ala Arg Lys Val Arg Leu Val Ala Ser Cys Lys Cys
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20 25 30

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35 40 45

Tyr Gly Ser Ser Asn Leu Glu Asp Gly Val Pro Ser Arg Phe Ser Gly

50 55 60

Ser Arg Tyr Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Glu Asp
65 70 75 80

Glu Asp Leu Ala Thr Tyr Phe Cys Leu Gln His Ser Tyr Leu Pro Tyr
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Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg Ala Asp Ala Ala
100 105 110

Pro Thr Val Ser Ile Phe Pro Pro Ser Ser Glu Gln Leu Thr Ser Gly
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Gly Ala Ser Val Val Cys Phe Leu Asn Asn Phe Tyr Pro Lys Asp Ile
130 135 140

Asn Val Lys Trp Lys Ile Asp Gly Ser Glu Arg Gln Asn Gly Val Leu
145 150 155 160

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gaagatctgg caacttattt ctgtctacaa catagttatc tcccgtacac gttcggaggg 300

gggaccaagc tggaataaaa acgggctgat gctgcaccaa ctgtatccat ctccccacca 360

tccagtgagc agttaacatc tggaggtgcc tcagtcgtgt gcttcttgaa caacttctac 420

cccaaagaca tcaagtcaa gtggaagatt gatggcagtg aacgacaaaa tggcgtcctg 480

aacagttgga ctgatcagga cagcaaagac agcacctaca gcatgagcag caccctcacg 540

ttgaccaagg acgagtatga acgacataac agctatacct gtgaggccac tcacaagaca 600

tcaacttcac ccattgtcaa gagcttcâac aggaatgagt gttag 645

<210> 9
<211> 236
<212> PRT

<213> 小家鼠

<400> 9

Met Asn Thr Arg Ala Pro Ala Glu Phe Leu Gly Phe Leu Leu Leu Trp
1 5 10 15
Phe Leu Gly Ala Arg Cys Asp Val Gln Met Ile Gln Ser Pro Ser Ser
20 25 30
Leu Ser Ala Ser Leu Gly Asp Ile Val Thr Met Thr Cys Gln Ala Ser
35 40 45
Gln Gly Thr Ser Ile Asn Leu Asn Trp Phe Gln Gln Lys Pro Gly Lys
50 55 60
Ala Pro Lys Leu Leu Ile Tyr Gly Ser Ser Asn Leu Glu Asp Gly Val
65 70 75 80
Pro Ser Arg Phe Ser Gly Ser Arg Tyr Gly Thr Asp Phe Thr Leu Thr
85 90 95
Ile Ser Ser Leu Glu Asp Glu Asp Leu Ala Thr Tyr Phe Cys Leu Gln
100 105 110
His Ser Tyr Leu Pro Tyr Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile
115 120 125
Lys Arg Ala Asp Ala Ala Pro Thr Val Ser Ile Phe Pro Pro Ser Ser
130 135 140
Glu Gln Leu Thr Ser Gly Gly Ala Ser Val Val Cys Phe Leu Asn Asn
145 150 155 160
Phe Tyr Pro Lys Asp Ile Asn Val Lys Trp Lys Ile Asp Gly Ser Glu
165 170 175
Arg Gln Asn Gly Val Leu Asn Ser Trp Thr Asp Gln Asp Ser Lys Asp
180 185 190
Ser Thr Tyr Ser Met Ser Ser Thr Leu Thr Leu Thr Lys Asp Glu Tyr
195 200 205
Glu Arg His Asn Ser Tyr Thr Cys Glu Ala Thr His Lys Thr Ser Thr
210 215 220
Ser Pro Ile Val Lys Ser Phe Asn Arg Asn Glu Cys
225 230 235

<210> 10

<211> 711

<212> DNA

<213> 小家鼠

<400> 10
atgaacacga gggccccgc tgagttccctt gggttcctgt tgctctggtt ttaggtgcc 60
agatgtgatg tccagatgat tcagtcctcca tcctccctgt ctgcatcttt gggagacata 120
gtcaccatga ctgcccaggc aagtcagggc actagcatta atttaactg gtttcagcaa 180

aaaccaggga aggtccttaa gctcctgata tatggttcaa gcaacttgga agatggggtc 240
ccatcaaggt tcaatggcag tagatatggg acagatttca ctctcacat cagcagcctg 300
gaggatgaag atctggcaac ttatttctgt ctacaacata gttatctccc gtacacgttc 360
ggagggggga ccaagctgga aataaaacgg gctgatgctg caccaactgt atccatcttc 420
ccaccatcca gtgagcagtt aacatctgga ggtgcctcag tegtgtgctt cttgaacaac 480
ttctacccca aagacatcaa tgtcaagtgg aagattgatg gcagtgaacg acaaaatggc 540
gtcctgaaca gtgggactga tcaggacagc aaagacagca cctacagcat gagcagcacc 600
ctcacgttga ccaaggacga gtaatgaacga cataacagct atacctgtga ggccactcac 660
aagacatcaa cttcacccat tgtcaagagc ttcaacagga atgagtgtta g 711

<210> 11
<211> 443
<212> PRT
<213> 小家鼠

<400> 11

Glu Val Gln Leu Gln Gln Ser Gly Pro Glu Leu Val Thr Pro Gly Ala
1 5 10 15
Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp His
20 25 30
Tyr Met Ser Trp Val Lys Gln Ser His Gly Lys Ser Leu Glu Trp Ile
35 40 45
Gly Asp Ile Asn Pro Tyr Ser Gly Glu Thr Thr Tyr Asn Gln Lys Phe
50 55 60
Lys Gly Thr Ala Thr Leu Thr Val Asp Lys Ser Ser Ser Ile Ala Tyr
65 70 75 80
Met Glu Ile Arg Gly Leu Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys
85 90 95
Ala Arg Asp Asp Tyr Asp Ala Ser Pro Phe Ala Tyr Trp Gly Gln Gly
100 105 110
Thr Leu Val Thr Val Ser Ala Ala Lys Thr Thr Pro Pro Ser Val Tyr
115 120 125
Pro Leu Ala Pro Gly Ser Ala Ala Gln Thr Asn Ser Met Val Thr Leu
130 135 140
Gly Cys Leu Val Lys Gly Tyr Phe Pro Glu Pro Val Thr Val Thr Trp
145 150 155 160
Asn Ser Gly Ser Leu Ser Ser Gly Val His Thr Phe Pro Ala Val Leu
165 170 175
Gln Ser Asp Leu Tyr Thr Leu Ser Ser Ser Val Thr Val Pro Ser Ser
180 185 190

Thr Trp Pro Ser Glu Thr Val Thr Cys Asn Val Ala His Pro Ala Ser
195 200 205

Ser Thr Lys Val Asp Lys Lys Ile Val Pro Arg Asp Cys Gly Cys Lys
210 215 220

Pro Cys Ile Cys Thr Val Pro Glu Val Ser Ser Val Phe Ile Phe Pro
225 230 235 240

Pro Lys Pro Lys Asp Val Leu Thr Ile Thr Leu Thr Pro Lys Val Thr
245 250 255

Cys Val Val Val Asp Ile Ser Lys Asp Asp Pro Glu Val Gln Phe Ser
260 265 270

Trp Phe Val Asp Asp Val Glu Val His Thr Ala Gln Thr Gln Pro Arg
275 280 285

Glu Glu Gln Phe Asn Ser Thr Phe Arg Ser Val Ser Glu Leu Pro Ile
290 295 300

Met His Gln Asp Trp Leu Asn Gly Lys Glu Phe Lys Cys Arg Val Asn
305 310 315 320

Ser Pro Ala Phe Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Thr Lys
325 330 335

Gly Arg Pro Lys Ala Pro Gln Val Tyr Thr Ile Pro Pro Pro Lys Glu
340 345 350

Gln Met Ala Lys Asp Lys Val Ser Leu Thr Cys Met Ile Thr Asp Phe
355 360 365

Phe Pro Glu Asp Ile Thr Val Glu Trp Gln Trp Asn Gly Gln Pro Ala
370 375 380

Glu Asn Tyr Lys Asn Thr Gln Pro Ile Met Asp Thr Asp Gly Ser Tyr
385 390 395 400

Phe Ile Tyr Ser Lys Leu Asn Val Gln Lys Ser Asn Trp Glu Ala Gly
405 410 415

Asn Thr Phe Thr Cys Ser Val Leu His Glu Gly Leu His Asn His His
420 425 430

Thr Glu Lys Ser Leu Ser His Ser Pro Gly Lys
435 440

<210> 12
<211> 1332
<212> DNA
<213> 小家鼠

<400> -12
gaggtccagc tgcaacagtc tggacctgaa ctgggtgacgc ctggggcttc agtgaagata 60
tcttgtaagg cttctggata cacattcact gaccactaca tgagctgggt gaagcagagt 120
catggaaaaa gccttgagtg gattggagat attaatccct attctgggtga aactacctac 180

aaccagaagt tcaagggcac ggccacattg actgtagaca agtcttccag tatagcctac 240
atggagatcc ggggcctgac atctgaggac tctgcagtct attactgtgc aagagatgat 300
tacgacgcct ctccgtttgc ttactggggc caagggactc tggtcactgt ctctgcagcc 360
aaaacgacac ccccatctgt ctatccactg gcccctggat ctgctgcccc aactaactcc 420
atggtgaccc tgggatgcct ggtcaagggc tatttccctg agccagtgc agtgacctgg 480
aactctggat cctgtgccag cgggtgtgac accttcccag ctgtcctgca gtctgacctc 540
tacactctga gcagctcagt gactgtcccc tccagcacct ggcccagcga gaccgtcacc 600
tgcaacgttg cccaccggc cagcagcacc aagggtggaca agaaaattgt gcccagggat 660
tgtggttgta agccttgcat atgtacagtc ccagaagtat catctgtctt caicttcccc 720
ccaaagccca aggatgtgct caccattact ctgactccta aggtcacgtg tgtgtggta 780
gacatcagca aggatgatcc cgaggtcag ttcagctggt ttgtagatga tgtggaggtg 840
cacacagctc agacgcaacc ccgggaggag cagttaaca gcactttccg ctgagtcagt 900
gaacttccca tcatgcacca ggactggctc aatggcaagg agttcaaatg cagggtcaac 960
agtccagctt tccctgcccc catcgagaaa accatctcca aaaccaaagg cagaccgaag 1020
gtccacagg tgtacacat tccacctccc aaggagcaga tggccaagga taaagtcagt 1080
ctgacctgca tgataacaga cttcttcctt gaagacatta ctgtggagtg gcagtggat 1140
gggcagccag cggagaacta caagaacact cagcccatca tggacacaga tggctcttac 1200
ttcatctaca gcaagctcaa tgtgcagaag agcaactggg aggcaggaaa tactttcacc 1260
tgctctgtgt tacatgaggg cctgcacaac caccatactg agaagagcct ctcccactct 1320
cctggtaaat ga 1332

<210> 13
<211> 462
<212> PRT
<213> 小家鼠

<400> 13

Met Arg Cys Arg Trp Ile Phe Leu Phe Leu Leu Ser Gly Thr Ala Gly
1 5 10 15

Val Leu Ser Glu Val Gln Leu Gln Gln Ser Gly Pro Glu Leu Val Thr
20 25 30

Pro Gly Ala Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Thr Phe
35 40 45

Thr Asp His Tyr Met Ser Trp Val Lys Gln Ser His Gly Lys Ser Leu
50 55 60

Glu Trp Ile Gly Asp Ile Asn Pro Tyr Ser Gly Glu Thr Thr Tyr Asn
65 70 75 80

Gln Lys Phe Lys Gly Thr Ala Thr Leu Thr Val Asp Lys Ser Ser Ser
85 90 95

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

Tyr Tyr Cys Ala Arg Asp Asp Tyr Asp Ala Ser Pro Phe Ala Tyr Trp
 115 120 125
 Gly Gln Gly Thr Leu Val Thr Val Ser Ala Ala Lys Thr Thr Pro Pro
 130 135 140
 Ser Val Tyr Pro Leu Ala Pro Gly Ser Ala Ala Gln Thr Asn Ser Met
 145 150 155 160
 Val Thr Leu Gly Cys Leu Val Lys Gly Tyr Phe Pro Glu Pro Val Thr
 165 170 175
 Val Thr Trp Asn Ser Gly Ser Leu Ser Ser Gly Val His Thr Phe Pro
 180 185 190
 Ala Val Leu Gln Ser Asp Leu Tyr Thr Leu Ser Ser Ser Val Thr Val
 195 200 205
 Pro Ser Ser Thr Trp Pro Ser Glu Thr Val Thr Cys Asn Val Ala His
 210 215 220
 Pro Ala Ser Ser Thr Lys Val Asp Lys Lys Ile Val Pro Arg Asp Cys
 225 230 235 240
 Gly Cys Lys Pro Cys Ile Cys Thr Val Pro Glu Val Ser Ser Val Phe
 245 250 255
 Ile Phe Pro Pro Lys Pro Lys Asp Val Leu Thr Ile Thr Leu Thr Pro
 260 265 270
 Lys Val Thr Cys Val Val Val Asp Ile Ser Lys Asp Asp Pro Glu Val
 275 280 285
 Gln Phe Ser Trp Phe Val Asp Asp Val Glu Val His Thr Ala Gln Thr
 290 295 300
 Gln Pro Arg Glu Glu Gln Phe Asn Ser Thr Phe Arg Ser Val Ser Glu
 305 310 315 320
 Leu Pro Ile Met His Gln Asp Trp Leu Asn Gly Lys Glu Phe Lys Cys
 325 330 335
 Arg Val Asn Ser Pro Ala Phe Pro Ala Pro Ile Glu Lys Thr Ile Ser
 340 345 350
 Lys Thr Lys Gly Arg Pro Lys Ala Pro Gln Val Tyr Thr Ile Pro Pro
 355 360 365
 Pro Lys Glu Gln Met Ala Lys Asp Lys Val Ser Leu Thr Cys Met Ile
 370 375 380
 Thr Asp Phe Phe Pro Glu Asp Ile Thr Val Glu Trp Gln Trp Asn Gly
 385 390 395 400
 Gln Pro Ala Glu Asn Tyr Lys Asn Thr Gln Pro Ile Met Asp Thr Asp

	405	410	415
Gly Ser Tyr Phe Ile Tyr Ser Lys Leu Asn Val Gln Lys Ser Asn Trp			
	420	425	430
Glu Ala Gly Asn Thr Phe Thr Cys Ser Val Leu His Glu Gly Leu His			
	435	440	445
Asn His His Thr Glu Lys Ser Leu Ser His Ser Pro Gly Lys			
	450	455	460

<210> 14
 <211> 1389
 <212> DNA
 <213> 小家鼠

<400> 14
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 gtccagctgc aacagtctgg acctgaactg gtgacgcctg gggcttcagt gaagatatct 120
 tgttaaggctt ctggatacac attcactgac cactacatga gctgggtgaa gcagagtcac 180
 ggaaaaagcc ttgagtggat tggagatatt aatccctatt ctggtgaaac tacctacaac 240
 cagaagttca agggcacggc cacattgact gtagacaagt ctccagtat agcctacatg 300
 gagatccgcg gcctgacatc tgaggactct gcagtctatt actgtgcaag agatgattac 360
 gacgcctctc cgtttgctta ctggggccaa gggactctgg tcaactgtctc tgcagccaaa 420
 acgacacccc catctgtcta tccactggcc cctggatctg ctgcccacaa taactccatg 480
 gtgaccctgg gatgcctggt caagggtctat ttccctgagc cagtgcacgt gacctggaac 540
 tctggatccc tgtccagcgg tgtgcacacc tcccagctg tctgcagtc tgacctctac 600
 actctgagca gctcagtgac tgtccctcc agcacctggc ccagcgagac cgtcacctgc 660
 aacgttgccc acccggccag cagcaccaag gtggacaaga aaattgtgcc cagggttgt 720
 ggttgtaagc ctgcatatg tacagtccca gaagtatcat ctgtcttcat cttccccca 780
 aagcccaagg atgtgctcac cattactctg actcctaagg tcacgtgtgt tgtggtagac 840
 atcagcaagg atgatccga ggtccagttc agctggttg tagatgatgt ggaggtgcac 900
 acagctcaga cgcaaccccg ggaggagcag ttcaacagca ctttccgctc agtcagtga 960
 ctcccatca tgcaccagga ctggctcaat ggcaaggagt tcaaatgcag ggtcaacagt 1020
 ccagctttcc ctgccccat cgagaaaacc atctccaaa ccaaaggcag accgaaggct 1080
 ccacaggtgt acaccattcc acctcccaag gacagatgg ccaaggataa agtcagtcgt 1140
 acctgcatga taacagactt cttccctgaa gacattactg tggagtgga gtggaatggg 1200
 cagccagcgg agaactacaa gaacactcag ccatcatgg acacagatgg ctcttacttc 1260
 atctacagca agctcaatgt gcagaagagc aactggggagg caggaaatac ttacacctgc 1320
 tctgtgttac atgagggcct gcacaaccac catactgaga agagcctctc ccactctcct 1380
 ggtaaatga 1389

<210> 15
 <211> 218
 <212> PRT
 <213> 小家鼠

<400> 15
Asp Ile Val Leu Thr Gln Ser Pro Ala Ser Leu Thr Val Ser Leu Gly
1 5 10 15
Leu Arg Ala Thr Ile Ser Cys Lys Ala Ser Gln Ser Val Asp Tyr Asp
20 25 30
Gly Asp Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro
35 40 45
Lys Leu Leu Ile Tyr Ala Ala Ser Asn Leu Glu Ser Gly Ile Pro Ala
50 55 60
Arg Phe Ser Gly Asn Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile His
65 70 75 80
Pro Val Glu Glu Glu Asp Ala Val Thr Tyr Tyr Cys Gln Gln Ser Asn
85 90 95
Glu Asp Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg
100 105 110
Ala Asp Ala Ala Pro Thr Val Ser Ile Phe Pro Pro Ser Ser Glu Gln
115 120 125
Leu Thr Ser Gly Gly Ala Ser Val Val Cys Phe Leu Asn Asn Phe Tyr
130 135 140
Pro Lys Asp Ile Asn Val Lys Trp Lys Ile Asp Gly Ser Glu Arg Gln
145 150 155 160
Asn Gly Val Leu Asn Ser Trp Thr Asp Gln Asp Ser Lys Asp Ser Thr
165 170 175
Tyr Ser Met Ser Ser Thr Leu Thr Leu Thr Lys Asp Glu Tyr Glu Arg
180 185 190
His Asn Ser Tyr Thr Cys Glu Ala Thr His Lys Thr Ser Thr Ser Pro
195 200 205
Ile Val Lys Ser Phe Asn Arg Asn Glu Cys
210 215

<210> 16
<211> 657
<212> DNA
<213> 小家鼠

<400> 16
gacattgtgc tgacccaatc tccagcttct tlgactgtgt ccttaggcct gagggccacc 60
atctcctgca aggccagcca aagtgttgat tatgatggtg atagttatat gaactggtac 120
cagcagaaac caggacagcc acccaaactc ctcatctatg ctgcatccaa tctagaatct 180
gggatcccag ccaggttttag tggcaatggg tctgggacag acttcaccct caacatccat 240
cctgtggagg aggaggatgc tgtaacctat tactgtcaac aaagtaatga ggatccgtgg 300
acgttcggtg gaggcaccaa gctggaaatc aaacgggctg atgctgcacc aactgtatcc 360

atcttccac catccagtga gcagtaaca tctggaggtg cctcagtcgt gtgcttcttg 420
 aacaacttct accccaaga catcaatgtc aagtggaaga ttgatggcag tgaacgacaa 480
 aatggcgicc tgaacagttg gactgatcag gacagcaaag acagcaccta cagcatgagc 540
 agcaccctca cggtgaccaa ggacgagtat gaacgacata acagctatac ctgtgaggcc 600
 actcacaaga catcaacttc acctatgtc aagagcttca acaggaatga gtgttag 657

<210> 17
 <211> 238
 <212> PRT
 <213> 小家鼠

<400> 17

Met Glu Thr Asp Thr Ile Leu Leu Trp Val Leu Leu Leu Trp Val Pro
 1 5 10 15

Gly Ser Thr Gly Asp Ile Val Leu Thr Gln Ser Pro Ala Ser Leu Thr
 20 25 30

Val Ser Leu Gly Leu Arg Ala Thr Ile Ser Cys Lys Ala Ser Gln Ser
 35 40 45

Val Asp Tyr Asp Gly Asp Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro
 50 55 60

Gly Gln Pro Pro Lys Leu Ile Tyr Ala Ala Ser Asn Leu Glu Ser
 65 70 75 80

Gly Ile Pro Ala Arg Phe Ser Gly Asn Gly Ser Gly Thr Asp Phe Thr
 85 90 95

Leu Asn Ile His Pro Val Glu Glu Glu Asp Ala Val Thr Tyr Tyr Cys
 100 105 110

Gln Gln Ser Asn Glu Asp Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu
 115 120 125

Glu Ile Lys Arg Ala Asp Ala Ala Pro Thr Val Ser Ile Phe Pro Pro
 130 135 140

Ser Ser Glu Gln Leu Thr Ser Gly Gly Ala Ser Val Val Cys Phe Leu
 145 150 155 160

Asn Asn Phe Tyr Pro Lys Asp Ile Asn Val Lys Trp Lys Ile Asp Gly
 165 170 175

Ser Glu Arg Gln Asn Gly Val Leu Asn Ser Trp Thr Asp Gln Asp Ser
 180 185 190

Lys Asp Ser Thr Tyr Ser Met Ser Ser Thr Leu Thr Leu Thr Lys Asp
 195 200 205

Glu Tyr Glu Arg His Asn Ser Tyr Thr Cys Glu Ala Thr His Lys Thr
 210 215 220

Ser Thr Ser Pro Ile Val Lys Ser Phe Asn Arg Asn Glu Cys
225 230 235

<210> 18
<211> 717
<212> DNA
<213> 小家鼠

<400> 18
atggagacag acacaatcct gctatgggtg ctgctgctct gggttccagg ctccactggt 60
gacattgtgc tgacccaatc tccagcttct ttgactgtgt ccttaggcct gagggccacc 120
atctcctgca aggccagcca aagtgtgat tatgatgggtg atagtataat gaactgggtac 180
cagcagaaac caggacagcc acccaaactc ctcatctatg ctgcatccaa tctagaatct 240
gggatcccag ccaggtttag tggcaatggg tctgggacag acttcaccct caacatccat 300
cctgtggagg agggaggatgc tgaacctat tactgtcaac aaagtaatga ggatccgtgg 360
acgttcggtg gaggcaccaa gctggaaatc aaacgggctg atgctgcacc aactgtatcc 420
atcttccac catccagtga gcagttaaca tctggagggtg cctcagtcgt gtgcttcttg 480
aacaacttct accccaaga catcaatgtc aagtggaga ttgatggcag tgaacgacaa 540
aatggcgtcc tgaacagttg gactgatcag gacagcaaag acagcaccta cagcatgagc 600
agcaccctca cgttgaccaa ggacgagtat gaacgacata acagctatac ctgtgaggcc 660
actcacaaga catcaacttc acccattgtc aagagcttca acaggaatga gtgttag 717

<210> 19
<211> 449
<212> PRT
<213> 小家鼠

<400> 19
Glu Val Gln Leu Gln Gln Ser Gly Pro Glu Leu Val Lys Pro Gly Thr
1 5 10 15
Ser Val Lys Met Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Cys
20 25 30
Tyr Met Asn Trp Val Lys Gln Ser His Gly Lys Ser Leu Glu Trp Ile
35 40 45
Gly Asp Ile Asn Pro Phe Asn Gly Gly Thr Thr Tyr Asn Gln Lys Phe
50 55 60
Lys Gly Lys Ala Thr Leu Thr Val Asp Lys Ser Ser Ser Thr Ala Tyr
65 70 75 80
Met Gln Leu Asn Ser Leu Thr Ser Asp Asp Ser Ala Val Tyr Tyr Cys
85 90 95
Ala Arg Ser His Tyr Tyr Phe Asp Gly Arg Val Pro Trp Asp Ala Met
100 105 110
Asp Tyr Trp Gly Gln Gly Thr Ser Val Thr Val Ser Ser Ala Lys Thr
115 120 125
Thr Pro Pro Ser Val Tyr Pro Leu Ala Pro Gly Ser Ala Ala Gln Thr

130	135	140
Asn Ser Met Val Thr	Leu Gly Cys Leu Val	Lys Gly Tyr Phe Pro Glu
145	150	155 160
Pro Val Thr Val Thr	Trp Asn Ser Gly Ser	Leu Ser Ser Gly Val His
	165	170 175
Thr Phe Pro Ala Val	Leu Gln Ser Asp	Leu Tyr Thr Leu Ser Ser Ser
	180	185 190
Val Thr Val Pro Ser	Ser Thr Trp Pro Ser	Glu Thr Val Thr Cys Asn
	195	200 205
Val Ala His Pro Ala	Ser Ser Thr Lys Val	Asp Lys Lys Ile Val Pro
	210	215 220
Arg Asp Cys Gly Cys	Lys Pro Cys Ile Cys	Thr Val Pro Glu Val Ser
225	230	235 240
Ser Val Phe Ile Phe	Pro Pro Lys Pro	Lys Asp Val Leu Thr Ile Thr
	245	250 255
Leu Thr Pro Lys Val	Thr Cys Val Val	Val Asp Ile Ser Lys Asp Asp
	260	265 270
Pro Glu Val Gln Phe	Ser Trp Phe Val Asp	Asp Val Glu Val His Thr
	275	280 285
Ala Gln Thr Gln Pro	Arg Glu Glu Gln Phe	Asn Ser Thr Phe Arg Ser
	290	295 300
Val Ser Glu Leu Pro	Ile Met His Gln Asp	Trp Leu Asn Gly Lys Glu
305	310	315 320
Phe Lys Cys Arg Val	Asn Ser Ala Ala	Phe Pro Ala Pro Ile Glu Lys
	325	330 335
Thr Ile Ser Lys Thr	Lys Gly Arg Pro	Lys Ala Pro Gln Val Tyr Thr
	340	345 350
Ile Pro Pro Pro Lys	Glu Gln Met Ala	Lys Asp Lys Val Ser Leu Thr
	355	360 365
Cys Met Ile Thr Asp	Phe Phe Pro Glu Asp	Ile Thr Val Glu Trp Gln
	370	375 380
Trp Asn Gly Gln Pro	Ala Glu Asn Tyr Lys	Asn Thr Gln Pro Ile Met
	385	390 395 400
Asp Thr Asp Gly Ser	Tyr Phe Ile Tyr	Ser Lys Leu Asn Val Gln Lys
	405	410 415
Ser Asn Trp Glu Ala	Gly Asn Thr Phe	Thr Cys Ser Val Leu His Glu
	420	425 430

Gly Leu His Asn His His Thr Glu Lys Ser Leu Ser His Ser Pro Gly
435 440 445

Lys

<210> 20
<211> 1350
<212> DNA
<213> 小家鼠

<400> 20
gagggtccagc tgcaacaatc tggacctgag ctggatgaagc ctgggacttc agtgaagatg 60
tcctgtaagg ctcttgata cacattcact gactgctaca tgaactgggt gaagcagagc 120
catgggaaga gccttgaatg gatggagat attaatcctt tcaacgggtg tactacctac 180
aaccagaagt tcaagggcaa ggccacattg actgtagaca aatcctccag cacagcctac 240
atgcagctca acagcctgac atctgacgac tctgcagtct attactgtgc aagatcccat 300
tattacttcg atggtagagt cccttgggat gctatggact actgggggtca aggaacctca 360
gtcacctgtc cctcagccaa aacgacaccc ccatctgtct atccactggc ccctggatct 420
gctgccccaa ctaactccat ggtgacctg ggatgcctgg tcaagggcta ttccctgag 480
ccagtgacag tgacctggaa ctctggatcc ctgtccagcg gtgtgcacac ctcccagct 540
gtcctgcagt ctgacctcta cactctgagc agctcagtga ctgtccctc cagcacctgg 600
cccagcgaga ccgtcacctg caacgttgcc caccggcca gcagcaccaa ggtggacaag 660
aaaattgtgc ccagggattg tggttgtaag ccttgcatat gtacagtccc agaagtatca 720
tctgtcttca tcttcccccc aaagcccaag gatgtgtca ccattactct gactcctaag 780
gtcacgtgtg ttgtggtaga catcagcaag gatgatcccg aggtccagtt cagctggttt 840
gtagatgatg tggaggtgca cacagctcag acgcaacccc gggaggagca gttcaacagc 900
actttccgct cagtcagtga acttcccatc atgcaccagg actggctcaa tggcaaggag 960
ttcaaatgca gggtaacag tgcagcttct cctgccccca tcgagaaaac catctccaaa 1020
accaaaggca gaccgaaggc tccacaggtg tacaccattc cacctcccaa ggagcagatg 1080
gccaaaggata aagtcagtct gacctgatg ataacagact tcttcctga agacattact 1140
gtggagtggc agtggaatgg gcagccagcg gagaactaca agaactca gccatcatg 1200
gacacagatg gctcttactt catctacagc aagctcaatg tgcagaagag caactgggag 1260
gcaggaaata ctltcacctg ctctgtgta catgagggcc tgcacaacca ccatactgag 1320
aagagcctct cccactctcc tggtaaatga 1350

<210> 21
<211> 468
<212> PRT
<213> 小家鼠

<400> 21

Met Gly Trp Asn Trp Ile Phe Leu Phe Leu Leu Ser Gly Thr Ala Gly
1 5 10 15

Val Tyr Ser Glu Val Gln Leu Gln Gln Ser Gly Pro Glu Leu Val Lys
20 25 30

Pro Gly Thr Ser Val Lys Met Ser Cys Lys Ala Ser Gly Tyr Thr Phe
 35 40 45
 Thr Asp Cys Tyr Met Asn Trp Val Lys Gln Ser His Gly Lys Ser Leu
 50 55 60
 Glu Trp Ile Gly Asp Ile Asn Pro Phe Asn Gly Gly Thr Thr Tyr Asn
 65 70 75 80
 Gln Lys Phe Lys Gly Lys Ala Thr Leu Thr Val Asp Lys Ser Ser Ser
 85 90 95
 Thr Ala Tyr Met Gln Leu Asn Ser Leu Thr Ser Asp Asp Ser Ala Val
 100 105 110
 Tyr Tyr Cys Ala Arg Ser His Tyr Tyr Phe Asp Gly Arg Val Pro Trp
 115 120 125
 Asp Ala Met Asp Tyr Trp Gly Gln Gly Thr Ser Val Thr Val Ser Ser
 130 135 140
 Ala Lys Thr Thr Pro Pro Ser Val Tyr Pro Leu Ala Pro Gly Ser Ala
 145 150 155 160
 Ala Gln Thr Asn Ser Met Val Thr Leu Gly Cys Leu Val Lys Gly Tyr
 165 170 175
 Phe Pro Glu Pro Val Thr Val Thr Trp Asn Ser Gly Ser Leu Ser Ser
 180 185 190
 Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Asp Leu Tyr Thr Leu
 195 200 205
 Ser Ser Ser Val Thr Val Pro Ser Ser Thr Trp Pro Ser Glu Thr Val
 210 215 220
 Thr Cys Asn Val Ala His Pro Ala Ser Ser Thr Lys Val Asp Lys Lys
 225 230 235 240
 Ile Val Pro Arg Asp Cys Gly Cys Lys Pro Cys Ile Cys Thr Val Pro
 245 250 255
 Glu Val Ser Ser Val Phe Ile Phe Pro Pro Lys Pro Lys Asp Val Leu
 260 265 270
 Thr Ile Thr Leu Thr Pro Lys Val Thr Cys Val Val Val Asp Ile Ser
 275 280 285
 Lys Asp Asp Pro Glu Val Gln Phe Ser Trp Phe Val Asp Asp Val Glu
 290 295 300
 Val His Thr Ala Gln Thr Gln Pro Arg Glu Glu Gln Phe Asn Ser Thr
 305 310 315 320
 Phe Arg Ser Val Ser Glu Leu Pro Ile Met His Gln Asp Trp Leu Asn
 325 330 335

Gly Lys Glu Phe Lys Cys Arg Val Asn Ser Ala Ala Phe Pro Ala Pro
340 345 350

Ile Glu Lys Thr Ile Ser Lys Thr Lys Gly Arg Pro Lys Ala Pro Gln
355 360 365

Val Tyr Thr Ile Pro Pro Pro Lys Glu Gln Met Ala Lys Asp Lys Val
370 375 380

Ser Leu Thr Cys Met Ile Thr Asp Phe Phe Pro Glu Asp Ile Thr Val
385 390 395 400

Glu Trp Gln Trp Asn Gly Gln Pro Ala Glu Asn Tyr Lys Asn Thr Gln
405 410 415

Pro Ile Met Asp Thr Asp Gly Ser Tyr Phe Ile Tyr Ser Lys Leu Asn
420 425 430

Val Gln Lys Ser Asn Trp Glu Ala Gly Asn Thr Phe Thr Cys Ser Val
435 440 445

Leu His Glu Gly Leu His Asn His His Thr Glu Lys Ser Leu Ser His
450 455 460

Ser Pro Gly Lys
465

<210> 22
<211> 1407
<212> DNA
<213> 小家鼠

<400> 22
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gtccagctgc aacaatctgg acctgagctg gtgaagcctg ggacttcagt gaagatgtcc 120
tgtaaggctt ctggatacac attcactgac tgctacatga actgggtgaa gcagagccat 180
gggaagagcc ttgaatggat tggagatatt aatcctttca acggtggtac tacctacaac 240
cagaagtcca agggcaaggc cacattgact gtagacaaat cctccagcac agcctacatg 300
cagctcaaca gcctgacatc tgacgactct gcagtctatt actgtgcaag atcccattat 360
tacttcgatg gtagagtccc ttgggatgct atggactact ggggtcaagg aacctcagtc 420
accgtctcct cagccaaaac gacaccccca tctgtctatc cactggcccc tggatctgct 480
gccccaaacta actccatggt gaccctggga tgccctggta agggctattt cctgagcca 540
gtgacagtga cctggaactc tggatccctg tccagcggig tgcacacctt cccagctgtc 600
ctgcagtctg acctctacac tctgagcagc tcagtactg tcccctccag cacctggccc 660
agcgagaccg tcacctgcaa cgttgcccac ccggccagca gcaccaaggt ggacaagaaa 720
attgtgccc a gggattgtgg ttgtaagcct tgcatatgta cagtcccaga agtatcatct 780
gtcttcatct tcccccaaa gcccaaggat gtgtcacca ttactctgac tcctaaggtc 840
acgtgtgttg tggtagacat cagcaaggat gatcccaggg tccagttcag ctggtttgta 900
gatgatgtgg aggtgcacac agctcagacg caaccccgagg aggagcagtt caacagcact 960

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ttccgctcag tcagtgaact tcccatcatg caccaggact ggctcaatgg caaggagttc 1020
aaatgcaggg tcaacagtgc agctttccct gcccccatcg agaaaacccat ctccaaaacc 1080
aaaggcagac cgaaggctcc acaggtgtac accattccac ctcccaagga gcagatggcc 1140
aaggataaag tcagtctgac ctgcatgata acagacttct tccctgaaga cattactgtg 1200
gagtggcagt ggaatgggca gccagcggag aactacaaga acactcagcc catcatggac 1260
acagatggct cttacttcat ctacagcaag ctcaatgtgc agaagagcaa ctgggaggca 1320
ggaaaatactt tcacctgtc tgtgttacat gagggcctgc acaaccacca tactgagaag 1380
agcctctccc actctcctgg taaatga 1407

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<210> 23
 <211> 217
 <212> PRT
 <213> 兔-小鼠嵌合体

<400> 23

Ala Gln Val Leu Thr Gln Thr Pro Ala Ser Val Ser Ala Ala Val Gly
1 5 10 15

Gly Thr Val Thr Ile Asn Cys Gln Ser Ser Gln Ser Val Tyr Asp Asn
20 25 30

Asn Trp Leu Ala Trp Phe Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu
35 40 45

Leu Ile Tyr Asp Ala Ser Asp Leu Ala Ser Gly Val Pro Ser Arg Phe
50 55 60

Ser Gly Ser Gly Ser Gly Thr Gln Phe Thr Leu Thr Ile Ser Gly Val
65 70 75 80

Gln Cys Ala Asp Ala Ala Thr Tyr Tyr Cys Gln Gly Ala Tyr Asn Asp
85 90 95

Val Ile Tyr Ala Phe Gly Gly Gly Thr Glu Val Val Val Lys Arg Thr
100 105 110

Asp Ala Ala Pro Thr Val Ser Ile Phe Pro Pro Ser Ser Glu Gln Leu
115 120 125

Thr Ser Gly Gly Ala Ser Val Val Cys Phe Leu Asn Asn Phe Tyr Pro
130 135 140

Lys Asp Ile Asn Val Lys Trp Lys Ile Asp Gly Ser Glu Arg Gln Asn
145 150 155 160

Gly Val Leu Asn Ser Trp Thr Asp Gln Asp Ser Lys Asp Ser Thr Tyr
165 170 175

Ser Met Ser Ser Thr Leu Thr Leu Thr Lys Asp Glu Tyr Glu Arg His
180 185 190

Asn Ser Tyr Thr Cys Glu Ala Thr His Lys Thr Ser Thr Ser Pro Ile
195 200 205

Val Lys Ser Phe Asn Arg Asn Glu Cys
210 215

<210> 24
<211> 654
<212> DNA
<213> 兔-小鼠嵌合體

<400> 24
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atcaattgcc agtccagtca gagggtttat gataacaact ggtagcctg gtttcagcag 120
aaaccagggc agcctcccaa gctcctgatt tatgatgcat ccgatctggc atctggggtc 180
ccatcgcggt tcagtggcag tggatctggg acacagttca ctctcaccat cagcggcgtg 240
cagtgtgccg atgctgccac ttactactgt caaggcgctt ataatgatgt tatttatgct 300
ttcggcggag ggaccgaggt ggtgggtcaaa cgtacggatg ctgcaccaac tglatccatc 360
ttcccaccat ccagttagca gttaacatct ggaggtgcct cagtcgtgtg ctcttgaac 420
aacttctacc ccaaagacat caatgtcaag tggaagattg atggcagtga acgacaaaat 480
ggcgtcctga acagttggac tgatcaggac agcaaagaca gcacctacag catgagcagc 540
accctcacgt tgaccaagga cgagtatgaa cgacataaca gctatactg tgaggccact 600
cacaagacat caacttcacc cattgtcaag agcttcaaca ggaatgagtg ttag 654

<210> 25
<211> 239
<212> PRT
<213> 兔-小鼠嵌合體

<400> 25
Met Asp Thr Arg Ala Pro Thr Gln Leu Leu Gly Leu Leu Leu Trp
1 5 10 15
Leu Pro Gly Ala Thr Phe Ala Gln Val Leu Thr Gln Thr Pro Ala Ser
20 25 30
Val Ser Ala Ala Val Gly Gly Thr Val Thr Ile Asn Cys Gln Ser Ser
35 40 45
Gln Ser Val Tyr Asp Asn Asn Trp Leu Ala Trp Phe Gln Gln Lys Pro
50 55 60
Gly Gln Pro Pro Lys Leu Leu Ile Tyr Asp Ala Ser Asp Leu Ala Ser
65 70 75 80
Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Gln Phe Thr
85 90 95
Leu Thr Ile Ser Gly Val Gln Cys Ala Asp Ala Ala Thr Tyr Tyr Cys
100 105 110
Gln Gly Ala Tyr Asn Asp Val Ile Tyr Ala Phe Gly Gly Gly Thr Glu
115 120 125
Val Val Val Lys Arg Thr Asp Ala Ala Pro Thr Val Ser Ile Phe Pro

130135140

Pro Ser Ser Glu Gln Leu Thr Ser Gly Gly Ala Ser Val Val Cys Phe
145150155160

Leu Asn Asn Phe Tyr Pro Lys Asp Ile Asn Val Lys Trp Lys Ile Asp
165170175

Gly Ser Glu Arg Gln Asn Gly Val Leu Asn Ser Trp Thr Asp Gln Asp
180185190

Ser Lys Asp Ser Thr Tyr Ser Met Ser Ser Thr Leu Thr Leu Thr Lys
195200205

Asp Glu Tyr Glu Arg His Asn Ser Tyr Thr Cys Glu Ala Thr His Lys
210215220

Thr Ser Thr Ser Pro Ile Val Lys Ser Phe Asn Arg Asn Glu Cys
225230235

<210> 26
<211> 720
<212> DNA
<213> 兔-小鼠嵌合体

<400> 26

atggacacga gggccccac tcagctgctg gggctcctgc tgctctggct cccaggtgcc60

acatttgcg aagtgtgac ccagactcca gcctccgtgt ctgcagctgt gggaggcaca120

gtcaccatca attgccagtc cagtcagagt gtttatgata acaactgggt agcctggttt180

cagcagaaac cagggcagcc tccaagctc ctgatttatg atgcattcga tctggcatct240

gggggcccat gcggtgtcag tggcagtga tctgggacac agttcactct caccatcagc300

ggcgtgcagt gtgccgatgc tgccacttac tactgtcaag gcgcttataa tgatgttatt360

tatgcttttc gcggagggac cgagggtgtg gtcaaacgta cggatgctgc accaactgta420

tccatcttcc caccatccag tgagcagtta acatctggag gtgcctcagt cgtgtgcttc480

ttgaacaact tctaccccaa agacatcaat gtcaagtga agattgatgg cagtgaacga540

caaatggcg tcctgaacag ttggactgat caggacagca aagacagcac ctacagcatg600

agcagcacc tcacgttgac caaggacgag tatgaacgac ataacagcta tacctgtgag660

gccactcaca agacatcaac ttcacccatt gtcaagagct tcaacaggaa tgagtgttag720

<210> 27
<211> 433
<212> PRT
<213> 人工序列

<220>
<223> 合成多肽

<220>
<221> MISC_FEATURE
<223> 人化抗体

<400> 27

Gln Ser Leu Glu Glu Ser Gly Gly Arg Leu Val Thr Pro Gly Thr Pro

151015

Leu Thr Leu Thr Cys Thr Ala Ser Gly Phe Ser Leu Ser Ser Tyr Trp
 20 25 30
 Met Asn Trp Val Arg Gln Ala Pro Gly Glu Gly Leu Glu Trp Ile Gly
 35 40 45
 Thr Ile Asp Ser Gly Gly Arg Thr Asp Tyr Ala Ser Trp Ala Lys Gly
 50 55 60
 Arg Phe Thr Ile Ser Arg Thr Ser Thr Thr Met Asp Leu Lys Met Thr
 65 70 75 80
 Ser Leu Thr Thr Gly Asp Thr Ala Arg Tyr Phe Cys Ala Arg Asn Trp
 85 90 95
 Asn Leu Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr
 100 105 110
 Lys Gly Pro Ser Val Tyr Pro Leu Ala Pro Gly Ser Ala Ala Gln Thr
 115 120 125
 Asn Ser Met Val Thr Leu Gly Cys Leu Val Lys Gly Tyr Phe Pro Glu
 130 135 140
 Pro Val Thr Val Thr Trp Asn Ser Gly Ser Leu Ser Ser Gly Val His
 145 150 155 160
 Thr Phe Pro Ala Val Leu Gln Ser Asp Leu Tyr Thr Leu Ser Ser Ser
 165 170 175
 Val Thr Val Pro Ser Ser Thr Trp Pro Ser Glu Thr Val Thr Cys Asn
 180 185 190
 Val Ala His Pro Ala Ser Ser Thr Lys Val Asp Lys Lys Ile Val Pro
 195 200 205
 Arg Asp Cys Gly Cys Lys Pro Cys Ile Cys Thr Val Pro Glu Val Ser
 210 215 220
 Ser Val Phe Ile Phe Pro Pro Lys Pro Lys Asp Val Leu Thr Ile Thr
 225 230 235 240
 Leu Thr Pro Lys Val Thr Cys Val Val Val Asp Ile Ser Lys Asp Asp
 245 250 255
 Pro Glu Val Gln Phe Ser Trp Phe Val Asp Asp Val Glu Val His Thr
 260 265 270
 Ala Gln Thr Gln Pro Arg Glu Glu Gln Phe Asn Ser Thr Phe Arg Ser
 275 280 285
 Val Ser Glu Leu Pro Ile Met His Gln Asp Trp Leu Asn Gly Lys Glu
 290 295 300
 Phe Lys Cys Arg Val Asn Ser Ala Ala Phe Pro Ala Pro Ile Glu Lys

305

310

315

320

Thr Ile Ser Lys Thr Lys Gly Arg Pro Lys Ala Pro Gln Val Tyr Thr

325330335

Ile Pro Pro Pro Lys Glu Gln Met Ala Lys Asp Lys Val Ser Leu Thr

340345350

Cys Met Ile Thr Asp Phe Phe Pro Glu Asp Ile Thr Val Glu Trp Gln

355360365

Trp Asn Gly Gln Pro Ala Glu Asn Tyr Lys Asn Thr Gln Pro Ile Met

370375380

Asn Thr Asn Gly Ser Tyr Phe Val Tyr Ser Lys Leu Asn Val Gln Lys

385390395400

Ser Asn Trp Glu Ala Gly Asn Thr Phe Thr Cys Ser Val Leu His Glu

405410415

Gly Leu His Asn His His Thr Glu Lys Ser Leu Ser His Ser Pro Gly

420425430

Lys

- <210> 28
- <211> 1302
- <212> DNA
- <213> 人工序列
- <220>
- <223> 合成聚核苷酸

- <220>
- <221> misc_feature
- <223> 人化抗体

<400> 28

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ggggaggggc tggaaatgat cggaaccatt gattctggig ttaggacgga ctacgcgagc180

tgggcaaaag gccgattcac catctccaga acctcgacta cgatggatct gaaaatgacc240

agtcctgacga ccggggacac ggcccgttat ttctgtgcca gaaattggaa cttgtggggc300

caaggcacc cgtgcaccgt ctcgagcgct tctacaaagg gcccatctgt ctatccactg360

gcccctggat ctgctgcca aactaactcc atggtgacct tgggatgcct ggtcaagggc420

tatttccctg agccagtac agtgacctgg aactctggat ccctgtccag cggtgtgcac480

accttcccag ctgtcctgca gtctgacctc tacactciga gcagctcagt gactgtcccc540

tccagcacct ggcccagcga gaccgtcacc tgcaacgttg cccacccggc cagcagcacc600

aagggtggaca agaaaattgt gcccagggat tgtggttgta agccttgcac atgtacagtc660

ccagaagtat catctgtctt catcttcccc ccaaagccca aggatgtgct caccattact720

ctgactccta aggtcacgtg tgttggtgta gacatcagca aggatgatcc cgagggtccag780

ttcagctggt ttgtagatga tgtggagggtg cacacagctc agacgcaacc ccgggaggag 840
cagttcaaca gcactttccg ctcagtcagt gaacttccca tcatgcacca ggactggctc 900
aatggcaagg agttcaaag cagggtcaac agtgcagctt tccctgcccc catcgagaaa 960
accatctcca aaaccaaagg cagaccgaag gctccacagg tgtacaccat tccacctccc 1020
aaggagcaga tggccaagga taaagtcagt ctgacctgca tgataacaga cttcttcctt 1080
gaagacatta ctgtggagtg gcagtggaaat gggcagccag cggagaacta caagaacact 1140
cagcccatca tggacacaga tggctcttac ttcgtctaca gcaagctcaa tgtgcagaag 1200
agcaactggg aggcaggaaa tactttcacc tgctctgtgt tacatgaggg cctgcacaac 1260
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<210> 29
<211> 452
<212> PRT
<213> 人工序列

<220>
<223> 合成多肽

<220>
<221> MISC_FEATURE
<223> 人化抗体

<400> 29

Met Glu Thr Gly Leu Arg Trp Leu Leu Leu Val Ala Val Leu Lys Gly
1 5 10 15
Val His Cys Gln Ser Leu Glu Glu Ser Gly Gly Arg Leu Val Thr Pro
20 25 30
Gly Thr Pro Leu Thr Leu Thr Cys Thr Ala Ser Gly Phe Ser Leu Ser
35 40 45
Ser Tyr Trp Met Asn Trp Val Arg Gln Ala Pro Gly Glu Gly Leu Glu
50 55 60
Trp Ile Gly Thr Ile Asp Ser Gly Gly Arg Thr Asp Tyr Ala Ser Trp
65 70 75 80
Ala Lys Gly Arg Phe Thr Ile Ser Arg Thr Ser Thr Thr Met Asp Leu
85 90 95
Lys Met Thr Ser Leu Thr Thr Gly Asp Thr Ala Arg Tyr Phe Cys Ala
100 105 110
Arg Asn Trp Asn Leu Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120 125
Ala Ser Thr Lys Gly Pro Ser Val Tyr Pro Leu Ala Pro Gly Ser Ala
130 135 140
Ala Gln Thr Asn Ser Met Val Thr Leu Gly Cys Leu Val Lys Gly Tyr
145 150 155 160
Phe Pro Glu Pro Val Thr Val Thr Trp Asn Ser Gly Ser Leu Ser Ser

[illegible]

<210> 30
<211> 1359
<212> DNA
<213> 人工序列

<220>
<223> 合成聚核苷酸

<220>
<221> misc_feature
<223> 人化抗体

<400> 30
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tcgctggagg agtccggggg tcgcttggtc acgcttgga caccctgac actcacctgc 120
acagccctcg gattctccct cagtagttat tggatgaact gggtccgcca ggctccaggg 180
gaggggctgg aatggatcgg aaccattgat tctggtggtg ggacggacta cgcgagctgg 240
gcaaaaggcc gattcaccat ctccagaacc tcgactacga tggatctgaa aatgaccagt 300
ctgacgaccg gggacacggc ccgttatttc tgtgccagaa attggaactt gtggggccaa 360
ggcaccctcg tcaccgtctc gagcgcttct acaaagggcc catctgtcta tccactggcc 420
cctggatctg ctgcccnaac taactccaatg gtgacctgg gatgcctggt caagggtat 480
ttccctgagc cagtgcagct gacctggaac tctggatccc tgtccagcgg tgtgcacacc 540
ttcccagctg tcctgcagtc tgacctctac actctgagca gctcagtgac tgtcccctcc 600
agcacctggc ccagcgagac cgtcacctgc aacgttgccc acccggccag cagcaccaag 660
gtggacaaga aaattgtgcc cagggattgt ggttgtaagc cttgcatatg tacagtcca 720
gaagtatcat ctgtcttcat ctcccccca aagcccaagg atgtgtcac cattactctg 780
actcctaagg tcacgttgtt tgtggtagac atcagcaagg atgatcccga ggtccagttc 840
agctggtttg tagatgatgt ggagggtgac acagctcaga cgcaaccccg ggaggagcag 900
ttcaacagca ctltccgctc agtcagtcaa ctccccatca tgcaccagga ctggctcaat 960
ggcaaggagt tcaaatgcag ggtcaacagt gcagctttcc ctgcccccat cgagaaaacc 1020
atctccaaaa ccaaggcag accgaaggct ccacagggtg acaccattcc acctccaag 1080
gagcagatgg ccaaggataa agtcagctcg acctgcatga taacagactt cttccctgaa 1140
gacattactg tggagtggca gtggaatggg cagccagcgg agaactacaa gaacactcag 1200
cccatcatgg acacagatgg ctcttacttc gtctacagca agctcaatgt gcagaagagc 1260
aactgggagg caggaaatac tttcacctgc tctgtgttac atgagggcct gcacaaccac 1320
catactgaga agagcctctc ccactctcct ggtaaatga 1359

<210> 31
<211> 213
<212> PRT
<213> 小家鼠

<400> 31
Gln Ile Val Leu Thr Gln Ser Pro Thr Ile Val Ser Ala Ser Pro Gly
1 5 10 15

Glu Lys Val Thr Leu Ile Cys Ser Ala Ser Ser Ser Val Ser Phe Val
20 25 30

Asp Trp Phe Gln Gln Lys Pro Gly Thr Ser Pro Lys Arg Trp Ile Tyr
35 40 45

Arg Thr Ser Asn Leu Gly Phe Gly Val Pro Ala Arg Phe Ser Gly Gly
50 55 60

Gly Ser Gly Thr Ser His Ser Leu Thr Ile Ser Arg Met Glu Ala Glu
65 70 75 80

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Arg Ser Thr Tyr Pro Pro Thr
85 90 95

Phe Gly Ala Gly Thr Lys Leu Glu Leu Lys Arg Ala Asp Ala Ala Pro
100 105 110

Thr Val Ser Ile Phe Pro Pro Ser Ser Glu Gln Leu Thr Ser Gly Gly
115 120 125

Ala Ser Val Val Cys Phe Leu Asn Asn Phe Tyr Pro Lys Asp Ile Asn
130 135 140

Val Lys Trp Lys Ile Asp Gly Ser Glu Arg Gln Asn Gly Val Leu Asn
145 150 155 160

Ser Trp Thr Asp Gln Asp Ser Lys Asp Ser Thr Tyr Ser Met Ser Ser
165 170 175

Thr Leu Thr Leu Thr Lys Asp Glu Tyr Glu Arg His Asn Ser Tyr Thr
180 185 190

Cys Glu Ala Thr His Lys Thr Ser Thr Ser Pro Ile Val Lys Ser Phe
195 200 205

Asn Arg Asn Glu Cys
210

<210> 32
<211> 642
<212> DNA
<213> 小家鼠

<400> 32
caaattgttc tcaccagtc tccaacaatc gtgtctgcat ctccagggga gaaggtcacc 60
ctaattctgca gtgccagttc aagtgttaagt ttcgtggact gggtccagca gaagccaggc 120
acttctccca aacgctggat ttacagaaca tccaacctgg gttttggagt ccttgctcgc 180
ttcagtggcg gtggatctgg gacctctcac tctctcaca tcagccgaat ggaggctgaa 240
gatgctgcca cttattactg ccagcaaagg agtacttacc caccacggtt cgggtgctggg 300
accaagctgg aactgaaacg ggctgatgct gcaccaactg tatccatctt cccaccatcc 360
agtgagcagt taacatctgg aggtgcctca gtcgtgtgct tcttgaacaa cttctacccc 420
aaagacatca atgtcaagtg gaagatgat ggacgtgaac gacaaaatgg cgtcctgaac 480
agttggactg atcaggacag caaagacagc acctacagca tgagcagcac cctcacgttg 540
accaaggacg agtatgaacg acataacagc tatacctgtg aggccactca caagacatca 600

acttcaccca ttgtcaagag cttcaacagg aatgagtgtt ag

642

<210> 33
<211> 235
<212> PRT
<213> 小家鼠

<400> 33

Met His Phe Gln Val Gln Ile Phe Ser Phe Leu Leu Ile Ser Ala Ser
1 5 10 15

Val Ile Val Ser Arg Gly Gln Ile Val Leu Thr Gln Ser Pro Thr Ile
20 25 30

Val Ser Ala Ser Pro Gly Glu Lys Val Thr Leu Ile Cys Ser Ala Ser
35 40 45

Ser Ser Val Ser Phe Val Asp Trp Phe Gln Gln Lys Pro Gly Thr Ser
50 55 60

Pro Lys Arg Trp Ile Tyr Arg Thr Ser Asn Leu Gly Phe Gly Val Pro
65 70 75 80

Ala Arg Phe Ser Gly Gly Gly Ser Gly Thr Ser His Ser Leu Thr Ile
85 90 95

Ser Arg Met Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Arg
100 105 110

Ser Thr Tyr Pro Pro Thr Phe Gly Ala Gly Thr Lys Leu Glu Leu Lys
115 120 125

Arg Ala Asp Ala Ala Pro Thr Val Ser Ile Phe Pro Pro Ser Ser Glu
130 135 140

Gln Leu Thr Ser Gly Gly Ala Ser Val Val Cys Phe Leu Asn Asn Phe
145 150 155 160

Tyr Pro Lys Asp Ile Asn Val Lys Trp Lys Ile Asp Gly Ser Glu Arg
165 170 175

Gln Asn Gly Val Leu Asn Ser Trp Thr Asp Gln Asp Ser Lys Asp Ser
180 185 190

Thr Tyr Ser Met Ser Ser Thr Leu Thr Leu Thr Lys Asp Glu Tyr Glu
195 200 205

Arg His Asn Ser Tyr Thr Cys Glu Ala Thr His Lys Thr Ser Thr Ser
210 215 220

Pro Ile Val Lys Ser Phe Asn Arg Asn Glu Cys
225 230 235

<210> 34
<211> 708
<212> DNA
<213> 小家鼠

<400> 34
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agagggcaaa ttgtttcac ccagttccca acaatcgtgt ctgcacttcc aggggagaag 120
gtcaccctaa tctgcagtgc cagttcaagt gtaagtttcg tggactggtt ccagcagaag 180
ccaggcactt ctcccaaacg ctggatttac agaacatcca acctgggttt tggagtcctt 240
gtctgcttca gtggcggtgg atctgggacc tctcactctc tcacaalcag ccgaatggag 300
gttgaagatg ctgccactta ttactgccag caaaggagta cttaccaccc cacttcgggt 360
gtctgggacca agcttggaact gaaacgggct gatgtctcac caactgtatc catcttccca 420
ccatccagtg agcagttaac atctggaggt gcctcagtcg tgtgcttctt gaacaacttc 480
taccctaaag acatcaatgt caagtggag attgatggca gtgaacgaca aaatggcgctc 540
ctgaacagtt ggactgatca ggacagcaaa gacagcacct acagcatgag cagcaccctc 600
acgttgacca aggacgagta tgaacgacat aacagctata cctgtgaggc cactcacaag 660
acatcaactt caccattgt caagagcttc aacaggaatg agtgtag 708

<210> 35
<211> 449
<212> PRT
<213> 小家鼠

<400> 35
Gln Val Thr Leu Lys Glu Ser Gly Pro Gly Ile Leu Gln Pro Ser Gln
1 5 10 15
Thr Leu Ser Leu Thr Cys Ser Phe Ser Gly Phe Ser Leu Ser Thr Ser
20 25 30
Gly Met Gly Val Gly Trp Ile Arg His Pro Ser Gly Lys Asn Leu Glu
35 40 45
Trp Leu Ala His Ile Trp Trp Asp Asp Val Lys Arg Tyr Asn Pro Val
50 55 60
Leu Lys Ser Arg Leu Thr Ile Ser Lys Asp Thr Ser Asn Ser Gln Val
65 70 75 80
Phe Leu Lys Ile Ala Asn Val Asp Thr Ala Asp Thr Ala Thr Tyr Tyr
85 90 95
Cys Ala Arg Ile Glu Asp Phe Asp Tyr Asp Glu Glu Tyr Tyr Ala Met
100 105 110
Asp Tyr Trp Gly Gln Gly Thr Ser Val Ile Val Ser Ser Ala Lys Thr
115 120 125
Thr Pro Pro Ser Val Tyr Pro Leu Ala Pro Gly Ser Ala Ala Gln Thr
130 135 140
Asn Ser Met Val Thr Leu Gly Cys Leu Val Lys Gly Tyr Phe Pro Glu
145 150 155 160
Pro Val Thr Val Thr Trp Asn Ser Gly Ser Leu Ser Ser Gly Val His
165 170 175

Thr Phe Pro Ala Val Leu Gln Ser Asp Leu Tyr Thr Leu Ser Ser Ser
180 185 190

Val Thr Val Pro Ser Ser Thr Trp Pro Ser Glu Thr Val Thr Cys Asn
195 200 205

Val Ala His Pro Ala Ser Ser Thr Lys Val Asp Lys Lys Ile Val Pro
210 215 220

Arg Asp Cys Gly Cys Lys Pro Cys Ile Cys Thr Val Pro Glu Val Ser
225 230 235 240

Ser Val Phe Ile Phe Pro Pro Lys Pro Lys Asp Val Leu Thr Ile Thr
245 250 255

Leu Thr Pro Lys Val Thr Cys Val Val Val Asp Ile Ser Lys Asp Asp
260 265 270

Pro Glu Val Gln Phe Ser Trp Phe Val Asp Asp Val Glu Val His Thr
275 280 285

Ala Gln Thr Gln Pro Arg Glu Glu Gln Phe Asn Ser Thr Phe Arg Ser
290 295 300

Val Ser Glu Leu Pro Ile Met His Gln Asp Trp Leu Asn Gly Lys Glu
305 310 315 320

Phe Lys Cys Arg Val Asn Ser Ala Ala Phe Pro Ala Pro Ile Glu Lys
325 330 335

Thr Ile Ser Lys Thr Lys Gly Arg Pro Lys Ala Pro Gln Val Tyr Thr
340 345 350

Ile Pro Pro Pro Lys Glu Gln Met Ala Lys Asp Lys Val Ser Leu Thr
355 360 365

Cys Met Ile Thr Asp Phe Phe Pro Glu Asp Ile Thr Val Glu Trp Gln
370 375 380

Trp Asn Gly Gln Pro Ala Glu Asn Tyr Lys Asn Thr Gln Pro Ile Met
385 390 395 400

Asp Thr Asp Gly Ser Tyr Phe Val Tyr Ser Lys Leu Asn Val Gln Lys
405 410 415

Ser Asn Trp Glu Ala Gly Asn Thr Phe Thr Cys Ser Val Leu His Glu
420 425 430

Gly Leu His Asn His His Thr Glu Lys Ser Leu Ser His Ser Pro Gly
435 440 445

Lys

<210> 36

<211> 1350
<212> DNA
<213> 小家鼠

<400> 36
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acttgttctt tctctgggtt ttcactgagc acttctggta tgggtgtagg ctggattcgt 120
caccatcag ggaagaatct ggagtggtc gcacacattt ggtgggatga tgtcaagcgc 180
tataaccag tctgaagag cgcacigact atctccaagg atacctcaa cagccaggta 240
ttctcaaga tcgccaatgt ggacactgca gatactgcca catactacig tgctcgaata 300
gaggactttg attacgacga ggagtattat gctatggact actggggta aggaacctca 360
gtcatcgctt cctcagcaa aacgacccc ccatctgtct atccactggc ccctggatct 420
gctgccccaa ctaactccat ggtgacctc ggatgcctgg tcaagggcta ttccctgag 480
ccagtgacag tgacctggaa ctctggatcc ctgtccagcg gtgtgcacac ctcccagct 540
gtccctcagt ctgacctcta cactctgagc agctcagtga ctgtccctc cagcacctgg 600
cccagcgaga cgtcacctg caacgttgcc cccccggca gcagcaccaa ggtggacaag 660
aaaattgtgc ccagggattg tggttgtaag ccttgcatat gtacagtccc agaagtatca 720
tctgtcttca tcttcccccc aaagcccaag gatgtgctca ccattactct gactcctaag 780
gtcacgtgtg ttgtggtaga catcagcaag gatgatcccg aggtccagti cagctgggtt 840
gtagatgatg tggagggtga cacagctcag acgcaacccc gggaggagca gttaacagc 900
actttccgct cagtcagtga acttcccatc atgcaccagg actgggtcaa tggcaaggag 960
ttcaaatgca ggggtcaacag tgcagctttc cctgccccca tcgagaaaac catctccaaa 1020
accaaaggca gaccgaaggc tccacagggtg tacaccattc cacttcccaa ggagcagatg 1080
gccaaggata aagtcagctt gacctgcatg ataacagact tcttccctga agacattact 1140
gtggagtggc agtggaatgg gcagccagcg gagaactaca agaacactca gccatcatg 1200
gacacagatg gctcttactt cgtctacagc aagctcaatg tgcagaagag caactgggag 1260
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aagagcctct cccactctcc tggtaaatga 1350

<210> 37
<211> 468
<212> PRT
<213> 小家鼠

<400> 37
Met Gly Arg Leu Thr Ser Ser Phe Leu Leu Leu Ile Val Pro Ala Tyr
1 5 10 15
Val Leu Ser Gln Val Thr Leu Lys Glu Ser Gly Pro Gly Ile Leu Gln
20 25 30
Pro Ser Gln Thr Leu Ser Leu Thr Cys Ser Phe Ser Gly Phe Ser Leu
35 40 45
Ser Thr Ser Gly Met Gly Val Gly Trp Ile Arg His Pro Ser Gly Lys
50 55 60

Asn Leu Glu Trp Leu Ala His Ile Trp Trp Asp Asp Val Lys Arg Tyr
 65 70 75 80
 Asn Pro Val Leu Lys Ser Arg Leu Thr Ile Ser Lys Asp Thr Ser Asn
 85 90 95
 Ser Gln Val Phe Leu Lys Ile Ala Asn Val Asp Thr Ala Asp Thr Ala
 100 105 110
 Thr Tyr Tyr Cys Ala Arg Ile Glu Asp Phe Asp Tyr Asp Glu Glu Tyr
 115 120 125
 Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Ser Val Ile Val Ser Ser
 130 135 140
 Ala Lys Thr Thr Pro Pro Ser Val Tyr Pro Leu Ala Pro Gly Ser Ala
 145 150 155 160
 Ala Gln Thr Asn Ser Met Val Thr Leu Gly Cys Leu Val Lys Gly Tyr
 165 170 175
 Phe Pro Glu Pro Val Thr Val Thr Trp Asn Ser Gly Ser Leu Ser Ser
 180 185 190
 Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Asp Leu Tyr Thr Leu
 195 200 205
 Ser Ser Ser Val Thr Val Pro Ser Ser Thr Trp Pro Ser Glu Thr Val
 210 215 220
 Thr Cys Asn Val Ala His Pro Ala Ser Ser Thr Lys Val Asp Lys Lys
 225 230 235 240
 Ile Val Pro Arg Asp Cys Gly Cys Lys Pro Cys Ile Cys Thr Val Pro
 245 250 255
 Glu Val Ser Ser Val Phe Ile Phe Pro Pro Lys Pro Lys Asp Val Leu
 260 265 270
 Thr Ile Thr Leu Thr Pro Lys Val Thr Cys Val Val Val Asp Ile Ser
 275 280 285
 Lys Asp Asp Pro Glu Val Gln Phe Ser Trp Phe Val Asp Asp Val Glu
 290 295 300
 Val His Thr Ala Gln Thr Gln Pro Arg Glu Glu Gln Phe Asn Ser Thr
 305 310 315 320
 Phe Arg Ser Val Ser Glu Leu Pro Ile Met His Gln Asp Trp Leu Asn
 325 330 335
 Gly Lys Glu Phe Lys Cys Arg Val Asn Ser Ala Ala Phe Pro Ala Pro
 340 345 350
 Ile Glu Lys Thr Ile Ser Lys Thr Lys Gly Arg Pro Lys Ala Pro Gln
 355 360 365

Val Tyr Thr Ile Pro Pro Pro Lys Glu Gln Met Ala Lys Asp Lys Val
370 375 380

Ser Leu Thr Cys Met Ile Thr Asp Phe Phe Pro Glu Asp Ile Thr Val
385 390 395 400

Glu Trp Gln Trp Asn Gly Gln Pro Ala Glu Asn Tyr Lys Asn Thr Gln
405 410 415

Pro Ile Met Asp Thr Asp Gly Ser Tyr Phe Val Tyr Ser Lys Leu Asn
420 425 430

Val Gln Lys Ser Asn Trp Glu Ala Gly Asn Thr Phe Thr Cys Ser Val
435 440 445

Leu His Glu Gly Leu His Asn His His Thr Glu Lys Ser Leu Ser His
450 455 460

Ser Pro Gly Lys
465

<210> 38
<211> 1407
<212> DNA
<213> 小家鼠

<400> 38
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gttactctga aagagtctgg cccctgggata ttgcagccct cccagaccct cagtcgtact 120
tgttctttct ctgggttttc actgagcact tctggtaagg gtgtaggctg gattcgtcac 180
ccatcaggga agaattctga gtggctggca cacatttggg gggatgatgt caagcgctat 240
aaccacgtcc tgaagagccg actgactatc tccaaggata cctccaacag ccaggttatc 300
ctcaagatcg ccaatgtgga cactgcagat actgccacat actactgtgc tcgaatagag 360
gactttgatt acgacgagga gtattatgct atggactact ggggtcaagg aacctcagtc 420
atcgtctcct cagccaaaac gacaccccca tctgtctatc cactggcccc tggatctgct 480
gccccaaacta actccatggt gaccctggga tgcctggica agggctatct cctgagcca 540
gtgacagtga cctggaactc tggatccctg tccagcggtg tgcacacctt cccagctgtc 600
ctgcagctcg acctctacac tctgagcagc tcagtgtactg tcccctccag cacctggccc 660
agcgagaccg tcacctgcaa cgttgcccac cggccagca gcaccaaggt ggacaagaaa 720
attgtgccca gggattgtgg ttgtaagcct tgcataigta cagtcccaga agtatcatct 780
gtcttcatct tcccccaaaa gcccaaggat gtgtcacca ttactctgac tcctaaggtc 840
acgtgtgttg tggtagacat cagcaaggat gatcccaggg tccagttcag ctggtttgta 900
gatgatgttg aggtgcacac agctcagacg caaccccggg aggagcagtt caacagcact 960
ttccgctcag tcagtgaact tccatcatg caccaggact ggctcaatgg caaggagttc 1020
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aaaggcagac cgaaggctcc acaggtgtac accattccac ctcccaagga gcagatggcc 1140
aaggataaag tcagtctgac ctgcatgata acagacttct tccctgaaga cattactgtg 1200

gagtggcagt ggaatgggca gccagcggag aactacaaga acaticagcc catcatggac 1260
acagatggct cttacttcgt ctacagcaag ctcaatgtgc agaagagcaa ctgggaggca 1320
ggaaatactt tcacctgcct tgtgttacat gagggcctgc acaaccacca tactgagaag 1380
agcctctccc actctcctgg taaatga 1407

<210> 39
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<212> PRT
<213> 小家鼠

<400> 39

Asp His Tyr Met Ser
1 5

<210> 40
<211> 17
<212> PRT
<213> 小家鼠

<400> 40

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

Gly

<210> 41
<211> 10
<212> PRT
<213> 小家鼠

<400> 41

Asp Asp Tyr Asp Ala Ser Pro Phe Ala Tyr
1 5 10

<210> 42
<211> 11
<212> PRT
<213> 小家鼠

<400> 42

Gln Ala Ser Gln Gly Thr Ser Ile Asn Leu Asn
1 5 10

<210> 43
<211> 7
<212> PRT
<213> 小家鼠

<400> 43

Gly Ser Ser Asn Leu Glu Asp
1 5

<210> 44
<211> 9
<212> PRT
<213> 小家鼠

<400> 44

Leu Gln His Ser Tyr Leu Pro Tyr Thr
1 5

<210> 45
<211> 5
<212> PRT
<213> 小家鼠

<400> 45

Asp Cys Tyr Met Asn
1 5

<210> 46
<211> 17
<212> PRT
<213> 小家鼠

<400> 46

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

Gly

<210> 47
<211> 16
<212> PRT
<213> 小家鼠

<400> 47

Ser His Tyr Tyr Phe Asp Gly Arg Val Pro Trp Asp Ala Met Asp Tyr
1 5 10 15

<210> 48
<211> 15
<212> PRT
<213> 小家鼠

<400> 48

Lys Ala Ser Gln Ser Val Asp Tyr Asp Gly Asp Ser Tyr Met Asn
1 5 10 15

<210> 49
<211> 7
<212> PRT
<213> 小家鼠

<400> 49

Ala Ala Ser Asn Leu Glu Ser
1 5

<210> 50
<211> 9
<212> PRT
<213> 小家鼠

<400> 50

Gln Gln Ser Asn Glu Asp Pro Trp Thr
1 5

<210> 51

<211> 5
<212> PRT
<213> 兔-小鼠嵌合體

<400> 51

Ser Tyr Trp Met Asn
1 5

<210> 52
<211> 16
<212> PRT
<213> 兔-小鼠嵌合體

<400> 52

Thr Ile Asp Ser Gly Gly Arg Thr Asp Tyr Ala Ser Trp Ala Lys Gly
1 5 10 15

<210> 53
<211> 4
<212> PRT
<213> 兔-小鼠嵌合體

<400> 53

Asn Trp Asn Leu
1

<210> 54
<211> 13
<212> PRT
<213> 兔-小鼠嵌合體

<400> 54

Gln Ser Ser Gln Ser Val Tyr Asp Asn Asn Trp Leu Ala
1 5 10

<210> 55
<211> 7
<212> PRT
<213> 兔-小鼠嵌合體

<400> 55

Asp Ala Ser Asp Leu Ala Ser
1 5

<210> 56
<211> 10
<212> PRT
<213> 兔-小鼠嵌合體

<400> 56

Gln Gly Ala Tyr Asn Asp Val Ile Tyr Ala
1 5 10

<210> 57
<211> 7
<212> PRT
<213> 小家鼠

<400> 57

Thr Ser Gly Met Gly Val Gly
1 5

<210> 58
 <211> 16
 <212> PRT
 <213> 小家鼠

<400> 58

His Ile Trp Trp Asp Asp Val Lys Arg Tyr Asn Pro Val Leu Lys Ser
 1 5 10 15

<210> 59
 <211> 14
 <212> PRT
 <213> 小家鼠

<400> 59

Glu Asp Phe Asp Tyr Asp Glu Glu Tyr Tyr Ala Met Asp Tyr
 1 5 10

<210> 60
 <211> 10
 <212> PRT
 <213> 小家鼠

<400> 60

Ser Ala Ser Ser Ser Val Ser Phe Val Asp
 1 5 10

<210> 61
 <211> 7
 <212> PRT
 <213> 小家鼠

<400> 61

Arg Thr Ser Asn Leu Gly Phe
 1 5

<210> 62
 <211> 9
 <212> PRT
 <213> 小家鼠

<400> 62

Gln Gln Arg Ser Thr Tyr Pro Pro Thr
 1 5

<210> 63
 <211> 20
 <212> PRT
 <213> 智人

<400> 63

Cys Gly Pro Ala Arg Leu Leu Pro Asn Ala Ile Gly Arg Gly Lys Trp
 1 5 10 15

Trp Arg Pro Ser
 20

<210> 64
 <211> 20
 <212> PRT
 <213> 智人

<400> 64

Gly Pro Ala Arg Leu Leu Pro Asn Ala Ile Gly Arg Gly Lys Trp Trp
1 5 10 15

Arg Pro Ser Gly
20

<210> 65
<211> 20
<212> PRT
<213> 智人

<400> 65

Pro Ala Arg Leu Leu Pro Asn Ala Ile Gly Arg Gly Lys Trp Trp Arg
1 5 10 15

Pro Ser Gly Pro
20

<210> 66
<211> 20
<212> PRT
<213> 智人

<400> 66

Ala Arg Leu Leu Pro Asn Ala Ile Gly Arg Gly Lys Trp Trp Arg Pro
1 5 10 15

Ser Gly Pro Asp
20

<210> 67
<211> 20
<212> PRT
<213> 智人

<400> 67

Arg Leu Leu Pro Asn Ala Ile Gly Arg Gly Lys Trp Trp Arg Pro Ser
1 5 10 15

Gly Pro Asp Phe
20

<210> 68
<211> 20
<212> PRT
<213> 智人

<400> 68

Leu Leu Pro Asn Ala Ile Gly Arg Gly Lys Trp Trp Arg Pro Ser Gly
1 5 10 15

Pro Asp Phe Arg
20

<210> 69
<211> 20
<212> PRT
<213> 智人

<400> 69
Leu Pro Asn Ala Ile Gly Arg Gly Lys Trp Trp Arg Pro Ser Gly Pro
1 5 10 15

Asp Phe Arg Cys
20

<210> 70
<211> 14
<212> PRT
<213> 智人

<400> 70
Ser Ala Lys Pro Val Thr Glu Leu Val Cys Ser Gly Gln Cys
1 5 10

<210> 71
<211> 7
<212> PRT
<213> 智人

<400> 71
Leu Val Ala Ser Cys Lys Cys
1 5

<210> 72
<211> 8
<212> PRT
<213> 智人

<400> 72
Cys Arg Glu Leu His Phe Thr Arg
1 5

<210> 73
<211> 7
<212> PRT
<213> 智人

<400> 73
Cys Ile Pro Asp Arg Tyr Arg
1 5

<210> 74
<211> 399
<212> DNA
<213> 人工序列

<220>
<223> 合成聚核苷酸

<220>
<221> misc_feature
<223> 人化抗体序列

<400> 74
atggacacga gggccccac tcagctgctg gggctcctgc tgccttggti cccagggtgcc 60
acatttgctc aagttctgac ccagagtcga agcagtcctc ccgccagcgt aggcgatcgt 120
gtgactatta cctgtcaatc tagtcagagc gtgtatgata acaattggct ggcgtggtag 180

cagcaaaaac cgggcaaagc cccgaagctg ctcatctatg acgcgctccga tctggctagc 240
gggtgtgcaa gccgtttcag tggcagtggc agcggctactg acittaccct cacaatttcg 300
tctctccagc cggaagattt cgccacttac tatgtcaag gtgcttaca cgaatgtgatt 360
tatgccttcg gtcagggcac taaagtagaa atcaaacgt . 399

<210> 75
<211> 133
<212> PRT
<213> 人工序列

<220>
<223> 合成多肽

<220>
<221> MISC_FEATURE
<223> 人化抗体序列

<400> 75
Met Asp Thr Arg Ala Pro Thr Gln Leu Leu Gly Leu Leu Leu Trp
1 5 10 15
Leu Pro Gly Ala Thr Phe Ala Gln Val Leu Thr Gln Ser Pro Ser Ser
20 25 30
Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Gln Ser Ser
35 40 45
Gln Ser Val Tyr Asp Asn Asn Trp Leu Ala Trp Tyr Gln Gln Lys Pro
50 55 60
Gly Lys Ala Pro Lys Leu Leu Ile Tyr Asp Ala Ser Asp Leu Ala Ser
65 70 75 80
Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr
85 90 95
Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys
100 105 110
Gln Gly Ala Tyr Asn Asp Val Ile Tyr Ala Phe Gly Gln Gly Thr Lys
115 120 125
Val Glu Ile Lys Arg
130

<210> 76
<211> 393
<212> DNA
<213> 人工序列

<220>
<223> 合成聚核苷酸

<220>
<221> misc_feature
<223> 人化抗体序列

<400> 76
atggagactg ggctgcgctg gcttctcctg gtcgctgtgc tcaaaggtgt ccactgtgag 60

gtgcagctgt tggagtctgg aggcgggctt gtccagcctg gagggagcct gcgtctctct 120
tgtgcagcaa gcggcttcag cttatcctct tactggatga atlgggtgcg gcaggcacct 180
gggaaggggcc tggagtgggi gggcaccatt gattccggag gccgtacaga ctacgcgtct 240
tgggcaaagg gccgtttcac catttccgc gacaactcca aaaataccat gtacctccag 300
atgaactctc tccgcgcaga ggacacagca cgttattact gtgcacgcaa ctggaatctg 360
tggggtaag gtactcttgi aacagtctcg agc 393

<210> 77
<211> 131
<212> PRT
<213> 人工序列

<220>
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<220>
<221> MISC_FEATURE
<223> 人化抗体序列

<400> 77
Met Glu Thr Gly Leu Arg Trp Leu Leu Leu Val Ala Val Leu Lys Gly
1 5 10 15
Val His Cys Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln
20 25 30
Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Ser Leu
35 40 45
Ser Ser Tyr Trp Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu
50 55 60
Glu Trp Val Gly Thr Ile Asp Ser Gly Gly Arg Thr Asp Tyr Ala Ser
65 70 75 80
Trp Ala Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr
85 90 95
Met Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Arg Tyr
100 105 110
Tyr Cys Ala Arg Asn Trp Asn Leu Trp Gly Gln Gly Thr Leu Val Thr
115 120 125
Val Ser Ser
130

<210> 78
<211> 11
<212> PRT
<213> 小家鼠

<400> 78
Arg Ala Ser Gln Asp Ile Ser Asn Tyr Leu Asn
1 5 10

<210> 79
<211> 7
<212> PRT
<213> 小家鼠

<400> 79

Tyr Thr Ser Arg Leu Leu Ser
1 5

<210> 80
<211> 9
<212> PRT
<213> 小家鼠

<400> 80

Gln Gln Gly Asp Thr Leu Pro Tyr Thr
1 5

<210> 81
<211> 11
<212> PRT
<213> 小家鼠

<400> 81

Arg Ala Ser Gln Asp Ile Ser Asn Tyr Leu Asn
1 5 10

<210> 82
<211> 24
<212> PRT
<213> 褐家鼠

<400> 82

Gln Gly Trp Gln Ala Phe Lys Asn Asp Ala Thr Glu Ile Ile Pro Gly
1 5 10 15

Leu Arg Glu Tyr Pro Glu Pro Pro
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<210> 83
<211> 20
<212> PRT
<213> 褐家鼠

<400> 83

Thr Glu Ile Ile Pro Gly Leu Arg Glu Tyr Pro Glu Pro Pro Gln Glu
1 5 10 15

Leu Glu Asn Asn
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<210> 84
<211> 20
<212> PRT
<213> 褐家鼠

<400> 84

Pro Glu Pro Pro Gln Glu Leu Glu Asn Asn Gln Thr Met Asn Arg Ala
1 5 10 15

Glu Asn Gly Gly
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<210> 85
<211> 20
<212> PRT
<213> 褐家鼠

<400> 85

Glu Asn Gly Gly Arg Pro Pro His His Pro Tyr Asp Thr Lys Asp Val
1 5 10 15

Ser Glu Tyr Ser
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<210> 86
<211> 14
<212> PRT
<213> 褐家鼠

<400> 86

Cys Arg Glu Leu His Tyr Thr Arg Phe Val Thr Asp Gly Pro
1 5 10

<210> 87
<211> 25
<212> PRT
<213> 褐家鼠

<400> 87

Cys Arg Glu Leu His Tyr Thr Arg Phe Val Thr Asp Gly Pro Ser Arg
1 5 10 15

Ser Ala Lys Pro Val Thr Glu Leu Val
20 25

<210> 88
<211> 23
<212> PRT
<213> 褐家鼠

<400> 88

Cys Arg Ser Ala Lys Pro Val Thr Glu Leu Val Ser Ser Gly Gln Ser
1 5 10 15

Gly Pro Arg Ala Arg Leu Leu
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<210> 89
<211> 25
<212> PRT
<213> 褐家鼠

<400> 89

Cys Gly Pro Ala Arg Leu Leu Pro Asn Ala Ile Gly Arg Val Lys Trp
1 5 10 15

Trp Arg Pro Asn Gly Pro Asp Phe Arg
20 25

<210> 90
 <211> 20
 <212> PRT
 <213> 褐家鼠

<400> 90

Arg Ala Gln Arg Val Gln Leu Leu Cys Pro Gly Gly Ala Ala Pro Arg
 1 5 10 15

Ser Arg Lys Val
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<210> 91
 <211> 16
 <212> PRT
 <213> 褐家鼠

<400> 91

Pro Gly Gly Ala Ala Pro Arg Ser Arg Lys Val Arg Leu Val Ala Ser
 1 5 10 15

<210> 92
 <211> 23
 <212> PRT
 <213> 褐家鼠

<400> 92

Lys Arg Leu Thr Arg Phe His Asn Gln Ser Glu Leu Lys Asp Phe Gly
 1 5 10 15

Pro Glu Thr Ala Arg Pro Gln
 20

<210> 93
 <211> 16
 <212> PRT
 <213> 褐家鼠

<400> 93

Ile Pro Asp Arg Tyr Ala Gln Arg Val Gln Leu Leu Ser Pro Gly Gly
 1 5 10 15

<210> 94
 <211> 24
 <212> PRT
 <213> 褐家鼠

<400> 94

Ser Glu Leu Lys Asp Phe Gly Pro Glu Thr Ala Arg Pro Gln Lys Gly
 1 5 10 15

Arg Lys Pro Arg Pro Arg Ala Arg
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<210> 95
 <211> 23
 <212> PRT
 <213> 褐家鼠

<400> 95

Lys Gly Arg Lys Pro Arg Pro Arg Ala Arg Gly Ala Lys Ala Asn Gln

1	5	10	15

Ala Glu Leu Glu Asn Ala Tyr
20

<210> 96
<211> 18
<212> PRT
<213> 褐家鼠

<400> 96

Pro Asn Ala Ile Gly Arg Val Lys Trp Trp Arg Pro Asn Gly Pro Asp
1 5 10 15

Phe Arg

<210> 97
<211> 22
<212> PRT
<213> 褐家鼠

<400> 97

Lys Trp Trp Arg Pro Asn Gly Pro Asp Phe Arg Cys Ile Pro Asp Arg
1 5 10 15

Tyr Arg Ala Gln Arg Val
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<210> 98
<211> 213
<212> PRT
<213> 褐家鼠

<400> 98

Met Gln Leu Ser Leu Ala Pro Cys Leu Ala Cys Leu Leu Val His Ala
1 5 10 15

Ala Phe Val Ala Val Glu Ser Gln Gly Trp Gln Ala Phe Lys Asn Asp
20 25 30

Ala Thr Glu Ile Ile Pro Gly Leu Arg Glu Tyr Pro Glu Pro Pro Gln
35 40 45

Glu Leu Glu Asn Asn Gln Thr Met Asn Arg Ala Glu Asn Gly Gly Arg
50 55 60

Pro Pro His His Pro Tyr Asp Thr Lys Asp Val Ser Glu Tyr Ser Cys
65 70 75 80

Arg Glu Leu His Tyr Thr Arg Phe Val Thr Asp Gly Pro Cys Arg Ser
85 90 95

Ala Lys Pro Val Thr Glu Leu Val Cys Ser Gly Gln Cys Gly Pro Ala
100 105 110

Arg Leu Leu Pro Asn Ala Ile Gly Arg Val Lys Trp Trp Arg Pro Asn
115 120 125

Gly Pro Asp Phe Arg Cys Ile Pro Asp Arg Tyr Arg Ala Gln Arg Val
130 135 140

Gln Leu Leu Cys Pro Gly Gly Ala Ala Pro Arg Ser Arg Lys Val Arg
145 150 155 160

Leu Val Ala Ser Cys Lys Cys Lys Arg Leu Thr Arg Phe His Asn Gln
165 170 175

Ser Glu Leu Lys Asp Phe Gly Pro Glu Thr Ala Arg Pro Gln Lys Gly
180 185 190

Arg Lys Pro Arg Pro Arg Ala Arg Gly Ala Lys Ala Asn Gln Ala Glu
195 200 205

Leu Glu Asn Ala Tyr
210

<210> 99
<211> 7
<212> PRT
<213> 小家鼠

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Tyr Thr Ser Arg Leu His Ser
1 5

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<400> 100

Gln Gln Gly Asp Thr Leu Pro Tyr Thr
1 5

<210> 101
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<400> 101

Arg Ala Ser Gln Val Ile Thr Asn Tyr Leu Tyr
1 5 10

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<400> 102

Tyr Thr Ser Arg Leu His Ser
1 5

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Gln Gln Gly Asp Thr Leu Pro Tyr Thr
1 5

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Arg Ala Ser Gln Asp Ile Ser Asn Tyr Leu Asn
1 5 10

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Tyr Thr Ser Arg Leu Leu Ser
1 5

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Gln Gln Gly Asp Thr Leu Pro Tyr Thr
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Arg Ala Ser Gln Asp Ile Ser Asn Tyr Leu Asn
1 5 10

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Tyr Thr Ser Arg Leu Phe Ser
1 5

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Gln Gln Gly Asp Thr Leu Pro Tyr Thr
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1 5

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Gln Gln Gly Asp Thr Leu Pro Tyr Thr
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<400> 113

Arg Ala Ser Gln Asp Ile Ser Asn Tyr Leu Asn
1 5 10

<210> 114

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Tyr Thr Ser Thr Leu Gln Ser
1 5

<210> 115

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Gln Gln Gly Asp Thr Leu Pro Tyr Thr
1 5

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<400> 116

Ser Val Ser Ser Ser Ile Ser Ser Ser Asn Leu His
1 5 10

<210> 117

<211> 213

<212> PRT
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<400> 117

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Glu Lys Val Thr Met Thr Cys Arg Ala Ser Ser Ser Val Tyr Tyr Met
20 25 30
His Trp Tyr Gln Gln Lys Pro Gly Ser Ser Pro Lys Pro Trp Ile Tyr
35 40 45
Ala Thr Ser Asn Leu Ala Ser Gly Val Pro Val Arg Phe Ser Gly Ser
50 55 60
Gly Ser Gly Thr Ser Tyr Ser Leu Thr Ile Thr Arg Val Glu Ala Glu
65 70 75 80
Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asp Pro Leu Thr
85 90 95
Phe Gly Ala Gly Thr Lys Leu Glu Leu Lys Arg Ala Asp Ala Ala Pro
100 105 110
Thr Val Ser Ile Phe Pro Pro Ser Ser Glu Gln Leu Thr Ser Gly Gly
115 120 125
Ala Ser Val Val Cys Phe Leu Asn Asn Phe Tyr Pro Lys Asp Ile Asn
130 135 140
Val Lys Trp Lys Ile Asp Gly Ser Glu Arg Gln Asn Gly Val Leu Asn
145 150 155 160
Ser Trp Thr Asp Gln Asp Ser Lys Asp Ser Thr Tyr Ser Met Ser Ser
165 170 175
Thr Leu Thr Leu Thr Lys Asp Glu Tyr Glu Arg His Asn Ser Tyr Thr
180 185 190
Cys Glu Ala Thr His Lys Thr Ser Thr Ser Pro Ile Val Lys Ser Phe
195 200 205

Asn Arg Asn Glu Cys
210

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tcctccccc aacctggat ttatgccaca tccaacctgg ctcttgaggt cctgttcgc 180
ttcagtgcca gtgggtcttg gacctcttac tctctcacia tcaccagagt ggaggctgaa 240

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gatgctgcca cttattactg ccagcagtgg agtagtgacc cactcacgtt cggtgctggg      300
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aaagacatca atgtcaagtg gaagattgat ggcagtgaac gacaaaatgg cgtcctgaac      480
agttggactg atcaggacag caaagacagc acctacagca tgagcagcac cctcacgttg      540
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 <213> 小家鼠

<400> 119

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Val Ile Met Ser Arg Gly Gln Ile Val Leu Ser Gln Ser Pro Ala Ile
20 25 30

Leu Ser Thr Ser Pro Gly Glu Lys Val Thr Met Thr Cys Arg Ala Ser
35 40 45

Ser Ser Val Tyr Tyr Met His Trp Tyr Gln Gln Lys Pro Gly Ser Ser
50 55 60

Pro Lys Pro Trp Ile Tyr Ala Thr Ser Asn Leu Ala Ser Gly Val Pro
65 70 75 80

Val Arg Phe Ser Gly Ser Gly Ser Gly Thr Ser Tyr Ser Leu Thr Ile
85 90 95

Thr Arg Val Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp
100 105 110

Ser Ser Asp Pro Leu Thr Phe Gly Ala Gly Thr Lys Leu Glu Leu Lys
115 120 125

Arg Ala Asp Ala Ala Pro Thr Val Ser Ile Phe Pro Pro Ser Ser Glu
130 135 140

Gln Leu Thr Ser Gly Gly Ala Ser Val Val Cys Phe Leu Asn Asn Phe
145 150 155 160

Tyr Pro Lys Asp Ile Asn Val Lys Trp Lys Ile Asp Gly Ser Glu Arg
165 170 175

Gln Asn Gly Val Leu Asn Ser Trp Thr Asp Gln Asp Ser Lys Asp Ser
180 185 190

Thr Tyr Ser Met Ser Ser Thr Leu Thr Leu Thr Lys Asp Glu Tyr Glu
195 200 205

Arg His Asn Ser Tyr Thr Cys Glu Ala Thr His Lys Thr Ser Thr Ser

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Pro Ile Val Lys Ser Phe Asn Arg Asn Glu Cys		
225	230	235
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Val Tyr Pro Leu Ala Pro Gly Ser Ala Ala Gln Thr Asn Ser Met Val
130 135 140

Thr Leu Gly Cys Leu Val Lys Gly Tyr Phe Pro Glu Pro Val Thr Val
145 150 155 160

Thr Trp Asn Ser Gly Ser Leu Ser Ser Gly Val His Thr Phe Pro Ala
165 170 175

Val Leu Gln Ser Asp Leu Tyr Thr Leu Ser Ser Ser Val Thr Val Pro
180 185 190

Ser Ser Thr Trp Pro Ser Glu Thr Val Thr Cys Asn Val Ala His Pro
195 200 205

Ala Ser Ser Thr Lys Val Asp Lys Lys Ile Val Pro Arg Asp Cys Gly
210 215 220

Cys Lys Pro Cys Ile Cys Thr Val Pro Glu Val Ser Ser Val Phe Ile
225 230 235 240

Phe Pro Pro Lys Pro Lys Asp Val Leu Thr Ile Thr Leu Thr Pro Lys
245 250 255

Val Thr Cys Val Val Val Asp Ile Ser Lys Asp Asp Pro Glu Val Gln
260 265 270

Phe Ser Trp Phe Val Asp Asp Val Glu Val His Thr Ala Gln Thr Gln
275 280 285

Pro Arg Glu Glu Gln Phe Asn Ser Thr Phe Arg Ser Val Ser Glu Leu
290 295 300

Pro Ile Met His Gln Asp Trp Leu Asn Gly Lys Glu Phe Lys Cys Arg
305 310 315 320

Val Asn Ser Ala Ala Phe Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys
325 330 335

Thr Lys Gly Arg Pro Lys Ala Pro Gln Val Tyr Thr Ile Pro Pro Pro
340 345 350

Lys Glu Gln Met Ala Lys Asp Lys Val Ser Leu Thr Cys Met Ile Thr
355 360 365

Asp Phe Phe Pro Glu Asp Ile Thr Val Glu Trp Gln Trp Asn Gly Gln
370 375 380

Pro Ala Glu Asn Tyr Lys Asn Thr Gln Pro Ile Met Asp Thr Asp Gly
385 390 395 400

Ser Tyr Phe Ile Tyr Ser Lys Leu Asn Val Gln Lys Ser Asn Trp Glu
405 410 415

Ala Gly Asn Thr Phe Thr Cys Ser Val Leu His Glu Gly Leu His Asn

420	425	430
His His Thr Glu Lys Ser Leu Ser His Ser Pro Gly Lys		
435	440	445
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tccitgcacag cttctggcct caacattaaa gactacttta tacactgggt gaagcagagg	120	
cctgaacagg gccitggagtg gatttgaagg cttgatcctg aggatggtga aagtgattat	180	
gccccgaagt tccaggacaa ggccattatg acagcagaca catcatcaa cacagcctat	240	
cttcagctca gaagcctgac atctgaggac actgccatct attattgtga gagagaggac	300	
tacgatggta cctacacctt ttttccttac tggggccaag ggactctggt cactgtctct	360	
gcagccaaaa cgacaccccc atctgtctat ccactggccc ctggatctgc tgcccaaact	420	
aactccatgg tgaccctggg atgcctggtc aagggtctatt tccctgagcc agtgacagtg	480	
acctggaact ctggatccct gtccagcggg gtgcacacct tcccagctgt cctgcagtct	540	
gacctctaca cttctgagcag ctcatgtact gtccctcca gcacctggcc cagcgagacc	600	
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agggattgtg gttgtgaagg ttgcatagt acagtcccag aagtatcatc tgtcttcatc	720	
ttcccccaa agcccaagga tgtgtctacc attactctga ctccaaaggt cacgtgtgtt	780	
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gagggtgcaca cagctcagac gcaaccccgaggaggagcagt tcaacagcac tttccgctca	900	
gtcagtgaac ttcccatcat gcaccaggac tggctcaatg gcaaggagtt caaatgcagg	960	
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gtcagtctga cctgcatgat aacagacttc ttccttgaag acattactgt ggagtggcag	1140	
tggaaatgggc agccagcgga gaactacaag aacactcagc ccatcatgga cacagatggc	1200	
tcttacttca tctacagcaa gctcaatgtg cagaagagca actgggaggc aggaaatact	1260	
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<210> 123 <211> 464 <212> PRT <213> 小家鼠		
<400> 123		
Met Lys Cys Ser Trp Val Ile Phe Phe Leu Met Ala Val Val Thr Gly		
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Val Asn Ser Glu Val Gln Val Gln Gln Ser Gly Pro Glu Leu Val Lys		
20	25	30

Pro Gly Ala Ser Val Lys Leu Ser Cys Thr Ala Ser Gly Phe Asn Ile
 35 40 45
 Lys Asp Tyr Phe Ile His Trp Val Lys Gln Arg Pro Glu Gln Gly Leu
 50 55 60
 Glu Trp Ile Gly Arg Leu Asp Pro Glu Asp Gly Glu Ser Asp Tyr Ala
 65 70 75 80
 Pro Lys Phe Gln Asp Lys Ala Ile Met Thr Ala Asp Thr Ser Ser Asn
 85 90 95
 Thr Ala Tyr Leu Gln Leu Arg Ser Leu Thr Ser Glu Asp Thr Ala Ile
 100 105 110
 Tyr Tyr Cys Glu Arg Glu Asp Tyr Asp Gly Thr Tyr Thr Phe Phe Pro
 115 120 125
 Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ala Ala Lys Thr Thr
 130 135 140
 Pro Pro Ser Val Tyr Pro Leu Ala Pro Gly Ser Ala Ala Gln Thr Asn
 145 150 155 160
 Ser Met Val Thr Leu Gly Cys Leu Val Lys Gly Tyr Phe Pro Glu Pro
 165 170 175
 Val Thr Val Thr Trp Asn Ser Gly Ser Leu Ser Ser Gly Val His Thr
 180 185 190
 Phe Pro Ala Val Leu Gln Ser Asp Leu Tyr Thr Leu Ser Ser Ser Val
 195 200 205
 Thr Val Pro Ser Ser Thr Trp Pro Ser Glu Thr Val Thr Cys Asn Val
 210 215 220
 Ala His Pro Ala Ser Ser Thr Lys Val Asp Lys Lys Ile Val Pro Arg
 225 230 235 240
 Asp Cys Gly Cys Lys Pro Cys Ile Cys Thr Val Pro Glu Val Ser Ser
 245 250 255
 Val Phe Ile Phe Pro Pro Lys Pro Lys Asp Val Leu Thr Ile Thr Leu
 260 265 270
 Thr Pro Lys Val Thr Cys Val Val Val Asp Ile Ser Lys Asp Asp Pro
 275 280 285
 Glu Val Gln Phe Ser Trp Phe Val Asp Asp Val Glu Val His Thr Ala
 290 295 300
 Gln Thr Gln Pro Arg Glu Glu Gln Phe Asn Ser Thr Phe Arg Ser Val
 305 310 315 320
 Ser Glu Leu Pro Ile Met His Gln Asp Trp Leu Asn Gly Lys Glu Phe
 325 330 335

Lys Cys Arg Val Asn Ser Ala Ala Phe Pro Ala Pro Ile Glu Lys Thr
340 345 350

Ile Ser Lys Thr Lys Gly Arg Pro Lys Ala Pro Gln Val Tyr Thr Ile
355 360 365

Pro Pro Pro Lys Glu Gln Met Ala Lys Asp Lys Val Ser Leu Thr Cys
370 375 380

Met Ile Thr Asp Phe Phe Pro Glu Asp Ile Thr Val Glu Trp Gln Trp
385 390 395 400

Asn Gly Gln Pro Ala Glu Asn Tyr Lys Asn Thr Gln Pro Ile Met Asp
405 410 415

Thr Asp Gly Ser Tyr Phe Ile Tyr Ser Lys Leu Asn Val Gln Lys Ser
420 425 430

Asn Trp Glu Ala Gly Asn Thr Phe Thr Cys Ser Val Leu His Glu Gly
435 440 445

Leu His Asn His His Thr Glu Lys Ser Leu Ser His Ser Pro Gly Lys
450 455 460

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<212> DNA
<213> 小家鼠

<400> 124	
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tgcacagctt ctggctcaa cattaaagac tactttatac actgggtgaa gcagaggcct	180
gaacagggcc tggagtggat tggaaggctt gatcctgagg atggtgaaag tgattatgcc	240
ccgaagtcc aggacaaggc cattatgaca gcagacacat catccaacac agcctatctt	300
cagctcagaa gcctgacatc tgaggacact gccatctatt atgtgagag agaggactac	360
gatggctacct acaccttttt tccctacttg ggccaaggga ctcgtgtcac tgtctctgca	420
gccaaaacga ccccccatc tgtctatcca ctggccccctg gatctgctgc ccaaactaac	480
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aacagtgcag ctttccctgc ccccatcgag aaaaccatct ccaaaaccaa aggcagaccg	1080

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aatgggcagc cagcggagaa ctacaagaac actcagccca tcatggacac agatggctct 1260
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<210> 125
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<212> PRT
<213> 小家鼠

<400> 125

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

His Leu His Trp Phe Gln Gln Lys Ser Asp Thr Ser Pro Lys Pro Trp
35 40 45

Ile Tyr Gly Thr Ser Asn Leu Ala Ser Gly Val Pro Val Arg Phe Ser
50 55 60

Gly Ser Gly Ser Gly Thr Ser Tyr Ser Leu Thr Ile Ser Ser Met Glu
65 70 75 80

Ala Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Tyr Pro
85 90 95

Leu Thr Phe Gly Ala Gly Thr Lys Leu Glu Leu Arg Arg Ala Asp Ala
100 105 110

Ala Pro Thr Val Ser Ile Phe Pro Pro Ser Ser Glu Gln Leu Thr Ser
115 120 125

Gly Gly Ala Ser Val Val Cys Phe Leu Asn Asn Phe Tyr Pro Lys Asp
130 135 140

Ile Asn Val Lys Trp Lys Ile Asp Gly Ser Glu Arg Gln Asn Gly Val
145 150 155 160

Leu Asn Ser Trp Thr Asp Gln Asp Ser Lys Asp Ser Thr Tyr Ser Met
165 170 175

Ser Ser Thr Leu Thr Leu Thr Lys Asp Glu Tyr Glu Arg His Asn Ser
180 185 190

Tyr Thr Cys Glu Ala Thr His Lys Thr Ser Thr Ser Pro Ile Val Lys
195 200 205

Ser Phe Asn Arg Asn Glu Cys
210 215

<210> 126
<211> 648
<212> DNA
<213> 小家鼠

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tcagacacct cccccaacc ctggatttat ggcacatcca acctggcttc tggagtcctt 180
gttcgcttca gtggcagtggt atctgggacc tcttattctc tcacaatcag cagcatggag 240
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<212> PRT
<213> 小家鼠

<400> 127
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Val Ile Leu Ser Ser Gly Glu Ile Val Leu Thr Gln Ser Pro Ala Leu
20 25 30
Met Ala Ala Ser Pro Gly Glu Lys Val Thr Ile Thr Cys Ser Val Ser
35 40 45
Ser Thr Ile Ser Ser Asn His Leu His Trp Phe Gln Gln Lys Ser Asp
50 55 60
Thr Ser Pro Lys Pro Trp Ile Tyr Gly Thr Ser Asn Leu Ala Ser Gly
65 70 75 80
Val Pro Val Arg Phe Ser Gly Ser Gly Ser Gly Thr Ser Tyr Ser Leu
85 90 95
Thr Ile Ser Ser Met Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys Gln
100 105 110
Gln Trp Ser Ser Tyr Pro Leu Thr Phe Gly Ala Gly Thr Lys Leu Glu
115 120 125
Leu Arg Arg Ala Asp Ala Ala Pro Thr Val Ser Ile Phe Pro Pro Ser
130 135 140
Ser Glu Gln Leu Thr Ser Gly Gly Ala Ser Val Val Cys Phe Leu Asn
145 150 155 160

Asn Phe Tyr Pro Lys Asp Ile Asn Val Lys Trp Lys Ile Asp Gly Ser
165 170 175

Glu Arg Gln Asn Gly Val Leu Asn Ser Trp Thr Asp Gln Asp Ser Lys
180 185 190

Asp Ser Thr Tyr Ser Met Ser Ser Thr Leu Thr Leu Thr Lys Asp Glu
195 200 205

Tyr Glu Arg His Asn Ser Tyr Thr Cys Glu Ala Thr His Lys Thr Ser
210 215 220

Thr Ser Pro Ile Val Lys Ser Phe Asn Arg Asn Glu Cys
225 230 235

<210> 128
<211> 714
<212> DNA
<213> 小家鼠

<400> 128
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gtcaccatca cctgcagtgt cagttcaact ataagttcca accacttgca ctggttccag 180
cagaagtcag acacctcccc caaaccttgg atttatggca catccaacct ggcttctgga 240
gtccctgttc gcttcagtgg cagtggatct gggacctctt attctctcac aatcagcagc 300
atggaggctg aggatgctgc cacttattac tgtcaacagt ggagtagtta cccactcacg 360
ttcggcgctg ggaccaagct ggagctgaga cgggctgatg ctgcaccaac tgtatccatc 420
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aacttctacc ccaaagacat caatgtcaag tggaagattg atggcagtga acgacaaaat 540
ggcgtcctga acagtggac tgatcaggac agcaaagaca gcacctacag catgagcagc 600
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<210> 129
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<212> PRT
<213> 小家鼠

<400> 129

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

Tyr Leu His Trp Met Arg Gln Arg Pro Glu Gln Gly Leu Asp Trp Ile
35 40 45

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

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

Leu Gln Leu Ser Gly Leu Thr Ser Glu Thr Thr Ala Val Tyr Tyr Cys
85 90 95

Ser Arg Glu Ala Asp Tyr Phe His Asp Gly Thr Ser Tyr Trp Tyr Phe
100 105 110

Asp Val Trp Gly Ala Gly Thr Thr Ile Thr Val Ser Ser Ala Lys Thr
115 120 125

Thr Pro Pro Ser Val Tyr Pro Leu Ala Pro Gly Ser Ala Ala Gln Thr
130 135 140

Asn Ser Met Val Thr Leu Gly Cys Leu Val Lys Gly Tyr Phe Pro Glu
145 150 155 160

Pro Val Thr Val Thr Trp Asn Ser Gly Ser Leu Ser Ser Gly Val His
165 170 175

Thr Phe Pro Ala Val Leu Gln Ser Asp Leu Tyr Thr Leu Ser Ser Ser
180 185 190

Val Thr Val Pro Ser Ser Thr Trp Pro Ser Glu Thr Val Thr Cys Asn
195 200 205

Val Ala His Pro Ala Ser Ser Thr Lys Val Asp Lys Lys Ile Val Pro
210 215 220

Arg Asp Cys Gly Cys Lys Pro Cys Ile Cys Thr Val Pro Glu Val Ser
225 230 235 240

Ser Val Phe Ile Phe Pro Pro Lys Pro Lys Asp Val Leu Thr Ile Thr
245 250 255

Leu Thr Pro Lys Val Thr Cys Val Val Val Asp Ile Ser Lys Asp Asp
260 265 270

Pro Glu Val Gln Phe Ser Trp Phe Val Asp Asp Val Glu Val His Thr
275 280 285

Ala Gln Thr Gln Pro Arg Glu Glu Gln Phe Asn Ser Thr Phe Arg Ser
290 295 300

Val Ser Glu Leu Pro Ile Met His Gln Asp Trp Leu Asn Gly Lys Glu
305 310 315 320

Phe Lys Cys Arg Val Asn Ser Ala Ala Phe Pro Ala Pro Ile Glu Lys
325 330 335

Thr Ile Ser Lys Thr Lys Gly Arg Pro Lys Ala Pro Gln Val Tyr Thr
340 345 350

Ile Pro Pro Pro Lys Glu Gln Met Ala Lys Asp Lys Val Ser Leu Thr
355 360 365

Cys Met Ile Thr Asp Phe Phe Pro Glu Asp Ile Thr Val Glu Trp Gln
370 375 380

Trp Asn Gly Gln Pro Ala Glu Asn Tyr Lys Asn Thr Gln Pro Ile Met
385 390 395 400

Asp Thr Asp Gly Ser Tyr Phe Ile Tyr Ser Lys Leu Asn Val Gln Lys
405 410 415

Ser Asn Trp Glu Ala Gly Asn Thr Phe Thr Cys Ser Val Leu His Glu
420 425 430

Gly Leu His Asn His His Thr Glu Lys Ser Leu Ser His Ser Pro Gly
435 440 445

Lys

<210> 130
<211> 1350
<212> DNA
<213> 小家鼠

<400> 130
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cctgaacagg gcctggactg gattggaagg attgatcctg agaatggtga tactttatat 180
gacccgaagt tccaggacaa ggccactctt acaacagaca catcctccaa cacagcctac 240
ctgcagctca gcggcctgac atctgagacc actgccgtct attactgttc tagagaggcg 300
gattatttcc acgatggtag ctctacttgg tacttcgatg tctggggcgc agggaccaca 360
atcacctgtc cctcagccaa aacgacaccc ccactgtct atccactggc ccctggatct 420
gtgcgccaaa ctaactccat ggtgacctg gtagcctgg tcaagggcta ttccctgag 480
ccagtgcagc tgacctggaa ctctggatcc ctgtccagcg gtgtgcacac ctcccagct 540
gtcctgcagt ctgacctcta cactctgagc agctcagtga ctgtccctc cagcacctgg 600
cccagcgaga ccgtcacctg caacgttgcc caccgggcca gcagcaccaa ggtggacaag 660
aaaaattgtc ccagggattg tggttgtaag ccttgcatat gtacagtccc agaagtatca 720
tctgtcttca tcttcccccc aaagcccaag gatgtgtcga ccattactct gactcctaag 780
gtcacglgtg ttgtggtaga catcagcaag gatgatcccg aggtccagtt cagctggttt 840
gtagatgatg tggagggtgca cacagctcag acgcaacccc gggaggagca gttcaacagc 900
actttccgtc cagtgcagtga acttcccatc atgcaccagg actggctcaa tggcaaggag 960
ttcaaatgca gggtaaacag tgcagctttc cctgccccca tcgagaaaac catctccaaa 1020
accaaaggca gaccgaaggc tccacaggtg tacaccattc cacctcccaa ggagcagatg 1080
gccaaaggata aagtcagtct gacctgcatg ataacagact tcttccctga agacattact 1140
gtggagtggc agtggaatgg gcagccagcg gagaactaca agaacactca gcccatcatg 1200
gacacagatg gctcttactt catctacagc aagctcaatg tgcagaagag caactgggag 1260
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aagagcctct cccactctcc tggtaaata

1350

<210> 131
<211> 468
<212> PRT
<213> 小家鼠

<400> 131

Met Lys Cys Ser Trp Val Ile Phe Phe Leu Met Ala Val Val Thr Gly
1 5 10 15

Val Asn Ser Glu Val Gln Leu Gln Gln Ser Gly Ala Glu Leu Val Arg
20 25 30

Pro Gly Ala Leu Val Lys Leu Ser Cys Thr Ala Ser Asp Phe Asn Ile
35 40 45

Lys Asp Phe Tyr Leu His Trp Met Arg Gln Arg Pro Glu Gln Gly Leu
50 55 60

Asp Trp Ile Gly Arg Ile Asp Pro Glu Asn Gly Asp Thr Leu Tyr Asp
65 70 75 80

Pro Lys Phe Gln Asp Lys Ala Thr Leu Thr Thr Asp Thr Ser Ser Asn
85 90 95

Thr Ala Tyr Leu Gln Leu Ser Gly Leu Thr Ser Glu Thr Thr Ala Val
100 105 110

Tyr Tyr Cys Ser Arg Glu Ala Asp Tyr Phe His Asp Gly Thr Ser Tyr
115 120 125

Trp Tyr Phe Asp Val Trp Gly Ala Gly Thr Thr Ile Thr Val Ser Ser
130 135 140

Ala Lys Thr Thr Pro Pro Ser Val Tyr Pro Leu Ala Pro Gly Ser Ala
145 150 155 160

Ala Gln Thr Asn Ser Met Val Thr Leu Gly Cys Leu Val Lys Gly Tyr
165 170 175

Phe Pro Glu Pro Val Thr Val Thr Trp Asn Ser Gly Ser Leu Ser Ser
180 185 190

Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Asp Leu Tyr Thr Leu
195 200 205

Ser Ser Ser Val Thr Val Pro Ser Ser Thr Trp Pro Ser Glu Thr Val
210 215 220

Thr Cys Asn Val Ala His Pro Ala Ser Ser Thr Lys Val Asp Lys Lys
225 230 235 240

Ile Val Pro Arg Asp Cys Gly Cys Lys Pro Cys Ile Cys Thr Val Pro
245 250 255

Glu Val Ser Ser Val Phe Ile Phe Pro Pro Lys Pro Lys Asp Val Leu
260 265 270

Thr Ile Thr Leu Thr Pro Lys Val Thr Cys Val Val Val Asp Ile Ser
275 280 285

Lys Asp Asp Pro Glu Val Gln Phe Ser Trp Phe Val Asp Asp Val Glu
290 295 300

Val His Thr Ala Gln Thr Gln Pro Arg Glu Glu Gln Phe Asn Ser Thr
305 310 315 320

Phe Arg Ser Val Ser Glu Leu Pro Ile Met His Gln Asp Trp Leu Asn
325 330 335

Gly Lys Glu Phe Lys Cys Arg Val Asn Ser Ala Ala Phe Pro Ala Pro
340 345 350

Ile Glu Lys Thr Ile Ser Lys Thr Lys Gly Arg Pro Lys Ala Pro Gln
355 360 365

Val Tyr Thr Ile Pro Pro Pro Lys Glu Gln Met Ala Lys Asp Lys Val
370 375 380

Ser Leu Thr Cys Met Ile Thr Asp Phe Phe Pro Glu Asp Ile Thr Val
385 390 395 400

Glu Trp Gln Trp Asn Gly Gln Pro Ala Glu Asn Tyr Lys Asn Thr Gln
405 410 415

Pro Ile Met Asp Thr Asp Gly Ser Tyr Phe Ile Tyr Ser Lys Leu Asn
420 425 430

Val Gln Lys Ser Asn Trp Glu Ala Gly Asn Thr Phe Thr Cys Ser Val
435 440 445

Leu His Glu Gly Leu His Asn His His Thr Glu Lys Ser Leu Ser His
450 455 460

Ser Pro Gly Lys
465

<210> 132
<211> 1407
<212> DNA
<213> 小家鼠

<400> 132
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gttcagctgc agcagtctgg ggctgaactt gtgaggccag gggccctagt caagttgtcc 120
tgcacagctt ctgacttcaa cattaaagac ttctatctac actggatgag gcagcggcct 180
gaacagggcc tggactggat tggaaggatt gatcctgaga atggtgatac tttatatgac 240
ccgaagtcc aggacaaggc cactcttaca acagacacat cctccaacac agcctacctg 300
cagctcagcg gcctgacatc tgagaccact gccgtctatt actgttctag agaggcggat 360
tatttccag atggtacctc ctactgttac ttcgatgtct ggggcgcagg gaccacaatc 420

accgtctcct cagccaaaac gacaccccca tctgtctatc cactggcccc tggatctgct 480
gccccaaacta actccatggt gaccttggga tgccttggtca agggctatit ccctgagcca 540
gtgacagtga ccttggaactc tggatccctg tccagcgggtg tgcacacctt cccagctgtc 600
ctgcagctctg acctctacac tctgagcagc tcagtactg tccccctccag cacctggccc 660
agcgagaccg tcacctgcaa cgttgccca cgggccagca gcaccaaggt ggacaagaaa 720
attgtgcccc gggattgtgg ttgtaagcct tgcataatga cagtccaga agtatcatct 780
gtcttcatct tccccccaaa gcccaaggat gtgtcacca ttactctgac tcctaaggtc 840
acgtgtgttg tggtagacat cagcaaggat gatcccgagg tccagttcag ctggtttgta 900
gatgatgttg aggtgcacac agctcagacg caaccccggg aggagcagti caacagcact 960
ttccgctcag tcagigaact tcccatcatg caccaggact ggctcaatgg caaggagttc 1020
aaatgcaggg tcaacagtgc agctttccct gcccccatcg agaaaacat ctccaaaacc 1080
aaaggcagac cgaaggctcc acagggtgtac accattccac ctccaagga gcagatggcc 1140
aaggataaag tcagtctgac ctgcatgata acagattct tccctgaaga cattactgtg 1200
gagtggcagt ggaatgggca gccagcggag aactacaaga acactcagcc catcatggac 1260
acagatggct cttacttcat ctacagcaag ctcaatgtgc agaagagcaa ctgggaggca 1320
ggaaatactt tcacctgtc tgtgttacat gagggcctgc acaaccacca tactgagaag 1380
agcctctccc actctcctgg taaatga 1407

<210> 133
<211> 214
<212> PRT
<213> 小家鼠

<400> 133

Asp Ile Gln Met Thr Gln Ile Thr Ser Ser Leu Ser Ala Ser Leu Gly
1 5 10 15
Asp Arg Val Ser Ile Ser Cys Arg Ala Ser Gln Asp Ile Ser Asn Tyr
20 25 30
Leu Asn Trp Tyr Gln Gln Lys Pro Asp Gly Thr Phe Lys Leu Leu Ile
35 40 45
Phe Tyr Thr Ser Arg Leu Leu Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60
Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Tyr Asn Leu Glu Gln
65 70 75 80
Glu Asp Phe Ala Thr Tyr Phe Cys Gln Gln Gly Asp Thr Leu Pro Tyr
85 90 95
Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg Ala Asp Ala Ala
100 105 110
Pro Thr Val Ser Ile Phe Pro Pro Ser Ser Glu Gln Leu Thr Ser Gly
115 120 125

Gly Ala Ser Val Val Cys Phe Leu Asn Asn Phe Tyr Pro Lys Asp Ile
130 135 140

Asn Val Lys Trp Lys Ile Asp Gly Ser Glu Arg Gln Asn Gly Val Leu
145 150 155 160

Asn Ser Trp Thr Asp Gln Asp Ser Lys Asp Ser Thr Tyr Ser Met Ser
165 170 175

Ser Thr Leu Thr Leu Thr Lys Asp Glu Tyr Glu Arg His Asn Ser Tyr
180 185 190

Thr Cys Glu Ala Thr His Lys Thr Ser Thr Ser Pro Ile Val Lys Ser
195 200 205

Phe Asn Arg Asn Glu Cys
210

<210> 134
<211> 645
<212> DNA
<213> 小家鼠

<400> 134
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atcagttgca gggcaagtca agacattagc aattatttaa actgggtatca gcagaaacca 120
gatggaactt ttaaactcct tatcttctac acatcaagat tactctcagg agtcccatca 180
aggttcagtg gcagtgggtc tggaacagat tattctctca ccatttaca cctggagcaa 240
gaagattttg ccacttactt ttgccaacag ggagatacgc ttccgtacac tticggaggg 300
gggaccaagc tggaaataaa acgggctgat gctgcaccaa ctgtatccat cttccacca 360
tccagtgagc agttaacatc tggagggtgcc tcagtcgtgt gcttcttgaa caacttctac 420
cccaaagaca tcaatgtcaa gtggaagatt gatggcagtg aacgacaaaa tggcgtcctg 480
aacagttgga ctgatcagga cagcaaagac agcacctaca gcatgagcag caccctcacg 540
ttgaccaagg acgagtatga acgacataac agctatacct glgaggccac tcacaagaca 600
tcaacttcac ccattgtcaa gagcttcaac aggaatgagt gttag 645

<210> 135
<211> 234
<212> PRT
<213> 小家鼠

<400> 135

Met Met Ser Ser Ala Gln Phe Leu Gly Leu Leu Leu Cys Phe Gln
1 5 10 15

Gly Thr Arg Cys Asp Ile Gln Met Thr Gln Ile Thr Ser Ser Leu Ser
20 25 30

Ala Ser Leu Gly Asp Arg Val Ser Ile Ser Cys Arg Ala Ser Gln Asp
35 40 45

Ile Ser Asn Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Asp Gly Thr Phe
50 55 60

Lys Leu Leu Ile Phe Tyr Thr Ser Arg Leu Leu Ser Gly Val Pro Ser
65707580

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Tyr
859095

Asn Leu Glu Gln Glu Asp Phe Ala Thr Tyr Phe Cys Gln Gln Gly Asp
100105110

Thr Leu Pro Tyr Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg
115120125

Ala Asp Ala Ala Pro Thr Val Ser Ile Phe Pro Pro Ser Ser Glu Gln
130135140

Leu Thr Ser Gly Gly Ala Ser Val Val Cys Phe Leu Asn Asn Phe Tyr
145150155160

Pro Lys Asp Ile Asn Val Lys Trp Lys Ile Asp Gly Ser Glu Arg Gln
165170175

Asn Gly Val Leu Asn Ser Trp Thr Asp Gln Asp Ser Lys Asp Ser Thr
180185190

Tyr Ser Met Ser Ser Thr Leu Thr Leu Thr Lys Asp Glu Tyr Glu Arg
195200205

His Asn Ser Tyr Thr Cys Glu Ala Thr His Lys Thr Ser Thr Ser Pro
210215220

Ile Val Lys Ser Phe Asn Arg Asn Glu Cys
225230

<210> 136
<211> 705
<212> DNA
<213> 小家鼠

<400> 136
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atcagttgca gggcaagtca agacattagc aattatttaa actgglatca gcagaaacca
gatggaactt ttaaactcct tatcttttac acatcaagat tactctcagg agtcccatca
aggttcagtg gcagtgggtc tggaacagat tattctctca ccatttaca cctggagcaa
gaagattttg ccacttactt ttgccaacag ggagatacgc ttccgtacac tttcggaggg
gggaccaagc tggaataaaa acgggctgat gctgcaccaa ctgtatccat ctccccacca
tccagtgagc agttaacatc tggagggtcc tcagtcgtgt gcctcttgaa caacttttac
cccaaagaca tcaatgtcaa gtggaagatt gatggcagtg aacgacaaaa tggcgtcctg
aacagttgga ctgatcagga cagcaaagac agcacctaca gcatgagcag caccctcacg
ttgaccaagg acgagtatga acgacataac agctatacct gtgaggccac tcacaagaca
tcaacttcac ccattgtcaa gagcttcaac aggaatgagt gttag

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<210> 137
 <211> 447
 <212> PRT
 <213> 小家鼠

<400> 137

Glu Val Gln Leu Gln Gln Ser Gly Pro Glu Leu Met Lys Pro Gly Ala
 1 5 10 15

Ser Val Lys Met Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Tyr
 20 25 30

Asn Met His Trp Val Lys Gln Asn Gln Gly Lys Thr Leu Glu Trp Ile
 35 40 45

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

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

Met Glu Leu Arg Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys
 85 90 95

Ala Arg Leu Gly Tyr Asp Asp Ile Tyr Asp Asp Trp Tyr Phe Asp Val
 100 105 110

Trp Gly Ala Gly Thr Thr Val Thr Val Ser Ser Ala Lys Thr Thr Pro
 115 120 125

Pro Ser Val Tyr Pro Leu Ala Pro Gly Ser Ala Ala Gln Thr Asn Ser
 130 135 140

Met Val Thr Leu Gly Cys Leu Val Lys Gly Tyr Phe Pro Glu Pro Val
 145 150 155 160

Thr Val Thr Trp Asn Ser Gly Ser Leu Ser Ser Gly Val His Thr Phe
 165 170 175

Pro Ala Val Leu Gln Ser Asp Leu Tyr Thr Leu Ser Ser Ser Val Thr
 180 185 190

Val Pro Ser Ser Thr Trp Pro Ser Glu Thr Val Thr Cys Asn Val Ala
 195 200 205

His Pro Ala Ser Ser Thr Lys Val Asp Lys Lys Ile Val Pro Arg Asp
 210 215 220

Cys Gly Cys Lys Pro Cys Ile Cys Thr Val Pro Glu Val Ser Ser Val
 225 230 235 240

Phe Ile Phe Pro Pro Lys Pro Lys Asp Val Leu Thr Ile Thr Leu Thr
 245 250 255

Pro Lys Val Thr Cys Val Val Val Asp Ile Ser Lys Asp Asp Pro Glu
 260 265 270

Val Gln Phe Ser Trp Phe Val Asp Asp Val Glu Val His Thr Ala Gln
275 280 285

Thr Gln Pro Arg Glu Glu Gln Phe Asn Ser Thr Phe Arg Ser Val Ser
290 295 300

Glu Leu Pro Ile Met His Gln Asp Trp Leu Asn Gly Lys Glu Phe Lys
305 310 315 320

Cys Arg Val Asn Ser Ala Ala Phe Pro Ala Pro Ile Glu Lys Thr Ile
325 330 335

Ser Lys Thr Lys Gly Arg Pro Lys Ala Pro Gln Val Tyr Thr Ile Pro
340 345 350

Pro Pro Lys Glu Gln Met Ala Lys Asp Lys Val Ser Leu Thr Cys Met
355 360 365

Ile Thr Asp Phe Phe Pro Glu Asp Ile Thr Val Glu Trp Gln Trp Asn
370 375 380

Gly Gln Pro Ala Glu Asn Tyr Lys Asn Thr Gln Pro Ile Met Asp Thr
385 390 395 400

Asp Gly Ser Tyr Phe Ile Tyr Ser Lys Leu Asn Val Gln Lys Ser Asn
405 410 415

Trp Glu Ala Gly Asn Thr Phe Thr Cys Ser Val Leu His Glu Gly Leu
420 425 430

His Asn His His Thr Glu Lys Ser Leu Ser His Ser Pro Gly Lys
435 440 445

<210> 138
<211> 1344
<212> DNA
<213> 小家鼠

<400> 138
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tcctgcaagg ctctgggata tacattcact gactacaaca tgcactgggt gaagcagaac 120
caaggaaaga ccctagagtg gataggagaa attaatccta acagtgggtg tgctggctac 180
aaccagaagt tcaagggcaa ggccacattg actgtagaca agtcctccac cacagcctac 240
atggagctcc gcagcctgac atctgaggac tctgcagtct attactgtgc aagattgggc 300
tacgatgata tctacgacga ctgggtacttc gatgtctggg gcgcagggac cacggtcacc 360
gtctcctcag ccaaaacgac acccccatct gtctatccac tggcccttg atctgtgccc 420
caaaactaact ccatggtgac cctgggatgc ctggtaagg gctatttccc tgagccagtg 480
acagtgacct ggaactctgg atccctgtcc agcgggtgtc acaccttccc agctgtcctg 540
cagtctgacc tctacactct gagcagctca gtgactgtcc cctccagcac ctggcccagc 600
gagaccgtca cctgcaacgt tgcccaccg gccagcagca ccaaggtgga caagaaaatt 660
gtgcccaggg attgtggttg taagccttgc atatgtacag tcccagaagt atcatctgtc 720

ttcatcttcc ccccaaagcc caaggatgtg ctcaccattt ctcctgactcc taaggtcacg 780
tgtgtgtggt tagacatcag caaggatgat cccgagggtc agttcagctg gttttagat 840
gatgtggagg tgcacacagc tcagacgcaa ccccgaggagg agcagttcaa cagcactttc 900
cgctcagtca gtgaacttcc catcatgcac caggactggc tcaatggcaa ggagttcaaa 960
tgcagggtca acagtgcagc ttccctgcc cccatcgaga aaaccatctc caaaaccaa 1020
ggcagaccga aggtccaca ggtgtacacc attccacctc ccaaggagca gatggccaag 1080
gataaagtca gtctgacctg catgataaca gacttcttcc ctgaagacat tactgtggag 1140
tggcagtgga atgggcagcc agcggagaac tacaagaaca ctcagcccat catggacaca 1200
gatggctctt attcatcta cagcaagctc aatgtgcaga agagcaactg ggaggcagga 1260
aatactttca cctgtctgt gtacatgag ggctgcaca accaccatac tgagaagagc 1320
ctctcccact ctctggtaa atga 1344

<210> 139
<211> 466
<212> PRT
<213> 小家鼠

<400> 139

Met Gly Trp Ser Trp Thr Phe Leu Phe Leu Leu Ser Gly Thr Ala Gly
1 5 10 15
Val Leu Ser Glu Val Gln Leu Gln Gln Ser Gly Pro Glu Leu Met Lys
20 25 30
Pro Gly Ala Ser Val Lys Met Ser Cys Lys Ala Ser Gly Tyr Thr Phe
35 40 45
Thr Asp Tyr Asn Met His Trp Val Lys Gln Asn Gln Gly Lys Thr Leu
50 55 60
Glu Trp Ile Gly Glu Ile Asn Pro Asn Ser Gly Gly Ala Gly Tyr Asn
65 70 75 80
Gln Lys Phe Lys Gly Lys Ala Thr Leu Thr Val Asp Lys Ser Ser Thr
85 90 95
Thr Ala Tyr Met Glu Leu Arg Ser Leu Thr Ser Glu Asp Ser Ala Val
100 105 110
Tyr Tyr Cys Ala Arg Leu Gly Tyr Asp Asp Ile Tyr Asp Asp Trp Tyr
115 120 125
Phe Asp Val Trp Gly Ala Gly Thr Thr Val Thr Val Ser Ser Ala Lys
130 135 140
Thr Thr Pro Pro Ser Val Tyr Pro Leu Ala Pro Gly Ser Ala Ala Gln
145 150 155 160
Thr Asn Ser Met Val Thr Leu Gly Cys Leu Val Lys Gly Tyr Phe Pro
165 170 175
Glu Pro Val Thr Val Thr Trp Asn Ser Gly Ser Leu Ser Ser Gly Val

180										185										190																																			
His	Thr	Phe	Pro	Ala	Val	Leu	Gln	Ser	Asp	Leu	Tyr	Thr	Leu	Ser	Ser																																								
		195					200					205																																											
Ser	Val	Thr	Val	Pro	Ser	Ser	Thr	Trp	Pro	Ser	Glu	Thr	Val	Thr	Cys																																								
		210					215				220																																												
Asn	Val	Ala	His	Pro	Ala	Ser	Ser	Thr	Lys	Val	Asp	Lys	Lys	Ile	Val																																								
		225			230					235					240																																								
Pro	Arg	Asp	Cys	Gly	Cys	Lys	Pro	Cys	Ile	Cys	Thr	Val	Pro	Glu	Val																																								
				245					250					255																																									
Ser	Ser	Val	Phe	Ile	Phe	Pro	Pro	Lys	Pro	Lys	Asp	Val	Leu	Thr	Ile																																								
			260					265					270																																										
Thr	Leu	Thr	Pro	Lys	Val	Thr	Cys	Val	Val	Val	Asp	Ile	Ser	Lys	Asp																																								
		275					280					285																																											
Asp	Pro	Glu	Val	Gln	Phe	Ser	Trp	Phe	Val	Asp	Asp	Val	Glu	Val	His																																								
		290				295					300																																												
Thr	Ala	Gln	Thr	Gln	Pro	Arg	Glu	Glu	Gln	Phe	Asn	Ser	Thr	Phe	Arg																																								
		305			310					315					320																																								
Ser	Val	Ser	Glu	Leu	Pro	Ile	Met	His	Gln	Asp	Trp	Leu	Asn	Gly	Lys																																								
				325					330					335																																									
Glu	Phe	Lys	Cys	Arg	Val	Asn	Ser	Ala	Ala	Phe	Pro	Ala	Pro	Ile	Glu																																								
			340					345					350																																										
Lys	Thr	Ile	Ser	Lys	Thr	Lys	Gly	Arg	Pro	Lys	Ala	Pro	Gln	Val	Tyr																																								
		355					360					365																																											
Thr	Ile	Pro	Pro	Pro	Lys	Glu	Gln	Met	Ala	Lys	Asp	Lys	Val	Ser	Leu																																								
		370				375					380																																												
Thr	Cys	Met	Ile	Thr	Asp	Phe	Phe	Pro	Glu	Asp	Ile	Thr	Val	Glu	Trp																																								
		385			390				395					400																																									
Gln	Trp	Asn	Gly	Gln	Pro	Ala	Glu	Asn	Tyr	Lys	Asn	Thr	Gln	Pro	Ile																																								
				405				410					415																																										
Met	Asp	Thr	Asp	Gly	Ser	Tyr	Phe	Ile	Tyr	Ser	Lys	Leu	Asn	Val	Gln																																								
			420				425					430																																											
Lys	Ser	Asn	Trp	Glu	Ala	Gly	Asn	Thr	Phe	Thr	Cys	Ser	Val	Leu	His																																								
		435				440					445																																												
Glu	Gly	Leu	His	Asn	His	His	Thr	Glu	Lys	Ser	Leu	Ser	His	Ser	Pro																																								
		450			455						460																																												
Gly	Lys																																																						
		465																																																					

<210> 140
<211> 1401
<212> DNA
<213> 小家鼠

<400> 140
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tgcaaggcct ctggatatac attcactgac tacaacatgc actgggtgaa gcagaaccaa 180
ggaaagacc tagagtggat aggagaaatt aatcctaaca gtggtggtgc tggctacaac 240
cagaagtcca agggcaaggc cacattgact gtagacaagt cctccaccac agcctacatg 300
gagctccgca gcctgacatc tgaggactct gcagtctatt actgtgcaag attgggctac 360
gatgatact acgacgactg gtacttcgat gtctggggcg cagggaccac ggtcaccgtc 420
tcctcagcca aaacgacacc cccatctgtc tatccactgg cccctggatc tgctgcccaa 480
actaactcca tggtagacct gggatgcctg gtcaagggtc atttccctga gccagtgcac 540
gtgacctgga actctggatc cctgtccagc ggtgtgcaca ccttcccagc tctctgcag 600
ctgacctct acactctgag cagctcagt actgtccct ccagcacctg gccagcgag 660
accgtacct gcaacgttc ccaccggcc agcagacca aggtggacaa gaaaattgtg 720
cccagggatt gtggttgtaa gccttgcata tglacagtc cagaagtatc atctgtcttc 780
atcttcccc caaagcccaa ggatgtgctc accattactc tgactcctaa ggtcacgtgt 840
gttgtggtag acatcagcaa ggatgatccc gaggtccagt tcagctggtt tglagatgat 900
gtggagggtc acacagctca gacgcaaccc cgggaggagc agttcaacag cactttccgc 960
tcagtcatg aacttcccat catgcaccag gactggctca atggcaagga gttcaaatgc 1020
agggtaaca gtgcagcttt cctgtccccc atcgagaaaa ccatctccaa aaccaaaggc 1080
agaccgaagg ctccacaggi gtacaccatt ccacctccca aggagcagat ggccaaggat 1140
aaagtcagtc tgacctgcat gataacagac ttcttccctg aagacattac tgtggagtgg 1200
cagtggaatg ggcagccagc ggagaactac aagaacactc agcccatcat ggacacagat 1260
ggctcttact tcatctacag caagctcaat gtgcagaaga gcaactggga ggcaggaaat 1320
actttacct gctctgtgtt acatgagggc ctgcacaacc accatactga gaagagcctc 1380
tccactctc ctggtaaatg a 1401

<210> 141
<211> 214
<212> PRT
<213> 人工序列

<220>
<223> 合成多肽

<220>
<221> MISC_FEATURE
<223> 人化抗体序列

<400> 141
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Ile Ser Asn Tyr

20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Tyr Thr Ser Arg Leu Leu Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Gly Asp Thr Leu Pro Tyr
85 90 95

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala
100 105 110

Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly
115 120 125

Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala
130 135 140

Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln
145 150 155 160

Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser
165 170 175

Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
180 185 190

Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
195 200 205

Phe Asn Arg Gly Glu Cys
210

<210> 142
<211> 642
<212> DNA
<213> 人工序列

<220>
<223> 合成聚核苷酸

<220>
<221> misc_feature
<223> 人化抗体序列

<400> 142
gacatccaga tgaccagtc tccatcctcc ctctccgcat ccgtaggcga ccgcgtaacc 60
ataacatgta gagcatctca agatatttcc aactatttga attggtacca acaaaaaccc 120
ggcaaagcac ctaaactcct catctactat acatcaagac tcctctccgg cgttccatca 180
cgattctcag gctccggctc cggcacagat ttacactca ctatttctc cctccaacca 240
gaagattttg caacctatta ctgtcaacaa ggcgatacac tccatacac attcggcggc 300

ggcacaaaag ttgaaattaa acgtacggtg gctgcaccat ctgtcttcat ctcccgcca 360
tctgatgagc agttgaaatc tggaactgcc tctgttgtgt gcctgctgaa taacttctat 420
cccagagagg ccaaagtaca gtggaaggig gataacgcc tccaatcggg taactcccag 480
gagagtgtca cagagcagga cagcaaggac agcacctaca gcctcagcag caccctgacg 540
ctgagcaaag cagactacga gaaacacaaa gtctacgcct gcgaagtcac ccacaggggc 600
ctgagctcgc ccgtcacaaa gagcttcaac aggggagagt gt 642

<210> 143
<211> 236
<212> PRT
<213> 人工序列

<220>
<223> 合成多肽

<220>
<221> MISC_FEATURE
<223> 人化抗体序列

<400> 143

Met Asp Met Arg Val Pro Ala Gln Leu Leu Gly Leu Leu Leu Leu Trp
1 5 10 15

Leu Arg Gly Ala Arg Cys Asp Ile Gln Met Thr Gln Ser Pro Ser Ser
20 25 30

Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser
35 40 45

Gln Asp Ile Ser Asn Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys
50 55 60

Ala Pro Lys Leu Leu Ile Tyr Tyr Thr Ser Arg Leu Leu Ser Gly Val
65 70 75 80

Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
85 90 95

Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln
100 105 110

Gly Asp Thr Leu Pro Tyr Thr Phe Gly Gly Gly Thr Lys Val Glu Ile
115 120 125

Lys Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp
130 135 140

Glu Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn
145 150 155 160

Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu
165 170 175

Gln Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp
180 185 190

Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr
195 200 205

Glu Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser
210 215 220

Ser Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
225 230 235

<210> 144
<211> 708
<212> DNA
<213> 人工序列

<220>
<223> 合成聚核苷酸

<220>
<221> misc_feature
<223> 人化抗体序列

<400> 144
atggacatga gggccccgc tcagctcctg gggctcctgc tactctggct ccgaggtgcc 60
agatgtgaca tccagatgac ccagtctcca tcttccctct ccgcatccgt aggcgaccgc 120
gtaaccataa catgtagagc atctcaagat atttccaact attgaattg gtaccaacaa 180
aaacccggca aagcacctaa actcctcatl tactatacat caagactcct ctccggcggt 240
ccatcacgat tctcaggctc cggtccggc acagatttca cactcactat ttcctccctc 300
caaccagaag attttgcaac ctattactgt caacaaggcg atacactccc atacacattc 360
ggcggcggca caaaagtiga aattaaacgt acggtggctg caccatctgt ctcatcttc 420
ccgccatctg atgagcagtt gaaatctgga actgcctctg ttgtgtgcct gctgaataac 480
ttctatccca gagaggccaa agtacagtgg aagggtggata acgcccacca atcgggtaac 540
tcccaggaga gtgtcacaga gcaggacagc aaggacagca cctacagcct cagcagcacc 600
ctgacgctga gcaaagcaga ctacgagaaa cacaaagtct acgcctgcga agtcacccat 660
cagggcctga gctcgcccggt cacaaagagc ttcaacaggg gagagtgt 708

<210> 145
<211> 449
<212> PRT
<213> 人工序列

<220>
<223> 合成多肽

<220>
<221> MISC_FEATURE
<223> 人化抗体序列

<400> 145

Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Tyr
20 25 30

Asn	Met	His	Trp	Val	Arg	Gln	Ala	Pro	Gly	Gln	Gly	Leu	Glu	Trp	Met
354045															
Gly	Glu	Ile	Asn	Pro	Asn	Ser	Gly	Gly	Ala	Gly	Tyr	Asn	Gln	Lys	Phe
505560															
Lys	Gly	Arg	Val	Thr	Met	Thr	Thr	Asp	Thr	Ser	Thr	Ser	Thr	Ala	Tyr
65707580															
Met	Glu	Leu	Arg	Ser	Leu	Arg	Ser	Asp	Asp	Thr	Ala	Val	Tyr	Tyr	Cys
859095															
Ala	Arg	Leu	Gly	Tyr	Asp	Asp	Ile	Tyr	Asp	Asp	Trp	Tyr	Phe	Asp	Val
100105110															
Trp	Gly	Gln	Gly	Thr	Thr	Val	Thr	Val	Ser	Ser	Ala	Ser	Thr	Lys	Gly
115120125															
Pro	Ser	Val	Phe	Pro	Leu	Ala	Pro	Cys	Ser	Arg	Ser	Thr	Ser	Glu	Ser
130135140															
Thr	Ala	Ala	Leu	Gly	Cys	Leu	Val	Lys	Asp	Tyr	Phe	Pro	Glu	Pro	Val
145150155160															
Thr	Val	Ser	Trp	Asn	Ser	Gly	Ala	Leu	Thr	Ser	Gly	Val	His	Thr	Phe
165170175															
Pro	Ala	Val	Leu	Gln	Ser	Ser	Gly	Leu	Tyr	Ser	Leu	Ser	Ser	Val	Val
180185190															
Thr	Val	Pro	Ser	Ser	Asn	Phe	Gly	Thr	Gln	Thr	Tyr	Thr	Cys	Asn	Val
195200205															
Asp	His	Lys	Pro	Ser	Asn	Thr	Lys	Val	Asp	Lys	Thr	Val	Glu	Arg	Lys
210215220															
Cys	Cys	Val	Glu	Cys	Pro	Pro	Cys	Pro	Ala	Pro	Pro	Val	Ala	Gly	Pro
225230235240															
Ser	Val	Phe	Leu	Phe	Pro	Pro	Lys	Pro	Lys	Asp	Thr	Leu	Met	Ile	Ser
245250255															
Arg	Thr	Pro	Glu	Val	Thr	Cys	Val	Val	Val	Asp	Val	Ser	His	Glu	Asp
260265270															
Pro	Glu	Val	Gln	Phe	Asn	Trp	Tyr	Val	Asp	Gly	Val	Glu	Val	His	Asn
275280285															
Ala	Lys	Thr	Lys	Pro	Arg	Glu	Glu	Gln	Phe	Asn	Ser	Thr	Phe	Arg	Val
290295300															
Val	Ser	Val	Leu	Thr	Val	Val	His	Gln	Asp	Trp	Leu	Asn	Gly	Lys	Glu
305310315320															
Tyr	Lys	Cys	Lys	Val	Ser	Asn	Lys	Gly	Leu	Pro	Ala	Pro	Ile	Glu	Lys
325330335															

Thr Ile Ser Lys Thr Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr
340 345 350

Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr
355 360 365

Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu
370 375 380

Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Met Leu
385 390 395 400

Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys
405 410 415

Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu
420 425 430

Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
435 440 445

Lys

<210> 146
<211> 1347
<212> DNA
<213> 人工序列

<220>
<223> 合成聚核苷酸

<220>
<221> misc_feature
<223> 人化抗体序列

<400> 146
gaggtgcagc tgggtgcagag cggcgccgag gtaaaaaaac caggagcaag cgttaaagtt 60
tcttgtaaag caagcggata tacatttaca gattacaaca tgcattgggt aagacaagcg 120
ccaggacaag gattggaatg gatgggcgaa attaaccta atagtggagg agcaggctac 180
aatcaaaaat tcaaaggagg agttacaatg acaacagaca caagcacttc aacagcatat 240
atggaactgc gatcacttag aagcgacgat acagctgtat actattgcgc acgacttggg 300
tatgatgata tataatgatga ctggtatttc gatgtttggg gccagggaac aacagttacc 360
gtctctagtg cctccaccaa gggcccatcg gtcttcccc tggcgccctg ctccaggagc 420
acctccgaga gcacagcggc cctgggctgc ctggtcaagg actacttccc cgaaccggtg 480
acgggtgctg ggaactcagg cgctctgacc agcggcgtgc acaccttccc agctgtccta 540
cagtcctcag gactctactc cctcagcagc gtggtgaccg tgccctccag caacttcggc 600
accagacct acacctgcaa cgtagatcac aagcccagca acaccaaggt ggacaagaca 660
gttgagcgca aatgttgtgt cgagtgcaca ccgtgcccag caccacctgt ggcaggaccg 720
tcagtcttcc tcttcccccc aaaaccaag gacacctca tgatctccc gacccttgag 780
gtcacgtgcg tgggtggtgga cgtgagccac gaagacccc aggtccagtt caactggtac 840

gtggacggcg tggagggtgca taatgccaag acaaagccac gggaggagca gttcaacagc 900
acgtttccgtg tggtcagcgt cctcaccgtt gtgcaccagg actggctgaa cggcaaggag 960
tacaagtigca aggtctccaa caaaggcctc ccagccccca tcgagaaaac catctccaaa 1020
accaaagggc agccccgaga accacagggtg tacaccctgc ccccatcccg ggaggagatg 1080
accaagaacc aggtcagcct gacctgcctg gtcaaaggct tctaccccag cgacatcgcc 1140
gtggagtggg agagcaatgg gcagccggag aacaactaca agaccacacc tcccatgctg 1200
gactccgacg gctcttctt cctctacagc aagctcaccg tggacaagag caggtggcag 1260
caggggaacg tcttctcatg ctccgtgatg catgaggctc tgcacaacca ctacacgcag 1320
aagagcctct ccctgtctcc gggtaaa 1347

<210> 147
<211> 468
<212> PRT
<213> 人工序列

<220>
<223> 合成多肽

<220>
<221> MISC_FEATURE
<223> 人化抗体序列

<400> 147

Met Asp Trp Thr Trp Arg Ile Leu Phe Leu Val Ala Ala Ala Thr Gly
1 5 10 15

Ala His Ser Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys
20 25 30

Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe
35 40 45

Thr Asp Tyr Asn Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu
50 55 60

Glu Trp Met Gly Glu Ile Asn Pro Asn Ser Gly Gly Ala Gly Tyr Asn
65 70 75 80

Gln Lys Phe Lys Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser
85 90 95

Thr Ala Tyr Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val
100 105 110

Tyr Tyr Cys Ala Arg Leu Gly Tyr Asp Asp Ile Tyr Asp Asp Trp Tyr
115 120 125

Phe Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser
130 135 140

Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr
145 150 155 160

Ser Glu Ser Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro

165	170	175
Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val 180 185 190		
His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser 195 200 205		
Ser Val Val Thr Val Pro Ser Ser Asn Phe Gly Thr Gln Thr Tyr Thr 210 215 220		
Cys Asn Val Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys Thr Val 225 230 235 240		
Glu Arg Lys Cys Cys Val Glu Cys Pro Pro Cys Pro Ala Pro Pro Val 245 250 255		
Ala Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu 260 265 270		
Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser 275 280 285		
His Glu Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu 290 295 300		
Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr 305 310 315 320		
Phe Arg Val Val Ser Val Leu Thr Val Val His Gln Asp Trp Leu Asn 325 330 335		
Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ala Pro 340 345 350		
Ile Glu Lys Thr Ile Ser Lys Thr Lys Gly Gln Pro Arg Glu Pro Gln 355 360 365		
Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val 370 375 380		
Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val 385 390 395 400		
Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro 405 410 415		
Pro Met Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr 420 425 430		
Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val 435 440 445		
Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu 450 455 460		

Ser Pro Gly Lys
465

<210> 148
<211> 1404
<212> DNA
<213> 小家鼠

<400> 148
atggactgga cctggaggat cctcttcttg gtggcagcag ccacaggagc ccactccgag 60
gtgcagctgg tgcagagcgg cgccgaggta aaaaaaccag gagcaagcgt taaagtttct 120
tgtaaagcaa gcggatatac atttacagat tacaacatgc attgggtaag acaagcgcca 180
ggacaaggat tggaatggat gggcgaaatt aaccctaata gtggaggagc aggctacaat 240
caaaaattca aaggagagat tacaatgaca acagacacaa gcacttcaac agcatatatg 300
gaactgcgat cacttagaag cgacgataca gctgtatact attgcgcacg acttgggtat 360
gatgatatat atgatgactg gtatttcgat gtttggggcc agggaacaac agttaccgtc 420
tctagtgcct ccaccaaggg cccatcggtc tccccctgg cgccclgctc caggagcacc 480
tccgagagca cagcggccct gggctgcctg gtcaaggact acttccccga accggtgacg 540
gtgtcgtgga actcaggcgc tctgaccagc ggcgtgcaca ctttcccagc tglcctacag 600
tcctcaggac tctactccct cagcagcgtg gtgaccgtgc cctccagcaa cttcggcacc 660
cagacctaca cctgcaacgt agatcacaaag cccagcaaca ccaagggtga caagacagtt 720
gagcgcaaat gttgtgtcga gtgcccaccg tgcacagcac cacctgtggc aggaccgta 780
gtcttctctt tcccccaaa acccaaggac accctcatga tctccggac cctgaggtc 840
acgtgcgtgg tgggtggacgt gagccacgaa gaccccgagg tccagttcaa ctggtacgtg 900
gacggcgtgg aggtgcataa tgccaagaca aagccacggg aggagcagtt caacagcacg 960
ttccgtgtgg tcagcgtcct caccgttgtg caccaggact ggctgaacgg caaggagtac 1020
aagtgcagg tctccaacaa aggcctccca gcccccacg agaaaacat ctccaaaacc 1080
aaagggcagc cccgagaacc acaggtgtac accctgcccc catcccggga ggagatgacc 1140
aagaaccagg tcagcctgac ctgcctggtc aaaggcttct accccagcga catcgccgtg 1200
gagtgggaga gcaatgggca gccggagaac aactacaaga ccacacctcc catgctggac 1260
tccgacggct ctttcttctt ctacagcaag ctaccgtgg acaagagcag gtggcagcag 1320
gggaacgtct tctcatgctc cgtgatgcat gaggcctctg acaaccacta cagcagaag 1380
agcctctccc tgtctccggg taaa 1404

<210> 149
<211> 214
<212> PRT
<213> 小家鼠

<400> 149

Asp Ile Gln Met Thr Gln Thr Thr Ser Ser Leu Ser Ala Ser Leu Gly
1 5 10 15

Asp Arg Val Thr Ile Ser Cys Arg Ala Ser Gln Asp Ile Ser Asn Tyr
20 25 30

Leu Asn Trp Phe Gln Gln Lys Pro Asp Gly Thr Leu Lys Leu Leu Ile

35

40

45

Phe Tyr Thr Ser Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Ser Asn Leu Glu Gln
65 70 75 80

Glu Asp Ile Ala Thr Tyr Phe Cys Gln Gln Gly Asp Thr Leu Pro Tyr
85 90 95

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Arg Arg Ala Asp Ala Ala
100 105 110

Pro Thr Val Ser Ile Phe Pro Pro Ser Ser Glu Gln Leu Thr Ser Gly
115 120 125

Gly Ala Ser Val Val Cys Phe Leu Asn Asn Phe Tyr Pro Lys Asp Ile
130 135 140

Asn Val Lys Trp Lys Ile Asp Gly Ser Glu Arg Gln Asn Gly Val Leu
145 150 155 160

Asn Ser Trp Thr Asp Gln Asp Ser Lys Asp Ser Thr Tyr Ser Met Ser
165 170 175

Ser Thr Leu Thr Leu Thr Lys Asp Glu Tyr Glu Arg His Asn Ser Tyr
180 185 190

Thr Cys Glu Ala Thr His Lys Thr Ser Thr Ser Pro Ile Val Lys Ser
195 200 205

Phe Asn Arg Asn Glu Cys
210

<210> 150
<211> 645
<212> DNA
<213> 小家鼠

<400> 150

gatataccaga tgacacagac tacatcctcc ctgtctgcct cctcgggaga cagagtcacc 60

atcagttgca gggcaagtca ggacattagc aattatttaa actggtttca gcagaaacca 120

gatggaactc ttaaaactcct gatcttctac acatcaagat tacactcagg agttccatca 180

aggttcagtg gcagtgggtc tggaacagat tattctctca ccattagcaa cctggagcaa 240

gaagatatig ccacttactt ttgccaacag ggtgatacgc ttccgtacac gttcgggggg 300

gggaccaagc tggaaataag acgggctgat gctgcaccaa ctgtatccat cttcccacca 360

tccagtgagc agttaacatc tggaggtgcc tcagtcgtgt gcttcttgaa caacttctac 420

cccaaagaca tcaatgtcaa gtggaagatt gatggcagtg aacgacaaaa tggcgtcctg 480

aacagttgga ctgatcagga cagcaaagac agcacctaca gcatgagcag caccctcacg 540

ttgaccaagg acgagtatga acgacataac agctatacct gtgaggccac tcacaagaca 600

tcaacttcac ccattgtcaa gagcttcaac aggaatgagt gttag 645

<210> 151
 <211> 234
 <212> PRT
 <213> 小家鼠

<400> 151

Met Met Ser Ser Ala Gln Phe Leu Gly Leu Leu Leu Leu Cys Phe Gln
 1 5 10 15

Gly Thr Arg Cys Asp Ile Gln Met Thr Gln Thr Thr Ser Ser Leu Ser
 20 25 30

Ala Ser Leu Gly Asp Arg Val Thr Ile Ser Cys Arg Ala Ser Gln Asp
 35 40 45

Ile Ser Asn Tyr Leu Asn Trp Phe Gln Gln Lys Pro Asp Gly Thr Leu
 50 55 60

Lys Leu Leu Ile Phe Tyr Thr Ser Arg Leu His Ser Gly Val Pro Ser
 65 70 75 80

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Ser
 85 90 95

Asn Leu Glu Gln Glu Asp Ile Ala Thr Tyr Phe Cys Gln Gln Gly Asp
 100 105 110

Thr Leu Pro Tyr Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Arg Arg
 115 120 125

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

Leu Thr Ser Gly Gly Ala Ser Val Val Cys Phe Leu Asn Asn Phe Tyr
 145 150 155 160

Pro Lys Asp Ile Asn Val Lys Trp Lys Ile Asp Gly Ser Glu Arg Gln
 165 170 175

Asn Gly Val Leu Asn Ser Trp Thr Asp Gln Asp Ser Lys Asp Ser Thr
 180 185 190

Tyr Ser Met Ser Ser Thr Leu Thr Leu Thr Lys Asp Glu Tyr Glu Arg
 195 200 205

His Asn Ser Tyr Thr Cys Glu Ala Thr His Lys Thr Ser Thr Ser Pro
 210 215 220

Ile Val Lys Ser Phe Asn Arg Asn Glu Cys
 225 230

<210> 152
 <211> 705
 <212> DNA
 <213> 小家鼠

<400> 152

atgatgtcct ctgctcagtt ccttggctct ctgttgctct gttttcaagg taccagatgt

60

gatatccaga tgacacagac tacatcctcc ctgtctgcct cctctgggaga cagagtcacc 120
atcagttgca gggcaagtca ggacattagc aattatttaa actggtttca gcagaaacca 180
gatggaactc ttaaactcct gatcttctac acatcaagat tacactcagg agttccatca 240
aggttcagtg gcagtgggtc tggaacagat tattctctca ccattagcaa cctggagcaa 300
gaagatatgg ccacttactt ttgccaacag ggtgatacgc ttccgtacac gttcgggggg 360
gggaccaagc tggaaataag acgggctgat gctgcaccaa ctglatccat cttcccacca 420
tccagtgagc agttaacatc tggaggtgcc tcagtcgtgt gcttcttgaa caacttctac 480
cccaaagaca tcaatgtcaa gtggaagatt gatggcagtg aacgacaaaa tggcgtcctg 540
aacagttgga ctgatcagga cagcaaagac agcacctaca gcatgagcag caccctcacg 600
ttgaccaagg acgagtatga acgacataac agctatacct gtgaggccac tcacaagaca 660
tcaacttcac ccattgtcaa gagcttcaac aggaatgagi gttag 705

<210> 153
<211> 447
<212> PRT
<213> 小家鼠

<400> 153

Glu Val Gln Leu Gln Gln Ser Gly Pro Glu Leu Met Lys Pro Gly Ala
1 5 10 15
Ser Val Lys Met Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Tyr
20 25 30
Asn Met His Trp Val Lys Gln Asn Gln Gly Lys Ser Leu Glu Trp Ile
35 40 45
Gly Glu Ile Asn Pro Asn Ser Gly Gly Ser Gly Tyr Asn Gln Lys Phe
50 55 60
Lys Gly Lys Ala Thr Leu Thr Val Asp Lys Ser Ser Ser Thr Ala Tyr
65 70 75 80
Met Glu Leu Arg Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys
85 90 95
Ala Arg Leu Val Tyr Asp Gly Ser Tyr Glu Asp Trp Tyr Phe Asp Val
100 105 110
Trp Gly Ala Gly Thr Thr Val Thr Val Ser Ser Ala Lys Thr Thr Pro
115 120 125
Pro Ser Val Tyr Pro Leu Ala Pro Gly Ser Ala Ala Gln Thr Asn Ser
130 135 140
Met Val Thr Leu Gly Cys Leu Val Lys Gly Tyr Phe Pro Glu Pro Val
145 150 155 160
Thr Val Thr Trp Asn Ser Gly Ser Leu Ser Ser Gly Val His Thr Phe
165 170 175

Pro Ala Val Leu Gln Ser Asp Leu Tyr Thr Leu Ser Ser Ser Val Thr
180 185 190

Val Pro Ser Ser Thr Trp Pro Ser Glu Thr Val Thr Cys Asn Val Ala
195 200 205

His Pro Ala Ser Ser Thr Lys Val Asp Lys Lys Ile Val Pro Arg Asp
210 215 220

Cys Gly Cys Lys Pro Cys Ile Cys Thr Val Pro Glu Val Ser Ser Val
225 230 235 240

Phe Ile Phe Pro Pro Lys Pro Lys Asp Val Leu Thr Ile Thr Leu Thr
245 250 255

Pro Lys Val Thr Cys Val Val Val Asp Ile Ser Lys Asp Asp Pro Glu
260 265 270

Val Gln Phe Ser Trp Phe Val Asp Asp Val Glu Val His Thr Ala Gln
275 280 285

Thr Gln Pro Arg Glu Glu Gln Phe Asn Ser Thr Phe Arg Ser Val Ser
290 295 300

Glu Leu Pro Ile Met His Gln Asp Trp Leu Asn Gly Lys Glu Phe Lys
305 310 315 320

Cys Arg Val Asn Ser Ala Ala Phe Pro Ala Pro Ile Glu Lys Thr Ile
325 330 335

Ser Lys Thr Lys Gly Arg Pro Lys Ala Pro Gln Val Tyr Thr Ile Pro
340 345 350

Pro Pro Lys Glu Gln Met Ala Lys Asp Lys Val Ser Leu Thr Cys Met
355 360 365

Ile Thr Asp Phe Phe Pro Glu Asp Ile Thr Val Glu Trp Gln Trp Asn
370 375 380

Gly Gln Pro Ala Glu Asn Tyr Lys Asn Thr Gln Pro Ile Met Asp Thr
385 390 395 400

Asp Gly Ser Tyr Phe Ile Tyr Ser Lys Leu Asn Val Gln Lys Ser Asn
405 410 415

Trp Glu Ala Gly Asn Thr Phe Thr Cys Ser Val Leu His Glu Gly Leu
420 425 430

His Asn His His Thr Glu Lys Ser Leu Ser His Ser Pro Gly Lys
435 440 445

<210> 154
<211> 1344
<212> DNA
<213> 小家鼠

<400> 154
gaggtccagc tgcaacagtc tggacctgaa ctaatgaagc ctggggcctc agtgaagatg

tccgtcaagg ctcttgata cacattcact gactacaaca tgcactgggt gaaacagaac 120
caaggaaaga gcctagagt gataggagaa attaatccta acagtgggtg tagtggtac 180
aaccaaaagt tcaaaggcaa ggccacatig actgtagaca agtcttcag cacagcctac 240
atggagctcc gcagcctgac atctgaggac tctgcagtct attactgtgc aagattggtc 300
tacgatggca gctacagga ctggctacttc gatgtctggg gcgcaggagc cacggtcacc 360
gtctctcag ccaaaacgac acccccatct gtctatccac tggcccctgg atctgtgcc 420
caaaactaact ccatggtgac cctgggagtc ctgggtcaagg gctatttccc tgagccagt 480
acagtgacct ggaactctgg atccctgtcc agcgggtgtc acaccttccc agctgtcctg 540
cagtctgacc tctacactct gagcagctca gtgactgtcc cctccagcac ctggcccagc 600
gagaccgtca cctgcaacgt tggccacccg gccagcagca ccaagggtga caagaaaatt 660
gtggccaggg attgtgggtg taagccttgc atatgtacag tcccagaagt atcatctgtc 720
ttcatcttcc ccccaaagcc caaggatgtg ctaccatta ctctgactcc taaggtcacg 780
tgtgttgg tagacatcag caaggatgat cccgagggtc agttcagctg gttttagat 840
gatgtggagg tgcacacagc tcagacgcaa cccggggagg agcagttcaa cagcactttc 900
cgctcagtc gtgaacttcc catcatgcac caggactggc tcaatggcaa ggagttcaaa 960
tgcagggtca acagtgcagc ttccctgcc cccatcgaga aaaccatctc caaaacaaa 1020
ggcagaccga aggtccaca ggtgtacacc attccacctc ccaaggagca gatggccaag 1080
gataaagtc gtctgacctg catgataaca gacttcttcc ctgaagacat tactgtggag 1140
tggcagtgga atgggcagcc agcggagaac tacaagaaca ctgagcccat catggacaca 1200
gatggctctt acctcatcta cagcaagctc aatgtgcaga agagcaactg ggaggcagga 1260
aatacttica cctgctctgt gttacatgag ggctgcaca accaccatac tgagaagagc 1320
ctctccact ctcttgtaa atga 1344

<210> 155
<211> 466
<212> PRT
<213> 小家鼠

<400> 155

Met Gly Trp Ser Trp Thr Phe Leu Phe Leu Leu Ser Gly Thr Ala Gly
1 5 10 15

Val Leu Ser Glu Val Gln Leu Gln Gln Ser Gly Pro Glu Leu Met Lys
20 25 30

Pro Gly Ala Ser Val Lys Met Ser Cys Lys Ala Ser Gly Tyr Thr Phe
35 40 45

Thr Asp Tyr Asn Met His Trp Val Lys Gln Asn Gln Gly Lys Ser Leu
50 55 60

Glu Trp Ile Gly Glu Ile Asn Pro Asn Ser Gly Gly Ser Gly Tyr Asn
65 70 75 80

Gln Lys Phe Lys Gly Lys Ala Thr Leu Thr Val Asp Lys Ser Ser Ser
85 90 95

Thr Ala Tyr Met Glu Leu Arg Ser Leu Thr Ser Glu Asp Ser Ala Val
100 105 110

Tyr Tyr Cys Ala Arg Leu Val Tyr Asp Gly Ser Tyr Glu Asp Trp Tyr
115 120 125

Phe Asp Val Trp Gly Ala Gly Thr Thr Val Thr Val Ser Ser Ala Lys
130 135 140

Thr Thr Pro Pro Ser Val Tyr Pro Leu Ala Pro Gly Ser Ala Ala Gln
145 150 155 160

Thr Asn Ser Met Val Thr Leu Gly Cys Leu Val Lys Gly Tyr Phe Pro
165 170 175

Glu Pro Val Thr Val Thr Trp Asn Ser Gly Ser Leu Ser Ser Gly Val
180 185 190

His Thr Phe Pro Ala Val Leu Gln Ser Asp Leu Tyr Thr Leu Ser Ser
195 200 205

Ser Val Thr Val Pro Ser Ser Thr Trp Pro Ser Glu Thr Val Thr Cys
210 215 220

Asn Val Ala His Pro Ala Ser Ser Thr Lys Val Asp Lys Lys Ile Val
225 230 235 240

Pro Arg Asp Cys Gly Cys Lys Pro Cys Ile Cys Thr Val Pro Glu Val
245 250 255

Ser Ser Val Phe Ile Phe Pro Pro Lys Pro Lys Asp Val Leu Thr Ile
260 265 270

Thr Leu Thr Pro Lys Val Thr Cys Val Val Val Asp Ile Ser Lys Asp
275 280 285

Asp Pro Glu Val Gln Phe Ser Trp Phe Val Asp Asp Val Glu Val His
290 295 300

Thr Ala Gln Thr Gln Pro Arg Glu Glu Gln Phe Asn Ser Thr Phe Arg
305 310 315 320

Ser Val Ser Glu Leu Pro Ile Met His Gln Asp Trp Leu Asn Gly Lys
325 330 335

Glu Phe Lys Cys Arg Val Asn Ser Ala Ala Phe Pro Ala Pro Ile Glu
340 345 350

Lys Thr Ile Ser Lys Thr Lys Gly Arg Pro Lys Ala Pro Gln Val Tyr
355 360 365

Thr Ile Pro Pro Pro Lys Glu Gln Met Ala Lys Asp Lys Val Ser Leu
370 375 380

Thr Cys Met Ile Thr Asp Phe Phe Pro Glu Asp Ile Thr Val Glu Trp

385		390		395		400
Gln Trp Asn Gly	Gln Pro Ala Glu Asn Tyr Lys Asn Thr Gln Pro Ile					
	405		410		415	
Met Asp Thr Asp Gly Ser Tyr Phe Ile Tyr Ser Lys Leu Asn Val Gln						
	420		425		430	
Lys Ser Asn Trp Glu Ala Gly Asn Thr Phe Thr Cys Ser Val Leu His						
	435		440		445	
Glu Gly Leu His Asn His His Thr Glu Lys Ser Leu Ser His Ser Pro						
	450		455		460	

Gly Lys
465

<210> 156
<211> 1401
<212> DNA
<213> 小家鼠

<400> 156	
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gtccagctgc aacagctctgg acctgaacta atgaagcctg gggcttcagt gaagatgtcc	120
tgcaaggctt ctggatacac attcactgac tacaacatgc actgggtgaa acagaaccaa	180
ggaaagagcc tagagtggat aggagaaatt aatcctaaca gtggtggtag tggctacaac	240
caaaagtcca aaggcaaggc cacattgact gtagacaagt cttccagcac agcctacatg	300
gagctccgca gcctgacatc tgaggactct gcagtctatt actgtgcaag attggtctac	360
gatggcagct acgaggactg gtacttcgat gctcggggcg cagggaccac ggtcacctgc	420
tcctcagcca aaacgacacc cccatctgtc tatccactgg cccctggatc tgcigcccaa	480
actaactcca tggtagacct gggatgcctg gtcaagggtt atttccctga gccagtgaca	540
gtgacctgga actctggatc cctgtccagc ggtgtgcaca ccttcccagc tgcctgcag	600
tctgacctct acactctgag cagctcagtg actgtccctt ccagcacctg gccagcgag	660
accgtcacct gcaacgttgc ccaccggcc agcagcacca aggtggacaa gaaaattgtg	720
cccagggatt gtggttgtaa gccttgcata tgtacagtc cagaagtatc atctgtcttc	780
atcttcccc caaagcccaa ggatgtgctc accattactc tgactcctaa ggtcacgtgt	840
gttgtggtag acatcagcaa ggatgatccc gaggtccagt tcagctgggt tglagatgat	900
gtggaggtgc acacagctca gacgcaacc cgggaggagc agttcaacag cactttccgc	960
tcagtcagtg aacttcccat catgcaccag gactggctca atggcaagga gttcaaatgc	1020
agggtcaaca gtgcagcttt cctgtcccc atcgagaaaa ccatctccaa aaccaaaggc	1080
agaccgaagg ctccacaggt gtacaccatt ccacctccca aggagcagat ggccaaggat	1140
aaagtcatgc tgacctgcat gataacagac ttcttccttg aagacattac tgtggagtgg	1200
cagtggatg ggcagccagc ggagaactac aagaacactc agcccatcat ggacacagat	1260
ggctcttact tcacttacag caagctcaat gtgcagaaga gcaactggga ggcaggaaat	1320
actttcacct gctctgtgtt acatgagggc ctgcacaacc accatactga gaagagcctc	1380

tcccactctc ctggtaaag a 1401

<210> 157
<211> 214
<212> PRT
<213> 小家鼠

<400> 157

Asp Ile Gln Met Thr Gln Thr Thr Ser Ser Leu Ser Ala Ser Leu Gly
1 5 10 15

Asp Arg Val Thr Ile Cys Cys Arg Ala Ser Gln Val Ile Thr Asn Tyr
20 25 30

Leu Tyr Trp Tyr Gln Gln Lys Pro Asp Gly Thr Phe Lys Leu Leu Ile
35 40 45

Tyr Tyr Thr Ser Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Ser Asn Leu Glu Gln
65 70 75 80

Glu Asp Ile Ala Thr Tyr Phe Cys Gln Gln Gly Asp Thr Leu Pro Tyr
85 90 95

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg Ala Asp Ala Ala
100 105 110

Pro Thr Val Ser Ile Phe Pro Pro Ser Ser Glu Gln Leu Thr Ser Gly
115 120 125

Gly Ala Ser Val Val Cys Phe Leu Asn Asn Phe Tyr Pro Lys Asp Ile
130 135 140

Asn Val Lys Trp Lys Ile Asp Gly Ser Glu Arg Gln Asn Gly Val Leu
145 150 155 160

Asn Ser Trp Thr Asp Gln Asp Ser Lys Asp Ser Thr Tyr Ser Met Ser
165 170 175

Ser Thr Leu Thr Leu Thr Lys Asp Glu Tyr Glu Arg His Asn Ser Tyr
180 185 190

Thr Cys Glu Ala Thr His Lys Thr Ser Thr Ser Pro Ile Val Lys Ser
195 200 205

Phe Asn Arg Asn Glu Cys
210

<210> 158
<211> 642
<212> DNA
<213> 小家鼠

<400> 158
gatatccaga tgacacagac tacatcctcc ctgtctgcct ctctggggaga cagagtcacc 60
atctgttgca gggcaagtca ggatcattacc aattatttat acttggtatca gcagaaacca 120

gatggaactt ttaaactcct gatctactac acatcaagat tacactcagg agtcccatca 180
 aggttcagtg gcagtgggtc tggaacagat tattctctca ccattagcaa cctggaacag 240
 gaagatattg ccacttactt ttgccaacag ggtgatacgc ttccgtacac gttcggaggg 300
 gggaccaagc tggaataaaa acgggctgat gctgcaccaa ctgtatccat cttcccacca 360
 tccagtgagc agttaacatc tggagggtgcc tcagtcgtgt gcttcttgaa caacttctac 420
 cccaaagaca tcaatgtcaa gtggaagatt gatggcagtg aacgacaaaa tggcgtcctg 480
 aacagtgtga ctgatcagga cagcaaagac agcacctaca gcatgagcag caccctcacg 540
 ttgaccaagg acgagtaiga acgacataac agctatacct gtgaggccac tcacaagaca 600
 tcaacttcac ccattgtcaa gagcttcaac aggaatgagt gt 642

<210> 159
 <211> 234
 <212> PRT
 <213> 小家鼠

<400> 159

Met Met Ser Ser Ala Gln Phe Leu Gly Leu Leu Leu Cys Phe Gln
 1 5 10 15

Gly Thr Arg Cys Asp Ile Gln Met Thr Gln Thr Thr Ser Ser Leu Ser
 20 25 30

Ala Ser Leu Gly Asp Arg Val Thr Ile Cys Cys Arg Ala Ser Gln Val
 35 40 45

Ile Thr Asn Tyr Leu Tyr Trp Tyr Gln Gln Lys Pro Asp Gly Thr Phe
 50 55 60

Lys Leu Leu Ile Tyr Tyr Thr Ser Arg Leu His Ser Gly Val Pro Ser
 65 70 75 80

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Ser
 85 90 95

Asn Leu Glu Gln Glu Asp Ile Ala Thr Tyr Phe Cys Gln Gln Gly Asp
 100 105 110

Thr Leu Pro Tyr Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg
 115 120 125

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

Leu Thr Ser Gly Gly Ala Ser Val Val Cys Phe Leu Asn Asn Phe Tyr
 145 150 155 160

Pro Lys Asp Ile Asn Val Lys Trp Lys Ile Asp Gly Ser Glu Arg Gln
 165 170 175

Asn Gly Val Leu Asn Ser Trp Thr Asp Gln Asp Ser Lys Asp Ser Thr
 180 185 190

Tyr Ser Met Ser Ser Thr Leu Thr Leu Thr Lys Asp Glu Tyr Glu Arg
195 200 205

His Asn Ser Tyr Thr Cys Glu Ala Thr His Lys Thr Ser Thr Ser Pro
210 215 220

Ile Val Lys Ser Phe Asn Arg Asn Glu Cys
225 230

<210> 160
<211> 702
<212> DNA
<213> 小家鼠

<400> 160
atgatgtcct ctgctcagtt ccttgggtctc ctgttgctct gttttcaagg taccagatgt 60
gatatccaga tgacacagac tacatctctc ctgtctgcct ctctgggaga cagagtcacc 120
atctgttgca gggcaagtca ggtcattacc aattatttat actggtatca gcagaaacca 180
gatggaactt ttaaactcct gatctactac acatcaagat tacactcagg agtcccatca 240
aggttcagtg gcagtgggtc tggaacagat tattctctca ccattagcaa cctggaacag 300
gaagatatig ccacttactt ttgccaacag ggtgatacgc ttccgtacac gttcggaggg 360
gggaccaagc tggaataaaa acgggctgat gctgcaccaa ctgtatccat cttcccacca 420
tccagtgagc agttaacatc tggaggtgcc tcagtcgtgt gcttcttgaa caacttctac 480
cccaaagaca tcaatgtcaa gtggaagatt gatggcagtg aacgacaaaa tggcgtcctg 540
aacagttgga ctgacagga cagcaaagac agcacctaca gcatgagcag caccctcacg 600
ttgaccaagg acgagtatga acgacataac agctatacct gtgaggccac tcacaagaca 660
tcaacttcac ccattgtcaa gagcttcaac aggaatgagt gt 702

<210> 161
<211> 447
<212> PRT
<213> 小家鼠

<400> 161
Glu Val Gln Leu Gln Gln Ser Gly Pro Glu Leu Met Lys Pro Gly Ala
1 5 10 15
Ser Val Lys Met Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Tyr
20 25 30
Asn Met His Trp Met Lys Gln Asn Gln Gly Lys Ser Leu Glu Trp Ile
35 40 45
Gly Glu Ile Asn Pro Asn Ser Gly Gly Ala Gly Tyr Asn Gln Gln Phe
50 55 60
Lys Gly Lys Ala Thr Leu Thr Val Asp Lys Ser Ser Arg Thr Ala Tyr
65 70 75 80
Met Glu Leu Arg Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys
85 90 95
Ala Arg Leu Gly Tyr Val Gly Asn Tyr Glu Asp Trp Tyr Phe Asp Val

100	105	110
Trp Gly Ala Gly Thr Thr Val Thr Val Ser Ser Ala Lys Thr Thr Pro 115 120 125		
Pro Ser Val Tyr Pro Leu Ala Pro Gly Ser Ala Ala Gln Thr Asn Ser 130 135 140		
Met Val Thr Leu Gly Cys Leu Val Lys Gly Tyr Phe Pro Glu Pro Val 145 150 155 160		
Thr Val Thr Trp Asn Ser Gly Ser Leu Ser Ser Gly Val His Thr Phe 165 170 175		
Pro Ala Val Leu Gln Ser Asp Leu Tyr Thr Leu Ser Ser Ser Val Thr 180 185 190		
Val Pro Ser Ser Thr Trp Pro Ser Glu Thr Val Thr Cys Asn Val Ala 195 200 205		
His Pro Ala Ser Ser Thr Lys Val Asp Lys Lys Ile Val Pro Arg Asp 210 215 220		
Cys Gly Cys Lys Pro Cys Ile Cys Thr Val Pro Glu Val Ser Ser Val 225 230 235 240		
Phe Ile Phe Pro Pro Lys Pro Lys Asp Val Leu Thr Ile Thr Leu Thr 245 250 255		
Pro Lys Val Thr Cys Val Val Val Asp Ile Ser Lys Asp Asp Pro Glu 260 265 270		
Val Gln Phe Ser Trp Phe Val Asp Asp Val Glu Val His Thr Ala Gln 275 280 285		
Thr Gln Pro Arg Glu Glu Gln Phe Asn Ser Thr Phe Arg Ser Val Ser 290 295 300		
Glu Leu Pro Ile Met His Gln Asp Trp Leu Asn Gly Lys Glu Phe Lys 305 310 315 320		
Cys Arg Val Asn Ser Ala Ala Phe Pro Ala Pro Ile Glu Lys Thr Ile 325 330 335		
Ser Lys Thr Lys Gly Arg Pro Lys Ala Pro Gln Val Tyr Thr Ile Pro 340 345 350		
Pro Pro Lys Glu Gln Met Ala Lys Asp Lys Val Ser Leu Thr Cys Met 355 360 365		
Ile Thr Asp Phe Phe Pro Glu Asp Ile Thr Val Glu Trp Gln Trp Asn 370 375 380		
Gly Gln Pro Ala Glu Asn Tyr Lys Asn Thr Gln Pro Ile Met Asp Thr 385 390 395 400		

Asp Gly Ser Tyr Phe Ile Tyr Ser Lys Leu Asn Val Gln Lys Ser Asn
405 410 415

Trp Glu Ala Gly Asn Thr Phe Thr Cys Ser Val Leu His Glu Gly Leu
420 425 430

His Asn His His Thr Glu Lys Ser Leu Ser His Ser Pro Gly Lys
435 440 445

<210> 162
<211> 1341
<212> DNA
<213> 小家鼠

<400> 162
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tcctgcaagg ctcttgata cacattcact gactacaaca tgcactggat gaagcagaac 120
caaggaaaga gcctagaatg gataggagaa attaataccta acagtggtagg tgctggctac 180
aaccagcagt tcaaaggcaa ggccacattg actgtagaca agtcctccag gacagcctac 240
atggagctcc gcagcctgac atctgaggac tctgcagctc attactgtgc aagattgggc 300
tacgttggta attacgagga ctggtacttc gatgtcggg gcgcagggac cacggtcacc 360
gtctctcag ccaaaacgac acccccatct gtctatccac tggccccctgg atctgctgcc 420
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acagtgacct ggaactctgg atccctgtcc agcgggtgtc acaccttccc agctgtcctg 540
cagttctgacc tctacactct gagcagctca gtgactgtcc cctccagcac ctggcccagc 600
gagaccgtca cctgcaacgt tgcccccccg gccagcagca ccaagggtga caagaaaatt 660
gtgcccaggg attgtggttg taagccttgc atatgtacag tcccagaagt atcatctgtc 720
ttcatcttcc ccccaaagcc caaggatgtg ctccaccatta ctctgactcc taaggtcacg 780
tgtgttgttg tagacatcag caaggatgat cccgagggtc agtcagctg gttttagat 840
gatgtggagg tgcacacagc tcagacgcaa ccccgaggagg agcagttcaa cagcactttc 900
cgctcagtca gtgaacttcc catcatgcac caggactggc tcaatggcaa ggagttcaaa 960
tgcagggtca acagtgcagc ttccctgtcc cccatcgaga aaacatctc caaaacaaa 1020
ggcagaccga aggtccaca ggtgtacacc attccacctc ccaaggagca gatggccaag 1080
gataaagtca gtctgacctg catgataaca gacttcttcc ctgaagacat tactgtggag 1140
tggcagtgga atgggcagcc agcggagaac tacaagaaca ctgagcccat catggacaca 1200
gatggctctt acttcatcta cagcaagctc aatgtgcaga agagcaactg ggaggcagga 1260
aatactttca cctgctctgt gtacatgag ggccctgcaca accaccatac tgagaagagc 1320
ctctcccact ctcttggtaa a 1341

<210> 163
<211> 466
<212> PRT
<213> 小家鼠

<400> 163
Met Gly Trp Ser Trp Thr Phe Leu Phe Leu Leu Ser Gly Thr Ala Gly
1 5 10 15

Val Leu Ser Glu Val Gln Leu Gln Gln Ser Gly Pro Glu Leu Met Lys
20 25 30

Pro Gly Ala Ser Val Lys Met Ser Cys Lys Ala Ser Gly Tyr Thr Phe
35 40 45

Thr Asp Tyr Asn Met His Trp Met Lys Gln Asn Gln Gly Lys Ser Leu
50 55 60

Glu Trp Ile Gly Glu Ile Asn Pro Asn Ser Gly Gly Ala Gly Tyr Asn
65 70 75 80

Gln Gln Phe Lys Gly Lys Ala Thr Leu Thr Val Asp Lys Ser Ser Arg
85 90 95

Thr Ala Tyr Met Glu Leu Arg Ser Leu Thr Ser Glu Asp Ser Ala Val
100 105 110

Tyr Tyr Cys Ala Arg Leu Gly Tyr Val Gly Asn Tyr Glu Asp Trp Tyr
115 120 125

Phe Asp Val Trp Gly Ala Gly Thr Thr Val Thr Val Ser Ser Ala Lys
130 135 140

Thr Thr Pro Pro Ser Val Tyr Pro Leu Ala Pro Gly Ser Ala Ala Gln
145 150 155 160

Thr Asn Ser Met Val Thr Leu Gly Cys Leu Val Lys Gly Tyr Phe Pro
165 170 175

Glu Pro Val Thr Val Thr Trp Asn Ser Gly Ser Leu Ser Ser Gly Val
180 185 190

His Thr Phe Pro Ala Val Leu Gln Ser Asp Leu Tyr Thr Leu Ser Ser
195 200 205

Ser Val Thr Val Pro Ser Ser Thr Trp Pro Ser Glu Thr Val Thr Cys
210 215 220

Asn Val Ala His Pro Ala Ser Ser Thr Lys Val Asp Lys Lys Ile Val
225 230 235 240

Pro Arg Asp Cys Gly Cys Lys Pro Cys Ile Cys Thr Val Pro Glu Val
245 250 255

Ser Ser Val Phe Ile Phe Pro Pro Lys Pro Lys Asp Val Leu Thr Ile
260 265 270

Thr Leu Thr Pro Lys Val Thr Cys Val Val Val Asp Ile Ser Lys Asp
275 280 285

Asp Pro Glu Val Gln Phe Ser Trp Phe Val Asp Asp Val Glu Val His
290 295 300

Thr Ala Gln Thr Gln Pro Arg Glu Glu Gln Phe Asn Ser Thr Phe Arg
305 310 315 320

Ser Val Ser Glu Leu Pro Ile Met His Gln Asp Trp Leu Asn Gly Lys
325 330 335

Glu Phe Lys Cys Arg Val Asn Ser Ala Ala Phe Pro Ala Pro Ile Glu
340 345 350

Lys Thr Ile Ser Lys Thr Lys Gly Arg Pro Lys Ala Pro Gln Val Tyr
355 360 365

Thr Ile Pro Pro Pro Lys Glu Gln Met Ala Lys Asp Lys Val Ser Leu
370 375 380

Thr Cys Met Ile Thr Asp Phe Phe Pro Glu Asp Ile Thr Val Glu Trp
385 390 395 400

Gln Trp Asn Gly Gln Pro Ala Glu Asn Tyr Lys Asn Thr Gln Pro Ile
405 410 415

Met Asp Thr Asp Gly Ser Tyr Phe Ile Tyr Ser Lys Leu Asn Val Gln
420 425 430

Lys Ser Asn Trp Glu Ala Gly Asn Thr Phe Thr Cys Ser Val Leu His
435 440 445

Glu Gly Leu His Asn His His Thr Glu Lys Ser Leu Ser His Ser Pro
450 455 460

Gly Lys
465

- <210> 164
- <211> 1398
- <212> DNA
- <213> 小家鼠

<400> 164
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gtccagctgc aacagtctgg acctgaacta atgaagcctg gggcttcagt gaagatgtcc 120
tgcaaggctt ctggatacac attcactgac tacaacatgc actggatgaa gcagaaccaa 180
ggaaagagcc tagaatggat aggagaaatt aatcctaaca gtggttggtgc tggctacaac 240
cagcagltta aaggcaaggc cacattgact gtagacaagt cctccaggac agcctacatg 300
gagctccgca gcctgacatc tgaggactct gcagtctatt actgtgcaag attgggctac 360
gttggttaatt acgaggactg gtacttcgat gtctggggcg cagggaccac ggtcaccgtc 420
tcctcagcca aaacgacacc cccatctgtc tatccactgg cccctggatc tgctgcccac 480
actaactcca tggtagacct gggatgcctg gtcaagggtt atttccctga gccagtgaca 540
gtgacctgga actctggatc ccgtgccagc ggtgtgcaca ccttcccagc tgtcctgcag 600
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accgtcacct gcaacgttgc ccaccggcc agcagcacca aggtggacaa gaaaattgtg 720
cccagggatt gtggttgtaa gccttgcata tgtacagtcc cagaagtatc atctgtcttc 780
atcttccccc caaagcccaa ggaatgtgtc accattactc tgactcctaa ggtcacgtgt 840

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gttgtggttag acatcagcaa ggatgatccc gaggtccagt tcagctgggt ttagatgat      900
gtggagggtgc acacagctca gacgcaaccc cgggaggagc agttcaacag cactttccgc      960
tcagtcagtg aacttcccat catgcaccag gactggctca atggcaagga gttcaaatgc      1020
agggtaaca gtgcagcttt ccctgcccc atcgagaaaa ccatctccaa aaccaaaggc      1080
agaccgaagg ctccacaggt gtacaccatt ccacctccca aggagcagat ggccaaggat      1140
aaagtcagtc tgacctgcat gataacagac ttcttccctg aagacattac tgtggagtgg      1200
cagtggaatg ggcagccagc ggagaactac aagaacactc agcccatcat ggacacagat      1260
ggctcttact tcacttacag caagctcaat gtgcagaaga gcaactggga ggcaggaaat      1320
actttcacct gtctgtgttt acatgagggc ctgcacaacc accatactga gaagagcctc      1380
tcccactctc ctggtaaa      1398

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<210> 165
 <211> 214
 <212> PRT
 <213> 小家鼠

<400> 165

Asp Ile Gln Met Thr Gln Thr Thr Ser Ser Leu Ser Ala Ser Leu Gly
1 5 10 15

Asp Arg Val Ser Ile Ser Cys Arg Ala Ser Gln Asp Ile Ser Asn Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Asp Gly Thr Phe Lys Leu Leu Ile
35 40 45

Phe Tyr Thr Ser Arg Leu Leu Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Tyr Asn Leu Glu Gln
65 70 75 80

Glu Asp Phe Ala Thr Tyr Phe Cys Gln Gln Gly Asp Thr Leu Pro Tyr
85 90 95

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg Ala Asp Ala Ala
100 105 110

Pro Thr Val Ser Ile Phe Pro Pro Ser Ser Glu Gln Leu Thr Ser Gly
115 120 125

Gly Ala Ser Val Val Cys Phe Leu Asn Asn Phe Tyr Pro Lys Asp Ile
130 135 140

Asn Val Lys Trp Lys Ile Asp Gly Ser Glu Arg Gln Asn Gly Val Leu
145 150 155 160

Asn Ser Trp Thr Asp Gln Asp Ser Lys Asp Ser Thr Tyr Ser Met Ser
165 170 175

Ser Thr Leu Thr Leu Thr Lys Asp Glu Tyr Glu Arg His Asn Ser Tyr
180 185 190

Thr Cys Glu Ala Thr His Lys Thr Ser Thr Ser Pro Ile Val Lys Ser
195 200 205

Phe Asn Arg Asn Glu Cys
210

<210> 166
<211> 645
<212> DNA
<213> 小家鼠

<400> 166
gatatccaga tgacacagac tacatcctcc ctgtctgcct ccttgggaga cagggctctcc 60
atcagttgca gggcaagtca agacattagc aattatttaa actgglatca gcagaaacca 120
gatggaactt ttaaactcct tatcttctac acatcaagat tactctcagg agtcccatca 180
aggttcagtg gcagtgggtc tggaaacagat tattctctca ccatttaciaa cctggagcaa 240
gaagatttgg ccacttactt ttgccaacag ggagatacgc ttccgtacac ttctggaggg 300
gggaccaaac tggaaataaa acgggctgat gctgcaccaa ctgtatccat cttcccacca 360
tccagtgagc agttaacatc tggagggtgcc tcagtcgtgt gcttcttgaa caacttctac 420
cccaaagaca tcaatgtcaa gtggaagatt gatggcagtg aacgacaaaa tggcgtcctg 480
aacagttgga ctgatcagga cagcaaagac agcacctaca gcatgagcag caccctcacg 540
ttgaccaagg acgagtatga acgacataac agctatacct gtgaggccac tcacaagaca 600
tcaacttcac ccattgtcaa gagcttcaac aggaatgagt gttag 645

<210> 167
<211> 234
<212> PRT
<213> 小家鼠

<400> 167

Met Met Ser Ser Ala Gln Phe Leu Gly Leu Leu Leu Leu Cys Phe Gln
1 5 10 15

Gly Thr Arg Cys Asp Ile Gln Met Thr Gln Thr Thr Ser Ser Leu Ser
20 25 30

Ala Ser Leu Gly Asp Arg Val Ser Ile Ser Cys Arg Ala Ser Gln Asp
35 40 45

Ile Ser Asn Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Asp Gly Thr Phe
50 55 60

Lys Leu Leu Ile Phe Tyr Thr Ser Arg Leu Leu Ser Gly Val Pro Ser
65 70 75 80

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Tyr
85 90 95

Asn Leu Glu Gln Glu Asp Phe Ala Thr Tyr Phe Cys Gln Gln Gly Asp
100 105 110

Thr Leu Pro Tyr Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg

115120125

Ala Asp Ala Ala Pro Thr Val Ser Ile Phe Pro Pro Ser Ser Glu Gln
130135140

Leu Thr Ser Gly Gly Ala Ser Val Val Cys Phe Leu Asn Asn Phe Tyr
145150155160

Pro Lys Asp Ile Asn Val Lys Trp Lys Ile Asp Gly Ser Glu Arg Gln
165170175

Asn Gly Val Leu Asn Ser Trp Thr Asp Gln Asp Ser Lys Asp Ser Thr
180185190

Tyr Ser Met Ser Ser Thr Leu Thr Leu Thr Lys Asp Glu Tyr Glu Arg
195200205

His Asn Ser Tyr Thr Cys Glu Ala Thr His Lys Thr Ser Thr Ser Pro
210215220

Ile Val Lys Ser Phe Asn Arg Asn Glu Cys
225230

<210> 168
<211> 705
<212> DNA
<213> 小家鼠

<400> 168

atgatgtcct ctgttcagtt ccttgggtctc ctgttgcctt gttttcaagg taccagatgt60

gatatccaga tgacacagac tacatcctcc ctgtctgcct ctctgggaga cagggtctcc120

atcagttgca gggcaagtca agacattagc aattatttaa acttggtatca gcagaaacca180

gatggaactt ttaaactcct tatcttctac acatcaagat tactctcagg agtcccatca240

aggttcagtg gcagtggtgc tggaacagat tattctctca ccatttaca cctggagcaa300

gaagattitg ccacttactt ttgccaacag ggagatacgc ttccgtacac tttcggaggg360

gggaccaaac tggaataaaa acgggtgat gctgcaccaa ctgtatccat ctcccca420

tccagtgagc agttaacatc tggaggtgcc tcagtcgtgt gcttcttgaa caacttctac480

cccaaagaca tcaatgtcaa gtggaagatt gatggcagtg aacgacaaaa tggcgtcctg540

aacagttgga ctgatcagga cagcaaagac agcacctaca gcatgagcag caccctcacg600

ttgaccaagg acgaglatga acgacataac agctatacct gtgaggccac tcacaagaca660

tcaacttcac ccattgtcaa gagcttcaac aggaatgagt gttag705

<210> 169
<211> 447
<212> PRT
<213> 小家鼠

<400> 169

Glu Val Gln Leu Gln Gln Ser Gly Pro Glu Leu Met Lys Pro Gly Ala
151015

Ser Val Lys Met Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Tyr
202530

Asn Met His Trp Val Lys Gln Asn Gln Gly Lys Thr Leu Asp Trp Ile
 35 40 45
 Gly Glu Ile Asn Pro Asn Ser Gly Gly Ala Gly Tyr Asn Gln Lys Phe
 50 55 60
 Lys Gly Lys Ala Thr Leu Thr Val Asp Lys Ser Ser Thr Thr Ala Tyr
 65 70 75 80
 Met Glu Leu Arg Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys
 85 90 95
 Ala Arg Leu Gly Tyr Asp Asp Ile Tyr Asp Asp Trp Tyr Phe Asp Val
 100 105 110
 Trp Gly Ala Gly Thr Thr Val Thr Val Ser Ser Ala Lys Thr Thr Pro
 115 120 125
 Pro Ser Val Tyr Pro Leu Ala Pro Gly Ser Ala Ala Gln Thr Asn Ser
 130 135 140
 Met Val Thr Leu Gly Cys Leu Val Lys Gly Tyr Phe Pro Glu Pro Val
 145 150 155 160
 Thr Val Thr Trp Asn Ser Gly Ser Leu Ser Ser Gly Val His Thr Phe
 165 170 175
 Pro Ala Val Leu Gln Ser Asp Leu Tyr Thr Leu Ser Ser Ser Val Thr
 180 185 190
 Val Pro Ser Ser Thr Trp Pro Ser Glu Thr Val Thr Cys Asn Val Ala
 195 200 205
 His Pro Ala Ser Ser Thr Lys Val Asp Lys Lys Ile Val Pro Arg Asp
 210 215 220
 Cys Gly Cys Lys Pro Cys Ile Cys Thr Val Pro Glu Val Ser Ser Val
 225 230 235 240
 Phe Ile Phe Pro Pro Lys Pro Lys Asp Val Leu Thr Ile Thr Leu Thr
 245 250 255
 Pro Lys Val Thr Cys Val Val Val Asp Ile Ser Lys Asp Asp Pro Glu
 260 265 270
 Val Gln Phe Ser Trp Phe Val Asp Asp Val Glu Val His Thr Ala Gln
 275 280 285
 Thr Gln Pro Arg Glu Glu Gln Phe Asn Ser Thr Phe Arg Ser Val Ser
 290 295 300
 Glu Leu Pro Ile Met His Gln Asp Trp Leu Asn Gly Lys Glu Phe Lys
 305 310 315 320
 Cys Arg Val Asn Ser Ala Ala Phe Pro Ala Pro Ile Glu Lys Thr Ile

325	330	335
Ser Lys Thr Lys Gly Arg Pro Lys Ala Pro Gln Val Tyr Thr Ile Pro		
340	345	350
Pro Pro Lys Glu Gln Met Ala Lys Asp Lys Val Ser Leu Thr Cys Met		
355	360	365
Ile Thr Asp Phe Phe Pro Glu Asp Ile Thr Val Glu Trp Gln Trp Asn		
370	375	380
Gly Gln Pro Ala Glu Asn Tyr Lys Asn Thr Gln Pro Ile Met Asp Thr		
385	390	400
Asp Gly Ser Tyr Phe Ile Tyr Ser Lys Leu Asn Val Gln Lys Ser Asn		
405	410	415
Trp Glu Ala Gly Asn Thr Phe Thr Cys Ser Val Leu His Glu Gly Leu		
420	425	430
His Asn His His Thr Glu Lys Ser Leu Ser His Ser Pro Gly Lys		
435	440	445

<210> 170
 <211> 1344
 <212> DNA
 <213> 小家鼠

<400> 170
 gaggtccaac tgcaacagtc tggacctgaa ctaatgaagc ctggggcttc agtgaagatg 60
 tcctgcaagg cttctggata tacattcact gactacaaca tgcactgggt gaagcagaac 120
 caaggaaaga ccctagactg gataggagaa attaataccta acagtgggtg tgctggctac 180
 aaccagaagt tcaagggcaa ggccacattg actgtagaca agtcctccac cacagcctac 240
 atggagctcc gcagcctgac atctgaggac tctgcagtct attactgtgc aagattgggc 300
 tacgatgata tctacgacga ctggtacttc gatgtctggg gcgcagggac cacggtcacc 360
 gtctcctcag ccaaaacgac acccccatct gtctatccac tggcccctgg atctgctgcc 420
 caaactaact ccatggtgac cctgggatgc ctggtcaagg gctatttccc tgagccagtg 480
 acagtgaact ggaactctgg atccctgtcc agcgggtgtgc acaccttccc agctgtcctg 540
 cagtctgacc tctacactct gaggagctca gtgactgtcc cctccagcac ctggcccagc 600
 gagaccgtca cctgcaacgt tgcccaccg gccagcagca ccaaggtgga caagaaaatt 660
 gtgcccaggg attgtggttg taagccttgc atatgtacag tcccagaagt atcatctgtc 720
 ttcatcttcc ccccaaagcc caaggatgtg ctaccatta ctctgactcc taaggtcacg 780
 tgtgtgtgg tagacatcag caaggatgat cccgaggtcc agttcagctg gttttagat 840
 gatgtggagg tgcacacagc tcagacgcaa cccggggagg agcagttcaa cagcactttc 900
 cgctcagtc gtgaacttcc catcatgcac caggactggc tcaatggcaa ggagttcaaa 960
 tgcagggtca acagtgcagc ttccctgcc cccatcgaga aaaccatctc caaaacaaa 1020
 ggagaccga aggtccaca ggtgtacacc attccactc ccaaggagca gatggccaag 1080
 gataaagtc gtctgacctg catgataaca gacttcttcc ctgaagacat tactgtggag 1140

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tggcagtgga atgggcagcc agcggagaac tacaagaaca ctcagcccat catggacaca 1200
gatggctctt acttcatcta cagcaagctc aatgtgcaga agagcaactg ggaggcagga 1260
aatactttca cctgctctgt gttacatgag ggcctgcaca accaccatac tgagaagagc 1320
ctctcccaact ctcttggtaa atga 1344

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<210> 171
 <211> 466
 <212> PRT
 <213> 小家鼠

<400> 171

Met Gly Trp Ser Trp Thr Phe Leu Phe Leu Leu Ser Gly Thr Ala Gly
1 5 10 15

Val Leu Ser Glu Val Gln Leu Gln Gln Ser Gly Pro Glu Leu Met Lys
20 25 30

Pro Gly Ala Ser Val Lys Met Ser Cys Lys Ala Ser Gly Tyr Thr Phe
35 40 45

Thr Asp Tyr Asn Met His Trp Val Lys Gln Asn Gln Gly Lys Thr Leu
50 55 60

Asp Trp Ile Gly Glu Ile Asn Pro Asn Ser Gly Gly Ala Gly Tyr Asn
65 70 75 80

Gln Lys Phe Lys Gly Lys Ala Thr Leu Thr Val Asp Lys Ser Ser Thr
85 90 95

Thr Ala Tyr Met Glu Leu Arg Ser Leu Thr Ser Glu Asp Ser Ala Val
100 105 110

Tyr Tyr Cys Ala Arg Leu Gly Tyr Asp Asp Ile Tyr Asp Asp Trp Tyr
115 120 125

Phe Asp Val Trp Gly Ala Gly Thr Thr Val Thr Val Ser Ser Ala Lys
130 135 140

Thr Thr Pro Pro Ser Val Tyr Pro Leu Ala Pro Gly Ser Ala Ala Gln
145 150 155 160

Thr Asn Ser Met Val Thr Leu Gly Cys Leu Val Lys Gly Tyr Phe Pro
165 170 175

Glu Pro Val Thr Val Thr Trp Asn Ser Gly Ser Leu Ser Ser Gly Val
180 185 190

His Thr Phe Pro Ala Val Leu Gln Ser Asp Leu Tyr Thr Leu Ser Ser
195 200 205

Ser Val Thr Val Pro Ser Ser Thr Trp Pro Ser Glu Thr Val Thr Cys
210 215 220

Asn Val Ala His Pro Ala Ser Ser Thr Lys Val Asp Lys Lys Ile Val
225 230 235 240

Pro Arg Asp Cys Gly Cys Lys Pro Cys Ile Cys Thr Val Pro Glu Val
245 250 255

Ser Ser Val Phe Ile Phe Pro Pro Lys Pro Lys Asp Val Leu Thr Ile
260 265 270

Thr Leu Thr Pro Lys Val Thr Cys Val Val Val Asp Ile Ser Lys Asp
275 280 285

Asp Pro Glu Val Gln Phe Ser Trp Phe Val Asp Asp Val Glu Val His
290 295 300

Thr Ala Gln Thr Gln Pro Arg Glu Glu Gln Phe Asn Ser Thr Phe Arg
305 310 315 320

Ser Val Ser Glu Leu Pro Ile Met His Gln Asp Trp Leu Asn Gly Lys
325 330 335

Glu Phe Lys Cys Arg Val Asn Ser Ala Ala Phe Pro Ala Pro Ile Glu
340 345 350

Lys Thr Ile Ser Lys Thr Lys Gly Arg Pro Lys Ala Pro Gln Val Tyr
355 360 365

Thr Ile Pro Pro Pro Lys Glu Gln Met Ala Lys Asp Lys Val Ser Leu
370 375 380

Thr Cys Met Ile Thr Asp Phe Phe Pro Glu Asp Ile Thr Val Glu Trp
385 390 395 400

Gln Trp Asn Gly Gln Pro Ala Glu Asn Tyr Lys Asn Thr Gln Pro Ile
405 410 415

Met Asp Thr Asp Gly Ser Tyr Phe Ile Tyr Ser Lys Leu Asn Val Gln
420 425 430

Lys Ser Asn Trp Glu Ala Gly Asn Thr Phe Thr Cys Ser Val Leu His
435 440 445

Glu Gly Leu His Asn His His Thr Glu Lys Ser Leu Ser His Ser Pro
450 455 460

Gly Lys
465

<210> 172
<211> 1401
<212> DNA
<213> 小家鼠

<400> 172
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gtccaactgc aacagtctgg acctgaacta atgaagcctg gggcttcagt gaagatgtcc 120
tgcaaggctt ctggatatac attcactgac tacaacatgc actgggtgaa gcagaaccaa 180
ggaaagaccc tagactggat aggagaaatt aatcctaaca gtggtggtgc tggctacaac 240

cagaagtcca agggcaaggc cacattgact gtagacaagt cctccaccac agcctacatg 300
gagctccgca gcctgacatc tgaggactct gcagtctatt actgtgcaag attgggctac 360
gatgatatct acgacgactg gtacttcgat gtctggggcg cagggaccac ggtcaccgic 420
tcctcagecca aaacgacacc cccatctgtc tatccactgg cccctggatc tgcigcccaa 480
actaactcca tggtagacct gggatgcctg gtaagggtt atttccctga gccagtgaca 540
gtgacctgga actctggatc cctgtccagc ggtgtgcaca ccttcccagc tgcctgcag 600
tctgacctct acactctgag cagctcagtg actgtccctt ccagcacctg gccagcgag 660
accgtcacct gcaacgttgc ccaccggcc agcagcacca aggtggacaa gaaaattgtg 720
cccagggatt gtggttgtaa gccttgcata tgtacagtcc cagaagtatc atctgtcttc 780
atcttcccc caaagcccaa ggatgtgtc accattactc tgactcctaa ggtcacgtgt 840
gttgtggtag acatcagcaa ggatgatccc gaggtccagt tcagctgggt tgtagatgat 900
gtggagggtc acacagctca gacgcaaccc cgggaggagc agttcaacag cactttccgc 960
tcagtcatgt aacttcccat catgcaccag gactggctca atggcaagga gttcaaatgc 1020
agggtaaca gtgcagcttt ccttgcctcc atcgagaaaa ccatctccaa aaccaaaggc 1080
agaccgaagg ctccacaggt gtacaccatt ccacctccca aggagcagat ggccaaggat 1140
aaagtcatgc tgacctgcat gataacagac ttcttcctg aagacattac tgtggagtgg 1200
cagtggaatg ggcagccagc ggagaactac aagaacactc agcccatcat ggacacagat 1260
ggctcttact tcattctacag caagctcaat gtgcagaaga gcaactggga ggcaggaaat 1320
actttcacct gctctgtgtt acatgagggc ctgcacaacc accatactga gaagagcctc 1380
tcccactctc ctggtaaatg a 1401

<210> 173
<211> 214
<212> PRT
<213> 小家鼠

<400> 173

Asp Ile Gln Met Thr Gln Ile Thr Ser Ser Leu Ser Ala Ser Leu Gly
1 5 10 15
Asp Arg Val Ser Ile Ser Cys Arg Ala Ser Gln Asp Ile Ser Asn Tyr
20 25 30
Leu Asn Trp Tyr Gln Gln Lys Pro Asp Gly Thr Phe Lys Leu Leu Ile
35 40 45
Phe Tyr Thr Ser Arg Leu Phe Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60
Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Tyr Asn Leu Glu Gln
65 70 75 80
Glu Asp Phe Ala Thr Tyr Phe Cys Gln Gln Gly Asp Thr Leu Pro Tyr
85 90 95
Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Arg Ala Asp Ala Ala
100 105 110

Pro Thr Val Ser Ile Phe Pro Pro Ser Ser Glu Gln Leu Thr Ser Gly
115 120 125

Gly Ala Ser Val Val Cys Phe Leu Asn Asn Phe Tyr Pro Lys Asp Ile
130 135 140

Asn Val Lys Trp Lys Ile Asp Gly Ser Glu Arg Gln Asn Gly Val Leu
145 150 155 160

Asn Ser Trp Thr Asp Gln Asp Ser Lys Asp Ser Thr Tyr Ser Met Ser
165 170 175

Ser Thr Leu Thr Leu Thr Lys Asp Glu Tyr Glu Arg His Asn Ser Tyr
180 185 190

Thr Cys Glu Ala Thr His Lys Thr Ser Thr Ser Pro Ile Val Lys Ser
195 200 205

Phe Asn Arg Asn Glu Cys
210

<210> 174
<211> 642
<212> DNA
<213> 小家鼠

<400> 174
gatatccaga tgacacagat tacatcctcc ctgtctgcct ctctgggaga cagggctctcc 60
atcagttgca gggcaagtca agacattagc aattatttaa attggtatca gcagaaacca 120
gatggaactt ttaaactcct tatctttctac acatcaagat tattttcagg agtcccatca 180
aggttcagtg gcagtggggc tggaacagat tattctctca ccatttaca cctggagcaa 240
gaagattttg ccacttactt ttgccaacag ggagatacgc ttccgtacac tticggagggg 300
gggaccaagg tggaaataaa acgggctgat gctgcaccaa ctgtatccat ctccccacca 360
tccagtgagc agttaacatc tggagggtgcc tcagtcgigt gcttcttgaa caacttctac 420
cccaaagaca tcaatgtcaa gtggaagatt gatggcagtg aacgacaaaa tggcgctctg 480
aacagttgga ctgatcagga cagcaaagac agcacctaca gcatgagcag caccctcagc 540
ttgaccaagg acgagtatga acgacataac agctatacct gtgaggccac tcacaagaca 600
tcaacttcac ccattgtcaa gagcttcaac aggaatgagt gt 642

<210> 175
<211> 234
<212> PRT
<213> 小家鼠

<400> 175
Met Met Ser Ser Ala Gln Phe Leu Gly Leu Leu Leu Cys Phe Gln
1 5 10 15

Gly Thr Arg Cys Asp Ile Gln Met Thr Gln Ile Thr Ser Ser Leu Ser
20 25 30

Ala Ser Leu Gly Asp Arg Val Ser Ile Ser Cys Arg Ala Ser Gln Asp
35 40 45

Ile Ser Asn Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Asp Gly Thr Phe
50 55 60

Lys Leu Leu Ile Phe Tyr Thr Ser Arg Leu Phe Ser Gly Val Pro Ser
65 70 75 80

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Tyr
85 90 95

Asn Leu Glu Gln Glu Asp Phe Ala Thr Tyr Phe Cys Gln Gln Gly Asp
100 105 110

Thr Leu Pro Tyr Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Arg
115 120 125

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

Leu Thr Ser Gly Gly Ala Ser Val Val Cys Phe Leu Asn Asn Phe Tyr
145 150 155 160

Pro Lys Asp Ile Asn Val Lys Trp Lys Ile Asp Gly Ser Glu Arg Gln
165 170 175

Asn Gly Val Leu Asn Ser Trp Thr Asp Gln Asp Ser Lys Asp Ser Thr
180 185 190

Tyr Ser Met Ser Ser Thr Leu Thr Leu Thr Lys Asp Glu Tyr Glu Arg
195 200 205

His Asn Ser Tyr Thr Cys Glu Ala Thr His Lys Thr Ser Thr Ser Pro
210 215 220

Ile Val Lys Ser Phe Asn Arg Asn Glu Cys
225 230

<210> 176
<211> 702
<212> DNA
<213> 小家鼠

<400> 176
atgatgtcct ctgctcagtt ccttggctct ctgttgcctt gttttcaagg taccagatgt 60
gatatccaga tgacacagat tacatcctcc ctgtctgcct ctctggggaga cagggtctcc 120
atcagttgca gggcaagtca agacattagc aattatttaa attggtatca gcagaaacca 180
gatggaactt ttaaactcct tatcttctac acatcaagat tattttcagg agtcccatca 240
aggttcagtg gcagtgggtc tggaacagat tattctctca ccatttaciaa cctggagcaa 300
gaagattttg ccacttactt ttgccaacag ggagatacgc ttccgtacac tticggaggg 360
gggaccaagg tggaataaaa acgggctgat gctgcaccaa ctgtatccat ctccccacca 420
tccagtgagc agttaacatc tggaggtgcc tcagtcgtgt gcttcttgaa caacttctac 480
cccaaagaca tcaatgtcaa gtggaagatt gatggcagtg aacgacaaaa tggcgtcctg 540
aacagttgga ctgatcagga cagcaaagac agcacctaca gcatgagcag caccctcacg 600

ttgaccaagg acgagtatga acgacataac agctatacct gtgaggccac tcacaagaca 660
tcaacttcac ccattgtcaa gagcttcaac aggaatgagt gt 702

<210> 177
<211> 450
<212> PRT
<213> 小家鼠

<400> 177

Glu Val Gln Leu Gln Gln Ser Gly Pro Glu Leu Met Lys Pro Gly Thr
1 5 10 15

Ser Val Lys Met Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Tyr
20 25 30

Asn Met His Trp Val Lys Gln Thr Gln Gly Lys Thr Leu Glu Trp Ile
35 40 45

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

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

Met Glu Leu Arg Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Leu Gly Tyr Asp Asp Ile Tyr Asp Asp Trp Tyr Phe Asp Val
100 105 110

Trp Gly Ala Gly Thr Thr Val Thr Val Ser Ser Ala Lys Thr Thr Ala
115 120 125

Pro Ser Val Tyr Pro Leu Ala Pro Val Cys Gly Asp Thr Thr Gly Ser
130 135 140

Ser Val Thr Leu Gly Cys Leu Val Lys Gly Tyr Phe Pro Glu Pro Val
145 150 155 160

Thr Leu Thr Trp Asn Ser Gly Ser Leu Ser Ser Asp Val His Thr Phe
165 170 175

Pro Ala Leu Leu Gln Ser Gly Leu Tyr Thr Leu Ser Ser Ser Val Thr
180 185 190

Val Thr Thr Trp Pro Ser Gln Thr Ile Thr Cys Asn Val Ala His Pro
195 200 205

Ala Ser Ser Thr Lys Val Asp Lys Lys Ile Glu Pro Arg Gly Ser Pro
210 215 220

Thr His Lys Pro Cys Pro Pro Cys Pro Ala Pro Asn Leu Leu Gly Gly
225 230 235 240

Pro Ser Val Phe Ile Phe Pro Pro Lys Ile Lys Asp Val Leu Met Ile
245 250 255

Ser Leu Ser Pro Met Val Thr Cys Val Val Val Asp Val Ser Glu Asp
260 265 270

Asp Pro Asp Val His Val Ser Trp Phe Val Asn Asn Val Glu Val His
275 280 285

Thr Ala Gln Thr Gln Thr His Arg Glu Asp Tyr Asn Ser Thr Ile Arg
290 295 300

Val Val Ser Ala Leu Pro Ile Gln His Gln Asp Trp Met Ser Gly Lys
305 310 315 320

Glu Phe Lys Cys Lys Val Asn Asn Lys Ala Leu Pro Ala Pro Ile Glu
325 330 335

Arg Thr Ile Ser Lys Pro Lys Gly Pro Val Arg Ala Pro Gln Val Tyr
340 345 350

Val Leu Pro Pro Pro Glu Glu Glu Met Thr Lys Lys Gln Val Thr Leu
355 360 365

Thr Cys Met Ile Thr Asp Phe Met Pro Glu Asp Ile Tyr Val Glu Trp
370 375 380

Thr Asn Asn Gly Gln Thr Glu Leu Asn Tyr Lys Asn Thr Glu Pro Val
385 390 395 400

Leu Asp Ser Asp Gly Ser Tyr Phe Met Tyr Ser Lys Leu Arg Val Glu
405 410 415

Lys Lys Asn Trp Val Glu Arg Asn Ser Tyr Ser Cys Ser Val Val His
420 425 430

Glu Gly Leu His Asn His His Thr Thr Lys Ser Phe Ser Arg Thr Pro
435 440 445

Gly Lys
450

<210> 178
<211> 1350
<212> DNA
<213> 小家鼠

<400> 178
gagggtccaac tgcaacagtc tggacctgaa ctaatgaagc ctgggacttc agtgaagatg 60
tcctgcaagg cttctggata tacattcact gactacaaca tgcactgggt gaagcagacc 120
caaggaaaga ccctagagtg gataggagaa attaatccta acagtgggtg tgcctggctac 180
aaccagaagt tcaagggcaa ggccacattg actgtagaca agtcctccac cacagcctac 240
atggagctcc gcagcctgac atctgaggac tctgcagtct attactgtgc aaaattgggc 300
tacgatgata tctacgacga ctggtatttc gatgtctggg gcgcagggac cacggtcacc 360
gtctcctcag ccaaacaac agcccatcg gtctatccac tggccctgt gtgtggagat 420
acaactggct cctcggtgac tctaggatgc ctggtaagg gtattttccc tgagccagtg 480

accctgacct ggaactctgg atccctgtcc agtgatgtgc acaccttccc agctctcctg 540
cagtctggcc tctacacct cagcagctca gtgactgtaa ccacctggcc cagccagacc 600
atcacctgca atgtggccca cccggcaagc agcaccaaag tggacaagaa aattgagccc 660
agaggggtccc caacacataa acccigtctt ccatgcccag ctcttaacct ctggggtgga 720
ccatccgtct tcatcttccc tccaaagatc aaggatgtac tcatgatctc cctgagcccc 780
atggtcacgt gtgtgggtgt ggatgtgagc gaggatgacc cagatgtcca tgtcagctgg 840
ttcgtgaaca acgtggaagt acacacagct cagacacaaa cccatagaga ggattacaac 900
agtactatcc ggggtggtcag tgccctcccc atccagcacc aggactggat gagtggcaag 960
gagttcaaat gcaagggtcaa caacaaagcc ctcccagcgc ccatcgagag aaccatctca 1020
aaacccaaag ggccagtaag agctccacag gtatatgtct tgccctccacc agaagaagag 1080
atgactaaga aacaggtcac tctgacctgc atgatcacag acttcatgcc tgaagacatt 1140
tacgtggagt ggaccaacaa cgggcaaaca gagctaaact acaagaacac tgaaccagtc 1200
ctggactctg atggttctta cttcatgtac agcaagctga gagtggaaaa gaagaactgg 1260
gtggaaagaa atagctactc ctgttcagtg gtccacgagg gtctgcacaa tcaccacacg 1320
actaagagct tctcccgac tccgggtaaa 1350

<210> 179
<211> 469
<212> PRT
<213> 小家鼠

<400> 179

Met Gly Trp Ser Trp Thr Phe Leu Phe Leu Leu Ser Gly Thr Ala Gly
1 5 10 15

Val Leu Ser Glu Val Gln Leu Gln Gln Ser Gly Pro Glu Leu Met Lys
20 25 30

Pro Gly Thr Ser Val Lys Met Ser Cys Lys Ala Ser Gly Tyr Thr Phe
35 40 45

Thr Asp Tyr Asn Met His Trp Val Lys Gln Thr Gln Gly Lys Thr Leu
50 55 60

Glu Trp Ile Gly Glu Ile Asn Pro Asn Ser Gly Gly Ala Gly Tyr Asn
65 70 75 80

Gln Lys Phe Lys Gly Lys Ala Thr Leu Thr Val Asp Lys Ser Ser Thr
85 90 95

Thr Ala Tyr Met Glu Leu Arg Ser Leu Thr Ser Glu Asp Ser Ala Val
100 105 110

Tyr Tyr Cys Ala Lys Leu Gly Tyr Asp Asp Ile Tyr Asp Asp Trp Tyr
115 120 125

Phe Asp Val Trp Gly Ala Gly Thr Thr Val Thr Val Ser Ser Ala Lys
130 135 140

Thr	Thr	Ala	Pro	Ser	Val	Tyr	Pro	Leu	Ala	Pro	Val	Cys	Gly	Asp	Thr	145	150	155	160
Thr	Gly	Ser	Ser	Val	Thr	Leu	Gly	Cys	Leu	Val	Lys	Gly	Tyr	Phe	Pro	165	170	175	
Glu	Pro	Val	Thr	Leu	Thr	Trp	Asn	Ser	Gly	Ser	Leu	Ser	Ser	Asp	Val	180	185	190	
His	Thr	Phe	Pro	Ala	Leu	Leu	Gln	Ser	Gly	Leu	Tyr	Thr	Leu	Ser	Ser	195	200	205	
Ser	Val	Thr	Val	Thr	Thr	Trp	Pro	Ser	Gln	Thr	Ile	Thr	Cys	Asn	Val	210	215	220	
Ala	His	Pro	Ala	Ser	Ser	Thr	Lys	Val	Asp	Lys	Lys	Ile	Glu	Pro	Arg	225	230	235	240
Gly	Ser	Pro	Thr	His	Lys	Pro	Cys	Pro	Pro	Cys	Pro	Ala	Pro	Asn	Leu	245	250	255	
Leu	Gly	Gly	Pro	Ser	Val	Phe	Ile	Phe	Pro	Pro	Lys	Ile	Lys	Asp	Val	260	265	270	
Leu	Met	Ile	Ser	Leu	Ser	Pro	Met	Val	Thr	Cys	Val	Val	Val	Asp	Val	275	280	285	
Ser	Glu	Asp	Asp	Pro	Asp	Val	His	Val	Ser	Trp	Phe	Val	Asn	Asn	Val	290	295	300	
Glu	Val	His	Thr	Ala	Gln	Thr	Gln	Thr	His	Arg	Glu	Asp	Tyr	Asn	Ser	305	310	315	320
Thr	Ile	Arg	Val	Val	Ser	Ala	Leu	Pro	Ile	Gln	His	Gln	Asp	Trp	Met	325	330	335	
Ser	Gly	Lys	Glu	Phe	Lys	Cys	Lys	Val	Asn	Asn	Lys	Ala	Leu	Pro	Ala	340	345	350	
Pro	Ile	Glu	Arg	Thr	Ile	Ser	Lys	Pro	Lys	Gly	Pro	Val	Arg	Ala	Pro	355	360	365	
Gln	Val	Tyr	Val	Leu	Pro	Pro	Pro	Glu	Glu	Glu	Met	Thr	Lys	Lys	Gln	370	375	380	
Val	Thr	Leu	Thr	Cys	Met	Ile	Thr	Asp	Phe	Met	Pro	Glu	Asp	Ile	Tyr	385	390	395	400
Val	Glu	Trp	Thr	Asn	Asn	Gly	Gln	Thr	Glu	Leu	Asn	Tyr	Lys	Asn	Thr	405	410	415	
Glu	Pro	Val	Leu	Asp	Ser	Asp	Gly	Ser	Tyr	Phe	Met	Tyr	Ser	Lys	Leu	420	425	430	
Arg	Val	Glu	Lys	Lys	Asn	Trp	Val	Glu	Arg	Asn	Ser	Tyr	Ser	Cys	Ser	435	440	445	

Val Val His Glu Gly Leu His Asn His His Thr Thr Lys Ser Phe Ser
450 455 460

Arg Thr Pro Gly Lys
465

<210> 180
<211> 1407
<212> DNA
<213> 小家鼠

<400> 180
atgggatgga gctggacctt tctcttcctc ctgtcaggaa ctgcaggtgt cctctctgag 60
gtccaactgc aacagtctgg acctgaacta atgaagcctg ggacttcagt gaagatgtcc 120
tgcaaggctt ctggatatac attcactgac tacaacatgc actgggtgaa gcagacccaa 180
ggaaagaccc tagagtggat aggagaaatt aatcctaaca gtggtggtgc tggctacaac 240
cagaagtcca agggcaaggc cacattgact gtagacaagt cctccaccac agcctacatg 300
gagctccgca gcctgacatc tgaggactct gcagtctatt actgtgcaaa attgggctac 360
gatgatatct acgacgactg gtatttcgat gtctggggcg cagggaccac ggtcaccgtc 420
tcctcagcca aaacaacagc cccatcggtc tatccactgg cccctgtgtg tggagataca 480
actggctcct cggtgactct aggatgcctg gtcaaggggt atttcctga gccagtgacc 540
ttgacctgga actctggatc cctgtccagt gatgtgcaca ccttcccagc tctcctgcag 600
tctggcctct acaccctcag cagctcagtg actgtaacca cctggcccag ccagaccatc 660
acctgcaatg tggcccaccc ggcaagcagc accaaagtgg acaagaaaat tgagcccaga 720
gggtcccca cacataaacc ctgtcctcca tgcccagctc ctaacctctt ggggtggacca 780
tccgtcttca tcttccctcc aaagatcaag gatgtactca tgatctccct gagccccatg 840
gtcacgtgtg tgggtggtgga tgtgagcgag gatgaccag atgtccatgt cagctggttc 900
gtgaacaacg tggaagtaca cacagctcag acacaaaccc atagagagga ttacaacagt 960
actatccggg tggtcagtg cctccccatc cagcaccagg actggatgag tggcaaggag 1020
ttcaaatgca aggtcaacaa caaagccctc ccagcgccca tcgagagaac catctcaaaa 1080
cccaaagggc cagtaagagc tccacaggta tatgtcttgc ctccaccaga agaagagatg 1140
actaagaaac aggtcactct gacctgcatg atcacagact tcatgcctga agacatttac 1200
gtggagtgga ccaacaacgg gcaaacagag ctaaactaca agaacactga accagtcctg 1260
gactctgatg gticttactt catgtacagc aagctgagag tggaaaagaa gaactgggtg 1320
gaaagaaata gctactcctg ttcagtggtc cagcagggtc tgcacaatca ccacacgact 1380
aagagcttct cccggactcc gggtaaa 1407

<210> 181
<211> 214
<212> PRT
<213> 小家鼠

<400> 181

Asp Ile Gln Met Thr Gln Thr Thr Ser Ser Leu Ser Ala Ser Leu Gly
1 5 10 15

Asp Arg Val Ser Ile Ser Cys Arg Ala Ser Gln Asp Ile Ser Asn Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Asp Gly Thr Phe Lys Leu Leu Ile
35 40 45

Phe Tyr Thr Ser Arg Leu Leu Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Tyr Asn Leu Glu Gln
65 70 75 80

Glu Asp Phe Ala Thr Tyr Phe Cys Gln Gln Gly Asp Thr Leu Pro Tyr
85 90 95

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg Ala Asp Ala Ala
100 105 110

Pro Thr Val Ser Ile Phe Pro Leu Ser Ser Glu Gln Leu Thr Ser Gly
115 120 125

Gly Ala Ser Val Val Cys Phe Leu Asn Asn Phe Tyr Pro Lys Asp Ile
130 135 140

Asn Val Lys Trp Lys Ile Asp Gly Ser Glu Arg Gln Asn Gly Val Leu
145 150 155 160

Asn Ser Trp Thr Asp Gln Asp Ser Lys Asp Ser Thr Tyr Ser Met Ser
165 170 175

Ser Thr Leu Thr Leu Thr Lys Asp Glu Tyr Glu Arg His Asn Ser Tyr
180 185 190

Thr Cys Glu Ala Thr His Lys Thr Ser Thr Ser Pro Ile Val Lys Ser
195 200 205

Phe Asn Arg Asn Glu Cys
210

<210> 182
<211> 645
<212> DNA
<213> 小家鼠

<400> 182
gatatccaga tgacacagac tacatctccc ctgtctgcct ctctgggaga cagggtctcc 60
atcagttgca gggcaagtca agacattagc aattatttaa actggtatca gcagaaacca 120
gatggaactt ttaaactcct tatcttctac acatcaagat tactctcagg agtcccatca 180
aggttcagtg gcagtggggc tggaacagat tattctctca ccatctacaa cctggagcaa 240
gaagattttg ccacttactt ttgccaacag ggagatacgc ttccgtacac ttctggaggg 300
gggaccaaac tggaaataaa acgggctgat gctgcaccaa ctglatccat ctctccacta 360
tccagtgagc agttaacatc tggaggtgcc tcagtcgtgt gcttcttgaa caacttctac 420
cccaaagaca tcaatgtcaa gtggaagatt gatggcagtg aacgacaaaa tggcgctctg 480
aacagttgga ctgatcagga cagcaaagac agcacctaca gcatgagcag caccctcacg 540

ttgaccaagg acgagtaiga acgacataac agctatacct gtgaggccac tcacaagaca 600
tcaacttcac ccattgtcaa gagcttcaac aggaatgagt gtttag 645

<210> 183
<211> 234
<212> PRT
<213> 小家鼠

<400> 183

Met Met Ser Ser Ala Gln Phe Leu Gly Leu Leu Leu Leu Cys Phe Gln
1 5 10 15

Gly Thr Arg Cys Asp Ile Gln Met Thr Gln Thr Thr Ser Ser Leu Ser
20 25 30

Ala Ser Leu Gly Asp Arg Val Ser Ile Ser Cys Arg Ala Ser Gln Asp
35 40 45

Ile Ser Asn Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Asp Gly Thr Phe
50 55 60

Lys Leu Leu Ile Phe Tyr Thr Ser Arg Leu Leu Ser Gly Val Pro Ser
65 70 75 80

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Tyr
85 90 95

Asn Leu Glu Gln Glu Asp Phe Ala Thr Tyr Phe Cys Gln Gln Gly Asp
100 105 110

Thr Leu Pro Tyr Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg
115 120 125

Ala Asp Ala Ala Pro Thr Val Ser Ile Phe Pro Leu Ser Ser Glu Gln
130 135 140

Leu Thr Ser Gly Gly Ala Ser Val Val Cys Phe Leu Asn Asn Phe Tyr
145 150 155 160

Pro Lys Asp Ile Asn Val Lys Trp Lys Ile Asp Gly Ser Glu Arg Gln
165 170 175

Asn Gly Val Leu Asn Ser Trp Thr Asp Gln Asp Ser Lys Asp Ser Thr
180 185 190

Tyr Ser Met Ser Ser Thr Leu Thr Leu Thr Lys Asp Glu Tyr Glu Arg
195 200 205

His Asn Ser Tyr Thr Cys Glu Ala Thr His Lys Thr Ser Thr Ser Pro
210 215 220

Ile Val Lys Ser Phe Asn Arg Asn Glu Cys
225 230

<210> 184
<211> 705

<212> DNA
<213> 小家鼠

<400> 184
atgatgtcct ctgtcagtt ccttggcttc ctgttgcct gtttcaagg taccagatgt 60
gatatccaga tgacacagac tacatcctcc ctgtctgcct ctctgggaga cagggtctcc 120
atcagttgca gggcaagtc agacattagc aattatttaa actggtatca gcagaaacca 180
gatggaactt ttaaactcct tatctcttac acatcaagat tactctcagg agtcccatca 240
aggttcagtg gcagtgggic tggaacagat tattctctca ccatitacaa cctggagcaa 300
gaagattttg ccacttacit ttgccaacag ggagatacgc ttccgtacac tticggaggg 360
gggaccaaac tggaaataaa acgggctgat gctgcaccaa ctgtatccat cticccacta 420
tccagtgagc agttaacatc tggagggtgcc tcagtcgtgt gcttcttgaa caacttctac 480
cccaaagaca tcaatgtcaa gtggaagatt gatggcagtg aacgacaaaa tggcgtcctg 540
aacagttgga ctgatcagga cagcaaagac agcacctaca gcatgagcag caccctcacg 600
ttgaccaagg acgagtatga acgacataac agctatacct gtgaggccac tcacaagaca 660
tcaacttcac ccattgtcaa gagcttcaac aggaatgagt gtttag 705

<210> 185
<211> 447
<212> PRT
<213> 小家鼠

<400> 185

Glu Val Gln Leu Gln Gln Ser Gly Pro Glu Leu Met Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Met Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Tyr
20 25 30

Asn Met His Trp Val Lys Gln Asn Gln Gly Lys Thr Leu Glu Trp Ile
35 40 45

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

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

Met Glu Leu Arg Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Leu Gly Tyr Asp Asp Ile Tyr Asp Asp Trp Tyr Phe Asp Val
100 105 110

Trp Gly Ala Gly Thr Thr Val Thr Val Ser Ser Ala Lys Thr Thr Pro
115 120 125

Pro Ser Val Tyr Pro Leu Ala Pro Gly Ser Ala Ala Gln Thr Asn Ser
130 135 140

Met Val Thr Leu Gly Cys Leu Val Lys Gly Tyr Phe Pro Glu Pro Val
145 150 155 160

Thr Val Thr Trp Asn Ser Gly Ser Leu Ser Ser Gly Val His Thr Phe
165 170 175

Pro Ala Val Leu Gln Ser Asp Leu Tyr Thr Leu Ser Ser Ser Val Thr
180 185 190

Val Pro Ser Ser Thr Trp Pro Ser Glu Thr Val Thr Cys Asn Val Ala
195 200 205

His Pro Ala Ser Ser Thr Lys Val Asp Lys Lys Ile Val Pro Arg Asp
210 215 220

Cys Gly Cys Lys Pro Cys Ile Cys Thr Val Pro Glu Val Ser Ser Val
225 230 235 240

Phe Ile Phe Pro Pro Lys Pro Lys Asp Val Leu Thr Ile Thr Leu Thr
245 250 255

Pro Lys Val Thr Cys Val Val Val Asp Ile Ser Lys Asp Asp Pro Glu
260 265 270

Val Gln Phe Ser Trp Phe Val Asp Asp Val Glu Val His Thr Ala Gln
275 280 285

Thr Gln Pro Arg Glu Glu Gln Phe Asn Ser Thr Phe Arg Ser Val Ser
290 295 300

Glu Leu Pro Ile Met His Gln Asp Trp Leu Asn Gly Lys Glu Phe Lys
305 310 315 320

Cys Arg Val Asn Ser Ala Ala Phe Pro Ala Pro Ile Glu Lys Thr Ile
325 330 335

Ser Lys Thr Lys Gly Arg Pro Lys Ala Pro Gln Val Tyr Thr Ile Pro
340 345 350

Pro Pro Lys Glu Gln Met Ala Lys Asp Lys Val Ser Leu Thr Cys Met
355 360 365

Ile Thr Asp Phe Phe Pro Glu Asp Ile Thr Val Glu Trp Gln Trp Asn
370 375 380

Gly Gln Pro Ala Glu Asn Tyr Lys Asn Thr Gln Pro Ile Met Asp Thr
385 390 395 400

Asp Gly Ser Tyr Phe Ile Tyr Ser Lys Leu Asn Val Gln Lys Ser Asn
405 410 415

Trp Glu Ala Gly Asn Thr Phe Thr Cys Ser Val Leu His Glu Gly Leu
420 425 430

His Asn His His Thr Glu Lys Ser Leu Ser His Ser Pro Gly Lys
435 440 445

<210> 186
<211> 1344

<212> DNA
<213> 小家鼠

<400> 186
gagggtccaac tgcaacagtc tggacctgaa ctaatgaagc ctgggggcttc agtgaagatg 60
tcctgcaagg cttctggata tacattcact gactacaaca tgcactgggt gaagcagaac 120
caaggaaaga ccctagaatg gataggagaa attaatccta acagtgggtg tgctggctac 180
aaccagaagt tcaagggcaa ggccacattg actgtagaca agtcctccac cacagcctac 240
atggagctcc gcagcctgac atctgaggac tctgcagtct attactgtgc aagattgggc 300
tacgatgata tctacgacga ctggtacttc gatgtctggg gcgcagggac cacggtcacc 360
gtctcctcag ccaaaacgac acccccatct gtctatccac tggccccctgg atctgtgcc 420
caaaactaact ccatggtgac cctgggatgc ctggtaagg gctatttccc tgagccagtg 480
acagtgacct ggaactctgg atccctgtcc agcgggtgtc acaccttccc agctgtcctg 540
cagtctgacc tctacactct gagcagctca gtgactgtcc cctccagcac ctggcccagc 600
gagaccgtca cctgcaacgt tggccaccg gccagcagca ccaagggtga caagaaaatt 660
gtgcccaggg atgtgggtg taagccttgc atatgtacag tcccagaagt atcatctgtc 720
ttcatcttcc ccccaaagcc caaggatgtg ctcaccatta cttgacttcc taaggtcacg 780
tgtgttgtgg tagacatcag caaggatgat cccgaggtcc agttcagctg gttttagat 840
gatgtggagg tgcacacagc tcagacgcaa ccccgggagg agcagttcaa cagcacttcc 900
cgctcagtca gtgaacttcc catcatgcac caggactggc tcaatggcaa ggagttcaaa 960
tgcagggtca acagtcgac tttccctgcc cccatcgaga aaaccatctc caaaacaaa 1020
ggcagaccga aggcctccaca ggtgtacacc attccacctc ccaaggagca gatggccaag 1080
gataaagtca gtctgacctg catgataaca gacttcttcc ctgaagacat tactgtggag 1140
tggcagtgga atgggcagcc agcggagaac tacaagaaca ctcagcccat catggacaca 1200
gatggctctt acttcatcta cagcaagctc aatgtgcaga agagcaactg ggaggcagga 1260
aatacttca cctgtctgt gttacatgag ggctgcaca accaccatac tgagaagagc 1320
ctctcccact ctcttggtta atga 1344

<210> 187
<211> 466
<212> PRT
<213> 小家鼠

<400> 187
Met Gly Trp Ser Trp Thr Phe Leu Phe Leu Leu Ser Gly Thr Ala Gly
1 5 10 15
Val Leu Ser Glu Val Gln Leu Gln Gln Ser Gly Pro Glu Leu Met Lys
20 25 30
Pro Gly Ala Ser Val Lys Met Ser Cys Lys Ala Ser Gly Tyr Thr Phe
35 40 45
Thr Asp Tyr Asn Met His Trp Val Lys Gln Asn Gln Gly Lys Thr Leu
50 55 60
Glu Trp Ile Gly Glu Ile Asn Pro Asn Ser Gly Gly Ala Gly Tyr Asn

65	70	75	80
Gln Lys Phe Lys Gly Lys Ala Thr Leu Thr Val Asp Lys Ser Ser Thr	85	90	95
Thr Ala Tyr Met Glu Leu Arg Ser Leu Thr Ser Glu Asp Ser Ala Val	100	105	110
Tyr Tyr Cys Ala Arg Leu Gly Tyr Asp Asp Ile Tyr Asp Asp Trp Tyr	115	120	125
Phe Asp Val Trp Gly Ala Gly Thr Thr Val Thr Val Ser Ser Ala Lys	130	135	140
Thr Thr Pro Pro Ser Val Tyr Pro Leu Ala Pro Gly Ser Ala Ala Gln	145	150	155
Thr Asn Ser Met Val Thr Leu Gly Cys Leu Val Lys Gly Tyr Phe Pro	165	170	175
Glu Pro Val Thr Val Thr Trp Asn Ser Gly Ser Leu Ser Ser Gly Val	180	185	190
His Thr Phe Pro Ala Val Leu Gln Ser Asp Leu Tyr Thr Leu Ser Ser	195	200	205
Ser Val Thr Val Pro Ser Ser Thr Trp Pro Ser Glu Thr Val Thr Cys	210	215	220
Asn Val Ala His Pro Ala Ser Ser Thr Lys Val Asp Lys Lys Ile Val	225	230	235
Pro Arg Asp Cys Gly Cys Lys Pro Cys Ile Cys Thr Val Pro Glu Val	245	250	255
Ser Ser Val Phe Ile Phe Pro Pro Lys Pro Lys Asp Val Leu Thr Ile	260	265	270
Thr Leu Thr Pro Lys Val Thr Cys Val Val Val Asp Ile Ser Lys Asp	275	280	285
Asp Pro Glu Val Gln Phe Ser Trp Phe Val Asp Asp Val Glu Val His	290	295	300
Thr Ala Gln Thr Gln Pro Arg Glu Glu Gln Phe Asn Ser Thr Phe Arg	305	310	315
Ser Val Ser Glu Leu Pro Ile Met His Gln Asp Trp Leu Asn Gly Lys	325	330	335
Glu Phe Lys Cys Arg Val Asn Ser Ala Ala Phe Pro Ala Pro Ile Glu	340	345	350
Lys Thr Ile Ser Lys Thr Lys Gly Arg Pro Lys Ala Pro Gln Val Tyr	355	360	365

Thr Ile Pro Pro Pro Lys Glu Gln Met Ala Lys Asp Lys Val Ser Leu
370 375 380

Thr Cys Met Ile Thr Asp Phe Phe Pro Glu Asp Ile Thr Val Glu Trp
385 390 395 400

Gln Trp Asn Gly Gln Pro Ala Glu Asn Tyr Lys Asn Thr Gln Pro Ile
405 410 415

Met Asp Thr Asp Gly Ser Tyr Phe Ile Tyr Ser Lys Leu Asn Val Gln
420 425 430

Lys Ser Asn Trp Glu Ala Gly Asn Thr Phe Thr Cys Ser Val Leu His
435 440 445

Glu Gly Leu His Asn His His Thr Glu Lys Ser Leu Ser His Ser Pro
450 455 460

Gly Lys
465

<210> 188
<211> 1401
<212> DNA
<213> 小家鼠

<400> 188
atgggatgga gctggacatt tctcttcctc ctgtcaggaa ctgcagggtgt cctctctgag 60
gtccaactgc aacagtctgg acctgaacta atgaagcctg gggcttcagt gaagatgtcc 120
tgcaaggctt ctggatatac attcactgac tacaacatgc actgggtgaa gcagaaccaa 180
ggaaagaccc tagaatggat aggagaaatt aatcctaaca gtgggtggtgc tggctacaac 240
cagaagttca agggcaaggc cacattgact gtagacaagt cctccaccac agcctacatg 300
gagctccgca gcctgacatc tgaggactct gcagtcattt actgtgcaag atggggctac 360
gatgatattt acgacgactg gtacttcgat gtctggggcg caggggaccac ggtcaccgtc 420
tcctcagcca aaacgacacc cccatctgtc tatccactgg cccctggatc tgcctgccaa 480
actaacicca tgggtgacct gggaatgctg gtcaagggtt atttccctga gccagtgaca 540
gtgacctgga actctggatc cctgtccagc ggtgtgcaca ccttcccagc tgcctgcag 600
tctgacctt acactctgag cagctcagtg actgtccctt ccagcacctg gccagcgag 660
accgtcacct gcaacgttgc ccaccgggc agcagcacca aggtggacaa gaaaattgtg 720
cccagggatt gtggttgtaa gccttgcata tgtacagtc cagaagtatc atctgtcttc 780
atcttcccc caaagcccaa ggaatgtgct accattactc tgactcctaa ggtcacgtgt 840
gttgtgtag acatcagcaa ggaatgatcc gaggtccagt tcagctggtt ttagatgat 900
gtggagggtc acacagctca gacgcaacct cgggaggagc agttcaacag cactttccgc 960
tcagtcagtg aacttcccat catgcaccag gactggtcct atggcaagga gtacaaatgc 1020
agggtcaaca gtgcagcttt ccttgcctcc atcgagaaaa ccatctccaa aaccaaggc 1080
agaccgaagg ctccacaggt gtacaccatt ccacctccca aggagcagat ggccaaggat 1140
aaagtcagtc tgacctgcat gataacagac ttcttccttg aagacattac tgtggagtgg 1200
cagtggaatg ggcagccagc ggagaactac aagaacactc agcccatcat ggacacagat 1260

ggctcttact tcatctacag caagctcaat gtgcagaaga gcaactggga ggcaggaaat 1320
actttcacct gctctgtgtt acatgagggc ctgcacaacc accatactga gaagagcctc 1380
tcccactctc ctggtaaatg a 1401

<210> 189
<211> 213
<212> PRT
<213> 小家鼠

<400> 189

Gln Ile Val Leu Ser Gln Ser Pro Ala Phe Leu Ser Val Ser Pro Gly
1 5 10 15

Asp Lys Val Thr Met Thr Cys Arg Ala Ser Ser Ser Ile Ser Tyr Ile
20 25 30

His Trp Phe Gln Gln Lys Pro Gly Ser Ser Pro Arg Ser Trp Ile Tyr
35 40 45

Ala Thr Ser Asn Leu Ala Ser Gly Val Pro Gly Arg Phe Ser Gly Ser
50 55 60

Gly Ser Gly Thr Ser Tyr Ser Leu Thr Ile Ser Arg Val Glu Ala Glu
65 70 75 80

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asp Pro Leu Thr
85 90 95

Phe Gly Ala Gly Thr Lys Leu Glu Leu Lys Arg Ala Asp Ala Ala Pro
100 105 110

Thr Val Ser Ile Phe Pro Pro Ser Ser Glu Gln Leu Thr Ser Gly Gly
115 120 125

Ala Ser Val Val Cys Phe Leu Asn Asn Phe Tyr Pro Lys Asp Ile Asn
130 135 140

Val Lys Trp Lys Ile Asp Gly Ser Glu Arg Gln Asn Gly Val Leu Asn
145 150 155 160

Ser Trp Thr Asp Gln Asp Ser Lys Asp Ser Thr Tyr Ser Met Ser Ser
165 170 175

Thr Leu Thr Leu Thr Lys Asp Glu Tyr Glu Arg His Asn Ser Tyr Thr
180 185 190

Cys Glu Ala Thr His Lys Thr Ser Thr Ser Pro Ile Val Lys Ser Phe
195 200 205

Asn Arg Asn Glu Cys
210

<210> 190
<211> 642
<212> DNA
<213> 小家鼠

<400> 190
 caaatgttgc tctcccagtc tccagcattc ctgtctgtat ctccagggga taaggtcaca 60
 atgacttgca gggccagctc aagtataagt tacatacact ggtttcagca gaagccagga 120
 tctccccca gatcctggat ttatgccaca tccaacctgg cttctggagt ccttggctgc 180
 ttcagtgcca gtgggtctgg gacctttac tctctcacia tcagcagagt ggaggttgag 240
 gatgctgcca cttattactg ccagcagtg agtagtgacc cactcacgtt cgggtctggg 300
 accaagctgg agctgaaacg ggcgatgct gcaccaacig tatccatctt cccaccatcc 360
 agtgagcagt taacatctgg aggtgcctca gtcgtgtgct tcttgaacaa cttctacccc 420
 aaagacatca atgtcaagtg gaagattgat ggcagtgaac gacaaaatgg cgtccctgaac 480
 agttggactg atcaggacag caaagacagc acctacagca tgagcagcac cctcacgtt 540
 accaaggacg agtatgaacg acataacagc tatacctgtg aggccactca caagacatca 600
 acttcaccca ttgtcaagag cttcaacagg aatgagtgtt ag 642

<210> 191
 <211> 235
 <212> PRT
 <213> 小家鼠

<400> 191
 Met Asp Phe Gln Val Gln Ile Phe Ser Phe Leu Leu Ile Ser Ala Ser 1 5 10 15
 Val Ile Met Ser Arg Gly Gln Ile Val Leu Ser Gln Ser Pro Ala Phe 20 25 30
 Leu Ser Val Ser Pro Gly Asp Lys Val Thr Met Thr Cys Arg Ala Ser 35 40 45
 Ser Ser Ile Ser Tyr Ile His Trp Phe Gln Gln Lys Pro Gly Ser Ser 50 55 60
 Pro Arg Ser Trp Ile Tyr Ala Thr Ser Asn Leu Ala Ser Gly Val Pro 65 70 75 80
 Gly Arg Phe Ser Gly Ser Gly Ser Gly Thr Ser Tyr Ser Leu Thr Ile 85 90 95
 Ser Arg Val Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp 100 105 110
 Ser Ser Asp Pro Leu Thr Phe Gly Ala Gly Thr Lys Leu Glu Leu Lys 115 120 125
 Arg Ala Asp Ala Ala Pro Thr Val Ser Ile Phe Pro Pro Ser Ser Glu 130 135 140
 Gln Leu Thr Ser Gly Gly Ala Ser Val Val Cys Phe Leu Asn Asn Phe 145 150 155 160
 Tyr Pro Lys Asp Ile Asn Val Lys Trp Lys Ile Asp Gly Ser Glu Arg 165 170 175

Gln Asn Gly Val Leu Asn Ser Trp Thr Asp Gln Asp Ser Lys Asp Ser
180 185 190

Thr Tyr Ser Met Ser Ser Thr Leu Thr Leu Thr Lys Asp Glu Tyr Glu
195 200 205

Arg His Asn Ser Tyr Thr Cys Glu Ala Thr His Lys Thr Ser Thr Ser
210 215 220

Pro Ile Val Lys Ser Phe Asn Arg Asn Glu Cys
225 230 235

<210> 192
<211> 708
<212> DNA
<213> 小家鼠

<400> 192
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agaggacaaa ttgttctctc ccagttctcca gcattccigt ctgtatctcc aggggataag 120
gtcacaatga cttgcagggc cagctcaagt ataagttaca tacactggtt tcagcagaag 180
ccaggatcct cccccagatc ctggatttat gccacatcca acctggcttc tggagtcct 240
ggtcgcttca gtggcagtggt gtcctgggacc tcttactctc tcacaatcag cagagtggag 300
gctgaggatg ctgccactta ttactgccag cagtggagta gigacccact cacgttcggt 360
gctgggacca agctggagct gaaacgggct gatgctgcac caactgiatc catcttccca 420
ccatccagtg agcagttaac atctggaggc gcctcagtcg tgtgcttctt gaacaacttc 480
taccceaaaag acatcaatgt caagtggag attgatggca gtgaacgaca aaatggcgtc 540
ctgaacagtt ggactgatca ggacagcaaa gacagcacct acagcatgag cagcaccctc 600
acgttgacca aggacgagta tgaacgacat aacagctata cctgtgaggc cactcacaag 660
acatcaactt caccatttgt caagagcttc aacaggaatg agtggttag 708

<210> 193
<211> 445
<212> PRT
<213> 小家鼠

<400> 193

Glu Val Gln Leu Gln Gln Ser Gly Ala Asp Leu Val Gln Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Thr Ala Ser Gly Phe Asp Ile Lys Asp Tyr
20 25 30

Tyr Ile His Trp Met Lys Gln Arg Pro Asp Gln Gly Leu Glu Trp Ile
35 40 45

Gly Arg Val Asp Pro Asp Asn Gly Glu Thr Glu Phe Ala Pro Lys Phe
50 55 60

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

Leu Gln Leu Arg Gly Leu Thr Ser Glu Asp Thr Ala Ile Tyr Tyr Cys
 85 90 95
 Gly Arg Glu Asp Tyr Asp Gly Thr Tyr Thr Trp Phe Pro Tyr Trp Gly
 100 105 110
 Gln Gly Thr Leu Val Thr Val Ser Ala Ala Lys Thr Thr Pro Pro Ser
 115 120 125
 Val Tyr Pro Leu Ala Pro Gly Ser Ala Ala Gln Thr Asn Ser Met Val
 130 135 140
 Thr Leu Gly Cys Leu Val Lys Gly Tyr Phe Pro Glu Pro Val Thr Val
 145 150 155 160
 Thr Trp Asn Ser Gly Ser Leu Ser Ser Gly Val His Thr Phe Pro Ala
 165 170 175
 Val Leu Gln Ser Asp Leu Tyr Thr Leu Ser Ser Ser Val Thr Val Pro
 180 185 190
 Ser Ser Thr Trp Pro Ser Glu Thr Val Thr Cys Asn Val Ala His Pro
 195 200 205
 Ala Ser Ser Thr Lys Val Asp Lys Lys Ile Val Pro Arg Asp Cys Gly
 210 215 220
 Cys Lys Pro Cys Ile Cys Thr Val Pro Glu Val Ser Ser Val Phe Ile
 225 230 235 240
 Phe Pro Pro Lys Pro Lys Asp Val Leu Thr Ile Thr Leu Thr Pro Lys
 245 250 255
 Val Thr Cys Val Val Val Asp Ile Ser Lys Asp Asp Pro Glu Val Gln
 260 265 270
 Phe Ser Trp Phe Val Asp Asp Val Glu Val His Thr Ala Gln Thr Gln
 275 280 285
 Pro Arg Glu Glu Gln Phe Asn Ser Thr Phe Arg Ser Val Ser Glu Leu
 290 295 300
 Pro Ile Met His Gln Asp Trp Leu Asn Gly Lys Glu Phe Lys Cys Arg
 305 310 315 320
 Val Asn Ser Ala Ala Phe Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys
 325 330 335
 Thr Lys Gly Arg Pro Lys Ala Pro Gln Val Tyr Thr Ile Pro Pro Pro
 340 345 350
 Lys Glu Gln Met Ala Lys Asp Lys Val Ser Leu Thr Cys Met Ile Thr
 355 360 365
 Asp Phe Phe Pro Glu Asp Ile Thr Val Glu Trp Gln Trp Asn Gly Gln
 370 375 380

Pro Ala Glu Asn Tyr Lys Asn Thr Gln Pro Ile Met Asp Thr Asp Gly
385 390 395 400

Ser Tyr Phe Ile Tyr Ser Lys Leu Asn Val Gln Lys Ser Asn Trp Glu
405 410 415

Ala Gly Asn Thr Phe Thr Cys Ser Val Leu His Glu Gly Leu His Asn
420 425 430

His His Thr Glu Lys Ser Leu Ser His Ser Pro Gly Lys
435 440 445

<210> 194
<211> 1338
<212> DNA
<213> 小家鼠

<400> 194
gaagttcagc tgcaacagtc tggggcagac cttgtgcagc caggggcctc agtcaaggltg 60
tcctgcacag cttctggcct cgacattaag gactactata tacactggat gaaacagagg 120
cctgaccagg gcctggagtg gattggaagg gttgatcctg acaatggtga gactgaattt 180
gccccgaagt tcccgggcaa ggccactttt acaacagaca cactctccaa cacagcctac 240
ctacaactca gaggcctgac atctgaggac actgccatct attactgtgg gagagaagac 300
tacgatggta cctacacctg gtttccttat tggggccaag ggactctggt cactgtctct 360
gcagccaaaa cgacaccccc atctgtctat ccactggccc ctggatctgc tgcccaaact 420
aactccatgg tgaccctggg atgcctggtc aagggtctatt tccctgagcc agtgacagtg 480
acctggaact ctggatccct gtccagcggg gtgcacacct tcccagctgt cctgcagict 540
gacctctaca ctctgagcag ctgagtgact gtccctcca gcacctggcc cagcgagacc 600
gtcacctgca acgttgccca cccggccagc agcaccaagg tggacaagaa aattgtgccc 660
agggattgtg gttgtaagcc ttgcatatgt acagtcccag aagtaicac tgtcttcac 720
ttcccccaa agcccaagga tgtgtcacc attactctga ctctaaggc cactgtgtt 780
gtggtagaca tcagcaagga tgatcccag gtccagttca gctggtttgt agatgatgtg 840
gaggtgcaca cagctcagac gcaaccccg gaggagcagt tcaacagcac ttccgctca 900
gtcagtgaac ttcccatcat gcaccaggac tggctcaatg gcaaggagtt caaatgcagg 960
gtcaacagtg cagctttccc tgcccccatc gagaaaacca tctccaaaac caaaggcaga 1020
ccgaaggctc cacaggtgta caccattcca cctcccaagg agcagatggc caaggataaa 1080
gtcagtciga cctgcatgat aacagacttc ttccctgaag acattactgt ggagtggcag 1140
tggaatgggc agccagcggg gaactacaag aacactcagc ccatcatgga cacagatggc 1200
tcttacttca tctacagcaa gctcaatgtg cagaagagca actgggaggc aggaataact 1260
ttcacctgct ctgtgttaca tgagggcctg cacaaccacc atactgagaa gagcctctcc 1320
cactctcctg gtaaatga 1338

<210> 195
<211> 464
<212> PRT
<213> 小家鼠

<400> 195

Met Lys Cys Ser Trp Val Ile Phe Phe Leu Met Ala Val Val Thr Gly
1 5 10 15

Val Asn Ser Glu Val Gln Leu Gln Gln Ser Gly Ala Asp Leu Val Gln
20 25 30

Pro Gly Ala Ser Val Lys Val Ser Cys Thr Ala Ser Gly Phe Asp Ile
35 40 45

Lys Asp Tyr Tyr Ile His Trp Met Lys Gln Arg Pro Asp Gln Gly Leu
50 55 60

Glu Trp Ile Gly Arg Val Asp Pro Asp Asn Gly Glu Thr Glu Phe Ala
65 70 75 80

Pro Lys Phe Pro Gly Lys Ala Thr Phe Thr Thr Asp Thr Ser Ser Asn
85 90 95

Thr Ala Tyr Leu Gln Leu Arg Gly Leu Thr Ser Glu Asp Thr Ala Ile
100 105 110

Tyr Tyr Cys Gly Arg Glu Asp Tyr Asp Gly Thr Tyr Thr Trp Phe Pro
115 120 125

Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ala Ala Lys Thr Thr
130 135 140

Pro Pro Ser Val Tyr Pro Leu Ala Pro Gly Ser Ala Ala Gln Thr Asn
145 150 155 160

Ser Met Val Thr Leu Gly Cys Leu Val Lys Gly Tyr Phe Pro Glu Pro
165 170 175

Val Thr Val Thr Trp Asn Ser Gly Ser Leu Ser Ser Gly Val His Thr
180 185 190

Phe Pro Ala Val Leu Gln Ser Asp Leu Tyr Thr Leu Ser Ser Ser Val
195 200 205

Thr Val Pro Ser Ser Thr Trp Pro Ser Glu Thr Val Thr Cys Asn Val
210 215 220

Ala His Pro Ala Ser Ser Thr Lys Val Asp Lys Lys Ile Val Pro Arg
225 230 235 240

Asp Cys Gly Cys Lys Pro Cys Ile Cys Thr Val Pro Glu Val Ser Ser
245 250 255

Val Phe Ile Phe Pro Pro Lys Pro Lys Asp Val Leu Thr Ile Thr Leu
260 265 270

Thr Pro Lys Val Thr Cys Val Val Val Asp Ile Ser Lys Asp Asp Pro
275 280 285

Glu Val Gln Phe Ser Trp Phe Val Asp Asp Val Glu Val His Thr Ala

290

295

300

Gln Thr Gln Pro Arg Glu Glu Gln Phe Asn Ser Thr Phe Arg Ser Val
305 310 315 320

Ser Glu Leu Pro Ile Met His Gln Asp Trp Leu Asn Gly Lys Glu Phe
325 330 335

Lys Cys Arg Val Asn Ser Ala Ala Phe Pro Ala Pro Ile Glu Lys Thr
340 345 350

Ile Ser Lys Thr Lys Gly Arg Pro Lys Ala Pro Gln Val Tyr Thr Ile
355 360 365

Pro Pro Pro Lys Glu Gln Met Ala Lys Asp Lys Val Ser Leu Thr Cys
370 375 380

Met Ile Thr Asp Phe Phe Pro Glu Asp Ile Thr Val Glu Trp Gln Trp
385 390 395 400

Asn Gly Gln Pro Ala Glu Asn Tyr Lys Asn Thr Gln Pro Ile Met Asp
405 410 415

Thr Asp Gly Ser Tyr Phe Ile Tyr Ser Lys Leu Asn Val Gln Lys Ser
420 425 430

Asn Trp Glu Ala Gly Asn Thr Phe Thr Cys Ser Val Leu His Glu Gly
435 440 445

Leu His Asn His His Thr Glu Lys Ser Leu Ser His Ser Pro Gly Lys
450 455 460

<210> 196
<211> 1395
<212> DNA
<213> 小家鼠

<400> 196

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gttcagctgc aacagtcttg ggagacctt gtgcagccag gggcctcagt caagggtgcc 120

tgcacagctt ctggcttcga cattaaggac tactatatac actggatgaa acagaggcct 180

gaccagggcc tggagtggat tggaggggtt gatcctgaca atggtgagac tgaatttgcc 240

ccgaagtcc cgggcaaggc cacttttaca acagacacat cctccaacac agcctacctt 300

caactcagag gcctgacatc tgaggacact gccatctatt actgtgggag agaagactac 360

gatggtacct acacctggtt tccttattgg ggccaaggga ctctgggtcac tgtctctgca 420

gccaaaacga ccccccaic tgtctatcca ctggccccctg gatctgctgc ccaaactaac 480

tccatggtga ccctgggatg cctgggtcaag ggctatttcc ctgagccagt gacagtgacc 540

tggaactctg gatccctgtc cagcgggtgtg cacaccttcc cagctgtcct gcagtctgac 600

ctctacactc tgagcagctc agtgactgtc cctccagca cctggcccag cgagaccgtc 660

acctgaacg ttgccaccgc ggccagcagc accaagggtg acaagaaaat tgtgccagg 720

gattgtggtt gtaagccttg catatgtaca gtcccagaag tatcatctgt cttcatcttc 780

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ccccaaagc ccaaggatgt gctcaccatt actctgactc ctaaggtcac gtgtgtgtg      840
gtagacatca gcaaggatga tcccagggtc cagttcagct ggttttaga tgatgtggag      900
gtgcacacag ctacagcgca accccgggag gagcagttca acagcacttt ccgctcagtc      960
agtgaacttc ccatcatgca ccaggactgg ctcaatggca aggagttaa atgcagggtc     1020
aacagtgcag ctttccctgc ccccatcgag aaaacatct ccaaaaccaa aggcagaccg     1080
aaggctccac aggtgtacac cattccacct cccaaggagc agatggccaa ggataaagtc     1140
agtctgacct gcatgataac agacttcttc cctgaagaca ttactgtgga gtggcagtgg     1200
aatgggcagc cagcggagaa ctacaagaac actcagccca tcatggacac agatggctct     1260
tacttcatct acagcaagct caatgtgcag aagagcaact gggaggcagg aaatacttct     1320
acctgctctg tgttacatga gggcctgcac aaccaccata ctgagaagag cctctccac     1380
tctcctggta aatga                                                         1395

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<210> 197
 <211> 214
 <212> PRT
 <213> 小家鼠

<400> 197

Asp Leu Gln Met Thr Gln Thr Thr Ser Ser Leu Ser Ala Ser Leu Gly
1 5 10 15

Asp Arg Val Thr Ile Ser Cys Arg Ala Ser Gln Asp Ile Ser Asn Tyr
20 25 30

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

Phe Tyr Thr Ser Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asn Tyr Ser Leu Thr Ile Thr Asn Leu Glu Gln
65 70 75 80

Asp Asp Ala Ala Thr Tyr Phe Cys Gln Gln Gly Asp Thr Leu Pro Tyr
85 90 95

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg Ala Asp Ala Ala
100 105 110

Pro Thr Val Ser Ile Phe Pro Pro Ser Ser Glu Gln Leu Thr Ser Gly
115 120 125

Gly Ala Ser Val Val Cys Phe Leu Asn Asn Phe Tyr Pro Lys Asp Ile
130 135 140

Asn Val Lys Trp Lys Ile Asp Gly Ser Glu Arg Gln Asn Gly Val Leu
145 150 155 160

Asn Ser Trp Thr Asp Gln Asp Ser Lys Asp Ser Thr Tyr Ser Met Ser
165 170 175

Ser Thr Leu Thr Leu Thr Lys Asp Glu Tyr Glu Arg His Asn Ser Tyr

180185190

Thr Cys Glu Ala Thr His Lys Thr Ser Thr Ser Pro Ile Val Lys Ser

195200205

Phe Asn Arg Asn Glu Cys
210

<210> 198
<211> 645
<212> DNA
<213> 小家鼠

<400> 198
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atcagttgca gggcaagtca ggacattagc aattatttaa actggtatca gcagaaacca 120
gatggaactg ttaagctcct gatcttctac acatcaacat tacagtcagg agtcccatcg 180
aggttcagtg gcagtgggtc tggaacaaat tattctctca ccattaccaa cctggagcaa 240
gatgatgctg ccacttactt ttgccaacag ggtgatacgc ttccgtacac gttcggaggg 300
gggaccaagc tggaaataaa acgggctgat gctgcaccaa ctgtatccat cttcccacca 360
tccagtgagc agttaacatc tggagggtgcc tcagtcgtgt gcttcttgaa caacttctac 420
cccaaagaca tcaatgtcaa gtggaagatt gatggcagtg aacgacaaaa tggcgtcctg 480
aacagttigga ctgatcagga cagcaaagac agcacctaca gcatgagcag caccctcacg 540
ttgaccaagg acgagtatga acgacataac agctatacct gtgaggccac tcacaagaca 600
tcaacttcac ccattgtcaa gagcttcaac aggaatgagt gttag 645

<210> 199
<211> 234
<212> PRT
<213> 小家鼠

<400> 199
Met Met Ser Ser Ala Gln Phe Leu Gly Leu Leu Leu Leu Cys Phe Gln
151015
Gly Ser Arg Cys Asp Leu Gln Met Thr Gln Thr Thr Ser Ser Leu Ser
202530
Ala Ser Leu Gly Asp Arg Val Thr Ile Ser Cys Arg Ala Ser Gln Asp
354045
Ile Ser Asn Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Asp Gly Thr Val
505560
Lys Leu Leu Ile Phe Tyr Thr Ser Thr Leu Gln Ser Gly Val Pro Ser
65707580
Arg Phe Ser Gly Ser Gly Ser Gly Thr Asn Tyr Ser Leu Thr Ile Thr
859095
Asn Leu Glu Gln Asp Asp Ala Ala Thr Tyr Phe Cys Gln Gln Gly Asp
100105110

Thr Leu Pro Tyr Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg
115 120 125

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

Leu Thr Ser Gly Gly Ala Ser Val Val Cys Phe Leu Asn Asn Phe Tyr
145 150 155 160

Pro Lys Asp Ile Asn Val Lys Trp Lys Ile Asp Gly Ser Glu Arg Gln
165 170 175

Asn Gly Val Leu Asn Ser Trp Thr Asp Gln Asp Ser Lys Asp Ser Thr
180 185 190

Tyr Ser Met Ser Ser Thr Leu Thr Leu Thr Lys Asp Glu Tyr Glu Arg
195 200 205

His Asn Ser Tyr Thr Cys Glu Ala Thr His Lys Thr Ser Thr Ser Pro
210 215 220

Ile Val Lys Ser Phe Asn Arg Asn Glu Cys
225 230

<210> 200
<211> 705
<212> DNA
<213> 小家鼠

<400> 200
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gatctccaga tgacacagac tacttctcc ctgtctgct ctctgggaga cagagtcacc 120
atcagttgca gggcaagtca ggacattagc aattatttaa actggtatca gcagaaacca 180
gatggaactg ttaagctcct gatcttctac acatcaacat tacagtcagg agtcccatcg 240
aggttcagtg gcagtgggtc tggaacaaat tatctctcga ccattaccaa cctggagcaa 300
gatgatgctg ccacttactt ttgccaacag ggtgatacgc ttccgtacac gttcggaggg 360
gggaccaagc tggaataaaa acgggctgat gctgcaccaa ctgtatccat cttcccacca 420
tccagtgagc agttaacatc tggagggtgc tcagtcgtgt gcttcttgaa caacttctac 480
cccaaagaca tcaatgtcaa gtggaagatt gatggcagtg aacgacaaaa tggcgtcctg 540
aacagttgga ctgatcagga cagcaaagac agcacctaca gcatgagcag caccctcacg 600
ttgaccaagg acgagiatga acgacataac agctatacct gtgaggccac tcacaagaca 660
tcaacttcac ccattgtcaa gagcttcaac aggaatgagt gttag 705

<210> 201
<211> 447
<212> PRT
<213> 小家鼠

<400> 201
Glu Val Gln Leu Gln Gln Ser Gly Pro Glu Leu Met Lys Pro Gly Ala
1 5 10 15
Ser Val Lys Met Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Tyr

20					25					30					
Asn	Met	His	Trp	Met	Lys	Gln	Asn	Gln	Gly	Lys	Ser	Leu	Glu	Trp	Ile
	35						40					45			
Gly	Glu	Ile	Asn	Pro	Asn	Ser	Gly	Gly	Ser	Gly	Tyr	Asn	Gln	Lys	Phe
	50					55					60				
Lys	Gly	Lys	Ala	Thr	Leu	Thr	Val	Asp	Lys	Ser	Ser	Ser	Thr	Ala	Tyr
	65					70					75				80
Met	Glu	Leu	Arg	Ser	Leu	Thr	Ser	Glu	Asp	Ser	Ala	Val	Tyr	Tyr	Cys
				85					90					95	
Ala	Arg	Leu	Gly	Tyr	Tyr	Gly	Asn	Tyr	Glu	Asp	Trp	Tyr	Phe	Asp	Val
			100					105					110		
Trp	Gly	Ala	Gly	Thr	Thr	Val	Thr	Val	Ser	Ser	Ala	Lys	Thr	Thr	Pro
			115					120					125		
Pro	Ser	Val	Tyr	Pro	Leu	Ala	Pro	Gly	Ser	Ala	Ala	Gln	Thr	Asn	Ser
				130				135					140		
Met	Val	Thr	Leu	Gly	Cys	Leu	Val	Lys	Gly	Tyr	Phe	Pro	Glu	Pro	Val
				145				150					155		160
Thr	Val	Thr	Trp	Asn	Ser	Gly	Ser	Leu	Ser	Ser	Gly	Val	His	Thr	Phe
				165					170					175	
Pro	Ala	Val	Leu	Gln	Ser	Asp	Leu	Tyr	Thr	Leu	Ser	Ser	Ser	Val	Thr
				180				185						190	
Val	Pro	Ser	Ser	Thr	Trp	Pro	Ser	Glu	Thr	Val	Thr	Cys	Asn	Val	Ala
				195				200					205		
His	Pro	Ala	Ser	Ser	Thr	Lys	Val	Asp	Lys	Lys	Ile	Val	Pro	Arg	Asp
				210				215					220		
Cys	Gly	Cys	Lys	Pro	Cys	Ile	Cys	Thr	Val	Pro	Glu	Val	Ser	Ser	Val
				225				230					235		240
Phe	Ile	Phe	Pro	Pro	Lys	Pro	Lys	Asp	Val	Leu	Thr	Ile	Thr	Leu	Thr
				245					250					255	
Pro	Lys	Val	Thr	Cys	Val	Val	Val	Asp	Ile	Ser	Lys	Asp	Asp	Pro	Glu
				260				265						270	
Val	Gln	Phe	Ser	Trp	Phe	Val	Asp	Asp	Val	Glu	Val	His	Thr	Ala	Gln
				275				280					285		
Thr	Gln	Pro	Arg	Glu	Glu	Gln	Phe	Asn	Ser	Thr	Phe	Arg	Ser	Val	Ser
				290				295					300		
Glu	Leu	Pro	Ile	Met	His	Gln	Asp	Trp	Leu	Asn	Gly	Lys	Glu	Phe	Lys
				305									315		320

Cys Arg Val Asn Ser Ala Ala Phe Pro Ala Pro Ile Glu Lys Thr Ile
325 330 335

Ser Lys Thr Lys Gly Arg Pro Lys Ala Pro Gln Val Tyr Thr Ile Pro
340 345 350

Pro Pro Lys Glu Gln Met Ala Lys Asp Lys Val Ser Leu Thr Cys Met
355 360 365

Ile Thr Asp Phe Phe Pro Glu Asp Ile Thr Val Glu Trp Gln Trp Asn
370 375 380

Gly Gln Pro Ala Glu Asn Tyr Lys Asn Thr Gln Pro Ile Met Asp Thr
385 390 395 400

Asp Gly Ser Tyr Phe Ile Tyr Ser Lys Leu Asn Val Gln Lys Ser Asn
405 410 415

Trp Glu Ala Gly Asn Thr Phe Thr Cys Ser Val Leu His Glu Gly Leu
420 425 430

His Asn His His Thr Glu Lys Ser Leu Ser His Ser Pro Gly Lys
435 440 445

<210> 202
<211> 1344
<212> DNA
<213> 小家鼠

<400> 202
gagggtccagt tgcaacagtc tggacctgaa ctaatgaagc ctggggcttc agtgaagatg 60
tcctgcaagg ctcttgata cacattcact gactacaaca tgcactggat gaagcagaac 120
caaggaaaga gcctagagtg gataggagag attaataccta acagtgggtg ttctggttac 180
aaccagaagt lcaaaggcaa ggccacattg actgtagaca agtcctccag cacagcctac 240
atggagctcc gcagcctgac atctgaggac tctgcagtct attactgtgc aagattgggc 300
tactatggta actacgagga ctggtatttc gatgtctggg gcgcagggac cacggtcacc 360
gtctcctctg ccaaaacgac acccccatct gtctatccac tggcccctgg atctgctgcc 420
caaactaact ccatggtgac cctgggatgc ctgggtcaagg gctatttccc tgagccagtg 480
acagtgcctt ggaactctgg atccctgtcc agcgggtgtgc acaccttccc agctgtcctg 540
cagtctgacc tctacactct gagcagctca gtgactgtcc cctccagcac ctggcccagc 600
gagaccgtca cctgcaacgt tgcccacccg gccagcagca ccaagggtga caagaaaatt 660
gtgcccaggg attgtggttg taagccttgc atatgtacag tcccagaagt atcatctgtc 720
ttcatcttcc ccccaaagcc caaggatgtg ctacacatta ctctgactcc taaggtcacg 780
tgtgttggtg tagacatcag caaggatgat cccgagggtc agttcagctg gttgttagat 840
gatgtggagg tgcacacagc tcagacgcaa ccccgaggag agcagttcaa cagcactttc 900
cgctcagtca gtgaacttcc catcatgcac caggactggc tcaatggcaa ggagttcaaa 960
tgcagggtca acagtgcagc ttccctgcc cccatcgaga aaaccatctc caaaacaaa 1020
ggcagaccga aggtccaca ggtgtacacc attccacctc ccaaggagca gatggccaag 1080
gataaagtca gtctgacctg catgataaca gacttcttcc ctgaagacat tactgtggag 1140

tggcagtga atgggcagcc agcggagaac tacaagaaca ctcagcccat catggacaca 1200
 gatggctctt acttcattcta cagcaagctc aatgtgcaga agagcaactg ggaggcagga 1260
 aatactttca cctgctctgt gtacatgag gccctgcaca accaccatac tgagaagagc 1320
 cctctccact ctcctggtaa atga 1344

<210> 203
 <211> 466
 <212> PRT
 <213> 小家鼠

<400> 203

Met Gly Trp Ser Trp Thr Phe Leu Phe Leu Leu Ser Gly Thr Ser Gly
1 5 10 15

Val Leu Ser Glu Val Gln Leu Gln Gln Ser Gly Pro Glu Leu Met Lys
20 25 30

Pro Gly Ala Ser Val Lys Met Ser Cys Lys Ala Ser Gly Tyr Thr Phe
35 40 45

Thr Asp Tyr Asn Met His Trp Met Lys Gln Asn Gln Gly Lys Ser Leu
50 55 60

Glu Trp Ile Gly Glu Ile Asn Pro Asn Ser Gly Gly Ser Gly Tyr Asn
65 70 75 80

Gln Lys Phe Lys Gly Lys Ala Thr Leu Thr Val Asp Lys Ser Ser Ser
85 90 95

Thr Ala Tyr Met Glu Leu Arg Ser Leu Thr Ser Glu Asp Ser Ala Val
100 105 110

Tyr Tyr Cys Ala Arg Leu Gly Tyr Tyr Gly Asn Tyr Glu Asp Trp Tyr
115 120 125

Phe Asp Val Trp Gly Ala Gly Thr Thr Val Thr Val Ser Ser Ala Lys
130 135 140

Thr Thr Pro Pro Ser Val Tyr Pro Leu Ala Pro Gly Ser Ala Ala Gln
145 150 155 160

Thr Asn Ser Met Val Thr Leu Gly Cys Leu Val Lys Gly Tyr Phe Pro
165 170 175

Glu Pro Val Thr Val Thr Trp Asn Ser Gly Ser Leu Ser Ser Gly Val
180 185 190

His Thr Phe Pro Ala Val Leu Gln Ser Asp Leu Tyr Thr Leu Ser Ser
195 200 205

Ser Val Thr Val Pro Ser Ser Thr Trp Pro Ser Glu Thr Val Thr Cys
210 215 220

Asn Val Ala His Pro Ala Ser Ser Thr Lys Val Asp Lys Lys Ile Val
225 230 235 240

Pro Arg Asp Cys Gly Cys Lys Pro Cys Ile Cys Thr Val Pro Glu Val
245 250 255

Ser Ser Val Phe Ile Phe Pro Pro Lys Pro Lys Asp Val Leu Thr Ile
260 265 270

Thr Leu Thr Pro Lys Val Thr Cys Val Val Val Asp Ile Ser Lys Asp
275 280 285

Asp Pro Glu Val Gln Phe Ser Trp Phe Val Asp Asp Val Glu Val His
290 295 300

Thr Ala Gln Thr Gln Pro Arg Glu Glu Gln Phe Asn Ser Thr Phe Arg
305 310 315 320

Ser Val Ser Glu Leu Pro Ile Met His Gln Asp Trp Leu Asn Gly Lys
325 330 335

Glu Phe Lys Cys Arg Val Asn Ser Ala Ala Phe Pro Ala Pro Ile Glu
340 345 350

Lys Thr Ile Ser Lys Thr Lys Gly Arg Pro Lys Ala Pro Gln Val Tyr
355 360 365

Thr Ile Pro Pro Pro Lys Glu Gln Met Ala Lys Asp Lys Val Ser Leu
370 375 380

Thr Cys Met Ile Thr Asp Phe Phe Pro Glu Asp Ile Thr Val Glu Trp
385 390 395 400

Gln Trp Asn Gly Gln Pro Ala Glu Asn Tyr Lys Asn Thr Gln Pro Ile
405 410 415

Met Asp Thr Asp Gly Ser Tyr Phe Ile Tyr Ser Lys Leu Asn Val Gln
420 425 430

Lys Ser Asn Trp Glu Ala Gly Asn Thr Phe Thr Cys Ser Val Leu His
435 440 445

Glu Gly Leu His Asn His His Thr Glu Lys Ser Leu Ser His Ser Pro
450 455 460

Gly Lys
465

- <210> 204
- <211> 1401
- <212> DNA
- <213> 小家鼠

<400> 204
atgggatgga gctggacatt tctcttcctc ctgtcaggaa cticgggtgt cctctctgag 60
gtccagttgc aacagtctgg acctgaacta atgaagcctg gggcttcagt gaagatgtcc 120
tgcaaggctt ctggatacac attcactgac tacaacatgc actggatgaa gcagaaccaa 180
ggaaagagcc tagagtggat aggagagatt aatcctaaca gtggtggttc tggttacaac 240

cagaagttca aaggcaaggc cacattgact gtagacaagt cctccagcac agcctacatg 300
gagctccgca gcctgacatc tgaggactct gcagtctatt actgtgcaag attgggctac 360
tatggtaact acgaggactg gtatttcgat gtcgtgggcg cagggaccac ggtcaccgtc 420
tcctctgccca aaacgacacc cccatctgtc tatccactgg cccctggatc tgcctgccc 480
actaactcca tgggtgacctt gggatgcctg gtcaagggtt atttccctga gccagtgaca 540
gtgacctgga actctggatc cctgtccagc ggtgtgcaca ccttcccagc tgcctgcag 600
tctgacctct acactctgag cagctcagtg actgtccctt ccagcacctg gccagcgag 660
accgtcacct gcaacgttgc ccaccggcc agcagcacca aggtggacaa gaaaattgtg 720
cccagggatt gtggttgtaa gccttgcata tgtacagtcc cagaagtatc atctgtcttc 780
atcttcccc caaagcccaa ggatgtgtc accattactc tgactcctaa ggtcacgtgt 840
gttgtggtag acatcagcaa ggatgatccc gaggtccagt tcagctggtt ttagatgat 900
gtggagggtc acacagctca gacgcaaccc cgggaggagc agttcaacag cactttccgc 960
tcagtcagtg aacttcccat catgcaccag gactggctca atggcaagga gttcaaatgc 1020
agggtcaaca gtgcagcttt ccttgccttc atcgagaaaa ccatctccaa aaccaaggc 1080
agaccgaagg ctccacaggt gtacaccatt ccacctccca aggagcagat ggccaaggat 1140
aaagtcatgc tgacctgat gataacagac ttcttccctg aagacattac tgtggagtgg 1200
cagtggaatg ggcagccagc ggagaactac aagaacactc agcccatcat ggacacagat 1260
ggctcttact tcatctacag caagctcaat gtgcagaaga gcaactggga ggcaggaaa 1320
actttcacct gctctgtgtt acatgagggc ctgcacaacc accatactga gaagagcctc 1380
tcccactctc ctggtaaaatg a 1401

<210> 205
<211> 215
<212> PRT
<213> 小家鼠

<400> 205

Gln Ile Val Leu Thr Gln Ser Pro Ala Ile Met Ser Ala Ser Pro Gly
1 5 10 15

Glu Lys Val Thr Met Thr Cys Arg Ala Ser Ser Ser Val Thr Ser Ser
20 25 30

Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly Ser Ser Pro Lys Leu Trp
35 40 45

Ile Tyr Ser Thr Ser Asn Leu Ala Ser Gly Val Pro Ala Arg Phe Ser
50 55 60

Gly Ser Gly Ser Gly Thr Ser Tyr Ser Leu Thr Ile Ser Ser Val Glu
65 70 75 80

Ala Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Tyr Asp Phe Phe Pro
85 90 95

Ser Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg Ala Asp Ala
100 105 110

Ala Pro Thr Val Ser Ile Phe Pro Pro Ser Ser Glu Gln Leu Thr Ser
115 120 125

Gly Gly Ala Ser Val Val Cys Phe Leu Asn Asn Phe Tyr Pro Lys Asp
130 135 140

Ile Asn Val Lys Trp Lys Ile Asp Gly Ser Glu Arg Gln Asn Gly Val
145 150 155 160

Leu Asn Ser Trp Thr Asp Gln Asp Ser Lys Asp Ser Thr Tyr Ser Met
165 170 175

Ser Ser Thr Leu Thr Leu Thr Lys Asp Glu Tyr Glu Arg His Asn Ser
180 185 190

Tyr Thr Cys Glu Ala Thr His Lys Thr Ser Thr Ser Pro Ile Val Lys
195 200 205

Ser Phe Asn Arg Asn Glu Cys
210 215

<210> 206
<211> 645
<212> DNA
<213> 小家鼠

<400> 206
cagattgttc tcaccagtc tccagcaatc atgtctgcat ctccaggga gaaggtcacc 60
atgacctgca gggccagctc aagtgttaact tccagttact tgaactggta ccagcagaag 120
ccaggatctt cccccaaact ctggatttat agcacatcca acctggcttc aggagtccca 180
gctcgttca gtggcagtgg gtctgggacc tcttactctc tcacaatcag cagtgtggag 240
gctgaggatg ctgccactta ttactgccag cagtatgatt ttttccatc gacgttcggt 300
ggaggcacca agctggaaat caagcgggct gatgtgcac caactgtatc catcttccca 360
ccatccagtg agcagttaac atctggaggt gcctcagtcg tgtgttctt gaacaacttc 420
taccctaaag acatcaatgt caagtgaag attgatggca gtgaacgaca aaatggcgtc 480
ctgaacagtt ggactgatca ggacagcaaa gacagcacct acagcatgag cagcaccttc 540
acgttgacca aggacgagta tgaacgacat aacagctata cctgtgaggc cactcacaag 600
acatcaactt caccatcgt caagagcttc aacaggaatg agtgt 645

<210> 207
<211> 237
<212> PRT
<213> 小家鼠

<400> 207

Met Asp Ser Gln Val Gln Ile Phe Ser Phe Leu Leu Ile Ser Ala Leu
1 5 10 15

Val Lys Met Ser Arg Gly Gln Ile Val Leu Thr Gln Ser Pro Ala Ile
20 25 30

Met Ser Ala Ser Pro Gly Glu Lys Val Thr Met Thr Cys Arg Ala Ser

35

40

45

Ser Ser Val Thr Ser Ser Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly
50 55 60

Ser Ser Pro Lys Leu Trp Ile Tyr Ser Thr Ser Asn Leu Ala Ser Gly
65 70 75 80

Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Ser Tyr Ser Leu
85 90 95

Thr Ile Ser Ser Val Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys Gln
100 105 110

Gln Tyr Asp Phe Phe Pro Ser Thr Phe Gly Gly Gly Thr Lys Leu Glu
115 120 125

Ile Lys Arg Ala Asp Ala Ala Pro Thr Val Ser Ile Phe Pro Pro Ser
130 135 140

Ser Glu Gln Leu Thr Ser Gly Gly Ala Ser Val Val Cys Phe Leu Asn
145 150 155 160

Asn Phe Tyr Pro Lys Asp Ile Asn Val Lys Trp Lys Ile Asp Gly Ser
165 170 175

Glu Arg Gln Asn Gly Val Leu Asn Ser Trp Thr Asp Gln Asp Ser Lys
180 185 190

Asp Ser Thr Tyr Ser Met Ser Ser Thr Leu Thr Leu Thr Lys Asp Glu
195 200 205

Tyr Glu Arg His Asn Ser Tyr Thr Cys Glu Ala Thr His Lys Thr Ser
210 215 220

Thr Ser Pro Ile Val Lys Ser Phe Asn Arg Asn Glu Cys
225 230 235

<210> 208
<211> 711
<212> DNA
<213> 小家鼠

<400> 208
atggattctc aagtcagat tticagcttc cttctaataca gtgccttagt caaaatgtcc 60
agaggacaga ttgttctcac ccagcttcca gcaatcatgt ctgcatctcc aggggagaag 120
gtcaccatga cctgcagggc cagctcaagt gtaacttcca gttacttgaa ctggtaccag 180
cagaagccag gatcttcccc caaactctgg atttatagca catccaacct ggcctcagga 240
gtcccagctc gcttcagtgg cagtgggtct gggacctctt actctctcac aatcagcagt 300
gtggaggctg aggatgctgc cacttattac tgccagcagt atgattttt cccatcgacg 360
ttcggtaggag gcaccaagct ggaaatcaag cgggctgaig ctgcaccaac tgtatccatc 420
ttcccacat ccagttagca gtaacatct ggagggtgcct cagtcgtgtg cttcttgaa 480
aacttctacc ccaaagacat caatgtcaag tggaagattg atggcagtga acgacaaaat 540

ggcgtcctga acagttggac tgatcaggac agcaaagaca gcacctacag catgagcagc 600
accctcacgt tgaccaagga cgagtatgaa cgacataaca gctataacctg tgaggccact 660
cacaagacat caacttcacc catcgtcaag agcttcaaca ggaatgagtg t 711

<210> 209
<211> 445
<212> PRT
<213> 小家鼠

<400> 209

Glu Val Gln Leu Gln Gln Ser Gly Pro Glu Leu Val Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Met Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Tyr
20 25 30

Tyr Met Asn Trp Val Lys Gln Ser His Gly Glu Ser Leu Glu Trp Ile
35 40 45

Gly Asp Ile Asn Pro Tyr Asn Asp Asp Thr Thr Tyr Asn His Lys Phe
50 55 60

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

Met Gln Leu Asn Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Glu Thr Ala Val Ile Thr Thr Asn Ala Met Asp Tyr Trp Gly
100 105 110

Gln Gly Thr Ser Val Thr Val Ser Ser Ala Lys Thr Thr Pro Pro Ser
115 120 125

Val Tyr Pro Leu Ala Pro Gly Ser Ala Ala Gln Thr Asn Ser Met Val
130 135 140

Thr Leu Gly Cys Leu Val Lys Gly Tyr Phe Pro Glu Pro Val Thr Val
145 150 155 160

Thr Trp Asn Ser Gly Ser Leu Ser Ser Gly Val His Thr Phe Pro Ala
165 170 175

Val Leu Gln Ser Asp Leu Tyr Thr Leu Ser Ser Ser Val Thr Val Pro
180 185 190

Ser Ser Thr Trp Pro Ser Glu Thr Val Thr Cys Asn Val Ala His Pro
195 200 205

Ala Ser Ser Thr Lys Val Asp Lys Lys Ile Val Pro Arg Asp Cys Gly
210 215 220

Cys Lys Pro Cys Ile Cys Thr Val Pro Glu Val Ser Ser Val Phe Ile
225 230 235 240

Phe Pro Pro Lys Pro Lys Asp Val Leu Thr Ile Thr Leu Thr Pro Lys

245 250 255

Val Thr Cys Val Val Val Asp Ile Ser Lys Asp Asp Pro Glu Val Gln
260 265 270

Phe Ser Trp Phe Val Asp Asp Val Glu Val His Thr Ala Gln Thr Gln
275 280 285

Pro Arg Glu Glu Gln Phe Asn Ser Thr Phe Arg Ser Val Ser Glu Leu
290 295 300

Pro Ile Met His Gln Asp Trp Leu Asn Gly Lys Glu Phe Lys Cys Arg
305 310 315 320

Val Asn Ser Ala Ala Phe Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys
325 330 335

Thr Lys Gly Arg Pro Lys Ala Pro Gln Val Tyr Thr Ile Pro Pro Pro
340 345 350

Lys Glu Gln Met Ala Lys Asp Lys Val Ser Leu Thr Cys Met Ile Thr
355 360 365

Asp Phe Phe Pro Glu Asp Ile Thr Val Glu Trp Gln Trp Asn Gly Gln
370 375 380

Pro Ala Glu Asn Tyr Lys Asn Thr Gln Pro Ile Met Asp Thr Asp Gly
385 390 395 400

Ser Tyr Phe Ile Tyr Ser Lys Leu Asn Val Gln Lys Ser Asn Trp Glu
405 410 415

Ala Gly Asn Thr Phe Thr Cys Ser Val Leu His Glu Gly Leu His Asn
420 425 430

His His Thr Glu Lys Ser Leu Ser His Ser Pro Gly Lys
435 440 445

<210> 210
<211> 1335
<212> DNA
<213> 小家鼠

<400> 210
gaggtccagc tgcaacaatc tggacctgag ctggtgaagc ctggggcttc agtgaagatg 60
tcctgtaagg cttctggata cacattcact gactactaca tgaactgggt gaagcagagc 120
catggagaga gccttgagtg gattggagat attaatcctt acaacgatga tactacctac 180
aaccacaagt tcaagggcaa ggccacattg actgtagaca aatcctccaa cacagcctac 240
atgcagctca acagccctgac atctgaggac tctgcagtct attactgtgc aagagagacg 300
gccgttatta ctacgaatgc tatggactac tggggicaag gaacctcagt caccgtctcc 360
tcagccaaaa cgacaccccc atctgtctat ccactggccc ctggatctgc tgcccaaact 420
aactccaatg tgaccttggg atgcctggtc aagggtctatt tccttgagcc agtgacagtg 480
acctggaact ctggatccct gtccagcggg gtgcacacct tcccagctgt cctgcagtct 540

gacctctaca ctctgagcag ctacgtgact gtccctcca gcacctggcc cagcgagacc 600
gtcacctgca acgttgccca cccggccagc agcaccaagg tggacaagaa aattgtgccc 660
agggattgtg gttgtaagcc ttgcatatgt acagtcaccag aagtatcacc tgtcttcacc 720
ttccccccaa agcccaagga tgtgtcacc attactctga ctccaaaggt cagctgtgtt 780
gtggtagaca tcagcaagga tgatcccag gtccagtcca gctggtttgt agatgatgtg 840
gaggtgcaca cagctcagac gcaaccccg gaggagcagt tcaacagcac tttccgtcca 900
gtcagtgaac ttcccatcat gcaccaggac tggctcaatg gcaaggagtt caaatgcagg 960
gtcaacagtg cagctttccc tgccccacc gagaaaacca tctccaaaac caaaggcaga 1020
ccgaaggctc cacagggtga caccattcca cctccaagg agcagatggc caaggataaa 1080
gtcagctcga cctgcatgat aacagacttc ttccctgaag acattactgt ggagtggcag 1140
tggaatgggc agccagcggg gaactacaag aacactcagc ccatcatgga cacagatggc 1200
tcttacttca tctacagcaa gctcaatgtg cagaagagca actggggaggc aggaataact 1260
ttcacctgct ctgtgttaca tgagggcctg cacaaccacc atactgagaa gagcctctcc 1320
cactctcctg gtaaa 1335

<210> 211
<211> 464
<212> PRT
<213> 小家鼠

<400> 211
Met Gly Trp Asn Trp Ile Phe Leu Phe Leu Leu Ser Gly Thr Ala Gly
1 5 10 15
Val Tyr Ser Glu Val Gln Leu Gln Gln Ser Gly Pro Glu Leu Val Lys
20 25 30
Pro Gly Ala Ser Val Lys Met Ser Cys Lys Ala Ser Gly Tyr Thr Phe
35 40 45
Thr Asp Tyr Tyr Met Asn Trp Val Lys Gln Ser His Gly Glu Ser Leu
50 55 60
Glu Trp Ile Gly Asp Ile Asn Pro Tyr Asn Asp Asp Thr Thr Tyr Asn
65 70 75 80
His Lys Phe Lys Gly Lys Ala Thr Leu Thr Val Asp Lys Ser Ser Asn
85 90 95
Thr Ala Tyr Met Gln Leu Asn Ser Leu Thr Ser Glu Asp Ser Ala Val
100 105 110
Tyr Tyr Cys Ala Arg Glu Thr Ala Val Ile Thr Thr Asn Ala Met Asp
115 120 125
Tyr Trp Gly Gln Gly Thr Ser Val Thr Val Ser Ser Ala Lys Thr Thr
130 135 140
Pro Pro Ser Val Tyr Pro Leu Ala Pro Gly Ser Ala Ala Gln Thr Asn
145 150 155 160

Ser Met Val Thr Leu Gly Cys Leu Val Lys Gly Tyr Phe Pro Glu Pro
165 170 175

Val Thr Val Thr Trp Asn Ser Gly Ser Leu Ser Ser Gly Val His Thr
180 185 190

Phe Pro Ala Val Leu Gln Ser Asp Leu Tyr Thr Leu Ser Ser Ser Val
195 200 205

Thr Val Pro Ser Ser Thr Trp Pro Ser Glu Thr Val Thr Cys Asn Val
210 215 220

Ala His Pro Ala Ser Ser Thr Lys Val Asp Lys Lys Ile Val Pro Arg
225 230 235 240

Asp Cys Gly Cys Lys Pro Cys Ile Cys Thr Val Pro Glu Val Ser Ser
245 250 255

Val Phe Ile Phe Pro Pro Lys Pro Lys Asp Val Leu Thr Ile Thr Leu
260 265 270

Thr Pro Lys Val Thr Cys Val Val Val Asp Ile Ser Lys Asp Asp Pro
275 280 285

Glu Val Gln Phe Ser Trp Phe Val Asp Asp Val Glu Val His Thr Ala
290 295 300

Gln Thr Gln Pro Arg Glu Glu Gln Phe Asn Ser Thr Phe Arg Ser Val
305 310 315 320

Ser Glu Leu Pro Ile Met His Gln Asp Trp Leu Asn Gly Lys Glu Phe
325 330 335

Lys Cys Arg Val Asn Ser Ala Ala Phe Pro Ala Pro Ile Glu Lys Thr
340 345 350

Ile Ser Lys Thr Lys Gly Arg Pro Lys Ala Pro Gln Val Tyr Thr Ile
355 360 365

Pro Pro Pro Lys Glu Gln Met Ala Lys Asp Lys Val Ser Leu Thr Cys
370 375 380

Met Ile Thr Asp Phe Phe Pro Glu Asp Ile Thr Val Glu Trp Gln Trp
385 390 395 400

Asn Gly Gln Pro Ala Glu Asn Tyr Lys Asn Thr Gln Pro Ile Met Asp
405 410 415

Thr Asp Gly Ser Tyr Phe Ile Tyr Ser Lys Leu Asn Val Gln Lys Ser
420 425 430

Asn Trp Glu Ala Gly Asn Thr Phe Thr Cys Ser Val Leu His Glu Gly
435 440 445

Leu His Asn His His Thr Glu Lys Ser Leu Ser His Ser Pro Gly Lys
450 455 460

<210> 212
<211> 1392
<212> DNA
<213> 小家鼠

<400> 212
atgggatgga actggatctt tctcttcctc ttgtcaggaa ctgcagggtg ctactctgag 60
gtccagctgc aacaatctgg acctgagctg gtgaagcctg gggcttcagt gaagatgtcc 120
tgtaaggctt ctggatacac attcactgac tactacatga actgggtgaa gcagagccat 180
ggagagagcc ttgagtggat tggagatatt aatccttaca acgatgatac tacctacaac 240
cacaagtica agggcaaggc cacattgact gtagacaaat cctccaacac agcctacatg 300
cagctcaaca gcctgacatc tgaggactct gcagtcctat actgtgcaag agagacggcc 360
gttattacta cgaatgctat ggactactgg ggtaaggaa cctcagtcac cgtctcctca 420
gccaaaacga caccctccatc tgtctatcca ctggccctg gatctgtcgc ccaaactaac 480
tccatgggtg ccctgggatg cctgggtcaag ggctatctcc ctgagccagt gacagtgacc 540
tggaactctg gatccctgtc cagcgggtgtg cacaccttcc cagctgtcct gcagctgac 600
ctctacactc tgagcagctc agtgactgtc ccctccagca cctggcccag cgagaccgtc 660
acctgcaacg ttgccacccc ggccagcagc accaagggtg acaagaaaaa tgtgcccagg 720
gattgtgggt glaagccttg catatgtaca gtcccagaag tatcatctgt cticactctc 780
cccccaaagc ccaaggatgt gctcaccatt actctgactc ctgaagtcac gtgtgtgtgtg 840
gtagacatca gcaaggatga tcccagggtc cagttcagct ggtttgtaga tgatgtggag 900
gtgcacacag ctgagacgca accccgggag gagcagtica acagcacttt ccgctcagtc 960
agtgaacttc ccatcatgca ccaggactgg ctcaatggca aggagttcaa atgcagggtc 1020
aacagtgcag ctttccctgc ccccatcgag aaaacatct ccaaaaccaa aggcagaccg 1080
aaggctccac aggtgtacac cattccacct cccaaggagc agatggccaa ggataaagtc 1140
agtctgacct gcatgataac agacttcttc cctgaagaca ttactgtgga gtggcagttg 1200
aatgggcagc cagcggagaa ctacaagaac actcagccca tcatggacac agatggctct 1260
tacttcatct acagcaagct caatgtgcag aagagcaact gggaggcagg aaatactttc 1320
acctgctctg tgttacatga gggcctgcac aaccaccata ctgagaagag cctctcccac 1380
tctcctggta aa 1392

<210> 213
<211> 215
<212> PRT
<213> 人工序列

<220>
<223> 合成多肽

<220>
<221> MISC_FEATURE
<223> 人化抗体序列

<400> 213
Asp Ile Gln Leu Thr Gln Ser Pro Ser Phe Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Ser Ser Val Thr Ser Ser
20 25 30

Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu
35 40 45

Ile Tyr Ser Thr Ser Asn Leu Ala Ser Gly Val Pro Ser Arg Phe Ser
50 55 60

Gly Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln
65 70 75 80

Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Asp Phe Phe Pro
85 90 95

Ser Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala
100 105 110

Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser
115 120 125

Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu
130 135 140

Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser
145 150 155 160

Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu
165 170 175

Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val
180 185 190

Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys
195 200 205

Ser Phe Asn Arg Gly Glu Cys
210 215

<210> 214
<211> 645
<212> DNA
<213> 人工序列

<220>
<223> 合成聚核苷酸

<220>
<221> misc_feature
<223> 人化抗体序列

<400> 214
gacatccagc tgacccagag ccccagcttc ctttccgcat ccgttggiga ccgagtaaca 60
atcacatgcc ggcctcatc ttcagttaca tcttcttata ttaattggta tcaacaaaaa 120
ccaggaaaag cacctaaact tcttatatac tctacatcta atctcgcatc aggagttccc 180
tctcgatttt caggatctgg atcaggcaca gaatttacac ttactataac atcactccaa 240

ccagaagact tcgccactta ttactgccaa caatacgatt ttttccaag cacattcgga 300
ggaggtagaa aagtagaaat caagcgtacg gtggctgcac catctgtctt catcttcccg 360
ccatctgatg agcagttgaa atctggaact gcctctgttg tgtgccctgct gaataacttc 420
tatcccagag aggccaaagt acagtgggaag gtggataacg ccctccaatc gggtaactcc 480
caggagagtg tcacagagca ggacagcaag gacagcacct acagccicag cagcaccctg 540
acgttgagca aagcagacta cgagaaacac aaagtctacg cctgcgaagt caccatcag 600
ggcctgagct cgcccgtcac aaagagcttc aacaggggag agtgt 645

<210> 215
<211> 237
<212> PRT
<213> 人工序列

<220>
<223> 合成多肽

<220>
<221> MISC_FEATURE
<223> 人化抗体序列

<400> 215

Met Asp Met Arg Val Pro Ala Gln Leu Leu Gly Leu Leu Leu Trp
1 5 10 15

Leu Pro Gly Ala Arg Cys Asp Ile Gln Leu Thr Gln Ser Pro Ser Phe
20 25 30

Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser
35 40 45

Ser Ser Val Thr Ser Ser Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly
50 55 60

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

Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Glu Phe Thr Leu
85 90 95

Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln
100 105 110

Gln Tyr Asp Phe Phe Pro Ser Thr Phe Gly Gly Gly Thr Lys Val Glu
115 120 125

Ile Lys Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser
130 135 140

Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn
145 150 155 160

Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala
165 170 175

Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys

180185190

Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp
195200205

Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu
210215220

Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
225230235

<210> 216
<211> 711
<212> DNA
<213> 人工序列

<220>
<223> 合成聚核苷酸

<220>
<221> misc_feature
<223> 人化抗体序列

<400> 216
atggacatga ggggtccccgc tcagctcctg gggctcctgc tactctggct cccaggtgcc 60
agatgtgaca tccagctgac ccagagcccc agcttccttt ccgcatccgt tggtgaccga 120
gtaacaatca catgccgcgc ctcatcttca gttacatctt cttatcttaa ttggtatcaa 180
caaaaaccag gaaaagcacc taaacttctt atatactcta catctaattt cgcatacagga 240
gttccctctc gattttcagg atctggatca ggcacagaat ttacattac tataatcatca 300
ctccaaccag aagacttcgc cacttattac tgccaacaat acgatttttt tccaagcaca 360
ttcggaggag gtacaaaagt agaaatcaag cgtacgggtg ctgcaccatc tgtcttcac 420
ttccccccat ctgatgagca gttgaaatct ggaactgcct ctgttgtgtg cctgctgaat 480
aacttctatc ccagagaggc caaagtacag tggaagggtg ataacgccct ccaatcgggt 540
aactcccagg agagtgtcac agagcaggac agcaaggaca gcacctacag cctcagcagc 600
accttgacgc tgagcaaagc agactacgag aaacacaaag tctacgcctg cgaagtcacc 660
catcaggggc tgagctcgcc cgtcacaaag agcttcaaca ggggagagtg t 711

<210> 217
<211> 447
<212> PRT
<213> 人工序列

<220>
<223> 合成多肽

<220>
<221> MISC_FEATURE
<223> 人化抗体序列

<400> 217
Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
151015

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Tyr
202530

Tyr Met Asn Trp Val Arg Gln Ala Pro Gly Gln Arg Leu Glu Trp Met
 35 40 45
 Gly Asp Ile Asn Pro Tyr Asn Asp Asp Thr Thr Tyr Asn His Lys Phe
 50 55 60
 Lys Gly Arg Val Thr Ile Thr Arg Asp Thr Ser Ala Ser Thr Ala Tyr
 65 70 75 80
 Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
 85 90 95
 Ala Arg Glu Thr Ala Val Ile Thr Thr Asn Ala Met Asp Tyr Trp Gly
 100 105 110
 Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser
 115 120 125
 Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser Thr Ala
 130 135 140
 Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val
 145 150 155 160
 Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala
 165 170 175
 Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val
 180 185 190
 Pro Ser Ser Asn Phe Gly Thr Gln Thr Tyr Thr Cys Asn Val Asp His
 195 200 205
 Lys Pro Ser Asn Thr Lys Val Asp Lys Thr Val Glu Arg Lys Cys Cys
 210 215 220
 Val Glu Cys Pro Pro Cys Pro Ala Pro Pro Val Ala Gly Pro Ser Val
 225 230 235 240
 Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr
 245 250 255
 Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu
 260 265 270
 Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys
 275 280 285
 Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Phe Arg Val Val Ser
 290 295 300
 Val Leu Thr Val Val His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys
 305 310 315 320
 Cys Lys Val Ser Asn Lys Gly Leu Pro Ala Pro Ile Glu Lys Thr Ile

325330335

Ser Lys Thr Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro
340345350

Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu
355360365

Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn
370375380

Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Met Leu Asp Ser
385390395400

Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg
405410415

Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu
420425430

His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
435440445

<210> 218
<211> 1341
<212> DNA
<213> 人工序列

<220>
<223> 合成聚核苷酸

<220>
<221> misc_feature
<223> 人化抗体序列

<400> 218

gaggtgcagc tgggtcagag cggcgccgag gtcaagaaac ctggagcaag cgtaaagggt60

agttgcaaag catctggata cacatttacc gactactaca tgaattgggt acgacaagcc120

cctggacaaa gacttgaatg gatgggagac attaacccctt ataacgacga cactacatac180

aatcataaat ttaaaggaag agttacaatt acaagagata catccgcacg aaccgcctat240

atggaacttt cctcatigag atctgaagac actgctgttt attactgtgc aagagaaact300

gccgttatta ctactaacgc tatggattac tgggggtcaag gaaccactgt taccgtctct360

agtgcctcca ccaagggccc atcgggtcttc cccctggcgc cctgtccag gagcacctcc420

gagagcacag cggccctggg ctgcctggtc aaggactact tccccgaacc ggtgacggtg480

tcgtggaact caggcgctct gaccagcggc gtgcacacct tcccagctgt cctacagtcc540

tcaggactct actccctcag cagcgtggtg accgtgccct ccagcaactt cggcacccag600

acctacacct gcaacgtaga tcacaagccc agcaacacca aggtggacaa gacagttgag660

cgcaaatgtt gtgtcgagtg cccaccgtgc ccagcaccac ctgtggcagg accgtcagtc720

tctctcttcc ccccaaaacc caaggacacc ctcatgatct cccggacccc tgaggtcacg780

tgcgtggtgg tggacgtgag ccacgaagac cccgaggtcc agttcaactg gtacgtggac840

ggcgtggagg tgcataatgc caagacaaag ccacgggagg agcagttcaa cagcacgttc900

cggtggtgca gcgtcctcac cgttgtgcac caggactggc tgaacggcaa ggagtacaag 960
tgcaagggtct ccaacaaagg cctcccagcc cccatcgaga aaaccatctc caaaacccaaa 1020
gggcagcccc gagaaccaca ggtgtacacc ctgcccccat cccgggagga gatgaccaag 1080
aaccagggtca gcctgacctg cctgggtcaaa ggcttctacc ccagcgacat cgccgtggag 1140
tgggagagca atgggcagcc ggagaacaac tacaagacca caccitcccat gctggactcc 1200
gacggctcct tcttctctta cagcaagctc accgtggaca agagcagggtg gcagcagggg 1260
aacgtcttct catgctccgt gatgcatgag gctctgcaca accactacac gcagaagagc 1320
ctctccctgt ctccgggtaa a 1341

<210> 219
<211> 466
<212> PRT
<213> 人工序列

<220>
<223> 合成多肽

<220>
<221> MISC_FEATURE
<223> 人化抗体序列

<400> 219

Met Asp Trp Thr Trp Arg Ile Leu Phe Leu Val Ala Ala Ala Thr Gly
1 5 10 15

Ala His Ser Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys
20 25 30

Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe
35 40 45

Thr Asp Tyr Tyr Met Asn Trp Val Arg Gln Ala Pro Gly Gln Arg Leu
50 55 60

Glu Trp Met Gly Asp Ile Asn Pro Tyr Asn Asp Asp Thr Thr Tyr Asn
65 70 75 80

His Lys Phe Lys Gly Arg Val Thr Ile Thr Arg Asp Thr Ser Ala Ser
85 90 95

Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val
100 105 110

Tyr Tyr Cys Ala Arg Glu Thr Ala Val Ile Thr Thr Asn Ala Met Asp
115 120 125

Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys
130 135 140

Gly Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu
145 150 155 160

Ser Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro
165 170 175

Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr
180 185 190

Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val
195 200 205

Val Thr Val Pro Ser Ser Asn Phe Gly Thr Gln Thr Tyr Thr Cys Asn
210 215 220

Val Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys Thr Val Glu Arg
225 230 235 240

Lys Cys Cys Val Glu Cys Pro Pro Cys Pro Ala Pro Pro Val Ala Gly
245 250 255

Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile
260 265 270

Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu
275 280 285

Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
290 295 300

Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Phe Arg
305 310 315 320

Val Val Ser Val Leu Thr Val Val His Gln Asp Trp Leu Asn Gly Lys
325 330 335

Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ala Pro Ile Glu
340 345 350

Lys Thr Ile Ser Lys Thr Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr
355 360 365

Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu
370 375 380

Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
385 390 395 400

Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Met
405 410 415

Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp
420 425 430

Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His
435 440 445

Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
450 455 460

Gly Lys
465

<210> 220
<211> 1398
<212> DNA
<213> 人工序列

<220>
<223> 合成聚核苷酸

<220>
<221> misc_feature
<223> 人化抗体序列

<400> 220
atggactgga cctggaggat cctcttcttg gtggcagcag ccacaggagc ccactccgag 60
gtgcagctgg tgcagagcgg cgccgaggtc aagaaacctg gagcaagcgt aaaggttagt 120
tgcaaagcat ctggatacac atttaccgac tactacatga attgggtacg acaagcccct 180
ggacaagac ttgaatggat gggagacatt aacccttata acgacgacac tacatacaat 240
cataaatlta aaggaagagt tacaattaca agagatacat ccgcatcaac cgcttatatg 300
gaactttctt catlgagatc tgaagacact gctgtttatt actgtgcaag agaaactgcc 360
gttattacta ctacgctat ggattactgg ggtcaaggaa ccactgttac cgtctctagt 420
gcctccacca agggcccatc ggtcttcccc ctggcgccct gctccaggag cacctccgag 480
agcacagcgg ccctgggctg cctgggtcaag gactacttcc ccgaaccggt gacgggtgctg 540
tggaactcag gcgctctgac cagcggcgtg cacaccttcc cagctgtcct acagtctca 600
ggactctact cctcagcag cgtggtgacc gtgccctcca gcaacttcgg caccagacc 660
tacacctgca acgtagatca caagcccagc aacaccaagg tggacaagac agttgagcgc 720
aaatgttgtg tcgagtgcgc accgtgcccc gcaccacctg tggcaggacc gtcagtcttc 780
ctcttcccc caaaacccaa ggacacctc atgatctccc ggacctctga ggtcacgtgc 840
gtgggtgggg acgtgagcca cgaagacccc gaggtccagt tcaactggta cgtggacggc 900
gtggagggtc ataatgcaa gacaaagcca cgggaggagc agttcaacag cacgttccgt 960
gtggtcagcg tcctcaccgt tgtgcaccag gactggctga acggcaagga gtacaagtgc 1020
aaggcttcca acaaaggcct ccagcccc atcgagaaaa ccatctccaa aaccaaaggg 1080
cagccccgag aaccacaggt gtacacctg ccccatccc gggaggagat gaccaagaac 1140
caggtcagcc tgacctgcct ggtcaaaggc ttctaccca gcgacatcgc cgtggagtgg 1200
gagagcaatg ggcagccgga gaacaactac aagaccacac ctcccatgct ggactccgac 1260
ggctccttct tcctctacag caagctcacc gtggacaaga gcaggtggca gcaggggaac 1320
gtcttctcat gctccgtgat gcatgaggct ctgcacaacc actacacgca gaagagcctc 1380
tcctgtctc cgggtaaa 1398

<210> 221
<211> 215
<212> PRT
<213> 人工序列

<220>
<223> 合成多肽

<220>

<221> MISC_FEATURE

<223> 人化抗體序列

<400> 221

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Ser Val Ser Ser Thr Ile Ser Ser Asn
20 25 30

His Leu His Trp Phe Gln Gln Lys Pro Gly Lys Ala Pro Lys Ser Leu
35 40 45

Ile Tyr Gly Thr Ser Asn Leu Ala Ser Gly Val Pro Ser Arg Phe Ser
50 55 60

Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln
65 70 75 80

Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Tyr Pro
85 90 95

Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala
100 105 110

Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser
115 120 125

Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu
130 135 140

Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser
145 150 155 160

Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu
165 170 175

Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val
180 185 190

Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys
195 200 205

Ser Phe Asn Arg Gly Glu Cys
210 215

<210> 222

<211> 645

<212> DNA

<213> 人工序列

<220>

<223> 合成聚核苷酸

<220>

<221> misc_feature

<223> 人化抗體序列

<400> 222

gacatccaga tgacccagtc tccatcctcc ctctcagcat ccgtaggcga tagagttaca 60
ataacatgca gcgtatcatc aactatatca tcaaatcadc ttcattgggtt ccaacagaaa 120
cccggaagac cacctaaatc acttatatac ggcacatcaa atctcgcatc aggcgttcct 180
tcaagatttt caggctctgg ctacaggcacc gactttactc ttacaatata ctccttccaa 240
cccgaagact tcgcaacctt ttactgtcaa caatgggtcct catatccaact cacatttgge 300
ggcggcacia aagtagaaat taaacgtacg gtggctgcac catctgtctt catcttcccg 360
ccatctgatg agcagttgaa atctggaact gcctctgttg tgtgcctgct gaataacttc 420
tatccagag aggccaaaagt acagtggaag gtggataacg ccttccaatc gggtaactcc 480
caggagagtg tcacagagca ggacagcaag gacagcacct acagcctcag cagcacctg 540
acgtgagca aagcagacta cgagaaacac aaagtctacg cctgcgaagt caccatcag 600
ggcctgagct cgcccgtcac aaagagcttc aacaggggag agtgt 645

<210> 223
<211> 237
<212> PRT
<213> 人工序列

<220>
<223> 合成多肽

<220>
<221> MISC_FEATURE
<223> 人化抗体序列

<400> 223

Met Asp Met Arg Val Pro Ala Gln Leu Leu Gly Leu Leu Leu Leu Trp
1 5 10 15

Leu Arg Gly Ala Arg Cys Asp Ile Gln Met Thr Gln Ser Pro Ser Ser
20 25 30

Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Ser Val Ser
35 40 45

Ser Thr Ile Ser Ser Asn His Leu His Trp Phe Gln Gln Lys Pro Gly
50 55 60

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

Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu
85 90 95

Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln
100 105 110

Gln Trp Ser Ser Tyr Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu
115 120 125

Ile Lys Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser
130 135 140

Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn

145150155160

Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala
165170175

Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys
180185190

Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp
195200205

Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu
210215220

Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
225230235

<210> 224
<211> 711
<212> DNA
<213> 人工序列

<220>
<223> 合成聚核苷酸

<220>
<221> misc_feature
<223> 人化抗体序列

<400> 224

atggacaiga gggccccgc tcagctcctg gggctcctgc tactctggct ccgaggtgcc60

agatgtgaca tccagatgac ccagtcacca tcctccctct cagcatccgt aggcgataga120

gttacaataa catgcagcgt atcatcaact atatcatcaa atcatcttca ttggttccaa180

cagaaacccg gcaaagcacc taaatcactt atatacggca catcaaatct cgcacacaggc240

gttccttcaa gattttcagg ctctggctca ggcaccgact ttactcttac aatactctcc300

ctccaacccg aagacttcgc aacctattac tgtcaacaat ggtcctcata tccactcaca360

tttggcggcg gcacaaaagt agaaattaaa cgtacgggtg ctgcaccatc tgtcttcac420

ttcccgccat ctgatgagca gtigaaatct ggaactgcct ctgttgtgtg cctgctgaat480

aacttctatc ccagagaggc caaagtacag tggaagggtg ataacgccct ccaatcgggt540

aactcccagg agagtgtcac agagcaggac agcaaggaca gcacctacag cctcagcagc600

acctgacgc tgagcaaagc agactacgag aaacacaaag tctacgcctg cgaagtcacc660

catcagggcc tgagctcgcc cgtcacaaag agcttcaaca ggggagagtg t711

<210> 225
<211> 451
<212> PRT
<213> 人工序列

<220>
<223> 合成多肽

<220>
<221> MISC_FEATURE
<223> 人化抗体序列

<400> 225

Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Asp Phe Asn Ile Lys Asp Phe
20 25 30

Tyr Leu His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

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

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

Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Glu Ala Asp Tyr Phe His Asp Gly Thr Ser Tyr Trp Tyr Phe
100 105 110

Asp Val Trp Gly Arg Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr
115 120 125

Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser
130 135 140

Glu Ser Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu
145 150 155 160

Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His
165 170 175

Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser
180 185 190

Val Val Thr Val Pro Ser Ser Asn Phe Gly Thr Gln Thr Tyr Thr Cys
195 200 205

Asn Val Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys Thr Val Glu
210 215 220

Arg Lys Cys Cys Val Glu Cys Pro Pro Cys Pro Ala Pro Pro Val Ala
225 230 235 240

Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
245 250 255

Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
260 265 270

Glu Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val
275 280 285

His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Phe

290295300

Arg Val Val Ser Val Leu Thr Val Val His Gln Asp Trp Leu Asn Gly
305310315320

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ala Pro Ile
325330335

Glu Lys Thr Ile Ser Lys Thr Lys Gly Gln Pro Arg Glu Pro Gln Val
340345350

Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser
355360365

Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
370375380

Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
385390395400

Met Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val
405410415

Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
420425430

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
435440445

Pro Gly Lys
450

<210> 226
<211> 1353
<212> DNA
<213> 人工序列

<220>
<223> 合成聚核苷酸

<400> 226

gaggatgcagc tggatgcagtc tggggctgag gtgaagaagc ctggggcctc agtgaaggtc60

tcctgcaagg cttctgactt caacattaaa gacttctatc tacactgggt gcgacaggcc120

cctggacaag ggcttgagtg gattggaagg attgatcctg agaatggiga tactttatat180

gacccgaagt tccaggacaa ggtcaccatg accacagaca cgtccaccag cacagcctac240

atggagctga ggagcctgag atctgacgac acggccgtgt attactgtgc gagagaggcg300

gattatttcc acgatgggtac ctccctactgg tacttcgatg tctggggccg tggcaccctg360

gtcaccgtct ctagtgcctc caccaagggc ccatcggtct tccccctggc gccctgctcc420

aggagcacct ccgagagcac agcggccctg ggctgcctgg tcaaggacta cttccccgaa480

ccggtgacgg tgtcgtggaa ctcaggcgct ctgaccagcg gcgtgcacac ctccccagct540

gtcctacagt cctcaggact ctactccctc agcagcgtag tgaccgtgcc ctccagcaac600

ttcggcaccc agacctacac ctgcaacgta gatcacaagc ccagcaacac caaggtaggac660

aagacagttg agcgcaaatg ttgtgtcgag tgcaccacct gccagcacc acctgtggca720

ggaccgtcag tcttcctctt cccccaaaa cccaaggaca ccctcatgat ctcccggacc 780
cctgagggtc cgtgcggtgt ggtggacgtg agccacgaag accccgaggt ccagttcaac 840
tggtacgtgg acggcgtgga ggtgcataat gccaagacaa agccacggga ggagcagttc 900
aacagcacgt tccgtgtgtt cagcgtcttc accgttgtgc accaggactg gctgaacggc 960
aaggagtaca agtgcaaggt ctccaacaaa ggcttcccag ccccatcga gaaaaccatc 1020
tccaaaacca aagggcagcc ccgagaacca cagggtgtaca ccctgcccc atcccgggag 1080
gagatgacca agaaccaggt cagcctgacc tgcctggtca aaggcttcta cccagcgac 1140
atgccgtgg agtgggagag caatgggcag ccggagaaca actacaagac cacacctccc 1200
atgtggact ccgacggctc cttcttcttc tacagcaagc tcaccgtgga caagagcagg 1260
tggcagcagg ggaacgtctt ctcatgtccc gtgatgatg aggcctctga caaccactac 1320
acgcagaaga gcctctccct gtctccgggt aaa 1353

<210> 227
<211> 470
<212> PRT
<213> 人工序列

<220>
<223> 合成多肽

<220>
<221> MISC_FEATURE
<223> 人化抗体序列

<400> 227

Met Asp Trp Thr Trp Arg Ile Leu Phe Leu Val Ala Ala Ala Thr Gly
1 5 10 15
Ala His Ser Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys
20 25 30
Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Asp Phe Asn Ile
35 40 45
Lys Asp Phe Tyr Leu His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu
50 55 60
Glu Trp Ile Gly Arg Ile Asp Pro Glu Asn Gly Asp Thr Leu Tyr Asp
65 70 75 80
Pro Lys Phe Gln Asp Lys Val Thr Met Thr Thr Asp Thr Ser Thr Ser
85 90 95
Thr Ala Tyr Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val
100 105 110
Tyr Tyr Cys Ala Arg Glu Ala Asp Tyr Phe His Asp Gly Thr Ser Tyr
115 120 125
Trp Tyr Phe Asp Val Trp Gly Arg Gly Thr Leu Val Thr Val Ser Ser
130 135 140

Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg
145 150 155 160

Ser Thr Ser Glu Ser Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr
165 170 175

Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser
180 185 190

Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser
195 200 205

Leu Ser Ser Val Val Thr Val Pro Ser Ser Asn Phe Gly Thr Gln Thr
210 215 220

Tyr Thr Cys Asn Val Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys
225 230 235 240

Thr Val Glu Arg Lys Cys Cys Val Glu Cys Pro Pro Cys Pro Ala Pro
245 250 255

Pro Val Ala Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
260 265 270

Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp
275 280 285

Val Ser His Glu Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp Gly
290 295 300

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn
305 310 315 320

Ser Thr Phe Arg Val Val Ser Val Leu Thr Val Val His Gln Asp Trp
325 330 335

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro
340 345 350

Ala Pro Ile Glu Lys Thr Ile Ser Lys Thr Lys Gly Gln Pro Arg Glu
355 360 365

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn
370 375 380

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
385 390 395 400

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
405 410 415

Thr Pro Pro Met Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys
420 425 430

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
435 440 445

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
450 455 460

Ser Leu Ser Pro Gly Lys
465 470

<210> 228
<211> 1410
<212> DNA
<213> 人工序列

<220>
<223> 合成聚核苷酸

<220>
<221> misc_feature
<223> 人化抗体序列

<400> 228
atggactgga cctggaggat cctcttcttg gtggcagcag ccacaggagc ccactccgag 60
gtgcagctgg tgcagtctgg ggctgaggtg aagaagcctg gggcctcagt gaaggctctc 120
tgcaaggctt ctgacttcaa cattaaagac ttctatctac actgggtgcg acaggccccct 180
ggacaagggc ttgagtggat tgggaaggatt gatcctgaga atggtgatac tttatatgac 240
ccgaagttcc aggacaaggi caccatgacc acagacacgt ccaccagcac agcctacatg 300
gagctgagga gcctgagatc tgacgacacg gccgtgtatt actgtgcgag agaggcggat 360
tatttccacg atggtiaccic ctactggtac ttcgatgtct ggggcctgtg caccctggtc 420
accgtctcta gtgccctccac caagggccca tcggtcttcc ccttggcgcc ctgtctccagg 480
agcacctccg agagcacagc ggccctgggc tgcctggta aggactactt ccccgaaaccg 540
gtgacggltg cgttgaactc aggcgctctg accagcggcg tgcacacett cccagctgtc 600
ctacagtcct caggactcta ctccctcagc agcgtggtga ccgtgccctc cagcaacttc 660
ggcaccaga cctacacctg caacgtagat cacaagccca gcaacaccaa ggtggacaag 720
acagttagc gcaaatgttg tgtcgagtgc ccaccgtgcc cagcaccacc tgtggcagga 780
ccgtcagict tcctcttccc ccaaaaaccc aaggacaccc tcatgatctc ccggacccct 840
gaggtcacgt gcgtgggtgg ggacgtgagc cacgaagacc ccgaggtcca gtccaactgg 900
tacgtggacg gcgtggaggt gcataatgcc aagacaaagc cacgggagga gcagttcaac 960
agcacgttcc gtgtggtcag cgtcctcacc gtgtgcacc aggactggct gaacggcaag 1020
gaglacaaat gcaaggcttc caacaaaggc ctcccagccc ccacgagaa aaccatctcc 1080
aaaaccaaag ggcagccccg agaaccacag gtgtacaccc tgccccatc ccgggaggag 1140
atgaccaaga accaggtcag cctgacctgc ctgggtcaaag gcttctaccc cagcgacatc 1200
gccgtggagt gggagagcaa tgggcagccg gagaacaact acaagaccac acctcccatg 1260
ctggactccg acggtctctt cttctcttac agcaagctca ccgtggacaa gagcaggtgg 1320
cagcagggga acgtcttctc atgtctccgt atgcatgagg ctctgcacaa ccactacacg 1380
cagaagagcc tctccctgtc tccgggtaaa 1410

<210> 229
<211> 213
<212> PRT

<213> 人工序列

<220>

<223> 合成多肽

<220>

<221> MISC_FEATURE

<223> 人化抗体序列

<400> 229

Asp Ile Gln Leu Thr Gln Ser Pro Ser Phe Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Ser Ser Ile Ser Tyr Ile
20 25 30

His Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr
35 40 45

Ala Thr Ser Asn Leu Ala Ser Gly Val Pro Ser Arg Phe Ser Gly Ser
50 55 60

Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu
65 70 75 80

Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asp Pro Leu Thr
85 90 95

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala Pro
100 105 110

Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr
115 120 125

Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys
130 135 140

Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu
145 150 155 160

Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser
165 170 175

Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala
180 185 190

Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe
195 200 205

Asn Arg Gly Glu Cys
210

<210> 230

<211> 639

<212> DNA

<213> 人工序列

<220>

<223> 合成聚核苷酸

<220>
<221> misc_feature
<223> 人化抗體序列

<400> 230
gacatccagt tgaccagtc tccatccttc ctgtctgcat ctgtaggaga cagagtcacc 60
atcacttgca gggccagctc aagtataagt tacatacact ggtatcagca aaaaccaggg 120
aaagccccta agctcctgat ctatgccaca tccaacctgg ctctggggt cccatcaagg 180
ttcagcggca gtggatctgg gacagaattc actctcaca tccagcagcct gcagcctgaa 240
gattttgcaa ctattactg tcagcagtg agtagtgacc cactcacgtt cggcggaggg 300
accaaggtgg agatcaaacg tacgggtggc gcaccatctg tcttcatctt cccgccatct 360
gatgagcagt tgaatctgg aactgcctct gtgtgtgccc tgcagaataa ctctatccc 420
agagaggcca aagtacagtg gaaggtggat aacgcccctc aatcgggtaa ctcccaggag 480
agtgtcacag agcaggacag caaggacagc acctacagcc tcagcagcac cctgacgctg 540
agcaaagcag actacgagaa acacaaagtc tacgcctgcg aagtcaccca tcagggcctg 600
agctcgcccg tcacaaagag cttcaacagg ggagagtgt 639

<210> 231
<211> 235
<212> PRT
<213> 人工序列

<220>
<223> 合成多肽

<220>
<221> MISC_FEATURE
<223> 人化抗體序列

<400> 231
Met Asp Met Arg Val Pro Ala Gln Leu Leu Gly Leu Leu Leu Leu Trp
1 5 10 15
Leu Pro Gly Ala Arg Cys Asp Ile Gln Leu Thr Gln Ser Pro Ser Phe
20 25 30
Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser
35 40 45
Ser Ser Ile Ser Tyr Ile His Trp Tyr Gln Gln Lys Pro Gly Lys Ala
50 55 60
Pro Lys Leu Leu Ile Tyr Ala Thr Ser Asn Leu Ala Ser Gly Val Pro
65 70 75 80
Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile
85 90 95
Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Trp
100 105 110
Ser Ser Asp Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
115 120 125

Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu
130 135 140

Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe
145 150 155 160

Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln
165 170 175

Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser
180 185 190

Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu
195 200 205

Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser
210 215 220

Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
225 230 235

<210> 232
<211> 705
<212> DNA
<213> 人工序列

<220>
<223> 合成聚核苷酸

<220>
<221> misc_feature
<223> 人化抗体序列

<400> 232
atggacatga gggccccgc tcagtcctg gggctcctgc tgctctggct ccaggtgcc 60
agatgtgaca tccagttgac ccagtcctca tccttcctgt ctgcatctgt aggagacaga 120
gtcaccatca ctgacagggc cagctcaagt ataagttaca tacactggta tcagcaaaaa 180
ccagggaaaag ccctaagct cctgatctat gccacatcca acctggcttc tgggggccca 240
tcaaggttca gcggcagltg atctgggaca gaattcactc tcacaatcag cagcctgcag 300
cctgaagatt ttgcaactta ttactgtcag cagtgaggta gtgacccact cacgttcggc 360
ggagggacca aggtggagat caaacgtacg gtggctgcac catctgtctt catcttcccg 420
ccatctgatg agcagttgaa atctggaact gcctctgttg tggcctgct gaataacttc 480
tatcccagag aggccaaagt acagtggaag gtggataacg ccctccaatc gggtaactcc 540
caggagagtg tcacagagca ggacagcaag gacagcacct acagcctcag cagcacctg 600
acgctgagca aagcagacta cgagaaacac aaagtctacg cctgcgaagt caccatcag 660
ggcctgagct cgcccgctcac aaagagcttc aacaggggag agtgt 705

<210> 233
<211> 447
<212> PRT
<213> 人工序列
<220>

<223> 合成多肽

<220>

<221> MISC_FEATURE

<223> 人化抗体序列

<400> 233

Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Phe Asp Ile Lys Asp Tyr
20 25 30

Tyr Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Arg Val Asp Pro Asp Asn Gly Glu Thr Glu Phe Ala Pro Lys Phe
50 55 60

Pro Gly Lys Val Thr Met Thr Thr Asp Thr Ser Ile Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Glu Asp Tyr Asp Gly Thr Tyr Thr Trp Phe Pro Tyr Trp Gly
100 105 110

Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser
115 120 125

Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser Thr Ala
130 135 140

Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val
145 150 155 160

Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala
165 170 175

Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val
180 185 190

Pro Ser Ser Asn Phe Gly Thr Gln Thr Tyr Thr Cys Asn Val Asp His
195 200 205

Lys Pro Ser Asn Thr Lys Val Asp Lys Thr Val Glu Arg Lys Cys Cys
210 215 220

Val Glu Cys Pro Pro Cys Pro Ala Pro Pro Val Ala Gly Pro Ser Val
225 230 235 240

Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr
245 250 255

Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu
260 265 270

Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys
275 280 285

Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Phe Arg Val Val Ser
290 295 300

Val Leu Thr Val Val His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys
305 310 315 320

Cys Lys Val Ser Asn Lys Gly Leu Pro Ala Pro Ile Glu Lys Thr Ile
325 330 335

Ser Lys Thr Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro
340 345 350

Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu
355 360 365

Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn
370 375 380

Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Met Leu Asp Ser
385 390 395 400

Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg
405 410 415

Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu
420 425 430

His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
435 440 445

- <210> 234
- <211> 1341
- <212> DNA
- <213> 人工序列

- <220>
- <223> 合成聚核苷酸

- <220>
- <221> misc_feature
- <223> 人化抗体序列

<400> 234
gagggtgcagc tgggtgcagtc tggggctgag gtgaagaagc ctggggcctc agtgaaggtc 60
tcctgcaagg ctctcggatt cgacattaag gactactata tacactgggt gcgacaggcc 120
cctggacaag ggcttgagtg gatcggaagg gtgatccig acaatgggtga gactgaattt 180
gccccgaagt tccccggcaa ggtcaccatg accacagaca cgtccatcag cacagcctac 240
atggagctga gcaggctgag atctgacgac acggccgtgt attactgtgc gagagaagac 300
tacgatggta cctacacctg gtttccttat tggggccaag ggactctggt caccgtctct 360
agtcctcca ccaaggggcc atcggtcttc cccctggcgc cctgctccag gaggacctcc 420
gagagcacag cggccctggg ctgcctggtc aaggactact tccccgaacc ggtgacggtg 480

tcgtggaact caggcgctct gaccagcggc gtgcacacct tcccagctgt cctacagtcc 540
tcaggactct actccctcag cagcgtggig accgtgccct ccagcaactt cggcaccacg 600
acctacacct gcaacgtaga tcacaagccc agcaacacca aggtggacaa gacagttgag 660
cgcaaatgtt gtgtcgagtg cccaccgtgc ccagcaccac ctgtggcagg accgtcagtc 720
ttctcttccc ccccaaaacc caaggacacc ctcatgatct cccggacccc tgaggtcacg 780
tgcgtggigg tggacgtgag ccacgaagac cccgagggtcc agttcaactg gtacgtggac 840
ggcgtggagg tgcataatgc caagacaaag ccacgggagg agcagttcaa cagcacgttc 900
cgtgtggica gcgtcctcac cgttgtgcac caggactggc tgaacggcaa ggagtacaag 960
tgcaaggctt ccaacaaagg cctcccagcc cccatcgaga aaaccatctc caaaacaaaa 1020
gggcagcccc gagaaccaca ggtgtacacc ctgccccat cccgggagga gatgaccaag 1080
aaccaggica gcctgacctg cctgggtcaaa ggcttctacc ccagcgacat cgcctggag 1140
tgggagagca atgggcagcc ggagaacaac tacaagacca cacctcccat gctggactcc 1200
gacggctcct tcttctctta cagcaagctc accgtggaca agagcagggtg gcagcagggg 1260
aacgtctctt catgctccgt gatgcatgag gctctgcaca accactacac gcagaagagc 1320
ctctccctgt ctccgggtaa a 1341

<210> 235
<211> 466
<212> PRT
<213> 人工序列

<220>
<223> 合成多肽

<220>
<221> MISC_FEATURE
<223> 人化抗体序列

<400> 235

Met Asp Trp Thr Trp Arg Ile Leu Phe Leu Val Ala Ala Ala Thr Gly
1 5 10 15
Ala His Ser Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys
20 25 30
Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Phe Asp Ile
35 40 45
Lys Asp Tyr Tyr Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu
50 55 60
Glu Trp Ile Gly Arg Val Asp Pro Asp Asn Gly Glu Thr Glu Phe Ala
65 70 75 80
Pro Lys Phe Pro Gly Lys Val Thr Met Thr Thr Asp Thr Ser Ile Ser
85 90 95
Thr Ala Tyr Met Glu Leu Ser Arg Leu Arg Ser Asp Asp Thr Ala Val
100 105 110

Tyr Tyr Cys Ala Arg Glu Asp Tyr Asp Gly Thr Tyr Thr Trp Phe Pro
 115 120 125
 Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys
 130 135 140
 Gly Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu
 145 150 155 160
 Ser Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro
 165 170 175
 Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr
 180 185 190
 Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val
 195 200 205
 Val Thr Val Pro Ser Ser Asn Phe Gly Thr Gln Thr Tyr Thr Cys Asn
 210 215 220
 Val Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys Thr Val Glu Arg
 225 230 235 240
 Lys Cys Cys Val Glu Cys Pro Pro Cys Pro Ala Pro Pro Val Ala Gly
 245 250 255
 Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile
 260 265 270
 Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu
 275 280 285
 Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
 290 295 300
 Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Phe Arg
 305 310 315 320
 Val Val Ser Val Leu Thr Val Val His Gln Asp Trp Leu Asn Gly Lys
 325 330 335
 Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ala Pro Ile Glu
 340 345 350
 Lys Thr Ile Ser Lys Thr Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr
 355 360 365
 Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu
 370 375 380
 Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
 385 390 395 400
 Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Met
 405 410 415

Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp
420 425 430

Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His
435 440 445

Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
450 455 460

Gly Lys
465

<210> 236
<211> 1398
<212> DNA
<213> 人工序列

<220>
<223> 合成聚核苷酸

<220>
<221> misc_feature
<223> 人化抗体序列

<400> 236
atggactgga cctggaggat cctcttcttg gtggcagcag ccacaggagc ccactccgag 60
gtgcagctgg tgcagctctg ggctgagggt aagaagcctg gggcctcagt gaaggctctc 120
tgcaaggctt ctggattcga cattaaggac tactatatac actgggtgcg acaggccctt 180
ggacaagggc ttgagtggat cggaagggtt gatcctgaca atggtgagac tgaatttgcc 240
ccgaagtcc cgaggcaaggt caccatgacc acagacacgt ccatcagcac agcctacatg 300
gagctgagca ggctgagatc tgacgacacg gccgtgtatt actgtgagag agaagactac 360
gatggtacct acacctgggt tccttatttg ggccaaggga ctctgggtcac cgtctctagt 420
gcctccacca agggcccatc ggtcttcccc ctggcgccct gctccaggag cacctccgag 480
agcacagcgg ccctgggctg cctgggtcaag gactacttcc ccgaaccggt gacgggtgtc 540
tggaactcag gcgctctgac cagcggcggt cacaccttcc cagctgtcct acagtccctc 600
ggactctact ccctcagcag cgtgggtgacc gtgccctcca gcaacttcgg caccagacc 660
tacacctgca acgtagatca caagcccagc aacaccaagg tggacaagac agttgagcgc 720
aaatgttgtg tcgagtgcct accgtgccc gacccacctg tggcaggacc gtcagtcttc 780
ctcttcccc caaaacccaa ggacaccctc atgatctccc ggaccctga ggtcacgtgc 840
gtggtggtgg acgtgagcca cgaagacccc gaggtccagt tcaactggta cgtggacggc 900
gtggaggtgc ataatgccaa gacaaagcca cgggaggagc agttcaacag cagttccgt 960
gtggtcagcg tcctcaccgt tgtgcaccag gactggctga acggcaagga gtacaagtgc 1020
aaggcttcca acaaaggcct ccagcccc atcgagaaaa ccatctccaa aaccaaaggg 1080
cagccccgag aaccacaggt gtacaccctg ccccatccc gggaggagat gaccaagaac 1140
caggtcagcc tgacctgcct ggtcaaaggc ttctacccca gcgacatcgc cgtggagtgg 1200
gagagcaatg ggcagccgga gaacaactac aagaccacac ctcccatgct ggactccgac 1260
ggctcttct tcctctacag caagctcacc gtggacaaga gcaggtggca gcagggaac 1320

gtctttctcat gctccgtgat gcatgaggct ctgcacaacc actacacgca gaagagcctc
tccctgtctc cgggtaaa

1380
1398

<210> 237
<211> 7
<212> PRT
<213> 小家鼠

<400> 237

Gly Thr Ser Asn Leu Ala Ser
1 5

<210> 238
<211> 8
<212> PRT
<213> 小家鼠

<400> 238

Gln Gln Trp Thr Thr Thr Tyr Thr
1 5

<210> 239
<211> 11
<212> PRT
<213> 小家鼠

<400> 239

Arg Ala Ser Gln Asp Ile Ser Ser Tyr Leu Asn
1 5 10

<210> 240
<211> 7
<212> PRT
<213> 小家鼠

<400> 240

Ser Thr Ser Arg Leu Asn Ser
1 5

<210> 241
<211> 8
<212> PRT
<213> 小家鼠

<400> 241

Gln Gln Asp Ile Lys His Pro Thr
1 5

<210> 242
<211> 11
<212> PRT
<213> 小家鼠

<400> 242

Lys Ala Ser Gln Asp Val Phe Thr Ala Val Ala
1 5 10

<210> 243
<211> 7
<212> PRT
<213> 小家鼠

<400> 243

Trp Ala Ser Thr Arg His Thr
1 5

<210> 244

<211> 9

<212> PRT

<213> 小家鼠

<400> 244

Gln Gln Tyr Ser Ser Tyr Pro Leu Thr
1 5

<210> 245

<211> 5

<212> PRT

<213> 小家鼠

<400> 245

Asp Tyr Asn Met His
1 5

<210> 246

<211> 17

<212> PRT

<213> 小家鼠

<400> 246

Glu Ile Asn Pro Asn Ser Gly Gly Ala Gly Tyr Asn Gln Lys Phe Lys
1 5 10 15

Gly

<210> 247

<211> 14

<212> PRT

<213> 小家鼠

<400> 247

Leu Gly Tyr Asp Asp Ile Tyr Asp Asp Trp Tyr Phe Asp Val
1 5 10

<210> 248

<211> 5

<212> PRT

<213> 小家鼠

<400> 248

Asp Tyr Asn Met His
1 5

<210> 249

<211> 17

<212> PRT

<213> 小家鼠

<400> 249

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

Gly

<210> 250
<211> 14
<212> PRT
<213> 小家鼠

<400> 250

Leu Val Tyr Asp Gly Ser Tyr Glu Asp Trp Tyr Phe Asp Val
1 5 10

<210> 251
<211> 5
<212> PRT
<213> 小家鼠

<400> 251

Asp Tyr Asn Met His
1 5

<210> 252
<211> 17
<212> PRT
<213> 小家鼠

<400> 252

Glu Ile Asn Pro Asn Ser Gly Gly Ala Gly Tyr Asn Gln Gln Phe Lys
1 5 10 15

Gly

<210> 253
<211> 14
<212> PRT
<213> 小家鼠

<400> 253

Leu Gly Tyr Val Gly Asn Tyr Glu Asp Trp Tyr Phe Asp Val
1 5 10

<210> 254
<211> 5
<212> PRT
<213> 小家鼠

<400> 254

Asp Tyr Asn Met His
1 5

<210> 255
<211> 17
<212> PRT
<213> 小家鼠

<400> 255

Glu Ile Asn Pro Asn Ser Gly Gly Ala Gly Tyr Asn Gln Lys Phe Lys
1 5 10 15

Gly

<210> 256
<211> 14
<212> PRT
<213> 小家鼠

<400> 256

Leu Gly Tyr Asp Asp Ile Tyr Asp Asp Trp Tyr Phe Asp Val
1 5 10

<210> 257
<211> 5
<212> PRT
<213> 小家鼠

<400> 257

Asp Tyr Asn Met His
1 5

<210> 258
<211> 17
<212> PRT
<213> 小家鼠

<400> 258

Glu Ile Asn Pro Asn Ser Gly Gly Ala Gly Tyr Asn Gln Lys Phe Lys
1 5 10 15

Gly

<210> 259
<211> 14
<212> PRT
<213> 小家鼠

<400> 259

Leu Gly Tyr Asp Asp Ile Tyr Asp Asp Trp Tyr Phe Asp Val
1 5 10

<210> 260
<211> 5
<212> PRT
<213> 小家鼠

<400> 260

Asp Tyr Asn Met His
1 5

<210> 261
<211> 17
<212> PRT
<213> 小家鼠

<400> 261

Glu Ile Asn Pro Asn Ser Gly Gly Ala Gly Tyr Asn Gln Lys Phe Lys
1 5 10 15

Gly

<210> 262
<211> 14
<212> PRT
<213> 小家鼠

<400> 262

Leu Gly Tyr Asp Asp Ile Tyr Asp Asp Trp Tyr Phe Asp Val
1 5 10

<210> 263
<211> 5
<212> PRT
<213> 小家鼠

<400> 263

Asp Tyr Asn Met His
1 5

<210> 264
<211> 17
<212> PRT
<213> 小家鼠

<400> 264

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

Gly

<210> 265
<211> 14
<212> PRT
<213> 小家鼠

<400> 265

Leu Gly Tyr Tyr Gly Asn Tyr Glu Asp Trp Tyr Phe Asp Val
1 5 10

<210> 266
<211> 5
<212> PRT
<213> 小家鼠

<400> 266

Asp Tyr Tyr Ile His
1 5

<210> 267
<211> 17
<212> PRT
<213> 小家鼠

<400> 267

Arg Ile Asp Pro Asp Asn Gly Glu Ser Thr Tyr Val Pro Lys Phe Gln
1 5 10 15

Gly

<210> 268
 <211> 13
 <212> PRT
 <213> 小家鼠

<400> 268

Glu Gly Leu Asp Tyr Gly Asp Tyr Tyr Ala Val Asp Tyr
 1 5 10

<210> 269
 <211> 5
 <212> PRT
 <213> 小家鼠

<400> 269

Asp Tyr Ile Met His
 1 5

<210> 270
 <211> 17
 <212> PRT
 <213> 小家鼠

<400> 270

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

Gly

<210> 271
 <211> 11
 <212> PRT
 <213> 小家鼠

<400> 271

Ser Ile Tyr Tyr Tyr Asp Ala Pro Phe Ala Tyr
 1 5 10

<210> 272
 <211> 5
 <212> PRT
 <213> 小家鼠

<400> 272

Asp Tyr Tyr Met His
 1 5

<210> 273
 <211> 17
 <212> PRT
 <213> 小家鼠

<400> 273

Arg Ile Asp Pro Glu Asn Gly Asp Ile Ile Tyr Asp Pro Lys Phe Gln
 1 5 10 15

Gly

<210> 274
 <211> 10
 <212> PRT
 <213> 小家鼠

<400> 274

Asp Ala Gly Asp Pro Ala Trp Phe Thr Tyr
 1 5 10

<210> 275
 <211> 10
 <212> PRT
 <213> 小家鼠

<400> 275

Arg Ala Ser Ser Ser Val Tyr Tyr Met His
 1 5 10

<210> 276
 <211> 7
 <212> PRT
 <213> 小家鼠

<400> 276

Ala Thr Ser Asn Leu Ala Ser
 1 5

<210> 277
 <211> 9
 <212> PRT
 <213> 小家鼠

<400> 277

Gln Gln Trp Ser Ser Asp Pro Leu Thr
 1 5

<210> 278
 <211> 12
 <212> PRT
 <213> 小家鼠

<400> 278

Ser Val Ser Ser Thr Ile Ser Ser Asn His Leu His
 1 5 10

<210> 279
 <211> 7
 <212> PRT
 <213> 小家鼠

<400> 279

Gly Thr Ser Asn Leu Ala Ser
 1 5

<210> 280
 <211> 9
 <212> PRT
 <213> 小家鼠

<400> 280

Gln Gln Trp Ser Ser Tyr Pro Leu Thr
1 5

<210> 281
<211> 10
<212> PRT
<213> 小家鼠

<400> 281

Arg Ala Ser Ser Ser Ile Ser Tyr Ile His
1 5 10

<210> 282
<211> 7
<212> PRT
<213> 小家鼠

<400> 282

Ala Thr Ser Asn Leu Ala Ser
1 5

<210> 283
<211> 9
<212> PRT
<213> 小家鼠

<400> 283

Gln Gln Trp Ser Ser Asp Pro Leu Thr
1 5

<210> 284
<211> 12
<212> PRT
<213> 小家鼠

<400> 284

Arg Ala Ser Ser Ser Val Thr Ser Ser Tyr Leu Asn
1 5 10

<210> 285
<211> 7
<212> PRT
<213> 小家鼠

<400> 285

Ser Thr Ser Asn Leu Ala Ser
1 5

<210> 286
<211> 9
<212> PRT
<213> 小家鼠

<400> 286

Gln Gln Tyr Asp Phe Phe Pro Ser Thr
1 5

<210> 287
<211> 5
<212> PRT
<213> 小家鼠

<400> 287

Asp Tyr Phe Ile His
1 5

<210> 288

<211> 17

<212> PRT

<213> 小家鼠

<400> 288

Arg Leu Asp Pro Glu Asp Gly Glu Ser Asp Tyr Ala Pro Lys Phe Gln
1 5 10 15

Asp

<210> 289

<211> 12

<212> PRT

<213> 小家鼠

<400> 289

Glu Asp Tyr Asp Gly Thr Tyr Thr Phe Phe Pro Tyr
1 5 10

<210> 290

<211> 5

<212> PRT

<213> 小家鼠

<400> 290

Asp Phe Tyr Leu His
1 5

<210> 291

<211> 17

<212> PRT

<213> 小家鼠

<400> 291

Arg Ile Asp Pro Glu Asn Gly Asp Thr Leu Tyr Asp Pro Lys Phe Gln
1 5 10 15

Asp

<210> 292

<211> 16

<212> PRT

<213> 小家鼠

<400> 292

Glu Ala Asp Tyr Phe His Asp Gly Thr Ser Tyr Trp Tyr Phe Asp Val
1 5 10 15

<210> 293

<211> 5

<212> PRT

<213> 小家鼠

<400> 293

Asp Tyr Tyr Ile His
1 5

<210> 294
<211> 17
<212> PRT
<213> 小家鼠

<400> 294

Arg Val Asp Pro Asp Asn Gly Glu Thr Glu Phe Ala Pro Lys Phe Pro
1 5 10 15

Gly

<210> 295
<211> 12
<212> PRT
<213> 小家鼠

<400> 295

Glu Asp Tyr Asp Gly Thr Tyr Thr Trp Phe Pro Tyr
1 5 10

<210> 296
<211> 5
<212> PRT
<213> 小家鼠

<400> 296

Asp Tyr Tyr Met Asn
1 5

<210> 297
<211> 17
<212> PRT
<213> 小家鼠

<400> 297

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

Gly

<210> 298
<211> 11
<212> PRT
<213> 小家鼠

<400> 298

Glu Thr Ala Val Ile Thr Thr Asn Ala Met Asp
1 5 10

<210> 299
<211> 130
<212> PRT
<213> 小家鼠

<400> 299

Met Asp Phe Gln Val Gln Ile Phe Ser Phe Met Leu Ile Ser Val Thr
1 5 10 15
Val Ile Leu Ser Ser Gly Glu Ile Val Leu Thr Gln Ser Pro Ala Leu
20 25 30
Met Ala Ala Ser Pro Gly Glu Lys Val Thr Ile Thr Cys Ser Val Ser
35 40 45
Ser Ser Ile Ser Ser Ser Asn Leu His Trp Ser Gln Gln Lys Ser Gly
50 55 60
Thr Ser Pro Lys Leu Trp Ile Tyr Gly Thr Ser Asn Leu Ala Ser Gly
65 70 75 80
Val Pro Val Arg Phe Ser Gly Ser Gly Ser Gly Thr Ser Tyr Ser Leu
85 90 95
Thr Ile Ser Ser Met Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys Gln
100 105 110
Gln Trp Thr Thr Thr Tyr Thr Phe Gly Ser Gly Thr Lys Leu Glu Leu
115 120 125
Lys Arg
130

<210> 300
<211> 390
<212> DNA
<213> 小家鼠

<400> 300
atggattttc aggtgcagat ttccagcttc atgctaataca gtgtcacagt catattgtcc 60
agtggagaaaa ttgtgtctcac ccagttctcca gcactcatgg ctgcatctcc aggggagaag 120
gtcaccatca cctgcagtgt cagctcagat ataagttcca gcaacttaca ctggtcccag 180
cagaagtcag gaacctcccc caaactctgg atttatggca catccaacct tgcttctgga 240
gtccctgttc gcttcagtgg cagtggatct gggacctctt attctctcac aatcagcagc 300
atggaggctg aagatgctgc cacttattac tgtcaacagt ggactactac gtatacgttc 360
ggatcggggga ccaagctgga gctgaaacgt 390

<210> 301
<211> 141
<212> PRT
<213> 小家鼠

<400> 301
Met Gly Trp Asn Trp Ile Ile Phe Phe Leu Met Ala Val Val Thr Gly
1 5 10 15
Val Asn Ser Glu Val Gln Leu Arg Gln Ser Gly Ala Asp Leu Val Lys
20 25 30
Pro Gly Ala Ser Val Lys Leu Ser Cys Thr Ala Ser Gly Phe Asn Ile
35 40 45

Lys Asp Tyr Tyr Ile His Trp Val Lys Gln Arg Pro Glu Gln Gly Leu
50 55 60

Glu Trp Ile Gly Arg Ile Asp Pro Asp Asn Gly Glu Ser Thr Tyr Val
65 70 75 80

Pro Lys Phe Gln Gly Lys Ala Thr Ile Thr Ala Asp Thr Ser Ser Asn
85 90 95

Thr Ala Tyr Leu Gln Leu Arg Ser Leu Thr Ser Glu Asp Thr Ala Ile
100 105 110

Tyr Tyr Cys Gly Arg Glu Gly Leu Asp Tyr Gly Asp Tyr Tyr Ala Val
115 120 125

Asp Tyr Trp Gly Gln Gly Thr Ser Val Thr Val Ser Ser
130 135 140

<210> 302
<211> 423
<212> DNA
<213> 小家鼠

<400> 302
atgggatgga actggatcat cttcttctcg atggcagtggt ttacaggggt caattcagag 60
gtgcagtigc ggcagtcctg ggcagacctt gtgaagccag gggcctcagt caagttgtcc 120
tgcacagctt ctggcttcaa cattaaagac tactatatac actgggtgaa gcagaggcct 180
gaacagggcc tggagtggat tggaggatt gatcctgata atgggtgaaag tacatatgtc 240
ccgaagticc agggcaaggc cactataaca gcagacacat catccaacac agcctaccta 300
caactcagaa gcctgacatc tgaggacact gccatctatt attgtgggag agaggggctc 360
gactatggtg actactatgc tgtggactac tgggggtcaag gaacctcggc cacagtctcg 420
agc 423

<210> 303
<211> 130
<212> PRT
<213> 人工序列

<220>
<223> 合成多肽

<220>
<221> MISC_FEATURE
<223> 人化抗体序列

<400> 303
Met Asp Met Arg Val Pro Ala Gln Leu Leu Gly Leu Leu Leu Leu Trp
1 5 10 15

Leu Pro Gly Ala Arg Cys Asp Ile Gln Leu Thr Gln Ser Pro Ser Phe
20 25 30

Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Ser Val Ser
35 40 45

Ser Ser Ile Ser Ser Ser Asn Leu His Trp Tyr Gln Gln Lys Pro Gly
50 55 60

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

Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Glu Phe Thr Leu
85 90 95

Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln
100 105 110

Gln Trp Thr Thr Thr Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile
115 120 125

Lys Arg
130

<210> 304
<211> 390
<212> DNA
<213> 人工序列

<220>
<223> 合成聚核苷酸

<220>
<221> misc_feature
<223> 人化抗体序列

<400> 304
atggatatgc gcgtgccggc gcagctgctg ggccctgctgc tgctgtggct gccgggcgcg 60
cgctgcgata ttcagctgac ccagagcccg agctttciga gcgcgagcgt gggcgatcgc 120
gtgaccattia cctgcagcgt gagcagcagc attagcagca gcaacctgca ttggtatcag 180
cagaaaccgg gcaaagcgcc gaaactgctg atttatggca ccagcaacct ggcgagcggc 240
gtgccgagcc gctttagcgg cagcggcagc ggcaccgaat ttaccctgac cattagcagc 300
ctgcagccgg aagattttgc gacctattat tgccagcagt ggaccaccac ctatacctt 360
ggccagggca ccaaactgga aattaaacgt 390

<210> 305
<211> 141
<212> PRT
<213> 人工序列

<220>
<223> 合成多肽

<220>
<221> MISC_FEATURE
<223> 人化抗体序列

<400> 305

Met Asp Trp Thr Trp Ser Ile Leu Phe Leu Val Ala Ala Pro Thr Gly
1 5 10 15

Ala His Ser Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys
20 25 30

Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Phe Asn Ile
35 40 45
Lys Asp Tyr Tyr Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu
50 55 60
Glu Trp Met Gly Arg Ile Asp Pro Asp Asn Gly Glu Ser Thr Tyr Val
65 70 75 80
Pro Lys Phe Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser
85 90 95
Thr Ala Tyr Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val
100 105 110
Tyr Tyr Cys Ala Arg Glu Gly Leu Asp Tyr Gly Asp Tyr Tyr Ala Val
115 120 125
Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
130 135 140

<210> 306
<211> 423
<212> DNA
<213> 人工序列

<220>
<223> 合成聚核苷酸

<220>
<221> misc_feature
<223> 人化抗体序列

<400> 306
atggattgga cctggagcat tctgtttctg gtggcggcgc cgaccggcgc gcatagcgaa 60
gtgcagctgg tgcagagcgg cgcggaagtg aaaaaaccgg gcgcgagcgt gaaagtgagc 120
tgcaaagcga gcggctttaa cattaaagat tattatattc attgggtgcg ccaggcgccg 180
ggccagggcc tggaatggat gggccgcatt gatccggata acggcgaaag cacctatgtg 240
ccgaaatttc agggccgcgt gaccatgacc accgatacca gcaccagcac cgcgtatatg 300
gaactgcgca gcctgcgcag cgatgatacc gcggtgtatt attgcgcgcg cgaaggcctg 360
gattatggcg attattatgc ggtggattat tggggccagg gcaccctggt gaccgtctcg 420
agc 423

<210> 307
<211> 127
<212> PRT
<213> 人工序列

<220>
<223> 合成多肽

<220>
<221> MISC_FEATURE
<223> 人化抗体序列

<400> 307

Met Met Ser Ser Ala Gln Phe Leu Gly Leu Leu Leu Cys Phe Gln
1 5 10 15

Gly Thr Arg Cys Asp Ile Gln Met Thr Gln Thr Thr Ser Ser Leu Ser
20 25 30

Ala Ser Leu Gly Asp Arg Val Asn Ile Ser Cys Arg Ala Ser Gln Asp
35 40 45

Ile Ser Ser Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Asp Gly Thr Val
50 55 60

Lys Leu Leu Ile Tyr Ser Thr Ser Arg Leu Asn Ser Gly Val Pro Ser
65 70 75 80

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Ser
85 90 95

Asn Leu Ala Gln Glu Asp Ile Ala Thr Tyr Phe Cys Gln Gln Asp Ile
100 105 110

Lys His Pro Thr Phe Gly Gly Gly Thr Lys Leu Glu Leu Lys Arg
115 120 125

<210> 308
<211> 381
<212> DNA
<213> 小家鼠

<400> 308
atgatgtcct ctgctcagtt ccttggtctc ctgttgcct gtttcaagg taccagatgt 60
gatatccaga tgacacagac tacatcctcc ctgtctgcct ctctgggaga cagagtcaac 120
atcagctgca gggcaagtca ggacattagc agttatttaa actggtatca gcagaaacca 180
gatggaactg taaactcct gatctactcc acatcaagat taaactcagg agtcccatca 240
aggttcagtg gcagtgggtc tgggacagat tattctctca ctattagcaa cctggcacia 300
gaagatattg ccacttacit ttgccaacag gatattaagc atccgacgtt cgggtggaggc 360
accaagtgtg agctgaaacg t 381

<210> 309
<211> 139
<212> PRT
<213> 小家鼠

<400> 309

Met Glu Trp Ile Trp Ile Phe Leu Phe Leu Leu Ser Gly Thr Ala Gly
1 5 10 15

Val His Ser Glu Val Gln Leu Gln Gln Ser Gly Pro Glu Leu Val Lys
20 25 30

Pro Gly Ala Ser Val Lys Met Ser Cys Lys Ala Ser Gly Phe Thr Phe
35 40 45

Thr Asp Tyr Ile Met His Trp Val Lys Gln Lys Pro Gly Gln Gly Leu
50 55 60

Glu Trp Ile Gly Tyr Ile Asn Pro Tyr Asn Asp Asp Thr Glu Tyr Asn
65 70 75 80

Glu Lys Phe Lys Gly Lys Ala Thr Leu Thr Ser Asp Lys Ser Ser Ser
85 90 95

Thr Ala Tyr Met Asp Leu Ser Ser Leu Thr Ser Glu Gly Ser Ala Val
100 105 110

Tyr Tyr Cys Ala Arg Ser Ile Tyr Tyr Tyr Asp Ala Pro Phe Ala Tyr
115 120 125

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
130 135

<210> 310
<211> 417
<212> DNA
<213> 小家鼠

<400> 310
atggaatgga tctggatatt tctcttcctc ctgtcaggaa ctgcagggtgt ccactctgag 60
gtccagctgc agcagttctgg acctgagctg gtaaagcctg gggcttcagt gaagatgtcc 120
tgcaaggctt ctgggttcac attcactgac tacattatgc actgggtgaa gcagaagcct 180
gggcagggcc ttgagtggat tggatatatt aatccttaca atgatgatac tgaatacaat 240
gagaagttca aaggcaaggc cacactgact tcagacaaat cctccagcac agcctacatg 300
gatctcagca gtctgacctc tgagggtctt gcggtctatt actgtgcaag atcgatttat 360
tactacgatg ccccgtttgc ttactggggc caagggaactc tggtcacagt ctcgagc 417

<210> 311
<211> 127
<212> PRT
<213> 人工序列

<220>
<223> 合成多肽

<220>
<221> MISC_FEATURE
<223> 人化抗体序列

<400> 311

Met Met Ser Ser Ala Gln Phe Leu Gly Leu Leu Leu Cys Phe Gln
1 5 10 15

Gly Thr Arg Cys Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser
20 25 30

Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp
35 40 45

Ile Ser Ser Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro
50 55 60

Lys Leu Leu Ile Tyr Ser Thr Ser Arg Leu Asn Ser Gly Val Pro Ser
65 70 75 80

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser
85 90 95

Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Asp Ile
100 105 110

Lys His Pro Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
115 120 125

<210> 312
<211> 381
<212> DNA
<213> 人工序列

<220>
<223> 合成聚核苷酸

<220>
<221> misc_feature
<223> 人化抗体序列

<400> 312
atgatgtcct ctgctcagtt ccttggtctc ctgttgctct gttttcaagg taccagatgt 60
gatatccaga tgaccagtc tccatcctcc ctgctgcat ctgtaggtga ccgtgtcacc 120
atcacttgcc gcgcaagtca ggatattagc agctatttaa attggtatca gcagaaacca 180
gggaaagccc ctaagctcct gatctattct acttcccggt tgaatagtgg ggtcccatca 240
cgcttcagtg gcagtggtctc tgggacagat ttcaacttca ccatcagcag tctgcaacct 300
gaagattttg caacttacta ctgtcaacag gatattaaac accctacgtt cggtcaaggc 360
accaaggtgg agatcaaacg t 381

<210> 313
<211> 139
<212> PRT
<213> 人工序列

<220>
<223> 合成多肽

<220>
<221> MISC_FEATURE
<223> 人化抗体序列

<400> 313

Met Glu Trp Ile Trp Ile Phe Leu Phe Leu Leu Ser Gly Thr Ala Gly
1 5 10 15

Val His Ser Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys
20 25 30

Pro Gly Ser Ser Val Lys Val Ser Cys Lys Ala Ser Gly Phe Thr Phe
35 40 45

Thr Asp Tyr Ile Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu
50 55 60

Glu Trp Met Gly Tyr Ile Asn Pro Tyr Asn Asp Asp Thr Glu Tyr Asn

65	70	75	80
Glu Lys Phe Lys	Gly Arg Val Thr Ile Thr	Ala Asp Lys Ser	Thr Ser
	85	90	95
Thr Ala Tyr Met	Glu Leu Ser Ser	Leu Arg Ser Glu Asp	Thr Ala Val
	100	105	110
Tyr Tyr Cys Ala Arg Ser	Ile Tyr Tyr Tyr Asp Ala	Pro Phe Ala Tyr	
	115	120	125
Trp Gly Gln Gly Thr	Leu Val Thr Val Ser Ser		
	130	135	

<210> 314
 <211> 107
 <212> PRT
 <213> 小家鼠

<400> 314

Asp Ile Gln Met	Thr Gln Thr Thr Ser	Ser Leu Ser Ala Ser	Leu Gly
1	5	10	15
Asp Arg Val Asn	Ile Ser Cys Arg	Ala Ser Gln Asp	Ile Ser Ser Tyr
	20	25	30
Leu Asn Trp Tyr	Gln Gln Lys Pro Asp Gly	Thr Val Lys Leu Leu	Ile
	35	40	45
Tyr Ser Thr Ser	Arg Leu Asn Ser Gly	Val Pro Ser Arg Phe	Ser Gly
	50	55	60
Ser Gly Ser Gly	Thr Asp Tyr Ser Leu Thr	Ile Ser Asn Leu Ala	Gln
	65	70	75
Glu Asp Ile Ala	Thr Tyr Phe Cys Gln Gln	Asp Ile Lys His Pro	Thr
	85	90	95
Phe Gly Gly Gly	Thr Lys Leu Glu Leu Lys	Arg	
	100	105	

<210> 315
 <211> 128
 <212> PRT
 <213> 小家鼠

<400> 315

Met Lys Ser Gln	Thr Gln Val Phe Val	Tyr Met Leu Leu Trp	Leu Ser
1	5	10	15
Gly Val Glu Gly	Asp Ile Val Met Thr	Gln Ser His Lys Phe	Met Ser
	20	25	30
Thr Ser Val Gly	Asp Arg Val Thr	Ile Thr Cys Lys Ala	Ser Gln Asp
	35	40	45
Val Phe Thr Ala	Val Ala Trp Tyr Gln Gln	Lys Pro Gly Gln	Ser Pro
	50	55	60

Lys Leu Leu Ile Tyr Trp Ala Ser Thr Arg His Thr Gly Val Pro Asp
65 70 75 80

Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser
85 90 95

Asn Val Gln Ser Glu Asp Leu Ala Asp Tyr Phe Cys Gln Gln Tyr Ser
100 105 110

Ser Tyr Pro Leu Thr Phe Gly Ala Gly Thr Lys Leu Glu Leu Lys Arg
115 120 125

<210> 316
<211> 381
<212> DNA
<213> 小家鼠

<400> 316
atgaagtcac agaccagggt cttgtatcac atgttgcgtt ggttgcctgg tgtgaagga 60
gacattgtga tgaccagtc tcacaaattc atgtccagct cagtaggaga cagggtcacc 120
atcacctgca aggccagtc ggaatgtctt actgctgtag cctgggtatca acagaaacca 180
ggacaatctc ctactact gatttactgg gcatccaccc ggcacactgg agtcctgat 240
cgcttcacag gcagtggtatc tgggacagat ttcactctca ccattagcaa tgtgcagct 300
gaagacttgg cagattatit ctgtcaacaa tatagcagct atcctctcac gticgggtgt 360
gggaccaagt tggagctgaa a 381

<210> 317
<211> 138
<212> PRT
<213> 小家鼠

<400> 317

Met Gly Trp Asn Trp Ile Ile Phe Phe Leu Met Ala Val Val Thr Gly
1 5 10 15

Val Asn Ser Glu Val Gln Leu Gln Gln Ser Gly Ala Glu Leu Val Arg
20 25 30

Pro Gly Ala Leu Val Lys Leu Ser Cys Lys Ala Ser Gly Phe Asn Ile
35 40 45

Lys Asp Tyr Tyr Met His Trp Val Lys Gln Arg Pro Glu Gln Gly Leu
50 55 60

Glu Trp Ile Gly Arg Ile Asp Pro Glu Asn Gly Asp Ile Ile Tyr Asp
65 70 75 80

Pro Lys Phe Gln Gly Lys Ala Ser Ile Thr Thr Asp Thr Ser Ser Asn
85 90 95

Thr Ala Tyr Leu Gln Leu Ser Ser Leu Thr Ser Glu Asp Thr Ala Val
100 105 110

Tyr Tyr Cys Ala Tyr Asp Ala Gly Asp Pro Ala Trp Phe Thr Tyr Trp

115	120	125
Gly Gln Gly Thr Leu Val Thr Val Ser Ser		
130	135	
<210> 318		
<211> 411		
<212> DNA		
<213> 小家鼠		
<400> 318		
atgggatgga actggatcat ctctctcctg atggcagtgg ttacaggggt caattcagag	60	
gttcagctgc agcagctctgg ggctgagctt gtgaggccag gggccttagt caagttgtcc	120	
tgcaaagctt ctggcttcaa tattaaagac tactatatgc actgggtgaa gcagaggcct	180	
gaacagggcc tggagtggat tggaaggatt gatcctgaga atggtgatat tatatatgac	240	
ccgaagtacc agggcaaggc cagtataaca acagacacat cctccaacac agcctacctg	300	
cagctcagca gcctgacgtc tgaggacact gccgtctatt actgtgctta cgatgctggt	360	
gaccccgccct ggtttactta ctggggccaa gggactctgg tcaccgtctc g	411	
<210> 319		
<211> 130		
<212> PRT		
<213> 小家鼠		
<400> 319		
Met Asp Met Arg Val Pro Ala Gln Leu Leu Gly Leu Leu Leu Leu Trp		
1 5 10 15		
Leu Arg Gly Ala Arg Cys Asp Ile Gln Met Thr Gln Ser Pro Ser Ser		
20 25 30		
Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Lys Ala Ser		
35 40 45		
Gln Asp Val Phe Thr Ala Val Ala Trp Tyr Gln Gln Lys Pro Gly Lys		
50 55 60		
Ala Pro Lys Leu Leu Ile Tyr Trp Ala Ser Thr Arg His Thr Gly Val		
65 70 75 80		
Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr		
85 90 95		
Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln		
100 105 110		
Tyr Ser Ser Tyr Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile		
115 120 125		
Lys Arg		
130		
<210> 320		
<211> 390		
<212> DNA		
<213> 小家鼠		

<400> 320
 atggatatgc gcgtagccggc gcagctgctg ggccctgctgc tgctgtggct gcgcggcgcg 60
 cgctgcgata tccagatgac ccagagcccc agcagcctga gcgcgagcgt gggcgatcgc 120
 gtgaccatta cctgcaaagc gagccaggat gtgtttaccg cggtaggcgtg gtatcagcag 180
 aaaccgggca aagcgccgaa actgctgatt tattgggcga gcacccgcca taccggcgtg 240
 ccgagtcgct ttagcggcag cggcagcggc accgatitaa cctgacccat tagcagcctg 300
 cagccggaag attttgcgac ctattattgc cagcagtata gcagctatcc gctgaccttt 360
 ggcggcggca ccaaagtgga aattaaacgt 390

<210> 321
 <211> 138
 <212> PRT
 <213> 人工序列

<220>
 <223> 合成多肽

<220>
 <221> MISC_FEATURE
 <223> 人化抗体序列

<400> 321
 Met Asp Trp Thr Trp Ser Ile Leu Phe Leu Val Ala Ala Pro Thr Gly
 1 5 10 15
 Ala His Ser Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys
 20 25 30
 Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Phe Asn Ile
 35 40 45
 Lys Asp Tyr Tyr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu
 50 55 60
 Glu Trp Ile Gly Arg Ile Asp Pro Glu Asn Gly Asp Ile Ile Tyr Asp
 65 70 75 80
 Pro Lys Phe Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser
 85 90 95
 Thr Ala Tyr Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val
 100 105 110
 Tyr Tyr Cys Ala Tyr Asp Ala Gly Asp Pro Ala Trp Phe Thr Tyr Trp
 115 120 125
 Gly Gln Gly Thr Leu Val Thr Val Ser Ser
 130 135

<210> 322
 <211> 414
 <212> DNA
 <213> 人工序列

<220>
 <223> 合成聚核苷酸

<220>
<221> misc_feature
<223> 人化抗体序列

<400> 322
atggattgga cctggagcat tctgtttctg gtggcggcgc cgaccggcgc gcatagcgaa 60
gtgcagctgg tgcagagcgg cgcggaagtg aaaaaaccgg gcgcgagcgt gaaagtgagc 120
tgcaaagcga gcggctttaa cattaagat tattatatgc attgggtgcg ccaggcgccg 180
ggccagggcc tggaatggat cggccgcatt gatccggaaa acggcgatat tatttatgat 240
ccgaaatttc agggccgcgt gaccatgacc accgatacca gcaccagcac cgcgtatatg 300
gaactgcgca gcctgcgcag cgatgatacc gcggtgtatt attgcgcgta tgatgcgggc 360
gatccggcgt ggtttaccta ttggggccag ggcaccctgg tgaccgtctc gagg 414

<210> 323
<211> 106
<212> PRT
<213> 小家鼠

<400> 323

Thr	Asp	Ala	Ala	Pro	Thr	Val	Ser	Ile	Phe	Pro	Pro	Ser	Ser	Glu	Gln
1				5					10					15	
Leu	Thr	Ser	Gly	Gly	Ala	Ser	Val	Val	Cys	Phe	Leu	Asn	Asn	Phe	Tyr
			20					25					30		
Pro	Lys	Asp	Ile	Asn	Val	Lys	Trp	Lys	Ile	Asp	Gly	Ser	Glu	Arg	Gln
		35					40					45			
Asn	Gly	Val	Leu	Asn	Ser	Trp	Thr	Asp	Gln	Asp	Ser	Lys	Asp	Ser	Thr
	50					55					60				
Tyr	Ser	Met	Ser	Ser	Thr	Leu	Thr	Leu	Thr	Lys	Asp	Glu	Tyr	Glu	Arg
65					70					75					80
His	Asn	Ser	Tyr	Thr	Cys	Glu	Ala	Thr	His	Lys	Thr	Ser	Thr	Ser	Pro
				85					90					95	
Ile	Val	Lys	Ser	Phe	Asn	Arg	Asn	Glu	Cys						
			100					105							

<210> 324
<211> 320
<212> PRT
<213> 小家鼠

<400> 324

Ala	Lys	Thr	Thr	Pro	Pro	Ser	Val	Tyr	Pro	Leu	Ala	Pro	Gly	Ser	Ala
1				5					10					15	
Ala	Gln	Thr	Asn	Ser	Met	Val	Thr	Leu	Gly	Cys	Leu	Val	Lys	Gly	Tyr
			20					25					30		
Phe	Pro	Glu	Pro	Val	Thr	Val	Thr	Trp	Asn	Ser	Gly	Ser	Leu	Ser	Ser
		35					40					45			

Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Asp Leu Tyr Thr Leu
 50 55 60
 Ser Ser Ser Val Thr Val Pro Ser Ser Thr Trp Pro Ser Glu Thr Val
 65 70 75 80
 Thr Cys Asn Val Ala His Pro Ala Ser Ser Thr Lys Val Asp Lys Lys
 85 90 95
 Ile Val Pro Arg Asp Cys Gly Cys Lys Pro Cys Ile Cys Thr Val Pro
 100 105 110
 Glu Val Ser Ser Val Phe Ile Phe Pro Pro Lys Pro Lys Asp Val Leu
 115 120 125
 Thr Ile Thr Leu Thr Pro Lys Val Thr Cys Val Val Val Asp Ile Ser
 130 135 140
 Lys Asp Asp Pro Glu Val Gln Phe Ser Trp Phe Val Asp Asp Val Glu
 145 150 155 160
 Val His Thr Ala Gln Thr Gln Pro Arg Glu Glu Gln Phe Asn Ser Thr
 165 170 175
 Phe Arg Ser Val Ser Glu Leu Pro Ile Met His Gln Asp Trp Leu Asn
 180 185 190
 Gly Lys Glu Phe Lys Cys Arg Val Asn Ser Ala Ala Phe Pro Ala Pro
 195 200 205
 Ile Glu Lys Thr Ile Ser Lys Thr Lys Gly Arg Pro Lys Ala Pro Gln
 210 215 220
 Val Tyr Thr Ile Pro Pro Pro Lys Glu Gln Met Ala Lys Asp Lys Val
 225 230 235 240
 Ser Leu Thr Cys Met Ile Thr Asp Phe Phe Pro Glu Asp Ile Thr Val
 245 250 255
 Glu Trp Gln Trp Asn Gly Gln Pro Ala Glu Asn Tyr Lys Asn Thr Gln
 260 265 270
 Pro Ile Met Asp Thr Asp Gly Ser Tyr Phe Val Tyr Ser Lys Leu Asn
 275 280 285
 Val Gln Lys Ser Asn Trp Glu Ala Gly Asn Thr Phe Thr Cys Ser Val
 290 295 300
 Leu His Glu Gly Leu His Asn His His Thr Glu Lys Ser Leu Ser His
 305 310 315 320

<210> 325
 <211> 106
 <212> PRT
 <213> 智人

<400> 325

Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln
1 5 10 15

Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr
20 25 30

Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser
35 40 45

Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr
50 55 60

Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys
65 70 75 80

His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro
85 90 95

Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
100 105

<210> 326
<211> 327
<212> PRT
<213> 智人

<400> 326

Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg
1 5 10 15

Ser Thr Ser Glu Ser Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr
20 25 30

Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser
35 40 45

Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser
50 55 60

Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Lys Thr
65 70 75 80

Tyr Thr Cys Asn Val Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys
85 90 95

Arg Val Glu Ser Lys Tyr Gly Pro Pro Cys Pro Pro Cys Pro Ala Pro
100 105 110

Glu Phe Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys
115 120 125

Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val
130 135 140

Asp Val Ser Gln Glu Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp
145 150 155 160

Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe
165 170 175

Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp
180 185 190

Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu
195 200 205

Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg
210 215 220

Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Gln Glu Glu Met Thr Lys
225 230 235 240

Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp
245 250 255

Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys
260 265 270

Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser
275 280 285

Arg Leu Thr Val Asp Lys Ser Arg Trp Gln Glu Gly Asn Val Phe Ser
290 295 300

Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser
305 310 315 320

Leu Ser Leu Ser Leu Gly Lys
325

<210> 327
<211> 120
<212> PRT
<213> 小家鼠

<400> 327

Glu Val Gln Leu Gln Gln Ser Gly Pro Glu Leu Val Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Met Ser Cys Lys Ala Ser Gly Phe Thr Phe Thr Asp Tyr
20 25 30

Ile Met His Trp Val Lys Gln Lys Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

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

Lys Gly Lys Ala Thr Leu Thr Ser Asp Lys Ser Ser Ser Thr Ala Tyr
65 70 75 80

Met Asp Leu Ser Ser Leu Thr Ser Glu Gly Ser Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Ser Ile Tyr Tyr Tyr Asp Ala Pro Phe Ala Tyr Trp Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 328
<211> 120
<212> PRT
<213> 小家鼠

<400> 328

Glu Val Gln Leu Gln Gln Ser Gly Pro Glu Leu Val Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Met Ser Cys Lys Ala Ser Gly Phe Thr Phe Thr Asp Tyr
20 25 30

Ile Met His Trp Val Lys Gln Lys Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

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

Lys Gly Lys Ala Thr Leu Thr Ser Asp Lys Ser Ser Ser Thr Ala Tyr
65 70 75 80

Met Asp Leu Ser Ser Leu Thr Ser Glu Gly Ser Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Ser Ile Tyr Tyr Tyr Asp Ala Pro Phe Ala Tyr Trp Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 329
<211> 120
<212> PRT
<213> 小家鼠

<400> 329

Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Phe Thr Phe Thr Asp Tyr
20 25 30

Ile Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

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

Lys Gly Arg Val Thr Ile Thr Ala Asp Lys Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Ser Ile Tyr Tyr Tyr Asp Ala Pro Phe Ala Tyr Trp Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 330
<211> 226
<212> PRT
<213> 小家鼠

<400> 330

Glu Val Gln Leu Gln Gln Ser Gly Pro Glu Leu Val Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Met Ser Cys Lys Ala Ser Gly Phe Thr Phe Thr Asp Tyr
20 25 30

Ile Met His Trp Val Lys Gln Lys Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

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

Lys Gly Lys Ala Thr Leu Thr Ser Asp Lys Ser Ser Ser Thr Ala Tyr
65 70 75 80

Met Asp Leu Ser Ser Leu Thr Ser Glu Gly Ser Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Ser Ile Tyr Tyr Tyr Asp Ala Pro Phe Ala Tyr Trp Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser Thr Val Ala Ala Pro Ser Val Phe
115 120 125

Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser Val
130 135 140

Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp
145 150 155 160

Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr
165 170 175

Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr
180 185 190

Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val
195 200 205

Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly
210 215 220

Glu Cys
225

<210> 331
<211> 447
<212> PRT
<213> 小家鼠

<400> 331

Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Phe Thr Phe Thr Asp Tyr
20 25 30

Ile Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

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

Lys Gly Arg Val Thr Ile Thr Ala Asp Lys Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Ser Ile Tyr Tyr Tyr Asp Ala Pro Phe Ala Tyr Trp Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val
115 120 125

Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser Thr Ala Ala
130 135 140

Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser
145 150 155 160

Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val
165 170 175

Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro
180 185 190

Ser Ser Ser Leu Gly Thr Lys Thr Tyr Thr Cys Asn Val Asp His Lys
195 200 205

Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Ser Lys Tyr Gly Pro
210 215 220

Pro Cys Pro Pro Cys Pro Ala Pro Glu Phe Leu Gly Gly Pro Ser Val
225 230 235 240

Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr
245 250 255

Pro Glu Val Thr Cys Val Val Val Asp Val Ser Gln Glu Asp Pro Glu
260 265 270

Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys
275 280 285

Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Tyr Arg Val Val Ser
290 295 300

Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys
305 310 315 320

Cys Lys Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile
325 330 335

Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro
340 345 350

Pro Ser Gln Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu
355 360 365

Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn
370 375 380

Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser
385 390 395 400

Asp Gly Ser Phe Phe Leu Tyr Ser Arg Leu Thr Val Asp Lys Ser Arg
405 410 415

Trp Gln Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu
420 425 430

His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Leu Gly Lys
435 440 445

<210> 332
<211> 107
<212> PRT
<213> 小家鼠

<400> 332

Asp Ile Gln Met Thr Gln Ile Thr Ser Ser Leu Ser Ala Ser Leu Gly
1 5 10 15

Asp Arg Val Ser Ile Ser Cys Arg Ala Ser Gln Asp Ile Ser Asn Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Asp Gly Thr Phe Lys Leu Leu Ile
35 40 45

Phe Tyr Thr Ser Arg Leu Leu Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Tyr Asn Leu Glu Gln
65 70 75 80

Glu Asp Phe Ala Thr Tyr Phe Cys Gln Gln Gly Asp Thr Leu Pro Tyr
 85 90 95
 Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
 100 105
 <210> 333
 <211> 324
 <212> PRT
 <213> 小家鼠
 <400> 333
 Ala Lys Thr Thr Pro Pro Ser Val Tyr Pro Leu Ala Pro Gly Ser Ala
 1 5 10 15
 Ala Gln Thr Asn Ser Met Val Thr Leu Gly Cys Leu Val Lys Gly Tyr
 20 25 30
 Phe Pro Glu Pro Val Thr Val Thr Trp Asn Ser Gly Ser Leu Ser Ser
 35 40 45
 Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Asp Leu Tyr Thr Leu
 50 55 60
 Ser Ser Ser Val Thr Val Pro Ser Ser Thr Trp Pro Ser Glu Thr Val
 65 70 75 80
 Thr Cys Asn Val Ala His Pro Ala Ser Ser Thr Lys Val Asp Lys Lys
 85 90 95
 Ile Val Pro Arg Asp Cys Gly Cys Lys Pro Cys Ile Cys Thr Val Pro
 100 105 110
 Glu Val Ser Ser Val Phe Ile Phe Pro Pro Lys Pro Lys Asp Val Leu
 115 120 125
 Thr Ile Thr Leu Thr Pro Lys Val Thr Cys Val Val Val Asp Ile Ser
 130 135 140
 Lys Asp Asp Pro Glu Val Gln Phe Ser Trp Phe Val Asp Asp Val Glu
 145 150 155 160
 Val His Thr Ala Gln Thr Gln Pro Arg Glu Glu Gln Phe Asn Ser Thr
 165 170 175
 Phe Arg Ser Val Ser Glu Leu Pro Ile Met His Gln Asp Trp Leu Asn
 180 185 190
 Gly Lys Glu Phe Lys Cys Arg Val Asn Ser Ala Ala Phe Pro Ala Pro
 195 200 205
 Ile Glu Lys Thr Ile Ser Lys Thr Lys Gly Arg Pro Lys Ala Pro Gln
 210 215 220
 Val Tyr Thr Ile Pro Pro Pro Lys Glu Gln Met Ala Lys Asp Lys Val
 225 230 235 240

Ser Leu Thr Cys Met Ile Thr Asp Phe Phe Pro Glu Asp Ile Thr Val
 245 250 255

Glu Trp Gln Trp Asn Gly Gln Pro Ala Glu Asn Tyr Lys Asn Thr Gln
 260 265 270

Pro Ile Met Asp Thr Asp Gly Ser Tyr Phe Ile Tyr Ser Lys Leu Asn
 275 280 285

Val Gln Lys Ser Asn Trp Glu Ala Gly Asn Thr Phe Thr Cys Ser Val
 290 295 300

Leu His Glu Gly Leu His Asn His His Thr Glu Lys Ser Leu Ser His
 305 310 315 320

Ser Pro Gly Lys

<210> 334
 <211> 213
 <212> PRT
 <213> 小家鼠

<400> 334

Asp Ile Gln Met Thr Gln Thr Thr Ser Ser Leu Ser Ala Ser Leu Gly
 1 5 10 15

Asp Arg Val Asn Ile Ser Cys Arg Ala Ser Gln Asp Ile Ser Ser Tyr
 20 25 30

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

Tyr Ser Thr Ser Arg Leu Asn Ser Gly Val Pro Ser Arg Phe Ser Gly
 50 55 60

Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Ser Asn Leu Ala Gln
 65 70 75 80

Glu Asp Ile Ala Thr Tyr Phe Cys Gln Gln Asp Ile Lys His Pro Thr
 85 90 95

Phe Gly Gly Gly Thr Lys Leu Glu Leu Lys Arg Thr Asp Ala Ala Pro
 100 105 110

Thr Val Ser Ile Phe Pro Pro Ser Ser Glu Gln Leu Thr Ser Gly Gly
 115 120 125

Ala Ser Val Val Cys Phe Leu Asn Asn Phe Tyr Pro Lys Asp Ile Asn
 130 135 140

Val Lys Trp Lys Ile Asp Gly Ser Glu Arg Gln Asn Gly Val Leu Asn
 145 150 155 160

Ser Trp Thr Asp Gln Asp Ser Lys Asp Ser Thr Tyr Ser Met Ser Ser
 165 170 175

Thr Leu Thr Leu Thr Lys Asp Glu Tyr Glu Arg His Asn Ser Tyr Thr
 180 185 190
 Cys Glu Ala Thr His Lys Thr Ser Thr Ser Pro Ile Val Lys Ser Phe
 195 200 205
 Asn Arg Asn Glu Cys
 210
 <210> 335
 <211> 444
 <212> PRT
 <213> 小家鼠
 <400> 335
 Glu Val Gln Leu Gln Gln Ser Gly Pro Glu Leu Val Lys Pro Gly Ala
 1 5 10 15
 Ser Val Lys Met Ser Cys Lys Ala Ser Gly Phe Thr Phe Thr Asp Tyr
 20 25 30
 Ile Met His Trp Val Lys Gln Lys Pro Gly Gln Gly Leu Glu Trp Ile
 35 40 45
 Gly Tyr Ile Asn Pro Tyr Asn Asp Asp Thr Glu Tyr Asn Glu Lys Phe
 50 55 60
 Lys Gly Lys Ala Thr Leu Thr Ser Asp Lys Ser Ser Ser Thr Ala Tyr
 65 70 75 80
 Met Asp Leu Ser Ser Leu Thr Ser Glu Gly Ser Ala Val Tyr Tyr Cys
 85 90 95
 Ala Arg Ser Ile Tyr Tyr Tyr Asp Ala Pro Phe Ala Tyr Trp Gly Gln
 100 105 110
 Gly Thr Leu Val Thr Val Ser Ser Ala Lys Thr Thr Pro Pro Ser Val
 115 120 125
 Tyr Pro Leu Ala Pro Gly Ser Ala Ala Gln Thr Asn Ser Met Val Thr
 130 135 140
 Leu Gly Cys Leu Val Lys Gly Tyr Phe Pro Glu Pro Val Thr Val Thr
 145 150 155 160
 Trp Asn Ser Gly Ser Leu Ser Ser Gly Val His Thr Phe Pro Ala Val
 165 170 175
 Leu Gln Ser Asp Leu Tyr Thr Leu Ser Ser Ser Val Thr Val Pro Ser
 180 185 190
 Ser Thr Trp Pro Ser Glu Thr Val Thr Cys Asn Val Ala His Pro Ala
 195 200 205
 Ser Ser Thr Lys Val Asp Lys Lys Ile Val Pro Arg Asp Cys Gly Cys
 210 215 220

Lys Pro Cys Ile Cys Thr Val Pro Glu Val Ser Ser Val Phe Ile Phe
225 230 235 240

Pro Pro Lys Pro Lys Asp Val Leu Thr Ile Thr Leu Thr Pro Lys Val
245 250 255

Thr Cys Val Val Val Asp Ile Ser Lys Asp Asp Pro Glu Val Gln Phe
260 265 270

Ser Trp Phe Val Asp Asp Val Glu Val His Thr Ala Gln Thr Gln Pro
275 280 285

Arg Glu Glu Gln Phe Asn Ser Thr Phe Arg Ser Val Ser Glu Leu Pro
290 295 300

Ile Met His Gln Asp Trp Leu Asn Gly Lys Glu Phe Lys Cys Arg Val
305 310 315 320

Asn Ser Ala Ala Phe Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Thr
325 330 335

Lys Gly Arg Pro Lys Ala Pro Gln Val Tyr Thr Ile Pro Pro Pro Lys
340 345 350

Glu Gln Met Ala Lys Asp Lys Val Ser Leu Thr Cys Met Ile Thr Asp
355 360 365

Phe Phe Pro Glu Asp Ile Thr Val Glu Trp Gln Trp Asn Gly Gln Pro
370 375 380

Ala Glu Asn Tyr Lys Asn Thr Gln Pro Ile Met Asp Thr Asp Gly Ser
385 390 395 400

Tyr Phe Val Tyr Ser Lys Leu Asn Val Gln Lys Ser Asn Trp Glu Ala
405 410 415

Gly Asn Thr Phe Thr Cys Ser Val Leu His Glu Gly Leu His Asn His
420 425 430

His Thr Glu Lys Ser Leu Ser His Ser Pro Gly Lys
435 440

<210> 336
<211> 108
<212> PRT
<213> 小家鼠

<400> 336

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Lys Ala Ser Gln Asp Val Phe Thr Ala
20 25 30

Val Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Trp Ala Ser Thr Arg His Thr Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Ser Ser Tyr Pro Leu
85 90 95

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 337
<211> 324
<212> DNA
<213> 小家鼠

<400> 337
gatatccaga tgaccagag cccgagcagc ctgagcgga gcgtgggga tcggtgacc 60
attacctgca aagcgagcca ggatgtgttt accgcggtgg cgtggtatca gcagaaaccg 120
ggcaaagcgc gaaactgct gatttattgg gcgagcagcc gccataccgg cgtgccgagt 180
cgcttttagcg gcagcggcag cggcaccgat ttaccctga ccattagcag cctgcagccg 240
gaagattttg cgacctatta ttgccagcag tatagcagct atccgctgac ctttggcggc 300
ggcaccaaag tggaaattaa acgt 324

<210> 338
<211> 119
<212> PRT
<213> 小家鼠

<400> 338

Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Phe Asn Ile Lys Asp Tyr
20 25 30

Tyr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

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

Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Tyr Asp Ala Gly Asp Pro Ala Trp Phe Thr Tyr Trp Gly Gln Gly
100 105 110

Thr Leu Val Thr Val Ser Ser
115

<210> 339

<211> 357
<212> DNA
<213> 小家鼠

<400> 339
gaaglgcagc tggcgcagag cggcgcggaa gtagaaaaac cgggcgcgag cgtgaaagtg 60
agctgcaaag cgagcggctt taacattaaa gattattata tgcatlgggt gcgccaggcg 120
ccgggccagg gcctggaatg gatcgccgcg atgatccgg aaaacggcga tattatttat 180
gatccgaaat ttcaggggcg cgtgaccatg accaccgata ccagcaccag caccgcgtat 240
atggaactgc gcagcctgcg cagcgatgat accgcggtgt attatlgcgc gtatgatgcg 300
ggcgatccgg cgtggtttac ctattggggc cagggcaccc tggtagaccgt ctcgagc 357

<210> 340
<211> 1395
<212> DNA
<213> 小家鼠

<400> 340
atggactgga cctggaggat cctcttcttg gtggcagcag ccacaggagc ccactccgag 60
gtgcagctgg tgcagctcgg ggctgagggt aagaagcctg ggtcctcgtt gaaggctctc 120
tgcaaggctt ctggttttac ctaccgcgac tatattatgc actgggtgcg tcaggccctt 180
ggccaaggcg ttgagtggat gggctatata aacccttata atgatgacac cgaatacaac 240
gagaagttca agggccgtgt cagcattacc gcggacaaat ccacgagcac agcctacatg 300
gagctgagca gcctgcgcgc tgaggacacg gccgtgtatt actgtgcgcg ttcgatttat 360
tactacgatg ccccgtttgc ttactggggc caagggactc tggtcaccgt ctctagtgc 420
tccaccaagg gcccatcggt ctccccctg gcgccctgct ccaggagcac ctccgagagc 480
acagcggccc tgggctgcct ggtcaaggac tacttccccg aaccgggtgac ggtgtcgttg 540
aactcaggcg ctctgaccag cggcgtgcac accttcccag ctgtcctaca gtccctcagga 600
ctctactccc tcagcagcgt ggtgaccgtg ccttccagca acttcggcac ccagacctac 660
acctgcaacg tagatcaca gccagcaac accaaggagg acaagacagt tgagcgcaaa 720
tgttgtgtcg agtccccacc gtgccagca ccacctgtgg caggaccgtc agtcttcttc 780
ttcccccaaa aaccaaggga caccctcatg atctcccggg cccctgaggt cacgtgcgtg 840
gtggtggacg tgagccacga agaccccgag gtccagttca actggtacgt ggacggcgtg 900
gagggtgcata atgccaagac aaagccacgg gaggagcagt tcaacagcac gttccgtgtg 960
gtcagcgicc tcaccgttgi gcaccaggac tggctgaacg gcaaggagta caagtgaag 1020
gtctccaaca aaggcctccc agccccatc gaaaaacca tctccaaaac caaagggcag 1080
ccccgagaac cacagggtga caccctgccc ccatcccggg aggagatgac caagaaccag 1140
gtcagcctga cctgcctggt caaaggctc taccacagcg acatcgccgt ggagtgaggag 1200
agcaatgggc agccggagaa caactacaag accacacctc ccatgctgga ctccgacggc 1260
tccttcttcc tctacagaa gctcaccgtg gacaagagca ggtggcagca ggggaacgtc 1320
ttctcatgct ccgtgatgca tgaggctctg cacaaccact acacgcagaa gagcctctcc 1380
ctgtctccgg gtaaa 1395

<210> 341
<211> 213

<212> PRT
<213> 小家鼠

<400> 341

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Ile Ser Ser Tyr
20 25 30
Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45
Tyr Ser Thr Ser Arg Leu Asn Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60
Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80
Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Asp Ile Lys His Pro Thr
85 90 95
Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala Pro
100 105 110
Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr
115 120 125
Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys
130 135 140
Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu
145 150 155 160
Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser
165 170 175
Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala
180 185 190
Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe
195 200 205
Asn Arg Gly Glu Cys ..
210

<210> 342
<211> 639
<212> DNA
<213> 小家鼠

<400> 342

gacatccaga tgaccacgtc tccatcctcc ctgtctgcat ctgtaggatga ccgtgtcacc	60
atcacttgcc gcgcaagtca ggatatttagc agctatttaa attggtatca gcagaaacca	120
gggaaagccc ctaagctcct gatctattct acttcccggt tgaatagtgg ggtcccatca	180
cgttcacgtg gcagtggtc tgggacagat ttactctca ccatcagcag tctgcaacct	240

gaagatttig caacttacta cigtcaacag gatattaaac accctacgtt cggtaaggc 300
 accaaggtgg agatcaaacg tacgggtggct gcaccatctg tcttcatctt cccgccatct 360
 gatgagcagt tgaaatctgg aactgcctct gttgtgtgcc tgctgaataa ctctatccc 420
 agagaggcca aagtacagtg gaaggtggat aacgccctcc aatcgggtaa ctcccaggag 480
 agtgtcacag agcaggacag caaggacagc acctacagcc tcagcagcac cctgacgctg 540
 agcaaagcag actacgagaa acacaaagtc tacgcctgcg aagtcaccca tcagggcctg 600
 agctcgcccg tcacaaagag ctccaacagg ggagagtgt 639

<210> 343
 <211> 235
 <212> PRT
 <213> 小家鼠

<400> 343

Met Asp Met Arg Val Pro Ala Gln Leu Leu Gly Leu Leu Leu Leu Trp
 1 5 10 15

Leu Arg Gly Ala Arg Cys Asp Ile Gln Met Thr Gln Ser Pro Ser Ser
 20 25 30

Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser
 35 40 45

Gln Asp Ile Ser Ser Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys
 50 55 60

Ala Pro Lys Leu Leu Ile Tyr Ser Thr Ser Arg Leu Asn Ser Gly Val
 65 70 75 80

Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
 85 90 95

Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln
 100 105 110

Asp Ile Lys His Pro Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
 115 120 125

Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu
 130 135 140

Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe
 145 150 155 160

Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln
 165 170 175

Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser
 180 185 190

Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu
 195 200 205

Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser

210	215	220
Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys		
225	230	235
<210> 344 <211> 705 <212> DNA <213> 小家鼠		
<400> 344 atggacatga ggggtgccgc tcagtcctg gggctcctgc tgcgtggct gagaggcgcc60 agatgtgaca tccagatgac ccagtcacca tcctccctgt ctgcatctgt aggtgaccgt120 gtcaccatca ctgtccgcgc aagtcaggat attagcagct atttaaattg gtatcagcag180 aaaccaggga aagccccata gctcctgac tattctactt cccgtttgaa tagtggggtc240 ccatcacgct tcagtggcag tggctctggg acagatttca ctctcaccat cagcagctctg300 caacctgaag attttgcaac ttactactgt caacaggata ttaaacaccc tacgttcggt360 caaggcacca aggtggagat caaacgtacg gtggctgcac catctgtctt catcttcccg420 ccatctgatg agcagttgaa atctggaact gcctctgttg tgtgcctgct gaataacttc480 tatcccagag aggccaaagt acagtggaag gtggataacg ccctccaatc gggtaacttc540 caggagagtg tcacagagca ggacagcaag gacagcacct acagcctcag cagcacctcg600 acgctgagca aagcagacta cgagaaacac aaagtctacg cctgcgaagt caccatcag660 ggcctgagct cgcccgctac aaagagcttc aacaggggag agtgt705		
<210> 345 <211> 446 <212> PRT <213> 小家鼠		
<400> 345 Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser 151015 Ser Val Lys Val Ser Cys Lys Ala Ser Gly Phe Thr Phe Thr Asp Tyr 202530 Ile Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met 354045 Gly Tyr Ile Asn Pro Tyr Asn Asp Asp Thr Glu Tyr Asn Glu Lys Phe 505560 Lys Gly Arg Val Thr Ile Thr Ala Asp Lys Ser Thr Ser Thr Ala Tyr 65707580 Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys 859095 Ala Arg Ser Ile Tyr Tyr Tyr Asp Ala Pro Phe Ala Tyr Trp Gly Gln 100105110 Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val 115120125		

Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser Thr Ala Ala
 130 135 140
 Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser
 145 150 155 160
 Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val
 165 170 175
 Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro
 180 185 190
 Ser Ser Asn Phe Gly Thr Gln Thr Tyr Thr Cys Asn Val Asp His Lys
 195 200 205
 Pro Ser Asn Thr Lys Val Asp Lys Thr Val Glu Arg Lys Cys Cys Val
 210 215 220
 Glu Cys Pro Pro Cys Pro Ala Pro Pro Val Ala Gly Pro Ser Val Phe
 225 230 235 240
 Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro
 245 250 255
 Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val
 260 265 270
 Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr
 275 280 285
 Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Phe Arg Val Val Ser Val
 290 295 300
 Leu Thr Val Val His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys
 305 310 315 320
 Lys Val Ser Asn Lys Gly Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser
 325 330 335
 Lys Thr Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro
 340 345 350
 Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val
 355 360 365
 Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly
 370 375 380
 Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Met Leu Asp Ser Asp
 385 390 395 400
 Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp
 405 410 415
 Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His

420	425	430
Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys		
435	440	445
<210> 346 <211> 1338 <212> DNA <213> 小家鼠		
<400> 346 gagggtgcagc tgggtgcagtc tggggctgag gtgaagaagc ctgggtcctc ggtgaaggtc 60 tccctgaagg ctcttggttt taccttcacc gactatatta tgcactgggt gcgtcaggcc 120 cctggccaag ggcttgagtg gatgggctat atcaaccctt ataatgatga caccgaatac 180 aacgagaagt tcaagggccg tgtcacgatt accgcggaca aatccacgag cacagcctac 240 atggagctga gcagcctgcg ctctgaggac acggccgtgt attactgtgc gcgttcgatt 300 tattactacg atgccccgtt tgcttactgg ggccaaggga ctctggtcac cgctcttagt 360 gcctccacca agggcccatc ggtcttcccc ctggcgccct gtccaggag cacctccgag 420 agcacagcgg ccctgggctg cctgggtcaag gactacttcc ccgaaccggt gacggtgtcg 480 tggaaactcag gcgctctgac cagcggcgtg cacaccttcc cagctgtcct acagtcctca 540 ggactctact ccctcagcag cgtgggtgacc gtgccctcca gcaacttcgg caccagacc 600 tacacctgca acgtagatca caagcccagc aacaccaagg tggacaagac agttgagcgc 660 aaatgtttgt togagtgcgc accgtgccca gcaccacctg tggcaggacc gtcagtcctc 720 ctcttcccc caaaacccaa ggacaccctc atgatctccc ggacccctga ggtcacgtgc 780 gtggtggtgg acgtgagcca cgaagacccc gaggtccagt tcaactggta cgtggacggc 840 gtggaggtgc ataatgccaa gacaaagcca cgggaggagc agttcaacag cacgttccgt 900 gtggtcagcg tccctaccgt tgtgcaccag gactggctga acggcaagga gtacaagtgc 960 aaggctcca acaaaggcct cccagccccc atcgagaaaa ccatctccaa aaccaaaggg 1020 cagccccgag aaccacaggt gtacaccctg ccccatccc gggaggagat gaccaagaac 1080 caggtcagcc tgacctgcct ggtcaaaggc ttctacccca gcgacatcgc cgtggagtgg 1140 gagagcaatg ggcagccgga gaacaactac aagaccacac ctcccatgct ggactccgac 1200 ggctccttct tctcttacag caagctcacc gtggacaaga gcaggtggca gcaggggaac 1260 gtctttctcat gctccgtgat gcatgaggct ctgcacaacc actacacgca gaagagcctc 1320 tccctgtctc cgggtaaa 1338		
<210> 347 <211> 465 <212> PRT <213> 小家鼠		
<400> 347 Met Asp Trp Thr Trp Arg Ile Leu Phe Leu Val Ala Ala Ala Thr Gly 1 5 10 15 Ala His Ser Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys 20 25 30		

Pro Gly Ser Ser Val Lys Val Ser Cys Lys Ala Ser Gly Phe Thr Phe
35 40 45

Thr Asp Tyr Ile Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu
50 55 60

Glu Trp Met Gly Tyr Ile Asn Pro Tyr Asn Asp Asp Thr Glu Tyr Asn
65 70 75 80

Glu Lys Phe Lys Gly Arg Val Thr Ile Thr Ala Asp Lys Ser Thr Ser
85 90 95

Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val
100 105 110

Tyr Tyr Cys Ala Arg Ser Ile Tyr Tyr Tyr Asp Ala Pro Phe Ala Tyr
115 120 125

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly
130 135 140

Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser
145 150 155 160

Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val
165 170 175

Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe
180 185 190

Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val
195 200 205

Thr Val Pro Ser Ser Asn Phe Gly Thr Gln Thr Tyr Thr Cys Asn Val
210 215 220

Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys Thr Val Glu Arg Lys
225 230 235 240

Cys Cys Val Glu Cys Pro Pro Cys Pro Ala Pro Pro Val Ala Gly Pro
245 250 255

Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser
260 265 270

Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp
275 280 285

Pro Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
290 295 300

Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Phe Arg Val
305 310 315 320

Val Ser Val Leu Thr Val Val His Gln Asp Trp Leu Asn Gly Lys Glu
325 330 335

Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ala Pro Ile Glu Lys
340 345 350

Thr Ile Ser Lys Thr Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr
355 360 365

Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr
370 375 380

Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu
385 390 395 400

Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Met Leu
405 410 415

Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys
420 425 430

Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu
435 440 445

Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
450 455 460

Lys
465

<210> 348
<211> 1395
<212> DNA
<213> 小家鼠

<400> 348
atggactgga cctggaggat cctcttcttg gtggcagcag ccacaggagc ccaactccgag 60
gtgcagctgg tgcagctcgg ggctgaggtg aagaagcctg ggtcctcggg gaaggctctcc 120
tgcaaggctt ctggttttac cttcaccgac tatattatgc actgggtgcg tcaggcccct 180
ggtaaggggc ttgagtggat gggctatatc aacccttata atgatgacac cgaatacaac 240
gagaagttca agggccgtgt cagcattacc gcggacaaat ccacgagcac agcctacatg 300
gagctgagca gccctgcgtc tgaggacacg gccgtgtatt actgtgcgcg ttcgatttat 360
tactacgatg ccccgtttgc ttactggggc caagggactc tggtcaccgt ctctagtgcc 420
tccaccaagg gcccatcggg cttccccctg gcgccctgct ccaggagcac ctccgagagc 480
acagcggccc tgggctgcct ggtcaaggac tacttccccg aaccgggtgac ggtgtcgtgg 540
aactcaggcg ctctgaccag cggcgtgcac accttcccag ctgtcctaca gtccctcagga 600
ctctactccc tcagcagcgt ggtgaccgtg ccctccagca acttcggcac ccagacctac 660
acctgcaacg tagatcacaa gccagcaac accaaggagg acaagacagt tgagcgcaaa 720
tgttgtgtcg agtgcccacc gtgccagca ccacctgtgg caggaccgtc agtcttccctc 780
ttcccccaa aacccaagga caccctcatg atctcccga cccctgaggt caggtgcgtg 840
gtggtggacg tgagccacga agaccccag gtccagtcca actgggtacgt ggacggcgtg 900
gaggtgcata atgccaagac aaagccacgg gaggagcagt tcaacagcac gttccgtgtg 960

gtcagcgtcc tcaccgttgt gcaccaggac tggctgaacg gcaaggagta caagtgaag 1020
gtctccaaca aaggcctccc agcccccata gagaaaacca tctccaaaac caaagggcag 1080
ccccgagaac cacagggtga caccctgccc ccatcccggg aggagatgac caagaaccag 1140
gtcagcctga cctgcctggg caaaggcttc taccccagcg acatcgccgt ggagtgggag 1200
agcaatgggc agccggagaa caactacaag accacacctc ccatgctgga ctccgacggc 1260
tccttcttcc tctacagcaa gctcaccgtg gacaagagca ggtggcagca ggggaacgtc 1320
ttctcatgct ccgtgatgca tgaggctctg cacaaccact acacgcagaa gagcctctcc 1380
ctgtctccgg gtaaa 1395

<210> 349
<211> 417
<212> DNA
<213> 小家鼠

<400> 349
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gtcagctgg tgcagtctgg ggtcagggtg aagaagcctg ggtcctcggg gaaggtctcc 120
tgcaaggctt ctggttttac cttaccgac tatattatgc actgggtgctg tcaggccctt 180
ggtaagggtc ttgagtggat gggctataac aaccttata atgatgacac cgaatacaac 240
gagaagtcca agggccgtgt cagcattacc ggggacaaat ccacgagcac agcctacatg 300
gagctgagca gcctgcgtc tgaggacacg gccgtgtatt actgtgcgctg ttgatttat 360
tactacgatg ccccgtttgc ttactggggc caagggactc tggtcacagt ctcgagc 417

<210> 350
<211> 218
<212> PRT
<213> 小家鼠

<400> 350
Asp Ile Val Leu Thr Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly
1 5 10 15
Gln Arg Ala Thr Ile Ala Cys Lys Ala Ser Gln Ser Val Asp Tyr Asp
20 25 30
Gly Thr Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro
35 40 45
Lys Leu Leu Ile Tyr Ala Ala Ser Asn Leu Glu Ser Glu Ile Pro Ala
50 55 60
Arg Phe Ser Gly Thr Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile His
65 70 75 80
Pro Val Glu Glu Glu Asp Ile Thr Thr Tyr Tyr Cys Gln Gln Ser Asn
85 90 95
Glu Asp Pro Phe Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg
100 105 110
Ala Asp Ala Ala Pro Thr Val Ser Ile Phe Pro Pro Ser Ser Glu Gln
115 120 125

Leu Thr Ser Gly Gly Ala Ser Val Val Cys Phe Leu Asn Asn Phe Tyr
130 135 140

Pro Lys Asp Ile Asn Val Lys Trp Lys Ile Asp Gly Ser Glu Arg Gln
145 150 155 160

Asn Gly Val Leu Asn Ser Trp Thr Asp Gln Asp Ser Lys Asp Ser Thr
165 170 175

Tyr Ser Met Ser Ser Thr Leu Thr Leu Thr Lys Asp Glu Tyr Glu Arg
180 185 190

His Asn Ser Tyr Thr Cys Glu Ala Thr His Lys Thr Ser Thr Ser Pro
195 200 205

Ile Val Lys Ser Phe Asn Arg Asn Glu Cys
210 215

<210> 351
<211> 15
<212> PRT
<213> 小家鼠

<400> 351

Lys Ala Ser Gln Ser Val Asp Tyr Asp Gly Thr Ser Tyr Met Asn
1 5 10 15

<210> 352
<211> 7
<212> PRT
<213> 小家鼠

<400> 352

Ala Ala Ser Asn Leu Glu Ser
1 5

<210> 353
<211> 9
<212> PRT
<213> 小家鼠

<400> 353

Gln Gln Ser Asn Glu Asp Pro Phe Thr
1 5

<210> 354
<211> 657
<212> DNA
<213> 小家鼠

<400> 354
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atcgccctgca aggccagcca aagtgttgat tatgatggta ctagttatat gaattggtac 120
caacagaaac caggacagcc acccaaactc ctcatctatg ctgcatccaa tctagaatct 180
gagatcccag ccaggttttag tggcactggg tctgggacag acttcaccct caacatccat 240
cctgtggagg aggaggatat cacaacctat tactgtcagc aaagtaatga ggatccgttc 300

acgttcggag gggggaccaa gttggaata aaacgggctg atgctgcacc aactgtatcc 360
atcttccac catccagtga gcagttaaca tctggaggtg cctcagtcgt gtgcttcttg 420
aacaacttct accccaaaga catcaatgtc aagtgggaaga ttgatggcag tgaacgacaa 480
aatggcgctc tgaacagttg gactgatcag gacagcaaag acagcaccta cagcatgagc 540
agcaccctca cgttgaccaa ggacgagtat gaacgacata acagctatac ctgtgaggcc 600
actcacaaga catcaacttc acccattgtc aagagcttca acaggaatga gtgttag 657

<210> 355
<211> 238
<212> PRT
<213> 小家鼠

<400> 355

Met Glu Thr Asp Thr Ile Leu Leu Trp Val Leu Leu Leu Trp Val Pro
1 5 10 15

Gly Ser Thr Gly Asp Ile Val Leu Thr Gln Ser Pro Ala Ser Leu Ala
20 25 30

Val Ser Leu Gly Gln Arg Ala Thr Ile Ala Cys Lys Ala Ser Gln Ser
35 40 45

Val Asp Tyr Asp Gly Thr Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro
50 55 60

Gly Gln Pro Pro Lys Leu Leu Ile Tyr Ala Ala Ser Asn Leu Glu Ser
65 70 75 80

Glu Ile Pro Ala Arg Phe Ser Gly Thr Gly Ser Gly Thr Asp Phe Thr
85 90 95

Leu Asn Ile His Pro Val Glu Glu Glu Asp Ile Thr Thr Tyr Tyr Cys
100 105 110

Gln Gln Ser Asn Glu Asp Pro Phe Thr Phe Gly Gly Gly Thr Lys Leu
115 120 125

Glu Ile Lys Arg Ala Asp Ala Ala Pro Thr Val Ser Ile Phe Pro Pro
130 135 140

Ser Ser Glu Gln Leu Thr Ser Gly Gly Ala Ser Val Val Cys Phe Leu
145 150 155 160

Asn Asn Phe Tyr Pro Lys Asp Ile Asn Val Lys Trp Lys Ile Asp Gly
165 170 175

Ser Glu Arg Gln Asn Gly Val Leu Asn Ser Trp Thr Asp Gln Asp Ser
180 185 190

Lys Asp Ser Thr Tyr Ser Met Ser Ser Thr Leu Thr Leu Thr Lys Asp
195 200 205

Glu Tyr Glu Arg His Asn Ser Tyr Thr Cys Glu Ala Thr His Lys Thr
210 215 220

Ser Thr Ser Pro Ile Val Lys Ser Phe Asn Arg Asn Glu Cys
225 230 235

<210> 356
<211> 717
<212> DNA
<213> 小家鼠

<400> 356
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gacattgtgt tgacccagtc tccagcttct ttggctgtgt ctctagggca gagggccacc 120
atcgctgca aggccagcca aagtgtgat tatgatggtg ctagtatat gaattggtac 180
caacagaaac caggacagcc acccaaactc ctcatctatg ctgcatcaa tctagaatct 240
gagatccag ccaggtttag tggcactggg tctgggacag acttcaccct caacatccat 300
cctgtggagg aggaggatat cacaacctat tactgtcagc aaagtaatga ggatccgttc 360
acgttcggag gggggaccaa gttggaata aaacgggctg atgctgcacc aactgtatcc 420
atcttccac catccagtga gcagttaaca tctggagggt cctcagtcgt gtgcttcttg 480
aacaacttct accccaaga catcaatgic aagtgaaga ttgatggcag tgaacgacaa 540
aatggcgctc tgaacagttg gactgatcag gacagcaaag acagcaccta cagcatgagc 600
agcaccctca cgttgaccaa ggacgagtat gaacgacata acagctatac ctgtgaggcc 660
actcacaaga catcaacttc acccatgtc aagagcttca acaggaatga gtgttag 717

<210> 357
<211> 442
<212> PRT
<213> 小家鼠

<400> 357

Gln Val Gln Leu Gln Gln Pro Gly Thr Glu Leu Val Arg Pro Gly Thr
1 5 10 15

Ser Val Lys Leu Ser Cys Lys Ala Ser Gly Tyr Ile Phe Thr Thr Tyr
20 25 30

Trp Met Asn Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Met Ile His Pro Ser Ala Ser Glu Ile Arg Leu Asp Gln Lys Phe
50 55 60

Lys Asp Lys Ala Thr Leu Thr Leu Asp Lys Ser Ser Ser Thr Ala Tyr
65 70 75 80

Met His Leu Ser Gly Pro Thr Ser Val Asp Ser Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Ser Gly Glu Trp Gly Ser Met Asp Tyr Trp Gly Gln Gly Thr
100 105 110

Ser Val Thr Val Ser Ser Ala Lys Thr Thr Pro Pro Ser Val Tyr Pro
115 120 125

Leu Ala Pro Gly Ser Ala Ala Gln Thr Asn Ser Met Val Thr Leu Gly
 130 135 140
 Cys Leu Val Lys Gly Tyr Phe Pro Glu Pro Val Thr Val Thr Trp Asn
 145 150 155 160
 Ser Gly Ser Leu Ser Ser Gly Val His Thr Phe Pro Ala Val Leu Gln
 165 170 175
 Ser Asp Leu Tyr Thr Leu Ser Ser Ser Val Thr Val Pro Ser Ser Thr
 180 185 190
 Trp Pro Ser Glu Thr Val Thr Cys Asn Val Ala His Pro Ala Ser Ser
 195 200 205
 Thr Lys Val Asp Lys Lys Ile Val Pro Arg Asp Cys Gly Cys Lys Pro
 210 215 220
 Cys Ile Cys Thr Val Pro Glu Val Ser Ser Val Phe Ile Phe Pro Pro
 225 230 235 240
 Lys Pro Lys Asp Val Leu Thr Ile Thr Leu Thr Pro Lys Val Thr Cys
 245 250 255
 Val Val Val Asp Ile Ser Lys Asp Asp Pro Glu Val Gln Phe Ser Trp
 260 265 270
 Phe Val Asp Asp Val Glu Val His Thr Ala Gln Thr Gln Pro Arg Glu
 275 280 285
 Glu Gln Phe Asn Ser Thr Phe Arg Ser Val Ser Glu Leu Pro Ile Met
 290 295 300
 His Gln Asp Trp Leu Asn Gly Lys Glu Phe Lys Cys Arg Val Asn Ser
 305 310 315 320
 Ala Ala Phe Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Thr Lys Gly
 325 330 335
 Arg Pro Lys Ala Pro Gln Val Tyr Thr Ile Pro Pro Pro Lys Glu Gln
 340 345 350
 Met Ala Lys Asp Lys Val Ser Leu Thr Cys Met Ile Thr Asp Phe Phe
 355 360 365
 Pro Glu Asp Ile Thr Val Glu Trp Gln Trp Asn Gly Gln Pro Ala Glu
 370 375 380
 Asn Tyr Lys Asn Thr Gln Pro Ile Met Asp Thr Asp Gly Ser Tyr Phe
 385 390 395 400
 Ile Tyr Ser Lys Leu Asn Val Gln Lys Ser Asn Trp Glu Ala Gly Asn
 405 410 415
 Thr Phe Thr Cys Ser Val Leu His Glu Gly Leu His Asn His His Thr
 420 425 430

Glu Lys Ser Leu Ser His Ser Pro Gly Lys
435 440

<210> 358
<211> 5
<212> PRT
<213> 小家鼠

<400> 358

Thr Tyr Trp Met Asn
1 5

<210> 359
<211> 17
<212> PRT
<213> 小家鼠

<400> 359

Met Ile His Pro Ser Ala Ser Glu Ile Arg Leu Asp Gln Lys Phe Lys
1 5 10 15

Asp

<210> 360
<211> 9
<212> PRT
<213> 小家鼠

<400> 360

Ser Gly Glu Trp Gly Ser Met Asp Tyr
1 5

<210> 361
<211> 1329
<212> DNA
<213> 小家鼠

<400> 361
cagggtccaac tacagcagcc tgggactgag ctggtgaggc ctggaacttc agtgaagttg 60
tcctgtaagg cttctggcta catcttcacc acctactgga tgaactgggt gaaacagagg 120
cctggacaag gccttgagtg gattggcatg attcatcctt ccgcaagtga aattaggttg 180
gatcagaaat tcaaggacaa ggccacattg actcttgaca aatcctccag cacagcctat 240
atgcacctca gcggcccgac atctgtggat tctgcgggtct attactgtgc aagatcaggg 300
gaatgggggt ctatggacta ctgggggtcaa ggaacctcag tcaccgtctc ctacgcaaaa 360
acgacacccc catctgtcta tccactggcc cctggatctg ctgccccaac taactccatg 420
gtgaccttgg gatgccttgt caagggctat ttccctgagc cagtgacagt gacctggaac 480
tctggatccc tgtccagcgg tgtgcacacc ttcccagctg tccctgcagt tgacctctac 540
actctgagca gctcagtgac tgtccccctc agcacctggc ccagcgagac cgtcacctgc 600
aacgttgccc acccggccag cagcaccaag gttgacaaga aaattgtgcc cagggattgt 660
ggttgtaagc ctgcatatg tacagtccea gaagtatcat ctgtcttcat ctcccccca 720
aagcccaagg atgtgtctac cattactctg actcctaagg tcacgttgtt tgtggtagac 780
atcagcaagg atgatccga ggtccagttc agctgggttt tagatgatgt ggaggtgcac 840

acagctcaga cgcaaccccg ggaggagcag ttcaacagca ctttccgctc agtcagtga 900
 cttcccatca tgcaccagga ctggctcaat ggcaaggagt tcaaatgcag ggtcaacagt 960
 gcagctttcc ctgcccccat cgagaaaacc atctccaaaa ccaaaggcag accgaaggct 1020
 ccacaggtgt acaccattcc acctcccaag gagcagatgg ccaaggataa agtcagtctg 1080
 acctgcatga taacagactt cttccctgaa gacattactg tggagtggca gtggaatggg 1140
 cagccagcgg agaactacaa gaacactcag cccatcatgg acacagatgg ctcttacttc 1200
 atctacagca agctcaatgt gcagaagagc aactggggagg caggaaatac ttacacctgc 1260
 tctgtgttac atgagggcct gcacaaccac catactgaga agagcctctc ccactctcct 1320
 ggtaaatga 1329

<210> 362
 <211> 461
 <212> PRT
 <213> 小家鼠

<400> 362

Met Gly Trp Ser Ser Ile Ile Leu Phe Leu Val Ala Thr Ala Thr Gly
 1 5 10 15
 Val His Ser Gln Val Gln Leu Gln Gln Pro Gly Thr Glu Leu Val Arg
 20 25 30
 Pro Gly Thr Ser Val Lys Leu Ser Cys Lys Ala Ser Gly Tyr Ile Phe
 35 40 45
 Thr Thr Tyr Trp Met Asn Trp Val Lys Gln Arg Pro Gly Gln Gly Leu
 50 55 60
 Glu Trp Ile Gly Met Ile His Pro Ser Ala Ser Glu Ile Arg Leu Asp
 65 70 75 80
 Gln Lys Phe Lys Asp Lys Ala Thr Leu Thr Leu Asp Lys Ser Ser Ser
 85 90 95
 Thr Ala Tyr Met His Leu Ser Gly Pro Thr Ser Val Asp Ser Ala Val
 100 105 110
 Tyr Tyr Cys Ala Arg Ser Gly Glu Trp Gly Ser Met Asp Tyr Trp Gly
 115 120 125
 Gln Gly Thr Ser Val Thr Val Ser Ser Ala Lys Thr Thr Pro Pro Ser
 130 135 140
 Val Tyr Pro Leu Ala Pro Gly Ser Ala Ala Gln Thr Asn Ser Met Val
 145 150 155 160
 Thr Leu Gly Cys Leu Val Lys Gly Tyr Phe Pro Glu Pro Val Thr Val
 165 170 175
 Thr Trp Asn Ser Gly Ser Leu Ser Ser Gly Val His Thr Phe Pro Ala
 180 185 190

Val Leu Gln Ser Asp Leu Tyr Thr Leu Ser Ser Ser Val Thr Val Pro
195 200 205

Ser Ser Thr Trp Pro Ser Glu Thr Val Thr Cys Asn Val Ala His Pro
210 215 220

Ala Ser Ser Thr Lys Val Asp Lys Lys Ile Val Pro Arg Asp Cys Gly
225 230 235 240

Cys Lys Pro Cys Ile Cys Thr Val Pro Glu Val Ser Ser Val Phe Ile
245 250 255

Phe Pro Pro Lys Pro Lys Asp Val Leu Thr Ile Thr Leu Thr Pro Lys
260 265 270

Val Thr Cys Val Val Val Asp Ile Ser Lys Asp Asp Pro Glu Val Gln
275 280 285

Phe Ser Trp Phe Val Asp Asp Val Glu Val His Thr Ala Gln Thr Gln
290 295 300

Pro Arg Glu Glu Gln Phe Asn Ser Thr Phe Arg Ser Val Ser Glu Leu
305 310 315 320

Pro Ile Met His Gln Asp Trp Leu Asn Gly Lys Glu Phe Lys Cys Arg
325 330 335

Val Asn Ser Ala Ala Phe Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys
340 345 350

Thr Lys Gly Arg Pro Lys Ala Pro Gln Val Tyr Thr Ile Pro Pro Pro
355 360 365

Lys Glu Gln Met Ala Lys Asp Lys Val Ser Leu Thr Cys Met Ile Thr
370 375 380

Asp Phe Phe Pro Glu Asp Ile Thr Val Glu Trp Gln Trp Asn Gly Gln
385 390 395 400

Pro Ala Glu Asn Tyr Lys Asn Thr Gln Pro Ile Met Asp Thr Asp Gly
405 410 415

Ser Tyr Phe Ile Tyr Ser Lys Leu Asn Val Gln Lys Ser Asn Trp Glu
420 425 430

Ala Gly Asn Thr Phe Thr Cys Ser Val Leu His Glu Gly Leu His Asn
435 440 445

His His Thr Glu Lys Ser Leu Ser His Ser Pro Gly Lys
450 455 460

<210> 363
<211> 1386
<212> DNA
<213> 小家鼠

<400> 363
atgggatgga gctctatcat cctcttcttg gtagcaacag ctacaggtgt ccactcccag

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gtccaactac agcagcctgg gactgagctg gtgaggcctg gaacttcagt gaagttgtcc 120
tgtaaggctt ctggctacat cltcaccacc tactggatga acitgggtgaa acagaggcct 180
ggacaaggcc ttgagtggat tggcatgatt catccttccg caagtgaat taggttggat 240
cagaaattca aggacaaggc cacattgact cttgacaaat cctccagcac agccttatatg 300
cacctcagcg gcccacatc tgtggattct gcggtctatt actgtgcaag atcaggggaa 360
tgggggtcta tggactactg gggicaagga acctcagtca cgtctcctc agccaaaacg 420
acacccccat ctgtctatcc actggccctt ggatctgtg cccaaactaa ctccatggtg 480
accctgggat gcctgggtcaa gggctatttc cctgagccag tgacagtgc ctggaactct 540
ggatccctgt ccagcgggtg gcacaccttc ccagctgtcc tgcagtctga cctctacact 600
ctgagcagct cagtactgt cccctccagc acctggccca gcgagaccgt cacttgcaac 660
gttgcccacc cggccagcag caccaagggt gacaagaaaa ttgtgccag ggattgtgtt 720
tgtaagcctt gcatagttac agtccagaa gtatcatctg tcttcactt cccccaaag 780
ccaaggatg tgctcacat tactctgact cctaaggta cgtgtgtgt ggtagacatc 840
agcaaggatg atcccaggt ccagttcagc tggttttag atgatgtga ggtgcacaca 900
gtcagacgc aaccccgga ggagcagttc aacagcactt tccgctcagt cagtgaactt 960
cccatcatgc accaggactg gctcaatggc aaggagtta aatgcagggt caacagtga 1020
gttttcctg ccccatcga gaaaaccatc tccaaaacca aaggcagacc gaaggctcca 1080
caggtgtaca ccattccacc tccaaggag cagatggcca aggataaagt cagtctgacc 1140
tgcatgataa cagacttctt cctgaagac attactgtg agtggcagt gaatgggcag 1200
ccagcggaga actacaagaa cctcagccc atcatggaca cagatggctc ttacttcac 1260
tacagcaagc tcaatgtgca gaagagcaac tgggaggcag gaaatactt cacctgctct 1320
gtgttacatg agggcctgca caaccacat actgagaaga gcctctccca ctctcctgtt 1380
aatga 1386

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<210> 364
 <211> 106
 <212> PRT
 <213> 小家鼠

<400> 364

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Ile Ser Ser Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Ser Thr Ser Arg Leu Asn Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Asp Ile Lys His Pro Thr
85 90 95

Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105

<210> 365
<211> 318
<212> DNA
<213> 小家鼠

<400> 365
gacatccaga tgacccagtc tccatcctcc ctgtctgcat ctgtaggtga ccgtgtcacc 60
atcacttgcc gcgcaagtca ggatattagc agctatttaa attggtatca gcagaaacca 120
gggaaagccc ctaagctcct gatctattct acttcccggt tgaatagtgg ggtcccatca 180
cgcttcagtg gcagtggctc tgggacagat ttactctca ccatcagcag tctgcaacct 240
gaagattttg caacttacta ctgtcaacag gatattaaac accctacgtt cgggtcaaggc 300
accaaggtgg agatcaaa 318

<210> 366
<211> 120
<212> PRT
<213> 小家鼠

<400> 366

Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Phe Thr Phe Thr Asp Tyr
20 25 30

Ile Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

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

Lys Gly Arg Val Thr Ile Thr Ala Asp Lys Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Ser Ile Tyr Tyr Tyr Asp Ala Pro Phe Ala Tyr Trp Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 367
<211> 360
<212> DNA
<213> 小家鼠

<400> 367
gagggtgcagc tgggtgcagtc tggggctgag gtgaagaagc ctgggtcctc ggtgaaggtc 60
tcctgcaagg ctcttggttt taccttcacc gactatatta tgcactgggt gcgtcaggcc 120

ccitggtcaag ggcttgagtg gatgggctat atcaaccctt ataatgatga caccgaatac 180
aacgagaagt tcaagggccg tgtcacgatt accgcggaca aatccacgag cacagcctac 240
atggagctga gcagccitcg ctctgaggac acggccgtgt attactgtgc gcgttcgatt 300
tattactacg atgccccgtt tgccttacitgg ggccaaggga ctctggtcac cgtctctagt 360

<210> 368
<211> 108
<212> PRT
<213> 小家鼠

<400> 368

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Lys Ala Ser Gln Asp Val Phe Thr Ala
20 25 30

Val Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Trp Ala Ser Thr Arg His Thr Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Ser Ser Tyr Pro Leu
85 90 95

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 369
<211> 324
<212> DNA
<213> 小家鼠

<400> 369

gatatccaga tgaccagag cccgagcagc ctgagcgcca gcgtgggcca tcgctgacc 60
attacctgca aagcgagcca ggatgtgttt accgcggtgg cgtgglatca gcagaaaccg 120
ggcaaagcgc cgaactgct gatttattgg gcgagcaccg gccataccgg cgtgccgagt 180
cgcttttagcg gcagcggcag cggcaccgat ttaccctga ccattagcag cctgcagccg 240
gaagattttg cgacctatta ttgccagcag tatagcagct atccgctgac ctttggcggc 300
ggcaccaaaag tggaaattaa acgt 324

<210> 370
<211> 119
<212> PRT
<213> 小家鼠

<400> 370

Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Phe Asn Ile Lys Asp Tyr
20 25 30
Tyr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45
Gly Arg Ile Asp Pro Glu Asn Gly Asp Ile Ile Tyr Asp Pro Lys Phe
50 55 60
Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
65 70 75 80
Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95
Ala Tyr Asp Ala Gly Asp Pro Ala Trp Phe Thr Tyr Trp Gly Gln Gly
100 105 110
Thr Leu Val Thr Val Ser Ser
115

<210> 371
<211> 357
<212> DNA
<213> 小家鼠

<400> 371
gaagtgcagc tgggtgcagag cggcgcgga gtaaaaaac cgggcgcgag cgtgaaagtg 60
agctgcaaag cgagcggtt taacattaaa gattattata tgcattgggt gcgccaggcg 120
ccgggccagg gcctggaatg gatcgccgc attgatccg aaaacggcga tattatttat 180
gatccgaaat ttcagggccg cgtgacctg accaccgata ccagcaccag caccgcgtat 240
atggaactgc gcagcctgcg cagcgatgat accgcggtgt attattgcgc gtatgatgcg 300
ggcgatccgg cgtggtttac ctattggggc cagggcaccc tggtgaccgt ctcgagc 357

<210> 372
<211> 108
<212> PRT
<213> 小家鼠

<400> 372
Asp Ile Gln Leu Thr Gln Ser Pro Ser Phe Leu Ser Ala Ser Val Gly
1 5 10 15
Asp Arg Val Thr Ile Thr Cys Ser Val Ser Ser Ser Ile Ser Ser Ser
20 25 30
Asn Leu His Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu
35 40 45
Ile Tyr Gly Thr Ser Asn Leu Ala Ser Gly Val Pro Ser Arg Phe Ser
50 55 60
Gly Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln
65 70 75 80
Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Trp Thr Thr Thr Tyr

85

90

95

Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Arg
100 105

<210> 373
<211> 324
<212> DNA
<213> 小家鼠

<400> 373
gatattcagc tgaccagag cccgagcttt ctgagcgca gcgtggcgca tcgctgacc 60
attacctgca gcgtgagcag cagcattagc agcagcaacc tgcattggta tcagcagaaa 120
ccgggcaaaag cgccgaaact gctgatttat ggcaccagca acctggcgag cggcgtgccg 180
agccgcttta gggcgagcgg cagcggcacc gaatttacc tgaccattag cagcctgcag 240
ccggaagatt ttgcgacctt ttattgccag cagtggacca ccacctatac ctttggccag 300
ggcaccaaac tggaaattaa acgt 324

<210> 374
<211> 122
<212> PRT
<213> 小家鼠

<400> 374

Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Phe Asn Ile Lys Asp Tyr
20 25 30

Tyr Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

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

Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Glu Gly Leu Asp Tyr Gly Asp Tyr Tyr Ala Val Asp Tyr Trp
100 105 110

Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 375
<211> 366
<212> DNA
<213> 小家鼠

<400> 375
gaagtgcagc tgggtcagag cggcgcgga gtaaaaaac cggcgcgag cgtgaaagtg 60
agctgcaaag cgagcggctt taacattaaa gattattata ttcattgggt gcgccaggcg 120

ccgggccagg gcctggaatg gatgggcccgc attgatccgg ataacggcga aagcacctat 180
gtgccgaaat ttcagggccg cgtgaccatg accaccgata ccagcaccag caccgcgtat 240
atggaactgc gcagcctgcg cagcgatgat accgcggtgt attattgcgc gcgcgaaggc 300
ctggattatg gcgattatta tgcggtggat tattggggcc agggcaccct ggtgaccgtc 360
tcgagc 366

<210> 376
<211> 107
<212> PRT
<213> 小家鼠

<400> 376

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Ile Ser Asn Tyr
20 25 30
Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45
Tyr Tyr Thr Ser Arg Leu Leu Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60
Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80
Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Gly Asp Thr Leu Pro Tyr
85 90 95
Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105

<210> 377
<211> 321
<212> DNA
<213> 小家鼠

<400> 377
gacatccaga tgaccagtc tccatcctcc ctctccgcat ccgtaggcga ccgcgtaacc 60
ataacatgta gagcatctca agatatctcc aactatttga attggtacca acaaaaaccc 120
ggcaaagcac ctaaactcct catttactat acatcaagac tcctctccgg cgttccatca 180
cgattctcag gctccggctc cggcacagat ttcacactca ctatttcctc cctccaacca 240
gaagattitg caacctatta ctgtcaacaa ggcgatacac tcccatacac attcggcggc 300
ggcacaaaag ttgaaattaa a 321

<210> 378
<211> 123
<212> PRT
<213> 小家鼠

<400> 378

Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Tyr
20 25 30

Asn Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

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

Lys Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Leu Gly Tyr Asp Asp Ile Tyr Asp Asp Trp Tyr Phe Asp Val
100 105 110

Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 379
<211> 369
<212> DNA
<213> 小家鼠

<400> 379
gaggtgcagc tgggtgcagag cggcgccgag gtaaaaaaac caggagcaag cgtaaagtt 60
tcttgtaaag caagcggata tacatttaca gattacaaca tgcattgggt aagacaagcg 120
ccaggacaag gattggaatg gatggcgcaa attaaccta atagtggagg agcaggctac 180
aatcaaaaat tcaaaggag agttacaatg acaacagaca caagcacttc aacagcatat 240
atggaactgc gatcacttag aagcgacgat acagctgtat actattgcgc acgactiggg 300
tatgatgata tatatgatga ctggtatttc gatgtttggg gccagggaac aacagtiacc 360
gtctctagt 369

<210> 380
<211> 108
<212> PRT
<213> 小家鼠

<400> 380

Asp Ile Gln Leu Thr Gln Ser Pro Ser Phe Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Ser Ser Val Thr Ser Ser
20 25 30

Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu
35 40 45

Ile Tyr Ser Thr Ser Asn Leu Ala Ser Gly Val Pro Ser Arg Phe Ser
50 55 60

Gly Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln
65 70 75 80

Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Asp Phe Phe Pro
85 90 95

Ser Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105

<210> 381
<211> 324
<212> DNA
<213> 小家鼠

<400> 381
gacatccagc tgaccagag cccagcttc cttccgcat ccgttggga ccgagtaaca 60
atcacatgcc gcgcctcatc ttcagttaca tcttcttata ttaattggta tcaacaaaaa 120
ccaggaaaag cacctaaact tcttatatac tctacatcta atctcgcatc aggagttccc 180
tctcgatttt caggatcigg atcaggcaca gaatttacac ttactatata atcaactcaa 240
ccagaagact tcgccactta ttactgcaa caatacgatt tttttccaag cacattcgga 300
ggaggtacaa aagtagaat caag 324

<210> 382
<211> 121
<212> PRT
<213> 小家鼠

<400> 382

Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Tyr
20 25 30

Tyr Met Asn Trp Val Arg Gln Ala Pro Gly Gln Arg Leu Glu Trp Met
35 40 45

Gly Asp Ile Asn Pro Tyr Asn Asp Asp Thr Thr Tyr Asn His Lys Phe
50 55 60

Lys Gly Arg Val Thr Ile Thr Arg Asp Thr Ser Ala Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Glu Thr Ala Val Ile Thr Thr Asn Ala Met Asp Tyr Trp Gly
100 105 110

Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 383
<211> 363
<212> DNA
<213> 小家鼠

<400> 383
gagggtgcagc tggtgcagag cggcgccgag gtcaagaaac ctggagcaag cgtaaagggt 60

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agttgcaaag catctggata cacatttacc gactactaca tgaattgggt acgacaagcc 120
cctggacaaa gacttgaatg gatgggagac attaacccctt ataacgacga cactacatac 180
aatcataaat ttaaaggaag agttacaatt acaagagata catccgcac aaccgcctat 240
atggaacttt cctcattgag atctgaagac actgctgttt attactgtgc aagagaaact 300
gccgttatta ctactaacgc tatggattac tggggicaag gaaccactgt taccgtctct 360
agt 363

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<210> 384
 <211> 108
 <212> PRT
 <213> 小家鼠

<400> 384

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
 1 5 10 15

Asp Arg Val Thr Ile Thr Cys Ser Val Ser Ser Thr Ile Ser Ser Asn
 20 25 30

His Leu His Trp Phe Gln Gln Lys Pro Gly Lys Ala Pro Lys Ser Leu
 35 40 45

Ile Tyr Gly Thr Ser Asn Leu Ala Ser Gly Val Pro Ser Arg Phe Ser
 50 55 60

Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln
 65 70 75 80

Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Tyr Pro
 85 90 95

Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
 100 105

<210> 385
 <211> 324
 <212> DNA
 <213> 小家鼠

<400> 385

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gacatccaga tgacccagtc tccatcctcc ctctcagcat ccgtaggcga tagagttaca 60
ataacatgca gcgtatcatc aactatatca tcaaatcatc ttcatgtggtt ccaacagaaa 120
cccggcaaag cacctaaatc acttatatac ggcacatcaa atctcgcac aggcgttcct 180
tcaagatttt caggctctgg ctccaggcacc gactttactc ttacaatac ctccctccaa 240
cccgaagact tcgcaacctt ttactgtcaa caatggctcct catatccact cacatttggc 300
ggcggcacaa aagtagaaat taaa 324

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<210> 386
 <211> 125
 <212> PRT
 <213> 小家鼠

<400> 386

Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15
Ser Val Lys Val Ser Cys Lys Ala Ser Asp Phe Asn Ile Lys Asp Phe
20 25 30
Tyr Leu His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45
Gly Arg Ile Asp Pro Glu Asn Gly Asp Thr Leu Tyr Asp Pro Lys Phe
50 55 60
Gln Asp Lys Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
65 70 75 80
Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95
Ala Arg Glu Ala Asp Tyr Phe His Asp Gly Thr Ser Tyr Trp Tyr Phe
100 105 110
Asp Val Trp Gly Arg Gly Thr Leu Val Thr Val Ser Ser
115 120 125

<210> 387
<211> 375
<212> DNA
<213> 小家鼠

<400> 387
gagggtgcagc tgggtgcagtc tggggctgag gtgaagaagc ctggggcctc agtgaaggtc 60
tcctgcaagg cttctgactt caacattaaa gacttctatc tacactgggt gcgacaggcc 120
cctggacaag ggcttgagtg gattggaagg atigatcctg agaatgggtga tactttatat 180
gacccgaagt tccaggacaa ggtcaccaatg accacagaca cgtccaccag cacagcctac 240
atggagctga ggagcctgag atctgacgac acggccgtgt attactgtgc gagagaggcg 300
gattatttcc acgatggtac ctctactgg tacttcgatg tctggggccg tggcacccctg 360
gtcacctgtct ctagt 375

<210> 388
<211> 106
<212> PRT
<213> 小家鼠

<400> 388
Asp Ile Gln Leu Thr Gln Ser Pro Ser Phe Leu Ser Ala Ser Val Gly
1 5 10 15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Ser Ser Ile Ser Tyr Ile
20 25 30
His Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr
35 40 45
Ala Thr Ser Asn Leu Ala Ser Gly Val Pro Ser Arg Phe Ser Gly Ser
50 55 60

Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu
65 70 75 80

Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asp Pro Leu Thr
85 90 95

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105

<210> 389
<211> 318
<212> DNA
<213> 小家鼠

<400> 389
gacatccagt tgaccagtc tccatccttc ctgtctgcat ctgtaggaga cagagtcacc 60
atcacttgca gggccagctc aagataagt tacatacact ggtatcagca aaaaccaggg 120
aaagccccta agctcctgat ctatgccaca tccaacctgg ctctgggggt cccatcaagg 180
ttcagcggca gtggatctgg gacagaattc acttcacaa tcagcagcct gcagcctgaa 240
gattttgcaa ctattactg tcagcagtgg agtagtgacc cactcacgtt cggcggaggg 300
accaagggtg agatcaaa 318

<210> 390
<211> 121
<212> PRT
<213> 小家鼠

<400> 390

Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Phe Asp Ile Lys Asp Tyr
20 25 30

Tyr Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Arg Val Asp Pro Asp Asn Gly Glu Thr Glu Phe Ala Pro Lys Phe
50 55 60

Pro Gly Lys Val Thr Met Thr Thr Asp Thr Ser Ile Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Glu Asp Tyr Asp Gly Thr Tyr Thr Trp Phe Pro Tyr Trp Gly
100 105 110

Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 391
<211> 363
<212> DNA
<213> 小家鼠

<400> 391
gagggtgcagc tggtgcagtc tggggctgag gtgaagaagc ctggggcctc agtgaaggtc 60
tcctgcaagg ctctctggatt cgacattaag gactactata tacactgggt gcgacaggcc 120
cctggacaag ggcttgagtg gatcggaagg gtgatcctg acaatggta gactgaattt 180
gccccgaagt tccccggcaa ggtcaccaig accacagaca cgtccatcag cacagcctac 240
atggagctga gcaggctgag atctgacgac acggccgtgt attactgtgc gagagaagac 300
tacgatggta cctacacctg gtttccctat lggggccaag ggactctggt caccgtctct 360
agt 363

<210> 392
<211> 448
<212> PRT
<213> 人工序列

<220>
<223> 合成多肽

<220>
<221> MISC_FEATURE
<223> 人化抗体序列

<400> 392
Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Tyr
20 25 30
Asn Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45
Gly Glu Ile Asn Pro Asn Ser Gly Gly Ala Gly Tyr Asn Gln Lys Phe
50 55 60
Lys Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
65 70 75 80
Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95
Ala Arg Leu Gly Tyr Asp Asp Ile Tyr Asp Asp Trp Tyr Phe Asp Val
100 105 110
Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly
115 120 125
Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser
130 135 140
Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val
145 150 155 160
Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe
165 170 175

Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val
180 185 190

Thr Val Pro Ser Ser Asn Phe Gly Thr Gln Thr Tyr Thr Cys Asn Val
195 200 205

Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys Thr Val Glu Arg Lys
210 215 220

Cys Cys Val Glu Cys Pro Pro Cys Pro Ala Pro Pro Val Ala Gly Pro
225 230 235 240

Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser
245 250 255

Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp
260 265 270

Pro Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
275 280 285

Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Phe Arg Val
290 295 300

Val Ser Val Leu Thr Val Val His Gln Asp Trp Leu Asn Gly Lys Glu
305 310 315 320

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

Thr Ile Ser Lys Thr Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr
340 345 350

Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr
355 360 365

Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu
370 375 380

Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Met Leu
385 390 395 400

Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys
405 410 415

Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu
420 425 430

Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
435 440 445

<210> 393
<211> 446
<212> PRT
<213> 人工序列

<220>

<223> 合成多肽

<220>

<221> MISC_FEATURE

<223> 人化抗体序列

<400> 393

Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Tyr
20 25 30

Tyr Met Asn Trp Val Arg Gln Ala Pro Gly Gln Arg Leu Glu Trp Met
35 40 45

Gly Asp Ile Asn Pro Tyr Asn Asp Asp Thr Thr Tyr Asn His Lys Phe
50 55 60

Lys Gly Arg Val Thr Ile Thr Arg Asp Thr Ser Ala Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Glu Thr Ala Val Ile Thr Thr Asn Ala Met Asp Tyr Trp Gly
100 105 110

Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser
115 120 125

Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser Thr Ala
130 135 140

Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val
145 150 155 160

Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala
165 170 175

Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val
180 185 190

Pro Ser Ser Asn Phe Gly Thr Gln Thr Tyr Thr Cys Asn Val Asp His
195 200 205

Lys Pro Ser Asn Thr Lys Val Asp Lys Thr Val Glu Arg Lys Cys Cys
210 215 220

Val Glu Cys Pro Pro Cys Pro Ala Pro Pro Val Ala Gly Pro Ser Val
225 230 235 240

Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr
245 250 255

Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu
260 265 270

Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys
275 280 285

Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Phe Arg Val Val Ser
290 295 300

Val Leu Thr Val Val His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys
305 310 315 320

Cys Lys Val Ser Asn Lys Gly Leu Pro Ala Pro Ile Glu Lys Thr Ile
325 330 335

Ser Lys Thr Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro
340 345 350

Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu
355 360 365

Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn
370 375 380

Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Met Leu Asp Ser
385 390 395 400

Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg
405 410 415

Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu
420 425 430

His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
435 440 445

<210> 394
<211> 450
<212> PRT
<213> 人工序列

<220>
<223> 合成多肽

<220>
<221> MISC_FEATURE
<223> 人化抗体序列

<400> 394

Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Asp Phe Asn Ile Lys Asp Phe
20 25 30

Tyr Leu His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

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

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

Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Glu Ala Asp Tyr Phe His Asp Gly Thr Ser Tyr Trp Tyr Phe
100 105 110

Asp Val Trp Gly Arg Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr
115 120 125

Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser
130 135 140

Glu Ser Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu
145 150 155 160

Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His
165 170 175

Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser
180 185 190

Val Val Thr Val Pro Ser Ser Asn Phe Gly Thr Gln Thr Tyr Thr Cys
195 200 205

Asn Val Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys Thr Val Glu
210 215 220

Arg Lys Cys Cys Val Glu Cys Pro Pro Cys Pro Ala Pro Pro Val Ala
225 230 235 240

Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
245 250 255

Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
260 265 270

Glu Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val
275 280 285

His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Phe
290 295 300

Arg Val Val Ser Val Leu Thr Val Val His Gln Asp Trp Leu Asn Gly
305 310 315 320

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

Glu Lys Thr Ile Ser Lys Thr Lys Gly Gln Pro Arg Glu Pro Gln Val
340 345 350

Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser

355	360	365
Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu		
370	375	380
Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro		
385	390	395
Met Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val		
405	410	415
Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met		
420	425	430
His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser		
435	440	445
Pro Gly		
450		
<210> 395		
<211> 446		
<212> PRT		
<213> 人工序列		
<220>		
<223> 合成多肽		
<220>		
<221> MISC_FEATURE		
<223> 人化抗体序列		
<400> 395		
Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala		
1	5	10
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Phe Asp Ile Lys Asp Tyr		
20	25	30
Tyr Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile		
35	40	45
Gly Arg Val Asp Pro Asp Asn Gly Glu Thr Glu Phe Ala Pro Lys Phe		
50	55	60
Pro Gly Lys Val Thr Met Thr Thr Asp Thr Ser Ile Ser Thr Ala Tyr		
65	70	75
Met Glu Leu Ser Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys		
85	90	95
Ala Arg Glu Asp Tyr Asp Gly Thr Tyr Thr Trp Phe Pro Tyr Trp Gly		
100	105	110
Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser		
115	120	125
Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser Thr Ala		

130	135	140
Ala Leu Gly Cys Leu Val 145	Lys Asp Tyr Phe 150	Pro Glu Pro Val Thr Val 155
Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala 165	170	175
Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val 180	185	190
Pro Ser Ser Asn Phe Gly Thr Gln Thr Tyr Thr Cys Asn Val Asp His 195	200	205
Lys Pro Ser Asn Thr Lys Val Asp Lys Thr Val Glu Arg Lys Cys Cys 210	215	220
Val Glu Cys Pro Pro Cys Pro Ala Pro Pro Val Ala Gly Pro Ser Val 225	230	235
Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr 245	250	255
Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu 260	265	270
Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys 275	280	285
Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Phe Arg Val Val Ser 290	295	300
Val Leu Thr Val Val His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys 305	310	315
Cys Lys Val Ser Asn Lys Gly Leu Pro Ala Pro Ile Glu Lys Thr Ile 325	330	335
Ser Lys Thr Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro 340	345	350
Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu 355	360	365
Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn 370	375	380
Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Met Leu Asp Ser 385	390	395
Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg 405	410	415
Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu 420	425	430

His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
435 440 445

<210> 396
<211> 445
<212> PRT
<213> 人工序列

<220>
<223> 合成多肽

<220>
<221> MISC_FEATURE
<223> 人化抗体序列

<400> 396

Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Phe Thr Phe Thr Asp Tyr
20 25 30

Ile Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

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

Lys Gly Arg Val Thr Ile Thr Ala Asp Lys Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Ser Ile Tyr Tyr Tyr Asp Ala Pro Phe Ala Tyr Trp Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val
115 120 125

Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser Thr Ala Ala
130 135 140

Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser
145 150 155 160

Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val
165 170 175

Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro
180 185 190

Ser Ser Asn Phe Gly Thr Gln Thr Tyr Thr Cys Asn Val Asp His Lys
195 200 205

Pro Ser Asn Thr Lys Val Asp Lys Thr Val Glu Arg Lys Cys Cys Val
210 215 220

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

五、中文發明摘要：

本發明係有關一種抑制骨再吸收之方法。該方法包含向人類投與使骨再吸收標記之含量減少之量的骨硬化素(sclerostin)抑制劑達至少2週。本發明亦提供一種監測抗骨硬化素療法之方法，該方法包含量測一或多種骨再吸收標記之含量，投與骨硬化素結合劑，隨後量測該等骨再吸收標記之含量。亦提供一種增加骨礦物質密度之方法；一種改善蝕骨細胞相關病症之影響之方法；一種藉由維持骨密度治療骨相關病症之方法；及一種治療患有低鈣血症或高鈣血症或處於患低鈣血症或高鈣血症風險中之人類、忌用副甲狀腺素或其類似物治療之人類或忌用雙膦酸鹽治療之人類的骨相關病症之方法。

六、英文發明摘要：

The invention is directed to a method of inhibiting bone resorption. The method comprises administering to a human an amount of sclerostin inhibitor that reduces a bone resorption marker level for at least 2 weeks. The invention also provides a method of monitoring anti-sclerostin therapy comprising measuring one or more bone resorption marker levels, administering a sclerostin binding agent, then measuring the bone resorption marker levels. Also provided is a method of increasing bone mineral density; a method of ameliorating the effects of an osteoclast-related disorder; a method of treating a bone-related disorder by maintaining bone density; and a method of treating a bone-related disorder in a human suffering from or at risk of hypocalcemia or hypercalcemia, a human in which treatment with a parathyroid hormone or analog thereof is contraindicated, or a human in which treatment with a bisphosphonate is contraindicated.

七、指定代表圖：

(一)本案指定代表圖為：第 (5) 圖。

(二)本代表圖之元件符號簡單說明：

(無元件符號說明)

八、本案若有化學式時，請揭示最能顯示發明特徵的化學式：

(無)

十、申請專利範圍：

1. 一種對 SEQ ID NO: 1 之骨硬化素展現小於或等於 1×10^{-9} M 之結合親和力之抗-骨硬化素抗體或其片段之用途，其係用於製備以約 70 mg 至約 450 mg 之量抑制骨再吸收之藥物。
2. 一種對 SEQ ID NO: 1 之骨硬化素展現小於或等於 1×10^{-9} M 之結合親和力之抗-骨硬化素抗體或其片段之用途，其係用於製備以約 70 mg 至約 450 mg 之量投與患有骨相關病症或處於患骨相關病症之風險中之人類之藥物。
3. 一種對 SEQ ID NO: 1 之骨硬化素展現小於或等於 1×10^{-9} M 之結合親和力之抗-骨硬化素抗體或其片段之用途，其係用於製備以約 70 mg 至約 450 mg 之量增加骨礦物質密度之藥物。
4. 一種對 SEQ ID NO: 1 之骨硬化素展現小於或等於 1×10^{-9} M 之結合親和力之抗-骨硬化素抗體或其片段之用途，其係用於製備治療骨相關病症之藥物，該藥物係以約 70 mg 至約 450 mg 之量治療第一段時間，接著以約 70 mg 至約 450 mg 之量治療第二段時間，以有效維持骨礦物質密度。
5. 如請求項 4 之用途，其中該第一段時間為 3 個月或更短。
6. 如請求項 4 或 5 之用途，其中該第二段時間為至少 6 個月。
7. 如請求項 1 及 3 至 5 之用途，其中該個體為人類。
8. 一種對 SEQ ID NO: 1 之骨硬化素展現小於或等於 1×10^{-9}

M之結合親和力之抗-骨硬化素抗體或其片段之用途，其係用於製備以約70 mg至約450 mg之量治療患有低鈣血症或高鈣血症或處於患低鈣血症或高鈣血症之風險中之人類的骨相關病症之藥物。

9. 如請求項8之用途，其中該低鈣血症或該高鈣血症係由慢性腎病、腎衰竭、原發性或繼發性副甲狀腺功能亢進、假副甲狀腺功能亢進、副甲狀腺功能減退、假副甲狀腺功能減退、鎂耗盡、重度高鎂血症、維生素D缺乏、高磷酸鹽血症、急性胰炎、骨饑餓症候群、螯合作用、成骨細胞轉移、膿毒病、手術、化學療法、瘤形成症候群、副甲狀腺功能減退、家族性低尿鈣高鈣血症、肉狀瘤病、肺結核、鉍中毒症、組織漿菌病、念珠菌病、球黴菌病、組織細胞增多病X、霍奇金氏或非霍奇金氏淋巴瘤(Hodgkin's or Non-Hodgkin's lymphoma)、克羅恩氏病(Crohn's disease)、韋格納肉牙腫病(Wegener's granulomatosis)、肺炎、聚矽氧誘發之肉芽瘤、噻嗪(thiazide)利尿劑或鋰之投與或行動不便引起。
10. 一種對SEQ ID NO: 1之骨硬化素展現小於或等於 1×10^{-9} M之結合親和力之抗-骨硬化素抗體或其片段之用途，其係用於製備治療(a)忌用副甲狀腺素或其類似物治療之人類或(b)忌用雙膦酸鹽治療之人類之骨相關病症的藥物。
11. 如請求項2、4、5及8中任一項之用途，其中該骨相關病症係選自由以下組成之群：軟骨發育不全、鎖骨顱骨發育不全、內生性軟骨瘤、纖維結構不良、高雪氏病

(Gaucher's Disease)、低磷酸鹽性佝僂病、馬凡氏症候群 (Marfan's syndrome)、多發性遺傳性外生骨疣、神經纖維瘤、成骨不全症、骨硬化病、脆弱性骨硬化、硬化病變、假關節、化膿性骨髓炎、牙周病、抗癲癇藥物誘發之骨流失、原發性和繼發性副甲狀腺功能亢進、家族性副甲狀腺功能亢進症候群、體重減輕誘發之骨流失、男性之骨質疏鬆症、絕經後骨流失、骨關節炎、腎性骨營養不良、浸潤性骨病症、口腔骨流失、頷骨壞死、青少年佩吉特氏病 (juvenile Paget's disease)、肢骨紋狀肥大、代謝性骨病、肥大細胞增多症、鐮刀型細胞貧血/疾病、器官移植相關骨流失、腎移植相關骨流失、全身性紅斑狼瘡、強直性脊椎炎、癲癇症、青少年關節炎皮疹、地中海貧血、黏多醣病、法布瑞疾病 (Fabry Disease)、特納症候群 (Turner Syndrome)、唐氏症候群 (Down Syndrome)、克林費特症候群 (Klinefelter Syndrome)、麻瘋病、佩特茲病 (Perthe's Disease)、青少年特發性脊柱側凸、嬰兒發作之多系統發炎性疾病、韋徹斯特症候群 (Winchester Syndrome)、曼克斯疾病 (Menkes Disease)、威爾遜氏病 (Wilson's Disease)、缺血性骨病 (諸如股骨頭缺血性壞死 (Legg-Calve-Perthes disease)、區域遷移性骨質疏鬆症)、貧血狀態、由類固醇引起之病狀、糖皮質激素誘發之骨流失、肝素誘發之骨流失、骨髓病症、壞血病、營養不良、鈣缺乏症、骨質疏鬆症、骨質減少、酒精中毒、慢性肝病、絕經後狀態、慢性發炎性病狀、類

風濕性關節炎、發炎性腸病、潰瘍性結腸炎、發炎性結腸炎、克羅恩氏病、月經過少、閉經、妊娠、糖尿病、甲狀腺功能亢進、甲狀腺病症、副甲狀腺病症、庫欣氏病(Cushing's disease)、肢端肥大症、性腺功能減退、行動不便或失能、反射性交感神經營養不良症候群、區域性骨質疏鬆症、骨軟化、與關節置換相關之骨流失、HIV相關骨流失、與生長激素損失相關之骨流失、與囊性纖維化相關之骨流失、化學療法相關骨流失、腫瘤誘發之骨流失、癌症相關骨流失、激素去除之骨流失、多發性骨髓瘤、藥物誘發之骨流失、神經性厭食、疾病相關面骨流失、疾病相關顱骨流失、疾病相關頷骨流失、疾病相關顱骨流失、與老化相關之骨流失、與老化相關之面骨流失、與老化相關之顱骨流失、與老化相關之頷骨流失、與老化相關之顱骨流失及與空間飛行相關之骨流失。

12. 如請求項1至5及8至10中任一項之用途，其中該抗-骨硬化素抗體或其片段之量為約70 mg至約210mg。
13. 如請求項1至5及8至10中任一項之用途，其中該抗-骨硬化素抗體或其片段之量為約70 mg。
14. 如請求項1至5及8至10中任一項之用途，其中該抗-骨硬化素抗體或其片段之量為約140 mg。
15. 如請求項1至5及8至10中任一項之用途，其中該抗-骨硬化素抗體或其片段之量為約210 mg。
16. 如請求項1至5及8至10中任一項之用途，其中該抗-骨硬

化素抗體或其片段之量係每兩週投與至該個體一次。

17. 如請求項1至5及8至10中任一項之用途，其中該抗-骨硬化素抗體或其片段之量係每月投與至該個體一次。
18. 如請求項1至5及8至10中任一項之用途，其中該抗-骨硬化素抗體或其片段交叉阻斷以下至少一種抗體與骨硬化素之結合：Ab-A、Ab-B、Ab-C、Ab-D、Ab-1、Ab-2、Ab-3、Ab-4、Ab-5、Ab-6、Ab-7、Ab-8、Ab-9、Ab-10、Ab-11、Ab-12、Ab-13、Ab-14、Ab-15、Ab-16、Ab-17、Ab-18、Ab-19、Ab-20、Ab-21、Ab-22、Ab-23及Ab-24。
19. 如請求項1至5及8至10中任一項之用途，其中該抗-骨硬化素抗體或其片段與骨硬化素之結合係受到以下至少一種抗體交叉阻斷：Ab-A、Ab-B、Ab-C、Ab-D、Ab-1、Ab-2、Ab-3、Ab-4、Ab-5、Ab-6、Ab-7、Ab-8、Ab-9、Ab-10、Ab-11、Ab-12、Ab-13、Ab-14、Ab-15、Ab-16、Ab-17、Ab-18、Ab-19、Ab-20、Ab-21、Ab-22、Ab-23及Ab-24。
20. 如請求項1至5及8至10中任一項之用途，其中該抗-骨硬化素抗體或其片段交叉阻斷包含SEQ ID NO: 209之重鏈及SEQ ID NO: 205之輕鏈之抗體Ab-13與骨硬化素之結合，及/或該抗-骨硬化素抗體或其片段與骨硬化素之結合係受到包含SEQ ID NO: 209之重鏈及SEQ ID NO: 205之輕鏈之抗體Ab-13之交叉阻斷。
21. 如請求項1至5及8至10中任一項之用途，其中該抗體或

其片段包含：a)SEQ ID NO: 54、55及56之CDR序列及SEQ ID NO: 51、52及53之CDR序列；b)SEQ ID NO: 60、61及62之CDR序列及SEQ ID NO: 57、58及59之CDR序列；c)SEQ ID NO: 48、49及50之CDR序列及SEQ ID NO: 45、46及47之CDR序列；d)SEQ ID NO: 42、43及44之CDR序列及SEQ ID NO: 39、40及41之CDR序列；e)SEQ ID NO: 275、276及277之CDR序列及SEQ ID NO: 287、288及289之CDR序列；f)SEQ ID NO: 278、279及280之CDR序列及SEQ ID NO: 290、291及292之CDR序列；g)SEQ ID NO: 78、79及80之CDR序列及SEQ ID NO: 245、246及247之CDR序列；h)SEQ ID NO: 81、99及100之CDR序列及SEQ ID NO: 248、249及250之CDR序列；i)SEQ ID NO: 101、102及103之CDR序列及SEQ ID NO: 251、252及253之CDR序列；j)SEQ ID NO: 104、105及106之CDR序列及SEQ ID NO: 254、255及256之CDR序列；k)SEQ ID NO: 107、108及109之CDR序列及SEQ ID NO: 257、258及259之CDR序列；l)SEQ ID NO: 110、111及112之CDR序列及SEQ ID NO: 260、261及262之CDR序列；m)SEQ ID NO: 281、282及283之CDR序列及SEQ ID NO: 293、294及295之CDR序列；n)SEQ ID NO: 113、114及115之CDR序列及SEQ ID NO: 263、264及265之CDR序列；o)SEQ ID NO: 284、285及286之CDR序列及SEQ ID NO: 296、297及298之CDR序列；p)SEQ ID NO: 116、237及238之CDR序列及SEQ ID NO: 266、267

及 268 之 CDR 序列；q)SEQ ID NO: 239、240 及 241 之 CDR 序列及 SEQ ID NO: 269、270 及 271 之 CDR 序列；r)SEQ ID NO: 242、243 及 244 之 CDR 序列及 SEQ ID NO: 272、273 及 274 之 CDR 序列；或 s)SEQ ID NO: 351、352 及 353 之 CDR 序列及 SEQ ID NO: 358、359 及 360 之 CDR 序列。

22. 如請求項 21 之用途，其中該抗體或其片段包含 CDR-H1、CDR-H2、CDR-H3、CDR-L1、CDR-L2 及 CDR-L3，其中 (a)CDR-H1 為 SEQ ID NO: 245，CDR-H2 為 SEQ ID NO: 246，CDR-H3 為 SEQ ID NO: 247，CDR-L1 為 SEQ ID NO: 78，CDR-L2 為 SEQ ID NO: 79 且 CDR-L3 為 SEQ ID NO: 80；或 (b)CDR-H1 為 SEQ ID NO: 269，CDR-H2 為 SEQ ID NO: 270，CDR-H3 為 SEQ ID NO: 271，CDR-L1 為 SEQ ID NO: 239，CDR-L2 為 SEQ ID NO: 240 且 CDR-L3 為 SEQ ID NO: 241。

23. 如請求項 22 之用途，其中該抗體或其片段包含 CDR-H1、CDR-H2、CDR-H3、CDR-L1、CDR-L2 及 CDR-L3，其中 CDR-H1 為 SEQ ID NO: 245，CDR-H2 為 SEQ ID NO: 246，CDR-H3 為 SEQ ID NO: 247，CDR-L1 為 SEQ ID NO: 78，CDR-L2 為 SEQ ID NO: 79 且 CDR-L3 為 SEQ ID NO: 80。

24. 如請求項 1 至 5 及 8 至 10 中任一項之用途，其中該抗-骨硬化素抗體包含重鏈及輕鏈。

25. 如請求項 23 之用途，其中該抗-骨硬化素抗體包含重鏈及輕鏈。

26. 如請求項1至5及8至10中任一項之用途，其中該抗-骨硬化素抗體為人類抗體、人化抗體、單株抗體或嵌合抗體。
27. 如請求項22之用途，其中該抗-骨硬化素抗體為人化抗體、單株抗體或嵌合抗體。
28. 如請求項25之用途，其中該抗-骨硬化素抗體為人化單株抗體。
29. 一種對SEQ ID NO: 1之骨硬化素展現小於或等於 1×10^{-7} M之結合親和力，且包含SEQ ID NO: 245之CDR-H1，SEQ ID NO: 246之CDR-H2，SEQ ID NO: 247之CDR-H3，SEQ ID NO: 78之CDR-L1為，SEQ ID NO: 79之CDR-L2及SEQ ID NO: 80之CDR-L3；或(b)SEQ ID NO: 269之CDR-H1，SEQ ID NO: 270之CDR-H2，SEQ ID NO: 271之CDR-H3，SEQ ID NO: 239之CDR-L1，SEQ ID NO: 240之CDR-L2及SEQ ID NO: 241之CDR-L3之抗體之用途，其係用於製備以約70 mg、約140 mg或約210mg之量投與患有骨相關病症或處於患骨相關病症之風險中之人類之藥物。
30. 如請求項2、8至10及29中任一項之用途，其中該人類為絕經後女性。
31. 如請求項30之用途，其中該人類患有骨質疏鬆症。
32. 如請求項29之用途，其中該抗體為人類抗體、人化抗體、單株抗體或嵌合抗體。
33. 如請求項29或32之用途，其中該抗體或其片段包含CDR-

H1、CDR-H2、CDR-H3、CDR-L1、CDR-L2及CDR-L3，其中CDR-H1為SEQ ID NO: 245，CDR-H2為SEQ ID NO: 246，CDR-H3為SEQ ID NO: 247，CDR-L1為SEQ ID NO: 78，CDR-L2為SEQ ID NO: 79且CDR-L3為SEQ ID NO: 80。

34. 如請求項32之用途，其中該抗體為人化抗體或嵌合抗體。

35. 如請求項34之用途，其中該抗體或其片段包含CDR-H1、CDR-H2、CDR-H3、CDR-L1、CDR-L2及CDR-L3，其中CDR-H1為SEQ ID NO: 245，CDR-H2為SEQ ID NO: 246，CDR-H3為SEQ ID NO: 247，CDR-L1為SEQ ID NO: 78，CDR-L2為SEQ ID NO: 79且CDR-L3為SEQ ID NO: 80。

36. 一種容器，其包含約70 mg至約450 mg之量的對SEQ ID NO: 1之骨硬化素展現小於或等於 1×10^{-9} M之結合親和力之抗骨硬化素抗體。