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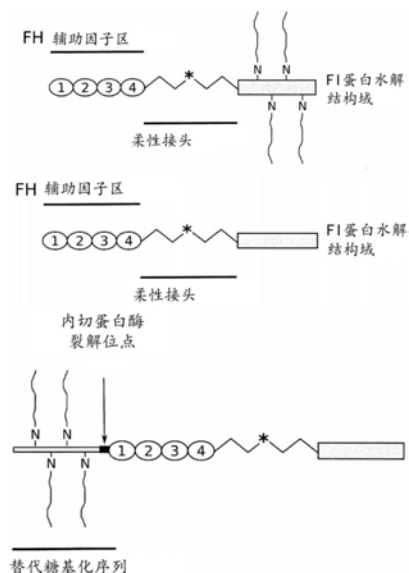
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(54)发明名称

C3b灭活多肽

(57)摘要

公开了包括C3b结合区和C3b灭活区的多肽，以及编码这样的多肽的核酸和载体。还公开的是包括这样的多肽的细胞和组合物，以及使用它们的用途和方法。



1. 一种多肽,其包括C3b结合区和C3b灭活区。
2. 根据权利要求1所述的多肽,其中所述C3b灭活区能够蛋白水解裂解C3b。
3. 根据权利要求1或权利要求2所述的多肽,其中所述C3b灭活区能够在位置1303和/或1320裂解C3 α '链。
4. 根据权利要求1到3中任一项所述的多肽,其中所述C3b灭活区包括与SEQ ID NO:9的氨基酸序列具有至少65%的序列同一性的氨基酸序列,或由其组成。
5. 根据权利要求1到4中任一项所述的多肽,其中所述C3b结合区在由补体因子I的辅助因子结合的区域中结合C3b。
6. 根据权利要求1到5中任一项所述的多肽,其中所述C3b结合区在由补体因子H、CR1、CD46、CD55或C4结合蛋白之一结合的区域中结合C3b。
7. 根据权利要求1到6中任一项所述的多肽,其中所述C3b结合区在由补体因子H结合的区域中、或在由补体受体1 (CR1) 结合的区域中结合C3b。
8. 根据权利要求1到7中任一项所述的多肽,其中所述C3b结合区在由补体因子H补体调控蛋白 (CCP) 结构域1-4结合的区域中、或者在由CR1 CCP结构域8-10或15-17结合的区域中结合C3b。
9. 根据权利要求1到8中任一项所述的多肽,其中所述C3b结合区包括与SEQ ID NO:11、13或14的氨基酸序列具有至少65%的序列同一性的氨基酸序列,或由其组成。
10. 根据权利要求1到9中任一项所述的多肽,其能够扩散跨越布鲁赫膜 (BrM) 。
11. 根据权利要求1到10中任一项所述的多肽,其中所述多肽不是糖基化的。
12. 根据权利要求1到11中任一项所述的多肽,其中所述C3b灭活区缺乏与SEQ ID NO:27的共有序列相符的氨基酸序列。
13. 根据权利要求1到12中任一项所述的多肽,其中所述多肽包括检测序列,其中所述检测序列包括蛋白水解酶的裂解位点或由其组成,并且其中利用所述蛋白水解酶的所述多肽的裂解引起非内源肽的产生。
14. 根据权利要求1到13中任一项所述的多肽,其包括与SEQ ID NO:32、33、34、35、36、37、49、50、51、52、53、54、55、56、57、58、59、60、61、69、70、71、72或73的氨基酸序列具有至少65%的序列同一性的氨基酸序列,或由其组成。
15. 根据权利要求1到14中任一项所述的多肽,其另外包括分泌途径序列。
16. 根据权利要求15所述的多肽,其中所述分泌途径序列包括与SEQ ID NO:27的共有序列相符的氨基酸序列的一个或多个拷贝,并且其中所述多肽另外包括用于除去所述分泌途径序列的裂解位点。
17. 根据权利要求16所述的多肽,其中所述用于除去所述分泌途径序列的裂解位点是弗林内切蛋白酶裂解位点。
18. 一种核酸,其编码根据权利要求1到17中任一项所述的多肽。
19. 一种载体,其包括权利要求18所述的核酸。
20. 一种细胞,其包括根据权利要求1到17中任一项所述的多肽、根据权利要求18所述的核酸、或根据权利要求19所述的载体。
21. 一种生产多肽的方法,其包括向细胞中导入根据权利要求18的核酸或根据权利要求19的载体,以及在适合于表达所述多肽的条件下培养所述细胞。

22. 一种细胞,其是通过根据权利要求21所述的方法所获得的或可获得的。

23. 一种药物组合物,其包括根据权利要求1到17中任一项所述的多肽、根据权利要求18所述的核酸、根据权利要求19所述的载体、或者根据权利要求20或权利要求22所述的细胞,以及药学可接受载体、佐剂、赋形剂或稀释剂。

24. 根据权利要求1到16中任一项所述的多肽、根据权利要求17所述的核酸、根据权利要求18所述的载体、根据权利要求19或权利要求21所述的细胞、或者根据权利要求22所述的药物组合物,其用于治疗或预防疾病或病症的方法中使用。

25. 根据权利要求1到17中任一项所述的多肽、根据权利要求18所述的核酸、根据权利要求19所述的载体、根据权利要求20或权利要求22所述的细胞、或者根据权利要求23所述的药物组合物在制造药物中的用途,所述药物用于治疗或预防疾病或病症。

26. 一种治疗或预防疾病或病症的方法,其包括向受试者施用根据权利要求1到17中任一项所述的多肽、根据权利要求18所述的核酸、根据权利要求19所述的载体、根据权利要求20或权利要求22所述的细胞、或者根据权利要求23所述的药物组合物。

27. 一种治疗或预防受试者中的疾病或病症的方法,其包括修饰所述受试者的至少一个细胞以表达或包括根据权利要求18的核酸或根据权利要求19的载体。

28. 根据权利要求24所述的多肽、核酸、载体、细胞或药物组合物的使用,根据权利要求25所述的用途,或根据权利要求26或根据权利要求27所述的方法,其中所述疾病或病症是其中C3b或含有C3b的复合物、与C3b或含有C3b的复合物相关联的活性/响应、或者与C3b或含有C3b的复合物相关联的活性/响应的产物为病理上牵连的疾病或病症。

29. 根据权利要求24到28中任一项所述的多肽、核酸、载体、细胞或药物组合物的使用、用途或方法,其中所述疾病或病症是年龄相关性黄斑变性 (AMD)。

30. 一种成套的试剂盒,其包括预定量的根据权利要求1到17的任一项所述的多肽、根据权利要求18所述的核酸、根据权利要求19所述的载体、根据权利要求20或权利要求22所述的细胞、或者根据权利要求23所述的药物组合物。

31. 一种检测样品中的多肽的方法,其包括:

(i) 使疑似含有根据权利要求13的多肽的样品,接触特异于所述检测序列的蛋白水解裂解位点的蛋白水解酶;和

(ii) 检测所述非内源肽的存在。

C3b灭活多肽

[0001] 本申请要求于2017年6月9日提交的GB1709222.2的优先权,为了所有目的,其内容和元素通过引用合并在本文中。

发明领域

[0002] 本发明涉及分子生物学、免疫学和药物领域。更具体地,本发明涉及一种多肽,其包括C3b结合区和C3b灭活区;编码所述多肽的核酸和载体;包括所述核酸/载体和/或产生所述多肽的细胞;包括所述多肽/核酸/载体/细胞的组合物;以及所述多肽/核酸/载体/细胞的治疗和预防用途,例如,治疗在其中病理性牵连C3b的疾病/病症。

[0003] 发明背景

[0004] 年龄相关性黄斑变性(age-related macular degeneration,AMD)是发达世界中失明的主要原因:据估计到2020年将有1.96亿人受到影响。疾病的早期阶段的特征在于在黄斑(对中央视敏度(central visual acuity)负责的视网膜的中心部分)中病变(称为脉络膜疣(drusen))的形成。这些脉络膜疣邻近于布鲁赫膜(Bruch's membrane,BrM)形成,布鲁赫膜是将眼睛的血液供应(脉络膜(choroid))与视网膜色素上皮细胞(retinal pigment epithelium,RPE)分开的膜,该视网膜色素上皮细胞支撑视力所必须的视杆细胞和视锥细胞。脉络膜疣引起RPE细胞功能障碍和死亡,随后引起视杆细胞和视锥细胞的死亡。AMD很大程度上是一种遗传疾病,其补体系统的基因中的突变与AMD的增加性风险强烈相关。的确,已经清楚的是,补体系统的过度活化在该疾病的发病机理中具有重要的作用。

[0005] 经由替代途径、标准途径和凝集素途径的补体系统的活化汇聚以形成C3转化酶。由替代途径形成的C3转化酶包括因子Bb和C3b。C3转化酶催化C3蛋白水解成C3a和C3b片段。C3b在表面上(例如,细胞/组织)的沉积启动补体级联的放大环路,最终引起细胞/组织破坏和局部炎症反应(所有这些都是早期AMD的特征)。

[0006] 非细胞结构、例如BrM上补体的活化由补体因子H(factor H,FH)和补体因子I(factor I,FI)来调节。因子I裂解和灭活C3b(iC3b不能与因子Bb组装成功能性C3转化酶),因而妨碍(stopping)补体活化,但是仅可在诸如因子H的辅助因子存在情况下这样做。

[0007] 过去5-10年,已经研究了几种用于AMD的补体类疗法。这些已经包括了将完整补体调节物、例如因子H或截短的因子H同种型FHL-1注射到眼睛中的尝试。使用这样的疗法很少成功,主要因为这些蛋白质不能到达目标区域,即,BrM/RPE细胞界面。

发明内容

[0008] 在一个方面中,本发明提供了一种多肽,其包括C3b结合区和C3b灭活区的多肽。

[0009] 在某些实施方式中,C3b灭活区能够蛋白水解裂解C3b。在某些实施方式中,C3b灭活区能够在位置1303和/或1320处裂解C3 α' 链。在某些实施方式中,C3b灭活区包括与SEQ ID NO:9的氨基酸序列具有至少65%的序列同一性的氨基酸序列,或由其组成。在某些实施方式中,C3b结合区在由补体因子I的辅助因子结合的区域中结合C3b。

[0010] 在某些实施方式中,C3b结合区在由补体因子H、CR1、CD46、CD55或C4-结合蛋白之

一结合的区域中结合C3b。在某些实施方式中,C3b结合区在由补体因子H结合的区域中、或在由补体受体1 (CR1) 结合的区域中结合C3b。在某些实施方式中,C3b结合区在由补体因子H补体调控蛋白 (CCP) 结构域1-4结合的区域中、或者在由CR1 CCP结构域8-10或15-17结合的区域中结合C3b。在某些实施方式中,C3b结合区包括与SEQ ID NO:11、13或14的氨基酸序列具有至少65%的序列同一性的氨基酸序列,或由其组成。

[0011] 在某些实施方式中,多肽能够扩散跨越布鲁赫膜 (BrM)。在某些实施方式中,多肽不是糖基化的。在某些实施方式中,C3b灭活区缺乏与SEQ ID NO:27的共有序列相符的氨基酸序列。

[0012] 在某些实施方式中,多肽包括检测序列,其中该检测序列包括蛋白水解酶的裂解位点或由其组成,并且其中利用蛋白水解酶的多肽的裂解引起非内源肽的产生。

[0013] 在某些实施方式中,多肽包括与SEQ ID NO:32、33、34、35、36、37、49、50、51、52、53、54、55、56、57、58、59、60、61、69、70、71、72或73的氨基酸序列具有至少65%的序列同一性的氨基酸序列,或由其组成。

[0014] 在某些实施方式中,多肽另外包括分泌途径序列。在某些实施方式中,该分泌途径序列包括与SEQ ID NO:27的共有序列相符的氨基酸序列的一个或多个拷贝,并且其中多肽另外包括用于除去分泌途径序列的裂解位点。在某些实施方式中,该用于除去分泌途径序列的裂解位点是内切蛋白酶裂解位点,例如,用于由RPE细胞表达的内切蛋白酶、例如弗林内切蛋白酶 (furin endoprotease) 的裂解位点。

[0015] 在另一个方面中,本发明提供了一种核酸,其编码根据本发明的多肽。

[0016] 在另一个方面中,本发明提供了一种载体,其包括本发明的核酸。

[0017] 在另一个方面中,本发明提供了一种细胞,其包括根据本发明的多肽、核酸或载体。

[0018] 在另一个方面中,本发明提供了一种生产多肽的方法,其包括向细胞中导入根据本发明的核酸或载体,以及在适合于表达多肽的条件下培养该细胞。

[0019] 在另一个方面中,本发明提供了一种细胞,其是通过根据本发明的生产多肽的方法所获得的或可获得的。

[0020] 在另一个方面中,本发明提供了一种药物组合物,其包括根据本发明的多肽、核酸、载体或细胞,以及药学可接受载体、佐剂、赋形剂或稀释剂。

[0021] 在另一个方面中,本发明提供了在治疗或预防疾病或病症的方法中使用的根据本发明的多肽、核酸、载体或药物组合物。

[0022] 在另一个方面中,本发明提供了根据本发明的多肽、核酸、载体或药物组合物在制造药物中的用途,该药物用于治疗或预防疾病或病症。

[0023] 在另一个方面中,本发明提供了一种治疗或预防疾病或病症的方法,其包括向受试者施用根据本发明的所述多肽、核酸、载体或药物组合物。

[0024] 在另一个方面中,本发明提供了一种治疗或预防受试者中的疾病或病症的方法,其包括修饰该受试者的至少一个细胞以表达或包括根据本发明的核酸或载体。

[0025] 在某些实施方式中,根据本发明的各个方面,所述疾病或病症是其中C3b或含有C3b的复合物、与C3b或含有C3b的复合物相关联的活性/响应、或者与C3b或含有C3b的复合物相关联的活性/响应的产物为病理上牵连的疾病或病症。在某些实施方式中,所述疾病或

病症是年龄相关性黄斑变性 (AMD)。

[0026] 在另一个方面中,本发明提供了成套的试剂盒,其包括预定量的根据本发明的多肽、核酸、载体、细胞、或药物组合物。

[0027] 在另一个方面中,本发明提供了一种检测样品中的多肽的方法,其包括:

[0028] (i) 使疑似含有本发明的多肽的样品接触特异于检测序列的蛋白水解裂解位点的蛋白水解酶;和

[0029] (ii) 检测所述非内源肽的存在。

[0030] 说明书

[0031] 本发明涉及一种多肽,其包含C3b结合区和C3b灭活区的多肽。多肽包含补体因子I和补体因子I的辅助因子(例如,如本文描述的,如补体因子H、补体受体1(CR1)等)两者的活性结构域,使得多肽可以将C3b酶促裂解为iC3b而无需第二种蛋白质。重要地,iC3b和它的降解产物C3dg及C3d都是调理素(opsonins),并且是碎片去除(debris removal)的重要介体(mediators)。

[0032] C3和C3b

[0033] 补体成分3(C3)是免疫系统蛋白质,该免疫系统蛋白质在先天免疫和补体系统中具有核心作用。例如,在Foley et al.J Thromb Haemostasis(2015)13:610-618中描述的C3的加工,通过引用以其整体合并在本文中。人C3(通用蛋白资源(Universal Protein Resource,UniProt):P01024;SEQ ID NO:1)包括有1663个氨基酸的序列(包括N-末端22个氨基酸的信号肽)。氨基酸23到667编码C3 β 链(SEQ ID NO:2),且氨基酸749到1663编码C3 α '链(SEQ ID NO:3)。C3 β 链和C3 α '链通过链间的二硫键(形成在C3 β 链的半胱氨酸559与C3 α '链的半胱氨酸816之间)缔合以形成C3b。C3a是77个氨基酸片段,其相应于C3的氨基酸位置672到748(SEQ ID NO:4),由通过标准途径和凝集素途径活化之后的C3的蛋白水解裂解产生。

[0034] C3b是强力调理素,靶向病原体、抗体-抗原免疫复合物和凋亡细胞,用于吞噬细胞和NK细胞的吞噬作用。C3b还涉及用于活化和放大补体反应转化酶酶复合物的形成。C3b与因子B缔合以形成C3bBb型C3转化酶(替代途径),并且可以与C4b和C2a缔合以形成C4b2a3b型C5转化酶(标准途径),或与C3bBb缔合以形成C3bBb3b型C5转化酶(替代途径)。

[0035] C3b可以通过在氨基酸位置1303和1320处 α '链的蛋白水解裂解被加工成不能参与转化酶组装的无活性形式、称为iC3b,以形成 α '链片段1(相应于C3的氨基酸位置749到1303;SEQ ID NO:5)和 α '链片段2(相应于C3的氨基酸位置1321到1663;SEQ ID NO:6),。iC3b包含C3 β 链、C3 α '链片段1和C3 α '链片段2(通过二硫键缔合)。 α '链的裂解还释放C3f,其相应于C3的氨基酸位置1304到1320(SEQ ID NO:7)。

[0036] 本文使用的“C3”是指来自任何物种的C3,并包括来自任何物种的C3的同种型、片段、变体或同源物。在某些实施方式中,所述C3是哺乳动物C3(例如,猕猴、人类和/或啮齿动物(例如,大鼠和/或鼠)C3)。C3的同种型、片段、变体或同源物任选地可以表征为与来自给定物种的不成熟或成熟C3、例如人类C3(SEQ ID NO:1)的氨基酸序列具有至少70%,优选地80%、85%、90%、91%、92%、93%、94%、95%、96%、97%、98%、99%或100%之一的氨基酸序列同一性。

[0037] 本文使用的“C3b”是指并包括来自任何物种的C3b的同种型、片段、变体或同源物。

在某些实施方式中,所述C3b是哺乳动物C3b(例如,猕猴、人类和/或啮齿动物(例如,大鼠和/或鼠)C3b)。

[0038] C3b的同种型、片段、变体或同源物任选地可以表征为包含C3 α '链片段1、C3 α '链片段2和C3 β ,其与来自给定物种、例如人类的相应多肽的氨基酸序列具有至少70%、优选地80%、85%、90%、91%、92%、93%、94%、95%、96%、97%、98%、99%或100%之一的氨基酸序列同一性。也就是说,C3b可以包括:与SEQ ID NO:5具有至少70%、优选地80%、85%、90%、91%、92%、93%、94%、95%、96%、97%、98%、99%或100%之一的氨基酸序列同一性的C3 α '链片段1;与SEQ ID NO:6具有至少70%、优选地80%、85%、90%、91%、92%、93%、94%、95%、96%、97%、98%、99%或100%之一的氨基酸序列同一性的C3 α '链片段2;和与SEQ ID NO:2具有至少70%、优选地80%、85%、90%、91%、92%、93%、94%、95%、96%、97%、98%、99%或100%之一的氨基酸序列同一性的C3 β 链。

[0039] C3b的同种型、片段、变体或同源物任选地可以是功能性同种型、片段、变体或同源物,例如,具有所述参考C3b的功能性质/活性,按照通过由对该功能性质/活性的适当试验来分析而确定的。例如,C3b的同种型、片段、变体或同源物可以以充当调理素起、和/或形成功能性C3/C5转化酶的能力为特征。

[0040] 补体因子I和补体因子I的辅助因子

[0041] 通过补体因子I(在人类中由基因CFI编码)执行C3b到iC3b的加工。人补体因子I(UniProt:P05156;SEQ ID NO:8)具有有583个氨基酸的序列(包括N-末端,18个氨基酸的信号肽)。前体多肽通过弗林蛋白酶裂解以产出成熟的补体因子I,其包括由链间二硫键连接的重链(氨基酸19到335)、和轻链(氨基酸340到583)。轻链的氨基酸340到574编码补体因子I(SEQ ID NO:9)的蛋白水解结构域,其是含有负责裂解C3b以产生iC3b的催化性三联体的丝氨酸蛋白酶(Ekdahl等.,J Immunol(1990)144(11):4269-74)。

[0042] 本文使用的“补体因子I”是指来自任何物种的补体因子I,并包括来自任何物种的补体因子I的同种型、片段、变体或同源物。在某些实施方式中,所述补体因子I是哺乳动物补体因子I(例如,猕猴、人类和/或啮齿动物(例如,大鼠和/或鼠)补体因子I)。

[0043] 补体因子I的同种型、片段、变体或同源物任选地可以表征为与来自给定物种的不成熟或成熟补体因子I、例如人补体因子I(SEQ ID NO:8)的氨基酸序列具有至少70%,优选地80%、85%、90%、91%、92%、93%、94%、95%、96%、97%、98%、99%或100%之一的氨基酸序列同一性。补体因子I的同种型、片段、变体或同源物可以任选地是功能性同种型、片段、变体或同源物,例如,具有所述参考补体因子I(例如,全长人补体因子I)的功能性质/活性,按照通过由对该功能性质/活性的适当试验来分析而确定的。例如,补体因子I的同种型、片段、变体或同源物可以展现丝氨酸蛋白酶活性和/或能够灭活C3b。

[0044] 补体因子I的片段可以是任何长度(根据氨基酸的数量),尽管任选地可以是成熟补体因子I的长度的至少25%,并且可以具有成熟补体因子I的长度的50%、75%、80%、85%、90%、91%、92%、93%、94%、95%、96%、97%、98%或99%之一的最大长度。补体因子I的片段可以具有10个氨基酸的最小长度,以及15、20、25、30、40、50、100、150、200、250、300、350、400、450、500、550或575个氨基酸中的一种的最大长度。

[0045] 在某些实施方式中,补体因子I与SEQ ID NO:8具有至少70%,优选地80%、85%、90%、91%、92%、93%、94%、95%、96%、97%、98%、99%或100%之一的氨基酸序列同一

性。

[0046] 通过补体因子I的辅助因子促进了由补体因子I蛋白水解裂解C3b产生iC3b。补体因子I的辅助因子通常结合C3b和/或补体因子I,并通过补体因子I强化将C3b加工成iC3b。能够充当补体因子I的辅助因子的分子包括补体因子H、补体受体1 (CR1)、CD46、CD55和C4结合蛋白质 (C4BP)、SPICE、牛痘补体酶抑制剂 (Vaccinia Inhibitor of Complement Enzymes, VCP (或VICE)) 和猴痘补体酶抑制剂 (Monkeypox Inhibitor of Complement Enzymes, MOPICE)。

[0047] 例如在Wu等, Nat Immunol (2009) 10 (7):728-733中评述了补体因子H的结构和功能,通过引用以其整体合并在本文中。人补体因子H (UniProt:P08603;SEQ ID NO:10) 具有有1233个氨基酸的序列 (包括N-末端,18个氨基酸的信号肽),且包括~60个氨基酸的20个补体调控蛋白 (complement control protein, CCP) 结构域:CCP1=位置19到82, CCP2=位置83到143, CCP3=位置144到207, CCP4=位置208到264, CCP5=位置265到322, CCP6=位置324到386, CCP7=位置387到444, CCP8=位置446到507, CCP9=位置515到566, CCP10=位置567到625, CCP11=位置628到686, CCP12=位置689到746, CCP13=位置751到805, CCP14=位置809到866, CCP15=位置868到928, CCP16=位置929到986, CCP17=位置987到1045, CCP18=位置1046到1104, CCP19=位置1107到1165, 以及CCP20=位置1170到1230。相应于位置19到264 (SEQ ID NO:11) 的补体因子H的前四个CCP结构域 (即, CCP1到CCP4), 对于C3b到iC3b的裂解的补体因子I辅助因子活性均为必须的且充分的。还已经显示了CCP 19到20与C3b和C3d接合 (Morgan等, Nat Struct Mol Biol (2011) 18 (4):463-470), 而CCP7和CCP19到20结合糖胺聚糖 (glycosaminoglycans, GAG) 和唾液酸, 并且涉及自身与非自身之间的分辨 (Schmidt等, J Immunol (2008) 181 (4):2610-2619; Kajander et al., PNAS (2011) 108 (7):2897-2902)。

[0048] 在例如Khera和Das, Mol Immunol (2009) 46 (5):761-772以及Jacquet等, J Immunol (2013) 190 (7):3721-3731中评述了补体受体1 (CR1) 的结构和功能, 这两篇通过引用以其整体合并在本文中。人CR1 (UniProt:P17927;SEQ ID NO:12) 具有有2039个氨基酸的序列 (包括N-末端,41个氨基酸的信号肽), 并且包含30个补体调控蛋白 (CCP) 结构域, N-末端28个CCP被组织到各包含7个CCP的四个长同源重复 (long homologous repeat, LHR) 结构域中:LHR-A、LHR-B、LHR-C和LHR-D。在LHR-B中的CCP 8-10 (UniProt:P17927位置491到684; SEQ ID NO:13) 中以及LHR-C中的CCP 15-17 (UniProt:P17927位置941到1134; SEQ ID NO:14) 中发现了CR1的C3b结合区。

[0049] 例如在Liszewski和Atkinson, Human Genomics (2015) 9:7以及Liszewski等, J Biol Chem (2000) 275:37692-37701中描述了CD46 (也称为膜辅助因子蛋白 (Membrane Co-factor Protein, MCP)) 的结构和功能, 这两篇通过引用以其整体合并在本文中。人CD46 (UniProt:P15529;SEQ ID NO:15) 具有有392个氨基酸的序列 (包括N-末端,34个氨基酸的信号肽), 包括309个氨基酸的细胞外结构域 (UniProt:P15529位置35到343)、23个氨基酸的跨膜结构域 (UniProt:P15529位置344到366) 和26个氨基酸的胞质结构域 (UniProt:P15529位置367到392)。CD46的细胞外结构域包含四个CCP:CCP1=位置35到95, CCP2=位置97到159, CCP3=位置160到225, 以及CCP4=位置226到285。已经显示了CD46与C3b的结合和辅助因子活性通过CCP 2到4来介导 (UniProt:P15529位置97到285, SEQ ID NO:16, 参见

Forneris et al., EMBO J 35 (10):1133-1149)。天花病毒蛋白质天花补体酶抑制剂 (Smallpox Inhibitor of Complement Enzymes, SPICE) 是一种病毒蛋白质, 其包括四个 CCP 结构域并显示出补体因子 I 的辅助因子活性 (Rosengard 等, PNAS (2002) 99:8808-8813), 与人 CD46 具有 ~40% 的序列同一性。

[0050] 例如 Brodbeck 等, Immunology (2000) 101 (1):104-111 描述了 CD55 (也称为衰变加速因子 (Decay Accelerating Factor, DAF)) 的结构和功能, 通过引用以其整体合并并在本文中。人 CD55 (UniProt:P08174; SEQ ID NO:17) 具有有 381 个氨基酸的序列 (包括 N-末端, 34 个氨基酸的信号肽), 并包括四个 CCP: CCP1 = 位置 35 到 96, CCP2 = 位置 96 到 160, CCP3 = 位置 161 到 222, 以及 CCP4 = 位置 223 到 285。已经显示了 CD55 与 C3b 的结合以及辅助因子活性通过 CCP 2 到 4 来介导 (UniProt:P08174 位置 96 到 285, SEQ ID NO:18, 参见 Forneris 等, EMBO J 35 (10):1133-1149)。

[0051] 在 Blom 等, J Biol Chem (2001) 276 (29):27136-27144 和 Fukui 等, J Biochem (2002) 132 (5):719-728 中描述了 C4-结合蛋白 (C4BP) 的结构和功能, 这两篇通过引用以其整体合并并在本文中。人 C4BP (UniProt:P04003; SEQ ID NO:19) 具有有 597 个氨基酸的序列 (包括 N-末端, 48 个氨基酸的信号肽), 包含 8 个 CCP: CCP1 = 位置 49 到 110, CCP2 = 位置 111 到 172, CCP3 = 位置 173 到 236, CCP4 = 位置 237 到 296, CCP5 = 位置 297 到 362, CCP6 = 位置 363 到 424, CCP7 = 位置 425 到 482, 以及 CCP8 = 位置 483 到 540。已经显示了补体因子 I 介导的 C3b 灭活的辅助因子活性需要 C4BP 的 CCP 2 到 4 (UniProt:P04003 位置 111 到 296, SEQ ID NO:20, 参见上文的 Fukui 等)。

[0052] 本文使用的“补体因子 H”、“补体受体 1 (CR1)”、“CD46”、“CD55”和“C4-结合蛋白 (C4BP)”是指来自任何物种的蛋白质, 包括来自任何物种的所述蛋白质的同种型、片段、变体或同源物。在某些实施方式中, 蛋白质是哺乳动物的 (例如, 猕猴、人类和/或啮齿动物 (例如, 大鼠和/或鼠))。

[0053] 称为 SPICE、VCP (或 VICE) 和 MOPICE 的天花、牛痘和猴痘的痘病毒 (poxviral) 补体抑制剂与补体因子 I 的辅助因子具有同源性, 并且在例如 Liszewski 等, J Immunol (2008) 181 (6):4199-4207 和 Liszewski 等, J Immunol (2009) 183 (5):3150-3159 中进行了评述。SPICE、VCP 和 MOPICE 的氨基酸序列分别在 SEQ ID NO:21、SEQ ID NO:22 和 SEQ ID NO:23 中显示。

[0054] 补体因子 I 的辅助因子的同种型、片段、变体或同源物任选地可以表征为与来自给定物种、例如人类的不成熟或成熟蛋白质的氨基酸序列具有至少 70%, 优选地 80%、85%、90%、91%、92%、93%、94%、95%、96%、97%、98%、99% 或 100% 之一的氨基酸序列同一性。辅助因子的同种型、片段、变体或同源物任选地可以是功能性的同种型、片段、变体或同源物, 例如, 具有参考蛋白质的功能性质/活性, 按照通过由对该功能性质/活性的适当试验来分析而确定的。例如, 给定补体因子 I 的辅助因子的同种型、片段、变体或同源物可以展示出补体因子 I 的辅助因子活性, 例如, 通过补体因子 I 强化 C3b 的灭活的能力。

[0055] 片段可以是任何长度 (氨基酸的数量), 尽管任选地可以是成熟蛋白质的长度的至少 25%, 并且可以具有成熟蛋白质的长度的 50%、75%、80%、85%、90%、91%、92%、93%、94%、95%、96%、97%、98% 或 99% 之一的最大长度。

[0056] 在某些实施方式中, 补体因子 H 与 SEQ ID NO:10 具有至少 70%, 优选地 80%、85%、

90%、91%、92%、93%、94%、95%、96%、97%、98%、99%或100%之一的氨基酸序列同一性。在某些实施方式中,补体受体1与SEQ ID NO:12具有至少70%,优选地80%、85%、90%、91%、92%、93%、94%、95%、96%、97%、98%、99%或100%之一的氨基酸序列同一性。在某些实施方式中,CD46与SEQ ID NO:15具有至少70%,优选地80%、85%、90%、91%、92%、93%、94%、95%、96%、97%、98%、99%或100%之一的氨基酸序列同一性。在某些实施方式中,CD55与SEQ ID NO:17具有至少70%,优选地80%、85%、90%、91%、92%、93%、94%、95%、96%、97%、98%、99%或100%之一的氨基酸序列同一性。在某些实施方式中,C4BP与SEQ ID NO:19具有至少70%,优选地80%、85%、90%、91%、92%、93%、94%、95%、96%、97%、98%、99%或100%之一的氨基酸序列同一性。在某些实施方式中,SPICE与SEQ ID NO:21具有至少70%,优选地80%、85%、90%、91%、92%、93%、94%、95%、96%、97%、98%、99%或100%之一的氨基酸序列同一性。在某些实施方式中,VCP与SEQ ID NO:22具有至少70%,优选地80%、85%、90%、91%、92%、93%、94%、95%、96%、97%、98%、99%或100%之一的氨基酸序列同一性。在某些实施方式中,MOPICE与SEQ ID NO:23具有至少70%,优选地80%、85%、90%、91%、92%、93%、94%、95%、96%、97%、98%、99%或100%之一的氨基酸序列同一性。

[0057] C3b结合区

[0058] 本发明的多肽包含C3b结合区。

[0059] 如本文使用的,“C3b结合区”是指能够结合C3b的区域。在某些实施方式中,C3b结合区能够特异性结合C3b。可以通过C3b结合区与C3b之间形成的非共价相互作用介导结合C3b,该非共价相互作用例如范德华力、静电相互作用、氢键键合和疏水相互作用。在某些实施方式中,C3b结合区比结合C3b以外的分子以更大的亲和力和/或以更长的持续时间结合C3b。

[0060] 推定的C3b结合区与C3b结合的能力可以使用本领域技术人员熟知的技术来分析,这些技术包括酶联免疫吸附测定(enzyme-linked immunosorbent assay,ELISA)ELISA、表面等离子体共振(Surface plasmon Resonance,SPR;参见Hearty等,Methods Mol Biol (2012) 907:411-442;或Rich等,Anal Biochem.2008 Feb 1;373(1):112-20)、生物层干涉技术(Bio-Layer Interferometry)(参见,例如Lad等,(2015)J Biomol Screen 20(4):498-507;或Concepcion等,Comb Chem High Throughput Screen.2009 Sep;12(8):791-800)、微尺度热泳(MicroScale Thermophoresis,MST)分析(参见,例如Jerabek-Willemsen等,Assay Drug Dev Technol.2011 Aug;9(4):342-353),或放射性标记抗原结合试验(radiolabelled antigen binding assay,RIA)。通过这样的分析,可以测定和定量与给定靶点的结合。在某些实施方式中,该结合可以是给定分析中检测到的响应。

[0061] 在某些实施方式中,C3b结合区在这样的试验中展现与C3b的结合比在这样的分析中检测到的与阴性对照分子结合信号水平大1倍,例如,>1.01、>1.02、>1.03、>1.04、>1.05、>1.06、>1.07、>1.08、>1.09、>1.1、>1.2、>1.3、>1.4、>1.5、>1.6、>1.7、>1.8、>1.9、>2、>3、>4、>5、>6、>7、>8、>9、>10、>15、>20、>25、>30、>35、>40、>45、>50、>60、>70、>80、>90、或>100倍之一。

[0062] 在某些实施方式中,C3b结合区能够以结合亲和力结合C3b,该结合亲和力类似于给定试验中由补体因子I的辅助因子(或其片段)展示的与C3b的结合亲和力。与参考结合亲

和力类似的结合亲和力可以是,例如在可比较的试验中由参考补体因子I的辅助因子展示的和C3b的结合水平的 $\pm 40\%$,例如,结合水平的 $\pm 35\%$ 、 $\pm 30\%$ 、 $\pm 25\%$ 、 $\pm 20\%$ 、 $\pm 15\%$ 、 $\pm 10\%$ 或 $\pm 5\%$ 之一。

[0063] 例如,C3b结合区可以包括能够结合C3b的核酸或氨基酸序列,或由其组成。在某些实施方式中,C3b结合区包含能够结合C3b的核酸适体,或由其组成。在某些实施方式中,C3b结合区包括能够结合C3b的氨基酸序列,或由其组成。在某些实施方式中,能够结合C3b的氨基酸序列包括C3b结合适体、C3b结合抗体、或C3b结合抗原结合片段(例如,C3结合scFv、小体(minibody)、Fab等)的氨基酸序列,或由其组成。能够结合C3b的核酸和肽适体以及抗体/片段是本领域已知的,并且C3b结合核酸/肽适体以及抗体/片段可以通过技术人员已知的方法产生。例如,在Yuce等,Analyst (2015) 140 (16) :5379-99中描述了选择和生产核酸和肽适体的方法,在Antibodies:A Laboratory Manual,Second Edition,2014;Edward A.Greenfield,Cold Spring Harbor Laboratory Press.中描述了用于产生抗体/片段的方法。

[0064] 在某些实施方式中,根据本发明的多肽的C3b结合区能够在由补体因子I的辅助因子结合的区域中结合C3b(即,结合相同的区域或重叠的区域)。在某些实施方式中,根据本发明的多肽的C3b结合区能够在由补体因子H、CR1、CD46、CD55、C4BP、SPICE、VCP或MOPICE结合的C3b的区域中结合C3b。

[0065] 在某些实施方式中,根据本发明的多肽的C3b结合区能够在由补体因子H结合的C3b的区域中结合C3b。在某些实施方式中,C3b结合区能够在由补体因子H、CCP 1到4(SEQ ID NO:11)结合的C3b的区域中结合C3b。

[0066] C3b结合区是否在由给定补体因子I的辅助因子(或其片段)结合的C3b的区域中结合C3b,可以通过技术人员已知的各种方法来确定,各种方法包括ELISA和表面等离子体共振(SPR)分析。确定C3b结合区是否在由给定补体因子I的辅助因子(或其片段)结合的区域中结合C3b的适当试验的实例是竞争性ELISA分析。

[0067] 例如,C3b结合区是否在由给定补体因子I的辅助因子(或其片段)结合的C3b区域中结合C3b,可以通过在辅助因子/片段和C3b之一或两者与包括C3b结合区或由其组成的肽/多肽孵育存在或在其之后,分析辅助因子/片段与C3b的相互作用来确定。在由给定辅助因子/片段结合的C3b区域中结合C3b的C3b结合区,通过观察到与不存在C3b结合区(或存在适当的对照肽/多肽)的相互作用水平相比较的、在存在C3b结合区-或在相互作用对之一或两者与该C3b结合区孵育之后-辅助因子/片段与C3b之间相互作用水平的降低/下降来鉴定。例如,可以使用重组相互作用对在体外进行适当分析。为了这种试验的目的,相互作用对之一或两者、和/或包括给定C3b结合区或由其组成的肽/多肽可以被标记,或与可检测实体(entity)一起使用,以检测和/或测量相互作用的水平。

[0068] 在某些实施方式中,C3b结合区充当补体因子I的辅助因子。补体因子I的辅助因子强化补体因子I裂解C3b。例如,补体因子I的辅助因子可以将C3b呈现出有利于补体因子I的蛋白水解裂解的有利方向。C3b结合区优选地不抑制补体因子I蛋白水解裂解C3b。

[0069] 例如,可以通过分析与不存在C3b结合区的情况下(或存在适当的对照肽/多肽的情况下)补体因子I蛋白水解裂解C3b水平或速率相比较的、存在包括C3b结合区或由其组成的肽/多肽的情况下(或与之孵育之后)适当试验中补体因子I蛋白水解裂解C3b的水平或速

率,来确定充当补体因子I的辅助因子的C3b结合区。通过检测存在包括C3b结合区或由其组成的肽/多肽的情况下(或与之孵育之后)补体因子I蛋白水解裂解C3b的水平或速率的提高,鉴定出充当补体因子I的辅助因子的C3b结合区。例如,通过检测补体因子I裂解C3b的一种或更多种产物、如iC3b或C3f,可以测定补体因子I蛋白水解裂解C3b的水平或速率。

[0070] 在某些实施方式中,根据本发明的多肽的C3b结合区包括补体因子H、CR1、CD46、CD55、C4BP、SPICE、VCP或MOPICE的一种或更多种的C3b结合区。在某些实施方式中,多肽的C3b结合区包括补体因子H或CR1的C3b结合区。在某些实施方式中,根据本发明的多肽的C3b结合区包括与SEQ ID NO:11、13、14、16、18、20、21、22或23之一的氨基酸序列具有至少60%,例如至少65%、70%、75%、80%、85%、90%、91%、92%、93%、94%、95%、96%、97%、98%、99%或100%之一的序列同一性的氨基酸序列,或由其组成。

[0071] 在某些实施方式中,根据本发明的多肽的C3b结合区包括与SEQ ID NO:11之一的氨基酸序列具有至少60%,例如至少65%、70%、75%、80%、85%、90%、91%、92%、93%、94%、95%、96%、97%、98%、99%或100%之一的序列同一性的氨基酸序列,或由其组成。在某些实施方式中,根据本发明的多肽的C3b结合区包括氨基酸序列SEQ ID NO:11,或由其组成。

[0072] 在某些实施方式中,根据本发明的多肽的C3b结合区包括与SEQ ID NO:13之一的氨基酸序列具有至少60%,例如至少65%、70%、75%、80%、85%、90%、91%、92%、93%、94%、95%、96%、97%、98%、99%或100%之一的序列同一性的氨基酸序列,或由其组成。在某些实施方式中,根据本发明的多肽的C3b结合区包括氨基酸序列SEQ ID NO:13,或由其组成。

[0073] 在某些实施方式中,根据本发明的所述多肽的所述C3b结合区包含与SEQ ID NO:14之一的氨基酸序列具有至少60%,例如至少65%、70%、75%、80%、85%、90%、91%、92%、93%、94%、95%、96%、97%、98%、99%或100%之一的序列同一性的氨基酸序列,或由其组成。在某些实施方式中,根据本发明的所述多肽的所述C3b结合区包含SEQ ID NO:14的氨基酸序列,或由其组成。

[0074] C3b灭活区

[0075] 本发明的多肽包括C3b灭活区。

[0076] 如本文使用的,“C3b灭活区”是指能够降低或防止C3b的生物学功能的区域。该C3b灭活区可以结合C3b,和/或可以引起C3b结构的物理改变。

[0077] 在某些实施方式中,C3b灭活区能够进行以下一种或更多种:降低/防止功能性C3bBb型C3转化酶的形成;降低/防止功能性C4b2a3b型C5转化酶的形成;降低/防止功能性C3bBb3b型C5转化酶的形成;降低C3bBb型C3转化酶活性;降低C4b2a3b型C5转化酶活性;降低C3bBb3b型C5转化酶活性;降低C3bBb型C3转化酶的量;降低C3bBb3b型C5转化酶的量;降低C4b2a3b型C5转化酶的量;降低C3b的量;提高iC3b的量;提高C3f的量;提高C3dg的量;提高C3d的量;降低C5b的量;降低C5a的量。

[0078] 推定的C3b灭活区降低/防止功能性转化酶的形成、或降低转化酶的量,例如可以通过在适当试验中分析转化酶的和/或转化酶活性来分析。例如,转化酶的和/或转化酶活性可以在存在肽/多肽的情况下-或对其进行孵育之后来分析,该肽/多肽包括推定的C3b灭活区或由其组成。通过观察与不存在推定的C3b结合区的情况下(或存在适当

的对照肽/多肽的情况下)转化酶和/或转化酶活性水平相比较的、存在推定的C3b灭活区的情况下-或与推定的C3b灭活区孵育之后-转化酶和/或转化酶活性水平降低/下降,来鉴定C3b灭活区。可以使用适合的读数、例如转化酶活性的产物来检测转化酶/转化酶活性水平。

[0079] 给定的转化酶C3b、iC3b、C3dg、C3d、C3f、C5b或C5a的量可以例如通过技术人员熟知的基于抗体的方法如免疫印迹(Western blot)、ELISA、质谱测定法或基于报告物的方法来分析。

[0080] 可以使用适当因子在体外进行适合的分析,例如可以重组产生该因子。

[0081] 在某些实施方式中,C3b灭活区能够不可逆地灭活C3b。在某些实施方式中,C3b灭活区能够蛋白水解裂解C3b。在某些实施方式中,C3b灭活区展现丝氨酸蛋白酶活性。在某些实施方式中,C3b灭活区能够蛋白水解裂解C3b以形成iC3b和C3f。在某些实施方式中,C3b灭活区能够裂解残基1303和/或1320处的C3b的C3 α '链。

[0082] 例如可以通过在适当的条件下将重组C3b与肽/多肽孵育以发生裂解的适合的时间、随后检测iC3b和/或C3f,来分析推定的C3b灭活区裂解C3b以形成iC3b和C3f的能力。

[0083] 例如,推定的C3b灭活区裂解C3b的能力可以通过Clark等J. Immunol (2014) 193, 4962-4970中描述的方法进行分析,通过引用以其整体合并在本文中。

[0084] 在某些实施方式中,根据本发明的多肽的C3b灭活区包括补体因子I的C3b灭活区。

[0085] 在某些实施方式中,根据本发明的多肽的C3b灭活区包括与SEQ ID NO:9之一的氨基酸序列具有至少60%,例如至少65%、70%、75%、80%、85%、90%、91%、92%、93%、94%、95%、96%、97%、98%、99%或100%之一的序列同一性的氨基酸序列,或由其组成。在某些实施方式中,根据本发明的多肽的C3b灭活区包括氨基酸序列SEQ ID NO:9,或由其组成。

[0086] 多肽的进一步的特征

[0087] 在某些实施方式中,本发明的多肽可以包括C3b结合区和C3b灭活区之间的接头(linker)。连接的C3b结合和C3b灭活区被有利地表达为单一多肽,因而它们的互补活性得以共存。

[0088] 该接头有利地被设计为足够短以提供多肽的有效表达和/或扩散,同时(通过接头的长度和/或组成)保持区域之间的连接的柔性度,使得它们能够进行它们各自的功能,即,使得C3b结合区能够结合C3b、且C3b灭活区能够灭活C3b。该接头可以包括氨基酸序列或由其组成,并且可以共价键合(例如,通过肽键)至C3b结合区和C3b灭活区的氨基酸序列的末端。

[0089] 接头可以是肽或多肽接头。接头可以是柔性接头。例如在Chen等,Adv Drug Deliv Rev (2013) 65 (10):1357-1369中描述的,柔性接头的氨基酸序列是技术人员已知的通过引用以其整体合并在本文中。在某些实施方式中,柔性接头序列包括丝氨酸和甘氨酸残基。在某些实施方式中,接头是肽/多肽,该肽/多肽由1-100、1-50、1-20、1-10或1-5个氨基酸残基组成。

[0090] 在某些实施方式中,所述接头包含基序(motif)GGGGS(SEQ ID NO:45)即“G₄S”的一个或多个拷贝。在某些实施方式中,接头包括SEQ ID NO:45的至少1个、至少2个、至少3个、至少4个、至少5个、至少6个、至少7个或至少8个拷贝。

[0091] 有益地,C3b结合区和C3b灭活区的连接提供了对C3b的有效捕获和灭活。

[0092] 可以在本发明的多肽的其他区域之间提供另外的接头。

[0093] 对于能够在体内跟踪、检测和定量药剂的水平和位置,例如分析生产、安帅气、最大浓度等的疗法的开发是有利的。因而,包含有助于本发明的多肽检测的部分是有用的,例如,能够使所述多肽与内源蛋白质(例如,内源补体因子H和/或内源的补体因子I的辅助因子)区分开。

[0094] 在本文中,“内源”蛋白质/肽是指由相关的细胞类型、组织或受试者(在用根据本发明的多肽、核酸、载体、细胞或药物组合物治疗之前)编码/表达的蛋白质/肽。“非内源”蛋白质/肽是指不由相关的细胞类型、组织或受试者(在用根据本发明的多肽、核酸、载体、细胞或药物组合物治疗之前)编码/表达的蛋白质/肽。

[0095] 因此,在某些实施方式中,本发明的多肽包括氨基酸序列,该氨基酸序列有助于检测例如含有多肽的生物样品中多肽(下文称为“检测序列”)。在某些实施方式中,所述检测序列包含氨基酸序列,或由其组成;该氨基酸序列有助于,例如在向受试者施用根据本发明的多肽、核酸、载体、细胞或药物组合物之后,检测获从受试者获取的样品中多肽,。

[0096] 例如,在某些实施方式中,检测序列包括不存在于内源人C3b结合蛋白和/或内源人C3b灭活蛋白中的氨基酸序列,或由其组成。在某些实施方式中,检测序列包括不存在于内源人蛋白中的氨基酸序列,或由其组成。

[0097] 在某些实施方式中,检测序列有助于用例如蛋白水解酶的酶处理的样品中多肽的检测。在某些实施方式中,检测序列包含蛋白酶的裂解位点,或由其组成。在某些实施方式中,检测序列在用蛋白酶处理之后提供了非内源肽的产生(其中“非内源肽”是指不由相关的宿主细胞/组织/受试者内源地产生的肽)。这样,本发明的多肽可以与内源蛋白质(例如,C3b结合蛋白和/或内源C3b灭活蛋白)区分开,因而可以被检测和定量。

[0098] 在某些实施方式中,检测序列提供了胰蛋白酶肽的产生,从而有助于用胰蛋白酶处理的样品中多肽的检测。

[0099] 在某些实施方式中,检测序列被包括在多肽的接头之中。在某些实施方式中,检测序列邻近接头(即,在所述接头的N-末端或C-末端的1-5、1-10、1-15、1-20或1-30个氨基酸残基之内)。在某些实施方式中,检测序列可以包括本发明的多肽的一个或多个其他区域的一个或多个氨基酸,例如,C3b结合区、接头、C3b灭活区等。

[0100] 例如,SEQ ID NO:32、33和34中显示的本发明的示范性多肽包括接头,该接头包括精氨酸残基,其在胰蛋白酶裂解多肽期间提供了两种特异性肽的产生:GDAVCTESGWRPLPSCEEGGGSR(SEQ ID NO:46)和GGGGSGGGGSIVGGK(SEQ ID NO:47)。

[0101] 在某些实施方式中,接头是肽/多肽,该肽/多肽包括SEQ ID NO:24的氨基酸序列或由其组成。在某些实施方式中,接头是肽/多肽,该肽/多肽包括SEQ ID NO:48的氨基酸序列或由其组成。在某些实施方式中,接头是肽/多肽,该肽/多肽包括SEQ ID NO:67的氨基酸序列或由其组成。在某些实施方式中,接头是肽/多肽,该肽/多肽包括SEQ ID NO:68的氨基酸序列或由其组成。

[0102] 在某些实施方式中,多肽可以缺乏与除C3b结合区以外的补体因子I的辅助因子(例如,补体因子H、CR1、CD46、CD55、C4BP、SPICE、VCP或MOPICE)具有大体上的序列同一性的氨基酸序列。也就是说,在某些实施方式中,多肽缺乏氨基酸序列,该氨基酸序列相应于除补体因子I的辅助因子C3b结合区以外的补体因子I的辅助因子氨基酸序列。

[0103] 如本文使用的,对应于参考氨基酸序列的氨基酸序列通常包括与参考序列至少60%,例如至少65%、70%、75%、80%、85%、90%、91%、92%、93%、94%、95%、96%、97%、98%、99%或100%之一的序列同一性。

[0104] 可以期望的是多肽缺乏除C3b结合功能以外的补体因子I的辅助因子的某些性质。例如,可以期望的是多肽缺乏区域,否则这些区域将抑制通过布鲁赫膜(BrM)的扩散、或将干扰天然辅助因子家族蛋白的活性,或否则将被病原细菌利用来破坏宿主免疫系统。

[0105] 在某些实施方式中,本发明的多肽缺乏氨基酸序列,该氨基酸序列对应于编码CCP 6-8的补体因子H的氨基酸序列。在某些实施方式中,多肽缺乏对应于SEQ ID NO:39的氨基酸序列。

[0106] 在某些实施方式中,本发明的多肽缺乏氨基酸序列,该氨基酸序列对应于编码CCP 19-20的补体因子H的氨基酸序列。在某些实施方式中,多肽缺乏对应于SEQ ID NO:40的氨基酸序列。

[0107] 在某些实施方式中,本发明的多肽缺乏氨基酸序列,该氨基酸序列对应于除补体因子HC3b结合区以外的补体因子H氨基酸序列。在某些实施方式中,多肽缺乏对应于SEQ ID NO:25的氨基酸序列。

[0108] 在某些实施方式中,本发明的多肽缺乏氨基酸序列,该氨基酸序列对应于除C3b结合区以外的补体因子H同种型FHL-1的氨基酸序列。在某些实施方式中,多肽缺乏对应于SEQ ID NO:41的氨基酸序列。

[0109] 在某些实施方式中,多肽可以缺乏氨基酸序列,该氨基酸序列与除蛋白水解结构域以外的补体因子I具有大体上序列同一性。也就是说,在某些实施方式中,多肽缺乏氨基酸序列,该氨基酸序列对应于除结构域以外的补体因子I的蛋白水解氨基酸序列。在某些实施方式中,多肽缺乏对应于SEQ ID NO:26的氨基酸序列。

[0110] 在某些实施方式中,本发明的多肽由300-1000个氨基酸组成,例如,350-900、400-850、450-800、500-750个氨基酸中的一种。

[0111] 在某些实施方式中,本发明的多肽缺乏一个或多个糖基化位点。在某些实施方式中,本发明的多肽缺乏一个或多个N-联糖基化位点(sites for N-linked glycosylation)。在某些实施方式中,多肽缺乏N-联聚糖。在某些实施方式中,多肽是无糖基的(aglycosyl)(即,不是糖基化的)。在某些实施方式中,多肽例如通过用糖苷酶(例如,肽N-糖苷酶)处理已经去糖基化。去糖基化优选地是非变性的。

[0112] Fenaille等,Glycobiology (2007) 17 (9) 932-944报道了补体因子H的位置217处的天冬酰胺(根据UniProt:P08603编号,在SEQ ID NO:10中显示)由于存在位置220处的脯氨酸残基(根据UniProt:P08603编号)因而不是糖基化的。

[0113] 在某些实施方式中,多肽缺乏与SEQ ID NO:66的共有序列相符的序列。在某些实施方式中,一个或多个C3b结合区和C3b灭活区缺乏与SEQ ID NO:66的共有序列相符的序列。在某些实施方式中,多肽包括C3b结合区和/或C3b灭活区,其中被确认为SEQ ID NO:66的共有序列的一个或多个序列被突变以除去N-糖基化位点。

[0114] 在某些实施方式中,多肽缺乏与SEQ ID NO:27的共有序列相符的序列。在某些实施方式中,一个或多个C3b结合区和C3b灭活区缺乏与SEQ ID NO:27的共有序列相符的序列。在某些实施方式中,多肽包括C3b结合区和/或C3b灭活区,其中被确认为SEQ ID NO:27

的共有序列的一个或多个序列被突变以除去N-糖基化位点。

[0115] 在某些实施方式中,C3b灭活区缺乏与SEQ ID NO:27的共有序列相符的序列。在某些实施方式中,C3b灭活区包含与SEQ ID NO:9之一的氨基酸序列具有至少60%、例如至少65%、70%、75%、80%、85%、90%、91%、92%、93%、94%、95%、96%、97%、98%、99%或100%之一的序列同一性的氨基酸序列,或由其组成,其中C3b灭活区包括替代物N464Q、N494Q和N536Q(根据UniProt:P05156编号)。

[0116] 在某些实施方式中,本发明的多肽可以另外包括分泌途径序列。如本文使用的,分泌途径序列是指导多肽的分泌的氨基酸序列。一旦多肽链跨越粗糙型内质网的输出被启动,分泌途径序列可以从成熟蛋白质上裂解。由哺乳动物细胞分泌的多肽通常具有与多肽的N-末端融合的信号肽,其从转译的多肽上裂解以产生多肽的“成熟”形式。

[0117] 在某些实施方式中,分泌途径序列包括一个或更多个糖基化位点。在某些实施方式中,分泌途径序列是糖基化的。在某些实施方式中,分泌途径序列包括一个或多个N-联糖基化位点。在某些实施方式中,分泌途径序列包括与SEQ ID NO:27的共有序列相符的一个或多个序列。

[0118] 在某些实施方式中,分泌途径序列可以包括前导序列(也称为信号肽或信号序列)或由其组成。前导序列通常由形成单个alpha螺旋的5-30个疏水性氨基酸的序列组成。分泌的蛋白质和细胞表面表达的蛋白质常包括前导序列。前导序列可以存在于新转译的多肽中(例如,在加工以除去前导序列之前)。对于许多蛋白质前导序列是已知的,并且该前导序列记录于数据库中例如基因银行(GenBank)、UniProt、蛋白序列数据库(Swiss-Prot)、TrEMBL、蛋白质信息资源(Protein Information Resource)、蛋白质资料库(Protein Data Bank)、Ensembl和英特普数据库(InterPro),和/或例如可以使用氨基酸序列分析工具如信号肽预测(SignalP)(Petersen等,2011 Nature Methods 8:785-786)或信号基本局部比对搜索工具(Signal-BLAST)(Frank and Sippl,2008Bioinformatics 24:2172-2176)来鉴定/预测。

[0119] 在某些实施方式中,本发明的多肽可以另外包括用于从多肽除去分泌途径序列的裂解位点。在某些实施方式中,用于从多肽除去分泌途径序列的裂解位点是内切蛋白酶的裂解位点。在某些实施方式中,裂解位点是用于通过细胞表达的内切蛋白酶,在该细胞中表达多肽。在某些实施方式中,裂解位点是信号肽酶裂解位点。在某些实施方式中,裂解位点是蛋白酶裂解位点,例如,用于通过细胞表达的内切蛋白酶的裂解位点,该细胞表达多肽。在某些实施方式中,裂解位点是用于通过RPE细胞表达的内切蛋白酶的裂解位点。在某些实施方式中,裂解位点是弗林内切蛋白酶裂解位点。在某些实施方式中,用于从多肽除去分泌途径序列的裂解位点包括与SEQ ID NO:28或29的共有序列相符的序列,或由其组成。

[0120] 在某些实施方式中,本发明的所述多肽可以包括进一步的功能性氨基酸序列。例如,多肽可以包括有助于多肽的表达、折叠、运输(trafficking)、加工、纯化或检测的氨基酸序列。例如,多肽可以包括任选地:在多肽的N-末端或C-末端处、在接头中、或接头的N-末端或C-末端处编码蛋白质标签,例如,His(例如,6×His;SEQ ID NO:30)、FLAG、Myc、GST、MBP、HA、E或生物素标签的序列。

[0121] 在某些实施方式中,本发明的多肽可以另外包括用于除去蛋白质标签的裂解位点。例如,可能希望的是在纯化之后除去用于多肽纯化的标签。在某些实施方式中,例如,所

述裂解位点可以是烟草蚀纹病毒 (Tobacco Etch Virus, TEV) 蛋白酶裂解位点, 例如, SEQ ID NO:31中所示的。

[0122] 如本文使用的, “多肽” 包括分子, 该分子包括超过一条多肽链, 所述多肽链可以 (例如, 共价地或非共价地) 缔合成复合物。也就是说, 本发明的含义内的 “多肽” 涵盖了包括一条或多条多肽链的分子。例如, 在某些实施方式中, 多肽可以是多多肽链复合物 (multi-polypeptide chain complex)。

[0123] 本发明的多肽可以设置有不同区域的特定组合和相对排列。

[0124] 在某些实施方式中, 本发明的多肽可以设置有根据以下之一的相对排列:

[0125] N端-[C3b结合区]-[接头区]-[C3b灭活区]-C端

[0126] N端-[分泌途径序列]-[内切蛋白酶裂解位点]-[C3b结合区]-[接头区]-[C3b灭活区]-C端

[0127] 可以在各种不同的实施方式中、且可以处在体外或体内表达/生产的不同阶段的本发明的多肽包括例如信号肽、蛋白质标签、用于其脱除的裂解位点、等。

[0128] 本发明的多肽可以包括本文描述的任何C3b结合区以及本文描述的任何C3b灭活区, 任选地与本文描述的本发明多肽一种或多种任何进一步特征组合 (例如, 信号肽、接头、检测序列、蛋白质标签、用于除去蛋白质标签的裂解位点、分泌途径序列、用于除去分泌途径序列的裂解位点)。

[0129] 本发明多肽的特定示例性实施方式的区域在下表中概括。

[0130]

成熟蛋白的名称	多肽的区域				SEQ ID NO
	信号肽	His 标签和 TEV 裂解位点	C3b 结合区和 C3b 灭活区	C3b 灭活区	
His-FH-FI	是	是	因子 H 辅助因子区	因子 I 蛋白水解结构域	32
His-nFH-FI	是	是	因子 H 辅助因子区	包括替代物 N464Q、N494Q 和 N536Q 的因子 I 蛋白水解结构域	33
His-FH-FI	否	是	因子 H 辅助因子区	因子 I 蛋白水解结构域	35
His-nFH-FI	否	是	因子 H 辅助因子区	包括替代物 N464Q、N494Q 和 N536Q 的因子 I 蛋白水解结构域	36
FH-FI	是	否	因子 H 辅助因子区	因子 I 蛋白水解结构域	69
nFH-FI	是	否	因子 H 辅助因子区	包括替代物 N464Q、N494Q 和 N536Q 的因子 I 蛋白水解结构域	34
FH-FI	否	否	因子 H 辅助因子区	因子 I 蛋白水解结构域	37
nFH-FI	否	否	因子 H 辅助因子区	包括替代物 N464Q、N494Q 和 N536Q 的因子 I 蛋白水解结构域	49
His-CR1a-FI	是	是	补体受体 1 辅助因子区 CCP 8-10	因子 I 蛋白水解结构域	50
His-nCR1a-FI	是	是	包括替代物 N509Q 和 N578Q 的补体受体 1 辅助因子区 CCP 8-10	包括替代物 N464Q、N494Q 和 N536Q 的因子 I 蛋白水解结构域	52
His-CR1a-FI	否	是	补体受体 1 辅助因子区 CCP 8-10	因子 I 蛋白水解结构域	54
His-nCR1a-FI	否	是	包括替代物 N509Q 和 N578Q 的补体受体 1 辅助因子区 CCP 8-10	包括替代物 N464Q、N494Q 和 N536Q 的因子 I 蛋白水解结构域	56
CR1a-FI	是	否	补体受体 1 辅助因子区 CCP 8-10	因子 I 蛋白水解结构域	70
nCR1a-FI	是	否	包括替代物 N509Q 和 N578Q 的补体受体 1 辅助因子区 CCP 8-10	包括替代物 N464Q、N494Q 和 N536Q 的因子 I 蛋白水解结构域	72
CR1a-FI	否	否	补体受体 1 辅助因子区 CCP 8-10	因子 I 蛋白水解结构域	58
nCR1a-FI	否	否	包括替代物 N509Q 和 N578Q 的补体受体 1 辅助因子区	包括替代物 N464Q、N494Q 和 N536Q 的因子 I 蛋白水解结构域	60

[0131]

			CCP 8-10		
His-CR1b-FI	是	是	补体受体 1 辅助因子区 CCP 15-17	因子 I 蛋白水解结构域	51
His-nCR1b-FI	是	是	包括替代物 N959Q 和 N1028Q 的补体受体 1 辅助因子区 CCP 15-17	包括替代物 N464Q、N494Q 和 N536Q 的因子 I 蛋白水解结构域	53
His-CR1b-FI	否	是	补体受体 1 辅助因子区 CCP 15-17	因子 I 蛋白水解结构域	55
His-nCR1b-FI	否	是	包括替代物 N959Q 和 N1028Q 的补体受体 1 辅助因子区 CCP 15-17	包括替代物 N464Q、N494Q 和 N536Q 的因子 I 蛋白水解结构域	57
CR1b-FI	是	否	补体受体 1 辅助因子区 CCP 15-17	因子 I 蛋白水解结构域	71
nCR1b-FI	是	否	包括替代物 N959Q 和 N1028Q 的补体受体 1 辅助因子区 CCP 15-17	包括替代物 N464Q、N494Q 和 N536Q 的因子 I 蛋白水解结构域	73
CR1b-FI	否	否	补体受体 1 辅助因子区 CCP 15-17	因子 I 蛋白水解结构域	59
nCR1b-FI	否	否	包括替代物 N959Q 和 N1028Q 的补体受体 1 辅助因子区 CCP 15-17	包括替代物 N464Q、N494Q 和 N536Q 的因子 I 蛋白水解结构域	61

[0132] 在某些实施方式中,根据本发明的多肽包括与SEQ ID NO:32、33、34、35、36、37、49或69的氨基酸序列具有至少60%、65%、70%、75%、80%、85%、86%、87%、88%、89%、90%、91%、92%、93%、94%、95%、96%、97%、98%、99%或100%的序列同一性的氨基酸序列,或由其组成。

[0133] 在某些实施方式中,根据本发明的多肽包括与SEQ ID NO:50、51、52、53、54、55、56、57、58、59、60、61、70、71、72或73的氨基酸序列具有至少60%、65%、70%、75%、80%、85%、86%、87%、88%、89%、90%、91%、92%、93%、94%、95%、96%、97%、98%、99%或100%的序列同一性的氨基酸序列,或由其组成。

[0134] 所述多肽的功能性质

[0135] 本发明的多肽可以通过参考一种或多种功能性质来表征。

[0136] 特别地,根据本发明的多肽可以具有一种或多种以下性质(正如通过在对所述性质的适当试验中进行分析所确定的):

[0137] 结合C3b;

[0138] 以与对C3b的结合亲和力相类似的亲和力来结合C3b,所述对C3b的结合亲和力通过补体因子I的辅助因子(或其片段)来展示;

[0139] 在由补体因子I的辅助因子(或其片段)结合的C3b的区域中结合C3b;

[0140] 灭活C3b;

[0141] 降低/防止功能性C3bBb型C3转化酶的形成;

[0142] 降低/防止功能性C3bBb3b型C5转化酶的形成;

[0143] 降低/防止功能性C4b2a3b型C5转化酶的形成;

- [0144] 降低C3bBb型C3转化酶活性；
- [0145] 降低C3bBb3b型C5转化酶活性；
- [0146] 降低C4b2a3b型C5转化酶活性；
- [0147] 降低C3bBb型C3转化酶的量；
- [0148] 降低C3bBb3b型C5转化酶的量；
- [0149] 降低C4b2a3b型C5转化酶的量；
- [0150] 降低C3b的量；
- [0151] 提高iC3b的量；
- [0152] 提高C3dg的量；
- [0153] 提高C3d的量；
- [0154] 提高C3f的量；
- [0155] 降低C5b的量；
- [0156] 降低C5a的量。
- [0157] 例如按上文所描述的，可以分析给定多肽是否具有前述段落中提及的功能性质。
- [0158] 在某些实施方式中，根据本发明的多肽具有扩散通过布鲁赫膜 (BrM) 的能力，如通过对所述性质的适当试验中分析所确定的。
- [0159] 布鲁赫膜 (BrM) 是位于视网膜和脉络膜之间的薄的 (2-4 μ m)、非细胞的、五层的细胞外基质，布鲁赫膜向前延伸到锯齿缘 (ora serrata)。布鲁赫膜位于代谢活性的视网膜色素上皮细胞 (RPE) 和毛细血管床 (脉络膜血管层 (choriocapillaris)) 之间，并起到RPE的基层和血管壁的一种主要功能的作用。例如在Curcio and Johnson, Structure, Function and Pathology of Bruch's Membrane, In: Ryan等 (2013), Retina, Vol.1, Part 2: Basic Science and Translation to Therapy. 5th ed. London: Elsevier, pp466-481中评述了BrM的结构和功能，通过引用以其整体合并在本文中。
- [0160] 例如，如在Clark等J. Immunol (2014) 193, 4962-4970中所描述的，例如可以在体外分析给定多肽扩散通过BrM的能力。简要地说，如在McHarg等, J Vis Exp (2015) 1-7中所描述的，可以从供体眼睛分离BrM，并且黄斑区可以安装在尤斯灌流室 (Ussing chamber) 中。一旦固定，5mm直径的黄斑区是两个相同区室之间唯一的屏障 (barrier)。BrM的两侧可以用磷酸缓冲液 (phosphate buffer, PBS) 洗涤，人血清可以用PBS 1:1稀释，并添加到BrM一侧的尤斯灌流区室中。要分析的多肽可以添加至PBS中的样品室，单独的PBS可以添加到BrM的另一侧的区室中 (扩散物室 (diffusate chamber))，该尤斯灌流室可以在室温下在样品室和扩散物室中温和搅动下孵育24小时。随后例如可以使用诸如ELISA分析或Western印迹的基于抗体的检测方法，分析来自每个室的样品中多肽的存在。扩散物室中多肽的检测表明该多肽能够扩散通过BrM。已知能够/不能够扩散通过BrM的适当阳性和阴性调控蛋白质可以包括在这样的实验中。
- [0161] 在某些实施方式中，本发明的多肽展现了与补体因子I相比扩散通过BrM的优越的能力。在某些实施方式中，本发明的多肽展现了与补体因子H相比扩散通过BrM的优越的能力。在某些实施方式中，本发明的多肽展现了与截短补体因子H同种型FHL-1 (UniProt: P08603-2; SEQ ID NO: 38) 相比扩散通过BrM的相似的能力。在某些实施方式中，本发明的多肽展现了与补体因子H同种型FHL-1相比扩散通过BrM的优越的能力。

[0162] 通过分析如上所述通过BrM的扩散,以及在实验结束时检测直到扩散物室的改进的扩散速率、和/或检测扩散物室中增加的多肽比例,可以鉴定与给定参考多肽相比展示了扩散通过BrM的优越能力的多肽。通过如上所述分析通过BrM的扩散、及检测直到扩散物扩散速率,和/或通过检测在实验结束时扩散物室中参考多肽的比例30%以内、例如25%、20%、15%或10%之一之内的扩散物室中多肽比例,可以鉴定与给定参考多肽相比展示了与扩散通过BrM的相类似能力的多肽;所述直到扩散物的扩散速率在参考多肽的扩散速率的30%之内。

[0163] 核酸、细胞、组合物和试剂盒

[0164] 本发明提供了编码根据本发明的多肽的核酸。在某些实施方式中,例如,所述核酸是从其他核酸或天然发生的生物材料中纯化或分离的。

[0165] 本发明还提供了包括编码根据本发明的多肽的核酸的载体。

[0166] 本文使用的“载体”是用作将外源核酸转译到细胞中的媒介物(vehicle)的核酸(DNA或RNA)。载体可以是用于在细胞中表达核酸的表达载体。这样的载体可以包括启动子序列,该启动子序列可操作的连接编码要表达的序列的核酸。载体还可以包括终止密码子和表达增强子(enhancer)。本领域已知的任何适合的载体、启动子、增强子和终止密码子可以用于从根据本发明的载体表达根据本发明的多肽。

[0167] 在本说明书中,术语“可操作地连接”可以包括该情形,在其中选定的核酸序列和调节核酸序列(例如,启动子和/或增强子)以将核苷酸序列的表达处于调节序列的影响或控制下的方式共价连接,(从而形成表达盒(expression cassette))。因此,如果调节序列能够影响核酸序列的转录,则调节序列与选定的核酸序列可操作地连接。在适当的情况下,产生的转录产物然后可以被转译成期望的多肽。

[0168] 优选提供根据本发明的核酸和/或载体以导入细胞,例如原代人免疫细胞(primary human immune cell)。例如,如Maus等,Annu Rev Immunol (2014) 32:189-225或Morgan and Boyerinas,Biomedicines 2016 4,9中描述的,适当的载体包括质粒、二元载体、DNA载体、mRNA载体、病毒载体(例如,gamma逆转录病毒载体(例如,鼠白血病病毒(murine Leukemia virus,MLV)-衍生载体、慢病毒载体、腺病毒载体、腺相关病毒载体、牛痘病毒载体和疱疹病毒载体)、转座子类载体、以及人造染色体(例如,酵母人造染色体)这两篇通过引用以其整体合并在本文中。在某些实施方式中,病毒载体可以是慢病毒、逆转录病毒、腺病毒或单纯性疱疹病毒载体。在某些实施方式中,慢病毒载体可以是第三代慢病毒载体(pELNS),或可以衍生自pELNS。在某些实施方式中,载体可以是编码短回文重复序列(Clustered Regularly Interspaced Short Palindromic Repeats,CRISPR)/CRISPR相关蛋白9(CRISPR associated protein 9,Cas9)的载体。

[0169] 在某些实施方式中,根据本发明的核酸包括编码多肽的核酸序列,或由其组成,该多肽具有与SEQ ID NO:32、33、34、35、36、37、或49的氨基酸序列具有至少60%、65%、70%、75%、80%、85%、86%、87%、88%、89%、90%、91%、92%、93%、94%、95%、96%、97%、98%、99%或100%的序列同一性的氨基酸序列。

[0170] 在某些实施方式中,由于密码子简并性(codon degeneracy),根据本发明的核酸包括与SEQ ID NO:42、43或44具有至少60%、65%、70%、75%、80%、85%、86%、87%、88%、89%、90%、91%、92%、93%、94%、95%、96%、97%、98%、99%或100%的序列同一

性的核酸序列,或编码与SEQ ID NO:42、43或44之一相同的氨基酸序列的核酸序列,或由其组成。

[0171] 在某些实施方式中,根据本发明的核酸包括编码多肽的核酸序列,或由其组成,该多肽具有与SEQ ID NO:50、51、52、53、54、55、56、57、58、59、60、61、70、71、72或73的氨基酸序列具有至少60%、65%、70%、75%、80%、85%、86%、87%、88%、89%、90%、91%、92%、93%、94%、95%、96%、97%、98%、99%或100%的序列同一性的氨基酸序列。

[0172] 在某些实施方式中,由于密码子简并性,根据本发明的核酸包括与SEQ ID NO:62、63、64或65具有至少60%、65%、70%、75%、80%、85%、86%、87%、88%、89%、90%、91%、92%、93%、94%、95%、96%、97%、98%、99%或100%的序列同一性的核酸序列,或编码与SEQ ID NO:62、63、64或65之一相同的氨基酸序列的核酸序列,或由其组成。

[0173] 本发明还提供了包括或表达根据本发明的多肽的细胞。还提供的是包括或表达根据本发明的核酸或载体的细胞。包括或表达根据本发明多肽、核酸或载体的细胞可以分泌根据本发明的多肽。也就是说,多肽、核酸或载体的表达可以引起来自细胞的根据本发明的多肽的溶性生产(soluble production)。

[0174] 所述细胞可以是真核细胞,例如哺乳动物细胞。该哺乳动物可以是人类或非人哺乳动物(例如,兔、豚鼠、大鼠、小鼠或其他啮齿动物(包括啮齿目中的任何动物)、猫、狗、猪、绵羊、山羊、牛(包括奶牛,例如,乳牛,或牛属中的任何动物)、马(包括马科中的任何动物)、驴和非人灵长类)。在某些实施方式中,所述细胞可以来自人类受试者、或可以已经获自人类受试者。

[0175] 在某些实施方式中,所述细胞是眼细胞。在某些实施方式中,所述细胞是视网膜、脉络膜、视网膜色素上皮细胞或黄斑的细胞。在某些实施方式中,所述细胞是视网膜细胞。在某些实施方式中,所述细胞是视网膜色素上皮细胞(RPE)。

[0176] 本发明还提供了用于产生包括根据本发明的核酸或载体的细胞的方法,该方法包括将根据本发明的核酸或载体导入细胞中。本发明还提供了用于产生包括或表达根据本发明的多肽的细胞的方法,该方法包括将根据本发明的核酸或载体导入细胞中。在某些实施方式中,该方法另外包括在适合于通过细胞表达所述核酸或载体的条件下培养细胞。在某些实施方式中,在体外或体内执行该方法。在某些实施方式中,在体内执行该方法。

[0177] 本发明还提供了通过根据本发明的用于产生细胞的方法获得的或可获得的细胞。

[0178] 本发明还提供了包含根据本发明的多肽、核酸、载体或细胞的组合物。

[0179] 根据本发明的多肽、核酸、载体和细胞可以配制为用于临床使用的药物组合物,并可以包含药学可接受载体、稀释剂、赋形剂或佐剂。

[0180] 根据本发明,还提供了用于生产药学上有用的组合物的方法,这样的生产方法可以包括选自以下的一个或多个步骤:分离如本文描述的多肽、细胞、核酸或载体;和/或将如本文描述的多肽、细胞、核酸或载体与药学可接受载体、佐剂、赋形剂或稀释剂混合。

[0181] 还提供了成套的试剂盒(a kit of parts)。在某些实施方式中,该试剂盒可以具有至少一个容器,所述容器具有预定量的根据本发明的多肽、核酸、载体、细胞或组合物。

[0182] 试剂盒可以将多肽、核酸、载体、细胞或组合物与用于给药的说明书一起提供给受试者以治疗特定疾病/病症。多肽、核酸、载体、细胞或组合物可以被配制成为适合于注射或输注。在某些实施方式中,多肽、核酸、载体、细胞或组合物可以被配制成为适合于静脉内、眼内、

视网膜下或结膜内注射,作为滴眼剂施用(即,眼部施用),或口服施用。

[0183] 在某些实施方式中,试剂盒可以包括用于生产根据本发明的细胞的材料。例如,试剂盒可以包括用于修饰细胞以表达或包括根据本发明的多肽、核酸或载体的材料,或用于向细胞中导入根据本发明的核酸或载体的材料。

[0184] 在某些实施方式中,试剂盒还可以包含至少一个容器,该容器具有预定量的另一种治疗剂(例如,用于治疗AMD的治疗药剂)。在这样的实施方式中,试剂盒还可以包含第二药物或药物组合物,使得所述两种药物或药物组合物可以同时施用或分别施用,以便它们提供对特定疾病或病症的组合治疗。

[0185] 蛋白质表达

[0186] 适合于在细胞中产生根据本发明的多肽的分子生物学技术是本领域熟知的,例如,在Sambrook等,Molecular Cloning:A Laboratory Manual,New York:Cold Spring Harbor Press,1989中阐述的那些。多肽可以从核酸序列表达。核酸序列可以包含在存在于细胞中的载体中,或可以掺入细胞的基因组中。

[0187] 适合于表达多肽的任何细胞可以用于生产根据本发明的蛋白质。细胞可以是原核细胞或真核细胞。适当的原核细胞包括大肠杆菌(E.coli)。真核细胞的实施例包括酵母细胞、植物细胞、昆虫细胞或哺乳动物细胞(例如,中国仓鼠卵巢(CHO)细胞)。在某些情况下,细胞不是原核细胞,因为某些原核细胞不允许如真核细胞的译后修饰。另外,在真核细胞中非常高的表达水平是可能的,使用适当标签蛋白质可以更容易地从真核细胞中纯化。还可以利用特定的质粒,其增强向细胞培养基中的蛋白质分泌。

[0188] 生产目标多肽(polypeptide of interest)的方法可以涉及培养或发酵被修饰以表达多肽的细胞。可以在生物反应器中执行培养或发酵,该生物反应器设置有适当的营养物、空气/氧气和/或生长因子的供应。可以通过将培养基/发酵液与细胞分割、提取蛋白质含量(protein content)、分离单个蛋白质以分离分泌的多肽来收集分泌的蛋白质。培养、发酵和分离技术是本领域技术人员熟知的。

[0189] 生物反应器包括可以在其中培养细胞的一个或多个容器。生物反应器中的培养可以连续地发生,反应物连续流动进入反应器,培养的细胞连续流出反应器。做为选择,培养可以分批发生。生物反应器监视并控制环境条件,例如pH值、氧气、进出的流速、和容器内的搅动,从而为培养中的细胞提供最佳条件。

[0190] 在表达多肽的细胞培养之后,优选分离多肽。可以使用本领域已知的从细胞培养物中分离多肽的任何适合的方法。为了从培养中分离目标多肽,必须首先从含有目标多肽的培养基中分离培养的细胞。如果目标多肽从细胞中分泌,那么可以通过离心将细胞从含有分泌的多肽的培养基中分离。如果目标多肽在细胞内收集,那么将必须在离心之前破坏细胞,例如使用超声、快速冻融或渗透性裂解。离心将产生含有培养的细胞、或培养的细胞的细胞碎片的沉淀,以及含有培养基和目标多肽的上清液。

[0191] 然后可取的是将目标多肽从上清液或培养基中分离,该上清液或培养基可能含有其他蛋白质或非蛋白质成分。从上清液或培养基中分离多肽成分的常见方法是通过沉淀。不同溶解度的多肽/蛋白质在不同浓度的诸如硫酸铵沉淀剂下沉淀。例如,在低浓度的沉淀试剂下,提取水溶性蛋白质。因而,通过添加浓度递增的沉淀试剂,可以区分不同溶解度的蛋白质。随后可以使用透析来从分离的蛋白质中除去硫酸铵。

[0192] 分离/纯化多肽的其他方法是本领域已知的,例如离子交换层析和大小层析。多肽还可以使用多肽上分子标签(例如,His、FLAG、Myc、GST、MBP、HA、E或生物素标签)的适当结合伴侣来亲和纯化。这些技术可以用作对沉淀的替代,或可以在沉淀之后进行。

[0193] 在某些情况下,还可能希望加工多肽,例如以除去氨基酸的序列、分子标签、部分等。

[0194] 在某些实施方式中,使用适当肽链内切酶处理以裂解和除去氨基酸序列。

[0195] 在某些实施方式中,使用酶处理来除去目标部分。在某些实施方式中,多肽被处理以除去聚糖(即,多肽去脱糖基化),例如,通过使用糖苷酶处理,例如使用肽:N-糖苷酶(PNGase)。

[0196] 一旦从培养中分离了目标多肽,可能希望浓缩所述蛋白质。浓缩目标蛋白质的许多方法是本领域已知的,例如通过超滤或冻干。

[0197] 在某些实施方式中,例如在向宿主中导入包括编码本发明的多肽的核酸或载体的细胞之后、或者在向宿主的细胞中导入编码本发明的多肽的核酸或载体之后,多肽的生产在体内发生。在这样的实施方式中,多肽被转录、转译和译后加工为成熟多肽。在某些实施方式中,多肽在所述宿主中期望的位置原位产生。

[0198] 补体系统和年龄相关性黄斑变性(AMD)

[0199] 例如,通过Zipfel等人在Lambris and Adamis(eds.), *Inflammation and Retinal Disease: Complement Biology and Pathology*, *Advances in Experimental Medicine and Biology* 703, Springer Science+Business Media, LLC (2010) 的章节2中评述了补体在AMD中的作用,通过引用以其整体合并在本文中。年龄相关性黄斑变性(AMD)显现为眼睛背部视网膜中心部分、黄斑的渐进性破坏,导致中央视敏度的损失。这是流行病(prevalent disease),其中预测数据(projected figures)预计到2020年全世界范围内有1.96亿9千6百万人患有某种形式的AMD;AMD占当前全世界所有失明登记的8.7%原因(Wong等Lancet Glob Heal (2014) 2:e106-16)。疾病的早期阶段可见黄斑中形态变化,包括首先脉络膜血管层中血管损失(Whitmore等, *Prog Retin Eye Res* (2015) 45:1-29),脉络膜血管层是布鲁赫膜(BrM)紧下方的有窗孔(fenestrated)的血管。这也是AMD之前补体活化和周转(turnover)提高的主要区域之一。

[0200] 早期AMD形式的标志性病变就在BrM之内,称为脉络膜疣。脉络膜疣由脂质和细胞碎屑的积累而形成,并包括补体活化产物的包裹物(Anderson等, *Prog Retin Eye Res* (2009) 29:95-112;Whitcup等, *Int J Inflam* (2013) 1-10)。BrM内脉络膜疣的存在破坏从脉络膜跨越细胞外基质进入RPE细胞的营养物流动,这导致细胞功能障碍和最终的死亡。由于RPE细胞单层支撑感觉神经视网膜的视杆细胞和视锥细胞,它们的细胞死亡导致光受体细胞的功能障碍,随后视敏度损失。这代表晚期AMD之一,称为地图状萎缩,或代表了约90%的病例的“干性”AMD,。在其余百分比的病例中,脉络膜疣的存在促进脉络膜新血管形成(choroidal neovascularisation, CNV),其中来自RPE细胞的血管内皮生长因子(vascular endothelial growth factor, VEGF)的合成增加促进了脉络膜/脉络膜血管层的过度血管生长,其突破BrM并渗入感觉神经视网膜。这被称为“湿性”AMD,虽然仅代表10%的病例,但是是晚期AMD的最恶性的形式。存在着对湿性AMD的治疗,其中向眼睛的玻璃体中注射抗VEGF抗体片段可以减缓或逆转这些血管的生长,然而它不能一开始就阻止它们的形成。干

性AMD仍是不可治疗的。

[0201] 与发生AMD的遗传风险相关联的主要单核苷酸多态性(single nucleotide polymorphisms, SNP)之一是补体因子H(complement factor H, CFH)基因中的一个,其引起补体的主要流体相调节物因子H(FH;参见例如Science (2005) 308:419-21)中的Y402H多态性,并且它是可替代的剪接变体因子H样蛋白1(factor H-like protein 1, FHL-1)。约30%的白种欧洲人血统(white European heritage)的个体具有这种多态性的至少一个拷贝,其中成为异质结合体提高了你的AMD的风险~3倍(Sofat等, Int J Epidemiol (2012) 41:250-262)。体现在第七补体调控蛋白(CCP)结构域中的Y402H多态性降低了FH/FHL-1与BrM的结合,考虑到BrM的非细胞性质,这些血源性(blood-borne)补体调节物的结合中的任何扰动将引起这一表面上的被阻抑的补体调节(Clark等, J Biol Chem (2010) 285:30192-202)。FH/FHL-1与BrM的结合受到硫酸酸化糖介导,该硫酸化糖包括糖胺聚糖(glycosaminoglycans, GAGs)硫酸乙酰肝素(heparan sulphate, HS)和硫酸皮肤素(dermatan sulphate, DS)。BrM中发现的GAG序列家族看起来比早先设想的具有更大的组织特异性,因为它们能够通过它们的CCP7结构域征募FH/FHL-1,而不是通过CCP 19-20中发现的FH的次级锚定位点(Clark等, J Immunol (2013) 190:2049-2057)。这可能是进化扭转(evolutionary twist),因为已经发现BrM内的补体的主要调节物是截短的FHL-1蛋白(Clark等J. Immunol (2014) 193, 4962-4970),该截短的FHL-1蛋白仅具有CCP7中的一个表面锚定位点并缺乏CCP 19-20;Y402H多态性不与肾脏疾病相关,在其中已知FH的CCP19-20结构域是主要的GAG介导的锚定位点(Clark等, J Immunol (2013) 190:2049-2057)。HS和DS的BrM表达水平的年龄相关的改变,其自身被认为是正常的老化过程的一部分,也已经与AMD相关联,并且可能某种程度上解释了遗传驱动的AMD的年龄相关性。

[0202] 存在着令人信服的数据,该数据表明潜在的(underlying)血管在AMD中也是重要的。不结合BrM的FH的C-末端CCP 19-20区域中的罕见突变(R1210C)具有与AMD有非常高水平的相关性,并且发现携带这种突变的FH蛋白与白蛋白共价结合(Sánchez-Corral等, Am J Hum Genet (2002) 71:1285-1295)。并且,某些研究表明,在地图状萎缩之前大汇合的脉络膜疣、以及RPE细胞中关联色素改变表明,首先从RPE细胞中的功能障碍产生干性AMD,伴有脉络膜内的次级效应(Bhutto and Lutty Mol Aspects Med (2012) 33:295-317)。相比之下,Whitmore等人报道了在所有形式的晚期AMD之前脉络膜血管层中的改变包括终端补体膜攻击复合物(membrane attack complex, MAC)的沉积,并争论了这是主要因素(primary event),RPE萎缩是次级的(Whitmore等, Prog Retin Eye Res (2015) 45:1-29)。这些改变是否是年龄相关的、是否由氧化应激驱动、或是否是RPE细胞功能障碍的结果尚待分晓,但是已知这些结构中天然发生的改变受到年龄的影响。

[0203] 治疗应用

[0204] 根据本发明的多肽、核酸、载体、细胞和药物组合物在治疗和预防方法中获得应用。

[0205] 本发明提供了根据本发明的多肽、核酸、载体、细胞或药物组合物,其在药物治疗或预防方法中使用。本发明还提供了根据本发明的多肽、核酸、载体、细胞或药物组合物在制造用于治疗或预防疾病或病症的药物中的用途。本发明还提供了治疗或预防疾病或病症的方法,该方法包括向受试者施用治疗有效量或预防有效量的根据本发明的多肽、核酸、载

体、细胞或药物组合物。

[0206] 特别地,根据本发明的所述多肽、核酸、载体、细胞和药物组合物在治疗或预防与补体失调、特别是与过度活化的补体响应相关联疾病/病症中获得应用。

[0207] 多肽、核酸、载体、细胞和药物组合物在治疗或预防疾病/病症中获得应用,该疾病/病症将会受益于以下一种或多种:C3bBb型C3转化酶、C3bBb3b型C5转化酶或C4b2a3b型C5转化酶的水平或活性的降低;C3b、C5b或C5a的水平的降低;或iC3b、C3f、C3dg或C3d的水平提高。

[0208] 例如,“治疗”可以是疾病/病症的发展或进展(progression)的降低,疾病/病症的症状的缓解,或疾病/病症的病理的降低。疾病/病症的治疗或缓解可以有效防止所述疾病/病症的进展,例如,防止病症的恶化或减慢发展速度。在某些实施方式中,治疗或缓解可以引起疾病/病症的改善,例如,所述疾病/病症的症状的降低,或所述疾病/病症的严重度/活性的某些其他相关物的降低。疾病/病症的防止/预防可以指病症恶化的防止、或疾病/病症发展的防止,例如,防止早期疾病/病症发展至晚期的、慢性的阶段。

[0209] 在某些实施方式中,待治疗或预防的疾病或病症是与C3b或含有C3b的复合物、与C3b或含有C3b的复合物相关联活性/响应、或者与C3b或含有C3b的复合物相关联活性/响应产物,相关联的疾病/病症。也就是说,在某些实施方式中,待治疗或预防的疾病或病症是一种疾病/病症,在其中C3b、含有C3b的复合物、与C3b或含有C3b的复合物相关联活性/响应、或者所述活性/响应产物,是病理上牵连的。在某些实施方式中,与对照状态相比,疾病/病症可以与C3b或含有C3b的复合物的水平提高、与C3b或含有C3b的复合物相关联活性/响应的水平提高、或者与C3b或含有C3b的复合物相关联活性/响应产物的水平提高,相关联。

[0210] 在某些实施方式中,失调可以是与FH、FHL-1、FI、FB、FD、CR1和/或CD46,与FH、FHL-1、FI、FB、FD、CR1和/或CD46相关联的活性/响应,或者与FH、FHL-1、FI、FB、FD、CR1和/或CD46相关联的活性/响应产物,相关联的失调。在某些实施方式中,失调是在其中FH、FHL-1、FI、FB、FD、CR1和/或CD46,与FH、FHL-1、FI、FB、FD、CR1和/或CD46相关联的活性/响应,或者与FH、FHL-1、FI、FB、FD、CR1和/或CD46相关联的活性/响应产物是病理上牵连的一种失调。在某些实施方式中,与对照状态相比,失调可以与FH、FHL-1、FI、FB、FD、CR1和/或CD46的水平降低,与FH、FHL-1、FI、FB、FD、CR1和/或CD46相关联的活性/响应的水平降低,或者与FH、FHL-1、FI、FB、FD、CR1和/或CD46相关联活性/响应产物的水平降低相关联。

[0211] 在某些实施方式中,与对照状态相比,失调与C3、C3b、C3转化酶和/或C3bBb的水平提高相关联。在某些实施方式中,与对照状态相比,失调与iC3b的水平下降相关联。

[0212] 治疗目的可以在于降低C3b或含有C3b的复合物的水平、与C3b或含有C3b的复合物相关联活性/响应、或者与C3b或含有C3b的复合物相关联活性/响应产物。在某些实施方式中,治疗的目的在于:降低C3bBb型C3转化酶、C3bBb3b型C5转化酶或C4b2a3b型C5转化酶的水平或活性;降低C3b、C5b或C5a的水平;或者提高iC3b、C3f、C3dg或C3d的水平。

[0213] 施用本发明的多肽、核酸、载体、细胞和组合物可以通过C3b的裂解引起C3b或含有C3b的复合物、与C3b或含有C3b的复合物相关联活性/响应、或者与C3b或含有C3b的复合物相关联活性/响应产物的水平降低。

[0214] 在某些实施方式中,治疗目的可以在于降低受试者中,例如在特定位置,在特定器官、组织、结构或细胞类型中,C3b或含有C3b的复合物、与C3b或含有C3b的复合物相关联活

性/响应、或者与C3b或含有C3b的复合物相关联活性/响应产物的水平。在某些实施方式中，治疗目的可以在于降低眼睛中，例如，视网膜、脉络膜、视网膜色素上皮细胞、黄斑和/或BrM/RPE细胞界面处，C3b或含有C3b的复合物、与C3b或含有C3b的复合物相关联活性/响应、或者与C3b或含有C3b的复合物相关联活性/响应产物的水平。

[0215] 在某些实施方式中，治疗可以包括修饰细胞或细胞种群以包括/表达本发明的多肽、核酸或载体。在某些实施方式中，治疗可以包括在体内修饰细胞/种群，用于原位产生本发明的多肽。

[0216] 在某些实施方式中，治疗可以包括向受试者施用细胞或细胞种群，所述细胞或细胞种群被修饰以包括/表达本发明的多肽、核酸或载体。在某些实施方式中，治疗可以包括在体内或体外细胞/种群的修饰。

[0217] 在某些实施方式中，治疗目的在于，例如通过施用根据本发明的细胞、或产生根据本发明的细胞，向受试者提供产生本发明的多肽的细胞或细胞种群。

[0218] 在某些实施方式中，细胞是眼睛的细胞。在某些实施方式中，细胞是视网膜、脉络膜、视网膜色素上皮细胞或黄斑的细胞。在某些实施方式中，所述细胞是视网膜细胞。在某些实施方式中，细胞是视网膜色素上皮细胞(RPE)。

[0219] 本发明提供了一种治疗或呈现受试者中的疾病或病症的方法，所述方法包括修饰至少一个细胞以表达或包括根据本发明的多肽、核酸或载体。

[0220] 可以根据技术人员公知的方法修饰根据本发明修饰的至少一个细胞。该修饰可以包括核酸转移以永久性或瞬时性表达所转移的核酸。任何适合的遗传工程平台可以用于修饰根据本发明的细胞。用于修饰细胞的适当的方法包括，使用遗传工程平台、例如gamma逆转录病毒载体、慢病毒载体、腺病毒载体、腺相关病毒(adeno-associated virus, AAV)载体、DNA转染、转位子类基因递送和RNA转染，例如在Maus等, *Annu Rev Immunol* (2014) 32: 189-225中描述的，其通过引用合并在本文中。

[0221] 待治疗的受试者可以是任何动物或人类。受试者优选地是哺乳动物，更优选地是人类。受试者可以是非人类哺乳动物，但更优选地是人类。受试者可以是雄性或雌性。受试者可以是患者。受试者可以已被诊断患有所需治疗的疾病或病症，或被怀疑患有这样的疾病或病症。

[0222] 例如，如通过使用适当试验分析受试者、或从受试者获取的样品(例如，细胞、组织、血液样品)所确定的，待治疗的受试者可以展现C3b或含有C3b的复合物、与C3b或含有C3b的复合物相关联活性/响应、或者与C3b或含有C3b的复合物相关联活性/响应产物的升高水平。

[0223] 受试者可以具有C3b或含有C3b的复合物的、或者与C3b或含有C3b的复合物相关联活性/响应的，正调节物/效应物的提高的表达或活性水平；或者可以具有与C3b或含有C3b的复合物相关联活性/响应产物提高的表达或活性水平。受试者可以具有由C3b或含有C3b的复合物上调的活性水平。

[0224] 受试者可以具有C3b或含有C3b的复合物的、或者与C3b或含有C3b的复合物相关联活性/响应的，正调节物/效应物的降低的表达或活性水平；或者可以具有与C3b或含有C3b的复合物相关联活性/响应产物的降低的表达或活性水平。受试者可以具有由C3b或含有C3b的复合物下调的活性水平。

[0225] 提高/降低可以与不存在相关疾病/病症的情况下的表达/活性水平相关,例如与在健康对照受试者中、或者获自健康对照受试者的样品中的表达/活性水平相关。

[0226] 在某些实施方式中,受试者可以处于发生(developing)/感染(contracting)疾病或病症的风险中。在某些实施方式中,受试者可以具有提高发生/感染疾病或病症风险的一种或多种发病诱因。

[0227] 在某些实施方式中,受试者可以具有年龄相关性黄斑变性(AMD)的一种或多种风险因素。在某些实施方式中,受试者可以具有一种或多种AMD关联遗传变体。例如在Clark等,J Clin Med (2015) 4 (1):18-31中描述了AMD关联遗传变体,通过引用以其整体合并在本文中。在某些实施方式中,受试者可以具有一种或多种以下的AMD关联遗传变体(或具有带有此类变体的 $LD=r^2 \geq 0.8$ 的变体):CHF中的Y402H(即rs1061170^C)、rs1410996^C、CFH中的I62V、CFH中的R53C、CFH中的D90G、CFH中的R1210C、或rs6685931^T。

[0228] 在某些实施方式中,基于确定受试者具有AMD的一种或多种风险因素、例如一种或多种AMD关联遗传变体,选择所述受试者用本发明的多肽、核酸、载体、细胞或组合物进行治疗或预防疗法。在某些实施方式中,受试者已被确定为具有一种或多种这样的风险因素。在某些实施方式中,本发明的方法涉及确定受试者是否具有一种或多种这样的风险因素。

[0229] 在某些实施方式中,待治疗或预防的疾病或病症可以是眼部疾病/病症。在某些实施方式中,待治疗或预防的疾病或病症可以选自AMD、干性(即,非渗出性)AMD、青光眼、自体免疫性葡萄膜炎(autoimmune uveitis)、脉络膜新生血管(CNV)和糖尿病性视网膜病。在某些实施方式中,待治疗或预防的疾病或病症是AMD。在某些实施方式中,待治疗或预防的疾病或病症是干性AMD。在某些实施方式中,待治疗的疾病或病症是湿性(渗出性)AMD。如本文使用的,术语“AMD”包括早期AMD、中期AMD、晚期/进展期(advanced)AMD、地图状萎缩(“干性”(即,非渗出性)AMD)、和“湿性”(即,渗出性)AMD,其每一种可以是就自身而言如本文描述的被检测、治疗和/或预防的失调。

[0230] 在某些实施方式中,失调可以选自溶血性尿毒综合症(Haemolytic Uremic Syndrome,HUS)、非典型性溶血性尿毒综合症(atypical Haemolytic Uremic Syndrome,aHUS)、自体免疫性葡萄膜炎、膜增殖性肾小球性肾炎II型(Membranoproliferative Glomerulonephritis Type II,MPGN II)、脓毒症(sepsis)、亨-舍二氏紫癜(Henoch-Schonlein purpura,HSP)、IgA肾病、阵发性睡眠性血红蛋白尿(paroxysmal nocturnal hemoglobinuria,PNH)、自身免疫性溶血性贫血(autoimmune hemolytic anemiaAIHA)、系统性红斑狼疮(systemic lupus erythematosus,SLE)、斯耶格伦氏综合征(Sjogren's syndrome,SS)、类风湿性关节炎(rheumatoid arthritis,RA)、C3肾炎因子肾小球性肾炎(C3 nephritic factor glomerulonephritis,C3 NF GN)、遗传性血管性水肿(hereditary angioedema,HAE)、获得性血管性水肿(acquired angioedema,AAE)、脑脊髓炎、动脉粥样硬化、多发性硬化(multiple sclerosis,MS)、帕金森氏病和阿尔茨海默氏病。在某些情况下,失调是神经学的和/或神经变性的失调。

[0231] 药物治疗的方法还可以涉及体内的、体外的、和过继免疫疗法,其包括使用自体的和/或异源的细胞、或者无限增殖化细胞系的那些方法。

[0232] 优选地,施用可以是“治疗有效量”,这足以显示对个体的益处。施用的实际量、以及施用的速率和时程,将取决于被治疗的疾病的性质和严重程度。治疗的处方、例如关于剂量

的判定等,在全科医师和其他医学医生的职责之内,一般考虑待治疗的病症、个体患者的病症、递送的位点、施用的方法和医师已知的其他因素。上述技术和方案的实施例可以在 Remington's Pharmaceutical Sciences, 20th Edition, 2000, pub. Lippincott, Williams & Wilkins 中找到。

[0233] 根据本发明的多肽、核酸、载体和细胞可以配制为药物组合物或临床应用药物,并可以包括药学可接受载体、稀释剂、赋形剂或佐剂。该组合物可以配制为局部的、胃肠外的、全身性、腔内的、静脉内的、动脉内的、肌肉内的、鞘内的、眼内的、结膜内的、视网膜下的、皮下的、真皮内的、鞘内的、口服的或经皮的施用途径,其可以包括注射或输注,或者作为滴眼剂施用(即,眼部施用)。适当制剂可以包括无菌的或等渗的基质中的多肽、核酸、载体或细胞。药物和药物组合物可以配制为液体形式、包括凝胶形式。液体制剂可以配制为通过注射或输注(例如,通过导管)施用至人体或动物体的选定器官或区域。

[0234] 施用的特定模式和/或位点可以根据期望C3b灭活的位置来选择。

[0235] 根据本发明,还提供了用于生产药学上有用的组合物的方法,这样的生产方法可以包括选自以下的一个或多个步骤:分离如本文描述的多肽、核酸、载体或细胞;和/或将如本文描述的多肽、核酸、载体或细胞与药学可接受载体、佐剂、赋形剂或稀释剂混合。

[0236] 例如,本发明的进一步的方面涉及配制或生产在药物治疗方法中使用的药物或药物组合物的方法,该方法包括通过将本文描述的多肽、核酸、载体或细胞与药学可接受载体、佐剂、赋形剂或稀释剂混合来配制药物组合物或药物。

[0237] 施用可以是单独的或与其他治疗结合(例如,其他治疗或预防性介入),取决于待治疗的病症同时地或顺序地施用。

[0238] 适合与本发明一起使用的其他治疗剂或治疗可以包括营养疗法、光动力学疗法(photodynamic therapy, PDT)、激光光凝术、抗VEGF(血管内皮生长因子)疗法和/或本领域已知的其他疗法,参见,例如Al-Zamil WM and Yassin SA, Clin Interv Aging. 2017 Aug 22; 12:1313-1330。抗VEGF疗法可以包括药剂,例如兰尼单抗(ranibizumab)(雷珠单抗(Lucentis),由基因泰克/诺华公司(Genentech/Novartis)制造)、阿瓦斯汀(Genentech)、贝伐单抗(标记外的(off-label)阿瓦斯汀)和阿柏西普(来自再生元公司/拜耳(Regeneron/Bayer)的艾力亚® (Eylea®)阿柏西普眼科溶液(VEGF Trap-Eye))。适于与本发明一起使用的其他药剂或技术包括培可他普兰-2 (APL-2) (阿佩利斯(Apellis))、腺病毒色素上皮衍生因子(Adenovirus Pigment epithelium-derived factor, AdPEDF)(真科生物(GenVec))、封装的细胞技术(encapsulated cell technology, ECT; 涅罗科技(Neurotech))、乳酸角鲨胺(EVIZON™, 纳来(GenAera))、OT-551(抗氧化剂滴眼剂, Othera)、醋酸阿奈可他(anecortave actate, 阿奈可他® (Retaane®), 爱尔康(Alcon))、贝伐西尼(bevasiranib, 干扰RNA(siRNA), 敏度制药(Acuity Pharmaceuticals))、哌加他尼钠(pegaptanib sodium, 哌加他尼钠® (Macugen®)) 和AAVCAGsCD59(临床试验标识符: NCT03144999)。

[0239] 根据本发明的多肽、核酸、载体、细胞或组合物以及治疗剂可以同时地或依序地施用。

[0240] 同时施用是指一起将多肽、核酸、载体、细胞或组合物与治疗药剂一起施用、例如

作为含有两种药剂(结合制品)的药物组合物,或紧接彼此之后给药,任选地通过相同的施用途,例如,施用到相同组织、动脉、静脉或其他血管。依序施用是指通过分开施用其他药剂在给定的时间间隔之后施用多肽、核酸、载体、细胞或组合物或治疗剂之一。不需要通过相同的途径施用两种药剂,尽管这在是在某些实施方式中的情况。该时间间隔可以是任何时间间隔。

[0241] 可以提供多肽、核酸、载体、细胞或组合物的多个剂量。该剂量的一个或多个、或者每个可以伴随另一种治疗剂的的同时的或依序的施用。

[0242] 多个剂量可以按照预定时间间隔分开,该预定时间间隔可以被选择为1、2、3、4、5、6、7、8、9、10、11、12、13、14、15、16、17、18、19、20、21、22、23、24、25、26、27、28、29、30或31天,或1、2、3、4、5或6个月中的一种。举例来说,剂量可以每7天、14天、21天或28天(加或减3、2或1天)给予一次。

[0243] 检测

[0244] 本发明还提供了检测样品中多肽的方法,该方法包括:

[0245] (i) 使疑似含有本发明的多肽的样品接触特异于多肽检测序列蛋白水解裂解位点的蛋白水解酶;和

[0246] (ii) 检测所述非内源肽的存在。

[0247] 如本文描述的,该方法在向受试者施用根据本发明的多肽、核酸、载体、细胞或药物组合物之后执行。

[0248] 该样品可以是获自受试者的任何生物样品。在某些实施方式中,样品是液体活检、例如眼液(泪液、水状液或玻璃体)、血液、血浆,等。在某些实施方式中,样品是细胞学样品或组织样品、例如手术样品,例如,眼部细胞/组织的样品。

[0249] 样品在条件下(例如温度、pH值,等)接触给定蛋白水解酶,并持续适合于给定酶的蛋白水解活性的一段时间。

[0250] 非内源肽的检测可以通过任何适当的手段,例如,通过质谱分析法,或采用特异性结合试剂的方法,例如Western印迹、ELISA等。在某些实施方式中,该方法还包括定量样品中的非内源肽量,以及任选地将非内源肽的量与样品中多肽的量或浓度相关联。

[0251] 在该方法的说明性实施方式中,疑似含有由氨基酸序列SEQ ID NO:37组成的多肽的样品在适当条件下与胰蛋白酶接触,并持续多肽的胰蛋白酶化的足够时间,随后通过检测肽SEQ ID NO:46和47之一或两者来确认根据SEQ ID NO:37的多肽的存在。

[0252] 序列同一性

[0253] 为了确定两种或多种氨基酸或核酸序列之间的百分比同一性的成对的和多重的序列比对(sequence alignment)可以以本领域技术人员已知的各种方式实现,例如,使用公众可获得的计算机软件例如ClustalOmega (Soding, J. 2005, Bioinformatics 21, 951-960)、T-coffee (Notredame等2000, J. Mol. Biol. (2000) 302, 205-217)、Kalign (Lassmann and Sonnhammer 2005, BMC Bioinformatics, 6 (298)) 和MAFFT (Katoh and Standley 2013, Molecular Biology and Evolution, 30 (4) 772-780)。当使用这样的软件时,优选地使用默认参数、例如对于空位罚分(gap penalty)和延伸罚分(extension penalty)。

[0254] 序列

[0255]

SEQ ID NO:	说明	序列
1	人 C3 (UniProt: P01024) 包括信号肽	MGPTSGPSLLLLLTHLPLALGSPMYSIITPNILRLESEETMVLEAHDAQG DVPVTVTVHDFPGKKLVLSSEKTVLTPATNHMGNTFTIPANREFKSEKG RNKFVTVQATFGTQVVEKVVLVSLQSGYLFIQTDKTIYTPGSTVLYRIFTV NHKLLPVGRTVMVNIENPEGIPVKQDSLSSQNQLGVLPWSWDIPELVNMG QWKIRAYYENSPQQVFSTEFVKEYVLPSEFVIVEPTEKFYIYNEKGLEV TITARFLYGKKVEGTAFVIFGIQDGEQRISLPESLKRIPIEDGSGEVLSRKV LLDGVQNPRAEDLVGKSLYVSATVILHSGSDMVQAERSGPIVTSPIYQIHF TKTPKYFKPGMPFDLMVFTNPDGSPAYRVPVAVQGEDTVQSLTQGDGV AKLSINTHPSQKPLSITVRTKKQELSEAEQATRTMQALPYSTVGNSNNYL HLSVLRTELRPGETLVNLFLLRMDRAHEAKIRYYTYLIMNKGRLKAGR QVREPGQDLVVLPLSITDFIPSFRLVAYYTLIGASGQREVVADSVWVDVK DSCVGSLLVVKSGQSEDRQVPVPGQQMTLKIEGDHGARVVLVAVDKGVFVL NKKNKLTQSKIWDVVEKADIGCTPGSGKDYAGVFSDAGLFTSSSGQQT AQRAELQCPQPAARRRRSVQLTEKRMDKVGKYPKELRKCCEDGMREN MRFSCQRRTRFISLGEACKKVFLDCCNYITELRRQHARASHLGLARSNLD EDIIAENIVSRSEFPESWLWNVEDLKEPPKNGISTKLMNIFLKDSITTWEI LAVSMSDDKKGICVADPFVETVMQDFFIDRLPYSVVRNEQVEIRAVLYNY RQNQELKVRVELLHNPAFCSLATTKRRHQQTVTIPKSSLSVPYVIVPLKT GLQEVEVKAAYVHHFISDGVRSKLVVPEGIRMNKTAVVRTLDPERLGR EGVQKEDIPPADLSDQVPDTESETRILLQGTPVAQMTEDAVDAERLKHLLV TPGSGCEQNMIGMTPTVIAVHYLDETEQWEKFGLEKRGGALELIKKGYT QQLAFRQPSSAFAAFVKRAPSTWLTAYVVKVFLAVNLIAIDSQVLCGAV KWLILEKQKPDGVFQEDAPVIHQEMIGGLRNNNEKDMALTAFLISLQEA KDICEEQVNSLPGSITKAGDFLEANYMNLQRSYTVAIAGYALAQMGRLK GPLLNKFLTTAKDKNRWEDPGKQLYNVEATSYALLALLQLKDFDFVPPV VRWLNEQRYYGGGYGSTQATFMVFQALAQYQKDAPDHQELNLDVSLQ LPSRSSKITHRIHWESASLLRSEETKENEGFTVTAEGKGQGTLSVVTMYH AKAKDQLTCNKFDLKVTIKPAPETEKRPQDAKNTMILEICTRYRGDQDAT MSILDISMMTGAPDTPDLKQLANGVDRIYSKYELDKAFSDRNTLIYLD KVSHSEDDCLAFKVHQYFNVELIQPGAVKVYAYYNLEESCTRFYHPEKE DGKLNKLCRDELCRAEENCFIQKSDDKVTLEERLDKACEPGVDYVYKT RLVKVQLSNDFDEYIMAIEQTIKSGSDEVQVGQQRFTISPIKCREALKLEE KKHLYLMWGLSSDFWGEKPNLSYIIGKDTWVEHWPEEDECQDEENQKQC QDLGAFTESMVVFGCPN
2	人 C3 β 链 (UniProt: P01024 残基	SPMYSIITPNILRLESEETMVLEAHDAQGDVPVTVTVHDFPGKKLVLSSEK TVLTPATNHMGNTFTIPANREFKSEKGRNKFVTVQATFGTQVVEKVVLV SLQSGYLFIQTDKTIYTPGSTVLYRIFTVNHKLLPVGRTVMVNIENPEGIPV

[0256]

	23-667)	KQDSLSSQNQLGVLPLSWDIPELVNMGQWKIRAYYENSPQQVFSTEFEV KEYVLPSPFEVIVEPTEKFYYIYNEKGLEVTITARFLYGKKVEGTAFVIFGIQ DGEQRISLPESLKRIPIEDGSGEVVLSRKVLLDGVQNPRAEDLVGKSLYVS ATVILHSGSDMVQAERSGIPIVTSPIYQIHFTKTPKYFKPGMPFDLMVFVTN PDGSPAYRVPVAVQGEDTVQSLTQGDGVAKLSINTHPKPLSITVVRTKKQ ELSEAEQATRTMQALPYSTVGNSNNYLHLSVLRTELRPGETLNVNFLLRM DRAHEAKIRYYTYLIMNKGRLLKAGRQVREPQQDLVVLPLSITTDIFPSFR LVAYYTLIGASGQREVVDASVWVDVKDSCVGSVLVKSQSEDQRQVPVPGQ QMTLKIEGDHGARVVLAVDKGVFVLNKKNKLTQSKIWDVVEKADIGCT PGSGKDYAGVFSDAGLTFTSSSGQQTAAQRAELQCPQAA
3	人 C3 α' 链 (UniProt : P01024 残基 749-1663)	SNLDEDIAEENIVSRSEFPESWLWNVEDLKEPPKNGISTKLMNIFLKDSIT TWEILAVSMSDDKKGICVADPFEVTVMQDFFIDLRLPYSVVRNEQVEIRAVL YNYRQNQELKVRVELLHNPFCSLATTKRRHQQTVTIPPSSSLVPPYVIVP LKTGLQEVEVKAAYVHHFISDGVRSLSLVPEGIRMNKTAVVRTLDPERL GREGVQKEDIPPADLSDQVPDTESETRILLQGTPVAQMTEDAVDAERLKH LIVTPSGCGEQNMIGMTPTVIAVHYLDETEQWEKFGLEKRQGALELIKKG YTQQLAFRQPSSAFAAFVKRAPSTWLTAYVVKVFLAVNLIAIDSQVLCG AVKWLILEKQKPDGVFQEDAPVIHQEMIGGLRNNNEKDMALTAFLISLQ EAKDICEEQVNSLPGSITKAGDFLEANYMNLQRSYTVAIAGYALAQMG LKGPLLNKFLTAKDKNRWEDPGKQLYNVEATSYALLALLQLKDFDFVP PVVRWLNEQRYYGGSYGSTQATFMVFQALAQYQKDAPDHQELNLDVS LQLPSRSSKITHRIHWESASLLRSEETKENEGFTVTAEGKGQGTLSVVTM YHAKAKDQLTCNKFDLKVITIKPAPETEKRPQDAKNTMILEICTRYRGDQD ATMSILDISMGTGFAPDITDLKQLANGVDYISKYELDKAFSDRNTLIY DKVSHSEDDCLAFKVHGYFNVELIQPGAVKVYAYYNLEESCTRFYHPEK EDGKLNKLCRDELRCRAEENCIFIQSDDKVTLERLDKACEPGVDYVYK TRLVKVQLSNDFDEYIMAIEQTIKSGSDEVQVGQRTFISPIKCREALKLE EKKHYLMWGLSSDFWGEKPNLSYIIGKDTWVEHWPEEDECQDEENQKQ CQDLGAFTESMVVFGCPN
4	人 C3a (UniProt : P01024 残基 672-748)	SVQLTEKRMDKVGKYPKELRKCCEDGMRENPMRFSCQRRTRFISLGEAC KKVFLDCCNYITELRRQHARASHLGLAR
5	人 C3 α' 链片段 1 (UniProt : P01024 残基 749-1303)	SNLDEDIAEENIVSRSEFPESWLWNVEDLKEPPKNGISTKLMNIFLKDSIT TWEILAVSMSDDKKGICVADPFEVTVMQDFFIDLRLPYSVVRNEQVEIRAVL YNYRQNQELKVRVELLHNPFCSLATTKRRHQQTVTIPPSSSLVPPYVIVP LKTGLQEVEVKAAYVHHFISDGVRSLSLVPEGIRMNKTAVVRTLDPERL GREGVQKEDIPPADLSDQVPDTESETRILLQGTPVAQMTEDAVDAERLKH LIVTPSGCGEQNMIGMTPTVIAVHYLDETEQWEKFGLEKRQGALELIKKG YTQQLAFRQPSSAFAAFVKRAPSTWLTAYVVKVFLAVNLIAIDSQVLCG AVKWLILEKQKPDGVFQEDAPVIHQEMIGGLRNNNEKDMALTAFLISLQ EAKDICEEQVNSLPGSITKAGDFLEANYMNLQRSYTVAIAGYALAQMG LKGPLLNKFLTAKDKNRWEDPGKQLYNVEATSYALLALLQLKDFDFVP PVVRWLNEQRYYGGSYGSTQATFMVFQALAQYQKDAPDHQELNLDVS LQLPSR

[0257]

6	人 C3 α' 链片段 2 (UniProt : P01024 残基 1321-1663)	SEETKENEGFTVTAEGKGQGTLSVVTMYHAKAKDQLTCNKFDLKVTIKP APETEKRPQDAKNTMILEICTRYRGDQDATMSILDISMMTGFAPDTDLLK QLANGVDRIYSKYELDKAFSDRNTLIYLDKVSHSEDDCLAFKVHQYFNV ELIQPGAVKVYAYYNLEESCTRFYHPEKEDGKLNKLCRDELCRAEENCF IQKSDDKVTLEERLDKACEPGVDYVYKTRLVKVQLSNDFDEYIMAIEQTI KSGSDEVQVGQQRFTFISPIKCREALKLEEKHYLMWGLSSDFWGEKPNL SYIIGKDTWVEHWPEEDECQDEENQKQCQDLGAFTESMVVFGCPN
7	人 C3f (UniProt : P01024 残基 1304-1320)	SSKITHRIHWESASLLR
8	人补体因子 I (UniProt : P05156)	MKLLHVFLFLCFHLRFCKVITYTSQEDLVEKKCLAKKYTHLSCDKVFCQ PWQRCIEGTCVCKLPYQCPKNGTAVCATNRRSFPTYCQKSLECLHPGTK FLNNGTCTAEGKFSVSLKHGNTDSEGIVEVKLVQDKTMFICKSSWSMR EANVACLDLGFQQGADTQRRFKLSDLINSTECLHVHCRGLETSLAECTF TKRRTMGYQDFADVVCYTQKADSPMDDFFQCVNGKYISQMKACDGIN CGDQSDCLCKACQKGFGHCKSGVCIPSQYQCNGEVDICITGEDEVGCAG FASVTQEETEILTADMDAERRRIKSLPKLSCGVKNRMHRRKRIVGGKR AQLGDLPWQVAIKDASGITCGGIYIGGCWILTAHCLRAASKTHRYQIWT VVDWIHPDLKRIVIEYVDRIIFHENYNAGTYQNDIALIEMKKDGNKKDCE LPRSIPACVPWSPYLFQPNDCIVSGWGREKDNERVFSLQWGEVKLISNC SKFYGNRFYEKEMECAGTYDGSIDACKGDSGGPLVCMANNVTYVWG VVSWGENCCKPEFPGVYTKVANYFDWISYHVGRPFISQYNV
9	人补体因子 I 蛋白水解结构域 (UniProt : P05156 残基 340-574)	IVGGKRAQLGDLPWQVAIKDASGITCGGIYIGGCWILTAHCLRAASKTHR YQIWTTVVDWIHPDLKRIVIEYVDRIIFHENYNAGTYQNDIALIEMKKDG NKKDCELPRSIPACVPWSPYLFQPNDCIVSGWGREKDNERVFSLQWGE VKLISNCSKFYGNRFYEKEMECAGTYDGSIDACKGDSGGPLVCMANN VTYVWGVVSWGENCCKPEFPGVYTKVANYFDWISYHVG
10	人补体因子 H (UniProt : P08603)	MRLAKIICMLWAICVAEDCNELPPRRNTEILTGSDQTYPEGTQAIYK CRPGYRSLGNVIMVCRKGEWVALNPLRKCQKRPCGHPGDTFGTFTLTG GNVFEYGVKAVYTCNEGYYQLLGEINYRECDTDGWTNDIPICEVVKCLPV TAPENGKIVSSAMEPDREYHFGQAVRFVCNSGYKIEGDEEMHCSDDGFW SKEPKCVEISCKSPDVINGSPISQIYKENERFQYKCNMGYEYSERGDA VCTESGWRPLPSCEEKSCDNPIYNGDYSPLRIKHRTGDEITYQCRNGFY ATRGNTAKCTSTGWIPAPRCTLPCDYPDIKHGGLYHENMRRPYFPVAVG KYYSYCYDEHFETPSGSYWDHIHCTQDGWSPAVPCLRKCYFPYLENGYN QNYGRKFVQGSIDVACHPGYALPKAQTTVTCMENGWSPTPRCIRVKTC SKSSIDIENGFISESQYTYALKEKAKYQCKLGYVTADGETSGSITCGKDG WSAQPTCIKSCDIPVFMNARTKNDFTWFKLNDTLDYECHDGYESNTGST TGSIVCGYNGWSDLPICYERECELPKIDVHLVPDRKKDQYKVGVLKFC KPGFTIVGPNSVQCYHFGLSPLPICKEVQSCGPPPELLNGNVKEKTKEE YGHSEVVEYYCNPRFLMKGPNIQCVDGWTTLPVCIVEESTCGDIPELE HGWAQLSSPPYYGDSVEFNCSESFTMIGHRSITCIHGVWTQLPQCVAID KLKKCKSSNLIILEEHLKKNKEFDHNSNIRYRCRGKEGWIHTVCINGRWD PEVNCSMAQIQLCPPPQIPNSHNMTTTLNRYRDGEKVSVLCQENYLIQEG

[0258]

		EEITCKDGRWQSIPLCVEKIPCSQPPQIEHGTINSSRSSQESYAHGTKLSYT CEGGFRISEENETTCYMGKWSSPPQCEGLPCKSPPEISHGVVAHMSDSYQ YGEEVTYKCFEGFGIDGPAIAKCLGEKWSHPPSCIKTDCLSLPSFENAIPM GEKKDVYKAGEQVTTYTCATYYKMDGASNVTICNSRWTGRPTCRDTSVCV NPPTVQNAYIVSRQMSKYPGGERVRYQCRSPYEMFGDEEVMCLNGNWT EPPQCKDSTGKCGPPPIDNGDITSFPLSVYAPASSVEYQCQONLYQLEGNK RITCRNGQWSEPPKCLHPCVISREIMENYNIALRWTAQKQLYSRTGESVEF VCKRGYRLSSRSHTLRTTCWDGKLEYPTCAKR
11	人补体因子 H 辅助因子区 (UniProt : P08603 残基 19-264)	EDCNELPPRRNTEILTGSWSDQTYPEGTQAIYKCRPGYRSLGNVIMVCRK GEWVALNPLRKCKRPGCHPGDTPFGTFTLTGGNVFEYGVKAVYTCNEG YQLLGEINYRECDTDGWTNDIPICEVVKCLPVTAPENGKIVSSAMEPDRE YHFGQAVRFVCNSGYKIEGDEEMHCSDDGFWSKEKPKCVEISCKSPDVIN GSPISQKIYKENERFQYKCNMGYEYSERGDAVCTESGWRPLPSC EE
12	人补体受体 1 (UniProt : P17927)	MGASSPRSEPVGPPAPGLPFCCGGSLAVVLLALPVAWGQCNAPEWLP FARPTNLTDDEFPIGTYLNYECPGYSGRPFSIICLNKSVWTGAKDRCCR KSCRNPDPVNGMVHVIGIQFGS QIKYSCTKGYRLIGSSSATCIIISGDTVI WDNETPICDRIPCGLPPTITNGDFISTNRENFHYGSVVTYRCNPGSGGRKV FELVGESYICTSNDDQVGIWSPAPQCIIPNKCTPPNVENGILVSDNRS LF SLNEVVEFRQCQPGFVMKGPRRVKCQALNKWEPELPSCSRVCQPPDVLH AERTQRDKDNFSPGQEVFYSCPEGYDLRGAASMRCTPQGDWSPAAPTCE VKSCDDFMGQLLNGRVLFVNLQLGAKVDFVCDEGFQKLGSSASYCVL AGMESLWNSSVPVCEQIFCPSPVIPNGRHTGKPLEVFPFGKTVNYTCDP HPDRGTSFDLIGESTIRCTSDPQNGVWSSPAPRCGILGHCQAPDHFLFAK LKTQTNASDFPIGTS LKYECPREYYGRPFSITCLDNLVWSSPKDVCKRKSC KTPDPVNGMVHVITDIQVGS RINYSCTTGHR LIGHSSAECILSGNAAHW STKPPICQRI PCGLPPTIANGDFISTNRENFHYGSVVTYRCNPGSGGRKVFE LVGEPYICTSNDDQVGIWSPAPQCIIPNKCTPPNVENGILVSDNRS LFSL NEVVEFRQCQPGFVMKGPRRVKCQALNKWEPELPSCSRVCQPPDVLHAE RTQRDKDNFSPGQEVFYSCPEGYDLRGAASMRCTPQGDWSPAAPTCEVK SCDDFMGQLLNGRVLFVNLQLGAKVDFVCDEGFQKLGSSASYCVLAG MESLWNSSVPVCEQIFCPSPVIPNGRHTGKPLEVFPFGKAVNYTCDPHPD RGTSFDLIGESTIRCTSDPQNGVWSSPAPRCGILGHCQAPDHFLFAKLKT QTNASDFPIGTS LKYECPREYYGRPFSITCLDNLVWSSPKDVCKRKSKCTP PDPVNGMVHVITDIQVGS RINYSCTTGHR LIGHSSAECILSGNTAHWSTKP PICQRI PCGLPPTIANGDFISTNRENFHYGSVVTYRCNLGSRGRKVFELVG EPSYICTSNDDQVGIWSPAPQCIIPNKCTPPNVENGILVSDNRS LFSLNEV VEFRQCQPGFVMKGPRRVKCQALNKWEPELPSCSRVCQPPPEILHGEHTPS HQDNFSPGQEVFYSCPEGYDLRGAASLHCTPQGDWSPEAPRAVKS CDD FLGQLPHGRVLFPLNLQLGAKVSFVCDEGFRLKGSSVSHCVLVGM RSLW NNSVPVCEHIFCPNPAILNGRHTGTPSGDIPYGKEISYTCDPHPDRGMTF NLIGESTIRCTSDPHGNGVWSSPAPRC ELSVRAGHCKTPEQFPFASPTIPIN DFEFPVGTSLNYECPGYFGKMFSISCL ENLVWSSVEDNCRKSCGPPPEP FNGMVHINTDTQFGSTVNYSCNEGFR LIGSPSTTCLVSGNNVTWDDKAPI CEIISCEPPPTISNGDFYSNNRTSFHNGTVV TYQCHTGP DGEQLFELVGERS IYCTSKDDQVGWSSPPPRCISTNKCTAPEVENAIRVPGNRSFFSLTEIIRFR

[0259]

		CQPGFVMVGSHTVQCQTNGRWGPKLPHCSRVCQPPPEILHGEHTLSHQD NFSPGQEVFYSCPSYDLRGAASLHCTPQGDWSPEAPRCTVKSCDDFLG QLPHGRVLLPLNLQLGAKVSFVCDEGFRLKGRSASHCVLAGMKALWNS SVPVCEQIFCPNPAILNGRHTGTPTFGDIPYGKEISYACDTHPDRGMTFNLI GESSIRCTSDPQNGVWSSPAPRCELSVPAACPHPPKIQNGHYIGGHVSLY LPGMTISYICDPGYLLVGKGFICTDQGIWSQLDHYCKEVNCSFPLFMNGI SKELEMKKVYHYGDYVTLKCEDGYTLEGSPWSQCQADDRWDPPLAKC TSRTHDALIVGTLSGTIFILLIIFLSWILKHRKGNNAHENPKEVAIHLHSQ GGSSVHPRTLQTNEENSRVLP
13	人类补体受体 1 CCP 8-10 (UniProt : P17927 残基 491 到 684)	GHCQAPDHFLFAKLKTQTNASDFPIGTSLKYECPREYYGRPFSITCLDNLV WSSPKDVCKRKCKTTPDPVNGMVHVITDIQVGSRYNSCTTGHLRIGH SAECILSGNAAHWSTKPPICQRIPCGLPPTIANGDFISTNRENFHYGSVVTY RCNPGSGGRKVFELVGESPIYCTSNDDQVGIWSGPAPQCII
14	人补体受体 1 CCP 15-17 (UniProt : P17927 残基 941 到 1134)	GHCQAPDHFLFAKLKTQTNASDFPIGTSLKYECPREYYGRPFSITCLDNLV WSSPKDVCKRKCKTTPDPVNGMVHVITDIQVGSRYNSCTTGHLRIGH SAECILSGNTAHWSTKPPICQRIPCGLPPTIANGDFISTNRENFHYGSVVTY RCNLGSRGRKVFELVGESPIYCTSNDDQVGIWSGPAPQCII
15	人 CD46 (UniProt : P15529)	MEPPGRRECPFPSWRFPGLLLAAMVLLLYSFSACEEPTFEAMELIGKP KPYEIGERVYDKCKKGYFYIPPLATHICTDRNHTWLPVSDDACYRETCP YIRDPLNGQAVPANGTYEFGYQMHFICNEGYYLIGEEILYCELGKSVAIWS GKPPICEKVLCTPPPKIKNGKHTFSEVEVFEYLDVATYSCDPAPGDPFSLI GESTIYCGDNSVWSRAAPECKVVKCRFPVVENGKQISGFGKKFYKATV MFECDKGFYLDGSDTIVCDSNSTWDPPVPKCLKVLPPSSTKPPALSHSVS TSSTTKSPASSASGPRPTYKPPVSNYPGYKPEEGILDSLVDVWVIAVIVIAI VVGVAICVVPYRYLQRRKKKGTYLTDETHREVKFTSL
16	人 CD46 CCP 2-4 (UniProt: P15529 残基 97 到 285)	ETCPYIRDPLNGQAVPANGTYEFGYQMHFICNEGYYLIGEEILYCELGKSV AIWSGKPPICEKVLCTPPPKIKNGKHTFSEVEVFEYLDVATYSCDPAPGPD PFSLIGESTIYCGDNSVWSRAAPECKVVKCRFPVVENGKQISGFGKKFYY KATVMFECDKGFYLDGSDTIVCDSNSTWDPPVPKCLK
17	人 CD55 (UniProt : P08174)	MTVARPSVPAALPLLGLPRLLLLVLLCLPAVWGDCGLPPDPNAQPALE GRTSFPEDTVITYKCEESFVKIPGEKDSVICLKGSQWSDIEEFCNRSCEVPT RLNSASLKQPYITQNYFPVGTVEYECRPGYRREPSLSPKLTCLQNLKWS TAVEFCKKKSCPNPGEIRNGQIDVPGGILFGATISFSCNTGYKLFGSTSSFC LISGSSVQWSDPLPECREIYCPAPPQIDNGIIQGERDHYGYRQSVTYACNK GFTMIGEHSIYCTVNNDGEWEGSGPPPECRGKSLTSKVPPTVQKPTTVNVP TTEVSPTSQKTTTTPNAQATRSTPVSRTTKHFHETTPNKGSGTTS GTT RLLSGSRPVTQAGMRWCDRSSLQSRTPGFKRSFHFSLPSSWYYRAHV FH VDRFAWDASNHGLADLAKEELRRKYTQVYRLFLVS
18	人 CD55 CCP 2-4 (UniProt : P08174 残基 96	RSCEVPTRLNSASLKQPYITQNYFPVGTVEYECRPGYRREPSLSPKLTCL QNLKWSTAVEFCKKKSCPNPGEIRNGQIDVPGGILFGATISFSCNTGYKLF GSTSSFC LISGSSVQWSDPLPECREIYCPAPPQIDNGIIQGERDHYGYRQSV TYACNK GFTMIGEHSIYCTVNNDGEWEGSGPPPECRG

[0260]

	到 285)	
19	人 C4BP (UniProt : P04003)	MHPPKTPSGALHRKRKMAAWPFSRLWKVSDPILFQMTLIAALLPAVLGN CGPPPTLSFAAPMDITLTETRFKGTTLKYTCLPGYVRSHSTQTLTNSDG EWVYNTFCIYKRCRHPGELRNGQVEIKTDLSFGSQIEFSCSEGFLIGSTTS RCEVQDRGVGWSHPLPQCEIVKCKPPDIRNGRHSGEENFYAYGFSVTYS CDPRFSLGHASISCTVENETIGVWRPSPPTCEKITCRKPDVSHGEMVSGF GPIYNYKDTIVFKCQKGFVLRGSSVIHCDADSKWNPSPPACEPNSCINLPD IPHASWETYPRPTKEDVYVVGTVLRYRCHPGYKPTTDEPTTVICQKNLR WTPYQGCEALCCPEPKLNNGEITQHRKSRPANHCYFYGDEISFSCHETS RFSaicQGDGTWSPRTPSCGDICNFPKIAHGHIYKQSSSYFFKEEIIYEC KGYILVGQAKLSCSYSHWSAPAPQCKALCRKPELVNGLSVDKDQYVEP ENVTIQCDSGYGVVGPQSITCSGNRTWYPEVPKCEWETPEGCEQVLTGK RLMQCLNPEDVKMALEVYKLSLEIEQLELQRDSARQSTLDKEL
20	人 C4BP CCP 2-4 (UniProt : P04003 残基 111 到 296)	KRCRHPGELRNGQVEIKTDLSFGSQIEFSCSEGFLIGSTTSRCEVQDRGV GWSHPLPQCEIVKCKPPDIRNGRHSGEENFYAYGFSVTYS CDPRFSLGHASISCTVENETIGVWRPSPPTCEKITCRKPDVSHGEMVSGFGPIYNYKDTI VFKCQKGFVLRGSSVIHCDADSKWNPSPPACEP
21	SPICE (PDB:5FOB_ C)	SCCTIPSRPINMKFKNSVETDANANYNIGDTIEYLCLPGYRKQKMGPIYA KCTGTGWTLFNQCIKRRCPSPRDIDNGHLDIGGVDFGSSITYSCNSGYLI GEYKSYCKLGSTGSMVWNPAPICESVKCQLPPSISNGRHNGYNDFYTD GSVVTYSCNSGYSLIGNSGVLCSSGGEWSNPPTCQIVKCPHTILNGYLSSG FKRSYSYNDNVDFTCYGYKLSGSSSSTCSPGNTWQPELPKCV
22	VCP (NCBI:YP_23 2907.1)	MKVESVTFLTLGIGCVLSCCTIPSRPINMKFKNSVETDANANYNIGDTIE YLCLPGYRKQKMGPIYAKCTGTGWTLFNQCIKRRCPSPRDIDNGQLDIGG VDFGSSITYSCNSGYHLIGESKSYCELSTGSMVWNPAPICESVKCQSP SISNGRHNGYEDFYTDGSVVTYSCNSGYSLIGNSGVLCSSGGEWSNPPTCQ IVKCPHTISNGYLSSGFKRSYSYNDNVDFKCKYGYKLSGSSSSTCSPGNT WKPELPKCV
23	MOPICE (GenBank:AA V84857.1)	MKVESVTFLTLGIGCVLSYCTIPSRPINMKFKNSVETDANYNIGDTIEYL CLPGYRKQKMGPIYAKCTGTGWTLFNQCIKRRCPSPRDIDNGQLDIGG VDFGSSITYSCNSGYHLIGESKSYCELSTGSMVWNPAPICESVKCQSP SISNGRHNGYEDFYIDGSIVTYSCNSGYSLIGNSGVMCSGGEWSNPPTCQIV KCPHPISNGKLLAA
24	G ₄ S-R-(G ₄ S) ₂ 接 头	GGGGSRRGGGSGGGGS
25	人补体因子 H 残基 264-1231	KSCDNPIPNGDYSPLRIKHRTGDEITYQCRNGFYPATRGNTAKCTSTGWI PAPRCTLKPCDYPDIKHGGLYHENMRRPYFPVAVGKYYSYCYDEHFETPS GSYWDHIHCTQDGWSPAAPCLRKCYFPYLENGYNQNYGRKFVQGKSIDV ACHPGYALPKAQTTCMENGWSPTPRCIRVKTCSKSSIDIENGFISESQY TYALKEKAKYQCKLGVTADGETSGSITCGKDGWSAQPTCIKSCDIPVF MNARTKNDFTWFKLNDTLDYECHDGYESNTGSTTGSIVCGYNGWSDLPI CYERECLEPKIDVHLPDRKKDQYKVGVLKFCKPGFTIVGPNSVQCYH FGLSPDLPICKEQVQSCGPPPELLNGNVKEKTKEEYGHSEVVEYYCNP

[0261]

		LMKGPNKIQCV DGEWTTLPVCIVEESTCGDIPELEHGWAQLSSPPYYYGDSVEFNCSSEFTMIGHRSITCIHGVWTQLPQCVAIDKLKCKSSNLIILEEHLKNKKEFDHNSNIRYRCRGKEGWIHTVCINGRWDPVNC SMAQIQLCPPP PQIPNSHNMTTTLNRYR DGEKVS VLCQENYLIQEGEITCKDGRWQSIPLCVEKIPCSQPPQIEHGTINSSRSQESYAHGTKLSYTCGGFRISEENETTCYMGKWSSPPQCEGLPCKSPPEISHGVVAHMSDSYQYGEEV TYKCFEGFGIDGPAIAKCLGEKWSHPPSCIKTDCLSLPSFENAIPMGEKKDVYKAGEQVTYTCATYYKMDGASNVT CINSRWTGRPTCRDTS CVNPPTVQNAYIVSRQMSKYPSGERVRYQCRSPYEMFGDEEVMCLNGNWTEPPQCKDSTGKCGPPPIDNGDITSFPLSVYAPASSVEYQCQONLYQLEGNK RITCRNGQWSEPPKCLHPCVISREIMENYNIALRWTAQKLYSRTGESVEFVCKRGYRLSSRSHLTRTTCWDGKLEYPTCAKR
26	人补体因子 I 残基 1 到 339	MKLLHVFLFLCFHLRFCKV TYTSQEDLVEKKCLAKKYTHLSCDKVFCQPWQRCIEGTCVCKLPYQCPKNGTAVCATNRRSFPTYCQKSL ECLHPGTF LNNGTCTAEGKFSVSLKHGNTDSEGIVEVKLV DQDKTMFICKSSWSMR EANVACLDLGFQQGADTQRRFKLSDLINSTECLHVHCRGLETSLAECTFTKRRTMGYQDFADVVCYTQKADSPMDDFFQCVNGKYISQMKACDGINDCGDQSD ELCCKACQGKG FHC KSGVCIPSQYQCNGEVD CITGEDEVGCAGFASVTQEETEILTADMDAERRRIKSLLPKLSCGVKNRMHIRRKR
27	N-连接的糖基化的共有序列	NX_1X_2 其中 X_1 = 除 P 外的任何氨基酸 X_2 = S 或 T
28	弗林内肽酶裂解位点 (最小的)	RX_3X_4R 其中 X_3 = 任何氨基酸 X_4 = 任何氨基酸
29	弗林内肽酶裂解位点 (优选的)	RX_5X_6R 其中 X_5 = 任何氨基酸 X_6 = K 或 R
30	6×His 标签	HHHHHH
31	烟草蚀纹病毒 (TEV) 蛋白酶裂解位点	ENLYFQG
32	His 标签的糖基化嵌合 FH-FI 蛋白氨基酸序列	MRLLAKIICLMLWAICVAHHHHHHGSS ENLYFQGSSGEDCNELPPRRNTEILTGSWSDQTYPEGTQAIYKCRPGYRSLGNIIMVCRKGEWVALNPLRKCCQKRPCGHPGDTPFGTFTLTGGNVFEYGVKAVYTCNEG YQLLGEINYRECDTDGWTNDIPICEVVKCLPVTAPENGKIVSSAMEPDREYHFGQAVRFVCNSGYKIEGDEEMHCSDDGFWSKEKPKC VEISCKSPDVINGSPISKIYKENERFYKYCNMGYEY SERGDAVCTESGWRPLPSCEE GGGGSRGGGSGGGGSIVGGKRAQLGDLPWQVAIKDASGITCGGIYIGGCWILTA AHCLRASKTHRYQIWTTVVVDWIHPDLKRIVIEYVDRIIFHENYNAGTYQNDIALIEMKKDGNKKDCELP RSIPAAVPWSPYLFQPN DTCIVSGWGREKDNERVFSLQWGE

[0262]

		VKLISNCSKFYGNRFYEKEMECAGTYDGSIDACKGDSGGPLVCMDANN VTYVWGVVSWGENCCKPEFPGVYTKVANYFDWISYHVGRPFISQYNV
33	His 标签的非糖 基化嵌合 FH-FI 蛋白氨基酸序 列	MRLAKIICLMLWAICVAHHHHHGSSENLYFQGSSGEDCNELPPRRNTEI LTGSWSDQTYPEGTQAIYKCRPGYRSLGNIIMVCRKGEWVALNPLRKCCQ KRPCGHPGDTPTFTLTGGNVFEYGVKAVYTCNEGYQLLGEINYRECD TDGWTNDIPICEVVKCLPVTAPENGKIVSSAMEPDREYHFGQAVRFVCNS GYKIEGDEEMHCSDDGFWSKEKPKCVEISCKSPDVINGSPISQKIYKENE RFQYKCNMGYEYSERGDVCTESGWRPLPSCEEGGGGSRGGGSGGGG SIVGGKRAQLGDLWPQVAIKDASGITCGGIYIGGCWILTAACHCLRASKTH RYQIWTTVVDWIHPDLKRIVIEYVDRIIFHENYNAGTYQNDIALIEMKKD GNKKDCELPSPAAVPWSPYLFQPQDTCIVSGWGREKDNERVFSLQWGE VKLISQCSKFYGNRFYEKEMECAGTYDGSIDACKGDSGGPLVCMDANQ VTYVWGVVSWGENCCKPEFPGVYTKVANYFDWISYHVGRPFISQYNV
34	非糖基化嵌合 FH-FI 蛋白氨基 酸序列	MRLAKIICLMLWAICVAEDCNELPPRRNTEILTGSWSDQTYPEGTQAIYK CRPGYRSLGNIIMVCRKGEWVALNPLRKCCQKRPCGHPGDTPTFTLTGG NVFEYGVKAVYTCNEGYQLLGEINYRECDTDGWTNDIPICEVVKCLPVT APENGKIVSSAMEPDREYHFGQAVRFVCNSGYKIEGDEEMHCSDDGFWS KEKPKCVEISCKSPDVINGSPISQKIYKENERFQYKCNMGYEYSERGDV CTESGWRPLPSCEEGGGGSRGGGSGGGGSIVGGKRAQLGDLWPQVAIK DASGITCGGIYIGGCWILTAACHCLRASKTHRYQIWTTVVDWIHPDLKRI EYVDRIIFHENYNAGTYQNDIALIEMKKDGNKKDCELPSPAAVPWSPY LFQPQDTCIVSGWGREKDNERVFSLQWGEVKLISQCSKFYGNRFYEKEM ECAGTYDGSIDACKGDSGGPLVCMDANQVTYVWGVVSWGENCCKPEF PGVYTKVANYFDWISYHVGRPFISQYNV
35	His 标签的糖基 化嵌合 FH-FI 蛋白质氨基酸 序列 (没有信号 肽)	HHHHHHGSSENLYFQGSSGEDCNELPPRRNTEILTGSWSDQTYPEGTQAI YKCRPGYRSLGNIIMVCRKGEWVALNPLRKCCQKRPCGHPGDTPTFTLT GGNVFEYGVKAVYTCNEGYQLLGEINYRECDTDGWTNDIPICEVVKCLP VTAPENGKIVSSAMEPDREYHFGQAVRFVCNSGYKIEGDEEMHCSDDGF WSKEKPKCVEISCKSPDVINGSPISQKIYKENERFQYKCNMGYEYSERGD AVCTESGWRPLPSCEEGGGGSRGGGSGGGGSIVGGKRAQLGDLWPQV AIKDASGITCGGIYIGGCWILTAACHCLRASKTHRYQIWTTVVDWIHPDLK RIVIEYVDRIIFHENYNAGTYQNDIALIEMKKDGNKKDCELPSPAAVPW SPYLFQPNQDTCIVSGWGREKDNERVFSLQWGEVKLISNCSKFYGNRFYEK EMECAGTYDGSIDACKGDSGGPLVCMDANNVTYVWGVVSWGENCCKP EFPVYTKVANYFDWISYHVGRPFISQYNV
36	His 标签的非糖 基化嵌合 FH-FI 蛋白氨基酸序 列 (没有信号 肽)	HHHHHHGSSENLYFQGSSGEDCNELPPRRNTEILTGSWSDQTYPEGTQAI YKCRPGYRSLGNIIMVCRKGEWVALNPLRKCCQKRPCGHPGDTPTFTLT GGNVFEYGVKAVYTCNEGYQLLGEINYRECDTDGWTNDIPICEVVKCLP VTAPENGKIVSSAMEPDREYHFGQAVRFVCNSGYKIEGDEEMHCSDDGF WSKEKPKCVEISCKSPDVINGSPISQKIYKENERFQYKCNMGYEYSERGD AVCTESGWRPLPSCEEGGGGSRGGGSGGGGSIVGGKRAQLGDLWPQV AIKDASGITCGGIYIGGCWILTAACHCLRASKTHRYQIWTTVVDWIHPDLK RIVIEYVDRIIFHENYNAGTYQNDIALIEMKKDGNKKDCELPSPAAVPW SPYLFQPQDTCIVSGWGREKDNERVFSLQWGEVKLISQCSKFYGNRFYEK EMECAGTYDGSIDACKGDSGGPLVCMDANQVTYVWGVVSWGENCCKP

[0263]

		EFPGVYTKVANYFDWISYHVGRPFISQYNV
37	非糖基化嵌合 FH-FI 蛋白氨基酸序列(没有信号肽)	EDCNELPPRRNTEILTGSWSDQTYPEGTQAIYKCRPGYRSLGNIMVCRK GEWVALNPLRKCQKRPCGHPGDTDFGTFTLTGGNVFEYGVKAVYTCNEG YQLLGEINYRECDTDGWTNDIPICEVVKCLPVTAPENGKIVSSAMEPDRE YHFGQAVRFVCNSGYKIEGDEEMHCSDDGFWSKEKPKCVEISCKSPDVIN GSPISQKIIYKENERFQYKCNMGYEYSERGDAVCTESGWRPLPSCEEGLG GSRGGGSGGGGSIVGGKRAQLGDLPWQVAIKDASGITCGGIYIGGCWIL TAAHCLRASKTHRYQIWTTVVWDWIHPDLKRIVIEYVDRIIFHENYNAGTY QNDIALIEMKKDGNKKDCELPSPAAVPWSPYLFQPDTCIVSGWGREK DNERVFSLQWGEVKLISQCSKFYGNRFYEKEMECAGTYDGSIDACKGDS GGPLVCMDANQVTYVWGVVSWGECGKPEFPVYTKVANYFDWISYH VGRPFISQYNV
38	补体因子 H 同种型 FHL-1 (UniProt : P08603-2)	MRLAKIICLMLWAICVAEDCNELPPRRNTEILTGSWSDQTYPEGTQAIYK CRPGYRSLGNVIMVCRKGEWVALNPLRKCQKRPCGHPGDTDFGTFTLTG GNVFEYGVKAVYTCNEGYQLLGEINYRECDTDGWTNDIPICEVVKCLPV TAPENGKIVSSAMEPDREYHFGQAVRFVCNSGYKIEGDEEMHCSDDGF SKEKPKCVEISCKSPDVINGSPISQKIIYKENERFQYKCNMGYEYSERGDA VCTESGWRPLPSCEEKSCDNPIYNGDYSPLRIKHRTGDEITYQCRNGFY PYPATRGNTAKCTSTGWIPAPRCTLKPCDYPDIKHGGLYHENMRRPYFPVAVG KYYSYCYDEHFETPSGSYWDHIHCTQDGWSPAVPCLRKCYFPYLENGYN QNYGRKFVQGKSIDVACHPGYALPKAQTTVTCMENGWSPTPRCIRVSFTL
39	补体因子 H CCP 6-8 (UniProt : P08603 残基 324 到 507)	PCDYPDIKHGGLYHENMRRPYFPVAVGKYYSYCYDEHFETPSGSYWDHI HCTQDGWSPAVPCLRKCYFPYLENGYNQNYGRKFVQGKSIDVACHPGYA LPKAQTTVTCMENGWSPTPRCIRVKTCSSIDIENGFISESQYTYALKEK AKYQCKLGYVTADGETSGSITCGKDGWSAQPTCIK
40	补体因子 H CCP 19-20 (UniProt : P08603 残基 1107 到 1230)	GKCGPPPIDNGDITSFPLSVYAPASSVEYQCQONLYQLEGNKRITCRNGQW SEPPKCLHPCVISREIMENYNIALRWTAQKLYSRTGESVEFVCKRGYRLS SRSHTLRITTCWDGKLEYPTCAK
41	补体因子 H 同种型 FHL-1 (UniProt : P08603-2 残基 265 到 449)	KSCDNPIYNGDYSPLRIKHRTGDEITYQCRNGFYPATRGNTAKCTSTGWI PAPRCTLKPCDYPDIKHGGLYHENMRRPYFPVAVGKYYSYCYDEHFETPS GSYWDHIHCTQDGWSPAVPCLRKCYFPYLENGYNQNYGRKFVQGKSIDV ACHPGYALPKAQTTVTCMENGWSPTPRCIRVSFTL
42	His 标签的糖基化嵌合 FH-FI 编码序列蛋白质	TATAGGGAGACCCAAGCTGGCTAGCGTTTAACTTAAGCTTGCCACCA TGAGACTGCTGGCCAAGATCATCTGCCTGATGCTGTGGGCCATCTGCG TGGCCCACCACCATCACCATCACGGCAGCAGCGAGAACCTGTACTTCC AAGGCAGCTCCGGCGAGGACTGCAATGAGCTGCCTCCTAGACGGAAC ACCGAGATCCTGACAGGCTCTTGGAGCGACCAGACATACCCTGAGGG AACCCAGGCCATCTACAAGTGCAGACCCGGCTACAGAAGCCTGGGCA ACATCATCATGGTCTGCCGAAAGGCGAGTGGGTGCGCCTGAATCCTC TGCGGAAGTGCCAGAAAAGACCCTGCGGACACCCTGGCGATACCCCT

[0264]

		TTCGGAACCTTTACTGACCGGCGGCAACGTGTTTCGAGTACGGCGTG AAAGCCGTGTACACCTGTAACGAGGGCTACCAGCTGCTGGGCGAGATC AACTACAGAGAGTGCATACCGACGGCTGGACCAACGACATCCCTATC TGCGAGGTGGTCAAGTGCCTGCCTGTGACAGCCCCTGAGAACGGCAA GATTGTGTCCAGCGCCATGGAACCCGACAGAGAGTACCACTTTGGCCA GGCCGTCAGATTTCGTGTGCAACAGCGGCTACAAGATCGAGGGCGACG AGGAAATGCACTGCAGCGACGATGGCTTCTGGTCCAAAGAAAAGCCT AAGTGCCTGGAAATCAGCTGCAAGAGCCCCGACGTGATCAACGGCAG CCCTATCAGCCAGAAGATTATCTACAAAGAGAACGAGCGGTTCCAGTA CAAGTGTAACATGGGCTACGAGTACAGCGAGAGGGGCGACGCCGTGT GTACAGAATCTGGATGGCGACCTCTGCCTAGCTGCGAAGAAGGTGGCG GAGGATCTAGAGGCGGAGGCGGAAGTGGCGGTGGTGGATCTATCGTT GGAGGCAAGAGAGCACAGCTGGGCGACCTTCCATGGCAGGTTGCCAT CAAGGATGCCAGCGGCATCACATGCGGCGGCATCTATATCGGCGGCTG CTGGATTCTGACCGCCGCTCATTGTCTGAGAGCCAGCAAGACCCACCG GTATCAGATCTGGACCACCGTGGTGGACTGGATTACCCCGACCTGAA GCGGATCGTGATCGAGTATGTGGACCGGATCATCTCCACGAGAATA CAACGCCGGCACCTACCAGAACGATATCGCCCTGATCGAGATGAAGAA GGACGGCAACAAGAAGGACTGCGAGCTGCCAGATCTATCCCTGCTG CTGTTCCCTGGAGCCCCCTACCTGTTCCAGCCTAACGATACCTGCATCGT GTCCGGCTGGGGCAGAGAGAAGGACAACGAAAGGGTGTTCAGCCTG CAGTGGGGCGAAGTGAAGCTGATCTCCAACCTGCAGCAAGTTCTACGG CAACCGGTTCTACGAGAAAGAAATGGAATGCGCCGGCACATACGACG GCTCCATCGATGCCTGTAAAGGCGATTCTGGCGGCCCTCTCGTGTGCAT GGATGCCAACAATGTGACCTACGTGTGGGGCGTCTGTCTGGGGAGA GAATTGTGGCAAGCCTGAGTTCCCCGGCGTGTACACAAAGGTGGCCA ACTACTTCGACTGGATCAGCTACCACGTGGGCAGACCCTTCATCAGCC AGTACAACGTTGCGGCCGCTCGAGTCTAGAGGGCCCGTTAAACCCGC TGATCA
43	His 标签的非糖基化嵌合 FH-FI 蛋白质编码序列	ATAGGGAGACCCAAGCTGGCTAGCGTTTAACTTAAGCTTGCCACCAT GAGACTGCTGGCCAAGATCATCTGCCTGATGCTGTGGGCCATCTGCGT GGCCCACCACCATCACCATCACGGCAGCAGCGAGAACCTGTACTTCCA AGGCAGCTCCGGCGAGGACTGCAATGAGCTGCCTCCTAGACGGAACA CCGAGATCCTGACAGGCTCTTGGAGCGACCAGACATACCCTGAGGGA ACCCAGGCCATCTACAAGTGCAGACCCGGCTACAGAAGCCTGGGCAA CATCATCATGGTCTGCCGAAAGGCGAGTGGGTCGCCCTGAATCCTCT GCGGAAGTGCCAGAAAAGACCCTGCGGACACCCTGGCGATACCCCTT TCGGAACCTTTACTGACCGGCGGCAACGTGTTTCGAGTACGGCGTGA AAGCCGTGTACACCTGTAACGAGGGCTACCAGCTGCTGGGCGAGATCA ACTACAGAGAGTGCATACCGACGGCTGGACCAACGACATCCCTATCT GCGAGGTGGTCAAGTGCCTGCCTGTGACAGCCCCTGAGAACGGCAAG ATTGTGTCCAGCGCCATGGAACCCGACAGAGAGTACCACTTTGGCCAG GCCGTCAGATTTCGTGTGCAACAGCGGCTACAAGATCGAGGGCGACGA GGAAATGCACTGCAGCGACGATGGCTTCTGGTCCAAAGAAAAGCCTA AGTGCCTGGAAATCAGCTGCAAGAGCCCCGACGTGATCAACGGCAGC

[0265]

		CCTATCAGCCAGAAGATTATCTACAAAGAGAACGAGCGGTTCCAGTAC AAGTGTAACATGGGCTACGAGTACAGCGAGAGGGGCGACGCCGTGTG TACAGAATCTGGATGGCGACCTCTGCCTAGCTGCGAAGAAGGTGGCGG AGGATCTAGAGGCGGAGGCGGAAGTGGCGGTGGTGGATCTATCGTTG GAGGCAAGAGAGCACAGCTGGGCGACCTTCCATGGCAGGTTGCCATC AAGGATGCCAGCGGCATCACATGCGGCGGCATCTATATCGGCGGCTGC TGGATTCTGACCGCCGCTCATTGTCTGAGAGCCAGCAAGACCCACCGG TATCAGATCTGGACCACCGTGGTGGACTGGATTACCCCCGACCTGAAG CGGATCGTGATCGAGTATGTGGACCGGATCATCTTCCACGAGAACTAC AACGCCGGCACCTACCAGAACGATATCGCCCTGATCGAGATGAAGAAG GACGGCAACAAGAAGGACTGCGAGCTGCCAGATCTATCCCTGCTGCT GTTCTTGGAGCCCCCTACCTGTTCCAGCCTCAAGATACCTGCATCGTGT CCGGCTGGGGCAGAGAGAAGGACAACGAAAGGTGTTTCAGCCTGCA GTGGGGCGAAGTGAAGCTGATCTCCAGTGCAGCAAGTTCTACGGCA ACCGGTTCTACGAGAAAGAAATGGAATGCGCCGGCACATACGACGGC TCCATCGATGCCTGTAAAGGCGATTCTGGCGGCCCTCTCGTGTGCATGG ATGCCAATCAAGTGACCTACGTGTGGGGCGTCGTGTCCTGGGGAGAGA ATTGTGGCAAGCCTGAGTTCCCCGGCGGTACACAAAGGTGGCCAACT ACTTCGACTGGATCAGCTACCACGTGGGCAGACCCTTCATCAGCCAGT ACAACGTTGCGGCCGCTCGAGTCTAGAGGGCCCCGTTTAAACCCGCTGA TCA
44	非糖基化嵌合 FH-FI 蛋白质编 码序列	TATAGGGAGACCCAAGCTGGCTAGCGTTTAAACTTAAGCTTGCCACCA TGAGACTGCTGGCCAAGATCATCTGCCTGATGCTGTGGGCCATCTGCG TGGCCGAGGATTGCAATGAGCTGCCTCCTCGGAGAAACACCGAGATCC TGACAGGCTCTTGGAGCGACACAGACATACCCTGAGGGAACCCAGGCC ATCTACAAGTGCAGACCCGGCTACAGAAGCCTGGGCAACATCATCATG GTCTGCCGGAAGGCGAGTGGGTCGCCCTGAATCCTCTGCGGAAGTG CCAGAAAAGACCCTGCGGACACCCTGGCGATACCCCTTTCGGAACCTT TACACTGACCGGCGGCAACGTGTTTCGAGTACGGCGTGAAAGCCGTGT ACACCTGTAACGAGGGCTACCAGCTGCTGGGCGAGATCAACTACAGA GAGTGCGATACCGACGGCTGGACCAACGACATCCCTATCTGCGAGGTG GTCAAGTGCCTGCCTGTGACAGCCCCTGAGAACGGCAAGATTGTGTCC AGCGCCATGGAACCCGACAGAGAGTACCCTTTGGCCAGGCCGTCAG ATTCGTGTGCAACAGCGGCTACAAGATCGAGGGCGACGAGGAAATGC ACTGCAGCGACGATGGCTTCTGGTCCAAAGAAAAGCCTAAGTGCGTG GAAATCAGCTGCAAGAGCCCCGACGTGATCAACGGCAGCCCTATCAGC CAGAAGATTATCTACAAAGAGAACGAGCGGTTCCAGTACAAGTGTAAC ATGGGCTACGAGTACAGCGAGAGGGGCGACGCCGTGTGTACAGAATC TGGATGGCGACCTCTGCCTAGCTGCGAAGAAGGTGGCGGAGGATCTA GAGGCGGAGGCGGAAGTGGCGGTGGTGGATCTATCGTTGGAGGCAAG AGAGCACAGCTGGGCGACCTGCCTTGGCAGGTTGCCATTAAGGATGCC AGCGGCATCACCTGTGGCGGCATCTATATCGGCGGCTGCTGGATTCTGA CCGCCGCTCATTGTCTGAGAGCCAGCAAGACCCACCGGTATCAGATCT GGACCACCGTGGTGGACTGGATTACCCCCGACCTGAAGCGGATCGTGA TCGAGTATGTGGACCGGATCATCTTCCACGAGAACTACAACGCCGGCA

[0266]

		CCTACCAGAACGATATCGCCCTGATCGAGATGAAGAAGGACGGCAACA AGAAGGACTGCGAGCTGCCAGATCTATCCCTGCTGCTGTTCTTGA GCCCCACCTGTTCCAGCCTCAAGATACCTGCATCGTGTCCGGCTGGG GCAGAGAGAAGGACAACGAAAGGGTGTTACGCTGCAGTGGGGCGA AGTGAAGCTGATCTCCCAGTGCAGCAAGTTCTACGGCAACCGTTCTA CGAGAAAGAAATGGAATGCGCCGGCACATACGACGGCTCCATCGATGC CTGTAAAGGCGATTCTGGCGGCCCTCTCGTGTGCATGGATGCCAATCA AGTGACCTACGTGTGGGGCGTCGTGTCCTGGGGAGAGAATTGTGGCA AGCCTGAGTTCCCCGGCGTGACACAAAGGTGGCCAACTACTTCGACT GGATCAGCTACCACGTGGGCAGACCCCTTCATCAGCCAGTACAACGTCT GAGCGGCCGCTCGAGTCTAGAGGGCCCCGTTAAACCCGCTGATCA
45	G4S 接头	GGGS
46	胰蛋白酶肽	GDAVCTESGWRPLPSCEEGGGS
47	胰蛋白酶肽	GGGSGGGGSIVGGK
48	G4S-K-(G4S) ₂ 接头	GGGSKGGGSGGGGS
49	糖基化嵌合 FH-FI 蛋白质氨 基酸序列 (没有 信号肽)	EDCNELPPRRNTEILTGSWSDQTYPEGTQAIYKCRPGYRSLGNIIMVCRK GEWVALNPLRKCKRPGCHPGDTPFGTFTLTGGNVFEYGVKAVYTCNEG YQLLGEINYRECDTDGWTNDIPICEVVKCLPVTAPENGKIVSSAMEPDRE YHFGQAVRFVNSGYKIEGDEEMHCSDDGFWSKEKPKCIVEISCKSPDVIN GSPISQKIIYKENERFQYKCNMGYYSERGDVCTESGWRPLPSCEEGG GSRGGGSGGGGSIVGGKRAQLGDLPWQVAIKDASGITCGGIYIGGCWIL TAAHCLRASKTTHRYQIWTTVVDWIHPDLKRIVIEYVDRIIFHENYNAGTY QNDIALIEMKKDGNKKDCELPSPAPVWSPYLFQPNDCIVSGWGREK DNERVFSLQWGEVKLISNCSKFYGNRFYEKEMECAGTYDGSIDACKGDS GGPLVCMDANNVTYVWGVVSWGENCGKPEFPGVYTKVANYFDWISYH VGRPFISQYNV
50	His 标签的糖基 化嵌合 CR1a-FI 蛋白质氨基酸 序列	MRLAKIICMLLWAICVAHHHHHHGSSENLYFQGSSGGHCQAPDHFLFAK LKTQTNASDFPIGTSKLYECRPEYYGRPFSITCLDNLVWSSPKDVCKRKSC KTPPDPVNGMVHVITDIQVGSRINYSCTTGHRILGHSSAECILSGNAAHW STKPPICQRIPCGLPPTIANGDFISTNRENFHYGSVVITYRCNPGSGGRKVF LVGEPSIYCTSNDDQVGIWSGPAPQCIIPNKATPPNVENGGGSRGGGSG GGGSIVGGKRAQLGDLPWQVAIKDASGITCGGIYIGGCWILTAAHCLRAS KTHRYQIWTTVVDWIHPDLKRIVIEYVDRIIFHENYNAGTYQNDIALIEM KKDGNKKDCELPSPAPVWSPYLFQPNDCIVSGWGREKDNERVFSLQ WGEVKLISNCSKFYGNRFYEKEMECAGTYDGSIDACKGDSGGPLVCMD ANNVTYVWGVVSWGENCGKPEFPGVYTKVANYFDWISYHVGRPFISQY NV
51	His 标签的糖基 化嵌合 CR1b-FI 蛋白质氨基酸 序列	MRLAKIICMLLWAICVAHHHHHHGSSENLYFQGSSGGHCQAPDHFLFAK LKTQTNASDFPIGTSKLYECRPEYYGRPFSITCLDNLVWSSPKDVCKRKSC KTPPDPVNGMVHVITDIQVGSRINYSCTTGHRILGHSSAECILSGNTAHWS TKPPICQRIPCGLPPTIANGDFISTNRENFHYGSVVITYRCNLGSRGRKVFEL VGEPSIYCTSNDDQVGIWSGPAPQCIIPNKATPPNVENGGGSRGGGSG GGGSIVGGKRAQLGDLPWQVAIKDASGITCGGIYIGGCWILTAAHCLRAS

[0267]

		KTHRYQIWTTVVDWIHPDLKRIVIEYVDRIIFHENYNAGTYQNDIALIEM KKDGNKKDCELPISIPAAVPWSPYLFQPNDDTCIVSGWGREKDNERVFSLQ WGEVKLISNCSKFYGNRFYEKEMECAGTYDGSIDACKGDSGGPLVCMD ANNVTYVWGVVSWGECGKPEFPGVYTKVANYFDWISYHVGRPFISQY NV
52	His 标签的非糖 基化嵌合 CR1a-FI 蛋白质 氨基酸序列	MRLAKIICLMLWAICVAHHHHHHGSSSENLYFQGSSGGHCQAPDHFLFAK LKTQTQASDFPIGTSKLYECRPEYYGRPFSITCLDNLVWSSPKDVCKRKSC KTPDPVNGMVHVITDIQVGSRIQYSCCTGHRIGHSSAECILSGNAAHW STKPPICQRIPCGLPPTIANGDFISTNRENPHYGSVVTYRCNPGSGGRKVFEL LVGEPISYCTSNDDQVGIWSPAPQCIIPNKATPPNVENGSGGSRGGGSG GGGSIVGGKRAQLGDLPWQVAIKDASGITCGGIYIGGCWILTAHCLRAS KTHRYQIWTTVVDWIHPDLKRIVIEYVDRIIFHENYNAGTYQNDIALIEM KKDGNKKDCELPISIPAAVPWSPYLFQPNDDTCIVSGWGREKDNERVFSLQ WGEVKLISQCSKFYGNRFYEKEMECAGTYDGSIDACKGDSGGPLVCMD ANQVTYVWGVVSWGECGKPEFPGVYTKVANYFDWISYHVGRPFISQY NV
53	His 标签的非糖 基化嵌合 CR1b-FI 蛋白质 氨基酸序列	MRLAKIICLMLWAICVAHHHHHHGSSSENLYFQGSSGGHCQAPDHFLFAK LKTQTQASDFPIGTSKLYECRPEYYGRPFSITCLDNLVWSSPKDVCKRKSC KTPDPVNGMVHVITDIQVGSRIQYSCCTGHRIGHSSAECILSGNAAHW STKPPICQRIPCGLPPTIANGDFISTNRENPHYGSVVTYRCNPGSGGRKVFEL LVGEPISYCTSNDDQVGIWSPAPQCIIPNKATPPNVENGSGGSRGGGSG GGGSIVGGKRAQLGDLPWQVAIKDASGITCGGIYIGGCWILTAHCLRAS KTHRYQIWTTVVDWIHPDLKRIVIEYVDRIIFHENYNAGTYQNDIALIEM KKDGNKKDCELPISIPAAVPWSPYLFQPNDDTCIVSGWGREKDNERVFSLQ WGEVKLISQCSKFYGNRFYEKEMECAGTYDGSIDACKGDSGGPLVCMD ANQVTYVWGVVSWGECGKPEFPGVYTKVANYFDWISYHVGRPFISQY NV
54	His 标签的糖基 化嵌合 CR1a-FI 蛋白质氨基酸 序列(没有信号 肽)	HHHHHHGSSSENLYFQGSSGGHCQAPDHFLFAKLKTQTNASDFPIGTSKLY ECRPEYYGRPFSITCLDNLVWSSPKDVCKRKSCKTPDPVNGMVHVITDI QVGSRIYSCCTGHRIGHSSAECILSGNAAHWSTKPPICQRIPCGLPPTIA NGDFISTNRENPHYGSVVTYRCNPGSGGRKVFELVGEPISYCTSNDDQVG IWSGPAPQCIIPNKATPPNVENGSGGSRGGGSGGGGSIVGGKRAQLGDL PWQVAIKDASGITCGGIYIGGCWILTAHCLRASKTHRYQIWTTVVDWIH PDLKRIVIEYVDRIIFHENYNAGTYQNDIALIEMKKDGNKKDCELPISIP AVPWSYLFQPNDDTCIVSGWGREKDNERVFSLQWGEVKLISNCSKFYGN RFYEKEMECAGTYDGSIDACKGDSGGPLVCMDANNVTYVWGVVSWG NCGKPEFPGVYTKVANYFDWISYHVGRPFISQYNV
55	His 标签的糖基 化嵌合 CR1b-FI 蛋白质氨基酸 序列(没有信号 肽)	HHHHHHGSSSENLYFQGSSGGHCQAPDHFLFAKLKTQTNASDFPIGTSKLY ECRPEYYGRPFSITCLDNLVWSSPKDVCKRKSCKTPDPVNGMVHVITDI QVGSRIYSCCTGHRIGHSSAECILSGNTAHWSTKPPICQRIPCGLPPTIA NGDFISTNRENPHYGSVVTYRCNLGSRGRKVFELVGEPISYCTSNDDQVG IWSGPAPQCIIPNKATPPNVENGSGGSRGGGSGGGGSIVGGKRAQLGDL PWQVAIKDASGITCGGIYIGGCWILTAHCLRASKTHRYQIWTTVVDWIH PDLKRIVIEYVDRIIFHENYNAGTYQNDIALIEMKKDGNKKDCELPISIP AVPWSYLFQPNDDTCIVSGWGREKDNERVFSLQWGEVKLISNCSKFYGN

[0268]

		RFYEKEMECAGTYDGSIDACKGDSGGPLVCMDANNVTYVWGVVSWGE NCGKPEFPGVYTKVANYFDWISYHVGRPFISQYNV
56	His 标签的非糖 基化嵌合 CR1a-FI 蛋白质 氨基酸序列 (没 有信号肽)	HHHHHHGSSSENYFQGSSGGHCQAPDHFLFAKLKTQTQASDFPIGTSKLY ECRPEYYGRPFSITCLDNLVWSSPKDVCKRKSCKTPDPVNGMVHVITDI QVGSRIQYSCTTGHRLLIGHSSAECILSGNAAHWSTKPPICQRI PCGLPPTIA NGDFISTNRENFHYGSVVTYRCNPGSGGRKVFELVGEPSIYCTSNDDQVG IWSGPAPQCIIPNKATPPNVENGSGSGGGSGGGGSIVGGKRAQLGDL PWQVAIKDASGITCGGIYIGGCWILTAACHCLRASKTHRYQIWTTVVWDWIH PDLKRIVIEYVDRIIFHENYNAGTYQNDIALIEMKKDGNKKDCELP RSIPA AVPWSPYLFQPQDTCIVSGWGREKDNERVFSLQWGEVKLISQCSKFYGN RFYEKEMECAGTYDGSIDACKGDSGGPLVCMDANQVTYVWGVVSWGE NCGKPEFPGVYTKVANYFDWISYHVGRPFISQYNV
57	His 标签的非糖 基化嵌合 CR1b-FI 蛋白质 氨基酸序列 (没 有信号肽)	HHHHHHGSSSENYFQGSSGGHCQAPDHFLFAKLKTQTQASDFPIGTSKLY ECRPEYYGRPFSITCLDNLVWSSPKDVCKRKSCKTPDPVNGMVHVITDI QVGSRIQYSCTTGHRLLIGHSSAECILSGNAAHWSTKPPICQRI PCGLPPTIA NGDFISTNRENFHYGSVVTYRCNPGSGGRKVFELVGEPSIYCTSNDDQVG IWSGPAPQCIIPNKATPPNVENGSGSGGGSGGGGSIVGGKRAQLGDL PWQVAIKDASGITCGGIYIGGCWILTAACHCLRASKTHRYQIWTTVVWDWIH PDLKRIVIEYVDRIIFHENYNAGTYQNDIALIEMKKDGNKKDCELP RSIPA AVPWSPYLFQPQDTCIVSGWGREKDNERVFSLQWGEVKLISQCSKFYGN RFYEKEMECAGTYDGSIDACKGDSGGPLVCMDANQVTYVWGVVSWGE NCGKPEFPGVYTKVANYFDWISYHVGRPFISQYNV
58	糖基化嵌合 CR1a-FI 蛋白质 氨基酸序列 (没 有信号肽)	GHCQAPDHFLFAKLKTQTNASDFPIGTSKLYECRPEYYGRPFSITCLDNLV WSSPKDVCKRKSCKTPDPVNGMVHVITDIQVGSRIYNSCTTGHRLLIGHS SAECILSGNAAHWSTKPPICQRI PCGLPPTIANGDFISTNRENFHYGSVVTY RCNPGSGGRKVFELVGEPSIYCTSNDDQVG IWSGPAPQCIIPNKATPPNVE NGGGGSRGGGSGGGGSIVGGKRAQLGDL PWQVAIKDASGITCGGIYIG GCWILTAACHCLRASKTHRYQIWTTVVWDWIHPDLKRIVIEYVDRIIFHENYN AGTYQNDIALIEMKKDGNKKDCELP RSIPAAVPWSPYLFQPNDTCIVSGW GREKDNERVFSLQWGEVKLISNCSKFYGNRFYEKEMECAGTYDGSIDAC KGDSGGPLVCMDANNVTYVWGVVSWGENCGKPEFPGVYTKVANYFD WISYHVGRPFISQYNV
59	糖基化嵌合 CR1b-FI 蛋白质 氨基酸序列 (没 有信号肽)	GHCQAPDHFLFAKLKTQTNASDFPIGTSKLYECRPEYYGRPFSITCLDNLV WSSPKDVCKRKSCKTPDPVNGMVHVITDIQVGSRIYNSCTTGHRLLIGHS SAECILSGNTAHWSTKPPICQRI PCGLPPTIANGDFISTNRENFHYGSVVTY RCNLGSRGRKVFELVGEPSIYCTSNDDQVG IWSGPAPQCIIPNKATPPNVE NGGGGSRGGGSGGGGSIVGGKRAQLGDL PWQVAIKDASGITCGGIYIG GCWILTAACHCLRASKTHRYQIWTTVVWDWIHPDLKRIVIEYVDRIIFHENYN AGTYQNDIALIEMKKDGNKKDCELP RSIPAAVPWSPYLFQPNDTCIVSGW GREKDNERVFSLQWGEVKLISNCSKFYGNRFYEKEMECAGTYDGSIDAC KGDSGGPLVCMDANNVTYVWGVVSWGENCGKPEFPGVYTKVANYFD WISYHVGRPFISQYNV
60	非糖基化嵌合 CR1a-FI 蛋白质 氨基酸序列 (没	GHCQAPDHFLFAKLKTQTQASDFPIGTSKLYECRPEYYGRPFSITCLDNLV WSSPKDVCKRKSCKTPDPVNGMVHVITDIQVGSRIQYSCTTGHRLLIGHS SAECILSGNAAHWSTKPPICQRI PCGLPPTIANGDFISTNRENFHYGSVVTY

[0269]

	有信号肽)	RCNPGSGGRKVFELVGEPSIYCTSNDDQVGIWSGPAPQCIIPNKATPPNVE NGGGGSRGGGSGGGGSIVGGKRAQLGDLPWQVAIKDASGITCGGIYIG GCWILTAACHCLRASKTHRYQIWTTVVVDWIHPDLKRIVIEYVDRIIFHENYN AGTYQNDIALIEMKKDGNKKDCELPRSIPAAVPWSPYLFQPDTCIVSGW GREKDNERNVSLQWGEVKLISQCSKFYGNRFYEKEMECAGTYDGSIDAC KGDSGGPLVCMDANQVTYVWGVVSWGENCGKPEFPGVYTKVANYFD WISYHVGRPFISQYNV
61	非糖基化嵌合 CR1b-FI 蛋白质 氨基酸序列 (没 有信号肽)	GHCQAPDHFLFAKLKTQTQASDFPIGTSKYECPREYYGRPFISITCLDNLV WSSPKDVCKRKSKCTPPDPVNGMVHVITDIQVGSRIQYSCTTGHRLLIGHS SAECILSGNAAHWSTKPPICQRI PCGLPPTIANGDFISTNRENFHYGVSVTY RCNPGSGGRKVFELVGEPSIYCTSNDDQVGIWSGPAPQCIIPNKATPPNVE NGGGGSRGGGSGGGGSIVGGKRAQLGDLPWQVAIKDASGITCGGIYIG GCWILTAACHCLRASKTHRYQIWTTVVVDWIHPDLKRIVIEYVDRIIFHENYN AGTYQNDIALIEMKKDGNKKDCELPRSIPAAVPWSPYLFQPDTCIVSGW GREKDNERNVSLQWGEVKLISQCSKFYGNRFYEKEMECAGTYDGSIDAC KGDSGGPLVCMDANQVTYVWGVVSWGENCGKPEFPGVYTKVANYFD WISYHVGRPFISQYNV
62	His 标签的糖基 化嵌合 CR1a-FI 蛋白质编码序 列	AAGCTTGCCACCATGAGACTGCTGGCCAAGATCATCTGCCTGATGCTG TGGGCCATCTGCGTGGCCCACCACCATCACCATCACGGCAGCAGCGAG AACCTGTACTTCCAAGGATCTTCTGGCGGCCACTGTCAGGCCCTGAT CACTTCCTGTTCCGCAAGCTGAAAACCCAGACCAACGCCAGCGACTT CCCTATCGGCACCAGCCTGAAGTACGAGTGCAGACCCGAGTACTACGG CAGACCCTTCAGCATCACCTGTCTGGACAACCTCGTGTGGTCTAGCCC CAAGGACGTGTGCAAGAGAAAGAGCTGCAAGACCCCTCCTGATCCTG TGAACGGCATGGTGCACGTGATCACCGACATCCAAGTGGGCAGCAGA ATCAACTACAGCTGCACCACCGGCCACAGACTGATCGGACACTCTAGC GCCGAGTGTATCCTGAGCGGCAATGCCGCACACTGGTCCACCAAGCCT CCAATCTGCCAGAGAATCCCTTGCGGCCTGCCTCCTACAATCGCCAAC GGCGATTTCATCAGCACCAACAGAGAGAACTTCCACTACGGCTCCGTG GTCACCTACAGATGCAATCCTGGCAGCGGCGGCAGAAAGGTGTTCTGA ACTTGTGGGCGAGCCAGCATCTACTGCACCAGCAACGATGACCAAGT CGGCATTTGGAGCGGCCCTGCTCCTCAGTGCATCATCCCCAACAAAGC CACACCTCCTAACGTGGAAAATGGCGGCGGAGGCTCTAGAGGTGGCG GAGGATCTGGCGGAGGCGGATCTATCGTTGGAGGAAAGAGAGCACAG CTGGGCGACCTGCCTTGGCAGGTTGCCATTAAGGATGCCAGCGGCATC ACATGCGGCGGCATCTATATCGGCGGCTGCTGGATTCTGACAGCCGCTC ATTGTCTGCGGGCCAGCAAGACCCACCGGTATCAGATTTGGACCAACG TGGTGGACTGGATTACCCCGACCTGAAGCGGATCGTGATCGAGTACG TGGACCGGATCATCTTCCACGAGAACTACAACGCCGGCACCTACCAGA ACGATATCGCCCTGATCGAGATGAAGAAGGACGGCAACAAGAAGGAC TGCGAGCTGCCTAGATCTATCCAGCCGCTGTTCTTGGAGCCCCTACC TGTTCCAGCCTAACGATACCTGCATCGTGTCCGGCTGGGGCAGAGAGA AGGACAACGAAAGGGTGTTACGCCTGCAGTGGGGCGAAGTGAAGCT GATCTCCAACCTGCAGCAAGTTCTACGGCAACCGGTTCTACGAGAAAGA AATGGAATGCGCCGGCACATACGACGGCTCCATCGATGCCTGTAAAGG

[0270]

		CGATTCTGGCGGACCCCTCGTGTGCATGGATGCCAACAATGTGACCTA CGTGTGGGGCGTCGTGTCTTGGGGAGAGAATTGTGGCAAGCCTGAGT TCCCCGGCGTGTACACCAAGGTGGCCAACCTACTTCGACTGGATCAGCT ACCACGTGGGCAGACCATTTCATCAGCCAGTACAACGTTGCGGCCGC
63	His 标签的糖基 化嵌合 CR1b-FI 蛋白质编码序 列	AAGCTTGCCACCATGAGACTGCTGGCCAAGATCATCTGCCTGATGCTG TGGGCCATCTGCGTGGGCCACCACCATCACCATCACGGCAGCAGCGAG AACCTGTACTTCCAAGGATCTTCTGGCGGCCACTGTCAGGCCCTGAT CACTTCCTGTTGCCAAGCTGAAAACCCAGACCAACGCCAGCGACTT CCCTATCGGCACCAGCCTGAAGTACGAGTGCAGACCCGAGTACTACGG CAGACCCCTCAGCATCACCTGTCTGGACAACCTCGTGTGGTCTAGCCC CAAGGACGTGTGCAAGAGAAAAGAGCTGCAAGACCCCTCCTGATCCTG TGAACGGCATGGTGCACGTGATCACCGACATCCAAGTGGGCAGCAGA ATCAACTACAGCTGCACCACCGGCCACAGACTGATCGGACACTCTAGC GCCGAGTGTATCCTGAGCGGCAACACAGCCCACTGGTCCACCAAGCCT CCAATCTGCCAGAGAATCCCTTGGCGCCTGCCTCTACAATCGCCAAC GGCGATTTCATCAGCACCAACAGAGAGAACTTCCACTACGGCTCCGTG GTCACCTACAGATGCAACCTGGGCTCCAGAGGCCGGAAGGTGTTTCA ACTGTGGGCGAGCCTAGCATCTACTGCACCAGCAACGACGACCAAGT CGGCATTTGGAGCGGACCTGCTCCTCAGTGCATCATCCCCAACAAGGC CACACCTCCTAACGTGGAAAATGGCGGCGGAGGCTCTAGAGGTGGCG GAGGATCTGGCGGAGGCGGATCTATCGTTGGAGGAAAAGAGAGCACAG CTGGGCGACCTGCCTTGGCAGGTTGCCATTAAGGATGCCAGCGGCATC ACATGCGGCGGCATCTATATCGGCGGCTGCTGGATTCTGACCGCCGCTC ATTGTCTGAGAGCCAGCAAGACCCACCGGTATCAGATCTGGACCACCG TGGTGGACTGGATTACCCCGACCTGAAGCGGATCGTGATCGAGTACG TGGACCGGATCATCTTCCACGAGAACTACAACGCCGGCACCTACCAGA ACGATATCGCCCTGATCGAGATGAAGAAGGACGGCAACAAGAAGGAC TGCGAGCTGCCTAGATCTATCCCTGCCGCTGTTTCTTGGAGCCCCCTACC TGTTCCAGCCTAACGATACCTGCATCGTGTCCGGCTGGGGCAGAGAGA AGGACAACGAAAGGGTGTTACGCCTGCAGTGGGGCGAAGTGAAGCT GATCTCCAACCTGCAGCAAGTTCTACGGCAACCGGTTCTACGAGAAAAG AATGGAATGCGCCGGCACATACGACGGCTCCATCGATGCCTGTAAAGG CGATTCTGGCGGACCCCTCGTGTGCATGGATGCCAACAATGTGACCTA CGTGTGGGGCGTCGTGTCTTGGGGAGAGAATTGTGGCAAGCCTGAGT TCCCCGGCGTGTACACCAAGGTGGCCAACCTACTTCGACTGGATCAGCT ACCACGTGGGCAGACCATTTCATCAGCCAGTACAACGTTGCGGCCGC
64	His 标签的非糖 基化嵌合 CR1a-FI 蛋白质 编码序列	AAGCTTGCCACCATGAGACTGCTGGCCAAGATCATCTGCCTGATGCTG TGGGCCATCTGCGTGGGCCACCACCATCACCATCACGGCAGCAGCGAG AACCTGTACTTCCAAGGATCTTCTGGCGGCCACTGTCAGGCCCTGAT CACTTCCTGTTGCCAAGCTGAAAACCCAGACACAGGCCAGCGACTT CCCTATCGGCACCAGCCTGAAGTACGAGTGCAGACCCGAGTACTACGG CAGACCCCTCAGCATCACCTGTCTGGACAACCTCGTGTGGTCTAGCCC CAAGGACGTGTGCAAGAGAAAAGAGCTGCAAGACCCCTCCTGATCCTG TGAACGGCATGGTGCACGTGATCACCGACATCCAAGTGGGCAGCAGA ATCCAGTACAGCTGCACCACAGGCCACAGACTGATCGGCCACTCTAGC

[0271]

		GCCGAGTGTATCCTGTCTGGCAATGCCGCTCACTGGTCCACCAAGCCT CCAATCTGCCAGAGAATCCCTTGCGGCCTGCCTCCTACAATCGCCAAC GGCGATTTCATCAGCACCAACAGAGAGAACTTCCACTACGGCTCCGTG GTCACCTACAGATGCAATCCTGGCAGCGGCGGCAGAAAGGTGTTCTGA ACTTGTGGGCGAGCCCAGCATCTACTGCACCAGCAACGATGACCAAGT CGGCATTTGGAGCGGCCCTGCTCCTCAGTGCATCATCCCCAACAAAGC CACACCTCCTAACGTGGAAAATGGCGGCGGAGGCTCTAGAGGTGGCG GAGGATCTGGCGGAGGCGGATCTATCGTTGGAGGAAAGAGAGCACAG CTGGGCGACCTGCCTTGGCAGGTTGCCATTAAGGATGCCAGCGGCATC ACATGCGGCGGCATCTATATCGGCGGCTGCTGGATTCTCACCGCCGCAC ATTGTCTGAGAGCCAGCAAGACCCACCGGTATCAGATCTGGACCACCG TGGTGGACTGGATTACCCCCGACCTGAAGCGGATCGTGATCGAGTACG TGGACCGGATCATCTTCCACGAGAACTACAACGCCGGCACCTACCAGA ACGATATCGCCCTGATCGAGATGAAGAAGGACGGCAACAAGAAGGAC TGCAGCTGCCCTAGATCTATCCAGCCGCTGTTCTTGGAGCCCCCTACC TGTTCCAGCCTCAAGATACCTGCATCGTGTCCGGCTGGGGCAGAGAGA AGGACAACGAAAGGGTGTTTCAGCCTGCAGTGGGGCGAAGTGAAGCT GATCTCCAGTGCAGCAAGTTCTACGGCAACCGGTTCTACGAGAAAGA AATGGAATGCGCCGGCACATACGACGGCTCCATCGATGCCTGTAAAGG CGATTCTGGCGGACCCCTCGTGTGCATGGATGCCAATCAAGTGACCTA CGTGTGGGGCGTCTGTCTCGGGGAGAGAATTGTGGCAAGCCTGAGT TCCCCGGCGTGTACACCAAGGTGGCCAACTACTTCGACTGGATCAGCT ACCACGTGGGCAGACCATTCTATCAGCCAGTACAACGTTGCGGCCGC
65	His 标签的非糖基化嵌合 CR1b-FI 蛋白质编码序列	AAGCTTGCCACCATGAGACTGCTGGCCAAGATCATCTGCCTGATGCTG TGGGCCATCTGCGTGGGCCACCACCATCACCATCACGGCAGCAGCGAG AACCTGTACTTCCAAGGATCTTCTGGCGGCCACTGTCAGGCCCTGAT CACTTCCTGTTGCGCAAGCTGAAAACCCAGACACAGGCCAGCGACTT CCCTATCGGCACCAGCCTGAAGTACGAGTGCAGACCCGAGTACTACGG CAGACCCCTCAGCATCACCTGTCTGGACAACCTCGTGTGGTCTAGCCC CAAGGACGTGTGCAAGAGAAAAGAGCTGCAAGACCCCTCCTGATCCTG TGAACGGCATGGTGCACGTGATCACCGACATCCAAGTGGGCAGCAGA ATCCAGTACAGCTGCACCACAGGCCACAGACTGATCGGCCACTCTAGC GCCGAGTGTATCCTGAGCGGAAACACAGCCCACTGGTCCACCAAGCC TCCAATCTGCCAGAGAATCCCTTGCGGCCTGCCTCCTACAATCGCCAA CGGCGATTTCATCAGCACCAACAGAGAGAACTTCCACTACGGCTCCGT GGTACCTACAGATGCAACCTGGGCTCCAGAGGCCGGAAGGTGTTCTG AACTTGTGGGCGAGCCTAGCATCTACTGCACCAGCAACGACGACCAA GTCGGCATTTGGAGCGGACCTGCTCCTCAGTGCATCATCCCCAACAAAG GCCACACCTCCTAACGTGGAAAATGGCGGCGGAGGCTCTAGAGGTGG CGGAGGATCTGGCGGAGGCGGATCTATCGTTGGAGGAAAGAGAGCAC AGCTGGGCGACCTGCCTTGGCAGGTTGCCATTAAGGATGCCAGCGGCA TCACATGCGGCGGCATCTATATCGGCGGCTGCTGGATTCTCACCGCCGC TCATTGTCTGAGAGCCAGCAAGACCCACCGGTATCAGATCTGGACCAC CGTGGTGGACTGGATTACCCCCGACCTGAAGCGGATCGTGATCGAGTA CGTGGACCGGATCATCTTCCACGAGAACTACAACGCCGGCACCTACCA

[0273]

		WSGPAPQCIIPNKATPPNVENGSGGSRGGGSGGGGSIVGGKRAQLGDLP WQVAIKDASGITCGGIYIGGCWILTAACHCLRASKTHRYQIWTTVVVDWIHP DLKRIVIEYVDRIIFHENYNAGTYQNDIALIEMKKDGNKKDCELPSPSIPAA VPWSPYLFQPNDDTCIVSGWGREKDNERVFSLQWGEVKLISNCSKFYGNR FYEKEMECAGTYDGSIDACKGDSGGPLVCMDDANNVTYVWGVVSWGEN CGKPEFPGVYTKVANYFDWISYHVGRPFISQYNV
72	非糖基化嵌合 CR1a-FI 蛋白质 氨基酸序列 (有 信号肽)	MRLAKIICLMLWAICVAGHCQAPDHFLFAKLKTQTQASDFPIGTSCLKYE CRPEYYGRPFISITCLDNLVWSSPKDVCKRKCKTTPDPVNGMVHVITDIQ VGSRIQYSCTTGHRLLIGHSSAECILSGNAAHWSTKPPICQRIPCGLPPTIAN GDFISTNRENHFYGSVVITYRCNPGSGGRKVFELVGEPISYCTSNDDQVGI WSGPAPQCIIPNKATPPNVENGSGGSRGGGSGGGGSIVGGKRAQLGDLP WQVAIKDASGITCGGIYIGGCWILTAACHCLRASKTHRYQIWTTVVVDWIHP DLKRIVIEYVDRIIFHENYNAGTYQNDIALIEMKKDGNKKDCELPSPSIPAA VPWSPYLFQPNDDTCIVSGWGREKDNERVFSLQWGEVKLISQCSKFYGNR FYEKEMECAGTYDGSIDACKGDSGGPLVCMDDANQVTYVWGVVSWGEN CGKPEFPGVYTKVANYFDWISYHVGRPFISQYNV
73	非糖基化嵌合 CR1b-FI 蛋白质 氨基酸序列 (有 信号肽)	MRLAKIICLMLWAICVAGHCQAPDHFLFAKLKTQTQASDFPIGTSCLKYE CRPEYYGRPFISITCLDNLVWSSPKDVCKRKCKTTPDPVNGMVHVITDIQ VGSRIQYSCTTGHRLLIGHSSAECILSGNAAHWSTKPPICQRIPCGLPPTIAN GDFISTNRENHFYGSVVITYRCNPGSGGRKVFELVGEPISYCTSNDDQVGI WSGPAPQCIIPNKATPPNVENGSGGSRGGGSGGGGSIVGGKRAQLGDLP WQVAIKDASGITCGGIYIGGCWILTAACHCLRASKTHRYQIWTTVVVDWIHP DLKRIVIEYVDRIIFHENYNAGTYQNDIALIEMKKDGNKKDCELPSPSIPAA VPWSPYLFQPNDDTCIVSGWGREKDNERVFSLQWGEVKLISQCSKFYGNR FYEKEMECAGTYDGSIDACKGDSGGPLVCMDDANQVTYVWGVVSWGEN CGKPEFPGVYTKVANYFDWISYHVGRPFISQYNV

[0274] 本发明包括所描述的方面和优选特征的组合,除非这样的组合明确不允许或被明确避免。

[0275] 本文使用的节标题仅是为了组织的目的,不能被解释为限制所描述的主题。

[0276] 现在将参考附图以举例的方式说明本发明的方面和实施方式。进一步方面和实施方式对于本领域技术人员而言将是明显的。本文中所提及的所有文献通过引用合并在本文中。

[0277] 在整个说明书包括随后的权利要求书中,除非上下文另外需要,否则词语“包括 (comprise)”和变体例如“包括 (comprises)”和“包括 (comprising)”,将被理解为暗指包括规定的整数 (integer) 或步骤、或者整数或步骤的组,但是不排除任何其他整数或步骤、或者整体或步骤的组。

[0278] 必须注意的是,如在本说明书和附随的权利要求中使用的,除非上下文明确指示,否则单数形式“一个 (a)”“一种 (an)”和“该 (the)”包括复数的对象。在文本中范围可以表示为从“约”一个特定值,和/或到“约”另一个特定值。当表述这样的范围时,另一实施方式包括从该一个特定值和/或到该其他特定值。类似地,当通过使用在先的“约”将值表示为近似值时,要理解的是,该特定值形成另一实施方式。

[0279] 在公开核酸序列的情况下,其反向互补物也被明确考虑。

[0280] 附图的简要说明

[0281] 现将参照附图讨论说明本发明的原理的实施方式和实验。

[0282] 图1. 包括补体因子H辅助因子区的C3b灭活多肽的示意图。C3b灭活多肽包括补体

因子H的C3b结合区(即,CCP 1-4);柔性接头、其包括工程化蛋白水解裂解位点(由*显示)以产生唯一的肽,该肽被设计为容许通过质谱分析法在生物样品中检测;以及补体因子I的蛋白水解结构域。图1A代表在补体因子I的蛋白水解结构域上包括N-聚糖的多肽。图1B代表多肽,在该多肽中补体因子I的蛋白水解结构域已经突变以除去N-糖基化位点。图1C代表多肽,在该多肽中补体因子I的蛋白水解结构域已经突变以除去N-糖基化位点,并且该多肽包括蛋白质的N-末端处的替代糖基化序列,以及用于从该蛋白质除去所述替代糖基化序列的内肽酶裂解位点。

[0283] 图2.显示了C3b分解的Western印迹分析结果的图片。*表示C3b分解的iC3b产物。“嵌合体(chimera)”是指图1A中示意性代表的多肽。

[0284] 图3.显示了即时蓝(Instant Blue)染色的凝胶的图片,该即时蓝染色的凝胶显示了图1A中示意性代表的多肽的酶去糖基化之后的条带移动(band shift)。“d嵌合体”是指去糖基化的多肽。

[0285] 图4.检测在扩散通过BrM之后在人全血清(whole human serum)中检测可溶补体蛋白存在的Western印迹图片(图4A),以及(图4B)即时蓝染色的凝胶,其显示了对于纯补体蛋白观察到与人全血清中所见的相同的扩散模式。

[0286] 图5.在存在来自BrM扩散试验的不同纯化蛋白或渗出物的情况下,C3b分解的即时蓝染色凝胶分析的图片。(A)显示了补体因子I扩散跨越BrM并分解C3b的能力的分析结果。(B)显示了天然补体因子I(dFI)的去糖基化以及产生的条带移动模式。(C)显示了取糖基化补体因子I扩散跨越BrM并分解C3b的能力的分析结果。

[0287] 图6.在分析扩散跨越BrM的能力之后,在样品室和扩散物室中,检测图1C示意性代表的去糖基化嵌合FH-FI多肽(dFH-FI)存在的Western印迹的结果的图片。

[0288] 图7.显示了使用图1A中示意性代表的嵌合FH-HI多肽去糖基化版本分析C3b分解的Western印迹结果的图片。

[0289] 图8.由布鲁赫膜(BrM)维持的眼睛中不同补体组(complementome)区域的示意图。

[0290] 图9.显示了通过Bio-Layer干涉度量法来测量的,糖基化的和去糖基化嵌合FH-FI多肽(9A)、以及FH和FHL-1(9B)对C3b的结合亲和力的表格和图片。

[0291] 图10.包括补体受体1辅助因子区的C3b灭活多肽的示意图。该C3b灭活多肽包括补体受体1的C3b结合区CCP 8-10或15-17;基序,其用于创建质谱分析兼容的检测肽(用“M”显示),柔性接头,其包括设计为容许通过质谱分析法在生物样品中检测的唯一胰蛋白酶肽(用*显示);以及补体因子I的蛋白水解结构域。图10A代表辅助因子和蛋白水解结构域上包括CR1 CCP 8-10以及N-聚糖的多肽(CR1a-FI)。图10B代表包括CR1 CCP 8-10的多肽,并且其中辅助因子和蛋白水解结构域已经突变以除去N-糖基化位点(nCR1a-FI)。图10C代表辅助因子和蛋白水解结构域上包括CR1 CCP 15-17以及N-聚糖的多肽(CR1b-FI)。图10D代表包括CR1 CCP 15-17的多肽,并且其中辅助因子和蛋白水解结构域已经突变以除去N-糖基化位点(nCR1b-FI)。

实施例

[0292] 在下面的实施例中,发明人描述了嵌合的C3b灭活多肽的设计,该多肽其包括补体因子H的C3b结合辅助因子区和补体因子I的C3b灭活蛋白水解区,以及去糖基化嵌合多肽扩

散跨越布鲁赫膜 (BrM) 并将C3b分解成iC3b的能力。

[0293] 实施例1:包括补体因子H辅助因子区的嵌合的C3b灭活多肽的产生

[0294] 编码SEQ ID NO:32、33和34中显示的氨基酸序列的DNA插入物(inserts)通过重组DNA技术制备,并克隆到载体中以产生用于嵌合蛋白质的重组表达的构建体。氨基酸序列及其特征如下所示。

[0295] His-FH-FI:

MRLAKIICLMLWAICVAHHHHHHGSSENLYFQGSSGEDCNELPPRRNTEIL
TGSWSDQTYPEGTQAIYKCRPGYRSLGNIIMVCRKGEWVALNPLRKCQK
RPCGHPGDTPFGTFTLTGGNVFEYGVKAVYTCNEGYQLLGEINYRECDTD
GWTNDIPICEVVKCLPVTAPENGKIVSSAMEPDREYHFGQAVRFVCNSGY
KIEGDEEMHCSDDGFWWSKEKPKCVEISCKSPDVINGSPISOKIIYKENERFO
YKCNMGYEYSERGDAVCTESGWRPLPSCEEGGGSRGGGGSGGGGSIV
[0296] GGKRAQLGDLPWQVAIKDASGITCGGIYIGGCWILTAHCLRASKTHRYQ
IWTTVVDWIHPDLKRIVIEYVDRIIFHENYNAGTYQNDIALIEMKKDGNK
KDCELPRSIPAAVPWSPYLFQPNDCIVSGWGREKDNERVFSLOWGEVKL
ISNCSKFYGNRFYEKEMECAGTYDGSIDACKGDSGGPLVCMDANNVTYV
WGVVSWGGENCGKPEFPGVYTKVANYFDWISYHVGRPFISQYNV (SEQ ID
NO: 32)

[0297] 信号肽;6×His标签;

烟草蚀纹病毒 (TEV) 蛋白酶裂解位点; 人补体因子

H 辅助因子区 (UniProt: P08603 残基 19-264); G4S-R-(G4S)₂ 接头; 人补体
因子 I 蛋白水解结构域 (UniProt: P05156 残基 340-574)。

[0298] His-nFH-FI:

MRLAKIICLMLWAICVAHHHHHHGSSENLYFQGSSGEDCNELPPRRNTEIL
TGSWSDQTYPEGTQAIYKCRPGYRSLGNIIMVCRKGEWVALNPLRKCQK
[0299] RPCGHPGDTPFGTFTLTGGNVFEYGVKAVYTCNEGYQLLGEINYRECDTD
GWTNDIPICEVVKCLPVTAPENGKIVSSAMEPDREYHFGQAVRFVCNSGY
KIEGDEEMHCSDDGFWWSKEKPKCVEISCKSPDVINGSPISOKIIYKENERFO

- YKCNMGYEYSERGDVCTESGWRPLPSCEE GGGGSRGGGGSGGGGSIV
GGKRAQLGDLPWQVAIKDASGITCGGIYIGGCWILTA AHCLRASKTHRYQ
IWTTVVDWIHPDLKRIVIEYVDRIIFHENYNAGTYQNDIALIEMKKDGNK
[0300] KDCELPR SIPAAVPWSPYLFQPDTCIVSGWGREKDNERVFSLOWGEVKL
ISQCSKFYGNRFYEKEME CAGTYDGSIDACKGDSGGPLVCMDANQVTYV
WGVVSWGENCGKPEFPGVYTKVANYFDWISYHVGRPFISQYNV (SEQ ID
NO: 33)
- [0301] 信号肽; 6×His 标签;
烟草蚀纹病毒 (TEV) 蛋白酶裂解位点; 人补体因子
H 辅助因子区 (UniProt: P08603 残基 19-264); G4S-R-(G4S)₂ 接头; 包括替
代物 N464Q、N494Q 和 N536Q 的人补体因子 I 蛋白水解结构域 (UniProt:
P05156 残基 340-574)。
- [0302] nFH-FI:
MRL LAKIICLMLWAICVAEDCNELPPRRNTEILTGSWSDQTYPEGTQAIYKC
RPGYRSLGNIIMVCRKGEWVALNPLRKCKRPGCHPGDTPFGTFTLTGGN
VF EYGVKAVYTCNEGYQLLGEINYRECDTDGWTNDIPICEVVKCLPVTAP
ENGKIVSSAMEPDREYHFGQAVRFVCNSGYKIEGDEEMHCSDDGFWSKE
- [0303] KPKCVEISCKSPDVINGSPISOKIIYKENERFOYKCNMGYEYSERGDVCT
ESGWRPLPSCEE GGGGSRGGGGSGGGGSIVGGKRAQLGDLPWQVAIKDA
SGITCGGIYIGGCWILTA AHCLRASKTHRYQIWTTVVDWIHPDLKRIVIEY
VDRIIFHENYNAGTYQNDIALIEMKKDGNKKDCELPR SIPAAVPWSPYLFQ
PQDTCIVSGWGREKDNERVFSLOWGEVKLISQCSKFYGNRFYEKEMECA
GTYDGSIDACKGDSGGPLVCMDANQVTYVWGVVSWGENCGKPEFPGV
- [0304] YTKVANYFDWISYHVGRPFISQYNV (SEQ ID NO: 34)
- [0305] 信号肽;
人补体因子 H 辅助因子区 (UniProt: P08603 残基 19-264);

G4S-R-(G4S)₂接头：包括替代物N464Q、N494Q和N536Q的人补体因子I蛋白水解结构域（UniProt: P05156残基340-574）。

[0306] 图1A显示了用TEV蛋白酶处理以除去N-末端6×His标签之后,具有氨基酸序列SEQ ID NO:32的蛋白FH-FI的示意图。

[0307] 图1B显示了在用EV蛋白酶处理除去N-末端6×His标签、和用肽:N-糖苷酶(PNGase)处理除去N-聚糖之后(即,d嵌合体),具有SEQ ID NO:32的氨基酸序列的蛋白FH-FI的示意图。

[0308] 设计编码SEQ ID NO:34中显示的序列的进一步FH-HI构建体,其另外包括N-末端替代糖基化序列和紧靠补体因子H辅助因子区上游的弗林内切蛋白酶裂解位点。由这一构建体编码的FH-FI蛋白的示意图在图1C中显示。有益地,图1C中示意性显示的多肽将由具有弗林内切蛋白酶内源表达的细胞以无糖基形式分泌。因而编码这一蛋白质的构建体对于产生能够在体内、例如在期望的位置、生产所述非糖基化多肽的细胞是有用的。

[0309] 实施例2:通过嵌合C3b灭活多肽将C3b分解成iC3b

[0310] 如在Clark等J.Immunol (2014) 193,4962-4970中描述的,在体外研究了嵌合C3b灭活FH-HI多肽分解C3b的能力。简要地说,在20μl的总体积中进行反应。纯化的C3b、因子I和因子H;纯化的C3b和嵌合FH-FI多肽;或者纯化的C3b和细胞培养基对照在PBS中混合在一起,在37℃下孵育15分钟。通过添加5μl的5×SDS还原样品缓冲液并在100℃煮沸10分钟来停止反应。

[0311] 随后通过Western印迹检测C3b和iC3b 68kDa iC3b产物。简要地说,样品在200V下在预制的4-12% NuPAGE Bis Tris SDS凝胶(赛默飞世尔科技(Thermo Fisher Scientific),奥特林厄姆(Altrincham),UK)中运行60分钟,以确保分辨任何紧密迁移的条带,然后使用半干的转移装置,在转移缓冲液(25mM三羟甲基氨基甲烷(Tris),192mM甘氨酸,10% (v/v) 甲醇)中在80mA下将凝胶转移到硝化纤维膜上1.5小时。在添加磷酸盐缓冲液(Phosphate Buffer Solution,PBS)、0.2% (v/v) 吐温-20(Tween-20) (PBS-T) 中的0.5μg/ml抗C3b抗体克隆755(剑桥生物科学(Cambridge Biosciences),剑桥(Cambridge),UK;目录号2072)在室温下持续2小时之前,膜在4℃下在PBS、10% (w/v) 奶、0.2% (w/v) 牛血清蛋白(Bull Serum Albumin,BSA)中封闭16小时。在添加1:2000稀释度的HRP结合的二抗在室温下持续2小时之前,将膜在PBS-T中洗涤2×30分钟。在添加SuperSignal West Pico化学发光底物(赛默飞世尔科技,目录号34080)在室温下持续3分钟之前,膜在PBS-T中洗涤2×30分钟,之后。通过在室温下将Super RX-N X射线底片(富士胶片(FujiFilm),目录号PPB5080)曝光于处理的膜持续5分钟,并在自动化X射线底片显影机上显影,来检测反应条带。

[0312] 图2显示了图1A中示意性代表的嵌合FH-FI多肽的C3b分解分析结果。发现FH-HI能够将C3b分解成iC3b,正如iC3b 68kDa条带(*)的检出所指示的。

[0313] 实施例3:嵌合C3b灭活多肽的去糖基化

[0314] 3.1嵌合C3b灭活多肽的取糖基化

[0315] 图1A中示意性代表的嵌合FH-FI多肽如下去糖基化以除去N-连接的聚糖。

[0316] 用几丁质结合结构域标记的Remove-iT聚糖酶F(PNGase F)(纽英伦(New England Biolabs),目录号P0706S)用于在非变性条件下(通过除去N-聚糖)对纯化的嵌合多肽去糖

基化。2μl的GlycoBuffer 2 (10×) 添加到20μg蛋白质中,总体积18μl。通过抽吸(aspiration)轻柔混合之后,添加5μl的PNGase F并通过抽吸小心地混合。反应保持在37℃的水浴中24小时。对于随后除去PNGase F,50μl的磁性几丁质珠子(纽英伦,目录号E8036S)在PBS中洗涤,并使用磁性艾本德(eppendorf)夹持器进行沉淀(pelleted)。收获的珠子应用于去糖基化反应,并在室温下孵育10分钟。使用磁力架沉淀磁性几丁质珠子和缩合的PNGase F,并收集含有去糖基化的蛋白质的上清液。通过凝胶电泳分析去糖基化的蛋白质。预制的4-12%NuPAGE Bis Tris SDS凝胶(赛默飞世尔科技,奥特林厄姆,UK)在200V下运行60分钟,以确保分辨任何靠近迁移的条带,用即时蓝染料(埃克斯德翁(Expedeon),哈斯顿(Harston),UK)在室温下对凝胶进行染色60分钟。

[0317] 图3显示,图1A中示意性代表的嵌合FH-FI多肽的脱糖基化引起条带移动。增加的条带迁移表明聚糖的损失,以及随后水动力学半径的降低。

[0318] 实施例4:嵌合C3b灭活多肽跨越布鲁赫膜的扩散

[0319] 4.1补体因子I和H不能扩散跨越布鲁赫膜

[0320] 分析了不同的补体蛋白质扩散跨越布鲁赫膜的能力。

[0321] 如Clark等J. Immunol (2014) 193,4962-4970描述的执行可溶蛋白质通过富集的黄斑BrM的被动扩散。简要地说,富集的BrM的黄斑区如McHarg等,J Vis Exp (2015) 1-7中所描述的从供体眼睛分离,并安装在尤斯灌流室(哈佛仪器(Harvard Apparatus),哈姆登(Hamden),USA)中;从其上除去BrM的眼睛组织没有显示AMD的宏观证据。安装后,5mm直径的黄斑区是两个相同的区室之间唯一的阻挡物。BrM的两侧用2ml的PBS在室温下洗涤5分钟。对于使用人全血清的实验,人血清(西格玛奥德里奇(Sigma-Aldrich),普尔(Poole),UK,目录号H4522)用PBS 1:1稀释,并将2ml添加到称为样品室的尤斯灌流室中。对于使用纯化的补体的实验,将纯化的蛋白质以PBS中100μg/ml添加到样品室中。1分钟后,如果没有检测到进入第二室的渗漏(这将指示膜完整性的损坏),则将2ml PBS单独添加到尤斯灌流室的第二区室中、称为扩散物室,在室温下放置24小时,每个室中柔和搅动以避免产生扩散蛋白质的梯度。随后通过凝胶电泳分析每个室的样品,用即时蓝染料(Expedeon,Harston,UK)在室温下染色60分钟,或者如上所述进行Western印迹。以下抗体用于Western印迹实验中:抗FI克隆271203(R&D系统,目录号MAB3307),抗FD克隆255706(R&D系统,目录号MAB1824);和抗FB克隆313011(R&D系统,目录号MAB2739),抗FH克隆OX23(艾博抗(ABcam)目录号ab17928),抗C3b克隆755(剑桥生物科学目录号2072)和Clark等J. Immunol (2014) 193,4962-4970中描述的多克隆抗FHL-1抗体。

[0322] 实验结果在图4A(人全血清)和4B(纯化的补体蛋白质)中显示。发现补体因子H、B、I和C3b不能扩散通过BrM,而因子D和FHL-1能够扩散跨越BrM。

[0323] 在基本上如上文实施例2中描述执行的C3b分解试验中,确认了补体因子I不能扩散跨越BrM和分解C3b。使用在PBS中混合在一起的2μg纯化的C3b和0.1μg FHL-1,以及0.04μg纯化的FI,或取自扩散实验的扩散物室的10μl样品,在20μl的总体积中进行反应,在该扩散实验中研究了纯化的FI跨越BrM的扩散。

[0324] 结果在图5A中显示。在存在FHL-1和FI的情况下可以观察到C3b的α链的分解。向来自扩散物室的样品添加FHL-1和C3b,表明没有C3bα链分解,即,不存在FI。通过直接向相同样品中添加纯化的FI、及随后C3bα链降解成它的构成物43kDa和68kDa iC3b分解产物,来确

认试验有效性。

[0325] 证明了补体因子I不存在于扩散物中,正如由“扩散物+、C3b+、FHL-1+、补充的FI-”泳道(即,图5A的凝胶的泳道8)中没有iC3b产物所证明的。这个实验还显示,单独的FHL-1不能分解C3b(图5A的凝胶的泳道7和8)。

[0326] 本发明人接下来研究了补体因子I的糖基化状态对于扩散跨越BrM的能力是否重要的。通过如上文实施例3.1中描述的用Remove-iT PNGase F处理补体因子I来制备去糖基化补体因子I(图5B中称为dFI)。去糖基化与条带移位相关联;重链条带糖基化程度最高,因而显示了最大的移动(图5B)。

[0327] 去糖基化补体因子I扩散跨越BrM和分解C3b的能力在C3b分解试验中分析,该C3b分解试验基本上如上文实施例2中描述的来执行。在20 μ l的总体积中进行反应,使用在PBS中混合在一起的2 μ g纯化的C3b和0.1 μ g FHL-1、以及取自扩散实验的扩散物室的10 μ l样品,在该扩散实验中研究了dFI跨越BrM的扩散。

[0328] 结果在图5C中显示。证明了去糖基化补体因子I存在于扩散物中并能够分解C3b,正如由在“扩散物+,C3b+,FHL-1+”泳道(即,图5C的凝胶的泳道7)中存在iC3b产物。

[0329] 4.2去糖基化嵌合FH-FI C3b灭活多肽扩散跨越布鲁赫膜。

[0330] 在如上文实施例4.1中描述的试验中分析如实施例3中描述制备的去糖基化嵌合FH-FI多肽扩散跨越BrM的能力。

[0331] 实验结果在图6中显示。显示了去糖基化嵌合FH-FI多肽(图6中命名为dFH-FI)能够扩散跨越BrM。

[0332] 实施例5:去糖基化嵌合FH-FI C3b灭活多肽保持C3b分解活性

[0333] 在如上文实施例2中描述的试验中分析如实施例3中描述制备的去糖基化嵌合FH-FI多肽将C3b分解成iC3b的能力。

[0334] 实验结果在图7中显示。显示了去糖基化嵌合FH-FI多肽(图7中命名为dFH-FI)能够分解将C3b分解成iC3b。

[0335] 实施例6:评估了非糖基化嵌合FH-FI多肽扩散跨越布鲁赫膜和维持C3b分解活性的能力

[0336] 在如上文实施例4.1描述的试验中分析了例如图1B中示意性代表的非糖基化嵌合FH-FI多肽扩散跨越BrM的能力。

[0337] 在如上文实施例2描述的试验中分析了例如图1B中示意性代表的非糖基化嵌合FH-FI多肽将C3b分解成iC3b的能力。

[0338] 实施例7:糖基化和脱糖基化嵌合FH-FI多肽展现对C3b的结合亲和力

[0339] 评估了糖基化嵌合FH-FI多肽(例如,图1A中示意性显示的)和脱糖基化嵌合FH-FI多肽(如实施例3中描述制备的)对C3b的结合亲和力。

[0340] 使用Bio-Layer干涉量度法计算亲和力测量结果。包括天然补体调节物和C3b结合多肽FH和FHL-1作为阳性对照。

[0341] 结果在图9A和9B中显示。嵌合FH-FI的糖基化和脱糖基化的形式二者显示了对C3b的结合亲和力(图9A)。糖基化嵌合FH-FI展现了在对C3b的最强结合,KD为 5.21×10^{-9} M。脱糖基化嵌合FH-FI较低强度地结合,KD为 4.76×10^{-8} M。两种嵌合FH-FI多肽比FH(KD 5.83×10^{-7} M)或FHL-1(KD 1.17×10^{-6} M)更强地结合C3b,在图9B中显示。

[0342] 实施例8:产生包括补体受体1辅助因子区的嵌合C3b灭活多肽

[0343] 设计编码SEQ ID NO:50、51、52和53中显示的氨基酸序列的DNA插入物,并通过重组DNA技术生产,且克隆到载体中,以产生用于嵌合蛋白质的重组表达的构建体。氨基酸序列及其特征如下。

[0344] His-CR1a-FI:

MRLLAKIICLMLWAICVAHHHHHHGSSSENLYFQGSSGGHCQAPDHFLFAKL
KTQTNASDFPIGTSLKYECRPEYYGRPFISITCLDNLVWSSPKDVCKRKSC
KTPDPVNGMVHVITDIQVGSRIYSCCTTGHRLIGHSSAECILSGNAAHWS
TKPPICQRIPCGLPPTIANGDFISTNRENFHYGSVVITYRCNPGSGGRKVFEL
VGEPISYCTSNDDQVGIWSGPAPOCIIIPNKATPPNVENGSGGSRGGGGSGG
GGSIYGGKRAQLGDLWPQVAIKDASGITCGGIYIGGCWILTAHCLRASK
THRYQIWTTVVVDWIHPDLKRIVIEYVDRIIFHENYNAGTYQNDIALIEMKK
DGNKKDCELPRSIPAAVPWSPYLFQPNDDTCIVSGWGREKDNERVESLOW
GEVKLISNCSKFYGNRFYEKEMECAGTYDGSIDACKGDSGGPLVCMDAN

[0346] NVTYVWGVVSWGENCGKPEFPGVYTKVANYFDWISYHVGRPFISQYNV

[0347] (SEQ ID NO:50)

[0348] 信号肽;6×His标签;

烟草蚀纹病毒 (TEV) 蛋白酶裂解位点; 人补体受体

1 辅助因子区 CCP 8-10 (UniProt: P17927 残基 491 到 684); 用于创建质谱
分析兼容的检测肽的基序; G4S-R-(G4S)₂ 接头; 人补体因子 I 蛋白水解结构
域 (UniProt: P05156 残基 340-574)。

[0349] His-CR1b-FI:

MRLLAKIICLMLWAICVAHHHHHHGSSSENLYFQGSSGGHCQAPDHFLFAKL
KTQTNASDFPIGTSLKYECPEYYGRPFSITCLDNLVWSSPKDVCKRKSC
KTPDPVNGMVHVITDIQVGSRINYSCTTGHRLIGHSSAECILSGNTAHWS
TKPPICQRIPCGLPPTIANGDFISTNRENFHYGSVVTYRCNLGSRGRKVFEL
VGPSIYCTSNDDQVGIWSGPAPQCIIPNKATPPNVENGGGGSRGGGGSGG
[0350] GGSIVGGKRAQLGDLPWQVAIKDASGITCGGIYIGGCWILTAAHCLRASK
THRYQIWTTVVDWIHPDLKRIVIEYVDRIIFHENYNAGTYQNDIALIEMKK
DGNKKDCELPRSIPAAVPWSPYLFQPNDTCIVSGWGREKDNERVFSLOW
GEVKLISNCSKFYGNRFYEKEMECAGTYDGSIDACKGDSGGPLVCMDAN
NVTYVWGVVSWGENCGKPEFPGVYTKVANYFDWISYHVGRPFISQYNV

(SEQ ID NO: 51)

[0351] 信号肽;6×His标签;

烟草蚀纹病毒 (TEV) 蛋白酶裂解位点; 人补体受体

1 辅助因子区 CCP 15-17 (UniProt: P17927 残基 941 到 1134); 用于创建质谱分析兼容的检测肽的基序; G4S-R-(G4S)₂ 接头; 人补体因子 I 蛋白水解结构域 (UniProt: P05156 残基 340-574)。

[0352] His-nCR1a-FI:

MRLLAKIICLMLWAICVAHHHHHHGSSSENLYFQGSSGGHCQAPDHFLFAKL
KTQTQASDFPIGTSLKYECPPEYYGRPFSITCLDNLVWSSPKDVCKRKSC
KTPDPVNGMVHVITDIQVGSRIQYSCTTGHRLIGHSSAECILSGNAAHWS
TKPPICQRIPCGLPPTIANGDFISTNRENFHYGSVVTYRCNPGSGGRKVFEL
VGEPSIYCTSNDDQVGIWSGPAPQCIIPNKATPPNVENGGGGSRGGGGSGG
[0353] GGSIVGGKRAQLGDLPWQVAIKDASGITCGGIYIGGCWILTAAHCLRASK
THRYQIWTTVVDWIHPDLKRIVIEYVDRIIFHENYNAGTYQNDIALIEMKK
DGNKKDCELPRSIPAAVPWSPYLFQPODTCIVSGWGREKDNERVFSLOW
GEVKLISQCSKFYGNRFYEKEMECAGTYDGSIDACKGDSGGPLVCMDAN
QVTYVWGVVSWGENCGKPEFPGVYTKVANYFDWISYHVGRPFISQYNV

(SEQ ID NO: 52)

[0354] 信号肽;6×His标签;

烟草蚀纹病毒 (TEV) 蛋白酶裂解位点; 包含代替物

N509Q 和 N578Q 的人补体受体 1 辅助因子区 CCP 8-10 (UniProt: P17927

残基 491 到 684); 用于创建质谱分析兼容的检测肽的基序;G4S-R-(G4S)₂ 接

头; 包括替代物 N464Q、N494Q 和 N536Q 的人补体因子 I 蛋白水解结构域

(UniProt: P05156 残基 340-574)。

[0355] His-nCR1b-FI:

MRLLAKIICLMLWAICVAHHHHHHGSSSENLVFQSSGGHCQAPDHFLFAKL
KTQTQASDFPIGTSLKYECPPEYYGRPFSTCLDNLVWSSPKDVCKRKSC
KTPDPVNGMVHVITDIQVGSRIQYSCTTGHRLIGHSSAECILSGNAAHWS
TKPPICQRI PCGLPPTIANGDFISTNRENFHYGSVVTYRCNPGSGGRKVFEL
VGEPsiYCTSNDDQVGIWSGPAPQCII PNKATPPNVENG GGGGSRGGGGSGG
 [0356] GGsIVGGKRAQLGDLPWQVAIKDASGITCGGIYIGGCWILTA AHCLRASK
THRYQIWTTVVVDWIHPDLKRIVIEYVDRIIFHENYNAGTYQNDIALIEMKK
DGNKKDCELPRSIPAAVPWSPYLFQPODTCIVSGWGREKDNERVFSLOW
GEVKLISQCSKFYGNRFYEKEME CAGTYDGSIDACKGDSGGPLVCMDAN
QVTYVWGVVSWGENCGKPEFPGVYTKVANYFDWISYHVGRPFISQYNV

(SEQ ID NO: 53)

[0357] 信号肽; 6×His标签; 烟草蚀纹病毒 (TEV) 蛋白酶裂解位点; 包
括替代物 N959Q 和 N1028Q 的人补体受体 1 辅助因子区 CCP 15-17
(UniProt: P17927 残基 941 到 1134); 用于创造质谱相容的检测多肽的
基序; G4S-R- (G4S)₂ 接头; 包含取代 N464Q、N494Q 和 N536Q 的人类
补体因子 I 蛋白水解结构域 (UniProt: P05156 残基 340-574)。

[0358] 图10A-10D显示了用TEV蛋白酶处理除去N-末端6×His标签之后, SEQ ID NO:50到53的蛋白质的示意图。

[0359] 实施例9: 评估了嵌合CR1a-FI和CR1b-FI多肽扩散跨越布鲁赫膜和维持C3b分解活性的能力

[0360] 在如上文实施例2描述的试验中分析了图10A和10C中示意性代表的嵌合CR1a-FI和CR1b-FI多肽将C3b分解成iC3b的能力。

[0361] 在如上文实施例4.1描述的试验中分析了图10A和10C中示意性代表的嵌合CR1a-FI和CR1b-FI多肽扩散跨越BrM的能力。

[0362] 如上文实施例3.1中描述的通过用Remove-iT PNGase F处理来制备图10A和10C中示意性代表的嵌合CR1a-FI和CR1b-FI多肽的去糖基化版本。去糖基化嵌合CR1a-FI和CR1b-FI多肽的示意图在图10B和10D中显示。

[0363] 在如上文实施例4.1描述的试验中分析了嵌合CR1a-FI和CR1b-FI多肽的去糖基化版本扩散跨越BrM的能力, 并在如上文实施例2描述的试验中分析了它们将C3b分解成iC3b的能力。

[0364] 实施例10: 嵌合C3b灭活多肽跨越布鲁赫膜的非糖基化的扩散

[0365] 在如上文实施例4.1描述的试验中分析了例如图10B和10D中示意性代表的非糖基

化嵌合nCR1a-FI和nCR1b-FI多肽扩散跨越BrM的能力。

[0366] 在如上文实施例2描述的试验中分析了例如图10C和10D中示意性代表的非糖基化嵌合nCR1a-FI和nCR1b-FI多肽将C3b分解成iC3b的能力。

SEQUENCE LISTING

<110> 曼彻斯特大学

<120> C3b灭活多肽

<130> RIC/MP7371487

<150> GB 1709222.2

<151> 2017-06-09

<160> 73

<170> PatentIn version 3.5

<210> 1

<211> 1663

<212> PRT

<213> 包括信号肽的人(智人)C3 (UniProt: P01024)

<400> 1

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

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Lys Glu Tyr Val Leu Pro Ser Phe Glu Val Ile Val Glu Pro Thr Glu		
225	230	235
Lys Phe Tyr Tyr Ile Tyr Asn Glu Lys Gly Leu Glu Val Thr Ile Thr		
245	250	255
Ala Arg Phe Leu Tyr Gly Lys Lys Val Glu Gly Thr Ala Phe Val Ile		
260	265	270
Phe Gly Ile Gln Asp Gly Glu Gln Arg Ile Ser Leu Pro Glu Ser Leu		
275	280	285
Lys Arg Ile Pro Ile Glu Asp Gly Ser Gly Glu Val Val Leu Ser Arg		
290	295	300
Lys Val Leu Leu Asp Gly Val Gln Asn Pro Arg Ala Glu Asp Leu Val		
305	310	315
Gly Lys Ser Leu Tyr Val Ser Ala Thr Val Ile Leu His Ser Gly Ser		
325	330	335
Asp Met Val Gln Ala Glu Arg Ser Gly Ile Pro Ile Val Thr Ser Pro		
340	345	350
Tyr Gln Ile His Phe Thr Lys Thr Pro Lys Tyr Phe Lys Pro Gly Met		
355	360	365
Pro Phe Asp Leu Met Val Phe Val Thr Asn Pro Asp Gly Ser Pro Ala		
370	375	380
Tyr Arg Val Pro Val Ala Val Gln Gly Glu Asp Thr Val Gln Ser Leu		
385	390	395
Thr Gln Gly Asp Gly Val Ala Lys Leu Ser Ile Asn Thr His Pro Ser		
405	410	415
Gln Lys Pro Leu Ser Ile Thr Val Arg Thr Lys Lys Gln Glu Leu Ser		
420	425	430
Glu Ala Glu Gln Ala Thr Arg Thr Met Gln Ala Leu Pro Tyr Ser Thr		
435	440	445
Val Gly Asn Ser Asn Asn Tyr Leu His Leu Ser Val Leu Arg Thr Glu		
450	455	460
Leu Arg Pro Gly Glu Thr Leu Asn Val Asn Phe Leu Leu Arg Met Asp		
465	470	475
Arg Ala His Glu Ala Lys Ile Arg Tyr Tyr Thr Tyr Leu Ile Met Asn		
485	490	495
Lys Gly Arg Leu Leu Lys Ala Gly Arg Gln Val Arg Glu Pro Gly Gln		
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Phe Arg Leu Val Ala Tyr Tyr Thr Leu Ile Gly Ala Ser Gly Gln Arg		
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Glu Val Val Ala Asp Ser Val Trp Val Asp Val Lys Asp Ser Cys Val		
545	550	555
Gly Ser Leu Val Val Lys Ser Gly Gln Ser Glu Asp Arg Gln Pro Val		
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Pro Gly Gln Gln Met Thr Leu Lys Ile Glu Gly Asp His Gly Ala Arg		
580	585	590
Val Val Leu Val Ala Val Asp Lys Gly Val Phe Val Leu Asn Lys Lys		
595	600	605
Asn Lys Leu Thr Gln Ser Lys Ile Trp Asp Val Val Glu Lys Ala Asp		
610	615	620
Ile Gly Cys Thr Pro Gly Ser Gly Lys Asp Tyr Ala Gly Val Phe Ser		
625	630	635
Asp Ala Gly Leu Thr Phe Thr Ser Ser Ser Gly Gln Gln Thr Ala Gln		
645	650	655
Arg Ala Glu Leu Gln Cys Pro Gln Pro Ala Ala Arg Arg Arg Arg Ser		
660	665	670
Val Gln Leu Thr Glu Lys Arg Met Asp Lys Val Gly Lys Tyr Pro Lys		
675	680	685
Glu Leu Arg Lys Cys Cys Glu Asp Gly Met Arg Glu Asn Pro Met Arg		
690	695	700
Phe Ser Cys Gln Arg Arg Thr Arg Phe Ile Ser Leu Gly Glu Ala Cys		
705	710	715
Lys Lys Val Phe Leu Asp Cys Cys Asn Tyr Ile Thr Glu Leu Arg Arg		
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Gln His Ala Arg Ala Ser His Leu Gly Leu Ala Arg Ser Asn Leu Asp		
740	745	750
Glu Asp Ile Ile Ala Glu Glu Asn Ile Val Ser Arg Ser Glu Phe Pro		
755	760	765
Glu Ser Trp Leu Trp Asn Val Glu Asp Leu Lys Glu Pro Pro Lys Asn		
770	775	780
Gly Ile Ser Thr Lys Leu Met Asn Ile Phe Leu Lys Asp Ser Ile Thr		
785	790	795
Thr Trp Glu Ile Leu Ala Val Ser Met Ser Asp Lys Lys Gly Ile Cys		
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Val Ala Asp Pro Phe Glu Val Thr Val Met Gln Asp Phe Phe Ile Asp		

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835		840		845	
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850		855		860	
Glu Leu Leu His Asn Pro Ala Phe Cys Ser Leu Ala Thr Thr Lys Arg					
865		870		875	880
Arg His Gln Gln Thr Val Thr Ile Pro Pro Lys Ser Ser Leu Ser Val					
	885		890		895
Pro Tyr Val Ile Val Pro Leu Lys Thr Gly Leu Gln Glu Val Glu Val					
900		905		910	
Lys Ala Ala Val Tyr His His Phe Ile Ser Asp Gly Val Arg Lys Ser					
915		920		925	
Leu Lys Val Val Pro Glu Gly Ile Arg Met Asn Lys Thr Val Ala Val					
930		935		940	
Arg Thr Leu Asp Pro Glu Arg Leu Gly Arg Glu Gly Val Gln Lys Glu					
945		950		955	960
Asp Ile Pro Pro Ala Asp Leu Ser Asp Gln Val Pro Asp Thr Glu Ser					
	965		970		975
Glu Thr Arg Ile Leu Leu Gln Gly Thr Pro Val Ala Gln Met Thr Glu					
980		985		990	
Asp Ala Val Asp Ala Glu Arg Leu Lys His Leu Ile Val Thr Pro Ser					
995		1000		1005	
Gly Cys Gly Glu Gln Asn Met Ile Gly Met Thr Pro Thr Val Ile					
1010		1015		1020	
Ala Val His Tyr Leu Asp Glu Thr Glu Gln Trp Glu Lys Phe Gly					
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Leu Glu Lys Arg Gln Gly Ala Leu Glu Leu Ile Lys Lys Gly Tyr					
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Thr Gln Gln Leu Ala Phe Arg Gln Pro Ser Ser Ala Phe Ala Ala					
1055		1060		1065	
Phe Val Lys Arg Ala Pro Ser Thr Trp Leu Thr Ala Tyr Val Val					
1070		1075		1080	
Lys Val Phe Ser Leu Ala Val Asn Leu Ile Ala Ile Asp Ser Gln					
1085		1090		1095	
Val Leu Cys Gly Ala Val Lys Trp Leu Ile Leu Glu Lys Gln Lys					
1100		1105		1110	
Pro Asp Gly Val Phe Gln Glu Asp Ala Pro Val Ile His Gln Glu					
1115		1120		1125	

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Thr Ala Phe Val Leu Ile Ser Leu Gln Glu Ala Lys Asp Ile Cys		
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Glu Glu Gln Val Asn Ser Leu Pro Gly Ser Ile Thr Lys Ala Gly		
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Asp Phe Leu Glu Ala Asn Tyr Met Asn Leu Gln Arg Ser Tyr Thr		
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Val Ala Ile Ala Gly Tyr Ala Leu Ala Gln Met Gly Arg Leu Lys		
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Gly Pro Leu Leu Asn Lys Phe Leu Thr Thr Ala Lys Asp Lys Asn		
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Arg Trp Glu Asp Pro Gly Lys Gln Leu Tyr Asn Val Glu Ala Thr		
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Ser Tyr Ala Leu Leu Ala Leu Leu Gln Leu Lys Asp Phe Asp Phe		
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Val Pro Pro Val Val Arg Trp Leu Asn Glu Gln Arg Tyr Tyr Gly		
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Gly Gly Tyr Gly Ser Thr Gln Ala Thr Phe Met Val Phe Gln Ala		
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Leu Ala Gln Tyr Gln Lys Asp Ala Pro Asp His Gln Glu Leu Asn		
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Leu Asp Val Ser Leu Gln Leu Pro Ser Arg Ser Ser Lys Ile Thr		
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His Arg Ile His Trp Glu Ser Ala Ser Leu Leu Arg Ser Glu Glu		
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Thr Lys Glu Asn Glu Gly Phe Thr Val Thr Ala Glu Gly Lys Gly		
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Gln Gly Thr Leu Ser Val Val Thr Met Tyr His Ala Lys Ala Lys		
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Pro Ala Pro Glu Thr Glu Lys Arg Pro Gln Asp Ala Lys Asn Thr		
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Met Ile Leu Glu Ile Cys Thr Arg Tyr Arg Gly Asp Gln Asp Ala		
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Thr Met Ser Ile Leu Asp Ile Ser Met Met Thr Gly Phe Ala Pro		
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Asp Thr Asp Asp Leu Lys Gln Leu Ala Asn Gly Val Asp Arg Tyr		

1415	1420	1425
Ile Ser Lys Tyr Glu Leu Asp Lys Ala Phe Ser Asp Arg Asn Thr		
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Leu Ile Ile Tyr Leu Asp Lys Val Ser His Ser Glu Asp Asp Cys		
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Leu Ala Phe Lys Val His Gln Tyr Phe Asn Val Glu Leu Ile Gln		
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Pro Gly Ala Val Lys Val Tyr Ala Tyr Tyr Asn Leu Glu Glu Ser		
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Lys Leu Cys Arg Asp Glu Leu Cys Arg Cys Ala Glu Glu Asn Cys		
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Phe Ile Gln Lys Ser Asp Asp Lys Val Thr Leu Glu Glu Arg Leu		
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Leu Val Lys Val Gln Leu Ser Asn Asp Phe Asp Glu Tyr Ile Met		
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Ser Asp Phe Trp Gly Glu Lys Pro Asn Leu Ser Tyr Ile Ile Gly		
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Lys Asp Thr Trp Val Glu His Trp Pro Glu Glu Asp Glu Cys Gln		
1625	1630	1635
Asp Glu Glu Asn Gln Lys Gln Cys Gln Asp Leu Gly Ala Phe Thr		
1640	1645	1650
Glu Ser Met Val Val Phe Gly Cys Pro Asn		
1655	1660	
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<211> 645		
<212> PRT		
<213> 人(智人)C3 β 链(UniProt: P01024 残基23-667)		
<400> 2		
Ser Pro Met Tyr Ser Ile Ile Thr Pro Asn Ile Leu Arg Leu Glu Ser		

1	5	10	15
Glu Glu Thr Met Val Leu Glu Ala His Asp Ala Gln Gly Asp Val Pro			
20	25	30	
Val Thr Val Thr Val His Asp Phe Pro Gly Lys Lys Leu Val Leu Ser			
35	40	45	
Ser Glu Lys Thr Val Leu Thr Pro Ala Thr Asn His Met Gly Asn Val			
50	55	60	
Thr Phe Thr Ile Pro Ala Asn Arg Glu Phe Lys Ser Glu Lys Gly Arg			
65	70	75	80
Asn Lys Phe Val Thr Val Gln Ala Thr Phe Gly Thr Gln Val Val Glu			
85	90	95	
Lys Val Val Leu Val Ser Leu Gln Ser Gly Tyr Leu Phe Ile Gln Thr			
100	105	110	
Asp Lys Thr Ile Tyr Thr Pro Gly Ser Thr Val Leu Tyr Arg Ile Phe			
115	120	125	
Thr Val Asn His Lys Leu Leu Pro Val Gly Arg Thr Val Met Val Asn			
130	135	140	
Ile Glu Asn Pro Glu Gly Ile Pro Val Lys Gln Asp Ser Leu Ser Ser			
145	150	155	160
Gln Asn Gln Leu Gly Val Leu Pro Leu Ser Trp Asp Ile Pro Glu Leu			
165	170	175	
Val Asn Met Gly Gln Trp Lys Ile Arg Ala Tyr Tyr Glu Asn Ser Pro			
180	185	190	
Gln Gln Val Phe Ser Thr Glu Phe Glu Val Lys Glu Tyr Val Leu Pro			
195	200	205	
Ser Phe Glu Val Ile Val Glu Pro Thr Glu Lys Phe Tyr Tyr Ile Tyr			
210	215	220	
Asn Glu Lys Gly Leu Glu Val Thr Ile Thr Ala Arg Phe Leu Tyr Gly			
225	230	235	240
Lys Lys Val Glu Gly Thr Ala Phe Val Ile Phe Gly Ile Gln Asp Gly			
245	250	255	
Glu Gln Arg Ile Ser Leu Pro Glu Ser Leu Lys Arg Ile Pro Ile Glu			
260	265	270	
Asp Gly Ser Gly Glu Val Val Leu Ser Arg Lys Val Leu Leu Asp Gly			
275	280	285	
Val Gln Asn Pro Arg Ala Glu Asp Leu Val Gly Lys Ser Leu Tyr Val			
290	295	300	
Ser Ala Thr Val Ile Leu His Ser Gly Ser Asp Met Val Gln Ala Glu			
305	310	315	320

Arg Ser Gly Ile Pro Ile Val Thr Ser Pro Tyr Gln Ile His Phe Thr		
325	330	335
Lys Thr Pro Lys Tyr Phe Lys Pro Gly Met Pro Phe Asp Leu Met Val		
340	345	350
Phe Val Thr Asn Pro Asp Gly Ser Pro Ala Tyr Arg Val Pro Val Ala		
355	360	365
Val Gln Gly Glu Asp Thr Val Gln Ser Leu Thr Gln Gly Asp Gly Val		
370	375	380
Ala Lys Leu Ser Ile Asn Thr His Pro Ser Gln Lys Pro Leu Ser Ile		
385	390	395
Thr Val Arg Thr Lys Lys Gln Glu Leu Ser Glu Ala Glu Gln Ala Thr		
405	410	415
Arg Thr Met Gln Ala Leu Pro Tyr Ser Thr Val Gly Asn Ser Asn Asn		
420	425	430
Tyr Leu His Leu Ser Val Leu Arg Thr Glu Leu Arg Pro Gly Glu Thr		
435	440	445
Leu Asn Val Asn Phe Leu Leu Arg Met Asp Arg Ala His Glu Ala Lys		
450	455	460
Ile Arg Tyr Tyr Thr Tyr Leu Ile Met Asn Lys Gly Arg Leu Leu Lys		
465	470	475
Ala Gly Arg Gln Val Arg Glu Pro Gly Gln Asp Leu Val Val Leu Pro		
485	490	495
Leu Ser Ile Thr Thr Asp Phe Ile Pro Ser Phe Arg Leu Val Ala Tyr		
500	505	510
Tyr Thr Leu Ile Gly Ala Ser Gly Gln Arg Glu Val Val Ala Asp Ser		
515	520	525
Val Trp Val Asp Val Lys Asp Ser Cys Val Gly Ser Leu Val Val Lys		
530	535	540
Ser Gly Gln Ser Glu Asp Arg Gln Pro Val Pro Gly Gln Gln Met Thr		
545	550	555
Leu Lys Ile Glu Gly Asp His Gly Ala Arg Val Val Leu Val Ala Val		
565	570	575
Asp Lys Gly Val Phe Val Leu Asn Lys Lys Asn Lys Leu Thr Gln Ser		
580	585	590
Lys Ile Trp Asp Val Val Glu Lys Ala Asp Ile Gly Cys Thr Pro Gly		
595	600	605
Ser Gly Lys Asp Tyr Ala Gly Val Phe Ser Asp Ala Gly Leu Thr Phe		
610	615	620
Thr Ser Ser Ser Gly Gln Gln Thr Ala Gln Arg Ala Glu Leu Gln Cys		

625	630	635	640
Pro Gln Pro Ala Ala			
	645		
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<213> 人(智人)C3 α' 链(UniProt: P01024 残基749-1663)			
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Ser Asn Leu Asp Glu Asp Ile Ile Ala Glu Glu Asn Ile Val Ser Arg			
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Ser Glu Phe Pro Glu Ser Trp Leu Trp Asn Val Glu Asp Leu Lys Glu			
	20	25	30
Pro Pro Lys Asn Gly Ile Ser Thr Lys Leu Met Asn Ile Phe Leu Lys			
	35	40	45
Asp Ser Ile Thr Thr Trp Glu Ile Leu Ala Val Ser Met Ser Asp Lys			
	50	55	60
Lys Gly Ile Cys Val Ala Asp Pro Phe Glu Val Thr Val Met Gln Asp			
65	70	75	80
Phe Phe Ile Asp Leu Arg Leu Pro Tyr Ser Val Val Arg Asn Glu Gln			
	85	90	95
Val Glu Ile Arg Ala Val Leu Tyr Asn Tyr Arg Gln Asn Gln Glu Leu			
	100	105	110
Lys Val Arg Val Glu Leu Leu His Asn Pro Ala Phe Cys Ser Leu Ala			
	115	120	125
Thr Thr Lys Arg Arg His Gln Gln Thr Val Thr Ile Pro Pro Lys Ser			
	130	135	140
Ser Leu Ser Val Pro Tyr Val Ile Val Pro Leu Lys Thr Gly Leu Gln			
145	150	155	160
Glu Val Glu Val Lys Ala Ala Val Tyr His His Phe Ile Ser Asp Gly			
	165	170	175
Val Arg Lys Ser Leu Lys Val Val Pro Glu Gly Ile Arg Met Asn Lys			
	180	185	190
Thr Val Ala Val Arg Thr Leu Asp Pro Glu Arg Leu Gly Arg Glu Gly			
	195	200	205
Val Gln Lys Glu Asp Ile Pro Pro Ala Asp Leu Ser Asp Gln Val Pro			
	210	215	220
Asp Thr Glu Ser Glu Thr Arg Ile Leu Leu Gln Gly Thr Pro Val Ala			
225	230	235	240
Gln Met Thr Glu Asp Ala Val Asp Ala Glu Arg Leu Lys His Leu Ile			

				245					250					255			
Val	Thr	Pro	Ser	Gly	Cys	Gly	Glu	Gln	Asn	Met	Ile	Gly	Met	Thr	Pro		
				260					265					270			
Thr	Val	Ile	Ala	Val	His	Tyr	Leu	Asp	Glu	Thr	Glu	Gln	Trp	Glu	Lys		
				275					280					285			
Phe	Gly	Leu	Glu	Lys	Arg	Gln	Gly	Ala	Leu	Glu	Leu	Ile	Lys	Lys	Gly		
				290					295					300			
Tyr	Thr	Gln	Gln	Leu	Ala	Phe	Arg	Gln	Pro	Ser	Ser	Ala	Phe	Ala	Ala		
305																	
				310										315			
Phe	Val	Lys	Arg	Ala	Pro	Ser	Thr	Trp	Leu	Thr	Ala	Tyr	Val	Val	Lys		
				325													
									330					335			
Val	Phe	Ser	Leu	Ala	Val	Asn	Leu	Ile	Ala	Ile	Asp	Ser	Gln	Val	Leu		
				340										350			
Cys	Gly	Ala	Val	Lys	Trp	Leu	Ile	Leu	Glu	Lys	Gln	Lys	Pro	Asp	Gly		
				355													
									360					365			
Val	Phe	Gln	Glu	Asp	Ala	Pro	Val	Ile	His	Gln	Glu	Met	Ile	Gly	Gly		
				370													
									375					380			
Leu	Arg	Asn	Asn	Asn	Glu	Lys	Asp	Met	Ala	Leu	Thr	Ala	Phe	Val	Leu		
385																	
				390													
									395					400			
Ile	Ser	Leu	Gln	Glu	Ala	Lys	Asp	Ile	Cys	Glu	Glu	Gln	Val	Asn	Ser		
				405													
									410					415			
Leu	Pro	Gly	Ser	Ile	Thr	Lys	Ala	Gly	Asp	Phe	Leu	Glu	Ala	Asn	Tyr		
				420													
									425					430			
Met	Asn	Leu	Gln	Arg	Ser	Tyr	Thr	Val	Ala	Ile	Ala	Gly	Tyr	Ala	Leu		
				435													
									440					445			
Ala	Gln	Met	Gly	Arg	Leu	Lys	Gly	Pro	Leu	Leu	Asn	Lys	Phe	Leu	Thr		
				450													
									455					460			
Thr	Ala	Lys	Asp	Lys	Asn	Arg	Trp	Glu	Asp	Pro	Gly	Lys	Gln	Leu	Tyr		
465																	
				470													
									475					480			
Asn	Val	Glu	Ala	Thr	Ser	Tyr	Ala	Leu	Leu	Ala	Leu	Leu	Gln	Leu	Lys		
				485													
									490					495			
Asp	Phe	Asp	Phe	Val	Pro	Pro	Val	Val	Arg	Trp	Leu	Asn	Glu	Gln	Arg		
				500													
									505					510			
Tyr	Tyr	Gly	Gly	Gly	Tyr	Gly	Ser	Thr	Gln	Ala	Thr	Phe	Met	Val	Phe		
				515													
									520					525			
Gln	Ala	Leu	Ala	Gln	Tyr	Gln	Lys	Asp	Ala	Pro	Asp	His	Gln	Glu	Leu		
				530													
									535					540			
Asn	Leu	Asp	Val	Ser	Leu	Gln	Leu	Pro	Ser	Arg	Ser	Ser	Lys	Ile	Thr		
545																	
				550													
									555								
														560			

His Arg Ile His Trp Glu Ser Ala Ser Leu Leu Arg Ser Glu Glu Thr		
	565	570 575
Lys Glu Asn Glu Gly Phe Thr Val Thr Ala Glu Gly Lys Gly Gln Gly		
	580	585 590
Thr Leu Ser Val Val Thr Met Tyr His Ala Lys Ala Lys Asp Gln Leu		
	595	600 605
Thr Cys Asn Lys Phe Asp Leu Lys Val Thr Ile Lys Pro Ala Pro Glu		
	610	615 620
Thr Glu Lys Arg Pro Gln Asp Ala Lys Asn Thr Met Ile Leu Glu Ile		
625	630	635 640
Cys Thr Arg Tyr Arg Gly Asp Gln Asp Ala Thr Met Ser Ile Leu Asp		
	645	650 655
Ile Ser Met Met Thr Gly Phe Ala Pro Asp Thr Asp Asp Leu Lys Gln		
	660	665 670
Leu Ala Asn Gly Val Asp Arg Tyr Ile Ser Lys Tyr Glu Leu Asp Lys		
	675	680 685
Ala Phe Ser Asp Arg Asn Thr Leu Ile Ile Tyr Leu Asp Lys Val Ser		
	690	695 700
His Ser Glu Asp Asp Cys Leu Ala Phe Lys Val His Gln Tyr Phe Asn		
705	710	715 720
Val Glu Leu Ile Gln Pro Gly Ala Val Lys Val Tyr Ala Tyr Tyr Asn		
	725	730 735
Leu Glu Glu Ser Cys Thr Arg Phe Tyr His Pro Glu Lys Glu Asp Gly		
	740	745 750
Lys Leu Asn Lys Leu Cys Arg Asp Glu Leu Cys Arg Cys Ala Glu Glu		
	755	760 765
Asn Cys Phe Ile Gln Lys Ser Asp Asp Lys Val Thr Leu Glu Glu Arg		
	770	775 780
Leu Asp Lys Ala Cys Glu Pro Gly Val Asp Tyr Val Tyr Lys Thr Arg		
785	790	795 800
Leu Val Lys Val Gln Leu Ser Asn Asp Phe Asp Glu Tyr Ile Met Ala		
	805	810 815
Ile Glu Gln Thr Ile Lys Ser Gly Ser Asp Glu Val Gln Val Gly Gln		
	820	825 830
Gln Arg Thr Phe Ile Ser Pro Ile Lys Cys Arg Glu Ala Leu Lys Leu		
	835	840 845
Glu Glu Lys Lys His Tyr Leu Met Trp Gly Leu Ser Ser Asp Phe Trp		
	850	855 860
Gly Glu Lys Pro Asn Leu Ser Tyr Ile Ile Gly Lys Asp Thr Trp Val		

865	870	875	880
Glu His Trp Pro Glu Glu Asp Glu Cys Gln Asp Glu Glu Asn Gln Lys			
	885	890	895
Gln Cys Gln Asp Leu Gly Ala Phe Thr Glu Ser Met Val Val Phe Gly			
	900	905	910
Cys Pro Asn			
915			
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<213> 人(智人)C3a (UniProt: P01024 残基672-748)			
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Lys Glu Leu Arg Lys Cys Cys Glu Asp Gly Met Arg Glu Asn Pro Met			
	20	25	30
Arg Phe Ser Cys Gln Arg Arg Thr Arg Phe Ile Ser Leu Gly Glu Ala			
	35	40	45
Cys Lys Lys Val Phe Leu Asp Cys Cys Asn Tyr Ile Thr Glu Leu Arg			
	50	55	60
Arg Gln His Ala Arg Ala Ser His Leu Gly Leu Ala Arg			
65	70	75	
<210> 5			
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<212> PRT			
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Ser Asn Leu Asp Glu Asp Ile Ile Ala Glu Glu Asn Ile Val Ser Arg			
1	5	10	15
Ser Glu Phe Pro Glu Ser Trp Leu Trp Asn Val Glu Asp Leu Lys Glu			
	20	25	30
Pro Pro Lys Asn Gly Ile Ser Thr Lys Leu Met Asn Ile Phe Leu Lys			
	35	40	45
Asp Ser Ile Thr Thr Trp Glu Ile Leu Ala Val Ser Met Ser Asp Lys			
	50	55	60
Lys Gly Ile Cys Val Ala Asp Pro Phe Glu Val Thr Val Met Gln Asp			
65	70	75	80
Phe Phe Ile Asp Leu Arg Leu Pro Tyr Ser Val Val Arg Asn Glu Gln			
	85	90	95

Val	Glu	Ile	Arg	Ala	Val	Leu	Tyr	Asn	Tyr	Arg	Gln	Asn	Gln	Glu	Leu	
100					105					110						
Lys	Val	Arg	Val	Glu	Leu	Leu	His	Asn	Pro	Ala	Phe	Cys	Ser	Leu	Ala	
115					120					125						
Thr	Thr	Lys	Arg	Arg	His	Gln	Gln	Thr	Val	Thr	Ile	Pro	Pro	Lys	Ser	
130					135					140						
Ser	Leu	Ser	Val	Pro	Tyr	Val	Ile	Val	Pro	Leu	Lys	Thr	Gly	Leu	Gln	
145					150					155					160	
Glu	Val	Glu	Val	Lys	Ala	Ala	Val	Tyr	His	His	Phe	Ile	Ser	Asp	Gly	
165					170					175						
Val	Arg	Lys	Ser	Leu	Lys	Val	Val	Pro	Glu	Gly	Ile	Arg	Met	Asn	Lys	
180					185					190						
Thr	Val	Ala	Val	Arg	Thr	Leu	Asp	Pro	Glu	Arg	Leu	Gly	Arg	Glu	Gly	
195					200					205						
Val	Gln	Lys	Glu	Asp	Ile	Pro	Pro	Ala	Asp	Leu	Ser	Asp	Gln	Val	Pro	
210					215					220						
Asp	Thr	Glu	Ser	Glu	Thr	Arg	Ile	Leu	Leu	Gln	Gly	Thr	Pro	Val	Ala	
225					230					235					240	
Gln	Met	Thr	Glu	Asp	Ala	Val	Asp	Ala	Glu	Arg	Leu	Lys	His	Leu	Ile	
245					250					255						
Val	Thr	Pro	Ser	Gly	Cys	Gly	Glu	Gln	Asn	Met	Ile	Gly	Met	Thr	Pro	
260					265					270						
Thr	Val	Ile	Ala	Val	His	Tyr	Leu	Asp	Glu	Thr	Glu	Gln	Trp	Glu	Lys	
275					280					285						
Phe	Gly	Leu	Glu	Lys	Arg	Gln	Gly	Ala	Leu	Glu	Leu	Ile	Lys	Lys	Gly	
290					295					300						
Tyr	Thr	Gln	Gln	Leu	Ala	Phe	Arg	Gln	Pro	Ser	Ser	Ala	Phe	Ala	Ala	
305					310					315					320	
Phe	Val	Lys	Arg	Ala	Pro	Ser	Thr	Trp	Leu	Thr	Ala	Tyr	Val	Val	Lys	
325					330					335						
Val	Phe	Ser	Leu	Ala	Val	Asn	Leu	Ile	Ala	Ile	Asp	Ser	Gln	Val	Leu	
340					345					350						
Cys	Gly	Ala	Val	Lys	Trp	Leu	Ile	Leu	Glu	Lys	Gln	Lys	Pro	Asp	Gly	
355					360					365						
Val	Phe	Gln	Glu	Asp	Ala	Pro	Val	Ile	His	Gln	Glu	Met	Ile	Gly	Gly	
370					375					380						
Leu	Arg	Asn	Asn	Asn	Glu	Lys	Asp	Met	Ala	Leu	Thr	Ala	Phe	Val	Leu	
385					390					395					400	
Ile	Ser	Leu	Gln	Glu	Ala	Lys	Asp	Ile	Cys	Glu	Glu	Gln	Val	Asn	Ser	

405	410	415
Leu Pro Gly Ser Ile Thr Lys Ala Gly Asp Phe Leu Glu Ala Asn Tyr		
420	425	430
Met Asn Leu Gln Arg Ser Tyr Thr Val Ala Ile Ala Gly Tyr Ala Leu		
435	440	445
Ala Gln Met Gly Arg Leu Lys Gly Pro Leu Leu Asn Lys Phe Leu Thr		
450	455	460
Thr Ala Lys Asp Lys Asn Arg Trp Glu Asp Pro Gly Lys Gln Leu Tyr		
465	470	475
Asn Val Glu Ala Thr Ser Tyr Ala Leu Leu Ala Leu Leu Gln Leu Lys		
485	490	495
Asp Phe Asp Phe Val Pro Pro Val Val Arg Trp Leu Asn Glu Gln Arg		
500	505	510
Tyr Tyr Gly Gly Gly Tyr Gly Ser Thr Gln Ala Thr Phe Met Val Phe		
515	520	525
Gln Ala Leu Ala Gln Tyr Gln Lys Asp Ala Pro Asp His Gln Glu Leu		
530	535	540
Asn Leu Asp Val Ser Leu Gln Leu Pro Ser Arg		
545	550	555
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<213> 人(智人)C3 α' 链片段2 (UniProt: P01024 残基1321-1663)		
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1	5	10
Lys Gly Gln Gly Thr Leu Ser Val Val Thr Met Tyr His Ala Lys Ala		
20	25	30
Lys Asp Gln Leu Thr Cys Asn Lys Phe Asp Leu Lys Val Thr Ile Lys		
35	40	45
Pro Ala Pro Glu Thr Glu Lys Arg Pro Gln Asp Ala Lys Asn Thr Met		
50	55	60
Ile Leu Glu Ile Cys Thr Arg Tyr Arg Gly Asp Gln Asp Ala Thr Met		
65	70	75
Ser Ile Leu Asp Ile Ser Met Met Thr Gly Phe Ala Pro Asp Thr Asp		
85	90	95
Asp Leu Lys Gln Leu Ala Asn Gly Val Asp Arg Tyr Ile Ser Lys Tyr		
100	105	110
Glu Leu Asp Lys Ala Phe Ser Asp Arg Asn Thr Leu Ile Ile Tyr Leu		

<211> 583

<212> PRT

<213> 人(智人)补体因子I (UniProt: P05156)

<400> 8

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

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Asp	Glu	Val	Gly	Cys	Ala	Gly	Phe	Ala	Ser	Val	Thr	Gln	Glu	Glu	Thr	290	295	300
Glu	Ile	Leu	Thr	Ala	Asp	Met	Asp	Ala	Glu	Arg	Arg	Arg	Ile	Lys	Ser	305	310	315
Leu	Leu	Pro	Lys	Leu	Ser	Cys	Gly	Val	Lys	Asn	Arg	Met	His	Ile	Arg	325	330	335
Arg	Lys	Arg	Ile	Val	Gly	Gly	Lys	Arg	Ala	Gln	Leu	Gly	Asp	Leu	Pro	340	345	350
Trp	Gln	Val	Ala	Ile	Lys	Asp	Ala	Ser	Gly	Ile	Thr	Cys	Gly	Gly	Ile	355	360	365
Tyr	Ile	Gly	Gly	Cys	Trp	Ile	Leu	Thr	Ala	Ala	His	Cys	Leu	Arg	Ala	370	375	380
Ser	Lys	Thr	His	Arg	Tyr	Gln	Ile	Trp	Thr	Thr	Val	Val	Asp	Trp	Ile	385	390	395
His	Pro	Asp	Leu	Lys	Arg	Ile	Val	Ile	Glu	Tyr	Val	Asp	Arg	Ile	Ile	405	410	415
Phe	His	Glu	Asn	Tyr	Asn	Ala	Gly	Thr	Tyr	Gln	Asn	Asp	Ile	Ala	Leu	420	425	430
Ile	Glu	Met	Lys	Lys	Asp	Gly	Asn	Lys	Lys	Asp	Cys	Glu	Leu	Pro	Arg	435	440	445
Ser	Ile	Pro	Ala	Cys	Val	Pro	Trp	Ser	Pro	Tyr	Leu	Phe	Gln	Pro	Asn	450	455	460
Asp	Thr	Cys	Ile	Val	Ser	Gly	Trp	Gly	Arg	Glu	Lys	Asp	Asn	Glu	Arg	465	470	475
Val	Phe	Ser	Leu	Gln	Trp	Gly	Glu	Val	Lys	Leu	Ile	Ser	Asn	Cys	Ser	485	490	495
Lys	Phe	Tyr	Gly	Asn	Arg	Phe	Tyr	Glu	Lys	Glu	Met	Glu	Cys	Ala	Gly	500	505	510
Thr	Tyr	Asp	Gly	Ser	Ile	Asp	Ala	Cys	Lys	Gly	Asp	Ser	Gly	Gly	Pro	515	520	525
Leu	Val	Cys	Met	Asp	Ala	Asn	Asn	Val	Thr	Tyr	Val	Trp	Gly	Val	Val	530	535	540
Ser	Trp	Gly	Glu	Asn	Cys	Gly	Lys	Pro	Glu	Phe	Pro	Gly	Val	Tyr	Thr	545	550	555
Lys	Val	Ala	Asn	Tyr	Phe	Asp	Trp	Ile	Ser	Tyr	His	Val	Gly	Arg	Pro	565	570	575
Phe	Ile	Ser	Gln	Tyr	Asn	Val										580		

<210> 9

<211> 235

<212> PRT

<213> 人(智人)补体因子I蛋白水解结构域(UniProt: P05156 残基340-574)

<400> 9

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

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<210> 10

<211> 1231

<212> PRT

<213> 人(智人)补体因子H (UniProt: P08603)

<400> 10

Met	Arg	Leu	Leu	Ala	Lys	Ile	Ile	Cys	Leu	Met	Leu	Trp	Ala	Ile	Cys
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Val	Ala	Glu	Asp	Cys	Asn	Glu	Leu	Pro	Pro	Arg	Arg	Asn	Thr	Glu	Ile
				20					25					30	
Leu	Thr	Gly	Ser	Trp	Ser	Asp	Gln	Thr	Tyr	Pro	Glu	Gly	Thr	Gln	Ala
				35					40					45	
Ile	Tyr	Lys	Cys	Arg	Pro	Gly	Tyr	Arg	Ser	Leu	Gly	Asn	Val	Ile	Met
Val	Cys	Arg	Lys	Gly	Glu	Trp	Val	Ala	Leu	Asn	Pro	Leu	Arg	Lys	Cys
65															
Gln	Lys	Arg	Pro	Cys	Gly	His	Pro	Gly	Asp	Thr	Pro	Phe	Gly	Thr	Phe
Thr	Leu	Thr	Gly	Gly	Asn	Val	Phe	Glu	Tyr	Gly	Val	Lys	Ala	Val	Tyr
Thr	Cys	Asn	Glu	Gly	Tyr	Gln	Leu	Leu	Gly	Glu	Ile	Asn	Tyr	Arg	Glu
Cys	Asp	Thr	Asp	Gly	Trp	Thr	Asn	Asp	Ile	Pro	Ile	Cys	Glu	Val	Val
Lys	Cys	Leu	Pro	Val	Thr	Ala	Pro	Glu	Asn	Gly	Lys	Ile	Val	Ser	Ser
145															
Ala	Met	Glu	Pro	Asp	Arg	Glu	Tyr	His	Phe	Gly	Gln	Ala	Val	Arg	Phe
Val	Cys	Asn	Ser	Gly	Tyr	Lys	Ile	Glu	Gly	Asp	Glu	Glu	Met	His	Cys
Ser	Asp	Asp	Gly	Phe	Trp	Ser	Lys	Glu	Lys	Pro	Lys	Cys	Val	Glu	Ile
Ser	Cys	Lys	Ser	Pro	Asp	Val	Ile	Asn	Gly	Ser	Pro	Ile	Ser	Gln	Lys
Ile	Ile	Tyr	Lys	Glu	Asn	Glu	Arg	Phe	Gln	Tyr	Lys	Cys	Asn	Met	Gly
225															
Tyr	Glu	Tyr	Ser	Glu	Arg	Gly	Asp	Ala	Val	Cys	Thr	Glu	Ser	Gly	Trp
Arg	Pro	Leu	Pro	Ser	Cys	Glu	Glu	Lys	Ser	Cys	Asp	Asn	Pro	Tyr	Ile
Pro	Asn	Gly	Asp	Tyr	Ser	Pro	Leu	Arg	Ile	Lys	His	Arg	Thr	Gly	Asp
Glu	Ile	Thr	Tyr	Gln	Cys	Arg	Asn	Gly	Phe	Tyr	Pro	Ala	Thr	Arg	Gly
Asn	Thr	Ala	Lys	Cys	Thr	Ser	Thr	Gly	Trp	Ile	Pro	Ala	Pro	Arg	Cys

305	310	315	320
Thr Leu Lys Pro Cys Asp Tyr Pro Asp Ile Lys His Gly Gly Leu Tyr			
	325	330	335
His Glu Asn Met Arg Arg Pro Tyr Phe Pro Val Ala Val Gly Lys Tyr			
	340	345	350
Tyr Ser Tyr Tyr Cys Asp Glu His Phe Glu Thr Pro Ser Gly Ser Tyr			
	355	360	365
Trp Asp His Ile His Cys Thr Gln Asp Gly Trp Ser Pro Ala Val Pro			
	370	375	380
Cys Leu Arg Lys Cys Tyr Phe Pro Tyr Leu Glu Asn Gly Tyr Asn Gln			
385	390	395	400
Asn Tyr Gly Arg Lys Phe Val Gln Gly Lys Ser Ile Asp Val Ala Cys			
	405	410	415
His Pro Gly Tyr Ala Leu Pro Lys Ala Gln Thr Thr Val Thr Cys Met			
	420	425	430
Glu Asn Gly Trp Ser Pro Thr Pro Arg Cys Ile Arg Val Lys Thr Cys			
	435	440	445
Ser Lys Ser Ser Ile Asp Ile Glu Asn Gly Phe Ile Ser Glu Ser Gln			
	450	455	460
Tyr Thr Tyr Ala Leu Lys Glu Lys Ala Lys Tyr Gln Cys Lys Leu Gly			
465	470	475	480
Tyr Val Thr Ala Asp Gly Glu Thr Ser Gly Ser Ile Thr Cys Gly Lys			
	485	490	495
Asp Gly Trp Ser Ala Gln Pro Thr Cys Ile Lys Ser Cys Asp Ile Pro			
	500	505	510
Val Phe Met Asn Ala Arg Thr Lys Asn Asp Phe Thr Trp Phe Lys Leu			
	515	520	525
Asn Asp Thr Leu Asp Tyr Glu Cys His Asp Gly Tyr Glu Ser Asn Thr			
	530	535	540
Gly Ser Thr Thr Gly Ser Ile Val Cys Gly Tyr Asn Gly Trp Ser Asp			
545	550	555	560
Leu Pro Ile Cys Tyr Glu Arg Glu Cys Glu Leu Pro Lys Ile Asp Val			
	565	570	575
His Leu Val Pro Asp Arg Lys Lys Asp Gln Tyr Lys Val Gly Glu Val			
	580	585	590
Leu Lys Phe Ser Cys Lys Pro Gly Phe Thr Ile Val Gly Pro Asn Ser			
	595	600	605
Val Gln Cys Tyr His Phe Gly Leu Ser Pro Asp Leu Pro Ile Cys Lys			
610	615	620	

Glu	Gln	Val	Gln	Ser	Cys	Gly	Pro	Pro	Pro	Glu	Leu	Leu	Asn	Gly	Asn	625	630	635	640
Val	Lys	Glu	Lys	Thr	Lys	Glu	Glu	Tyr	Gly	His	Ser	Glu	Val	Val	Glu	645	650	655	
Tyr	Tyr	Cys	Asn	Pro	Arg	Phe	Leu	Met	Lys	Gly	Pro	Asn	Lys	Ile	Gln	660	665	670	
Cys	Val	Asp	Gly	Glu	Trp	Thr	Thr	Leu	Pro	Val	Cys	Ile	Val	Glu	Glu	675	680	685	
Ser	Thr	Cys	Gly	Asp	Ile	Pro	Glu	Leu	Glu	His	Gly	Trp	Ala	Gln	Leu	690	695	700	
Ser	Ser	Pro	Pro	Tyr	Tyr	Tyr	Gly	Asp	Ser	Val	Glu	Phe	Asn	Cys	Ser	705	710	715	720
Glu	Ser	Phe	Thr	Met	Ile	Gly	His	Arg	Ser	Ile	Thr	Cys	Ile	His	Gly	725	730	735	
Val	Trp	Thr	Gln	Leu	Pro	Gln	Cys	Val	Ala	Ile	Asp	Lys	Leu	Lys	Lys	740	745	750	
Cys	Lys	Ser	Ser	Asn	Leu	Ile	Ile	Leu	Glu	Glu	His	Leu	Lys	Asn	Lys	755	760	765	
Lys	Glu	Phe	Asp	His	Asn	Ser	Asn	Ile	Arg	Tyr	Arg	Cys	Arg	Gly	Lys	770	775	780	
Glu	Gly	Trp	Ile	His	Thr	Val	Cys	Ile	Asn	Gly	Arg	Trp	Asp	Pro	Glu	785	790	795	800
Val	Asn	Cys	Ser	Met	Ala	Gln	Ile	Gln	Leu	Cys	Pro	Pro	Pro	Pro	Gln	805	810	815	
Ile	Pro	Asn	Ser	His	Asn	Met	Thr	Thr	Thr	Leu	Asn	Tyr	Arg	Asp	Gly	820	825	830	
Glu	Lys	Val	Ser	Val	Leu	Cys	Gln	Glu	Asn	Tyr	Leu	Ile	Gln	Glu	Gly	835	840	845	
Glu	Glu	Ile	Thr	Cys	Lys	Asp	Gly	Arg	Trp	Gln	Ser	Ile	Pro	Leu	Cys	850	855	860	
Val	Glu	Lys	Ile	Pro	Cys	Ser	Gln	Pro	Pro	Gln	Ile	Glu	His	Gly	Thr	865	870	875	880
Ile	Asn	Ser	Ser	Arg	Ser	Ser	Gln	Glu	Ser	Tyr	Ala	His	Gly	Thr	Lys	885	890	895	
Leu	Ser	Tyr	Thr	Cys	Glu	Gly	Gly	Phe	Arg	Ile	Ser	Glu	Glu	Asn	Glu	900	905	910	
Thr	Thr	Cys	Tyr	Met	Gly	Lys	Trp	Ser	Ser	Pro	Pro	Gln	Cys	Glu	Gly	915	920	925	
Leu	Pro	Cys	Lys	Ser	Pro	Pro	Glu	Ile	Ser	His	Gly	Val	Val	Ala	His				

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Met Ser Asp Ser Tyr Gln Tyr Gly Glu Glu Val Thr Tyr Lys Cys Phe		
945	950	955
Glu Gly Phe Gly Ile Asp Gly Pro Ala Ile Ala Lys Cys Leu Gly Glu		
965	970	975
Lys Trp Ser His Pro Pro Ser Cys Ile Lys Thr Asp Cys Leu Ser Leu		
980	985	990
Pro Ser Phe Glu Asn Ala Ile Pro Met Gly Glu Lys Lys Asp Val Tyr		
995	1000	1005
Lys Ala Gly Glu Gln Val Thr Tyr Thr Cys Ala Thr Tyr Tyr Lys		
1010	1015	1020
Met Asp Gly Ala Ser Asn Val Thr Cys Ile Asn Ser Arg Trp Thr		
1025	1030	1035
Gly Arg Pro Thr Cys Arg Asp Thr Ser Cys Val Asn Pro Pro Thr		
1040	1045	1050
Val Gln Asn Ala Tyr Ile Val Ser Arg Gln Met Ser Lys Tyr Pro		
1055	1060	1065
Ser Gly Glu Arg Val Arg Tyr Gln Cys Arg Ser Pro Tyr Glu Met		
1070	1075	1080
Phe Gly Asp Glu Glu Val Met Cys Leu Asn Gly Asn Trp Thr Glu		
1085	1090	1095
Pro Pro Gln Cys Lys Asp Ser Thr Gly Lys Cys Gly Pro Pro Pro		
1100	1105	1110
Pro Ile Asp Asn Gly Asp Ile Thr Ser Phe Pro Leu Ser Val Tyr		
1115	1120	1125
Ala Pro Ala Ser Ser Val Glu Tyr Gln Cys Gln Asn Leu Tyr Gln		
1130	1135	1140
Leu Glu Gly Asn Lys Arg Ile Thr Cys Arg Asn Gly Gln Trp Ser		
1145	1150	1155
Glu Pro Pro Lys Cys Leu His Pro Cys Val Ile Ser Arg Glu Ile		
1160	1165	1170
Met Glu Asn Tyr Asn Ile Ala Leu Arg Trp Thr Ala Lys Gln Lys		
1175	1180	1185
Leu Tyr Ser Arg Thr Gly Glu Ser Val Glu Phe Val Cys Lys Arg		
1190	1195	1200
Gly Tyr Arg Leu Ser Ser Arg Ser His Thr Leu Arg Thr Thr Cys		
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Trp Asp Gly Lys Leu Glu Tyr Pro Thr Cys Ala Lys Arg		
1220	1225	1230

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<212> PRT

<213> 人(智人)补体因子H辅助因子区(UniProt: P08603 残基19-264)

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Lys Cys Arg Pro Gly Tyr Arg Ser Leu Gly Asn Val Ile Met Val Cys
          35          40          45
Arg Lys Gly Glu Trp Val Ala Leu Asn Pro Leu Arg Lys Cys Gln Lys
          50          55          60
Arg Pro Cys Gly His Pro Gly Asp Thr Pro Phe Gly Thr Phe Thr Leu
65          70          75          80
Thr Gly Gly Asn Val Phe Glu Tyr Gly Val Lys Ala Val Tyr Thr Cys
          85          90          95
Asn Glu Gly Tyr Gln Leu Leu Gly Glu Ile Asn Tyr Arg Glu Cys Asp
          100          105          110
Thr Asp Gly Trp Thr Asn Asp Ile Pro Ile Cys Glu Val Val Lys Cys
          115          120          125
Leu Pro Val Thr Ala Pro Glu Asn Gly Lys Ile Val Ser Ser Ala Met
          130          135          140
Glu Pro Asp Arg Glu Tyr His Phe Gly Gln Ala Val Arg Phe Val Cys
145          150          155          160
Asn Ser Gly Tyr Lys Ile Glu Gly Asp Glu Glu Met His Cys Ser Asp
          165          170          175
Asp Gly Phe Trp Ser Lys Glu Lys Pro Lys Cys Val Glu Ile Ser Cys
          180          185          190
Lys Ser Pro Asp Val Ile Asn Gly Ser Pro Ile Ser Gln Lys Ile Ile
          195          200          205
Tyr Lys Glu Asn Glu Arg Phe Gln Tyr Lys Cys Asn Met Gly Tyr Glu
          210          215          220
Tyr Ser Glu Arg Gly Asp Ala Val Cys Thr Glu Ser Gly Trp Arg Pro
225          230          235          240
Leu Pro Ser Cys Glu Glu
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<210> 12

<211> 2039

<212> PRT

<213> 人(智人)补体受体1(UniProt: P17927)

<400> 12

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

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Glu	Leu	Pro	Ser	Cys	Ser	Arg	Val	Cys	Gln	Pro	Pro	Pro	Asp	Val	Leu
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His	Ala	Glu	Arg	Thr	Gln	Arg	Asp	Lys	Asp	Asn	Phe	Ser	Pro	Gly	Gln
305					310					315					320
Glu	Val	Phe	Tyr	Ser	Cys	Glu	Pro	Gly	Tyr	Asp	Leu	Arg	Gly	Ala	Ala
				325					330					335	
Ser	Met	Arg	Cys	Thr	Pro	Gln	Gly	Asp	Trp	Ser	Pro	Ala	Ala	Pro	Thr
		340						345					350		
Cys	Glu	Val	Lys	Ser	Cys	Asp	Asp	Phe	Met	Gly	Gln	Leu	Leu	Asn	Gly
		355					360					365			
Arg	Val	Leu	Phe	Pro	Val	Asn	Leu	Gln	Leu	Gly	Ala	Lys	Val	Asp	Phe
		370				375					380				
Val	Cys	Asp	Glu	Gly	Phe	Gln	Leu	Lys	Gly	Ser	Ser	Ala	Ser	Tyr	Cys
385					390					395					400
Val	Leu	Ala	Gly	Met	Glu	Ser	Leu	Trp	Asn	Ser	Ser	Val	Pro	Val	Cys
				405					410					415	
Glu	Gln	Ile	Phe	Cys	Pro	Ser	Pro	Pro	Val	Ile	Pro	Asn	Gly	Arg	His
		420							425				430		
Thr	Gly	Lys	Pro	Leu	Glu	Val	Phe	Pro	Phe	Gly	Lys	Thr	Val	Asn	Tyr
		435					440					445			
Thr	Cys	Asp	Pro	His	Pro	Asp	Arg	Gly	Thr	Ser	Phe	Asp	Leu	Ile	Gly
		450				455					460				
Glu	Ser	Thr	Ile	Arg	Cys	Thr	Ser	Asp	Pro	Gln	Gly	Asn	Gly	Val	Trp
465					470					475					480
Ser	Ser	Pro	Ala	Pro	Arg	Cys	Gly	Ile	Leu	Gly	His	Cys	Gln	Ala	Pro
				485					490					495	
Asp	His	Phe	Leu	Phe	Ala	Lys	Leu	Lys	Thr	Gln	Thr	Asn	Ala	Ser	Asp
		500						505					510		
Phe	Pro	Ile	Gly	Thr	Ser	Leu	Lys	Tyr	Glu	Cys	Arg	Pro	Glu	Tyr	Tyr
		515					520						525		
Gly	Arg	Pro	Phe	Ser	Ile	Thr	Cys	Leu	Asp	Asn	Leu	Val	Trp	Ser	Ser
		530				535					540				
Pro	Lys	Asp	Val	Cys	Lys	Arg	Lys	Ser	Cys	Lys	Thr	Pro	Pro	Asp	Pro
545					550					555					560
Val	Asn	Gly	Met	Val	His	Val	Ile	Thr	Asp	Ile	Gln	Val	Gly	Ser	Arg
				565					570				575		
Ile	Asn	Tyr	Ser	Cys	Thr	Thr	Gly	His	Arg	Leu	Ile	Gly	His	Ser	Ser
		580						585					590		
Ala	Glu	Cys	Ile	Leu	Ser	Gly	Asn	Ala	Ala	His	Trp	Ser	Thr	Lys	Pro

595	600	605
Pro Ile Cys Gln Arg Ile	Pro Cys Gly Leu Pro	Pro Thr Ile Ala Asn
610	615	620
Gly Asp Phe Ile Ser Thr	Asn Arg Glu Asn Phe	His Tyr Gly Ser Val
625	630	635
Val Thr Tyr Arg Cys Asn	Pro Gly Ser Gly Gly	Arg Lys Val Phe Glu
645	650	655
Leu Val Gly Glu Pro Ser	Ile Tyr Cys Thr Ser	Asn Asp Asp Gln Val
660	665	670
Gly Ile Trp Ser Gly Pro	Ala Pro Gln Cys Ile	Ile Pro Asn Lys Cys
675	680	685
Thr Pro Pro Asn Val Glu	Asn Gly Ile Leu Val	Ser Asp Asn Arg Ser
690	695	700
Leu Phe Ser Leu Asn Glu	Val Val Glu Phe Arg	Cys Gln Pro Gly Phe
705	710	715
Val Met Lys Gly Pro Arg	Arg Val Lys Cys Gln	Ala Leu Asn Lys Trp
725	730	735
Glu Pro Glu Leu Pro Ser	Cys Ser Arg Val Cys	Gln Pro Pro Pro Asp
740	745	750
Val Leu His Ala Glu Arg	Thr Gln Arg Asp Lys	Asp Asn Phe Ser Pro
755	760	765
Gly Gln Glu Val Phe Tyr	Ser Cys Glu Pro Gly	Tyr Asp Leu Arg Gly
770	775	780
Ala Ala Ser Met Arg Cys	Thr Pro Gln Gly Asp	Trp Ser Pro Ala Ala
785	790	795
Pro Thr Cys Glu Val Lys	Ser Cys Asp Asp Phe	Met Gly Gln Leu Leu
805	810	815
Asn Gly Arg Val Leu Phe	Pro Val Asn Leu Gln	Leu Gly Ala Lys Val
820	825	830
Asp Phe Val Cys Asp Glu	Gly Phe Gln Leu Lys	Gly Ser Ser Ala Ser
835	840	845
Tyr Cys Val Leu Ala Gly	Met Glu Ser Leu Trp	Asn Ser Ser Val Pro
850	855	860
Val Cys Glu Gln Ile Phe	Cys Pro Ser Pro Pro	Val Ile Pro Asn Gly
865	870	875
Arg His Thr Gly Lys Pro	Leu Glu Val Phe Pro	Phe Gly Lys Ala Val
885	890	895
Asn Tyr Thr Cys Asp Pro	His Pro Asp Arg Gly	Thr Ser Phe Asp Leu
900	905	910

Ile Gly Glu Ser Thr Ile Arg Cys Thr Ser Asp Pro Gln Gly Asn Gly		
915	920	925
Val Trp Ser Ser Pro Ala Pro Arg Cys Gly Ile Leu Gly His Cys Gln		
930	935	940
Ala Pro Asp His Phe Leu Phe Ala Lys Leu Lys Thr Gln Thr Asn Ala		
945	950	955
Ser Asp Phe Pro Ile Gly Thr Ser Leu Lys Tyr Glu Cys Arg Pro Glu		
965	970	975
Tyr Tyr Gly Arg Pro Phe Ser Ile Thr Cys Leu Asp Asn Leu Val Trp		
980	985	990
Ser Ser Pro Lys Asp Val Cys Lys Arg Lys Ser Cys Lys Thr Pro Pro		
995	1000	1005
Asp Pro Val Asn Gly Met Val His Val Ile Thr Asp Ile Gln Val		
1010	1015	1020
Gly Ser Arg Ile Asn Tyr Ser Cys Thr Thr Gly His Arg Leu Ile		
1025	1030	1035
Gly His Ser Ser Ala Glu Cys Ile Leu Ser Gly Asn Thr Ala His		
1040	1045	1050
Trp Ser Thr Lys Pro Pro Ile Cys Gln Arg Ile Pro Cys Gly Leu		
1055	1060	1065
Pro Pro Thr Ile Ala Asn Gly Asp Phe Ile Ser Thr Asn Arg Glu		
1070	1075	1080
Asn Phe His Tyr Gly Ser Val Val Thr Tyr Arg Cys Asn Leu Gly		
1085	1090	1095
Ser Arg Gly Arg Lys Val Phe Glu Leu Val Gly Glu Pro Ser Ile		
1100	1105	1110
Tyr Cys Thr Ser Asn Asp Asp Gln Val Gly Ile Trp Ser Gly Pro		
1115	1120	1125
Ala Pro Gln Cys Ile Ile Pro Asn Lys Cys Thr Pro Pro Asn Val		
1130	1135	1140
Glu Asn Gly Ile Leu Val Ser Asp Asn Arg Ser Leu Phe Ser Leu		
1145	1150	1155
Asn Glu Val Val Glu Phe Arg Cys Gln Pro Gly Phe Val Met Lys		
1160	1165	1170
Gly Pro Arg Arg Val Lys Cys Gln Ala Leu Asn Lys Trp Glu Pro		
1175	1180	1185
Glu Leu Pro Ser Cys Ser Arg Val Cys Gln Pro Pro Pro Glu Ile		
1190	1195	1200
Leu His Gly Glu His Thr Pro Ser His Gln Asp Asn Phe Ser Pro		

1205	1210	1215
Gly Gln Glu Val Phe Tyr	Ser Cys Glu Pro Gly	Tyr Asp Leu Arg
1220	1225	1230
Gly Ala Ala Ser Leu His	Cys Thr Pro Gln Gly	Asp Trp Ser Pro
1235	1240	1245
Glu Ala Pro Arg Cys Ala	Val Lys Ser Cys Asp	Asp Phe Leu Gly
1250	1255	1260
Gln Leu Pro His Gly Arg	Val Leu Phe Pro Leu	Asn Leu Gln Leu
1265	1270	1275
Gly Ala Lys Val Ser Phe	Val Cys Asp Glu Gly	Phe Arg Leu Lys
1280	1285	1290
Gly Ser Ser Val Ser His	Cys Val Leu Val Gly	Met Arg Ser Leu
1295	1300	1305
Trp Asn Asn Ser Val Pro	Val Cys Glu His Ile	Phe Cys Pro Asn
1310	1315	1320
Pro Pro Ala Ile Leu Asn	Gly Arg His Thr Gly	Thr Pro Ser Gly
1325	1330	1335
Asp Ile Pro Tyr Gly Lys	Glu Ile Ser Tyr Thr	Cys Asp Pro His
1340	1345	1350
Pro Asp Arg Gly Met Thr	Phe Asn Leu Ile Gly	Glu Ser Thr Ile
1355	1360	1365
Arg Cys Thr Ser Asp Pro	His Gly Asn Gly Val	Trp Ser Ser Pro
1370	1375	1380
Ala Pro Arg Cys Glu Leu	Ser Val Arg Ala Gly	His Cys Lys Thr
1385	1390	1395
Pro Glu Gln Phe Pro Phe	Ala Ser Pro Thr Ile	Pro Ile Asn Asp
1400	1405	1410
Phe Glu Phe Pro Val Gly	Thr Ser Leu Asn Tyr	Glu Cys Arg Pro
1415	1420	1425
Gly Tyr Phe Gly Lys Met	Phe Ser Ile Ser Cys	Leu Glu Asn Leu
1430	1435	1440
Val Trp Ser Ser Val Glu	Asp Asn Cys Arg Arg	Lys Ser Cys Gly
1445	1450	1455
Pro Pro Pro Glu Pro Phe	Asn Gly Met Val His	Ile Asn Thr Asp
1460	1465	1470
Thr Gln Phe Gly Ser Thr	Val Asn Tyr Ser Cys	Asn Glu Gly Phe
1475	1480	1485
Arg Leu Ile Gly Ser Pro	Ser Thr Thr Cys Leu	Val Ser Gly Asn
1490	1495	1500

Asn Val Thr Trp Asp Lys Lys Ala Pro Ile Cys Glu Ile Ile Ser		
1505	1510	1515
Cys Glu Pro Pro Pro Thr Ile Ser Asn Gly Asp Phe Tyr Ser Asn		
1520	1525	1530
Asn Arg Thr Ser Phe His Asn Gly Thr Val Val Thr Tyr Gln Cys		
1535	1540	1545
His Thr Gly Pro Asp Gly Glu Gln Leu Phe Glu Leu Val Gly Glu		
1550	1555	1560
Arg Ser Ile Tyr Cys Thr Ser Lys Asp Asp Gln Val Gly Val Trp		
1565	1570	1575
Ser Ser Pro Pro Pro Arg Cys Ile Ser Thr Asn Lys Cys Thr Ala		
1580	1585	1590
Pro Glu Val Glu Asn Ala Ile Arg Val Pro Gly Asn Arg Ser Phe		
1595	1600	1605
Phe Ser Leu Thr Glu Ile Ile Arg Phe Arg Cys Gln Pro Gly Phe		
1610	1615	1620
Val Met Val Gly Ser His Thr Val Gln Cys Gln Thr Asn Gly Arg		
1625	1630	1635
Trp Gly Pro Lys Leu Pro His Cys Ser Arg Val Cys Gln Pro Pro		
1640	1645	1650
Pro Glu Ile Leu His Gly Glu His Thr Leu Ser His Gln Asp Asn		
1655	1660	1665
Phe Ser Pro Gly Gln Glu Val Phe Tyr Ser Cys Glu Pro Ser Tyr		
1670	1675	1680
Asp Leu Arg Gly Ala Ala Ser Leu His Cys Thr Pro Gln Gly Asp		
1685	1690	1695
Trp Ser Pro Glu Ala Pro Arg Cys Thr Val Lys Ser Cys Asp Asp		
1700	1705	1710
Phe Leu Gly Gln Leu Pro His Gly Arg Val Leu Leu Pro Leu Asn		
1715	1720	1725
Leu Gln Leu Gly Ala Lys Val Ser Phe Val Cys Asp Glu Gly Phe		
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Arg Leu Lys Gly Arg Ser Ala Ser His Cys Val Leu Ala Gly Met		
1745	1750	1755
Lys Ala Leu Trp Asn Ser Ser Val Pro Val Cys Glu Gln Ile Phe		
1760	1765	1770
Cys Pro Asn Pro Pro Ala Ile Leu Asn Gly Arg His Thr Gly Thr		
1775	1780	1785
Pro Phe Gly Asp Ile Pro Tyr Gly Lys Glu Ile Ser Tyr Ala Cys		

1790	1795	1800
Asp Thr His Pro Asp Arg	Gly Met Thr Phe Asn	Leu Ile Gly Glu
1805	1810	1815
Ser Ser Ile Arg Cys Thr	Ser Asp Pro Gln Gly	Asn Gly Val Trp
1820	1825	1830
Ser Ser Pro Ala Pro Arg	Cys Glu Leu Ser Val	Pro Ala Ala Cys
1835	1840	1845
Pro His Pro Pro Lys Ile	Gln Asn Gly His Tyr	Ile Gly Gly His
1850	1855	1860
Val Ser Leu Tyr Leu Pro	Gly Met Thr Ile Ser	Tyr Ile Cys Asp
1865	1870	1875
Pro Gly Tyr Leu Leu Val	Gly Lys Gly Phe Ile	Phe Cys Thr Asp
1880	1885	1890
Gln Gly Ile Trp Ser Gln	Leu Asp His Tyr Cys	Lys Glu Val Asn
1895	1900	1905
Cys Ser Phe Pro Leu Phe	Met Asn Gly Ile Ser	Lys Glu Leu Glu
1910	1915	1920
Met Lys Lys Val Tyr His	Tyr Gly Asp Tyr Val	Thr Leu Lys Cys
1925	1930	1935
Glu Asp Gly Tyr Thr Leu	Glu Gly Ser Pro Trp	Ser Gln Cys Gln
1940	1945	1950
Ala Asp Asp Arg Trp Asp	Pro Pro Leu Ala Lys	Cys Thr Ser Arg
1955	1960	1965
Thr His Asp Ala Leu Ile	Val Gly Thr Leu Ser	Gly Thr Ile Phe
1970	1975	1980
Phe Ile Leu Leu Ile Ile	Phe Leu Ser Trp Ile	Ile Leu Lys His
1985	1990	1995
Arg Lys Gly Asn Asn Ala	His Glu Asn Pro Lys	Glu Val Ala Ile
2000	2005	2010
His Leu His Ser Gln Gly	Gly Ser Ser Val His	Pro Arg Thr Leu
2015	2020	2025
Gln Thr Asn Glu Glu Asn	Ser Arg Val Leu Pro	
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Gly His Cys Gln Ala Pro	Asp His Phe Leu Phe	Ala Lys Leu Lys Thr

1	5	10	15
Gln Thr Asn Ala Ser Asp Phe Pro Ile Gly Thr Ser Leu Lys Tyr Glu			
20	25	30	
Cys Arg Pro Glu Tyr Tyr Gly Arg Pro Phe Ser Ile Thr Cys Leu Asp			
35	40	45	
Asn Leu Val Trp Ser Ser Pro Lys Asp Val Cys Lys Arg Lys Ser Cys			
50	55	60	
Lys Thr Pro Pro Asp Pro Val Asn Gly Met Val His Val Ile Thr Asp			
65	70	75	80
Ile Gln Val Gly Ser Arg Ile Asn Tyr Ser Cys Thr Thr Gly His Arg			
85	90	95	
Leu Ile Gly His Ser Ser Ala Glu Cys Ile Leu Ser Gly Asn Ala Ala			
100	105	110	
His Trp Ser Thr Lys Pro Pro Ile Cys Gln Arg Ile Pro Cys Gly Leu			
115	120	125	
Pro Pro Thr Ile Ala Asn Gly Asp Phe Ile Ser Thr Asn Arg Glu Asn			
130	135	140	
Phe His Tyr Gly Ser Val Val Thr Tyr Arg Cys Asn Pro Gly Ser Gly			
145	150	155	160
Gly Arg Lys Val Phe Glu Leu Val Gly Glu Pro Ser Ile Tyr Cys Thr			
165	170	175	
Ser Asn Asp Asp Gln Val Gly Ile Trp Ser Gly Pro Ala Pro Gln Cys			
180	185	190	
Ile Ile			
<210> 14			
<211> 194			
<212> PRT			
<213> 人(智人)补体受体1 CCP 15-17 (UniProt: P17927 残基941到1134)			
<400> 14			
Gly His Cys Gln Ala Pro Asp His Phe Leu Phe Ala Lys Leu Lys Thr			
1	5	10	15
Gln Thr Asn Ala Ser Asp Phe Pro Ile Gly Thr Ser Leu Lys Tyr Glu			
20	25	30	
Cys Arg Pro Glu Tyr Tyr Gly Arg Pro Phe Ser Ile Thr Cys Leu Asp			
35	40	45	
Asn Leu Val Trp Ser Ser Pro Lys Asp Val Cys Lys Arg Lys Ser Cys			
50	55	60	
Lys Thr Pro Pro Asp Pro Val Asn Gly Met Val His Val Ile Thr Asp			
65	70	75	80

Ile	Gln	Val	Gly	Ser	Arg	Ile	Asn	Tyr	Ser	Cys	Thr	Thr	Gly	His	Arg
				85					90					95	
Leu	Ile	Gly	His	Ser	Ser	Ala	Glu	Cys	Ile	Leu	Ser	Gly	Asn	Thr	Ala
				100					105					110	
His	Trp	Ser	Thr	Lys	Pro	Pro	Ile	Cys	Gln	Arg	Ile	Pro	Cys	Gly	Leu
				115					120					125	
Pro	Pro	Thr	Ile	Ala	Asn	Gly	Asp	Phe	Ile	Ser	Thr	Asn	Arg	Glu	Asn
				130					135					140	
Phe	His	Tyr	Gly	Ser	Val	Val	Thr	Tyr	Arg	Cys	Asn	Leu	Gly	Ser	Arg
145					150					155					160
Gly	Arg	Lys	Val	Phe	Glu	Leu	Val	Gly	Glu	Pro	Ser	Ile	Tyr	Cys	Thr
				165					170					175	
Ser	Asn	Asp	Asp	Gln	Val	Gly	Ile	Trp	Ser	Gly	Pro	Ala	Pro	Gln	Cys
				180					185					190	
Ile	Ile														
<210>	15														
<211>	392														
<212>	PRT														
<213>	人(智人)CD46 (UniProt: P15529)														
<400>	15														
Met	Glu	Pro	Pro	Gly	Arg	Arg	Glu	Cys	Pro	Phe	Pro	Ser	Trp	Arg	Phe
1				5					10					15	
Pro	Gly	Leu	Leu	Leu	Ala	Ala	Met	Val	Leu	Leu	Leu	Tyr	Ser	Phe	Ser
				20					25					30	
Asp	Ala	Cys	Glu	Glu	Pro	Pro	Thr	Phe	Glu	Ala	Met	Glu	Leu	Ile	Gly
				35					40					45	
Lys	Pro	Lys	Pro	Tyr	Tyr	Glu	Ile	Gly	Glu	Arg	Val	Asp	Tyr	Lys	Cys
				50					55					60	
Lys	Lys	Gly	Tyr	Phe	Tyr	Ile	Pro	Pro	Leu	Ala	Thr	His	Thr	Ile	Cys
65					70					75					80
Asp	Arg	Asn	His	Thr	Trp	Leu	Pro	Val	Ser	Asp	Asp	Ala	Cys	Tyr	Arg
				85						90				95	
Glu	Thr	Cys	Pro	Tyr	Ile	Arg	Asp	Pro	Leu	Asn	Gly	Gln	Ala	Val	Pro
				100					105					110	
Ala	Asn	Gly	Thr	Tyr	Glu	Phe	Gly	Tyr	Gln	Met	His	Phe	Ile	Cys	Asn
				115					120					125	
Glu	Gly	Tyr	Tyr	Leu	Ile	Gly	Glu	Glu	Ile	Leu	Tyr	Cys	Glu	Leu	Lys
				130					135					140	
Gly	Ser	Val	Ala	Ile	Trp	Ser	Gly	Lys	Pro	Pro	Ile	Cys	Glu	Lys	Val

145	150	155	160
Leu Cys Thr Pro Pro Pro Lys Ile Lys Asn Gly Lys His Thr Phe Ser			
	165	170	175
Glu Val Glu Val Phe Glu Tyr Leu Asp Ala Val Thr Tyr Ser Cys Asp			
	180	185	190
Pro Ala Pro Gly Pro Asp Pro Phe Ser Leu Ile Gly Glu Ser Thr Ile			
	195	200	205
Tyr Cys Gly Asp Asn Ser Val Trp Ser Arg Ala Ala Pro Glu Cys Lys			
	210	215	220
Val Val Lys Cys Arg Phe Pro Val Val Glu Asn Gly Lys Gln Ile Ser			
225	230	235	240
Gly Phe Gly Lys Lys Phe Tyr Tyr Lys Ala Thr Val Met Phe Glu Cys			
	245	250	255
Asp Lys Gly Phe Tyr Leu Asp Gly Ser Asp Thr Ile Val Cys Asp Ser			
	260	265	270
Asn Ser Thr Trp Asp Pro Pro Val Pro Lys Cys Leu Lys Val Leu Pro			
	275	280	285
Pro Ser Ser Thr Lys Pro Pro Ala Leu Ser His Ser Val Ser Thr Ser			
	290	295	300
Ser Thr Thr Lys Ser Pro Ala Ser Ser Ala Ser Gly Pro Arg Pro Thr			
305	310	315	320
Tyr Lys Pro Pro Val Ser Asn Tyr Pro Gly Tyr Pro Lys Pro Glu Glu			
	325	330	335
Gly Ile Leu Asp Ser Leu Asp Val Trp Val Ile Ala Val Ile Val Ile			
	340	345	350
Ala Ile Val Val Gly Val Ala Val Ile Cys Val Val Pro Tyr Arg Tyr			
	355	360	365
Leu Gln Arg Arg Lys Lys Lys Gly Thr Tyr Leu Thr Asp Glu Thr His			
	370	375	380
Arg Glu Val Lys Phe Thr Ser Leu			
385	390		
<210> 16			
<211> 189			
<212> PRT			
<213> 人(智人)CD46 CCP 2-4 (UniProt: P15529 残基97到285)			
<400> 16			
Glu Thr Cys Pro Tyr Ile Arg Asp Pro Leu Asn Gly Gln Ala Val Pro			
1	5	10	15
Ala Asn Gly Thr Tyr Glu Phe Gly Tyr Gln Met His Phe Ile Cys Asn			

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

<210> 17

<211> 440

<212> PRT

<213> 人(智人)CD55 (UniProt: P08174)

<400> 17

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

95

Gly Leu Ala Asp Leu Ala Lys Glu Glu Leu Arg Arg Lys Tyr Thr Gln
 420 425 430

Val Tyr Arg Leu Phe Leu Val Ser
 435 440

<210> 18

<211> 190

<212> PRT

<213> 人(智人)CD55 CCP 2-4 (UniProt: P08174 残基96到285)

<400> 18

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

Pro Tyr Ile Thr Gln Asn Tyr Phe Pro Val Gly Thr Val Val Glu Tyr
 20 25 30

Glu Cys Arg Pro Gly Tyr Arg Arg Glu Pro Ser Leu Ser Pro Lys Leu
 35 40 45

Thr Cys Leu Gln Asn Leu Lys Trp Ser Thr Ala Val Glu Phe Cys Lys
 50 55 60

Lys Lys Ser Cys Pro Asn Pro Gly Glu Ile Arg Asn Gly Gln Ile Asp
 65 70 75 80

Val Pro Gly Gly Ile Leu Phe Gly Ala Thr Ile Ser Phe Ser Cys Asn
 85 90 95

Thr Gly Tyr Lys Leu Phe Gly Ser Thr Ser Ser Phe Cys Leu Ile Ser
 100 105 110

Gly Ser Ser Val Gln Trp Ser Asp Pro Leu Pro Glu Cys Arg Glu Ile
 115 120 125

Tyr Cys Pro Ala Pro Pro Gln Ile Asp Asn Gly Ile Ile Gln Gly Glu
 130 135 140

Arg Asp His Tyr Gly Tyr Arg Gln Ser Val Thr Tyr Ala Cys Asn Lys
 145 150 155 160

Gly Phe Thr Met Ile Gly Glu His Ser Ile Tyr Cys Thr Val Asn Asn
 165 170 175

Asp Glu Gly Glu Trp Ser Gly Pro Pro Pro Glu Cys Arg Gly
 180 185 190

<210> 19

<211> 597

<212> PRT

<213> 人(智人)C4BP (UniProt: P04003)

<400> 19

Met His Pro Pro Lys Thr Pro Ser Gly Ala Leu His Arg Lys Arg Lys

1	5	10	15
Met Ala Ala Trp	Pro Phe Ser Arg	Leu Trp Lys Val	Ser Asp Pro Ile
20	25	30	
Leu Phe Gln Met	Thr Leu Ile Ala	Ala Leu Leu Pro	Ala Val Leu Gly
35	40	45	
Asn Cys Gly Pro	Pro Pro Thr Leu	Ser Phe Ala Ala	Pro Met Asp Ile
50	55	60	
Thr Leu Thr Glu	Thr Arg Phe Lys	Thr Gly Thr Thr	Leu Lys Tyr Thr
65	70	75	80
Cys Leu Pro Gly	Tyr Val Arg Ser	His Ser Thr Gln	Thr Leu Thr Cys
85	90	95	
Asn Ser Asp Gly	Glu Trp Val Tyr	Asn Thr Phe Cys	Ile Tyr Lys Arg
100	105	110	
Cys Arg His Pro	Gly Glu Leu Arg	Asn Gly Gln Val	Glu Ile Lys Thr
115	120	125	
Asp Leu Ser Phe	Gly Ser Gln Ile	Glu Phe Ser Cys	Ser Glu Gly Phe
130	135	140	
Phe Leu Ile Gly	Ser Thr Thr Ser	Arg Cys Glu Val	Gln Asp Arg Gly
145	150	155	160
Val Gly Trp Ser	His Pro Leu Pro	Gln Cys Glu Ile	Val Lys Cys Lys
165	170	175	
Pro Pro Pro Asp	Ile Arg Asn Gly	Arg His Ser Gly	Glu Glu Asn Phe
180	185	190	
Tyr Ala Tyr Gly	Phe Ser Val Thr	Tyr Ser Cys Asp	Pro Arg Phe Ser
195	200	205	
Leu Leu Gly His	Ala Ser Ile Ser	Cys Thr Val Glu	Asn Glu Thr Ile
210	215	220	
Gly Val Trp Arg	Pro Ser Pro Pro	Thr Cys Glu Lys	Ile Thr Cys Arg
225	230	235	240
Lys Pro Asp Val	Ser His Gly Glu	Met Val Ser Gly	Phe Gly Pro Ile
245	250	255	
Tyr Asn Tyr Lys	Asp Thr Ile Val	Phe Lys Cys Gln	Lys Gly Phe Val
260	265	270	
Leu Arg Gly Ser	Ser Val Ile His	Cys Asp Ala Asp	Ser Lys Trp Asn
275	280	285	
Pro Ser Pro Pro	Ala Cys Glu Pro	Asn Ser Cys Ile	Asn Leu Pro Asp
290	295	300	
Ile Pro His Ala	Ser Trp Glu Thr	Tyr Pro Arg Pro	Thr Lys Glu Asp
305	310	315	320

Val	Tyr	Val	Val	Gly	Thr	Val	Leu	Arg	Tyr	Arg	Cys	His	Pro	Gly	Tyr	
				325					330					335		
Lys	Pro	Thr	Thr	Asp	Glu	Pro	Thr	Thr	Val	Ile	Cys	Gln	Lys	Asn	Leu	
				340					345					350		
Arg	Trp	Thr	Pro	Tyr	Gln	Gly	Cys	Glu	Ala	Leu	Cys	Cys	Pro	Glu	Pro	
				355					360					365		
Lys	Leu	Asn	Asn	Gly	Glu	Ile	Thr	Gln	His	Arg	Lys	Ser	Arg	Pro	Ala	
				370					375					380		
Asn	His	Cys	Val	Tyr	Phe	Tyr	Gly	Asp	Glu	Ile	Ser	Phe	Ser	Cys	His	
385					390					395					400	
Glu	Thr	Ser	Arg	Phe	Ser	Ala	Ile	Cys	Gln	Gly	Asp	Gly	Thr	Trp	Ser	
				405					410					415		
Pro	Arg	Thr	Pro	Ser	Cys	Gly	Asp	Ile	Cys	Asn	Phe	Pro	Pro	Lys	Ile	
				420					425					430		
Ala	His	Gly	His	Tyr	Lys	Gln	Ser	Ser	Ser	Tyr	Ser	Phe	Phe	Lys	Glu	
				435					440					445		
Glu	Ile	Ile	Tyr	Glu	Cys	Asp	Lys	Gly	Tyr	Ile	Leu	Val	Gly	Gln	Ala	
				450					455					460		
Lys	Leu	Ser	Cys	Ser	Tyr	Ser	His	Trp	Ser	Ala	Pro	Ala	Pro	Gln	Cys	
465					470					475					480	
Lys	Ala	Leu	Cys	Arg	Lys	Pro	Glu	Leu	Val	Asn	Gly	Arg	Leu	Ser	Val	
				485					490					495		
Asp	Lys	Asp	Gln	Tyr	Val	Glu	Pro	Glu	Asn	Val	Thr	Ile	Gln	Cys	Asp	
				500					505					510		
Ser	Gly	Tyr	Gly	Val	Val	Gly	Pro	Gln	Ser	Ile	Thr	Cys	Ser	Gly	Asn	
				515					520					525		
Arg	Thr	Trp	Tyr	Pro	Glu	Val	Pro	Lys	Cys	Glu	Trp	Glu	Thr	Pro	Glu	
				530					535					540		
Gly	Cys	Glu	Gln	Val	Leu	Thr	Gly	Lys	Arg	Leu	Met	Gln	Cys	Leu	Pro	
545					550					555					560	
Asn	Pro	Glu	Asp	Val	Lys	Met	Ala	Leu	Glu	Val	Tyr	Lys	Leu	Ser	Leu	
				565					570					575		
Glu	Ile	Glu	Gln	Leu	Glu	Leu	Gln	Arg	Asp	Ser	Ala	Arg	Gln	Ser	Thr	
				580					585					590		
Leu	Asp	Lys	Glu	Leu												
				595												
<210> 20																
<211> 186																
<212> PRT																

<213> 人(智人)C4BP CCP 2-4 (UniProt: P04003 残基111到296)

<400> 20

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

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<210> 21

<211> 245

<212> PRT

<213> 人(智人)SPICE (PDB: 5FOB_C)

<400> 21

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

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Lys Arg Arg Cys Pro Ser Pro Arg Asp Ile Asp Asn Gly His Leu Asp
 65 70 75 80
 Ile Gly Gly Val Asp Phe Gly Ser Ser Ile Thr Tyr Ser Cys Asn Ser
 85 90 95
 Gly Tyr Tyr Leu Ile Gly Glu Tyr Lys Ser Tyr Cys Lys Leu Gly Ser
 100 105 110
 Thr Gly Ser Met Val Trp Asn Pro Lys Ala Pro Ile Cys Glu Ser Val
 115 120 125
 Lys Cys Gln Leu Pro Pro Ser Ile Ser Asn Gly Arg His Asn Gly Tyr
 130 135 140
 Asn Asp Phe Tyr Thr Asp Gly Ser Val Val Thr Tyr Ser Cys Asn Ser
 145 150 155 160
 Gly Tyr Ser Leu Ile Gly Asn Ser Gly Val Leu Cys Ser Gly Gly Glu
 165 170 175
 Trp Ser Asn Pro Pro Thr Cys Gln Ile Val Lys Cys Pro His Pro Thr
 180 185 190
 Ile Leu Asn Gly Tyr Leu Ser Ser Gly Phe Lys Arg Ser Tyr Ser Tyr
 195 200 205
 Asn Asp Asn Val Asp Phe Thr Cys Lys Tyr Gly Tyr Lys Leu Ser Gly
 210 215 220
 Ser Ser Ser Ser Thr Cys Ser Pro Gly Asn Thr Trp Gln Pro Glu Leu
 225 230 235 240
 Pro Lys Cys Val Arg
 245

<210> 22

<211> 263

<212> PRT

<213> 人(智人)VCP (NCBI: YP_232907.1)

<400> 22

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

Cys Ile Lys Arg Arg Cys Pro Ser Pro Arg Asp Ile Asp Asn Gly Gln
 85 90 95
 Leu Asp Ile Gly Gly Val Asp Phe Gly Ser Ser Ile Thr Tyr Ser Cys
 100 105 110
 Asn Ser Gly Tyr His Leu Ile Gly Glu Ser Lys Ser Tyr Cys Glu Leu
 115 120 125
 Gly Ser Thr Gly Ser Met Val Trp Asn Pro Glu Ala Pro Ile Cys Glu
 130 135 140
 Ser Val Lys Cys Gln Ser Pro Pro Ser Ile Ser Asn Gly Arg His Asn
 145 150 155 160
 Gly Tyr Glu Asp Phe Tyr Thr Asp Gly Ser Val Val Thr Tyr Ser Cys
 165 170 175
 Asn Ser Gly Tyr Ser Leu Ile Gly Asn Ser Gly Val Leu Cys Ser Gly
 180 185 190
 Gly Glu Trp Ser Asp Pro Pro Thr Cys Gln Ile Val Lys Cys Pro His
 195 200 205
 Pro Thr Ile Ser Asn Gly Tyr Leu Ser Ser Gly Phe Lys Arg Ser Tyr
 210 215 220
 Ser Tyr Asn Asp Asn Val Asp Phe Lys Cys Lys Tyr Gly Tyr Lys Leu
 225 230 235 240
 Ser Gly Ser Ser Ser Ser Thr Cys Ser Pro Gly Asn Thr Trp Lys Pro
 245 250 255
 Glu Leu Pro Lys Cys Val Arg
 260

<210> 23

<211> 216

<212> PRT

<213> 人(智人)MOPICE (GenBank: AAV84857.1)

<400> 23

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

Lys Arg Arg Cys Pro Ser Pro Arg Asp Ile Asp Asn Gly Gln Leu Asp
 85 90 95
 Ile Gly Gly Val Asp Phe Gly Ser Ser Ile Thr Tyr Ser Cys Asn Ser
 100 105 110
 Gly Tyr His Leu Ile Gly Glu Ser Lys Ser Tyr Cys Glu Leu Gly Ser
 115 120 125
 Thr Gly Ser Met Val Trp Asn Pro Glu Ala Pro Ile Cys Glu Ser Val
 130 135 140
 Lys Cys Gln Ser Pro Pro Ser Ile Ser Asn Gly Arg His Asn Gly Tyr
 145 150 155 160
 Glu Asp Phe Tyr Ile Asp Gly Ser Ile Val Thr Tyr Ser Cys Asn Ser
 165 170 175
 Gly Tyr Ser Leu Ile Gly Asn Ser Gly Val Met Cys Ser Gly Gly Glu
 180 185 190
 Trp Ser Asn Pro Pro Thr Cys Gln Ile Val Lys Cys Pro His Pro Ile
 195 200 205
 Ser Asn Gly Lys Leu Leu Ala Ala
 210 215

<210> 24

<211> 16

<212> PRT

<213> 人工序列

<220>

<223> G4S-R- (G4S) 2接头

<400> 24

Gly Gly Gly Gly Ser Arg Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
 1 5 10 15

<210> 25

<211> 967

<212> PRT

<213> 人(智人)补体因子H 残基264-1231

<400> 25

Lys Ser Cys Asp Asn Pro Tyr Ile Pro Asn Gly Asp Tyr Ser Pro Leu
 1 5 10 15
 Arg Ile Lys His Arg Thr Gly Asp Glu Ile Thr Tyr Gln Cys Arg Asn
 20 25 30
 Gly Phe Tyr Pro Ala Thr Arg Gly Asn Thr Ala Lys Cys Thr Ser Thr
 35 40 45
 Gly Trp Ile Pro Ala Pro Arg Cys Thr Leu Lys Pro Cys Asp Tyr Pro

50	55	60
Asp Ile Lys His Gly Gly Leu Tyr His Glu Asn Met Arg Arg Pro Tyr		
65	70	75
Phe Pro Val Ala Val Gly Lys Tyr Tyr Ser Tyr Tyr Cys Asp Glu His		80
	85	90
Phe Glu Thr Pro Ser Gly Ser Tyr Trp Asp His Ile His Cys Thr Gln		95
	100	105
Asp Gly Trp Ser Pro Ala Val Pro Cys Leu Arg Lys Cys Tyr Phe Pro		110
	115	120
Tyr Leu Glu Asn Gly Tyr Asn Gln Asn Tyr Gly Arg Lys Phe Val Gln		125
	130	135
Gly Lys Ser Ile Asp Val Ala Cys His Pro Gly Tyr Ala Leu Pro Lys		140
145	150	155
Ala Gln Thr Thr Val Thr Cys Met Glu Asn Gly Trp Ser Pro Thr Pro		160
	165	170
Arg Cys Ile Arg Val Lys Thr Cys Ser Lys Ser Ser Ile Asp Ile Glu		175
	180	185
Asn Gly Phe Ile Ser Glu Ser Gln Tyr Thr Tyr Ala Leu Lys Glu Lys		190
	195	200
Ala Lys Tyr Gln Cys Lys Leu Gly Tyr Val Thr Ala Asp Gly Glu Thr		205
	210	215
Ser Gly Ser Ile Thr Cys Gly Lys Asp Gly Trp Ser Ala Gln Pro Thr		220
225	230	235
Cys Ile Lys Ser Cys Asp Ile Pro Val Phe Met Asn Ala Arg Thr Lys		240
	245	250
Asn Asp Phe Thr Trp Phe Lys Leu Asn Asp Thr Leu Asp Tyr Glu Cys		255
	260	265
His Asp Gly Tyr Glu Ser Asn Thr Gly Ser Thr Thr Gly Ser Ile Val		270
	275	280
Cys Gly Tyr Asn Gly Trp Ser Asp Leu Pro Ile Cys Tyr Glu Arg Glu		285
	290	295
Cys Glu Leu Pro Lys Ile Asp Val His Leu Val Pro Asp Arg Lys Lys		300
305	310	315
Asp Gln Tyr Lys Val Gly Glu Val Leu Lys Phe Ser Cys Lys Pro Gly		320
	325	330
Phe Thr Ile Val Gly Pro Asn Ser Val Gln Cys Tyr His Phe Gly Leu		335
	340	345
Ser Pro Asp Leu Pro Ile Cys Lys Glu Gln Val Gln Ser Cys Gly Pro		350
	355	360
		365

Pro	Pro	Glu	Leu	Leu	Asn	Gly	Asn	Val	Lys	Glu	Lys	Thr	Lys	Glu	Glu	370	375	380
Tyr	Gly	His	Ser	Glu	Val	Val	Glu	Tyr	Tyr	Cys	Asn	Pro	Arg	Phe	Leu	385	390	395
Met	Lys	Gly	Pro	Asn	Lys	Ile	Gln	Cys	Val	Asp	Gly	Glu	Trp	Thr	Thr	405	410	415
Leu	Pro	Val	Cys	Ile	Val	Glu	Glu	Ser	Thr	Cys	Gly	Asp	Ile	Pro	Glu	420	425	430
Leu	Glu	His	Gly	Trp	Ala	Gln	Leu	Ser	Ser	Pro	Pro	Tyr	Tyr	Tyr	Gly	435	440	445
Asp	Ser	Val	Glu	Phe	Asn	Cys	Ser	Glu	Ser	Phe	Thr	Met	Ile	Gly	His	450	455	460
Arg	Ser	Ile	Thr	Cys	Ile	His	Gly	Val	Trp	Thr	Gln	Leu	Pro	Gln	Cys	465	470	475
Val	Ala	Ile	Asp	Lys	Leu	Lys	Lys	Cys	Lys	Ser	Ser	Asn	Leu	Ile	Ile	485	490	495
Leu	Glu	Glu	His	Leu	Lys	Asn	Lys	Lys	Glu	Phe	Asp	His	Asn	Ser	Asn	500	505	510
Ile	Arg	Tyr	Arg	Cys	Arg	Gly	Lys	Glu	Gly	Trp	Ile	His	Thr	Val	Cys	515	520	525
Ile	Asn	Gly	Arg	Trp	Asp	Pro	Glu	Val	Asn	Cys	Ser	Met	Ala	Gln	Ile	530	535	540
Gln	Leu	Cys	Pro	Pro	Pro	Pro	Gln	Ile	Pro	Asn	Ser	His	Asn	Met	Thr	545	550	555
Thr	Thr	Leu	Asn	Tyr	Arg	Asp	Gly	Glu	Lys	Val	Ser	Val	Leu	Cys	Gln	565	570	575
Glu	Asn	Tyr	Leu	Ile	Gln	Glu	Gly	Glu	Glu	Ile	Thr	Cys	Lys	Asp	Gly	580	585	590
Arg	Trp	Gln	Ser	Ile	Pro	Leu	Cys	Val	Glu	Lys	Ile	Pro	Cys	Ser	Gln	595	600	605
Pro	Pro	Gln	Ile	Glu	His	Gly	Thr	Ile	Asn	Ser	Ser	Arg	Ser	Ser	Gln	610	615	620
Glu	Ser	Tyr	Ala	His	Gly	Thr	Lys	Leu	Ser	Tyr	Thr	Cys	Glu	Gly	Gly	625	630	635
Phe	Arg	Ile	Ser	Glu	Glu	Asn	Glu	Thr	Thr	Cys	Tyr	Met	Gly	Lys	Trp	645	650	655
Ser	Ser	Pro	Pro	Gln	Cys	Glu	Gly	Leu	Pro	Cys	Lys	Ser	Pro	Pro	Glu	660	665	670
Ile	Ser	His	Gly	Val	Val	Ala	His	Met	Ser	Asp	Ser	Tyr	Gln	Tyr	Gly			

675	680	685
Glu Glu Val Thr Tyr Lys Cys Phe Glu Gly Phe Gly Ile Asp Gly Pro		
690	695	700
Ala Ile Ala Lys Cys Leu Gly Glu Lys Trp Ser His Pro Pro Ser Cys		
705	710	715
Ile Lys Thr Asp Cys Leu Ser Leu Pro Ser Phe Glu Asn Ala Ile Pro		
725	730	735
Met Gly Glu Lys Lys Asp Val Tyr Lys Ala Gly Glu Gln Val Thr Tyr		
740	745	750
Thr Cys Ala Thr Tyr Tyr Lys Met Asp Gly Ala Ser Asn Val Thr Cys		
755	760	765
Ile Asn Ser Arg Trp Thr Gly Arg Pro Thr Cys Arg Asp Thr Ser Cys		
770	775	780
Val Asn Pro Pro Thr Val Gln Asn Ala Tyr Ile Val Ser Arg Gln Met		
785	790	795
Ser Lys Tyr Pro Ser Gly Glu Arg Val Arg Tyr Gln Cys Arg Ser Pro		
805	810	815
Tyr Glu Met Phe Gly Asp Glu Glu Val Met Cys Leu Asn Gly Asn Trp		
820	825	830
Thr Glu Pro Pro Gln Cys Lys Asp Ser Thr Gly Lys Cys Gly Pro Pro		
835	840	845
Pro Pro Ile Asp Asn Gly Asp Ile Thr Ser Phe Pro Leu Ser Val Tyr		
850	855	860
Ala Pro Ala Ser Ser Val Glu Tyr Gln Cys Gln Asn Leu Tyr Gln Leu		
865	870	875
Glu Gly Asn Lys Arg Ile Thr Cys Arg Asn Gly Gln Trp Ser Glu Pro		
885	890	895
Pro Lys Cys Leu His Pro Cys Val Ile Ser Arg Glu Ile Met Glu Asn		
900	905	910
Tyr Asn Ile Ala Leu Arg Trp Thr Ala Lys Gln Lys Leu Tyr Ser Arg		
915	920	925
Thr Gly Glu Ser Val Glu Phe Val Cys Lys Arg Gly Tyr Arg Leu Ser		
930	935	940
Ser Arg Ser His Thr Leu Arg Thr Thr Cys Trp Asp Gly Lys Leu Glu		
945	950	955
Tyr Pro Thr Cys Ala Lys Arg		
965		

<210> 26

<211> 339

<212> PRT

<213> 人(智人)补体因子I 残基1到339

<400> 26

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Met Lys Leu Leu His Val Phe Leu Leu Phe Leu Cys Phe His Leu Arg
1           5           10           15
Phe Cys Lys Val Thr Tyr Thr Ser Gln Glu Asp Leu Val Glu Lys Lys
           20           25           30
Cys Leu Ala Lys Lys Tyr Thr His Leu Ser Cys Asp Lys Val Phe Cys
           35           40           45
Gln Pro Trp Gln Arg Cys Ile Glu Gly Thr Cys Val Cys Lys Leu Pro
           50           55           60
Tyr Gln Cys Pro Lys Asn Gly Thr Ala Val Cys Ala Thr Asn Arg Arg
65           70           75           80
Ser Phe Pro Thr Tyr Cys Gln Gln Lys Ser Leu Glu Cys Leu His Pro
           85           90           95
Gly Thr Lys Phe Leu Asn Asn Gly Thr Cys Thr Ala Glu Gly Lys Phe
           100          105          110
Ser Val Ser Leu Lys His Gly Asn Thr Asp Ser Glu Gly Ile Val Glu
           115          120          125
Val Lys Leu Val Asp Gln Asp Lys Thr Met Phe Ile Cys Lys Ser Ser
           130          135          140
Trp Ser Met Arg Glu Ala Asn Val Ala Cys Leu Asp Leu Gly Phe Gln
145          150          155          160
Gln Gly Ala Asp Thr Gln Arg Arg Phe Lys Leu Ser Asp Leu Ser Ile
           165          170          175
Asn Ser Thr Glu Cys Leu His Val His Cys Arg Gly Leu Glu Thr Ser
           180          185          190
Leu Ala Glu Cys Thr Phe Thr Lys Arg Arg Thr Met Gly Tyr Gln Asp
           195          200          205
Phe Ala Asp Val Val Cys Tyr Thr Gln Lys Ala Asp Ser Pro Met Asp
           210          215          220
Asp Phe Phe Gln Cys Val Asn Gly Lys Tyr Ile Ser Gln Met Lys Ala
225          230          235          240
Cys Asp Gly Ile Asn Asp Cys Gly Asp Gln Ser Asp Glu Leu Cys Cys
           245          250          255
Lys Ala Cys Gln Gly Lys Gly Phe His Cys Lys Ser Gly Val Cys Ile
           260          265          270
Pro Ser Gln Tyr Gln Cys Asn Gly Glu Val Asp Cys Ile Thr Gly Glu
           275          280          285

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Asp Glu Val Gly Cys Ala Gly Phe Ala Ser Val Thr Gln Glu Glu Thr
290 295 300
Glu Ile Leu Thr Ala Asp Met Asp Ala Glu Arg Arg Arg Ile Lys Ser
305 310 315 320
Leu Leu Pro Lys Leu Ser Cys Gly Val Lys Asn Arg Met His Ile Arg
325 330 335

Arg Lys Arg

<210> 27

<211> 3

<212> PRT

<213> 人工序列

<220>

<223> N-连接的糖基化共有序列

<220>

<221> MISC_FEATURE

<222> (2) .. (2)

<223> Xaa = 除P外的任何氨基酸

<220>

<221> MISC_FEATURE

<222> (3) .. (3)

<223> Xaa = S或T

<400> 27

Asn Xaa Xaa

1

<210> 28

<211> 4

<212> PRT

<213> 人工序列

<220>

<223> 弗林内肽酶裂解位点(最小)

<220>

<221> MISC_FEATURE

<222> (2) .. (2)

<223> Xaa = 任何氨基酸

<220>

<221> MISC_FEATURE

<222> (3) .. (3)

<223> Xaa = 任何氨基酸

<400> 28

Arg Xaa Xaa Arg

1

<210> 29

<211> 4

<212> PRT

<213> 人工序列

<220>

<223> 弗林内肽酶裂解位点 (优选的)

<220>

<221> MISC_FEATURE

<222> (2) .. (2)

<223> Xaa = 任何氨基酸

<220>

<221> MISC_FEATURE

<222> (3) .. (3)

<223> Xaa = K或R

<400> 29

Arg Xaa Xaa Arg

1

<210> 30

<211> 6

<212> PRT

<213> 人工序列

<220>

<223> 6xHis标签

<400> 30

His His His His His His

1

5

<210> 31

<211> 7

<212> PRT

<213> 人工序列

<220>

<223> 烟草蚀纹病毒 (TEV) 蛋白酶裂解位点

<400> 31

Glu Asn Leu Tyr Phe Gln Gly

1

5

<210> 32

<211> 543

<212> PRT

<213> 人工序列

<220>

<223> His-标签的糖基化嵌合FH-FI蛋白氨基酸序列

<400> 32

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Met Arg Leu Leu Ala Lys Ile Ile Cys Leu Met Leu Trp Ala Ile Cys
1           5           10           15
Val Ala His His His His His His Gly Ser Ser Glu Asn Leu Tyr Phe
           20           25           30
Gln Gly Ser Ser Gly Glu Asp Cys Asn Glu Leu Pro Pro Arg Arg Asn
           35           40           45
Thr Glu Ile Leu Thr Gly Ser Trp Ser Asp Gln Thr Tyr Pro Glu Gly
           50           55           60
Thr Gln Ala Ile Tyr Lys Cys Arg Pro Gly Tyr Arg Ser Leu Gly Asn
65           70           75           80
Ile Ile Met Val Cys Arg Lys Gly Glu Trp Val Ala Leu Asn Pro Leu
           85           90           95
Arg Lys Cys Gln Lys Arg Pro Cys Gly His Pro Gly Asp Thr Pro Phe
           100          105          110
Gly Thr Phe Thr Leu Thr Gly Gly Asn Val Phe Glu Tyr Gly Val Lys
           115          120          125
Ala Val Tyr Thr Cys Asn Glu Gly Tyr Gln Leu Leu Gly Glu Ile Asn
           130          135          140
Tyr Arg Glu Cys Asp Thr Asp Gly Trp Thr Asn Asp Ile Pro Ile Cys
145          150          155          160
Glu Val Val Lys Cys Leu Pro Val Thr Ala Pro Glu Asn Gly Lys Ile
           165          170          175
Val Ser Ser Ala Met Glu Pro Asp Arg Glu Tyr His Phe Gly Gln Ala
           180          185          190
Val Arg Phe Val Cys Asn Ser Gly Tyr Lys Ile Glu Gly Asp Glu Glu
           195          200          205
Met His Cys Ser Asp Asp Gly Phe Trp Ser Lys Glu Lys Pro Lys Cys
           210          215          220
Val Glu Ile Ser Cys Lys Ser Pro Asp Val Ile Asn Gly Ser Pro Ile
225          230          235          240
Ser Gln Lys Ile Ile Tyr Lys Glu Asn Glu Arg Phe Gln Tyr Lys Cys
           245          250          255
Asn Met Gly Tyr Glu Tyr Ser Glu Arg Gly Asp Ala Val Cys Thr Glu
           260          265          270

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Ser Gly Trp Arg Pro Leu Pro Ser Cys Glu Glu Gly Gly Gly Gly Ser		
275	280	285
Arg Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Ile Val Gly Gly Lys		
290	295	300
Arg Ala Gln Leu Gly Asp Leu Pro Trp Gln Val Ala Ile Lys Asp Ala		
305	310	315 320
Ser Gly Ile Thr Cys Gly Gly Ile Tyr Ile Gly Gly Cys Trp Ile Leu		
	325	330 335
Thr Ala Ala His Cys Leu Arg Ala Ser Lys Thr His Arg Tyr Gln Ile		
	340	345 350
Trp Thr Thr Val Val Asp Trp Ile His Pro Asp Leu Lys Arg Ile Val		
	355	360 365
Ile Glu Tyr Val Asp Arg Ile Ile Phe His Glu Asn Tyr Asn Ala Gly		
	370 375	380
Thr Tyr Gln Asn Asp Ile Ala Leu Ile Glu Met Lys Lys Asp Gly Asn		
385	390	395 400
Lys Lys Asp Cys Glu Leu Pro Arg Ser Ile Pro Ala Ala Val Pro Trp		
	405	410 415
Ser Pro Tyr Leu Phe Gln Pro Asn Asp Thr Cys Ile Val Ser Gly Trp		
	420	425 430
Gly Arg Glu Lys Asp Asn Glu Arg Val Phe Ser Leu Gln Trp Gly Glu		
	435	440 445
Val Lys Leu Ile Ser Asn Cys Ser Lys Phe Tyr Gly Asn Arg Phe Tyr		
	450	455 460
Glu Lys Glu Met Glu Cys Ala Gly Thr Tyr Asp Gly Ser Ile Asp Ala		
465	470	475 480
Cys Lys Gly Asp Ser Gly Gly Pro Leu Val Cys Met Asp Ala Asn Asn		
	485	490 495
Val Thr Tyr Val Trp Gly Val Val Ser Trp Gly Glu Asn Cys Gly Lys		
	500	505 510
Pro Glu Phe Pro Gly Val Tyr Thr Lys Val Ala Asn Tyr Phe Asp Trp		
	515	520 525
Ile Ser Tyr His Val Gly Arg Pro Phe Ile Ser Gln Tyr Asn Val		
	530	535 540
<210> 33		
<211> 543		
<212> PRT		
<213> 人工序列		
<220>		

<223> His-标签的非糖基化嵌合FH-FI蛋白氨基酸序列

<400> 33

Met	Arg	Leu	Leu	Ala	Lys	Ile	Ile	Cys	Leu	Met	Leu	Trp	Ala	Ile	Cys
1				5				10					15		
Val	Ala	His	His	His	His	His	His	Gly	Ser	Ser	Glu	Asn	Leu	Tyr	Phe
			20					25					30		
Gln	Gly	Ser	Ser	Gly	Glu	Asp	Cys	Asn	Glu	Leu	Pro	Pro	Arg	Arg	Asn
			35				40						45		
Thr	Glu	Ile	Leu	Thr	Gly	Ser	Trp	Ser	Asp	Gln	Thr	Tyr	Pro	Glu	Gly
			50				55				60				
Thr	Gln	Ala	Ile	Tyr	Lys	Cys	Arg	Pro	Gly	Tyr	Arg	Ser	Leu	Gly	Asn
65					70					75					80
Ile	Ile	Met	Val	Cys	Arg	Lys	Gly	Glu	Trp	Val	Ala	Leu	Asn	Pro	Leu
				85					90					95	
Arg	Lys	Cys	Gln	Lys	Arg	Pro	Cys	Gly	His	Pro	Gly	Asp	Thr	Pro	Phe
			100					105					110		
Gly	Thr	Phe	Thr	Leu	Thr	Gly	Gly	Asn	Val	Phe	Glu	Tyr	Gly	Val	Lys
			115					120					125		
Ala	Val	Tyr	Thr	Cys	Asn	Glu	Gly	Tyr	Gln	Leu	Leu	Gly	Glu	Ile	Asn
			130				135					140			
Tyr	Arg	Glu	Cys	Asp	Thr	Asp	Gly	Trp	Thr	Asn	Asp	Ile	Pro	Ile	Cys
145					150					155					160
Glu	Val	Val	Lys	Cys	Leu	Pro	Val	Thr	Ala	Pro	Glu	Asn	Gly	Lys	Ile
				165					170					175	
Val	Ser	Ser	Ala	Met	Glu	Pro	Asp	Arg	Glu	Tyr	His	Phe	Gly	Gln	Ala
			180					185					190		
Val	Arg	Phe	Val	Cys	Asn	Ser	Gly	Tyr	Lys	Ile	Glu	Gly	Asp	Glu	Glu
			195					200					205		
Met	His	Cys	Ser	Asp	Asp	Gly	Phe	Trp	Ser	Lys	Glu	Lys	Pro	Lys	Cys
			210				215					220			
Val	Glu	Ile	Ser	Cys	Lys	Ser	Pro	Asp	Val	Ile	Asn	Gly	Ser	Pro	Ile
225					230					235					240
Ser	Gln	Lys	Ile	Ile	Tyr	Lys	Glu	Asn	Glu	Arg	Phe	Gln	Tyr	Lys	Cys
				245					250					255	
Asn	Met	Gly	Tyr	Glu	Tyr	Ser	Glu	Arg	Gly	Asp	Ala	Val	Cys	Thr	Glu
			260					265					270		
Ser	Gly	Trp	Arg	Pro	Leu	Pro	Ser	Cys	Glu	Glu	Gly	Gly	Gly	Gly	Ser
			275					280					285		
Arg	Gly	Gly	Gly	Gly	Ser	Gly	Gly	Gly	Gly	Ser	Ile	Val	Gly	Gly	Lys

290	295	300
Arg Ala Gln Leu Gly Asp	Leu Pro Trp Gln Val Ala	Ile Lys Asp Ala
305	310	315
Ser Gly Ile Thr Cys Gly Gly	Ile Tyr Ile Gly Gly Cys	Trp Ile Leu
325	330	335
Thr Ala Ala His Cys Leu Arg	Ala Ser Lys Thr His Arg	Tyr Gln Ile
340	345	350
Trp Thr Thr Val Val Asp	Trp Ile His Pro Asp	Leu Lys Arg Ile Val
355	360	365
Ile Glu Tyr Val Asp Arg	Ile Ile Phe His Glu	Asn Tyr Asn Ala Gly
370	375	380
Thr Tyr Gln Asn Asp Ile	Ala Leu Ile Glu Met	Lys Lys Asp Gly Asn
385	390	395
Lys Lys Asp Cys Glu Leu	Pro Arg Ser Ile Pro	Ala Ala Val Pro Trp
405	410	415
Ser Pro Tyr Leu Phe Gln	Pro Gln Asp Thr Cys	Ile Val Ser Gly Trp
420	425	430
Gly Arg Glu Lys Asp Asn	Glu Arg Val Phe Ser	Leu Gln Trp Gly Glu
435	440	445
Val Lys Leu Ile Ser Gln	Cys Ser Lys Phe Tyr	Gly Asn Arg Phe Tyr
450	455	460
Glu Lys Glu Met Glu Cys	Ala Gly Thr Tyr Asp	Gly Ser Ile Asp Ala
465	470	475
Cys Lys Gly Asp Ser Gly	Gly Pro Leu Val Cys	Met Asp Ala Asn Gln
485	490	495
Val Thr Tyr Val Trp Gly	Val Val Ser Trp Gly	Glu Asn Cys Gly Lys
500	505	510
Pro Glu Phe Pro Gly Val	Tyr Thr Lys Val Ala	Asn Tyr Phe Asp Trp
515	520	525
Ile Ser Tyr His Val Gly	Arg Pro Phe Ile Ser	Gln Tyr Asn Val
530	535	540
<210> 34		
<211> 524		
<212> PRT		
<213> 人工序列		
<220>		
<223> 非糖基化嵌合FH-FI蛋白氨基酸序列		
<400> 34		
Met Arg Leu Leu Ala Lys	Ile Ile Cys Leu Met	Leu Trp Ala Ile Cys

1	5	10	15
Val Ala Glu Asp Cys Asn Glu Leu Pro Pro Arg Arg Asn Thr Glu Ile			
20	25	30	
Leu Thr Gly Ser Trp Ser Asp Gln Thr Tyr Pro Glu Gly Thr Gln Ala			
35	40	45	
Ile Tyr Lys Cys Arg Pro Gly Tyr Arg Ser Leu Gly Asn Ile Ile Met			
50	55	60	
Val Cys Arg Lys Gly Glu Trp Val Ala Leu Asn Pro Leu Arg Lys Cys			
65	70	75	80
Gln Lys Arg Pro Cys Gly His Pro Gly Asp Thr Pro Phe Gly Thr Phe			
85	90	95	
Thr Leu Thr Gly Gly Asn Val Phe Glu Tyr Gly Val Lys Ala Val Tyr			
100	105	110	
Thr Cys Asn Glu Gly Tyr Gln Leu Leu Gly Glu Ile Asn Tyr Arg Glu			
115	120	125	
Cys Asp Thr Asp Gly Trp Thr Asn Asp Ile Pro Ile Cys Glu Val Val			
130	135	140	
Lys Cys Leu Pro Val Thr Ala Pro Glu Asn Gly Lys Ile Val Ser Ser			
145	150	155	160
Ala Met Glu Pro Asp Arg Glu Tyr His Phe Gly Gln Ala Val Arg Phe			
165	170	175	
Val Cys Asn Ser Gly Tyr Lys Ile Glu Gly Asp Glu Glu Met His Cys			
180	185	190	
Ser Asp Asp Gly Phe Trp Ser Lys Glu Lys Pro Lys Cys Val Glu Ile			
195	200	205	
Ser Cys Lys Ser Pro Asp Val Ile Asn Gly Ser Pro Ile Ser Gln Lys			
210	215	220	
Ile Ile Tyr Lys Glu Asn Glu Arg Phe Gln Tyr Lys Cys Asn Met Gly			
225	230	235	240
Tyr Glu Tyr Ser Glu Arg Gly Asp Ala Val Cys Thr Glu Ser Gly Trp			
245	250	255	
Arg Pro Leu Pro Ser Cys Glu Glu Gly Gly Gly Ser Arg Gly Gly			
260	265	270	
Gly Gly Ser Gly Gly Gly Gly Ser Ile Val Gly Gly Lys Arg Ala Gln			
275	280	285	
Leu Gly Asp Leu Pro Trp Gln Val Ala Ile Lys Asp Ala Ser Gly Ile			
290	295	300	
Thr Cys Gly Gly Ile Tyr Ile Gly Gly Cys Trp Ile Leu Thr Ala Ala			
305	310	315	320

His Cys Leu Arg Ala Ser Lys Thr His Arg Tyr Gln Ile Trp Thr Thr																			
Val Val Asp Trp Ile His Pro Asp Leu Lys Arg Ile Val Ile Glu Tyr																			
Val Asp Arg Ile Ile Phe His Glu Asn Tyr Asn Ala Gly Thr Tyr Gln																			
Asn Asp Ile Ala Leu Ile Glu Met Lys Lys Asp Gly Asn Lys Lys Asp																			
Cys Glu Leu Pro Arg Ser Ile Pro Ala Ala Val Pro Trp Ser Pro Tyr																			
Leu Phe Gln Pro Gln Asp Thr Cys Ile Val Ser Gly Trp Gly Arg Glu																			
Lys Asp Asn Glu Arg Val Phe Ser Leu Gln Trp Gly Glu Val Lys Leu																			
Ile Ser Gln Cys Ser Lys Phe Tyr Gly Asn Arg Phe Tyr Glu Lys Glu																			
Met Glu Cys Ala Gly Thr Tyr Asp Gly Ser Ile Asp Ala Cys Lys Gly																			
Asp Ser Gly Gly Pro Leu Val Cys Met Asp Ala Asn Gln Val Thr Tyr																			
Val Trp Gly Val Val Ser Trp Gly Glu Asn Cys Gly Lys Pro Glu Phe																			
Pro Gly Val Tyr Thr Lys Val Ala Asn Tyr Phe Asp Trp Ile Ser Tyr																			
His Val Gly Arg Pro Phe Ile Ser Gln Tyr Asn Val																			
<210> 35																			
<211> 525																			
<212> PRT																			
<213> 人工序列																			
<220>																			
<223> His-标签的糖基化嵌合FH-FI蛋白氨基酸序列(无信号肽)																			
<400> 35																			
His His His His His His Gly Ser Ser Glu Asn Leu Tyr Phe Gln Gly																			
1																			
Ser Ser Gly Glu Asp Cys Asn Glu Leu Pro Pro Arg Arg Asn Thr Glu																			
Ile Leu Thr Gly Ser Trp Ser Asp Gln Thr Tyr Pro Glu Gly Thr Gln																			

Ala Ile Tyr Lys Cys Arg Pro Gly Tyr Arg Ser Leu Gly Asn Ile Ile		
50	55	60
Met Val Cys Arg Lys Gly Glu Trp Val Ala Leu Asn Pro Leu Arg Lys		
65	70	75 80
Cys Gln Lys Arg Pro Cys Gly His Pro Gly Asp Thr Pro Phe Gly Thr		
85	90	95
Phe Thr Leu Thr Gly Gly Asn Val Phe Glu Tyr Gly Val Lys Ala Val		
100	105	110
Tyr Thr Cys Asn Glu Gly Tyr Gln Leu Leu Gly Glu Ile Asn Tyr Arg		
115	120	125
Glu Cys Asp Thr Asp Gly Trp Thr Asn Asp Ile Pro Ile Cys Glu Val		
130	135	140
Val Lys Cys Leu Pro Val Thr Ala Pro Glu Asn Gly Lys Ile Val Ser		
145	150	155 160
Ser Ala Met Glu Pro Asp Arg Glu Tyr His Phe Gly Gln Ala Val Arg		
165	170	175
Phe Val Cys Asn Ser Gly Tyr Lys Ile Glu Gly Asp Glu Glu Met His		
180	185	190
Cys Ser Asp Asp Gly Phe Trp Ser Lys Glu Lys Pro Lys Cys Val Glu		
195	200	205
Ile Ser Cys Lys Ser Pro Asp Val Ile Asn Gly Ser Pro Ile Ser Gln		
210	215	220
Lys Ile Ile Tyr Lys Glu Asn Glu Arg Phe Gln Tyr Lys Cys Asn Met		
225	230	235 240
Gly Tyr Glu Tyr Ser Glu Arg Gly Asp Ala Val Cys Thr Glu Ser Gly		
245	250	255
Trp Arg Pro Leu Pro Ser Cys Glu Glu Gly Gly Gly Gly Ser Arg Gly		
260	265	270
Gly Gly Gly Ser Gly Gly Gly Gly Ser Ile Val Gly Gly Lys Arg Ala		
275	280	285
Gln Leu Gly Asp Leu Pro Trp Gln Val Ala Ile Lys Asp Ala Ser Gly		
290	295	300
Ile Thr Cys Gly Gly Ile Tyr Ile Gly Gly Cys Trp Ile Leu Thr Ala		
305	310	315 320
Ala His Cys Leu Arg Ala Ser Lys Thr His Arg Tyr Gln Ile Trp Thr		
325	330	335
Thr Val Val Asp Trp Ile His Pro Asp Leu Lys Arg Ile Val Ile Glu		
340	345	350
Tyr Val Asp Arg Ile Ile Phe His Glu Asn Tyr Asn Ala Gly Thr Tyr		

355	360	365
Gln Asn Asp Ile Ala Leu Ile	Glu Met Lys Lys Asp Gly Asn Lys Lys	
370	375	380
Asp Cys Glu Leu Pro Arg Ser Ile Pro Ala Ala Val Pro Trp Ser Pro		
385	390	395
400		
Tyr Leu Phe Gln Pro Asn Asp Thr Cys Ile Val Ser Gly Trp Gly Arg		
405	410	415
Glu Lys Asp Asn Glu Arg Val Phe Ser Leu Gln Trp Gly Glu Val Lys		
420	425	430
Leu Ile Ser Asn Cys Ser Lys Phe Tyr Gly Asn Arg Phe Tyr Glu Lys		
435	440	445
Glu Met Glu Cys Ala Gly Thr Tyr Asp Gly Ser Ile Asp Ala Cys Lys		
450	455	460
Gly Asp Ser Gly Gly Pro Leu Val Cys Met Asp Ala Asn Asn Val Thr		
465	470	475
480		
Tyr Val Trp Gly Val Val Ser Trp Gly Glu Asn Cys Gly Lys Pro Glu		
485	490	495
Phe Pro Gly Val Tyr Thr Lys Val Ala Asn Tyr Phe Asp Trp Ile Ser		
500	505	510
Tyr His Val Gly Arg Pro Phe Ile Ser Gln Tyr Asn Val		
515	520	525
<210> 36		
<400> 36		
000		
<210> 37		
<211> 506		
<212> PRT		
<213> 人工序列		
<220>		
<223> 非糖基化嵌合FH-FI蛋白氨基酸序列(无信号肽)		
<400> 37		
Glu Asp Cys Asn Glu Leu Pro Pro Arg Arg Asn Thr Glu Ile Leu Thr		
1	5	10
15		
Gly Ser Trp Ser Asp Gln Thr Tyr Pro Glu Gly Thr Gln Ala Ile Tyr		
20	25	30
Lys Cys Arg Pro Gly Tyr Arg Ser Leu Gly Asn Ile Ile Met Val Cys		
35	40	45
Arg Lys Gly Glu Trp Val Ala Leu Asn Pro Leu Arg Lys Cys Gln Lys		
50	55	60

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

370	375	380
Gln Pro Gln Asp Thr Cys Ile Val Ser Gly Trp Gly Arg Glu Lys Asp		
385	390	395
Asn Glu Arg Val Phe Ser Leu Gln Trp Gly Glu Val Lys Leu Ile Ser		400
	405	410
Gln Cys Ser Lys Phe Tyr Gly Asn Arg Phe Tyr Glu Lys Glu Met Glu		415
	420	425
Cys Ala Gly Thr Tyr Asp Gly Ser Ile Asp Ala Cys Lys Gly Asp Ser		430
	435	440
Gly Gly Pro Leu Val Cys Met Asp Ala Asn Gln Val Thr Tyr Val Trp		445
	450	455
Gly Val Val Ser Trp Gly Glu Asn Cys Gly Lys Pro Glu Phe Pro Gly		460
465	470	475
Val Tyr Thr Lys Val Ala Asn Tyr Phe Asp Trp Ile Ser Tyr His Val		480
	485	490
Gly Arg Pro Phe Ile Ser Gln Tyr Asn Val		495
	500	505
<210> 38		
<211> 449		
<212> PRT		
<213> 人工序列		
<220>		
<223> 补体因子H同种型FHL-1 (UniProt: P08603-2)		
<400> 38		
Met Arg Leu Leu Ala Lys Ile Ile Cys Leu Met Leu Trp Ala Ile Cys		
1	5	10
Val Ala Glu Asp Cys Asn Glu Leu Pro Pro Arg Arg Asn Thr Glu Ile		15
	20	25
Leu Thr Gly Ser Trp Ser Asp Gln Thr Tyr Pro Glu Gly Thr Gln Ala		30
	35	40
Ile Tyr Lys Cys Arg Pro Gly Tyr Arg Ser Leu Gly Asn Val Ile Met		45
	50	55
Val Cys Arg Lys Gly Glu Trp Val Ala Leu Asn Pro Leu Arg Lys Cys		60
65	70	75
Gln Lys Arg Pro Cys Gly His Pro Gly Asp Thr Pro Phe Gly Thr Phe		80
	85	90
Thr Leu Thr Gly Gly Asn Val Phe Glu Tyr Gly Val Lys Ala Val Tyr		95
	100	105
Thr Cys Asn Glu Gly Tyr Gln Leu Leu Gly Glu Ile Asn Tyr Arg Glu		110

115	120	125
Cys Asp Thr Asp Gly Trp Thr Asn Asp Ile Pro Ile Cys Glu Val Val		
130	135	140
Lys Cys Leu Pro Val Thr Ala Pro Glu Asn Gly Lys Ile Val Ser Ser		
145	150	155
Ala Met Glu Pro Asp Arg Glu Tyr His Phe Gly Gln Ala Val Arg Phe		
165	170	175
Val Cys Asn Ser Gly Tyr Lys Ile Glu Gly Asp Glu Glu Met His Cys		
180	185	190
Ser Asp Asp Gly Phe Trp Ser Lys Glu Lys Pro Lys Cys Val Glu Ile		
195	200	205
Ser Cys Lys Ser Pro Asp Val Ile Asn Gly Ser Pro Ile Ser Gln Lys		
210	215	220
Ile Ile Tyr Lys Glu Asn Glu Arg Phe Gln Tyr Lys Cys Asn Met Gly		
225	230	235
Tyr Glu Tyr Ser Glu Arg Gly Asp Ala Val Cys Thr Glu Ser Gly Trp		
245	250	255
Arg Pro Leu Pro Ser Cys Glu Glu Lys Ser Cys Asp Asn Pro Tyr Ile		
260	265	270
Pro Asn Gly Asp Tyr Ser Pro Leu Arg Ile Lys His Arg Thr Gly Asp		
275	280	285
Glu Ile Thr Tyr Gln Cys Arg Asn Gly Phe Tyr Pro Ala Thr Arg Gly		
290	295	300
Asn Thr Ala Lys Cys Thr Ser Thr Gly Trp Ile Pro Ala Pro Arg Cys		
305	310	315
Thr Leu Lys Pro Cys Asp Tyr Pro Asp Ile Lys His Gly Gly Leu Tyr		
325	330	335
His Glu Asn Met Arg Arg Pro Tyr Phe Pro Val Ala Val Gly Lys Tyr		
340	345	350
Tyr Ser Tyr Tyr Cys Asp Glu His Phe Glu Thr Pro Ser Gly Ser Tyr		
355	360	365
Trp Asp His Ile His Cys Thr Gln Asp Gly Trp Ser Pro Ala Val Pro		
370	375	380
Cys Leu Arg Lys Cys Tyr Phe Pro Tyr Leu Glu Asn Gly Tyr Asn Gln		
385	390	395
Asn Tyr Gly Arg Lys Phe Val Gln Gly Lys Ser Ile Asp Val Ala Cys		
405	410	415
His Pro Gly Tyr Ala Leu Pro Lys Ala Gln Thr Thr Val Thr Cys Met		
420	425	430

Glu Asn Gly Trp Ser Pro Thr Pro Arg Cys Ile Arg Val Ser Phe Thr
 435 440 445

Leu

<210> 39

<211> 184

<212> PRT

<213> 人工序列

<220>

<223> 补体因子H CCP 6-8 (UniProt: P08603 残基324到507)

<400> 39

Pro Cys Asp Tyr Pro Asp Ile Lys His Gly Gly Leu Tyr His Glu Asn
 1 5 10 15

Met Arg Arg Pro Tyr Phe Pro Val Ala Val Gly Lys Tyr Tyr Ser Tyr
 20 25 30

Tyr Cys Asp Glu His Phe Glu Thr Pro Ser Gly Ser Tyr Trp Asp His
 35 40 45

Ile His Cys Thr Gln Asp Gly Trp Ser Pro Ala Val Pro Cys Leu Arg
 50 55 60

Lys Cys Tyr Phe Pro Tyr Leu Glu Asn Gly Tyr Asn Gln Asn Tyr Gly
 65 70 75 80

Arg Lys Phe Val Gln Gly Lys Ser Ile Asp Val Ala Cys His Pro Gly
 85 90 95

Tyr Ala Leu Pro Lys Ala Gln Thr Thr Val Thr Cys Met Glu Asn Gly
 100 105 110

Trp Ser Pro Thr Pro Arg Cys Ile Arg Val Lys Thr Cys Ser Lys Ser
 115 120 125

Ser Ile Asp Ile Glu Asn Gly Phe Ile Ser Glu Ser Gln Tyr Thr Tyr
 130 135 140

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

Ala Asp Gly Glu Thr Ser Gly Ser Ile Thr Cys Gly Lys Asp Gly Trp
 165 170 175

Ser Ala Gln Pro Thr Cys Ile Lys
 180

<210> 40

<211> 124

<212> PRT

<213> 人工序列

<220>

<223> 补体因子H CCP 19-20 (UniProt: P08603 残基1107到1230)

<400> 40

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

<210> 41

<211> 185

<212> PRT

<213> 人工序列

<220>

<223> 补体因子H同种型FHL-1 (UniProt: P08603-2 残基265到449)

<400> 41

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

Asp Gly Trp Ser Pro Ala Val Pro Cys Leu Arg Lys Cys Tyr Phe Pro
115 120 125
Tyr Leu Glu Asn Gly Tyr Asn Gln Asn Tyr Gly Arg Lys Phe Val Gln
130 135 140
Gly Lys Ser Ile Asp Val Ala Cys His Pro Gly Tyr Ala Leu Pro Lys
145 150 155 160
Ala Gln Thr Thr Val Thr Cys Met Glu Asn Gly Trp Ser Pro Thr Pro
165 170 175
Arg Cys Ile Arg Val Ser Phe Thr Leu
180 185

<210> 42

<211> 1719

<212> DNA

<213> 人工序列

<220>

<223> His-标签的糖基化嵌合FH-FI蛋白质编码序列

<400> 42

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tatagggaga cccaagctgg ctagcgttta aacttaagct tgccaccatg agactgctgg 60
ccaagatcat ctgcctgatg ctgtgggcca tctgcgtggc ccaccaccat caccatcacg 120
gcagcagcga gaacctgtac ttccaaggca gctccggcga ggactgcaat gagctgcctc 180
ctagacggaa caccgagatc ctgacaggct cttggagcga ccagacatac cctgagggaa 240
cccaggccat ctacaagtgc agacccggct acagaagcct gggcaacatc atcatggtct 300
gccggaaagg cgagtgggtc gccctgaatc ctctgcggaa gtgccagaaa agaccctgcg 360
gacaccctgg cgatacccct ttcggaacct ttacactgac cggcggcaac gtgttcgagt 420
acggcgtgaa agccgtgtac acctgtaacg agggctacca gctgctgggc gagatcaact 480
acagagagtg cgataccgac ggctggacca acgacatccc tatctgcgag gtggtcaagt 540
gcctgcctgt gacagcccct gagaacggca agattgtgtc cagcgccatg gaacccgaca 600
gagagtacca ctttggccag gccgtcagat tcgtgtgcaa cagcggctac aagatcgagg 660
gcgacgagga aatgcactgc agcgacgatg gcttctggtc caaagaaaag cctaagtgcg 720
tggaatatcag ctgcaagagc cccgacgtga tcaacggcag ccctatcagc cagaagatta 780
tctacaaaaga gaacgagcgg ttccagtaca agtghtaacat gggctacgag tacagcgaga 840
ggggcgacgc cgtgtgtaca gaatctggat ggcgacctct gcctagctgc gaagaaggtg 900
gcggaggatc tagaggcgga ggcggaagtg gcggtggtgg atctatcggt ggaggcaaga 960
gagcacagct gggcgacctt ccatggcagg ttgccatcaa ggatgccagc ggcacacat 1020
gcggcggcac ctatatcggc ggctgctgga ttctgaccgc cgctcattgt ctgagagcca 1080
gcaagaccca ccggtatcag atctggacca ccgtggtgga ctggattcac cccgacctga 1140
agcggatcgt gatcgagtat gtggaccgga tcatcttcca cgagaactac aacgccggca 1200
cctaccagaa cgatatcgcc ctgatcgaga tgaagaagga cggcaacaag aaggactgcg 1260
agctgcccag atctatccct gctgctgttc cttggagccc ctacctgttc cagcctaacg 1320

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atacctgcat cgtgtccggc tggggcagag agaaggacaa cgaaagggtg ttcagcctgc 1380
 agtggggcgca agtgaagctg atctccaact gcagcaagtt ctacggcaac cggttctacg 1440
 agaaagaaat ggaatgcgcc ggcacatacg acggctccat cgatgcctgt aaaggcgatt 1500
 ctggcggccc tctcgtgtgc atggatgcca acaatgtgac ctacgtgtgg ggcgtcgtgt 1560
 cctggggaga gaattgtggc aagcctgagt tccccggcgt gtacacaaag gtggccaact 1620
 acttcgactg gatcagctac cacgtgggca gacccttcat cagccagtac aacgttgcgg 1680
 ccgctcgagt ctagagggcc cgtttaaacc cgctgatca 1719

<210> 43

<211> 1718

<212> DNA

<213> 人工序列

<220>

<223> His-标签的非糖基化嵌合FH-FI蛋白质编码序列

<400> 43

ataggagac ccaagctggc tagcgtttaa acttaagctt gccaccatga gactgctggc 60
 caagatcatc tgcctgatgc tgtgggccat ctgcgtggcc caccaccatc accatcacgg 120
 cagcagcgag aacctgtact tccaaggcag ctccggcgag gactgcaatg agctgcctcc 180
 tagacggaac accgagatcc tgacaggctc ttggagcgac cagacatacc ctgagggaac 240
 ccaggccatc tacaagtga gacccggcta cagaagcctg ggcaacatca tcatggtctg 300
 ccggaaaggc gagtgggtcg ccctgaatcc tctgcggaag tgccagaaaa gaccctgcgg 360
 acaccctggc gatacccctt tcggaacctt tacactgacc ggcggcaacg tgttcgagta 420
 cggcgtgaaa gccgtgtaca cctgtaacga gggctaccag ctgctgggcg agatcaacta 480
 cagagagtgc gataccgacg gctggaccaa cgacatccct atctgcgagg tggtaagtgc 540
 cctgcctgtg acagcccctg agaacggcaa gatttgttcc agcgccatgg aaccgcacag 600
 agagtaccac tttggccagg ccgtcagatt cgtgtgcaac agcggctaca agatcgaggg 660
 cgacgaggaa atgcactgca gcgacgatgg cttctggtcc aaagaaaagc ctaagtgcgt 720
 ggaaatcagc tgcaagagcc ccgacgtgat caacggcagc cctatcagcc agaagattat 780
 ctacaaagag aacgagcggc tccagtacaa gtgtaacatg ggctacgagt acagcgagag 840
 gggcgacgcc gtgtgtacag aatctggatg gcgacctctg cctagctgcg aagaaggtgg 900
 cggaggatct agaggcggag gcggaagtgg cgggtggtga tctatcgttg gaggcaagag 960
 agcacagctg ggcgaccttc catggcaggt tgccatcaag gatgccagcg gcatcacatg 1020
 cggcggcacg tatatcgggc gctgctggat tctgaccgcc gctcattgtc tgagagccag 1080
 caagaccac cggtatcaga tctggaccac cgtggtggac tggattcacc ccgacctgaa 1140
 gcggatcgtg atcgagtatg tggaccgat catcttccac gagaactaca acgcccgcac 1200
 ctaccagaac gatatcgccc tgatcgagat gaagaaggac ggcaacaaga aggactgcga 1260
 gctgcccaga tctatccctg ctgctgttcc ttggagcccc tacctgttcc agcctcaaga 1320
 tacctgcacg gtgtccggct ggggcagaga gaaggacaac gaaagggtgt tcagcctgca 1380
 gtggggcgaa gtgaagctga tctcccagtg cagcaagttc tacggcaacc ggttctacga 1440
 gaaagaaatg gaatgcgccg gcacatacga cggctccatc gatgcctgta aaggcgattc 1500

tggcggccct ctcgtgtgca tggatgccaa tcaagtgacc tacgtgtggg gcgtcgtgtc 1560
 ctggggagag aattgtggca agcctgagtt ccccggcgtg tacacaaagg tggccaacta 1620
 cttcgactgg atcagctacc acgtgggcag acccttcac agccagtaca acgttgccgc 1680
 cgctcgagtc tagagggccc gtttaaacc gctgatca 1718

<210> 44

<211> 1665

<212> DNA

<213> 人工序列

<220>

<223> 非糖基化嵌合FH-FI蛋白质编码序列

<400> 44

tatagggaga cccaagctgg ctagcgttta aacttaagct tgccaccatg agactgctgg 60
 ccaagatcat ctgcctgatg ctgtgggcca tctgcgtggc cgaggattgc aatgagctgc 120
 ctccctcgag aaacaccgag atcctgacag gctcttggag cgaccagaca taccctgagg 180
 gaaccaggc catctacaag tgcagacccg gctacagaag cctgggcaac atcatcatgg 240
 tctgccggaa aggcgagtgg gtcgccctga atcctctgcg gaagtgccag aaaagaccct 300
 gcggacaccc tggcgatacc cctttcgaa cctttacact gaccggcggc aacgtgttcg 360
 agtacggcgt gaaagccgtg tacacctgta acgagggcta ccagctgctg ggcgagatca 420
 actacagaga gtgcgatacc gacggctgga ccaacgacat ccctatctgc gaggtggtca 480
 agtgccctgcc tgtgacagcc cctgagaacg gcaagattgt gtccagcgcc atggaaccgc 540
 acagagagta ccactttggc caggccgtca gattcgtgtg caacagcggc tacaagatcg 600
 agggcgacga ggaaatgcac tgcagcgacg atggcttctg gtccaaagaa aagcctaagt 660
 gcgtggaaat cagctgcaag agccccgacg tgatcaacgg cagccctatc agccagaaga 720
 ttatctacaa agagaacgag cggttccagt acaagtgtaa catgggctac gagtacagcg 780
 agagggggcga cgccgtgtgt acagaatctg gatggcgacc tctgcctagc tgcgaagaag 840
 gtggcggagg atctagaggc ggaggcggaa gtggcggtgg tggatctatc gttggaggca 900
 agagagcaca gctgggcgac ctgccttggc aggttgccat taaggatgcc agcggcatca 960
 cctgtggcgg catctatatc ggcggtgct ggattctgac cgccgctcat tgtctgagag 1020
 ccagcaagac ccaccggtat cagatctgga ccaccgtggt ggactggatt caccgacg 1080
 tgaagcggat cgtgatcgag tatgtggacc ggatcatctt ccacgagaac tacaacgccg 1140
 gcacctacca gaacgatatc gccctgatcg agatgaagaa ggacggcaac aagaaggact 1200
 gcgagctgcc cagatctatc cctgctgctg ttcttggag ccctacctg ttccagcctc 1260
 aagatacctg catcgtgtcc ggctggggca gagagaagga caacgaaagg gtgttcagcc 1320
 tgcagtgggg cgaagtgaag ctgatctccc agtgacgaa gttctacggc aaccggttct 1380
 acgagaaaga aatggaatgc gccggcaca acgacggctc catcgatgcc tgtaaaggcg 1440
 attctggcgg ccctctcgtg tgcattgatg ccaatcaagt gacctacgtg tggggcgctc 1500
 tgtcctgggg agagaattgt ggcaagcctg agttccccgg cgtgtacaca aaggtggcca 1560
 actacttcga ctggatcagc taccacgtgg gcagaccctt catcagccag tacaacgtct 1620
 gagcggccgc tcgagtctag agggcccggt taaaccgct gatca 1665

<210> 45

<211> 5

<212> PRT

<213> 人工序列

<220>

<223> G4S接头

<400> 45

Gly Gly Gly Gly Ser

1 5

<210> 46

<211> 24

<212> PRT

<213> 人工序列

<220>

<223> 胰蛋白酶肽

<400> 46

Gly Asp Ala Val Cys Thr Glu Ser Gly Trp Arg Pro Leu Pro Ser Cys

1 5 10 15

Glu Glu Gly Gly Gly Gly Ser Arg

20

<210> 47

<211> 15

<212> PRT

<213> 人工序列

<220>

<223> 胰蛋白酶肽

<400> 47

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Ile Val Gly Gly Lys

1 5 10 15

<210> 48

<211> 16

<212> PRT

<213> 人工序列

<220>

<223> G4S-K- (G4S) 2接头

<400> 48

Gly Gly Gly Gly Ser Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser

1 5 10 15

<210> 49

<211> 506

<212> PRT

<213> 人工序列

<220>

<223> 糖基化嵌合FH-FI蛋白氨基酸序列(无信号肽)

<400> 49

Glu	Asp	Cys	Asn	Glu	Leu	Pro	Pro	Arg	Arg	Asn	Thr	Glu	Ile	Leu	Thr
1				5				10						15	
Gly	Ser	Trp	Ser	Asp	Gln	Thr	Tyr	Pro	Glu	Gly	Thr	Gln	Ala	Ile	Tyr
			20					25						30	
Lys	Cys	Arg	Pro	Gly	Tyr	Arg	Ser	Leu	Gly	Asn	Ile	Ile	Met	Val	Cys
			35					40						45	
Arg	Lys	Gly	Glu	Trp	Val	Ala	Leu	Asn	Pro	Leu	Arg	Lys	Cys	Gln	Lys
			50					55						60	
Arg	Pro	Cys	Gly	His	Pro	Gly	Asp	Thr	Pro	Phe	Gly	Thr	Phe	Thr	Leu
65					70					75					80
Thr	Gly	Gly	Asn	Val	Phe	Glu	Tyr	Gly	Val	Lys	Ala	Val	Tyr	Thr	Cys
				85						90					95
Asn	Glu	Gly	Tyr	Gln	Leu	Leu	Gly	Glu	Ile	Asn	Tyr	Arg	Glu	Cys	Asp
				100						105					110
Thr	Asp	Gly	Trp	Thr	Asn	Asp	Ile	Pro	Ile	Cys	Glu	Val	Val	Lys	Cys
				115						120					125
Leu	Pro	Val	Thr	Ala	Pro	Glu	Asn	Gly	Lys	Ile	Val	Ser	Ser	Ala	Met
				130						135					140
Glu	Pro	Asp	Arg	Glu	Tyr	His	Phe	Gly	Gln	Ala	Val	Arg	Phe	Val	Cys
145					150					155					160
Asn	Ser	Gly	Tyr	Lys	Ile	Glu	Gly	Asp	Glu	Glu	Met	His	Cys	Ser	Asp
				165						170					175
Asp	Gly	Phe	Trp	Ser	Lys	Glu	Lys	Pro	Lys	Cys	Val	Glu	Ile	Ser	Cys
				180						185					190
Lys	Ser	Pro	Asp	Val	Ile	Asn	Gly	Ser	Pro	Ile	Ser	Gln	Lys	Ile	Ile
				195						200					205
Tyr	Lys	Glu	Asn	Glu	Arg	Phe	Gln	Tyr	Lys	Cys	Asn	Met	Gly	Tyr	Glu
				210						215					220
Tyr	Ser	Glu	Arg	Gly	Asp	Ala	Val	Cys	Thr	Glu	Ser	Gly	Trp	Arg	Pro
225					230					235					240
Leu	Pro	Ser	Cys	Glu	Glu	Gly	Gly	Gly	Gly	Ser	Arg	Gly	Gly	Gly	Gly
				245						250					255
Ser	Gly	Gly	Gly	Gly	Ser	Ile	Val	Gly	Gly	Lys	Arg	Ala	Gln	Leu	Gly

260	265	270
Asp Leu Pro Trp Gln Val Ala Ile Lys Asp Ala Ser Gly Ile Thr Cys		
275	280	285
Gly Gly Ile Tyr Ile Gly Gly Cys Trp Ile Leu Thr Ala Ala His Cys		
290	295	300
Leu Arg Ala Ser Lys Thr His Arg Tyr Gln Ile Trp Thr Thr Val Val		
305	310	315
Asp Trp Ile His Pro Asp Leu Lys Arg Ile Val Ile Glu Tyr Val Asp		
325	330	335
Arg Ile Ile Phe His Glu Asn Tyr Asn Ala Gly Thr Tyr Gln Asn Asp		
340	345	350
Ile Ala Leu Ile Glu Met Lys Lys Asp Gly Asn Lys Lys Asp Cys Glu		
355	360	365
Leu Pro Arg Ser Ile Pro Ala Ala Val Pro Trp Ser Pro Tyr Leu Phe		
370	375	380
Gln Pro Asn Asp Thr Cys Ile Val Ser Gly Trp Gly Arg Glu Lys Asp		
385	390	395
Asn Glu Arg Val Phe Ser Leu Gln Trp Gly Glu Val Lys Leu Ile Ser		
405	410	415
Asn Cys Ser Lys Phe Tyr Gly Asn Arg Phe Tyr Glu Lys Glu Met Glu		
420	425	430
Cys Ala Gly Thr Tyr Asp Gly Ser Ile Asp Ala Cys Lys Gly Asp Ser		
435	440	445
Gly Gly Pro Leu Val Cys Met Asp Ala Asn Asn Val Thr Tyr Val Trp		
450	455	460
Gly Val Val Ser Trp Gly Glu Asn Cys Gly Lys Pro Glu Phe Pro Gly		
465	470	475
Val Tyr Thr Lys Val Ala Asn Tyr Phe Asp Trp Ile Ser Tyr His Val		
485	490	495
Gly Arg Pro Phe Ile Ser Gln Tyr Asn Val		
500	505	
<210> 50		
<211> 502		
<212> PRT		
<213> 人工序列		
<220>		
<223> His-标签的糖基化嵌合CR1a-FI蛋白氨基酸序列		
<400> 50		
Met Arg Leu Leu Ala Lys Ile Ile Cys Leu Met Leu Trp Ala Ile Cys		

1													5													10													15												
Val	Ala	His	His	His	His	His	His	His	Gly	Ser	Ser	Glu	Asn	Leu	Tyr	Phe																																			
																20																	25																	30	
Gln	Gly	Ser	Ser	Gly	Gly	His	Cys	Gln	Ala	Pro	Asp	His	Phe	Leu	Phe																																				
																35																	40																	45	
Ala	Lys	Leu	Lys	Thr	Gln	Thr	Asn	Ala	Ser	Asp	Phe	Pro	Ile	Gly	Thr																																				
																50																	55																	60	
Ser	Leu	Lys	Tyr	Glu	Cys	Arg	Pro	Glu	Tyr	Tyr	Gly	Arg	Pro	Phe	Ser																																				
65																	70																	75																	80
Ile	Thr	Cys	Leu	Asp	Asn	Leu	Val	Trp	Ser	Ser	Pro	Lys	Asp	Val	Cys																																				
																85																	90																	95	
Lys	Arg	Lys	Ser	Cys	Lys	Thr	Pro	Pro	Asp	Pro	Val	Asn	Gly	Met	Val																																				
																100																	105																	110	
His	Val	Ile	Thr	Asp	Ile	Gln	Val	Gly	Ser	Arg	Ile	Asn	Tyr	Ser	Cys																																				
																115																	120																	125	
Thr	Thr	Gly	His	Arg	Leu	Ile	Gly	His	Ser	Ser	Ala	Glu	Cys	Ile	Leu																																				
																130																	135																	140	
Ser	Gly	Asn	Ala	Ala	His	Trp	Ser	Thr	Lys	Pro	Pro	Ile	Cys	Gln	Arg																																				
145																	150																	155																	160
Ile	Pro	Cys	Gly	Leu	Pro	Pro	Thr	Ile	Ala	Asn	Gly	Asp	Phe	Ile	Ser																																				
																165																	170																	175	
Thr	Asn	Arg	Glu	Asn	Phe	His	Tyr	Gly	Ser	Val	Val	Thr	Tyr	Arg	Cys																																				
																180																	185																	190	
Asn	Pro	Gly	Ser	Gly	Gly	Arg	Lys	Val	Phe	Glu	Leu	Val	Gly	Glu	Pro																																				
																195																	200																	205	
Ser	Ile	Tyr	Cys	Thr	Ser	Asn	Asp	Asp	Gln	Val	Gly	Ile	Trp	Ser	Gly																																				
																210																	215																	220	
Pro	Ala	Pro	Gln	Cys	Ile	Ile	Pro	Asn	Lys	Ala	Thr	Pro	Pro	Asn	Val																																				
225																	230																	235																	240
Glu	Asn	Gly	Gly	Gly	Gly	Ser	Arg	Gly	Gly	Gly	Gly	Ser	Gly	Gly	Gly																																				
																245																	250																	255	
Gly	Ser	Ile	Val	Gly	Gly	Lys	Arg	Ala	Gln	Leu	Gly	Asp	Leu	Pro	Trp																																				
																260																	265																	270	
Gln	Val	Ala	Ile	Lys	Asp	Ala	Ser	Gly	Ile	Thr	Cys	Gly	Gly	Ile	Tyr																																				
																275																	280																	285	
Ile	Gly	Gly	Cys	Trp	Ile	Leu	Thr	Ala	Ala	His	Cys	Leu	Arg	Ala	Ser																																				
																290																	295																	300	
Lys	Thr	His	Arg	Tyr	Gln	Ile	Trp	Thr	Thr	Val	Val	Asp	Trp	Ile	His																																				
305																	310																	315																	320

Pro Asp Leu Lys Arg Ile Val Ile Glu Tyr Val Asp Arg Ile Ile Phe
 325 330 335
 His Glu Asn Tyr Asn Ala Gly Thr Tyr Gln Asn Asp Ile Ala Leu Ile
 340 345 350
 Glu Met Lys Lys Asp Gly Asn Lys Lys Asp Cys Glu Leu Pro Arg Ser
 355 360 365
 Ile Pro Ala Ala Val Pro Trp Ser Pro Tyr Leu Phe Gln Pro Asn Asp
 370 375 380
 Thr Cys Ile Val Ser Gly Trp Gly Arg Glu Lys Asp Asn Glu Arg Val
 385 390 395 400
 Phe Ser Leu Gln Trp Gly Glu Val Lys Leu Ile Ser Asn Cys Ser Lys
 405 410 415
 Phe Tyr Gly Asn Arg Phe Tyr Glu Lys Glu Met Glu Cys Ala Gly Thr
 420 425 430
 Tyr Asp Gly Ser Ile Asp Ala Cys Lys Gly Asp Ser Gly Gly Pro Leu
 435 440 445
 Val Cys Met Asp Ala Asn Asn Val Thr Tyr Val Trp Gly Val Val Ser
 450 455 460
 Trp Gly Glu Asn Cys Gly Lys Pro Glu Phe Pro Gly Val Tyr Thr Lys
 465 470 475 480
 Val Ala Asn Tyr Phe Asp Trp Ile Ser Tyr His Val Gly Arg Pro Phe
 485 490 495
 Ile Ser Gln Tyr Asn Val
 500

<210> 51

<211> 502

<212> PRT

<213> 人工序列

<220>

<223> His-标签的糖基化嵌合CR1b-FI蛋白氨基酸序列

<400> 51

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

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

370	375	380
Thr Cys Ile Val Ser Gly Trp Gly Arg Glu Lys Asp Asn Glu Arg Val		
385	390	395
Phe Ser Leu Gln Trp Gly Glu Val Lys Leu Ile Ser Asn Cys Ser Lys		400
	405	410
Phe Tyr Gly Asn Arg Phe Tyr Glu Lys Glu Met Glu Cys Ala Gly Thr		415
	420	425
Tyr Asp Gly Ser Ile Asp Ala Cys Lys Gly Asp Ser Gly Gly Pro Leu		430
	435	440
Val Cys Met Asp Ala Asn Asn Val Thr Tyr Val Trp Gly Val Val Ser		445
	450	455
Trp Gly Glu Asn Cys Gly Lys Pro Glu Phe Pro Gly Val Tyr Thr Lys		460
465	470	475
Val Ala Asn Tyr Phe Asp Trp Ile Ser Tyr His Val Gly Arg Pro Phe		480
	485	490
Ile Ser Gln Tyr Asn Val		495
	500	

<210> 52

<211> 502

<212> PRT

<213> 人工序列

<220>

<223> His-标签的非糖基化嵌合CR1a-FI蛋白氨基酸序列

<400> 52

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

115	120	125
Thr Thr Gly His Arg Leu Ile Gly His Ser Ser Ala Glu Cys Ile Leu		
130	135	140
Ser Gly Asn Ala Ala His Trp Ser Thr Lys Pro Pro Ile Cys Gln Arg		
145	150	155
Ile Pro Cys Gly Leu Pro Pro Thr Ile Ala Asn Gly Asp Phe Ile Ser		
165	170	175
Thr Asn Arg Glu Asn Phe His Tyr Gly Ser Val Val Thr Tyr Arg Cys		
180	185	190
Asn Pro Gly Ser Gly Gly Arg Lys Val Phe Glu Leu Val Gly Glu Pro		
195	200	205
Ser Ile Tyr Cys Thr Ser Asn Asp Asp Gln Val Gly Ile Trp Ser Gly		
210	215	220
Pro Ala Pro Gln Cys Ile Ile Pro Asn Lys Ala Thr Pro Pro Asn Val		
225	230	235
Glu Asn Gly Gly Gly Gly Ser Arg Gly Gly Gly Gly Ser Gly Gly Gly		
245	250	255
Gly Ser Ile Val Gly Gly Lys Arg Ala Gln Leu Gly Asp Leu Pro Trp		
260	265	270
Gln Val Ala Ile Lys Asp Ala Ser Gly Ile Thr Cys Gly Gly Ile Tyr		
275	280	285
Ile Gly Gly Cys Trp Ile Leu Thr Ala Ala His Cys Leu Arg Ala Ser		
290	295	300
Lys Thr His Arg Tyr Gln Ile Trp Thr Thr Val Val Asp Trp Ile His		
305	310	315
Pro Asp Leu Lys Arg Ile Val Ile Glu Tyr Val Asp Arg Ile Ile Phe		
325	330	335
His Glu Asn Tyr Asn Ala Gly Thr Tyr Gln Asn Asp Ile Ala Leu Ile		
340	345	350
Glu Met Lys Lys Asp Gly Asn Lys Lys Asp Cys Glu Leu Pro Arg Ser		
355	360	365
Ile Pro Ala Ala Val Pro Trp Ser Pro Tyr Leu Phe Gln Pro Gln Asp		
370	375	380
Thr Cys Ile Val Ser Gly Trp Gly Arg Glu Lys Asp Asn Glu Arg Val		
385	390	395
Phe Ser Leu Gln Trp Gly Glu Val Lys Leu Ile Ser Gln Cys Ser Lys		
405	410	415
Phe Tyr Gly Asn Arg Phe Tyr Glu Lys Glu Met Glu Cys Ala Gly Thr		
420	425	430

Tyr Asp Gly Ser Ile Asp Ala Cys Lys Gly Asp Ser Gly Gly Pro Leu
 435 440 445
 Val Cys Met Asp Ala Asn Gln Val Thr Tyr Val Trp Gly Val Val Ser
 450 455 460
 Trp Gly Glu Asn Cys Gly Lys Pro Glu Phe Pro Gly Val Tyr Thr Lys
 465 470 475 480
 Val Ala Asn Tyr Phe Asp Trp Ile Ser Tyr His Val Gly Arg Pro Phe
 485 490 495
 Ile Ser Gln Tyr Asn Val
 500

<210> 53

<211> 502

<212> PRT

<213> 人工序列

<220>

<223> His-标签的非糖基化嵌合CR1b-FI蛋白氨基酸序列

<400> 53

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

Thr Asn Arg Glu Asn Phe His Tyr Gly Ser Val Val Thr Tyr Arg Cys		
180	185	190
Asn Pro Gly Ser Gly Gly Arg Lys Val Phe Glu Leu Val Gly Glu Pro		
195	200	205
Ser Ile Tyr Cys Thr Ser Asn Asp Asp Gln Val Gly Ile Trp Ser Gly		
210	215	220
Pro Ala Pro Gln Cys Ile Ile Pro Asn Lys Ala Thr Pro Pro Asn Val		
225	230	235
Glu Asn Gly Gly Gly Gly Ser Arg Gly Gly Gly Ser Gly Gly Gly		
245	250	255
Gly Ser Ile Val Gly Gly Lys Arg Ala Gln Leu Gly Asp Leu Pro Trp		
260	265	270
Gln Val Ala Ile Lys Asp Ala Ser Gly Ile Thr Cys Gly Gly Ile Tyr		
275	280	285
Ile Gly Gly Cys Trp Ile Leu Thr Ala Ala His Cys Leu Arg Ala Ser		
290	295	300
Lys Thr His Arg Tyr Gln Ile Trp Thr Thr Val Val Asp Trp Ile His		
305	310	315
Pro Asp Leu Lys Arg Ile Val Ile Glu Tyr Val Asp Arg Ile Ile Phe		
325	330	335
His Glu Asn Tyr Asn Ala Gly Thr Tyr Gln Asn Asp Ile Ala Leu Ile		
340	345	350
Glu Met Lys Lys Asp Gly Asn Lys Lys Asp Cys Glu Leu Pro Arg Ser		
355	360	365
Ile Pro Ala Ala Val Pro Trp Ser Pro Tyr Leu Phe Gln Pro Gln Asp		
370	375	380
Thr Cys Ile Val Ser Gly Trp Gly Arg Glu Lys Asp Asn Glu Arg Val		
385	390	395
Phe Ser Leu Gln Trp Gly Glu Val Lys Leu Ile Ser Gln Cys Ser Lys		
405	410	415
Phe Tyr Gly Asn Arg Phe Tyr Glu Lys Glu Met Glu Cys Ala Gly Thr		
420	425	430
Tyr Asp Gly Ser Ile Asp Ala Cys Lys Gly Asp Ser Gly Gly Pro Leu		
435	440	445
Val Cys Met Asp Ala Asn Gln Val Thr Tyr Val Trp Gly Val Val Ser		
450	455	460
Trp Gly Glu Asn Cys Gly Lys Pro Glu Phe Pro Gly Val Tyr Thr Lys		
465	470	475
Val Ala Asn Tyr Phe Asp Trp Ile Ser Tyr His Val Gly Arg Pro Phe		

485	490	495
Ile Ser Gln Tyr Asn Val		
500		
<210> 54		
<211> 484		
<212> PRT		
<213> 人工序列		
<220>		
<223> His-标签的糖基化嵌合CR1a-FI蛋白氨基酸序列(无信号肽)		
<400> 54		
His His His His His His Gly Ser Ser Glu Asn Leu Tyr Phe Gln Gly		
1 5 10 15		
Ser Ser Gly Gly His Cys Gln Ala Pro Asp His Phe Leu Phe Ala Lys		
20 25 30		
Leu Lys Thr Gln Thr Asn Ala Ser Asp Phe Pro Ile Gly Thr Ser Leu		
35 40 45		
Lys Tyr Glu Cys Arg Pro Glu Tyr Tyr Gly Arg Pro Phe Ser Ile Thr		
50 55 60		
Cys Leu Asp Asn Leu Val Trp Ser Ser Pro Lys Asp Val Cys Lys Arg		
65 70 75 80		
Lys Ser Cys Lys Thr Pro Pro Asp Pro Val Asn Gly Met Val His Val		
85 90 95		
Ile Thr Asp Ile Gln Val Gly Ser Arg Ile Asn Tyr Ser Cys Thr Thr		
100 105 110		
Gly His Arg Leu Ile Gly His Ser Ser Ala Glu Cys Ile Leu Ser Gly		
115 120 125		
Asn Ala Ala His Trp Ser Thr Lys Pro Pro Ile Cys Gln Arg Ile Pro		
130 135 140		
Cys Gly Leu Pro Pro Thr Ile Ala Asn Gly Asp Phe Ile Ser Thr Asn		
145 150 155 160		
Arg Glu Asn Phe His Tyr Gly Ser Val Val Thr Tyr Arg Cys Asn Pro		
165 170 175		
Gly Ser Gly Gly Arg Lys Val Phe Glu Leu Val Gly Glu Pro Ser Ile		
180 185 190		
Tyr Cys Thr Ser Asn Asp Asp Gln Val Gly Ile Trp Ser Gly Pro Ala		
195 200 205		
Pro Gln Cys Ile Ile Pro Asn Lys Ala Thr Pro Pro Asn Val Glu Asn		
210 215 220		
Gly Gly Gly Gly Ser Arg Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser		

225	230	235	240
Ile Val Gly Gly Lys Arg Ala Gln Leu Gly Asp Leu Pro Trp Gln Val			
	245	250	255
Ala Ile Lys Asp Ala Ser Gly Ile Thr Cys Gly Gly Ile Tyr Ile Gly			
	260	265	270
Gly Cys Trp Ile Leu Thr Ala Ala His Cys Leu Arg Ala Ser Lys Thr			
	275	280	285
His Arg Tyr Gln Ile Trp Thr Thr Val Val Asp Trp Ile His Pro Asp			
	290	295	300
Leu Lys Arg Ile Val Ile Glu Tyr Val Asp Arg Ile Ile Phe His Glu			
305	310	315	320
Asn Tyr Asn Ala Gly Thr Tyr Gln Asn Asp Ile Ala Leu Ile Glu Met			
	325	330	335
Lys Lys Asp Gly Asn Lys Lys Asp Cys Glu Leu Pro Arg Ser Ile Pro			
	340	345	350
Ala Ala Val Pro Trp Ser Pro Tyr Leu Phe Gln Pro Asn Asp Thr Cys			
	355	360	365
Ile Val Ser Gly Trp Gly Arg Glu Lys Asp Asn Glu Arg Val Phe Ser			
	370	375	380
Leu Gln Trp Gly Glu Val Lys Leu Ile Ser Asn Cys Ser Lys Phe Tyr			
385	390	395	400
Gly Asn Arg Phe Tyr Glu Lys Glu Met Glu Cys Ala Gly Thr Tyr Asp			
	405	410	415
Gly Ser Ile Asp Ala Cys Lys Gly Asp Ser Gly Gly Pro Leu Val Cys			
	420	425	430
Met Asp Ala Asn Asn Val Thr Tyr Val Trp Gly Val Val Ser Trp Gly			
	435	440	445
Glu Asn Cys Gly Lys Pro Glu Phe Pro Gly Val Tyr Thr Lys Val Ala			
	450	455	460
Asn Tyr Phe Asp Trp Ile Ser Tyr His Val Gly Arg Pro Phe Ile Ser			
465	470	475	480
Gln Tyr Asn Val			
<210> 55			
<211> 484			
<212> PRT			
<213> 人工序列			
<220>			
<223> His-标签的糖基化嵌合CR1b-FI蛋白氨基酸序列(无信号肽)			
<400> 55			

His	His	His	His	His	His	Gly	Ser	Ser	Glu	Asn	Leu	Tyr	Phe	Gln	Gly
1				5					10					15	
Ser	Ser	Gly	Gly	His	Cys	Gln	Ala	Pro	Asp	His	Phe	Leu	Phe	Ala	Lys
			20					25						30	
Leu	Lys	Thr	Gln	Thr	Asn	Ala	Ser	Asp	Phe	Pro	Ile	Gly	Thr	Ser	Leu
			35					40						45	
Lys	Tyr	Glu	Cys	Arg	Pro	Glu	Tyr	Tyr	Gly	Arg	Pro	Phe	Ser	Ile	Thr
			50					55						60	
Cys	Leu	Asp	Asn	Leu	Val	Trp	Ser	Ser	Pro	Lys	Asp	Val	Cys	Lys	Arg
65					70					75					80
Lys	Ser	Cys	Lys	Thr	Pro	Pro	Asp	Pro	Val	Asn	Gly	Met	Val	His	Val
					85					90					95
Ile	Thr	Asp	Ile	Gln	Val	Gly	Ser	Arg	Ile	Asn	Tyr	Ser	Cys	Thr	Thr
					100					105				110	
Gly	His	Arg	Leu	Ile	Gly	His	Ser	Ser	Ala	Glu	Cys	Ile	Leu	Ser	Gly
					115					120				125	
Asn	Thr	Ala	His	Trp	Ser	Thr	Lys	Pro	Pro	Ile	Cys	Gln	Arg	Ile	Pro
					130					135				140	
Cys	Gly	Leu	Pro	Pro	Thr	Ile	Ala	Asn	Gly	Asp	Phe	Ile	Ser	Thr	Asn
145						150				155					160
Arg	Glu	Asn	Phe	His	Tyr	Gly	Ser	Val	Val	Thr	Tyr	Arg	Cys	Asn	Leu
					165					170					175
Gly	Ser	Arg	Gly	Arg	Lys	Val	Phe	Glu	Leu	Val	Gly	Glu	Pro	Ser	Ile
					180					185				190	
Tyr	Cys	Thr	Ser	Asn	Asp	Asp	Gln	Val	Gly	Ile	Trp	Ser	Gly	Pro	Ala
					195					200				205	
Pro	Gln	Cys	Ile	Ile	Pro	Asn	Lys	Ala	Thr	Pro	Pro	Asn	Val	Glu	Asn
					210					215				220	
Gly	Gly	Gly	Gly	Ser	Arg	Gly	Gly	Gly	Gly	Ser	Gly	Gly	Gly	Gly	Ser
225						230				235					240
Ile	Val	Gly	Gly	Lys	Arg	Ala	Gln	Leu	Gly	Asp	Leu	Pro	Trp	Gln	Val
					245					250					255
Ala	Ile	Lys	Asp	Ala	Ser	Gly	Ile	Thr	Cys	Gly	Gly	Ile	Tyr	Ile	Gly
					260					265				270	
Gly	Cys	Trp	Ile	Leu	Thr	Ala	Ala	His	Cys	Leu	Arg	Ala	Ser	Lys	Thr
					275					280				285	
His	Arg	Tyr	Gln	Ile	Trp	Thr	Thr	Val	Val	Asp	Trp	Ile	His	Pro	Asp
					290					295				300	
Leu	Lys	Arg	Ile	Val	Ile	Glu	Tyr	Val	Asp	Arg	Ile	Ile	Phe	His	Glu

305	310	315	320
Asn Tyr Asn Ala Gly Thr Tyr Gln Asn Asp Ile Ala Leu Ile Glu Met			
	325	330	335
Lys Lys Asp Gly Asn Lys Lys Asp Cys Glu Leu Pro Arg Ser Ile Pro			
	340	345	350
Ala Ala Val Pro Trp Ser Pro Tyr Leu Phe Gln Pro Asn Asp Thr Cys			
	355	360	365
Ile Val Ser Gly Trp Gly Arg Glu Lys Asp Asn Glu Arg Val Phe Ser			
	370	375	380
Leu Gln Trp Gly Glu Val Lys Leu Ile Ser Asn Cys Ser Lys Phe Tyr			
385	390	395	400
Gly Asn Arg Phe Tyr Glu Lys Glu Met Glu Cys Ala Gly Thr Tyr Asp			
	405	410	415
Gly Ser Ile Asp Ala Cys Lys Gly Asp Ser Gly Gly Pro Leu Val Cys			
	420	425	430
Met Asp Ala Asn Asn Val Thr Tyr Val Trp Gly Val Val Ser Trp Gly			
	435	440	445
Glu Asn Cys Gly Lys Pro Glu Phe Pro Gly Val Tyr Thr Lys Val Ala			
	450	455	460
Asn Tyr Phe Asp Trp Ile Ser Tyr His Val Gly Arg Pro Phe Ile Ser			
465	470	475	480
Gln Tyr Asn Val			
<210> 56			
<211> 484			
<212> PRT			
<213> 人工序列			
<220>			
<223> His-标签的非糖基化嵌合CR1a-FI蛋白氨基酸序列(无信号肽)			
<400> 56			
His His His His His His Gly Ser Ser Glu Asn Leu Tyr Phe Gln Gly			
1	5	10	15
Ser Ser Gly Gly His Cys Gln Ala Pro Asp His Phe Leu Phe Ala Lys			
	20	25	30
Leu Lys Thr Gln Thr Gln Ala Ser Asp Phe Pro Ile Gly Thr Ser Leu			
	35	40	45
Lys Tyr Glu Cys Arg Pro Glu Tyr Tyr Gly Arg Pro Phe Ser Ile Thr			
	50	55	60
Cys Leu Asp Asn Leu Val Trp Ser Ser Pro Lys Asp Val Cys Lys Arg			
65	70	75	80

Lys	Ser	Cys	Lys	Thr	Pro	Pro	Asp	Pro	Val	Asn	Gly	Met	Val	His	Val
85				90				95							
Ile	Thr	Asp	Ile	Gln	Val	Gly	Ser	Arg	Ile	Gln	Tyr	Ser	Cys	Thr	Thr
100				105				110							
Gly	His	Arg	Leu	Ile	Gly	His	Ser	Ser	Ala	Glu	Cys	Ile	Leu	Ser	Gly
115				120				125							
Asn	Ala	Ala	His	Trp	Ser	Thr	Lys	Pro	Pro	Ile	Cys	Gln	Arg	Ile	Pro
130				135				140							
Cys	Gly	Leu	Pro	Pro	Thr	Ile	Ala	Asn	Gly	Asp	Phe	Ile	Ser	Thr	Asn
145				150				155				160			
Arg	Glu	Asn	Phe	His	Tyr	Gly	Ser	Val	Val	Thr	Tyr	Arg	Cys	Asn	Pro
165				170				175							
Gly	Ser	Gly	Gly	Arg	Lys	Val	Phe	Glu	Leu	Val	Gly	Glu	Pro	Ser	Ile
180				185				190							
Tyr	Cys	Thr	Ser	Asn	Asp	Asp	Gln	Val	Gly	Ile	Trp	Ser	Gly	Pro	Ala
195				200				205							
Pro	Gln	Cys	Ile	Ile	Pro	Asn	Lys	Ala	Thr	Pro	Pro	Asn	Val	Glu	Asn
210				215				220							
Gly	Gly	Gly	Gly	Ser	Arg	Gly	Gly	Gly	Gly	Ser	Gly	Gly	Gly	Gly	Ser
225				230				235				240			
Ile	Val	Gly	Gly	Lys	Arg	Ala	Gln	Leu	Gly	Asp	Leu	Pro	Trp	Gln	Val
245				250				255							
Ala	Ile	Lys	Asp	Ala	Ser	Gly	Ile	Thr	Cys	Gly	Gly	Ile	Tyr	Ile	Gly
260				265				270							
Gly	Cys	Trp	Ile	Leu	Thr	Ala	Ala	His	Cys	Leu	Arg	Ala	Ser	Lys	Thr
275				280				285							
His	Arg	Tyr	Gln	Ile	Trp	Thr	Thr	Val	Val	Asp	Trp	Ile	His	Pro	Asp
290				295				300							
Leu	Lys	Arg	Ile	Val	Ile	Glu	Tyr	Val	Asp	Arg	Ile	Ile	Phe	His	Glu
305				310				315				320			
Asn	Tyr	Asn	Ala	Gly	Thr	Tyr	Gln	Asn	Asp	Ile	Ala	Leu	Ile	Glu	Met
325				330				335							
Lys	Lys	Asp	Gly	Asn	Lys	Lys	Asp	Cys	Glu	Leu	Pro	Arg	Ser	Ile	Pro
340				345				350							
Ala	Ala	Val	Pro	Trp	Ser	Pro	Tyr	Leu	Phe	Gln	Pro	Gln	Asp	Thr	Cys
355				360				365							
Ile	Val	Ser	Gly	Trp	Gly	Arg	Glu	Lys	Asp	Asn	Glu	Arg	Val	Phe	Ser
370				375				380							
Leu	Gln	Trp	Gly	Glu	Val	Lys	Leu	Ile	Ser	Gln	Cys	Ser	Lys	Phe	Tyr

385	390	395	400
Gly Asn Arg Phe Tyr Glu Lys Glu Met Glu Cys Ala Gly Thr Tyr Asp			
	405	410	415
Gly Ser Ile Asp Ala Cys Lys Gly Asp Ser Gly Gly Pro Leu Val Cys			
	420	425	430
Met Asp Ala Asn Gln Val Thr Tyr Val Trp Gly Val Val Ser Trp Gly			
	435	440	445
Glu Asn Cys Gly Lys Pro Glu Phe Pro Gly Val Tyr Thr Lys Val Ala			
	450	455	460
Asn Tyr Phe Asp Trp Ile Ser Tyr His Val Gly Arg Pro Phe Ile Ser			
465	470	475	480
Gln Tyr Asn Val			
<210> 57			
<211> 484			
<212> PRT			
<213> 人工序列			
<220>			
<223> His-标签的非糖基化嵌合CR1b-FI蛋白氨基酸序列(无信号肽)			
<400> 57			
His His His His His His Gly Ser Ser Glu Asn Leu Tyr Phe Gln Gly			
1	5	10	15
Ser Ser Gly Gly His Cys Gln Ala Pro Asp His Phe Leu Phe Ala Lys			
	20	25	30
Leu Lys Thr Gln Thr Gln Ala Ser Asp Phe Pro Ile Gly Thr Ser Leu			
	35	40	45
Lys Tyr Glu Cys Arg Pro Glu Tyr Tyr Gly Arg Pro Phe Ser Ile Thr			
	50	55	60
Cys Leu Asp Asn Leu Val Trp Ser Ser Pro Lys Asp Val Cys Lys Arg			
65	70	75	80
Lys Ser Cys Lys Thr Pro Pro Asp Pro Val Asn Gly Met Val His Val			
	85	90	95
Ile Thr Asp Ile Gln Val Gly Ser Arg Ile Gln Tyr Ser Cys Thr Thr			
	100	105	110
Gly His Arg Leu Ile Gly His Ser Ser Ala Glu Cys Ile Leu Ser Gly			
	115	120	125
Asn Ala Ala His Trp Ser Thr Lys Pro Pro Ile Cys Gln Arg Ile Pro			
	130	135	140
Cys Gly Leu Pro Pro Thr Ile Ala Asn Gly Asp Phe Ile Ser Thr Asn			
145	150	155	160

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

465	470	475	480
Gln Tyr Asn Val			
<210> 58			
<211> 465			
<212> PRT			
<213> 人工序列			
<220>			
<223> 糖基化嵌合CR1a-FI蛋白氨基酸序列(无信号肽)			
<400> 58			
Gly His Cys Gln Ala Pro Asp His Phe Leu Phe Ala Lys Leu Lys Thr			
1	5	10	15
Gln Thr Asn Ala Ser Asp Phe Pro Ile Gly Thr Ser Leu Lys Tyr Glu			
	20	25	30
Cys Arg Pro Glu Tyr Tyr Gly Arg Pro Phe Ser Ile Thr Cys Leu Asp			
	35	40	45
Asn Leu Val Trp Ser Ser Pro Lys Asp Val Cys Lys Arg Lys Ser Cys			
	50	55	60
Lys Thr Pro Pro Asp Pro Val Asn Gly Met Val His Val Ile Thr Asp			
65	70	75	80
Ile Gln Val Gly Ser Arg Ile Asn Tyr Ser Cys Thr Thr Gly His Arg			
	85	90	95
Leu Ile Gly His Ser Ser Ala Glu Cys Ile Leu Ser Gly Asn Ala Ala			
	100	105	110
His Trp Ser Thr Lys Pro Pro Ile Cys Gln Arg Ile Pro Cys Gly Leu			
	115	120	125
Pro Pro Thr Ile Ala Asn Gly Asp Phe Ile Ser Thr Asn Arg Glu Asn			
	130	135	140
Phe His Tyr Gly Ser Val Val Thr Tyr Arg Cys Asn Pro Gly Ser Gly			
145	150	155	160
Gly Arg Lys Val Phe Glu Leu Val Gly Glu Pro Ser Ile Tyr Cys Thr			
	165	170	175
Ser Asn Asp Asp Gln Val Gly Ile Trp Ser Gly Pro Ala Pro Gln Cys			
	180	185	190
Ile Ile Pro Asn Lys Ala Thr Pro Pro Asn Val Glu Asn Gly Gly Gly			
	195	200	205
Gly Ser Arg Gly Gly Gly Gly Ser Gly Gly Gly Ser Ile Val Gly			
	210	215	220
Gly Lys Arg Ala Gln Leu Gly Asp Leu Pro Trp Gln Val Ala Ile Lys			
225	230	235	240

Asp	Ala	Ser	Gly	Ile	Thr	Cys	Gly	Gly	Ile	Tyr	Ile	Gly	Gly	Cys	Trp
				245				250				255			
Ile	Leu	Thr	Ala	Ala	His	Cys	Leu	Arg	Ala	Ser	Lys	Thr	His	Arg	Tyr
				260				265				270			
Gln	Ile	Trp	Thr	Thr	Val	Val	Asp	Trp	Ile	His	Pro	Asp	Leu	Lys	Arg
				275				280				285			
Ile	Val	Ile	Glu	Tyr	Val	Asp	Arg	Ile	Ile	Phe	His	Glu	Asn	Tyr	Asn
				290				295				300			
Ala	Gly	Thr	Tyr	Gln	Asn	Asp	Ile	Ala	Leu	Ile	Glu	Met	Lys	Lys	Asp
305				310				315				320			
Gly	Asn	Lys	Lys	Asp	Cys	Glu	Leu	Pro	Arg	Ser	Ile	Pro	Ala	Ala	Val
				325				330				335			
Pro	Trp	Ser	Pro	Tyr	Leu	Phe	Gln	Pro	Asn	Asp	Thr	Cys	Ile	Val	Ser
				340				345				350			
Gly	Trp	Gly	Arg	Glu	Lys	Asp	Asn	Glu	Arg	Val	Phe	Ser	Leu	Gln	Trp
				355				360				365			
Gly	Glu	Val	Lys	Leu	Ile	Ser	Asn	Cys	Ser	Lys	Phe	Tyr	Gly	Asn	Arg
370				375				380							
Phe	Tyr	Glu	Lys	Glu	Met	Glu	Cys	Ala	Gly	Thr	Tyr	Asp	Gly	Ser	Ile
385				390				395				400			
Asp	Ala	Cys	Lys	Gly	Asp	Ser	Gly	Gly	Pro	Leu	Val	Cys	Met	Asp	Ala
				405				410				415			
Asn	Asn	Val	Thr	Tyr	Val	Trp	Gly	Val	Val	Ser	Trp	Gly	Glu	Asn	Cys
				420				425				430			
Gly	Lys	Pro	Glu	Phe	Pro	Gly	Val	Tyr	Thr	Lys	Val	Ala	Asn	Tyr	Phe
				435				440				445			
Asp	Trp	Ile	Ser	Tyr	His	Val	Gly	Arg	Pro	Phe	Ile	Ser	Gln	Tyr	Asn
450				455				460							
Val															
465															
<210> 59															
<211> 465															
<212> PRT															
<213> 人工序列															
<220>															
<223> 糖基化嵌合CR1b-FI蛋白氨基酸序列(无信号肽)															
<400> 59															
Gly	His	Cys	Gln	Ala	Pro	Asp	His	Phe	Leu	Phe	Ala	Lys	Leu	Lys	Thr
1					5					10					15

Gln	Thr	Asn	Ala	Ser	Asp	Phe	Pro	Ile	Gly	Thr	Ser	Leu	Lys	Tyr	Glu			
			20					25					30					
Cys	Arg	Pro	Glu	Tyr	Tyr	Gly	Arg	Pro	Phe	Ser	Ile	Thr	Cys	Leu	Asp			
		35					40					45						
Asn	Leu	Val	Trp	Ser	Ser	Pro	Lys	Asp	Val	Cys	Lys	Arg	Lys	Ser	Cys			
		50				55					60							
Lys	Thr	Pro	Pro	Asp	Pro	Val	Asn	Gly	Met	Val	His	Val	Ile	Thr	Asp			
65					70				75						80			
Ile	Gln	Val	Gly	Ser	Arg	Ile	Asn	Tyr	Ser	Cys	Thr	Thr	Gly	His	Arg			
				85				90						95				
Leu	Ile	Gly	His	Ser	Ser	Ala	Glu	Cys	Ile	Leu	Ser	Gly	Asn	Thr	Ala			
			100					105					110					
His	Trp	Ser	Thr	Lys	Pro	Pro	Ile	Cys	Gln	Arg	Ile	Pro	Cys	Gly	Leu			
		115					120					125						
Pro	Pro	Thr	Ile	Ala	Asn	Gly	Asp	Phe	Ile	Ser	Thr	Asn	Arg	Glu	Asn			
		130				135					140							
Phe	His	Tyr	Gly	Ser	Val	Val	Thr	Tyr	Arg	Cys	Asn	Leu	Gly	Ser	Arg			
145					150				155						160			
Gly	Arg	Lys	Val	Phe	Glu	Leu	Val	Gly	Glu	Pro	Ser	Ile	Tyr	Cys	Thr			
				165				170						175				
Ser	Asn	Asp	Asp	Gln	Val	Gly	Ile	Trp	Ser	Gly	Pro	Ala	Pro	Gln	Cys			
				180				185					190					
Ile	Ile	Pro	Asn	Lys	Ala	Thr	Pro	Pro	Asn	Val	Glu	Asn	Gly	Gly	Gly			
		195					200					205						
Gly	Ser	Arg	Gly	Gly	Gly	Gly	Ser	Gly	Gly	Gly	Gly	Ser	Ile	Val	Gly			
		210				215					220							
Gly	Lys	Arg	Ala	Gln	Leu	Gly	Asp	Leu	Pro	Trp	Gln	Val	Ala	Ile	Lys			
225					230				235						240			
Asp	Ala	Ser	Gly	Ile	Thr	Cys	Gly	Gly	Ile	Tyr	Ile	Gly	Gly	Cys	Trp			
				245				250						255				
Ile	Leu	Thr	Ala	Ala	His	Cys	Leu	Arg	Ala	Ser	Lys	Thr	His	Arg	Tyr			
			260					265					270					
Gln	Ile	Trp	Thr	Thr	Val	Val	Asp	Trp	Ile	His	Pro	Asp	Leu	Lys	Arg			
		275					280					285						
Ile	Val	Ile	Glu	Tyr	Val	Asp	Arg	Ile	Ile	Phe	His	Glu	Asn	Tyr	Asn			
		290				295				300								
Ala	Gly	Thr	Tyr	Gln	Asn	Asp	Ile	Ala	Leu	Ile	Glu	Met	Lys	Lys	Asp			
305					310				315						320			
Gly	Asn	Lys	Lys	Asp	Cys	Glu	Leu	Pro	Arg	Ser	Ile	Pro	Ala	Ala	Val			

325	330	335
Pro Trp Ser Pro Tyr Leu Phe Gln Pro Asn Asp Thr Cys Ile Val Ser		
340	345	350
Gly Trp Gly Arg Glu Lys Asp Asn Glu Arg Val Phe Ser Leu Gln Trp		
355	360	365
Gly Glu Val Lys Leu Ile Ser Asn Cys Ser Lys Phe Tyr Gly Asn Arg		
370	375	380
Phe Tyr Glu Lys Glu Met Glu Cys Ala Gly Thr Tyr Asp Gly Ser Ile		
385	390	395
Asp Ala Cys Lys Gly Asp Ser Gly Gly Pro Leu Val Cys Met Asp Ala		
405	410	415
Asn Asn Val Thr Tyr Val Trp Gly Val Val Ser Trp Gly Glu Asn Cys		
420	425	430
Gly Lys Pro Glu Phe Pro Gly Val Tyr Thr Lys Val Ala Asn Tyr Phe		
435	440	445
Asp Trp Ile Ser Tyr His Val Gly Arg Pro Phe Ile Ser Gln Tyr Asn		
450	455	460

Val

465

<210> 60

<211> 465

<212> PRT

<213> 人工序列

<220>

<223> 非糖基化嵌合CR1a-FI蛋白氨基酸序列(无信号肽)

<400> 60

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

	100		105		110
His Trp Ser Thr Lys Pro Pro Ile Cys Gln Arg Ile Pro Cys Gly Leu					
115			120		125
Pro Pro Thr Ile Ala Asn Gly Asp Phe Ile Ser Thr Asn Arg Glu Asn					
130			135		140
Phe His Tyr Gly Ser Val Val Thr Tyr Arg Cys Asn Pro Gly Ser Gly					
145			150		155
Gly Arg Lys Val Phe Glu Leu Val Gly Glu Pro Ser Ile Tyr Cys Thr					
165			170		175
Ser Asn Asp Asp Gln Val Gly Ile Trp Ser Gly Pro Ala Pro Gln Cys					
180			185		190
Ile Ile Pro Asn Lys Ala Thr Pro Pro Asn Val Glu Asn Gly Gly Gly					
195			200		205
Gly Ser Arg Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Ile Val Gly					
210			215		220
Gly Lys Arg Ala Gln Leu Gly Asp Leu Pro Trp Gln Val Ala Ile Lys					
225			230		235
Asp Ala Ser Gly Ile Thr Cys Gly Gly Ile Tyr Ile Gly Gly Cys Trp					
245			250		255
Ile Leu Thr Ala Ala His Cys Leu Arg Ala Ser Lys Thr His Arg Tyr					
260			265		270
Gln Ile Trp Thr Thr Val Val Asp Trp Ile His Pro Asp Leu Lys Arg					
275			280		285
Ile Val Ile Glu Tyr Val Asp Arg Ile Ile Phe His Glu Asn Tyr Asn					
290			295		300
Ala Gly Thr Tyr Gln Asn Asp Ile Ala Leu Ile Glu Met Lys Lys Asp					
305			310		315
Gly Asn Lys Lys Asp Cys Glu Leu Pro Arg Ser Ile Pro Ala Ala Val					
325			330		335
Pro Trp Ser Pro Tyr Leu Phe Gln Pro Gln Asp Thr Cys Ile Val Ser					
340			345		350
Gly Trp Gly Arg Glu Lys Asp Asn Glu Arg Val Phe Ser Leu Gln Trp					
355			360		365
Gly Glu Val Lys Leu Ile Ser Gln Cys Ser Lys Phe Tyr Gly Asn Arg					
370			375		380
Phe Tyr Glu Lys Glu Met Glu Cys Ala Gly Thr Tyr Asp Gly Ser Ile					
385			390		395
Asp Ala Cys Lys Gly Asp Ser Gly Gly Pro Leu Val Cys Met Asp Ala					
405			410		415

Asn Gln Val Thr Tyr Val Trp Gly Val Val Ser Trp Gly Glu Asn Cys
 420 425 430
 Gly Lys Pro Glu Phe Pro Gly Val Tyr Thr Lys Val Ala Asn Tyr Phe
 435 440 445
 Asp Trp Ile Ser Tyr His Val Gly Arg Pro Phe Ile Ser Gln Tyr Asn
 450 455 460
 Val
 465
 <210> 61
 <211> 465
 <212> PRT
 <213> 人工序列
 <220>
 <223> 非糖基化嵌合CR1b-FI蛋白氨基酸序列(无信号肽)
 <400> 61
 Gly His Cys Gln Ala Pro Asp His Phe Leu Phe Ala Lys Leu Lys Thr
 1 5 10 15
 Gln Thr Gln Ala Ser Asp Phe Pro Ile Gly Thr Ser Leu Lys Tyr Glu
 20 25 30
 Cys Arg Pro Glu Tyr Tyr Gly Arg Pro Phe Ser Ile Thr Cys Leu Asp
 35 40 45
 Asn Leu Val Trp Ser Ser Pro Lys Asp Val Cys Lys Arg Lys Ser Cys
 50 55 60
 Lys Thr Pro Pro Asp Pro Val Asn Gly Met Val His Val Ile Thr Asp
 65 70 75 80
 Ile Gln Val Gly Ser Arg Ile Gln Tyr Ser Cys Thr Thr Gly His Arg
 85 90 95
 Leu Ile Gly His Ser Ser Ala Glu Cys Ile Leu Ser Gly Asn Ala Ala
 100 105 110
 His Trp Ser Thr Lys Pro Pro Ile Cys Gln Arg Ile Pro Cys Gly Leu
 115 120 125
 Pro Pro Thr Ile Ala Asn Gly Asp Phe Ile Ser Thr Asn Arg Glu Asn
 130 135 140
 Phe His Tyr Gly Ser Val Val Thr Tyr Arg Cys Asn Pro Gly Ser Gly
 145 150 155 160
 Gly Arg Lys Val Phe Glu Leu Val Gly Glu Pro Ser Ile Tyr Cys Thr
 165 170 175
 Ser Asn Asp Asp Gln Val Gly Ile Trp Ser Gly Pro Ala Pro Gln Cys
 180 185 190

Ile Ile Pro Asn Lys Ala Thr Pro Pro Asn Val Glu Asn Gly Gly Gly		
195	200	205
Gly Ser Arg Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Ile Val Gly		
210	215	220
Gly Lys Arg Ala Gln Leu Gly Asp Leu Pro Trp Gln Val Ala Ile Lys		
225	230	235
240		
Asp Ala Ser Gly Ile Thr Cys Gly Gly Ile Tyr Ile Gly Gly Cys Trp		
245	250	255
Ile Leu Thr Ala Ala His Cys Leu Arg Ala Ser Lys Thr His Arg Tyr		
260	265	270
Gln Ile Trp Thr Thr Val Val Asp Trp Ile His Pro Asp Leu Lys Arg		
275	280	285
Ile Val Ile Glu Tyr Val Asp Arg Ile Ile Phe His Glu Asn Tyr Asn		
290	295	300
Ala Gly Thr Tyr Gln Asn Asp Ile Ala Leu Ile Glu Met Lys Lys Asp		
305	310	315
320		
Gly Asn Lys Lys Asp Cys Glu Leu Pro Arg Ser Ile Pro Ala Ala Val		
325	330	335
Pro Trp Ser Pro Tyr Leu Phe Gln Pro Gln Asp Thr Cys Ile Val Ser		
340	345	350
Gly Trp Gly Arg Glu Lys Asp Asn Glu Arg Val Phe Ser Leu Gln Trp		
355	360	365
Gly Glu Val Lys Leu Ile Ser Gln Cys Ser Lys Phe Tyr Gly Asn Arg		
370	375	380
Phe Tyr Glu Lys Glu Met Glu Cys Ala Gly Thr Tyr Asp Gly Ser Ile		
385	390	395
400		
Asp Ala Cys Lys Gly Asp Ser Gly Gly Pro Leu Val Cys Met Asp Ala		
405	410	415
Asn Gln Val Thr Tyr Val Trp Gly Val Val Ser Trp Gly Glu Asn Cys		
420	425	430
Gly Lys Pro Glu Phe Pro Gly Val Tyr Thr Lys Val Ala Asn Tyr Phe		
435	440	445
Asp Trp Ile Ser Tyr His Val Gly Arg Pro Phe Ile Ser Gln Tyr Asn		
450	455	460
Val		
465		
<210> 62		
<211> 1526		
<212> DNA		

<213> 人工序列

<220>

<223> His-标签的糖基化嵌合CR1a-FI蛋白质编码序列

<400> 62

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aagcttgcca ccatgagact gctggccaag atcatctgcc tgatgctgtg ggccatctgc 60
gtggcccacc accatcacca tcacggcagc agcgagaacc tgtacttcca aggatcttct 120
ggcggccact gtcaggcccc tgatcacttc ctgttcgccca agctgaaaac ccagaccaac 180
gccagcgact tccctatcgg caccagcctg aagtacgagt gcagaccgga gtactacggc 240
agacccttca gcatcacctg tctggacaac ctcgtgtggt ctagcccca ggacgtgtgc 300
aagagaaaaga gctgcaagac cctcctgat cctgtgaacg gcatggtgca cgtgatcacc 360
gacatccaag tgggcagcag aatcaactac agctgcacca ccggccacag actgatcgga 420
cactctagcg ccgagtgtat cctgagcggc aatgccgcac actgggtccac caagcctcca 480
atctgccaga gaatcccttg cggcctgcct cctacaatcg ccaacggcga tttcatcage 540
accaacagag agaacttcca ctacggctcc gtggtcacct acagatgcaa tcctggcagc 600
ggcggcagaa aggtgttcga acttgtgggc gagcccagca tctactgcac cagcaacgat 660
gaccaagtcg gcatttggag cggccctgct cctcagtga tcatcccca caaagccaca 720
cctcctaacg tggaaaatgg cggcggaggc tctagagggt gcggaggatc tggcggaggc 780
ggatctatcg ttggaggaaa gagagcacag ctgggcgacc tgccttggca ggttgccatt 840
aaggatgcca gcggcatcac atgcggcggc atctatatcg gcggctgctg gattctgaca 900
gccgctcatt gtctgcgggc cagcaagacc caccggtatc agatttggac caccgtggtg 960
gactggattc accccgacct gaagcggatc gtgatcgagt acgtggaccg gatcatcttc 1020
cacgagaact acaacgccgg cacctaccag aacgatatcg ccctgatcga gatgaagaag 1080
gacggcaaca agaaggactg cgagctgcct agatctatcc cagccgctgt tccttggagc 1140
ccctacctgt tccagcctaa cgatactgc atcgtgtccg gctggggcag agagaaggac 1200
aacgaaaggg tgttcagcct gcagtggggc gaagtgaagc tgatctccaa ctgcagcaag 1260
ttctacggca accggttcta cgagaaagaa atggaatgcg ccggcacata cgacggctcc 1320
atcgatgcct gtaaaggcga ttctggcgga cccctcgtgt gcatggatgc caacaatgtg 1380
acctacgtgt ggggcgtcgt gtcctgggga gagaattgtg gcaagcctga gttccccggc 1440
gtgtacacca aggtggccaa ctacttcgac tggatcagct accacgtggg cagaccattc 1500
atcagccagt acaacgttgc ggccgc 1526
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<210> 63

<211> 1526

<212> DNA

<213> 人工序列

<220>

<223> His-标签的糖基化嵌合CR1b-FI蛋白质编码序列

<400> 63

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aagcttgcca ccatgagact gctggccaag atcatctgcc tgatgctgtg ggccatctgc 60
gtggcccacc accatcacca tcacggcagc agcgagaacc tgtacttcca aggatcttct 120
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ggcgccact gtcaggcccc tgatcacttc ctgttcgcca agctgaaaac ccagaccaac 180
 gccagcgact tccctatcgg caccagcctg aagtacgagt gcagaccgga gtactacggc 240
 agacccttca gcatcacctg tctggacaac ctctgtgtgt ctagcccca ggacgtgtgc 300
 aagagaaaga gctgcaagac ccctcctgat cctgtgaacg gcatggtgca cgtgatcacc 360
 gacatccaag tgggcagcag aatcaactac agctgcacca ccggccacag actgatcgga 420
 cactctagcg ccgagtgtat cctgagcggc aacacagccc actggtccac caagcctcca 480
 atctgccaga gaatcccttg cggcctgcct cctacaatcg ccaacggcga tttcatcagc 540
 accaacagag agaacttcca ctacggctcc gtggtcacct acagatgcaa cctgggctcc 600
 agaggccgga aggtgttcga acttgtgggc gagcctagca tctactgcac cagcaacgac 660
 gaccaagtcg gcatttggag cggacctgct cctcagtgc tcatcccca caaggccaca 720
 cctcctaacg tggaaaatgg cggcggaggc tctagagggt gcgaggatc tggcggaggc 780
 ggatctatcg ttggaggaaa gagagcacag ctgggcgacc tgccttggca ggttgccatt 840
 aaggatgcca gcggcatcac atgcggcggc atctatatcg gcggtgctg gattctgacc 900
 gccgctcatt gtctgagagc cagcaagacc caccggtatc agatctggac caccgtggtg 960
 gactggattc accccgacct gaagcggatc gtgatcgagt acgtggaccg gatcatcttc 1020
 cacgagaact acaacgccgg cacctaccag aacgatatcg ccctgatcga gatgaagaag 1080
 gacggcaaca agaaggactg cgagctgcct agatctatcc ctgccgtgt tccttggagc 1140
 ccctacctgt tccagcctaa cgatacctgc atcgtgtccg gctggggcag agagaaggac 1200
 aacgaaaggg tgttcagcct gcagtggggc gaagtgaagc tgatctccaa ctgcagcaag 1260
 ttctacggca accggttcta cgagaaagaa atggaatgcg ccggcacata cgacggctcc 1320
 atcgaatgct gtaaaggcga ttctggcgga cccctcgtgt gcatggatgc caacaatgtg 1380
 acctacgtgt ggggcgtcgt gtcctgggga gagaattgtg gcaagcctga gttccccggc 1440
 gtgtacacca aggtggccaa ctacttcgac tggatcagct accacgtggg cagaccattc 1500
 atcagccagt acaacgttgc ggccgc 1526

<210> 64

<211> 1526

<212> DNA

<213> 人工序列

<220>

<223> His-标签的非糖基化嵌合CR1a-FI蛋白质编码序列

<400> 64

aagcttgcca ccatgagact gctggccaag atcatctgcc tgatgctgtg ggccatctgc 60
 gtggcccacc accatcacca tcacggcagc agcgagaacc tgtacttcca aggatcttct 120
 ggcgccact gtcaggcccc tgatcacttc ctgttcgcca agctgaaaac ccagacacag 180
 gccagcgact tccctatcgg caccagcctg aagtacgagt gcagaccgga gtactacggc 240
 agacccttca gcatcacctg tctggacaac ctctgtgtgt ctagcccca ggacgtgtgc 300
 aagagaaaga gctgcaagac ccctcctgat cctgtgaacg gcatggtgca cgtgatcacc 360
 gacatccaag tgggcagcag aatccagtac agctgcacca caggccacag actgatcggc 420
 cactctagcg ccgagtgtat cctgtctggc aatgccgctc actggtccac caagcctcca 480

atctgccaga gaatcccttg cggcctgcct cctacaatcg ccaacggcga tttcatcage 540
 accaacagag agaacttcca ctacggctcc gtggtcacct acagatgcaa tcctggcage 600
 ggcggcagaa aggtgttcga acttgtgggc gagcccagca tctactgcac cagcaacgat 660
 gaccaagtcg gcatttggag cggccctgct cctcagtga tcatcccca caaagccaca 720
 cctcctaacg tggaaaatgg cggcggaggc tctagagggt gcggaggatc tggcggaggc 780
 ggatctatcg ttggaggaaa gagagcacag ctgggcgacc tgccttggca ggttgccatt 840
 aaggatgcca gcggcatcac atgcggcggc atctatatcg gcggctgctg gattctcacc 900
 gccgcacatt gtctgagagc cagcaagacc caccggtatc agatctggac caccgtggtg 960
 gactggattc accccgacct gaagcggatc gtgatcgagt acgtggaccg gatcatcttc 1020
 cacgagaact acaacgccgg cacctaccag aacgatatcg cctgatcga gatgaagaag 1080
 gacggcaaca agaaggactg cgagctgcct agatctatcc cagccgctgt tccttggagc 1140
 ccctacctgt tccagcctca agatactgc atcgtgtccg gctggggcag agagaaggac 1200
 aacgaaaggg tgttcagcct gcagtggggc gaagtgaagc tgatctcca gtgcagcaag 1260
 ttctacggca accggttcta cgagaaagaa atggaatgcg ccggcacata cgacggctcc 1320
 atcgatgcct gtaaaggcga ttctggcgga cccctcgtgt gcattgatgc caatcaagtg 1380
 acctacgtgt ggggcgtcgt gtctgggga gagaattgtg gcaagcctga gttccccggc 1440
 gtgtacacca aggtggccaa ctacttcgac tggatcagct accacgtggg cagaccattc 1500
 atcagccagt acaacgttgc ggccgc 1526

<210> 65

<211> 1526

<212> DNA

<213> 人工序列

<220>

<223> His-标签的非糖基化嵌合CR1b-FI蛋白质编码序列

<400> 65

aagcttgcca ccatgagact gctggccaag atcatctgcc tgatgctgtg ggccatctgc 60
 gtggcccacc accatcacca tcacggcagc agcgagaacc tgtacttcca aggatcttct 120
 ggcggccact gtcaggcccc tgatcacttc ctgttcgcca agctgaaaac ccagacacag 180
 gccagcgact tccctatcgg caccagcctg aagtacgagt gcagaccga gtactacggc 240
 agacccttca gcatcacctg tctggacaac ctctgtgtgt ctagcccca ggacgtgtgc 300
 aagagaaaaga gctgcaagac cctcctgat cctgtgaacg gcatggtgca cgtgatcacc 360
 gacatccaag tgggcagcag aatccagtac agctgcacca caggccacag actgatcggc 420
 cactctagcg ccgagtgtat cctgagcgga aacacagccc actggtccac caagcctcca 480
 atctgccaga gaatcccttg cggcctgcct cctacaatcg ccaacggcga tttcatcage 540
 accaacagag agaacttcca ctacggctcc gtggtcacct acagatgcaa cctgggctcc 600
 agaggccgga aggtgttcga acttgtgggc gagcctagca tctactgcac cagcaacgac 660
 gaccaagtcg gcatttggag cggacctgct cctcagtga tcatcccca caaggccaca 720
 cctcctaacg tggaaaatgg cggcggaggc tctagagggt gcggaggatc tggcggaggc 780
 ggatctatcg ttggaggaaa gagagcacag ctgggcgacc tgccttggca ggttgccatt 840

aaggatgcca gcggcacac atgcggcggc atctatatcg gcggctgctg gattctcacc 900
gccgctcatt gtctgagagc cagcaagacc caccggtatc agatctggac caccgtggtg 960
gactggattc accccgacct gaagcggatc gtgatcgagt acgtggaccg gatcatcttc 1020
cacgagaact acaacgcccg cacctaccag aacgatatcg ccctgatcga gatgaagaag 1080
gacggcaaca agaaggactg cgagctgcct agatctatcc ctgccgctgt tccttgagc 1140
ccctacctgt tccagcctca agatactgc atcgtgtccg gctggggcag agagaaggac 1200
aacgaaaggg tgttcagcct gcagtggggc gaagtgaagc tgatctccca gtgcagcaag 1260
ttctacggca accggttcta cgagaaagaa atggaatgcg ccggcacata cgacggctcc 1320
atcgatgcct gtaaaggcga ttctggcgga cccctcgtgt gcatggatgc caatcaagtg 1380
acctacgtgt ggggcgtcgt gtctgggga gagaattgtg gcaagcctga gttccccggc 1440
gtgtacacca aggtggccaa ctacttcgac tggatcagct accacgtggg cagaccattc 1500
atcagccagt acaacgttgc ggccgc 1526

<210> 66

<211> 4

<212> PRT

<213> 人工序列

<220>

<223> N-连接的糖基化的共有序列

<220>

<221> MISC_FEATURE

<222> (2) .. (2)

<223> Xaa = 除P外的任何氨基酸

<220>

<221> MISC_FEATURE

<222> (3) .. (3)

<223> Xaa = S或T

<220>

<221> MISC_FEATURE

<222> (4) .. (4)

<223> Xaa = 除P外的任何氨基酸

<400> 66

Asn Xaa Xaa Xaa

1

<210> 67

<211> 26

<212> PRT

<213> 人工序列

<220>

<223> G4S-R- (G4S) 4接头

<400> 67

Gly Gly Gly Gly Ser Arg Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
 1 5 10 15
 Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
 20 25

<210> 68

<211> 26

<212> PRT

<213> 人工序列

<220>

<223> G4S-K- (G4S) 4接头

<400> 68

Gly Gly Gly Gly Ser Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
 1 5 10 15
 Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
 20 25

<210> 69

<211> 524

<212> PRT

<213> 人工序列

<220>

<223> 糖基化的嵌合FH-FI蛋白氨基酸序列(有信号肽)

<400> 69

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

Cys Asp Thr Asp Gly Trp Thr Asn Asp Ile Pro Ile Cys Glu Val Val		
130	135	140
Lys Cys Leu Pro Val Thr Ala Pro Glu Asn Gly Lys Ile Val Ser Ser		
145	150	155
Ala Met Glu Pro Asp Arg Glu Tyr His Phe Gly Gln Ala Val Arg Phe		
	165	170
Val Cys Asn Ser Gly Tyr Lys Ile Glu Gly Asp Glu Glu Met His Cys		
	180	185
Ser Asp Asp Gly Phe Trp Ser Lys Glu Lys Pro Lys Cys Val Glu Ile		
	195	200
Ser Cys Lys Ser Pro Asp Val Ile Asn Gly Ser Pro Ile Ser Gln Lys		
	210	215
Ile Ile Tyr Lys Glu Asn Glu Arg Phe Gln Tyr Lys Cys Asn Met Gly		
225	230	235
Tyr Glu Tyr Ser Glu Arg Gly Asp Ala Val Cys Thr Glu Ser Gly Trp		
	245	250
Arg Pro Leu Pro Ser Cys Glu Glu Gly Gly Gly Ser Arg Gly Gly		
	260	265
Gly Gly Ser Gly Gly Gly Gly Ser Ile Val Gly Gly Lys Arg Ala Gln		
	275	280
Leu Gly Asp Leu Pro Trp Gln Val Ala Ile Lys Asp Ala Ser Gly Ile		
	290	295
Thr Cys Gly Gly Ile Tyr Ile Gly Gly Cys Trp Ile Leu Thr Ala Ala		
305	310	315
His Cys Leu Arg Ala Ser Lys Thr His Arg Tyr Gln Ile Trp Thr Thr		
	325	330
Val Val Asp Trp Ile His Pro Asp Leu Lys Arg Ile Val Ile Glu Tyr		
	340	345
Val Asp Arg Ile Ile Phe His Glu Asn Tyr Asn Ala Gly Thr Tyr Gln		
	355	360
Asn Asp Ile Ala Leu Ile Glu Met Lys Lys Asp Gly Asn Lys Lys Asp		
	370	375
Cys Glu Leu Pro Arg Ser Ile Pro Ala Ala Val Pro Trp Ser Pro Tyr		
385	390	395
Leu Phe Gln Pro Asn Asp Thr Cys Ile Val Ser Gly Trp Gly Arg Glu		
	405	410
Lys Asp Asn Glu Arg Val Phe Ser Leu Gln Trp Gly Glu Val Lys Leu		
	420	425
Ile Ser Asn Cys Ser Lys Phe Tyr Gly Asn Arg Phe Tyr Glu Lys Glu		

435	440	445
Met Glu Cys Ala Gly Thr Tyr Asp Gly Ser Ile Asp Ala Cys Lys Gly		
450	455	460
Asp Ser Gly Gly Pro Leu Val Cys Met Asp Ala Asn Asn Val Thr Tyr		
465	470	475
Val Trp Gly Val Val Ser Trp Gly Glu Asn Cys Gly Lys Pro Glu Phe		480
485	490	495
Pro Gly Val Tyr Thr Lys Val Ala Asn Tyr Phe Asp Trp Ile Ser Tyr		
500	505	510
His Val Gly Arg Pro Phe Ile Ser Gln Tyr Asn Val		
515	520	
<210> 70		
<211> 483		
<212> PRT		
<213> 人工序列		
<220>		
<223> 糖基化嵌合CR1a-FI蛋白氨基酸序列(有信号肽)		
<400> 70		
Met Arg Leu Leu Ala Lys Ile Ile Cys Leu Met Leu Trp Ala Ile Cys		
1	5	10
Val Ala Gly His Cys Gln Ala Pro Asp His Phe Leu Phe Ala Lys Leu		15
20	25	30
Lys Thr Gln Thr Asn Ala Ser Asp Phe Pro Ile Gly Thr Ser Leu Lys		
35	40	45
Tyr Glu Cys Arg Pro Glu Tyr Tyr Gly Arg Pro Phe Ser Ile Thr Cys		
50	55	60
Leu Asp Asn Leu Val Trp Ser Ser Pro Lys Asp Val Cys Lys Arg Lys		
65	70	75
Ser Cys Lys Thr Pro Pro Asp Pro Val Asn Gly Met Val His Val Ile		80
85	90	95
Thr Asp Ile Gln Val Gly Ser Arg Ile Asn Tyr Ser Cys Thr Thr Gly		
100	105	110
His Arg Leu Ile Gly His Ser Ser Ala Glu Cys Ile Leu Ser Gly Asn		
115	120	125
Ala Ala His Trp Ser Thr Lys Pro Pro Ile Cys Gln Arg Ile Pro Cys		
130	135	140
Gly Leu Pro Pro Thr Ile Ala Asn Gly Asp Phe Ile Ser Thr Asn Arg		
145	150	155
Glu Asn Phe His Tyr Gly Ser Val Val Thr Tyr Arg Cys Asn Pro Gly		160

	165		170		175
Ser Gly Gly Arg Lys Val Phe Glu Leu Val Gly Glu Pro Ser Ile Tyr					
	180		185		190
Cys Thr Ser Asn Asp Asp Gln Val Gly Ile Trp Ser Gly Pro Ala Pro					
	195		200		205
Gln Cys Ile Ile Pro Asn Lys Ala Thr Pro Pro Asn Val Glu Asn Gly					
	210		215		220
Gly Gly Gly Ser Arg Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Ile					
225		230		235	240
Val Gly Gly Lys Arg Ala Gln Leu Gly Asp Leu Pro Trp Gln Val Ala					
	245		250		255
Ile Lys Asp Ala Ser Gly Ile Thr Cys Gly Gly Ile Tyr Ile Gly Gly					
	260		265		270
Cys Trp Ile Leu Thr Ala Ala His Cys Leu Arg Ala Ser Lys Thr His					
	275		280		285
Arg Tyr Gln Ile Trp Thr Thr Val Val Asp Trp Ile His Pro Asp Leu					
	290		295		300
Lys Arg Ile Val Ile Glu Tyr Val Asp Arg Ile Ile Phe His Glu Asn					
305		310		315	320
Tyr Asn Ala Gly Thr Tyr Gln Asn Asp Ile Ala Leu Ile Glu Met Lys					
	325		330		335
Lys Asp Gly Asn Lys Lys Asp Cys Glu Leu Pro Arg Ser Ile Pro Ala					
	340		345		350
Ala Val Pro Trp Ser Pro Tyr Leu Phe Gln Pro Asn Asp Thr Cys Ile					
	355		360		365
Val Ser Gly Trp Gly Arg Glu Lys Asp Asn Glu Arg Val Phe Ser Leu					
	370		375		380
Gln Trp Gly Glu Val Lys Leu Ile Ser Asn Cys Ser Lys Phe Tyr Gly					
385		390		395	400
Asn Arg Phe Tyr Glu Lys Glu Met Glu Cys Ala Gly Thr Tyr Asp Gly					
	405		410		415
Ser Ile Asp Ala Cys Lys Gly Asp Ser Gly Gly Pro Leu Val Cys Met					
	420		425		430
Asp Ala Asn Asn Val Thr Tyr Val Trp Gly Val Val Ser Trp Gly Glu					
	435		440		445
Asn Cys Gly Lys Pro Glu Phe Pro Gly Val Tyr Thr Lys Val Ala Asn					
	450		455		460
Tyr Phe Asp Trp Ile Ser Tyr His Val Gly Arg Pro Phe Ile Ser Gln					
465		470		475	480

Tyr Asn Val

<210> 71

<211> 483

<212> PRT

<213> 人工序列

<220>

<223> 糖基化嵌合CR1b-FI蛋白氨基酸序列(有信号肽)

<400> 71

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Met Arg Leu Leu Ala Lys Ile Ile Cys Leu Met Leu Trp Ala Ile Cys
1           5           10           15
Val Ala Gly His Cys Gln Ala Pro Asp His Phe Leu Phe Ala Lys Leu
          20           25           30
Lys Thr Gln Thr Asn Ala Ser Asp Phe Pro Ile Gly Thr Ser Leu Lys
          35           40           45
Tyr Glu Cys Arg Pro Glu Tyr Tyr Gly Arg Pro Phe Ser Ile Thr Cys
          50           55           60
Leu Asp Asn Leu Val Trp Ser Ser Pro Lys Asp Val Cys Lys Arg Lys
65           70           75           80
Ser Cys Lys Thr Pro Pro Asp Pro Val Asn Gly Met Val His Val Ile
          85           90           95
Thr Asp Ile Gln Val Gly Ser Arg Ile Asn Tyr Ser Cys Thr Thr Gly
          100          105          110
His Arg Leu Ile Gly His Ser Ser Ala Glu Cys Ile Leu Ser Gly Asn
          115          120          125
Thr Ala His Trp Ser Thr Lys Pro Pro Ile Cys Gln Arg Ile Pro Cys
          130          135          140
Gly Leu Pro Pro Thr Ile Ala Asn Gly Asp Phe Ile Ser Thr Asn Arg
145          150          155          160
Glu Asn Phe His Tyr Gly Ser Val Val Thr Tyr Arg Cys Asn Leu Gly
          165          170          175
Ser Arg Gly Arg Lys Val Phe Glu Leu Val Gly Glu Pro Ser Ile Tyr
          180          185          190
Cys Thr Ser Asn Asp Asp Gln Val Gly Ile Trp Ser Gly Pro Ala Pro
          195          200          205
Gln Cys Ile Ile Pro Asn Lys Ala Thr Pro Pro Asn Val Glu Asn Gly
          210          215          220
Gly Gly Gly Ser Arg Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Ile
225          230          235          240
Val Gly Gly Lys Arg Ala Gln Leu Gly Asp Leu Pro Trp Gln Val Ala

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	245	250	255
Ile Lys Asp Ala Ser Gly Ile Thr Cys Gly Gly Ile Tyr Ile Gly Gly			
260	265	270	
Cys Trp Ile Leu Thr Ala Ala His Cys Leu Arg Ala Ser Lys Thr His			
275	280	285	
Arg Tyr Gln Ile Trp Thr Thr Val Val Asp Trp Ile His Pro Asp Leu			
290	295	300	
Lys Arg Ile Val Ile Glu Tyr Val Asp Arg Ile Ile Phe His Glu Asn			
305	310	315	320
Tyr Asn Ala Gly Thr Tyr Gln Asn Asp Ile Ala Leu Ile Glu Met Lys			
325	330	335	
Lys Asp Gly Asn Lys Lys Asp Cys Glu Leu Pro Arg Ser Ile Pro Ala			
340	345	350	
Ala Val Pro Trp Ser Pro Tyr Leu Phe Gln Pro Asn Asp Thr Cys Ile			
355	360	365	
Val Ser Gly Trp Gly Arg Glu Lys Asp Asn Glu Arg Val Phe Ser Leu			
370	375	380	
Gln Trp Gly Glu Val Lys Leu Ile Ser Asn Cys Ser Lys Phe Tyr Gly			
385	390	395	400
Asn Arg Phe Tyr Glu Lys Glu Met Glu Cys Ala Gly Thr Tyr Asp Gly			
405	410	415	
Ser Ile Asp Ala Cys Lys Gly Asp Ser Gly Gly Pro Leu Val Cys Met			
420	425	430	
Asp Ala Asn Asn Val Thr Tyr Val Trp Gly Val Val Ser Trp Gly Glu			
435	440	445	
Asn Cys Gly Lys Pro Glu Phe Pro Gly Val Tyr Thr Lys Val Ala Asn			
450	455	460	
Tyr Phe Asp Trp Ile Ser Tyr His Val Gly Arg Pro Phe Ile Ser Gln			
465	470	475	480
Tyr Asn Val			
<210> 72			
<211> 483			
<212> PRT			
<213> 人工序列			
<220>			
<223> 非糖基化嵌合CR1a-FI蛋白氨基酸序列(有信号肽)			
<400> 72			
Met Arg Leu Leu Ala Lys Ile Ile Cys Leu Met Leu Trp Ala Ile Cys			
1	5	10	15

Val	Ala	Gly	His	Cys	Gln	Ala	Pro	Asp	His	Phe	Leu	Phe	Ala	Lys	Leu
20				25				30							
Lys	Thr	Gln	Thr	Gln	Ala	Ser	Asp	Phe	Pro	Ile	Gly	Thr	Ser	Leu	Lys
35				40				45							
Tyr	Glu	Cys	Arg	Pro	Glu	Tyr	Tyr	Gly	Arg	Pro	Phe	Ser	Ile	Thr	Cys
50				55				60							
Leu	Asp	Asn	Leu	Val	Trp	Ser	Ser	Pro	Lys	Asp	Val	Cys	Lys	Arg	Lys
65				70				75				80			
Ser	Cys	Lys	Thr	Pro	Pro	Asp	Pro	Val	Asn	Gly	Met	Val	His	Val	Ile
85				90				95							
Thr	Asp	Ile	Gln	Val	Gly	Ser	Arg	Ile	Gln	Tyr	Ser	Cys	Thr	Thr	Gly
100				105				110							
His	Arg	Leu	Ile	Gly	His	Ser	Ser	Ala	Glu	Cys	Ile	Leu	Ser	Gly	Asn
115				120				125							
Ala	Ala	His	Trp	Ser	Thr	Lys	Pro	Pro	Ile	Cys	Gln	Arg	Ile	Pro	Cys
130				135				140							
Gly	Leu	Pro	Pro	Thr	Ile	Ala	Asn	Gly	Asp	Phe	Ile	Ser	Thr	Asn	Arg
145				150				155				160			
Glu	Asn	Phe	His	Tyr	Gly	Ser	Val	Val	Thr	Tyr	Arg	Cys	Asn	Pro	Gly
165				170				175							
Ser	Gly	Gly	Arg	Lys	Val	Phe	Glu	Leu	Val	Gly	Glu	Pro	Ser	Ile	Tyr
180				185				190							
Cys	Thr	Ser	Asn	Asp	Asp	Gln	Val	Gly	Ile	Trp	Ser	Gly	Pro	Ala	Pro
195				200				205							
Gln	Cys	Ile	Ile	Pro	Asn	Lys	Ala	Thr	Pro	Pro	Asn	Val	Glu	Asn	Gly
210				215				220							
Gly	Gly	Gly	Ser	Arg	Gly	Gly	Gly	Gly	Ser	Gly	Gly	Gly	Gly	Ser	Ile
225				230				235				240			
Val	Gly	Gly	Lys	Arg	Ala	Gln	Leu	Gly	Asp	Leu	Pro	Trp	Gln	Val	Ala
245				250				255							
Ile	Lys	Asp	Ala	Ser	Gly	Ile	Thr	Cys	Gly	Gly	Ile	Tyr	Ile	Gly	Gly
260				265				270							
Cys	Trp	Ile	Leu	Thr	Ala	Ala	His	Cys	Leu	Arg	Ala	Ser	Lys	Thr	His
275				280				285							
Arg	Tyr	Gln	Ile	Trp	Thr	Thr	Val	Val	Asp	Trp	Ile	His	Pro	Asp	Leu
290				295				300							
Lys	Arg	Ile	Val	Ile	Glu	Tyr	Val	Asp	Arg	Ile	Ile	Phe	His	Glu	Asn
305				310				315				320			
Tyr	Asn	Ala	Gly	Thr	Tyr	Gln	Asn	Asp	Ile	Ala	Leu	Ile	Glu	Met	Lys

	325		330		335
Lys Asp Gly Asn Lys Lys Asp Cys Glu Leu Pro Arg Ser Ile Pro Ala					
	340		345		350
Ala Val Pro Trp Ser Pro Tyr Leu Phe Gln Pro Gln Asp Thr Cys Ile					
	355		360		365
Val Ser Gly Trp Gly Arg Glu Lys Asp Asn Glu Arg Val Phe Ser Leu					
	370		375		380
Gln Trp Gly Glu Val Lys Leu Ile Ser Gln Cys Ser Lys Phe Tyr Gly					
385		390		395	400
Asn Arg Phe Tyr Glu Lys Glu Met Glu Cys Ala Gly Thr Tyr Asp Gly					
	405		410		415
Ser Ile Asp Ala Cys Lys Gly Asp Ser Gly Gly Pro Leu Val Cys Met					
	420		425		430
Asp Ala Asn Gln Val Thr Tyr Val Trp Gly Val Val Ser Trp Gly Glu					
	435		440		445
Asn Cys Gly Lys Pro Glu Phe Pro Gly Val Tyr Thr Lys Val Ala Asn					
	450		455		460
Tyr Phe Asp Trp Ile Ser Tyr His Val Gly Arg Pro Phe Ile Ser Gln					
465		470		475	480
Tyr Asn Val					
<210> 73					
<211> 483					
<212> PRT					
<213> 人工序列					
<220>					
<223> 非糖基化嵌合CR1b-FI蛋白氨基酸序列(有信号肽)					
<400> 73					
Met Arg Leu Leu Ala Lys Ile Ile Cys Leu Met Leu Trp Ala Ile Cys					
1	5		10		15
Val Ala Gly His Cys Gln Ala Pro Asp His Phe Leu Phe Ala Lys Leu					
	20		25		30
Lys Thr Gln Thr Gln Ala Ser Asp Phe Pro Ile Gly Thr Ser Leu Lys					
	35		40		45
Tyr Glu Cys Arg Pro Glu Tyr Tyr Gly Arg Pro Phe Ser Ile Thr Cys					
	50		55		60
Leu Asp Asn Leu Val Trp Ser Ser Pro Lys Asp Val Cys Lys Arg Lys					
65		70		75	80
Ser Cys Lys Thr Pro Pro Asp Pro Val Asn Gly Met Val His Val Ile					
	85		90		95

Thr	Asp	Ile	Gln	Val	Gly	Ser	Arg	Ile	Gln	Tyr	Ser	Cys	Thr	Thr	Gly
His	Arg	Leu	Ile	Gly	His	Ser	Ser	Ala	Glu	Cys	Ile	Leu	Ser	Gly	Asn
Ala	Ala	His	Trp	Ser	Thr	Lys	Pro	Pro	Ile	Cys	Gln	Arg	Ile	Pro	Cys
Gly	Leu	Pro	Pro	Thr	Ile	Ala	Asn	Gly	Asp	Phe	Ile	Ser	Thr	Asn	Arg
Glu	Asn	Phe	His	Tyr	Gly	Ser	Val	Val	Thr	Tyr	Arg	Cys	Asn	Pro	Gly
Ser	Gly	Gly	Arg	Lys	Val	Phe	Glu	Leu	Val	Gly	Glu	Pro	Ser	Ile	Tyr
Cys	Thr	Ser	Asn	Asp	Asp	Gln	Val	Gly	Ile	Trp	Ser	Gly	Pro	Ala	Pro
Gln	Cys	Ile	Ile	Pro	Asn	Lys	Ala	Thr	Pro	Pro	Asn	Val	Glu	Asn	Gly
Gly	Gly	Gly	Ser	Arg	Gly	Gly	Gly	Gly	Ser	Gly	Gly	Gly	Gly	Ser	Ile
Val	Gly	Gly	Lys	Arg	Ala	Gln	Leu	Gly	Asp	Leu	Pro	Trp	Gln	Val	Ala
Ile	Lys	Asp	Ala	Ser	Gly	Ile	Thr	Cys	Gly	Gly	Ile	Tyr	Ile	Gly	Gly
Cys	Trp	Ile	Leu	Thr	Ala	Ala	His	Cys	Leu	Arg	Ala	Ser	Lys	Thr	His
Arg	Tyr	Gln	Ile	Trp	Thr	Thr	Val	Val	Asp	Trp	Ile	His	Pro	Asp	Leu
Lys	Arg	Ile	Val	Ile	Glu	Tyr	Val	Asp	Arg	Ile	Ile	Phe	His	Glu	Asn
Tyr	Asn	Ala	Gly	Thr	Tyr	Gln	Asn	Asp	Ile	Ala	Leu	Ile	Glu	Met	Lys
Lys	Asp	Gly	Asn	Lys	Lys	Asp	Cys	Glu	Leu	Pro	Arg	Ser	Ile	Pro	Ala
Ala	Val	Pro	Trp	Ser	Pro	Tyr	Leu	Phe	Gln	Pro	Gln	Asp	Thr	Cys	Ile
Val	Ser	Gly	Trp	Gly	Arg	Glu	Lys	Asp	Asn	Glu	Arg	Val	Phe	Ser	Leu
Gln	Trp	Gly	Glu	Val	Lys	Leu	Ile	Ser	Gln	Cys	Ser	Lys	Phe	Tyr	Gly
Asn	Arg	Phe	Tyr	Glu	Lys	Glu	Met	Glu	Cys	Ala	Gly	Thr	Tyr	Asp	Gly

405							410							415													
Ser	Ile	Asp	Ala	Cys	Lys	Gly	Asp	Ser	Gly	Gly	Pro	Leu	Val	Cys	Met												
420							425							430													
Asp	Ala	Asn	Gln	Val	Thr	Tyr	Val	Trp	Gly	Val	Val	Ser	Trp	Gly	Glu												
435							440							445													
Asn	Cys	Gly	Lys	Pro	Glu	Phe	Pro	Gly	Val	Tyr	Thr	Lys	Val	Ala	Asn												
450							455							460													
Tyr	Phe	Asp	Trp	Ile	Ser	Tyr	His	Val	Gly	Arg	Pro	Phe	Ile	Ser	Gln												
465							470							475							480						
Tyr							Asn							Val													

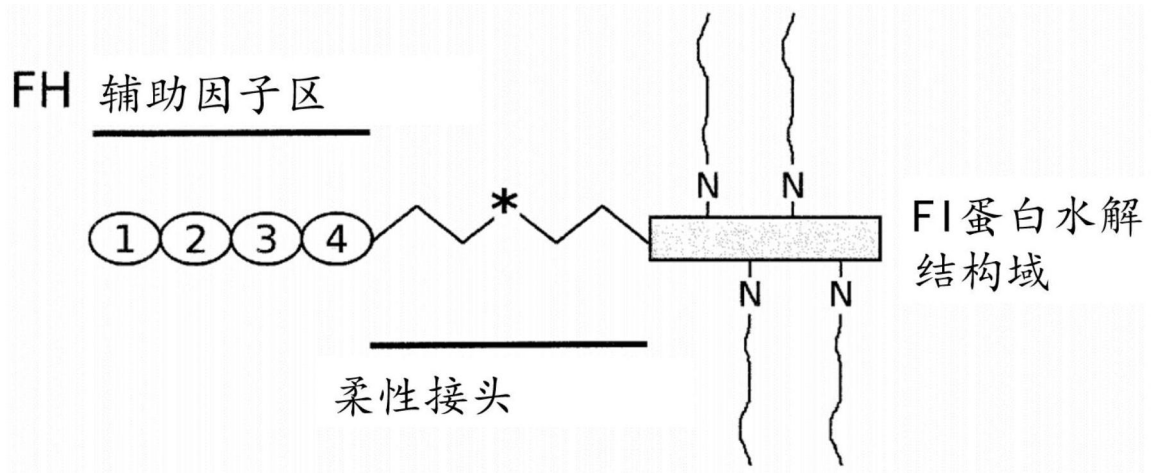


图1A

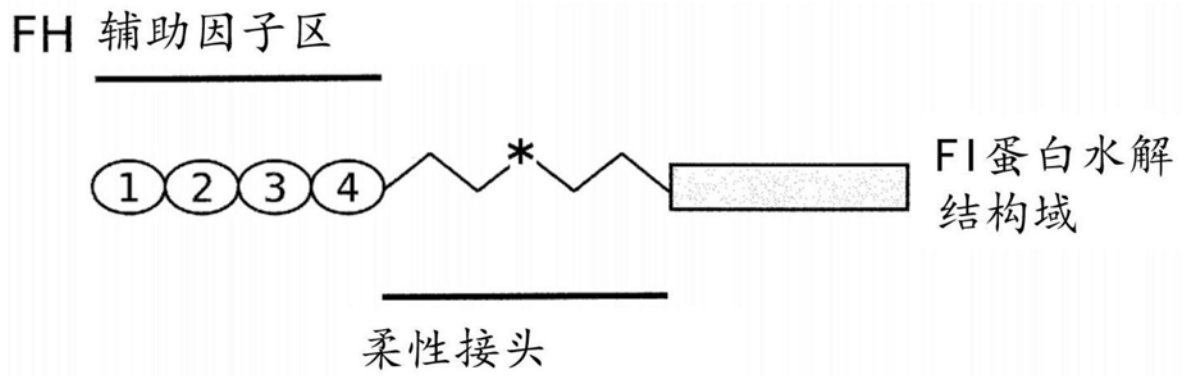


图1B

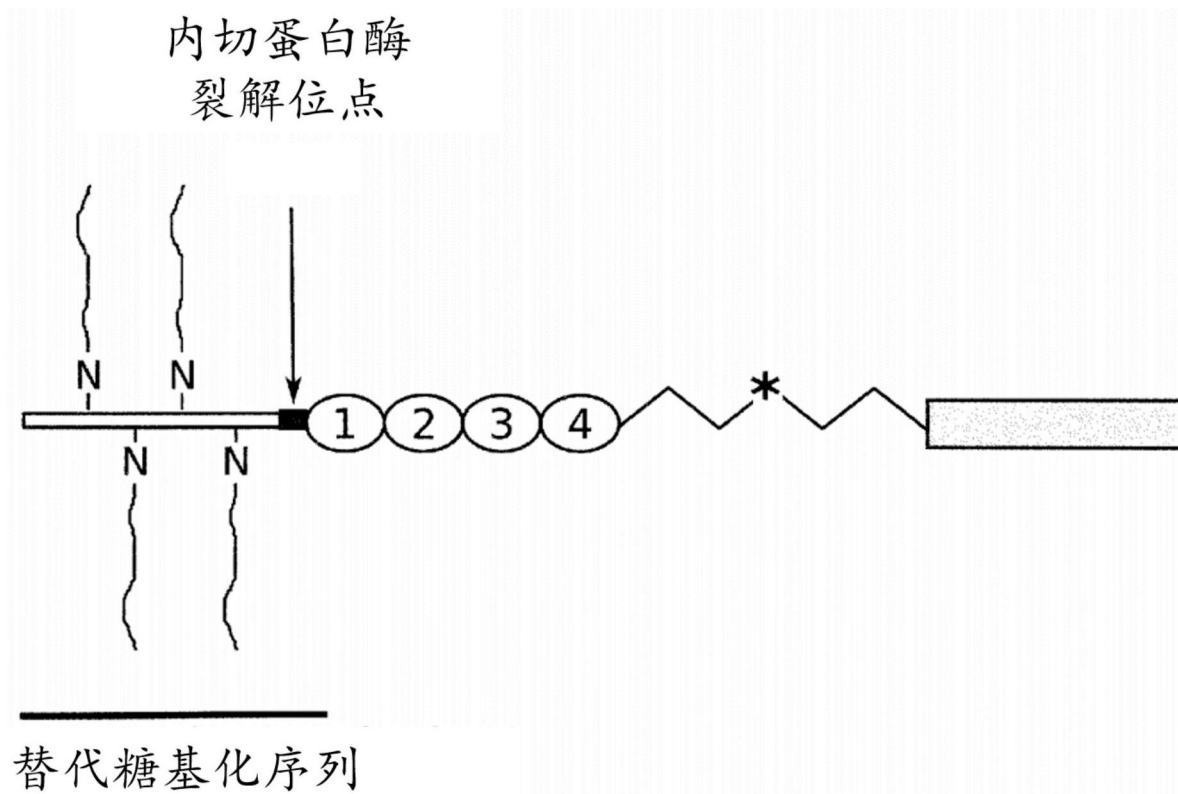


图1C

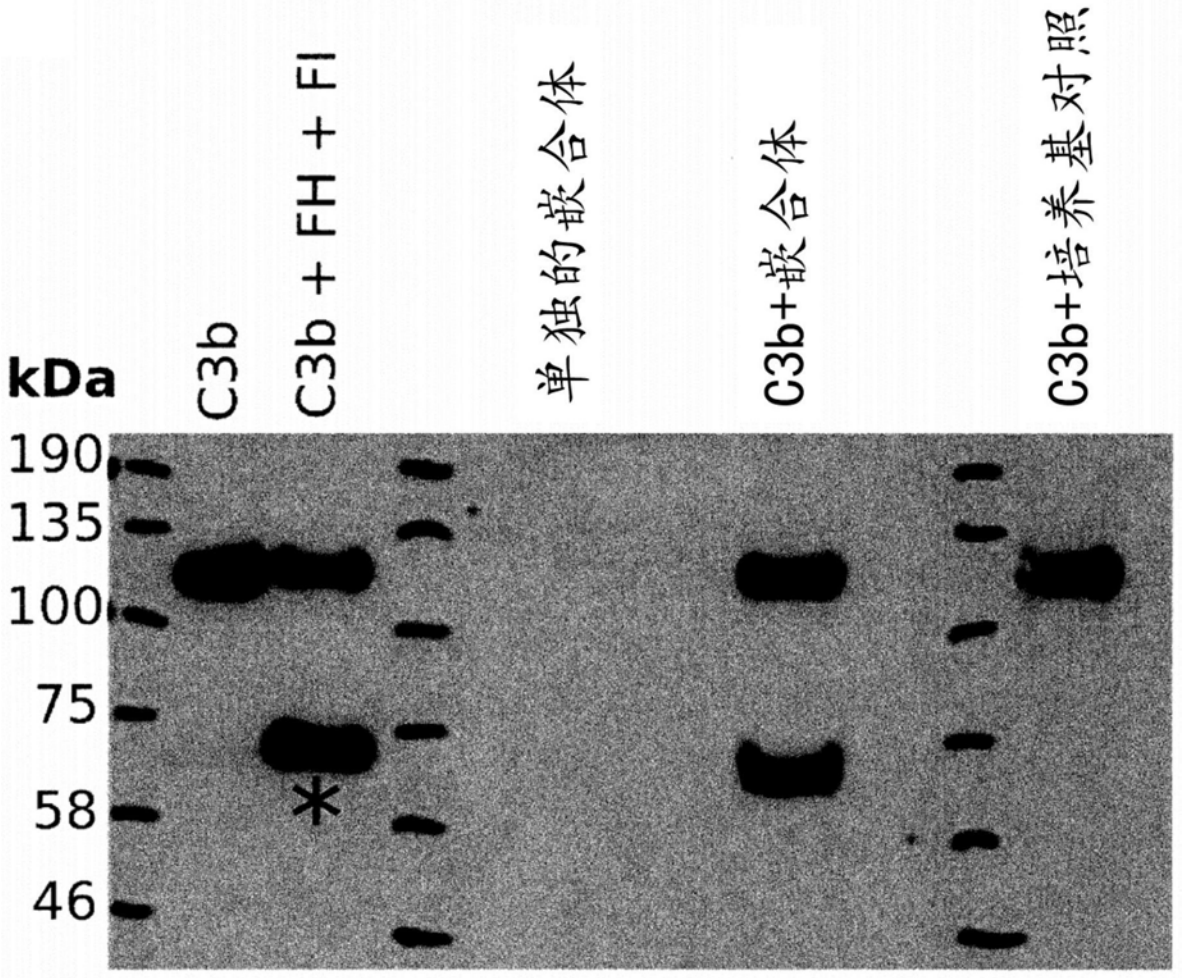


图2

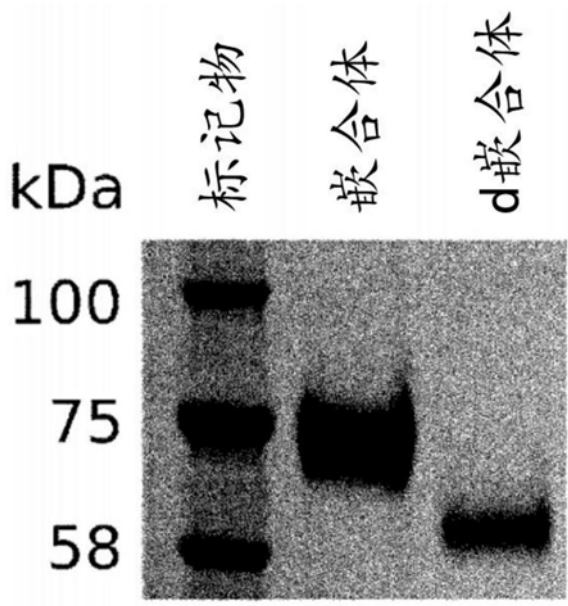


图3

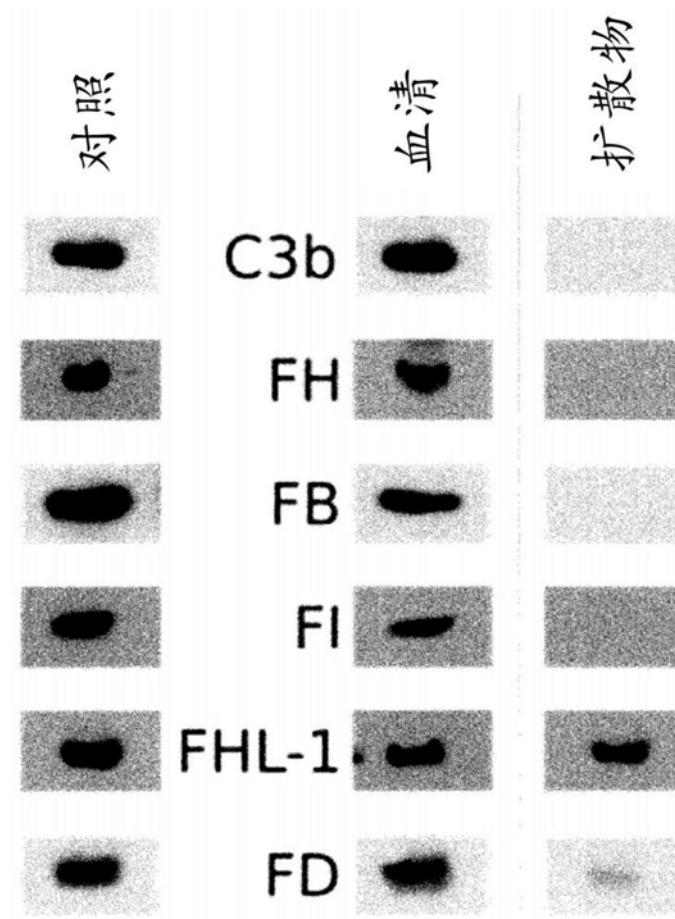


图4A

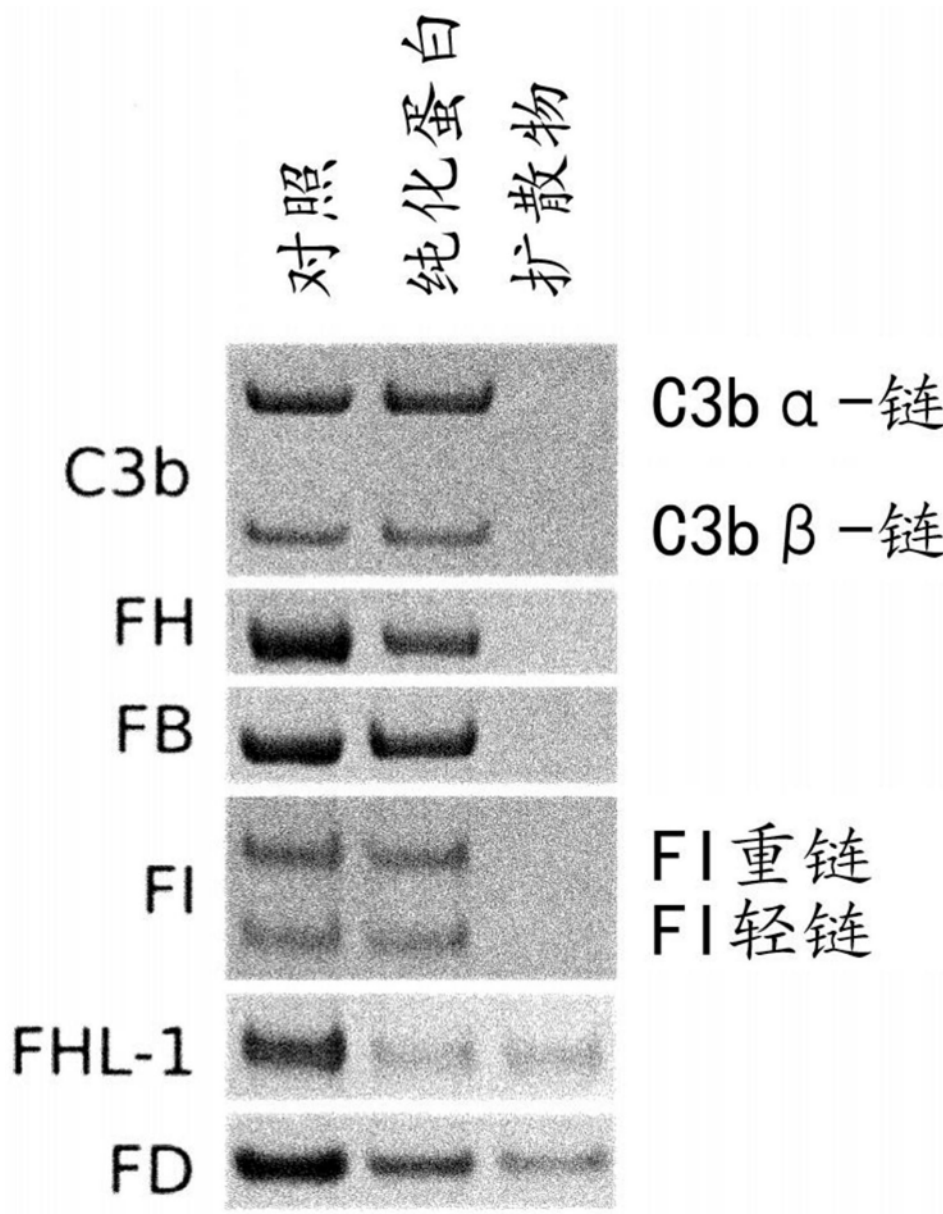


图4B

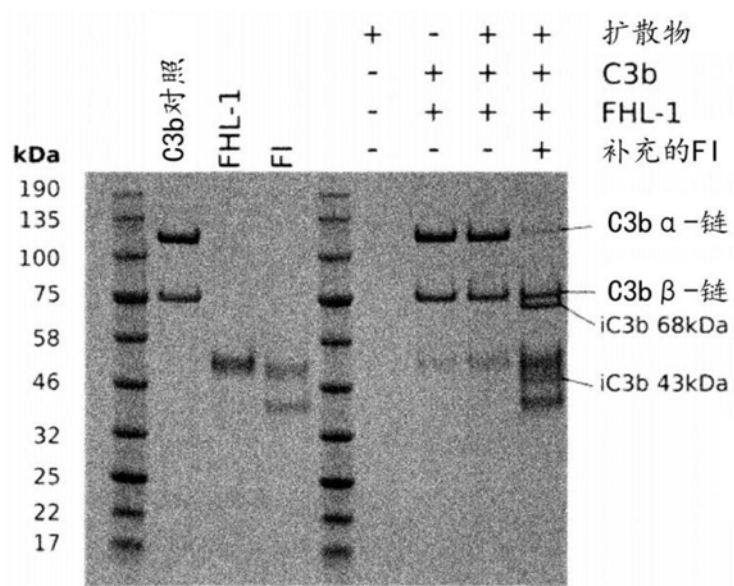


图5A

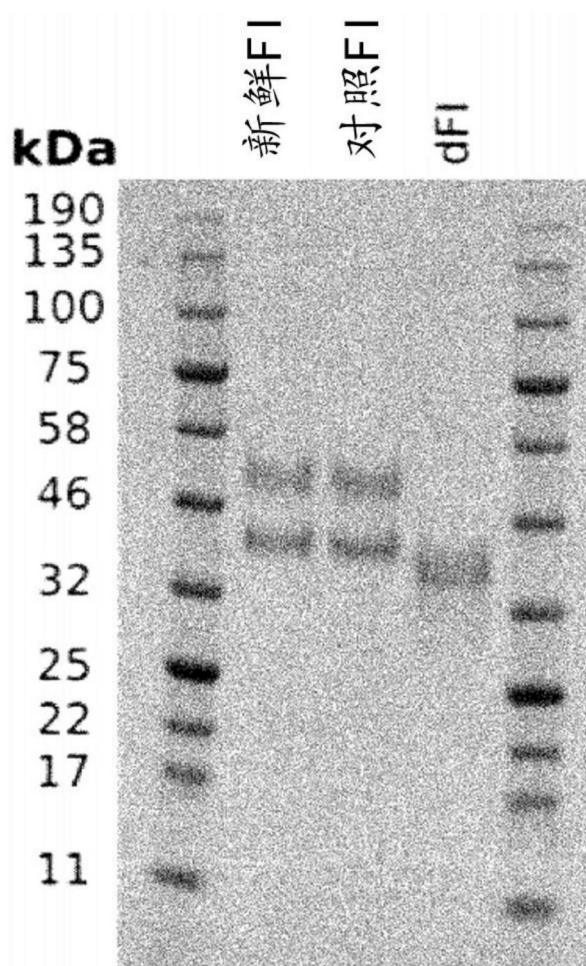


图5B

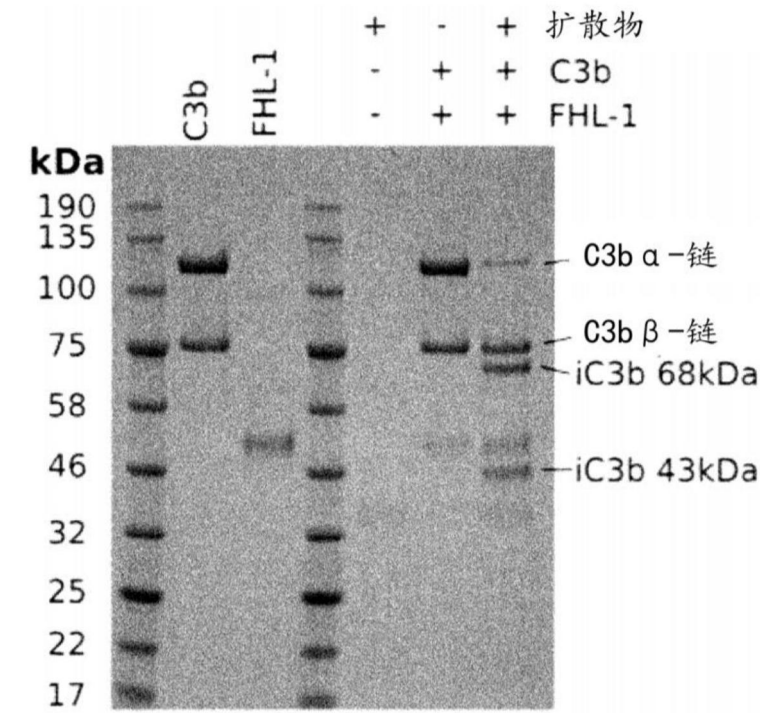


图5C

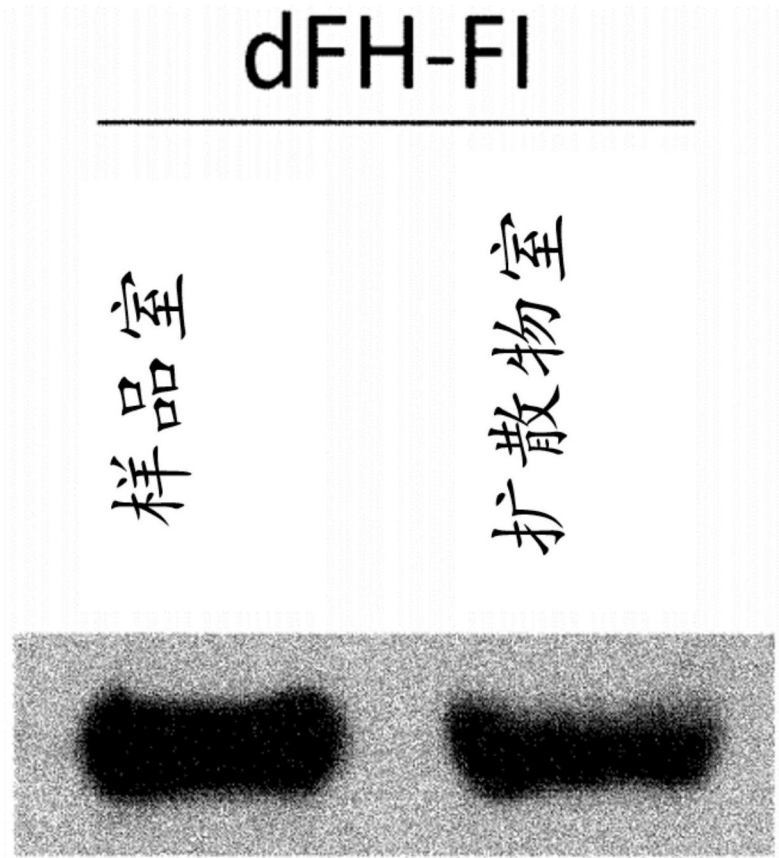


图6

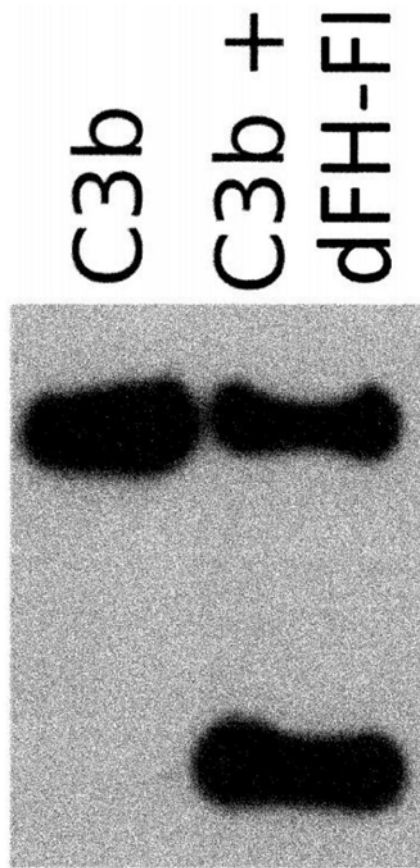


图7

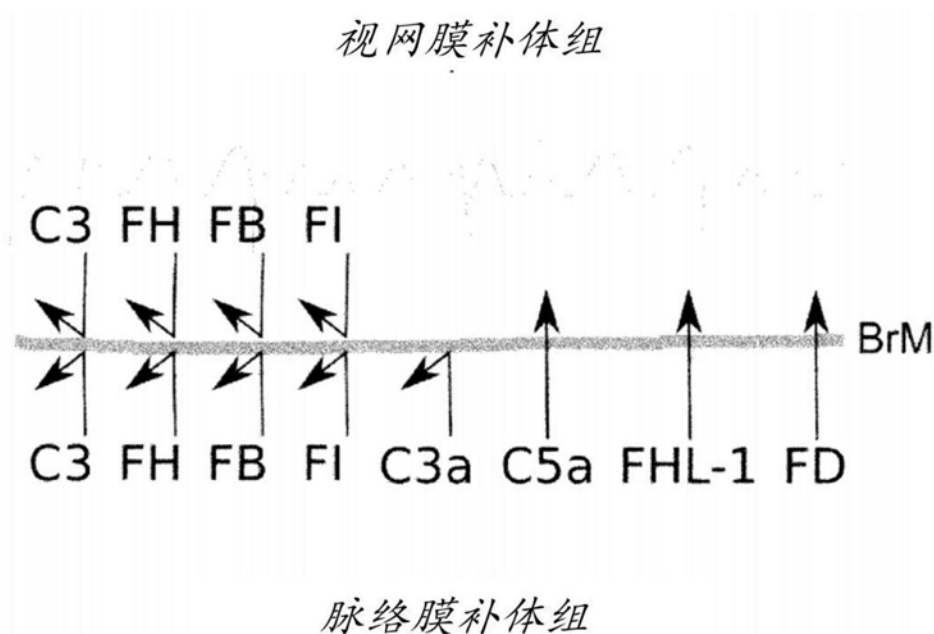


图8

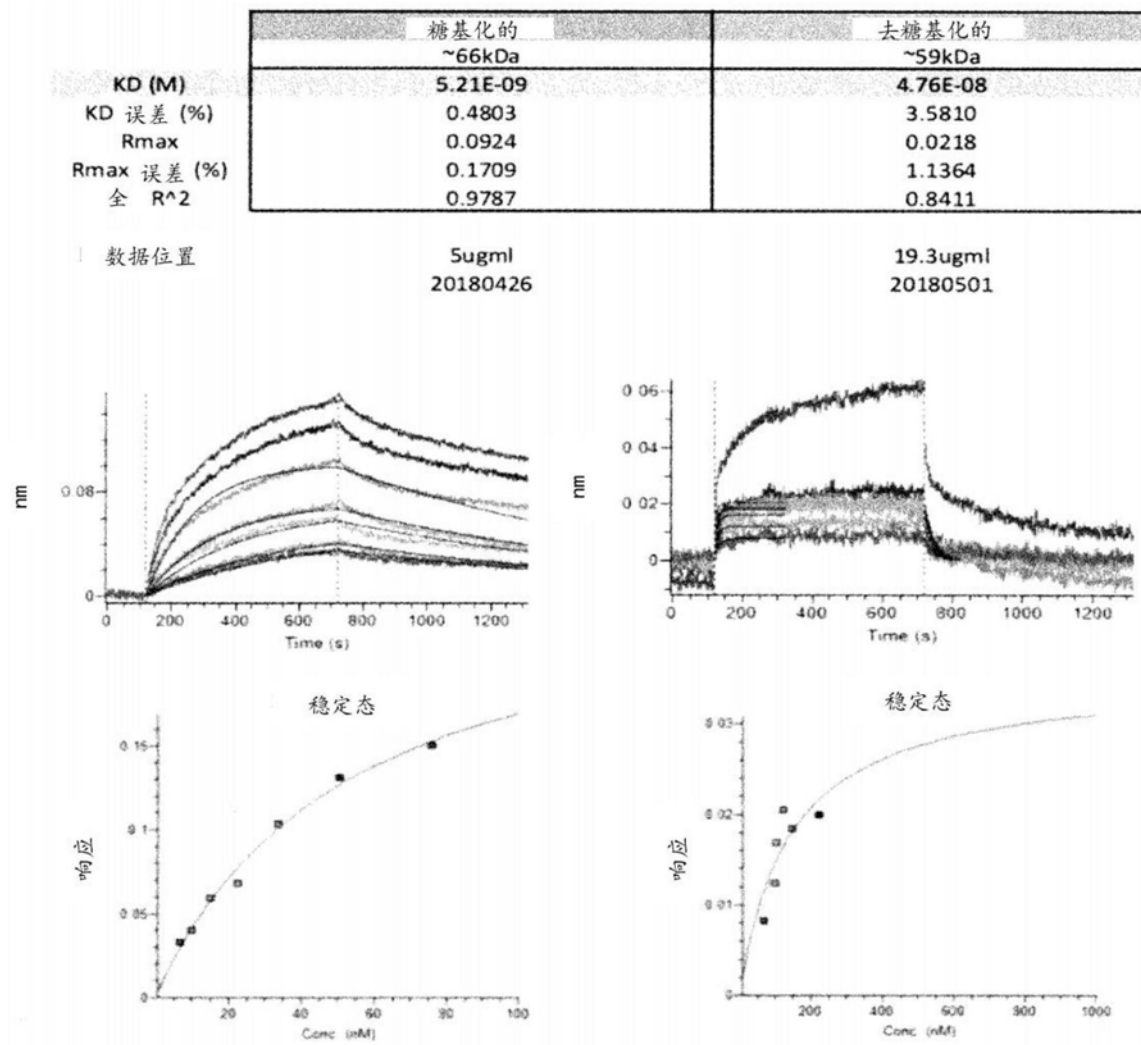


图9A

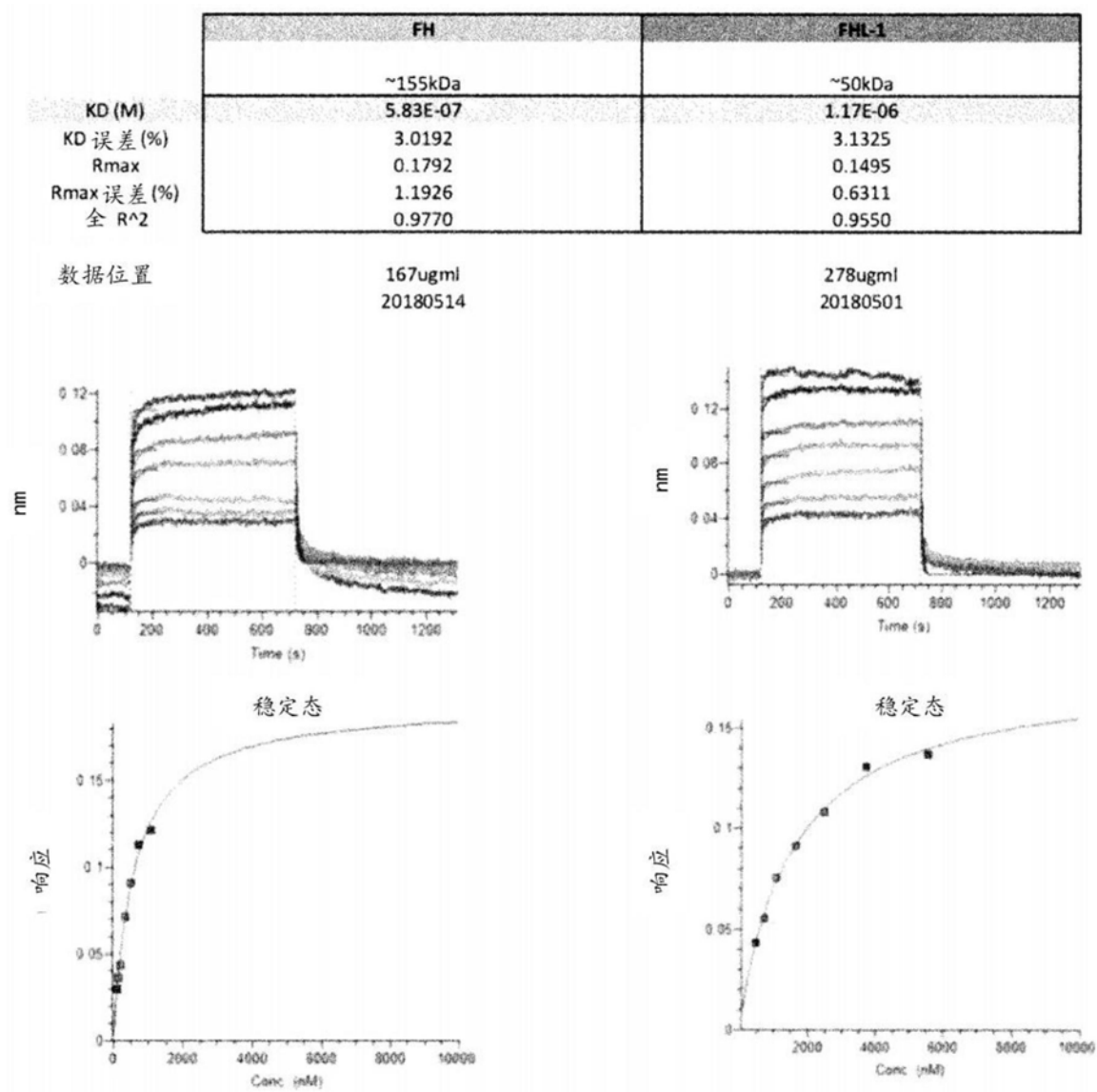


图9B

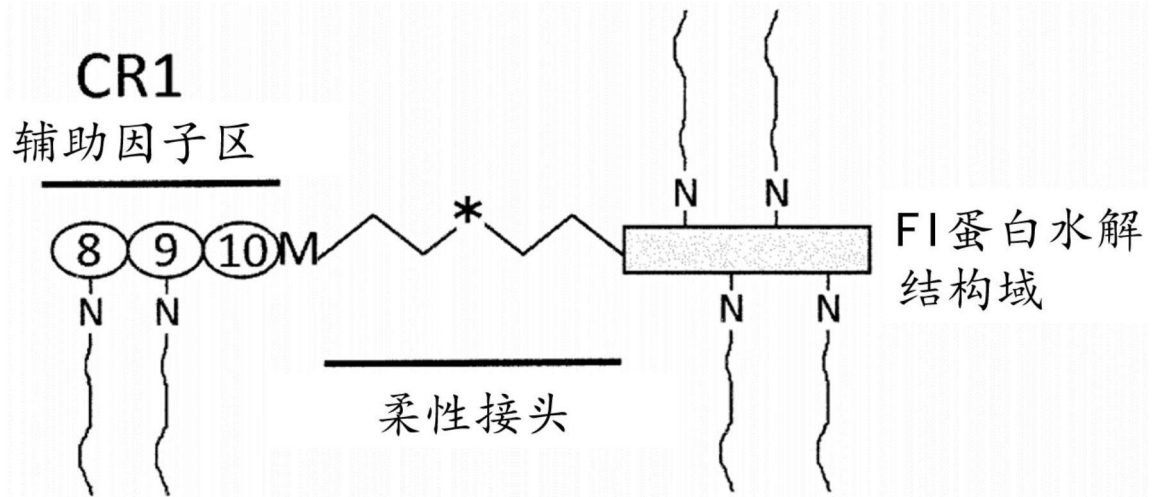


图10A

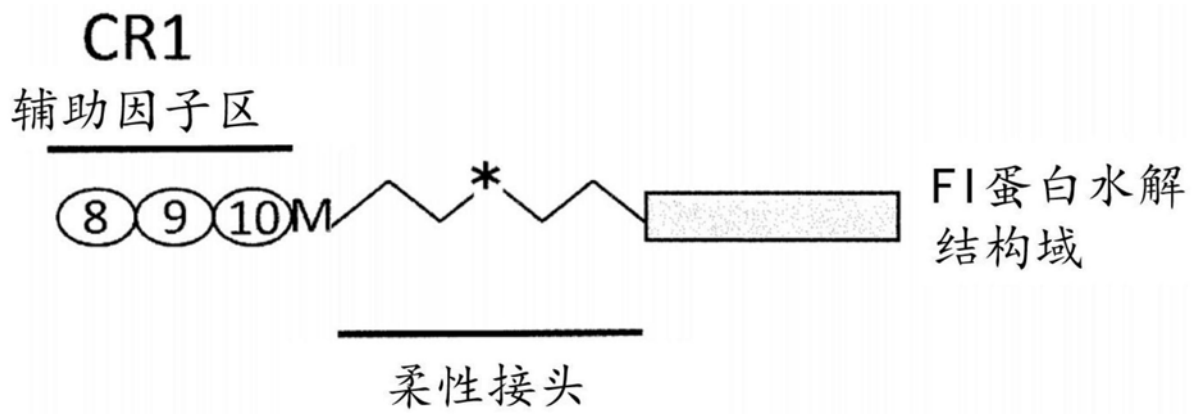


图10B

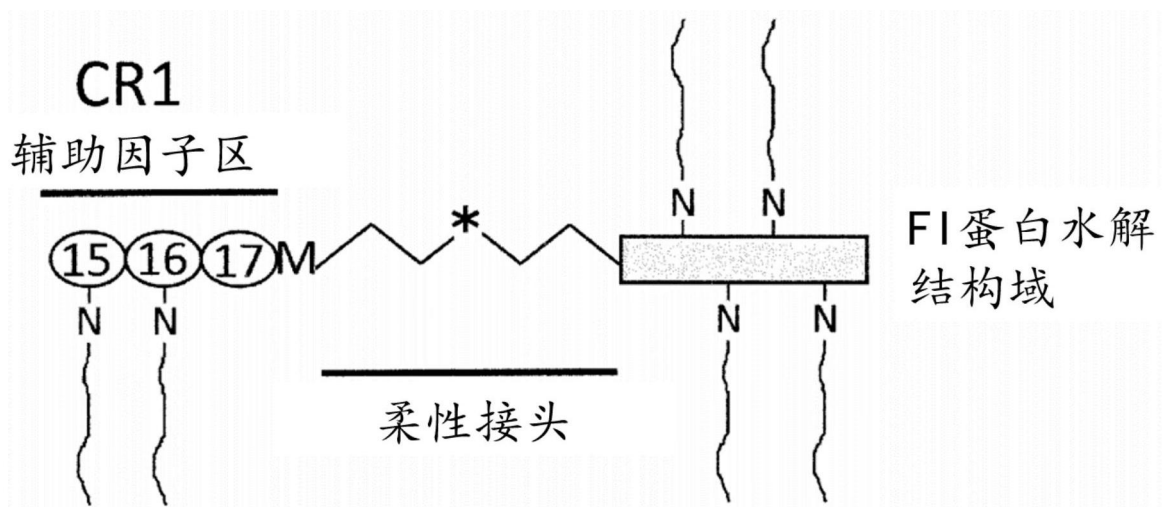


图10C

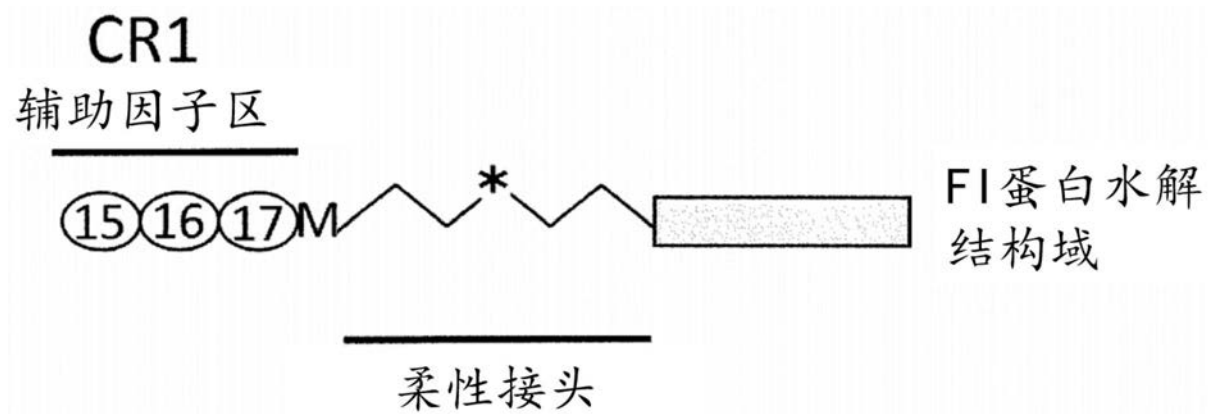


图10D