(19)国家知识产权局

(12)发明专利

(10)授权公告号 CN 113785052 B
(45)授权公告日 2024.06.28

(21)申请号 202080020112.7

(22)申请日 2020.02.18

(65)同一申请的已公布的文献号
申请公布号 CN 113785052 A

(43)申请公布日 2021.12.10

(30)优先权数据
19157932.5 2019.02.19 EP

(85)PCT国际申请进入国家阶段日
2021.09.09

(86)PCT国际申请的申请数据
PCT/EP2020/054197 2020.02.18

(87)PCT国际申请的公布数据
WO2020/169577 EN 2020.08.27

(73)专利权人 维也纳兽医大学
地址 奥地利维也纳
专利权人 维也纳自然资源与生命科学大学

(72)发明人 T·伯姆 B·伊尔马 N·博特 E·格卢多瓦茨

(74)专利代理机构 广州嘉权专利商标事务所有限公司 44205
专利代理师 黄琳娟

(51)Int.Cl.
C12N 9/06(2006.01)
A61K 38/44(2006.01)
C12N 15/53(2006.01)

(56)对比文件
WO 2023122254 A2,2023.06.29
McGrath 等.“Structure and Inhibition of Human Diamine Oxidase”.《BIOCHEMISTRY》.2009,第48卷(第41期),摘要,第9810页左栏注释,第9816页右栏第3段.
Gludovacz 等.“Glycosylation site Asn168 is important for slow in vivo clearance of recombinant human diamine oxidase heparin-binding motif mutants”.《GLYCOBIOLOGY》.2022,第32卷(第5期),404-413.
王清.“拟南芥二胺氧化酶(CuAOζ)及其转录因子MYB响应生长素信号的分子机理”.《中国优秀硕士学位论文全文数据库 基础科学辑》.2019,(第7期),A006-123.

审查员 刘魏

权利要求书2页 说明书31页
序列表205页 附图61页

(54)发明名称

新重组二胺氧化酶及其治疗以过量组胺为特征的疾病的用途

(57)摘要

本发明涉及具有降低的糖胺聚糖结合亲和力的重组人二胺氧化酶(DAO),其中所述DAO在糖胺聚糖(GAG)结合结构域中包含至少一个氨基酸修饰。本发明还涉及所述DAO在治疗与过量组胺相关的病症中,特别地在慢性变应性疾病中,更特别地在过敏反应、过敏性休克、慢性荨麻疹、急性荨麻疹、哮喘、枯草热、变应性鼻炎、变应性结膜炎、组胺中毒、头痛、特应性皮炎炎性疾病、肥大细胞增多症、肥大细胞激活综合征(MCAS)、先兆子痫、妊娠剧吐、早产、消化性溃疡、酸返流、瘙痒症和败血症中的用途。

CN 113785052 B

1.重组人二胺氧化酶(DAO),所述重组人二胺氧化酶(DAO)与相应的野生型人DAO相比具有降低的糖胺聚糖结合亲和力,其中所述重组人DAO在参考SEQ ID NO:1的编号的糖胺聚糖(GAG)结合结构域的第568-575位的氨基酸上发生取代;其中所述氨基酸取代选自R568S、K575T、R568S+R571T、R568S+K575T和R568S+R571T+C123A。

2.根据权利要求1所述的重组DAO,所述重组DAO包含氨基酸序列SEQ ID NO:10、11或16。

3.重组人二胺氧化酶(DAO),所述重组人DAO在权利要求1所述的重组人DAO的基础上还在参考SEQ ID NO:1中在第123位氨基酸的溶剂可及的半胱氨酸(cys123)上发生取代,其中cys123被丙氨酸取代。

4.根据权利要求1或3所述的重组人DAO,其参考SEQ ID NO:1在第168位还包含N168Q的氨基酸取代。

5.融合多肽,所述融合多肽包含权利要求1至4中任一项所述的重组人DAO和人IgG或人血清白蛋白(HSA)的Fc结构域,其中所述融合多肽保留重组人DAO的功能活性。

6.编码权利要求1至4中任一项所述的重组人DAO的分离的核苷酸序列,所述核苷酸序列包含序列SEQ ID NO:18-19、21、24、26-27、29或32。

7.包含权利要求6所述的核苷酸序列的重组载体,所述载体是细菌、酵母、杆状病毒、植物或哺乳动物表达载体。

8.表达盒,所述表达盒包含权利要求6所述的核苷酸序列,所述核苷酸序列可操作地连接至调节元件。

9.包含权利要求1至4中任一项所述的重组人DAO的重组宿主细胞或宿主细胞系,其中所述宿主细胞选自由以下项组成的组:CHO细胞、Vero细胞、MDCK细胞、毕赤酵母细胞、SF9细胞。

10.表达系统,所述表达系统包含权利要求7所述的载体或权利要求8所述的表达盒和权利要求9的宿主细胞或宿主细胞系。

11.用于产生根据权利要求1至4所述的重组人DAO的方法,所述方法包括以下步骤:

i.将编码权利要求1至4中任一项所述的重组人DAO的核苷酸序列克隆到表达载体中,

ii.用所述载体转化宿主细胞,

iii.在表达所述重组人DAO的条件下培养转化的宿主细胞,

iv.从宿主细胞培养物中分离所述重组人DAO。

12.根据权利要求11中所述的重组人DAO的方法,步骤iv中,通过分解所述宿主细胞从宿主细胞培养物中分离所述重组人DAO。

13.根据权利要求11或12中所述的重组DAO的方法,所述重组人DAO的方法还包括v.纯化所述重组人DAO。

14.药物组合物,所述药物组合物包含权利要求1至4中任一项所述的重组人DAO和一种或多种赋形剂。

15.根据权利要求1至4中任一项所述的重组人DAO用于制造药剂的用途,所述药剂用于治疗慢性变应性疾病。

16.根据权利要求1至4中任一项所述的重组人DAO用于制造药剂的用途,所述药剂用于治疗过敏反应、过敏性休克、慢性荨麻疹、急性荨麻疹、哮喘、枯草热、变应性鼻炎、变应性结

膜炎、组胺中毒、特应性皮炎炎性疾病、肥大细胞增多症、消化性溃疡、瘙痒症和败血症。

新重组二胺氧化酶及其治疗以过量组胺为特征的疾病的用途

技术领域

[0001] 本发明涉及具有降低的糖胺聚糖结合亲和力的重组二胺氧化酶(diamine oxidase)(DAO),其中所述DAO在糖胺聚糖(glycosaminoglycan)(GAG)结合结构域中包含至少一个氨基酸修饰。

[0002] 本发明还涉及所述DAO在治疗与过量组胺相关的病症中,特别地在治疗慢性变应性疾病中和/或在治疗高风险妊娠中,更特别地在治疗过敏反应、过敏性休克、慢性荨麻疹、急性荨麻疹、哮喘、枯草热、变应性鼻炎、变应性结膜炎、组胺中毒、头痛、特应性皮炎炎性疾病、肥大细胞增多症、肥大细胞激活综合征(MCAS)、先兆子痫、妊娠剧吐、早产、消化性溃疡、酸返流、瘙痒症和败血症中的用途。

背景技术

[0003] 组胺(2-(1H-咪唑-4-基)乙胺)是一种有机含氮化合物,其参与局部免疫反应,调节肠道生理功能并且充当脑、脊髓和子宫的神经递质。组胺参与炎症反应并且具有作为瘙痒介质的核心作用。作为对外来病原体的免疫反应的一部分,组胺由嗜碱性粒细胞以及由在附近结缔组织中发现的肥大细胞产生。它以非活性形式储存在肥大细胞和嗜碱性白细胞的异染颗粒中,其中它可用于立即释放。组胺也可以在炎症过程中由嗜中性粒细胞和巨噬细胞新鲜合成。在其释放后,组胺是强大的生理和病理介质,其与在体内许多不同细胞上表达的四种受体(H_1-H_4)结合。组胺与其受体的结合是非常特异性的。结合后,诱导许多下游活性。急性变态反应,诸如枯草热、流鼻涕、眼睛发痒或在更严重的情况下伴有呼吸困难的哮喘;急性和慢性荨麻疹和超敏反应,也称为过敏反应,例如由药物(尤其是抗生素或放射造影剂)、由花生或黄蜂过敏等引起的过敏反应,由血液中的组织肥大细胞和嗜碱性粒细胞介导,从而释放出若干种介质,其中组胺是最具活性的介质之一。组胺诱导的症状包括过敏反应,一种超敏反应,其具有血压下降、昏厥和呼吸问题等其他症状;支气管痉挛;潮红(皮肤变红);瘙痒症(瘙痒);心动过速(高脉冲率);晕厥(昏厥);低血压(血压低);上腹痛和腹痛;恶心;呕吐;腹泻;疲劳;记忆丧失;抑郁和头痛等。血液中过量的组胺(>10ng/ml;症状在1至3ng/ml开始)会危及生命。血液中大约100ng/ml的组胺浓度可能导致心脏骤停。特别是在妊娠期间,高组胺血症可能导致特定的妊娠并发症,诸如先兆子痫、自然流产、早产和妊娠剧吐(Brew O.和Sullivan M.H.F.,J.Reprod.Immunol.,72(2006),94-107,Maintz L.等人,Human Reproduction Update,14,5,2008,485-495)。

[0004] 肥大细胞和嗜碱性粒细胞是具有许多不同功能的免疫系统细胞。尽管如此,肥大细胞和组胺在许多疾病中起着重要作用,所述疾病如肥大细胞激活综合征、MCAS(即,无法耐受红酒或奶酪或其他食物中的组胺;在文献中通常被描述为组胺不耐受)、特应性皮炎(也称为神经性皮炎,一种皮肤疾病)、肥大细胞增多症(皮肤和/或内脏器官(如骨髓或肝脏或脾脏)中的肥大细胞数量增加)、消化性溃疡(由过量组胺然后酸释放引起的胃或十二指肠粘膜的损伤)、酸返流、头痛、瘙痒症以及可能地甚至败血症等其他疾病。在某些疾病条件下,在例如嗜中性粒细胞和巨噬细胞中诱导的组氨酸脱羧酶也可以新合成组胺。

[0005] 此外,组胺也可以通过吸入或口服(例如,通过摄入含组胺食品,诸如奶酪、酒、鱼罐头和酸菜)从外部进入体内。组胺也可以由微生物组的细菌产生。

[0006] 对抗组胺受体H_1和H_2的活性的抗组胺药已经可用了几十年,并且它们被假设为在治疗诸如流鼻涕以及皮肤和眼睛瘙痒的症状方面是有效的。抗组胺药是全球最频繁开出的药物之一。尽管如此,彻底的数据分析已清楚地显示,抗组胺药的功效在若干种病理条件下是受限的。例如,约25%的慢性荨麻疹患者对抗组胺药有抗性并且遭受低生活质量。用抗组胺药治疗超敏反应被广泛实践,但缺失高质量的功效数据,并且在一些文件中指出缺乏功效。过敏反应指南不一定推荐使用组胺H_1受体阻断剂进行治疗,因为益处证据尚不清楚。不鼓励在过敏反应中使用组胺H_2受体拮抗剂,因为它可能使症状恶化。

[0007] 抗组胺药的这种受限功效并不是令人惊讶的。若干项研究已经显示,抗组胺药只能阻断2至3倍增加的组胺浓度的作用,但当组胺浓度增加超过所述浓度时有效性会小得多。在过敏反应或超敏反应过程中,循环中的组胺浓度在正常人中可能增加超过100倍并且在肥大细胞增多症患者中甚至更多。在稳态非过敏性条件下,肥大细胞增多症患者具有持续5至15倍增加的组胺及其代谢物水平。身体不能足够快地降解过多的组胺,并且各种症状的发展是合乎逻辑的结果。

[0008] 在哺乳动物生物体中,组胺被两种酶降解:二胺氧化酶(二胺氧化酶,DAO,EC 1.4.3.6)和组胺-N-甲基转移酶(HNMT或简称NMT,EC 2.1.1.8)。NMT催化N-甲基化为N-甲基-组胺。

[0009] McGrath AP等人(Biochemistry,2009,48(41),9810-9822)中综述了人DAO的结构和抑制作用。DAO催化组胺氧化脱氨基为咪唑乙醛。DAO最初被鉴定为从切碎的肺和肝脏样品中清除外源性组胺的酶并且因此被称为组胺酶(Best CH.,J.Physiol.,1929,67,256-263)。随后,被鉴定为二胺氧化酶的蛋白质被称为阿米洛利(amiloride)结合蛋白,并且错误地牵涉到阿米洛利敏感性Na^+通道。一些数据库仍将AOC1指定为ABP1。原作者(Novotny WF等人,J.Biol.Chem.,1994,269,9921-9925)后来指出DAO和ABP1实际上是同一种蛋白质,所述原作者还报道了人基因的克隆,对应于751个氨基酸残基的蛋白质。已经在昆虫细胞中实现了重组人DAO(hDAO)的过表达(Elmore BO.等人,J.Biol.Inorg.Chem.,2002,7,565-579)。虽然Elmore等人进一步报道了DAO含有肝素结合共有序列(残基568-575),但不能从此结构推导出肝素结合结构域真正结合肝素。12聚体(mer)肝素分子长约5nm(50 Å)并且DAO中圆形肝素结合结构域的直径约25 Å。肝素12聚体的分子量=284*12=3408Da。LMWH不与DAO强结合,但具有5000Da(18个糖单位)的平均分子量。只有HMWH与DAO结合,其平均分子量为15000Da,但这对应于在一行中15000/284=52个糖单位。

[0010] 大量重组hDAO的可用性使得能够在体外鉴定其优选的底物,显示出对二胺的明显偏向。具体地,组胺和1-甲基组胺两种非典型二胺是优异的底物。各含有替代存在于典型的二胺底物(如亚精胺、腐胺或尸胺)中的一个伯胺的咪唑基团。hDAO是用于降解外源性组胺的前线酶,并且已显示降低的DAO水平与组胺不耐受直接相关(Maintz L.等人,Am.J.Clin.Nutr.,2007,85,1185-1196)。已经在多种异源性妊娠并发症(诸如糖尿病、先兆流产和过期流产以及滋养层障碍)中发现DAO的活性降低(Maintz L.,等人,2008)。

[0011] 在胃肠道中,DAO会降解饮食中的组胺,以避免和保护身体免受血液中浓度增加的影响。尽管如此,除了在妊娠期间外,DAO抗原以及因此其活性在血浆中是低的或甚至不存

在(Boehm T.等人,Clinical Biochemistry 50,2017,444-451)。在妊娠期间,DAO活性增加超过100倍。

[0012] WO 02/43745中公开了全身使用植物源DAO以治疗组胺介导的疾病。然而,由于在植物中频繁出现过敏原,主要鉴于WO 02/43745中公开的豆科植物具有高的致敏潜力的事实,因此从植物中直接分离的酶的施用是一个大问题。

[0013] WO 2006/003213A1描述了动物来源的或重组产生的DAO的特定施用配制品。

[0014] Gludovacz E.等人(J Biotechnol.2016,227:120-130)公布了在CHO细胞中重组野生型(wt)人(rh)DAO的表达和纯化。尽管如此,在大鼠中,wt rhDAO的α分布半衰期小于10分钟,并且占注射的蛋白质的量的超过80%。β-消除半衰期约3小时。生物制剂从大鼠到人外推的比例因子约4至8,并且因此,重组wt DAO的PK曲线不适合临床前和临床开发。DAO的三个糖基化位点已突变,但聚糖突变未改善PK曲线。Gludovacz E.等人(J.Biol.Chem.2018,293(3),1070-1087)公布了聚糖突变对DAO的表达和活性的影响。

[0015] 数据库UniProt登录号G3QJ02,2011,XP-002792064公开了来自大猩猩(Gorilla gorilla)的二胺氧化酶序列。

[0016] 数据库UniProt登录号Q9SXW5,2000公开了来自豌豆(Pisum sativum)的二胺氧化酶序列。

[0017] WO 2012/028891A1报道了来自植物源的组胺酶。因为释放的组胺不能被抗组胺药有效地阻断或失活,因此用于使过量组胺快速失活的新治疗和预防方法将为遭受高循环组胺浓度的患者带来显著益处。许多患者遭受增加的组胺浓度持续数小时。在过敏反应和由于肾脏过滤和血流量减少而引起的低血压期间,组胺的半衰期甚至增加。

[0018] 因此,对于改善的与过量组胺相关的病症的治疗,存在高且未满足的需求。

发明内容

[0019] 在病理条件下,目前可用的抗组胺药不能有效地拮抗过量的组胺。增加的组胺水平会引起烦人的、严重的、使人衰弱的、危及生命的症状并且偶尔会引起死亡。

[0020] 本发明的一个目的是提供用于去除过量组胺以及治疗和预防组胺诱导的疾病和病症的改善的方案。

[0021] 本发明通过提供重组经修饰的DAO以增加个体体内活性DAO的浓度从而分别帮助或实现组胺的降解来解决所述目的。

[0022] 如本文所述的重组人DAO的施用可以在急性、亚急性、亚慢性、慢性和预防性病症下降解过量的组胺,从而显著有益于患有或即将患有抗组胺药不足以有效降解过量组胺浓度的若干种疾病的患者。这为遭受过量组胺的受试者建立了全新的治疗选择。

[0023] 根据本发明,提供了重组人二胺氧化酶(DAO),其与相应野生型人DAO的GAG结合亲和力相比具有降低的糖胺聚糖(GAG)结合亲和力,其中所述DAO在糖胺聚糖(GAG)结合结构域中包含至少一个氨基酸修饰,特别地所述GAG结合结构域参考SEQ ID NO:1的编号在第568-575位包含所述氨基酸。

[0024] 特别地,GAG结合结构域是肝素/硫酸乙酰肝素结合结构域。

[0025] 特别地,氨基酸修饰导致DAO的GAG结合亲和力降低,同时保留其针对组胺的酶活性。

[0026] 根据一个具体实施方案,所述DAO的GAG结合结构域的至少一个氨基酸修饰是氨基酸取代、缺失、插入或与化学部分偶联。

[0027] 根据本发明的一个具体实施方案,本发明的重组DAO在GAG结合结构域中包含2、3、4、5、6、7或8个氨基酸修饰。特别地,所述氨基酸残基被其他氨基酸残基取代,特别地精氨酸或赖氨酸被丝氨酸或苏氨酸取代。

[0028] 根据一个替代实施方案,所述重组DAO包含氨基酸序列X1FX2X3X4LPX5的GAG结合结构域,其中

[0029] X1可以是任何氨基酸,特别地其为A或S,更特别地其为S;

[0030] X2可以是任何氨基酸,特别地其为K;

[0031] X3可以是任何氨基酸,特别地其为A或T,更特别地其为T,

[0032] X4可以是任何氨基酸,特别地其为K,并且

[0033] X5可以是任何氨基酸,特别地其为K或T,更特别地其为T。

[0034] 在又一个具体实施方案中,所述重组DAO包含选自由以下项组成的组的氨基酸序列:SFKAKLPK(SEQ ID NO:33)、AFKAKLPT(SEQ ID NO:34)、AFKTKLPK(SEQ ID NO:35)、SFKTKLPK(SEQ ID NO:36)、AFKTKLPT(SEQ ID NO:37)、SFKAKLPK(SEQ ID NO:38)。

[0035] 根据一个具体实施方案,如本文公开的重组DAO进一步包含参考SEQ ID No.1的编号在第123氨基酸位的溶剂可及的半胱氨酸(cys123)的至少一个修饰,特别地所述半胱氨酸的修饰是氨基酸取代、缺失或与化学部分的缀合。

[0036] 在一个优选的实施方案中,根据DAO的SEQ ID 1的编号,cys123被丙氨酸取代(cys123ala,C123A)。

[0037] 本发明的DAO特别地显示从血浆的清除率降低。本发明特别地提供了重组DAO,所述重组DAO与野生型DAO相比具有显著增加的血浆半衰期,特别地所述半衰期与野生型DAO相比增加至少1.5倍、特别是至少2倍。

[0038] 在替代或又一个实施方案中,所述DAO与野生型DAO相比具有至少10倍增加的AUC。

[0039] 根据本文提供的一个实施方案,与野生型DAO相比,内皮细胞对重组DAO的内化减少至少10%、25%、50%、60%、70%、80%、特别是90%。

[0040] 根据又一个实施方案,与野生型DAO相比,如本文所述的DAO的GAG结合亲和力、特别是肝素/硫酸乙酰肝素结合亲和力减少至少10%、25%、50%、60%、70%、80%、特别是90%。

[0041] 本文还提供了重组DAO或其功能衍生物或类似物,其包含氨基酸序列SEQ ID NO:2、3、4、5、6、7、8、9、10、11、12、13、14、15或16或与SEQ ID NO:2、3、4、5、6、7、8、9、10、11、12、13、14、15或16中的任一个具有至少90%的序列同一性。

[0042] 人DAO还具有多个N-糖基化位点,其在内质网中的分泌和停留中发挥作用。特别地,在Asn-168处的聚糖主要被双触角至四触角分支唾液酸化。

[0043] 根据一个实施方案,本文所述的重组DAO进一步包含修饰,特别是参考SEQ ID NO 1在第168位的氨基酸取代。特别地,所述修饰是在第168位的单一修饰。更特别地,Asn被Gln替代。特别地,所述修饰增加本文所述的DAO的PK。更特别地,所述DAO包含氨基酸序列SEQ ID NO:106。

[0044] 本文还提供了重组DAO或其功能衍生物或类似物,其由SEQ ID NO:17、18、19、20、

21、22、23、24、25、26、27、28、29、30、31或32中的任一个或与SEQ ID NO:17、18、19、20、21、22、23、24、25、26、27、28、29、30、31或32中的任一个具有至少90％的序列同一性的编码。

[0045] 本文还提供了编码如本文所述的DAO或其功能类似物或衍生物的分离的核苷酸序列,其特别地包含序列SEQ ID NO:17、18、19、20、21、22、23、24、25、26、27、28、29、30、31或32或其片段。

[0046] 根据本发明的一个具体实施方案,本文提供了融合多肽,所述融合多肽包含本文所述的重组DAO和人IgG或人血清白蛋白(HSA)的Fc结构域或其片段,其中所述融合多肽保留所述重组DAO的功能活性。

[0047] 本文还提供了融合多肽,所述融合多肽包含本文所述的重组DAO和人IgG的Fc结构域,所述融合多肽包含SEQ ID No:56至70中的任一个或与SEQ ID NO:56至70中的任一个具有至少90％的序列同一性的序列。

[0048] 本文还提供了融合多肽,所述融合多肽包含本文所述的重组DAO和人IgG的Fc结构域或其功能衍生物或类似物,所述融合多肽由SEQ ID NO:72至102中的任一个或与SEQ ID NO:72至102中的任一个具有至少90％的序列同一性的编码。

[0049] 本文进一步提供了重组载体,所述重组载体包含本文所述的核苷酸序列,特别地所述载体是细菌、酵母、杆状病毒、植物或哺乳动物表达载体。

[0050] 根据一个实施方案,本文提供了表达盒,所述表达盒包含所述核苷酸序列,所述核苷酸序列可操作地连接至调节元件。

[0051] 根据一个实施方案,本文提供了细菌、酵母、杆状病毒、植物或哺乳动物源的重组宿主细胞或宿主细胞系,其包含本文所述的重组DAO,其中所述宿主细胞特别地选自由以下项组成的组:CHO细胞、Vero细胞、MDCK细胞、毕赤酵母(Pichia pastoris)细胞和SF9细胞。

[0052] 本文进一步提供了表达系统,所述表达系统包含所述载体或所述表达盒和本文所述的宿主细胞或宿主细胞系。

[0053] 根据一个实施方案,本文还提供了用于生产本文所述的重组DAO的方法,所述方法包括以下步骤:

[0054] i.将编码所述DAO的核苷酸序列克隆到表达载体中,

[0055] ii.用所述载体转化宿主细胞,

[0056] iii.在表达所述DAO的条件下培养转化的宿主细胞,

[0057] iv.从宿主细胞培养物中分离所述DAO,任选地通过分解所述宿主细胞,以及任选地

[0058] v.纯化所述DAO。

[0059] 根据一个实施方案,提供了药物组合物,所述药物组合物包含所述重组DAO和任选地一种或多种赋形剂。

[0060] 特别地,所述药物组合物可以静脉内、肌内和皮下或经由其他肠胃外施用途径如腹膜内或鞘内来应用。

[0061] 在又一个实施方案中,提供了所述重组DAO用于制备药物组合物的用途。

[0062] 特别地,所述重组DAO被提供用于治疗与过量组胺相关的病症,特别地用于治疗慢性变应性疾病或与组胺增加或DAO活性降低相关的疾病,更特别地用于治疗过敏反应、过敏性休克、慢性荨麻疹、急性荨麻疹、哮喘、枯草热、变应性鼻炎、变应性结膜炎、组胺中毒、头

痛、特应性皮炎炎性疾病、肥大细胞增多症、肥大细胞激活综合征(MCAS)、先兆子痫、妊娠剧吐、早产、消化性溃疡、酸返流、瘙痒症和败血症。

[0063] 在本发明的一个实施方案中,所述重组DAO的用途包括用于制造药剂,所述药剂用于治疗与过量组胺相关的病症,特别地用于治疗慢性变应性疾病或与组胺增加或DAO活性降低相关的疾病,更特别地用于治疗过敏反应、过敏性休克、慢性荨麻疹、急性荨麻疹、哮喘、枯草热、变应性鼻炎、变应性结膜炎、组胺中毒、头痛、特应性皮炎炎性疾病、肥大细胞增多症、肥大细胞激活综合征(MCAS)、先兆子痫、妊娠剧吐、早产、消化性溃疡、酸返流、瘙痒症和败血症。

[0064] 在一个替代实施方案中,本文提供了靶特异性配体,所述靶特异性配体特异性结合至DAO的GAG结合结构域,特别是结合至参考SEQ ID No.1的编号在第568-575位的氨基酸中的一个或多个。

[0065] 可替代地,本文提供了靶特异性配体,所述靶特异性配体特异性抑制肝素/硫酸乙酰肝素结合至DAO的GAG结合结构域,特别是结合至参考SEQ ID No.1的编号在第568-575位的氨基酸中的任一个或多个。

[0066] 特别地,所述配体选自由以下项组成的组:核酸、小分子抑制剂或抗原结合蛋白。

[0067] 在一个替代实施方案中,所述配体是抗原结合蛋白,特别地选自由以下项组成的组:

[0068] -抗体或抗体片段,诸如以下中的任意:Fab;Fd;scFv;双体抗体;三体抗体;Fv四聚体;微型抗体;纳米抗体;单结构域抗体,如VH、VHH、IgNAR或V-NAR;

[0069] -抗体模拟物,诸如Adnectins™、Affibodies®、Affilins®、Affimers®、Affitin、α体、适体、Anticalin、Avimer、DARPins®、Fynomers®、Kunitz结构域肽、单体或NanoCLAMPS;或

[0070] -包含一个或多个免疫球蛋白折叠结构域、抗体结构域或抗体模拟物的融合蛋白。

[0071] 根据一个实施方案,本文提供了用于鉴定调节所述DAO的肝素结合的化合物的方法,其包括以下步骤:

[0072] (a)构建由DAO序列SEQ ID No.1的氨基酸的结构坐标定义的GAG结合结构域的计算机模型,

[0073] (b)通过选自由以下项组成的组的方法选择潜在的调节化合物:

[0074] (i)将分子片段组装成所述化合物,

[0075] (ii)从小分子数据库中选择化合物,以及

[0076] (iii)所述化合物的从头配体设计;

[0077] (c)采用计算手段在所述化合物与GAG结合结构域的计算机模型之间进行拟合程序操作,以提供在肝素结合结构域中所述化合物的能量最小化构型;以及

[0078] (d)评价所述拟合操作的结果以量化所述化合物与肝素/硫酸乙酰肝素结合结构域之间的缔合,从而评价所述化合物与所述肝素结合结构域缔合的能力。

附图说明

[0079] 图1:野生型DAO和经修饰的DAO的氨基酸和核苷酸序列。参考氨基酸序列:粗体字母是指与wt序列相比的取代;下划线字母是指分泌信号;粗体斜体字母是指Fc,粗体、斜体

且下划线字母是指来自IgG1铰链区的接头序列;

[0080] 图2:重组人DAO野生型和肝素/硫酸乙酰肝素突变体的肝素-琼脂糖洗脱曲线;

[0081] 图3:与DAO_WT相比,以低50％的盐浓度从肝素-琼脂糖洗脱Hepmut 1、4和7变体;

[0082] 图4:在与DAO_WT和Hepmut变体一起孵育后SK-Hep1细胞裂解物的蛋白质印迹;

[0083] 图5:与DAO_WT相比,Hepmut4变体显示出与SK-Hep1细胞的结合减少;

[0084] 图6:DAO_WT和Hepmut4的等温滴定量热法;

[0085] 图7:示出了线性(a)和log y-标度(b)。静脉内注射1mg/kg DAO变体后,与野生型DAO蛋白相比,Hepmut4使AUC(曲线下面积)增加超过19倍;

[0086] 图8:在腹膜内注射后,与DAO_WT蛋白相比,Hepmut4使AUC增加超过16倍;

[0087] 图9:使用1mg/kg DAO野生型和不同Hepmut变体的测量值的平均值;

[0088] 图10:与以1mg/kg施用的DAO野生型蛋白相比,肝素/硫酸乙酰肝素结合结构域突变体的清除慢;

[0089] 图11:与DAO野生型蛋白相比,肝素结合结构域突变体的清除慢;

[0090] 图12:与以1mg/kg施用的DAO野生型蛋白相比,肝素结合结构域突变体的清除慢;

[0091] 图13:与以1mg/kg施用的DAO野生型蛋白相比,肝素结合结构域突变体的清除慢。线性y-轴标度;

[0092] 图14:与以1mg/kg施用的DAO野生型蛋白相比,肝素结合结构域突变体的清除慢。示出了前90分钟;线性y-轴标度;

[0093] 图15:与分别在6或4只大鼠中以1mg/kg施用的Fc-Hepmut4相比,Fc-DAO野生型的清除快速。示出了平均值与标准偏差;线性y-轴标度;

[0094] 图16:与分别在6或4只大鼠中以1mg/kg施用的Fc-Hepmut4相比,Fc-DAO野生型的清除快速。示出了平均值与标准偏差;Log y-轴标度;

[0095] 图17:Fc-DAO-Hepmut4示出了在静脉内施用1mg/kg后AUC的强烈增加;Log y-轴标度;

[0096] 图18:Fc-DAO-Hepmut4示出了在静脉内施用1mg/kg后AUC的强烈增加;线性y-轴标度;

[0097] 图19:DAO突变体的蛋白质印迹;

[0098] 图20:DAO_WT与cys123突变之间的DAO活性没有相关差异。

具体实施方式

[0099] 除非另有指示或定义,否则本文中使用的所有术语均具有其在本领域中的通常含义,这对技术人员来说是清楚的。例如参考标准手册,诸如Sambrook等人,“Molecular Cloning:A Laboratory Manual”(第2版),第1-3卷,冷泉港实验室出版社(Cold Spring Harbor Laboratory Press)(1989);Lewin,“Genes IV”,牛津大学出版社(Oxford University Press),纽约,(1990),和Janeway等人,“Immunobiology”(第5版或更新的版本,Garland Science,纽约,2001)。

[0100] 权利要求的主题具体涉及人造产品或采用或生产此类人造产品的方法,所述人造产品可以是天然(野生型)产品的变体。尽管与天然结构可能存在一定程度的序列同一性,但应充分理解,本发明的材料、方法和用途(例如,特别是指分离的核酸序列、氨基酸序列、

融合构建体、表达构建体、转化的宿主细胞和经修饰的蛋白质)是“人造的”或合成的,并且因此不被视为“自然法则”的结果。

[0101] 如本文所用,术语“包含”、“含有”、“具有”和“包括”可以同义使用并且应被理解为开放性限定,允许其他成员或部分或要素。“由...组成”被认为是组成限定特征的最封闭的限定,其中没有其他要素。因此,“包含”更广泛并且含有“由...组成”限定。

[0102] 如本文所用的术语“约”是指相同的值或相差给定值的+/-5%的值。

[0103] 人DAO单体包含约751个氨基酸并且形成具有酶活性的二聚体。在DAO二聚体中的14个半胱氨酸中,其中10个参与S-S形成并且4个不参与。特别地,半胱氨酸123和633不参与二硫键的形成。

[0104] 如本文所用,氨基酸是指由六十四种三联密码子编码的二十种天然存在的氨基酸。这20种氨基酸可以分为具有中性电荷、正电荷和负电荷的氨基酸:

[0105] 下面示出了“中性”氨基酸连同其相应的三字母和单字母代码和极性:

[0106] 丙氨酸:(Ala,A)极性,中性;

[0107] 天冬酰胺:(Asn,N)极性,中性;

[0108] 半胱氨酸:(Cys,C)非极性,中性;

[0109] 谷氨酰胺:(Gln,Q)极性,中性;

[0110] 甘氨酸:(Gly,G)非极性,中性;

[0111] 异亮氨酸:(Ile,I)非极性,中性;

[0112] 亮氨酸:(Leu,L)非极性,中性;

[0113] 甲硫氨酸:(Met,M)非极性,中性;

[0114] 苯丙氨酸:(Phe,F)非极性,中性;

[0115] 脯氨酸:(Pro,P)非极性,中性;

[0116] 丝氨酸:(Ser,S)极性,中性;

[0117] 苏氨酸:(Thr,T)极性,中性;

[0118] 色氨酸:(Trp,W)非极性,中性;

[0119] 酪氨酸:(Tyr,Y)极性,中性;

[0120] 缬氨酸:(Val,V)非极性,中性;和

[0121] 组氨酸:(His,H)极性,正(10%)中性(90%)。

[0122] “带正”电荷的氨基酸是:

[0123] 精氨酸:(Arg,R)极性,正;和

[0124] 赖氨酸:(Lys,K)极性,正。

[0125] “带负”电荷的氨基酸是:

[0126] 天冬氨酸:(Asp,D)极性,负;和

[0127] 谷氨酸:(Glu,E)极性,负。

[0128] 本发明DAO的术语“修饰”是指任何氨基酸序列改变,包括但不限于氨基酸取代、添加、缺失、突变和插入。修饰也可以是化学选择性修饰。此类修饰可以是与化学部分的缀合或偶联,其中在两个分子之间形成稳定的共价连接,所述分子中的至少一个是生物分子。此类缀合可以用一个或多个氨基酸残基形成,诸如但不限于与马来酰亚胺、碘乙酰胺、异乙酰胺、2-硫代吡啶、3-芳基丙腈、苯甲酰氟、异硫氰酸酯、异氰酸酯、重氮盐、PTAD、NaIO4或PLP

的缀合。

[0129] 游离半胱氨酸很少出现在蛋白质表面上,并且对于化学选择性修饰是优异的选择。特别地,在如本文所述的经修饰的DAO的第123和633氨基酸位的Cys是溶剂可及的。通过特定地取代溶剂可及的cys123,特别是通过将cys123交换为ala123,如此产生的DAO变得无法形成导致更高阶聚集体的二硫键或其他分子相互作用。在CHO细胞中表达重组DAO后,一定百分比的DAO分子(约20%至30%)不仅形成二聚体,而且还形成四聚体、六聚体和甚至八聚体。这些更高阶的寡聚体已被描述,并且可以被认为是具有未知功能的天然变体。不清楚它们是在折叠和从ER转运到高尔基体并且分泌到细胞外环境中期间形成的,还是一般只在细胞外环境中形成的。尽管如此,这些四聚体和更大的寡聚体使本文所述的重组DAO的最优配制品的表达、纯化、表征、标准化和选择复杂化。通过使DAO表面上的相对溶剂可及的半胱氨酸突变,特别是通过使Cys123突变,在宿主细胞、特别是CHO细胞的上清液中仅发现DAO二聚体。

[0130] 另外,根据又一个具体实施方案,在第633氨基酸位的半胱氨酸也可以如本文针对cys123所述进行修饰。Cys633也不参与二硫键的形成。

[0131] 在碱性条件下,半胱氨酸残基可以被去质子化以产生硫醇盐亲核试剂,所述硫醇盐亲核试剂将与软亲电试剂(诸如马来酰亚胺和碘乙酰胺)反应。其结果是,形成碳-硫键。半胱氨酸残基的另一种修饰涉及二硫键的形成。还原的半胱氨酸残基与外源性二硫化物反应,在蛋白质上产生新的二硫键。通常使用过量的二硫化物来驱动反应,诸如2-硫代吡啶酮和3-羧基-4-硝基苯硫酚。缺电子炔烃被证明在其他亲核氨基酸残基的存在下选择性地与蛋白质的半胱氨酸残基反应。根据炔烃取代,这些反应可以产生可裂解的(当使用炔酮衍生物时)或水解稳定的生物缀合物(当使用3-芳基丙炔腈时)。

[0132] 在术语修饰内,还包括用非天然氨基酸取代天然氨基酸。通用遗传密码不编码非天然氨基酸。通常,它们可以作为代谢产物在自然界中被发现,尤其是在植物和细菌中。此类非天然氨基酸可以选自但不限于D-氨基酸、同源氨基酸、N-甲基氨基酸、α甲基氨基酸、β^2氨基酸、β^3氨基酸、β^3同源氨基酸、ACHC、类肽或重氨基酸,特别是被13C和/或15N原子取代的,特别是E-乙酰基-赖氨酸、丙氨酸(3-氨基-丙酸)、6-氨基己酸、?-氨基丁酸、瓜氨酸、乙酰胺基甲基保护的半胱氨酸、二甲基-赖氨酸、羟脯氨酸、巯基丙酸、甲基-赖氨酸、3-硝基-酪氨酸、正亮氨酸、焦谷氨酸、苄氧羰基。

[0133] 如本文所用,术语“GAG结合结构域”是指具有DAO的区域,其参与与所有四类糖胺聚糖(包括肝素/硫酸乙酰肝素、软骨素/硫酸皮肤素、硫酸角蛋白和透明质酸)的结合或相互作用。与肝素/硫酸乙酰肝素的结合是优选的。肝素存在于肥大细胞中。硫酸乙酰肝素存在于几乎所有细胞上,诸如内皮细胞。

[0134] 术语“GAG结合”是指DAO与糖胺聚糖,特别是与肝素或硫酸乙酰肝素的相互作用/结合。GAG主要通过在带负电荷的硫酸基团和糖醛酸与蛋白质中带正电荷的氨基酸之间的静电相互作用与许多不同类别的蛋白质结合。肝素结合亲和力可以通过技术人员已知的任何方法来确定。多种方法可用于分析GAG-蛋白质相互作用,并且一些会提供K_d值的直接测量。一种常见的方法涉及蛋白质在含有共价连接的GAG链(通常是肝素)的琼脂糖柱上的亲和分级。用不同浓度的氯化钠洗脱结合的蛋白质,并且洗脱所需的浓度总体上与K_d成比例。高亲和力相互作用需要至少1M NaCl来置换结合的配体,其转化为10^{-7}-10^{-9}M的K_d值(在生理

盐浓度下通过平衡结合确定)。具有低亲和力(10^{-4}-10^{-6}M)的蛋白质在“正常”条件(0.15M NaCl)下不结合或仅需要0.3-0.5M NaCl来洗脱。此方法基于GAG-蛋白质相互作用是完全离子性的假设,并且在比较不同的GAG结合蛋白时可以提供相对亲和力的评估。替代方法可以是但不限于亲和共电泳、分析超速离心、圆二色性、竞争ELISA、荧光显微术、离子迁移质谱法、等温滴定量热法、激光散射、NMR、表面等离子体共振和X射线,并且从而提供详细的热力学数据(ΔH[焓变]、ΔS[熵变]、ΔCp[摩尔热容变化]等)、动力学数据(缔合和解离速率)、以及在GAG-蛋白质相互作用中原子接触的高分辨率数据(Esko JD.等人,Essentials of Glycobiology,第3版,第38章,2017)。

[0135] 特别地,如本文所述的DAO突变体具有减弱的或显示出降低的与肝素和/或硫酸乙酰肝素的结合。特别地,与野生型DAO相比,所述重组DAO的肝素/硫酸乙酰肝素结合亲和力减少至少10%、25%、50%、60%、70%、80%、特别是90%。根据特定方法,使用肝素-琼脂糖色谱法确定结合亲和力,其中在低盐浓度下孵育DAO变体并且随着盐浓度增加而被洗脱。将具有DAO蛋白峰(使用在280nm处的吸光度测量)的盐浓度用作洗脱DAO的mM盐浓度。

[0136] 与被内化的野生型DAO相比,本发明的DAO进一步显示出降低的到内皮细胞中的内化。特别地,与野生型DAO相比,被内皮细胞的内化减少至少10%、25%、50%、60%、70%、80%、特别是90%。

[0137] 特别地,GAG结合结构域参考SEQ ID NO:1的编号在第568-575位包含氨基酸。在所述结构域内,可以修饰1、2、3、4、5、6、7个或所有氨基酸。

[0138] DAO单体在一级氨基酸序列中含有24个赖氨酸和44个精氨酸,其中大部分在分子表面上。其他赖氨酸和精氨酸很可能参与肝素结合。除了包括在第568-575位的氨基酸的GAG结合结构域之外,在DAO表面上的其他赖氨酸或精氨酸也可能参与肝素/硫酸乙酰肝素结合。

[0139] 这些赖氨酸和/或精氨酸中的一种或多种的修饰可以进一步降低所述重组DAO的肝素/硫酸乙酰肝素结合。

[0140] DAO的术语“酶活性”是指所述多肽催化适当的底物(如腐胺或组胺)氧化脱氨基为氨基丁醛或咪唑乙醛的能力。酶活性的保留意指本发明的DAO具有与相应野生型DAO相同或相似的酶活性。为野生型活性的至少80%、特别是至少90%的酶活性被解释为与野生型DAO相似的酶活性。

[0141] 为了确定DAO的酶活性,可以使用本领域已知的任何方法。这些方法可以是但不限于使用辣根过氧化物酶(HRP)介导的鲁米诺氧化的测定(Bartko J.等人,Alcohol.2016年8月;54:51-9);如Holmstedt B.O.和Tham R.(Acta Physiol.Scand.,1959,45,152-163)和Bardsley W.G.等人,(Biochem.J.1972,127,875-879)所述的分光光度法;质谱法(Gludovacz E.等人,2016);液体闪烁计数(Okuyama T.和Kobayashi Y.,Archives Biochem.Biophys.,19661,95,242-250);滴定、测压、荧光测定、生物或放射性测定方法(Zeller EA.,The enzymes,(J.B.Sumner和K Maybäck 编辑)第II卷,A部分,第536页,Academic Press,纽约1951;Shore P.A.等人,J.Pharmacol.,Exptl.Therap.127,1959,182;Ahlark A.,Acta Physiol.Scand.Suppl.,1944,28,9)。

[0142] 术语“功能变体”或“功能活性变体”还包括天然存在的等位基因变体,以及突变体或任何其他非天然存在的变体。如本领域已知的,等位基因变体是核酸或肽的替代形式,其

特征在于具有一个或多个核苷酸或一个或多个氨基酸的取代、缺失或添加,其基本上不改变所述核酸或多肽的生物功能。

[0143] 功能变体可以通过多肽或核苷酸序列的序列改变,例如通过一个或多个点突变来获得,其中当与本发明组合使用时,序列改变保留或改善未改变的多肽或核苷酸序列的功能。此类序列改变可以包括但不限于(保守)取代、添加、缺失、突变和插入。保守取代是在其侧链和化学特性上相关的氨基酸家族内发生的取代。此类家族的例子是具有碱性侧链、酸性侧链、非极性脂族侧链、非极性芳族侧链、不带电荷的极性侧链、小侧链、大侧链等的氨基酸。

[0144] 点突变特别地被理解为多核苷酸的工程改造,其导致表达这样的氨基酸序列,所述氨基酸序列与非工程改造的氨基酸序列的不同之处在于对于不同氨基酸取代或交换、缺失或插入一个或多个单一(非连续)或双联氨基酸。

[0145] 在一个替代实施方案中,可以通过重组手段在多肽内的任何位置将GAG结合结构域引入DAO中。相应结构域可以由氨基酸序列X1FX2X3X4LPX5构成,X1是任何氨基酸,特别是A或S,更特别地是S;X2是任何氨基酸,特别是K;X3是任何氨基酸,特别是A或T,更特别地是T,X4是任何氨基酸,特别是K,并且X5是任何氨基酸,特别是K或T,更特别地是T。在一个具体实施方案中,将氨基酸序列SFKAKLPK(SEQ ID NO:33)、AFKAKLPT(SEQ ID NO:34)、AFKTKLPK(SEQ ID NO:35)、SFKTKLPK(SEQ ID NO:36)、AFKTKLPT(SEQ ID NO:37)、SFKAKLPK(SEQ ID NO:38)中的一个或多个引入本文所述的DAO多肽中。

[0146] 如本文所用的术语“序列同一性”应理解为两个氨基酸序列之间或两个核苷酸序列之间的相关性,并且通过序列同一性或序列互补性的程度来描述。与亲本核苷酸或氨基酸序列相比,变体、同源物或直向同源物的序列同一性指示两个或更多个序列的同一性程度。两个或更多个氨基酸序列可以在相应位置具有相同或保守的氨基酸残基,在一定程度上,高达100%。两个或更多个核苷酸序列可以在相应位置具有相同或保守的碱基对,在一定程度上,高达100%。

[0147] 序列相似性搜索是一种用于鉴定具有过量(例如,至少50%)序列同一性的同源物的有效且可靠的策略。经常使用的序列相似性搜索工具是例如BLAST、FASTA和HMMER。

[0148] 序列相似性搜索可以通过检测过量相似性和反映共同祖先的统计上显著的相似性来鉴定此类同源蛋白质或多核苷酸。同源物可以包括直向同源物,其在本文中被理解为不同生物体中的相同蛋白质,例如不同不同生物体或物种中此类蛋白质的变体。

[0149] 为了确定两个互补序列的互补性%,需要将两个序列之一转化为其互补序列,然后可以使用以上提及的算法将互补性%计算为第一序列与第二转化序列之间的同一性%。

[0150] 关于本文所述的氨基酸序列、同源物和直向同源物的“同一性百分比(%)”被定义为在比对序列并且引入空位(如果需要)以实现最大百分比序列同一性并且不考虑任何保守取代作为序列同一性的一部分后,候选序列中与特定多肽序列中的氨基酸残基相同的氨基酸残基的百分比。本领域技术人员可以确定用于测量比对的适当参数,包括为了在被比较的序列的全长上实现最大比对所需要的任何算法。

[0151] 出于本文所述的目的,两个氨基酸序列之间的序列同一性使用NCBI BLAST程序2.2.29版(2014年1月06日)来确定,其中blastp设置为以下示例性参数:程序:blastp,字长:6,期望值:10,Hitlist大小:100,Gapcosts:11.1,矩阵:BLOSUM62,过滤字符串:F,遗传

密码:1,窗口大小:40,阈:21,基于组成的统计:2。

[0152] 关于核苷酸序列,例如核酸分子或其一部分,特别是编码DNA序列的“同一性百分比(%)”被定义为在比对序列并且引入空位(如果需要)以实现最大百分比序列同一性并且不考虑任何保守取代作为序列同一性的一部分后,候选DNA序列中与DNA序列中的核苷酸相同的核苷酸的百分比。可以以本领域技术内的各种方式,例如使用公开可用的计算机软件,来实现用于确定核苷酸序列同一性百分比目的的比对。本领域技术人员可以确定用于测量比对的适当参数,包括为了在被比较的序列的全长上实现最大比对所需要的任何算法。

[0153] 最佳比对可以使用用于比对序列的任何合适算法来确定,所述算法的非限制性例子包括史密斯-沃特曼(Smith-Waterman)算法、尼德曼-温施(Needleman-Wunsch)算法、基于巴罗斯-惠勒(Burrows-Wheeler)转换的算法(例如,巴罗斯-惠勒比对器)、ClustalW、Clustal X、BLAT、Novoalign(Novocraft Technologies;可访问novocraft.com)、ELAND(Illumina,圣地亚哥,加利福尼亚州)、SOAP(可访问soap.genomies.org.cn)和Maq(可访问maq.sourceforge.net)。

[0154] 如本文所述的DAO可以包含氨基酸序列SEQ ID NO:2至16和与SEQ ID NO:2至16中的任一个具有90％、95％、99％的序列同一性的其任何功能变体。

[0155] 所述重组DAO与野生型DAO相比具有增加的血浆半衰期,特别地所述半衰期与野生型DAO相比增加至少1.5倍、特别是至少2倍。

[0156] 药物的作用或物理存在的持续时间被称为其半衰期。这是在体内或全血或血浆中药物的浓度或量减少一半所需的时间段。药物的半衰期通常被认为与血浆或血清中的药物量有关。药物的血浆或血清半衰期取决于药物从血浆或血清中消除得有多快。药物分子可能从体内被消除,或者它可以转位到另一种体液隔室,诸如细胞内液,或者它可以在血液中被破坏。从血浆中去除药物被称为清除,并且药物在各种身体组织中的分布被称为分布容积。

[0157] 血浆药物浓度-时间曲线下面积(AUC)反映了在施用一剂药物(即,本文所述的重组DAO)后对药物的实际身体暴露并且以μg/min/ml表示。此曲线下面积取决于药物从体内消除的速率和施用剂量。身体消除的药物的总量可以通过从时间零(施用药物的时间)到无限时间,将在每个时间间隔内消除的量相加或积分来评估。此总量对应于到达体循环的施用剂量的分数。当药物遵循线性动力学时,AUC与剂量成正比。AUC与药物的清除率成反比。即清除率越高,药物在体循环中的时间越短,并且血浆药物浓度下降越快。因此,在这种情况下,对药物的身体暴露和浓度-时间曲线下面积较小。

[0158] 与野生型DAO相比,如本文所述的重组DAO具有至少2倍、至少5倍、10倍、至少15倍、至少20倍、至少25倍、至少30倍增加的AUC。

[0159] 术语“表达”按以下方式理解。含有表达产物(例如像如本文所述的融合蛋白)的所希望的编码序列的核酸分子可以用于表达目的。用这些序列转化或转染的宿主能够产生编码的蛋白质。为了实现转化,可以将表达系统包含在载体中;然而,相关DNA也可以整合到宿主染色体中。特别地,所述术语是指在例如用于表达由被载体携带并且引入宿主细胞中的外来DNA编码的蛋白质的合适条件下的宿主细胞和相容载体。

[0160] 编码DNA是编码特定多肽或蛋白质的特定氨基酸序列的DNA序列。启动子DNA是启动、调节或以其他方式介导或控制编码DNA的表达的DNA序列。启动子DNA和编码DNA可以来

自同一个基因或来自不同的基因,并且可以来自相同或不同的生物体。重组克隆载体通常包含一个或多个用于克隆或表达的复制系统、一个或多个用于在宿主中的选择(例如,抗生素抗性)的标记、一个或多个核定位信号(NLS)和一个或多个表达盒。

[0161] 如本文所用的“表达载体”被定义为克隆的重组核苷酸序列(即,重组基因)的转录及其mRNA在合适的宿主生物体中的翻译所需的DNA序列。为了获得表达,典型地将编码所希望的表达产物(诸如本文所述的DAO序列)的序列克隆到含有用于指导转录的启动子的表达载体中。合适的细菌和真核启动子是本领域众所周知的。用于指导核酸的表达的启动子取决于具体应用。例如,强组成型启动子典型地用于融合蛋白的表达和纯化。相比之下,当体内施用表达产物用于基因调节时,可以使用组成型启动子或诱导型启动子,取决于表达产物的具体用途。另外,用于施用的优选启动子可以是弱启动子。启动子还可以包括对反式激活有反应的元件,例如缺氧反应元件、Gal4反应元件和lac阻遏物反应元件。表达载体包含表达盒并且另外通常包含在宿主细胞中自主复制的起点或基因组整合位点、一个或多个选择标记(例如,氨基酸合成基因或赋予对诸如博莱霉素(zeocin)、卡那霉素、G418或潮霉素的抗生素的抗性的基因)、许多限制性酶切位点、合适的启动子序列和转录终止子,所述组分可操作地连接在一起。

[0162] “表达盒”是指编码表达产物的DNA编码序列或DNA区段,其可以在限定的限制性位点被插入载体中。表达盒限制位点被设计用于确保将表达盒插入正确的阅读框中。通常,在载体DNA的一个或多个限制性位点处插入外来DNA,并且然后由载体与可传播的载体DNA一起携带到宿主细胞中。具有插入或添加的DNA的DNA区段或序列,诸如表达载体,也可以被称为“DNA构建体”。

[0163] 任何合适的宿主细胞或细胞系可以用于表达允许正确折叠、翻译后修饰和酶活性的重组DAO。特别地,重组宿主细胞可以选自CHO细胞、COS细胞、Vero细胞、MDCK细胞、毕赤酵母细胞、SF9细胞、人细胞系诸如HEK和HeLa。

[0164] 如本文所用的术语“载体”包含自主复制的核苷酸序列以及基因组整合核苷酸序列。一种常见的载体类型是“质粒”,质粒通常是一种自足式双链DNA分子,所述分子可以容易地接受另外的(外来)DNA并且所述分子可以容易地被引入合适的宿主细胞中。质粒载体通常含有编码DNA和启动子DNA,并且具有一个或多个适用于插入外来DNA的限制性位点。特别地,术语“载体(vector)”或“质粒”是指一种载体(vehicle),通过所述载体可以将DNA或RNA序列(例如,外来基因)引入宿主细胞中以便转化宿主并且促进引入的序列的表达(例如,转录和翻译)。将载体转染到细胞中并且在稳定转染的情况下DNA可以通过同源重组整合到基因组中,或者可以瞬时转染细胞。特别地,所述载体是细菌、酵母、杆状病毒、植物或哺乳动物表达载体。

[0165] 可以使用用于将外来核苷酸序列引入宿主细胞中的任何已知程序。这些包括使用磷酸钙转染、聚凝胺、原生质体融合、电穿孔、核转染、脂质体、微注射、裸DNA、质粒载体、病毒载体(附加型和整合型两者)以及用于将克隆的基因组DNA、cDNA、合成DNA或其他外来遗传物质引入宿主细胞中的任何其他众所周知的方法(参见例如,Sambrook等人)。

[0166] 哺乳动物表达载体的例子包括腺病毒载体、pSV和pCMV系列质粒载体、牛痘和逆转录病毒载体以及杆状病毒。巨细胞病毒(CMV)和SV40的启动子通常用于哺乳动物表达载体以驱动基因表达。还已知的是非病毒启动子,诸如延伸因子(EF)-1启动子。

[0167] 使用上述载体和宿主细胞,本发明提供了用于生产重组DAO的方法,所述方法包括以下顺序的步骤:将编码DAO的核苷酸序列克隆到表达载体中,用所述载体转化宿主细胞、特别是哺乳动物细胞,在表达DAO的条件下培养转化的宿主细胞,从宿主细胞培养物中分离DAO,任选地通过分解宿主细胞或从细胞培养物上清液中分离DAO,并且任选地纯化DAO。

[0168] 进一步描述了一种药物组合物,其包含本文提供的重组DAO。根据一个具体实施方案,包含如本文所述的DAO或其功能变体的此类药物组合物用于治疗与过量组胺(特别是过量组胺>1ng/ml血浆浓度)相关的任何病症,特别地用于治疗慢性变应性疾病,更特别地用于治疗过敏反应、过敏性休克、慢性荨麻疹、急性荨麻疹、哮喘、枯草热、变应性鼻炎、变应性结膜炎、组胺中毒、头痛、瘙痒、呕吐、心动过速、低血压、心脏骤停、特应性皮炎炎性疾病、肥大细胞增多症、肥大细胞激活综合征(MCAS)、先兆子痫、妊娠剧吐、早产、消化性溃疡、酸返流、瘙痒症和败血症。

[0169] 特别地,当用于诊断或疗法时,本文所述的药物组合物进一步包含药学上可接受的载体或赋形剂,例如像增量剂。这些药物组合物可以根据本发明作为推注注射或输注或通过连续输注进行施用。适用于促进此类施用手段的药物载体是本领域众所周知的。

[0170] 药学上可接受的载体通常包括与本发明提供的DAO生理学相容的任何和所有合适的溶剂、分散介质、包衣、等渗和吸收延迟剂等。药学上可接受的载体的其他例子包括无菌水、盐水、磷酸盐缓冲盐水、右旋糖、甘油、乙醇等以及其任何组合。

[0171] 另外的药学上可接受的载体是本领域已知的并且描述于例如,Remington's Pharmaceutical Sciences(Gennaro,AR编辑,Mack Publishing Co,1985)。液体配制品可以是溶液、乳液或悬浮液,并且可以包含赋形剂,诸如悬浮剂、增溶剂、表面活性剂、防腐剂和螯合剂。

[0172] 如用于肠胃外施用的示例性配制品包括适合于以例如溶液、乳液或悬浮液的形式皮下、肌内或静脉内注射的那些。

[0173] 本文所述的DAO特别地以治疗有效量施用,所述治疗有效量意指当施用于受试者(例如,患有癌症的患者)时足以产生有益或希望的结果(包括临床结果)的量或活性。因此,有效量或其同义量取决于其应用的背景。有效量旨在意指足以治疗、预防或抑制此类疾病或障碍的化合物的量。

[0174] 将对应于此类有效量的化合物(即,本文所述的重组DAO)量将根据各种因素而变化,所述因素诸如所给予的药物或化合物、药物配制品、施用途径、疾病或障碍的类型、所治疗的受试者或宿主的身份等,尽管如此但仍可以由本领域技术人员常规地确定。

[0175] 根据本发明的一个具体实施方案,提供了融合多肽,其中重组DAO与第二部分缀合,所述第二部分可以是但不限于Fc或人血清白蛋白(HSA)。

[0176] 根据一个具体实施方案,与Fc缀合的DAO包含SEQ ID NO:40至70中的任一个或与SEQ ID NO:40至70中的任一个具有至少80%,特别是至少85%、90%、95%、99%序列同一性的其功能片段。

[0177] 根据一个具体实施方案,与Fc缀合的DAO由SEQ ID NO:72至102中的任一个或与SEQ ID NO:72至102中的任一个具有至少80%,特别地至少85%、90%、95%、99%序列同一性的其片段编码。

[0178] 在本发明背景下的术语"融合多肽"涉及主要(但不一定)通过肽键彼此连接的氨

基酸的序列。根据本发明的融合多肽,术语“融合”是指这样的事实,即至少两种不同来源的氨基酸序列(即,如本文定义的经修饰的DAO)和第二部分(特别是人IgG或白蛋白的Fc结构域)通过共价键直接地或经由氨基酸接头或间隔子彼此连接,从而接入(桥接、缀合、共价结合)所述氨基酸序列。融合可以通过化学缀合或通过本领域众所周知的基因工程方法进行。

[0179] 在一些实施方案中,如本文定义的DAO多肽通过其C末端共价连接至人IgG的Fc结构域或HSA。即,在一些实施方案中,在N末端至C末端方向上,根据本发明的融合多肽包含DAO多肽和Fc结构域组分或HSA。

[0180] 在其他实施方案中,如本文定义的DAO多肽通过其N末端共价连接至人IgG的Fc结构域或HSA。即,在一些实施方案中,在N末端至C末端方向上,本发明的融合多肽包含Fc结构域组分或HSA和DAO多肽。

[0181] 如本文所用的术语“多肽”是指通过肽键连接的氨基酸残基。多肽序列一般从含有游离氨基的N末端到含有游离羧基的C末端进行报告。多肽也可以称为氨基酸序列、肽或蛋白质,并且可以例如通过甘露糖基化、糖基化、酰胺化、羧化或磷酸化进行修饰。

[0182] 术语“共价连接(covalently linked)”或“共价连接(covalently linking)”意指所指示的结构域通过共价键连接(connected)或连接(linked)。

[0183] 具体地,如本文所用,术语“Fc融合多肽”包括包含全长Fc结构域的本公开文本的DAO以及包含Fc结构域片段(例如,全CH2结构域、全CH3结构域、CH2片段、CH3片段或其组合)的蛋白质。Fc融合蛋白还可以包含铰链区的全部或部分。

[0184] 如本文所用,Fc区包括包含除第一恒定区免疫球蛋白结构域之外的抗体恒定区的多肽及其片段。因此,Fc是指IgA、IgD和IgG的最后两个恒定区免疫球蛋白结构域,以及IgE和IgM的最后三个恒定区免疫球蛋白结构域,以及任选地在这些结构域的N末端的柔性铰链区。对于IgA和IgM,Fc区可以包含J链。对于IgG,Fc包含免疫球蛋白结构域Cgamma2和Cgamma3(Cγ2和Cγ3)以及任选地在Cgamma1(Cγ1)与Cgamma2(Cγ2)之间的铰链区。尽管Fc区的边界可以变化,但人IgG重链Fc区通常被定义为在其羧基末端包含残基C226或P230,其中编号是根据如在Kabat(Kabat等人,Sequences of Proteins of Immunological Interest,第5版Public Health Service,National Institutes of Health,马里兰州贝塞斯达(1991))中所阐述的EU索引的。Fc可以是指呈分离的此区域,或在抗体、抗体片段或Fc融合蛋白的背景下的此区域。

[0185] 与本文所述DAO多肽融合的HSA序列可以包含野生型序列或与野生型序列(SEQ ID NO.103)90%、特别是至少95%、更特别地至少99%、更特别地至少99.9%序列同一性的。任选地,在DAO与HSA之间含有接头序列,特别地包含2至约10个氨基酸残基。

[0186] 根据一个具体实施方案,抑制DAO的GAG结合,特别是肝素/硫酸乙酰肝素结合,从而导致DAO的内化降低并且在身体的循环中DAO的量增加,这可以通过AUC来确定。通过修饰如本文所述的DAO,DAO确实显示出显著降低的肝素/硫酸乙酰肝素结合。

[0187] 在身体的循环中增加DAO的另一个选择是提供一种与肝素/硫酸乙酰肝素结合结构域特异性结合的靶特异性配体。特别地,抗体或抗体片段或任何配体可以在接近肝素结合结构域处结合至DAO并且从而阻断接近肝素结合结构域。可替代地,它是融合蛋白,其中所述融合蛋白的部分覆盖并且阻断肝素结合结构域的功能,并且因此具有与直接结合至肝素结合结构域的突变或抗体相同的效果。

[0188] 作为替代方案,肝素/硫酸乙酰肝素结合至DAO的GAG结合结构域受到抑制。配体可以是抗原结合蛋白,特别地选自由以下项组成的组:抗体或抗体片段,诸如以下中的任意:Fab、Fd、scFv、双体抗体、三体抗体、Fv四聚体、微型抗体、纳米抗体、单结构域抗体(如VH、VHH、IgNAR或V-NAR);抗体模拟物,诸如Adnectins™(与抗体可变结构域共享具有多样化环的β-折叠夹心折叠,但在一级序列上与抗体不同并且具有无二硫键的单结构域结构)、Affibodies®(由基于蛋白A的一个IgG结合结构域的支架的三螺旋束构成的小的简单蛋白质)、Affilins®(结构上源自人泛素,通过修饰这些蛋白质的表面暴露氨基酸构建,并且通过展示技术(诸如噬菌体展示和筛选)分离。Affilin在其对抗原的亲和力和特异性方面类似于抗体,但在结构上不同,这使其成为一种类型的抗体模拟物)、Affimers®(以与抗体相似的特异性和亲和力的特异性和亲和力结合靶分子的小蛋白质)、Affitin(具有选择性结合抗原的能力的人工蛋白)、α体、适体、Anticalin、Avimer、DARPins®(基因工程化抗体模拟蛋白,其典型地展现出高度特异性和高亲和力的靶蛋白结合)、Fynomers®(源自Fyn激酶的人SH3结构域的小结合蛋白(7kDa),其可以经工程化以产生靶向特定蛋白质的特异性和高亲和力结合结构域)、Kunitz结构域肽、单体或NanoCLAMPS(CLostridal抗体模拟蛋白);或包含一个或多个免疫球蛋白折叠结构域、抗体结构域或抗体模拟物的融合蛋白。

[0189] 进一步提供了用于鉴定调节所述DAO的肝素结合的化合物的方法,所述方法包括以下步骤:

[0190] (a)构建由DAO序列SEQ ID No.1的氨基酸的结构坐标定义的GAG结合结构域的计算机模型,

[0191] (b)通过选自由以下项组成的组的方法选择潜在的调节化合物:

[0192] (i)将分子片段组装成所述化合物,

[0193] (ii)从小分子数据库中选择化合物,以及

[0194] (iii)所述化合物的从头配体设计;

[0195] (c)采用计算手段在所述化合物与GAG结合结构域的计算机模型之间进行拟合程序操作,以提供在肝素结合结构域中所述化合物的能量最小化构型;以及

[0196] (d)评价所述拟合操作的结果以量化所述化合物与肝素/硫酸乙酰肝素结合结构域之间的缔合,从而评价所述化合物与所述肝素/硫酸肝素结合结构域缔合的能力。

[0197] 术语“结构坐标”是指一组值,所述值限定了参考轴系统,一个或多个氨基酸残基的位置。所述术语是指限定一种或多种分子的三维结构的数据集(例如,笛卡尔坐标、温度因子和占有率)。结构坐标可以稍微修改,并且仍然渲染几乎相同的三维结构。一组独特的结构坐标的量度是所得结构的均方根偏差。彼此偏差小于3 Å、2 Å、1.5 Å、1.0 Å或0.5 Å的均方根偏差的渲染三维结构(特别是肝素/硫酸肝素结合结构域的三维结构)的结构坐标可以被本领域普通技术人员视为非常相似。

[0198] 如本文所用,术语“构建计算机模型”包括基于原子结构信息和相互作用模型的分子结构和/或功能的定量和定性分析。术语“建模”包括常规的基于数值的分子动力学和能量最小化模型、交互式计算机图形模型、改良的分子力学模型、距离几何和其他基于结构的约束模型。

[0199] 术语“拟合程序操作”是指利用化学实体、酶活性中心、结合口袋、分子或分子复合

物或其一部分的结构坐标来将化学实体与酶活性中心、结合口袋、分子或分子复合物或其一部分缔合的操作。这可以通过在酶活性中心中定位、旋转或平移化学实体以匹配酶活性中心的形状和静电互补性来实现。可以优化共价相互作用;非共价相互作用,诸如氢键、静电、疏水、范德华相互作用和非互补静电相互作用,诸如排斥电荷-电荷、偶极-偶极和电荷-偶极相互作用。可替代地,可以最小化化学实体与酶活性中心结合的变形能。

[0200] 以下项目是本文提供的本发明的特定实施方案。

[0201] 1具有降低的糖胺聚糖结合亲和力的重组二胺氧化酶(DAO),其中所述DAO在糖胺聚糖(GAG)结合结构域中包含至少一个氨基酸修饰。

[0202] 2根据项目1所述的重组DAO,其进一步包含参考SEQ ID No.1的编号在第123氨基酸位的溶剂可及的半胱氨酸的至少一个修饰,特别地所述半胱氨酸的修饰是氨基酸取代、缺失或与化学部分的偶联。

[0203] 3根据项目1或2所述的重组DAO,其中根据SEQ ID 1的编号在第123位的半胱氨酸被丙氨酸取代。

[0204] 4根据项目1至3中任一项所述的重组DAO,其中所述GAG结合结构域是肝素/硫酸乙酰肝素结合结构域。

[0205] 5根据项目1至4中任一项所述的重组DAO,其中所述GAG结合结构域中的至少一个氨基酸修饰是氨基酸取代、缺失、插入或与化学部分的偶联。

[0206] 6根据项目1至5中任一项所述的重组DAO,其在所述GAG结合结构域中包含2、3、4、5、6、7或8个氨基酸取代。

[0207] 7根据项目1至6中任一项所述的重组DAO,其中所述GAG结合结构域参考SEQ ID NO:1的编号在第568-575位包含所述氨基酸。

[0208] 8根据项目1至7中任一项所述的重组DAO,其包含氨基酸序列X1FX2X3X4LPX5的GAG结合结构域,其中

[0209] X1可以是任何氨基酸,特别地其为A或S,更特别地其为S;

[0210] X2可以是任何氨基酸,特别地其为K;

[0211] X3可以是任何氨基酸,特别地其为A或T,更特别地其为T,

[0212] X4可以是任何氨基酸,特别地其为K,并且

[0213] X5可以是任何氨基酸,特别地其为K或T,更特别地其为T。

[0214] 9根据项目7或8所述的重组DAO,其包含选自由以下项组成的组的氨基酸序列:SFKAKLPK(SEQ ID NO:33)、AFKAKLPT(SEQ ID NO:34)、AFKTKLPK(SEQ ID NO:35)、SFKTKLPK(SEQ ID NO:36)、AFKTKLPT(SEQ ID NO:37)、SFKAKLPK(SEQ ID NO:38)。

[0215] 10根据项目1至9中任一项所述的重组DAO,其中所述DAO与野生型DAO相比具有增加的血浆半衰期,特别地所述半衰期与野生型DAO相比增加至少1.5倍、特别是至少2倍。

[0216] 11根据项目1至10中任一项所述的重组DAO,其中所述DAO与野生型DAO相比具有至少10倍增加的AUC。

[0217] 12根据项目1至11中任一项所述的重组DAO,其中与野生型DAO相比,被内皮细胞的内化减少至少10%、25%、50%、60%、70%、80%、特别是90%。

[0218] 13根据项目1至12中任一项所述的重组DAO,其中与野生型DAO相比,GAG结合亲和力、特别是肝素/硫酸乙酰肝素结合亲和力减少至少10%、25%、50%、60%、70%、80%、特

别是90％。

[0219] 14根据项目1至13中任一项所述的重组DAO,其包含氨基酸序列SEQ ID NO:2至16。

[0220] 15融合多肽,所述融合多肽包含根据项目1至14中任一项所述的重组DAO和人IgG或人血清白蛋白(HSA)的Fc结构域,其中所述融合多肽保留所述重组DAO的功能活性。

[0221] 16编码项目1至15中任一项所述的DAO的分离的核苷酸序列,其特别地包含序列SEQ ID NO:17至32。

[0222] 17包含项目16所述的核苷酸序列的重组载体,特别地所述载体是细菌、酵母、杆状病毒、植物或哺乳动物表达载体。

[0223] 18表达盒,其包含根据项目17所述的核苷酸序列,所述核苷酸序列可操作地连接至调节元件。

[0224] 19包含根据项目1至15中任一项所述的重组DAO的重组宿主细胞或宿主细胞系,其中所述宿主细胞选自由以下项组成的组:CHO细胞、Vero细胞、MDCK细胞、毕赤酵母细胞、SF9细胞。

[0225] 20表达系统,其包含根据项目17所述的载体或根据项目18所述的表达盒和根据项目19所述的宿主细胞或宿主细胞系。

[0226] 21用于生产根据项目1至15所述的重组DAO的方法,所述方法包括以下步骤:

[0227] i.将编码根据项目1至15中任一项所述的DAO的核苷酸序列克隆到表达载体中,

[0228] ii.用所述载体转化宿主细胞,

[0229] iii.在表达所述DAO的条件下培养转化的宿主细胞,

[0230] iv.从宿主细胞培养物中分离所述DAO,任选地通过分解所述宿主细胞,以及任选地

[0231] v.纯化所述DAO。

[0232] 22药物组合物,其包含根据项目1至15中任一项所述的重组DAO和任选地一种或多种赋形剂。

[0233] 23根据项目1至15所述的重组DAO用于制备药物组合物的用途。

[0234] 24根据项目1至15中任一项所述的重组DAO,其用于治疗与过量组胺相关的病症,特别地用于治疗慢性变应性疾病,更特别地用于治疗过敏反应、过敏性休克、慢性荨麻疹、急性荨麻疹、哮喘、枯草热、变应性鼻炎、变应性结膜炎、组胺中毒、头痛、特应性皮炎炎性疾病、肥大细胞增多症、肥大细胞激活综合征(MCAS)、先兆子痫、妊娠剧吐、早产、消化性溃疡、酸返流、瘙痒症和败血症。

[0235] 25根据项目1至15中任一项所述的重组DAO用于制造药剂的用途,所述药剂用于治疗与过量组胺相关的病症,特别地用于治疗慢性变应性疾病,更特别地用于治疗过敏反应、过敏性休克、慢性荨麻疹、急性荨麻疹、哮喘、枯草热、变应性鼻炎、变应性结膜炎、组胺中毒、头痛、特应性皮炎炎性疾病、肥大细胞增多症、消化性溃疡、酸返流、瘙痒症和败血症。

[0236] 26靶特异性配体,其特异性结合至DAO的GAG结合结构域,特别是结合至参考SEQ ID No.1的编号在第568-575位的氨基酸中的一个或多个。

[0237] 27靶特异性配体,其特异性抑制肝素/硫酸乙酰肝素结合至DAO的GAG结合结构域,特别是结合至参考SEQ ID No.1的编号在第568-575位的氨基酸中的任一个或多个。

[0238] 28根据项目26或27所述的靶特异性配体,其中所述配体选自由以下项组成的组:

核酸、小分子抑制剂或抗原结合蛋白。

[0239] 29根据项目28所述的靶特异性配体,其中所述配体是抗原结合蛋白,特别地选自由以下项组成的组:

[0240] -抗体或抗体片段,诸如以下中的任意:Fab;Fd;scFv;双体抗体;三体抗体;Fv四聚体;微型抗体;纳米抗体;单结构域抗体,如VH、VHH、IgNAR或V-NAR;

[0241] -抗体模拟物,诸如Adnectins™、Affibodies®、Affilins®、Affimers®、Affitin、α体、适体、Anticalin、Avimer、DARPins®、Fynomers®、Kunitz结构域肽、单体或NanoCLAMPS;或

[0242] -包含一个或多个免疫球蛋白折叠结构域、抗体结构域或抗体模拟物的融合蛋白。

[0243] 30用于鉴定调节所述DAO的肝素结合的化合物的方法,其包括以下步骤:

[0244] (a)构建由DAO序列SEQ ID No.1的氨基酸的结构坐标定义的GAG结合结构域的计算机模型,

[0245] (b)通过选自由以下项组成的组的方法选择潜在的调节化合物:

[0246] (i)将分子片段组装成所述化合物,

[0247] (ii)从小分子数据库中选择化合物,以及

[0248] (iii)所述化合物的从头配体设计;

[0249] (c)采用计算手段在所述化合物与GAG结合结构域的计算机模型之间进行拟合程序操作,以提供在肝素结合结构域中所述化合物的能量最小化构型;以及

[0250] (d)评价所述拟合操作的结果以量化所述化合物与肝素/硫酸乙酰肝素结合结构域之间的缔合,从而评价所述化合物与所述肝素结合结构域缔合的能力。

[0251] 本文所述的实施例是对本发明的说明,而不旨在对其进行限制。已经根据本发明描述了本发明的不同实施方案。在不脱离本发明的精神和范围的情况下,可以对本文所述和说明的技术进行许多修改和变化。因此,应当理解,所述实施例仅是说明性的并且不限制本发明的范围。

[0252] 实施例

[0253] 实施例1

[0254] 具有经修饰的GAG结合结构域的DAO:

[0255] 概述:DAO的GAG结合(肝素/硫酸乙酰肝素-结合结构域)中的氨基酸发生突变。在DAO的肝素结合结构域突变后,用这些突变体进行动物研究。在大鼠中,短的α半衰期可以几乎消除,并且β半衰期增加至6小时。α半衰期是指由于药物从中央室到外周室的重新分布过程导致的血浆浓度下降的速率,β半衰期是指由于由代谢或排泄引起的药物消除的过程导致的下降速率。曲线下面积(AUC)增加超过20倍。在大鼠中6小时的半衰期外推至在人中24至48小时,并且这对于治疗具有过量组胺的急性和亚急性病症是必然足够的。例如,过敏反应或MCAS事件持续几个小时到1至2天,并且在10%-20%的患者中过敏反应可能是双相的,意味着可能在24小时内发生第二次发作。已经测试了若干种突变,并且在肝素结合结构域方面的独特双突变体显示出在药代动力学(PK)参数方面最明显的改善。由于DAO是二聚体并且肝素结合结构域形成由两个单体构成的环结构,因此四个突变的位置彼此接近。尽管如此,DAO野生型和DAO突变体的表达、稳定性和活性是相同的。

[0256] 具有经修饰的半胱氨酸的DAO

[0257] 当在CHO细胞中表达DAO时,一定百分比的DAO分子(约20％至30％)不仅形成二聚体,而且还形成四聚体、六聚体和甚至八聚体。这些更高阶的寡聚体可以被认为是具有未知功能的天然变体。不清楚它们是在折叠和从ER转运到高尔基体并且分泌到细胞外环境中期间形成的,还是一般只在细胞外环境中形成的。尽管如此,这些四聚体和更大的寡聚体使rhDAO的最优配制品的表达、纯化、表征、标准化和选择复杂化。因此,DAO表面上相对溶剂可及的半胱氨酸发生突变,并且在此突变体中,在CHO细胞的上清液中仅发现DAO二聚体。

[0258] 在肝素/硫酸乙酰肝素结合结构域中具有2个点突变以及在不同的半胱氨酸处具有单一突变的DAO构建体是具体的实施方案。

[0259] 下表示出了重组DAO。苏氨酸和丝氨酸突变优于丙氨酸和甘氨酸,以将赖氨酸和精氨酸与极性氨基酸交换。这有助于保持确认不变。

[0260] 表1:在GAG结合结构域中精氨酸和赖氨酸交换为丝氨酸和苏氨酸的DAO突变

[0261]

		氨基酸				
DAO 变体		568	570	571	572	575
WT		精氨酸	赖氨酸	精氨酸	赖氨酸	赖氨酸
Hepmut1	Arg_568_Ser	丝氨酸	赖氨酸	精氨酸	赖氨酸	赖氨酸
Hepmut2	Lys_575_Thr	精氨酸	赖氨酸	精氨酸	赖氨酸	苏氨酸
Hepmut3		精氨酸	赖氨酸	苏氨酸	赖氨酸	赖氨酸
Hepmut4	Arg_568_Ser; Arg_571_Thr	丝氨酸	赖氨酸	苏氨酸	赖氨酸	赖氨酸
Hepmut5		精氨酸	赖氨酸	苏氨酸	赖氨酸	苏氨酸

[0262]

Hepmut7	Arg_568_Ser; Lys_575_Thr	丝氨酸	赖氨酸	精氨酸	赖氨酸	苏氨酸

[0263] Hepmut4突变显示出与肝素的结合的最强丧失。Hepmut6是用Gly/Gln/Thr替代570/571/572的三重突变,其存在于啮齿动物中。啮齿动物序列中的谷氨酰胺也可以结合带负电荷的硫酸盐,并且有时可以替代精氨酸或赖氨酸。到目前为止,所有动物实验均是在啮齿动物(小鼠和大鼠)中进行的。

[0264] 以下是来自肝素-琼脂糖实验的数据,所述实验使用KCl和NaCl从肝素-琼脂糖洗脱纯化DAO野生型和Hepmut变体。肝素不可逆地偶联至琼脂糖,并且在低盐浓度下孵育纯化DAO,然后是递增浓度的KCl或NaCl的线性梯度。将具有DAO蛋白峰(使用在280nm处的吸光度测量)的盐浓度用作洗脱DAO的mM盐浓度。

[0265] 图2示出了重组人DAO野生型(WT)和肝素突变体的肝素-琼脂糖洗脱曲线。与DAO_WT相比,Hepmut变体更早被洗脱,将纯化DAO_WT和hepmut变体加载到使用50mM HEPES缓冲剂pH 7.4和0.2ml/min的流速的HiTrap肝素HP(高性能)1ml柱上。使用0％至70％50mM HEPES(含1M氯化钠,pH 7.4)的线性梯度与60分钟的梯度时间进行洗脱;rh＝重组人。对于

KCl洗脱,将纯化rhDAO变体加载到使用10mM磷酸钾缓冲剂pH 7.2和0.2ml/min的流速的HiTrap肝素HP 1ml柱上。使用0％至100％10mM磷酸钾缓冲剂(含1M氯化钾,pH 7.2)的线性梯度与60分钟的梯度时间进行洗脱。洗脱曲线未示出,但以下示出了在峰洗脱时的盐浓度。

[0266] 表2和图3示出了原始结果,但也基于使用DAO野生型蛋白的数据进行了归一化。计算来自两个盐实验的平均值和标准偏差(SD)并且以条形图呈现。条上方的数字对应于表中的数字。对于DAO_WT,它们代表洗脱的盐浓度。对于突变,示出了与DAO_WT盐浓度的差异。

[0267] DAO_WT在372mM NaCl或310mM KCl盐浓度下从肝素琼脂糖洗脱。Hepmut在显著更低的盐浓度下洗脱。NaCl与KCl洗脱曲线之间的相关系数R是97％,其中p值为0.0056。因此,将两个曲线组合并且计算平均值与SD似乎是合理的。平均值+/-SD由条高度(平均值)和误差条(+/-SD)表示。

[0268] 表2:在不同的NaCl或KCl浓度下从肝素-琼脂糖洗脱DAO_WT和hepmut变体

[0269]

	KCl Conc.[mM]	NaCl Conc.[mM]	DAO_WT 结合 KCl %	DAO_WT 结合 NaCl %	平 均 值%	SD %
DAO_WT	310	372	100%	100%	100%	0,0%
Hepmut1	172	186	56%	50%	53%	3,9%

[0270]

Hepmut2	233	317	75%	85%	80%	7,3%
Hepmut4	138	175	44%	47%	46%	1,8%
Hepmut7	164	197	53%	53%	53%	0,1%
WT = 野生型; Conc. = 浓度; SD = 标准偏差						

[0271] 图3示出了与DAO_WT相比,以低50％的盐浓度从肝素-琼脂糖洗脱的Hepmut 1、4和7变体。数据来自表2。

[0272] 表3示出了对于NaCl和KCl,来自DAO_WT与突变体的Δ盐浓度。例如,200mM意指与DAO_WT相比,从肝素-琼脂糖洗脱突变体所需的NaCl少200mM。

[0273] 表3:与DAO野生型蛋白相比,Hepmut变体以显著更低的NaCl或KCl浓度从肝素-琼脂糖洗脱

[0274]

	Δ mM KCl DAO	Δ mM NaCl DAO
DAO_WT	0	0
Hepmut1	138	186
Hepmut2	78	55
Hepmut4	172	197
Hepmut7	147	175

[0275] 基于这些数据,Hepmut4可能是最弱肝素结合突变体,但与Hepmut1和Hepmut7的差异不显著。使Hepmut2中的单一赖氨酸残基突变会降低对肝素-琼脂糖的亲和力。

[0276] 血清和血浆含有约145至150mM Na+和K+的组合以及100mM Cl-离子。从肝素-琼脂糖上Hepmut1、4和7变体的洗脱接近血清中离子的生理浓度,并且因此,这些突变体应该是在体内最小活性的,并且这是如下图所示的体外使用细胞以及在大鼠和小鼠体内的情况。

[0277] 这些数据清楚地显示,DAO经由肝素/硫酸乙酰肝素结合结构域结合肝素。为了将这些结果置于更大的背景下,在DAO序列中的48个赖氨酸和88个精氨酸氨基酸(并且其中大多数是表面暴露的)中1至2个精氨酸/赖氨酸残基的突变几乎革除了肝素结合,尽管使用具有两个精氨酸突变的Hepmut4,仅2/88＝2.3%的精氨酸残基已突变。

[0278] 与Hepmut变体相比,DAO_WT在小鼠和大鼠中的清除显著更快。假设肝素-结合结构域参与降低的曲线下面积(AUC)值。肝素结合突变体显示出在较低盐浓度下从肝素-琼脂糖上洗脱,意味着肝素或硫酸乙酰肝素结合降低。

[0279] 在接下来的一组实验中,发现DAO不仅与内皮细胞结合,而且实际上被内化到内皮细胞中,并且显示出在细胞内的囊泡染色。Hepmut变体不再被内皮细胞内化。内皮细胞是在静脉内施用后第一种暴露于DAO的细胞(血细胞除外)。它们与血液直接接触。他们在皮下施用后也暴露于DAO,因为DAO将经由淋巴系统运输到血液室中。

[0280] 在与DAO_WT和Hepmut变体一起孵育后,SK-Hep1细胞(一种来自患有肝癌的患者的内皮细胞样永生细胞系)的免疫荧光显微术显示,Hepmut变体的内化受到抑制。将SK-Hep1细胞与20μg/ml的纯化重组人DAO一起孵育60分钟,并且将Hepmut变体(阴性对照＝未添加rhDAO)在37℃下孵育,用150mM甘氨酸缓冲剂(含150mM氯化钠,pH 3.0)洗涤两次并且用PBS洗涤一次以去除膜结合的DAO。固定和透化后,将细胞与在兔中产生的抗ABP1(ABP1＝阿米洛利结合蛋白1,DAO的替代名称)抗体(Sigma Aldrich)的1:500稀释液一起孵育。将Alexa Fluor 488驴抗兔(H+L)(Jackson Research,711-545-152)的1:500稀释液用作第二抗体。将DAPI用于细胞核的复染。在配备有HCX PL APO 63x/1.30甘油浸没物镜和滤光片组A4(用于DAPI)和L5(用于Alexa Fluor 488)(莱卡微系统(Leica Microsystems))的倒置DMI-6000B显微镜上通过荧光显微术分析细胞。使用HUVEC＝人脐静脉内皮细胞(用于EC研究的原型内皮细胞(EC))获得了类似的结果。

[0281] Hepmut4和Hepmut7变体显示出向SK-Hep1细胞中的摄取强烈减少,而Hepmut1引起一些类似于DAO_WT的囊泡样染色的染色。这些结果不仅证明Hepmut DAO变体会阻断向EC中的摄取,而且还首次证明DAO被细胞内化。已经显示DAO与EC的表面结合,并且DAO已定位于细胞内部,但细胞与DAO的孵育以及DAO_WT被内化的证据意味着DAO受体的存在。已证实DAO结合至存在于EC上的硫酸乙酰肝素糖胺聚糖(肝素仅存在于人体中的肥大细胞中),并且Hepmut变体不再能够有效结合并且因此未被内化。这也反映在本文所述的体内大鼠和小鼠数据中。

[0282] 上面讨论的免疫荧光数据也反映在蛋白质印迹数据中。Hepmut4和Hepmut7与DAO_WT和Hepmut1的蛋白质印迹信号存在超过6倍的差异。这些数据与免疫荧光数据一致。Hepmut4和Hepmut7未被SK-Hep1细胞内化。

[0283] 图4示出了在与DAO_WT和Hepmut变体一起孵育后SK-Hep1细胞裂解物的蛋白质印迹,A.泳道1:阴性对照,2:rhDAO_WT,3:rhDAO-Hepmut1,4:rhDAO-Hepmut4,5:rhDAO-Hepmut7。在37℃下将SK-Hep1细胞与20μg/ml的相应的纯化DAO变体(阴性对照＝未添加rhDAO)一起孵育60分钟,用150mM甘氨酸缓冲剂(含150mM氯化钠,pH 3.0)洗涤两次并且用PBS洗涤一次以去除膜结合的DAO。然后将细胞用RIPA缓冲剂裂解并且进行超声处理。将细胞裂解物加载到SDS-PAGE凝胶上,然后印迹到PVDF膜上。将膜在封闭后与来自用纯化rhDAO免疫的兔的血清IgG级分的1:1000稀释液一起孵育。此步骤之后是用β-肌动蛋白mABAC-15

(英杰公司(Invitrogen))的1:5000稀释液孵育。将IRDye®800CW山羊抗兔IgG(H+L)第二抗体和IRDye®680RD山羊抗小鼠IgG(H+L)(Li-Cor)的1:5000稀释液用作第二抗体。使用Odyssey红外成像系统(Li-Cor)在700和800nm下扫描膜。B.参考纯化rhDAO_WT(未示出)确定条带强度,并且用于计算内化的rhDAO的量。

[0284] 在体外测定中,DAO_WT和Hepmut4变体与SK-Hep1细胞的结合低约5倍。将DAO在糖胺聚糖上用Alexa488荧光染料标记,并且与SK-HEP1细胞一起孵育。此测定在微量滴定板中进行。在洗涤和细胞裂解后测量荧光信号。

[0285] 在图5中,与DAO_WT相比,Hepmut4变体显示出与SK-Hep1细胞的结合减少。

[0286] 使SK-Hep1细胞在96孔板中生长,并且在37℃下与0至8μg/ml Alexa488标记的rhDAO_WT和rhDAO-Hepmut4一起孵育60分钟。将细胞用150mM甘氨酸缓冲剂(含150mM氯化钠,pH 3.0)洗涤两次并且用PBS洗涤一次以去除膜结合的DAO。使用RIPA缓冲剂裂解细胞后,使用Tecan酶标仪确定荧光强度。示出了三次重复的平均值与平均值的标准误差(SEM)。

[0287] 还使用等温滴定量热法(ITC)(一种用于确定无标记结合亲和力的现有技术仪器)测试DAO_WT和Hepmut4与高分子量和低分子量肝素(HMWH、LMWH)的结合。

[0288] 图6提供了DAO_WT和Hepmut4的ITC数据。

[0289] 使12.5μM纯化rhDAO_WT和12.0μM纯化rhDAO-Hepmut4经受等温滴定量热法(MicroCal PEAQ-ITC,Malvern),使用25x1μl的160μM高分子量(HMWH,Gilvasan,平均分子量=15kDa)和低分子量肝素(LMWH,依诺肝素(Lovenox),平均分子量=4.5kDa)注射液。缓冲剂是50mM HEPES,含150mM KCl pH 7.3。仅观察到rhDAO_WT和HMWH的结合,并且K_D值为423nM。

[0290] DAO蛋白和两种肝素分子这两种组分未改变并且未固定化。这允许确定真实的结合亲和力。肝素-琼脂糖代表一种多价基质,其中分子从一个肝素分子滑向另一个。DAO_WT以423nM的K_d与HMWH结合,而Hepmut4不与HMWH结合。DAO_WT也不结合至LMWH。

[0291] 向C57BL6小鼠静脉内注射DAO_WT和Hepmut4

[0292] 将DAO_WT和Hepmut4蛋白以1mg/kg注射到体重约20克的C57BL6小鼠的尾静脉中。两种纯化DAO变体的蛋白质浓度和酶活性是可比较的。蛋白质纯化如最近公布的方式进行(Gludovacz 2016)。示出了线性和log y-轴标度。

[0293] 图7中示出了线性(a)和log y-标度(b)。静脉内注射1mg/kg DAO变体后,与野生型DAO蛋白相比,Hepmut4使AUC(曲线下面积)增加超过19倍。示出了测量值(每个时间点n=3至4只小鼠)+/-标准偏差。使用我们内部开发的人DAO ELISA测量DAO浓度,所述人DAO ELISA不识别小鼠或大鼠DAO(Boehm 2017)。半衰期和AUC数据总结在下表中。

[0294] 表4:静脉内施用后,与DAO_WT处理的小鼠相比,Hepmut4的AUC增加19倍

[0295]

	半衰期分钟*	AUCμg*min/ml§
DAO_WT	76,1	76
Hepmut4	192,1	1468
Hepmut4与DAO_WT的比率	2,5	19,4

[0296] *从60至1680分钟计算

[0297] §AUC=曲线下面积;从10至1680分钟计算

[0298] 从60至1680分钟计算半衰期,以排除使用DAO_WT的快速α分布半衰期,其约10分钟。使用Hepmut4变体,这种从循环中非常快速的DAO消除或多或少不再存在。使用从60至1680的单指数衰减函数,存在高度曲线拟合。

[0299] 向C57BL6小鼠腹膜内注射DAO_WT和Hepmut4

[0300] 将DAO_WT和Hepmut4蛋白以1mg/kg腹膜内注射到体重21克的小鼠中。如图8中所示,在腹膜内注射后,与DAO_WT蛋白相比,Hepmut4使AUC(曲线下面积)增加超过16倍。每个时间点代表3只小鼠的平均值,并且因此使用总共15只小鼠DAO_WT和15只小鼠Hepmut4。示出了平均值与标准偏差。使用最近发布的人DAO ELISA(Boehm 2017)测量DAO浓度。AUC数据总结在下表中。不包括半衰期数据,因为我们将需要假设DAO_WT和Hepmut4从腹膜内空间的吸收是相同的,并且情况可能并非如此。

[0301] 表5:与DAO_WT处理的小鼠相比,Hepmut4的AUC增加16倍。

[0302]

	AUCμg*min/ml§
DAO_WT	41,2
Hepmut4	666,3
Hepmut4与DAO_WT的比率	16,2

[0303] §AUC=曲线下面积;从0至1440分钟计算

[0304] 向大鼠静脉内注射DAO_WT以及Hepmut1、4和7

[0305] 图9示出了使用1mg/kg DAO野生型和不同Hepmut变体的测量值的平均值+/-标准偏差(SD)。与以1mg/kg施用的DAO野生型蛋白相比,肝素结合结构域突变体的清除慢。DAO_WT n=9;Hepmut1 n=4;Hepmut4 n=5;Hepmut7 n=4;线性y-轴标度。示出了平均值与SD。

[0306] 图10展示了与以1mg/kg施用的DAO野生型蛋白相比,肝素结合结构域突变体的清除慢。DAO_WT n=9;Hepmut1 n=4;Hepmut4 n=5;Hepmut7 n=4;Log y-轴标度。示出了平均值与SD。

[0307] DAO_WT和Hepmut7示出了快速的α半衰期,并且使用两个方程来导出最佳拟合曲线。尽管如此,与DAO_WT相比,Hepmut7的α半衰期显著更长。半衰期在以下示出。对于Hepmut1和Hepmut4,单指数衰减显示出最佳拟合,具有最高调节的R平方和最低p值。这也可以在具有原始数据的图中看出。

[0308] 图11中示出了使用不同的导出的指数方程的曲线。这些曲线已用于计算稍后示出的AUC和半衰期。

[0309] 图11:与以1mg/kg施用的DAO野生型蛋白相比,肝素结合结构域突变体的清除慢。DAO_WT n=9;Hepmut1 n=4;Hepmut4 n=5;Hepmut7 n=4;Log y-轴标度;这些曲线是使用最佳拟合指数方程生成的。

[0310] 图12、13和14示出了看到使用DAO野生型蛋白的快速清除的前90分钟。

[0311] 图12示出了与以1mg/kg施用的DAO野生型蛋白相比,肝素结合结构域突变体的清除慢。DAO_WT n=9;Hepmut1 n=4;Hepmut4 n=5;Hepmut7 n=4;Log y-轴标度;仅示出了前90分钟。

[0312] 下面是这些图的线性y-轴形式。

[0313] 图13示出了与以1mg/kg施用的DAO野生型蛋白相比,肝素结合结构域突变体的清除慢。DAO_WT n=9;Hepmut1 n=4;Hepmut4 n=5;Hepmut7 n=4。所述曲线是使用最佳拟

合指数方程生成的;线性y-轴标度。

[0314] 图14示出了与以1mg/kg施用的DAO野生型蛋白相比,肝素结合结构域突变体的清除慢。DAO_WT n＝9;Hepmut1 n＝4;Hepmut4 n＝5;Hepmut7 n＝4;仅示出了前90分钟;线性y-轴标度。

[0315] 由于在DAO_WT处理的大鼠中的α半衰期快速,因此我们计算从0分钟而且还有从5分钟至240和1440分钟的AUC。在10分钟内的数据点很可能变化相当大。数据总结在下表中。

[0316] 表6:与DAO_WT处理的大鼠相比,肝素结合突变体的AUC增加

[0317]

	DAO 野生型(n=9)	Hepmut1 (n=4)	Hepmut4 (n=5)	Hepmut7 (n=4)	
AUC_0-1440	270	1554	3829	2165	μg/ml/min
AUC_0-240	238	797	1550	1010	μg/ml/min
AUC_5-1440	116	1531	3788	2113	μg/ml/min

[0318]

AUC_5-240	84	774	1509	958	μg/ml/min

[0319] 对于Hepmut变体,0至1440分钟或5至1440分钟没有任何相关差异,但对于DAO野生型蛋白,在5分钟开始AUC显著降低。使用最佳拟合指数方程计算的DAO浓度高于理论DAO浓度,并且因此不可能。使用从0至1440分钟的时间窗口也清楚地看到AUC的强增长。

[0320] 同样在这组实验中,Hepmut4变体显示出最强的效果。这也反映在半衰期数据中。

[0321] 表7:与DAO_WT处理的大鼠相比,肝素结合突变体的AUC增加在3倍与33倍之间,其中Hepmut4显示出最大的增加。

[0322]

	DAO 野生型(n=9)	Hepmut1 (n=4)	Hepmut4 (n=5)	Hepmut7 (n=4)
AUC_0-1440	1,0	5,8	14,2	8,0
AUC_0-240	1,0	3,4	6,5	4,2
AUC_5-1440	1,0	13,2	32,6	18,2
AUC_5-240	1,0	9,2	17,9	11,4

[0323] 表8:DAO野生型的非常快速的α半衰期消除以及肝素结合突变体的β半衰期的增加。

[0324]

	$t_{1/2}$α分钟	$t_{1/2}$β分钟
DAO_WT	1,9	162
Hepmut1	na	214
Hepmut4	na	343
Hepmut7	42	297

[0325] na＝不适用

[0326] 总之,在静脉内注射1mg/kg体重后,假定的DAO肝素结合结构域中的突变强烈增加

了在大鼠中的AUC。表现最好的突变体是去除2个精氨酸的双突变体Hepmut4。这很好地拟合于预测和肝素-琼脂糖洗脱数据。

[0327] 实施例2

[0328] 具有经修饰的GAG结合结构域的Fc-DAO:

[0329] 还测试Fc-DAO融合变体,其中肝素结合突变和PK参数进一步改善,其中β半衰期是9小时并且AUC增加。去除参与与Fc_γ受体高亲和力相互作用的氨基酸,并且参与与FcRN相互作用的氨基酸没有改变。

[0330] 向大鼠静脉内注射Fc-DAO_WT和Fc-DAO-Hepmut4

[0331] 以下是在静脉内注射1mg/kg Fc-DAO野生型和Fc-Hepmut4蛋白后来自6只和4只大鼠的使用线性和log标度的结果。我们仅使用Fc-DAO野生型测量4小时。尽管如此,可以使用导出的指数函数以外推到1680分钟,就像使用Fc-Hepmut4变体测量的那样(参见下文)。与DAO野生型蛋白类似,Fc-DAO融合蛋白显示出非常快速的α分布半衰期。大部分融合变体在20分钟内从血浆中去除。之后,使用30、120和240时间点值计算,半衰期约120分钟。

[0332] Fc-Hepmut4在血浆中稳定得多。DAO清除机制相比于Fc部分明显占主导地位。人IgG在大鼠中的半衰期是若干天,并且此半衰期主要由Fc部分与FcRN受体的结合决定。

[0333] 图15示出了与分别在6或4只大鼠中以1mg/kg施用的Fc-Hepmut4相比,Fc-DAO野生型的清除快速。示出了平均值与标准偏差;线性y-轴标度。

[0334] 图16示出了与分别在6或4只大鼠中以1mg/kg施用的Fc-Hepmut4相比,Fc-DAO野生型的清除快速。示出了平均值与标准偏差;Log y-轴标度。

[0335] 两个数据集都可以最佳拟合于单指数衰减函数,其中p值小于0.001并且调节的R平方值>97%。对于Fc-DAO野生型蛋白,基于来自时间点30、120和240分钟的数据,30分钟后的半衰期计算为120分钟。二因子衰减指数曲线拟合不收敛。使用最佳拟合方程将Fc-DAO数据外推至24小时。曲线在以下示出。

[0336] 在图17中,Fc-DAO-Hepmut4示出了在静脉内施用1mg/kg后AUC的强烈增加;Log y-轴标度。

[0337] 在图18中,Fc-DAO-Hepmut4示出了在静脉内施用1mg/kg后AUC的强烈增加;线性y-轴标度。

[0338] 计算在静脉内注射后从0和5分钟至240或1440分钟的曲线下面积。第一分钟的曲线拟合导致在Fc-DAO数据中在0分钟时的值非常高,并且因此我们还计算在5分钟开始的AUC。

[0339] 表9:与Fc-DAO_WT处理的大鼠相比,Fc-Hepmut4的AUC强烈增加

[0340]

	Fc-DAO 野生型（n=6）	Fc-Hepmut4（n=4）	
AUC_0-1440	157	2751	μg/ml/min
AUC_0-240	142	1057	μg/ml/min
AUC_5-1440	69	2723	μg/ml/min
AUC_5-240	54	1028	μg/ml/min

[0341] AUC的比率示出在下一个表中,然后是具有计算的半衰期的表。

[0342] 表10:相比于Fc-DAO_WT,Fc-Hepmut4的AUC大7至40倍

[0343]

	Fc_DAO 野生型(n=6)	Fc_Hepmut4（n=4）
AUC_0-1440	1,0	17,6
AUC_0-240	1,0	7,4
AUC_5-1440	1,0	39,5
AUC_5-240	1,0	19,0

[0344] 表11:在Fc-Hepmut大鼠中,Fc-DAO_WT的快速α半衰期被消除

[0345]

	$t_{1/2}\alpha$,分钟	$t_{1/2}\beta$,分钟*
Fc_DAO_WT	1,7	120
Fc_Hepmut4	na	268

[0346] *在静脉内注射后30分钟时开始

[0347] 与Fc-DAO相比,Fc-Hepmut4变体在血浆中更稳定。这与使用非融合DAO变体的小鼠和大鼠的数据一致。尽管如此,与IgG抗体相比,Fc-Hepmut4的半衰期仍然相当短。DAO清除相比于较慢的Fc清除机制似乎仍然占主导地位。

[0348] 实施例3

[0349] 具有经修饰的GAG结合结构域和经修饰的cys123的DAO:

[0350] 半胱氨酸123和633不参与DAO二聚体的二硫键形成。

[0351] 蛋白质残基的相对可及表面积或相对溶剂可及性(RSA)是残基溶剂暴露的量度。其可以由下式计算:RSA=ASA/MaxASA,其中ASA为溶剂可及表面积,并且MaxASA为最大可能溶剂可及的残基的表面积。ASA和MaxASA均通常以$Å^2$测量。

[0352] RSA Cys123

[0353] $Cys123 = 93.84\ Å^2$可及/$148\ Å^2 = 63.4\%$(单体B)

[0354] $Cys123 = 90.72\ Å^2$可及/$148\ Å^2 = 61.3\%$(单体A),平均值=62.4%

[0355] RSA Cys633

[0356] Cys633=34.62可及/148=23.4%(单体B)

[0357] Cys633＝33.49可及/148＝22.6％(单体A),平均值＝23％

[0358] Cys123在表面上,并且这是不寻常的。半胱氨酸氨基酸是蛋白质中最稀有和“最少且最高”保守的氨基酸(Marino SM和Gladyshev VN,J Mol Biol.2010Dec 17;404(5):902-16),很可能是因为它可用于氧化。DAO会产生过氧化氢,过氧化氢可能引起确切地cys123的这种氧化,并且因此它可能形成可能严重干扰功能的二硫键。它在酶中作为催化氨基酸是高度保守的,并且如果参与二硫键形成,则在DAO中也是如此。Cys633在结构内部更深并且不易可及,并且可能不会在聚集体形成中发挥作用。它可能在高DAO浓度下发挥作用。

[0359] 因为DAO二聚体具有两个可及Cys123氨基酸,一个二聚体可以与另一个二聚体形成二硫桥,从而产生四聚体,但它也可以与两个二聚体相互作用形成六聚体等。对于二聚体,缺乏完全基于氨基酸(732)的分泌信号的DAO的分子量将为166872Da。四聚体将为333744Da,六聚体为500617Da,并且八聚体为667489Da,但聚糖将使其增加很可能约25％(Elmore,2002)。DAO单体或二聚体的高度约65 Å,但在四聚体中增加到130 Å,在六聚体和八聚体中分别增加到195 Å和260 Å。我们没有关于DAO多聚体堆栈结构的数据。聚集体可以是刚性的或柔性的。这些聚集体具有必然更大的免疫原性,因为新表位可能在两个二聚体之间产生并且重复2或3次,对功效和安全性产生潜在和可能的负面影响(参见下文)。

[0360] 表12:使用25％聚糖重量的DAO单体至八聚体的分子量

[0361]

	732 氨基酸（aa）	732 aa + 聚糖 25%	DAO 高度 nm	DAO 长度 nm
单体	83436	104295	6.5	10.0
二聚体	166872	208590	6.5	10.0
四聚体	333744	417180	13.0	10.0
六聚体	500616	625770	19.5	10.0
八聚体	667488	834360	26.0	10.0

[0362] 已经描述了更高阶的DAO聚集体。Paolucci等人(Biochimie 1971;53(6):735-49)公布了人胎盘DAO的分子量由以下构成:1-4倍数的125kDa+/-5或换句话说125、250、375和500kDa。Tufvesson(Scand J Clin Lab Invest.1978年9月;38(5):463-72)又公布了在从人羊水中纯化后245和485kDa的DAO分子量,对应于二聚体和四聚体。Wilfingseder等人(Inflamm Res.2002年4月;51增刊1:S89-90)使用蛋白质印迹显示出人胎盘DAO的“复合形成”。

[0363] 将不同的DAO表达质粒转染到ExpiCHO细胞中进行瞬时表达。培养7天后,直接对上清液进行蛋白质印迹。结果示出在图19中。

[0364] 图19:泳道1:HiMark标准;泳道2:阴性对照(空质粒);泳道3:rhDAO_WT;泳道4:rhDAOΔ123;泳道5:rhFc-DAO;泳道6:rhFc-DAOΔ123;泳道7:rhDAO-Hepmut4;泳道8:rhDAO-Hepmut4Δ123;泳道9:rhFc-DAO-Hepmut4;泳道10:rhFc-DAO-Hepmut4Δ123。rhFc＝具有DAO的重组人Fc融合蛋白;加载15μl每种培养上清液。在非还原条件下进行SDS-PAGE。抗体:MUV兔血清#408,1:5000。

[0365] Cys123向Ala123的突变完全阻止了重组人野生型DAO和Hepmut4变体的四聚化和

更高阶聚集体的形成。在rhFc-DAO融合构建体中没有影响。这意味着这些Fc融合变体的聚集体形成是由Cys123引起的,但更可能是由Fc部分引起的,所述Fc部分也含有半胱氨酸。

[0366] 在使用巯基乙醇的还原条件下,二硫键打开,并且在野生型DAO和Hepmut或融合变体中均未看到四聚体或更高阶聚集体。分子量在71与117之间,并且仅基于氨基酸就可以预测为83.436Da。这些数据清楚地证明了cys123向ala123的突变完全阻止了DAO的四聚化和更高阶的n聚体变体。不涉及Cys633。

[0367] 使用ImageJ软件确定每个泳道的信号强度,以粗略地量化较高级n聚体变体的百分比。为了比较WT和相应的cys123突变体泳道,选择同样大小的区域(如所指示)并且生成信号谱。计算每个泳道的曲线下面积(AUC)。

[0368] 表13:在两个重复中ala123突变对聚集体形成的影响的量化

[0369]

	重复 1		重复 2	
	信号	百分比	信号	百分比
rhDAO_WT	77693	100%	68048	100%
rhDAO_Ala123	66523	86%	57007	84%
rhDAO_Hepmut4	76456	100%	67066	100%
rhDAO_Hepmut4_Ala123	56045	73%	55377	83%
rhDAO WT - Ala123	11170	14%	11041	16%
Hepmut4 WT - Ala123	20411	27%	11689	17%
平均值	**19%**			
SD	**5,5%**			
rhFc-DAO	70709	100%	64270	100%
rhFc-DAO_Ala123	61878	88%	69892	109%
rhFc-DAO-Hepmut4	56134	100%	66383	100%
rhFc-DAO-Hepmut4_Ala123	57673	103%	82826	125%
rhFc-DAO WT - Ala123	8831	12%	-5622	-9%
rhFc-Hepmut4 WT - Ala123	-1538	-3%	-16443	-25%

[0370]

平均值	**-6%**
SD	**15,4%**

[0371] Cys123与Ala123突变之间的平均(SD)差异是平均结合来自重复1和2的数据的,对于WT和Hepmut4突变体约19%(5.5%)。对于Fc-DAO变体,平均(SD)差异是-6%(15.4%)或换句话说cys123向ala123的突变没有不同。

[0372] 因此,ala123突变总体上对于制造和质量控制、而且还对于免疫原性的降低具有显著优势,并且因此这种突变也是在临床上高度相关的。众所周知,聚集体具有更大的免疫原性,并且因此使用这种突变将降低rhDAO的免疫原性。

[0373] 使用如Bartko(Alcohol.2016年8月;54:51-9.)或Gludovacz 2016中所述的标准DAO活性测定来测试上清液的DAO活性。已证实,cys123向ala123的突变对DAO活性没有影响。在图20中,呈现了DAO活性。将WT DAO、Hepmut4或Fc变体设置为100%并且与cys123向ala123的突变体进行比较。显示DAO_WT与cys123突变之间的DAO活性没有显著差异。

[0374] 实施例4

[0375] Asn168糖基化突变体的产生

[0376] Asn-168的定点诱变

[0377] 为了将N-糖基化位点处的天冬酰胺Asn-168(AAT)用谷氨酰胺(CAG)替代,使用定点诱变使DAO表达质粒中的相应密码子(Gludovacz E.等人,2016,J.Biotechnol.,227,120-130)发生突变。因此,使用以下5-磷酸化引物进行PCR:Asn-168,CAGaccacaggcttctcattc(正向,SEQ ID NO:104)和gaggaagaactgatgcag(反向,SEQ ID NO:105)。使用Phusion聚合酶(Thermo Fisher Scientific):退火温度:56.3℃;延伸时间,4min,30个循环。进行最终质粒的连接(T4 DNA连接酶,New England Biolabs)和扩增。通过DNA测序(Eurofins MWG Operon)验证序列的正确性。所有克隆技术均根据Green M.R.和Sambrook,J.(2012),Molecular Cloning:A Laboratory Manual第4版冷泉港实验室出版社,纽约州冷泉港;并且根据制造商的说明进行。

[0378] 向大鼠和小鼠静脉内施用rhDAO、竞争蛋白和糖基化突变体

[0379] 用于处理大鼠和小鼠的实验方案经当地动物福利委员会(local Animal Welfare Committee)和联邦科学、研究和经济部(Federal Ministry of Science,Research and Economy)(GZ 66.009/0152-WF/V/3b/2014)批准并且完全根据ARRIVE指南(Kilkenny,C等人,Br.J.Pharmacol.(2010)160,1577-1579)进行。为了将血管通路口植入颈静脉(Vena jugularis)中(具有可拆卸硅胶导管的啮齿动物血管通路口,Hugo-Sachs Elektronic-Harvard Apparatus),通过腹膜内注射氯胺酮(100mg/kg)和甲苯噻嗪(5mg/kg)将大鼠麻醉。插管后,通过连续容量控制通气(O_2-空气混合物+1.5%异氟烷)维持麻醉。将在手术区域的毛皮去毛,并且随后用碘溶液(Betaisodona,Mundipharma)消毒。皮下施用安乃近(Metamizol)(100mg/kg)用于镇痛。在动物的背部制造大约1cm的皮肤切口,以将血管通路口的球囊置于皮下。将口用盐水冲洗,然后用肩胛骨之间用缝合线固定球囊。在左颈静脉(V.jugularis sinistra)部位制造第二皮肤切口以解剖颈静脉用于导管插入术。在暴露的左颈静脉处安置小切口,并且将导管插入并且用丝线(7-0)固定。将皮下组织和皮肤用简单的间断缝合线(4-0)闭合。手术在无菌条件下进行。平均手术时间大约2小时。通过随意饮用含哌腈米特(piritramid)和葡萄糖的水(在250mL饮用水中30mg哌腈米特和10mL 10%葡萄糖)提供术后镇痛。在实验过程中,向血管通路口中填充在0.9%NaCl中含有10μg/mL阿加曲班(Argatra 100mg/mL;Mitsubishi Pharma)、0.3μg/mL组织纤溶酶原激活剂(阿替普酶(Alteplase)、艾通立(Actilyse),勃林格殷格翰公司(Boehringer Ingelheim))和0.38%柠檬酸钠的溶液以防止凝结。

[0380] 在短的异氟烷麻醉下在预先确定的时间点进行静脉抽血(0.5mL)到含有用于抗凝的柠檬酸钠的管中。在4小时内制备血浆并且储存在-32℃直至分析。向动物提供使用生理盐水溶液(0.9%NaCl)的流体替换(0.5mL)。在深度氯胺酮-甲苯噻嗪(35mg和5mg/kg)麻醉下最后一次抽血时间点后,通过过度剂量的戊巴比妥(300mg/kg)将动物处死。包括体重大

约400克的雄性大鼠(斯普拉格-杜勒(Sprague-Dawley))和体重大约20g的雌性小鼠(C57BL/6N)。

[0381] 从商业供应商(Janvier Labs,法国勒热内圣里勒(Le Genest-Saint-Isle)和奥地利欣贝格(Himberg),维也纳医科大学,实验动物科学与遗传学部)购买雄性斯普拉格-杜勒大鼠。将动物圈养在受控和标准化的条件下(人工L/D周期12:12,室温22℃±2℃,湿度45±10%)。将动物保持在两只的组中(模克隆(Makrolon)3笼),并且提供环境丰富性。使动物随意获取水和大鼠用完全饲料(Alleinfutter für Ratten und Mäuse sniff R/M-H; sniff Spezialdiäten GmbH)。

[0382] 从商业供应商(查尔斯河实验室(Charles River Laboratories),德国苏尔茨费尔德(Sulzfeld)和奥地利欣贝格,维也纳医科大学,实验动物科学与遗传学部)获得雌性小鼠(C57BL/6N)。将动物圈养在受控和标准化的条件下(人工L/D周期12:12,室温22℃±2℃,湿度45±10%)。将动物保持在五只的组中(模克隆2长笼),并且随意获取水和如上所述大鼠用完全饲料(用于小鼠)。

[0383] 在静脉内施用后rhDAO在大鼠和小鼠中的快速血浆清除

[0384] 将纯化rhDAO、野生型rhDAO和含有突变HepMut 1至HepMut 7中的任一个或HepMut1至HepMut4中的任一个的进一步包含Cys123和/或Asn168Gln突变的rhDAO以1mg/kg静脉内施用于大鼠和小鼠,并且在指示的时间点抽取血样。使用最近公布的人DAO ELISA(Boehm T.等人,2017,Clin.Biochem.,50,444-451)测量DAO抗原浓度。分布(α)和消除(β)半衰期在大鼠中分别是大约3和230分钟并且在小鼠中分别是大约11和110分钟。在大鼠中,超过90%的注射剂量在10分钟内从血浆库中去除。在小鼠中的快速清除有些稍慢。

[0001] 序列表

[0002] <110> 维也纳兽医大学

[0003] 维也纳自然资源与生命科学大学

[0004] <120> 新重组二胺氧化酶及其治疗以过量组胺为特征的疾病的用途

[0005] <130> MU008P

[0006] <150> EP 19157932.5

[0007] <151> 2019-02-19

[0008] <160> 106

[0009] <170> PatentIn 版本 3.5

[0010] <210> 1

[0011] <211> 751

[0012] <212> PRT

[0013] <213> 智人

[0014] <400> 1

[0015] Met Pro Ala Leu Gly Trp Ala Val Ala Ala Ile Leu Met Leu Gln Thr

[0016] 1 5 10 15

[0017] Ala Met Ala Glu Pro Ser Pro Gly Thr Leu Pro Arg Lys Ala Gly Val

[0018] 20 25 30

[0019] Phe Ser Asp Leu Ser Asn Gln Glu Leu Lys Ala Val His Ser Phe Leu

[0020] 35 40 45

[0021] Trp Ser Lys Lys Glu Leu Arg Leu Gln Pro Ser Ser Thr Thr Thr Met

[0022] 50 55 60

[0023] Ala Lys Asn Thr Val Phe Leu Ile Glu Met Leu Leu Pro Lys Lys Tyr

[0024] 65 70 75 80

[0025] His Val Leu Arg Phe Leu Asp Lys Gly Glu Arg His Pro Val Arg Glu

[0026] 85 90 95

[0027] Ala Arg Ala Val Ile Phe Phe Gly Asp Gln Glu His Pro Asn Val Thr

[0028] 100 105 110

[0029] Glu Phe Ala Val Gly Pro Leu Pro Gly Pro Cys Tyr Met Arg Ala Leu

[0030] 115 120 125

[0031] Ser Pro Arg Pro Gly Tyr Gln Ser Ser Trp Ala Ser Arg Pro Ile Ser

[0032] 130 135 140

[0033] Thr Ala Glu Tyr Ala Leu Leu Tyr His Thr Leu Gln Glu Ala Thr Lys

[0034] 145 150 155 160

[0035] Pro Leu His Gln Phe Phe Leu Asn Thr Thr Gly Phe Ser Phe Gln Asp

[0036] 165 170 175

[0037] Cys His Asp Arg Cys Leu Ala Phe Thr Asp Val Ala Pro Arg Gly Val

[0038] 180 185 190

[0039] Ala Ser Gly Gln Arg Arg Ser Trp Leu Ile Ile Gln Arg Tyr Val Glu

[0040] 195 200 205

[0041] Gly Tyr Phe Leu His Pro Thr Gly Leu Glu Leu Leu Val Asp His Gly

[0042] 210 215 220

[0043] Ser Thr Asp Ala Gly His Trp Ala Val Glu Gln Val Trp Tyr Asn Gly

[0044] 225 230 235 240

[0045] Lys Phe Tyr Gly Ser Pro Glu Glu Leu Ala Arg Lys Tyr Ala Asp Gly

[0046] 245 250 255

[0047] Glu Val Asp Val Val Val Leu Glu Asp Pro Leu Pro Gly Gly Lys Gly

[0048] 260 265 270

[0049] His Asp Ser Thr Glu Glu Pro Pro Leu Phe Ser Ser His Lys Pro Arg

[0050] 275 280 285

[0051] Gly Asp Phe Pro Ser Pro Ile His Val Ser Gly Pro Arg Leu Val Gln

[0052] 290 295 300

[0053] Pro His Gly Pro Arg Phe Arg Leu Glu Gly Asn Ala Val Leu Tyr Gly

[0054] 305 310 315 320

[0055] Gly Trp Ser Phe Ala Phe Arg Leu Arg Ser Ser Ser Gly Leu Gln Val

[0056] 325 330 335

[0057] Leu Asn Val His Phe Gly Gly Glu Arg Ile Ala Tyr Glu Val Ser Val

[0058] 340 345 350

[0059] Gln Glu Ala Val Ala Leu Tyr Gly Gly His Thr Pro Ala Gly Met Gln

[0060] 355 360 365

[0061] Thr Lys Tyr Leu Asp Val Gly Trp Gly Leu Gly Ser Val Thr His Glu

[0062] 370 375 380

[0063] Leu Ala Pro Gly Ile Asp Cys Pro Glu Thr Ala Thr Phe Leu Asp Thr

[0064] 385 390 395 400

[0065] Phe His Tyr Tyr Asp Ala Asp Asp Pro Val His Tyr Pro Arg Ala Leu

[0066] 405 410 415

[0067] Cys Leu Phe Glu Met Pro Thr Gly Val Pro Leu Arg Arg His Phe Asn

[0068] 420 425 430

[0069] Ser Asn Phe Lys Gly Gly Phe Asn Phe Tyr Ala Gly Leu Lys Gly Gln

[0070] 435 440 445

[0071] Val Leu Val Leu Arg Thr Thr Ser Thr Val Tyr Asn Tyr Asp Tyr Ile

[0072] 450 455 460

[0073] Trp Asp Phe Ile Phe Tyr Pro Asn Gly Val Met Glu Ala Lys Met His

[0074] 465 470 475 480

[0075] Ala Thr Gly Tyr Val His Ala Thr Phe Tyr Thr Pro Glu Gly Leu Arg

[0076] 485 490 495

[0077] His Gly Thr Arg Leu His Thr His Leu Ile Gly Asn Ile His Thr His

[0078] 500 505 510

[0079] Leu Val His Tyr Arg Val Asp Leu Asp Val Ala Gly Thr Lys Asn Ser

[0080] 515 520 525

[0081] Phe Gln Thr Leu Gln Met Lys Leu Glu Asn Ile Thr Asn Pro Trp Ser

[0082] 530 535 540

[0083] Pro Arg His Arg Val Val Gln Pro Thr Leu Glu Gln Thr Gln Tyr Ser

[0084] 545 550 555 560
[0085] Trp Glu Arg Gln Ala Ala Phe Arg Phe Lys Arg Lys Leu Pro Lys Tyr
[0086] 565 570 575
[0087] Leu Leu Phe Thr Ser Pro Gln Glu Asn Pro Trp Gly His Lys Arg Ser
[0088] 580 585 590
[0089] Tyr Arg Leu Gln Ile His Ser Met Ala Asp Gln Val Leu Pro Pro Gly
[0090] 595 600 605
[0091] Trp Gln Glu Glu Gln Ala Ile Thr Trp Ala Arg Tyr Pro Leu Ala Val
[0092] 610 615 620
[0093] Thr Lys Tyr Arg Glu Ser Glu Leu Cys Ser Ser Ser Ile Tyr His Gln
[0094] 625 630 635 640
[0095] Asn Asp Pro Trp His Pro Pro Val Val Phe Glu Gln Phe Leu His Asn
[0096] 645 650 655
[0097] Asn Glu Asn Ile Glu Asn Glu Asp Leu Val Ala Trp Val Thr Val Gly
[0098] 660 665 670
[0099] Phe Leu His Ile Pro His Ser Glu Asp Ile Pro Asn Thr Ala Thr Pro
[0100] 675 680 685
[0101] Gly Asn Ser Val Gly Phe Leu Leu Arg Pro Phe Asn Phe Phe Pro Glu
[0102] 690 695 700
[0103] Asp Pro Ser Leu Ala Ser Arg Asp Thr Val Ile Val Trp Pro Arg Asp
[0104] 705 710 715 720
[0105] Asn Gly Pro Asn Tyr Val Gln Arg Trp Ile Pro Glu Asp Arg Asp Cys
[0106] 725 730 735
[0107] Ser Met Pro Pro Pro Phe Ser Tyr Asn Gly Thr Tyr Arg Pro Val
[0108] 740 745 750
[0109] <210> 2
[0110] <211> 751
[0111] <212> PRT
[0112] <213> 人工序列
[0113] <220>
[0114] <223> hDAO-Hepmut1
[0115] <400> 2
[0116] Met Pro Ala Leu Gly Trp Ala Val Ala Ala Ile Leu Met Leu Gln Thr
[0117] 1 5 10 15
[0118] Ala Met Ala Glu Pro Ser Pro Gly Thr Leu Pro Arg Lys Ala Gly Val
[0119] 20 25 30
[0120] Phe Ser Asp Leu Ser Asn Gln Glu Leu Lys Ala Val His Ser Phe Leu
[0121] 35 40 45
[0122] Trp Ser Lys Lys Glu Leu Arg Leu Gln Pro Ser Ser Thr Thr Thr Met
[0123] 50 55 60
[0124] Ala Lys Asn Thr Val Phe Leu Ile Glu Met Leu Leu Pro Lys Lys Tyr
[0125] 65 70 75 80

[0126] His Val Leu Arg Phe Leu Asp Lys Gly Glu Arg His Pro Val Arg Glu
[0127] 85 90 95
[0128] Ala Arg Ala Val Ile Phe Phe Gly Asp Gln Glu His Pro Asn Val Thr
[0129] 100 105 110
[0130] Glu Phe Ala Val Gly Pro Leu Pro Gly Pro Cys Tyr Met Arg Ala Leu
[0131] 115 120 125
[0132] Ser Pro Arg Pro Gly Tyr Gln Ser Ser Trp Ala Ser Arg Pro Ile Ser
[0133] 130 135 140
[0134] Thr Ala Glu Tyr Ala Leu Leu Tyr His Thr Leu Gln Glu Ala Thr Lys
[0135] 145 150 155 160
[0136] Pro Leu His Gln Phe Phe Leu Asn Thr Thr Gly Phe Ser Phe Gln Asp
[0137] 165 170 175
[0138] Cys His Asp Arg Cys Leu Ala Phe Thr Asp Val Ala Pro Arg Gly Val
[0139] 180 185 190
[0140] Ala Ser Gly Gln Arg Arg Ser Trp Leu Ile Ile Gln Arg Tyr Val Glu
[0141] 195 200 205
[0142] Gly Tyr Phe Leu His Pro Thr Gly Leu Glu Leu Leu Val Asp His Gly
[0143] 210 215 220
[0144] Ser Thr Asp Ala Gly His Trp Ala Val Glu Gln Val Trp Tyr Asn Gly
[0145] 225 230 235 240
[0146] Lys Phe Tyr Gly Ser Pro Glu Glu Leu Ala Arg Lys Tyr Ala Asp Gly
[0147] 245 250 255
[0148] Glu Val Asp Val Val Val Leu Glu Asp Pro Leu Pro Gly Gly Lys Gly
[0149] 260 265 270
[0150] His Asp Ser Thr Glu Glu Pro Pro Leu Phe Ser Ser His Lys Pro Arg
[0151] 275 280 285
[0152] Gly Asp Phe Pro Ser Pro Ile His Val Ser Gly Pro Arg Leu Val Gln
[0153] 290 295 300
[0154] Pro His Gly Pro Arg Phe Arg Leu Glu Gly Asn Ala Val Leu Tyr Gly
[0155] 305 310 315 320
[0156] Gly Trp Ser Phe Ala Phe Arg Leu Arg Ser Ser Ser Gly Leu Gln Val
[0157] 325 330 335
[0158] Leu Asn Val His Phe Gly Gly Glu Arg Ile Ala Tyr Glu Val Ser Val
[0159] 340 345 350
[0160] Gln Glu Ala Val Ala Leu Tyr Gly Gly His Thr Pro Ala Gly Met Gln
[0161] 355 360 365
[0162] Thr Lys Tyr Leu Asp Val Gly Trp Gly Leu Gly Ser Val Thr His Glu
[0163] 370 375 380
[0164] Leu Ala Pro Gly Ile Asp Cys Pro Glu Thr Ala Thr Phe Leu Asp Thr
[0165] 385 390 395 400
[0166] Phe His Tyr Tyr Asp Ala Asp Asp Pro Val His Tyr Pro Arg Ala Leu
[0167] 405 410 415

[0168] Cys Leu Phe Glu Met Pro Thr Gly Val Pro Leu Arg Arg His Phe Asn
[0169] 420 425 430
[0170] Ser Asn Phe Lys Gly Gly Phe Asn Phe Tyr Ala Gly Leu Lys Gly Gln
[0171] 435 440 445
[0172] Val Leu Val Leu Arg Thr Thr Ser Thr Val Tyr Asn Tyr Asp Tyr Ile
[0173] 450 455 460
[0174] Trp Asp Phe Ile Phe Tyr Pro Asn Gly Val Met Glu Ala Lys Met His
[0175] 465 470 475 480
[0176] Ala Thr Gly Tyr Val His Ala Thr Phe Tyr Thr Pro Glu Gly Leu Arg
[0177] 485 490 495
[0178] His Gly Thr Arg Leu His Thr His Leu Ile Gly Asn Ile His Thr His
[0179] 500 505 510
[0180] Leu Val His Tyr Arg Val Asp Leu Asp Val Ala Gly Thr Lys Asn Ser
[0181] 515 520 525
[0182] Phe Gln Thr Leu Gln Met Lys Leu Glu Asn Ile Thr Asn Pro Trp Ser
[0183] 530 535 540
[0184] Pro Arg His Arg Val Val Gln Pro Thr Leu Glu Gln Thr Gln Tyr Ser
[0185] 545 550 555 560
[0186] Trp Glu Arg Gln Ala Ala Phe Ser Phe Lys Arg Lys Leu Pro Lys Tyr
[0187] 565 570 575
[0188] Leu Leu Phe Thr Ser Pro Gln Glu Asn Pro Trp Gly His Lys Arg Ser
[0189] 580 585 590
[0190] Tyr Arg Leu Gln Ile His Ser Met Ala Asp Gln Val Leu Pro Pro Gly
[0191] 595 600 605
[0192] Trp Gln Glu Glu Gln Ala Ile Thr Trp Ala Arg Tyr Pro Leu Ala Val
[0193] 610 615 620
[0194] Thr Lys Tyr Arg Glu Ser Glu Leu Cys Ser Ser Ser Ile Tyr His Gln
[0195] 625 630 635 640
[0196] Asn Asp Pro Trp His Pro Pro Val Val Phe Glu Gln Phe Leu His Asn
[0197] 645 650 655
[0198] Asn Glu Asn Ile Glu Asn Glu Asp Leu Val Ala Trp Val Thr Val Gly
[0199] 660 665 670
[0200] Phe Leu His Ile Pro His Ser Glu Asp Ile Pro Asn Thr Ala Thr Pro
[0201] 675 680 685
[0202] Gly Asn Ser Val Gly Phe Leu Leu Arg Pro Phe Asn Phe Phe Pro Glu
[0203] 690 695 700
[0204] Asp Pro Ser Leu Ala Ser Arg Asp Thr Val Ile Val Trp Pro Arg Asp
[0205] 705 710 715 720
[0206] Asn Gly Pro Asn Tyr Val Gln Arg Trp Ile Pro Glu Asp Arg Asp Cys
[0207] 725 730 735
[0208] Ser Met Pro Pro Pro Phe Ser Tyr Asn Gly Thr Tyr Arg Pro Val
[0209] 740 745 750

[0210] <210> 3

[0211] <211> 751

[0212] <212> PRT

[0213] <213> 人工序列

[0214] <220>

[0215] <223> hDAO-Hepmut2

[0216] <400> 3

[0217] Met Pro Ala Leu Gly Trp Ala Val Ala Ala Ile Leu Met Leu Gln Thr

[0218] 1 5 10 15

[0219] Ala Met Ala Glu Pro Ser Pro Gly Thr Leu Pro Arg Lys Ala Gly Val

[0220] 20 25 30

[0221] Phe Ser Asp Leu Ser Asn Gln Glu Leu Lys Ala Val His Ser Phe Leu

[0222] 35 40 45

[0223] Trp Ser Lys Lys Glu Leu Arg Leu Gln Pro Ser Ser Thr Thr Thr Met

[0224] 50 55 60

[0225] Ala Lys Asn Thr Val Phe Leu Ile Glu Met Leu Leu Pro Lys Lys Tyr

[0226] 65 70 75 80

[0227] His Val Leu Arg Phe Leu Asp Lys Gly Glu Arg His Pro Val Arg Glu

[0228] 85 90 95

[0229] Ala Arg Ala Val Ile Phe Phe Gly Asp Gln Glu His Pro Asn Val Thr

[0230] 100 105 110

[0231] Glu Phe Ala Val Gly Pro Leu Pro Gly Pro Cys Tyr Met Arg Ala Leu

[0232] 115 120 125

[0233] Ser Pro Arg Pro Gly Tyr Gln Ser Ser Trp Ala Ser Arg Pro Ile Ser

[0234] 130 135 140

[0235] Thr Ala Glu Tyr Ala Leu Leu Tyr His Thr Leu Gln Glu Ala Thr Lys

[0236] 145 150 155 160

[0237] Pro Leu His Gln Phe Phe Leu Asn Thr Thr Gly Phe Ser Phe Gln Asp

[0238] 165 170 175

[0239] Cys His Asp Arg Cys Leu Ala Phe Thr Asp Val Ala Pro Arg Gly Val

[0240] 180 185 190

[0241] Ala Ser Gly Gln Arg Arg Ser Trp Leu Ile Ile Gln Arg Tyr Val Glu

[0242] 195 200 205

[0243] Gly Tyr Phe Leu His Pro Thr Gly Leu Glu Leu Leu Val Asp His Gly

[0244] 210 215 220

[0245] Ser Thr Asp Ala Gly His Trp Ala Val Glu Gln Val Trp Tyr Asn Gly

[0246] 225 230 235 240

[0247] Lys Phe Tyr Gly Ser Pro Glu Glu Leu Ala Arg Lys Tyr Ala Asp Gly

[0248] 245 250 255

[0249] Glu Val Asp Val Val Val Leu Glu Asp Pro Leu Pro Gly Gly Lys Gly

[0250] 260 265 270

[0251] His Asp Ser Thr Glu Glu Pro Pro Leu Phe Ser Ser His Lys Pro Arg

[0252] 275 280 285

[0253] Gly Asp Phe Pro Ser Pro Ile His Val Ser Gly Pro Arg Leu Val Gln

[0254] 290 295 300

[0255] Pro His Gly Pro Arg Phe Arg Leu Glu Gly Asn Ala Val Leu Tyr Gly

[0256] 305 310 315 320

[0257] Gly Trp Ser Phe Ala Phe Arg Leu Arg Ser Ser Ser Gly Leu Gln Val

[0258] 325 330 335

[0259] Leu Asn Val His Phe Gly Gly Glu Arg Ile Ala Tyr Glu Val Ser Val

[0260] 340 345 350

[0261] Gln Glu Ala Val Ala Leu Tyr Gly Gly His Thr Pro Ala Gly Met Gln

[0262] 355 360 365

[0263] Thr Lys Tyr Leu Asp Val Gly Trp Gly Leu Gly Ser Val Thr His Glu

[0264] 370 375 380

[0265] Leu Ala Pro Gly Ile Asp Cys Pro Glu Thr Ala Thr Phe Leu Asp Thr

[0266] 385 390 395 400

[0267] Phe His Tyr Tyr Asp Ala Asp Asp Pro Val His Tyr Pro Arg Ala Leu

[0268] 405 410 415

[0269] Cys Leu Phe Glu Met Pro Thr Gly Val Pro Leu Arg Arg His Phe Asn

[0270] 420 425 430

[0271] Ser Asn Phe Lys Gly Gly Phe Asn Phe Tyr Ala Gly Leu Lys Gly Gln

[0272] 435 440 445

[0273] Val Leu Val Leu Arg Thr Thr Ser Thr Val Tyr Asn Tyr Asp Tyr Ile

[0274] 450 455 460

[0275] Trp Asp Phe Ile Phe Tyr Pro Asn Gly Val Met Glu Ala Lys Met His

[0276] 465 470 475 480

[0277] Ala Thr Gly Tyr Val His Ala Thr Phe Tyr Thr Pro Glu Gly Leu Arg

[0278] 485 490 495

[0279] His Gly Thr Arg Leu His Thr His Leu Ile Gly Asn Ile His Thr His

[0280] 500 505 510

[0281] Leu Val His Tyr Arg Val Asp Leu Asp Val Ala Gly Thr Lys Asn Ser

[0282] 515 520 525

[0283] Phe Gln Thr Leu Gln Met Lys Leu Glu Asn Ile Thr Asn Pro Trp Ser

[0284] 530 535 540

[0285] Pro Arg His Arg Val Val Gln Pro Thr Leu Glu Gln Thr Gln Tyr Ser

[0286] 545 550 555 560

[0287] Trp Glu Arg Gln Ala Ala Phe Arg Phe Lys Arg Lys Leu Pro Thr Tyr

[0288] 565 570 575

[0289] Leu Leu Phe Thr Ser Pro Gln Glu Asn Pro Trp Gly His Lys Arg Ser

[0290] 580 585 590

[0291] Tyr Arg Leu Gln Ile His Ser Met Ala Asp Gln Val Leu Pro Pro Gly

[0292] 595 600 605

[0293] Trp Gln Glu Glu Gln Ala Ile Thr Trp Ala Arg Tyr Pro Leu Ala Val

[0294] 610 615 620
[0295] Thr Lys Tyr Arg Glu Ser Glu Leu Cys Ser Ser Ser Ile Tyr His Gln
[0296] 625 630 635 640
[0297] Asn Asp Pro Trp His Pro Pro Val Val Phe Glu Gln Phe Leu His Asn
[0298] 645 650 655
[0299] Asn Glu Asn Ile Glu Asn Glu Asp Leu Val Ala Trp Val Thr Val Gly
[0300] 660 665 670
[0301] Phe Leu His Ile Pro His Ser Glu Asp Ile Pro Asn Thr Ala Thr Pro
[0302] 675 680 685
[0303] Gly Asn Ser Val Gly Phe Leu Leu Arg Pro Phe Asn Phe Phe Pro Glu
[0304] 690 695 700
[0305] Asp Pro Ser Leu Ala Ser Arg Asp Thr Val Ile Val Trp Pro Arg Asp
[0306] 705 710 715 720
[0307] Asn Gly Pro Asn Tyr Val Gln Arg Trp Ile Pro Glu Asp Arg Asp Cys
[0308] 725 730 735
[0309] Ser Met Pro Pro Pro Phe Ser Tyr Asn Gly Thr Tyr Arg Pro Val
[0310] 740 745 750
[0311] <210> 4
[0312] <211> 751
[0313] <212> PRT
[0314] <213> 人工序列
[0315] <220>
[0316] <223> hDAO-Hepmut3
[0317] <400> 4
[0318] Met Pro Ala Leu Gly Trp Ala Val Ala Ala Ile Leu Met Leu Gln Thr
[0319] 1 5 10 15
[0320] Ala Met Ala Glu Pro Ser Pro Gly Thr Leu Pro Arg Lys Ala Gly Val
[0321] 20 25 30
[0322] Phe Ser Asp Leu Ser Asn Gln Glu Leu Lys Ala Val His Ser Phe Leu
[0323] 35 40 45
[0324] Trp Ser Lys Lys Glu Leu Arg Leu Gln Pro Ser Ser Thr Thr Thr Met
[0325] 50 55 60
[0326] Ala Lys Asn Thr Val Phe Leu Ile Glu Met Leu Leu Pro Lys Lys Tyr
[0327] 65 70 75 80
[0328] His Val Leu Arg Phe Leu Asp Lys Gly Glu Arg His Pro Val Arg Glu
[0329] 85 90 95
[0330] Ala Arg Ala Val Ile Phe Phe Gly Asp Gln Glu His Pro Asn Val Thr
[0331] 100 105 110
[0332] Glu Phe Ala Val Gly Pro Leu Pro Gly Pro Cys Tyr Met Arg Ala Leu
[0333] 115 120 125
[0334] Ser Pro Arg Pro Gly Tyr Gln Ser Ser Trp Ala Ser Arg Pro Ile Ser
[0335] 130 135 140

[0336] Thr Ala Glu Tyr Ala Leu Leu Tyr His Thr Leu Gln Glu Ala Thr Lys
[0337] 145 150 155 160
[0338] Pro Leu His Gln Phe Phe Leu Asn Thr Thr Gly Phe Ser Phe Gln Asp
[0339] 165 170 175
[0340] Cys His Asp Arg Cys Leu Ala Phe Thr Asp Val Ala Pro Arg Gly Val
[0341] 180 185 190
[0342] Ala Ser Gly Gln Arg Arg Ser Trp Leu Ile Ile Gln Arg Tyr Val Glu
[0343] 195 200 205
[0344] Gly Tyr Phe Leu His Pro Thr Gly Leu Glu Leu Leu Val Asp His Gly
[0345] 210 215 220
[0346] Ser Thr Asp Ala Gly His Trp Ala Val Glu Gln Val Trp Tyr Asn Gly
[0347] 225 230 235 240
[0348] Lys Phe Tyr Gly Ser Pro Glu Glu Leu Ala Arg Lys Tyr Ala Asp Gly
[0349] 245 250 255
[0350] Glu Val Asp Val Val Val Leu Glu Asp Pro Leu Pro Gly Gly Lys Gly
[0351] 260 265 270
[0352] His Asp Ser Thr Glu Glu Pro Pro Leu Phe Ser Ser His Lys Pro Arg
[0353] 275 280 285
[0354] Gly Asp Phe Pro Ser Pro Ile His Val Ser Gly Pro Arg Leu Val Gln
[0355] 290 295 300
[0356] Pro His Gly Pro Arg Phe Arg Leu Glu Gly Asn Ala Val Leu Tyr Gly
[0357] 305 310 315 320
[0358] Gly Trp Ser Phe Ala Phe Arg Leu Arg Ser Ser Ser Gly Leu Gln Val
[0359] 325 330 335
[0360] Leu Asn Val His Phe Gly Gly Glu Arg Ile Ala Tyr Glu Val Ser Val
[0361] 340 345 350
[0362] Gln Glu Ala Val Ala Leu Tyr Gly Gly His Thr Pro Ala Gly Met Gln
[0363] 355 360 365
[0364] Thr Lys Tyr Leu Asp Val Gly Trp Gly Leu Gly Ser Val Thr His Glu
[0365] 370 375 380
[0366] Leu Ala Pro Gly Ile Asp Cys Pro Glu Thr Ala Thr Phe Leu Asp Thr
[0367] 385 390 395 400
[0368] Phe His Tyr Tyr Asp Ala Asp Asp Pro Val His Tyr Pro Arg Ala Leu
[0369] 405 410 415
[0370] Cys Leu Phe Glu Met Pro Thr Gly Val Pro Leu Arg Arg His Phe Asn
[0371] 420 425 430
[0372] Ser Asn Phe Lys Gly Gly Phe Asn Phe Tyr Ala Gly Leu Lys Gly Gln
[0373] 435 440 445
[0374] Val Leu Val Leu Arg Thr Thr Ser Thr Val Tyr Asn Tyr Asp Tyr Ile
[0375] 450 455 460
[0376] Trp Asp Phe Ile Phe Tyr Pro Asn Gly Val Met Glu Ala Lys Met His
[0377] 465 470 475 480

[0378] Ala Thr Gly Tyr Val His Ala Thr Phe Tyr Thr Pro Glu Gly Leu Arg
[0379] 485 490 495
[0380] His Gly Thr Arg Leu His Thr His Leu Ile Gly Asn Ile His Thr His
[0381] 500 505 510
[0382] Leu Val His Tyr Arg Val Asp Leu Asp Val Ala Gly Thr Lys Asn Ser
[0383] 515 520 525
[0384] Phe Gln Thr Leu Gln Met Lys Leu Glu Asn Ile Thr Asn Pro Trp Ser
[0385] 530 535 540
[0386] Pro Arg His Arg Val Val Gln Pro Thr Leu Glu Gln Thr Gln Tyr Ser
[0387] 545 550 555 560
[0388] Trp Glu Arg Gln Ala Ala Phe Arg Phe Lys Thr Lys Leu Pro Lys Tyr
[0389] 565 570 575
[0390] Leu Leu Phe Thr Ser Pro Gln Glu Asn Pro Trp Gly His Lys Arg Ser
[0391] 580 585 590
[0392] Tyr Arg Leu Gln Ile His Ser Met Ala Asp Gln Val Leu Pro Pro Gly
[0393] 595 600 605
[0394] Trp Gln Glu Glu Gln Ala Ile Thr Trp Ala Arg Tyr Pro Leu Ala Val
[0395] 610 615 620
[0396] Thr Lys Tyr Arg Glu Ser Glu Leu Cys Ser Ser Ser Ile Tyr His Gln
[0397] 625 630 635 640
[0398] Asn Asp Pro Trp His Pro Pro Val Val Phe Glu Gln Phe Leu His Asn
[0399] 645 650 655
[0400] Asn Glu Asn Ile Glu Asn Glu Asp Leu Val Ala Trp Val Thr Val Gly
[0401] 660 665 670
[0402] Phe Leu His Ile Pro His Ser Glu Asp Ile Pro Asn Thr Ala Thr Pro
[0403] 675 680 685
[0404] Gly Asn Ser Val Gly Phe Leu Leu Arg Pro Phe Asn Phe Phe Pro Glu
[0405] 690 695 700
[0406] Asp Pro Ser Leu Ala Ser Arg Asp Thr Val Ile Val Trp Pro Arg Asp
[0407] 705 710 715 720
[0408] Asn Gly Pro Asn Tyr Val Gln Arg Trp Ile Pro Glu Asp Arg Asp Cys
[0409] 725 730 735
[0410] Ser Met Pro Pro Pro Phe Ser Tyr Asn Gly Thr Tyr Arg Pro Val
[0411] 740 745 750
[0412] <210> 5
[0413] <211> 751
[0414] <212> PRT
[0415] <213> 人工序列
[0416] <220>
[0417] <223> hDAO-Hepmut4
[0418] <400> 5
[0419] Met Pro Ala Leu Gly Trp Ala Val Ala Ala Ile Leu Met Leu Gln Thr

[0420] 1 5 10 15

[0421] Ala Met Ala Glu Pro Ser Pro Gly Thr Leu Pro Arg Lys Ala Gly Val

[0422] 20 25 30

[0423] Phe Ser Asp Leu Ser Asn Gln Glu Leu Lys Ala Val His Ser Phe Leu

[0424] 35 40 45

[0425] Trp Ser Lys Lys Glu Leu Arg Leu Gln Pro Ser Ser Thr Thr Thr Met

[0426] 50 55 60

[0427] Ala Lys Asn Thr Val Phe Leu Ile Glu Met Leu Leu Pro Lys Lys Tyr

[0428] 65 70 75 80

[0429] His Val Leu Arg Phe Leu Asp Lys Gly Glu Arg His Pro Val Arg Glu

[0430] 85 90 95

[0431] Ala Arg Ala Val Ile Phe Phe Gly Asp Gln Glu His Pro Asn Val Thr

[0432] 100 105 110

[0433] Glu Phe Ala Val Gly Pro Leu Pro Gly Pro Cys Tyr Met Arg Ala Leu

[0434] 115 120 125

[0435] Ser Pro Arg Pro Gly Tyr Gln Ser Ser Trp Ala Ser Arg Pro Ile Ser

[0436] 130 135 140

[0437] Thr Ala Glu Tyr Ala Leu Leu Tyr His Thr Leu Gln Glu Ala Thr Lys

[0438] 145 150 155 160

[0439] Pro Leu His Gln Phe Phe Leu Asn Thr Thr Gly Phe Ser Phe Gln Asp

[0440] 165 170 175

[0441] Cys His Asp Arg Cys Leu Ala Phe Thr Asp Val Ala Pro Arg Gly Val

[0442] 180 185 190

[0443] Ala Ser Gly Gln Arg Arg Ser Trp Leu Ile Ile Gln Arg Tyr Val Glu

[0444] 195 200 205

[0445] Gly Tyr Phe Leu His Pro Thr Gly Leu Glu Leu Leu Val Asp His Gly

[0446] 210 215 220

[0447] Ser Thr Asp Ala Gly His Trp Ala Val Glu Gln Val Trp Tyr Asn Gly

[0448] 225 230 235 240

[0449] Lys Phe Tyr Gly Ser Pro Glu Glu Leu Ala Arg Lys Tyr Ala Asp Gly

[0450] 245 250 255

[0451] Glu Val Asp Val Val Val Leu Glu Asp Pro Leu Pro Gly Gly Lys Gly

[0452] 260 265 270

[0453] His Asp Ser Thr Glu Glu Pro Pro Leu Phe Ser Ser His Lys Pro Arg

[0454] 275 280 285

[0455] Gly Asp Phe Pro Ser Pro Ile His Val Ser Gly Pro Arg Leu Val Gln

[0456] 290 295 300

[0457] Pro His Gly Pro Arg Phe Arg Leu Glu Gly Asn Ala Val Leu Tyr Gly

[0458] 305 310 315 320

[0459] Gly Trp Ser Phe Ala Phe Arg Leu Arg Ser Ser Ser Gly Leu Gln Val

[0460] 325 330 335

[0461] Leu Asn Val His Phe Gly Gly Glu Arg Ile Ala Tyr Glu Val Ser Val

[0462] 340 345 350

[0463] Gln Glu Ala Val Ala Leu Tyr Gly Gly His Thr Pro Ala Gly Met Gln

[0464] 355 360 365

[0465] Thr Lys Tyr Leu Asp Val Gly Trp Gly Leu Gly Ser Val Thr His Glu

[0466] 370 375 380

[0467] Leu Ala Pro Gly Ile Asp Cys Pro Glu Thr Ala Thr Phe Leu Asp Thr

[0468] 385 390 395 400

[0469] Phe His Tyr Tyr Asp Ala Asp Asp Pro Val His Tyr Pro Arg Ala Leu

[0470] 405 410 415

[0471] Cys Leu Phe Glu Met Pro Thr Gly Val Pro Leu Arg Arg His Phe Asn

[0472] 420 425 430

[0473] Ser Asn Phe Lys Gly Gly Phe Asn Phe Tyr Ala Gly Leu Lys Gly Gln

[0474] 435 440 445

[0475] Val Leu Val Leu Arg Thr Thr Ser Thr Val Tyr Asn Tyr Asp Tyr Ile

[0476] 450 455 460

[0477] Trp Asp Phe Ile Phe Tyr Pro Asn Gly Val Met Glu Ala Lys Met His

[0478] 465 470 475 480

[0479] Ala Thr Gly Tyr Val His Ala Thr Phe Tyr Thr Pro Glu Gly Leu Arg

[0480] 485 490 495

[0481] His Gly Thr Arg Leu His Thr His Leu Ile Gly Asn Ile His Thr His

[0482] 500 505 510

[0483] Leu Val His Tyr Arg Val Asp Leu Asp Val Ala Gly Thr Lys Asn Ser

[0484] 515 520 525

[0485] Phe Gln Thr Leu Gln Met Lys Leu Glu Asn Ile Thr Asn Pro Trp Ser

[0486] 530 535 540

[0487] Pro Arg His Arg Val Val Gln Pro Thr Leu Glu Gln Thr Gln Tyr Ser

[0488] 545 550 555 560

[0489] Trp Glu Arg Gln Ala Ala Phe Ser Phe Lys Thr Lys Leu Pro Lys Tyr

[0490] 565 570 575

[0491] Leu Leu Phe Thr Ser Pro Gln Glu Asn Pro Trp Gly His Lys Arg Ser

[0492] 580 585 590

[0493] Tyr Arg Leu Gln Ile His Ser Met Ala Asp Gln Val Leu Pro Pro Gly

[0494] 595 600 605

[0495] Trp Gln Glu Glu Gln Ala Ile Thr Trp Ala Arg Tyr Pro Leu Ala Val

[0496] 610 615 620

[0497] Thr Lys Tyr Arg Glu Ser Glu Leu Cys Ser Ser Ser Ile Tyr His Gln

[0498] 625 630 635 640

[0499] Asn Asp Pro Trp His Pro Pro Val Val Phe Glu Gln Phe Leu His Asn

[0500] 645 650 655

[0501] Asn Glu Asn Ile Glu Asn Glu Asp Leu Val Ala Trp Val Thr Val Gly

[0502] 660 665 670

[0503] Phe Leu His Ile Pro His Ser Glu Asp Ile Pro Asn Thr Ala Thr Pro

[0504] 675 680 685
[0505] Gly Asn Ser Val Gly Phe Leu Leu Arg Pro Phe Asn Phe Phe Pro Glu
[0506] 690 695 700
[0507] Asp Pro Ser Leu Ala Ser Arg Asp Thr Val Ile Val Trp Pro Arg Asp
[0508] 705 710 715 720
[0509] Asn Gly Pro Asn Tyr Val Gln Arg Trp Ile Pro Glu Asp Arg Asp Cys
[0510] 725 730 735
[0511] Ser Met Pro Pro Pro Phe Ser Tyr Asn Gly Thr Tyr Arg Pro Val
[0512] 740 745 750
[0513] <210> 6
[0514] <211> 751
[0515] <212> PRT
[0516] <213> 人工序列
[0517] <220>
[0518] <223> hDAO-Hepmut5
[0519] <400> 6
[0520] Met Pro Ala Leu Gly Trp Ala Val Ala Ala Ile Leu Met Leu Gln Thr
[0521] 1 5 10 15
[0522] Ala Met Ala Glu Pro Ser Pro Gly Thr Leu Pro Arg Lys Ala Gly Val
[0523] 20 25 30
[0524] Phe Ser Asp Leu Ser Asn Gln Glu Leu Lys Ala Val His Ser Phe Leu
[0525] 35 40 45
[0526] Trp Ser Lys Lys Glu Leu Arg Leu Gln Pro Ser Ser Thr Thr Thr Met
[0527] 50 55 60
[0528] Ala Lys Asn Thr Val Phe Leu Ile Glu Met Leu Leu Pro Lys Lys Tyr
[0529] 65 70 75 80
[0530] His Val Leu Arg Phe Leu Asp Lys Gly Glu Arg His Pro Val Arg Glu
[0531] 85 90 95
[0532] Ala Arg Ala Val Ile Phe Phe Gly Asp Gln Glu His Pro Asn Val Thr
[0533] 100 105 110
[0534] Glu Phe Ala Val Gly Pro Leu Pro Gly Pro Cys Tyr Met Arg Ala Leu
[0535] 115 120 125
[0536] Ser Pro Arg Pro Gly Tyr Gln Ser Ser Trp Ala Ser Arg Pro Ile Ser
[0537] 130 135 140
[0538] Thr Ala Glu Tyr Ala Leu Leu Tyr His Thr Leu Gln Glu Ala Thr Lys
[0539] 145 150 155 160
[0540] Pro Leu His Gln Phe Phe Leu Asn Thr Thr Gly Phe Ser Phe Gln Asp
[0541] 165 170 175
[0542] Cys His Asp Arg Cys Leu Ala Phe Thr Asp Val Ala Pro Arg Gly Val
[0543] 180 185 190
[0544] Ala Ser Gly Gln Arg Arg Ser Trp Leu Ile Ile Gln Arg Tyr Val Glu
[0545] 195 200 205

[0546] Gly Tyr Phe Leu His Pro Thr Gly Leu Glu Leu Leu Val Asp His Gly
[0547] 210 215 220
[0548] Ser Thr Asp Ala Gly His Trp Ala Val Glu Gln Val Trp Tyr Asn Gly
[0549] 225 230 235 240
[0550] Lys Phe Tyr Gly Ser Pro Glu Glu Leu Ala Arg Lys Tyr Ala Asp Gly
[0551] 245 250 255
[0552] Glu Val Asp Val Val Val Leu Glu Asp Pro Leu Pro Gly Gly Lys Gly
[0553] 260 265 270
[0554] His Asp Ser Thr Glu Glu Pro Pro Leu Phe Ser Ser His Lys Pro Arg
[0555] 275 280 285
[0556] Gly Asp Phe Pro Ser Pro Ile His Val Ser Gly Pro Arg Leu Val Gln
[0557] 290 295 300
[0558] Pro His Gly Pro Arg Phe Arg Leu Glu Gly Asn Ala Val Leu Tyr Gly
[0559] 305 310 315 320
[0560] Gly Trp Ser Phe Ala Phe Arg Leu Arg Ser Ser Ser Gly Leu Gln Val
[0561] 325 330 335
[0562] Leu Asn Val His Phe Gly Gly Glu Arg Ile Ala Tyr Glu Val Ser Val
[0563] 340 345 350
[0564] Gln Glu Ala Val Ala Leu Tyr Gly Gly His Thr Pro Ala Gly Met Gln
[0565] 355 360 365
[0566] Thr Lys Tyr Leu Asp Val Gly Trp Gly Leu Gly Ser Val Thr His Glu
[0567] 370 375 380
[0568] Leu Ala Pro Gly Ile Asp Cys Pro Glu Thr Ala Thr Phe Leu Asp Thr
[0569] 385 390 395 400
[0570] Phe His Tyr Tyr Asp Ala Asp Asp Pro Val His Tyr Pro Arg Ala Leu
[0571] 405 410 415
[0572] Cys Leu Phe Glu Met Pro Thr Gly Val Pro Leu Arg Arg His Phe Asn
[0573] 420 425 430
[0574] Ser Asn Phe Lys Gly Gly Phe Asn Phe Tyr Ala Gly Leu Lys Gly Gln
[0575] 435 440 445
[0576] Val Leu Val Leu Arg Thr Thr Ser Thr Val Tyr Asn Tyr Asp Tyr Ile
[0577] 450 455 460
[0578] Trp Asp Phe Ile Phe Tyr Pro Asn Gly Val Met Glu Ala Lys Met His
[0579] 465 470 475 480
[0580] Ala Thr Gly Tyr Val His Ala Thr Phe Tyr Thr Pro Glu Gly Leu Arg
[0581] 485 490 495
[0582] His Gly Thr Arg Leu His Thr His Leu Ile Gly Asn Ile His Thr His
[0583] 500 505 510
[0584] Leu Val His Tyr Arg Val Asp Leu Asp Val Ala Gly Thr Lys Asn Ser
[0585] 515 520 525
[0586] Phe Gln Thr Leu Gln Met Lys Leu Glu Asn Ile Thr Asn Pro Trp Ser
[0587] 530 535 540

[0588] Pro Arg His Arg Val Val Gln Pro Thr Leu Glu Gln Thr Gln Tyr Ser
[0589] 545 550 555 560
[0590] Trp Glu Arg Gln Ala Ala Phe Arg Phe Lys Thr Lys Leu Pro Thr Tyr
[0591] 565 570 575
[0592] Leu Leu Phe Thr Ser Pro Gln Glu Asn Pro Trp Gly His Lys Arg Ser
[0593] 580 585 590
[0594] Tyr Arg Leu Gln Ile His Ser Met Ala Asp Gln Val Leu Pro Pro Gly
[0595] 595 600 605
[0596] Trp Gln Glu Glu Gln Ala Ile Thr Trp Ala Arg Tyr Pro Leu Ala Val
[0597] 610 615 620
[0598] Thr Lys Tyr Arg Glu Ser Glu Leu Cys Ser Ser Ser Ile Tyr His Gln
[0599] 625 630 635 640
[0600] Asn Asp Pro Trp His Pro Pro Val Val Phe Glu Gln Phe Leu His Asn
[0601] 645 650 655
[0602] Asn Glu Asn Ile Glu Asn Glu Asp Leu Val Ala Trp Val Thr Val Gly
[0603] 660 665 670
[0604] Phe Leu His Ile Pro His Ser Glu Asp Ile Pro Asn Thr Ala Thr Pro
[0605] 675 680 685
[0606] Gly Asn Ser Val Gly Phe Leu Leu Arg Pro Phe Asn Phe Phe Pro Glu
[0607] 690 695 700
[0608] Asp Pro Ser Leu Ala Ser Arg Asp Thr Val Ile Val Trp Pro Arg Asp
[0609] 705 710 715 720
[0610] Asn Gly Pro Asn Tyr Val Gln Arg Trp Ile Pro Glu Asp Arg Asp Cys
[0611] 725 730 735
[0612] Ser Met Pro Pro Pro Phe Ser Tyr Asn Gly Thr Tyr Arg Pro Val
[0613] 740 745 750
[0614] <210> 7
[0615] <211> 751
[0616] <212> PRT
[0617] <213> 人工序列
[0618] <220>
[0619] <223> hDAO-Hepmut6
[0620] <400> 7
[0621] Met Pro Ala Leu Gly Trp Ala Val Ala Ala Ile Leu Met Leu Gln Thr
[0622] 1 5 10 15
[0623] Ala Met Ala Glu Pro Ser Pro Gly Thr Leu Pro Arg Lys Ala Gly Val
[0624] 20 25 30
[0625] Phe Ser Asp Leu Ser Asn Gln Glu Leu Lys Ala Val His Ser Phe Leu
[0626] 35 40 45
[0627] Trp Ser Lys Lys Glu Leu Arg Leu Gln Pro Ser Ser Thr Thr Thr Met
[0628] 50 55 60
[0629] Ala Lys Asn Thr Val Phe Leu Ile Glu Met Leu Leu Pro Lys Lys Tyr

[0630] 65 70 75 80

[0631] His Val Leu Arg Phe Leu Asp Lys Gly Glu Arg His Pro Val Arg Glu

[0632] 85 90 95

[0633] Ala Arg Ala Val Ile Phe Phe Gly Asp Gln Glu His Pro Asn Val Thr

[0634] 100 105 110

[0635] Glu Phe Ala Val Gly Pro Leu Pro Gly Pro Cys Tyr Met Arg Ala Leu

[0636] 115 120 125

[0637] Ser Pro Arg Pro Gly Tyr Gln Ser Ser Trp Ala Ser Arg Pro Ile Ser

[0638] 130 135 140

[0639] Thr Ala Glu Tyr Ala Leu Leu Tyr His Thr Leu Gln Glu Ala Thr Lys

[0640] 145 150 155 160

[0641] Pro Leu His Gln Phe Phe Leu Asn Thr Thr Gly Phe Ser Phe Gln Asp

[0642] 165 170 175

[0643] Cys His Asp Arg Cys Leu Ala Phe Thr Asp Val Ala Pro Arg Gly Val

[0644] 180 185 190

[0645] Ala Ser Gly Gln Arg Arg Ser Trp Leu Ile Ile Gln Arg Tyr Val Glu

[0646] 195 200 205

[0647] Gly Tyr Phe Leu His Pro Thr Gly Leu Glu Leu Leu Val Asp His Gly

[0648] 210 215 220

[0649] Ser Thr Asp Ala Gly His Trp Ala Val Glu Gln Val Trp Tyr Asn Gly

[0650] 225 230 235 240

[0651] Lys Phe Tyr Gly Ser Pro Glu Glu Leu Ala Arg Lys Tyr Ala Asp Gly

[0652] 245 250 255

[0653] Glu Val Asp Val Val Val Leu Glu Asp Pro Leu Pro Gly Gly Lys Gly

[0654] 260 265 270

[0655] His Asp Ser Thr Glu Glu Pro Pro Leu Phe Ser Ser His Lys Pro Arg

[0656] 275 280 285

[0657] Gly Asp Phe Pro Ser Pro Ile His Val Ser Gly Pro Arg Leu Val Gln

[0658] 290 295 300

[0659] Pro His Gly Pro Arg Phe Arg Leu Glu Gly Asn Ala Val Leu Tyr Gly

[0660] 305 310 315 320

[0661] Gly Trp Ser Phe Ala Phe Arg Leu Arg Ser Ser Ser Gly Leu Gln Val

[0662] 325 330 335

[0663] Leu Asn Val His Phe Gly Gly Glu Arg Ile Ala Tyr Glu Val Ser Val

[0664] 340 345 350

[0665] Gln Glu Ala Val Ala Leu Tyr Gly Gly His Thr Pro Ala Gly Met Gln

[0666] 355 360 365

[0667] Thr Lys Tyr Leu Asp Val Gly Trp Gly Leu Gly Ser Val Thr His Glu

[0668] 370 375 380

[0669] Leu Ala Pro Gly Ile Asp Cys Pro Glu Thr Ala Thr Phe Leu Asp Thr

[0670] 385 390 395 400

[0671] Phe His Tyr Tyr Asp Ala Asp Asp Pro Val His Tyr Pro Arg Ala Leu

[0672] 405 410 415

[0673] Cys Leu Phe Glu Met Pro Thr Gly Val Pro Leu Arg Arg His Phe Asn

[0674] 420 425 430

[0675] Ser Asn Phe Lys Gly Gly Phe Asn Phe Tyr Ala Gly Leu Lys Gly Gln

[0676] 435 440 445

[0677] Val Leu Val Leu Arg Thr Thr Ser Thr Val Tyr Asn Tyr Asp Tyr Ile

[0678] 450 455 460

[0679] Trp Asp Phe Ile Phe Tyr Pro Asn Gly Val Met Glu Ala Lys Met His

[0680] 465 470 475 480

[0681] Ala Thr Gly Tyr Val His Ala Thr Phe Tyr Thr Pro Glu Gly Leu Arg

[0682] 485 490 495

[0683] His Gly Thr Arg Leu His Thr His Leu Ile Gly Asn Ile His Thr His

[0684] 500 505 510

[0685] Leu Val His Tyr Arg Val Asp Leu Asp Val Ala Gly Thr Lys Asn Ser

[0686] 515 520 525

[0687] Phe Gln Thr Leu Gln Met Lys Leu Glu Asn Ile Thr Asn Pro Trp Ser

[0688] 530 535 540

[0689] Pro Arg His Arg Val Val Gln Pro Thr Leu Glu Gln Thr Gln Tyr Ser

[0690] 545 550 555 560

[0691] Trp Glu Arg Gln Ala Ala Phe Arg Phe Gly Gln Thr Leu Pro Lys Tyr

[0692] 565 570 575

[0693] Leu Leu Phe Thr Ser Pro Gln Glu Asn Pro Trp Gly His Lys Arg Ser

[0694] 580 585 590

[0695] Tyr Arg Leu Gln Ile His Ser Met Ala Asp Gln Val Leu Pro Pro Gly

[0696] 595 600 605

[0697] Trp Gln Glu Glu Gln Ala Ile Thr Trp Ala Arg Tyr Pro Leu Ala Val

[0698] 610 615 620

[0699] Thr Lys Tyr Arg Glu Ser Glu Leu Cys Ser Ser Ser Ile Tyr His Gln

[0700] 625 630 635 640

[0701] Asn Asp Pro Trp His Pro Pro Val Val Phe Glu Gln Phe Leu His Asn

[0702] 645 650 655

[0703] Asn Glu Asn Ile Glu Asn Glu Asp Leu Val Ala Trp Val Thr Val Gly

[0704] 660 665 670

[0705] Phe Leu His Ile Pro His Ser Glu Asp Ile Pro Asn Thr Ala Thr Pro

[0706] 675 680 685

[0707] Gly Asn Ser Val Gly Phe Leu Leu Arg Pro Phe Asn Phe Phe Pro Glu

[0708] 690 695 700

[0709] Asp Pro Ser Leu Ala Ser Arg Asp Thr Val Ile Val Trp Pro Arg Asp

[0710] 705 710 715 720

[0711] Asn Gly Pro Asn Tyr Val Gln Arg Trp Ile Pro Glu Asp Arg Asp Cys

[0712] 725 730 735

[0713] Ser Met Pro Pro Pro Phe Ser Tyr Asn Gly Thr Tyr Arg Pro Val

[0714] 740 745 750

[0715] <210> 8

[0716] <211> 751

[0717] <212> PRT

[0718] <213> 人工序列

[0719] <220>

[0720] <223> hDAO-Hepmut7

[0721] <400> 8

[0722] Met Pro Ala Leu Gly Trp Ala Val Ala Ala Ile Leu Met Leu Gln Thr

[0723] 1 5 10 15

[0724] Ala Met Ala Glu Pro Ser Pro Gly Thr Leu Pro Arg Lys Ala Gly Val

[0725] 20 25 30

[0726] Phe Ser Asp Leu Ser Asn Gln Glu Leu Lys Ala Val His Ser Phe Leu

[0727] 35 40 45

[0728] Trp Ser Lys Lys Glu Leu Arg Leu Gln Pro Ser Ser Thr Thr Thr Met

[0729] 50 55 60

[0730] Ala Lys Asn Thr Val Phe Leu Ile Glu Met Leu Leu Pro Lys Lys Tyr

[0731] 65 70 75 80

[0732] His Val Leu Arg Phe Leu Asp Lys Gly Glu Arg His Pro Val Arg Glu

[0733] 85 90 95

[0734] Ala Arg Ala Val Ile Phe Phe Gly Asp Gln Glu His Pro Asn Val Thr

[0735] 100 105 110

[0736] Glu Phe Ala Val Gly Pro Leu Pro Gly Pro Cys Tyr Met Arg Ala Leu

[0737] 115 120 125

[0738] Ser Pro Arg Pro Gly Tyr Gln Ser Ser Trp Ala Ser Arg Pro Ile Ser

[0739] 130 135 140

[0740] Thr Ala Glu Tyr Ala Leu Leu Tyr His Thr Leu Gln Glu Ala Thr Lys

[0741] 145 150 155 160

[0742] Pro Leu His Gln Phe Phe Leu Asn Thr Thr Gly Phe Ser Phe Gln Asp

[0743] 165 170 175

[0744] Cys His Asp Arg Cys Leu Ala Phe Thr Asp Val Ala Pro Arg Gly Val

[0745] 180 185 190

[0746] Ala Ser Gly Gln Arg Arg Ser Trp Leu Ile Ile Gln Arg Tyr Val Glu

[0747] 195 200 205

[0748] Gly Tyr Phe Leu His Pro Thr Gly Leu Glu Leu Leu Val Asp His Gly

[0749] 210 215 220

[0750] Ser Thr Asp Ala Gly His Trp Ala Val Glu Gln Val Trp Tyr Asn Gly

[0751] 225 230 235 240

[0752] Lys Phe Tyr Gly Ser Pro Glu Glu Leu Ala Arg Lys Tyr Ala Asp Gly

[0753] 245 250 255

[0754] Glu Val Asp Val Val Val Leu Glu Asp Pro Leu Pro Gly Gly Lys Gly

[0755] 260 265 270

[0756] His Asp Ser Thr Glu Glu Pro Pro Leu Phe Ser Ser His Lys Pro Arg
[0757] 275 280 285
[0758] Gly Asp Phe Pro Ser Pro Ile His Val Ser Gly Pro Arg Leu Val Gln
[0759] 290 295 300
[0760] Pro His Gly Pro Arg Phe Arg Leu Glu Gly Asn Ala Val Leu Tyr Gly
[0761] 305 310 315 320
[0762] Gly Trp Ser Phe Ala Phe Arg Leu Arg Ser Ser Ser Gly Leu Gln Val
[0763] 325 330 335
[0764] Leu Asn Val His Phe Gly Gly Glu Arg Ile Ala Tyr Glu Val Ser Val
[0765] 340 345 350
[0766] Gln Glu Ala Val Ala Leu Tyr Gly Gly His Thr Pro Ala Gly Met Gln
[0767] 355 360 365
[0768] Thr Lys Tyr Leu Asp Val Gly Trp Gly Leu Gly Ser Val Thr His Glu
[0769] 370 375 380
[0770] Leu Ala Pro Gly Ile Asp Cys Pro Glu Thr Ala Thr Phe Leu Asp Thr
[0771] 385 390 395 400
[0772] Phe His Tyr Tyr Asp Ala Asp Asp Pro Val His Tyr Pro Arg Ala Leu
[0773] 405 410 415
[0774] Cys Leu Phe Glu Met Pro Thr Gly Val Pro Leu Arg Arg His Phe Asn
[0775] 420 425 430
[0776] Ser Asn Phe Lys Gly Gly Phe Asn Phe Tyr Ala Gly Leu Lys Gly Gln
[0777] 435 440 445
[0778] Val Leu Val Leu Arg Thr Thr Ser Thr Val Tyr Asn Tyr Asp Tyr Ile
[0779] 450 455 460
[0780] Trp Asp Phe Ile Phe Tyr Pro Asn Gly Val Met Glu Ala Lys Met His
[0781] 465 470 475 480
[0782] Ala Thr Gly Tyr Val His Ala Thr Phe Tyr Thr Pro Glu Gly Leu Arg
[0783] 485 490 495
[0784] His Gly Thr Arg Leu His Thr His Leu Ile Gly Asn Ile His Thr His
[0785] 500 505 510
[0786] Leu Val His Tyr Arg Val Asp Leu Asp Val Ala Gly Thr Lys Asn Ser
[0787] 515 520 525
[0788] Phe Gln Thr Leu Gln Met Lys Leu Glu Asn Ile Thr Asn Pro Trp Ser
[0789] 530 535 540
[0790] Pro Arg His Arg Val Val Gln Pro Thr Leu Glu Gln Thr Gln Tyr Ser
[0791] 545 550 555 560
[0792] Trp Glu Arg Gln Ala Ala Phe Ser Phe Lys Arg Lys Leu Pro Thr Tyr
[0793] 565 570 575
[0794] Leu Leu Phe Thr Ser Pro Gln Glu Asn Pro Trp Gly His Lys Arg Ser
[0795] 580 585 590
[0796] Tyr Arg Leu Gln Ile His Ser Met Ala Asp Gln Val Leu Pro Pro Gly
[0797] 595 600 605

[0798] Trp Gln Glu Glu Gln Ala Ile Thr Trp Ala Arg Tyr Pro Leu Ala Val
[0799] 610 615 620
[0800] Thr Lys Tyr Arg Glu Ser Glu Leu Cys Ser Ser Ser Ile Tyr His Gln
[0801] 625 630 635 640
[0802] Asn Asp Pro Trp His Pro Pro Val Val Phe Glu Gln Phe Leu His Asn
[0803] 645 650 655
[0804] Asn Glu Asn Ile Glu Asn Glu Asp Leu Val Ala Trp Val Thr Val Gly
[0805] 660 665 670
[0806] Phe Leu His Ile Pro His Ser Glu Asp Ile Pro Asn Thr Ala Thr Pro
[0807] 675 680 685
[0808] Gly Asn Ser Val Gly Phe Leu Leu Arg Pro Phe Asn Phe Phe Pro Glu
[0809] 690 695 700
[0810] Asp Pro Ser Leu Ala Ser Arg Asp Thr Val Ile Val Trp Pro Arg Asp
[0811] 705 710 715 720
[0812] Asn Gly Pro Asn Tyr Val Gln Arg Trp Ile Pro Glu Asp Arg Asp Cys
[0813] 725 730 735
[0814] Ser Met Pro Pro Pro Phe Ser Tyr Asn Gly Thr Tyr Arg Pro Val
[0815] 740 745 750
[0816] <210> 9
[0817] <211> 751
[0818] <212> PRT
[0819] <213> 人工序列
[0820] <220>
[0821] <223> hDAO-Cysmut
[0822] <400> 9
[0823] Met Pro Ala Leu Gly Trp Ala Val Ala Ala Ile Leu Met Leu Gln Thr
[0824] 1 5 10 15
[0825] Ala Met Ala Glu Pro Ser Pro Gly Thr Leu Pro Arg Lys Ala Gly Val
[0826] 20 25 30
[0827] Phe Ser Asp Leu Ser Asn Gln Glu Leu Lys Ala Val His Ser Phe Leu
[0828] 35 40 45
[0829] Trp Ser Lys Lys Glu Leu Arg Leu Gln Pro Ser Ser Thr Thr Thr Met
[0830] 50 55 60
[0831] Ala Lys Asn Thr Val Phe Leu Ile Glu Met Leu Leu Pro Lys Lys Tyr
[0832] 65 70 75 80
[0833] His Val Leu Arg Phe Leu Asp Lys Gly Glu Arg His Pro Val Arg Glu
[0834] 85 90 95
[0835] Ala Arg Ala Val Ile Phe Phe Gly Asp Gln Glu His Pro Asn Val Thr
[0836] 100 105 110
[0837] Glu Phe Ala Val Gly Pro Leu Pro Gly Pro Ala Tyr Met Arg Ala Leu
[0838] 115 120 125
[0839] Ser Pro Arg Pro Gly Tyr Gln Ser Ser Trp Ala Ser Arg Pro Ile Ser

[0840] 130 135 140

[0841] Thr Ala Glu Tyr Ala Leu Leu Tyr His Thr Leu Gln Glu Ala Thr Lys

[0842] 145 150 155 160

[0843] Pro Leu His Gln Phe Phe Leu Asn Thr Thr Gly Phe Ser Phe Gln Asp

[0844] 165 170 175

[0845] Cys His Asp Arg Cys Leu Ala Phe Thr Asp Val Ala Pro Arg Gly Val

[0846] 180 185 190

[0847] Ala Ser Gly Gln Arg Arg Ser Trp Leu Ile Ile Gln Arg Tyr Val Glu

[0848] 195 200 205

[0849] Gly Tyr Phe Leu His Pro Thr Gly Leu Glu Leu Leu Val Asp His Gly

[0850] 210 215 220

[0851] Ser Thr Asp Ala Gly His Trp Ala Val Glu Gln Val Trp Tyr Asn Gly

[0852] 225 230 235 240

[0853] Lys Phe Tyr Gly Ser Pro Glu Glu Leu Ala Arg Lys Tyr Ala Asp Gly

[0854] 245 250 255

[0855] Glu Val Asp Val Val Val Leu Glu Asp Pro Leu Pro Gly Gly Lys Gly

[0856] 260 265 270

[0857] His Asp Ser Thr Glu Glu Pro Pro Leu Phe Ser Ser His Lys Pro Arg

[0858] 275 280 285

[0859] Gly Asp Phe Pro Ser Pro Ile His Val Ser Gly Pro Arg Leu Val Gln

[0860] 290 295 300

[0861] Pro His Gly Pro Arg Phe Arg Leu Glu Gly Asn Ala Val Leu Tyr Gly

[0862] 305 310 315 320

[0863] Gly Trp Ser Phe Ala Phe Arg Leu Arg Ser Ser Ser Gly Leu Gln Val

[0864] 325 330 335

[0865] Leu Asn Val His Phe Gly Gly Glu Arg Ile Ala Tyr Glu Val Ser Val

[0866] 340 345 350

[0867] Gln Glu Ala Val Ala Leu Tyr Gly Gly His Thr Pro Ala Gly Met Gln

[0868] 355 360 365

[0869] Thr Lys Tyr Leu Asp Val Gly Trp Gly Leu Gly Ser Val Thr His Glu

[0870] 370 375 380

[0871] Leu Ala Pro Gly Ile Asp Cys Pro Glu Thr Ala Thr Phe Leu Asp Thr

[0872] 385 390 395 400

[0873] Phe His Tyr Tyr Asp Ala Asp Asp Pro Val His Tyr Pro Arg Ala Leu

[0874] 405 410 415

[0875] Cys Leu Phe Glu Met Pro Thr Gly Val Pro Leu Arg Arg His Phe Asn

[0876] 420 425 430

[0877] Ser Asn Phe Lys Gly Gly Phe Asn Phe Tyr Ala Gly Leu Lys Gly Gln

[0878] 435 440 445

[0879] Val Leu Val Leu Arg Thr Thr Ser Thr Val Tyr Asn Tyr Asp Tyr Ile

[0880] 450 455 460

[0881] Trp Asp Phe Ile Phe Tyr Pro Asn Gly Val Met Glu Ala Lys Met His

[0882] 465 470 475 480
[0883] Ala Thr Gly Tyr Val His Ala Thr Phe Tyr Thr Pro Glu Gly Leu Arg
[0884] 485 490 495
[0885] His Gly Thr Arg Leu His Thr His Leu Ile Gly Asn Ile His Thr His
[0886] 500 505 510
[0887] Leu Val His Tyr Arg Val Asp Leu Asp Val Ala Gly Thr Lys Asn Ser
[0888] 515 520 525
[0889] Phe Gln Thr Leu Gln Met Lys Leu Glu Asn Ile Thr Asn Pro Trp Ser
[0890] 530 535 540
[0891] Pro Arg His Arg Val Val Gln Pro Thr Leu Glu Gln Thr Gln Tyr Ser
[0892] 545 550 555 560
[0893] Trp Glu Arg Gln Ala Ala Phe Arg Phe Lys Arg Lys Leu Pro Lys Tyr
[0894] 565 570 575
[0895] Leu Leu Phe Thr Ser Pro Gln Glu Asn Pro Trp Gly His Lys Arg Ser
[0896] 580 585 590
[0897] Tyr Arg Leu Gln Ile His Ser Met Ala Asp Gln Val Leu Pro Pro Gly
[0898] 595 600 605
[0899] Trp Gln Glu Glu Gln Ala Ile Thr Trp Ala Arg Tyr Pro Leu Ala Val
[0900] 610 615 620
[0901] Thr Lys Tyr Arg Glu Ser Glu Leu Cys Ser Ser Ser Ile Tyr His Gln
[0902] 625 630 635 640
[0903] Asn Asp Pro Trp His Pro Pro Val Val Phe Glu Gln Phe Leu His Asn
[0904] 645 650 655
[0905] Asn Glu Asn Ile Glu Asn Glu Asp Leu Val Ala Trp Val Thr Val Gly
[0906] 660 665 670
[0907] Phe Leu His Ile Pro His Ser Glu Asp Ile Pro Asn Thr Ala Thr Pro
[0908] 675 680 685
[0909] Gly Asn Ser Val Gly Phe Leu Leu Arg Pro Phe Asn Phe Phe Pro Glu
[0910] 690 695 700
[0911] Asp Pro Ser Leu Ala Ser Arg Asp Thr Val Ile Val Trp Pro Arg Asp
[0912] 705 710 715 720
[0913] Asn Gly Pro Asn Tyr Val Gln Arg Trp Ile Pro Glu Asp Arg Asp Cys
[0914] 725 730 735
[0915] Ser Met Pro Pro Pro Phe Ser Tyr Asn Gly Thr Tyr Arg Pro Val
[0916] 740 745 750
[0917] <210> 10
[0918] <211> 751
[0919] <212> PRT
[0920] <213> 人工序列
[0921] <220>
[0922] <223> hDAO-Hepmut1-Cysmut
[0923] <400> 10

[0924] Met Pro Ala Leu Gly Trp Ala Val Ala Ala Ile Leu Met Leu Gln Thr
[0925] 1 5 10 15
[0926] Ala Met Ala Glu Pro Ser Pro Gly Thr Leu Pro Arg Lys Ala Gly Val
[0927] 20 25 30
[0928] Phe Ser Asp Leu Ser Asn Gln Glu Leu Lys Ala Val His Ser Phe Leu
[0929] 35 40 45
[0930] Trp Ser Lys Lys Glu Leu Arg Leu Gln Pro Ser Ser Thr Thr Thr Met
[0931] 50 55 60
[0932] Ala Lys Asn Thr Val Phe Leu Ile Glu Met Leu Leu Pro Lys Lys Tyr
[0933] 65 70 75 80
[0934] His Val Leu Arg Phe Leu Asp Lys Gly Glu Arg His Pro Val Arg Glu
[0935] 85 90 95
[0936] Ala Arg Ala Val Ile Phe Phe Gly Asp Gln Glu His Pro Asn Val Thr
[0937] 100 105 110
[0938] Glu Phe Ala Val Gly Pro Leu Pro Gly Pro Ala Tyr Met Arg Ala Leu
[0939] 115 120 125
[0940] Ser Pro Arg Pro Gly Tyr Gln Ser Ser Trp Ala Ser Arg Pro Ile Ser
[0941] 130 135 140
[0942] Thr Ala Glu Tyr Ala Leu Leu Tyr His Thr Leu Gln Glu Ala Thr Lys
[0943] 145 150 155 160
[0944] Pro Leu His Gln Phe Phe Leu Asn Thr Thr Gly Phe Ser Phe Gln Asp
[0945] 165 170 175
[0946] Cys His Asp Arg Cys Leu Ala Phe Thr Asp Val Ala Pro Arg Gly Val
[0947] 180 185 190
[0948] Ala Ser Gly Gln Arg Arg Ser Trp Leu Ile Ile Gln Arg Tyr Val Glu
[0949] 195 200 205
[0950] Gly Tyr Phe Leu His Pro Thr Gly Leu Glu Leu Leu Val Asp His Gly
[0951] 210 215 220
[0952] Ser Thr Asp Ala Gly His Trp Ala Val Glu Gln Val Trp Tyr Asn Gly
[0953] 225 230 235 240
[0954] Lys Phe Tyr Gly Ser Pro Glu Glu Leu Ala Arg Lys Tyr Ala Asp Gly
[0955] 245 250 255
[0956] Glu Val Asp Val Val Val Leu Glu Asp Pro Leu Pro Gly Gly Lys Gly
[0957] 260 265 270
[0958] His Asp Ser Thr Glu Glu Pro Pro Leu Phe Ser Ser His Lys Pro Arg
[0959] 275 280 285
[0960] Gly Asp Phe Pro Ser Pro Ile His Val Ser Gly Pro Arg Leu Val Gln
[0961] 290 295 300
[0962] Pro His Gly Pro Arg Phe Arg Leu Glu Gly Asn Ala Val Leu Tyr Gly
[0963] 305 310 315 320
[0964] Gly Trp Ser Phe Ala Phe Arg Leu Arg Ser Ser Ser Gly Leu Gln Val
[0965] 325 330 335

[0966] Leu Asn Val His Phe Gly Gly Glu Arg Ile Ala Tyr Glu Val Ser Val
[0967] 340 345 350
[0968] Gln Glu Ala Val Ala Leu Tyr Gly Gly His Thr Pro Ala Gly Met Gln
[0969] 355 360 365
[0970] Thr Lys Tyr Leu Asp Val Gly Trp Gly Leu Gly Ser Val Thr His Glu
[0971] 370 375 380
[0972] Leu Ala Pro Gly Ile Asp Cys Pro Glu Thr Ala Thr Phe Leu Asp Thr
[0973] 385 390 395 400
[0974] Phe His Tyr Tyr Asp Ala Asp Asp Pro Val His Tyr Pro Arg Ala Leu
[0975] 405 410 415
[0976] Cys Leu Phe Glu Met Pro Thr Gly Val Pro Leu Arg Arg His Phe Asn
[0977] 420 425 430
[0978] Ser Asn Phe Lys Gly Gly Phe Asn Phe Tyr Ala Gly Leu Lys Gly Gln
[0979] 435 440 445
[0980] Val Leu Val Leu Arg Thr Thr Ser Thr Val Tyr Asn Tyr Asp Tyr Ile
[0981] 450 455 460
[0982] Trp Asp Phe Ile Phe Tyr Pro Asn Gly Val Met Glu Ala Lys Met His
[0983] 465 470 475 480
[0984] Ala Thr Gly Tyr Val His Ala Thr Phe Tyr Thr Pro Glu Gly Leu Arg
[0985] 485 490 495
[0986] His Gly Thr Arg Leu His Thr His Leu Ile Gly Asn Ile His Thr His
[0987] 500 505 510
[0988] Leu Val His Tyr Arg Val Asp Leu Asp Val Ala Gly Thr Lys Asn Ser
[0989] 515 520 525
[0990] Phe Gln Thr Leu Gln Met Lys Leu Glu Asn Ile Thr Asn Pro Trp Ser
[0991] 530 535 540
[0992] Pro Arg His Arg Val Val Gln Pro Thr Leu Glu Gln Thr Gln Tyr Ser
[0993] 545 550 555 560
[0994] Trp Glu Arg Gln Ala Ala Phe Ser Phe Lys Arg Lys Leu Pro Lys Tyr
[0995] 565 570 575
[0996] Leu Leu Phe Thr Ser Pro Gln Glu Asn Pro Trp Gly His Lys Arg Ser
[0997] 580 585 590
[0998] Tyr Arg Leu Gln Ile His Ser Met Ala Asp Gln Val Leu Pro Pro Gly
[0999] 595 600 605
[1000] Trp Gln Glu Glu Gln Ala Ile Thr Trp Ala Arg Tyr Pro Leu Ala Val
[1001] 610 615 620
[1002] Thr Lys Tyr Arg Glu Ser Glu Leu Cys Ser Ser Ser Ile Tyr His Gln
[1003] 625 630 635 640
[1004] Asn Asp Pro Trp His Pro Pro Val Val Phe Glu Gln Phe Leu His Asn
[1005] 645 650 655
[1006] Asn Glu Asn Ile Glu Asn Glu Asp Leu Val Ala Trp Val Thr Val Gly
[1007] 660 665 670

[1008] Phe Leu His Ile Pro His Ser Glu Asp Ile Pro Asn Thr Ala Thr Pro
[1009] 675 680 685
[1010] Gly Asn Ser Val Gly Phe Leu Leu Arg Pro Phe Asn Phe Phe Pro Glu
[1011] 690 695 700
[1012] Asp Pro Ser Leu Ala Ser Arg Asp Thr Val Ile Val Trp Pro Arg Asp
[1013] 705 710 715 720
[1014] Asn Gly Pro Asn Tyr Val Gln Arg Trp Ile Pro Glu Asp Arg Asp Cys
[1015] 725 730 735
[1016] Ser Met Pro Pro Pro Phe Ser Tyr Asn Gly Thr Tyr Arg Pro Val
[1017] 740 745 750
[1018] <210> 11
[1019] <211> 751
[1020] <212> PRT
[1021] <213> 人工序列
[1022] <220>
[1023] <223> hDAO-Hepmut2-Cysmut
[1024] <400> 11
[1025] Met Pro Ala Leu Gly Trp Ala Val Ala Ala Ile Leu Met Leu Gln Thr
[1026] 1 5 10 15
[1027] Ala Met Ala Glu Pro Ser Pro Gly Thr Leu Pro Arg Lys Ala Gly Val
[1028] 20 25 30
[1029] Phe Ser Asp Leu Ser Asn Gln Glu Leu Lys Ala Val His Ser Phe Leu
[1030] 35 40 45
[1031] Trp Ser Lys Lys Glu Leu Arg Leu Gln Pro Ser Ser Thr Thr Thr Met
[1032] 50 55 60
[1033] Ala Lys Asn Thr Val Phe Leu Ile Glu Met Leu Leu Pro Lys Lys Tyr
[1034] 65 70 75 80
[1035] His Val Leu Arg Phe Leu Asp Lys Gly Glu Arg His Pro Val Arg Glu
[1036] 85 90 95
[1037] Ala Arg Ala Val Ile Phe Phe Gly Asp Gln Glu His Pro Asn Val Thr
[1038] 100 105 110
[1039] Glu Phe Ala Val Gly Pro Leu Pro Gly Pro Ala Tyr Met Arg Ala Leu
[1040] 115 120 125
[1041] Ser Pro Arg Pro Gly Tyr Gln Ser Ser Trp Ala Ser Arg Pro Ile Ser
[1042] 130 135 140
[1043] Thr Ala Glu Tyr Ala Leu Leu Tyr His Thr Leu Gln Glu Ala Thr Lys
[1044] 145 150 155 160
[1045] Pro Leu His Gln Phe Phe Leu Asn Thr Thr Gly Phe Ser Phe Gln Asp
[1046] 165 170 175
[1047] Cys His Asp Arg Cys Leu Ala Phe Thr Asp Val Ala Pro Arg Gly Val
[1048] 180 185 190
[1049] Ala Ser Gly Gln Arg Arg Ser Trp Leu Ile Ile Gln Arg Tyr Val Glu

[1050] 195 200 205
[1051] Gly Tyr Phe Leu His Pro Thr Gly Leu Glu Leu Leu Val Asp His Gly
[1052] 210 215 220
[1053] Ser Thr Asp Ala Gly His Trp Ala Val Glu Gln Val Trp Tyr Asn Gly
[1054] 225 230 235 240
[1055] Lys Phe Tyr Gly Ser Pro Glu Glu Leu Ala Arg Lys Tyr Ala Asp Gly
[1056] 245 250 255
[1057] Glu Val Asp Val Val Val Leu Glu Asp Pro Leu Pro Gly Gly Lys Gly
[1058] 260 265 270
[1059] His Asp Ser Thr Glu Glu Pro Pro Leu Phe Ser Ser His Lys Pro Arg
[1060] 275 280 285
[1061] Gly Asp Phe Pro Ser Pro Ile His Val Ser Gly Pro Arg Leu Val Gln
[1062] 290 295 300
[1063] Pro His Gly Pro Arg Phe Arg Leu Glu Gly Asn Ala Val Leu Tyr Gly
[1064] 305 310 315 320
[1065] Gly Trp Ser Phe Ala Phe Arg Leu Arg Ser Ser Ser Gly Leu Gln Val
[1066] 325 330 335
[1067] Leu Asn Val His Phe Gly Gly Glu Arg Ile Ala Tyr Glu Val Ser Val
[1068] 340 345 350
[1069] Gln Glu Ala Val Ala Leu Tyr Gly Gly His Thr Pro Ala Gly Met Gln
[1070] 355 360 365
[1071] Thr Lys Tyr Leu Asp Val Gly Trp Gly Leu Gly Ser Val Thr His Glu
[1072] 370 375 380
[1073] Leu Ala Pro Gly Ile Asp Cys Pro Glu Thr Ala Thr Phe Leu Asp Thr
[1074] 385 390 395 400
[1075] Phe His Tyr Tyr Asp Ala Asp Asp Pro Val His Tyr Pro Arg Ala Leu
[1076] 405 410 415
[1077] Cys Leu Phe Glu Met Pro Thr Gly Val Pro Leu Arg Arg His Phe Asn
[1078] 420 425 430
[1079] Ser Asn Phe Lys Gly Gly Phe Asn Phe Tyr Ala Gly Leu Lys Gly Gln
[1080] 435 440 445
[1081] Val Leu Val Leu Arg Thr Thr Ser Thr Val Tyr Asn Tyr Asp Tyr Ile
[1082] 450 455 460
[1083] Trp Asp Phe Ile Phe Tyr Pro Asn Gly Val Met Glu Ala Lys Met His
[1084] 465 470 475 480
[1085] Ala Thr Gly Tyr Val His Ala Thr Phe Tyr Thr Pro Glu Gly Leu Arg
[1086] 485 490 495
[1087] His Gly Thr Arg Leu His Thr His Leu Ile Gly Asn Ile His Thr His
[1088] 500 505 510
[1089] Leu Val His Tyr Arg Val Asp Leu Asp Val Ala Gly Thr Lys Asn Ser
[1090] 515 520 525
[1091] Phe Gln Thr Leu Gln Met Lys Leu Glu Asn Ile Thr Asn Pro Trp Ser

[1092] 530 535 540
[1093] Pro Arg His Arg Val Val Gln Pro Thr Leu Glu Gln Thr Gln Tyr Ser
[1094] 545 550 555 560
[1095] Trp Glu Arg Gln Ala Ala Phe Arg Phe Lys Arg Lys Leu Pro Thr Tyr
[1096] 565 570 575
[1097] Leu Leu Phe Thr Ser Pro Gln Glu Asn Pro Trp Gly His Lys Arg Ser
[1098] 580 585 590
[1099] Tyr Arg Leu Gln Ile His Ser Met Ala Asp Gln Val Leu Pro Pro Gly
[1100] 595 600 605
[1101] Trp Gln Glu Glu Gln Ala Ile Thr Trp Ala Arg Tyr Pro Leu Ala Val
[1102] 610 615 620
[1103] Thr Lys Tyr Arg Glu Ser Glu Leu Cys Ser Ser Ser Ile Tyr His Gln
[1104] 625 630 635 640
[1105] Asn Asp Pro Trp His Pro Pro Val Val Phe Glu Gln Phe Leu His Asn
[1106] 645 650 655
[1107] Asn Glu Asn Ile Glu Asn Glu Asp Leu Val Ala Trp Val Thr Val Gly
[1108] 660 665 670
[1109] Phe Leu His Ile Pro His Ser Glu Asp Ile Pro Asn Thr Ala Thr Pro
[1110] 675 680 685
[1111] Gly Asn Ser Val Gly Phe Leu Leu Arg Pro Phe Asn Phe Phe Pro Glu
[1112] 690 695 700
[1113] Asp Pro Ser Leu Ala Ser Arg Asp Thr Val Ile Val Trp Pro Arg Asp
[1114] 705 710 715 720
[1115] Asn Gly Pro Asn Tyr Val Gln Arg Trp Ile Pro Glu Asp Arg Asp Cys
[1116] 725 730 735
[1117] Ser Met Pro Pro Pro Phe Ser Tyr Asn Gly Thr Tyr Arg Pro Val
[1118] 740 745 750
[1119] <210> 12
[1120] <211> 751
[1121] <212> PRT
[1122] <213> 人工序列
[1123] <220>
[1124] <223> hDAO-Hepmut3-Cysmut
[1125] <400> 12
[1126] Met Pro Ala Leu Gly Trp Ala Val Ala Ala Ile Leu Met Leu Gln Thr
[1127] 1 5 10 15
[1128] Ala Met Ala Glu Pro Ser Pro Gly Thr Leu Pro Arg Lys Ala Gly Val
[1129] 20 25 30
[1130] Phe Ser Asp Leu Ser Asn Gln Glu Leu Lys Ala Val His Ser Phe Leu
[1131] 35 40 45
[1132] Trp Ser Lys Lys Glu Leu Arg Leu Gln Pro Ser Ser Thr Thr Thr Met
[1133] 50 55 60

[1134] Ala Lys Asn Thr Val Phe Leu Ile Glu Met Leu Leu Pro Lys Lys Tyr
[1135] 65 70 75 80
[1136] His Val Leu Arg Phe Leu Asp Lys Gly Glu Arg His Pro Val Arg Glu
[1137] 85 90 95
[1138] Ala Arg Ala Val Ile Phe Phe Gly Asp Gln Glu His Pro Asn Val Thr
[1139] 100 105 110
[1140] Glu Phe Ala Val Gly Pro Leu Pro Gly Pro Ala Tyr Met Arg Ala Leu
[1141] 115 120 125
[1142] Ser Pro Arg Pro Gly Tyr Gln Ser Ser Trp Ala Ser Arg Pro Ile Ser
[1143] 130 135 140
[1144] Thr Ala Glu Tyr Ala Leu Leu Tyr His Thr Leu Gln Glu Ala Thr Lys
[1145] 145 150 155 160
[1146] Pro Leu His Gln Phe Phe Leu Asn Thr Thr Gly Phe Ser Phe Gln Asp
[1147] 165 170 175
[1148] Cys His Asp Arg Cys Leu Ala Phe Thr Asp Val Ala Pro Arg Gly Val
[1149] 180 185 190
[1150] Ala Ser Gly Gln Arg Arg Ser Trp Leu Ile Ile Gln Arg Tyr Val Glu
[1151] 195 200 205
[1152] Gly Tyr Phe Leu His Pro Thr Gly Leu Glu Leu Leu Val Asp His Gly
[1153] 210 215 220
[1154] Ser Thr Asp Ala Gly His Trp Ala Val Glu Gln Val Trp Tyr Asn Gly
[1155] 225 230 235 240
[1156] Lys Phe Tyr Gly Ser Pro Glu Glu Leu Ala Arg Lys Tyr Ala Asp Gly
[1157] 245 250 255
[1158] Glu Val Asp Val Val Val Leu Glu Asp Pro Leu Pro Gly Gly Lys Gly
[1159] 260 265 270
[1160] His Asp Ser Thr Glu Glu Pro Pro Leu Phe Ser Ser His Lys Pro Arg
[1161] 275 280 285
[1162] Gly Asp Phe Pro Ser Pro Ile His Val Ser Gly Pro Arg Leu Val Gln
[1163] 290 295 300
[1164] Pro His Gly Pro Arg Phe Arg Leu Glu Gly Asn Ala Val Leu Tyr Gly
[1165] 305 310 315 320
[1166] Gly Trp Ser Phe Ala Phe Arg Leu Arg Ser Ser Ser Gly Leu Gln Val
[1167] 325 330 335
[1168] Leu Asn Val His Phe Gly Gly Glu Arg Ile Ala Tyr Glu Val Ser Val
[1169] 340 345 350
[1170] Gln Glu Ala Val Ala Leu Tyr Gly Gly His Thr Pro Ala Gly Met Gln
[1171] 355 360 365
[1172] Thr Lys Tyr Leu Asp Val Gly Trp Gly Leu Gly Ser Val Thr His Glu
[1173] 370 375 380
[1174] Leu Ala Pro Gly Ile Asp Cys Pro Glu Thr Ala Thr Phe Leu Asp Thr
[1175] 385 390 395 400

[1176] Phe His Tyr Tyr Asp Ala Asp Asp Pro Val His Tyr Pro Arg Ala Leu
[1177] 405 410 415
[1178] Cys Leu Phe Glu Met Pro Thr Gly Val Pro Leu Arg Arg His Phe Asn
[1179] 420 425 430
[1180] Ser Asn Phe Lys Gly Gly Phe Asn Phe Tyr Ala Gly Leu Lys Gly Gln
[1181] 435 440 445
[1182] Val Leu Val Leu Arg Thr Thr Ser Thr Val Tyr Asn Tyr Asp Tyr Ile
[1183] 450 455 460
[1184] Trp Asp Phe Ile Phe Tyr Pro Asn Gly Val Met Glu Ala Lys Met His
[1185] 465 470 475 480
[1186] Ala Thr Gly Tyr Val His Ala Thr Phe Tyr Thr Pro Glu Gly Leu Arg
[1187] 485 490 495
[1188] His Gly Thr Arg Leu His Thr His Leu Ile Gly Asn Ile His Thr His
[1189] 500 505 510
[1190] Leu Val His Tyr Arg Val Asp Leu Asp Val Ala Gly Thr Lys Asn Ser
[1191] 515 520 525
[1192] Phe Gln Thr Leu Gln Met Lys Leu Glu Asn Ile Thr Asn Pro Trp Ser
[1193] 530 535 540
[1194] Pro Arg His Arg Val Val Gln Pro Thr Leu Glu Gln Thr Gln Tyr Ser
[1195] 545 550 555 560
[1196] Trp Glu Arg Gln Ala Ala Phe Arg Phe Lys Thr Lys Leu Pro Lys Tyr
[1197] 565 570 575
[1198] Leu Leu Phe Thr Ser Pro Gln Glu Asn Pro Trp Gly His Lys Arg Ser
[1199] 580 585 590
[1200] Tyr Arg Leu Gln Ile His Ser Met Ala Asp Gln Val Leu Pro Pro Gly
[1201] 595 600 605
[1202] Trp Gln Glu Glu Gln Ala Ile Thr Trp Ala Arg Tyr Pro Leu Ala Val
[1203] 610 615 620
[1204] Thr Lys Tyr Arg Glu Ser Glu Leu Cys Ser Ser Ser Ile Tyr His Gln
[1205] 625 630 635 640
[1206] Asn Asp Pro Trp His Pro Pro Val Val Phe Glu Gln Phe Leu His Asn
[1207] 645 650 655
[1208] Asn Glu Asn Ile Glu Asn Glu Asp Leu Val Ala Trp Val Thr Val Gly
[1209] 660 665 670
[1210] Phe Leu His Ile Pro His Ser Glu Asp Ile Pro Asn Thr Ala Thr Pro
[1211] 675 680 685
[1212] Gly Asn Ser Val Gly Phe Leu Leu Arg Pro Phe Asn Phe Phe Pro Glu
[1213] 690 695 700
[1214] Asp Pro Ser Leu Ala Ser Arg Asp Thr Val Ile Val Trp Pro Arg Asp
[1215] 705 710 715 720
[1216] Asn Gly Pro Asn Tyr Val Gln Arg Trp Ile Pro Glu Asp Arg Asp Cys
[1217] 725 730 735

[1218] Ser Met Pro Pro Pro Phe Ser Tyr Asn Gly Thr Tyr Arg Pro Val
[1219] 740 745 750
[1220] <210> 13
[1221] <211> 751
[1222] <212> PRT
[1223] <213> 人工序列
[1224] <220>
[1225] <223> hDAO-Hepmut4-Cysmut
[1226] <400> 13
[1227] Met Pro Ala Leu Gly Trp Ala Val Ala Ala Ile Leu Met Leu Gln Thr
[1228] 1 5 10 15
[1229] Ala Met Ala Glu Pro Ser Pro Gly Thr Leu Pro Arg Lys Ala Gly Val
[1230] 20 25 30
[1231] Phe Ser Asp Leu Ser Asn Gln Glu Leu Lys Ala Val His Ser Phe Leu
[1232] 35 40 45
[1233] Trp Ser Lys Lys Glu Leu Arg Leu Gln Pro Ser Ser Thr Thr Thr Met
[1234] 50 55 60
[1235] Ala Lys Asn Thr Val Phe Leu Ile Glu Met Leu Leu Pro Lys Lys Tyr
[1236] 65 70 75 80
[1237] His Val Leu Arg Phe Leu Asp Lys Gly Glu Arg His Pro Val Arg Glu
[1238] 85 90 95
[1239] Ala Arg Ala Val Ile Phe Phe Gly Asp Gln Glu His Pro Asn Val Thr
[1240] 100 105 110
[1241] Glu Phe Ala Val Gly Pro Leu Pro Gly Pro Ala Tyr Met Arg Ala Leu
[1242] 115 120 125
[1243] Ser Pro Arg Pro Gly Tyr Gln Ser Ser Trp Ala Ser Arg Pro Ile Ser
[1244] 130 135 140
[1245] Thr Ala Glu Tyr Ala Leu Leu Tyr His Thr Leu Gln Glu Ala Thr Lys
[1246] 145 150 155 160
[1247] Pro Leu His Gln Phe Phe Leu Asn Thr Thr Gly Phe Ser Phe Gln Asp
[1248] 165 170 175
[1249] Cys His Asp Arg Cys Leu Ala Phe Thr Asp Val Ala Pro Arg Gly Val
[1250] 180 185 190
[1251] Ala Ser Gly Gln Arg Arg Ser Trp Leu Ile Ile Gln Arg Tyr Val Glu
[1252] 195 200 205
[1253] Gly Tyr Phe Leu His Pro Thr Gly Leu Glu Leu Leu Val Asp His Gly
[1254] 210 215 220
[1255] Ser Thr Asp Ala Gly His Trp Ala Val Glu Gln Val Trp Tyr Asn Gly
[1256] 225 230 235 240
[1257] Lys Phe Tyr Gly Ser Pro Glu Glu Leu Ala Arg Lys Tyr Ala Asp Gly
[1258] 245 250 255
[1259] Glu Val Asp Val Val Val Leu Glu Asp Pro Leu Pro Gly Gly Lys Gly

[1260] 260 265 270
[1261] His Asp Ser Thr Glu Glu Pro Pro Leu Phe Ser Ser His Lys Pro Arg
[1262] 275 280 285
[1263] Gly Asp Phe Pro Ser Pro Ile His Val Ser Gly Pro Arg Leu Val Gln
[1264] 290 295 300
[1265] Pro His Gly Pro Arg Phe Arg Leu Glu Gly Asn Ala Val Leu Tyr Gly
[1266] 305 310 315 320
[1267] Gly Trp Ser Phe Ala Phe Arg Leu Arg Ser Ser Ser Gly Leu Gln Val
[1268] 325 330 335
[1269] Leu Asn Val His Phe Gly Gly Glu Arg Ile Ala Tyr Glu Val Ser Val
[1270] 340 345 350
[1271] Gln Glu Ala Val Ala Leu Tyr Gly Gly His Thr Pro Ala Gly Met Gln
[1272] 355 360 365
[1273] Thr Lys Tyr Leu Asp Val Gly Trp Gly Leu Gly Ser Val Thr His Glu
[1274] 370 375 380
[1275] Leu Ala Pro Gly Ile Asp Cys Pro Glu Thr Ala Thr Phe Leu Asp Thr
[1276] 385 390 395 400
[1277] Phe His Tyr Tyr Asp Ala Asp Asp Pro Val His Tyr Pro Arg Ala Leu
[1278] 405 410 415
[1279] Cys Leu Phe Glu Met Pro Thr Gly Val Pro Leu Arg Arg His Phe Asn
[1280] 420 425 430
[1281] Ser Asn Phe Lys Gly Gly Phe Asn Phe Tyr Ala Gly Leu Lys Gly Gln
[1282] 435 440 445
[1283] Val Leu Val Leu Arg Thr Thr Ser Thr Val Tyr Asn Tyr Asp Tyr Ile
[1284] 450 455 460
[1285] Trp Asp Phe Ile Phe Tyr Pro Asn Gly Val Met Glu Ala Lys Met His
[1286] 465 470 475 480
[1287] Ala Thr Gly Tyr Val His Ala Thr Phe Tyr Thr Pro Glu Gly Leu Arg
[1288] 485 490 495
[1289] His Gly Thr Arg Leu His Thr His Leu Ile Gly Asn Ile His Thr His
[1290] 500 505 510
[1291] Leu Val His Tyr Arg Val Asp Leu Asp Val Ala Gly Thr Lys Asn Ser
[1292] 515 520 525
[1293] Phe Gln Thr Leu Gln Met Lys Leu Glu Asn Ile Thr Asn Pro Trp Ser
[1294] 530 535 540
[1295] Pro Arg His Arg Val Val Gln Pro Thr Leu Glu Gln Thr Gln Tyr Ser
[1296] 545 550 555 560
[1297] Trp Glu Arg Gln Ala Ala Phe Ser Phe Lys Thr Lys Leu Pro Lys Tyr
[1298] 565 570 575
[1299] Leu Leu Phe Thr Ser Pro Gln Glu Asn Pro Trp Gly His Lys Arg Ser
[1300] 580 585 590
[1301] Tyr Arg Leu Gln Ile His Ser Met Ala Asp Gln Val Leu Pro Pro Gly

595 600 605

Trp Gln Glu Glu Gln Ala Ile Thr Trp Ala Arg Tyr Pro Leu Ala Val
610 615 620

Thr Lys Tyr Arg Glu Ser Glu Leu Cys Ser Ser Ser Ile Tyr His Gln
625 630 635 640

Asn Asp Pro Trp His Pro Pro Val Val Phe Glu Gln Phe Leu His Asn
645 650 655

Asn Glu Asn Ile Glu Asn Glu Asp Leu Val Ala Trp Val Thr Val Gly
660 665 670

Phe Leu His Ile Pro His Ser Glu Asp Ile Pro Asn Thr Ala Thr Pro
675 680 685

Gly Asn Ser Val Gly Phe Leu Leu Arg Pro Phe Asn Phe Phe Pro Glu
690 695 700

Asp Pro Ser Leu Ala Ser Arg Asp Thr Val Ile Val Trp Pro Arg Asp
705 710 715 720

Asn Gly Pro Asn Tyr Val Gln Arg Trp Ile Pro Glu Asp Arg Asp Cys
725 730 735

Ser Met Pro Pro Pro Phe Ser Tyr Asn Gly Thr Tyr Arg Pro Val
740 745 750

<210> 14

<211> 751

<212> PRT

<213> 人工序列

<220>

<223> hDAO-Hepmut5-Cysmut

<400> 14

Met Pro Ala Leu Gly Trp Ala Val Ala Ala Ile Leu Met Leu Gln Thr
1 5 10 15

Ala Met Ala Glu Pro Ser Pro Gly Thr Leu Pro Arg Lys Ala Gly Val
20 25 30

Phe Ser Asp Leu Ser Asn Gln Glu Leu Lys Ala Val His Ser Phe Leu
35 40 45

Trp Ser Lys Lys Glu Leu Arg Leu Gln Pro Ser Ser Thr Thr Thr Met
50 55 60

Ala Lys Asn Thr Val Phe Leu Ile Glu Met Leu Leu Pro Lys Lys Tyr
65 70 75 80

His Val Leu Arg Phe Leu Asp Lys Gly Glu Arg His Pro Val Arg Glu
85 90 95

Ala Arg Ala Val Ile Phe Phe Gly Asp Gln Glu His Pro Asn Val Thr
100 105 110

Glu Phe Ala Val Gly Pro Leu Pro Gly Pro Ala Tyr Met Arg Ala Leu
115 120 125

[1344] Ser Pro Arg Pro Gly Tyr Gln Ser Ser Trp Ala Ser Arg Pro Ile Ser
[1345] 130 135 140
[1346] Thr Ala Glu Tyr Ala Leu Leu Tyr His Thr Leu Gln Glu Ala Thr Lys
[1347] 145 150 155 160
[1348] Pro Leu His Gln Phe Phe Leu Asn Thr Thr Gly Phe Ser Phe Gln Asp
[1349] 165 170 175
[1350] Cys His Asp Arg Cys Leu Ala Phe Thr Asp Val Ala Pro Arg Gly Val
[1351] 180 185 190
[1352] Ala Ser Gly Gln Arg Arg Ser Trp Leu Ile Ile Gln Arg Tyr Val Glu
[1353] 195 200 205
[1354] Gly Tyr Phe Leu His Pro Thr Gly Leu Glu Leu Leu Val Asp His Gly
[1355] 210 215 220
[1356] Ser Thr Asp Ala Gly His Trp Ala Val Glu Gln Val Trp Tyr Asn Gly
[1357] 225 230 235 240
[1358] Lys Phe Tyr Gly Ser Pro Glu Glu Leu Ala Arg Lys Tyr Ala Asp Gly
[1359] 245 250 255
[1360] Glu Val Asp Val Val Val Leu Glu Asp Pro Leu Pro Gly Gly Lys Gly
[1361] 260 265 270
[1362] His Asp Ser Thr Glu Glu Pro Pro Leu Phe Ser Ser His Lys Pro Arg
[1363] 275 280 285
[1364] Gly Asp Phe Pro Ser Pro Ile His Val Ser Gly Pro Arg Leu Val Gln
[1365] 290 295 300
[1366] Pro His Gly Pro Arg Phe Arg Leu Glu Gly Asn Ala Val Leu Tyr Gly
[1367] 305 310 315 320
[1368] Gly Trp Ser Phe Ala Phe Arg Leu Arg Ser Ser Ser Gly Leu Gln Val
[1369] 325 330 335
[1370] Leu Asn Val His Phe Gly Gly Glu Arg Ile Ala Tyr Glu Val Ser Val
[1371] 340 345 350
[1372] Gln Glu Ala Val Ala Leu Tyr Gly Gly His Thr Pro Ala Gly Met Gln
[1373] 355 360 365
[1374] Thr Lys Tyr Leu Asp Val Gly Trp Gly Leu Gly Ser Val Thr His Glu
[1375] 370 375 380
[1376] Leu Ala Pro Gly Ile Asp Cys Pro Glu Thr Ala Thr Phe Leu Asp Thr
[1377] 385 390 395 400
[1378] Phe His Tyr Tyr Asp Ala Asp Asp Pro Val His Tyr Pro Arg Ala Leu
[1379] 405 410 415
[1380] Cys Leu Phe Glu Met Pro Thr Gly Val Pro Leu Arg Arg His Phe Asn
[1381] 420 425 430
[1382] Ser Asn Phe Lys Gly Gly Phe Asn Phe Tyr Ala Gly Leu Lys Gly Gln
[1383] 435 440 445
[1384] Val Leu Val Leu Arg Thr Thr Ser Thr Val Tyr Asn Tyr Asp Tyr Ile
[1385] 450 455 460

[1386] Trp Asp Phe Ile Phe Tyr Pro Asn Gly Val Met Glu Ala Lys Met His
[1387] 465 470 475 480
[1388] Ala Thr Gly Tyr Val His Ala Thr Phe Tyr Thr Pro Glu Gly Leu Arg
[1389] 485 490 495
[1390] His Gly Thr Arg Leu His Thr His Leu Ile Gly Asn Ile His Thr His
[1391] 500 505 510
[1392] Leu Val His Tyr Arg Val Asp Leu Asp Val Ala Gly Thr Lys Asn Ser
[1393] 515 520 525
[1394] Phe Gln Thr Leu Gln Met Lys Leu Glu Asn Ile Thr Asn Pro Trp Ser
[1395] 530 535 540
[1396] Pro Arg His Arg Val Val Gln Pro Thr Leu Glu Gln Thr Gln Tyr Ser
[1397] 545 550 555 560
[1398] Trp Glu Arg Gln Ala Ala Phe Arg Phe Lys Thr Lys Leu Pro Thr Tyr
[1399] 565 570 575
[1400] Leu Leu Phe Thr Ser Pro Gln Glu Asn Pro Trp Gly His Lys Arg Ser
[1401] 580 585 590
[1402] Tyr Arg Leu Gln Ile His Ser Met Ala Asp Gln Val Leu Pro Pro Gly
[1403] 595 600 605
[1404] Trp Gln Glu Glu Gln Ala Ile Thr Trp Ala Arg Tyr Pro Leu Ala Val
[1405] 610 615 620
[1406] Thr Lys Tyr Arg Glu Ser Glu Leu Cys Ser Ser Ser Ile Tyr His Gln
[1407] 625 630 635 640
[1408] Asn Asp Pro Trp His Pro Pro Val Val Phe Glu Gln Phe Leu His Asn
[1409] 645 650 655
[1410] Asn Glu Asn Ile Glu Asn Glu Asp Leu Val Ala Trp Val Thr Val Gly
[1411] 660 665 670
[1412] Phe Leu His Ile Pro His Ser Glu Asp Ile Pro Asn Thr Ala Thr Pro
[1413] 675 680 685
[1414] Gly Asn Ser Val Gly Phe Leu Leu Arg Pro Phe Asn Phe Phe Pro Glu
[1415] 690 695 700
[1416] Asp Pro Ser Leu Ala Ser Arg Asp Thr Val Ile Val Trp Pro Arg Asp
[1417] 705 710 715 720
[1418] Asn Gly Pro Asn Tyr Val Gln Arg Trp Ile Pro Glu Asp Arg Asp Cys
[1419] 725 730 735
[1420] Ser Met Pro Pro Pro Phe Ser Tyr Asn Gly Thr Tyr Arg Pro Val
[1421] 740 745 750
[1422] <210> 15
[1423] <211> 751
[1424] <212> PRT
[1425] <213> 人工序列
[1426] <220>
[1427] <223> hDAO-Hepmut6-Cysmut

[1428] <400> 15

[1429] Met Pro Ala Leu Gly Trp Ala Val Ala Ala Ile Leu Met Leu Gln Thr
[1430] 1 5 10 15
[1431] Ala Met Ala Glu Pro Ser Pro Gly Thr Leu Pro Arg Lys Ala Gly Val
[1432] 20 25 30
[1433] Phe Ser Asp Leu Ser Asn Gln Glu Leu Lys Ala Val His Ser Phe Leu
[1434] 35 40 45
[1435] Trp Ser Lys Lys Glu Leu Arg Leu Gln Pro Ser Ser Thr Thr Thr Met
[1436] 50 55 60
[1437] Ala Lys Asn Thr Val Phe Leu Ile Glu Met Leu Leu Pro Lys Lys Tyr
[1438] 65 70 75 80
[1439] His Val Leu Arg Phe Leu Asp Lys Gly Glu Arg His Pro Val Arg Glu
[1440] 85 90 95
[1441] Ala Arg Ala Val Ile Phe Phe Gly Asp Gln Glu His Pro Asn Val Thr
[1442] 100 105 110
[1443] Glu Phe Ala Val Gly Pro Leu Pro Gly Pro Ala Tyr Met Arg Ala Leu
[1444] 115 120 125
[1445] Ser Pro Arg Pro Gly Tyr Gln Ser Ser Trp Ala Ser Arg Pro Ile Ser
[1446] 130 135 140
[1447] Thr Ala Glu Tyr Ala Leu Leu Tyr His Thr Leu Gln Glu Ala Thr Lys
[1448] 145 150 155 160
[1449] Pro Leu His Gln Phe Phe Leu Asn Thr Thr Gly Phe Ser Phe Gln Asp
[1450] 165 170 175
[1451] Cys His Asp Arg Cys Leu Ala Phe Thr Asp Val Ala Pro Arg Gly Val
[1452] 180 185 190
[1453] Ala Ser Gly Gln Arg Arg Ser Trp Leu Ile Ile Gln Arg Tyr Val Glu
[1454] 195 200 205
[1455] Gly Tyr Phe Leu His Pro Thr Gly Leu Glu Leu Leu Val Asp His Gly
[1456] 210 215 220
[1457] Ser Thr Asp Ala Gly His Trp Ala Val Glu Gln Val Trp Tyr Asn Gly
[1458] 225 230 235 240
[1459] Lys Phe Tyr Gly Ser Pro Glu Glu Leu Ala Arg Lys Tyr Ala Asp Gly
[1460] 245 250 255
[1461] Glu Val Asp Val Val Val Leu Glu Asp Pro Leu Pro Gly Gly Lys Gly
[1462] 260 265 270
[1463] His Asp Ser Thr Glu Glu Pro Pro Leu Phe Ser Ser His Lys Pro Arg
[1464] 275 280 285
[1465] Gly Asp Phe Pro Ser Pro Ile His Val Ser Gly Pro Arg Leu Val Gln
[1466] 290 295 300
[1467] Pro His Gly Pro Arg Phe Arg Leu Glu Gly Asn Ala Val Leu Tyr Gly
[1468] 305 310 315 320
[1469] Gly Trp Ser Phe Ala Phe Arg Leu Arg Ser Ser Ser Gly Leu Gln Val

[1470] 325 330 335
[1471] Leu Asn Val His Phe Gly Gly Glu Arg Ile Ala Tyr Glu Val Ser Val
[1472] 340 345 350
[1473] Gln Glu Ala Val Ala Leu Tyr Gly Gly His Thr Pro Ala Gly Met Gln
[1474] 355 360 365
[1475] Thr Lys Tyr Leu Asp Val Gly Trp Gly Leu Gly Ser Val Thr His Glu
[1476] 370 375 380
[1477] Leu Ala Pro Gly Ile Asp Cys Pro Glu Thr Ala Thr Phe Leu Asp Thr
[1478] 385 390 395 400
[1479] Phe His Tyr Tyr Asp Ala Asp Asp Pro Val His Tyr Pro Arg Ala Leu
[1480] 405 410 415
[1481] Cys Leu Phe Glu Met Pro Thr Gly Val Pro Leu Arg Arg His Phe Asn
[1482] 420 425 430
[1483] Ser Asn Phe Lys Gly Gly Phe Asn Phe Tyr Ala Gly Leu Lys Gly Gln
[1484] 435 440 445
[1485] Val Leu Val Leu Arg Thr Thr Ser Thr Val Tyr Asn Tyr Asp Tyr Ile
[1486] 450 455 460
[1487] Trp Asp Phe Ile Phe Tyr Pro Asn Gly Val Met Glu Ala Lys Met His
[1488] 465 470 475 480
[1489] Ala Thr Gly Tyr Val His Ala Thr Phe Tyr Thr Pro Glu Gly Leu Arg
[1490] 485 490 495
[1491] His Gly Thr Arg Leu His Thr His Leu Ile Gly Asn Ile His Thr His
[1492] 500 505 510
[1493] Leu Val His Tyr Arg Val Asp Leu Asp Val Ala Gly Thr Lys Asn Ser
[1494] 515 520 525
[1495] Phe Gln Thr Leu Gln Met Lys Leu Glu Asn Ile Thr Asn Pro Trp Ser
[1496] 530 535 540
[1497] Pro Arg His Arg Val Val Gln Pro Thr Leu Glu Gln Thr Gln Tyr Ser
[1498] 545 550 555 560
[1499] Trp Glu Arg Gln Ala Ala Phe Arg Phe Gly Gln Thr Leu Pro Lys Tyr
[1500] 565 570 575
[1501] Leu Leu Phe Thr Ser Pro Gln Glu Asn Pro Trp Gly His Lys Arg Ser
[1502] 580 585 590
[1503] Tyr Arg Leu Gln Ile His Ser Met Ala Asp Gln Val Leu Pro Pro Gly
[1504] 595 600 605
[1505] Trp Gln Glu Glu Gln Ala Ile Thr Trp Ala Arg Tyr Pro Leu Ala Val
[1506] 610 615 620
[1507] Thr Lys Tyr Arg Glu Ser Glu Leu Cys Ser Ser Ser Ile Tyr His Gln
[1508] 625 630 635 640
[1509] Asn Asp Pro Trp His Pro Pro Val Val Phe Glu Gln Phe Leu His Asn
[1510] 645 650 655
[1511] Asn Glu Asn Ile Glu Asn Glu Asp Leu Val Ala Trp Val Thr Val Gly

[1512] 660 665 670
[1513] Phe Leu His Ile Pro His Ser Glu Asp Ile Pro Asn Thr Ala Thr Pro
[1514] 675 680 685
[1515] Gly Asn Ser Val Gly Phe Leu Leu Arg Pro Phe Asn Phe Phe Pro Glu
[1516] 690 695 700
[1517] Asp Pro Ser Leu Ala Ser Arg Asp Thr Val Ile Val Trp Pro Arg Asp
[1518] 705 710 715 720
[1519] Asn Gly Pro Asn Tyr Val Gln Arg Trp Ile Pro Glu Asp Arg Asp Cys
[1520] 725 730 735
[1521] Ser Met Pro Pro Pro Phe Ser Tyr Asn Gly Thr Tyr Arg Pro Val
[1522] 740 745 750
[1523] <210> 16
[1524] <211> 751
[1525] <212> PRT
[1526] <213> 人工序列
[1527] <220>
[1528] <223> hDAO-Hepmut7-Cysmut
[1529] <400> 16
[1530] Met Pro Ala Leu Gly Trp Ala Val Ala Ala Ile Leu Met Leu Gln Thr
[1531] 1 5 10 15
[1532] Ala Met Ala Glu Pro Ser Pro Gly Thr Leu Pro Arg Lys Ala Gly Val
[1533] 20 25 30
[1534] Phe Ser Asp Leu Ser Asn Gln Glu Leu Lys Ala Val His Ser Phe Leu
[1535] 35 40 45
[1536] Trp Ser Lys Lys Glu Leu Arg Leu Gln Pro Ser Ser Thr Thr Thr Met
[1537] 50 55 60
[1538] Ala Lys Asn Thr Val Phe Leu Ile Glu Met Leu Leu Pro Lys Lys Tyr
[1539] 65 70 75 80
[1540] His Val Leu Arg Phe Leu Asp Lys Gly Glu Arg His Pro Val Arg Glu
[1541] 85 90 95
[1542] Ala Arg Ala Val Ile Phe Phe Gly Asp Gln Glu His Pro Asn Val Thr
[1543] 100 105 110
[1544] Glu Phe Ala Val Gly Pro Leu Pro Gly Pro Ala Tyr Met Arg Ala Leu
[1545] 115 120 125
[1546] Ser Pro Arg Pro Gly Tyr Gln Ser Ser Trp Ala Ser Arg Pro Ile Ser
[1547] 130 135 140
[1548] Thr Ala Glu Tyr Ala Leu Leu Tyr His Thr Leu Gln Glu Ala Thr Lys
[1549] 145 150 155 160
[1550] Pro Leu His Gln Phe Phe Leu Asn Thr Thr Gly Phe Ser Phe Gln Asp
[1551] 165 170 175
[1552] Cys His Asp Arg Cys Leu Ala Phe Thr Asp Val Ala Pro Arg Gly Val
[1553] 180 185 190

[1554] Ala Ser Gly Gln Arg Arg Ser Trp Leu Ile Ile Gln Arg Tyr Val Glu
[1555] 195 200 205
[1556] Gly Tyr Phe Leu His Pro Thr Gly Leu Glu Leu Leu Val Asp His Gly
[1557] 210 215 220
[1558] Ser Thr Asp Ala Gly His Trp Ala Val Glu Gln Val Trp Tyr Asn Gly
[1559] 225 230 235 240
[1560] Lys Phe Tyr Gly Ser Pro Glu Glu Leu Ala Arg Lys Tyr Ala Asp Gly
[1561] 245 250 255
[1562] Glu Val Asp Val Val Val Leu Glu Asp Pro Leu Pro Gly Gly Lys Gly
[1563] 260 265 270
[1564] His Asp Ser Thr Glu Glu Pro Pro Leu Phe Ser Ser His Lys Pro Arg
[1565] 275 280 285
[1566] Gly Asp Phe Pro Ser Pro Ile His Val Ser Gly Pro Arg Leu Val Gln
[1567] 290 295 300
[1568] Pro His Gly Pro Arg Phe Arg Leu Glu Gly Asn Ala Val Leu Tyr Gly
[1569] 305 310 315 320
[1570] Gly Trp Ser Phe Ala Phe Arg Leu Arg Ser Ser Ser Gly Leu Gln Val
[1571] 325 330 335
[1572] Leu Asn Val His Phe Gly Gly Glu Arg Ile Ala Tyr Glu Val Ser Val
[1573] 340 345 350
[1574] Gln Glu Ala Val Ala Leu Tyr Gly Gly His Thr Pro Ala Gly Met Gln
[1575] 355 360 365
[1576] Thr Lys Tyr Leu Asp Val Gly Trp Gly Leu Gly Ser Val Thr His Glu
[1577] 370 375 380
[1578] Leu Ala Pro Gly Ile Asp Cys Pro Glu Thr Ala Thr Phe Leu Asp Thr
[1579] 385 390 395 400
[1580] Phe His Tyr Tyr Asp Ala Asp Asp Pro Val His Tyr Pro Arg Ala Leu
[1581] 405 410 415
[1582] Cys Leu Phe Glu Met Pro Thr Gly Val Pro Leu Arg Arg His Phe Asn
[1583] 420 425 430
[1584] Ser Asn Phe Lys Gly Gly Phe Asn Phe Tyr Ala Gly Leu Lys Gly Gln
[1585] 435 440 445
[1586] Val Leu Val Leu Arg Thr Thr Ser Thr Val Tyr Asn Tyr Asp Tyr Ile
[1587] 450 455 460
[1588] Trp Asp Phe Ile Phe Tyr Pro Asn Gly Val Met Glu Ala Lys Met His
[1589] 465 470 475 480
[1590] Ala Thr Gly Tyr Val His Ala Thr Phe Tyr Thr Pro Glu Gly Leu Arg
[1591] 485 490 495
[1592] His Gly Thr Arg Leu His Thr His Leu Ile Gly Asn Ile His Thr His
[1593] 500 505 510
[1594] Leu Val His Tyr Arg Val Asp Leu Asp Val Ala Gly Thr Lys Asn Ser
[1595] 515 520 525

[1596] Phe Gln Thr Leu Gln Met Lys Leu Glu Asn Ile Thr Asn Pro Trp Ser
[1597] 530 535 540
[1598] Pro Arg His Arg Val Val Gln Pro Thr Leu Glu Gln Thr Gln Tyr Ser
[1599] 545 550 555 560
[1600] Trp Glu Arg Gln Ala Ala Phe Ser Phe Lys Arg Lys Leu Pro Thr Tyr
[1601] 565 570 575
[1602] Leu Leu Phe Thr Ser Pro Gln Glu Asn Pro Trp Gly His Lys Arg Ser
[1603] 580 585 590
[1604] Tyr Arg Leu Gln Ile His Ser Met Ala Asp Gln Val Leu Pro Pro Gly
[1605] 595 600 605
[1606] Trp Gln Glu Glu Gln Ala Ile Thr Trp Ala Arg Tyr Pro Leu Ala Val
[1607] 610 615 620
[1608] Thr Lys Tyr Arg Glu Ser Glu Leu Cys Ser Ser Ser Ile Tyr His Gln
[1609] 625 630 635 640
[1610] Asn Asp Pro Trp His Pro Pro Val Val Phe Glu Gln Phe Leu His Asn
[1611] 645 650 655
[1612] Asn Glu Asn Ile Glu Asn Glu Asp Leu Val Ala Trp Val Thr Val Gly
[1613] 660 665 670
[1614] Phe Leu His Ile Pro His Ser Glu Asp Ile Pro Asn Thr Ala Thr Pro
[1615] 675 680 685
[1616] Gly Asn Ser Val Gly Phe Leu Leu Arg Pro Phe Asn Phe Phe Pro Glu
[1617] 690 695 700
[1618] Asp Pro Ser Leu Ala Ser Arg Asp Thr Val Ile Val Trp Pro Arg Asp
[1619] 705 710 715 720
[1620] Asn Gly Pro Asn Tyr Val Gln Arg Trp Ile Pro Glu Asp Arg Asp Cys
[1621] 725 730 735
[1622] Ser Met Pro Pro Pro Phe Ser Tyr Asn Gly Thr Tyr Arg Pro Val
[1623] 740 745 750
[1624] <210> 17
[1625] <211> 2256
[1626] <212> DNA
[1627] <213> 智人
[1628] <400> 17
[1629] atgccggccc tgggctgggc cgtggctgcc atcctgatgc tgcagacggc catggcggag 60
[1630] ccctccccgg ggactctgcc caggaaggca ggggtgtttt cagacctaag caaccaagag 120
[1631] ctgaaggcag tgcacagctt cctctggtcc aagaaggagc tgaggctgca gccctccagt 180
[1632] accaccacca tggccaagaa caccgtgttt ctcatcgaga tgctgctgcc caagaagtac 240
[1633] catgtgctga ggtttctgga taaaggtgaa aggcatcctg tgcgggaagc ccgtgccgtc 300
[1634] atcttctttg gtgaccagga gcatcccaat gtcaccgagt ttgctgtggg gcccctgcca 360
[1635] gggccctgct acatgcgagc actgtccccc aggcctgggt accagtcctc ctgggcatcg 420
[1636] aggcccatct ccacagcaga gtatgccctc ctctaccaca ccctgcagga agccaccaag 480
[1637] cccctgcatc agttcttcct caataccaca ggcttctcat tccaagactg ccatgacaga 540

[1638] tgcctggcct tcaccgatgt ggcccccggg ggtgtggctt ctggccagcg ccgcagttgg 600
[1639] cttatcatac agcgctatgt agaaggctac tttctgcacc ccactgggct ggagctcctc 660
[1640] gtggatcatg ggagcacaga tgctgggcac tgggccgtgg agcaggtgtg gtacaacggg 720
[1641] aagttctatg ggagcccaga ggaactggct cggaagtatg cagatggaga ggtggacgtg 780
[1642] gtggtcctgg aggacccgct gcctgggggc aaggggcatg acagcacaga ggagccgccc 840
[1643] ctcttctcct cccacaagcc ccgcggggac ttccccagcc ccatccatgt gagcggcccc 900
[1644] cgcttggtcc agccccacgg ccctcgcttc aggctggagg gcaacgctgt gctctacggc 960
[1645] ggctggagct ttgccttccg gctgcgctcc tcctccgggc tgcaggtcct gaacgtgcac 1020
[1646] ttcggcggag agcgcattgc ctatgaggtc agcgtgcaag aggcagtggc gctgtatgga 1080
[1647] ggacacacac ctgcaggcat gcagaccaag tacctcgatg tcggctgggg cctgggcagc 1140
[1648] gtcactcatg agttagcccc cggcatcgac tgcccggaga ccgccacctt cctggacact 1200
[1649] ttccactact atgatgccga tgacccggtc cattatcccc gagccctctg cctctttgaa 1260
[1650] atgcccacag gggtgcccct tcggcggcac tttaattcca actttaaagg tggcttcaac 1320
[1651] ttctatgcgg ggctgaaggg ccaggtgctg gtgctgcgga caacttcaac tgtctacaat 1380
[1652] tatgattaca tttgggactt tatcttctac cccaacgggg tgatggaggc caagatgcat 1440
[1653] gccactggct acgtccacgc caccttctac acccccgagg ggctgcgcca cggcactcgc 1500
[1654] ctgcacaccc acctgattgg caacatacac actcacttgg tgcactaccg cgtagacctg 1560
[1655] gatgtggcag gcaccaagaa cagcttccag acactgcaga tgaagctaga aaacatcacc 1620
[1656] aacccctgga gcccaagaca ccgcgtggtc cagccaactc tggagcagac gcagtactcc 1680
[1657] tgggagcgcc aggcggcctt ccgcttcaaa aggaagctgc ccaagtacct gctctttacc 1740
[1658] agcccccagg agaacccctg gggccacaag cgcagctacc gcctgcagat ccactccatg 1800
[1659] gccgaccagg tgctgccccc aggctggcag gaggagcagg ccatcacctg ggcaaggtac 1860
[1660] cccctggcag tgaccaagta ccgggagtcg gagctgtgca gcagcagcat ctaccaccag 1920
[1661] aacgacccct ggcacccgcc cgtggtcttt gagcagtttc ttcacaacaa cgagaacatt 1980
[1662] gaaaatgagg acctggtggc ctgggtgacg gtgggcttcc tgcacatccc ccactcagag 2040
[1663] gacattccca acacagccac acctgggaac tccgtgggct tcctgctccg gccattcaac 2100
[1664] ttcttcccag aggacccctc cctggcatcc agagacactg tgatcgtgtg gcctcgggac 2160
[1665] aacggcccca actacgtcca gcgctggatc cctgaggaca gggactgctc gatgcctccc 2220
[1666] ccttttagct acaatgggac ctatagacct gtgtga 2256
[1667] <210> 18
[1668] <211> 2256
[1669] <212> DNA
[1670] <213> 人工序列
[1671] <220>
[1672] <223> hDAO-Hepmut1
[1673] <400> 18
[1674] atgccggccc tgggctgggc cgtggctgcc atcctgatgc tgcagacggc catggcggag 60
[1675] ccctccccgg ggactctgcc caggaaggca ggggtgtttt cagacctaag caaccaagag 120
[1676] ctgaaggcag tgcacagctt cctctggtcc aagaaggagc tgaggctgca gccctccagt 180
[1677] accaccacca tggccaagaa caccgtgttt ctcatcgaga tgctgctgcc caagaagtac 240
[1678] catgtgctga ggtttctgga taaaggtgaa aggcatcctg tgcgggaagc ccgtgccgtc 300
[1679] atcttctttg gtgaccagga gcatcccaat gtcaccgagt ttgctgtggg gcccctgcca 360

[1680] gggccctgct acatgcgagc actgtccccc aggcctgggt accagtcctc ctgggcatcg 420
[1681] aggcccatct ccacagcaga gtatgccctc ctctaccaca ccctgcagga agccaccaag 480
[1682] cccctgcatc agttcttcct caataccaca ggcttctcat tccaagactg ccatgacaga 540
[1683] tgcctggcct tcaccgatgt ggcccccccgg ggtgtggctt ctggccagcg ccgcagttgg 600
[1684] cttatcatac agcgctatgt agaaggctac tttctgcacc ccactgggct ggagctcctc 660
[1685] gtggatcatg ggagcacaga tgctgggcac tgggccgtgg agcaggtgtg gtacaacggg 720
[1686] aagttctatg ggagcccaga ggaactggct cggaagtatg cagatggaga ggtggacgtg 780
[1687] gtggtcctgg aggacccgct gcctgggggc aaggggcatg acagcacaga ggagccgccc 840
[1688] ctcttctcct cccacaagcc ccgcggggac ttccccagcc ccatccatgt gagcggcccc 900
[1689] cgcttggtcc agccccacgg ccctcgcttc aggctggagg gcaacgctgt gctctacggc 960
[1690] ggctggagct ttgccttccg gctgcgctcc tcctccgggc tgcaggtcct gaacgtgcac 1020
[1691] ttcggcggag agcgcattgc ctatgaggtc agcgtgcaag aggcagtggc gctgtatgga 1080
[1692] ggacacacac ctgcaggcat gcagaccaag tacctcgatg tcggctgggg cctgggcagc 1140
[1693] gtcactcatg agttagcccc cggcatcgac tgcccggaga ccgccacctt cctggacact 1200
[1694] ttccactact atgatgccga tgacccggtc cattatcccc gagccctctg cctctttgaa 1260
[1695] atgcccacag gggtgcccct tcggcggcac tttaattcca actttaaagg tggcttcaac 1320
[1696] ttctatgcgg ggctgaaggg ccaggtgctg gtgctgcgga caacttcaac tgtctacaat 1380
[1697] tatgattaca tttgggactt tatcttctac cccaacgggg tgatggaggc caagatgcat 1440
[1698] gccactggct acgtccacgc caccttctac acccccgagg ggctgcgcca cggcactcgc 1500
[1699] ctgcacaccc acctgattgg caacatacac actcacttgg tgcactaccg cgtagacctg 1560
[1700] gatgtggcag gcaccaagaa cagcttccag acactgcaga tgaagctaga aaacatcacc 1620
[1701] aacccctgga gcccaagaca ccgcgtggtc cagccaactc tggagcagac gcagtactcc 1680
[1702] tgggagcgcc aggcggcctt cagcttcaaa aggaagctgc ccaagtacct gctctttacc 1740
[1703] agcccccagg agaacccctg gggccacaag cgcagctacc gcctgcagat ccactccatg 1800
[1704] gccgaccagg tgctgccccc aggctggcag gaggagcagg ccatcacctg ggcaaggtac 1860
[1705] cccctggcag tgaccaagta ccgggagtcg gagctgtgca gcagcagcat ctaccaccag 1920
[1706] aacgacccct ggcacccgcc cgtggtcttt gagcagtttc ttcacaacaa cgagaacatt 1980
[1707] gaaaatgagg acctggtggc ctgggtgacg gtgggcttcc tgcacatccc ccactcagag 2040
[1708] gacattccca acacagccac acctgggaac tccgtgggct tcctgctccg gccattcaac 2100
[1709] ttcttcccag aggacccctc cctggcatcc agagacactg tgatcgtgtg gcctcgggac 2160
[1710] aacggcccca actacgtcca gcgctggatc cctgaggaca gggactgctc gatgcctccc 2220
[1711] ccttttagct acaatgggac ctatagacct gtgtga 2256
[1712] <210> 19
[1713] <211> 2256
[1714] <212> DNA
[1715] <213> 人工序列
[1716] <220>
[1717] <223> hDAO-Hepmut2
[1718] <400> 19
[1719] atgccggccc tgggctgggc cgtggctgcc atcctgatgc tgcagacggc catggcggag 60
[1720] ccctccccgg ggactctgcc caggaaggca ggggtgtttt cagacctaag caaccaagag 120
[1721] ctgaaggcag tgcacagctt cctctggtcc aagaaggagc tgaggctgca gccctccagt 180

[1722] accaccacca tggccaagaa caccgtgttt ctcatcgaga tgctgctgcc caagaagtac 240
[1723] catgtgctga ggtttctgga taaaggtgaa aggcatcctg tgcgggaagc ccgtgccgtc 300
[1724] atcttctttg gtgaccagga gcatcccaat gtcaccgagt ttgctgtggg gcccctgcca 360
[1725] gggccctgct acatgcgagc actgtccccc aggcctgggt accagtcctc ctgggcatcg 420
[1726] aggcccatct ccacagcaga gtatgccctc ctctaccaca ccctgcagga agccaccaag 480
[1727] cccctgcatc agttcttcct caataccaca ggcttctcat tccaagactg ccatgacaga 540
[1728] tgcctggcct tcaccgatgt ggcccccccgg ggtgtggctt ctggccagcg ccgcagttgg 600
[1729] cttatcatac agcgctatgt agaaggctac tttctgcacc ccactgggct ggagctcctc 660
[1730] gtggatcatg ggagcacaga tgctgggcac tgggccgtgg agcaggtgtg gtacaacggg 720
[1731] aagttctatg ggagcccaga ggaactggct cggaagtatg cagatggaga ggtggacgtg 780
[1732] gtggtcctgg aggacccgct gcctgggggc aaggggcatg acagcacaga ggagccgccc 840
[1733] ctcttctcct cccacaagcc ccgcggggac ttccccagcc ccatccatgt gagcggcccc 900
[1734] cgcttggtcc agccccacgg ccctcgcttc aggctggagg gcaacgctgt gctctacggc 960
[1735] ggctggagct ttgccttccg gctgcgctcc tcctccgggc tgcaggtcct gaacgtgcac 1020
[1736] ttcggcggag agcgcattgc ctatgaggtc agcgtgcaag aggcagtggc gctgtatgga 1080
[1737] ggacacacac ctgcaggcat gcagaccaag tacctcgatg tcggctgggg cctgggcagc 1140
[1738] gtcactcatg agttagcccc cggcatcgac tgcccggaga ccgccacctt cctggacact 1200
[1739] ttccactact atgatgccga tgacccggtc cattatcccc gagccctctg cctctttgaa 1260
[1740] atgcccacag gggtgcccct tcggcggcac tttaattcca actttaaagg tggcttcaac 1320
[1741] ttctatgcgg ggctgaaggg ccaggtgctg gtgctgcgga caacttcaac tgtctacaat 1380
[1742] tatgattaca tttgggactt tatcttctac cccaacgggg tgatggaggc caagatgcat 1440
[1743] gccactggct acgtccacgc caccttctac acccccgagg ggctgcgcca cggcactcgc 1500
[1744] ctgcacaccc acctgattgg caacatacac actcacttgg tgcactaccg cgtagacctg 1560
[1745] gatgtggcag gcaccaagaa cagcttccag acactgcaga tgaagctaga aaacatcacc 1620
[1746] aacccctgga gcccaagaca ccgcgtggtc cagccaactc tggagcagac gcagtactcc 1680
[1747] tgggagcgcc aggcggcctt ccgcttcaaa aggaagctgc ccacgtacct gctctttacc 1740
[1748] agcccccagg agaacccctg gggccacaag cgcagctacc gcctgcagat ccactccatg 1800
[1749] gccgaccagg tgctgccccc aggctggcag gaggagcagg ccatcacctg ggcaaggtac 1860
[1750] cccctggcag tgaccaagta ccgggagtcg gagctgtgca gcagcagcat ctaccaccag 1920
[1751] aacgacccct ggcacccgcc cgtggtcttt gagcagtttc ttcacaacaa cgagaacatt 1980
[1752] gaaaatgagg acctggtggc ctgggtgacg gtgggcttcc tgcacatccc ccactcagag 2040
[1753] gacattccca acacagccac acctgggaac tccgtgggct tcctgctccg gccattcaac 2100
[1754] ttcttcccag aggacccctc cctggcatcc agagacactg tgatcgtgtg gcctcgggac 2160
[1755] aacggcccca actacgtcca gcgctggatc cctgaggaca gggactgctc gatgcctccc 2220
[1756] ccttttagct acaatgggac ctatagacct gtgtga 2256
[1757] <210> 20
[1758] <211> 2256
[1759] <212> DNA
[1760] <213> 人工序列
[1761] <220>
[1762] <223> hDAO-Hepmut3
[1763] <400> 20

[1764] atgccggccc tgggctgggc cgtggctgcc atcctgatgc tgcagacggc catggcggag 60
[1765] ccctccccgg ggactctgcc caggaaggca ggggtgtttt cagacctaag caaccaagag 120
[1766] ctgaaggcag tgcacagctt cctctggtcc aagaaggagc tgaggctgca gccctccagt 180
[1767] accaccacca tggccaagaa caccgtgttt ctcatcgaga tgctgctgcc caagaagtac 240
[1768] catgtgctga ggtttctgga taaaggtgaa aggcatcctg tgcgggaagc ccgtgccgtc 300
[1769] atcttctttg gtgaccagga gcatcccaat gtcaccgagt ttgctgtggg gcccctgcca 360
[1770] gggccctgct acatgcgagc actgtccccc aggcctgggt accagtcctc ctgggcatcg 420
[1771] aggcccatct ccacagcaga gtatgccctc ctctaccaca ccctgcagga agccaccaag 480
[1772] cccctgcatc agttcttcct caataccaca ggcttctcat tccaagactg ccatgacaga 540
[1773] tgcctggcct tcaccgatgt ggcccccccgg ggtgtggctt ctggccagcg ccgcagttgg 600
[1774] cttatcatac agcgctatgt agaaggctac tttctgcacc ccactgggct ggagctcctc 660
[1775] gtggatcatg ggagcacaga tgctgggcac tgggccgtgg agcaggtgtg gtacaacggg 720
[1776] aagttctatg ggagcccaga ggaactggct cggaagtatg cagatggaga ggtggacgtg 780
[1777] gtggtcctgg aggacccgct gcctgggggc aaggggcatg acagcacaga ggagccgccc 840
[1778] ctcttctcct cccacaagcc ccgcggggac ttccccagcc ccatccatgt gagcggcccc 900
[1779] cgcttggtcc agccccacgg ccctcgcttc aggctggagg gcaacgctgt gctctacggc 960
[1780] ggctggagct ttgccttccg gctgcgctcc tcctccgggc tgcaggtcct gaacgtgcac 1020
[1781] ttcggcggag agcgcattgc ctatgaggtc agcgtgcaag aggcagtggc gctgtatgga 1080
[1782] ggacacacac ctgcaggcat gcagaccaag tacctcgatg tcggctgggg cctgggcagc 1140
[1783] gtcactcatg agttagcccc cggcatcgac tgcccggaga ccgccacctt cctggacact 1200
[1784] ttccactact atgatgccga tgacccggtc cattatcccc gagccctctg cctctttgaa 1260
[1785] atgcccacag gggtgcccct tcggcggcac tttaattcca actttaaagg tggcttcaac 1320
[1786] ttctatgcgg ggctgaaggg ccaggtgctg gtgctgcgga caacttcaac tgtctacaat 1380
[1787] tatgattaca tttgggactt tatcttctac cccaacgggg tgatggaggc caagatgcat 1440
[1788] gccactggct acgtccacgc caccttctac acccccgagg ggctgcgcca cggcactcgc 1500
[1789] ctgcacaccc acctgattgg caacatacac actcacttgg tgcactaccg cgtagacctg 1560
[1790] gatgtggcag gcaccaagaa cagcttccag acactgcaga tgaagctaga aaacatcacc 1620
[1791] aacccctgga gcccaagaca ccgcgtggtc cagccaactc tggagcagac gcagtactcc 1680
[1792] tgggagcgcc aggcggcctt ccgcttcaaa acgaagctgc ccaagtacct gctctttacc 1740
[1793] agcccccagg agaacccctg gggccacaag cgcagctacc gcctgcagat ccactccatg 1800
[1794] gccgaccagg tgctgccccc aggctggcag gaggagcagg ccatcacctg ggcaaggtac 1860
[1795] cccctggcag tgaccaagta ccgggagtcg gagctgtgca gcagcagcat ctaccaccag 1920
[1796] aacgacccct ggcacccgcc cgtggtcttt gagcagtttc ttcacaacaa cgagaacatt 1980
[1797] gaaaatgagg acctggtggc ctgggtgacg gtgggcttcc tgcacatccc ccactcagag 2040
[1798] gacattccca acacagccac acctgggaac tccgtgggct tcctgctccg gccattcaac 2100
[1799] ttcttcccag aggacccctc cctggcatcc agagacactg tgatcgtgtg gcctcgggac 2160
[1800] aacggcccca actacgtcca gcgctggatc cctgaggaca gggactgctc gatgcctccc 2220
[1801] ccttttagct acaatgggac ctatagacct gtgtga 2256
[1802] <210> 21
[1803] <211> 2256
[1804] <212> DNA
[1805] <213> 人工序列

[1806] <220>

[1807] <223> hDAO-Hepmut4

[1808] <400> 21

[1809] atgccggccc tgggctgggc cgtggctgcc atcctgatgc tgcagacggc catggcggag 60

[1810] ccctccccgg ggactctgcc caggaaggca ggggtgtttt cagacctaag caaccaagag 120

[1811] ctgaaggcag tgcacagctt cctctggtcc aagaaggagc tgaggctgca gccctccagt 180

[1812] accaccacca tggccaagaa caccgtgttt ctcatcgaga tgctgctgcc caagaagtac 240

[1813] catgtgctga ggtttctgga taaaggtgaa aggcatcctg tgcgggaagc ccgtgccgtc 300

[1814] atcttctttg gtgaccagga gcatcccaat gtcaccgagt ttgctgtggg gcccctgcca 360

[1815] gggccctgct acatgcgagc actgtccccc aggcctgggt accagtcctc ctgggcatcg 420

[1816] aggcccatct ccacagcaga gtatgccctc ctctaccaca ccctgcagga agccaccaag 480

[1817] cccctgcatc agttcttcct caataccaca ggcttctcat tccaagactg ccatgacaga 540

[1818] tgcctggcct tcaccgatgt ggcccccccgg ggtgtggctt ctggccagcg ccgcagttgg 600

[1819] cttatcatac agcgctatgt agaaggctac tttctgcacc ccactgggct ggagctcctc 660

[1820] gtggatcatg ggagcacaga tgctgggcac tgggccgtgg agcaggtgtg gtacaacggg 720

[1821] aagttctatg ggagcccaga ggaactggct cggaagtatg cagatggaga ggtggacgtg 780

[1822] gtggtcctgg aggacccgct gcctgggggc aaggggcatg acagcacaga ggagccgccc 840

[1823] ctcttctcct cccacaagcc ccgcggggac ttccccagcc ccatccatgt gagcggcccc 900

[1824] cgcttggtcc agccccacgg ccctcgcttc aggctggagg gcaacgctgt gctctacggc 960

[1825] ggctggagct ttgccttccg gctgcgctcc tcctccgggc tgcaggtcct gaacgtgcac 1020

[1826] ttcggcggag agcgcattgc ctatgaggtc agcgtgcaag aggcagtggc gctgtatgga 1080

[1827] ggacacacac ctgcaggcat gcagaccaag tacctcgatg tcggctgggg cctgggcagc 1140

[1828] gtcactcatg agttagcccc cggcatcgac tgcccggaga ccgccacctt cctggacact 1200

[1829] ttccactact atgatgccga tgacccggtc cattatcccc gagccctctg cctctttgaa 1260

[1830] atgcccacag gggtgcccct tcggcggcac tttaattcca actttaaagg tggcttcaac 1320

[1831] ttctatgcgg ggctgaaggg ccaggtgctg gtgctgcgga caacttcaac tgtctacaat 1380

[1832] tatgattaca tttgggactt tatcttctac cccaacgggg tgatggaggc caagatgcat 1440

[1833] gccactggct acgtccacgc caccttctac acccccgagg ggctgcgcca cggcactcgc 1500

[1834] ctgcacaccc acctgattgg caacatacac actcacttgg tgcactaccg cgtagacctg 1560

[1835] gatgtggcag gcaccaagaa cagcttccag acactgcaga tgaagctaga aaacatcacc 1620

[1836] aacccctgga gcccaagaca ccgcgtggtc cagccaactc tggagcagac gcagtactcc 1680

[1837] tgggagcgcc aggcggcctt cagcttcaaa acgaagctgc ccaagtacct gctctttacc 1740

[1838] agcccccagg agaacccctg gggccacaag cgcagctacc gcctgcagat ccactccatg 1800

[1839] gccgaccagg tgctgccccc aggctggcag gaggagcagg ccatcacctg ggcaaggtac 1860

[1840] cccctggcag tgaccaagta ccgggagtcg gagctgtgca gcagcagcat ctaccaccag 1920

[1841] aacgacccct ggcacccgcc cgtggtcttt gagcagtttc ttcacaacaa cgagaacatt 1980

[1842] gaaaatgagg acctggtggc ctgggtgacg gtgggcttcc tgcacatccc ccactcagag 2040

[1843] gacattccca acacagccac acctgggaac tccgtgggct tcctgctccg gccattcaac 2100

[1844] ttcttcccag aggacccctc cctggcatcc agagacactg tgatcgtgtg gcctcgggac 2160

[1845] aacggcccca actacgtcca gcgctggatc cctgaggaca gggactgctc gatgcctccc 2220

[1846] ccttttagct acaatgggac ctatagacct gtgtga 2256

[1847] <210> 22

[1848] <211> 2256

[1849] <212> DNA

[1850] <213> 人工序列

[1851] <220>

[1852] <223> hDAO-Hepmut5

[1853] <400> 22

[1854] atgccggccc tgggctgggc cgtggctgcc atcctgatgc tgcagacggc catggcggag 60

[1855] ccctccccgg ggactctgcc caggaaggca ggggtgtttt cagacctaag caaccaagag 120

[1856] ctgaaggcag tgcacagctt cctctggtcc aagaaggagc tgaggctgca gccctccagt 180

[1857] accaccacca tggccaagaa caccgtgttt ctcatcgaga tgctgctgcc caagaagtac 240

[1858] catgtgctga ggtttctgga taaaggtgaa aggcatcctg tgcgggaagc ccgtgccgtc 300

[1859] atcttctttg gtgaccagga gcatcccaat gtcaccgagt ttgctgtggg gcccctgcca 360

[1860] gggccctgct acatgcgagc actgtccccc aggcctgggt accagtcctc ctgggcatcg 420

[1861] aggcccatct ccacagcaga gtatgccctc ctctaccaca ccctgcagga agccaccaag 480

[1862] cccctgcatc agttcttcct caataccaca ggcttctcat tccaagactg ccatgacaga 540

[1863] tgcctggcct tcaccgatgt ggcccccccgg ggtgtggctt ctggccagcg ccgcagttgg 600

[1864] cttatcatac agcgctatgt agaaggctac tttctgcacc ccactgggct ggagctcctc 660

[1865] gtggatcatg ggagcacaga tgctgggcac tgggccgtgg agcaggtgtg gtacaacggg 720

[1866] aagttctatg ggagcccaga ggaactggct cggaagtatg cagatggaga ggtggacgtg 780

[1867] gtggtcctgg aggacccgct gcctgggggc aaggggcatg acagcacaga ggagccgccc 840

[1868] ctcttctcct cccacaagcc ccgcggggac ttccccagcc ccatccatgt gagcggcccc 900

[1869] cgcttggtcc agccccacgg ccctcgcttc aggctggagg gcaacgctgt gctctacggc 960

[1870] ggctggagct ttgccttccg gctgcgctcc tcctccgggc tgcaggtcct gaacgtgcac 1020

[1871] ttcggcggag agcgcattgc ctatgaggtc agcgtgcaag aggcagtggc gctgtatgga 1080

[1872] ggacacacac ctgcaggcat gcagaccaag tacctcgatg tcggctgggg cctgggcagc 1140

[1873] gtcactcatg agttagcccc cggcatcgac tgcccggaga ccgccacctt cctggacact 1200

[1874] ttccactact atgatgccga tgacccggtc cattatcccc gagccctctg cctctttgaa 1260

[1875] atgcccacag gggtgcccct tcggcggcac tttaattcca actttaaagg tggcttcaac 1320

[1876] ttctatgcgg ggctgaaggg ccaggtgctg gtgctgcgga caacttcaac tgtctacaat 1380

[1877] tatgattaca tttgggactt tatcttctac cccaacgggg tgatggaggc caagatgcat 1440

[1878] gccactggct acgtccacgc caccttctac acccccgagg ggctgcgcca cggcactcgc 1500

[1879] ctgcacaccc acctgattgg caacatacac actcacttgg tgcactaccg cgtagacctg 1560

[1880] gatgtggcag gcaccaagaa cagcttccag acactgcaga tgaagctaga aaacatcacc 1620

[1881] aacccctgga gcccaagaca ccgcgtggtc cagccaactc tggagcagac gcagtactcc 1680

[1882] tgggagcgcc aggcggcctt ccgcttcaaa acgaagctgc ccacgtacct gctctttacc 1740

[1883] agcccccagg agaacccctg gggccacaag cgcagctacc gcctgcagat ccactccatg 1800

[1884] gccgaccagg tgctgccccc aggctggcag gaggagcagg ccatcacctg ggcaaggtac 1860

[1885] cccctggcag tgaccaagta ccgggagtcg gagctgtgca gcagcagcat ctaccaccag 1920

[1886] aacgacccct ggcacccgcc cgtggtcttt gagcagtttc ttcacaacaa cgagaacatt 1980

[1887] gaaaatgagg acctggtggc ctgggtgacg gtgggcttcc tgcacatccc ccactcagag 2040

[1888] gacattccca acacagccac acctgggaac tccgtgggct tcctgctccg gccattcaac 2100

[1889] ttcttcccag aggacccctc cctggcatcc agagacactg tgatcgtgtg gcctcgggac 2160

[1890] aacggcccca actacgtcca gcgctggatc cctgaggaca gggactgctc gatgcctccc 2220

[1891] ccttttagct acaatgggac ctatagacct gtgtga 2256

[1892] <210> 23

[1893] <211> 2256

[1894] <212> DNA

[1895] <213> 人工序列

[1896] <220>

[1897] <223> hDAO-Hepmut6

[1898] <400> 23

[1899] atgccggccc tgggctgggc cgtggctgcc atcctgatgc tgcagacggc catggcggag 60

[1900] ccctccccgg ggactctgcc caggaaggca ggggtgtttt cagacctaag caaccaagag 120

[1901] ctgaaggcag tgcacagctt cctctggtcc aagaaggagc tgaggctgca gccctccagt 180

[1902] accaccacca tggccaagaa caccgtgttt ctcatcgaga tgctgctgcc caagaagtac 240

[1903] catgtgctga ggtttctgga taaaggtgaa aggcatcctg tgcgggaagc ccgtgccgtc 300

[1904] atcttctttg gtgaccagga gcatcccaat gtcaccgagt ttgctgtggg gcccctgcca 360

[1905] gggccctgct acatgcgagc actgtccccc aggcctgggt accagtcctc ctgggcatcg 420

[1906] aggcccatct ccacagcaga gtatgccctc ctctaccaca ccctgcagga agccaccaag 480

[1907] cccctgcatc agttcttcct caataccaca ggcttctcat tccaagactg ccatgacaga 540

[1908] tgcctggcct tcaccgatgt ggcccccccgg ggtgtggctt ctggccagcg ccgcagttgg 600

[1909] cttatcatac agcgctatgt agaaggctac tttctgcacc ccactgggct ggagctcctc 660

[1910] gtggatcatg ggagcacaga tgctgggcac tgggccgtgg agcaggtgtg gtacaacggg 720

[1911] aagttctatg ggagcccaga ggaactggct cggaagtatg cagatggaga ggtggacgtg 780

[1912] gtggtcctgg aggacccgct gcctgggggc aaggggcatg acagcacaga ggagccgccc 840

[1913] ctcttctcct cccacaagcc ccgcggggac ttccccagcc ccatccatgt gagcggcccc 900

[1914] cgcttggtcc agccccacgg ccctcgcttc aggctggagg gcaacgctgt gctctacggc 960

[1915] ggctggagct ttgccttccg gctgcgctcc tcctccgggc tgcaggtcct gaacgtgcac 1020

[1916] ttcggcggag agcgcattgc ctatgaggtc agcgtgcaag aggcagtggc gctgtatgga 1080

[1917] ggacacacac ctgcaggcat gcagaccaag tacctcgatg tcggctgggg cctgggcagc 1140

[1918] gtcactcatg agttagcccc cggcatcgac tgcccggaga ccgccacctt cctggacact 1200

[1919] ttccactact atgatgccga tgacccggtc cattatcccc gagccctctg cctctttgaa 1260

[1920] atgcccacag gggtgcccct tcggcggcac tttaattcca actttaaagg tggcttcaac 1320

[1921] ttctatgcgg ggctgaaggg ccaggtgctg gtgctgcgga caacttcaac tgtctacaat 1380

[1922] tatgattaca tttgggactt tatcttctac cccaacgggg tgatggaggc caagatgcat 1440

[1923] gccactggct acgtccacgc caccttctac acccccgagg ggctgcgcca cggcactcgc 1500

[1924] ctgcacaccc acctgattgg caacatacac actcacttgg tgcactaccg cgtagacctg 1560

[1925] gatgtggcag gcaccaagaa cagcttccag acactgcaga tgaagctaga aaacatcacc 1620

[1926] aacccctgga gcccaagaca ccgcgtggtc cagccaactc tggagcagac gcagtactcc 1680

[1927] tgggagcgcc aggcggcctt ccgcttcgga cagacgctgc ccaagtacct gctctttacc 1740

[1928] agcccccagg agaacccctg gggccacaag cgcagctacc gcctgcagat ccactccatg 1800

[1929] gccgaccagg tgctgccccc aggctggcag gaggagcagg ccatcacctg ggcaaggtac 1860

[1930] cccctggcag tgaccaagta ccgggagtcg gagctgtgca gcagcagcat ctaccaccag 1920

[1931] aacgacccct ggcacccgcc cgtggtcttt gagcagtttc ttcacaacaa cgagaacatt 1980

[1932] gaaaatgagg acctggtggc ctgggtgacg gtgggcttcc tgcacatccc ccactcagag 2040
[1933] gacattccca acacagccac acctgggaac tccgtgggct tcctgctccg gccattcaac 2100
[1934] ttcttcccag aggacccctc cctggcatcc agagacactg tgatcgtgtg gcctcgggac 2160
[1935] aacggcccca actacgtcca gcgctggatc cctgaggaca gggactgctc gatgcctccc 2220
[1936] ccttttagct acaatgggac ctatagacct gtgtga 2256
[1937] <210> 24
[1938] <211> 2256
[1939] <212> DNA
[1940] <213> 人工序列
[1941] <220>
[1942] <223> hDAO-Hepmut7
[1943] <400> 24
[1944] atgccggccc tgggctgggc cgtggctgcc atcctgatgc tgcagacggc catggcggag 60
[1945] ccctccccgg ggactctgcc caggaaggca ggggtgtttt cagacctaag caaccaagag 120
[1946] ctgaaggcag tgcacagctt cctctggtcc aagaaggagc tgaggctgca gccctccagt 180
[1947] accaccacca tggccaagaa caccgtgttt ctcatcgaga tgctgctgcc caagaagtac 240
[1948] catgtgctga ggtttctgga taaaggtgaa aggcatcctg tgcgggaagc ccgtgccgtc 300
[1949] atcttctttg gtgaccagga gcatcccaat gtcaccgagt ttgctgtggg gcccctgcca 360
[1950] gggccctgct acatgcgagc actgtccccc aggcctgggt accagtcctc ctgggcatcg 420
[1951] aggcccatct ccacagcaga gtatgccctc ctctaccaca ccctgcagga agccaccaag 480
[1952] cccctgcatc agttcttcct caataccaca ggcttctcat tccaagactg ccatgacaga 540
[1953] tgcctggcct tcaccgatgt ggcccccccgg ggtgtggctt ctggccagcg ccgcagttgg 600
[1954] cttatcatac agcgctatgt agaaggctac tttctgcacc ccactgggct ggagctcctc 660
[1955] gtggatcatg ggagcacaga tgctgggcac tgggccgtgg agcaggtgtg gtacaacggg 720
[1956] aagttctatg ggagcccaga ggaactggct cggaagtatg cagatggaga ggtggacgtg 780
[1957] gtggtcctgg aggacccgct gcctgggggc aaggggcatg acagcacaga ggagccgccc 840
[1958] ctcttctcct cccacaagcc ccgcggggac ttccccagcc ccatccatgt gagcggcccc 900
[1959] cgcttggtcc agccccacgg ccctcgcttc aggctggagg gcaacgctgt gctctacggc 960
[1960] ggctggagct ttgccttccg gctgcgctcc tcctccgggc tgcaggtcct gaacgtgcac 1020
[1961] ttcggcggag agcgcattgc ctatgaggtc agcgtgcaag aggcagtggc gctgtatgga 1080
[1962] ggacacacac ctgcaggcat gcagaccaag tacctcgatg tcggctgggg cctgggcagc 1140
[1963] gtcactcatg agttagcccc cggcatcgac tgcccggaga ccgccacctt cctggacact 1200
[1964] ttccactact atgatgccga tgacccggtc cattatcccc gagccctctg cctctttgaa 1260
[1965] atgcccacag gggtgcccct tcggcggcac tttaattcca actttaaagg tggcttcaac 1320
[1966] ttctatgcgg ggctgaaggg ccaggtgctg gtgctgcgga caacttcaac tgtctacaat 1380
[1967] tatgattaca tttgggactt tatcttctac cccaacgggg tgatggaggc caagatgcat 1440
[1968] gccactggct acgtccacgc caccttctac acccccgagg ggctgcgcca cggcactcgc 1500
[1969] ctgcacaccc acctgattgg caacatacac actcacttgg tgcactaccg cgtagacctg 1560
[1970] gatgtggcag gcaccaagaa cagcttccag acactgcaga tgaagctaga aaacatcacc 1620
[1971] aacccctgga gcccaagaca ccgcgtggtc cagccaactc tggagcagac gcagtactcc 1680
[1972] tgggagcgcc aggcggcctt cagcttcaaa aggaagctgc ccacgtacct gctctttacc 1740
[1973] agcccccagg agaacccctg gggccacaag cgcagctacc gcctgcagat ccactccatg 1800

[1974] gccgaccagg tgctgccccc aggctggcag gaggagcagg ccatcacctg ggcaaggtac 1860
[1975] cccctggcag tgaccaagta ccgggagtcg gagctgtgca gcagcagcat ctaccaccag 1920
[1976] aacgacccct ggcacccgcc cgtggtcttt gagcagtttc ttcacaacaa cgagaacatt 1980
[1977] gaaaatgagg acctggtggc ctgggtgacg gtgggcttcc tgcacatccc ccactcagag 2040
[1978] gacattccca acacagccac acctgggaac tccgtgggct tcctgctccg gccattcaac 2100
[1979] ttcttcccag aggacccctc cctggcatcc agagacactg tgatcgtgtg gcctcgggac 2160
[1980] aacggcccca actacgtcca gcgctggatc cctgaggaca gggactgctc gatgcctccc 2220
[1981] ccttttagct acaatgggac ctatagacct gtgtga 2256
[1982] <210> 25
[1983] <211> 2256
[1984] <212> DNA
[1985] <213> 人工序列
[1986] <220>
[1987] <223> hDAO-Cysmut
[1988] <400> 25
[1989] atgccggccc tgggctgggc cgtggctgcc atcctgatgc tgcagacggc catggcggag 60
[1990] ccctccccgg ggactctgcc caggaaggca ggggtgtttt cagacctaag caaccaagag 120
[1991] ctgaaggcag tgcacagctt cctctggtcc aagaaggagc tgaggctgca gccctccagt 180
[1992] accaccacca tggccaagaa caccgtgttt ctcatcgaga tgctgctgcc caagaagtac 240
[1993] catgtgctga ggtttctgga taaaggtgaa aggcatcctg tgcgggaagc ccgtgccgtc 300
[1994] atcttctttg gtgaccagga gcatcccaat gtcaccgagt ttgctgtggg gcccctgcca 360
[1995] gggcccgcct acatgcgagc actgtccccc aggcctgggt accagtcctc ctgggcatcg 420
[1996] aggcccatct ccacagcaga gtatgccctc ctctaccaca ccctgcagga agccaccaag 480
[1997] cccctgcatc agttcttcct caataccaca ggcttctcat tccaagactg ccatgacaga 540
[1998] tgcctggcct tcaccgatgt ggcccccccgg ggtgtggctt ctggccagcg ccgcagttgg 600
[1999] cttatcatac agcgctatgt agaaggctac tttctgcacc ccactgggct ggagctcctc 660
[2000] gtggatcatg ggagcacaga tgctgggcac tgggccgtgg agcaggtgtg gtacaacggg 720
[2001] aagttctatg ggagcccaga ggaactggct cggaagtatg cagatggaga ggtggacgtg 780
[2002] gtggtcctgg aggacccgct gcctgggggc aaggggcatg acagcacaga ggagccgccc 840
[2003] ctcttctcct cccacaagcc ccgcggggac ttccccagcc ccatccatgt gagcggcccc 900
[2004] cgcttggtcc agccccacgg ccctcgcttc aggctggagg gcaacgctgt gctctacggc 960
[2005] ggctggagct ttgccttccg gctgcgctcc tcctccgggc tgcaggtcct gaacgtgcac 1020
[2006] ttcggcggag agcgcattgc ctatgaggtc agcgtgcaag aggcagtggc gctgtatgga 1080
[2007] ggacacacac ctgcaggcat gcagaccaag tacctcgatg tcggctgggg cctgggcagc 1140
[2008] gtcactcatg agttagcccc cggcatcgac tgcccggaga ccgccacctt cctggacact 1200
[2009] ttccactact atgatgccga tgacccggtc cattatcccc gagccctctg cctctttgaa 1260
[2010] atgcccacag gggtgcccct tcggcggcac tttaattcca actttaaagg tggcttcaac 1320
[2011] ttctatgcgg ggctgaaggg ccaggtgctg gtgctgcgga caacttcaac tgtctacaat 1380
[2012] tatgattaca tttgggactt tatcttctac cccaacgggg tgatggaggc caagatgcat 1440
[2013] gccactggct acgtccacgc caccttctac acccccgagg ggctgcgcca cggcactcgc 1500
[2014] ctgcacaccc acctgattgg caacatacac actcacttgg tgcactaccg cgtagacctg 1560
[2015] gatgtggcag gcaccaagaa cagcttccag acactgcaga tgaagctaga aaacatcacc 1620

[2016] aacccctgga gcccaagaca ccgcgtggtc cagccaactc tggagcagac gcagtactcc 1680
[2017] tgggagcgcc aggcggcctt ccgcttcaaa aggaagctgc ccaagtacct gctctttacc 1740
[2018] agcccccagg agaacccctg gggccacaag cgcagctacc gcctgcagat ccactccatg 1800
[2019] gccgaccagg tgctgccccc aggctggcag gaggagcagg ccatcacctg ggcaaggtac 1860
[2020] cccctggcag tgaccaagta ccgggagtcg gagctgtgca gcagcagcat ctaccaccag 1920
[2021] aacgacccct ggcacccgcc cgtggtcttt gagcagtttc ttcacaacaa cgagaacatt 1980
[2022] gaaaatgagg acctggtggc ctgggtgacg gtgggcttcc tgcacatccc ccactcagag 2040
[2023] gacattccca acacagccac acctgggaac tccgtgggct tcctgctccg gccattcaac 2100
[2024] ttcttcccag aggacccctc cctggcatcc agagacactg tgatcgtgtg gcctcgggac 2160
[2025] aacggcccca actacgtcca gcgctggatc cctgaggaca gggactgctc gatgcctccc 2220
[2026] ccttttagct acaatgggac ctatagacct gtgtga 2256
[2027] <210> 26
[2028] <211> 2256
[2029] <212> DNA
[2030] <213> 人工序列
[2031] <220>
[2032] <223> hDAO-Hepmut1-Cysmut
[2033] <400> 26
[2034] atgccggccc tgggctgggc cgtggctgcc atcctgatgc tgcagacggc catggcggag 60
[2035] ccctccccgg ggactctgcc caggaaggca ggggtgtttt cagacctaag caaccaagag 120
[2036] ctgaaggcag tgcacagctt cctctggtcc aagaaggagc tgaggctgca gccctccagt 180
[2037] accaccacca tggccaagaa caccgtgttt ctcatcgaga tgctgctgcc caagaagtac 240
[2038] catgtgctga ggtttctgga taaaggtgaa aggcatcctg tgcgggaagc ccgtgccgtc 300
[2039] atcttctttg gtgaccagga gcatcccaat gtcaccgagt ttgctgtggg gcccctgcca 360
[2040] gggcccgcct acatgcgagc actgtccccc aggcctgggt accagtcctc ctgggcatcg 420
[2041] aggcccatct ccacagcaga gtatgccctc ctctaccaca ccctgcagga agccaccaag 480
[2042] cccctgcatc agttcttcct caataccaca ggcttctcat tccaagactg ccatgacaga 540
[2043] tgcctggcct tcaccgatgt ggcccccccgg ggtgtggctt ctggccagcg ccgcagttgg 600
[2044] cttatcatac agcgctatgt agaaggctac tttctgcacc ccactgggct ggagctcctc 660
[2045] gtggatcatg ggagcacaga tgctgggcac tgggccgtgg agcaggtgtg gtacaacggg 720
[2046] aagttctatg ggagcccaga ggaactggct cggaagtatg cagatggaga ggtggacgtg 780
[2047] gtggtcctgg aggacccgct gcctgggggc aaggggcatg acagcacaga ggagccgccc 840
[2048] ctcttctcct cccacaagcc ccgcggggac ttccccagcc ccatccatgt gagcggcccc 900
[2049] cgcttggtcc agccccacgg ccctcgcttc aggctggagg gcaacgctgt gctctacggc 960
[2050] ggctggagct ttgccttccg gctgcgctcc tcctccgggc tgcaggtcct gaacgtgcac 1020
[2051] ttcggcggag agcgcattgc ctatgaggtc agcgtgcaag aggcagtggc gctgtatgga 1080
[2052] ggacacacac ctgcaggcat gcagaccaag tacctcgatg tcggctgggg cctgggcagc 1140
[2053] gtcactcatg agttagcccc cggcatcgac tgcccggaga ccgccacctt cctggacact 1200
[2054] ttccactact atgatgccga tgacccggtc cattatcccc gagccctctg cctctttgaa 1260
[2055] atgcccacag gggtgcccct tcggcggcac tttaattcca actttaaagg tggcttcaac 1320
[2056] ttctatgcgg ggctgaaggg ccaggtgctg gtgctgcgga caacttcaac tgtctacaat 1380
[2057] tatgattaca tttgggactt tatcttctac cccaacgggg tgatggaggc caagatgcat 1440

[2058] gccactggct acgtccacgc caccttctac acccccgagg ggctgcgcca cggcactcgc 1500
[2059] ctgcacaccc acctgattgg caacatacac actcacttgg tgcactaccg cgtagacctg 1560
[2060] gatgtggcag gcaccaagaa cagcttccag acactgcaga tgaagctaga aaacatcacc 1620
[2061] aacccctgga gcccaagaca ccgcgtggtc cagccaactc tggagcagac gcagtactcc 1680
[2062] tgggagcgcc aggcggcctt cagcttcaaa aggaagctgc ccaagtacct gctctttacc 1740
[2063] agcccccagg agaacccctg gggccacaag cgcagctacc gcctgcagat ccactccatg 1800
[2064] gccgaccagg tgctgccccc aggctggcag gaggagcagg ccatcacctg ggcaaggtac 1860
[2065] cccctggcag tgaccaagta ccgggagtcg gagctgtgca gcagcagcat ctaccaccag 1920
[2066] aacgacccct ggcacccgcc cgtggtcttt gagcagtttc ttcacaacaa cgagaacatt 1980
[2067] gaaaatgagg acctggtggc ctgggtgacg gtgggcttcc tgcacatccc ccactcagag 2040
[2068] gacattccca acacagccac acctgggaac tccgtgggct tcctgctccg gccattcaac 2100
[2069] ttcttcccag aggacccctc cctggcatcc agagacactg tgatcgtgtg gcctcgggac 2160
[2070] aacggcccca actacgtcca gcgctggatc cctgaggaca gggactgctc gatgcctccc 2220
[2071] ccttttagct acaatgggac ctatagacct gtgtga 2256
[2072] <210> 27
[2073] <211> 2256
[2074] <212> DNA
[2075] <213> 人工序列
[2076] <220>
[2077] <223> hDAO-Hepmut2-Cysmut
[2078] <400> 27
[2079] atgccggccc tgggctgggc cgtggctgcc atcctgatgc tgcagacggc catggcggag 60
[2080] ccctccccgg ggactctgcc caggaaggca ggggtgtttt cagacctaag caaccaagag 120
[2081] ctgaaggcag tgcacagctt cctctggtcc aagaaggagc tgaggctgca gccctccagt 180
[2082] accaccacca tggccaagaa caccgtgttt ctcatcgaga tgctgctgcc caagaagtac 240
[2083] catgtgctga ggtttctgga taaaggtgaa aggcatcctg tgcgggaagc ccgtgccgtc 300
[2084] atcttctttg gtgaccagga gcatcccaat gtcaccgagt ttgctgtggg gcccctgcca 360
[2085] gggcccgcct acatgcgagc actgtccccc aggcctgggt accagtcctc ctgggcatcg 420
[2086] aggcccatct ccacagcaga gtatgccctc ctctaccaca ccctgcagga agccaccaag 480
[2087] cccctgcatc agttcttcct caataccaca ggcttctcat tccaagactg ccatgacaga 540
[2088] tgcctggcct tcaccgatgt ggcccccccgg ggtgtggctt ctggccagcg ccgcagttgg 600
[2089] cttatcatac agcgctatgt agaaggctac tttctgcacc ccactgggct ggagctcctc 660
[2090] gtggatcatg ggagcacaga tgctgggcac tgggccgtgg agcaggtgtg gtacaacggg 720
[2091] aagttctatg ggagcccaga ggaactggct cggaagtatg cagatggaga ggtggacgtg 780
[2092] gtggtcctgg aggacccgct gcctgggggc aaggggcatg acagcacaga ggagccgccc 840
[2093] ctcttctcct cccacaagcc ccgcggggac ttccccagcc ccatccatgt gagcggcccc 900
[2094] cgcttggtcc agccccacgg ccctcgcttc aggctggagg gcaacgctgt gctctacggc 960
[2095] ggctggagct ttgccttccg gctgcgctcc tcctccgggc tgcaggtcct gaacgtgcac 1020
[2096] ttcggcggag agcgcattgc ctatgaggtc agcgtgcaag aggcagtggc gctgtatgga 1080
[2097] ggacacacac ctgcaggcat gcagaccaag tacctcgatg tcggctgggg cctgggcagc 1140
[2098] gtcactcatg agttagcccc cggcatcgac tgcccggaga ccgccacctt cctggacact 1200
[2099] ttccactact atgatgccga tgacccggtc cattatcccc gagccctctg cctctttgaa 1260

[2100] atgcccacag gggtgcccct tcggcggcac tttaattcca actttaaagg tggcttcaac 1320
[2101] ttctatgcgg ggctgaaggg ccaggtgctg gtgctgcgga caacttcaac tgtctacaat 1380
[2102] tatgattaca tttgggactt tatcttctac cccaacgggg tgatggaggc caagatgcat 1440
[2103] gccactggct acgtccacgc caccttctac acccccgagg ggctgcgcca cggcactcgc 1500
[2104] ctgcacaccc acctgattgg caacatacac actcacttgg tgcactaccg cgtagacctg 1560
[2105] gatgtggcag gcaccaagaa cagcttccag acactgcaga tgaagctaga aaacatcacc 1620
[2106] aacccctgga gcccaagaca ccgcgtggtc cagccaactc tggagcagac gcagtactcc 1680
[2107] tgggagcgcc aggcggcctt ccgcttcaaa aggaagctgc ccacgtacct gctctttacc 1740
[2108] agcccccagg agaacccctg gggccacaag cgcagctacc gcctgcagat ccactccatg 1800
[2109] gccgaccagg tgctgccccc aggctggcag gaggagcagg ccatcacctg ggcaaggtac 1860
[2110] cccctggcag tgaccaagta ccgggagtcg gagctgtgca gcagcagcat ctaccaccag 1920
[2111] aacgacccct ggcacccgcc cgtggtcttt gagcagtttc ttcacaacaa cgagaacatt 1980
[2112] gaaaatgagg acctggtggc ctgggtgacg gtgggcttcc tgcacatccc ccactcagag 2040
[2113] gacattccca acacagccac acctgggaac tccgtgggct tcctgctccg gccattcaac 2100
[2114] ttcttcccag aggacccctc cctggcatcc agagacactg tgatcgtgtg gcctcgggac 2160
[2115] aacggcccca actacgtcca gcgctggatc cctgaggaca gggactgctc gatgcctccc 2220
[2116] ccttttagct acaatgggac ctatagacct gtgtga 2256
[2117] <210> 28
[2118] <211> 2256
[2119] <212> DNA
[2120] <213> 人工序列
[2121] <220>
[2122] <223> hDAO-Hepmut3-Cysmut
[2123] <400> 28
[2124] atgccggccc tgggctgggc cgtggctgcc atcctgatgc tgcagacggc catggcggag 60
[2125] ccctccccgg ggactctgcc caggaaggca ggggtgtttt cagacctaag caaccaagag 120
[2126] ctgaaggcag tgcacagctt cctctggtcc aagaaggagc tgaggctgca gccctccagt 180
[2127] accaccacca tggccaagaa caccgtgttt ctcatcgaga tgctgctgcc caagaagtac 240
[2128] catgtgctga ggtttctgga taaaggtgaa aggcatcctg tgcgggaagc ccgtgccgtc 300
[2129] atcttctttg gtgaccagga gcatcccaat gtcaccgagt ttgctgtggg gcccctgcca 360
[2130] gggcccgcct acatgcgagc actgtccccc aggcctgggt accagtcctc ctgggcatcg 420
[2131] aggcccatct ccacagcaga gtatgccctc ctctaccaca ccctgcagga agccaccaag 480
[2132] cccctgcatc agttcttcct caataccaca ggcttctcat tccaagactg ccatgacaga 540
[2133] tgcctggcct tcaccgatgt ggcccccccgg ggtgtggctt ctggccagcg ccgcagttgg 600
[2134] cttatcatac agcgctatgt agaaggctac tttctgcacc ccactgggct ggagctcctc 660
[2135] gtggatcatg ggagcacaga tgctgggcac tgggccgtgg agcaggtgtg gtacaacggg 720
[2136] aagttctatg ggagcccaga ggaactggct cggaagtatg cagatggaga ggtggacgtg 780
[2137] gtggtcctgg aggacccgct gcctgggggc aaggggcatg acagcacaga ggagccgccc 840
[2138] ctcttctcct cccacaagcc ccgcggggac ttccccagcc ccatccatgt gagcggcccc 900
[2139] cgcttggtcc agccccacgg ccctcgcttc aggctggagg gcaacgctgt gctctacggc 960
[2140] ggctggagct ttgccttccg gctgcgctcc tcctccgggc tgcaggtcct gaacgtgcac 1020
[2141] ttcggcggag agcgcattgc ctatgaggtc agcgtgcaag aggcagtggc gctgtatgga 1080

[2142] ggacacacac ctgcaggcat gcagaccaag tacctcgatg tcggctgggg cctgggcagc 1140
[2143] gtcactcatg agttagcccc cggcatcgac tgcccggaga ccgccacctt cctggacact 1200
[2144] ttccactact atgatgccga tgacccggtc cattatcccc gagccctctg cctctttgaa 1260
[2145] atgcccacag gggtgcccct tcggcggcac tttaattcca actttaaagg tggcttcaac 1320
[2146] ttctatgcgg ggctgaaggg ccaggtgctg gtgctgcgga caacttcaac tgtctacaat 1380
[2147] tatgattaca tttgggactt tatcttctac cccaacgggg tgatggaggc caagatgcat 1440
[2148] gccactggct acgtccacgc caccttctac acccccgagg ggctgcgcca cggcactcgc 1500
[2149] ctgcacaccc acctgattgg caacatacac actcacttgg tgcactaccg cgtagacctg 1560
[2150] gatgtggcag gcaccaagaa cagcttccag acactgcaga tgaagctaga aaacatcacc 1620
[2151] aacccctgga gcccaagaca ccgcgtggtc cagccaactc tggagcagac gcagtactcc 1680
[2152] tgggagcgcc aggcggcctt ccgcttcaaa acgaagctgc ccaagtacct gctctttacc 1740
[2153] agcccccagg agaacccctg gggccacaag cgcagctacc gcctgcagat ccactccatg 1800
[2154] gccgaccagg tgctgccccc aggctggcag gaggagcagg ccatcacctg ggcaaggtac 1860
[2155] cccctggcag tgaccaagta ccgggagtcg gagctgtgca gcagcagcat ctaccaccag 1920
[2156] aacgacccct ggcacccgcc cgtggtcttt gagcagtttc ttcacaacaa cgagaacatt 1980
[2157] gaaaatgagg acctggtggc ctgggtgacg gtgggcttcc tgcacatccc ccactcagag 2040
[2158] gacattccca acacagccac acctgggaac tccgtgggct tcctgctccg gccattcaac 2100
[2159] ttcttcccag aggacccctc cctggcatcc agagacactg tgatcgtgtg gcctcgggac 2160
[2160] aacggcccca actacgtcca gcgctggatc cctgaggaca gggactgctc gatgcctccc 2220
[2161] ccttttagct acaatgggac ctatagacct gtgtga 2256
[2162] <210> 29
[2163] <211> 2256
[2164] <212> DNA
[2165] <213> 人工序列
[2166] <220>
[2167] <223> hDAO-Hepmut4-Cysmut
[2168] <400> 29
[2169] atgccggccc tgggctgggc cgtggctgcc atcctgatgc tgcagacggc catggcggag 60
[2170] ccctccccgg ggactctgcc caggaaggca ggggtgtttt cagacctaag caaccaagag 120
[2171] ctgaaggcag tgcacagctt cctctggtcc aagaaggagc tgaggctgca gccctccagt 180
[2172] accaccacca tggccaagaa caccgtgttt ctcatcgaga tgctgctgcc caagaagtac 240
[2173] catgtgctga ggtttctgga taaaggtgaa aggcatcctg tgcgggaagc ccgtgccgtc 300
[2174] atcttctttg gtgaccagga gcatcccaat gtcaccgagt ttgctgtggg gcccctgcca 360
[2175] gggcccgcct acatgcgagc actgtccccc aggcctgggt accagtcctc ctgggcatcg 420
[2176] aggcccatct ccacagcaga gtatgccctc ctctaccaca ccctgcagga agccaccaag 480
[2177] cccctgcatc agttcttcct caataccaca ggcttctcat tccaagactg ccatgacaga 540
[2178] tgcctggcct tcaccgatgt ggcccccccgg ggtgtggctt ctggccagcg ccgcagttgg 600
[2179] cttatcatac agcgctatgt agaaggctac tttctgcacc ccactgggct ggagctcctc 660
[2180] gtggatcatg ggagcacaga tgctgggcac tgggccgtgg agcaggtgtg gtacaacggg 720
[2181] aagttctatg ggagcccaga ggaactggct cggaagtatg cagatggaga ggtggacgtg 780
[2182] gtggtcctgg aggacccgct gcctgggggc aaggggcatg acagcacaga ggagccgccc 840
[2183] ctcttctcct cccacaagcc ccgcggggac ttccccagcc ccatccatgt gagcggcccc 900

[2184] cgcttggtcc agccccacgg ccctcgcttc aggctggagg gcaacgctgt gctctacggc 960
[2185] ggctggagct ttgccttccg gctgcgctcc tcctccgggc tgcaggtcct gaacgtgcac 1020
[2186] ttcggcggag agcgcattgc ctatgaggtc agcgtgcaag aggcagtggc gctgtatgga 1080
[2187] ggacacacac ctgcaggcat gcagaccaag tacctcgatg tcggctgggg cctgggcagc 1140
[2188] gtcactcatg agttagcccc cggcatcgac tgcccggaga ccgccacctt cctggacact 1200
[2189] ttccactact atgatgccga tgacccggtc cattatcccc gagccctctg cctctttgaa 1260
[2190] atgcccacag gggtgcccct tcggcggcac tttaattcca actttaaagg tggcttcaac 1320
[2191] ttctatgcgg ggctgaaggg ccaggtgctg gtgctgcgga caacttcaac tgtctacaat 1380
[2192] tatgattaca tttgggactt tatcttctac cccaacgggg tgatggaggc caagatgcat 1440
[2193] gccactggct acgtccacgc caccttctac acccccgagg ggctgcgcca cggcactcgc 1500
[2194] ctgcacaccc acctgattgg caacatacac actcacttgg tgcactaccg cgtagacctg 1560
[2195] gatgtggcag gcaccaagaa cagcttccag acactgcaga tgaagctaga aaacatcacc 1620
[2196] aacccctgga gcccaagaca ccgcgtggtc cagccaactc tggagcagac gcagtactcc 1680
[2197] tgggagcgcc aggcggcctt cagcttcaaa acgaagctgc ccaagtacct gctctttacc 1740
[2198] agcccccagg agaacccctg gggccacaag cgcagctacc gcctgcagat ccactccatg 1800
[2199] gccgaccagg tgctgccccc aggctggcag gaggagcagg ccatcacctg ggcaaggtac 1860
[2200] cccctggcag tgaccaagta ccgggagtcg gagctgtgca gcagcagcat ctaccaccag 1920
[2201] aacgacccct ggcacccgcc cgtggtcttt gagcagtttc ttcacaacaa cgagaacatt 1980
[2202] gaaaatgagg acctggtggc ctgggtgacg gtgggcttcc tgcacatccc ccactcagag 2040
[2203] gacattccca acacagccac acctgggaac tccgtgggct tcctgctccg gccattcaac 2100
[2204] ttcttcccag aggacccctc cctggcatcc agagacactg tgatcgtgtg gcctcgggac 2160
[2205] aacggcccca actacgtcca gcgctggatc cctgaggaca gggactgctc gatgcctccc 2220
[2206] ccttttagct acaatgggac ctatagacct gtgtga 2256
[2207] <210> 30
[2208] <211> 2256
[2209] <212> DNA
[2210] <213> 人工序列
[2211] <220>
[2212] <223> hDAO-Hepmut5-Cysmut
[2213] <400> 30
[2214] atgccggccc tgggctgggc cgtggctgcc atcctgatgc tgcagacggc catggcggag 60
[2215] ccctccccgg ggactctgcc caggaaggca ggggtgtttt cagacctaag caaccaagag 120
[2216] ctgaaggcag tgcacagctt cctctggtcc aagaaggagc tgaggctgca gccctccagt 180
[2217] accaccacca tggccaagaa caccgtgttt ctcatcgaga tgctgctgcc caagaagtac 240
[2218] catgtgctga ggtttctgga taaaggtgaa aggcatcctg tgcgggaagc ccgtgccgtc 300
[2219] atcttctttg gtgaccagga gcatcccaat gtcaccgagt ttgctgtggg gcccctgcca 360
[2220] gggcccgcct acatgcgagc actgtccccc aggcctgggt accagtcctc ctgggcatcg 420
[2221] aggcccatct ccacagcaga gtatgccctc ctctaccaca ccctgcagga agccaccaag 480
[2222] cccctgcatc agttcttcct caataccaca ggcttctcat tccaagactg ccatgacaga 540
[2223] tgcctggcct tcaccgatgt ggcccccccgg ggtgtggctt ctggccagcg ccgcagttgg 600
[2224] cttatcatac agcgctatgt agaaggctac tttctgcacc ccactgggct ggagctcctc 660
[2225] gtggatcatg ggagcacaga tgctgggcac tgggccgtgg agcaggtgtg gtacaacggg 720

[2226] aagttctatg ggagcccaga ggaactggct cggaagtatg cagatggaga ggtggacgtg 780
[2227] gtggtcctgg aggacccgct gcctgggggc aaggggcatg acagcacaga ggagccgccc 840
[2228] ctcttctcct cccacaagcc ccgcggggac ttccccagcc ccatccatgt gagcggcccc 900
[2229] cgcttggtcc agccccacgg ccctcgcttc aggctggagg gcaacgctgt gctctacggc 960
[2230] ggctggagct ttgccttccg gctgcgctcc tcctccgggc tgcaggtcct gaacgtgcac 1020
[2231] ttcggcggag agcgcattgc ctatgaggtc agcgtgcaag aggcagtggc gctgtatgga 1080
[2232] ggacacacac ctgcaggcat gcagaccaag tacctcgatg tcggctgggg cctgggcagc 1140
[2233] gtcactcatg agttagcccc cggcatcgac tgcccggaga ccgccacctt cctggacact 1200
[2234] ttccactact atgatgccga tgacccggtc cattatcccc gagccctctg cctctttgaa 1260
[2235] atgcccacag gggtgcccct tcggcggcac tttaattcca actttaaagg tggcttcaac 1320
[2236] ttctatgcgg ggctgaaggg ccaggtgctg gtgctgcgga caacttcaac tgtctacaat 1380
[2237] tatgattaca tttgggactt tatcttctac cccaacgggg tgatggaggc caagatgcat 1440
[2238] gccactggct acgtccacgc caccttctac acccccgagg ggctgcgcca cggcactcgc 1500
[2239] ctgcacaccc acctgattgg caacatacac actcacttgg tgcactaccg cgtagacctg 1560
[2240] gatgtggcag gcaccaagaa cagcttccag acactgcaga tgaagctaga aaacatcacc 1620
[2241] aacccctgga gcccaagaca ccgcgtggtc cagccaactc tggagcagac gcagtactcc 1680
[2242] tgggagcgcc aggcggcctt ccgcttcaaa acgaagctgc ccacgtacct gctctttacc 1740
[2243] agcccccagg agaacccctg gggccacaag cgcagctacc gcctgcagat ccactccatg 1800
[2244] gccgaccagg tgctgccccc aggctggcag gaggagcagg ccatcacctg ggcaaggtac 1860
[2245] cccctggcag tgaccaagta ccgggagtcg gagctgtgca gcagcagcat ctaccaccag 1920
[2246] aacgacccct ggcacccgcc cgtggtcttt gagcagtttc ttcacaacaa cgagaacatt 1980
[2247] gaaaatgagg acctggtggc ctgggtgacg gtgggcttcc tgcacatccc ccactcagag 2040
[2248] gacattccca acacagccac acctgggaac tccgtgggct tcctgctccg gccattcaac 2100
[2249] ttcttcccag aggacccctc cctggcatcc agagacactg tgatcgtgtg gcctcgggac 2160
[2250] aacggcccca actacgtcca gcgctggatc cctgaggaca gggactgctc gatgcctccc 2220
[2251] ccttttagct acaatgggac ctatagacct gtgtga 2256
[2252] <210> 31
[2253] <211> 2256
[2254] <212> DNA
[2255] <213> 人工序列
[2256] <220>
[2257] <223> hDAO-Hepmut6-Cysmut
[2258] <400> 31
[2259] atgccggccc tgggctgggc cgtggctgcc atcctgatgc tgcagacggc catggcggag 60
[2260] ccctccccgg ggactctgcc caggaaggca ggggtgtttt cagacctaag caaccaagag 120
[2261] ctgaaggcag tgcacagctt cctctggtcc aagaaggagc tgaggctgca gccctccagt 180
[2262] accaccacca tggccaagaa caccgtgttt ctcatcgaga tgctgctgcc caagaagtac 240
[2263] catgtgctga ggtttctgga taaaggtgaa aggcatcctg tgcgggaagc ccgtgccgtc 300
[2264] atcttctttg gtgaccagga gcatcccaat gtcaccgagt ttgctgtggg gcccctgcca 360
[2265] gggcccgcct acatgcgagc actgtccccc aggcctgggt accagtcctc ctgggcatcg 420
[2266] aggcccatct ccacagcaga gtatgccctc ctctaccaca ccctgcagga agccaccaag 480
[2267] cccctgcatc agttcttcct caataccaca ggcttctcat tccaagactg ccatgacaga 540

[2268] tgcctggcct tcaccgatgt ggcccccggg ggtgtggctt ctggccagcg ccgcagttgg 600
[2269] cttatcatac agcgctatgt agaaggctac tttctgcacc ccactgggct ggagctcctc 660
[2270] gtggatcatg ggagcacaga tgctgggcac tgggccgtgg agcaggtgtg gtacaacggg 720
[2271] aagttctatg ggagcccaga ggaactggct cggaagtatg cagatggaga ggtggacgtg 780
[2272] gtggtcctgg aggacccgct gcctgggggc aaggggcatg acagcacaga ggagccgccc 840
[2273] ctcttctcct cccacaagcc ccgcggggac ttccccagcc ccatccatgt gagcggcccc 900
[2274] cgcttggtcc agccccacgg ccctcgcttc aggctggagg gcaacgctgt gctctacggc 960
[2275] ggctggagct ttgccttccg gctgcgctcc tcctccgggc tgcaggtcct gaacgtgcac 1020
[2276] ttcggcggag agcgcattgc ctatgaggtc agcgtgcaag aggcagtggc gctgtatgga 1080
[2277] ggacacacac ctgcaggcat gcagaccaag tacctcgatg tcggctgggg cctgggcagc 1140
[2278] gtcactcatg agttagcccc cggcatcgac tgcccggaga ccgccacctt cctggacact 1200
[2279] ttccactact atgatgccga tgacccggtc cattatcccc gagccctctg cctctttgaa 1260
[2280] atgcccacag gggtgcccct tcggcggcac tttaattcca actttaaagg tggcttcaac 1320
[2281] ttctatgcgg ggctgaaggg ccaggtgctg gtgctgcgga caacttcaac tgtctacaat 1380
[2282] tatgattaca tttgggactt tatcttctac cccaacgggg tgatggaggc caagatgcat 1440
[2283] gccactggct acgtccacgc caccttctac acccccgagg ggctgcgcca cggcactcgc 1500
[2284] ctgcacaccc acctgattgg caacatacac actcacttgg tgcactaccg cgtagacctg 1560
[2285] gatgtggcag gcaccaagaa cagcttccag acactgcaga tgaagctaga aaacatcacc 1620
[2286] aacccctgga gcccaagaca ccgcgtggtc cagccaactc tggagcagac gcagtactcc 1680
[2287] tgggagcgcc aggcggcctt ccgcttcgga cagacgctgc ccaagtacct gctctttacc 1740
[2288] agcccccagg agaacccctg gggccacaag cgcagctacc gcctgcagat ccactccatg 1800
[2289] gccgaccagg tgctgccccc aggctggcag gaggagcagg ccatcacctg ggcaaggtac 1860
[2290] cccctggcag tgaccaagta ccgggagtcg gagctgtgca gcagcagcat ctaccaccag 1920
[2291] aacgacccct ggcacccgcc cgtggtcttt gagcagtttc ttcacaacaa cgagaacatt 1980
[2292] gaaaatgagg acctggtggc ctgggtgacg gtgggcttcc tgcacatccc ccactcagag 2040
[2293] gacattccca acacagccac acctgggaac tccgtgggct tcctgctccg gccattcaac 2100
[2294] ttcttcccag aggacccctc cctggcatcc agagacactg tgatcgtgtg gcctcgggac 2160
[2295] aacggcccca actacgtcca gcgctggatc cctgaggaca gggactgctc gatgcctccc 2220
[2296] ccttttagct acaatgggac ctatagacct gtgtga 2256
[2297] <210> 32
[2298] <211> 2256
[2299] <212> DNA
[2300] <213> 人工序列
[2301] <220>
[2302] <223> hDAO-Hepmut7-Cysmut
[2303] <400> 32
[2304] atgccggccc tgggctgggc cgtggctgcc atcctgatgc tgcagacggc catggcggag 60
[2305] ccctccccgg ggactctgcc caggaaggca ggggtgtttt cagacctaag caaccaagag 120
[2306] ctgaaggcag tgcacagctt cctctggtcc aagaaggagc tgaggctgca gccctccagt 180
[2307] accaccacca tggccaagaa caccgtgttt ctcatcgaga tgctgctgcc caagaagtac 240
[2308] catgtgctga ggtttctgga taaaggtgaa aggcatcctg tgcgggaagc ccgtgccgtc 300
[2309] atcttctttg gtgaccagga gcatcccaat gtcaccgagt ttgctgtggg gcccctgcca 360

[2310] gggcccgcct acatgcgagc actgtccccc aggcctgggt accagtcctc ctgggcatcg 420
[2311] aggcccatct ccacagcaga gtatgccctc ctctaccaca ccctgcagga agccaccaag 480
[2312] cccctgcatc agttcttcct caataccaca ggcttctcat tccaagactg ccatgacaga 540
[2313] tgcctggcct tcaccgatgt ggcccccccgg ggtgtggctt ctggccagcg ccgcagttgg 600
[2314] cttatcatac agcgctatgt agaaggctac tttctgcacc ccactgggct ggagctcctc 660
[2315] gtggatcatg ggagcacaga tgctgggcac tgggccgtgg agcaggtgtg gtacaacggg 720
[2316] aagttctatg ggagcccaga ggaactggct cggaagtatg cagatggaga ggtggacgtg 780
[2317] gtggtcctgg aggacccgct gcctgggggc aaggggcatg acagcacaga ggagccgccc 840
[2318] ctcttctcct cccacaagcc ccgcggggac ttccccagcc ccatccatgt gagcggcccc 900
[2319] cgcttggtcc agccccacgg ccctcgcttc aggctggagg gcaacgctgt gctctacggc 960
[2320] ggctggagct ttgccttccg gctgcgctcc tcctccgggc tgcaggtcct gaacgtgcac 1020
[2321] ttcggcggag agcgcattgc ctatgaggtc agcgtgcaag aggcagtggc gctgtatgga 1080
[2322] ggacacacac ctgcaggcat gcagaccaag tacctcgatg tcggctgggg cctgggcagc 1140
[2323] gtcactcatg agttagcccc cggcatcgac tgcccggaga ccgccacctt cctggacact 1200
[2324] ttccactact atgatgccga tgacccggtc cattatcccc gagccctctg cctctttgaa 1260
[2325] atgcccacag gggtgcccct tcggcggcac tttaattcca actttaaagg tggcttcaac 1320
[2326] ttctatgcgg ggctgaaggg ccaggtgctg gtgctgcgga caacttcaac tgtctacaat 1380
[2327] tatgattaca tttgggactt tatcttctac cccaacgggg tgatggaggc caagatgcat 1440
[2328] gccactggct acgtccacgc caccttctac acccccgagg ggctgcgcca cggcactcgc 1500
[2329] ctgcacaccc acctgattgg caacatacac actcacttgg tgcactaccg cgtagacctg 1560
[2330] gatgtggcag gcaccaagaa cagcttccag acactgcaga tgaagctaga aaacatcacc 1620
[2331] aacccctgga gcccaagaca ccgcgtggtc cagccaactc tggagcagac gcagtactcc 1680
[2332] tgggagcgcc aggcggcctt cagcttcaaa aggaagctgc ccacgtacct gctctttacc 1740
[2333] agcccccagg agaacccctg gggccacaag cgcagctacc gcctgcagat ccactccatg 1800
[2334] gccgaccagg tgctgccccc aggctggcag gaggagcagg ccatcacctg ggcaaggtac 1860
[2335] cccctggcag tgaccaagta ccgggagtcg gagctgtgca gcagcagcat ctaccaccag 1920
[2336] aacgacccct ggcacccgcc cgtggtcttt gagcagtttc ttcacaacaa cgagaacatt 1980
[2337] gaaaatgagg acctggtggc ctgggtgacg gtgggcttcc tgcacatccc ccactcagag 2040
[2338] gacattccca acacagccac acctgggaac tccgtgggct tcctgctccg gccattcaac 2100
[2339] ttcttcccag aggacccctc cctggcatcc agagacactg tgatcgtgtg gcctcgggac 2160
[2340] aacggcccca actacgtcca gcgctggatc cctgaggaca gggactgctc gatgcctccc 2220
[2341] ccttttagct acaatgggac ctatagacct gtgtga 2256
[2342] <210> 33
[2343] <211> 8
[2344] <212> PRT
[2345] <213> 人工序列
[2346] <220>
[2347] <223> DAO 多肽
[2348] <400> 33
[2349] Ser Phe Lys Ala Lys Leu Pro Lys
[2350] 1 5
[2351] <210> 34

[2352] <211> 8
[2353] <212> PRT
[2354] <213> 人工序列
[2355] <220>
[2356] <223> DAO 多肽
[2357] <400> 34
[2358] Ala Phe Lys Ala Lys Leu Pro Thr
[2359] 1 5
[2360] <210> 35
[2361] <211> 8
[2362] <212> PRT
[2363] <213> 人工序列
[2364] <220>
[2365] <223> DAO 多肽
[2366] <400> 35
[2367] Ala Phe Lys Thr Lys Leu Pro Lys
[2368] 1 5
[2369] <210> 36
[2370] <211> 8
[2371] <212> PRT
[2372] <213> 人工序列
[2373] <220>
[2374] <223> DAO 多肽
[2375] <400> 36
[2376] Ser Phe Lys Thr Lys Leu Pro Lys
[2377] 1 5
[2378] <210> 37
[2379] <211> 8
[2380] <212> PRT
[2381] <213> 人工序列
[2382] <220>
[2383] <223> DAO 多肽
[2384] <400> 37
[2385] Ala Phe Lys Thr Lys Leu Pro Thr
[2386] 1 5
[2387] <210> 38
[2388] <211> 8
[2389] <212> PRT
[2390] <213> 人工序列
[2391] <220>
[2392] <223> DAO 多肽
[2393] <400> 38

[2394] Ser Phe Lys Ala Lys Leu Pro Lys
[2395] 1 5
[2396] <210> 39
[2397] <211> 983
[2398] <212> PRT
[2399] <213> 人工序列
[2400] <220>
[2401] <223> Fc-hDAO
[2402] <400> 39
[2403] Met Pro Ala Leu Gly Trp Ala Val Ala Ala Ile Leu Met Leu Gln Thr
[2404] 1 5 10 15
[2405] Ala Met Ala Glu Cys Pro Pro Cys Pro Ala Pro Pro Val Ala Gly Pro
[2406] 20 25 30
[2407] Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser
[2408] 35 40 45
[2409] Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp
[2410] 50 55 60
[2411] Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
[2412] 65 70 75 80
[2413] Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val
[2414] 85 90 95
[2415] Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu
[2416] 100 105 110
[2417] Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys
[2418] 115 120 125
[2419] Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr
[2420] 130 135 140
[2421] Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr
[2422] 145 150 155 160
[2423] Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu
[2424] 165 170 175
[2425] Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu
[2426] 180 185 190
[2427] Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys
[2428] 195 200 205
[2429] Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu
[2430] 210 215 220
[2431] Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
[2432] 225 230 235 240
[2433] Lys Glu Pro Lys Ser Ala Asp Lys Thr His Thr Glu Pro Ser Pro Gly
[2434] 245 250 255
[2435] Thr Leu Pro Arg Lys Ala Gly Val Phe Ser Asp Leu Ser Asn Gln Glu

[2436] 260 265 270
[2437] Leu Lys Ala Val His Ser Phe Leu Trp Ser Lys Lys Glu Leu Arg Leu
[2438] 275 280 285
[2439] Gln Pro Ser Ser Thr Thr Thr Met Ala Lys Asn Thr Val Phe Leu Ile
[2440] 290 295 300
[2441] Glu Met Leu Leu Pro Lys Lys Tyr His Val Leu Arg Phe Leu Asp Lys
[2442] 305 310 315 320
[2443] Gly Glu Arg His Pro Val Arg Glu Ala Arg Ala Val Ile Phe Phe Gly
[2444] 325 330 335
[2445] Asp Gln Glu His Pro Asn Val Thr Glu Phe Ala Val Gly Pro Leu Pro
[2446] 340 345 350
[2447] Gly Pro Cys Tyr Met Arg Ala Leu Ser Pro Arg Pro Gly Tyr Gln Ser
[2448] 355 360 365
[2449] Ser Trp Ala Ser Arg Pro Ile Ser Thr Ala Glu Tyr Ala Leu Leu Tyr
[2450] 370 375 380
[2451] His Thr Leu Gln Glu Ala Thr Lys Pro Leu His Gln Phe Phe Leu Asn
[2452] 385 390 395 400
[2453] Thr Thr Gly Phe Ser Phe Gln Asp Cys His Asp Arg Cys Leu Ala Phe
[2454] 405 410 415
[2455] Thr Asp Val Ala Pro Arg Gly Val Ala Ser Gly Gln Arg Arg Ser Trp
[2456] 420 425 430
[2457] Leu Ile Ile Gln Arg Tyr Val Glu Gly Tyr Phe Leu His Pro Thr Gly
[2458] 435 440 445
[2459] Leu Glu Leu Leu Val Asp His Gly Ser Thr Asp Ala Gly His Trp Ala
[2460] 450 455 460
[2461] Val Glu Gln Val Trp Tyr Asn Gly Lys Phe Tyr Gly Ser Pro Glu Glu
[2462] 465 470 475 480
[2463] Leu Ala Arg Lys Tyr Ala Asp Gly Glu Val Asp Val Val Val Leu Glu
[2464] 485 490 495
[2465] Asp Pro Leu Pro Gly Gly Lys Gly His Asp Ser Thr Glu Glu Pro Pro
[2466] 500 505 510
[2467] Leu Phe Ser Ser His Lys Pro Arg Gly Asp Phe Pro Ser Pro Ile His
[2468] 515 520 525
[2469] Val Ser Gly Pro Arg Leu Val Gln Pro His Gly Pro Arg Phe Arg Leu
[2470] 530 535 540
[2471] Glu Gly Asn Ala Val Leu Tyr Gly Gly Trp Ser Phe Ala Phe Arg Leu
[2472] 545 550 555 560
[2473] Arg Ser Ser Ser Gly Leu Gln Val Leu Asn Val His Phe Gly Gly Glu
[2474] 565 570 575
[2475] Arg Ile Ala Tyr Glu Val Ser Val Gln Glu Ala Val Ala Leu Tyr Gly
[2476] 580 585 590
[2477] Gly His Thr Pro Ala Gly Met Gln Thr Lys Tyr Leu Asp Val Gly Trp

[2478] 595 600 605
[2479] Gly Leu Gly Ser Val Thr His Glu Leu Ala Pro Gly Ile Asp Cys Pro
[2480] 610 615 620
[2481] Glu Thr Ala Thr Phe Leu Asp Thr Phe His Tyr Tyr Asp Ala Asp Asp
[2482] 625 630 635 640
[2483] Pro Val His Tyr Pro Arg Ala Leu Cys Leu Phe Glu Met Pro Thr Gly
[2484] 645 650 655
[2485] Val Pro Leu Arg Arg His Phe Asn Ser Asn Phe Lys Gly Gly Phe Asn
[2486] 660 665 670
[2487] Phe Tyr Ala Gly Leu Lys Gly Gln Val Leu Val Leu Arg Thr Thr Ser
[2488] 675 680 685
[2489] Thr Val Tyr Asn Tyr Asp Tyr Ile Trp Asp Phe Ile Phe Tyr Pro Asn
[2490] 690 695 700
[2491] Gly Val Met Glu Ala Lys Met His Ala Thr Gly Tyr Val His Ala Thr
[2492] 705 710 715 720
[2493] Phe Tyr Thr Pro Glu Gly Leu Arg His Gly Thr Arg Leu His Thr His
[2494] 725 730 735
[2495] Leu Ile Gly Asn Ile His Thr His Leu Val His Tyr Arg Val Asp Leu
[2496] 740 745 750
[2497] Asp Val Ala Gly Thr Lys Asn Ser Phe Gln Thr Leu Gln Met Lys Leu
[2498] 755 760 765
[2499] Glu Asn Ile Thr Asn Pro Trp Ser Pro Arg His Arg Val Val Gln Pro
[2500] 770 775 780
[2501] Thr Leu Glu Gln Thr Gln Tyr Ser Trp Glu Arg Gln Ala Ala Phe Arg
[2502] 785 790 795 800
[2503] Phe Lys Arg Lys Leu Pro Lys Tyr Leu Leu Phe Thr Ser Pro Gln Glu
[2504] 805 810 815
[2505] Asn Pro Trp Gly His Lys Arg Ser Tyr Arg Leu Gln Ile His Ser Met
[2506] 820 825 830
[2507] Ala Asp Gln Val Leu Pro Pro Gly Trp Gln Glu Glu Gln Ala Ile Thr
[2508] 835 840 845
[2509] Trp Ala Arg Tyr Pro Leu Ala Val Thr Lys Tyr Arg Glu Ser Glu Leu
[2510] 850 855 860
[2511] Cys Ser Ser Ser Ile Tyr His Gln Asn Asp Pro Trp His Pro Pro Val
[2512] 865 870 875 880
[2513] Val Phe Glu Gln Phe Leu His Asn Asn Glu Asn Ile Glu Asn Glu Asp
[2514] 885 890 895
[2515] Leu Val Ala Trp Val Thr Val Gly Phe Leu His Ile Pro His Ser Glu
[2516] 900 905 910
[2517] Asp Ile Pro Asn Thr Ala Thr Pro Gly Asn Ser Val Gly Phe Leu Leu
[2518] 915 920 925
[2519] Arg Pro Phe Asn Phe Phe Pro Glu Asp Pro Ser Leu Ala Ser Arg Asp

[2520] 930 935 940
[2521] Thr Val Ile Val Trp Pro Arg Asp Asn Gly Pro Asn Tyr Val Gln Arg
[2522] 945 950 955 960
[2523] Trp Ile Pro Glu Asp Arg Asp Cys Ser Met Pro Pro Pro Phe Ser Tyr
[2524] 965 970 975
[2525] Asn Gly Thr Tyr Arg Pro Val
[2526] 980
[2527] <210> 40
[2528] <211> 983
[2529] <212> PRT
[2530] <213> 人工序列
[2531] <220>
[2532] <223> Fc-hDAO-Hepmut1
[2533] <400> 40
[2534] Met Pro Ala Leu Gly Trp Ala Val Ala Ala Ile Leu Met Leu Gln Thr
[2535] 1 5 10 15
[2536] Ala Met Ala Glu Cys Pro Pro Cys Pro Ala Pro Pro Val Ala Gly Pro
[2537] 20 25 30
[2538] Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser
[2539] 35 40 45
[2540] Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp
[2541] 50 55 60
[2542] Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
[2543] 65 70 75 80
[2544] Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val
[2545] 85 90 95
[2546] Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu
[2547] 100 105 110
[2548] Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys
[2549] 115 120 125
[2550] Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr
[2551] 130 135 140
[2552] Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr
[2553] 145 150 155 160
[2554] Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu
[2555] 165 170 175
[2556] Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu
[2557] 180 185 190
[2558] Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys
[2559] 195 200 205
[2560] Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu
[2561] 210 215 220

[2562] Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
[2563] 225 230 235 240
[2564] Lys Glu Pro Lys Ser Ala Asp Lys Thr His Thr Glu Pro Ser Pro Gly
[2565] 245 250 255
[2566] Thr Leu Pro Arg Lys Ala Gly Val Phe Ser Asp Leu Ser Asn Gln Glu
[2567] 260 265 270
[2568] Leu Lys Ala Val His Ser Phe Leu Trp Ser Lys Lys Glu Leu Arg Leu
[2569] 275 280 285
[2570] Gln Pro Ser Ser Thr Thr Thr Met Ala Lys Asn Thr Val Phe Leu Ile
[2571] 290 295 300
[2572] Glu Met Leu Leu Pro Lys Lys Tyr His Val Leu Arg Phe Leu Asp Lys
[2573] 305 310 315 320
[2574] Gly Glu Arg His Pro Val Arg Glu Ala Arg Ala Val Ile Phe Phe Gly
[2575] 325 330 335
[2576] Asp Gln Glu His Pro Asn Val Thr Glu Phe Ala Val Gly Pro Leu Pro
[2577] 340 345 350
[2578] Gly Pro Cys Tyr Met Arg Ala Leu Ser Pro Arg Pro Gly Tyr Gln Ser
[2579] 355 360 365
[2580] Ser Trp Ala Ser Arg Pro Ile Ser Thr Ala Glu Tyr Ala Leu Leu Tyr
[2581] 370 375 380
[2582] His Thr Leu Gln Glu Ala Thr Lys Pro Leu His Gln Phe Phe Leu Asn
[2583] 385 390 395 400
[2584] Thr Thr Gly Phe Ser Phe Gln Asp Cys His Asp Arg Cys Leu Ala Phe
[2585] 405 410 415
[2586] Thr Asp Val Ala Pro Arg Gly Val Ala Ser Gly Gln Arg Arg Ser Trp
[2587] 420 425 430
[2588] Leu Ile Ile Gln Arg Tyr Val Glu Gly Tyr Phe Leu His Pro Thr Gly
[2589] 435 440 445
[2590] Leu Glu Leu Leu Val Asp His Gly Ser Thr Asp Ala Gly His Trp Ala
[2591] 450 455 460
[2592] Val Glu Gln Val Trp Tyr Asn Gly Lys Phe Tyr Gly Ser Pro Glu Glu
[2593] 465 470 475 480
[2594] Leu Ala Arg Lys Tyr Ala Asp Gly Glu Val Asp Val Val Val Leu Glu
[2595] 485 490 495
[2596] Asp Pro Leu Pro Gly Gly Lys Gly His Asp Ser Thr Glu Glu Pro Pro
[2597] 500 505 510
[2598] Leu Phe Ser Ser His Lys Pro Arg Gly Asp Phe Pro Ser Pro Ile His
[2599] 515 520 525
[2600] Val Ser Gly Pro Arg Leu Val Gln Pro His Gly Pro Arg Phe Arg Leu
[2601] 530 535 540
[2602] Glu Gly Asn Ala Val Leu Tyr Gly Gly Trp Ser Phe Ala Phe Arg Leu
[2603] 545 550 555 560

[2604] Arg Ser Ser Ser Gly Leu Gln Val Leu Asn Val His Phe Gly Gly Glu
[2605] 565 570 575
[2606] Arg Ile Ala Tyr Glu Val Ser Val Gln Glu Ala Val Ala Leu Tyr Gly
[2607] 580 585 590
[2608] Gly His Thr Pro Ala Gly Met Gln Thr Lys Tyr Leu Asp Val Gly Trp
[2609] 595 600 605
[2610] Gly Leu Gly Ser Val Thr His Glu Leu Ala Pro Gly Ile Asp Cys Pro
[2611] 610 615 620
[2612] Glu Thr Ala Thr Phe Leu Asp Thr Phe His Tyr Tyr Asp Ala Asp Asp
[2613] 625 630 635 640
[2614] Pro Val His Tyr Pro Arg Ala Leu Cys Leu Phe Glu Met Pro Thr Gly
[2615] 645 650 655
[2616] Val Pro Leu Arg Arg His Phe Asn Ser Asn Phe Lys Gly Gly Phe Asn
[2617] 660 665 670
[2618] Phe Tyr Ala Gly Leu Lys Gly Gln Val Leu Val Leu Arg Thr Thr Ser
[2619] 675 680 685
[2620] Thr Val Tyr Asn Tyr Asp Tyr Ile Trp Asp Phe Ile Phe Tyr Pro Asn
[2621] 690 695 700
[2622] Gly Val Met Glu Ala Lys Met His Ala Thr Gly Tyr Val His Ala Thr
[2623] 705 710 715 720
[2624] Phe Tyr Thr Pro Glu Gly Leu Arg His Gly Thr Arg Leu His Thr His
[2625] 725 730 735
[2626] Leu Ile Gly Asn Ile His Thr His Leu Val His Tyr Arg Val Asp Leu
[2627] 740 745 750
[2628] Asp Val Ala Gly Thr Lys Asn Ser Phe Gln Thr Leu Gln Met Lys Leu
[2629] 755 760 765
[2630] Glu Asn Ile Thr Asn Pro Trp Ser Pro Arg His Arg Val Val Gln Pro
[2631] 770 775 780
[2632] Thr Leu Glu Gln Thr Gln Tyr Ser Trp Glu Arg Gln Ala Ala Phe Ser
[2633] 785 790 795 800
[2634] Phe Lys Arg Lys Leu Pro Lys Tyr Leu Leu Phe Thr Ser Pro Gln Glu
[2635] 805 810 815
[2636] Asn Pro Trp Gly His Lys Arg Ser Tyr Arg Leu Gln Ile His Ser Met
[2637] 820 825 830
[2638] Ala Asp Gln Val Leu Pro Pro Gly Trp Gln Glu Glu Gln Ala Ile Thr
[2639] 835 840 845
[2640] Trp Ala Arg Tyr Pro Leu Ala Val Thr Lys Tyr Arg Glu Ser Glu Leu
[2641] 850 855 860
[2642] Cys Ser Ser Ser Ile Tyr His Gln Asn Asp Pro Trp His Pro Pro Val
[2643] 865 870 875 880
[2644] Val Phe Glu Gln Phe Leu His Asn Asn Glu Asn Ile Glu Asn Glu Asp
[2645] 885 890 895

[2646] Leu Val Ala Trp Val Thr Val Gly Phe Leu His Ile Pro His Ser Glu
[2647] 900 905 910
[2648] Asp Ile Pro Asn Thr Ala Thr Pro Gly Asn Ser Val Gly Phe Leu Leu
[2649] 915 920 925
[2650] Arg Pro Phe Asn Phe Phe Pro Glu Asp Pro Ser Leu Ala Ser Arg Asp
[2651] 930 935 940
[2652] Thr Val Ile Val Trp Pro Arg Asp Asn Gly Pro Asn Tyr Val Gln Arg
[2653] 945 950 955 960
[2654] Trp Ile Pro Glu Asp Arg Asp Cys Ser Met Pro Pro Pro Phe Ser Tyr
[2655] 965 970 975
[2656] Asn Gly Thr Tyr Arg Pro Val
[2657] 980
[2658] <210> 41
[2659] <211> 983
[2660] <212> PRT
[2661] <213> 人工序列
[2662] <220>
[2663] <223> Fc-hDAO-Hepmut2
[2664] <400> 41
[2665] Met Pro Ala Leu Gly Trp Ala Val Ala Ala Ile Leu Met Leu Gln Thr
[2666] 1 5 10 15
[2667] Ala Met Ala Glu Cys Pro Pro Cys Pro Ala Pro Pro Val Ala Gly Pro
[2668] 20 25 30
[2669] Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser
[2670] 35 40 45
[2671] Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp
[2672] 50 55 60
[2673] Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
[2674] 65 70 75 80
[2675] Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val
[2676] 85 90 95
[2677] Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu
[2678] 100 105 110
[2679] Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys
[2680] 115 120 125
[2681] Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr
[2682] 130 135 140
[2683] Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr
[2684] 145 150 155 160
[2685] Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu
[2686] 165 170 175
[2687] Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu

[2688] 180 185 190
[2689] Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys
[2690] 195 200 205
[2691] Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu
[2692] 210 215 220
[2693] Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
[2694] 225 230 235 240
[2695] Lys Glu Pro Lys Ser Ala Asp Lys Thr His Thr Glu Pro Ser Pro Gly
[2696] 245 250 255
[2697] Thr Leu Pro Arg Lys Ala Gly Val Phe Ser Asp Leu Ser Asn Gln Glu
[2698] 260 265 270
[2699] Leu Lys Ala Val His Ser Phe Leu Trp Ser Lys Lys Glu Leu Arg Leu
[2700] 275 280 285
[2701] Gln Pro Ser Ser Thr Thr Thr Met Ala Lys Asn Thr Val Phe Leu Ile
[2702] 290 295 300
[2703] Glu Met Leu Leu Pro Lys Lys Tyr His Val Leu Arg Phe Leu Asp Lys
[2704] 305 310 315 320
[2705] Gly Glu Arg His Pro Val Arg Glu Ala Arg Ala Val Ile Phe Phe Gly
[2706] 325 330 335
[2707] Asp Gln Glu His Pro Asn Val Thr Glu Phe Ala Val Gly Pro Leu Pro
[2708] 340 345 350
[2709] Gly Pro Cys Tyr Met Arg Ala Leu Ser Pro Arg Pro Gly Tyr Gln Ser
[2710] 355 360 365
[2711] Ser Trp Ala Ser Arg Pro Ile Ser Thr Ala Glu Tyr Ala Leu Leu Tyr
[2712] 370 375 380
[2713] His Thr Leu Gln Glu Ala Thr Lys Pro Leu His Gln Phe Phe Leu Asn
[2714] 385 390 395 400
[2715] Thr Thr Gly Phe Ser Phe Gln Asp Cys His Asp Arg Cys Leu Ala Phe
[2716] 405 410 415
[2717] Thr Asp Val Ala Pro Arg Gly Val Ala Ser Gly Gln Arg Arg Ser Trp
[2718] 420 425 430
[2719] Leu Ile Ile Gln Arg Tyr Val Glu Gly Tyr Phe Leu His Pro Thr Gly
[2720] 435 440 445
[2721] Leu Glu Leu Leu Val Asp His Gly Ser Thr Asp Ala Gly His Trp Ala
[2722] 450 455 460
[2723] Val Glu Gln Val Trp Tyr Asn Gly Lys Phe Tyr Gly Ser Pro Glu Glu
[2724] 465 470 475 480
[2725] Leu Ala Arg Lys Tyr Ala Asp Gly Glu Val Asp Val Val Val Leu Glu
[2726] 485 490 495
[2727] Asp Pro Leu Pro Gly Gly Lys Gly His Asp Ser Thr Glu Glu Pro Pro
[2728] 500 505 510
[2729] Leu Phe Ser Ser His Lys Pro Arg Gly Asp Phe Pro Ser Pro Ile His

[2730] 515 520 525
[2731] Val Ser Gly Pro Arg Leu Val Gln Pro His Gly Pro Arg Phe Arg Leu
[2732] 530 535 540
[2733] Glu Gly Asn Ala Val Leu Tyr Gly Gly Trp Ser Phe Ala Phe Arg Leu
[2734] 545 550 555 560
[2735] Arg Ser Ser Ser Gly Leu Gln Val Leu Asn Val His Phe Gly Gly Glu
[2736] 565 570 575
[2737] Arg Ile Ala Tyr Glu Val Ser Val Gln Glu Ala Val Ala Leu Tyr Gly
[2738] 580 585 590
[2739] Gly His Thr Pro Ala Gly Met Gln Thr Lys Tyr Leu Asp Val Gly Trp
[2740] 595 600 605
[2741] Gly Leu Gly Ser Val Thr His Glu Leu Ala Pro Gly Ile Asp Cys Pro
[2742] 610 615 620
[2743] Glu Thr Ala Thr Phe Leu Asp Thr Phe His Tyr Tyr Asp Ala Asp Asp
[2744] 625 630 635 640
[2745] Pro Val His Tyr Pro Arg Ala Leu Cys Leu Phe Glu Met Pro Thr Gly
[2746] 645 650 655
[2747] Val Pro Leu Arg Arg His Phe Asn Ser Asn Phe Lys Gly Gly Phe Asn
[2748] 660 665 670
[2749] Phe Tyr Ala Gly Leu Lys Gly Gln Val Leu Val Leu Arg Thr Thr Ser
[2750] 675 680 685
[2751] Thr Val Tyr Asn Tyr Asp Tyr Ile Trp Asp Phe Ile Phe Tyr Pro Asn
[2752] 690 695 700
[2753] Gly Val Met Glu Ala Lys Met His Ala Thr Gly Tyr Val His Ala Thr
[2754] 705 710 715 720
[2755] Phe Tyr Thr Pro Glu Gly Leu Arg His Gly Thr Arg Leu His Thr His
[2756] 725 730 735
[2757] Leu Ile Gly Asn Ile His Thr His Leu Val His Tyr Arg Val Asp Leu
[2758] 740 745 750
[2759] Asp Val Ala Gly Thr Lys Asn Ser Phe Gln Thr Leu Gln Met Lys Leu
[2760] 755 760 765
[2761] Glu Asn Ile Thr Asn Pro Trp Ser Pro Arg His Arg Val Val Gln Pro
[2762] 770 775 780
[2763] Thr Leu Glu Gln Thr Gln Tyr Ser Trp Glu Arg Gln Ala Ala Phe Arg
[2764] 785 790 795 800
[2765] Phe Lys Arg Lys Leu Pro Thr Tyr Leu Leu Phe Thr Ser Pro Gln Glu
[2766] 805 810 815
[2767] Asn Pro Trp Gly His Lys Arg Ser Tyr Arg Leu Gln Ile His Ser Met
[2768] 820 825 830
[2769] Ala Asp Gln Val Leu Pro Pro Gly Trp Gln Glu Glu Gln Ala Ile Thr
[2770] 835 840 845
[2771] Trp Ala Arg Tyr Pro Leu Ala Val Thr Lys Tyr Arg Glu Ser Glu Leu

[2772] 850 855 860
[2773] Cys Ser Ser Ser Ile Tyr His Gln Asn Asp Pro Trp His Pro Pro Val
[2774] 865 870 875 880
[2775] Val Phe Glu Gln Phe Leu His Asn Asn Glu Asn Ile Glu Asn Glu Asp
[2776] 885 890 895
[2777] Leu Val Ala Trp Val Thr Val Gly Phe Leu His Ile Pro His Ser Glu
[2778] 900 905 910
[2779] Asp Ile Pro Asn Thr Ala Thr Pro Gly Asn Ser Val Gly Phe Leu Leu
[2780] 915 920 925
[2781] Arg Pro Phe Asn Phe Phe Pro Glu Asp Pro Ser Leu Ala Ser Arg Asp
[2782] 930 935 940
[2783] Thr Val Ile Val Trp Pro Arg Asp Asn Gly Pro Asn Tyr Val Gln Arg
[2784] 945 950 955 960
[2785] Trp Ile Pro Glu Asp Arg Asp Cys Ser Met Pro Pro Pro Phe Ser Tyr
[2786] 965 970 975
[2787] Asn Gly Thr Tyr Arg Pro Val
[2788] 980
[2789] <210> 42
[2790] <211> 983
[2791] <212> PRT
[2792] <213> 人工序列
[2793] <220>
[2794] <223> Fc-hDAO-Hepmut3
[2795] <400> 42
[2796] Met Pro Ala Leu Gly Trp Ala Val Ala Ala Ile Leu Met Leu Gln Thr
[2797] 1 5 10 15
[2798] Ala Met Ala Glu Cys Pro Pro Cys Pro Ala Pro Pro Val Ala Gly Pro
[2799] 20 25 30
[2800] Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser
[2801] 35 40 45
[2802] Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp
[2803] 50 55 60
[2804] Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
[2805] 65 70 75 80
[2806] Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val
[2807] 85 90 95
[2808] Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu
[2809] 100 105 110
[2810] Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys
[2811] 115 120 125
[2812] Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr
[2813] 130 135 140

[2814] Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr
[2815] 145 150 155 160
[2816] Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu
[2817] 165 170 175
[2818] Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu
[2819] 180 185 190
[2820] Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys
[2821] 195 200 205
[2822] Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu
[2823] 210 215 220
[2824] Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
[2825] 225 230 235 240
[2826] Lys Glu Pro Lys Ser Ala Asp Lys Thr His Thr Glu Pro Ser Pro Gly
[2827] 245 250 255
[2828] Thr Leu Pro Arg Lys Ala Gly Val Phe Ser Asp Leu Ser Asn Gln Glu
[2829] 260 265 270
[2830] Leu Lys Ala Val His Ser Phe Leu Trp Ser Lys Lys Glu Leu Arg Leu
[2831] 275 280 285
[2832] Gln Pro Ser Ser Thr Thr Thr Met Ala Lys Asn Thr Val Phe Leu Ile
[2833] 290 295 300
[2834] Glu Met Leu Leu Pro Lys Lys Tyr His Val Leu Arg Phe Leu Asp Lys
[2835] 305 310 315 320
[2836] Gly Glu Arg His Pro Val Arg Glu Ala Arg Ala Val Ile Phe Phe Gly
[2837] 325 330 335
[2838] Asp Gln Glu His Pro Asn Val Thr Glu Phe Ala Val Gly Pro Leu Pro
[2839] 340 345 350
[2840] Gly Pro Cys Tyr Met Arg Ala Leu Ser Pro Arg Pro Gly Tyr Gln Ser
[2841] 355 360 365
[2842] Ser Trp Ala Ser Arg Pro Ile Ser Thr Ala Glu Tyr Ala Leu Leu Tyr
[2843] 370 375 380
[2844] His Thr Leu Gln Glu Ala Thr Lys Pro Leu His Gln Phe Phe Leu Asn
[2845] 385 390 395 400
[2846] Thr Thr Gly Phe Ser Phe Gln Asp Cys His Asp Arg Cys Leu Ala Phe
[2847] 405 410 415
[2848] Thr Asp Val Ala Pro Arg Gly Val Ala Ser Gly Gln Arg Arg Ser Trp
[2849] 420 425 430
[2850] Leu Ile Ile Gln Arg Tyr Val Glu Gly Tyr Phe Leu His Pro Thr Gly
[2851] 435 440 445
[2852] Leu Glu Leu Leu Val Asp His Gly Ser Thr Asp Ala Gly His Trp Ala
[2853] 450 455 460
[2854] Val Glu Gln Val Trp Tyr Asn Gly Lys Phe Tyr Gly Ser Pro Glu Glu
[2855] 465 470 475 480

[2856] Leu Ala Arg Lys Tyr Ala Asp Gly Glu Val Asp Val Val Val Leu Glu
[2857] 485 490 495
[2858] Asp Pro Leu Pro Gly Gly Lys Gly His Asp Ser Thr Glu Glu Pro Pro
[2859] 500 505 510
[2860] Leu Phe Ser Ser His Lys Pro Arg Gly Asp Phe Pro Ser Pro Ile His
[2861] 515 520 525
[2862] Val Ser Gly Pro Arg Leu Val Gln Pro His Gly Pro Arg Phe Arg Leu
[2863] 530 535 540
[2864] Glu Gly Asn Ala Val Leu Tyr Gly Gly Trp Ser Phe Ala Phe Arg Leu
[2865] 545 550 555 560
[2866] Arg Ser Ser Ser Gly Leu Gln Val Leu Asn Val His Phe Gly Gly Glu
[2867] 565 570 575
[2868] Arg Ile Ala Tyr Glu Val Ser Val Gln Glu Ala Val Ala Leu Tyr Gly
[2869] 580 585 590
[2870] Gly His Thr Pro Ala Gly Met Gln Thr Lys Tyr Leu Asp Val Gly Trp
[2871] 595 600 605
[2872] Gly Leu Gly Ser Val Thr His Glu Leu Ala Pro Gly Ile Asp Cys Pro
[2873] 610 615 620
[2874] Glu Thr Ala Thr Phe Leu Asp Thr Phe His Tyr Tyr Asp Ala Asp Asp
[2875] 625 630 635 640
[2876] Pro Val His Tyr Pro Arg Ala Leu Cys Leu Phe Glu Met Pro Thr Gly
[2877] 645 650 655
[2878] Val Pro Leu Arg Arg His Phe Asn Ser Asn Phe Lys Gly Gly Phe Asn
[2879] 660 665 670
[2880] Phe Tyr Ala Gly Leu Lys Gly Gln Val Leu Val Leu Arg Thr Thr Ser
[2881] 675 680 685
[2882] Thr Val Tyr Asn Tyr Asp Tyr Ile Trp Asp Phe Ile Phe Tyr Pro Asn
[2883] 690 695 700
[2884] Gly Val Met Glu Ala Lys Met His Ala Thr Gly Tyr Val His Ala Thr
[2885] 705 710 715 720
[2886] Phe Tyr Thr Pro Glu Gly Leu Arg His Gly Thr Arg Leu His Thr His
[2887] 725 730 735
[2888] Leu Ile Gly Asn Ile His Thr His Leu Val His Tyr Arg Val Asp Leu
[2889] 740 745 750
[2890] Asp Val Ala Gly Thr Lys Asn Ser Phe Gln Thr Leu Gln Met Lys Leu
[2891] 755 760 765
[2892] Glu Asn Ile Thr Asn Pro Trp Ser Pro Arg His Arg Val Val Gln Pro
[2893] 770 775 780
[2894] Thr Leu Glu Gln Thr Gln Tyr Ser Trp Glu Arg Gln Ala Ala Phe Arg
[2895] 785 790 795 800
[2896] Phe Lys Thr Lys Leu Pro Lys Tyr Leu Leu Phe Thr Ser Pro Gln Glu
[2897] 805 810 815

[2898] Asn Pro Trp Gly His Lys Arg Ser Tyr Arg Leu Gln Ile His Ser Met
[2899] 820 825 830
[2900] Ala Asp Gln Val Leu Pro Pro Gly Trp Gln Glu Glu Gln Ala Ile Thr
[2901] 835 840 845
[2902] Trp Ala Arg Tyr Pro Leu Ala Val Thr Lys Tyr Arg Glu Ser Glu Leu
[2903] 850 855 860
[2904] Cys Ser Ser Ser Ile Tyr His Gln Asn Asp Pro Trp His Pro Pro Val
[2905] 865 870 875 880
[2906] Val Phe Glu Gln Phe Leu His Asn Asn Glu Asn Ile Glu Asn Glu Asp
[2907] 885 890 895
[2908] Leu Val Ala Trp Val Thr Val Gly Phe Leu His Ile Pro His Ser Glu
[2909] 900 905 910
[2910] Asp Ile Pro Asn Thr Ala Thr Pro Gly Asn Ser Val Gly Phe Leu Leu
[2911] 915 920 925
[2912] Arg Pro Phe Asn Phe Phe Pro Glu Asp Pro Ser Leu Ala Ser Arg Asp
[2913] 930 935 940
[2914] Thr Val Ile Val Trp Pro Arg Asp Asn Gly Pro Asn Tyr Val Gln Arg
[2915] 945 950 955 960
[2916] Trp Ile Pro Glu Asp Arg Asp Cys Ser Met Pro Pro Pro Phe Ser Tyr
[2917] 965 970 975
[2918] Asn Gly Thr Tyr Arg Pro Val
[2919] 980
[2920] <210> 43
[2921] <211> 983
[2922] <212> PRT
[2923] <213> 人工序列
[2924] <220>
[2925] <223> Fc-hDAO-Hepmut4
[2926] <400> 43
[2927] Met Pro Ala Leu Gly Trp Ala Val Ala Ala Ile Leu Met Leu Gln Thr
[2928] 1 5 10 15
[2929] Ala Met Ala Glu Cys Pro Pro Cys Pro Ala Pro Pro Val Ala Gly Pro
[2930] 20 25 30
[2931] Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser
[2932] 35 40 45
[2933] Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp
[2934] 50 55 60
[2935] Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
[2936] 65 70 75 80
[2937] Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val
[2938] 85 90 95
[2939] Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu

[2940] 100 105 110
[2941] Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys
[2942] 115 120 125
[2943] Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr
[2944] 130 135 140
[2945] Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr
[2946] 145 150 155 160
[2947] Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu
[2948] 165 170 175
[2949] Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu
[2950] 180 185 190
[2951] Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys
[2952] 195 200 205
[2953] Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu
[2954] 210 215 220
[2955] Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
[2956] 225 230 235 240
[2957] Lys Glu Pro Lys Ser Ala Asp Lys Thr His Thr Glu Pro Ser Pro Gly
[2958] 245 250 255
[2959] Thr Leu Pro Arg Lys Ala Gly Val Phe Ser Asp Leu Ser Asn Gln Glu
[2960] 260 265 270
[2961] Leu Lys Ala Val His Ser Phe Leu Trp Ser Lys Lys Glu Leu Arg Leu
[2962] 275 280 285
[2963] Gln Pro Ser Ser Thr Thr Thr Met Ala Lys Asn Thr Val Phe Leu Ile
[2964] 290 295 300
[2965] Glu Met Leu Leu Pro Lys Lys Tyr His Val Leu Arg Phe Leu Asp Lys
[2966] 305 310 315 320
[2967] Gly Glu Arg His Pro Val Arg Glu Ala Arg Ala Val Ile Phe Phe Gly
[2968] 325 330 335
[2969] Asp Gln Glu His Pro Asn Val Thr Glu Phe Ala Val Gly Pro Leu Pro
[2970] 340 345 350
[2971] Gly Pro Cys Tyr Met Arg Ala Leu Ser Pro Arg Pro Gly Tyr Gln Ser
[2972] 355 360 365
[2973] Ser Trp Ala Ser Arg Pro Ile Ser Thr Ala Glu Tyr Ala Leu Leu Tyr
[2974] 370 375 380
[2975] His Thr Leu Gln Glu Ala Thr Lys Pro Leu His Gln Phe Phe Leu Asn
[2976] 385 390 395 400
[2977] Thr Thr Gly Phe Ser Phe Gln Asp Cys His Asp Arg Cys Leu Ala Phe
[2978] 405 410 415
[2979] Thr Asp Val Ala Pro Arg Gly Val Ala Ser Gly Gln Arg Arg Ser Trp
[2980] 420 425 430
[2981] Leu Ile Ile Gln Arg Tyr Val Glu Gly Tyr Phe Leu His Pro Thr Gly

[2982] 435 440 445
[2983] Leu Glu Leu Leu Val Asp His Gly Ser Thr Asp Ala Gly His Trp Ala
[2984] 450 455 460
[2985] Val Glu Gln Val Trp Tyr Asn Gly Lys Phe Tyr Gly Ser Pro Glu Glu
[2986] 465 470 475 480
[2987] Leu Ala Arg Lys Tyr Ala Asp Gly Glu Val Asp Val Val Val Leu Glu
[2988] 485 490 495
[2989] Asp Pro Leu Pro Gly Gly Lys Gly His Asp Ser Thr Glu Glu Pro Pro
[2990] 500 505 510
[2991] Leu Phe Ser Ser His Lys Pro Arg Gly Asp Phe Pro Ser Pro Ile His
[2992] 515 520 525
[2993] Val Ser Gly Pro Arg Leu Val Gln Pro His Gly Pro Arg Phe Arg Leu
[2994] 530 535 540
[2995] Glu Gly Asn Ala Val Leu Tyr Gly Gly Trp Ser Phe Ala Phe Arg Leu
[2996] 545 550 555 560
[2997] Arg Ser Ser Ser Gly Leu Gln Val Leu Asn Val His Phe Gly Gly Glu
[2998] 565 570 575
[2999] Arg Ile Ala Tyr Glu Val Ser Val Gln Glu Ala Val Ala Leu Tyr Gly
[3000] 580 585 590
[3001] Gly His Thr Pro Ala Gly Met Gln Thr Lys Tyr Leu Asp Val Gly Trp
[3002] 595 600 605
[3003] Gly Leu Gly Ser Val Thr His Glu Leu Ala Pro Gly Ile Asp Cys Pro
[3004] 610 615 620
[3005] Glu Thr Ala Thr Phe Leu Asp Thr Phe His Tyr Tyr Asp Ala Asp Asp
[3006] 625 630 635 640
[3007] Pro Val His Tyr Pro Arg Ala Leu Cys Leu Phe Glu Met Pro Thr Gly
[3008] 645 650 655
[3009] Val Pro Leu Arg Arg His Phe Asn Ser Asn Phe Lys Gly Gly Phe Asn
[3010] 660 665 670
[3011] Phe Tyr Ala Gly Leu Lys Gly Gln Val Leu Val Leu Arg Thr Thr Ser
[3012] 675 680 685
[3013] Thr Val Tyr Asn Tyr Asp Tyr Ile Trp Asp Phe Ile Phe Tyr Pro Asn
[3014] 690 695 700
[3015] Gly Val Met Glu Ala Lys Met His Ala Thr Gly Tyr Val His Ala Thr
[3016] 705 710 715 720
[3017] Phe Tyr Thr Pro Glu Gly Leu Arg His Gly Thr Arg Leu His Thr His
[3018] 725 730 735
[3019] Leu Ile Gly Asn Ile His Thr His Leu Val His Tyr Arg Val Asp Leu
[3020] 740 745 750
[3021] Asp Val Ala Gly Thr Lys Asn Ser Phe Gln Thr Leu Gln Met Lys Leu
[3022] 755 760 765
[3023] Glu Asn Ile Thr Asn Pro Trp Ser Pro Arg His Arg Val Val Gln Pro

[3024] 770 775 780
[3025] Thr Leu Glu Gln Thr Gln Tyr Ser Trp Glu Arg Gln Ala Ala Phe Ser
[3026] 785 790 795 800
[3027] Phe Lys Thr Lys Leu Pro Lys Tyr Leu Leu Phe Thr Ser Pro Gln Glu
[3028] 805 810 815
[3029] Asn Pro Trp Gly His Lys Arg Ser Tyr Arg Leu Gln Ile His Ser Met
[3030] 820 825 830
[3031] Ala Asp Gln Val Leu Pro Pro Gly Trp Gln Glu Glu Gln Ala Ile Thr
[3032] 835 840 845
[3033] Trp Ala Arg Tyr Pro Leu Ala Val Thr Lys Tyr Arg Glu Ser Glu Leu
[3034] 850 855 860
[3035] Cys Ser Ser Ser Ile Tyr His Gln Asn Asp Pro Trp His Pro Pro Val
[3036] 865 870 875 880
[3037] Val Phe Glu Gln Phe Leu His Asn Asn Glu Asn Ile Glu Asn Glu Asp
[3038] 885 890 895
[3039] Leu Val Ala Trp Val Thr Val Gly Phe Leu His Ile Pro His Ser Glu
[3040] 900 905 910
[3041] Asp Ile Pro Asn Thr Ala Thr Pro Gly Asn Ser Val Gly Phe Leu Leu
[3042] 915 920 925
[3043] Arg Pro Phe Asn Phe Phe Pro Glu Asp Pro Ser Leu Ala Ser Arg Asp
[3044] 930 935 940
[3045] Thr Val Ile Val Trp Pro Arg Asp Asn Gly Pro Asn Tyr Val Gln Arg
[3046] 945 950 955 960
[3047] Trp Ile Pro Glu Asp Arg Asp Cys Ser Met Pro Pro Pro Phe Ser Tyr
[3048] 965 970 975
[3049] Asn Gly Thr Tyr Arg Pro Val
[3050] 980
[3051] <210> 44
[3052] <211> 983
[3053] <212> PRT
[3054] <213> 人工序列
[3055] <220>
[3056] <223> Fc-hDAO-Hepmut5
[3057] <400> 44
[3058] Met Pro Ala Leu Gly Trp Ala Val Ala Ala Ile Leu Met Leu Gln Thr
[3059] 1 5 10 15
[3060] Ala Met Ala Glu Cys Pro Pro Cys Pro Ala Pro Pro Val Ala Gly Pro
[3061] 20 25 30
[3062] Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser
[3063] 35 40 45
[3064] Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp
[3065] 50 55 60

[3066] Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
[3067] 65 70 75 80
[3068] Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val
[3069] 85 90 95
[3070] Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu
[3071] 100 105 110
[3072] Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys
[3073] 115 120 125
[3074] Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr
[3075] 130 135 140
[3076] Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr
[3077] 145 150 155 160
[3078] Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu
[3079] 165 170 175
[3080] Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu
[3081] 180 185 190
[3082] Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys
[3083] 195 200 205
[3084] Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu
[3085] 210 215 220
[3086] Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
[3087] 225 230 235 240
[3088] Lys Glu Pro Lys Ser Ala Asp Lys Thr His Thr Glu Pro Ser Pro Gly
[3089] 245 250 255
[3090] Thr Leu Pro Arg Lys Ala Gly Val Phe Ser Asp Leu Ser Asn Gln Glu
[3091] 260 265 270
[3092] Leu Lys Ala Val His Ser Phe Leu Trp Ser Lys Lys Glu Leu Arg Leu
[3093] 275 280 285
[3094] Gln Pro Ser Ser Thr Thr Thr Met Ala Lys Asn Thr Val Phe Leu Ile
[3095] 290 295 300
[3096] Glu Met Leu Leu Pro Lys Lys Tyr His Val Leu Arg Phe Leu Asp Lys
[3097] 305 310 315 320
[3098] Gly Glu Arg His Pro Val Arg Glu Ala Arg Ala Val Ile Phe Phe Gly
[3099] 325 330 335
[3100] Asp Gln Glu His Pro Asn Val Thr Glu Phe Ala Val Gly Pro Leu Pro
[3101] 340 345 350
[3102] Gly Pro Cys Tyr Met Arg Ala Leu Ser Pro Arg Pro Gly Tyr Gln Ser
[3103] 355 360 365
[3104] Ser Trp Ala Ser Arg Pro Ile Ser Thr Ala Glu Tyr Ala Leu Leu Tyr
[3105] 370 375 380
[3106] His Thr Leu Gln Glu Ala Thr Lys Pro Leu His Gln Phe Phe Leu Asn
[3107] 385 390 395 400

[3108] Thr Thr Gly Phe Ser Phe Gln Asp Cys His Asp Arg Cys Leu Ala Phe
[3109] 405 410 415
[3110] Thr Asp Val Ala Pro Arg Gly Val Ala Ser Gly Gln Arg Arg Ser Trp
[3111] 420 425 430
[3112] Leu Ile Ile Gln Arg Tyr Val Glu Gly Tyr Phe Leu His Pro Thr Gly
[3113] 435 440 445
[3114] Leu Glu Leu Leu Val Asp His Gly Ser Thr Asp Ala Gly His Trp Ala
[3115] 450 455 460
[3116] Val Glu Gln Val Trp Tyr Asn Gly Lys Phe Tyr Gly Ser Pro Glu Glu
[3117] 465 470 475 480
[3118] Leu Ala Arg Lys Tyr Ala Asp Gly Glu Val Asp Val Val Val Leu Glu
[3119] 485 490 495
[3120] Asp Pro Leu Pro Gly Gly Lys Gly His Asp Ser Thr Glu Glu Pro Pro
[3121] 500 505 510
[3122] Leu Phe Ser Ser His Lys Pro Arg Gly Asp Phe Pro Ser Pro Ile His
[3123] 515 520 525
[3124] Val Ser Gly Pro Arg Leu Val Gln Pro His Gly Pro Arg Phe Arg Leu
[3125] 530 535 540
[3126] Glu Gly Asn Ala Val Leu Tyr Gly Gly Trp Ser Phe Ala Phe Arg Leu
[3127] 545 550 555 560
[3128] Arg Ser Ser Ser Gly Leu Gln Val Leu Asn Val His Phe Gly Gly Glu
[3129] 565 570 575
[3130] Arg Ile Ala Tyr Glu Val Ser Val Gln Glu Ala Val Ala Leu Tyr Gly
[3131] 580 585 590
[3132] Gly His Thr Pro Ala Gly Met Gln Thr Lys Tyr Leu Asp Val Gly Trp
[3133] 595 600 605
[3134] Gly Leu Gly Ser Val Thr His Glu Leu Ala Pro Gly Ile Asp Cys Pro
[3135] 610 615 620
[3136] Glu Thr Ala Thr Phe Leu Asp Thr Phe His Tyr Tyr Asp Ala Asp Asp
[3137] 625 630 635 640
[3138] Pro Val His Tyr Pro Arg Ala Leu Cys Leu Phe Glu Met Pro Thr Gly
[3139] 645 650 655
[3140] Val Pro Leu Arg Arg His Phe Asn Ser Asn Phe Lys Gly Gly Phe Asn
[3141] 660 665 670
[3142] Phe Tyr Ala Gly Leu Lys Gly Gln Val Leu Val Leu Arg Thr Thr Ser
[3143] 675 680 685
[3144] Thr Val Tyr Asn Tyr Asp Tyr Ile Trp Asp Phe Ile Phe Tyr Pro Asn
[3145] 690 695 700
[3146] Gly Val Met Glu Ala Lys Met His Ala Thr Gly Tyr Val His Ala Thr
[3147] 705 710 715 720
[3148] Phe Tyr Thr Pro Glu Gly Leu Arg His Gly Thr Arg Leu His Thr His
[3149] 725 730 735

[3150] Leu Ile Gly Asn Ile His Thr His Leu Val His Tyr Arg Val Asp Leu
[3151] 740 745 750
[3152] Asp Val Ala Gly Thr Lys Asn Ser Phe Gln Thr Leu Gln Met Lys Leu
[3153] 755 760 765
[3154] Glu Asn Ile Thr Asn Pro Trp Ser Pro Arg His Arg Val Val Gln Pro
[3155] 770 775 780
[3156] Thr Leu Glu Gln Thr Gln Tyr Ser Trp Glu Arg Gln Ala Ala Phe Arg
[3157] 785 790 795 800
[3158] Phe Lys Thr Lys Leu Pro Thr Tyr Leu Leu Phe Thr Ser Pro Gln Glu
[3159] 805 810 815
[3160] Asn Pro Trp Gly His Lys Arg Ser Tyr Arg Leu Gln Ile His Ser Met
[3161] 820 825 830
[3162] Ala Asp Gln Val Leu Pro Pro Gly Trp Gln Glu Glu Gln Ala Ile Thr
[3163] 835 840 845
[3164] Trp Ala Arg Tyr Pro Leu Ala Val Thr Lys Tyr Arg Glu Ser Glu Leu
[3165] 850 855 860
[3166] Cys Ser Ser Ser Ile Tyr His Gln Asn Asp Pro Trp His Pro Pro Val
[3167] 865 870 875 880
[3168] Val Phe Glu Gln Phe Leu His Asn Asn Glu Asn Ile Glu Asn Glu Asp
[3169] 885 890 895
[3170] Leu Val Ala Trp Val Thr Val Gly Phe Leu His Ile Pro His Ser Glu
[3171] 900 905 910
[3172] Asp Ile Pro Asn Thr Ala Thr Pro Gly Asn Ser Val Gly Phe Leu Leu
[3173] 915 920 925
[3174] Arg Pro Phe Asn Phe Phe Pro Glu Asp Pro Ser Leu Ala Ser Arg Asp
[3175] 930 935 940
[3176] Thr Val Ile Val Trp Pro Arg Asp Asn Gly Pro Asn Tyr Val Gln Arg
[3177] 945 950 955 960
[3178] Trp Ile Pro Glu Asp Arg Asp Cys Ser Met Pro Pro Pro Phe Ser Tyr
[3179] 965 970 975
[3180] Asn Gly Thr Tyr Arg Pro Val
[3181] 980
[3182] <210> 45
[3183] <211> 983
[3184] <212> PRT
[3185] <213> 人工序列
[3186] <220>
[3187] <223> Fc-hDAO-Hepmut6
[3188] <400> 45
[3189] Met Pro Ala Leu Gly Trp Ala Val Ala Ala Ile Leu Met Leu Gln Thr
[3190] 1 5 10 15
[3191] Ala Met Ala Glu Cys Pro Pro Cys Pro Ala Pro Pro Val Ala Gly Pro

[3192] 20 25 30
[3193] Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser
[3194] 35 40 45
[3195] Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp
[3196] 50 55 60
[3197] Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
[3198] 65 70 75 80
[3199] Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val
[3200] 85 90 95
[3201] Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu
[3202] 100 105 110
[3203] Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys
[3204] 115 120 125
[3205] Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr
[3206] 130 135 140
[3207] Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr
[3208] 145 150 155 160
[3209] Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu
[3210] 165 170 175
[3211] Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu
[3212] 180 185 190
[3213] Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys
[3214] 195 200 205
[3215] Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu
[3216] 210 215 220
[3217] Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
[3218] 225 230 235 240
[3219] Lys Glu Pro Lys Ser Ala Asp Lys Thr His Thr Glu Pro Ser Pro Gly
[3220] 245 250 255
[3221] Thr Leu Pro Arg Lys Ala Gly Val Phe Ser Asp Leu Ser Asn Gln Glu
[3222] 260 265 270
[3223] Leu Lys Ala Val His Ser Phe Leu Trp Ser Lys Lys Glu Leu Arg Leu
[3224] 275 280 285
[3225] Gln Pro Ser Ser Thr Thr Thr Met Ala Lys Asn Thr Val Phe Leu Ile
[3226] 290 295 300
[3227] Glu Met Leu Leu Pro Lys Lys Tyr His Val Leu Arg Phe Leu Asp Lys
[3228] 305 310 315 320
[3229] Gly Glu Arg His Pro Val Arg Glu Ala Arg Ala Val Ile Phe Phe Gly
[3230] 325 330 335
[3231] Asp Gln Glu His Pro Asn Val Thr Glu Phe Ala Val Gly Pro Leu Pro
[3232] 340 345 350
[3233] Gly Pro Cys Tyr Met Arg Ala Leu Ser Pro Arg Pro Gly Tyr Gln Ser

[3234] 355 360 365
[3235] Ser Trp Ala Ser Arg Pro Ile Ser Thr Ala Glu Tyr Ala Leu Leu Tyr
[3236] 370 375 380
[3237] His Thr Leu Gln Glu Ala Thr Lys Pro Leu His Gln Phe Phe Leu Asn
[3238] 385 390 395 400
[3239] Thr Thr Gly Phe Ser Phe Gln Asp Cys His Asp Arg Cys Leu Ala Phe
[3240] 405 410 415
[3241] Thr Asp Val Ala Pro Arg Gly Val Ala Ser Gly Gln Arg Arg Ser Trp
[3242] 420 425 430
[3243] Leu Ile Ile Gln Arg Tyr Val Glu Gly Tyr Phe Leu His Pro Thr Gly
[3244] 435 440 445
[3245] Leu Glu Leu Leu Val Asp His Gly Ser Thr Asp Ala Gly His Trp Ala
[3246] 450 455 460
[3247] Val Glu Gln Val Trp Tyr Asn Gly Lys Phe Tyr Gly Ser Pro Glu Glu
[3248] 465 470 475 480
[3249] Leu Ala Arg Lys Tyr Ala Asp Gly Glu Val Asp Val Val Val Leu Glu
[3250] 485 490 495
[3251] Asp Pro Leu Pro Gly Gly Lys Gly His Asp Ser Thr Glu Glu Pro Pro
[3252] 500 505 510
[3253] Leu Phe Ser Ser His Lys Pro Arg Gly Asp Phe Pro Ser Pro Ile His
[3254] 515 520 525
[3255] Val Ser Gly Pro Arg Leu Val Gln Pro His Gly Pro Arg Phe Arg Leu
[3256] 530 535 540
[3257] Glu Gly Asn Ala Val Leu Tyr Gly Gly Trp Ser Phe Ala Phe Arg Leu
[3258] 545 550 555 560
[3259] Arg Ser Ser Ser Gly Leu Gln Val Leu Asn Val His Phe Gly Gly Glu
[3260] 565 570 575
[3261] Arg Ile Ala Tyr Glu Val Ser Val Gln Glu Ala Val Ala Leu Tyr Gly
[3262] 580 585 590
[3263] Gly His Thr Pro Ala Gly Met Gln Thr Lys Tyr Leu Asp Val Gly Trp
[3264] 595 600 605
[3265] Gly Leu Gly Ser Val Thr His Glu Leu Ala Pro Gly Ile Asp Cys Pro
[3266] 610 615 620
[3267] Glu Thr Ala Thr Phe Leu Asp Thr Phe His Tyr Tyr Asp Ala Asp Asp
[3268] 625 630 635 640
[3269] Pro Val His Tyr Pro Arg Ala Leu Cys Leu Phe Glu Met Pro Thr Gly
[3270] 645 650 655
[3271] Val Pro Leu Arg Arg His Phe Asn Ser Asn Phe Lys Gly Gly Phe Asn
[3272] 660 665 670
[3273] Phe Tyr Ala Gly Leu Lys Gly Gln Val Leu Val Leu Arg Thr Thr Ser
[3274] 675 680 685
[3275] Thr Val Tyr Asn Tyr Asp Tyr Ile Trp Asp Phe Ile Phe Tyr Pro Asn

[3276] 690 695 700

[3277] Gly Val Met Glu Ala Lys Met His Ala Thr Gly Tyr Val His Ala Thr

[3278] 705 710 715 720

[3279] Phe Tyr Thr Pro Glu Gly Leu Arg His Gly Thr Arg Leu His Thr His

[3280] 725 730 735

[3281] Leu Ile Gly Asn Ile His Thr His Leu Val His Tyr Arg Val Asp Leu

[3282] 740 745 750

[3283] Asp Val Ala Gly Thr Lys Asn Ser Phe Gln Thr Leu Gln Met Lys Leu

[3284] 755 760 765

[3285] Glu Asn Ile Thr Asn Pro Trp Ser Pro Arg His Arg Val Val Gln Pro

[3286] 770 775 780

[3287] Thr Leu Glu Gln Thr Gln Tyr Ser Trp Glu Arg Gln Ala Ala Phe Arg

[3288] 785 790 795 800

[3289] Phe Gly Gln Thr Leu Pro Lys Tyr Leu Leu Phe Thr Ser Pro Gln Glu

[3290] 805 810 815

[3291] Asn Pro Trp Gly His Lys Arg Ser Tyr Arg Leu Gln Ile His Ser Met

[3292] 820 825 830

[3293] Ala Asp Gln Val Leu Pro Pro Gly Trp Gln Glu Glu Gln Ala Ile Thr

[3294] 835 840 845

[3295] Trp Ala Arg Tyr Pro Leu Ala Val Thr Lys Tyr Arg Glu Ser Glu Leu

[3296] 850 855 860

[3297] Cys Ser Ser Ser Ile Tyr His Gln Asn Asp Pro Trp His Pro Pro Val

[3298] 865 870 875 880

[3299] Val Phe Glu Gln Phe Leu His Asn Asn Glu Asn Ile Glu Asn Glu Asp

[3300] 885 890 895

[3301] Leu Val Ala Trp Val Thr Val Gly Phe Leu His Ile Pro His Ser Glu

[3302] 900 905 910

[3303] Asp Ile Pro Asn Thr Ala Thr Pro Gly Asn Ser Val Gly Phe Leu Leu

[3304] 915 920 925

[3305] Arg Pro Phe Asn Phe Phe Pro Glu Asp Pro Ser Leu Ala Ser Arg Asp

[3306] 930 935 940

[3307] Thr Val Ile Val Trp Pro Arg Asp Asn Gly Pro Asn Tyr Val Gln Arg

[3308] 945 950 955 960

[3309] Trp Ile Pro Glu Asp Arg Asp Cys Ser Met Pro Pro Pro Phe Ser Tyr

[3310] 965 970 975

[3311] Asn Gly Thr Tyr Arg Pro Val

[3312] 980

[3313] <210> 46

[3314] <211> 983

[3315] <212> PRT

[3316] <213> 人工序列

[3317] <220>

[3318] <223> Fc-hDAO-Hepmut7

[3319] <400> 46

[3320] Met Pro Ala Leu Gly Trp Ala Val Ala Ala Ile Leu Met Leu Gln Thr
[3321] 1 5 10 15

[3322] Ala Met Ala Glu Cys Pro Pro Cys Pro Ala Pro Pro Val Ala Gly Pro
[3323] 20 25 30

[3324] Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser
[3325] 35 40 45

[3326] Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp
[3327] 50 55 60

[3328] Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
[3329] 65 70 75 80

[3330] Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val
[3331] 85 90 95

[3332] Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu
[3333] 100 105 110

[3334] Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys
[3335] 115 120 125

[3336] Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr
[3337] 130 135 140

[3338] Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr
[3339] 145 150 155 160

[3340] Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu
[3341] 165 170 175

[3342] Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu
[3343] 180 185 190

[3344] Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys
[3345] 195 200 205

[3346] Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu
[3347] 210 215 220

[3348] Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
[3349] 225 230 235 240

[3350] Lys Glu Pro Lys Ser Ala Asp Lys Thr His Thr Glu Pro Ser Pro Gly
[3351] 245 250 255

[3352] Thr Leu Pro Arg Lys Ala Gly Val Phe Ser Asp Leu Ser Asn Gln Glu
[3353] 260 265 270

[3354] Leu Lys Ala Val His Ser Phe Leu Trp Ser Lys Lys Glu Leu Arg Leu
[3355] 275 280 285

[3356] Gln Pro Ser Ser Thr Thr Thr Met Ala Lys Asn Thr Val Phe Leu Ile
[3357] 290 295 300

[3358] Glu Met Leu Leu Pro Lys Lys Tyr His Val Leu Arg Phe Leu Asp Lys
[3359] 305 310 315 320

[3360] Gly Glu Arg His Pro Val Arg Glu Ala Arg Ala Val Ile Phe Phe Gly
[3361] 325 330 335
[3362] Asp Gln Glu His Pro Asn Val Thr Glu Phe Ala Val Gly Pro Leu Pro
[3363] 340 345 350
[3364] Gly Pro Cys Tyr Met Arg Ala Leu Ser Pro Arg Pro Gly Tyr Gln Ser
[3365] 355 360 365
[3366] Ser Trp Ala Ser Arg Pro Ile Ser Thr Ala Glu Tyr Ala Leu Leu Tyr
[3367] 370 375 380
[3368] His Thr Leu Gln Glu Ala Thr Lys Pro Leu His Gln Phe Phe Leu Asn
[3369] 385 390 395 400
[3370] Thr Thr Gly Phe Ser Phe Gln Asp Cys His Asp Arg Cys Leu Ala Phe
[3371] 405 410 415
[3372] Thr Asp Val Ala Pro Arg Gly Val Ala Ser Gly Gln Arg Arg Ser Trp
[3373] 420 425 430
[3374] Leu Ile Ile Gln Arg Tyr Val Glu Gly Tyr Phe Leu His Pro Thr Gly
[3375] 435 440 445
[3376] Leu Glu Leu Leu Val Asp His Gly Ser Thr Asp Ala Gly His Trp Ala
[3377] 450 455 460
[3378] Val Glu Gln Val Trp Tyr Asn Gly Lys Phe Tyr Gly Ser Pro Glu Glu
[3379] 465 470 475 480
[3380] Leu Ala Arg Lys Tyr Ala Asp Gly Glu Val Asp Val Val Val Leu Glu
[3381] 485 490 495
[3382] Asp Pro Leu Pro Gly Gly Lys Gly His Asp Ser Thr Glu Glu Pro Pro
[3383] 500 505 510
[3384] Leu Phe Ser Ser His Lys Pro Arg Gly Asp Phe Pro Ser Pro Ile His
[3385] 515 520 525
[3386] Val Ser Gly Pro Arg Leu Val Gln Pro His Gly Pro Arg Phe Arg Leu
[3387] 530 535 540
[3388] Glu Gly Asn Ala Val Leu Tyr Gly Gly Trp Ser Phe Ala Phe Arg Leu
[3389] 545 550 555 560
[3390] Arg Ser Ser Ser Gly Leu Gln Val Leu Asn Val His Phe Gly Gly Glu
[3391] 565 570 575
[3392] Arg Ile Ala Tyr Glu Val Ser Val Gln Glu Ala Val Ala Leu Tyr Gly
[3393] 580 585 590
[3394] Gly His Thr Pro Ala Gly Met Gln Thr Lys Tyr Leu Asp Val Gly Trp
[3395] 595 600 605
[3396] Gly Leu Gly Ser Val Thr His Glu Leu Ala Pro Gly Ile Asp Cys Pro
[3397] 610 615 620
[3398] Glu Thr Ala Thr Phe Leu Asp Thr Phe His Tyr Tyr Asp Ala Asp Asp
[3399] 625 630 635 640
[3400] Pro Val His Tyr Pro Arg Ala Leu Cys Leu Phe Glu Met Pro Thr Gly
[3401] 645 650 655

[3402] Val Pro Leu Arg Arg His Phe Asn Ser Asn Phe Lys Gly Gly Phe Asn
[3403] 660 665 670
[3404] Phe Tyr Ala Gly Leu Lys Gly Gln Val Leu Val Leu Arg Thr Thr Ser
[3405] 675 680 685
[3406] Thr Val Tyr Asn Tyr Asp Tyr Ile Trp Asp Phe Ile Phe Tyr Pro Asn
[3407] 690 695 700
[3408] Gly Val Met Glu Ala Lys Met His Ala Thr Gly Tyr Val His Ala Thr
[3409] 705 710 715 720
[3410] Phe Tyr Thr Pro Glu Gly Leu Arg His Gly Thr Arg Leu His Thr His
[3411] 725 730 735
[3412] Leu Ile Gly Asn Ile His Thr His Leu Val His Tyr Arg Val Asp Leu
[3413] 740 745 750
[3414] Asp Val Ala Gly Thr Lys Asn Ser Phe Gln Thr Leu Gln Met Lys Leu
[3415] 755 760 765
[3416] Glu Asn Ile Thr Asn Pro Trp Ser Pro Arg His Arg Val Val Gln Pro
[3417] 770 775 780
[3418] Thr Leu Glu Gln Thr Gln Tyr Ser Trp Glu Arg Gln Ala Ala Phe Ser
[3419] 785 790 795 800
[3420] Phe Lys Arg Lys Leu Pro Thr Tyr Leu Leu Phe Thr Ser Pro Gln Glu
[3421] 805 810 815
[3422] Asn Pro Trp Gly His Lys Arg Ser Tyr Arg Leu Gln Ile His Ser Met
[3423] 820 825 830
[3424] Ala Asp Gln Val Leu Pro Pro Gly Trp Gln Glu Glu Gln Ala Ile Thr
[3425] 835 840 845
[3426] Trp Ala Arg Tyr Pro Leu Ala Val Thr Lys Tyr Arg Glu Ser Glu Leu
[3427] 850 855 860
[3428] Cys Ser Ser Ser Ile Tyr His Gln Asn Asp Pro Trp His Pro Pro Val
[3429] 865 870 875 880
[3430] Val Phe Glu Gln Phe Leu His Asn Asn Glu Asn Ile Glu Asn Glu Asp
[3431] 885 890 895
[3432] Leu Val Ala Trp Val Thr Val Gly Phe Leu His Ile Pro His Ser Glu
[3433] 900 905 910
[3434] Asp Ile Pro Asn Thr Ala Thr Pro Gly Asn Ser Val Gly Phe Leu Leu
[3435] 915 920 925
[3436] Arg Pro Phe Asn Phe Phe Pro Glu Asp Pro Ser Leu Ala Ser Arg Asp
[3437] 930 935 940
[3438] Thr Val Ile Val Trp Pro Arg Asp Asn Gly Pro Asn Tyr Val Gln Arg
[3439] 945 950 955 960
[3440] Trp Ile Pro Glu Asp Arg Asp Cys Ser Met Pro Pro Pro Phe Ser Tyr
[3441] 965 970 975
[3442] Asn Gly Thr Tyr Arg Pro Val
[3443] 980

[3444] <210> 47

[3445] <211> 983

[3446] <212> PRT

[3447] <213> 人工序列

[3448] <220>

[3449] <223> Fc-hDAO-Cysmut

[3450] <400> 47

[3451] Met Pro Ala Leu Gly Trp Ala Val Ala Ala Ile Leu Met Leu Gln Thr

[3452] 1 5 10 15

[3453] Ala Met Ala Glu Cys Pro Pro Cys Pro Ala Pro Pro Val Ala Gly Pro

[3454] 20 25 30

[3455] Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser

[3456] 35 40 45

[3457] Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp

[3458] 50 55 60

[3459] Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn

[3460] 65 70 75 80

[3461] Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val

[3462] 85 90 95

[3463] Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu

[3464] 100 105 110

[3465] Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys

[3466] 115 120 125

[3467] Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr

[3468] 130 135 140

[3469] Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr

[3470] 145 150 155 160

[3471] Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu

[3472] 165 170 175

[3473] Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu

[3474] 180 185 190

[3475] Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys

[3476] 195 200 205

[3477] Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu

[3478] 210 215 220

[3479] Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly

[3480] 225 230 235 240

[3481] Lys Glu Pro Lys Ser Ala Asp Lys Thr His Thr Glu Pro Ser Pro Gly

[3482] 245 250 255

[3483] Thr Leu Pro Arg Lys Ala Gly Val Phe Ser Asp Leu Ser Asn Gln Glu

[3484] 260 265 270

[3485] Leu Lys Ala Val His Ser Phe Leu Trp Ser Lys Lys Glu Leu Arg Leu

[3486] 275 280 285
[3487] Gln Pro Ser Ser Thr Thr Thr Met Ala Lys Asn Thr Val Phe Leu Ile
[3488] 290 295 300
[3489] Glu Met Leu Leu Pro Lys Lys Tyr His Val Leu Arg Phe Leu Asp Lys
[3490] 305 310 315 320
[3491] Gly Glu Arg His Pro Val Arg Glu Ala Arg Ala Val Ile Phe Phe Gly
[3492] 325 330 335
[3493] Asp Gln Glu His Pro Asn Val Thr Glu Phe Ala Val Gly Pro Leu Pro
[3494] 340 345 350
[3495] Gly Pro Ala Tyr Met Arg Ala Leu Ser Pro Arg Pro Gly Tyr Gln Ser
[3496] 355 360 365
[3497] Ser Trp Ala Ser Arg Pro Ile Ser Thr Ala Glu Tyr Ala Leu Leu Tyr
[3498] 370 375 380
[3499] His Thr Leu Gln Glu Ala Thr Lys Pro Leu His Gln Phe Phe Leu Asn
[3500] 385 390 395 400
[3501] Thr Thr Gly Phe Ser Phe Gln Asp Cys His Asp Arg Cys Leu Ala Phe
[3502] 405 410 415
[3503] Thr Asp Val Ala Pro Arg Gly Val Ala Ser Gly Gln Arg Arg Ser Trp
[3504] 420 425 430
[3505] Leu Ile Ile Gln Arg Tyr Val Glu Gly Tyr Phe Leu His Pro Thr Gly
[3506] 435 440 445
[3507] Leu Glu Leu Leu Val Asp His Gly Ser Thr Asp Ala Gly His Trp Ala
[3508] 450 455 460
[3509] Val Glu Gln Val Trp Tyr Asn Gly Lys Phe Tyr Gly Ser Pro Glu Glu
[3510] 465 470 475 480
[3511] Leu Ala Arg Lys Tyr Ala Asp Gly Glu Val Asp Val Val Val Leu Glu
[3512] 485 490 495
[3513] Asp Pro Leu Pro Gly Gly Lys Gly His Asp Ser Thr Glu Glu Pro Pro
[3514] 500 505 510
[3515] Leu Phe Ser Ser His Lys Pro Arg Gly Asp Phe Pro Ser Pro Ile His
[3516] 515 520 525
[3517] Val Ser Gly Pro Arg Leu Val Gln Pro His Gly Pro Arg Phe Arg Leu
[3518] 530 535 540
[3519] Glu Gly Asn Ala Val Leu Tyr Gly Gly Trp Ser Phe Ala Phe Arg Leu
[3520] 545 550 555 560
[3521] Arg Ser Ser Ser Gly Leu Gln Val Leu Asn Val His Phe Gly Gly Glu
[3522] 565 570 575
[3523] Arg Ile Ala Tyr Glu Val Ser Val Gln Glu Ala Val Ala Leu Tyr Gly
[3524] 580 585 590
[3525] Gly His Thr Pro Ala Gly Met Gln Thr Lys Tyr Leu Asp Val Gly Trp
[3526] 595 600 605
[3527] Gly Leu Gly Ser Val Thr His Glu Leu Ala Pro Gly Ile Asp Cys Pro

[3528] 610 615 620
[3529] Glu Thr Ala Thr Phe Leu Asp Thr Phe His Tyr Tyr Asp Ala Asp Asp
[3530] 625 630 635 640
[3531] Pro Val His Tyr Pro Arg Ala Leu Cys Leu Phe Glu Met Pro Thr Gly
[3532] 645 650 655
[3533] Val Pro Leu Arg Arg His Phe Asn Ser Asn Phe Lys Gly Gly Phe Asn
[3534] 660 665 670
[3535] Phe Tyr Ala Gly Leu Lys Gly Gln Val Leu Val Leu Arg Thr Thr Ser
[3536] 675 680 685
[3537] Thr Val Tyr Asn Tyr Asp Tyr Ile Trp Asp Phe Ile Phe Tyr Pro Asn
[3538] 690 695 700
[3539] Gly Val Met Glu Ala Lys Met His Ala Thr Gly Tyr Val His Ala Thr
[3540] 705 710 715 720
[3541] Phe Tyr Thr Pro Glu Gly Leu Arg His Gly Thr Arg Leu His Thr His
[3542] 725 730 735
[3543] Leu Ile Gly Asn Ile His Thr His Leu Val His Tyr Arg Val Asp Leu
[3544] 740 745 750
[3545] Asp Val Ala Gly Thr Lys Asn Ser Phe Gln Thr Leu Gln Met Lys Leu
[3546] 755 760 765
[3547] Glu Asn Ile Thr Asn Pro Trp Ser Pro Arg His Arg Val Val Gln Pro
[3548] 770 775 780
[3549] Thr Leu Glu Gln Thr Gln Tyr Ser Trp Glu Arg Gln Ala Ala Phe Arg
[3550] 785 790 795 800
[3551] Phe Lys Arg Lys Leu Pro Lys Tyr Leu Leu Phe Thr Ser Pro Gln Glu
[3552] 805 810 815
[3553] Asn Pro Trp Gly His Lys Arg Ser Tyr Arg Leu Gln Ile His Ser Met
[3554] 820 825 830
[3555] Ala Asp Gln Val Leu Pro Pro Gly Trp Gln Glu Glu Gln Ala Ile Thr
[3556] 835 840 845
[3557] Trp Ala Arg Tyr Pro Leu Ala Val Thr Lys Tyr Arg Glu Ser Glu Leu
[3558] 850 855 860
[3559] Cys Ser Ser Ser Ile Tyr His Gln Asn Asp Pro Trp His Pro Pro Val
[3560] 865 870 875 880
[3561] Val Phe Glu Gln Phe Leu His Asn Asn Glu Asn Ile Glu Asn Glu Asp
[3562] 885 890 895
[3563] Leu Val Ala Trp Val Thr Val Gly Phe Leu His Ile Pro His Ser Glu
[3564] 900 905 910
[3565] Asp Ile Pro Asn Thr Ala Thr Pro Gly Asn Ser Val Gly Phe Leu Leu
[3566] 915 920 925
[3567] Arg Pro Phe Asn Phe Phe Pro Glu Asp Pro Ser Leu Ala Ser Arg Asp
[3568] 930 935 940
[3569] Thr Val Ile Val Trp Pro Arg Asp Asn Gly Pro Asn Tyr Val Gln Arg

[3570] 945 950 955 960
[3571] Trp Ile Pro Glu Asp Arg Asp Cys Ser Met Pro Pro Pro Phe Ser Tyr
[3572] 965 970 975
[3573] Asn Gly Thr Tyr Arg Pro Val
[3574] 980
[3575] <210> 48
[3576] <211> 983
[3577] <212> PRT
[3578] <213> 人工序列
[3579] <220>
[3580] <223> Fc-hDAO-Hepmut1-Cysmut
[3581] <400> 48
[3582] Met Pro Ala Leu Gly Trp Ala Val Ala Ala Ile Leu Met Leu Gln Thr
[3583] 1 5 10 15
[3584] Ala Met Ala Glu Cys Pro Pro Cys Pro Ala Pro Pro Val Ala Gly Pro
[3585] 20 25 30
[3586] Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser
[3587] 35 40 45
[3588] Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp
[3589] 50 55 60
[3590] Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
[3591] 65 70 75 80
[3592] Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val
[3593] 85 90 95
[3594] Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu
[3595] 100 105 110
[3596] Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys
[3597] 115 120 125
[3598] Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr
[3599] 130 135 140
[3600] Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr
[3601] 145 150 155 160
[3602] Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu
[3603] 165 170 175
[3604] Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu
[3605] 180 185 190
[3606] Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys
[3607] 195 200 205
[3608] Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu
[3609] 210 215 220
[3610] Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
[3611] 225 230 235 240

[3612] Lys Glu Pro Lys Ser Ala Asp Lys Thr His Thr Glu Pro Ser Pro Gly
[3613] 245 250 255
[3614] Thr Leu Pro Arg Lys Ala Gly Val Phe Ser Asp Leu Ser Asn Gln Glu
[3615] 260 265 270
[3616] Leu Lys Ala Val His Ser Phe Leu Trp Ser Lys Lys Glu Leu Arg Leu
[3617] 275 280 285
[3618] Gln Pro Ser Ser Thr Thr Thr Met Ala Lys Asn Thr Val Phe Leu Ile
[3619] 290 295 300
[3620] Glu Met Leu Leu Pro Lys Lys Tyr His Val Leu Arg Phe Leu Asp Lys
[3621] 305 310 315 320
[3622] Gly Glu Arg His Pro Val Arg Glu Ala Arg Ala Val Ile Phe Phe Gly
[3623] 325 330 335
[3624] Asp Gln Glu His Pro Asn Val Thr Glu Phe Ala Val Gly Pro Leu Pro
[3625] 340 345 350
[3626] Gly Pro Ala Tyr Met Arg Ala Leu Ser Pro Arg Pro Gly Tyr Gln Ser
[3627] 355 360 365
[3628] Ser Trp Ala Ser Arg Pro Ile Ser Thr Ala Glu Tyr Ala Leu Leu Tyr
[3629] 370 375 380
[3630] His Thr Leu Gln Glu Ala Thr Lys Pro Leu His Gln Phe Phe Leu Asn
[3631] 385 390 395 400
[3632] Thr Thr Gly Phe Ser Phe Gln Asp Cys His Asp Arg Cys Leu Ala Phe
[3633] 405 410 415
[3634] Thr Asp Val Ala Pro Arg Gly Val Ala Ser Gly Gln Arg Arg Ser Trp
[3635] 420 425 430
[3636] Leu Ile Ile Gln Arg Tyr Val Glu Gly Tyr Phe Leu His Pro Thr Gly
[3637] 435 440 445
[3638] Leu Glu Leu Leu Val Asp His Gly Ser Thr Asp Ala Gly His Trp Ala
[3639] 450 455 460
[3640] Val Glu Gln Val Trp Tyr Asn Gly Lys Phe Tyr Gly Ser Pro Glu Glu
[3641] 465 470 475 480
[3642] Leu Ala Arg Lys Tyr Ala Asp Gly Glu Val Asp Val Val Val Leu Glu
[3643] 485 490 495
[3644] Asp Pro Leu Pro Gly Gly Lys Gly His Asp Ser Thr Glu Glu Pro Pro
[3645] 500 505 510
[3646] Leu Phe Ser Ser His Lys Pro Arg Gly Asp Phe Pro Ser Pro Ile His
[3647] 515 520 525
[3648] Val Ser Gly Pro Arg Leu Val Gln Pro His Gly Pro Arg Phe Arg Leu
[3649] 530 535 540
[3650] Glu Gly Asn Ala Val Leu Tyr Gly Gly Trp Ser Phe Ala Phe Arg Leu
[3651] 545 550 555 560
[3652] Arg Ser Ser Ser Gly Leu Gln Val Leu Asn Val His Phe Gly Gly Glu
[3653] 565 570 575

[3654] Arg Ile Ala Tyr Glu Val Ser Val Gln Glu Ala Val Ala Leu Tyr Gly
[3655] 580 585 590
[3656] Gly His Thr Pro Ala Gly Met Gln Thr Lys Tyr Leu Asp Val Gly Trp
[3657] 595 600 605
[3658] Gly Leu Gly Ser Val Thr His Glu Leu Ala Pro Gly Ile Asp Cys Pro
[3659] 610 615 620
[3660] Glu Thr Ala Thr Phe Leu Asp Thr Phe His Tyr Tyr Asp Ala Asp Asp
[3661] 625 630 635 640
[3662] Pro Val His Tyr Pro Arg Ala Leu Cys Leu Phe Glu Met Pro Thr Gly
[3663] 645 650 655
[3664] Val Pro Leu Arg Arg His Phe Asn Ser Asn Phe Lys Gly Gly Phe Asn
[3665] 660 665 670
[3666] Phe Tyr Ala Gly Leu Lys Gly Gln Val Leu Val Leu Arg Thr Thr Ser
[3667] 675 680 685
[3668] Thr Val Tyr Asn Tyr Asp Tyr Ile Trp Asp Phe Ile Phe Tyr Pro Asn
[3669] 690 695 700
[3670] Gly Val Met Glu Ala Lys Met His Ala Thr Gly Tyr Val His Ala Thr
[3671] 705 710 715 720
[3672] Phe Tyr Thr Pro Glu Gly Leu Arg His Gly Thr Arg Leu His Thr His
[3673] 725 730 735
[3674] Leu Ile Gly Asn Ile His Thr His Leu Val His Tyr Arg Val Asp Leu
[3675] 740 745 750
[3676] Asp Val Ala Gly Thr Lys Asn Ser Phe Gln Thr Leu Gln Met Lys Leu
[3677] 755 760 765
[3678] Glu Asn Ile Thr Asn Pro Trp Ser Pro Arg His Arg Val Val Gln Pro
[3679] 770 775 780
[3680] Thr Leu Glu Gln Thr Gln Tyr Ser Trp Glu Arg Gln Ala Ala Phe Ser
[3681] 785 790 795 800
[3682] Phe Lys Arg Lys Leu Pro Lys Tyr Leu Leu Phe Thr Ser Pro Gln Glu
[3683] 805 810 815
[3684] Asn Pro Trp Gly His Lys Arg Ser Tyr Arg Leu Gln Ile His Ser Met
[3685] 820 825 830
[3686] Ala Asp Gln Val Leu Pro Pro Gly Trp Gln Glu Glu Gln Ala Ile Thr
[3687] 835 840 845
[3688] Trp Ala Arg Tyr Pro Leu Ala Val Thr Lys Tyr Arg Glu Ser Glu Leu
[3689] 850 855 860
[3690] Cys Ser Ser Ser Ile Tyr His Gln Asn Asp Pro Trp His Pro Pro Val
[3691] 865 870 875 880
[3692] Val Phe Glu Gln Phe Leu His Asn Asn Glu Asn Ile Glu Asn Glu Asp
[3693] 885 890 895
[3694] Leu Val Ala Trp Val Thr Val Gly Phe Leu His Ile Pro His Ser Glu
[3695] 900 905 910

[3696] Asp Ile Pro Asn Thr Ala Thr Pro Gly Asn Ser Val Gly Phe Leu Leu
[3697] 915 920 925
[3698] Arg Pro Phe Asn Phe Phe Pro Glu Asp Pro Ser Leu Ala Ser Arg Asp
[3699] 930 935 940
[3700] Thr Val Ile Val Trp Pro Arg Asp Asn Gly Pro Asn Tyr Val Gln Arg
[3701] 945 950 955 960
[3702] Trp Ile Pro Glu Asp Arg Asp Cys Ser Met Pro Pro Pro Phe Ser Tyr
[3703] 965 970 975
[3704] Asn Gly Thr Tyr Arg Pro Val
[3705] 980
[3706] <210> 49
[3707] <211> 983
[3708] <212> PRT
[3709] <213> 人工序列
[3710] <220>
[3711] <223> Fc-hDAO-Hepmut2-Cysmut
[3712] <400> 49
[3713] Met Pro Ala Leu Gly Trp Ala Val Ala Ala Ile Leu Met Leu Gln Thr
[3714] 1 5 10 15
[3715] Ala Met Ala Glu Cys Pro Pro Cys Pro Ala Pro Pro Val Ala Gly Pro
[3716] 20 25 30
[3717] Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser
[3718] 35 40 45
[3719] Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp
[3720] 50 55 60
[3721] Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
[3722] 65 70 75 80
[3723] Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val
[3724] 85 90 95
[3725] Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu
[3726] 100 105 110
[3727] Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys
[3728] 115 120 125
[3729] Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr
[3730] 130 135 140
[3731] Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr
[3732] 145 150 155 160
[3733] Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu
[3734] 165 170 175
[3735] Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu
[3736] 180 185 190
[3737] Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys

[3738] 195 200 205

[3739] Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu

[3740] 210 215 220

[3741] Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly

[3742] 225 230 235 240

[3743] Lys Glu Pro Lys Ser Ala Asp Lys Thr His Thr Glu Pro Ser Pro Gly

[3744] 245 250 255

[3745] Thr Leu Pro Arg Lys Ala Gly Val Phe Ser Asp Leu Ser Asn Gln Glu

[3746] 260 265 270

[3747] Leu Lys Ala Val His Ser Phe Leu Trp Ser Lys Lys Glu Leu Arg Leu

[3748] 275 280 285

[3749] Gln Pro Ser Ser Thr Thr Thr Met Ala Lys Asn Thr Val Phe Leu Ile

[3750] 290 295 300

[3751] Glu Met Leu Leu Pro Lys Lys Tyr His Val Leu Arg Phe Leu Asp Lys

[3752] 305 310 315 320

[3753] Gly Glu Arg His Pro Val Arg Glu Ala Arg Ala Val Ile Phe Phe Gly

[3754] 325 330 335

[3755] Asp Gln Glu His Pro Asn Val Thr Glu Phe Ala Val Gly Pro Leu Pro

[3756] 340 345 350

[3757] Gly Pro Ala Tyr Met Arg Ala Leu Ser Pro Arg Pro Gly Tyr Gln Ser

[3758] 355 360 365

[3759] Ser Trp Ala Ser Arg Pro Ile Ser Thr Ala Glu Tyr Ala Leu Leu Tyr

[3760] 370 375 380

[3761] His Thr Leu Gln Glu Ala Thr Lys Pro Leu His Gln Phe Phe Leu Asn

[3762] 385 390 395 400

[3763] Thr Thr Gly Phe Ser Phe Gln Asp Cys His Asp Arg Cys Leu Ala Phe

[3764] 405 410 415

[3765] Thr Asp Val Ala Pro Arg Gly Val Ala Ser Gly Gln Arg Arg Ser Trp

[3766] 420 425 430

[3767] Leu Ile Ile Gln Arg Tyr Val Glu Gly Tyr Phe Leu His Pro Thr Gly

[3768] 435 440 445

[3769] Leu Glu Leu Leu Val Asp His Gly Ser Thr Asp Ala Gly His Trp Ala

[3770] 450 455 460

[3771] Val Glu Gln Val Trp Tyr Asn Gly Lys Phe Tyr Gly Ser Pro Glu Glu

[3772] 465 470 475 480

[3773] Leu Ala Arg Lys Tyr Ala Asp Gly Glu Val Asp Val Val Val Leu Glu

[3774] 485 490 495

[3775] Asp Pro Leu Pro Gly Gly Lys Gly His Asp Ser Thr Glu Glu Pro Pro

[3776] 500 505 510

[3777] Leu Phe Ser Ser His Lys Pro Arg Gly Asp Phe Pro Ser Pro Ile His

[3778] 515 520 525

[3779] Val Ser Gly Pro Arg Leu Val Gln Pro His Gly Pro Arg Phe Arg Leu

[3780] 530 535 540

[3781] Glu Gly Asn Ala Val Leu Tyr Gly Gly Trp Ser Phe Ala Phe Arg Leu

[3782] 545 550 555 560

[3783] Arg Ser Ser Ser Gly Leu Gln Val Leu Asn Val His Phe Gly Gly Glu

[3784] 565 570 575

[3785] Arg Ile Ala Tyr Glu Val Ser Val Gln Glu Ala Val Ala Leu Tyr Gly

[3786] 580 585 590

[3787] Gly His Thr Pro Ala Gly Met Gln Thr Lys Tyr Leu Asp Val Gly Trp

[3788] 595 600 605

[3789] Gly Leu Gly Ser Val Thr His Glu Leu Ala Pro Gly Ile Asp Cys Pro

[3790] 610 615 620

[3791] Glu Thr Ala Thr Phe Leu Asp Thr Phe His Tyr Tyr Asp Ala Asp Asp

[3792] 625 630 635 640

[3793] Pro Val His Tyr Pro Arg Ala Leu Cys Leu Phe Glu Met Pro Thr Gly

[3794] 645 650 655

[3795] Val Pro Leu Arg Arg His Phe Asn Ser Asn Phe Lys Gly Gly Phe Asn

[3796] 660 665 670

[3797] Phe Tyr Ala Gly Leu Lys Gly Gln Val Leu Val Leu Arg Thr Thr Ser

[3798] 675 680 685

[3799] Thr Val Tyr Asn Tyr Asp Tyr Ile Trp Asp Phe Ile Phe Tyr Pro Asn

[3800] 690 695 700

[3801] Gly Val Met Glu Ala Lys Met His Ala Thr Gly Tyr Val His Ala Thr

[3802] 705 710 715 720

[3803] Phe Tyr Thr Pro Glu Gly Leu Arg His Gly Thr Arg Leu His Thr His

[3804] 725 730 735

[3805] Leu Ile Gly Asn Ile His Thr His Leu Val His Tyr Arg Val Asp Leu

[3806] 740 745 750

[3807] Asp Val Ala Gly Thr Lys Asn Ser Phe Gln Thr Leu Gln Met Lys Leu

[3808] 755 760 765

[3809] Glu Asn Ile Thr Asn Pro Trp Ser Pro Arg His Arg Val Val Gln Pro

[3810] 770 775 780

[3811] Thr Leu Glu Gln Thr Gln Tyr Ser Trp Glu Arg Gln Ala Ala Phe Arg

[3812] 785 790 795 800

[3813] Phe Lys Arg Lys Leu Pro Thr Tyr Leu Leu Phe Thr Ser Pro Gln Glu

[3814] 805 810 815

[3815] Asn Pro Trp Gly His Lys Arg Ser Tyr Arg Leu Gln Ile His Ser Met

[3816] 820 825 830

[3817] Ala Asp Gln Val Leu Pro Pro Gly Trp Gln Glu Glu Gln Ala Ile Thr

[3818] 835 840 845

[3819] Trp Ala Arg Tyr Pro Leu Ala Val Thr Lys Tyr Arg Glu Ser Glu Leu

[3820] 850 855 860

[3821] Cys Ser Ser Ser Ile Tyr His Gln Asn Asp Pro Trp His Pro Pro Val

[3822] 865 870 875 880
[3823] Val Phe Glu Gln Phe Leu His Asn Asn Glu Asn Ile Glu Asn Glu Asp
[3824] 885 890 895
[3825] Leu Val Ala Trp Val Thr Val Gly Phe Leu His Ile Pro His Ser Glu
[3826] 900 905 910
[3827] Asp Ile Pro Asn Thr Ala Thr Pro Gly Asn Ser Val Gly Phe Leu Leu
[3828] 915 920 925
[3829] Arg Pro Phe Asn Phe Phe Pro Glu Asp Pro Ser Leu Ala Ser Arg Asp
[3830] 930 935 940
[3831] Thr Val Ile Val Trp Pro Arg Asp Asn Gly Pro Asn Tyr Val Gln Arg
[3832] 945 950 955 960
[3833] Trp Ile Pro Glu Asp Arg Asp Cys Ser Met Pro Pro Pro Phe Ser Tyr
[3834] 965 970 975
[3835] Asn Gly Thr Tyr Arg Pro Val
[3836] 980
[3837] <210> 50
[3838] <211> 983
[3839] <212> PRT
[3840] <213> 人工序列
[3841] <220>
[3842] <223> Fc-hDAO-Hepmut3-Cysmut
[3843] <400> 50
[3844] Met Pro Ala Leu Gly Trp Ala Val Ala Ala Ile Leu Met Leu Gln Thr
[3845] 1 5 10 15
[3846] Ala Met Ala Glu Cys Pro Pro Cys Pro Ala Pro Pro Val Ala Gly Pro
[3847] 20 25 30
[3848] Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser
[3849] 35 40 45
[3850] Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp
[3851] 50 55 60
[3852] Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
[3853] 65 70 75 80
[3854] Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val
[3855] 85 90 95
[3856] Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu
[3857] 100 105 110
[3858] Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys
[3859] 115 120 125
[3860] Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr
[3861] 130 135 140
[3862] Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr
[3863] 145 150 155 160

[3864] Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu
[3865] 165 170 175
[3866] Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu
[3867] 180 185 190
[3868] Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys
[3869] 195 200 205
[3870] Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu
[3871] 210 215 220
[3872] Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
[3873] 225 230 235 240
[3874] Lys Glu Pro Lys Ser Ala Asp Lys Thr His Thr Glu Pro Ser Pro Gly
[3875] 245 250 255
[3876] Thr Leu Pro Arg Lys Ala Gly Val Phe Ser Asp Leu Ser Asn Gln Glu
[3877] 260 265 270
[3878] Leu Lys Ala Val His Ser Phe Leu Trp Ser Lys Lys Glu Leu Arg Leu
[3879] 275 280 285
[3880] Gln Pro Ser Ser Thr Thr Thr Met Ala Lys Asn Thr Val Phe Leu Ile
[3881] 290 295 300
[3882] Glu Met Leu Leu Pro Lys Lys Tyr His Val Leu Arg Phe Leu Asp Lys
[3883] 305 310 315 320
[3884] Gly Glu Arg His Pro Val Arg Glu Ala Arg Ala Val Ile Phe Phe Gly
[3885] 325 330 335
[3886] Asp Gln Glu His Pro Asn Val Thr Glu Phe Ala Val Gly Pro Leu Pro
[3887] 340 345 350
[3888] Gly Pro Ala Tyr Met Arg Ala Leu Ser Pro Arg Pro Gly Tyr Gln Ser
[3889] 355 360 365
[3890] Ser Trp Ala Ser Arg Pro Ile Ser Thr Ala Glu Tyr Ala Leu Leu Tyr
[3891] 370 375 380
[3892] His Thr Leu Gln Glu Ala Thr Lys Pro Leu His Gln Phe Phe Leu Asn
[3893] 385 390 395 400
[3894] Thr Thr Gly Phe Ser Phe Gln Asp Cys His Asp Arg Cys Leu Ala Phe
[3895] 405 410 415
[3896] Thr Asp Val Ala Pro Arg Gly Val Ala Ser Gly Gln Arg Arg Ser Trp
[3897] 420 425 430
[3898] Leu Ile Ile Gln Arg Tyr Val Glu Gly Tyr Phe Leu His Pro Thr Gly
[3899] 435 440 445
[3900] Leu Glu Leu Leu Val Asp His Gly Ser Thr Asp Ala Gly His Trp Ala
[3901] 450 455 460
[3902] Val Glu Gln Val Trp Tyr Asn Gly Lys Phe Tyr Gly Ser Pro Glu Glu
[3903] 465 470 475 480
[3904] Leu Ala Arg Lys Tyr Ala Asp Gly Glu Val Asp Val Val Val Leu Glu
[3905] 485 490 495

[3906] Asp Pro Leu Pro Gly Gly Lys Gly His Asp Ser Thr Glu Glu Pro Pro
[3907] 500 505 510
[3908] Leu Phe Ser Ser His Lys Pro Arg Gly Asp Phe Pro Ser Pro Ile His
[3909] 515 520 525
[3910] Val Ser Gly Pro Arg Leu Val Gln Pro His Gly Pro Arg Phe Arg Leu
[3911] 530 535 540
[3912] Glu Gly Asn Ala Val Leu Tyr Gly Gly Trp Ser Phe Ala Phe Arg Leu
[3913] 545 550 555 560
[3914] Arg Ser Ser Ser Gly Leu Gln Val Leu Asn Val His Phe Gly Gly Glu
[3915] 565 570 575
[3916] Arg Ile Ala Tyr Glu Val Ser Val Gln Glu Ala Val Ala Leu Tyr Gly
[3917] 580 585 590
[3918] Gly His Thr Pro Ala Gly Met Gln Thr Lys Tyr Leu Asp Val Gly Trp
[3919] 595 600 605
[3920] Gly Leu Gly Ser Val Thr His Glu Leu Ala Pro Gly Ile Asp Cys Pro
[3921] 610 615 620
[3922] Glu Thr Ala Thr Phe Leu Asp Thr Phe His Tyr Tyr Asp Ala Asp Asp
[3923] 625 630 635 640
[3924] Pro Val His Tyr Pro Arg Ala Leu Cys Leu Phe Glu Met Pro Thr Gly
[3925] 645 650 655
[3926] Val Pro Leu Arg Arg His Phe Asn Ser Asn Phe Lys Gly Gly Phe Asn
[3927] 660 665 670
[3928] Phe Tyr Ala Gly Leu Lys Gly Gln Val Leu Val Leu Arg Thr Thr Ser
[3929] 675 680 685
[3930] Thr Val Tyr Asn Tyr Asp Tyr Ile Trp Asp Phe Ile Phe Tyr Pro Asn
[3931] 690 695 700
[3932] Gly Val Met Glu Ala Lys Met His Ala Thr Gly Tyr Val His Ala Thr
[3933] 705 710 715 720
[3934] Phe Tyr Thr Pro Glu Gly Leu Arg His Gly Thr Arg Leu His Thr His
[3935] 725 730 735
[3936] Leu Ile Gly Asn Ile His Thr His Leu Val His Tyr Arg Val Asp Leu
[3937] 740 745 750
[3938] Asp Val Ala Gly Thr Lys Asn Ser Phe Gln Thr Leu Gln Met Lys Leu
[3939] 755 760 765
[3940] Glu Asn Ile Thr Asn Pro Trp Ser Pro Arg His Arg Val Val Gln Pro
[3941] 770 775 780
[3942] Thr Leu Glu Gln Thr Gln Tyr Ser Trp Glu Arg Gln Ala Ala Phe Arg
[3943] 785 790 795 800
[3944] Phe Lys Thr Lys Leu Pro Lys Tyr Leu Leu Phe Thr Ser Pro Gln Glu
[3945] 805 810 815
[3946] Asn Pro Trp Gly His Lys Arg Ser Tyr Arg Leu Gln Ile His Ser Met
[3947] 820 825 830

[3948] Ala Asp Gln Val Leu Pro Pro Gly Trp Gln Glu Glu Gln Ala Ile Thr
[3949] 835 840 845
[3950] Trp Ala Arg Tyr Pro Leu Ala Val Thr Lys Tyr Arg Glu Ser Glu Leu
[3951] 850 855 860
[3952] Cys Ser Ser Ser Ile Tyr His Gln Asn Asp Pro Trp His Pro Pro Val
[3953] 865 870 875 880
[3954] Val Phe Glu Gln Phe Leu His Asn Asn Glu Asn Ile Glu Asn Glu Asp
[3955] 885 890 895
[3956] Leu Val Ala Trp Val Thr Val Gly Phe Leu His Ile Pro His Ser Glu
[3957] 900 905 910
[3958] Asp Ile Pro Asn Thr Ala Thr Pro Gly Asn Ser Val Gly Phe Leu Leu
[3959] 915 920 925
[3960] Arg Pro Phe Asn Phe Phe Pro Glu Asp Pro Ser Leu Ala Ser Arg Asp
[3961] 930 935 940
[3962] Thr Val Ile Val Trp Pro Arg Asp Asn Gly Pro Asn Tyr Val Gln Arg
[3963] 945 950 955 960
[3964] Trp Ile Pro Glu Asp Arg Asp Cys Ser Met Pro Pro Pro Phe Ser Tyr
[3965] 965 970 975
[3966] Asn Gly Thr Tyr Arg Pro Val
[3967] 980
[3968] <210> 51
[3969] <211> 983
[3970] <212> PRT
[3971] <213> 人工序列
[3972] <220>
[3973] <223> Fc-hDAO-Hepmut4-Cysmut
[3974] <400> 51
[3975] Met Pro Ala Leu Gly Trp Ala Val Ala Ala Ile Leu Met Leu Gln Thr
[3976] 1 5 10 15
[3977] Ala Met Ala Glu Cys Pro Pro Cys Pro Ala Pro Pro Val Ala Gly Pro
[3978] 20 25 30
[3979] Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser
[3980] 35 40 45
[3981] Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp
[3982] 50 55 60
[3983] Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
[3984] 65 70 75 80
[3985] Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val
[3986] 85 90 95
[3987] Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu
[3988] 100 105 110
[3989] Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys

[3990] 115 120 125
[3991] Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr
[3992] 130 135 140
[3993] Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr
[3994] 145 150 155 160
[3995] Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu
[3996] 165 170 175
[3997] Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu
[3998] 180 185 190
[3999] Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys
[4000] 195 200 205
[4001] Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu
[4002] 210 215 220
[4003] Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
[4004] 225 230 235 240
[4005] Lys Glu Pro Lys Ser Ala Asp Lys Thr His Thr Glu Pro Ser Pro Gly
[4006] 245 250 255
[4007] Thr Leu Pro Arg Lys Ala Gly Val Phe Ser Asp Leu Ser Asn Gln Glu
[4008] 260 265 270
[4009] Leu Lys Ala Val His Ser Phe Leu Trp Ser Lys Lys Glu Leu Arg Leu
[4010] 275 280 285
[4011] Gln Pro Ser Ser Thr Thr Thr Met Ala Lys Asn Thr Val Phe Leu Ile
[4012] 290 295 300
[4013] Glu Met Leu Leu Pro Lys Lys Tyr His Val Leu Arg Phe Leu Asp Lys
[4014] 305 310 315 320
[4015] Gly Glu Arg His Pro Val Arg Glu Ala Arg Ala Val Ile Phe Phe Gly
[4016] 325 330 335
[4017] Asp Gln Glu His Pro Asn Val Thr Glu Phe Ala Val Gly Pro Leu Pro
[4018] 340 345 350
[4019] Gly Pro Ala Tyr Met Arg Ala Leu Ser Pro Arg Pro Gly Tyr Gln Ser
[4020] 355 360 365
[4021] Ser Trp Ala Ser Arg Pro Ile Ser Thr Ala Glu Tyr Ala Leu Leu Tyr
[4022] 370 375 380
[4023] His Thr Leu Gln Glu Ala Thr Lys Pro Leu His Gln Phe Phe Leu Asn
[4024] 385 390 395 400
[4025] Thr Thr Gly Phe Ser Phe Gln Asp Cys His Asp Arg Cys Leu Ala Phe
[4026] 405 410 415
[4027] Thr Asp Val Ala Pro Arg Gly Val Ala Ser Gly Gln Arg Arg Ser Trp
[4028] 420 425 430
[4029] Leu Ile Ile Gln Arg Tyr Val Glu Gly Tyr Phe Leu His Pro Thr Gly
[4030] 435 440 445
[4031] Leu Glu Leu Leu Val Asp His Gly Ser Thr Asp Ala Gly His Trp Ala

[4032] 450 455 460

[4033] Val Glu Gln Val Trp Tyr Asn Gly Lys Phe Tyr Gly Ser Pro Glu Glu

[4034] 465 470 475 480

[4035] Leu Ala Arg Lys Tyr Ala Asp Gly Glu Val Asp Val Val Val Leu Glu

[4036] 485 490 495

[4037] Asp Pro Leu Pro Gly Gly Lys Gly His Asp Ser Thr Glu Glu Pro Pro

[4038] 500 505 510

[4039] Leu Phe Ser Ser His Lys Pro Arg Gly Asp Phe Pro Ser Pro Ile His

[4040] 515 520 525

[4041] Val Ser Gly Pro Arg Leu Val Gln Pro His Gly Pro Arg Phe Arg Leu

[4042] 530 535 540

[4043] Glu Gly Asn Ala Val Leu Tyr Gly Gly Trp Ser Phe Ala Phe Arg Leu

[4044] 545 550 555 560

[4045] Arg Ser Ser Ser Gly Leu Gln Val Leu Asn Val His Phe Gly Gly Glu

[4046] 565 570 575

[4047] Arg Ile Ala Tyr Glu Val Ser Val Gln Glu Ala Val Ala Leu Tyr Gly

[4048] 580 585 590

[4049] Gly His Thr Pro Ala Gly Met Gln Thr Lys Tyr Leu Asp Val Gly Trp

[4050] 595 600 605

[4051] Gly Leu Gly Ser Val Thr His Glu Leu Ala Pro Gly Ile Asp Cys Pro

[4052] 610 615 620

[4053] Glu Thr Ala Thr Phe Leu Asp Thr Phe His Tyr Tyr Asp Ala Asp Asp

[4054] 625 630 635 640

[4055] Pro Val His Tyr Pro Arg Ala Leu Cys Leu Phe Glu Met Pro Thr Gly

[4056] 645 650 655

[4057] Val Pro Leu Arg Arg His Phe Asn Ser Asn Phe Lys Gly Gly Phe Asn

[4058] 660 665 670

[4059] Phe Tyr Ala Gly Leu Lys Gly Gln Val Leu Val Leu Arg Thr Thr Ser

[4060] 675 680 685

[4061] Thr Val Tyr Asn Tyr Asp Tyr Ile Trp Asp Phe Ile Phe Tyr Pro Asn

[4062] 690 695 700

[4063] Gly Val Met Glu Ala Lys Met His Ala Thr Gly Tyr Val His Ala Thr

[4064] 705 710 715 720

[4065] Phe Tyr Thr Pro Glu Gly Leu Arg His Gly Thr Arg Leu His Thr His

[4066] 725 730 735

[4067] Leu Ile Gly Asn Ile His Thr His Leu Val His Tyr Arg Val Asp Leu

[4068] 740 745 750

[4069] Asp Val Ala Gly Thr Lys Asn Ser Phe Gln Thr Leu Gln Met Lys Leu

[4070] 755 760 765

[4071] Glu Asn Ile Thr Asn Pro Trp Ser Pro Arg His Arg Val Val Gln Pro

[4072] 770 775 780

[4073] Thr Leu Glu Gln Thr Gln Tyr Ser Trp Glu Arg Gln Ala Ala Phe Ser

[4074] 785 790 795 800
[4075] Phe Lys Thr Lys Leu Pro Lys Tyr Leu Leu Phe Thr Ser Pro Gln Glu
[4076] 805 810 815
[4077] Asn Pro Trp Gly His Lys Arg Ser Tyr Arg Leu Gln Ile His Ser Met
[4078] 820 825 830
[4079] Ala Asp Gln Val Leu Pro Pro Gly Trp Gln Glu Glu Gln Ala Ile Thr
[4080] 835 840 845
[4081] Trp Ala Arg Tyr Pro Leu Ala Val Thr Lys Tyr Arg Glu Ser Glu Leu
[4082] 850 855 860
[4083] Cys Ser Ser Ser Ile Tyr His Gln Asn Asp Pro Trp His Pro Pro Val
[4084] 865 870 875 880
[4085] Val Phe Glu Gln Phe Leu His Asn Asn Glu Asn Ile Glu Asn Glu Asp
[4086] 885 890 895
[4087] Leu Val Ala Trp Val Thr Val Gly Phe Leu His Ile Pro His Ser Glu
[4088] 900 905 910
[4089] Asp Ile Pro Asn Thr Ala Thr Pro Gly Asn Ser Val Gly Phe Leu Leu
[4090] 915 920 925
[4091] Arg Pro Phe Asn Phe Phe Pro Glu Asp Pro Ser Leu Ala Ser Arg Asp
[4092] 930 935 940
[4093] Thr Val Ile Val Trp Pro Arg Asp Asn Gly Pro Asn Tyr Val Gln Arg
[4094] 945 950 955 960
[4095] Trp Ile Pro Glu Asp Arg Asp Cys Ser Met Pro Pro Pro Phe Ser Tyr
[4096] 965 970 975
[4097] Asn Gly Thr Tyr Arg Pro Val
[4098] 980
[4099] <210> 52
[4100] <211> 983
[4101] <212> PRT
[4102] <213> 人工序列
[4103] <220>
[4104] <223> Fc-hDAO-Hepmut5-Cysmut
[4105] <400> 52
[4106] Met Pro Ala Leu Gly Trp Ala Val Ala Ala Ile Leu Met Leu Gln Thr
[4107] 1 5 10 15
[4108] Ala Met Ala Glu Cys Pro Pro Cys Pro Ala Pro Pro Val Ala Gly Pro
[4109] 20 25 30
[4110] Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser
[4111] 35 40 45
[4112] Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp
[4113] 50 55 60
[4114] Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
[4115] 65 70 75 80

[4116] Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val
[4117] 85 90 95
[4118] Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu
[4119] 100 105 110
[4120] Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys
[4121] 115 120 125
[4122] Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr
[4123] 130 135 140
[4124] Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr
[4125] 145 150 155 160
[4126] Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu
[4127] 165 170 175
[4128] Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu
[4129] 180 185 190
[4130] Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys
[4131] 195 200 205
[4132] Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu
[4133] 210 215 220
[4134] Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
[4135] 225 230 235 240
[4136] Lys Glu Pro Lys Ser Ala Asp Lys Thr His Thr Glu Pro Ser Pro Gly
[4137] 245 250 255
[4138] Thr Leu Pro Arg Lys Ala Gly Val Phe Ser Asp Leu Ser Asn Gln Glu
[4139] 260 265 270
[4140] Leu Lys Ala Val His Ser Phe Leu Trp Ser Lys Lys Glu Leu Arg Leu
[4141] 275 280 285
[4142] Gln Pro Ser Ser Thr Thr Thr Met Ala Lys Asn Thr Val Phe Leu Ile
[4143] 290 295 300
[4144] Glu Met Leu Leu Pro Lys Lys Tyr His Val Leu Arg Phe Leu Asp Lys
[4145] 305 310 315 320
[4146] Gly Glu Arg His Pro Val Arg Glu Ala Arg Ala Val Ile Phe Phe Gly
[4147] 325 330 335
[4148] Asp Gln Glu His Pro Asn Val Thr Glu Phe Ala Val Gly Pro Leu Pro
[4149] 340 345 350
[4150] Gly Pro Ala Tyr Met Arg Ala Leu Ser Pro Arg Pro Gly Tyr Gln Ser
[4151] 355 360 365
[4152] Ser Trp Ala Ser Arg Pro Ile Ser Thr Ala Glu Tyr Ala Leu Leu Tyr
[4153] 370 375 380
[4154] His Thr Leu Gln Glu Ala Thr Lys Pro Leu His Gln Phe Phe Leu Asn
[4155] 385 390 395 400
[4156] Thr Thr Gly Phe Ser Phe Gln Asp Cys His Asp Arg Cys Leu Ala Phe
[4157] 405 410 415

[4158] Thr Asp Val Ala Pro Arg Gly Val Ala Ser Gly Gln Arg Arg Ser Trp
[4159] 420 425 430
[4160] Leu Ile Ile Gln Arg Tyr Val Glu Gly Tyr Phe Leu His Pro Thr Gly
[4161] 435 440 445
[4162] Leu Glu Leu Leu Val Asp His Gly Ser Thr Asp Ala Gly His Trp Ala
[4163] 450 455 460
[4164] Val Glu Gln Val Trp Tyr Asn Gly Lys Phe Tyr Gly Ser Pro Glu Glu
[4165] 465 470 475 480
[4166] Leu Ala Arg Lys Tyr Ala Asp Gly Glu Val Asp Val Val Val Leu Glu
[4167] 485 490 495
[4168] Asp Pro Leu Pro Gly Gly Lys Gly His Asp Ser Thr Glu Glu Pro Pro
[4169] 500 505 510
[4170] Leu Phe Ser Ser His Lys Pro Arg Gly Asp Phe Pro Ser Pro Ile His
[4171] 515 520 525
[4172] Val Ser Gly Pro Arg Leu Val Gln Pro His Gly Pro Arg Phe Arg Leu
[4173] 530 535 540
[4174] Glu Gly Asn Ala Val Leu Tyr Gly Gly Trp Ser Phe Ala Phe Arg Leu
[4175] 545 550 555 560
[4176] Arg Ser Ser Ser Gly Leu Gln Val Leu Asn Val His Phe Gly Gly Glu
[4177] 565 570 575
[4178] Arg Ile Ala Tyr Glu Val Ser Val Gln Glu Ala Val Ala Leu Tyr Gly
[4179] 580 585 590
[4180] Gly His Thr Pro Ala Gly Met Gln Thr Lys Tyr Leu Asp Val Gly Trp
[4181] 595 600 605
[4182] Gly Leu Gly Ser Val Thr His Glu Leu Ala Pro Gly Ile Asp Cys Pro
[4183] 610 615 620
[4184] Glu Thr Ala Thr Phe Leu Asp Thr Phe His Tyr Tyr Asp Ala Asp Asp
[4185] 625 630 635 640
[4186] Pro Val His Tyr Pro Arg Ala Leu Cys Leu Phe Glu Met Pro Thr Gly
[4187] 645 650 655
[4188] Val Pro Leu Arg Arg His Phe Asn Ser Asn Phe Lys Gly Gly Phe Asn
[4189] 660 665 670
[4190] Phe Tyr Ala Gly Leu Lys Gly Gln Val Leu Val Leu Arg Thr Thr Ser
[4191] 675 680 685
[4192] Thr Val Tyr Asn Tyr Asp Tyr Ile Trp Asp Phe Ile Phe Tyr Pro Asn
[4193] 690 695 700
[4194] Gly Val Met Glu Ala Lys Met His Ala Thr Gly Tyr Val His Ala Thr
[4195] 705 710 715 720
[4196] Phe Tyr Thr Pro Glu Gly Leu Arg His Gly Thr Arg Leu His Thr His
[4197] 725 730 735
[4198] Leu Ile Gly Asn Ile His Thr His Leu Val His Tyr Arg Val Asp Leu
[4199] 740 745 750

[4200] Asp Val Ala Gly Thr Lys Asn Ser Phe Gln Thr Leu Gln Met Lys Leu
[4201] 755 760 765
[4202] Glu Asn Ile Thr Asn Pro Trp Ser Pro Arg His Arg Val Val Gln Pro
[4203] 770 775 780
[4204] Thr Leu Glu Gln Thr Gln Tyr Ser Trp Glu Arg Gln Ala Ala Phe Arg
[4205] 785 790 795 800
[4206] Phe Lys Thr Lys Leu Pro Thr Tyr Leu Leu Phe Thr Ser Pro Gln Glu
[4207] 805 810 815
[4208] Asn Pro Trp Gly His Lys Arg Ser Tyr Arg Leu Gln Ile His Ser Met
[4209] 820 825 830
[4210] Ala Asp Gln Val Leu Pro Pro Gly Trp Gln Glu Glu Gln Ala Ile Thr
[4211] 835 840 845
[4212] Trp Ala Arg Tyr Pro Leu Ala Val Thr Lys Tyr Arg Glu Ser Glu Leu
[4213] 850 855 860
[4214] Cys Ser Ser Ser Ile Tyr His Gln Asn Asp Pro Trp His Pro Pro Val
[4215] 865 870 875 880
[4216] Val Phe Glu Gln Phe Leu His Asn Asn Glu Asn Ile Glu Asn Glu Asp
[4217] 885 890 895
[4218] Leu Val Ala Trp Val Thr Val Gly Phe Leu His Ile Pro His Ser Glu
[4219] 900 905 910
[4220] Asp Ile Pro Asn Thr Ala Thr Pro Gly Asn Ser Val Gly Phe Leu Leu
[4221] 915 920 925
[4222] Arg Pro Phe Asn Phe Phe Pro Glu Asp Pro Ser Leu Ala Ser Arg Asp
[4223] 930 935 940
[4224] Thr Val Ile Val Trp Pro Arg Asp Asn Gly Pro Asn Tyr Val Gln Arg
[4225] 945 950 955 960
[4226] Trp Ile Pro Glu Asp Arg Asp Cys Ser Met Pro Pro Pro Phe Ser Tyr
[4227] 965 970 975
[4228] Asn Gly Thr Tyr Arg Pro Val
[4229] 980
[4230] <210> 53
[4231] <211> 983
[4232] <212> PRT
[4233] <213> 人工序列
[4234] <220>
[4235] <223> Fc-hDAO-Hepmut6-Cysmut
[4236] <400> 53
[4237] Met Pro Ala Leu Gly Trp Ala Val Ala Ala Ile Leu Met Leu Gln Thr
[4238] 1 5 10 15
[4239] Ala Met Ala Glu Cys Pro Pro Cys Pro Ala Pro Pro Val Ala Gly Pro
[4240] 20 25 30
[4241] Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser

[4242] 35 40 45
[4243] Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp
[4244] 50 55 60
[4245] Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
[4246] 65 70 75 80
[4247] Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val
[4248] 85 90 95
[4249] Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu
[4250] 100 105 110
[4251] Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys
[4252] 115 120 125
[4253] Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr
[4254] 130 135 140
[4255] Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr
[4256] 145 150 155 160
[4257] Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu
[4258] 165 170 175
[4259] Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu
[4260] 180 185 190
[4261] Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys
[4262] 195 200 205
[4263] Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu
[4264] 210 215 220
[4265] Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
[4266] 225 230 235 240
[4267] Lys Glu Pro Lys Ser Ala Asp Lys Thr His Thr Glu Pro Ser Pro Gly
[4268] 245 250 255
[4269] Thr Leu Pro Arg Lys Ala Gly Val Phe Ser Asp Leu Ser Asn Gln Glu
[4270] 260 265 270
[4271] Leu Lys Ala Val His Ser Phe Leu Trp Ser Lys Lys Glu Leu Arg Leu
[4272] 275 280 285
[4273] Gln Pro Ser Ser Thr Thr Thr Met Ala Lys Asn Thr Val Phe Leu Ile
[4274] 290 295 300
[4275] Glu Met Leu Leu Pro Lys Lys Tyr His Val Leu Arg Phe Leu Asp Lys
[4276] 305 310 315 320
[4277] Gly Glu Arg His Pro Val Arg Glu Ala Arg Ala Val Ile Phe Phe Gly
[4278] 325 330 335
[4279] Asp Gln Glu His Pro Asn Val Thr Glu Phe Ala Val Gly Pro Leu Pro
[4280] 340 345 350
[4281] Gly Pro Ala Tyr Met Arg Ala Leu Ser Pro Arg Pro Gly Tyr Gln Ser
[4282] 355 360 365
[4283] Ser Trp Ala Ser Arg Pro Ile Ser Thr Ala Glu Tyr Ala Leu Leu Tyr

[4284] 370 375 380

[4285] His Thr Leu Gln Glu Ala Thr Lys Pro Leu His Gln Phe Phe Leu Asn

[4286] 385 390 395 400

[4287] Thr Thr Gly Phe Ser Phe Gln Asp Cys His Asp Arg Cys Leu Ala Phe

[4288] 405 410 415

[4289] Thr Asp Val Ala Pro Arg Gly Val Ala Ser Gly Gln Arg Arg Ser Trp

[4290] 420 425 430

[4291] Leu Ile Ile Gln Arg Tyr Val Glu Gly Tyr Phe Leu His Pro Thr Gly

[4292] 435 440 445

[4293] Leu Glu Leu Leu Val Asp His Gly Ser Thr Asp Ala Gly His Trp Ala

[4294] 450 455 460

[4295] Val Glu Gln Val Trp Tyr Asn Gly Lys Phe Tyr Gly Ser Pro Glu Glu

[4296] 465 470 475 480

[4297] Leu Ala Arg Lys Tyr Ala Asp Gly Glu Val Asp Val Val Val Leu Glu

[4298] 485 490 495

[4299] Asp Pro Leu Pro Gly Gly Lys Gly His Asp Ser Thr Glu Glu Pro Pro

[4300] 500 505 510

[4301] Leu Phe Ser Ser His Lys Pro Arg Gly Asp Phe Pro Ser Pro Ile His

[4302] 515 520 525

[4303] Val Ser Gly Pro Arg Leu Val Gln Pro His Gly Pro Arg Phe Arg Leu

[4304] 530 535 540

[4305] Glu Gly Asn Ala Val Leu Tyr Gly Gly Trp Ser Phe Ala Phe Arg Leu

[4306] 545 550 555 560

[4307] Arg Ser Ser Ser Gly Leu Gln Val Leu Asn Val His Phe Gly Gly Glu

[4308] 565 570 575

[4309] Arg Ile Ala Tyr Glu Val Ser Val Gln Glu Ala Val Ala Leu Tyr Gly

[4310] 580 585 590

[4311] Gly His Thr Pro Ala Gly Met Gln Thr Lys Tyr Leu Asp Val Gly Trp

[4312] 595 600 605

[4313] Gly Leu Gly Ser Val Thr His Glu Leu Ala Pro Gly Ile Asp Cys Pro

[4314] 610 615 620

[4315] Glu Thr Ala Thr Phe Leu Asp Thr Phe His Tyr Tyr Asp Ala Asp Asp

[4316] 625 630 635 640

[4317] Pro Val His Tyr Pro Arg Ala Leu Cys Leu Phe Glu Met Pro Thr Gly

[4318] 645 650 655

[4319] Val Pro Leu Arg Arg His Phe Asn Ser Asn Phe Lys Gly Gly Phe Asn

[4320] 660 665 670

[4321] Phe Tyr Ala Gly Leu Lys Gly Gln Val Leu Val Leu Arg Thr Thr Ser

[4322] 675 680 685

[4323] Thr Val Tyr Asn Tyr Asp Tyr Ile Trp Asp Phe Ile Phe Tyr Pro Asn

[4324] 690 695 700

[4325] Gly Val Met Glu Ala Lys Met His Ala Thr Gly Tyr Val His Ala Thr

[4326] 705 710 715 720
[4327] Phe Tyr Thr Pro Glu Gly Leu Arg His Gly Thr Arg Leu His Thr His
[4328] 725 730 735
[4329] Leu Ile Gly Asn Ile His Thr His Leu Val His Tyr Arg Val Asp Leu
[4330] 740 745 750
[4331] Asp Val Ala Gly Thr Lys Asn Ser Phe Gln Thr Leu Gln Met Lys Leu
[4332] 755 760 765
[4333] Glu Asn Ile Thr Asn Pro Trp Ser Pro Arg His Arg Val Val Gln Pro
[4334] 770 775 780
[4335] Thr Leu Glu Gln Thr Gln Tyr Ser Trp Glu Arg Gln Ala Ala Phe Arg
[4336] 785 790 795 800
[4337] Phe Gly Gln Thr Leu Pro Lys Tyr Leu Leu Phe Thr Ser Pro Gln Glu
[4338] 805 810 815
[4339] Asn Pro Trp Gly His Lys Arg Ser Tyr Arg Leu Gln Ile His Ser Met
[4340] 820 825 830
[4341] Ala Asp Gln Val Leu Pro Pro Gly Trp Gln Glu Glu Gln Ala Ile Thr
[4342] 835 840 845
[4343] Trp Ala Arg Tyr Pro Leu Ala Val Thr Lys Tyr Arg Glu Ser Glu Leu
[4344] 850 855 860
[4345] Cys Ser Ser Ser Ile Tyr His Gln Asn Asp Pro Trp His Pro Pro Val
[4346] 865 870 875 880
[4347] Val Phe Glu Gln Phe Leu His Asn Asn Glu Asn Ile Glu Asn Glu Asp
[4348] 885 890 895
[4349] Leu Val Ala Trp Val Thr Val Gly Phe Leu His Ile Pro His Ser Glu
[4350] 900 905 910
[4351] Asp Ile Pro Asn Thr Ala Thr Pro Gly Asn Ser Val Gly Phe Leu Leu
[4352] 915 920 925
[4353] Arg Pro Phe Asn Phe Phe Pro Glu Asp Pro Ser Leu Ala Ser Arg Asp
[4354] 930 935 940
[4355] Thr Val Ile Val Trp Pro Arg Asp Asn Gly Pro Asn Tyr Val Gln Arg
[4356] 945 950 955 960
[4357] Trp Ile Pro Glu Asp Arg Asp Cys Ser Met Pro Pro Pro Phe Ser Tyr
[4358] 965 970 975
[4359] Asn Gly Thr Tyr Arg Pro Val
[4360] 980
[4361] <210> 54
[4362] <211> 983
[4363] <212> PRT
[4364] <213> 人工序列
[4365] <220>
[4366] <223> Fc-hDAO-Hepmut7-Cysmut
[4367] <400> 54

[4368] Met Pro Ala Leu Gly Trp Ala Val Ala Ala Ile Leu Met Leu Gln Thr
[4369] 1 5 10 15
[4370] Ala Met Ala Glu Cys Pro Pro Cys Pro Ala Pro Pro Val Ala Gly Pro
[4371] 20 25 30
[4372] Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser
[4373] 35 40 45
[4374] Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp
[4375] 50 55 60
[4376] Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
[4377] 65 70 75 80
[4378] Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val
[4379] 85 90 95
[4380] Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu
[4381] 100 105 110
[4382] Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys
[4383] 115 120 125
[4384] Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr
[4385] 130 135 140
[4386] Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr
[4387] 145 150 155 160
[4388] Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu
[4389] 165 170 175
[4390] Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu
[4391] 180 185 190
[4392] Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys
[4393] 195 200 205
[4394] Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu
[4395] 210 215 220
[4396] Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
[4397] 225 230 235 240
[4398] Lys Glu Pro Lys Ser Ala Asp Lys Thr His Thr Glu Pro Ser Pro Gly
[4399] 245 250 255
[4400] Thr Leu Pro Arg Lys Ala Gly Val Phe Ser Asp Leu Ser Asn Gln Glu
[4401] 260 265 270
[4402] Leu Lys Ala Val His Ser Phe Leu Trp Ser Lys Lys Glu Leu Arg Leu
[4403] 275 280 285
[4404] Gln Pro Ser Ser Thr Thr Thr Met Ala Lys Asn Thr Val Phe Leu Ile
[4405] 290 295 300
[4406] Glu Met Leu Leu Pro Lys Lys Tyr His Val Leu Arg Phe Leu Asp Lys
[4407] 305 310 315 320
[4408] Gly Glu Arg His Pro Val Arg Glu Ala Arg Ala Val Ile Phe Phe Gly
[4409] 325 330 335

[4410] Asp Gln Glu His Pro Asn Val Thr Glu Phe Ala Val Gly Pro Leu Pro
[4411] 340 345 350
[4412] Gly Pro Ala Tyr Met Arg Ala Leu Ser Pro Arg Pro Gly Tyr Gln Ser
[4413] 355 360 365
[4414] Ser Trp Ala Ser Arg Pro Ile Ser Thr Ala Glu Tyr Ala Leu Leu Tyr
[4415] 370 375 380
[4416] His Thr Leu Gln Glu Ala Thr Lys Pro Leu His Gln Phe Phe Leu Asn
[4417] 385 390 395 400
[4418] Thr Thr Gly Phe Ser Phe Gln Asp Cys His Asp Arg Cys Leu Ala Phe
[4419] 405 410 415
[4420] Thr Asp Val Ala Pro Arg Gly Val Ala Ser Gly Gln Arg Arg Ser Trp
[4421] 420 425 430
[4422] Leu Ile Ile Gln Arg Tyr Val Glu Gly Tyr Phe Leu His Pro Thr Gly
[4423] 435 440 445
[4424] Leu Glu Leu Leu Val Asp His Gly Ser Thr Asp Ala Gly His Trp Ala
[4425] 450 455 460
[4426] Val Glu Gln Val Trp Tyr Asn Gly Lys Phe Tyr Gly Ser Pro Glu Glu
[4427] 465 470 475 480
[4428] Leu Ala Arg Lys Tyr Ala Asp Gly Glu Val Asp Val Val Val Leu Glu
[4429] 485 490 495
[4430] Asp Pro Leu Pro Gly Gly Lys Gly His Asp Ser Thr Glu Glu Pro Pro
[4431] 500 505 510
[4432] Leu Phe Ser Ser His Lys Pro Arg Gly Asp Phe Pro Ser Pro Ile His
[4433] 515 520 525
[4434] Val Ser Gly Pro Arg Leu Val Gln Pro His Gly Pro Arg Phe Arg Leu
[4435] 530 535 540
[4436] Glu Gly Asn Ala Val Leu Tyr Gly Gly Trp Ser Phe Ala Phe Arg Leu
[4437] 545 550 555 560
[4438] Arg Ser Ser Ser Gly Leu Gln Val Leu Asn Val His Phe Gly Gly Glu
[4439] 565 570 575
[4440] Arg Ile Ala Tyr Glu Val Ser Val Gln Glu Ala Val Ala Leu Tyr Gly
[4441] 580 585 590
[4442] Gly His Thr Pro Ala Gly Met Gln Thr Lys Tyr Leu Asp Val Gly Trp
[4443] 595 600 605
[4444] Gly Leu Gly Ser Val Thr His Glu Leu Ala Pro Gly Ile Asp Cys Pro
[4445] 610 615 620
[4446] Glu Thr Ala Thr Phe Leu Asp Thr Phe His Tyr Tyr Asp Ala Asp Asp
[4447] 625 630 635 640
[4448] Pro Val His Tyr Pro Arg Ala Leu Cys Leu Phe Glu Met Pro Thr Gly
[4449] 645 650 655
[4450] Val Pro Leu Arg Arg His Phe Asn Ser Asn Phe Lys Gly Gly Phe Asn
[4451] 660 665 670

[4452] Phe Tyr Ala Gly Leu Lys Gly Gln Val Leu Val Leu Arg Thr Thr Ser
[4453] 675 680 685
[4454] Thr Val Tyr Asn Tyr Asp Tyr Ile Trp Asp Phe Ile Phe Tyr Pro Asn
[4455] 690 695 700
[4456] Gly Val Met Glu Ala Lys Met His Ala Thr Gly Tyr Val His Ala Thr
[4457] 705 710 715 720
[4458] Phe Tyr Thr Pro Glu Gly Leu Arg His Gly Thr Arg Leu His Thr His
[4459] 725 730 735
[4460] Leu Ile Gly Asn Ile His Thr His Leu Val His Tyr Arg Val Asp Leu
[4461] 740 745 750
[4462] Asp Val Ala Gly Thr Lys Asn Ser Phe Gln Thr Leu Gln Met Lys Leu
[4463] 755 760 765
[4464] Glu Asn Ile Thr Asn Pro Trp Ser Pro Arg His Arg Val Val Gln Pro
[4465] 770 775 780
[4466] Thr Leu Glu Gln Thr Gln Tyr Ser Trp Glu Arg Gln Ala Ala Phe Ser
[4467] 785 790 795 800
[4468] Phe Lys Arg Lys Leu Pro Thr Tyr Leu Leu Phe Thr Ser Pro Gln Glu
[4469] 805 810 815
[4470] Asn Pro Trp Gly His Lys Arg Ser Tyr Arg Leu Gln Ile His Ser Met
[4471] 820 825 830
[4472] Ala Asp Gln Val Leu Pro Pro Gly Trp Gln Glu Glu Gln Ala Ile Thr
[4473] 835 840 845
[4474] Trp Ala Arg Tyr Pro Leu Ala Val Thr Lys Tyr Arg Glu Ser Glu Leu
[4475] 850 855 860
[4476] Cys Ser Ser Ser Ile Tyr His Gln Asn Asp Pro Trp His Pro Pro Val
[4477] 865 870 875 880
[4478] Val Phe Glu Gln Phe Leu His Asn Asn Glu Asn Ile Glu Asn Glu Asp
[4479] 885 890 895
[4480] Leu Val Ala Trp Val Thr Val Gly Phe Leu His Ile Pro His Ser Glu
[4481] 900 905 910
[4482] Asp Ile Pro Asn Thr Ala Thr Pro Gly Asn Ser Val Gly Phe Leu Leu
[4483] 915 920 925
[4484] Arg Pro Phe Asn Phe Phe Pro Glu Asp Pro Ser Leu Ala Ser Arg Asp
[4485] 930 935 940
[4486] Thr Val Ile Val Trp Pro Arg Asp Asn Gly Pro Asn Tyr Val Gln Arg
[4487] 945 950 955 960
[4488] Trp Ile Pro Glu Asp Arg Asp Cys Ser Met Pro Pro Pro Phe Ser Tyr
[4489] 965 970 975
[4490] Asn Gly Thr Tyr Arg Pro Val
[4491] 980
[4492] <210> 55
[4493] <211> 982

[4494] <212> PRT
[4495] <213> 人工序列
[4496] <220>
[4497] <223> hDAO-Fc
[4498] <400> 55
[4499] Met Pro Ala Leu Gly Trp Ala Val Ala Ala Ile Leu Met Leu Gln Thr
[4500] 1 5 10 15
[4501] Ala Met Ala Glu Pro Ser Pro Gly Thr Leu Pro Arg Lys Ala Gly Val
[4502] 20 25 30
[4503] Phe Ser Asp Leu Ser Asn Gln Glu Leu Lys Ala Val His Ser Phe Leu
[4504] 35 40 45
[4505] Trp Ser Lys Lys Glu Leu Arg Leu Gln Pro Ser Ser Thr Thr Thr Met
[4506] 50 55 60
[4507] Ala Lys Asn Thr Val Phe Leu Ile Glu Met Leu Leu Pro Lys Lys Tyr
[4508] 65 70 75 80
[4509] His Val Leu Arg Phe Leu Asp Lys Gly Glu Arg His Pro Val Arg Glu
[4510] 85 90 95
[4511] Ala Arg Ala Val Ile Phe Phe Gly Asp Gln Glu His Pro Asn Val Thr
[4512] 100 105 110
[4513] Glu Phe Ala Val Gly Pro Leu Pro Gly Pro Cys Tyr Met Arg Ala Leu
[4514] 115 120 125
[4515] Ser Pro Arg Pro Gly Tyr Gln Ser Ser Trp Ala Ser Arg Pro Ile Ser
[4516] 130 135 140
[4517] Thr Ala Glu Tyr Ala Leu Leu Tyr His Thr Leu Gln Glu Ala Thr Lys
[4518] 145 150 155 160
[4519] Pro Leu His Gln Phe Phe Leu Asn Thr Thr Gly Phe Ser Phe Gln Asp
[4520] 165 170 175
[4521] Cys His Asp Arg Cys Leu Ala Phe Thr Asp Val Ala Pro Arg Gly Val
[4522] 180 185 190
[4523] Ala Ser Gly Gln Arg Arg Ser Trp Leu Ile Ile Gln Arg Tyr Val Glu
[4524] 195 200 205
[4525] Gly Tyr Phe Leu His Pro Thr Gly Leu Glu Leu Leu Val Asp His Gly
[4526] 210 215 220
[4527] Ser Thr Asp Ala Gly His Trp Ala Val Glu Gln Val Trp Tyr Asn Gly
[4528] 225 230 235 240
[4529] Lys Phe Tyr Gly Ser Pro Glu Glu Leu Ala Arg Lys Tyr Ala Asp Gly
[4530] 245 250 255
[4531] Glu Val Asp Val Val Val Leu Glu Asp Pro Leu Pro Gly Gly Lys Gly
[4532] 260 265 270
[4533] His Asp Ser Thr Glu Glu Pro Pro Leu Phe Ser Ser His Lys Pro Arg
[4534] 275 280 285
[4535] Gly Asp Phe Pro Ser Pro Ile His Val Ser Gly Pro Arg Leu Val Gln

[4536] 290 295 300

[4537] Pro His Gly Pro Arg Phe Arg Leu Glu Gly Asn Ala Val Leu Tyr Gly

[4538] 305 310 315 320

[4539] Gly Trp Ser Phe Ala Phe Arg Leu Arg Ser Ser Ser Gly Leu Gln Val

[4540] 325 330 335

[4541] Leu Asn Val His Phe Gly Gly Glu Arg Ile Ala Tyr Glu Val Ser Val

[4542] 340 345 350

[4543] Gln Glu Ala Val Ala Leu Tyr Gly Gly His Thr Pro Ala Gly Met Gln

[4544] 355 360 365

[4545] Thr Lys Tyr Leu Asp Val Gly Trp Gly Leu Gly Ser Val Thr His Glu

[4546] 370 375 380

[4547] Leu Ala Pro Gly Ile Asp Cys Pro Glu Thr Ala Thr Phe Leu Asp Thr

[4548] 385 390 395 400

[4549] Phe His Tyr Tyr Asp Ala Asp Asp Pro Val His Tyr Pro Arg Ala Leu

[4550] 405 410 415

[4551] Cys Leu Phe Glu Met Pro Thr Gly Val Pro Leu Arg Arg His Phe Asn

[4552] 420 425 430

[4553] Ser Asn Phe Lys Gly Gly Phe Asn Phe Tyr Ala Gly Leu Lys Gly Gln

[4554] 435 440 445

[4555] Val Leu Val Leu Arg Thr Thr Ser Thr Val Tyr Asn Tyr Asp Tyr Ile

[4556] 450 455 460

[4557] Trp Asp Phe Ile Phe Tyr Pro Asn Gly Val Met Glu Ala Lys Met His

[4558] 465 470 475 480

[4559] Ala Thr Gly Tyr Val His Ala Thr Phe Tyr Thr Pro Glu Gly Leu Arg

[4560] 485 490 495

[4561] His Gly Thr Arg Leu His Thr His Leu Ile Gly Asn Ile His Thr His

[4562] 500 505 510

[4563] Leu Val His Tyr Arg Val Asp Leu Asp Val Ala Gly Thr Lys Asn Ser

[4564] 515 520 525

[4565] Phe Gln Thr Leu Gln Met Lys Leu Glu Asn Ile Thr Asn Pro Trp Ser

[4566] 530 535 540

[4567] Pro Arg His Arg Val Val Gln Pro Thr Leu Glu Gln Thr Gln Tyr Ser

[4568] 545 550 555 560

[4569] Trp Glu Arg Gln Ala Ala Phe Arg Phe Lys Arg Lys Leu Pro Lys Tyr

[4570] 565 570 575

[4571] Leu Leu Phe Thr Ser Pro Gln Glu Asn Pro Trp Gly His Lys Arg Ser

[4572] 580 585 590

[4573] Tyr Arg Leu Gln Ile His Ser Met Ala Asp Gln Val Leu Pro Pro Gly

[4574] 595 600 605

[4575] Trp Gln Glu Glu Gln Ala Ile Thr Trp Ala Arg Tyr Pro Leu Ala Val

[4576] 610 615 620

[4577] Thr Lys Tyr Arg Glu Ser Glu Leu Cys Ser Ser Ser Ile Tyr His Gln

[4578] 625 630 635 640
[4579] Asn Asp Pro Trp His Pro Pro Val Val Phe Glu Gln Phe Leu His Asn
[4580] 645 650 655
[4581] Asn Glu Asn Ile Glu Asn Glu Asp Leu Val Ala Trp Val Thr Val Gly
[4582] 660 665 670
[4583] Phe Leu His Ile Pro His Ser Glu Asp Ile Pro Asn Thr Ala Thr Pro
[4584] 675 680 685
[4585] Gly Asn Ser Val Gly Phe Leu Leu Arg Pro Phe Asn Phe Phe Pro Glu
[4586] 690 695 700
[4587] Asp Pro Ser Leu Ala Ser Arg Asp Thr Val Ile Val Trp Pro Arg Asp
[4588] 705 710 715 720
[4589] Asn Gly Pro Asn Tyr Val Gln Arg Trp Ile Pro Glu Asp Arg Asp Cys
[4590] 725 730 735
[4591] Ser Met Pro Pro Pro Phe Ser Tyr Asn Gly Thr Tyr Arg Pro Val Glu
[4592] 740 745 750
[4593] Pro Lys Ser Ala Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro
[4594] 755 760 765
[4595] Pro Val Ala Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
[4596] 770 775 780
[4597] Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp
[4598] 785 790 795 800
[4599] Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
[4600] 805 810 815
[4601] Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
[4602] 820 825 830
[4603] Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
[4604] 835 840 845
[4605] Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro
[4606] 850 855 860
[4607] Ser Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
[4608] 865 870 875 880
[4609] Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn
[4610] 885 890 895
[4611] Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
[4612] 900 905 910
[4613] Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
[4614] 915 920 925
[4615] Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys
[4616] 930 935 940
[4617] Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
[4618] 945 950 955 960
[4619] Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu

[4620] 965 970 975
[4621] Ser Leu Ser Pro Gly Lys
[4622] 980
[4623] <210> 56
[4624] <211> 982
[4625] <212> PRT
[4626] <213> 人工序列
[4627] <220>
[4628] <223> hDAO-Fc-Hepmut1
[4629] <400> 56
[4630] Met Pro Ala Leu Gly Trp Ala Val Ala Ala Ile Leu Met Leu Gln Thr
[4631] 1 5 10 15
[4632] Ala Met Ala Glu Pro Ser Pro Gly Thr Leu Pro Arg Lys Ala Gly Val
[4633] 20 25 30
[4634] Phe Ser Asp Leu Ser Asn Gln Glu Leu Lys Ala Val His Ser Phe Leu
[4635] 35 40 45
[4636] Trp Ser Lys Lys Glu Leu Arg Leu Gln Pro Ser Ser Thr Thr Thr Met
[4637] 50 55 60
[4638] Ala Lys Asn Thr Val Phe Leu Ile Glu Met Leu Leu Pro Lys Lys Tyr
[4639] 65 70 75 80
[4640] His Val Leu Arg Phe Leu Asp Lys Gly Glu Arg His Pro Val Arg Glu
[4641] 85 90 95
[4642] Ala Arg Ala Val Ile Phe Phe Gly Asp Gln Glu His Pro Asn Val Thr
[4643] 100 105 110
[4644] Glu Phe Ala Val Gly Pro Leu Pro Gly Pro Cys Tyr Met Arg Ala Leu
[4645] 115 120 125
[4646] Ser Pro Arg Pro Gly Tyr Gln Ser Ser Trp Ala Ser Arg Pro Ile Ser
[4647] 130 135 140
[4648] Thr Ala Glu Tyr Ala Leu Leu Tyr His Thr Leu Gln Glu Ala Thr Lys
[4649] 145 150 155 160
[4650] Pro Leu His Gln Phe Phe Leu Asn Thr Thr Gly Phe Ser Phe Gln Asp
[4651] 165 170 175
[4652] Cys His Asp Arg Cys Leu Ala Phe Thr Asp Val Ala Pro Arg Gly Val
[4653] 180 185 190
[4654] Ala Ser Gly Gln Arg Arg Ser Trp Leu Ile Ile Gln Arg Tyr Val Glu
[4655] 195 200 205
[4656] Gly Tyr Phe Leu His Pro Thr Gly Leu Glu Leu Leu Val Asp His Gly
[4657] 210 215 220
[4658] Ser Thr Asp Ala Gly His Trp Ala Val Glu Gln Val Trp Tyr Asn Gly
[4659] 225 230 235 240
[4660] Lys Phe Tyr Gly Ser Pro Glu Glu Leu Ala Arg Lys Tyr Ala Asp Gly
[4661] 245 250 255

[4662] Glu Val Asp Val Val Val Leu Glu Asp Pro Leu Pro Gly Gly Lys Gly
[4663] 260 265 270
[4664] His Asp Ser Thr Glu Glu Pro Pro Leu Phe Ser Ser His Lys Pro Arg
[4665] 275 280 285
[4666] Gly Asp Phe Pro Ser Pro Ile His Val Ser Gly Pro Arg Leu Val Gln
[4667] 290 295 300
[4668] Pro His Gly Pro Arg Phe Arg Leu Glu Gly Asn Ala Val Leu Tyr Gly
[4669] 305 310 315 320
[4670] Gly Trp Ser Phe Ala Phe Arg Leu Arg Ser Ser Ser Gly Leu Gln Val
[4671] 325 330 335
[4672] Leu Asn Val His Phe Gly Gly Glu Arg Ile Ala Tyr Glu Val Ser Val
[4673] 340 345 350
[4674] Gln Glu Ala Val Ala Leu Tyr Gly Gly His Thr Pro Ala Gly Met Gln
[4675] 355 360 365
[4676] Thr Lys Tyr Leu Asp Val Gly Trp Gly Leu Gly Ser Val Thr His Glu
[4677] 370 375 380
[4678] Leu Ala Pro Gly Ile Asp Cys Pro Glu Thr Ala Thr Phe Leu Asp Thr
[4679] 385 390 395 400
[4680] Phe His Tyr Tyr Asp Ala Asp Asp Pro Val His Tyr Pro Arg Ala Leu
[4681] 405 410 415
[4682] Cys Leu Phe Glu Met Pro Thr Gly Val Pro Leu Arg Arg His Phe Asn
[4683] 420 425 430
[4684] Ser Asn Phe Lys Gly Gly Phe Asn Phe Tyr Ala Gly Leu Lys Gly Gln
[4685] 435 440 445
[4686] Val Leu Val Leu Arg Thr Thr Ser Thr Val Tyr Asn Tyr Asp Tyr Ile
[4687] 450 455 460
[4688] Trp Asp Phe Ile Phe Tyr Pro Asn Gly Val Met Glu Ala Lys Met His
[4689] 465 470 475 480
[4690] Ala Thr Gly Tyr Val His Ala Thr Phe Tyr Thr Pro Glu Gly Leu Arg
[4691] 485 490 495
[4692] His Gly Thr Arg Leu His Thr His Leu Ile Gly Asn Ile His Thr His
[4693] 500 505 510
[4694] Leu Val His Tyr Arg Val Asp Leu Asp Val Ala Gly Thr Lys Asn Ser
[4695] 515 520 525
[4696] Phe Gln Thr Leu Gln Met Lys Leu Glu Asn Ile Thr Asn Pro Trp Ser
[4697] 530 535 540
[4698] Pro Arg His Arg Val Val Gln Pro Thr Leu Glu Gln Thr Gln Tyr Ser
[4699] 545 550 555 560
[4700] Trp Glu Arg Gln Ala Ala Phe Ser Phe Lys Arg Lys Leu Pro Lys Tyr
[4701] 565 570 575
[4702] Leu Leu Phe Thr Ser Pro Gln Glu Asn Pro Trp Gly His Lys Arg Ser
[4703] 580 585 590

[4704] Tyr Arg Leu Gln Ile His Ser Met Ala Asp Gln Val Leu Pro Pro Gly
[4705] 595 600 605
[4706] Trp Gln Glu Glu Gln Ala Ile Thr Trp Ala Arg Tyr Pro Leu Ala Val
[4707] 610 615 620
[4708] Thr Lys Tyr Arg Glu Ser Glu Leu Cys Ser Ser Ser Ile Tyr His Gln
[4709] 625 630 635 640
[4710] Asn Asp Pro Trp His Pro Pro Val Val Phe Glu Gln Phe Leu His Asn
[4711] 645 650 655
[4712] Asn Glu Asn Ile Glu Asn Glu Asp Leu Val Ala Trp Val Thr Val Gly
[4713] 660 665 670
[4714] Phe Leu His Ile Pro His Ser Glu Asp Ile Pro Asn Thr Ala Thr Pro
[4715] 675 680 685
[4716] Gly Asn Ser Val Gly Phe Leu Leu Arg Pro Phe Asn Phe Phe Pro Glu
[4717] 690 695 700
[4718] Asp Pro Ser Leu Ala Ser Arg Asp Thr Val Ile Val Trp Pro Arg Asp
[4719] 705 710 715 720
[4720] Asn Gly Pro Asn Tyr Val Gln Arg Trp Ile Pro Glu Asp Arg Asp Cys
[4721] 725 730 735
[4722] Ser Met Pro Pro Pro Phe Ser Tyr Asn Gly Thr Tyr Arg Pro Val Glu
[4723] 740 745 750
[4724] Pro Lys Ser Ala Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro
[4725] 755 760 765
[4726] Pro Val Ala Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
[4727] 770 775 780
[4728] Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp
[4729] 785 790 795 800
[4730] Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
[4731] 805 810 815
[4732] Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
[4733] 820 825 830
[4734] Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
[4735] 835 840 845
[4736] Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro
[4737] 850 855 860
[4738] Ser Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
[4739] 865 870 875 880
[4740] Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn
[4741] 885 890 895
[4742] Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
[4743] 900 905 910
[4744] Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
[4745] 915 920 925

[4746] Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys
[4747] 930 935 940
[4748] Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
[4749] 945 950 955 960
[4750] Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
[4751] 965 970 975
[4752] Ser Leu Ser Pro Gly Lys
[4753] 980
[4754] <210> 57
[4755] <211> 982
[4756] <212> PRT
[4757] <213> 人工序列
[4758] <220>
[4759] <223> hDAO-Fc-Hepmut2
[4760] <400> 57
[4761] Met Pro Ala Leu Gly Trp Ala Val Ala Ala Ile Leu Met Leu Gln Thr
[4762] 1 5 10 15
[4763] Ala Met Ala Glu Pro Ser Pro Gly Thr Leu Pro Arg Lys Ala Gly Val
[4764] 20 25 30
[4765] Phe Ser Asp Leu Ser Asn Gln Glu Leu Lys Ala Val His Ser Phe Leu
[4766] 35 40 45
[4767] Trp Ser Lys Lys Glu Leu Arg Leu Gln Pro Ser Ser Thr Thr Thr Met
[4768] 50 55 60
[4769] Ala Lys Asn Thr Val Phe Leu Ile Glu Met Leu Leu Pro Lys Lys Tyr
[4770] 65 70 75 80
[4771] His Val Leu Arg Phe Leu Asp Lys Gly Glu Arg His Pro Val Arg Glu
[4772] 85 90 95
[4773] Ala Arg Ala Val Ile Phe Phe Gly Asp Gln Glu His Pro Asn Val Thr
[4774] 100 105 110
[4775] Glu Phe Ala Val Gly Pro Leu Pro Gly Pro Cys Tyr Met Arg Ala Leu
[4776] 115 120 125
[4777] Ser Pro Arg Pro Gly Tyr Gln Ser Ser Trp Ala Ser Arg Pro Ile Ser
[4778] 130 135 140
[4779] Thr Ala Glu Tyr Ala Leu Leu Tyr His Thr Leu Gln Glu Ala Thr Lys
[4780] 145 150 155 160
[4781] Pro Leu His Gln Phe Phe Leu Asn Thr Thr Gly Phe Ser Phe Gln Asp
[4782] 165 170 175
[4783] Cys His Asp Arg Cys Leu Ala Phe Thr Asp Val Ala Pro Arg Gly Val
[4784] 180 185 190
[4785] Ala Ser Gly Gln Arg Arg Ser Trp Leu Ile Ile Gln Arg Tyr Val Glu
[4786] 195 200 205
[4787] Gly Tyr Phe Leu His Pro Thr Gly Leu Glu Leu Leu Val Asp His Gly

[4788] 210 215 220
[4789] Ser Thr Asp Ala Gly His Trp Ala Val Glu Gln Val Trp Tyr Asn Gly
[4790] 225 230 235 240
[4791] Lys Phe Tyr Gly Ser Pro Glu Glu Leu Ala Arg Lys Tyr Ala Asp Gly
[4792] 245 250 255
[4793] Glu Val Asp Val Val Val Leu Glu Asp Pro Leu Pro Gly Gly Lys Gly
[4794] 260 265 270
[4795] His Asp Ser Thr Glu Glu Pro Pro Leu Phe Ser Ser His Lys Pro Arg
[4796] 275 280 285
[4797] Gly Asp Phe Pro Ser Pro Ile His Val Ser Gly Pro Arg Leu Val Gln
[4798] 290 295 300
[4799] Pro His Gly Pro Arg Phe Arg Leu Glu Gly Asn Ala Val Leu Tyr Gly
[4800] 305 310 315 320
[4801] Gly Trp Ser Phe Ala Phe Arg Leu Arg Ser Ser Ser Gly Leu Gln Val
[4802] 325 330 335
[4803] Leu Asn Val His Phe Gly Gly Glu Arg Ile Ala Tyr Glu Val Ser Val
[4804] 340 345 350
[4805] Gln Glu Ala Val Ala Leu Tyr Gly Gly His Thr Pro Ala Gly Met Gln
[4806] 355 360 365
[4807] Thr Lys Tyr Leu Asp Val Gly Trp Gly Leu Gly Ser Val Thr His Glu
[4808] 370 375 380
[4809] Leu Ala Pro Gly Ile Asp Cys Pro Glu Thr Ala Thr Phe Leu Asp Thr
[4810] 385 390 395 400
[4811] Phe His Tyr Tyr Asp Ala Asp Asp Pro Val His Tyr Pro Arg Ala Leu
[4812] 405 410 415
[4813] Cys Leu Phe Glu Met Pro Thr Gly Val Pro Leu Arg Arg His Phe Asn
[4814] 420 425 430
[4815] Ser Asn Phe Lys Gly Gly Phe Asn Phe Tyr Ala Gly Leu Lys Gly Gln
[4816] 435 440 445
[4817] Val Leu Val Leu Arg Thr Thr Ser Thr Val Tyr Asn Tyr Asp Tyr Ile
[4818] 450 455 460
[4819] Trp Asp Phe Ile Phe Tyr Pro Asn Gly Val Met Glu Ala Lys Met His
[4820] 465 470 475 480
[4821] Ala Thr Gly Tyr Val His Ala Thr Phe Tyr Thr Pro Glu Gly Leu Arg
[4822] 485 490 495
[4823] His Gly Thr Arg Leu His Thr His Leu Ile Gly Asn Ile His Thr His
[4824] 500 505 510
[4825] Leu Val His Tyr Arg Val Asp Leu Asp Val Ala Gly Thr Lys Asn Ser
[4826] 515 520 525
[4827] Phe Gln Thr Leu Gln Met Lys Leu Glu Asn Ile Thr Asn Pro Trp Ser
[4828] 530 535 540
[4829] Pro Arg His Arg Val Val Gln Pro Thr Leu Glu Gln Thr Gln Tyr Ser

[4830] 545 550 555 560
[4831] Trp Glu Arg Gln Ala Ala Phe Arg Phe Lys Arg Lys Leu Pro Thr Tyr
[4832] 565 570 575
[4833] Leu Leu Phe Thr Ser Pro Gln Glu Asn Pro Trp Gly His Lys Arg Ser
[4834] 580 585 590
[4835] Tyr Arg Leu Gln Ile His Ser Met Ala Asp Gln Val Leu Pro Pro Gly
[4836] 595 600 605
[4837] Trp Gln Glu Glu Gln Ala Ile Thr Trp Ala Arg Tyr Pro Leu Ala Val
[4838] 610 615 620
[4839] Thr Lys Tyr Arg Glu Ser Glu Leu Cys Ser Ser Ser Ile Tyr His Gln
[4840] 625 630 635 640
[4841] Asn Asp Pro Trp His Pro Pro Val Val Phe Glu Gln Phe Leu His Asn
[4842] 645 650 655
[4843] Asn Glu Asn Ile Glu Asn Glu Asp Leu Val Ala Trp Val Thr Val Gly
[4844] 660 665 670
[4845] Phe Leu His Ile Pro His Ser Glu Asp Ile Pro Asn Thr Ala Thr Pro
[4846] 675 680 685
[4847] Gly Asn Ser Val Gly Phe Leu Leu Arg Pro Phe Asn Phe Phe Pro Glu
[4848] 690 695 700
[4849] Asp Pro Ser Leu Ala Ser Arg Asp Thr Val Ile Val Trp Pro Arg Asp
[4850] 705 710 715 720
[4851] Asn Gly Pro Asn Tyr Val Gln Arg Trp Ile Pro Glu Asp Arg Asp Cys
[4852] 725 730 735
[4853] Ser Met Pro Pro Pro Phe Ser Tyr Asn Gly Thr Tyr Arg Pro Val Glu
[4854] 740 745 750
[4855] Pro Lys Ser Ala Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro
[4856] 755 760 765
[4857] Pro Val Ala Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
[4858] 770 775 780
[4859] Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp
[4860] 785 790 795 800
[4861] Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
[4862] 805 810 815
[4863] Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
[4864] 820 825 830
[4865] Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
[4866] 835 840 845
[4867] Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro
[4868] 850 855 860
[4869] Ser Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
[4870] 865 870 875 880
[4871] Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn

[4872] 885 890 895
[4873] Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
[4874] 900 905 910
[4875] Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
[4876] 915 920 925
[4877] Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys
[4878] 930 935 940
[4879] Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
[4880] 945 950 955 960
[4881] Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
[4882] 965 970 975
[4883] Ser Leu Ser Pro Gly Lys
[4884] 980
[4885] <210> 58
[4886] <211> 982
[4887] <212> PRT
[4888] <213> 人工序列
[4889] <220>
[4890] <223> hDAO-Fc-Hepmut3
[4891] <400> 58
[4892] Met Pro Ala Leu Gly Trp Ala Val Ala Ala Ile Leu Met Leu Gln Thr
[4893] 1 5 10 15
[4894] Ala Met Ala Glu Pro Ser Pro Gly Thr Leu Pro Arg Lys Ala Gly Val
[4895] 20 25 30
[4896] Phe Ser Asp Leu Ser Asn Gln Glu Leu Lys Ala Val His Ser Phe Leu
[4897] 35 40 45
[4898] Trp Ser Lys Lys Glu Leu Arg Leu Gln Pro Ser Ser Thr Thr Thr Met
[4899] 50 55 60
[4900] Ala Lys Asn Thr Val Phe Leu Ile Glu Met Leu Leu Pro Lys Lys Tyr
[4901] 65 70 75 80
[4902] His Val Leu Arg Phe Leu Asp Lys Gly Glu Arg His Pro Val Arg Glu
[4903] 85 90 95
[4904] Ala Arg Ala Val Ile Phe Phe Gly Asp Gln Glu His Pro Asn Val Thr
[4905] 100 105 110
[4906] Glu Phe Ala Val Gly Pro Leu Pro Gly Pro Cys Tyr Met Arg Ala Leu
[4907] 115 120 125
[4908] Ser Pro Arg Pro Gly Tyr Gln Ser Ser Trp Ala Ser Arg Pro Ile Ser
[4909] 130 135 140
[4910] Thr Ala Glu Tyr Ala Leu Leu Tyr His Thr Leu Gln Glu Ala Thr Lys
[4911] 145 150 155 160
[4912] Pro Leu His Gln Phe Phe Leu Asn Thr Thr Gly Phe Ser Phe Gln Asp
[4913] 165 170 175

[4914] Cys His Asp Arg Cys Leu Ala Phe Thr Asp Val Ala Pro Arg Gly Val
[4915] 180 185 190
[4916] Ala Ser Gly Gln Arg Arg Ser Trp Leu Ile Ile Gln Arg Tyr Val Glu
[4917] 195 200 205
[4918] Gly Tyr Phe Leu His Pro Thr Gly Leu Glu Leu Leu Val Asp His Gly
[4919] 210 215 220
[4920] Ser Thr Asp Ala Gly His Trp Ala Val Glu Gln Val Trp Tyr Asn Gly
[4921] 225 230 235 240
[4922] Lys Phe Tyr Gly Ser Pro Glu Glu Leu Ala Arg Lys Tyr Ala Asp Gly
[4923] 245 250 255
[4924] Glu Val Asp Val Val Val Leu Glu Asp Pro Leu Pro Gly Gly Lys Gly
[4925] 260 265 270
[4926] His Asp Ser Thr Glu Glu Pro Pro Leu Phe Ser Ser His Lys Pro Arg
[4927] 275 280 285
[4928] Gly Asp Phe Pro Ser Pro Ile His Val Ser Gly Pro Arg Leu Val Gln
[4929] 290 295 300
[4930] Pro His Gly Pro Arg Phe Arg Leu Glu Gly Asn Ala Val Leu Tyr Gly
[4931] 305 310 315 320
[4932] Gly Trp Ser Phe Ala Phe Arg Leu Arg Ser Ser Ser Gly Leu Gln Val
[4933] 325 330 335
[4934] Leu Asn Val His Phe Gly Gly Glu Arg Ile Ala Tyr Glu Val Ser Val
[4935] 340 345 350
[4936] Gln Glu Ala Val Ala Leu Tyr Gly Gly His Thr Pro Ala Gly Met Gln
[4937] 355 360 365
[4938] Thr Lys Tyr Leu Asp Val Gly Trp Gly Leu Gly Ser Val Thr His Glu
[4939] 370 375 380
[4940] Leu Ala Pro Gly Ile Asp Cys Pro Glu Thr Ala Thr Phe Leu Asp Thr
[4941] 385 390 395 400
[4942] Phe His Tyr Tyr Asp Ala Asp Asp Pro Val His Tyr Pro Arg Ala Leu
[4943] 405 410 415
[4944] Cys Leu Phe Glu Met Pro Thr Gly Val Pro Leu Arg Arg His Phe Asn
[4945] 420 425 430
[4946] Ser Asn Phe Lys Gly Gly Phe Asn Phe Tyr Ala Gly Leu Lys Gly Gln
[4947] 435 440 445
[4948] Val Leu Val Leu Arg Thr Thr Ser Thr Val Tyr Asn Tyr Asp Tyr Ile
[4949] 450 455 460
[4950] Trp Asp Phe Ile Phe Tyr Pro Asn Gly Val Met Glu Ala Lys Met His
[4951] 465 470 475 480
[4952] Ala Thr Gly Tyr Val His Ala Thr Phe Tyr Thr Pro Glu Gly Leu Arg
[4953] 485 490 495
[4954] His Gly Thr Arg Leu His Thr His Leu Ile Gly Asn Ile His Thr His
[4955] 500 505 510

[4956] Leu Val His Tyr Arg Val Asp Leu Asp Val Ala Gly Thr Lys Asn Ser
[4957] 515 520 525
[4958] Phe Gln Thr Leu Gln Met Lys Leu Glu Asn Ile Thr Asn Pro Trp Ser
[4959] 530 535 540
[4960] Pro Arg His Arg Val Val Gln Pro Thr Leu Glu Gln Thr Gln Tyr Ser
[4961] 545 550 555 560
[4962] Trp Glu Arg Gln Ala Ala Phe Arg Phe Lys Thr Lys Leu Pro Lys Tyr
[4963] 565 570 575
[4964] Leu Leu Phe Thr Ser Pro Gln Glu Asn Pro Trp Gly His Lys Arg Ser
[4965] 580 585 590
[4966] Tyr Arg Leu Gln Ile His Ser Met Ala Asp Gln Val Leu Pro Pro Gly
[4967] 595 600 605
[4968] Trp Gln Glu Glu Gln Ala Ile Thr Trp Ala Arg Tyr Pro Leu Ala Val
[4969] 610 615 620
[4970] Thr Lys Tyr Arg Glu Ser Glu Leu Cys Ser Ser Ser Ile Tyr His Gln
[4971] 625 630 635 640
[4972] Asn Asp Pro Trp His Pro Pro Val Val Phe Glu Gln Phe Leu His Asn
[4973] 645 650 655
[4974] Asn Glu Asn Ile Glu Asn Glu Asp Leu Val Ala Trp Val Thr Val Gly
[4975] 660 665 670
[4976] Phe Leu His Ile Pro His Ser Glu Asp Ile Pro Asn Thr Ala Thr Pro
[4977] 675 680 685
[4978] Gly Asn Ser Val Gly Phe Leu Leu Arg Pro Phe Asn Phe Phe Pro Glu
[4979] 690 695 700
[4980] Asp Pro Ser Leu Ala Ser Arg Asp Thr Val Ile Val Trp Pro Arg Asp
[4981] 705 710 715 720
[4982] Asn Gly Pro Asn Tyr Val Gln Arg Trp Ile Pro Glu Asp Arg Asp Cys
[4983] 725 730 735
[4984] Ser Met Pro Pro Pro Phe Ser Tyr Asn Gly Thr Tyr Arg Pro Val Glu
[4985] 740 745 750
[4986] Pro Lys Ser Ala Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro
[4987] 755 760 765
[4988] Pro Val Ala Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
[4989] 770 775 780
[4990] Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp
[4991] 785 790 795 800
[4992] Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
[4993] 805 810 815
[4994] Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
[4995] 820 825 830
[4996] Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
[4997] 835 840 845

[4998] Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro
[4999] 850 855 860
[5000] Ser Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
[5001] 865 870 875 880
[5002] Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn
[5003] 885 890 895
[5004] Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
[5005] 900 905 910
[5006] Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
[5007] 915 920 925
[5008] Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys
[5009] 930 935 940
[5010] Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
[5011] 945 950 955 960
[5012] Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
[5013] 965 970 975
[5014] Ser Leu Ser Pro Gly Lys
[5015] 980
[5016] <210> 59
[5017] <211> 982
[5018] <212> PRT
[5019] <213> 人工序列
[5020] <220>
[5021] <223> hDAO-Fc-Hepmut4
[5022] <400> 59
[5023] Met Pro Ala Leu Gly Trp Ala Val Ala Ala Ile Leu Met Leu Gln Thr
[5024] 1 5 10 15
[5025] Ala Met Ala Glu Pro Ser Pro Gly Thr Leu Pro Arg Lys Ala Gly Val
[5026] 20 25 30
[5027] Phe Ser Asp Leu Ser Asn Gln Glu Leu Lys Ala Val His Ser Phe Leu
[5028] 35 40 45
[5029] Trp Ser Lys Lys Glu Leu Arg Leu Gln Pro Ser Ser Thr Thr Thr Met
[5030] 50 55 60
[5031] Ala Lys Asn Thr Val Phe Leu Ile Glu Met Leu Leu Pro Lys Lys Tyr
[5032] 65 70 75 80
[5033] His Val Leu Arg Phe Leu Asp Lys Gly Glu Arg His Pro Val Arg Glu
[5034] 85 90 95
[5035] Ala Arg Ala Val Ile Phe Phe Gly Asp Gln Glu His Pro Asn Val Thr
[5036] 100 105 110
[5037] Glu Phe Ala Val Gly Pro Leu Pro Gly Pro Cys Tyr Met Arg Ala Leu
[5038] 115 120 125
[5039] Ser Pro Arg Pro Gly Tyr Gln Ser Ser Trp Ala Ser Arg Pro Ile Ser

[5040] 130 135 140

[5041] Thr Ala Glu Tyr Ala Leu Leu Tyr His Thr Leu Gln Glu Ala Thr Lys

[5042] 145 150 155 160

[5043] Pro Leu His Gln Phe Phe Leu Asn Thr Thr Gly Phe Ser Phe Gln Asp

[5044] 165 170 175

[5045] Cys His Asp Arg Cys Leu Ala Phe Thr Asp Val Ala Pro Arg Gly Val

[5046] 180 185 190

[5047] Ala Ser Gly Gln Arg Arg Ser Trp Leu Ile Ile Gln Arg Tyr Val Glu

[5048] 195 200 205

[5049] Gly Tyr Phe Leu His Pro Thr Gly Leu Glu Leu Leu Val Asp His Gly

[5050] 210 215 220

[5051] Ser Thr Asp Ala Gly His Trp Ala Val Glu Gln Val Trp Tyr Asn Gly

[5052] 225 230 235 240

[5053] Lys Phe Tyr Gly Ser Pro Glu Glu Leu Ala Arg Lys Tyr Ala Asp Gly

[5054] 245 250 255

[5055] Glu Val Asp Val Val Val Leu Glu Asp Pro Leu Pro Gly Gly Lys Gly

[5056] 260 265 270

[5057] His Asp Ser Thr Glu Glu Pro Pro Leu Phe Ser Ser His Lys Pro Arg

[5058] 275 280 285

[5059] Gly Asp Phe Pro Ser Pro Ile His Val Ser Gly Pro Arg Leu Val Gln

[5060] 290 295 300

[5061] Pro His Gly Pro Arg Phe Arg Leu Glu Gly Asn Ala Val Leu Tyr Gly

[5062] 305 310 315 320

[5063] Gly Trp Ser Phe Ala Phe Arg Leu Arg Ser Ser Ser Gly Leu Gln Val

[5064] 325 330 335

[5065] Leu Asn Val His Phe Gly Gly Glu Arg Ile Ala Tyr Glu Val Ser Val

[5066] 340 345 350

[5067] Gln Glu Ala Val Ala Leu Tyr Gly Gly His Thr Pro Ala Gly Met Gln

[5068] 355 360 365

[5069] Thr Lys Tyr Leu Asp Val Gly Trp Gly Leu Gly Ser Val Thr His Glu

[5070] 370 375 380

[5071] Leu Ala Pro Gly Ile Asp Cys Pro Glu Thr Ala Thr Phe Leu Asp Thr

[5072] 385 390 395 400

[5073] Phe His Tyr Tyr Asp Ala Asp Asp Pro Val His Tyr Pro Arg Ala Leu

[5074] 405 410 415

[5075] Cys Leu Phe Glu Met Pro Thr Gly Val Pro Leu Arg Arg His Phe Asn

[5076] 420 425 430

[5077] Ser Asn Phe Lys Gly Gly Phe Asn Phe Tyr Ala Gly Leu Lys Gly Gln

[5078] 435 440 445

[5079] Val Leu Val Leu Arg Thr Thr Ser Thr Val Tyr Asn Tyr Asp Tyr Ile

[5080] 450 455 460

[5081] Trp Asp Phe Ile Phe Tyr Pro Asn Gly Val Met Glu Ala Lys Met His

[5082] 465 470 475 480
[5083] Ala Thr Gly Tyr Val His Ala Thr Phe Tyr Thr Pro Glu Gly Leu Arg
[5084] 485 490 495
[5085] His Gly Thr Arg Leu His Thr His Leu Ile Gly Asn Ile His Thr His
[5086] 500 505 510
[5087] Leu Val His Tyr Arg Val Asp Leu Asp Val Ala Gly Thr Lys Asn Ser
[5088] 515 520 525
[5089] Phe Gln Thr Leu Gln Met Lys Leu Glu Asn Ile Thr Asn Pro Trp Ser
[5090] 530 535 540
[5091] Pro Arg His Arg Val Val Gln Pro Thr Leu Glu Gln Thr Gln Tyr Ser
[5092] 545 550 555 560
[5093] Trp Glu Arg Gln Ala Ala Phe Ser Phe Lys Thr Lys Leu Pro Lys Tyr
[5094] 565 570 575
[5095] Leu Leu Phe Thr Ser Pro Gln Glu Asn Pro Trp Gly His Lys Arg Ser
[5096] 580 585 590
[5097] Tyr Arg Leu Gln Ile His Ser Met Ala Asp Gln Val Leu Pro Pro Gly
[5098] 595 600 605
[5099] Trp Gln Glu Glu Gln Ala Ile Thr Trp Ala Arg Tyr Pro Leu Ala Val
[5100] 610 615 620
[5101] Thr Lys Tyr Arg Glu Ser Glu Leu Cys Ser Ser Ser Ile Tyr His Gln
[5102] 625 630 635 640
[5103] Asn Asp Pro Trp His Pro Pro Val Val Phe Glu Gln Phe Leu His Asn
[5104] 645 650 655
[5105] Asn Glu Asn Ile Glu Asn Glu Asp Leu Val Ala Trp Val Thr Val Gly
[5106] 660 665 670
[5107] Phe Leu His Ile Pro His Ser Glu Asp Ile Pro Asn Thr Ala Thr Pro
[5108] 675 680 685
[5109] Gly Asn Ser Val Gly Phe Leu Leu Arg Pro Phe Asn Phe Phe Pro Glu
[5110] 690 695 700
[5111] Asp Pro Ser Leu Ala Ser Arg Asp Thr Val Ile Val Trp Pro Arg Asp
[5112] 705 710 715 720
[5113] Asn Gly Pro Asn Tyr Val Gln Arg Trp Ile Pro Glu Asp Arg Asp Cys
[5114] 725 730 735
[5115] Ser Met Pro Pro Pro Phe Ser Tyr Asn Gly Thr Tyr Arg Pro Val Glu
[5116] 740 745 750
[5117] Pro Lys Ser Ala Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro
[5118] 755 760 765
[5119] Pro Val Ala Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
[5120] 770 775 780
[5121] Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp
[5122] 785 790 795 800
[5123] Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly

[5124] 805 810 815
[5125] Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
[5126] 820 825 830
[5127] Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
[5128] 835 840 845
[5129] Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro
[5130] 850 855 860
[5131] Ser Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
[5132] 865 870 875 880
[5133] Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn
[5134] 885 890 895
[5135] Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
[5136] 900 905 910
[5137] Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
[5138] 915 920 925
[5139] Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys
[5140] 930 935 940
[5141] Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
[5142] 945 950 955 960
[5143] Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
[5144] 965 970 975
[5145] Ser Leu Ser Pro Gly Lys
[5146] 980
[5147] <210> 60
[5148] <211> 982
[5149] <212> PRT
[5150] <213> 人工序列
[5151] <220>
[5152] <223> hDAO-Fc-Hepmut5
[5153] <400> 60
[5154] Met Pro Ala Leu Gly Trp Ala Val Ala Ala Ile Leu Met Leu Gln Thr
[5155] 1 5 10 15
[5156] Ala Met Ala Glu Pro Ser Pro Gly Thr Leu Pro Arg Lys Ala Gly Val
[5157] 20 25 30
[5158] Phe Ser Asp Leu Ser Asn Gln Glu Leu Lys Ala Val His Ser Phe Leu
[5159] 35 40 45
[5160] Trp Ser Lys Lys Glu Leu Arg Leu Gln Pro Ser Ser Thr Thr Thr Met
[5161] 50 55 60
[5162] Ala Lys Asn Thr Val Phe Leu Ile Glu Met Leu Leu Pro Lys Lys Tyr
[5163] 65 70 75 80
[5164] His Val Leu Arg Phe Leu Asp Lys Gly Glu Arg His Pro Val Arg Glu
[5165] 85 90 95

[5166] Ala Arg Ala Val Ile Phe Phe Gly Asp Gln Glu His Pro Asn Val Thr
[5167] 100 105 110
[5168] Glu Phe Ala Val Gly Pro Leu Pro Gly Pro Cys Tyr Met Arg Ala Leu
[5169] 115 120 125
[5170] Ser Pro Arg Pro Gly Tyr Gln Ser Ser Trp Ala Ser Arg Pro Ile Ser
[5171] 130 135 140
[5172] Thr Ala Glu Tyr Ala Leu Leu Tyr His Thr Leu Gln Glu Ala Thr Lys
[5173] 145 150 155 160
[5174] Pro Leu His Gln Phe Phe Leu Asn Thr Thr Gly Phe Ser Phe Gln Asp
[5175] 165 170 175
[5176] Cys His Asp Arg Cys Leu Ala Phe Thr Asp Val Ala Pro Arg Gly Val
[5177] 180 185 190
[5178] Ala Ser Gly Gln Arg Arg Ser Trp Leu Ile Ile Gln Arg Tyr Val Glu
[5179] 195 200 205
[5180] Gly Tyr Phe Leu His Pro Thr Gly Leu Glu Leu Leu Val Asp His Gly
[5181] 210 215 220
[5182] Ser Thr Asp Ala Gly His Trp Ala Val Glu Gln Val Trp Tyr Asn Gly
[5183] 225 230 235 240
[5184] Lys Phe Tyr Gly Ser Pro Glu Glu Leu Ala Arg Lys Tyr Ala Asp Gly
[5185] 245 250 255
[5186] Glu Val Asp Val Val Val Leu Glu Asp Pro Leu Pro Gly Gly Lys Gly
[5187] 260 265 270
[5188] His Asp Ser Thr Glu Glu Pro Pro Leu Phe Ser Ser His Lys Pro Arg
[5189] 275 280 285
[5190] Gly Asp Phe Pro Ser Pro Ile His Val Ser Gly Pro Arg Leu Val Gln
[5191] 290 295 300
[5192] Pro His Gly Pro Arg Phe Arg Leu Glu Gly Asn Ala Val Leu Tyr Gly
[5193] 305 310 315 320
[5194] Gly Trp Ser Phe Ala Phe Arg Leu Arg Ser Ser Ser Gly Leu Gln Val
[5195] 325 330 335
[5196] Leu Asn Val His Phe Gly Gly Glu Arg Ile Ala Tyr Glu Val Ser Val
[5197] 340 345 350
[5198] Gln Glu Ala Val Ala Leu Tyr Gly Gly His Thr Pro Ala Gly Met Gln
[5199] 355 360 365
[5200] Thr Lys Tyr Leu Asp Val Gly Trp Gly Leu Gly Ser Val Thr His Glu
[5201] 370 375 380
[5202] Leu Ala Pro Gly Ile Asp Cys Pro Glu Thr Ala Thr Phe Leu Asp Thr
[5203] 385 390 395 400
[5204] Phe His Tyr Tyr Asp Ala Asp Asp Pro Val His Tyr Pro Arg Ala Leu
[5205] 405 410 415
[5206] Cys Leu Phe Glu Met Pro Thr Gly Val Pro Leu Arg Arg His Phe Asn
[5207] 420 425 430

[5208] Ser Asn Phe Lys Gly Gly Phe Asn Phe Tyr Ala Gly Leu Lys Gly Gln
[5209] 435 440 445
[5210] Val Leu Val Leu Arg Thr Thr Ser Thr Val Tyr Asn Tyr Asp Tyr Ile
[5211] 450 455 460
[5212] Trp Asp Phe Ile Phe Tyr Pro Asn Gly Val Met Glu Ala Lys Met His
[5213] 465 470 475 480
[5214] Ala Thr Gly Tyr Val His Ala Thr Phe Tyr Thr Pro Glu Gly Leu Arg
[5215] 485 490 495
[5216] His Gly Thr Arg Leu His Thr His Leu Ile Gly Asn Ile His Thr His
[5217] 500 505 510
[5218] Leu Val His Tyr Arg Val Asp Leu Asp Val Ala Gly Thr Lys Asn Ser
[5219] 515 520 525
[5220] Phe Gln Thr Leu Gln Met Lys Leu Glu Asn Ile Thr Asn Pro Trp Ser
[5221] 530 535 540
[5222] Pro Arg His Arg Val Val Gln Pro Thr Leu Glu Gln Thr Gln Tyr Ser
[5223] 545 550 555 560
[5224] Trp Glu Arg Gln Ala Ala Phe Arg Phe Lys Thr Lys Leu Pro Thr Tyr
[5225] 565 570 575
[5226] Leu Leu Phe Thr Ser Pro Gln Glu Asn Pro Trp Gly His Lys Arg Ser
[5227] 580 585 590
[5228] Tyr Arg Leu Gln Ile His Ser Met Ala Asp Gln Val Leu Pro Pro Gly
[5229] 595 600 605
[5230] Trp Gln Glu Glu Gln Ala Ile Thr Trp Ala Arg Tyr Pro Leu Ala Val
[5231] 610 615 620
[5232] Thr Lys Tyr Arg Glu Ser Glu Leu Cys Ser Ser Ser Ile Tyr His Gln
[5233] 625 630 635 640
[5234] Asn Asp Pro Trp His Pro Pro Val Val Phe Glu Gln Phe Leu His Asn
[5235] 645 650 655
[5236] Asn Glu Asn Ile Glu Asn Glu Asp Leu Val Ala Trp Val Thr Val Gly
[5237] 660 665 670
[5238] Phe Leu His Ile Pro His Ser Glu Asp Ile Pro Asn Thr Ala Thr Pro
[5239] 675 680 685
[5240] Gly Asn Ser Val Gly Phe Leu Leu Arg Pro Phe Asn Phe Phe Pro Glu
[5241] 690 695 700
[5242] Asp Pro Ser Leu Ala Ser Arg Asp Thr Val Ile Val Trp Pro Arg Asp
[5243] 705 710 715 720
[5244] Asn Gly Pro Asn Tyr Val Gln Arg Trp Ile Pro Glu Asp Arg Asp Cys
[5245] 725 730 735
[5246] Ser Met Pro Pro Pro Phe Ser Tyr Asn Gly Thr Tyr Arg Pro Val Glu
[5247] 740 745 750
[5248] Pro Lys Ser Ala Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro
[5249] 755 760 765

[5250] Pro Val Ala Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
[5251] 770 775 780
[5252] Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp
[5253] 785 790 795 800
[5254] Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
[5255] 805 810 815
[5256] Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
[5257] 820 825 830
[5258] Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
[5259] 835 840 845
[5260] Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro
[5261] 850 855 860
[5262] Ser Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
[5263] 865 870 875 880
[5264] Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn
[5265] 885 890 895
[5266] Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
[5267] 900 905 910
[5268] Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
[5269] 915 920 925
[5270] Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys
[5271] 930 935 940
[5272] Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
[5273] 945 950 955 960
[5274] Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
[5275] 965 970 975
[5276] Ser Leu Ser Pro Gly Lys
[5277] 980
[5278] <210> 61
[5279] <211> 982
[5280] <212> PRT
[5281] <213> 人工序列
[5282] <220>
[5283] <223> hDAO-Fc-Hepmut6
[5284] <400> 61
[5285] Met Pro Ala Leu Gly Trp Ala Val Ala Ala Ile Leu Met Leu Gln Thr
[5286] 1 5 10 15
[5287] Ala Met Ala Glu Pro Ser Pro Gly Thr Leu Pro Arg Lys Ala Gly Val
[5288] 20 25 30
[5289] Phe Ser Asp Leu Ser Asn Gln Glu Leu Lys Ala Val His Ser Phe Leu
[5290] 35 40 45
[5291] Trp Ser Lys Lys Glu Leu Arg Leu Gln Pro Ser Ser Thr Thr Thr Met

[5292] 50 55 60

[5293] Ala Lys Asn Thr Val Phe Leu Ile Glu Met Leu Leu Pro Lys Lys Tyr

[5294] 65 70 75 80

[5295] His Val Leu Arg Phe Leu Asp Lys Gly Glu Arg His Pro Val Arg Glu

[5296] 85 90 95

[5297] Ala Arg Ala Val Ile Phe Phe Gly Asp Gln Glu His Pro Asn Val Thr

[5298] 100 105 110

[5299] Glu Phe Ala Val Gly Pro Leu Pro Gly Pro Cys Tyr Met Arg Ala Leu

[5300] 115 120 125

[5301] Ser Pro Arg Pro Gly Tyr Gln Ser Ser Trp Ala Ser Arg Pro Ile Ser

[5302] 130 135 140

[5303] Thr Ala Glu Tyr Ala Leu Leu Tyr His Thr Leu Gln Glu Ala Thr Lys

[5304] 145 150 155 160

[5305] Pro Leu His Gln Phe Phe Leu Asn Thr Thr Gly Phe Ser Phe Gln Asp

[5306] 165 170 175

[5307] Cys His Asp Arg Cys Leu Ala Phe Thr Asp Val Ala Pro Arg Gly Val

[5308] 180 185 190

[5309] Ala Ser Gly Gln Arg Arg Ser Trp Leu Ile Ile Gln Arg Tyr Val Glu

[5310] 195 200 205

[5311] Gly Tyr Phe Leu His Pro Thr Gly Leu Glu Leu Leu Val Asp His Gly

[5312] 210 215 220

[5313] Ser Thr Asp Ala Gly His Trp Ala Val Glu Gln Val Trp Tyr Asn Gly

[5314] 225 230 235 240

[5315] Lys Phe Tyr Gly Ser Pro Glu Glu Leu Ala Arg Lys Tyr Ala Asp Gly

[5316] 245 250 255

[5317] Glu Val Asp Val Val Val Leu Glu Asp Pro Leu Pro Gly Gly Lys Gly

[5318] 260 265 270

[5319] His Asp Ser Thr Glu Glu Pro Pro Leu Phe Ser Ser His Lys Pro Arg

[5320] 275 280 285

[5321] Gly Asp Phe Pro Ser Pro Ile His Val Ser Gly Pro Arg Leu Val Gln

[5322] 290 295 300

[5323] Pro His Gly Pro Arg Phe Arg Leu Glu Gly Asn Ala Val Leu Tyr Gly

[5324] 305 310 315 320

[5325] Gly Trp Ser Phe Ala Phe Arg Leu Arg Ser Ser Ser Gly Leu Gln Val

[5326] 325 330 335

[5327] Leu Asn Val His Phe Gly Gly Glu Arg Ile Ala Tyr Glu Val Ser Val

[5328] 340 345 350

[5329] Gln Glu Ala Val Ala Leu Tyr Gly Gly His Thr Pro Ala Gly Met Gln

[5330] 355 360 365

[5331] Thr Lys Tyr Leu Asp Val Gly Trp Gly Leu Gly Ser Val Thr His Glu

[5332] 370 375 380

[5333] Leu Ala Pro Gly Ile Asp Cys Pro Glu Thr Ala Thr Phe Leu Asp Thr

[5334] 385 390 395 400
[5335] Phe His Tyr Tyr Asp Ala Asp Asp Pro Val His Tyr Pro Arg Ala Leu
[5336] 405 410 415
[5337] Cys Leu Phe Glu Met Pro Thr Gly Val Pro Leu Arg Arg His Phe Asn
[5338] 420 425 430
[5339] Ser Asn Phe Lys Gly Gly Phe Asn Phe Tyr Ala Gly Leu Lys Gly Gln
[5340] 435 440 445
[5341] Val Leu Val Leu Arg Thr Thr Ser Thr Val Tyr Asn Tyr Asp Tyr Ile
[5342] 450 455 460
[5343] Trp Asp Phe Ile Phe Tyr Pro Asn Gly Val Met Glu Ala Lys Met His
[5344] 465 470 475 480
[5345] Ala Thr Gly Tyr Val His Ala Thr Phe Tyr Thr Pro Glu Gly Leu Arg
[5346] 485 490 495
[5347] His Gly Thr Arg Leu His Thr His Leu Ile Gly Asn Ile His Thr His
[5348] 500 505 510
[5349] Leu Val His Tyr Arg Val Asp Leu Asp Val Ala Gly Thr Lys Asn Ser
[5350] 515 520 525
[5351] Phe Gln Thr Leu Gln Met Lys Leu Glu Asn Ile Thr Asn Pro Trp Ser
[5352] 530 535 540
[5353] Pro Arg His Arg Val Val Gln Pro Thr Leu Glu Gln Thr Gln Tyr Ser
[5354] 545 550 555 560
[5355] Trp Glu Arg Gln Ala Ala Phe Arg Phe Gly Gln Thr Leu Pro Lys Tyr
[5356] 565 570 575
[5357] Leu Leu Phe Thr Ser Pro Gln Glu Asn Pro Trp Gly His Lys Arg Ser
[5358] 580 585 590
[5359] Tyr Arg Leu Gln Ile His Ser Met Ala Asp Gln Val Leu Pro Pro Gly
[5360] 595 600 605
[5361] Trp Gln Glu Glu Gln Ala Ile Thr Trp Ala Arg Tyr Pro Leu Ala Val
[5362] 610 615 620
[5363] Thr Lys Tyr Arg Glu Ser Glu Leu Cys Ser Ser Ser Ile Tyr His Gln
[5364] 625 630 635 640
[5365] Asn Asp Pro Trp His Pro Pro Val Val Phe Glu Gln Phe Leu His Asn
[5366] 645 650 655
[5367] Asn Glu Asn Ile Glu Asn Glu Asp Leu Val Ala Trp Val Thr Val Gly
[5368] 660 665 670
[5369] Phe Leu His Ile Pro His Ser Glu Asp Ile Pro Asn Thr Ala Thr Pro
[5370] 675 680 685
[5371] Gly Asn Ser Val Gly Phe Leu Leu Arg Pro Phe Asn Phe Phe Pro Glu
[5372] 690 695 700
[5373] Asp Pro Ser Leu Ala Ser Arg Asp Thr Val Ile Val Trp Pro Arg Asp
[5374] 705 710 715 720
[5375] Asn Gly Pro Asn Tyr Val Gln Arg Trp Ile Pro Glu Asp Arg Asp Cys

[5376] 725 730 735
[5377] Ser Met Pro Pro Pro Phe Ser Tyr Asn Gly Thr Tyr Arg Pro Val Glu
[5378] 740 745 750
[5379] Pro Lys Ser Ala Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro
[5380] 755 760 765
[5381] Pro Val Ala Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
[5382] 770 775 780
[5383] Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp
[5384] 785 790 795 800
[5385] Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
[5386] 805 810 815
[5387] Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
[5388] 820 825 830
[5389] Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
[5390] 835 840 845
[5391] Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro
[5392] 850 855 860
[5393] Ser Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
[5394] 865 870 875 880
[5395] Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn
[5396] 885 890 895
[5397] Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
[5398] 900 905 910
[5399] Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
[5400] 915 920 925
[5401] Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys
[5402] 930 935 940
[5403] Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
[5404] 945 950 955 960
[5405] Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
[5406] 965 970 975
[5407] Ser Leu Ser Pro Gly Lys
[5408] 980
[5409] <210> 62
[5410] <211> 982
[5411] <212> PRT
[5412] <213> 人工序列
[5413] <220>
[5414] <223> hDAO-Fc-Hepmut7
[5415] <400> 62
[5416] Met Pro Ala Leu Gly Trp Ala Val Ala Ala Ile Leu Met Leu Gln Thr
[5417] 1 5 10 15

[5418] Ala Met Ala Glu Pro Ser Pro Gly Thr Leu Pro Arg Lys Ala Gly Val
[5419] 20 25 30
[5420] Phe Ser Asp Leu Ser Asn Gln Glu Leu Lys Ala Val His Ser Phe Leu
[5421] 35 40 45
[5422] Trp Ser Lys Lys Glu Leu Arg Leu Gln Pro Ser Ser Thr Thr Thr Met
[5423] 50 55 60
[5424] Ala Lys Asn Thr Val Phe Leu Ile Glu Met Leu Leu Pro Lys Lys Tyr
[5425] 65 70 75 80
[5426] His Val Leu Arg Phe Leu Asp Lys Gly Glu Arg His Pro Val Arg Glu
[5427] 85 90 95
[5428] Ala Arg Ala Val Ile Phe Phe Gly Asp Gln Glu His Pro Asn Val Thr
[5429] 100 105 110
[5430] Glu Phe Ala Val Gly Pro Leu Pro Gly Pro Cys Tyr Met Arg Ala Leu
[5431] 115 120 125
[5432] Ser Pro Arg Pro Gly Tyr Gln Ser Ser Trp Ala Ser Arg Pro Ile Ser
[5433] 130 135 140
[5434] Thr Ala Glu Tyr Ala Leu Leu Tyr His Thr Leu Gln Glu Ala Thr Lys
[5435] 145 150 155 160
[5436] Pro Leu His Gln Phe Phe Leu Asn Thr Thr Gly Phe Ser Phe Gln Asp
[5437] 165 170 175
[5438] Cys His Asp Arg Cys Leu Ala Phe Thr Asp Val Ala Pro Arg Gly Val
[5439] 180 185 190
[5440] Ala Ser Gly Gln Arg Arg Ser Trp Leu Ile Ile Gln Arg Tyr Val Glu
[5441] 195 200 205
[5442] Gly Tyr Phe Leu His Pro Thr Gly Leu Glu Leu Leu Val Asp His Gly
[5443] 210 215 220
[5444] Ser Thr Asp Ala Gly His Trp Ala Val Glu Gln Val Trp Tyr Asn Gly
[5445] 225 230 235 240
[5446] Lys Phe Tyr Gly Ser Pro Glu Glu Leu Ala Arg Lys Tyr Ala Asp Gly
[5447] 245 250 255
[5448] Glu Val Asp Val Val Val Leu Glu Asp Pro Leu Pro Gly Gly Lys Gly
[5449] 260 265 270
[5450] His Asp Ser Thr Glu Glu Pro Pro Leu Phe Ser Ser His Lys Pro Arg
[5451] 275 280 285
[5452] Gly Asp Phe Pro Ser Pro Ile His Val Ser Gly Pro Arg Leu Val Gln
[5453] 290 295 300
[5454] Pro His Gly Pro Arg Phe Arg Leu Glu Gly Asn Ala Val Leu Tyr Gly
[5455] 305 310 315 320
[5456] Gly Trp Ser Phe Ala Phe Arg Leu Arg Ser Ser Ser Gly Leu Gln Val
[5457] 325 330 335
[5458] Leu Asn Val His Phe Gly Gly Glu Arg Ile Ala Tyr Glu Val Ser Val
[5459] 340 345 350

[5460] Gln Glu Ala Val Ala Leu Tyr Gly Gly His Thr Pro Ala Gly Met Gln
[5461] 355 360 365
[5462] Thr Lys Tyr Leu Asp Val Gly Trp Gly Leu Gly Ser Val Thr His Glu
[5463] 370 375 380
[5464] Leu Ala Pro Gly Ile Asp Cys Pro Glu Thr Ala Thr Phe Leu Asp Thr
[5465] 385 390 395 400
[5466] Phe His Tyr Tyr Asp Ala Asp Asp Pro Val His Tyr Pro Arg Ala Leu
[5467] 405 410 415
[5468] Cys Leu Phe Glu Met Pro Thr Gly Val Pro Leu Arg Arg His Phe Asn
[5469] 420 425 430
[5470] Ser Asn Phe Lys Gly Gly Phe Asn Phe Tyr Ala Gly Leu Lys Gly Gln
[5471] 435 440 445
[5472] Val Leu Val Leu Arg Thr Thr Ser Thr Val Tyr Asn Tyr Asp Tyr Ile
[5473] 450 455 460
[5474] Trp Asp Phe Ile Phe Tyr Pro Asn Gly Val Met Glu Ala Lys Met His
[5475] 465 470 475 480
[5476] Ala Thr Gly Tyr Val His Ala Thr Phe Tyr Thr Pro Glu Gly Leu Arg
[5477] 485 490 495
[5478] His Gly Thr Arg Leu His Thr His Leu Ile Gly Asn Ile His Thr His
[5479] 500 505 510
[5480] Leu Val His Tyr Arg Val Asp Leu Asp Val Ala Gly Thr Lys Asn Ser
[5481] 515 520 525
[5482] Phe Gln Thr Leu Gln Met Lys Leu Glu Asn Ile Thr Asn Pro Trp Ser
[5483] 530 535 540
[5484] Pro Arg His Arg Val Val Gln Pro Thr Leu Glu Gln Thr Gln Tyr Ser
[5485] 545 550 555 560
[5486] Trp Glu Arg Gln Ala Ala Phe Ser Phe Lys Arg Lys Leu Pro Thr Tyr
[5487] 565 570 575
[5488] Leu Leu Phe Thr Ser Pro Gln Glu Asn Pro Trp Gly His Lys Arg Ser
[5489] 580 585 590
[5490] Tyr Arg Leu Gln Ile His Ser Met Ala Asp Gln Val Leu Pro Pro Gly
[5491] 595 600 605
[5492] Trp Gln Glu Glu Gln Ala Ile Thr Trp Ala Arg Tyr Pro Leu Ala Val
[5493] 610 615 620
[5494] Thr Lys Tyr Arg Glu Ser Glu Leu Cys Ser Ser Ser Ile Tyr His Gln
[5495] 625 630 635 640
[5496] Asn Asp Pro Trp His Pro Pro Val Val Phe Glu Gln Phe Leu His Asn
[5497] 645 650 655
[5498] Asn Glu Asn Ile Glu Asn Glu Asp Leu Val Ala Trp Val Thr Val Gly
[5499] 660 665 670
[5500] Phe Leu His Ile Pro His Ser Glu Asp Ile Pro Asn Thr Ala Thr Pro
[5501] 675 680 685

[5502] Gly Asn Ser Val Gly Phe Leu Leu Arg Pro Phe Asn Phe Phe Pro Glu
[5503] 690 695 700
[5504] Asp Pro Ser Leu Ala Ser Arg Asp Thr Val Ile Val Trp Pro Arg Asp
[5505] 705 710 715 720
[5506] Asn Gly Pro Asn Tyr Val Gln Arg Trp Ile Pro Glu Asp Arg Asp Cys
[5507] 725 730 735
[5508] Ser Met Pro Pro Pro Phe Ser Tyr Asn Gly Thr Tyr Arg Pro Val Glu
[5509] 740 745 750
[5510] Pro Lys Ser Ala Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro
[5511] 755 760 765
[5512] Pro Val Ala Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
[5513] 770 775 780
[5514] Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp
[5515] 785 790 795 800
[5516] Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
[5517] 805 810 815
[5518] Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
[5519] 820 825 830
[5520] Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
[5521] 835 840 845
[5522] Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro
[5523] 850 855 860
[5524] Ser Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
[5525] 865 870 875 880
[5526] Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn
[5527] 885 890 895
[5528] Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
[5529] 900 905 910
[5530] Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
[5531] 915 920 925
[5532] Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys
[5533] 930 935 940
[5534] Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
[5535] 945 950 955 960
[5536] Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
[5537] 965 970 975
[5538] Ser Leu Ser Pro Gly Lys
[5539] 980
[5540] <210> 63
[5541] <211> 982
[5542] <212> PRT
[5543] <213> 人工序列

[5544] <220>

[5545] <223> hDAO-Fc-Cysmut

[5546] <400> 63

[5547] Met Pro Ala Leu Gly Trp Ala Val Ala Ala Ile Leu Met Leu Gln Thr

[5548] 1 5 10 15

[5549] Ala Met Ala Glu Pro Ser Pro Gly Thr Leu Pro Arg Lys Ala Gly Val

[5550] 20 25 30

[5551] Phe Ser Asp Leu Ser Asn Gln Glu Leu Lys Ala Val His Ser Phe Leu

[5552] 35 40 45

[5553] Trp Ser Lys Lys Glu Leu Arg Leu Gln Pro Ser Ser Thr Thr Thr Met

[5554] 50 55 60

[5555] Ala Lys Asn Thr Val Phe Leu Ile Glu Met Leu Leu Pro Lys Lys Tyr

[5556] 65 70 75 80

[5557] His Val Leu Arg Phe Leu Asp Lys Gly Glu Arg His Pro Val Arg Glu

[5558] 85 90 95

[5559] Ala Arg Ala Val Ile Phe Phe Gly Asp Gln Glu His Pro Asn Val Thr

[5560] 100 105 110

[5561] Glu Phe Ala Val Gly Pro Leu Pro Gly Pro Ala Tyr Met Arg Ala Leu

[5562] 115 120 125

[5563] Ser Pro Arg Pro Gly Tyr Gln Ser Ser Trp Ala Ser Arg Pro Ile Ser

[5564] 130 135 140

[5565] Thr Ala Glu Tyr Ala Leu Leu Tyr His Thr Leu Gln Glu Ala Thr Lys

[5566] 145 150 155 160

[5567] Pro Leu His Gln Phe Phe Leu Asn Thr Thr Gly Phe Ser Phe Gln Asp

[5568] 165 170 175

[5569] Cys His Asp Arg Cys Leu Ala Phe Thr Asp Val Ala Pro Arg Gly Val

[5570] 180 185 190

[5571] Ala Ser Gly Gln Arg Arg Ser Trp Leu Ile Ile Gln Arg Tyr Val Glu

[5572] 195 200 205

[5573] Gly Tyr Phe Leu His Pro Thr Gly Leu Glu Leu Leu Val Asp His Gly

[5574] 210 215 220

[5575] Ser Thr Asp Ala Gly His Trp Ala Val Glu Gln Val Trp Tyr Asn Gly

[5576] 225 230 235 240

[5577] Lys Phe Tyr Gly Ser Pro Glu Glu Leu Ala Arg Lys Tyr Ala Asp Gly

[5578] 245 250 255

[5579] Glu Val Asp Val Val Val Leu Glu Asp Pro Leu Pro Gly Gly Lys Gly

[5580] 260 265 270

[5581] His Asp Ser Thr Glu Glu Pro Pro Leu Phe Ser Ser His Lys Pro Arg

[5582] 275 280 285

[5583] Gly Asp Phe Pro Ser Pro Ile His Val Ser Gly Pro Arg Leu Val Gln

[5584] 290 295 300

[5585] Pro His Gly Pro Arg Phe Arg Leu Glu Gly Asn Ala Val Leu Tyr Gly

[5586] 305 310 315 320
[5587] Gly Trp Ser Phe Ala Phe Arg Leu Arg Ser Ser Ser Gly Leu Gln Val
[5588] 325 330 335
[5589] Leu Asn Val His Phe Gly Gly Glu Arg Ile Ala Tyr Glu Val Ser Val
[5590] 340 345 350
[5591] Gln Glu Ala Val Ala Leu Tyr Gly Gly His Thr Pro Ala Gly Met Gln
[5592] 355 360 365
[5593] Thr Lys Tyr Leu Asp Val Gly Trp Gly Leu Gly Ser Val Thr His Glu
[5594] 370 375 380
[5595] Leu Ala Pro Gly Ile Asp Cys Pro Glu Thr Ala Thr Phe Leu Asp Thr
[5596] 385 390 395 400
[5597] Phe His Tyr Tyr Asp Ala Asp Asp Pro Val His Tyr Pro Arg Ala Leu
[5598] 405 410 415
[5599] Cys Leu Phe Glu Met Pro Thr Gly Val Pro Leu Arg Arg His Phe Asn
[5600] 420 425 430
[5601] Ser Asn Phe Lys Gly Gly Phe Asn Phe Tyr Ala Gly Leu Lys Gly Gln
[5602] 435 440 445
[5603] Val Leu Val Leu Arg Thr Thr Ser Thr Val Tyr Asn Tyr Asp Tyr Ile
[5604] 450 455 460
[5605] Trp Asp Phe Ile Phe Tyr Pro Asn Gly Val Met Glu Ala Lys Met His
[5606] 465 470 475 480
[5607] Ala Thr Gly Tyr Val His Ala Thr Phe Tyr Thr Pro Glu Gly Leu Arg
[5608] 485 490 495
[5609] His Gly Thr Arg Leu His Thr His Leu Ile Gly Asn Ile His Thr His
[5610] 500 505 510
[5611] Leu Val His Tyr Arg Val Asp Leu Asp Val Ala Gly Thr Lys Asn Ser
[5612] 515 520 525
[5613] Phe Gln Thr Leu Gln Met Lys Leu Glu Asn Ile Thr Asn Pro Trp Ser
[5614] 530 535 540
[5615] Pro Arg His Arg Val Val Gln Pro Thr Leu Glu Gln Thr Gln Tyr Ser
[5616] 545 550 555 560
[5617] Trp Glu Arg Gln Ala Ala Phe Arg Phe Lys Arg Lys Leu Pro Lys Tyr
[5618] 565 570 575
[5619] Leu Leu Phe Thr Ser Pro Gln Glu Asn Pro Trp Gly His Lys Arg Ser
[5620] 580 585 590
[5621] Tyr Arg Leu Gln Ile His Ser Met Ala Asp Gln Val Leu Pro Pro Gly
[5622] 595 600 605
[5623] Trp Gln Glu Glu Gln Ala Ile Thr Trp Ala Arg Tyr Pro Leu Ala Val
[5624] 610 615 620
[5625] Thr Lys Tyr Arg Glu Ser Glu Leu Cys Ser Ser Ser Ile Tyr His Gln
[5626] 625 630 635 640
[5627] Asn Asp Pro Trp His Pro Pro Val Val Phe Glu Gln Phe Leu His Asn

[5628] 645 650 655
[5629] Asn Glu Asn Ile Glu Asn Glu Asp Leu Val Ala Trp Val Thr Val Gly
[5630] 660 665 670
[5631] Phe Leu His Ile Pro His Ser Glu Asp Ile Pro Asn Thr Ala Thr Pro
[5632] 675 680 685
[5633] Gly Asn Ser Val Gly Phe Leu Leu Arg Pro Phe Asn Phe Phe Pro Glu
[5634] 690 695 700
[5635] Asp Pro Ser Leu Ala Ser Arg Asp Thr Val Ile Val Trp Pro Arg Asp
[5636] 705 710 715 720
[5637] Asn Gly Pro Asn Tyr Val Gln Arg Trp Ile Pro Glu Asp Arg Asp Cys
[5638] 725 730 735
[5639] Ser Met Pro Pro Pro Phe Ser Tyr Asn Gly Thr Tyr Arg Pro Val Glu
[5640] 740 745 750
[5641] Pro Lys Ser Ala Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro
[5642] 755 760 765
[5643] Pro Val Ala Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
[5644] 770 775 780
[5645] Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp
[5646] 785 790 795 800
[5647] Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
[5648] 805 810 815
[5649] Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
[5650] 820 825 830
[5651] Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
[5652] 835 840 845
[5653] Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro
[5654] 850 855 860
[5655] Ser Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
[5656] 865 870 875 880
[5657] Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn
[5658] 885 890 895
[5659] Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
[5660] 900 905 910
[5661] Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
[5662] 915 920 925
[5663] Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys
[5664] 930 935 940
[5665] Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
[5666] 945 950 955 960
[5667] Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
[5668] 965 970 975
[5669] Ser Leu Ser Pro Gly Lys

[5670] 980

[5671] <210> 64

[5672] <211> 982

[5673] <212> PRT

[5674] <213> 人工序列

[5675] <220>

[5676] <223> hDAO-Fc-Hepmut1-Cysmut

[5677] <400> 64

[5678] Met Pro Ala Leu Gly Trp Ala Val Ala Ala Ile Leu Met Leu Gln Thr

[5679] 1 5 10 15

[5680] Ala Met Ala Glu Pro Ser Pro Gly Thr Leu Pro Arg Lys Ala Gly Val

[5681] 20 25 30

[5682] Phe Ser Asp Leu Ser Asn Gln Glu Leu Lys Ala Val His Ser Phe Leu

[5683] 35 40 45

[5684] Trp Ser Lys Lys Glu Leu Arg Leu Gln Pro Ser Ser Thr Thr Thr Met

[5685] 50 55 60

[5686] Ala Lys Asn Thr Val Phe Leu Ile Glu Met Leu Leu Pro Lys Lys Tyr

[5687] 65 70 75 80

[5688] His Val Leu Arg Phe Leu Asp Lys Gly Glu Arg His Pro Val Arg Glu

[5689] 85 90 95

[5690] Ala Arg Ala Val Ile Phe Phe Gly Asp Gln Glu His Pro Asn Val Thr

[5691] 100 105 110

[5692] Glu Phe Ala Val Gly Pro Leu Pro Gly Pro Ala Tyr Met Arg Ala Leu

[5693] 115 120 125

[5694] Ser Pro Arg Pro Gly Tyr Gln Ser Ser Trp Ala Ser Arg Pro Ile Ser

[5695] 130 135 140

[5696] Thr Ala Glu Tyr Ala Leu Leu Tyr His Thr Leu Gln Glu Ala Thr Lys

[5697] 145 150 155 160

[5698] Pro Leu His Gln Phe Phe Leu Asn Thr Thr Gly Phe Ser Phe Gln Asp

[5699] 165 170 175

[5700] Cys His Asp Arg Cys Leu Ala Phe Thr Asp Val Ala Pro Arg Gly Val

[5701] 180 185 190

[5702] Ala Ser Gly Gln Arg Arg Ser Trp Leu Ile Ile Gln Arg Tyr Val Glu

[5703] 195 200 205

[5704] Gly Tyr Phe Leu His Pro Thr Gly Leu Glu Leu Leu Val Asp His Gly

[5705] 210 215 220

[5706] Ser Thr Asp Ala Gly His Trp Ala Val Glu Gln Val Trp Tyr Asn Gly

[5707] 225 230 235 240

[5708] Lys Phe Tyr Gly Ser Pro Glu Glu Leu Ala Arg Lys Tyr Ala Asp Gly

[5709] 245 250 255

[5710] Glu Val Asp Val Val Val Leu Glu Asp Pro Leu Pro Gly Gly Lys Gly

[5711] 260 265 270

[5712] His Asp Ser Thr Glu Glu Pro Pro Leu Phe Ser Ser His Lys Pro Arg
[5713] 275 280 285
[5714] Gly Asp Phe Pro Ser Pro Ile His Val Ser Gly Pro Arg Leu Val Gln
[5715] 290 295 300
[5716] Pro His Gly Pro Arg Phe Arg Leu Glu Gly Asn Ala Val Leu Tyr Gly
[5717] 305 310 315 320
[5718] Gly Trp Ser Phe Ala Phe Arg Leu Arg Ser Ser Ser Gly Leu Gln Val
[5719] 325 330 335
[5720] Leu Asn Val His Phe Gly Gly Glu Arg Ile Ala Tyr Glu Val Ser Val
[5721] 340 345 350
[5722] Gln Glu Ala Val Ala Leu Tyr Gly Gly His Thr Pro Ala Gly Met Gln
[5723] 355 360 365
[5724] Thr Lys Tyr Leu Asp Val Gly Trp Gly Leu Gly Ser Val Thr His Glu
[5725] 370 375 380
[5726] Leu Ala Pro Gly Ile Asp Cys Pro Glu Thr Ala Thr Phe Leu Asp Thr
[5727] 385 390 395 400
[5728] Phe His Tyr Tyr Asp Ala Asp Asp Pro Val His Tyr Pro Arg Ala Leu
[5729] 405 410 415
[5730] Cys Leu Phe Glu Met Pro Thr Gly Val Pro Leu Arg Arg His Phe Asn
[5731] 420 425 430
[5732] Ser Asn Phe Lys Gly Gly Phe Asn Phe Tyr Ala Gly Leu Lys Gly Gln
[5733] 435 440 445
[5734] Val Leu Val Leu Arg Thr Thr Ser Thr Val Tyr Asn Tyr Asp Tyr Ile
[5735] 450 455 460
[5736] Trp Asp Phe Ile Phe Tyr Pro Asn Gly Val Met Glu Ala Lys Met His
[5737] 465 470 475 480
[5738] Ala Thr Gly Tyr Val His Ala Thr Phe Tyr Thr Pro Glu Gly Leu Arg
[5739] 485 490 495
[5740] His Gly Thr Arg Leu His Thr His Leu Ile Gly Asn Ile His Thr His
[5741] 500 505 510
[5742] Leu Val His Tyr Arg Val Asp Leu Asp Val Ala Gly Thr Lys Asn Ser
[5743] 515 520 525
[5744] Phe Gln Thr Leu Gln Met Lys Leu Glu Asn Ile Thr Asn Pro Trp Ser
[5745] 530 535 540
[5746] Pro Arg His Arg Val Val Gln Pro Thr Leu Glu Gln Thr Gln Tyr Ser
[5747] 545 550 555 560
[5748] Trp Glu Arg Gln Ala Ala Phe Ser Phe Lys Arg Lys Leu Pro Lys Tyr
[5749] 565 570 575
[5750] Leu Leu Phe Thr Ser Pro Gln Glu Asn Pro Trp Gly His Lys Arg Ser
[5751] 580 585 590
[5752] Tyr Arg Leu Gln Ile His Ser Met Ala Asp Gln Val Leu Pro Pro Gly
[5753] 595 600 605

[5754] Trp Gln Glu Glu Gln Ala Ile Thr Trp Ala Arg Tyr Pro Leu Ala Val
[5755] 610 615 620
[5756] Thr Lys Tyr Arg Glu Ser Glu Leu Cys Ser Ser Ser Ile Tyr His Gln
[5757] 625 630 635 640
[5758] Asn Asp Pro Trp His Pro Pro Val Val Phe Glu Gln Phe Leu His Asn
[5759] 645 650 655
[5760] Asn Glu Asn Ile Glu Asn Glu Asp Leu Val Ala Trp Val Thr Val Gly
[5761] 660 665 670
[5762] Phe Leu His Ile Pro His Ser Glu Asp Ile Pro Asn Thr Ala Thr Pro
[5763] 675 680 685
[5764] Gly Asn Ser Val Gly Phe Leu Leu Arg Pro Phe Asn Phe Phe Pro Glu
[5765] 690 695 700
[5766] Asp Pro Ser Leu Ala Ser Arg Asp Thr Val Ile Val Trp Pro Arg Asp
[5767] 705 710 715 720
[5768] Asn Gly Pro Asn Tyr Val Gln Arg Trp Ile Pro Glu Asp Arg Asp Cys
[5769] 725 730 735
[5770] Ser Met Pro Pro Pro Phe Ser Tyr Asn Gly Thr Tyr Arg Pro Val Glu
[5771] 740 745 750
[5772] Pro Lys Ser Ala Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro
[5773] 755 760 765
[5774] Pro Val Ala Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
[5775] 770 775 780
[5776] Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp
[5777] 785 790 795 800
[5778] Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
[5779] 805 810 815
[5780] Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
[5781] 820 825 830
[5782] Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
[5783] 835 840 845
[5784] Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro
[5785] 850 855 860
[5786] Ser Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
[5787] 865 870 875 880
[5788] Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn
[5789] 885 890 895
[5790] Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
[5791] 900 905 910
[5792] Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
[5793] 915 920 925
[5794] Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys
[5795] 930 935 940

[5796] Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
[5797] 945 950 955 960
[5798] Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
[5799] 965 970 975
[5800] Ser Leu Ser Pro Gly Lys
[5801] 980
[5802] <210> 65
[5803] <211> 982
[5804] <212> PRT
[5805] <213> 人工序列
[5806] <220>
[5807] <223> hDAO-Fc-Hepmut2-Cysmut
[5808] <400> 65
[5809] Met Pro Ala Leu Gly Trp Ala Val Ala Ala Ile Leu Met Leu Gln Thr
[5810] 1 5 10 15
[5811] Ala Met Ala Glu Pro Ser Pro Gly Thr Leu Pro Arg Lys Ala Gly Val
[5812] 20 25 30
[5813] Phe Ser Asp Leu Ser Asn Gln Glu Leu Lys Ala Val His Ser Phe Leu
[5814] 35 40 45
[5815] Trp Ser Lys Lys Glu Leu Arg Leu Gln Pro Ser Ser Thr Thr Thr Met
[5816] 50 55 60
[5817] Ala Lys Asn Thr Val Phe Leu Ile Glu Met Leu Leu Pro Lys Lys Tyr
[5818] 65 70 75 80
[5819] His Val Leu Arg Phe Leu Asp Lys Gly Glu Arg His Pro Val Arg Glu
[5820] 85 90 95
[5821] Ala Arg Ala Val Ile Phe Phe Gly Asp Gln Glu His Pro Asn Val Thr
[5822] 100 105 110
[5823] Glu Phe Ala Val Gly Pro Leu Pro Gly Pro Ala Tyr Met Arg Ala Leu
[5824] 115 120 125
[5825] Ser Pro Arg Pro Gly Tyr Gln Ser Ser Trp Ala Ser Arg Pro Ile Ser
[5826] 130 135 140
[5827] Thr Ala Glu Tyr Ala Leu Leu Tyr His Thr Leu Gln Glu Ala Thr Lys
[5828] 145 150 155 160
[5829] Pro Leu His Gln Phe Phe Leu Asn Thr Thr Gly Phe Ser Phe Gln Asp
[5830] 165 170 175
[5831] Cys His Asp Arg Cys Leu Ala Phe Thr Asp Val Ala Pro Arg Gly Val
[5832] 180 185 190
[5833] Ala Ser Gly Gln Arg Arg Ser Trp Leu Ile Ile Gln Arg Tyr Val Glu
[5834] 195 200 205
[5835] Gly Tyr Phe Leu His Pro Thr Gly Leu Glu Leu Leu Val Asp His Gly
[5836] 210 215 220
[5837] Ser Thr Asp Ala Gly His Trp Ala Val Glu Gln Val Trp Tyr Asn Gly

[5838] 225 230 235 240
[5839] Lys Phe Tyr Gly Ser Pro Glu Glu Leu Ala Arg Lys Tyr Ala Asp Gly
[5840] 245 250 255
[5841] Glu Val Asp Val Val Val Leu Glu Asp Pro Leu Pro Gly Gly Lys Gly
[5842] 260 265 270
[5843] His Asp Ser Thr Glu Glu Pro Pro Leu Phe Ser Ser His Lys Pro Arg
[5844] 275 280 285
[5845] Gly Asp Phe Pro Ser Pro Ile His Val Ser Gly Pro Arg Leu Val Gln
[5846] 290 295 300
[5847] Pro His Gly Pro Arg Phe Arg Leu Glu Gly Asn Ala Val Leu Tyr Gly
[5848] 305 310 315 320
[5849] Gly Trp Ser Phe Ala Phe Arg Leu Arg Ser Ser Ser Gly Leu Gln Val
[5850] 325 330 335
[5851] Leu Asn Val His Phe Gly Gly Glu Arg Ile Ala Tyr Glu Val Ser Val
[5852] 340 345 350
[5853] Gln Glu Ala Val Ala Leu Tyr Gly Gly His Thr Pro Ala Gly Met Gln
[5854] 355 360 365
[5855] Thr Lys Tyr Leu Asp Val Gly Trp Gly Leu Gly Ser Val Thr His Glu
[5856] 370 375 380
[5857] Leu Ala Pro Gly Ile Asp Cys Pro Glu Thr Ala Thr Phe Leu Asp Thr
[5858] 385 390 395 400
[5859] Phe His Tyr Tyr Asp Ala Asp Asp Pro Val His Tyr Pro Arg Ala Leu
[5860] 405 410 415
[5861] Cys Leu Phe Glu Met Pro Thr Gly Val Pro Leu Arg Arg His Phe Asn
[5862] 420 425 430
[5863] Ser Asn Phe Lys Gly Gly Phe Asn Phe Tyr Ala Gly Leu Lys Gly Gln
[5864] 435 440 445
[5865] Val Leu Val Leu Arg Thr Thr Ser Thr Val Tyr Asn Tyr Asp Tyr Ile
[5866] 450 455 460
[5867] Trp Asp Phe Ile Phe Tyr Pro Asn Gly Val Met Glu Ala Lys Met His
[5868] 465 470 475 480
[5869] Ala Thr Gly Tyr Val His Ala Thr Phe Tyr Thr Pro Glu Gly Leu Arg
[5870] 485 490 495
[5871] His Gly Thr Arg Leu His Thr His Leu Ile Gly Asn Ile His Thr His
[5872] 500 505 510
[5873] Leu Val His Tyr Arg Val Asp Leu Asp Val Ala Gly Thr Lys Asn Ser
[5874] 515 520 525
[5875] Phe Gln Thr Leu Gln Met Lys Leu Glu Asn Ile Thr Asn Pro Trp Ser
[5876] 530 535 540
[5877] Pro Arg His Arg Val Val Gln Pro Thr Leu Glu Gln Thr Gln Tyr Ser
[5878] 545 550 555 560
[5879] Trp Glu Arg Gln Ala Ala Phe Arg Phe Lys Arg Lys Leu Pro Thr Tyr

[5880] 565 570 575
[5881] Leu Leu Phe Thr Ser Pro Gln Glu Asn Pro Trp Gly His Lys Arg Ser
[5882] 580 585 590
[5883] Tyr Arg Leu Gln Ile His Ser Met Ala Asp Gln Val Leu Pro Pro Gly
[5884] 595 600 605
[5885] Trp Gln Glu Glu Gln Ala Ile Thr Trp Ala Arg Tyr Pro Leu Ala Val
[5886] 610 615 620
[5887] Thr Lys Tyr Arg Glu Ser Glu Leu Cys Ser Ser Ser Ile Tyr His Gln
[5888] 625 630 635 640
[5889] Asn Asp Pro Trp His Pro Pro Val Val Phe Glu Gln Phe Leu His Asn
[5890] 645 650 655
[5891] Asn Glu Asn Ile Glu Asn Glu Asp Leu Val Ala Trp Val Thr Val Gly
[5892] 660 665 670
[5893] Phe Leu His Ile Pro His Ser Glu Asp Ile Pro Asn Thr Ala Thr Pro
[5894] 675 680 685
[5895] Gly Asn Ser Val Gly Phe Leu Leu Arg Pro Phe Asn Phe Phe Pro Glu
[5896] 690 695 700
[5897] Asp Pro Ser Leu Ala Ser Arg Asp Thr Val Ile Val Trp Pro Arg Asp
[5898] 705 710 715 720
[5899] Asn Gly Pro Asn Tyr Val Gln Arg Trp Ile Pro Glu Asp Arg Asp Cys
[5900] 725 730 735
[5901] Ser Met Pro Pro Pro Phe Ser Tyr Asn Gly Thr Tyr Arg Pro Val Glu
[5902] 740 745 750
[5903] Pro Lys Ser Ala Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro
[5904] 755 760 765
[5905] Pro Val Ala Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
[5906] 770 775 780
[5907] Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp
[5908] 785 790 795 800
[5909] Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
[5910] 805 810 815
[5911] Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
[5912] 820 825 830
[5913] Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
[5914] 835 840 845
[5915] Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro
[5916] 850 855 860
[5917] Ser Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
[5918] 865 870 875 880
[5919] Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn
[5920] 885 890 895
[5921] Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile

[5922] 900 905 910
[5923] Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
[5924] 915 920 925
[5925] Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys
[5926] 930 935 940
[5927] Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
[5928] 945 950 955 960
[5929] Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
[5930] 965 970 975
[5931] Ser Leu Ser Pro Gly Lys
[5932] 980
[5933] <210> 66
[5934] <211> 982
[5935] <212> PRT
[5936] <213> 人工序列
[5937] <220>
[5938] <223> hDAO-Fc-Hepmut3-Cysmut
[5939] <400> 66
[5940] Met Pro Ala Leu Gly Trp Ala Val Ala Ala Ile Leu Met Leu Gln Thr
[5941] 1 5 10 15
[5942] Ala Met Ala Glu Pro Ser Pro Gly Thr Leu Pro Arg Lys Ala Gly Val
[5943] 20 25 30
[5944] Phe Ser Asp Leu Ser Asn Gln Glu Leu Lys Ala Val His Ser Phe Leu
[5945] 35 40 45
[5946] Trp Ser Lys Lys Glu Leu Arg Leu Gln Pro Ser Ser Thr Thr Thr Met
[5947] 50 55 60
[5948] Ala Lys Asn Thr Val Phe Leu Ile Glu Met Leu Leu Pro Lys Lys Tyr
[5949] 65 70 75 80
[5950] His Val Leu Arg Phe Leu Asp Lys Gly Glu Arg His Pro Val Arg Glu
[5951] 85 90 95
[5952] Ala Arg Ala Val Ile Phe Phe Gly Asp Gln Glu His Pro Asn Val Thr
[5953] 100 105 110
[5954] Glu Phe Ala Val Gly Pro Leu Pro Gly Pro Ala Tyr Met Arg Ala Leu
[5955] 115 120 125
[5956] Ser Pro Arg Pro Gly Tyr Gln Ser Ser Trp Ala Ser Arg Pro Ile Ser
[5957] 130 135 140
[5958] Thr Ala Glu Tyr Ala Leu Leu Tyr His Thr Leu Gln Glu Ala Thr Lys
[5959] 145 150 155 160
[5960] Pro Leu His Gln Phe Phe Leu Asn Thr Thr Gly Phe Ser Phe Gln Asp
[5961] 165 170 175
[5962] Cys His Asp Arg Cys Leu Ala Phe Thr Asp Val Ala Pro Arg Gly Val
[5963] 180 185 190

[5964] Ala Ser Gly Gln Arg Arg Ser Trp Leu Ile Ile Gln Arg Tyr Val Glu
[5965] 195 200 205
[5966] Gly Tyr Phe Leu His Pro Thr Gly Leu Glu Leu Leu Val Asp His Gly
[5967] 210 215 220
[5968] Ser Thr Asp Ala Gly His Trp Ala Val Glu Gln Val Trp Tyr Asn Gly
[5969] 225 230 235 240
[5970] Lys Phe Tyr Gly Ser Pro Glu Glu Leu Ala Arg Lys Tyr Ala Asp Gly
[5971] 245 250 255
[5972] Glu Val Asp Val Val Val Leu Glu Asp Pro Leu Pro Gly Gly Lys Gly
[5973] 260 265 270
[5974] His Asp Ser Thr Glu Glu Pro Pro Leu Phe Ser Ser His Lys Pro Arg
[5975] 275 280 285
[5976] Gly Asp Phe Pro Ser Pro Ile His Val Ser Gly Pro Arg Leu Val Gln
[5977] 290 295 300
[5978] Pro His Gly Pro Arg Phe Arg Leu Glu Gly Asn Ala Val Leu Tyr Gly
[5979] 305 310 315 320
[5980] Gly Trp Ser Phe Ala Phe Arg Leu Arg Ser Ser Ser Gly Leu Gln Val
[5981] 325 330 335
[5982] Leu Asn Val His Phe Gly Gly Glu Arg Ile Ala Tyr Glu Val Ser Val
[5983] 340 345 350
[5984] Gln Glu Ala Val Ala Leu Tyr Gly Gly His Thr Pro Ala Gly Met Gln
[5985] 355 360 365
[5986] Thr Lys Tyr Leu Asp Val Gly Trp Gly Leu Gly Ser Val Thr His Glu
[5987] 370 375 380
[5988] Leu Ala Pro Gly Ile Asp Cys Pro Glu Thr Ala Thr Phe Leu Asp Thr
[5989] 385 390 395 400
[5990] Phe His Tyr Tyr Asp Ala Asp Asp Pro Val His Tyr Pro Arg Ala Leu
[5991] 405 410 415
[5992] Cys Leu Phe Glu Met Pro Thr Gly Val Pro Leu Arg Arg His Phe Asn
[5993] 420 425 430
[5994] Ser Asn Phe Lys Gly Gly Phe Asn Phe Tyr Ala Gly Leu Lys Gly Gln
[5995] 435 440 445
[5996] Val Leu Val Leu Arg Thr Thr Ser Thr Val Tyr Asn Tyr Asp Tyr Ile
[5997] 450 455 460
[5998] Trp Asp Phe Ile Phe Tyr Pro Asn Gly Val Met Glu Ala Lys Met His
[5999] 465 470 475 480
[6000] Ala Thr Gly Tyr Val His Ala Thr Phe Tyr Thr Pro Glu Gly Leu Arg
[6001] 485 490 495
[6002] His Gly Thr Arg Leu His Thr His Leu Ile Gly Asn Ile His Thr His
[6003] 500 505 510
[6004] Leu Val His Tyr Arg Val Asp Leu Asp Val Ala Gly Thr Lys Asn Ser
[6005] 515 520 525

[6006] Phe Gln Thr Leu Gln Met Lys Leu Glu Asn Ile Thr Asn Pro Trp Ser
[6007] 530 535 540
[6008] Pro Arg His Arg Val Val Gln Pro Thr Leu Glu Gln Thr Gln Tyr Ser
[6009] 545 550 555 560
[6010] Trp Glu Arg Gln Ala Ala Phe Arg Phe Lys Thr Lys Leu Pro Lys Tyr
[6011] 565 570 575
[6012] Leu Leu Phe Thr Ser Pro Gln Glu Asn Pro Trp Gly His Lys Arg Ser
[6013] 580 585 590
[6014] Tyr Arg Leu Gln Ile His Ser Met Ala Asp Gln Val Leu Pro Pro Gly
[6015] 595 600 605
[6016] Trp Gln Glu Glu Gln Ala Ile Thr Trp Ala Arg Tyr Pro Leu Ala Val
[6017] 610 615 620
[6018] Thr Lys Tyr Arg Glu Ser Glu Leu Cys Ser Ser Ser Ile Tyr His Gln
[6019] 625 630 635 640
[6020] Asn Asp Pro Trp His Pro Pro Val Val Phe Glu Gln Phe Leu His Asn
[6021] 645 650 655
[6022] Asn Glu Asn Ile Glu Asn Glu Asp Leu Val Ala Trp Val Thr Val Gly
[6023] 660 665 670
[6024] Phe Leu His Ile Pro His Ser Glu Asp Ile Pro Asn Thr Ala Thr Pro
[6025] 675 680 685
[6026] Gly Asn Ser Val Gly Phe Leu Leu Arg Pro Phe Asn Phe Phe Pro Glu
[6027] 690 695 700
[6028] Asp Pro Ser Leu Ala Ser Arg Asp Thr Val Ile Val Trp Pro Arg Asp
[6029] 705 710 715 720
[6030] Asn Gly Pro Asn Tyr Val Gln Arg Trp Ile Pro Glu Asp Arg Asp Cys
[6031] 725 730 735
[6032] Ser Met Pro Pro Pro Phe Ser Tyr Asn Gly Thr Tyr Arg Pro Val Glu
[6033] 740 745 750
[6034] Pro Lys Ser Ala Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro
[6035] 755 760 765
[6036] Pro Val Ala Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
[6037] 770 775 780
[6038] Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp
[6039] 785 790 795 800
[6040] Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
[6041] 805 810 815
[6042] Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
[6043] 820 825 830
[6044] Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
[6045] 835 840 845
[6046] Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro
[6047] 850 855 860

[6048] Ser Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
[6049] 865 870 875 880
[6050] Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn
[6051] 885 890 895
[6052] Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
[6053] 900 905 910
[6054] Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
[6055] 915 920 925
[6056] Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys
[6057] 930 935 940
[6058] Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
[6059] 945 950 955 960
[6060] Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
[6061] 965 970 975
[6062] Ser Leu Ser Pro Gly Lys
[6063] 980
[6064] <210> 67
[6065] <211> 982
[6066] <212> PRT
[6067] <213> 人工序列
[6068] <220>
[6069] <223> hDAO-Fc-Hepmut4-Cysmut
[6070] <400> 67
[6071] Met Pro Ala Leu Gly Trp Ala Val Ala Ala Ile Leu Met Leu Gln Thr
[6072] 1 5 10 15
[6073] Ala Met Ala Glu Pro Ser Pro Gly Thr Leu Pro Arg Lys Ala Gly Val
[6074] 20 25 30
[6075] Phe Ser Asp Leu Ser Asn Gln Glu Leu Lys Ala Val His Ser Phe Leu
[6076] 35 40 45
[6077] Trp Ser Lys Lys Glu Leu Arg Leu Gln Pro Ser Ser Thr Thr Thr Met
[6078] 50 55 60
[6079] Ala Lys Asn Thr Val Phe Leu Ile Glu Met Leu Leu Pro Lys Lys Tyr
[6080] 65 70 75 80
[6081] His Val Leu Arg Phe Leu Asp Lys Gly Glu Arg His Pro Val Arg Glu
[6082] 85 90 95
[6083] Ala Arg Ala Val Ile Phe Phe Gly Asp Gln Glu His Pro Asn Val Thr
[6084] 100 105 110
[6085] Glu Phe Ala Val Gly Pro Leu Pro Gly Pro Ala Tyr Met Arg Ala Leu
[6086] 115 120 125
[6087] Ser Pro Arg Pro Gly Tyr Gln Ser Ser Trp Ala Ser Arg Pro Ile Ser
[6088] 130 135 140
[6089] Thr Ala Glu Tyr Ala Leu Leu Tyr His Thr Leu Gln Glu Ala Thr Lys

[6090] 145 150 155 160
[6091] Pro Leu His Gln Phe Phe Leu Asn Thr Thr Gly Phe Ser Phe Gln Asp
[6092] 165 170 175
[6093] Cys His Asp Arg Cys Leu Ala Phe Thr Asp Val Ala Pro Arg Gly Val
[6094] 180 185 190
[6095] Ala Ser Gly Gln Arg Arg Ser Trp Leu Ile Ile Gln Arg Tyr Val Glu
[6096] 195 200 205
[6097] Gly Tyr Phe Leu His Pro Thr Gly Leu Glu Leu Leu Val Asp His Gly
[6098] 210 215 220
[6099] Ser Thr Asp Ala Gly His Trp Ala Val Glu Gln Val Trp Tyr Asn Gly
[6100] 225 230 235 240
[6101] Lys Phe Tyr Gly Ser Pro Glu Glu Leu Ala Arg Lys Tyr Ala Asp Gly
[6102] 245 250 255
[6103] Glu Val Asp Val Val Val Leu Glu Asp Pro Leu Pro Gly Gly Lys Gly
[6104] 260 265 270
[6105] His Asp Ser Thr Glu Glu Pro Pro Leu Phe Ser Ser His Lys Pro Arg
[6106] 275 280 285
[6107] Gly Asp Phe Pro Ser Pro Ile His Val Ser Gly Pro Arg Leu Val Gln
[6108] 290 295 300
[6109] Pro His Gly Pro Arg Phe Arg Leu Glu Gly Asn Ala Val Leu Tyr Gly
[6110] 305 310 315 320
[6111] Gly Trp Ser Phe Ala Phe Arg Leu Arg Ser Ser Ser Gly Leu Gln Val
[6112] 325 330 335
[6113] Leu Asn Val His Phe Gly Gly Glu Arg Ile Ala Tyr Glu Val Ser Val
[6114] 340 345 350
[6115] Gln Glu Ala Val Ala Leu Tyr Gly Gly His Thr Pro Ala Gly Met Gln
[6116] 355 360 365
[6117] Thr Lys Tyr Leu Asp Val Gly Trp Gly Leu Gly Ser Val Thr His Glu
[6118] 370 375 380
[6119] Leu Ala Pro Gly Ile Asp Cys Pro Glu Thr Ala Thr Phe Leu Asp Thr
[6120] 385 390 395 400
[6121] Phe His Tyr Tyr Asp Ala Asp Asp Pro Val His Tyr Pro Arg Ala Leu
[6122] 405 410 415
[6123] Cys Leu Phe Glu Met Pro Thr Gly Val Pro Leu Arg Arg His Phe Asn
[6124] 420 425 430
[6125] Ser Asn Phe Lys Gly Gly Phe Asn Phe Tyr Ala Gly Leu Lys Gly Gln
[6126] 435 440 445
[6127] Val Leu Val Leu Arg Thr Thr Ser Thr Val Tyr Asn Tyr Asp Tyr Ile
[6128] 450 455 460
[6129] Trp Asp Phe Ile Phe Tyr Pro Asn Gly Val Met Glu Ala Lys Met His
[6130] 465 470 475 480
[6131] Ala Thr Gly Tyr Val His Ala Thr Phe Tyr Thr Pro Glu Gly Leu Arg

[6132] 485 490 495
[6133] His Gly Thr Arg Leu His Thr His Leu Ile Gly Asn Ile His Thr His
[6134] 500 505 510
[6135] Leu Val His Tyr Arg Val Asp Leu Asp Val Ala Gly Thr Lys Asn Ser
[6136] 515 520 525
[6137] Phe Gln Thr Leu Gln Met Lys Leu Glu Asn Ile Thr Asn Pro Trp Ser
[6138] 530 535 540
[6139] Pro Arg His Arg Val Val Gln Pro Thr Leu Glu Gln Thr Gln Tyr Ser
[6140] 545 550 555 560
[6141] Trp Glu Arg Gln Ala Ala Phe Ser Phe Lys Thr Lys Leu Pro Lys Tyr
[6142] 565 570 575
[6143] Leu Leu Phe Thr Ser Pro Gln Glu Asn Pro Trp Gly His Lys Arg Ser
[6144] 580 585 590
[6145] Tyr Arg Leu Gln Ile His Ser Met Ala Asp Gln Val Leu Pro Pro Gly
[6146] 595 600 605
[6147] Trp Gln Glu Glu Gln Ala Ile Thr Trp Ala Arg Tyr Pro Leu Ala Val
[6148] 610 615 620
[6149] Thr Lys Tyr Arg Glu Ser Glu Leu Cys Ser Ser Ser Ile Tyr His Gln
[6150] 625 630 635 640
[6151] Asn Asp Pro Trp His Pro Pro Val Val Phe Glu Gln Phe Leu His Asn
[6152] 645 650 655
[6153] Asn Glu Asn Ile Glu Asn Glu Asp Leu Val Ala Trp Val Thr Val Gly
[6154] 660 665 670
[6155] Phe Leu His Ile Pro His Ser Glu Asp Ile Pro Asn Thr Ala Thr Pro
[6156] 675 680 685
[6157] Gly Asn Ser Val Gly Phe Leu Leu Arg Pro Phe Asn Phe Phe Pro Glu
[6158] 690 695 700
[6159] Asp Pro Ser Leu Ala Ser Arg Asp Thr Val Ile Val Trp Pro Arg Asp
[6160] 705 710 715 720
[6161] Asn Gly Pro Asn Tyr Val Gln Arg Trp Ile Pro Glu Asp Arg Asp Cys
[6162] 725 730 735
[6163] Ser Met Pro Pro Pro Phe Ser Tyr Asn Gly Thr Tyr Arg Pro Val Glu
[6164] 740 745 750
[6165] Pro Lys Ser Ala Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro
[6166] 755 760 765
[6167] Pro Val Ala Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
[6168] 770 775 780
[6169] Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp
[6170] 785 790 795 800
[6171] Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
[6172] 805 810 815
[6173] Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn

[6174] 820 825 830
[6175] Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
[6176] 835 840 845
[6177] Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro
[6178] 850 855 860
[6179] Ser Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
[6180] 865 870 875 880
[6181] Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn
[6182] 885 890 895
[6183] Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
[6184] 900 905 910
[6185] Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
[6186] 915 920 925
[6187] Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys
[6188] 930 935 940
[6189] Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
[6190] 945 950 955 960
[6191] Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
[6192] 965 970 975
[6193] Ser Leu Ser Pro Gly Lys
[6194] 980
[6195] <210> 68
[6196] <211> 982
[6197] <212> PRT
[6198] <213> 人工序列
[6199] <220>
[6200] <223> hDAO-Fc-Hepmut5-Cysmut
[6201] <400> 68
[6202] Met Pro Ala Leu Gly Trp Ala Val Ala Ala Ile Leu Met Leu Gln Thr
[6203] 1 5 10 15
[6204] Ala Met Ala Glu Pro Ser Pro Gly Thr Leu Pro Arg Lys Ala Gly Val
[6205] 20 25 30
[6206] Phe Ser Asp Leu Ser Asn Gln Glu Leu Lys Ala Val His Ser Phe Leu
[6207] 35 40 45
[6208] Trp Ser Lys Lys Glu Leu Arg Leu Gln Pro Ser Ser Thr Thr Thr Met
[6209] 50 55 60
[6210] Ala Lys Asn Thr Val Phe Leu Ile Glu Met Leu Leu Pro Lys Lys Tyr
[6211] 65 70 75 80
[6212] His Val Leu Arg Phe Leu Asp Lys Gly Glu Arg His Pro Val Arg Glu
[6213] 85 90 95
[6214] Ala Arg Ala Val Ile Phe Phe Gly Asp Gln Glu His Pro Asn Val Thr
[6215] 100 105 110

[6216] Glu Phe Ala Val Gly Pro Leu Pro Gly Pro Ala Tyr Met Arg Ala Leu
[6217] 115 120 125
[6218] Ser Pro Arg Pro Gly Tyr Gln Ser Ser Trp Ala Ser Arg Pro Ile Ser
[6219] 130 135 140
[6220] Thr Ala Glu Tyr Ala Leu Leu Tyr His Thr Leu Gln Glu Ala Thr Lys
[6221] 145 150 155 160
[6222] Pro Leu His Gln Phe Phe Leu Asn Thr Thr Gly Phe Ser Phe Gln Asp
[6223] 165 170 175
[6224] Cys His Asp Arg Cys Leu Ala Phe Thr Asp Val Ala Pro Arg Gly Val
[6225] 180 185 190
[6226] Ala Ser Gly Gln Arg Arg Ser Trp Leu Ile Ile Gln Arg Tyr Val Glu
[6227] 195 200 205
[6228] Gly Tyr Phe Leu His Pro Thr Gly Leu Glu Leu Leu Val Asp His Gly
[6229] 210 215 220
[6230] Ser Thr Asp Ala Gly His Trp Ala Val Glu Gln Val Trp Tyr Asn Gly
[6231] 225 230 235 240
[6232] Lys Phe Tyr Gly Ser Pro Glu Glu Leu Ala Arg Lys Tyr Ala Asp Gly
[6233] 245 250 255
[6234] Glu Val Asp Val Val Val Leu Glu Asp Pro Leu Pro Gly Gly Lys Gly
[6235] 260 265 270
[6236] His Asp Ser Thr Glu Glu Pro Pro Leu Phe Ser Ser His Lys Pro Arg
[6237] 275 280 285
[6238] Gly Asp Phe Pro Ser Pro Ile His Val Ser Gly Pro Arg Leu Val Gln
[6239] 290 295 300
[6240] Pro His Gly Pro Arg Phe Arg Leu Glu Gly Asn Ala Val Leu Tyr Gly
[6241] 305 310 315 320
[6242] Gly Trp Ser Phe Ala Phe Arg Leu Arg Ser Ser Ser Gly Leu Gln Val
[6243] 325 330 335
[6244] Leu Asn Val His Phe Gly Gly Glu Arg Ile Ala Tyr Glu Val Ser Val
[6245] 340 345 350
[6246] Gln Glu Ala Val Ala Leu Tyr Gly Gly His Thr Pro Ala Gly Met Gln
[6247] 355 360 365
[6248] Thr Lys Tyr Leu Asp Val Gly Trp Gly Leu Gly Ser Val Thr His Glu
[6249] 370 375 380
[6250] Leu Ala Pro Gly Ile Asp Cys Pro Glu Thr Ala Thr Phe Leu Asp Thr
[6251] 385 390 395 400
[6252] Phe His Tyr Tyr Asp Ala Asp Asp Pro Val His Tyr Pro Arg Ala Leu
[6253] 405 410 415
[6254] Cys Leu Phe Glu Met Pro Thr Gly Val Pro Leu Arg Arg His Phe Asn
[6255] 420 425 430
[6256] Ser Asn Phe Lys Gly Gly Phe Asn Phe Tyr Ala Gly Leu Lys Gly Gln
[6257] 435 440 445

[6258] Val Leu Val Leu Arg Thr Thr Ser Thr Val Tyr Asn Tyr Asp Tyr Ile
[6259] 450 455 460
[6260] Trp Asp Phe Ile Phe Tyr Pro Asn Gly Val Met Glu Ala Lys Met His
[6261] 465 470 475 480
[6262] Ala Thr Gly Tyr Val His Ala Thr Phe Tyr Thr Pro Glu Gly Leu Arg
[6263] 485 490 495
[6264] His Gly Thr Arg Leu His Thr His Leu Ile Gly Asn Ile His Thr His
[6265] 500 505 510
[6266] Leu Val His Tyr Arg Val Asp Leu Asp Val Ala Gly Thr Lys Asn Ser
[6267] 515 520 525
[6268] Phe Gln Thr Leu Gln Met Lys Leu Glu Asn Ile Thr Asn Pro Trp Ser
[6269] 530 535 540
[6270] Pro Arg His Arg Val Val Gln Pro Thr Leu Glu Gln Thr Gln Tyr Ser
[6271] 545 550 555 560
[6272] Trp Glu Arg Gln Ala Ala Phe Arg Phe Lys Thr Lys Leu Pro Thr Tyr
[6273] 565 570 575
[6274] Leu Leu Phe Thr Ser Pro Gln Glu Asn Pro Trp Gly His Lys Arg Ser
[6275] 580 585 590
[6276] Tyr Arg Leu Gln Ile His Ser Met Ala Asp Gln Val Leu Pro Pro Gly
[6277] 595 600 605
[6278] Trp Gln Glu Glu Gln Ala Ile Thr Trp Ala Arg Tyr Pro Leu Ala Val
[6279] 610 615 620
[6280] Thr Lys Tyr Arg Glu Ser Glu Leu Cys Ser Ser Ser Ile Tyr His Gln
[6281] 625 630 635 640
[6282] Asn Asp Pro Trp His Pro Pro Val Val Phe Glu Gln Phe Leu His Asn
[6283] 645 650 655
[6284] Asn Glu Asn Ile Glu Asn Glu Asp Leu Val Ala Trp Val Thr Val Gly
[6285] 660 665 670
[6286] Phe Leu His Ile Pro His Ser Glu Asp Ile Pro Asn Thr Ala Thr Pro
[6287] 675 680 685
[6288] Gly Asn Ser Val Gly Phe Leu Leu Arg Pro Phe Asn Phe Phe Pro Glu
[6289] 690 695 700
[6290] Asp Pro Ser Leu Ala Ser Arg Asp Thr Val Ile Val Trp Pro Arg Asp
[6291] 705 710 715 720
[6292] Asn Gly Pro Asn Tyr Val Gln Arg Trp Ile Pro Glu Asp Arg Asp Cys
[6293] 725 730 735
[6294] Ser Met Pro Pro Pro Phe Ser Tyr Asn Gly Thr Tyr Arg Pro Val Glu
[6295] 740 745 750
[6296] Pro Lys Ser Ala Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro
[6297] 755 760 765
[6298] Pro Val Ala Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
[6299] 770 775 780

[6300] Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp
[6301] 785 790 795 800
[6302] Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
[6303] 805 810 815
[6304] Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
[6305] 820 825 830
[6306] Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
[6307] 835 840 845
[6308] Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro
[6309] 850 855 860
[6310] Ser Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
[6311] 865 870 875 880
[6312] Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn
[6313] 885 890 895
[6314] Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
[6315] 900 905 910
[6316] Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
[6317] 915 920 925
[6318] Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys
[6319] 930 935 940
[6320] Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
[6321] 945 950 955 960
[6322] Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
[6323] 965 970 975
[6324] Ser Leu Ser Pro Gly Lys
[6325] 980
[6326] <210> 69
[6327] <211> 982
[6328] <212> PRT
[6329] <213> 人工序列
[6330] <220>
[6331] <223> hDAO-Fc-Hepmut6-Cysmut
[6332] <400> 69
[6333] Met Pro Ala Leu Gly Trp Ala Val Ala Ala Ile Leu Met Leu Gln Thr
[6334] 1 5 10 15
[6335] Ala Met Ala Glu Pro Ser Pro Gly Thr Leu Pro Arg Lys Ala Gly Val
[6336] 20 25 30
[6337] Phe Ser Asp Leu Ser Asn Gln Glu Leu Lys Ala Val His Ser Phe Leu
[6338] 35 40 45
[6339] Trp Ser Lys Lys Glu Leu Arg Leu Gln Pro Ser Ser Thr Thr Thr Met
[6340] 50 55 60
[6341] Ala Lys Asn Thr Val Phe Leu Ile Glu Met Leu Leu Pro Lys Lys Tyr

[6342] 65 70 75 80
[6343] His Val Leu Arg Phe Leu Asp Lys Gly Glu Arg His Pro Val Arg Glu
[6344] 85 90 95
[6345] Ala Arg Ala Val Ile Phe Phe Gly Asp Gln Glu His Pro Asn Val Thr
[6346] 100 105 110
[6347] Glu Phe Ala Val Gly Pro Leu Pro Gly Pro Ala Tyr Met Arg Ala Leu
[6348] 115 120 125
[6349] Ser Pro Arg Pro Gly Tyr Gln Ser Ser Trp Ala Ser Arg Pro Ile Ser
[6350] 130 135 140
[6351] Thr Ala Glu Tyr Ala Leu Leu Tyr His Thr Leu Gln Glu Ala Thr Lys
[6352] 145 150 155 160
[6353] Pro Leu His Gln Phe Phe Leu Asn Thr Thr Gly Phe Ser Phe Gln Asp
[6354] 165 170 175
[6355] Cys His Asp Arg Cys Leu Ala Phe Thr Asp Val Ala Pro Arg Gly Val
[6356] 180 185 190
[6357] Ala Ser Gly Gln Arg Arg Ser Trp Leu Ile Ile Gln Arg Tyr Val Glu
[6358] 195 200 205
[6359] Gly Tyr Phe Leu His Pro Thr Gly Leu Glu Leu Leu Val Asp His Gly
[6360] 210 215 220
[6361] Ser Thr Asp Ala Gly His Trp Ala Val Glu Gln Val Trp Tyr Asn Gly
[6362] 225 230 235 240
[6363] Lys Phe Tyr Gly Ser Pro Glu Glu Leu Ala Arg Lys Tyr Ala Asp Gly
[6364] 245 250 255
[6365] Glu Val Asp Val Val Val Leu Glu Asp Pro Leu Pro Gly Gly Lys Gly
[6366] 260 265 270
[6367] His Asp Ser Thr Glu Glu Pro Pro Leu Phe Ser Ser His Lys Pro Arg
[6368] 275 280 285
[6369] Gly Asp Phe Pro Ser Pro Ile His Val Ser Gly Pro Arg Leu Val Gln
[6370] 290 295 300
[6371] Pro His Gly Pro Arg Phe Arg Leu Glu Gly Asn Ala Val Leu Tyr Gly
[6372] 305 310 315 320
[6373] Gly Trp Ser Phe Ala Phe Arg Leu Arg Ser Ser Ser Gly Leu Gln Val
[6374] 325 330 335
[6375] Leu Asn Val His Phe Gly Gly Glu Arg Ile Ala Tyr Glu Val Ser Val
[6376] 340 345 350
[6377] Gln Glu Ala Val Ala Leu Tyr Gly Gly His Thr Pro Ala Gly Met Gln
[6378] 355 360 365
[6379] Thr Lys Tyr Leu Asp Val Gly Trp Gly Leu Gly Ser Val Thr His Glu
[6380] 370 375 380
[6381] Leu Ala Pro Gly Ile Asp Cys Pro Glu Thr Ala Thr Phe Leu Asp Thr
[6382] 385 390 395 400
[6383] Phe His Tyr Tyr Asp Ala Asp Asp Pro Val His Tyr Pro Arg Ala Leu

[6384] 405 410 415
[6385] Cys Leu Phe Glu Met Pro Thr Gly Val Pro Leu Arg Arg His Phe Asn
[6386] 420 425 430
[6387] Ser Asn Phe Lys Gly Gly Phe Asn Phe Tyr Ala Gly Leu Lys Gly Gln
[6388] 435 440 445
[6389] Val Leu Val Leu Arg Thr Thr Ser Thr Val Tyr Asn Tyr Asp Tyr Ile
[6390] 450 455 460
[6391] Trp Asp Phe Ile Phe Tyr Pro Asn Gly Val Met Glu Ala Lys Met His
[6392] 465 470 475 480
[6393] Ala Thr Gly Tyr Val His Ala Thr Phe Tyr Thr Pro Glu Gly Leu Arg
[6394] 485 490 495
[6395] His Gly Thr Arg Leu His Thr His Leu Ile Gly Asn Ile His Thr His
[6396] 500 505 510
[6397] Leu Val His Tyr Arg Val Asp Leu Asp Val Ala Gly Thr Lys Asn Ser
[6398] 515 520 525
[6399] Phe Gln Thr Leu Gln Met Lys Leu Glu Asn Ile Thr Asn Pro Trp Ser
[6400] 530 535 540
[6401] Pro Arg His Arg Val Val Gln Pro Thr Leu Glu Gln Thr Gln Tyr Ser
[6402] 545 550 555 560
[6403] Trp Glu Arg Gln Ala Ala Phe Arg Phe Gly Gln Thr Leu Pro Lys Tyr
[6404] 565 570 575
[6405] Leu Leu Phe Thr Ser Pro Gln Glu Asn Pro Trp Gly His Lys Arg Ser
[6406] 580 585 590
[6407] Tyr Arg Leu Gln Ile His Ser Met Ala Asp Gln Val Leu Pro Pro Gly
[6408] 595 600 605
[6409] Trp Gln Glu Glu Gln Ala Ile Thr Trp Ala Arg Tyr Pro Leu Ala Val
[6410] 610 615 620
[6411] Thr Lys Tyr Arg Glu Ser Glu Leu Cys Ser Ser Ser Ile Tyr His Gln
[6412] 625 630 635 640
[6413] Asn Asp Pro Trp His Pro Pro Val Val Phe Glu Gln Phe Leu His Asn
[6414] 645 650 655
[6415] Asn Glu Asn Ile Glu Asn Glu Asp Leu Val Ala Trp Val Thr Val Gly
[6416] 660 665 670
[6417] Phe Leu His Ile Pro His Ser Glu Asp Ile Pro Asn Thr Ala Thr Pro
[6418] 675 680 685
[6419] Gly Asn Ser Val Gly Phe Leu Leu Arg Pro Phe Asn Phe Phe Pro Glu
[6420] 690 695 700
[6421] Asp Pro Ser Leu Ala Ser Arg Asp Thr Val Ile Val Trp Pro Arg Asp
[6422] 705 710 715 720
[6423] Asn Gly Pro Asn Tyr Val Gln Arg Trp Ile Pro Glu Asp Arg Asp Cys
[6424] 725 730 735
[6425] Ser Met Pro Pro Pro Phe Ser Tyr Asn Gly Thr Tyr Arg Pro Val Glu

[6426] 740 745 750
[6427] Pro Lys Ser Ala Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro
[6428] 755 760 765
[6429] Pro Val Ala Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
[6430] 770 775 780
[6431] Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp
[6432] 785 790 795 800
[6433] Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
[6434] 805 810 815
[6435] Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
[6436] 820 825 830
[6437] Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
[6438] 835 840 845
[6439] Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro
[6440] 850 855 860
[6441] Ser Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
[6442] 865 870 875 880
[6443] Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn
[6444] 885 890 895
[6445] Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
[6446] 900 905 910
[6447] Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
[6448] 915 920 925
[6449] Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys
[6450] 930 935 940
[6451] Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
[6452] 945 950 955 960
[6453] Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
[6454] 965 970 975
[6455] Ser Leu Ser Pro Gly Lys
[6456] 980
[6457] <210> 70
[6458] <211> 982
[6459] <212> PRT
[6460] <213> 人工序列
[6461] <220>
[6462] <223> hDAO-Fc-Hepmut7-Cysmut
[6463] <400> 70
[6464] Met Pro Ala Leu Gly Trp Ala Val Ala Ala Ile Leu Met Leu Gln Thr
[6465] 1 5 10 15
[6466] Ala Met Ala Glu Pro Ser Pro Gly Thr Leu Pro Arg Lys Ala Gly Val
[6467] 20 25 30

[6468] Phe Ser Asp Leu Ser Asn Gln Glu Leu Lys Ala Val His Ser Phe Leu
[6469] 35 40 45
[6470] Trp Ser Lys Lys Glu Leu Arg Leu Gln Pro Ser Ser Thr Thr Thr Met
[6471] 50 55 60
[6472] Ala Lys Asn Thr Val Phe Leu Ile Glu Met Leu Leu Pro Lys Lys Tyr
[6473] 65 70 75 80
[6474] His Val Leu Arg Phe Leu Asp Lys Gly Glu Arg His Pro Val Arg Glu
[6475] 85 90 95
[6476] Ala Arg Ala Val Ile Phe Phe Gly Asp Gln Glu His Pro Asn Val Thr
[6477] 100 105 110
[6478] Glu Phe Ala Val Gly Pro Leu Pro Gly Pro Ala Tyr Met Arg Ala Leu
[6479] 115 120 125
[6480] Ser Pro Arg Pro Gly Tyr Gln Ser Ser Trp Ala Ser Arg Pro Ile Ser
[6481] 130 135 140
[6482] Thr Ala Glu Tyr Ala Leu Leu Tyr His Thr Leu Gln Glu Ala Thr Lys
[6483] 145 150 155 160
[6484] Pro Leu His Gln Phe Phe Leu Asn Thr Thr Gly Phe Ser Phe Gln Asp
[6485] 165 170 175
[6486] Cys His Asp Arg Cys Leu Ala Phe Thr Asp Val Ala Pro Arg Gly Val
[6487] 180 185 190
[6488] Ala Ser Gly Gln Arg Arg Ser Trp Leu Ile Ile Gln Arg Tyr Val Glu
[6489] 195 200 205
[6490] Gly Tyr Phe Leu His Pro Thr Gly Leu Glu Leu Leu Val Asp His Gly
[6491] 210 215 220
[6492] Ser Thr Asp Ala Gly His Trp Ala Val Glu Gln Val Trp Tyr Asn Gly
[6493] 225 230 235 240
[6494] Lys Phe Tyr Gly Ser Pro Glu Glu Leu Ala Arg Lys Tyr Ala Asp Gly
[6495] 245 250 255
[6496] Glu Val Asp Val Val Val Leu Glu Asp Pro Leu Pro Gly Gly Lys Gly
[6497] 260 265 270
[6498] His Asp Ser Thr Glu Glu Pro Pro Leu Phe Ser Ser His Lys Pro Arg
[6499] 275 280 285
[6500] Gly Asp Phe Pro Ser Pro Ile His Val Ser Gly Pro Arg Leu Val Gln
[6501] 290 295 300
[6502] Pro His Gly Pro Arg Phe Arg Leu Glu Gly Asn Ala Val Leu Tyr Gly
[6503] 305 310 315 320
[6504] Gly Trp Ser Phe Ala Phe Arg Leu Arg Ser Ser Ser Gly Leu Gln Val
[6505] 325 330 335
[6506] Leu Asn Val His Phe Gly Gly Glu Arg Ile Ala Tyr Glu Val Ser Val
[6507] 340 345 350
[6508] Gln Glu Ala Val Ala Leu Tyr Gly Gly His Thr Pro Ala Gly Met Gln
[6509] 355 360 365

[6510] Thr Lys Tyr Leu Asp Val Gly Trp Gly Leu Gly Ser Val Thr His Glu
[6511] 370 375 380
[6512] Leu Ala Pro Gly Ile Asp Cys Pro Glu Thr Ala Thr Phe Leu Asp Thr
[6513] 385 390 395 400
[6514] Phe His Tyr Tyr Asp Ala Asp Asp Pro Val His Tyr Pro Arg Ala Leu
[6515] 405 410 415
[6516] Cys Leu Phe Glu Met Pro Thr Gly Val Pro Leu Arg Arg His Phe Asn
[6517] 420 425 430
[6518] Ser Asn Phe Lys Gly Gly Phe Asn Phe Tyr Ala Gly Leu Lys Gly Gln
[6519] 435 440 445
[6520] Val Leu Val Leu Arg Thr Thr Ser Thr Val Tyr Asn Tyr Asp Tyr Ile
[6521] 450 455 460
[6522] Trp Asp Phe Ile Phe Tyr Pro Asn Gly Val Met Glu Ala Lys Met His
[6523] 465 470 475 480
[6524] Ala Thr Gly Tyr Val His Ala Thr Phe Tyr Thr Pro Glu Gly Leu Arg
[6525] 485 490 495
[6526] His Gly Thr Arg Leu His Thr His Leu Ile Gly Asn Ile His Thr His
[6527] 500 505 510
[6528] Leu Val His Tyr Arg Val Asp Leu Asp Val Ala Gly Thr Lys Asn Ser
[6529] 515 520 525
[6530] Phe Gln Thr Leu Gln Met Lys Leu Glu Asn Ile Thr Asn Pro Trp Ser
[6531] 530 535 540
[6532] Pro Arg His Arg Val Val Gln Pro Thr Leu Glu Gln Thr Gln Tyr Ser
[6533] 545 550 555 560
[6534] Trp Glu Arg Gln Ala Ala Phe Ser Phe Lys Arg Lys Leu Pro Thr Tyr
[6535] 565 570 575
[6536] Leu Leu Phe Thr Ser Pro Gln Glu Asn Pro Trp Gly His Lys Arg Ser
[6537] 580 585 590
[6538] Tyr Arg Leu Gln Ile His Ser Met Ala Asp Gln Val Leu Pro Pro Gly
[6539] 595 600 605
[6540] Trp Gln Glu Glu Gln Ala Ile Thr Trp Ala Arg Tyr Pro Leu Ala Val
[6541] 610 615 620
[6542] Thr Lys Tyr Arg Glu Ser Glu Leu Cys Ser Ser Ser Ile Tyr His Gln
[6543] 625 630 635 640
[6544] Asn Asp Pro Trp His Pro Pro Val Val Phe Glu Gln Phe Leu His Asn
[6545] 645 650 655
[6546] Asn Glu Asn Ile Glu Asn Glu Asp Leu Val Ala Trp Val Thr Val Gly
[6547] 660 665 670
[6548] Phe Leu His Ile Pro His Ser Glu Asp Ile Pro Asn Thr Ala Thr Pro
[6549] 675 680 685
[6550] Gly Asn Ser Val Gly Phe Leu Leu Arg Pro Phe Asn Phe Phe Pro Glu
[6551] 690 695 700

[6552] Asp Pro Ser Leu Ala Ser Arg Asp Thr Val Ile Val Trp Pro Arg Asp
[6553] 705 710 715 720
[6554] Asn Gly Pro Asn Tyr Val Gln Arg Trp Ile Pro Glu Asp Arg Asp Cys
[6555] 725 730 735
[6556] Ser Met Pro Pro Pro Phe Ser Tyr Asn Gly Thr Tyr Arg Pro Val Glu
[6557] 740 745 750
[6558] Pro Lys Ser Ala Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro
[6559] 755 760 765
[6560] Pro Val Ala Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
[6561] 770 775 780
[6562] Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp
[6563] 785 790 795 800
[6564] Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
[6565] 805 810 815
[6566] Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
[6567] 820 825 830
[6568] Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
[6569] 835 840 845
[6570] Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro
[6571] 850 855 860
[6572] Ser Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
[6573] 865 870 875 880
[6574] Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn
[6575] 885 890 895
[6576] Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
[6577] 900 905 910
[6578] Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
[6579] 915 920 925
[6580] Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys
[6581] 930 935 940
[6582] Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
[6583] 945 950 955 960
[6584] Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
[6585] 965 970 975
[6586] Ser Leu Ser Pro Gly Lys
[6587] 980
[6588] <210> 71
[6589] <211> 2952
[6590] <212> DNA
[6591] <213> 人工序列
[6592] <220>
[6593] <223> Fc-hDAO

[6594] <400> 71

[6595] atgccggccc tgggctgggc cgtggctgcc atcctgatgc tgcagacggc catggcggag 60

[6596] tgccccccct gccccgcccc ccccgtggcc ggcccctccg tgttcctgtt ccccccccaag 120

[6597] cccaaggaca ccctgatgat ctccaggacc cccgaggtga cctgcgtggt ggtggacgtg 180

[6598] tcccacgagg accccgaggt gaagttcaac tggtacgtgg acggcgtgga ggtgcacaac 240

[6599] gccaagacca agcccaggga ggagcagtac aactccacct acagggtggt gtccgtgctg 300

[6600] accgtgctgc accaggactg gctgaacggc aaggagtaca agtgcaaggt gtccaacaag 360

[6601] ggcctgccct cctccatcga gaagaccatc tccaaggcca agggccagcc cagggagccc 420

[6602] caggtgtaca ccctgccccc ctccagggag gagatgacca agaaccaggt gtccctgacc 480

[6603] tgcctggtga agggcttcta cccctccgac atcgccgtgg agtgggagtc caacggccag 540

[6604] cccgagaaca actacaagac cacccccccc gtgctggact ccgacggctc cttcttcctg 600

[6605] tactccaagc tgaccgtgga caagtccagg tggcagcagg gcaacgtgtt ctcctgctcc 660

[6606] gtgatgcacg aggccctgca caaccactac acccagaagt ccctgtccct gtcccccggc 720

[6607] aaggagccca agtccgccga caagacccac accgagccct ccccggggac tctgcccagg 780

[6608] aaggcagggg tgttttcaga cctaagcaac caagagctga aggcagtgca cagcttcctc 840

[6609] tggtccaaga aggagctgag gctgcagccc tccagtacca ccaccatggc caagaacacc 900

[6610] gtgtttctca tcgagatgct gctgcccaag aagtaccatg tgctgaggtt tctggataaa 960

[6611] ggtgaaaggc atcctgtgcg ggaagcccgt gccgtcatct tctttggtga ccaggagcat 1020

[6612] cccaatgtca ccgagtttgc tgtggggccc ctgccaggcc cctgctacat gcgagcactg 1080

[6613] tcccccaggc ctgggtacca gtcctcctgg gcatcgaggc ccatctccac agcagagtat 1140

[6614] gccctcctct accacaccct gcaggaagcc accaagcccc tgcatcagtt cttcctcaat 1200

[6615] accacaggct tctcattcca agactgccat gacagatgcc tggccttcac cgatgtggcc 1260

[6616] ccccggggtg tggcttctgg ccagcgccgc agttggctta tcatacagcg ctatgtagaa 1320

[6617] ggctactttc tgcaccccac tgggctggag ctcctcgtgg atcatgggag cacagatgct 1380

[6618] gggcactggg ccgtggagca ggtgtggtac aacgggaagt tctatgggag cccagaggaa 1440

[6619] ctggctcgga agtatgcaga tggagaggtg gacgtggtgg tcctggagga cccgctgcct 1500

[6620] gggggcaagg ggcatgacag cacagaggag ccgcccctct tctcctccca caagccccgc 1560

[6621] ggggacttcc ccagccccat ccatgtgagc ggcccccgct tggtccagcc ccacggccct 1620

[6622] cgcttcaggc tggagggcaa cgctgtgctc tacggcggct ggagctttgc cttccggctg 1680

[6623] cgctcctcct ccgggctgca ggtcctgaac gtgcacttcg gcggagagcg cattgcctat 1740

[6624] gaggtcagcg tgcaagaggc agtggcgctg tatggaggac acacacctgc aggcatgcag 1800

[6625] accaagtacc tcgatgtcgg ctggggcctg ggcagcgtca ctcatgagtt agcccccggc 1860

[6626] atcgactgcc cggagaccgc caccttcctg gacactttcc actactatga tgccgatgac 1920

[6627] ccggtccatt atccccgagc cctctgcctc tttgaaatgc ccacaggggt gcccccttcgg 1980

[6628] cggcacttta attccaactt taaaggtggc ttcaacttct atgcggggct gaagggccag 2040

[6629] gtgctggtgc tgcggacaac ttcaactgtc tacaattatg attacatttg ggactttatc 2100

[6630] ttctacccca acggggtgat ggaggccaag atgcatgcca ctggctacgt ccacgccacc 2160

[6631] ttctacaccc ccgaggggct gcgccacggc actcgcctgc acacccacct gattggcaac 2220

[6632] atacacactc acttggtgca ctaccgcgta gacctggatg tggcaggcac caagaacagc 2280

[6633] ttccagacac tgcagatgaa gctagaaaac atcaccaacc cctggagccc aagacaccgc 2340

[6634] gtggtccagc caactctgga gcagacgcag tactcctggg agcgccaggc ggccttccgc 2400

[6635] ttcaaaagga agctgcccaa gtacctgctc tttaccagcc cccaggagaa cccctggggc 2460

[6636] cacaagcgca gctaccgcct gcagatccac tccatggccg accaggtgct gcccccaggc 2520
[6637] tggcaggagg agcaggccat cacctgggca aggtaccccc tggcagtgac caagtaccgg 2580
[6638] gagtcggagc tgtgcagcag cagcatctac caccagaacg acccctggca cccgcccgtg 2640
[6639] gtctttgagc agtttcttca caacaacgag aacattgaaa atgaggacct ggtggcctgg 2700
[6640] gtgacggtgg gcttcctgca catcccccac tcagaggaca ttcccaacac agccacacct 2760
[6641] gggaactccg tgggcttcct gctccggcca ttcaacttct tcccagagga ccctccctg 2820
[6642] gcatccagag acactgtgat cgtgtggcct cgggacaacg gccccaacta cgtccagcgc 2880
[6643] tggatccctg aggacaggga ctgctcgatg cctccccctt ttagctacaa tgggacctat 2940
[6644] agacctgtgt ga 2952
[6645] <210> 72
[6646] <211> 2952
[6647] <212> DNA
[6648] <213> 人工序列
[6649] <220>
[6650] <223> Fc-hDAO-Hepmut1
[6651] <400> 72
[6652] atgccggccc tgggctgggc cgtggctgcc atcctgatgc tgcagacggc catggcggag 60
[6653] tgcccccct gccccgcccc ccccgtggcc ggcccctccg tgttcctgtt ccccccccaag 120
[6654] cccaaggaca ccctgatgat ctccaggacc cccgaggtga cctgcgtggt ggtggacgtg 180
[6655] tcccacgagg accccgaggt gaagttcaac tggtacgtgg acggcgtgga ggtgcacaac 240
[6656] gccaagacca agcccaggga ggagcagtac aactccacct acagggtggt gtccgtgctg 300
[6657] accgtgctgc accaggactg gctgaacggc aaggagtaca agtgcaaggt gtccaacaag 360
[6658] ggcctgccct cctccatcga gaagaccatc tccaaggcca agggccagcc cagggagccc 420
[6659] caggtgtaca ccctgccccc ctccagggag gagatgacca agaaccaggt gtccctgacc 480
[6660] tgcctggtga agggcttcta cccctccgac atcgccgtgg agtgggagtc caacggccag 540
[6661] cccgagaaca actacaagac cacccccccc gtgctggact ccgacggctc cttcttcctg 600
[6662] tactccaagc tgaccgtgga caagtccagg tggcagcagg gcaacgtgtt ctcctgctcc 660
[6663] gtgatgcacg aggccctgca caaccactac acccagaagt ccctgtccct gtcccccggc 720
[6664] aaggagccca agtccgccga caagacccac accgagccct ccccggggac tctgcccagg 780
[6665] aaggcagggg tgttttcaga cctaagcaac caagagctga aggcagtgca cagcttcctc 840
[6666] tggtccaaga aggagctgag gctgcagccc tccagtacca ccaccatggc caagaacacc 900
[6667] gtgtttctca tcgagatgct gctgcccaag aagtaccatg tgctgaggtt tctggataaa 960
[6668] ggtgaaaggc atcctgtgcg ggaagcccgt gccgtcatct tctttggtga ccaggagcat 1020
[6669] cccaatgtca ccgagtttgc tgtggggccc ctgccaggcc cctgctacat gcgagcactg 1080
[6670] tcccccaggc ctgggtacca gtcctcctgg gcatcgaggc ccatctccac agcagagtat 1140
[6671] gccctcctct accacaccct gcaggaagcc accaagcccc tgcatcagtt cttcctcaat 1200
[6672] accacaggct tctcattcca agactgccat gacagatgcc tggccttcac cgatgtggcc 1260
[6673] ccccggggtg tggcttctgg ccagcgccgc agttggctta tcatacagcg ctatgtagaa 1320
[6674] ggctactttc tgcaccccac tgggctggag ctcctcgtgg atcatgggag cacagatgct 1380
[6675] gggcactggg ccgtggagca ggtgtggtac aacgggaagt tctatgggag cccagaggaa 1440
[6676] ctggctcgga agtatgcaga tggagaggtg gacgtggtgg tcctggagga cccgctgcct 1500
[6677] gggggcaagg ggcatgacag cacagaggag ccgcccctct tctcctccca caagccccgc 1560

[6678] ggggacttcc ccagccccat ccatgtgagc ggcccccgct tggtccagcc ccacggccct 1620
[6679] cgcttcaggc tggagggcaa cgctgtgctc tacggcggct ggagctttgc cttccggctg 1680
[6680] cgctcctcct ccgggctgca ggtcctgaac gtgcacttcg gcggagagcg cattgcctat 1740
[6681] gaggtcagcg tgcaagaggc agtggcgctg tatggaggac acacacctgc aggcatgcag 1800
[6682] accaagtacc tcgatgtcgg ctggggcctg ggcagcgtca ctcatgagtt agcccccggc 1860
[6683] atcgactgcc cggagaccgc caccttcctg gacactttcc actactatga tgccgatgac 1920
[6684] ccggtccatt atccccgagc cctctgcctc tttgaaatgc ccacaggggt gcccccttcgg 1980
[6685] cggcacttta attccaactt taaaggtggc ttcaacttct atgcggggct gaagggccag 2040
[6686] gtgctggtgc tgcggacaac ttcaactgtc tacaattatg attacatttg ggactttatc 2100
[6687] ttctacccca acggggtgat ggaggccaag atgcatgcca ctggctacgt ccacgccacc 2160
[6688] ttctacaccc ccgaggggct gcgccacggc actcgcctgc acacccacct gattggcaac 2220
[6689] atacacactc acttggtgca ctaccgcgta gacctggatg tggcaggcac caagaacagc 2280
[6690] ttccagacac tgcagatgaa gctagaaaac atcaccaacc cctggagccc aagacaccgc 2340
[6691] gtggtccagc caactctgga gcagacgcag tactcctggg agcgccaggc ggccttcagc 2400
[6692] ttcaaaagga agctgcccaa gtacctgctc tttaccagcc cccaggagaa cccctggggc 2460
[6693] cacaagcgca gctaccgcct gcagatccac tccatggccg accaggtgct gcccccaggc 2520
[6694] tggcaggagg agcaggccat cacctgggca aggtaccccc tggcagtgac caagtaccgg 2580
[6695] gagtcggagc tgtgcagcag cagcatctac caccagaacg acccctggca cccgcccgtg 2640
[6696] gtctttgagc agtttcttca caacaacgag aacattgaaa atgaggacct ggtggcctgg 2700
[6697] gtgacggtgg gcttcctgca catcccccac tcagaggaca ttcccaacac agccacacct 2760
[6698] gggaactccg tgggcttcct gctccggcca ttcaacttct tcccagagga ccctccctg 2820
[6699] gcatccagag acactgtgat cgtgtggcct cgggacaacg gccccaacta cgtccagcgc 2880
[6700] tggatccctg aggacaggga ctgctcgatg cctccccctt ttagctacaa tgggacctat 2940
[6701] agacctgtgt ga 2952
[6702] <210> 73
[6703] <211> 2952
[6704] <212> DNA
[6705] <213> 人工序列
[6706] <220>
[6707] <223> Fc-hDAO-Hepmut2
[6708] <400> 73
[6709] atgccggccc tgggctgggc cgtggctgcc atcctgatgc tgcagacggc catggcggag 60
[6710] tgcccccct gccccgcccc ccccgtggcc ggcccctccg tgttcctgtt ccccccccaag 120
[6711] cccaaggaca ccctgatgat ctccaggacc cccgaggtga cctgcgtggt ggtggacgtg 180
[6712] tcccacgagg accccgaggt gaagttcaac tggtacgtgg acggcgtgga ggtgcacaac 240
[6713] gccaagacca agcccaggga ggagcagtac aactccacct acagggtggt gtccgtgctg 300
[6714] accgtgctgc accaggactg gctgaacggc aaggagtaca agtgcaaggt gtccaacaag 360
[6715] ggcctgccct cctccatcga gaagaccatc tccaaggcca agggccagcc cagggagccc 420
[6716] caggtgtaca ccctgccccc ctccagggag gagatgacca agaaccaggt gtccctgacc 480
[6717] tgcctggtga agggcttcta cccctccgac atcgccgtgg agtgggagtc caacggccag 540
[6718] cccgagaaca actacaagac cacccccccc gtgctggact ccgacggctc cttcttcctg 600
[6719] tactccaagc tgaccgtgga caagtccagg tggcagcagg gcaacgtgtt ctcctgctcc 660

[6720] gtgatgcacg aggccctgca caaccactac acccagaagt ccctgtccct gtcccccggc 720
[6721] aaggagccca agtccgccga caagacccac accgagccct ccccggggac tctgcccagg 780
[6722] aaggcagggg tgttttcaga cctaagcaac caagagctga aggcagtgca cagcttcctc 840
[6723] tggtccaaga aggagctgag gctgcagccc tccagtacca ccaccatggc caagaacacc 900
[6724] gtgtttctca tcgagatgct gctgcccaag aagtaccatg tgctgaggtt tctggataaa 960
[6725] ggtgaaaggc atcctgtgcg ggaagcccgt gccgtcatct tctttggtga ccaggagcat 1020
[6726] cccaatgtca ccgagtttgc tgtggggccc ctgccaggcc cctgctacat gcgagcactg 1080
[6727] tcccccaggc ctgggtacca gtcctcctgg gcatcgaggc ccatctccac agcagagtat 1140
[6728] gccctcctct accacaccct gcaggaagcc accaagcccc tgcatcagtt cttcctcaat 1200
[6729] accacaggct tctcattcca agactgccat gacagatgcc tggccttcac cgatgtggcc 1260
[6730] ccccggggtg tggcttctgg ccagcgccgc agttggctta tcatacagcg ctatgtagaa 1320
[6731] ggctactttc tgcaccccac tgggctggag ctcctcgtgg atcatgggag cacagatgct 1380
[6732] gggcactggg ccgtggagca ggtgtggtac aacgggaagt tctatgggag cccagaggaa 1440
[6733] ctggctcgga agtatgcaga tggagaggtg gacgtggtgg tcctggagga cccgctgcct 1500
[6734] gggggcaagg ggcatgacag cacagaggag ccgcccctct tctcctccca caagccccgc 1560
[6735] ggggacttcc ccagccccat ccatgtgagc ggcccccgct tggtccagcc ccacggccct 1620
[6736] cgcttcaggc tggagggcaa cgctgtgctc tacggcggct ggagctttgc cttccggctg 1680
[6737] cgctcctcct ccgggctgca ggtcctgaac gtgcacttcg gcggagagcg cattgcctat 1740
[6738] gaggtcagcg tgcaagaggc agtggcgctg tatggaggac acacacctgc aggcatgcag 1800
[6739] accaagtacc tcgatgtcgg ctggggcctg ggcagcgtca ctcatgagtt agcccccggc 1860
[6740] atcgactgcc cggagaccgc caccttcctg gacactttcc actactatga tgccgatgac 1920
[6741] ccggtccatt atccccgagc cctctgcctc tttgaaatgc ccacaggggt gcccccttcgg 1980
[6742] cggcacttta attccaactt taaaggtggc ttcaacttct atgcggggct gaagggccag 2040
[6743] gtgctggtgc tgcggacaac ttcaactgtc tacaattatg attacatttg ggactttatc 2100
[6744] ttctacccca acggggtgat ggaggccaag atgcatgcca ctggctacgt ccacgccacc 2160
[6745] ttctacaccc ccgaggggct gcgccacggc actcgcctgc acacccacct gattggcaac 2220
[6746] atacacactc acttggtgca ctaccgcgta gacctggatg tggcaggcac caagaacagc 2280
[6747] ttccagacac tgcagatgaa gctagaaaac atcaccaacc cctggagccc aagacaccgc 2340
[6748] gtggtccagc caactctgga gcagacgcag tactcctggg agcgccaggc ggccttccgc 2400
[6749] ttcaaaagga agctgcccac gtacctgctc tttaccagcc cccaggagaa cccctggggc 2460
[6750] cacaagcgca gctaccgcct gcagatccac tccatggccg accaggtgct gcccccaggc 2520
[6751] tggcaggagg agcaggccat cacctgggca aggtaccccc tggcagtgac caagtaccgg 2580
[6752] gagtcggagc tgtgcagcag cagcatctac caccagaacg acccctggca cccgcccgtg 2640
[6753] gtctttgagc agtttcttca caacaacgag aacattgaaa atgaggacct ggtggcctgg 2700
[6754] gtgacggtgg gcttcctgca catcccccac tcagaggaca ttcccaacac agccacacct 2760
[6755] gggaactccg tgggcttcct gctccggcca ttcaacttct tcccagagga cccctccctg 2820
[6756] gcatccagag acactgtgat cgtgtggcct cgggacaacg gccccaacta cgtccagcgc 2880
[6757] tggatccctg aggacaggga ctgctcgatg cctccccctt ttagctacaa tgggacctat 2940
[6758] agacctgtgt ga 2952
[6759] <210> 74
[6760] <211> 2952
[6761] <212> DNA

[6762] <213> 人工序列

[6763] <220>

[6764] <223> Fc-hDAO-Hepmut3

[6765] <400> 74

[6766] atgccggccc tgggctgggc cgtggctgcc atcctgatgc tgcagacggc catggcggag 60

[6767] tgccccccct gccccgcccc ccccgtggcc ggcccctccg tgttcctgtt ccccccccaag 120

[6768] cccaaggaca ccctgatgat ctccaggacc cccgaggtga cctgcgtggt ggtggacgtg 180

[6769] tcccacgagg accccgaggt gaagttcaac tggtacgtgg acggcgtgga ggtgcacaac 240

[6770] gccaagacca agcccaggga ggagcagtac aactccacct acagggtggt gtccgtgctg 300

[6771] accgtgctgc accaggactg gctgaacggc aaggagtaca agtgcaaggt gtccaacaag 360

[6772] ggcctgccct cctccatcga gaagaccatc tccaaggcca agggccagcc cagggagccc 420

[6773] caggtgtaca ccctgccccc ctccagggag gagatgacca agaaccaggt gtccctgacc 480

[6774] tgcctggtga agggcttcta cccctccgac atcgccgtgg agtgggagtc caacggccag 540

[6775] cccgagaaca actacaagac cacccccccc gtgctggact ccgacggctc cttcttcctg 600

[6776] tactccaagc tgaccgtgga caagtccagg tggcagcagg gcaacgtgtt ctcctgctcc 660

[6777] gtgatgcacg aggccctgca caaccactac acccagaagt ccctgtccct gtcccccggc 720

[6778] aaggagccca agtccgccga caagacccac accgagccct ccccggggac tctgcccagg 780

[6779] aaggcagggg tgttttcaga cctaagcaac caagagctga aggcagtgca cagcttcctc 840

[6780] tggtccaaga aggagctgag gctgcagccc tccagtacca ccaccatggc caagaacacc 900

[6781] gtgtttctca tcgagatgct gctgcccaag aagtaccatg tgctgaggtt tctggataaa 960

[6782] ggtgaaaggc atcctgtgcg ggaagcccgt gccgtcatct tctttggtga ccaggagcat 1020

[6783] cccaatgtca ccgagtttgc tgtggggccc ctgccaggcc cctgctacat gcgagcactg 1080

[6784] tcccccaggc ctgggtacca gtcctcctgg gcatcgaggc ccatctccac agcagagtat 1140

[6785] gccctcctct accacaccct gcaggaagcc accaagcccc tgcatcagtt cttcctcaat 1200

[6786] accacaggct tctcattcca agactgccat gacagatgcc tggccttcac cgatgtggcc 1260

[6787] ccccggggtg tggcttctgg ccagcgccgc agttggctta tcatacagcg ctatgtagaa 1320

[6788] ggctactttc tgcaccccac tgggctggag ctcctcgtgg atcatgggag cacagatgct 1380

[6789] gggcactggg ccgtggagca ggtgtggtac aacgggaagt tctatgggag cccagaggaa 1440

[6790] ctggctcgga agtatgcaga tggagaggtg gacgtggtgg tcctggagga cccgctgcct 1500

[6791] gggggcaagg ggcatgacag cacagaggag ccgcccctct tctcctccca caagccccgc 1560

[6792] ggggacttcc ccagccccat ccatgtgagc ggcccccgct tggtccagcc ccacggccct 1620

[6793] cgcttcaggc tggagggcaa cgctgtgctc tacggcggct ggagctttgc cttccggctg 1680

[6794] cgctcctcct ccgggctgca ggtcctgaac gtgcacttcg gcggagagcg cattgcctat 1740

[6795] gaggtcagcg tgcaagaggc agtggcgctg tatggaggac acacacctgc aggcatgcag 1800

[6796] accaagtacc tcgatgtcgg ctggggcctg ggcagcgtca ctcatgagtt agcccccggc 1860

[6797] atcgactgcc cggagaccgc caccttcctg gacactttcc actactatga tgccgatgac 1920

[6798] ccggtccatt atccccgagc cctctgcctc tttgaaatgc ccacaggggt gccccttcgg 1980

[6799] cggcacttta attccaactt taaaggtggc ttcaacttct atgcggggct gaagggccag 2040

[6800] gtgctggtgc tgcggacaac ttcaactgtc tacaattatg attacatttg ggactttatc 2100

[6801] ttctacccca acggggtgat ggaggccaag atgcatgcca ctggctacgt ccacgccacc 2160

[6802] ttctacaccc ccgaggggct gcgccacggc actcgcctgc acacccacct gattggcaac 2220

[6803] atacacactc acttggtgca ctaccgcgta gacctggatg tggcaggcac caagaacagc 2280

[6804] ttccagacac tgcagatgaa gctagaaaac atcaccaacc cctggagccc aagacaccgc 2340
[6805] gtggtccagc caactctgga gcagacgcag tactcctggg agcgccaggc ggccttccgc 2400
[6806] ttcaaaacga agctgcccaa gtacctgctc tttaccagcc cccaggagaa cccctggggc 2460
[6807] cacaagcgca gctaccgcct gcagatccac tccatggccg accaggtgct gcccccaggc 2520
[6808] tggcaggagg agcaggccat cacctgggca aggtaccccc tggcagtgac caagtaccgg 2580
[6809] gagtcggagc tgtgcagcag cagcatctac caccagaacg acccctggca cccgcccgtg 2640
[6810] gtctttgagc agtttcttca caacaacgag aacattgaaa atgaggacct ggtggcctgg 2700
[6811] gtgacggtgg gcttcctgca catcccccac tcagaggaca ttcccaacac agccacacct 2760
[6812] gggaactccg tgggcttcct gctccggcca ttcaacttct tcccagagga ccctccctg 2820
[6813] gcatccagag acactgtgat cgtgtggcct cgggacaacg gccccaacta cgtccagcgc 2880
[6814] tggatccctg aggacaggga ctgctcgatg cctccccctt ttagctacaa tgggacctat 2940
[6815] agacctgtgt ga 2952
[6816] <210> 75
[6817] <211> 2952
[6818] <212> DNA
[6819] <213> 人工序列
[6820] <220>
[6821] <223> Fc-hDAO-Hepmut4
[6822] <400> 75
[6823] atgccggccc tgggctgggc cgtggctgcc atcctgatgc tgcagacggc catggcggag 60
[6824] tgcccccct gccccgcccc ccccgtggcc ggcccctccg tgttcctgtt ccccccaag 120
[6825] cccaaggaca ccctgatgat ctccaggacc cccgaggtga cctgcgtggt ggtggacgtg 180
[6826] tcccacgagg accccgaggt gaagttcaac tggtacgtgg acggcgtgga ggtgcacaac 240
[6827] gccaagacca agcccaggga ggagcagtac aactccacct acagggtggt gtccgtgctg 300
[6828] accgtgctgc accaggactg gctgaacggc aaggagtaca agtgcaaggt gtccaacaag 360
[6829] ggcctgccct cctccatcga gaagaccatc tccaaggcca agggccagcc cagggagccc 420
[6830] caggtgtaca ccctgccccc ctccagggag gagatgacca agaaccaggt gtccctgacc 480
[6831] tgcctggtga agggcttcta cccctccgac atcgccgtgg agtgggagtc caacggccag 540
[6832] cccgagaaca actacaagac cacccccccc gtgctggact ccgacggctc cttcttcctg 600
[6833] tactccaagc tgaccgtgga caagtccagg tggcagcagg gcaacgtgtt ctcctgctcc 660
[6834] gtgatgcacg aggccctgca caaccactac acccagaagt ccctgtccct gtcccccggc 720
[6835] aaggagccca agtccgccga caagacccac accgagccct ccccggggac tctgcccagg 780
[6836] aaggcagggg tgttttcaga cctaagcaac caagagctga aggcagtgca cagcttcctc 840
[6837] tggtccaaga aggagctgag gctgcagccc tccagtacca ccaccatggc caagaacacc 900
[6838] gtgtttctca tcgagatgct gctgcccaag aagtaccatg tgctgaggtt tctggataaa 960
[6839] ggtgaaaggc atcctgtgcg ggaagcccgt gccgtcatct tctttggtga ccaggagcat 1020
[6840] cccaatgtca ccgagtttgc tgtggggccc ctgccaggcc cctgctacat gcgagcactg 1080
[6841] tcccccaggc ctgggtacca gtcctcctgg gcatcgaggc ccatctccac agcagagtat 1140
[6842] gccctcctct accacaccct gcaggaagcc accaagcccc tgcatcagtt cttcctcaat 1200
[6843] accacaggct tctcattcca agactgccat gacagatgcc tggccttcac cgatgtggcc 1260
[6844] ccccggggtg tggcttctgg ccagcgccgc agttggctta tcatacagcg ctatgtagaa 1320
[6845] ggctactttc tgcaccccac tgggctggag ctcctcgtgg atcatgggag cacagatgct 1380

[6846] gggcactggg ccgtggagca ggtgtggtac aacgggaagt tctatgggag cccagaggaa 1440
[6847] ctggctcgga agtatgcaga tggagaggtg gacgtggtgg tcctggagga cccgctgcct 1500
[6848] gggggcaagg ggcatgacag cacagaggag ccgcccctct tctcctccca caagccccgc 1560
[6849] ggggacttcc ccagccccat ccatgtgagc ggcccccgct tggtccagcc ccacggccct 1620
[6850] cgcttcaggc tggagggcaa cgctgtgctc tacggcggct ggagctttgc cttccggctg 1680
[6851] cgctcctcct ccgggctgca ggtcctgaac gtgcacttcg gcggagagcg cattgcctat 1740
[6852] gaggtcagcg tgcaagaggc agtggcgctg tatggaggac acacacctgc aggcatgcag 1800
[6853] accaagtacc tcgatgtcgg ctggggcctg ggcagcgtca ctcatgagtt agcccccggc 1860
[6854] atcgactgcc cggagaccgc caccttcctg gacactttcc actactatga tgccgatgac 1920
[6855] ccggtccatt atccccgagc cctctgcctc tttgaaatgc ccacaggggt gcccccttcgg 1980
[6856] cggcacttta attccaactt taaaggtggc ttcaacttct atgcggggct gaagggccag 2040
[6857] gtgctggtgc tgcggacaac ttcaactgtc tacaattatg attacatttg ggactttatc 2100
[6858] ttctacccca acggggtgat ggaggccaag atgcatgcca ctggctacgt ccacgccacc 2160
[6859] ttctacaccc ccgaggggct gcgccacggc actcgcctgc acacccacct gattggcaac 2220
[6860] atacacactc acttggtgca ctaccgcgta gacctggatg tggcaggcac caagaacagc 2280
[6861] ttccagacac tgcagatgaa gctagaaaac atcaccaacc cctggagccc aagacaccgc 2340
[6862] gtggtccagc caactctgga gcagacgcag tactcctggg agcgccaggc ggccttcagc 2400
[6863] ttcaaaacga agctgcccaa gtacctgctc tttaccagcc cccaggagaa ccccctggggc 2460
[6864] cacaagcgca gctaccgcct gcagatccac tccatggccg accaggtgct gcccccaggc 2520
[6865] tggcaggagg agcaggccat cacctgggca aggtaccccc tggcagtgac caagtaccgg 2580
[6866] gagtcggagc tgtgcagcag cagcatctac caccagaacg acccctggca cccgcccgtg 2640
[6867] gtctttgagc agtttcttca caacaacgag aacattgaaa atgaggacct ggtggcctgg 2700
[6868] gtgacggtgg gcttcctgca catcccccac tcagaggaca ttcccaacac agccacacct 2760
[6869] gggaactccg tgggcttcct gctccggcca ttcaacttct tcccagagga cccctccctg 2820
[6870] gcatccagag acactgtgat cgtgtggcct cgggacaacg gccccaacta cgtccagcgc 2880
[6871] tggatccctg aggacaggga ctgctcgatg cctccccctt ttagctacaa tgggacctat 2940
[6872] agacctgtgt ga 2952
[6873] <210> 76
[6874] <211> 2952
[6875] <212> DNA
[6876] <213> 人工序列
[6877] <220>
[6878] <223> Fc-hDAO-Hepmut5
[6879] <400> 76
[6880] atgccggccc tgggctgggc cgtggctgcc atcctgatgc tgcagacggc catggcggag 60
[6881] tgccccccct gccccgcccc ccccgtggcc ggcccctccg tgttcctgtt ccccccccaag 120
[6882] cccaaggaca ccctgatgat ctccaggacc cccgaggtga cctgcgtggt ggtggacgtg 180
[6883] tcccacgagg accccgaggt gaagttcaac tggtacgtgg acggcgtgga ggtgcacaac 240
[6884] gccaagacca agcccaggga ggagcagtac aactccacct acagggtggt gtccgtgctg 300
[6885] accgtgctgc accaggactg gctgaacggc aaggagtaca agtgcaaggt gtccaacaag 360
[6886] ggcctgccct cctccatcga gaagaccatc tccaaggcca agggccagcc cagggagccc 420
[6887] caggtgtaca ccctgccccc ctccagggag gagatgacca agaaccaggt gtccctgacc 480

[6888] tgcctggtga agggcttcta cccctccgac atcgccgtgg agtgggagtc caacggccag 540
[6889] cccgagaaca actacaagac cacccccccc gtgctggact ccgacggctc cttcttcctg 600
[6890] tactccaagc tgaccgtgga caagtccagg tggcagcagg gcaacgtgtt ctcctgctcc 660
[6891] gtgatgcacg aggccctgca caaccactac acccagaagt ccctgtccct gtcccccggc 720
[6892] aaggagccca agtccgccga caagacccac accgagccct ccccggggac tctgcccagg 780
[6893] aaggcagggg tgttttcaga cctaagcaac caagagctga aggcagtgca cagcttcctc 840
[6894] tggtccaaga aggagctgag gctgcagccc tccagtacca ccaccatggc caagaacacc 900
[6895] gtgtttctca tcgagatgct gctgcccaag aagtaccatg tgctgaggtt tctggataaa 960
[6896] ggtgaaaggc atcctgtgcg ggaagcccgt gccgtcatct tctttggtga ccaggagcat 1020
[6897] cccaatgtca ccgagtttgc tgtggggccc ctgccaggcc cctgctacat gcgagcactg 1080
[6898] tcccccaggc ctgggtacca gtcctcctgg gcatcgaggc ccatctccac agcagagtat 1140
[6899] gccctcctct accacaccct gcaggaagcc accaagcccc tgcatcagtt cttcctcaat 1200
[6900] accacaggct tctcattcca agactgccat gacagatgcc tggccttcac cgatgtggcc 1260
[6901] ccccggggtg tggcttctgg ccagcgccgc agttggctta tcatacagcg ctatgtagaa 1320
[6902] ggctactttc tgcaccccac tgggctggag ctcctcgtgg atcatgggag cacagatgct 1380
[6903] gggcactggg ccgtggagca ggtgtggtac aacgggaagt tctatgggag cccagaggaa 1440
[6904] ctggctcgga agtatgcaga tggagaggtg gacgtggtgg tcctggagga cccgctgcct 1500
[6905] gggggcaagg ggcatgacag cacagaggag ccgcccctct tctcctccca caagccccgc 1560
[6906] ggggacttcc ccagccccat ccatgtgagc ggcccccgct tggtccagcc ccacggccct 1620
[6907] cgcttcaggc tggagggcaa cgctgtgctc tacggcggct ggagctttgc cttccggctg 1680
[6908] cgctcctcct ccgggctgca ggtcctgaac gtgcacttcg gcggagagcg cattgcctat 1740
[6909] gaggtcagcg tgcaagaggc agtggcgctg tatggaggac acacacctgc aggcatgcag 1800
[6910] accaagtacc tcgatgtcgg ctggggcctg ggcagcgtca ctcatgagtt agcccccggc 1860
[6911] atcgactgcc cggagaccgc caccttcctg gacactttcc actactatga tgccgatgac 1920
[6912] ccggtccatt atccccgagc cctctgcctc tttgaaatgc ccacaggggt gcccccttcgg 1980
[6913] cggcacttta attccaactt taaaggtggc ttcaacttct atgcggggct gaagggccag 2040
[6914] gtgctggtgc tgcggacaac ttcaactgtc tacaattatg attacatttg ggactttatc 2100
[6915] ttctacccca acggggtgat ggaggccaag atgcatgcca ctggctacgt ccacgccacc 2160
[6916] ttctacaccc ccgaggggct gcgccacggc actcgcctgc acacccacct gattggcaac 2220
[6917] atacacactc acttggtgca ctaccgcgta gacctggatg tggcaggcac caagaacagc 2280
[6918] ttccagacac tgcagatgaa gctagaaaac atcaccaacc cctggagccc aagacaccgc 2340
[6919] gtggtccagc caactctgga gcagacgcag tactcctggg agcgccaggc ggccttccgc 2400
[6920] ttcaaaacga agctgcccac gtacctgctc tttaccagcc cccaggagaa cccctggggc 2460
[6921] cacaagcgca gctaccgcct gcagatccac tccatggccg accaggtgct gcccccaggc 2520
[6922] tggcaggagg agcaggccat cacctgggca aggtaccccc tggcagtgac caagtaccgg 2580
[6923] gagtcggagc tgtgcagcag cagcatctac caccagaacg acccctggca cccgcccgtg 2640
[6924] gtctttgagc agtttcttca caacaacgag aacattgaaa atgaggacct ggtggcctgg 2700
[6925] gtgacggtgg gcttcctgca catcccccac tcagaggaca ttcccaacac agccacacct 2760
[6926] gggaactccg tgggcttcct gctccggcca ttcaacttct tcccagagga ccctccctg 2820
[6927] gcatccagag acactgtgat cgtgtggcct cgggacaacg gccccaacta cgtccagcgc 2880
[6928] tggatccctg aggacaggga ctgctcgatg cctccccctt ttagctacaa tgggacctat 2940
[6929] agacctgtgt ga 2952

[6930] <210> 77

[6931] <211> 2952

[6932] <212> DNA

[6933] <213> 人工序列

[6934] <220>

[6935] <223> Fc-hDAO-Hepmut6

[6936] <400> 77

[6937] atgccggccc tgggctgggc cgtggctgcc atcctgatgc tgcagacggc catggcggag 60

[6938] tgccccccct gccccgcccc ccccgtggcc ggcccctccg tgttcctgtt ccccccccaag 120

[6939] cccaaggaca ccctgatgat ctccaggacc cccgaggtga cctgcgtggt ggtggacgtg 180

[6940] tcccacgagg accccgaggt gaagttcaac tggtacgtgg acggcgtgga ggtgcacaac 240

[6941] gccaagacca agcccaggga ggagcagtac aactccacct acagggtggt gtccgtgctg 300

[6942] accgtgctgc accaggactg gctgaacggc aaggagtaca agtgcaaggt gtccaacaag 360

[6943] ggcctgccct cctccatcga gaagaccatc tccaaggcca agggccagcc cagggagccc 420

[6944] caggtgtaca ccctgccccc ctccagggag gagatgacca agaaccaggt gtccctgacc 480

[6945] tgcctggtga agggcttcta cccctccgac atcgccgtgg agtgggagtc caacggccag 540

[6946] cccgagaaca actacaagac cacccccccc gtgctggact ccgacggctc cttcttcctg 600

[6947] tactccaagc tgaccgtgga caagtccagg tggcagcagg gcaacgtgtt ctcctgctcc 660

[6948] gtgatgcacg aggccctgca caaccactac acccagaagt ccctgtccct gtcccccggc 720

[6949] aaggagccca agtccgccga caagacccac accgagccct ccccggggac tctgcccagg 780

[6950] aaggcagggg tgttttcaga cctaagcaac caagagctga aggcagtgca cagcttcctc 840

[6951] tggtccaaga aggagctgag gctgcagccc tccagtacca ccaccatggc caagaacacc 900

[6952] gtgtttctca tcgagatgct gctgcccaag aagtaccatg tgctgaggtt tctggataaa 960

[6953] ggtgaaaggc atcctgtgcg ggaagcccgt gccgtcatct tctttggtga ccaggagcat 1020

[6954] cccaatgtca ccgagtttgc tgtggggccc ctgccaggcc cctgctacat gcgagcactg 1080

[6955] tcccccaggc ctgggtacca gtcctcctgg gcatcgaggc ccatctccac agcagagtat 1140

[6956] gccctcctct accacaccct gcaggaagcc accaagcccc tgcatcagtt cttcctcaat 1200

[6957] accacaggct tctcattcca agactgccat gacagatgcc tggccttcac cgatgtggcc 1260

[6958] ccccggggtg tggcttctgg ccagcgccgc agttggctta tcatacagcg ctatgtagaa 1320

[6959] ggctactttc tgcaccccac tgggctggag ctcctcgtgg atcatgggag cacagatgct 1380

[6960] gggcactggg ccgtggagca ggtgtggtac aacgggaagt tctatgggag cccagaggaa 1440

[6961] ctggctcgga agtatgcaga tggagaggtg gacgtggtgg tcctggagga cccgctgcct 1500

[6962] gggggcaagg ggcatgacag cacagaggag ccgcccctct tctcctccca caagccccgc 1560

[6963] ggggacttcc ccagccccat ccatgtgagc ggcccccgct tggtccagcc ccacggccct 1620

[6964] cgcttcaggc tggagggcaa cgctgtgctc tacggcggct ggagctttgc cttccggctg 1680

[6965] cgctcctcct ccgggctgca ggtcctgaac gtgcacttcg gcggagagcg cattgcctat 1740

[6966] gaggtcagcg tgcaagaggc agtggcgctg tatggaggac acacacctgc aggcatgcag 1800

[6967] accaagtacc tcgatgtcgg ctggggcctg ggcagcgtca ctcatgagtt agcccccggc 1860

[6968] atcgactgcc cggagaccgc caccttcctg gacactttcc actactatga tgccgatgac 1920

[6969] ccggtccatt atccccgagc cctctgcctc tttgaaatgc ccacaggggt gccccttcgg 1980

[6970] cggcacttta attccaactt taaaggtggc ttcaacttct atgcggggct gaagggccag 2040

[6971] gtgctggtgc tgcggacaac ttcaactgtc tacaattatg attacatttg ggactttatc 2100

[6972] ttctacccca acggggtgat ggaggccaag atgcatgcca ctggctacgt ccacgccacc 2160
[6973] ttctacaccc ccgaggggct gcgccacggc actcgcctgc acacccacct gattggcaac 2220
[6974] atacacactc acttggtgca ctaccgcgta gacctggatg tggcaggcac caagaacagc 2280
[6975] ttccagacac tgcagatgaa gctagaaaac atcaccaacc cctggagccc aagacaccgc 2340
[6976] gtggtccagc caactctgga gcagacgcag tactcctggg agcgccaggc ggccttccgc 2400
[6977] ttcggacaga cgctgcccaa gtacctgctc tttaccagcc cccaggagaa cccctggggc 2460
[6978] cacaagcgca gctaccgcct gcagatccac tccatggccg accaggtgct gcccccaggc 2520
[6979] tggcaggagg agcaggccat cacctgggca aggtaccccc tggcagtgac caagtaccgg 2580
[6980] gagtcggagc tgtgcagcag cagcatctac caccagaacg acccctggca cccgcccgtg 2640
[6981] gtctttgagc agtttcttca caacaacgag aacattgaaa atgaggacct ggtggcctgg 2700
[6982] gtgacggtgg gcttcctgca catcccccac tcagaggaca ttcccaacac agccacacct 2760
[6983] gggaactccg tgggcttcct gctccggcca ttcaacttct tcccagagga cccctccctg 2820
[6984] gcatccagag acactgtgat cgtgtggcct cgggacaacg gccccaacta cgtccagcgc 2880
[6985] tggatccctg aggacaggga ctgctcgatg cctccccctt ttagctacaa tgggacctat 2940
[6986] agacctgtgt ga 2952
[6987] <210> 78
[6988] <211> 2952
[6989] <212> DNA
[6990] <213> 人工序列
[6991] <220>
[6992] <223> Fc-hDAO-Hepmut7
[6993] <400> 78
[6994] atgccggccc tgggctgggc cgtggctgcc atcctgatgc tgcagacggc catggcggag 60
[6995] tgcccccccc gccccgcccc ccccgtggcc ggcccctccg tgttcctgtt ccccccccaag 120
[6996] cccaaggaca ccctgatgat ctccaggacc cccgaggtga cctgcgtggt ggtggacgtg 180
[6997] tcccacgagg accccgaggt gaagttcaac tggtacgtgg acggcgtgga ggtgcacaac 240
[6998] gccaagacca agcccaggga ggagcagtac aactccacct acagggtggt gtccgtgctg 300
[6999] accgtgctgc accaggactg gctgaacggc aaggagtaca agtgcaaggt gtccaacaag 360
[7000] ggcctgccct cctccatcga gaagaccatc tccaaggcca agggccagcc cagggagccc 420
[7001] caggtgtaca ccctgccccc ctccagggag gagatgacca agaaccaggt gtccctgacc 480
[7002] tgcctggtga agggcttcta cccctccgac atcgccgtgg agtgggagtc caacggccag 540
[7003] cccgagaaca actacaagac cacccccccc gtgctggact ccgacggctc cttcttcctg 600
[7004] tactccaagc tgaccgtgga caagtccagg tggcagcagg gcaacgtgtt ctcctgctcc 660
[7005] gtgatgcacg aggccctgca caaccactac acccagaagt ccctgtccct gtcccccggc 720
[7006] aaggagccca agtccgccga caagacccac accgagccct ccccggggac tctgcccagg 780
[7007] aaggcagggg tgttttcaga cctaagcaac caagagctga aggcagtgca cagcttcctc 840
[7008] tggtccaaga aggagctgag gctgcagccc tccagtacca ccaccatggc caagaacacc 900
[7009] gtgtttctca tcgagatgct gctgcccaag aagtaccatg tgctgaggtt tctggataaa 960
[7010] ggtgaaaggc atcctgtgcg ggaagcccgt gccgtcatct tctttggtga ccaggagcat 1020
[7011] cccaatgtca ccgagtttgc tgtggggccc ctgccaggcc cctgctacat gcgagcactg 1080
[7012] tcccccaggc ctgggtacca gtcctcctgg gcatcgaggc ccatctccac agcagagtat 1140
[7013] gccctcctct accacaccct gcaggaagcc accaagcccc tgcatcagtt cttcctcaat 1200

[7014] accacaggct tctcattcca agactgccat gacagatgcc tggccttcac cgatgtggcc 1260
[7015] ccccggggtg tggcttctgg ccagcgccgc agttggctta tcatacagcg ctatgtagaa 1320
[7016] ggctactttc tgcaccccac tgggctggag ctcctcgtgg atcatgggag cacagatgct 1380
[7017] gggcactggg ccgtggagca ggtgtggtac aacgggaagt tctatgggag cccagaggaa 1440
[7018] ctggctcgga agtatgcaga tggagaggtg gacgtggtgg tcctggagga cccgctgcct 1500
[7019] gggggcaagg ggcatgacag cacagaggag ccgcccctct tctcctccca caagccccgc 1560
[7020] ggggacttcc ccagccccat ccatgtgagc ggcccccgct tggtccagcc ccacggccct 1620
[7021] cgcttcaggc tggagggcaa cgctgtgctc tacggcggct ggagctttgc cttccggctg 1680
[7022] cgctcctcct ccgggctgca ggtcctgaac gtgcacttcg gcggagagcg cattgcctat 1740
[7023] gaggtcagcg tgcaagaggc agtggcgctg tatggaggac acacacctgc aggcatgcag 1800
[7024] accaagtacc tcgatgtcgg ctggggcctg ggcagcgtca ctcatgagtt agcccccggc 1860
[7025] atcgactgcc cggagaccgc caccttcctg gacactttcc actactatga tgccgatgac 1920
[7026] ccggtccatt atccccgagc cctctgcctc tttgaaatgc ccacaggggt gcccccttcgg 1980
[7027] cggcacttta attccaactt taaaggtggc ttcaacttct atgcggggct gaagggccag 2040
[7028] gtgctggtgc tgcggacaac ttcaactgtc tacaattatg attacatttg ggactttatc 2100
[7029] ttctacccca acggggtgat ggaggccaag atgcatgcca ctggctacgt ccacgccacc 2160
[7030] ttctacaccc ccgaggggct gcgccacggc actcgcctgc acacccacct gattggcaac 2220
[7031] atacacactc acttggtgca ctaccgcgta gacctggatg tggcaggcac caagaacagc 2280
[7032] ttccagacac tgcagatgaa gctagaaaac atcaccaacc cctggagccc aagacaccgc 2340
[7033] gtggtccagc caactctgga gcagacgcag tactcctggg agcgccaggc ggccttcagc 2400
[7034] ttcaaaagga agctgcccac gtacctgctc tttaccagcc cccaggagaa cccctggggc 2460
[7035] cacaagcgca gctaccgcct gcagatccac tccatggccg accaggtgct gcccccaggc 2520
[7036] tggcaggagg agcaggccat cacctgggca aggtaccccc tggcagtgac caagtaccgg 2580
[7037] gagtcggagc tgtgcagcag cagcatctac caccagaacg acccctggca cccgcccgtg 2640
[7038] gtctttgagc agtttcttca caacaacgag aacattgaaa atgaggacct ggtggcctgg 2700
[7039] gtgacggtgg gcttcctgca catcccccac tcagaggaca ttcccaacac agccacacct 2760
[7040] gggaactccg tgggcttcct gctccggcca ttcaacttct tcccagagga ccctccctg 2820
[7041] gcatccagag acactgtgat cgtgtggcct cgggacaacg gccccaacta cgtccagcgc 2880
[7042] tggatccctg aggacaggga ctgctcgatg cctccccctt ttagctacaa tgggacctat 2940
[7043] agacctgtgt ga 2952
[7044] <210> 79
[7045] <211> 2952
[7046] <212> DNA
[7047] <213> 人工序列
[7048] <220>
[7049] <223> Fc-hDAO-Cysmut
[7050] <400> 79
[7051] atgccggccc tgggctgggc cgtggctgcc atcctgatgc tgcagacggc catggcggag 60
[7052] tgccccccct gccccgcccc ccccgtggcc ggcccctccg tgttcctgtt ccccccccaag 120
[7053] cccaaggaca ccctgatgat ctccaggacc cccgaggtga cctgcgtggt ggtggacgtg 180
[7054] tcccacgagg accccgaggt gaagttcaac tggtacgtgg acggcgtgga ggtgcacaac 240
[7055] gccaagacca agcccaggga ggagcagtac aactccacct acagggtggt gtccgtgctg 300

[7056] accgtgctgc accaggactg gctgaacggc aaggagtaca agtgcaaggt gtccaacaag 360
[7057] ggcctgccct cctccatcga gaagaccatc tccaaggcca agggccagcc cagggagccc 420
[7058] caggtgtaca ccctgccccc ctccagggag gagatgacca agaaccaggt gtccctgacc 480
[7059] tgcctggtga agggcttcta cccctccgac atcgccgtgg agtgggagtc caacggccag 540
[7060] cccgagaaca actacaagac cacccccccc gtgctggact ccgacggctc cttcttcctg 600
[7061] tactccaagc tgaccgtgga caagtccagg tggcagcagg gcaacgtgtt ctcctgctcc 660
[7062] gtgatgcacg aggccctgca caaccactac acccagaagt ccctgtccct gtcccccggc 720
[7063] aaggagccca agtccgccga caagacccac accgagccct ccccggggac tctgcccagg 780
[7064] aaggcagggg tgttttcaga cctaagcaac caagagctga aggcagtgca cagcttcctc 840
[7065] tggtccaaga aggagctgag gctgcagccc tccagtacca ccaccatggc caagaacacc 900
[7066] gtgtttctca tcgagatgct gctgcccaag aagtaccatg tgctgaggtt tctggataaa 960
[7067] ggtgaaaggc atcctgtgcg ggaagcccgt gccgtcatct tctttggtga ccaggagcat 1020
[7068] cccaatgtca ccgagtttgc tgtggggccc ctgccaggcc ccgcctacat gcgagcactg 1080
[7069] tcccccaggc ctgggtacca gtcctcctgg gcatcgaggc ccatctccac agcagagtat 1140
[7070] gccctcctct accacaccct gcaggaagcc accaagcccc tgcatcagtt cttcctcaat 1200
[7071] accacaggct tctcattcca agactgccat gacagatgcc tggccttcac cgatgtggcc 1260
[7072] ccccggggtg tggcttctgg ccagcgccgc agttggctta tcatacagcg ctatgtagaa 1320
[7073] ggctactttc tgcaccccac tgggctggag ctcctcgtgg atcatgggag cacagatgct 1380
[7074] gggcactggg ccgtggagca ggtgtggtac aacgggaagt tctatgggag cccagaggaa 1440
[7075] ctggctcgga agtatgcaga tggagaggtg gacgtggtgg tcctggagga cccgctgcct 1500
[7076] gggggcaagg ggcatgacag cacagaggag ccgcccctct tctcctccca caagccccgc 1560
[7077] ggggacttcc ccagccccat ccatgtgagc ggcccccgct tggtccagcc ccacggccct 1620
[7078] cgcttcaggc tggagggcaa cgctgtgctc tacggcggct ggagctttgc cttccggctg 1680
[7079] cgctcctcct ccgggctgca ggtcctgaac gtgcacttcg gcggagagcg cattgcctat 1740
[7080] gaggtcagcg tgcaagaggc agtggcgctg tatggaggac acacacctgc aggcatgcag 1800
[7081] accaagtacc tcgatgtcgg ctggggcctg ggcagcgtca ctcatgagtt agcccccggc 1860
[7082] atcgactgcc cggagaccgc caccttcctg gacactttcc actactatga tgccgatgac 1920
[7083] ccggtccatt atccccgagc cctctgcctc tttgaaatgc ccacaggggt gcccccttcgg 1980
[7084] cggcacttta attccaactt taaaggtggc ttcaacttct atgcggggct gaagggccag 2040
[7085] gtgctggtgc tgcggacaac ttcaactgtc tacaattatg attacatttg ggactttatc 2100
[7086] ttctacccca acggggtgat ggaggccaag atgcatgcca ctggctacgt ccacgccacc 2160
[7087] ttctacaccc ccgaggggct gcgccacggc actcgcctgc acacccacct gattggcaac 2220
[7088] atacacactc acttggtgca ctaccgcgta gacctggatg tggcaggcac caagaacagc 2280
[7089] ttccagacac tgcagatgaa gctagaaaac atcaccaacc cctggagccc aagacaccgc 2340
[7090] gtggtccagc caactctgga gcagacgcag tactcctggg agcgccaggc ggccttccgc 2400
[7091] ttcaaaagga agctgcccaa gtacctgctc tttaccagcc cccaggagaa cccctggggc 2460
[7092] cacaagcgca gctaccgcct gcagatccac tccatggccg accaggtgct gcccccaggc 2520
[7093] tggcaggagg agcaggccat cacctgggca aggtaccccc tggcagtgac caagtaccgg 2580
[7094] gagtcggagc tgtgcagcag cagcatctac caccagaacg acccctggca cccgcccgtg 2640
[7095] gtctttgagc agtttcttca caacaacgag aacattgaaa atgaggacct ggtggcctgg 2700
[7096] gtgacggtgg gcttcctgca catcccccac tcagaggaca ttcccaacac agccacacct 2760
[7097] gggaactccg tgggcttcct gctccggcca ttcaacttct tcccagagga cccctccctg 2820

[7098] gcatccagag acactgtgat cgtgtggcct cgggacaacg gccccaacta cgtccagcgc 2880
[7099] tggatccctg aggacaggga ctgctcgatg cctccccctt ttagctacaa tgggacctat 2940
[7100] agacctgtgt ga 2952
[7101] <210> 80
[7102] <211> 2952
[7103] <212> DNA
[7104] <213> 人工序列
[7105] <220>
[7106] <223> Fc-hDAO-Hepmut1-Cysmut
[7107] <400> 80
[7108] atgccggccc tgggctgggc cgtggctgcc atcctgatgc tgcagacggc catggcggag 60
[7109] tgcccccccc gccccgcccc ccccgtggcc ggcccctccg tgttcctgtt ccccccccaag 120
[7110] cccaaggaca ccctgatgat ctccaggacc cccgaggtga cctgcgtggt ggtggacgtg 180
[7111] tcccacgagg accccgaggt gaagttcaac tggtacgtgg acggcgtgga ggtgcacaac 240
[7112] gccaagacca agcccaggga ggagcagtac aactccacct acagggtggt gtccgtgctg 300
[7113] accgtgctgc accaggactg gctgaacggc aaggagtaca agtgcaaggt gtccaacaag 360
[7114] ggcctgccct cctccatcga gaagaccatc tccaaggcca agggccagcc cagggagccc 420
[7115] caggtgtaca ccctgccccc ctccagggag gagatgacca agaaccaggt gtccctgacc 480
[7116] tgcctggtga agggcttcta cccctccgac atcgccgtgg agtgggagtc caacggccag 540
[7117] cccgagaaca actacaagac cacccccccc gtgctggact ccgacggctc cttcttcctg 600
[7118] tactccaagc tgaccgtgga caagtccagg tggcagcagg gcaacgtgtt ctcctgctcc 660
[7119] gtgatgcacg aggccctgca caaccactac acccagaagt ccctgtccct gtcccccggc 720
[7120] aaggagccca agtccgccga caagacccac accgagccct ccccggggac tctgcccagg 780
[7121] aaggcagggg tgttttcaga cctaagcaac caagagctga aggcagtgca cagcttcctc 840
[7122] tggtccaaga aggagctgag gctgcagccc tccagtacca ccaccatggc caagaacacc 900
[7123] gtgtttctca tcgagatgct gctgcccaag aagtaccatg tgctgaggtt tctggataaa 960
[7124] ggtgaaaggc atcctgtgcg ggaagcccgt gccgtcatct tctttggtga ccaggagcat 1020
[7125] cccaatgtca ccgagtttgc tgtggggccc ctgccaggcc ccgcctacat gcgagcactg 1080
[7126] tcccccaggc ctgggtacca gtcctcctgg gcatcgaggc ccatctccac agcagagtat 1140
[7127] gccctcctct accacaccct gcaggaagcc accaagcccc tgcatcagtt cttcctcaat 1200
[7128] accacaggct tctcattcca agactgccat gacagatgcc tggccttcac cgatgtggcc 1260
[7129] ccccggggtg tggcttctgg ccagcgccgc agttggctta tcatacagcg ctatgtagaa 1320
[7130] ggctactttc tgcaccccac tgggctggag ctcctcgtgg atcatgggag cacagatgct 1380
[7131] gggcactggg ccgtggagca ggtgtggtac aacgggaagt tctatgggag cccagaggaa 1440
[7132] ctggctcgga agtatgcaga tggagaggtg gacgtggtgg tcctggagga cccgctgcct 1500
[7133] gggggcaagg ggcatgacag cacagaggag ccgcccctct tctcctccca caagccccgc 1560
[7134] ggggacttcc ccagccccat ccatgtgagc ggcccccgct tggtccagcc ccacggccct 1620
[7135] cgcttcaggc tggagggcaa cgctgtgctc tacggcggct ggagctttgc cttccggctg 1680
[7136] cgctcctcct ccgggctgca ggtcctgaac gtgcacttcg gcggagagcg cattgcctat 1740
[7137] gaggtcagcg tgcaagaggc agtggcgctg tatggaggac acacacctgc aggcatgcag 1800
[7138] accaagtacc tcgatgtcgg ctggggcctg ggcagcgtca ctcatgagtt agcccccggc 1860
[7139] atcgactgcc cggagaccgc caccttcctg gacactttcc actactatga tgccgatgac 1920

[7140] ccggtccatt atccccgagc cctctgcctc tttgaaatgc ccacaggggt gccccttcgg 1980
[7141] cggcacttta attccaactt taaaggtggc ttcaacttct atgcggggct gaagggccag 2040
[7142] gtgctggtgc tgcggacaac ttcaactgtc tacaattatg attacatttg ggactttatc 2100
[7143] ttctacccca acggggtgat ggaggccaag atgcatgcca ctggctacgt ccacgccacc 2160
[7144] ttctacaccc ccgaggggct gcgccacggc actcgcctgc acacccacct gattggcaac 2220
[7145] atacacactc acttggtgca ctaccgcgta gacctggatg tggcaggcac caagaacagc 2280
[7146] ttccagacac tgcagatgaa gctagaaaac atcaccaacc cctggagccc aagacaccgc 2340
[7147] gtggtccagc caactctgga gcagacgcag tactcctggg agcgccaggc ggccttcagc 2400
[7148] ttcaaaagga agctgcccaa gtacctgctc tttaccagcc cccaggagaa cccctggggc 2460
[7149] cacaagcgca gctaccgcct gcagatccac tccatggccg accaggtgct gcccccaggc 2520
[7150] tggcaggagg agcaggccat cacctgggca aggtaccccc tggcagtgac caagtaccgg 2580
[7151] gagtcggagc tgtgcagcag cagcatctac caccagaacg acccctggca cccgcccgtg 2640
[7152] gtctttgagc agtttcttca caacaacgag aacattgaaa atgaggacct ggtggcctgg 2700
[7153] gtgacggtgg gcttcctgca catcccccac tcagaggaca ttcccaacac agccacacct 2760
[7154] gggaactccg tgggcttcct gctccggcca ttcaacttct tcccagagga ccctccctg 2820
[7155] gcatccagag acactgtgat cgtgtggcct cgggacaacg gccccaacta cgtccagcgc 2880
[7156] tggatccctg aggacaggga ctgctcgatg cctccccctt ttagctacaa tgggacctat 2940
[7157] agacctgtgt ga 2952
[7158] <210> 81
[7159] <211> 2952
[7160] <212> DNA
[7161] <213> 人工序列
[7162] <220>
[7163] <223> Fc-hDAO-Hepmut2-Cysmut
[7164] <400> 81
[7165] atgccggccc tgggctgggc cgtggctgcc atcctgatgc tgcagacggc catggcggag 60
[7166] tgccccccct gccccgcccc ccccgtggcc ggcccctccg tgttcctgtt ccccccccaag 120
[7167] cccaaggaca ccctgatgat ctccaggacc cccgaggtga cctgcgtggt ggtggacgtg 180
[7168] tcccacgagg accccgaggt gaagttcaac tggtacgtgg acggcgtgga ggtgcacaac 240
[7169] gccaagacca agcccaggga ggagcagtac aactccacct acagggtggt gtccgtgctg 300
[7170] accgtgctgc accaggactg gctgaacggc aaggagtaca agtgcaaggt gtccaacaag 360
[7171] ggcctgccct cctccatcga gaagaccatc tccaaggcca agggccagcc cagggagccc 420
[7172] caggtgtaca ccctgccccc ctccagggag gagatgacca agaaccaggt gtccctgacc 480
[7173] tgcctggtga agggcttcta cccctccgac atcgccgtgg agtgggagtc caacggccag 540
[7174] cccgagaaca actacaagac cacccccccc gtgctggact ccgacggctc cttcttcctg 600
[7175] tactccaagc tgaccgtgga caagtccagg tggcagcagg gcaacgtgtt ctcctgctcc 660
[7176] gtgatgcacg aggccctgca caaccactac acccagaagt ccctgtccct gtcccccggc 720
[7177] aaggagccca agtccgccga caagacccac accgagccct ccccggggac tctgcccagg 780
[7178] aaggcagggg tgttttcaga cctaagcaac caagagctga aggcagtgca cagcttcctc 840
[7179] tggtccaaga aggagctgag gctgcagccc tccagtacca ccaccatggc caagaacacc 900
[7180] gtgtttctca tcgagatgct gctgcccaag aagtaccatg tgctgaggtt tctggataaa 960
[7181] ggtgaaaggc atcctgtgcg ggaagcccgt gccgtcatct tctttggtga ccaggagcat 1020

[7182] cccaatgtca ccgagtttgc tgtggggccc ctgccaggcc ccgcctacat gcgagcactg 1080
[7183] tcccccaggc ctgggtacca gtcctcctgg gcatcgaggc ccatctccac agcagagtat 1140
[7184] gccctcctct accacaccct gcaggaagcc accaagcccc tgcatcagtt cttcctcaat 1200
[7185] accacaggct tctcattcca agactgccat gacagatgcc tggccttcac cgatgtggcc 1260
[7186] ccccggggtg tggcttctgg ccagcgccgc agttggctta tcatacagcg ctatgtagaa 1320
[7187] ggctactttc tgcaccccac tgggctggag ctcctcgtgg atcatgggag cacagatgct 1380
[7188] gggcactggg ccgtggagca ggtgtggtac aacgggaagt tctatgggag cccagaggaa 1440
[7189] ctggctcgga agtatgcaga tggagaggtg gacgtggtgg tcctggagga cccgctgcct 1500
[7190] gggggcaagg ggcatgacag cacagaggag ccgcccctct tctcctccca caagccccgc 1560
[7191] ggggacttcc ccagccccat ccatgtgagc ggcccccgct tggtccagcc ccacggccct 1620
[7192] cgcttcaggc tggagggcaa cgctgtgctc tacggcggct ggagctttgc cttccggctg 1680
[7193] cgctcctcct ccgggctgca ggtcctgaac gtgcacttcg gcggagagcg cattgcctat 1740
[7194] gaggtcagcg tgcaagaggc agtggcgctg tatggaggac acacacctgc aggcatgcag 1800
[7195] accaagtacc tcgatgtcgg ctggggcctg ggcagcgtca ctcatgagtt agcccccggc 1860
[7196] atcgactgcc cggagaccgc caccttcctg gacactttcc actactatga tgccgatgac 1920
[7197] ccggtccatt atccccgagc cctctgcctc tttgaaatgc ccacaggggt gcccccttcgg 1980
[7198] cggcacttta attccaactt taaaggtggc ttcaacttct atgcggggct gaagggccag 2040
[7199] gtgctggtgc tgcggacaac ttcaactgtc tacaattatg attacatttg ggactttatc 2100
[7200] ttctacccca acggggtgat ggaggccaag atgcatgcca ctggctacgt ccacgccacc 2160
[7201] ttctacaccc ccgaggggct gcgccacggc actcgcctgc acacccacct gattggcaac 2220
[7202] atacacactc acttggtgca ctaccgcgta gacctggatg tggcaggcac caagaacagc 2280
[7203] ttccagacac tgcagatgaa gctagaaaac atcaccaacc cctggagccc aagacaccgc 2340
[7204] gtggtccagc caactctgga gcagacgcag tactcctggg agcgccaggc ggccttccgc 2400
[7205] ttcaaaagga agctgcccac gtacctgctc tttaccagcc cccaggagaa cccctggggc 2460
[7206] cacaagcgca gctaccgcct gcagatccac tccatggccg accaggtgct gcccccaggc 2520
[7207] tggcaggagg agcaggccat cacctgggca aggtaccccc tggcagtgac caagtaccgg 2580
[7208] gagtcggagc tgtgcagcag cagcatctac caccagaacg acccctggca cccgcccgtg 2640
[7209] gtctttgagc agtttcttca caacaacgag aacattgaaa atgaggacct ggtggcctgg 2700
[7210] gtgacggtgg gcttcctgca catcccccac tcagaggaca ttcccaacac agccacacct 2760
[7211] gggaactccg tgggcttcct gctccggcca ttcaacttct tcccagagga ccctccctg 2820
[7212] gcatccagag acactgtgat cgtgtggcct cgggacaacg gccccaacta cgtccagcgc 2880
[7213] tggatccctg aggacaggga ctgctcgatg cctccccctt ttagctacaa tgggacctat 2940
[7214] agacctgtgt ga 2952
[7215] <210> 82
[7216] <211> 2952
[7217] <212> DNA
[7218] <213> 人工序列
[7219] <220>
[7220] <223> Fc-hDAO-Hepmut3-Cysmut
[7221] <400> 82
[7222] atgccggccc tgggctgggc cgtggctgcc atcctgatgc tgcagacggc catggcggag 60
[7223] tgccccccct gccccgcccc ccccgtggcc ggcccctccg tgttcctgtt ccccccccaag 120

[7224] cccaaggaca ccctgatgat ctccaggacc cccgaggtga cctgcgtggt ggtggacgtg 180
[7225] tcccacgagg accccgaggt gaagttcaac tggtacgtgg acggcgtgga ggtgcacaac 240
[7226] gccaagacca agcccaggga ggagcagtac aactccacct acagggtggt gtccgtgctg 300
[7227] accgtgctgc accaggactg gctgaacggc aaggagtaca agtgcaaggt gtccaacaag 360
[7228] ggcctgccct cctccatcga gaagaccatc tccaaggcca agggccagcc cagggagccc 420
[7229] caggtgtaca ccctgccccc ctccagggag gagatgacca agaaccaggt gtccctgacc 480
[7230] tgcctggtga agggcttcta cccctccgac atcgccgtgg agtgggagtc caacggccag 540
[7231] cccgagaaca actacaagac cacccccccc gtgctggact ccgacggctc cttcttcctg 600
[7232] tactccaagc tgaccgtgga caagtccagg tggcagcagg gcaacgtgtt ctcctgctcc 660
[7233] gtgatgcacg aggccctgca caaccactac acccagaagt ccctgtccct gtcccccggc 720
[7234] aaggagccca agtccgccga caagacccac accgagccct ccccggggac tctgcccagg 780
[7235] aaggcagggg tgttttcaga cctaagcaac caagagctga aggcagtgca cagcttcctc 840
[7236] tggtccaaga aggagctgag gctgcagccc tccagtacca ccaccatggc caagaacacc 900
[7237] gtgtttctca tcgagatgct gctgcccaag aagtaccatg tgctgaggtt tctggataaa 960
[7238] ggtgaaaggc atcctgtgcg ggaagcccgt gccgtcatct tctttggtga ccaggagcat 1020
[7239] cccaatgtca ccgagtttgc tgtggggccc ctgccaggcc ccgcctacat gcgagcactg 1080
[7240] tcccccaggc ctgggtacca gtcctcctgg gcatcgaggc ccatctccac agcagagtat 1140
[7241] gccctcctct accacaccct gcaggaagcc accaagcccc tgcatcagtt cttcctcaat 1200
[7242] accacaggct tctcattcca agactgccat gacagatgcc tggccttcac cgatgtggcc 1260
[7243] ccccggggtg tggcttctgg ccagcgccgc agttggctta tcatacagcg ctatgtagaa 1320
[7244] ggctactttc tgcaccccac tgggctggag ctcctcgtgg atcatgggag cacagatgct 1380
[7245] gggcactggg ccgtggagca ggtgtggtac aacgggaagt tctatgggag cccagaggaa 1440
[7246] ctggctcgga agtatgcaga tggagaggtg gacgtggtgg tcctggagga cccgctgcct 1500
[7247] gggggcaagg ggcatgacag cacagaggag ccgcccctct tctcctccca caagccccgc 1560
[7248] ggggacttcc ccagccccat ccatgtgagc ggcccccgct tggtccagcc ccacggccct 1620
[7249] cgcttcaggc tggagggcaa cgctgtgctc tacggcggct ggagctttgc cttccggctg 1680
[7250] cgctcctcct ccgggctgca ggtcctgaac gtgcacttcg gcggagagcg cattgcctat 1740
[7251] gaggtcagcg tgcaagaggc agtggcgctg tatggaggac acacacctgc aggcatgcag 1800
[7252] accaagtacc tcgatgtcgg ctggggcctg ggcagcgtca ctcatgagtt agcccccggc 1860
[7253] atcgactgcc cggagaccgc caccttcctg gacactttcc actactatga tgccgatgac 1920
[7254] ccggtccatt atccccgagc cctctgcctc tttgaaatgc ccacaggggt gcccccttcgg 1980
[7255] cggcacttta attccaactt taaaggtggc ttcaacttct atgcggggct gaagggccag 2040
[7256] gtgctggtgc tgcggacaac ttcaactgtc tacaattatg attacatttg ggactttatc 2100
[7257] ttctacccca acggggtgat ggaggccaag atgcatgcca ctggctacgt ccacgccacc 2160
[7258] ttctacaccc ccgaggggct gcgccacggc actcgcctgc acacccacct gattggcaac 2220
[7259] atacacactc acttggtgca ctaccgcgta gacctggatg tggcaggcac caagaacagc 2280
[7260] ttccagacac tgcagatgaa gctagaaaac atcaccaacc cctggagccc aagacaccgc 2340
[7261] gtggtccagc caactctgga gcagacgcag tactcctggg agcgccaggc ggccttccgc 2400
[7262] ttcaaaacga agctgcccaa gtacctgctc tttaccagcc cccaggagaa cccctggggc 2460
[7263] cacaagcgca gctaccgcct gcagatccac tccatggccg accaggtgct gcccccaggc 2520
[7264] tggcaggagg agcaggccat cacctgggca aggtaccccc tggcagtgac caagtaccgg 2580
[7265] gagtcggagc tgtgcagcag cagcatctac caccagaacg acccctggca cccgcccgtg 2640

[7266] gtctttgagc agtttcttca caacaacgag aacattgaaa atgaggacct ggtggcctgg 2700
[7267] gtgacggtgg gcttcctgca catcccccac tcagaggaca ttcccaacac agccacacct 2760
[7268] gggaactccg tgggcttcct gctccggcca ttcaacttct tcccagagga ccccctccctg 2820
[7269] gcatccagag acactgtgat cgtgtggcct cgggacaacg gccccaacta cgtccagcgc 2880
[7270] tggatccctg aggacaggga ctgctcgatg cctccccctt ttagctacaa tgggacctat 2940
[7271] agacctgtgt ga 2952
[7272] <210> 83
[7273] <211> 2952
[7274] <212> DNA
[7275] <213> 人工序列
[7276] <220>
[7277] <223> Fc-hDAO-Hepmut4-Cysmut
[7278] <400> 83
[7279] atgccggccc tgggctgggc cgtggctgcc atcctgatgc tgcagacggc catggcggag 60
[7280] tgccccccct gccccgcccc ccccgtggcc ggcccctccg tgttcctgtt ccccccccaag 120
[7281] cccaaggaca ccctgatgat ctccaggacc cccgaggtga cctgcgtggt ggtggacgtg 180
[7282] tcccacgagg accccgaggt gaagttcaac tggtacgtgg acggcgtgga ggtgcacaac 240
[7283] gccaagacca agcccaggga ggagcagtac aactccacct acagggtggt gtccgtgctg 300
[7284] accgtgctgc accaggactg gctgaacggc aaggagtaca agtgcaaggt gtccaacaag 360
[7285] ggcctgccct cctccatcga gaagaccatc tccaaggcca agggccagcc cagggagccc 420
[7286] caggtgtaca ccctgccccc ctccagggag gagatgacca agaaccaggt gtccctgacc 480
[7287] tgcctggtga agggcttcta cccctccgac atcgccgtgg agtgggagtc caacggccag 540
[7288] cccgagaaca actacaagac cacccccccc gtgctggact ccgacggctc cttcttcctg 600
[7289] tactccaagc tgaccgtgga caagtccagg tggcagcagg gcaacgtgtt ctcctgctcc 660
[7290] gtgatgcacg aggccctgca caaccactac acccagaagt ccctgtccct gtcccccggc 720
[7291] aaggagccca agtccgccga caagacccac accgagccct ccccggggac tctgcccagg 780
[7292] aaggcagggg tgttttcaga cctaagcaac caagagctga aggcagtgca cagcttcctc 840
[7293] tggtccaaga aggagctgag gctgcagccc tccagtacca ccaccatggc caagaacacc 900
[7294] gtgtttctca tcgagatgct gctgcccaag aagtaccatg tgctgaggtt tctggataaa 960
[7295] ggtgaaaggc atcctgtgcg ggaagcccgt gccgtcatct tctttggtga ccaggagcat 1020
[7296] cccaatgtca ccgagtttgc tgtggggccc ctgccaggcc ccgcctacat gcgagcactg 1080
[7297] tccccccaggc ctgggtacca gtcctcctgg gcatcgaggc ccatctccac agcagagtat 1140
[7298] gccctcctct accacaccct gcaggaagcc accaagcccc tgcatcagtt cttcctcaat 1200
[7299] accacaggct tctcattcca agactgccat gacagatgcc tggccttcac cgatgtggcc 1260
[7300] ccccggggtg tggcttctgg ccagcgccgc agttggctta tcatacagcg ctatgtagaa 1320
[7301] ggctactttc tgcaccccac tgggctggag ctcctcgtgg atcatgggag cacagatgct 1380
[7302] gggcactggg ccgtggagca ggtgtggtac aacgggaagt tctatgggag cccagaggaa 1440
[7303] ctggctcgga agtatgcaga tggagaggtg gacgtggtgg tcctggagga cccgctgcct 1500
[7304] gggggcaagg ggcatgacag cacagaggag ccgcccctct tctcctccca caagccccgc 1560
[7305] ggggacttcc ccagccccat ccatgtgagc ggcccccgct tggtccagcc ccacggccct 1620
[7306] cgcttcaggc tggagggcaa cgctgtgctc tacggcggct ggagctttgc cttccggctg 1680
[7307] cgctcctcct ccgggctgca ggtcctgaac gtgcacttcg gcggagagcg cattgcctat 1740

[7308] gaggtcagcg tgcaagaggc agtggcgctg tatggaggac acacacctgc aggcatgcag 1800
[7309] accaagtacc tcgatgtcgg ctggggcctg ggcagcgtca ctcatgagtt agcccccggc 1860
[7310] atcgactgcc cggagaccgc caccttcctg gacactttcc actactatga tgccgatgac 1920
[7311] ccggtccatt atccccgagc cctctgcctc tttgaaatgc ccacaggggt gcccccttcgg 1980
[7312] cggcacttta attccaactt taaaggtggc ttcaacttct atgcggggct gaagggccag 2040
[7313] gtgctggtgc tgcggacaac ttcaactgtc tacaattatg attacatttg ggactttatc 2100
[7314] ttctacccca acggggtgat ggaggccaag atgcatgcca ctggctacgt ccacgccacc 2160
[7315] ttctacaccc ccgaggggct gcgccacggc actcgcctgc acacccacct gattggcaac 2220
[7316] atacacactc acttggtgca ctaccgcgta gacctggatg tggcaggcac caagaacagc 2280
[7317] ttccagacac tgcagatgaa gctagaaaac atcaccaacc cctggagccc aagacaccgc 2340
[7318] gtggtccagc caactctgga gcagacgcag tactcctggg agcgccaggc ggccttcagc 2400
[7319] ttcaaaacga agctgcccaa gtacctgctc tttaccagcc cccaggagaa cccctggggc 2460
[7320] cacaagcgca gctaccgcct gcagatccac tccatggccg accaggtgct gcccccaggc 2520
[7321] tggcaggagg agcaggccat cacctgggca aggtaccccc tggcagtgac caagtaccgg 2580
[7322] gagtcggagc tgtgcagcag cagcatctac caccagaacg acccctggca cccgcccgtg 2640
[7323] gtctttgagc agtttcttca caacaacgag aacattgaaa atgaggacct ggtggcctgg 2700
[7324] gtgacggtgg gcttcctgca catcccccac tcagaggaca ttcccaacac agccacacct 2760
[7325] gggaactccg tgggcttcct gctccggcca ttcaacttct tcccagagga ccctccctg 2820
[7326] gcatccagag acactgtgat cgtgtggcct cgggacaacg gccccaacta cgtccagcgc 2880
[7327] tggatccctg aggacaggga ctgctcgatg cctccccctt ttagctacaa tgggacctat 2940
[7328] agacctgtgt ga 2952
[7329] <210> 84
[7330] <211> 2952
[7331] <212> DNA
[7332] <213> 人工序列
[7333] <220>
[7334] <223> Fc-hDAO-Hepmut5-Cysmut
[7335] <400> 84
[7336] atgccggccc tgggctgggc cgtggctgcc atcctgatgc tgcagacggc catggcggag 60
[7337] tgccccccct gccccgcccc ccccgtggcc ggcccctccg tgttcctgtt ccccccccaag 120
[7338] cccaaggaca ccctgatgat ctccaggacc cccgaggtga cctgcgtggt ggtggacgtg 180
[7339] tcccacgagg accccgaggt gaagttcaac tggtacgtgg acggcgtgga ggtgcacaac 240
[7340] gccaagacca agcccaggga ggagcagtac aactccacct acagggtggt gtccgtgctg 300
[7341] accgtgctgc accaggactg gctgaacggc aaggagtaca agtgcaaggt gtccaacaag 360
[7342] ggcctgccct cctccatcga gaagaccatc tccaaggcca agggccagcc cagggagccc 420
[7343] caggtgtaca ccctgccccc ctccagggag gagatgacca agaaccaggt gtccctgacc 480
[7344] tgcctggtga agggcttcta cccctccgac atcgccgtgg agtgggagtc caacggccag 540
[7345] cccgagaaca actacaagac cacccccccc gtgctggact ccgacggctc cttcttcctg 600
[7346] tactccaagc tgaccgtgga caagtccagg tggcagcagg gcaacgtgtt ctcctgctcc 660
[7347] gtgatgcacg aggccctgca caaccactac acccagaagt ccctgtccct gtcccccggc 720
[7348] aaggagccca agtccgccga caagacccac accgagccct ccccggggac tctgcccagg 780
[7349] aaggcagggg tgttttcaga cctaagcaac caagagctga aggcagtgca cagcttcctc 840

[7350] tggtccaaga aggagctgag gctgcagccc tccagtacca ccaccatggc caagaacacc 900

[7351] gtgtttctca tcgagatgct gctgcccaag aagtaccatg tgctgaggtt tctggataaa 960

[7352] ggtgaaaggc atcctgtgcg ggaagcccgt gccgtcatct tctttggtga ccaggagcat 1020

[7353] cccaatgtca ccgagtttgc tgtggggccc ctgccaggcc ccgcctacat gcgagcactg 1080

[7354] tcccccaggc ctgggtacca gtcctcctgg gcatcgaggc ccatctccac agcagagtat 1140

[7355] gccctcctct accacaccct gcaggaagcc accaagcccc tgcatcagtt cttcctcaat 1200

[7356] accacaggct tctcattcca agactgccat gacagatgcc tggccttcac cgatgtggcc 1260

[7357] ccccggggtg tggcttctgg ccagcgccgc agttggctta tcatacagcg ctatgtagaa 1320

[7358] ggctactttc tgcaccccac tgggctggag ctcctcgtgg atcatgggag cacagatgct 1380

[7359] gggcactggg ccgtggagca ggtgtggtac aacgggaagt tctatgggag cccagaggaa 1440

[7360] ctggctcgga agtatgcaga tggagaggtg gacgtggtgg tcctggagga cccgctgcct 1500

[7361] gggggcaagg ggcatgacag cacagaggag ccgcccctct tctcctccca caagccccgc 1560

[7362] ggggacttcc ccagccccat ccatgtgagc ggcccccgct tggtccagcc ccacggccct 1620

[7363] cgcttcaggc tggagggcaa cgctgtgctc tacggcggct ggagctttgc cttccggctg 1680

[7364] cgctcctcct ccgggctgca ggtcctgaac gtgcacttcg gcggagagcg cattgcctat 1740

[7365] gaggtcagcg tgcaagaggc agtggcgctg tatggaggac acacacctgc aggcatgcag 1800

[7366] accaagtacc tcgatgtcgg ctggggcctg ggcagcgtca ctcatgagtt agcccccggc 1860

[7367] atcgactgcc cggagaccgc caccttcctg gacactttcc actactatga tgccgatgac 1920

[7368] ccggtccatt atccccgagc cctctgcctc tttgaaatgc ccacaggggt gcccccttcgg 1980

[7369] cggcacttta attccaactt taaaggtggc ttcaacttct atgcggggct gaagggccag 2040

[7370] gtgctggtgc tgcggacaac ttcaactgtc tacaattatg attacatttg ggactttatc 2100

[7371] ttctacccca acggggtgat ggaggccaag atgcatgcca ctggctacgt ccacgccacc 2160

[7372] ttctacaccc ccgaggggct gcgccacggc actcgcctgc acacccacct gattggcaac 2220

[7373] atacacactc acttggtgca ctaccgcgta gacctggatg tggcaggcac caagaacagc 2280

[7374] ttccagacac tgcagatgaa gctagaaaac atcaccaacc cctggagccc aagacaccgc 2340

[7375] gtggtccagc caactctgga gcagacgcag tactcctggg agcgccaggc ggccttccgc 2400

[7376] ttcaaaacga agctgcccac gtacctgctc tttaccagcc cccaggagaa cccctggggc 2460

[7377] cacaagcgca gctaccgcct gcagatccac tccatggccg accaggtgct gcccccaggc 2520

[7378] tggcaggagg agcaggccat cacctgggca aggtaccccc tggcagtgac caagtaccgg 2580

[7379] gagtcggagc tgtgcagcag cagcatctac caccagaacg acccctggca cccgcccgtg 2640

[7380] gtctttgagc agtttcttca caacaacgag aacattgaaa atgaggacct ggtggcctgg 2700

[7381] gtgacggtgg gcttcctgca catcccccac tcagaggaca ttcccaacac agccacacct 2760

[7382] gggaactccg tgggcttcct gctccggcca ttcaacttct tcccagagga ccctccctg 2820

[7383] gcatccagag acactgtgat cgtgtggcct cgggacaacg gccccaacta cgtccagcgc 2880

[7384] tggatccctg aggacaggga ctgctcgatg cctccccctt ttagctacaa tgggacctat 2940

[7385] agacctgtgt ga 2952

[7386] <210> 85

[7387] <211> 2952

[7388] <212> DNA

[7389] <213> 人工序列

[7390] <220>

[7391] <223> Fc-hDAO-Hepmut6-Cysmut

[7392] <400> 85

[7393] atgccggccc tgggctgggc cgtggctgcc atcctgatgc tgcagacggc catggcggag 60

[7394] tgccccccct gccccgcccc ccccgtggcc ggcccctccg tgttcctgtt ccccccccaag 120

[7395] cccaaggaca ccctgatgat ctccaggacc cccgaggtga cctgcgtggt ggtggacgtg 180

[7396] tcccacgagg accccgaggt gaagttcaac tggtacgtgg acggcgtgga ggtgcacaac 240

[7397] gccaagacca agcccaggga ggagcagtac aactccacct acagggtggt gtccgtgctg 300

[7398] accgtgctgc accaggactg gctgaacggc aaggagtaca agtgcaaggt gtccaacaag 360

[7399] ggcctgccct cctccatcga gaagaccatc tccaaggcca agggccagcc cagggagccc 420

[7400] caggtgtaca ccctgccccc ctccagggag gagatgacca agaaccaggt gtccctgacc 480

[7401] tgcctggtga agggcttcta cccctccgac atcgccgtgg agtgggagtc caacggccag 540

[7402] cccgagaaca actacaagac cacccccccc gtgctggact ccgacggctc cttcttcctg 600

[7403] tactccaagc tgaccgtgga caagtccagg tggcagcagg gcaacgtgtt ctcctgctcc 660

[7404] gtgatgcacg aggccctgca caaccactac acccagaagt ccctgtccct gtcccccggc 720

[7405] aaggagccca agtccgccga caagacccac accgagccct ccccggggac tctgcccagg 780

[7406] aaggcagggg tgttttcaga cctaagcaac caagagctga aggcagtgca cagcttcctc 840

[7407] tggtccaaga aggagctgag gctgcagccc tccagtacca ccaccatggc caagaacacc 900

[7408] gtgtttctca tcgagatgct gctgcccaag aagtaccatg tgctgaggtt tctggataaa 960

[7409] ggtgaaaggc atcctgtgcg ggaagcccgt gccgtcatct tctttggtga ccaggagcat 1020

[7410] cccaatgtca ccgagtttgc tgtggggccc ctgccaggcc ccgcctacat gcgagcactg 1080

[7411] tcccccaggc ctgggtacca gtcctcctgg gcatcgaggc ccatctccac agcagagtat 1140

[7412] gccctcctct accacaccct gcaggaagcc accaagcccc tgcatcagtt cttcctcaat 1200

[7413] accacaggct tctcattcca agactgccat gacagatgcc tggccttcac cgatgtggcc 1260

[7414] ccccggggtg tggcttctgg ccagcgccgc agttggctta tcatacagcg ctatgtagaa 1320

[7415] ggctactttc tgcaccccac tgggctggag ctcctcgtgg atcatgggag cacagatgct 1380

[7416] gggcactggg ccgtggagca ggtgtggtac aacgggaagt tctatgggag cccagaggaa 1440

[7417] ctggctcgga agtatgcaga tggagaggtg gacgtggtgg tcctggagga cccgctgcct 1500

[7418] gggggcaagg ggcatgacag cacagaggag ccgcccctct tctcctccca caagccccgc 1560

[7419] ggggacttcc ccagccccat ccatgtgagc ggcccccgct tggtccagcc ccacggccct 1620

[7420] cgcttcaggc tggagggcaa cgctgtgctc tacggcggct ggagctttgc cttccggctg 1680

[7421] cgctcctcct ccgggctgca ggtcctgaac gtgcacttcg gcggagagcg cattgcctat 1740

[7422] gaggtcagcg tgcaagaggc agtggcgctg tatggaggac acacacctgc aggcatgcag 1800

[7423] accaagtacc tcgatgtcgg ctggggcctg ggcagcgtca ctcatgagtt agcccccggc 1860

[7424] atcgactgcc cggagaccgc caccttcctg gacactttcc actactatga tgccgatgac 1920

[7425] ccggtccatt atccccgagc cctctgcctc tttgaaatgc ccacaggggt gcccccttcgg 1980

[7426] cggcacttta attccaactt taaaggtggc ttcaacttct atgcggggct gaagggccag 2040

[7427] gtgctggtgc tgcggacaac ttcaactgtc tacaattatg attacatttg ggactttatc 2100

[7428] ttctacccca acggggtgat ggaggccaag atgcatgcca ctggctacgt ccacgccacc 2160

[7429] ttctacaccc ccgaggggct gcgccacggc actcgcctgc acacccacct gattggcaac 2220

[7430] atacacactc acttggtgca ctaccgcgta gacctggatg tggcaggcac caagaacagc 2280

[7431] ttccagacac tgcagatgaa gctagaaaac atcaccaacc cctggagccc aagacaccgc 2340

[7432] gtggtccagc caactctgga gcagacgcag tactcctggg agcgccaggc ggccttccgc 2400

[7433] ttcggacaga cgctgcccaa gtacctgctc tttaccagcc cccaggagaa cccctggggc 2460

[7434] cacaagcgca gctaccgcct gcagatccac tccatggccg accaggtgct gcccccaggc 2520
[7435] tggcaggagg agcaggccat cacctgggca aggtaccccc tggcagtgac caagtaccgg 2580
[7436] gagtcggagc tgtgcagcag cagcatctac caccagaacg acccctggca cccgcccgtg 2640
[7437] gtctttgagc agtttcttca caacaacgag aacattgaaa atgaggacct ggtggcctgg 2700
[7438] gtgacggtgg gcttcctgca catcccccac tcagaggaca ttcccaacac agccacacct 2760
[7439] gggaactccg tgggcttcct gctccggcca ttcaacttct tcccagagga ccctccctg 2820
[7440] gcatccagag acactgtgat cgtgtggcct cgggacaacg gccccaacta cgtccagcgc 2880
[7441] tggatccctg aggacaggga ctgctcgatg cctccccctt ttagctacaa tgggacctat 2940
[7442] agacctgtgt ga 2952
[7443] <210> 86
[7444] <211> 2952
[7445] <212> DNA
[7446] <213> 人工序列
[7447] <220>
[7448] <223> Fc-hDAO-Hepmut7-Cysmut
[7449] <400> 86
[7450] atgccggccc tgggctgggc cgtggctgcc atcctgatgc tgcagacggc catggcggag 60
[7451] tgccccccct gccccgcccc ccccgtggcc ggcccctccg tgttcctgtt ccccccccaag 120
[7452] cccaaggaca ccctgatgat ctccaggacc cccgaggtga cctgcgtggt ggtggacgtg 180
[7453] tcccacgagg accccgaggt gaagttcaac tggtacgtgg acggcgtgga ggtgcacaac 240
[7454] gccaagacca agcccaggga ggagcagtac aactccacct acagggtggt gtccgtgctg 300
[7455] accgtgctgc accaggactg gctgaacggc aaggagtaca agtgcaaggt gtccaacaag 360
[7456] ggcctgccct cctccatcga gaagaccatc tccaaggcca agggccagcc cagggagccc 420
[7457] caggtgtaca ccctgccccc ctccagggag gagatgacca agaaccaggt gtccctgacc 480
[7458] tgcctggtga agggcttcta cccctccgac atcgccgtgg agtgggagtc caacggccag 540
[7459] cccgagaaca actacaagac cacccccccc gtgctggact ccgacggctc cttcttcctg 600
[7460] tactccaagc tgaccgtgga caagtccagg tggcagcagg gcaacgtgtt ctcctgctcc 660
[7461] gtgatgcacg aggccctgca caaccactac acccagaagt ccctgtccct gtcccccggc 720
[7462] aaggagccca agtccgccga caagacccac accgagccct ccccggggac tctgcccagg 780
[7463] aaggcagggg tgttttcaga cctaagcaac caagagctga aggcagtgca cagcttcctc 840
[7464] tggtccaaga aggagctgag gctgcagccc tccagtacca ccaccatggc caagaacacc 900
[7465] gtgtttctca tcgagatgct gctgcccaag aagtaccatg tgctgaggtt tctggataaa 960
[7466] ggtgaaaggc atcctgtgcg ggaagcccgt gccgtcatct tctttggtga ccaggagcat 1020
[7467] cccaatgtca ccgagtttgc tgtggggccc ctgccaggcc ccgcctacat gcgagcactg 1080
[7468] tcccccaggc ctgggtacca gtcctcctgg gcatcgaggc ccatctccac agcagagtat 1140
[7469] gccctcctct accacaccct gcaggaagcc accaagcccc tgcatcagtt cttcctcaat 1200
[7470] accacaggct tctcattcca agactgccat gacagatgcc tggccttcac cgatgtggcc 1260
[7471] ccccggggtg tggcttctgg ccagcgccgc agttggctta tcatacagcg ctatgtagaa 1320
[7472] ggctactttc tgcaccccac tgggctggag ctcctcgtgg atcatgggag cacagatgct 1380
[7473] gggcactggg ccgtggagca ggtgtggtac aacgggaagt tctatgggag cccagaggaa 1440
[7474] ctggctcgga agtatgcaga tggagaggtg gacgtggtgg tcctggagga cccgctgcct 1500
[7475] gggggcaagg ggcatgacag cacagaggag ccgcccctct tctcctccca caagccccgc 1560

[7476] ggggacttcc ccagccccat ccatgtgagc ggcccccgct tggtccagcc ccacggccct 1620
[7477] cgcttcaggc tggagggcaa cgctgtgctc tacggcggct ggagctttgc cttccggctg 1680
[7478] cgctcctcct ccgggctgca ggtcctgaac gtgcacttcg gcggagagcg cattgcctat 1740
[7479] gaggtcagcg tgcaagaggc agtggcgctg tatggaggac acacacctgc aggcatgcag 1800
[7480] accaagtacc tcgatgtcgg ctggggcctg ggcagcgtca ctcatgagtt agcccccggc 1860
[7481] atcgactgcc cggagaccgc caccttcctg gacactttcc actactatga tgccgatgac 1920
[7482] ccggtccatt atccccgagc cctctgcctc tttgaaatgc ccacaggggt gcccccttcgg 1980
[7483] cggcacttta attccaactt taaaggtggc ttcaacttct atgcggggct gaagggccag 2040
[7484] gtgctggtgc tgcggacaac ttcaactgtc tacaattatg attacatttg ggactttatc 2100
[7485] ttctacccca acggggtgat ggaggccaag atgcatgcca ctggctacgt ccacgccacc 2160
[7486] ttctacaccc ccgaggggct gcgccacggc actcgcctgc acacccacct gattggcaac 2220
[7487] atacacactc acttggtgca ctaccgcgta gacctggatg tggcaggcac caagaacagc 2280
[7488] ttccagacac tgcagatgaa gctagaaaac atcaccaacc cctggagccc aagacaccgc 2340
[7489] gtggtccagc caactctgga gcagacgcag tactcctggg agcgccaggc ggccttcagc 2400
[7490] ttcaaaagga agctgcccac gtacctgctc tttaccagcc cccaggagaa cccctggggc 2460
[7491] cacaagcgca gctaccgcct gcagatccac tccatggccg accaggtgct gcccccaggc 2520
[7492] tggcaggagg agcaggccat cacctgggca aggtaccccc tggcagtgac caagtaccgg 2580
[7493] gagtcggagc tgtgcagcag cagcatctac caccagaacg acccctggca cccgcccgtg 2640
[7494] gtctttgagc agtttcttca caacaacgag aacattgaaa atgaggacct ggtggcctgg 2700
[7495] gtgacggtgg gcttcctgca catcccccac tcagaggaca ttcccaacac agccacacct 2760
[7496] gggaactccg tgggcttcct gctccggcca ttcaacttct tcccagagga cccctccctg 2820
[7497] gcatccagag acactgtgat cgtgtggcct cgggacaacg gccccaacta cgtccagcgc 2880
[7498] tggatccctg aggacaggga ctgctcgatg cctccccctt ttagctacaa tgggacctat 2940
[7499] agacctgtgt ga 2952
[7500] <210> 87
[7501] <211> 2949
[7502] <212> DNA
[7503] <213> 人工序列
[7504] <220>
[7505] <223> hDAO-Fc
[7506] <400> 87
[7507] atgccggccc tgggctgggc cgtggctgcc atcctgatgc tgcagacggc catggcggag 60
[7508] ccctccccgg ggactctgcc caggaaggca ggggtgtttt cagacctaag caaccaagag 120
[7509] ctgaaggcag tgcacagctt cctctggtcc aagaaggagc tgaggctgca gccctccagt 180
[7510] accaccacca tggccaagaa caccgtgttt ctcatcgaga tgctgctgcc caagaagtac 240
[7511] catgtgctga ggtttctgga taaaggtgaa aggcatcctg tgcgggaagc ccgtgccgtc 300
[7512] atcttctttg gtgaccagga gcatcccaat gtcaccgagt ttgctgtggg gcccctgcca 360
[7513] gggccctgct acatgcgagc actgtccccc aggcctgggt accagtcctc ctgggcatcg 420
[7514] aggcccatct ccacagcaga gtatgccctc ctctaccaca ccctgcagga agccaccaag 480
[7515] cccctgcatc agttcttcct caataccaca ggcttctcat tccaagactg ccatgacaga 540
[7516] tgcctggcct tcaccgatgt ggcccccccgg ggtgtggctt ctggccagcg ccgcagttgg 600
[7517] cttatcatac agcgctatgt agaaggctac tttctgcacc ccactgggct ggagctcctc 660

[7518] gtggatcatg ggagcacaga tgctgggcac tgggccgtgg agcaggtgtg gtacaacggg 720
[7519] aagttctatg ggagcccaga ggaactggct cggaagtatg cagatggaga ggtggacgtg 780
[7520] gtggtcctgg aggacccgct gcctgggggc aaggggcatg acagcacaga ggagccgccc 840
[7521] ctcttctcct cccacaagcc ccgcggggac ttccccagcc ccatccatgt gagcggcccc 900
[7522] cgcttggtcc agccccacgg ccctcgcttc aggctggagg gcaacgctgt gctctacggc 960
[7523] ggctggagct ttgccttccg gctgcgctcc tcctccgggc tgcaggtcct gaacgtgcac 1020
[7524] ttcggcggag agcgcattgc ctatgaggtc agcgtgcaag aggcagtggc gctgtatgga 1080
[7525] ggacacacac ctgcaggcat gcagaccaag tacctcgatg tcggctgggg cctgggcagc 1140
[7526] gtcactcatg agttagcccc cggcatcgac tgcccggaga ccgccacctt cctggacact 1200
[7527] ttccactact atgatgccga tgacccggtc cattatcccc gagccctctg cctctttgaa 1260
[7528] atgcccacag gggtgcccct tcggcggcac tttaattcca actttaaagg tggcttcaac 1320
[7529] ttctatgcgg ggctgaaggg ccaggtgctg gtgctgcgga caacttcaac tgtctacaat 1380
[7530] tatgattaca tttgggactt tatcttctac cccaacgggg tgatggaggc caagatgcat 1440
[7531] gccactggct acgtccacgc caccttctac acccccgagg ggctgcgcca cggcactcgc 1500
[7532] ctgcacaccc acctgattgg caacatacac actcacttgg tgcactaccg cgtagacctg 1560
[7533] gatgtggcag gcaccaagaa cagcttccag acactgcaga tgaagctaga aaacatcacc 1620
[7534] aacccctgga gcccaagaca ccgcgtggtc cagccaactc tggagcagac gcagtactcc 1680
[7535] tgggagcgcc aggcggcctt ccgcttcaaa aggaagctgc ccaagtacct gctctttacc 1740
[7536] agcccccagg agaacccctg gggccacaag cgcagctacc gcctgcagat ccactccatg 1800
[7537] gccgaccagg tgctgccccc aggctggcag gaggagcagg ccatcacctg ggcaaggtac 1860
[7538] cccctggcag tgaccaagta ccgggagtcg gagctgtgca gcagcagcat ctaccaccag 1920
[7539] aacgacccct ggcacccgcc cgtggtcttt gagcagtttc ttcacaacaa cgagaacatt 1980
[7540] gaaaatgagg acctggtggc ctgggtgacg gtgggcttcc tgcacatccc ccactcagag 2040
[7541] gacattccca acacagccac acctgggaac tccgtgggct tcctgctccg gccattcaac 2100
[7542] ttcttcccag aggacccctc cctggcatcc agagacactg tgatcgtgtg gcctcgggac 2160
[7543] aacggcccca actacgtcca gcgctggatc cctgaggaca gggactgctc gatgcctccc 2220
[7544] ccttttagct acaatgggac ctatagacct gtggagccca agtccgccga caagacccac 2280
[7545] acctgccccc cctgccccgc ccccccgtg gccggccct ccgtgttcct gttcccccc 2340
[7546] aagcccaagg acaccctgat gatctccagg acccccgagg tgacctgcgt ggtggtggac 2400
[7547] gtgtcccacg aggaccccga ggtgaagttc aactggtacg tggacggcgt ggaggtgcac 2460
[7548] aacgccaaga ccaagcccag ggaggagcag tacaactcca cctacagggt ggtgtccgtg 2520
[7549] ctgaccgtgc tgcaccagga ctggctgaac ggcaaggagt acaagtgcaa ggtgtccaac 2580
[7550] aagggcctgc cctcctccat cgagaagacc atctccaagg ccaagggcca gcccagggag 2640
[7551] ccccaggtgt acaccctgcc cccctccagg gaggagatga ccaagaacca ggtgtccctg 2700
[7552] acctgcctgg tgaagggctt ctacccctcc gacatcgccg tggagtggga gtccaacggc 2760
[7553] cagcccgaga acaactacaa gaccaccccc cccgtgctgg actccgacgg ctccttcttc 2820
[7554] ctgtactcca agctgaccgt ggacaagtcc aggtggcagc agggcaacgt gttctcctgc 2880
[7555] tccgtgatgc acgaggccct gcacaaccac tacacccaga agtccctgtc cctgtccccc 2940
[7556] ggcaagtga 2949
[7557] <210> 88
[7558] <211> 2949
[7559] <212> DNA

[7560] <213> 人工序列

[7561] <220>

[7562] <223> hDAO-Fc-Hepmut1

[7563] <400> 88

[7564] atgccggccc tgggctgggc cgtggctgcc atcctgatgc tgcagacggc catggcggag 60

[7565] ccctccccgg ggactctgcc caggaaggca ggggtgtttt cagacctaag caaccaagag 120

[7566] ctgaaggcag tgcacagctt cctctggtcc aagaaggagc tgaggctgca gccctccagt 180

[7567] accaccacca tggccaagaa caccgtgttt ctcatcgaga tgctgctgcc caagaagtac 240

[7568] catgtgctga ggtttctgga taaaggtgaa aggcatcctg tgcgggaagc ccgtgccgtc 300

[7569] atcttctttg gtgaccagga gcatcccaat gtcaccgagt ttgctgtggg gcccctgcca 360

[7570] gggccctgct acatgcgagc actgtccccc aggcctgggt accagtcctc ctgggcatcg 420

[7571] aggcccatct ccacagcaga gtatgccctc ctctaccaca ccctgcagga agccaccaag 480

[7572] cccctgcatc agttcttcct caataccaca ggcttctcat tccaagactg ccatgacaga 540

[7573] tgcctggcct tcaccgatgt ggcccccccgg ggtgtggctt ctggccagcg ccgcagttgg 600

[7574] cttatcatac agcgctatgt agaaggctac tttctgcacc ccactgggct ggagctcctc 660

[7575] gtggatcatg ggagcacaga tgctgggcac tgggccgtgg agcaggtgtg gtacaacggg 720

[7576] aagttctatg ggagcccaga ggaactggct cggaagtatg cagatggaga ggtggacgtg 780

[7577] gtggtcctgg aggacccgct gcctgggggc aaggggcatg acagcacaga ggagccgccc 840

[7578] ctcttctcct cccacaagcc ccgcggggac ttccccagcc ccatccatgt gagcggcccc 900

[7579] cgcttggtcc agccccacgg ccctcgcttc aggctggagg gcaacgctgt gctctacggc 960

[7580] ggctggagct ttgccttccg gctgcgctcc tcctccgggc tgcaggtcct gaacgtgcac 1020

[7581] ttcggcggag agcgcattgc ctatgaggtc agcgtgcaag aggcagtggc gctgtatgga 1080

[7582] ggacacacac ctgcaggcat gcagaccaag tacctcgatg tcggctgggg cctgggcagc 1140

[7583] gtcactcatg agttagcccc cggcatcgac tgcccggaga ccgccacctt cctggacact 1200

[7584] ttccactact atgatgccga tgacccggtc cattatcccc gagccctctg cctctttgaa 1260

[7585] atgcccacag gggtgcccct tcggcggcac tttaattcca actttaaagg tggcttcaac 1320

[7586] ttctatgcgg ggctgaaggg ccaggtgctg gtgctgcgga caacttcaac tgtctacaat 1380

[7587] tatgattaca tttgggactt tatcttctac cccaacgggg tgatggaggc caagatgcat 1440

[7588] gccactggct acgtccacgc caccttctac acccccgagg ggctgcgcca cggcactcgc 1500

[7589] ctgcacaccc acctgattgg caacatacac actcacttgg tgcactaccg cgtagacctg 1560

[7590] gatgtggcag gcaccaagaa cagcttccag acactgcaga tgaagctaga aaacatcacc 1620

[7591] aacccctgga gcccaagaca ccgcgtggtc cagccaactc tggagcagac gcagtactcc 1680

[7592] tgggagcgcc aggcggcctt cagcttcaaa aggaagctgc ccaagtacct gctctttacc 1740

[7593] agcccccagg agaacccctg gggccacaag cgcagctacc gcctgcagat ccactccatg 1800

[7594] gccgaccagg tgctgccccc aggctggcag gaggagcagg ccatcacctg ggcaaggtac 1860

[7595] cccctggcag tgaccaagta ccgggagtcg gagctgtgca gcagcagcat ctaccaccag 1920

[7596] aacgacccct ggcacccgcc cgtggtcttt gagcagtttc ttcacaacaa cgagaacatt 1980

[7597] gaaaatgagg acctggtggc ctgggtgacg gtgggcttcc tgcacatccc ccactcagag 2040

[7598] gacattccca acacagccac acctgggaac tccgtgggct tcctgctccg gccattcaac 2100

[7599] ttcttcccag aggacccctc cctggcatcc agagacactg tgatcgtgtg gcctcgggac 2160

[7600] aacggcccca actacgtcca gcgctggatc cctgaggaca gggactgctc gatgcctccc 2220

[7601] ccttttagct acaatgggac ctatagacct gtggagccca agtccgccga caagacccac 2280

[7602] acctgccccc cctgccccgc ccccccgtg gccggcccct ccgtgttcct gttccccccc 2340
[7603] aagcccaagg acaccctgat gatctccagg acccccgagg tgacctgcgt ggtggtggac 2400
[7604] gtgtcccacg aggaccccga ggtgaagttc aactggtacg tggacggcgt ggaggtgcac 2460
[7605] aacgccaaga ccaagcccag ggaggagcag tacaactcca cctacagggt ggtgtccgtg 2520
[7606] ctgaccgtgc tgcaccagga ctggctgaac ggcaaggagt acaagtgcaa ggtgtccaac 2580
[7607] aagggcctgc cctcctccat cgagaagacc atctccaagg ccaagggcca gcccagggag 2640
[7608] ccccaggtgt acaccctgcc cccctccagg gaggagatga ccaagaacca ggtgtccctg 2700
[7609] acctgcctgg tgaagggctt ctacccctcc gacatcgccg tggagtggga gtccaacggc 2760
[7610] cagcccgaga acaactacaa gaccaccccc cccgtgctgg actccgacgg ctccttcttc 2820
[7611] ctgtactcca agctgaccgt ggacaagtcc aggtggcagc agggcaacgt gttctcctgc 2880
[7612] tccgtgatgc acgaggccct gcacaaccac tacacccaga agtccctgtc cctgtccccc 2940
[7613] ggcaagtga 2949
[7614] <210> 89
[7615] <211> 2949
[7616] <212> DNA
[7617] <213> 人工序列
[7618] <220>
[7619] <223> hDAO-Fc-Hepmut2
[7620] <400> 89
[7621] atgccggccc tgggctgggc cgtggctgcc atcctgatgc tgcagacggc catggcggag 60
[7622] ccctccccgg ggactctgcc caggaaggca ggggtgtttt cagacctaag caaccaagag 120
[7623] ctgaaggcag tgcacagctt cctctggtcc aagaaggagc tgaggctgca gccctccagt 180
[7624] accaccacca tggccaagaa caccgtgttt ctcatcgaga tgctgctgcc caagaagtac 240
[7625] catgtgctga ggtttctgga taaaggtgaa aggcatcctg tgcgggaagc ccgtgccgtc 300
[7626] atcttctttg gtgaccagga gcatcccaat gtcaccgagt ttgctgtggg gcccctgcca 360
[7627] gggccctgct acatgcgagc actgtccccc aggcctgggt accagtcctc ctgggcatcg 420
[7628] aggcccatct ccacagcaga gtatgccctc ctctaccaca ccctgcagga agccaccaag 480
[7629] cccctgcatc agttcttcct caataccaca ggcttctcat tccaagactg ccatgacaga 540
[7630] tgcctggcct tcaccgatgt ggcccccccgg ggtgtggctt ctggccagcg ccgcagttgg 600
[7631] cttatcatac agcgctatgt agaaggctac tttctgcacc ccactgggct ggagctcctc 660
[7632] gtggatcatg ggagcacaga tgctgggcac tgggccgtgg agcaggtgtg gtacaacggg 720
[7633] aagttctatg ggagcccaga ggaactggct cggaagtatg cagatggaga ggtggacgtg 780
[7634] gtggtcctgg aggacccgct gcctgggggc aaggggcatg acagcacaga ggagccgccc 840
[7635] ctcttctcct cccacaagcc ccgcggggac ttccccagcc ccatccatgt gagcggcccc 900
[7636] cgcttggtcc agccccacgg ccctcgcttc aggctggagg gcaacgctgt gctctacggc 960
[7637] ggctggagct ttgccttccg gctgcgctcc tcctccgggc tgcaggtcct gaacgtgcac 1020
[7638] ttcggcggag agcgcattgc ctatgaggtc agcgtgcaag aggcagtggc gctgtatgga 1080
[7639] ggacacacac ctgcaggcat gcagaccaag tacctcgatg tcggctgggg cctgggcagc 1140
[7640] gtcactcatg agttagcccc cggcatcgac tgcccggaga ccgccacctt cctggacact 1200
[7641] ttccactact atgatgccga tgacccggtc cattatcccc gagccctctg cctctttgaa 1260
[7642] atgcccacag gggtgcccct tcggcggcac tttaattcca actttaaagg tggcttcaac 1320
[7643] ttctatgcgg ggctgaaggg ccaggtgctg gtgctgcgga caacttcaac tgtctacaat 1380

[7644] tatgattaca tttgggactt tatcttctac cccaacgggg tgatggaggc caagatgcat 1440
[7645] gccactggct acgtccacgc caccttctac acccccgagg ggctgcgcca cggcactcgc 1500
[7646] ctgcacaccc acctgattgg caacatacac actcacttgg tgcactaccg cgtagacctg 1560
[7647] gatgtggcag gcaccaagaa cagcttccag acactgcaga tgaagctaga aaacatcacc 1620
[7648] aacccctgga gcccaagaca ccgcgtggtc cagccaactc tggagcagac gcagtactcc 1680
[7649] tgggagcgcc aggcggcctt ccgcttcaaa aggaagctgc ccacgtacct gctctttacc 1740
[7650] agcccccagg agaacccctg gggccacaag cgcagctacc gcctgcagat ccactccatg 1800
[7651] gccgaccagg tgctgccccc aggctggcag gaggagcagg ccatcacctg ggcaaggtac 1860
[7652] cccctggcag tgaccaagta ccgggagtcg gagctgtgca gcagcagcat ctaccaccag 1920
[7653] aacgacccct ggcacccgcc cgtggtcttt gagcagtttc ttcacaacaa cgagaacatt 1980
[7654] gaaaatgagg acctggtggc ctgggtgacg gtgggcttcc tgcacatccc ccactcagag 2040
[7655] gacattccca acacagccac acctgggaac tccgtgggct tcctgctccg gccattcaac 2100
[7656] ttcttcccag aggacccctc cctggcatcc agagacactg tgatcgtgtg gcctcgggac 2160
[7657] aacggcccca actacgtcca gcgctggatc cctgaggaca gggactgctc gatgcctccc 2220
[7658] ccttttagct acaatgggac ctatagacct gtggagccca agtccgccga caagacccac 2280
[7659] acctgccccc cctgccccgc ccccccctgg gccggcccct ccgtgttcct gttcccccca 2340
[7660] aagcccaagg acaccctgat gatctccagg acccccgagg tgacctgcgt ggtggtggac 2400
[7661] gtgtcccacg aggaccccga ggtgaagttc aactggtacg tggacggcgt ggaggtgcac 2460
[7662] aacgccaaga ccaagcccag ggaggagcag tacaactcca cctacagggt ggtgtccgtg 2520
[7663] ctgaccgtgc tgcaccagga ctggctgaac ggcaaggagt acaagtgcaa ggtgtccaac 2580
[7664] aagggcctgc cctcctccat cgagaagacc atctccaagg ccaagggcca gcccagggag 2640
[7665] ccccaggtgt acaccctgcc cccctccagg gaggagatga ccaagaacca ggtgtccctg 2700
[7666] acctgcctgg tgaagggctt ctacccctcc gacatcgccg tggagtggga gtccaacggc 2760
[7667] cagcccgaga acaactacaa gaccaccccc cccgtgctgg actccgacgg ctccttcttc 2820
[7668] ctgtactcca agctgaccgt ggacaagtcc aggtggcagc agggcaacgt gttctcctgc 2880
[7669] tccgtgatgc acgaggccct gcacaaccac tacacccaga agtccctgtc cctgtccccc 2940
[7670] ggcaagtga 2949
[7671] <210> 90
[7672] <211> 2949
[7673] <212> DNA
[7674] <213> 人工序列
[7675] <220>
[7676] <223> hDAO-Fc-Hepmut3
[7677] <400> 90
[7678] atgccggccc tgggctgggc cgtggctgcc atcctgatgc tgcagacggc catggcggag 60
[7679] ccctccccgg ggactctgcc caggaaggca ggggtgtttt cagacctaag caaccaagag 120
[7680] ctgaaggcag tgcacagctt cctctggtcc aagaaggagc tgaggctgca gccctccagt 180
[7681] accaccacca tggccaagaa caccgtgttt ctcatcgaga tgctgctgcc caagaagtac 240
[7682] catgtgctga ggtttctgga taaaggtgaa aggcatcctg tgcgggaagc ccgtgccgtc 300
[7683] atcttctttg gtgaccagga gcatcccaat gtcaccgagt ttgctgtggg gcccctgcca 360
[7684] gggccctgct acatgcgagc actgtccccc aggcctgggt accagtcctc ctgggcatcg 420
[7685] aggcccatct ccacagcaga gtatgccctc ctctaccaca ccctgcagga agccaccaag 480

[7686] cccctgcatc agttcttcct caataccaca ggcttctcat tccaagactg ccatgacaga 540
[7687] tgcctggcct tcaccgatgt ggcccccccgg ggtgtggctt ctggccagcg ccgcagttgg 600
[7688] cttatcatac agcgctatgt agaaggctac tttctgcacc ccactgggct ggagctcctc 660
[7689] gtggatcatg ggagcacaga tgctgggcac tgggccgtgg agcaggtgtg gtacaacggg 720
[7690] aagttctatg ggagcccaga ggaactggct cggaagtatg cagatggaga ggtggacgtg 780
[7691] gtggtcctgg aggacccgct gcctgggggc aaggggcatg acagcacaga ggagccgccc 840
[7692] ctcttctcct cccacaagcc ccgcggggac ttccccagcc ccatccatgt gagcggcccc 900
[7693] cgcttggtcc agccccacgg ccctcgcttc aggctggagg gcaacgctgt gctctacggc 960
[7694] ggctggagct ttgccttccg gctgcgctcc tcctccgggc tgcaggtcct gaacgtgcac 1020
[7695] ttcggcggag agcgcattgc ctatgaggtc agcgtgcaag aggcagtggc gctgtatgga 1080
[7696] ggacacacac ctgcaggcat gcagaccaag tacctcgatg tcggctgggg cctgggcagc 1140
[7697] gtcactcatg agttagcccc cggcatcgac tgcccggaga ccgccacctt cctggacact 1200
[7698] ttccactact atgatgccga tgacccggtc cattatcccc gagccctctg cctctttgaa 1260
[7699] atgcccacag gggtgcccct tcggcggcac tttaattcca actttaaagg tggcttcaac 1320
[7700] ttctatgcgg ggctgaaggg ccaggtgctg gtgctgcgga caacttcaac tgtctacaat 1380
[7701] tatgattaca tttgggactt tatcttctac cccaacgggg tgatggaggc caagatgcat 1440
[7702] gccactggct acgtccacgc caccttctac acccccgagg ggctgcgcca cggcactcgc 1500
[7703] ctgcacaccc acctgattgg caacatacac actcacttgg tgcactaccg cgtagacctg 1560
[7704] gatgtggcag gcaccaagaa cagcttccag acactgcaga tgaagctaga aaacatcacc 1620
[7705] aacccctgga gcccaagaca ccgcgtggtc cagccaactc tggagcagac gcagtactcc 1680
[7706] tgggagcgcc aggcggcctt ccgcttcaaa acgaagctgc ccaagtacct gctctttacc 1740
[7707] agcccccagg agaacccctg gggccacaag cgcagctacc gcctgcagat ccactccatg 1800
[7708] gccgaccagg tgctgccccc aggctggcag gaggagcagg ccatcacctg ggcaaggtac 1860
[7709] cccctggcag tgaccaagta ccgggagtcg gagctgtgca gcagcagcat ctaccaccag 1920
[7710] aacgacccct ggcacccgcc cgtggtcttt gagcagtttc ttcacaacaa cgagaacatt 1980
[7711] gaaaatgagg acctggtggc ctgggtgacg gtgggcttcc tgcacatccc ccactcagag 2040
[7712] gacattccca acacagccac acctgggaac tccgtgggct tcctgctccg gccattcaac 2100
[7713] ttcttcccag aggacccctc cctggcatcc agagacactg tgatcgtgtg gcctcgggac 2160
[7714] aacggcccca actacgtcca gcgctggatc cctgaggaca gggactgctc gatgcctccc 2220
[7715] ccttttagct acaatgggac ctatagacct gtggagccca agtccgccga caagacccac 2280
[7716] acctgccccc cctgccccgc ccccccccgtg gccggcccct ccgtgttcct gttccccccc 2340
[7717] aagcccaagg acaccctgat gatctccagg acccccgagg tgacctgcgt ggtggtggac 2400
[7718] gtgtcccacg aggaccccga ggtgaagttc aactggtacg tggacggcgt ggaggtgcac 2460
[7719] aacgccaaga ccaagcccag ggaggagcag tacaactcca cctacagggt ggtgtccgtg 2520
[7720] ctgaccgtgc tgcaccagga ctggctgaac ggcaaggagt acaagtgcaa ggtgtccaac 2580
[7721] aagggcctgc cctcctccat cgagaagacc atctccaagg ccaagggcca gcccagggag 2640
[7722] ccccaggtgt acaccctgcc cccctccagg gaggagatga ccaagaacca ggtgtccctg 2700
[7723] acctgcctgg tgaagggctt ctacccctcc gacatcgccg tggagtggga gtccaacggc 2760
[7724] cagcccgaga acaactacaa gaccaccccc cccgtgctgg actccgacgg ctccttcttc 2820
[7725] ctgtactcca agctgaccgt ggacaagtcc aggtggcagc agggcaacgt gttctcctgc 2880
[7726] tccgtgatgc acgaggccct gcacaaccac tacacccaga agtccctgtc cctgtccccc 2940
[7727] ggcaagtga 2949

[7728] <210> 91

[7729] <211> 2949

[7730] <212> DNA

[7731] <213> 人工序列

[7732] <220>

[7733] <223> hDAO-Fc-Hepmut4

[7734] <400> 91

[7735] atgccggccc tgggctgggc cgtggctgcc atcctgatgc tgcagacggc catggcggag 60

[7736] ccctccccgg ggactctgcc caggaaggca ggggtgtttt cagacctaag caaccaagag 120

[7737] ctgaaggcag tgcacagctt cctctggtcc aagaaggagc tgaggctgca gccctccagt 180

[7738] accaccacca tggccaagaa caccgtgttt ctcatcgaga tgctgctgcc caagaagtac 240

[7739] catgtgctga ggtttctgga taaaggtgaa aggcatcctg tgcgggaagc ccgtgccgtc 300

[7740] atcttctttg gtgaccagga gcatcccaat gtcaccgagt ttgctgtggg gcccctgcca 360

[7741] gggccctgct acatgcgagc actgtccccc aggcctgggt accagtcctc ctgggcatcg 420

[7742] aggcccatct ccacagcaga gtatgccctc ctctaccaca ccctgcagga agccaccaag 480

[7743] cccctgcatc agttcttcct caataccaca ggcttctcat tccaagactg ccatgacaga 540

[7744] tgcctggcct tcaccgatgt ggcccccccgg ggtgtggctt ctggccagcg ccgcagttgg 600

[7745] cttatcatac agcgctatgt agaaggctac tttctgcacc ccactgggct ggagctcctc 660

[7746] gtggatcatg ggagcacaga tgctgggcac tgggccgtgg agcaggtgtg gtacaacggg 720

[7747] aagttctatg ggagcccaga ggaactggct cggaagtatg cagatggaga ggtggacgtg 780

[7748] gtggtcctgg aggacccgct gcctgggggc aaggggcatg acagcacaga ggagccgccc 840

[7749] ctcttctcct cccacaagcc ccgcggggac ttccccagcc ccatccatgt gagcggcccc 900

[7750] cgcttggtcc agccccacgg ccctcgcttc aggctggagg gcaacgctgt gctctacggc 960

[7751] ggctggagct ttgccttccg gctgcgctcc tcctccgggc tgcaggtcct gaacgtgcac 1020

[7752] ttcggcggag agcgcattgc ctatgaggtc agcgtgcaag aggcagtggc gctgtatgga 1080

[7753] ggacacacac ctgcaggcat gcagaccaag tacctcgatg tcggctgggg cctgggcagc 1140

[7754] gtcactcatg agttagcccc cggcatcgac tgcccggaga ccgccacctt cctggacact 1200

[7755] ttccactact atgatgccga tgacccggtc cattatcccc gagccctctg cctctttgaa 1260

[7756] atgcccacag gggtgcccct tcggcggcac tttaattcca actttaaagg tggcttcaac 1320

[7757] ttctatgcgg ggctgaaggg ccaggtgctg gtgctgcgga caacttcaac tgtctacaat 1380

[7758] tatgattaca tttgggactt tatcttctac cccaacgggg tgatggaggc caagatgcat 1440

[7759] gccactggct acgtccacgc caccttctac acccccgagg ggctgcgcca cggcactcgc 1500

[7760] ctgcacaccc acctgattgg caacatacac actcacttgg tgcactaccg cgtagacctg 1560

[7761] gatgtggcag gcaccaagaa cagcttccag acactgcaga tgaagctaga aaacatcacc 1620

[7762] aacccctgga gcccaagaca ccgcgtggtc cagccaactc tggagcagac gcagtactcc 1680

[7763] tgggagcgcc aggcggcctt cagcttcaaa acgaagctgc ccaagtacct gctctttacc 1740

[7764] agcccccagg agaacccctg gggccacaag cgcagctacc gcctgcagat ccactccatg 1800

[7765] gccgaccagg tgctgccccc aggctggcag gaggagcagg ccatcacctg ggcaaggtac 1860

[7766] cccctggcag tgaccaagta ccgggagtcg gagctgtgca gcagcagcat ctaccaccag 1920

[7767] aacgacccct ggcacccgcc cgtggtcttt gagcagtttc ttcacaacaa cgagaacatt 1980

[7768] gaaaatgagg acctggtggc ctgggtgacg gtgggcttcc tgcacatccc ccactcagag 2040

[7769] gacattccca acacagccac acctgggaac tccgtgggct tcctgctccg gccattcaac 2100

[7770] ttcttcccag aggacccctc cctggcatcc agagacactg tgatcgtgtg gcctcgggac 2160
[7771] aacggcccca actacgtcca gcgctggatc cctgaggaca gggactgctc gatgcctccc 2220
[7772] ccttttagct acaatgggac ctatagacct gtggagccca agtccgccga caagacccac 2280
[7773] acctgccccc cctgccccgc ccccccgtg gccggcccct ccgtgttcct gttccccccc 2340
[7774] aagcccaagg acaccctgat gatctccagg acccccgagg tgacctgcgt ggtggtggac 2400
[7775] gtgtcccacg aggaccccga ggtgaagttc aactggtacg tggacggcgt ggaggtgcac 2460
[7776] aacgccaaga ccaagcccag ggaggagcag tacaactcca cctacagggt ggtgtccgtg 2520
[7777] ctgaccgtgc tgcaccagga ctggctgaac ggcaaggagt acaagtgcaa ggtgtccaac 2580
[7778] aagggcctgc cctcctccat cgagaagacc atctccaagg ccaagggcca gccccagggag 2640
[7779] ccccaggtgt acaccctgcc cccctccagg gaggagatga ccaagaacca ggtgtccctg 2700
[7780] acctgcctgg tgaagggctt ctacccctcc gacatcgccg tggagtggga gtccaacggc 2760
[7781] cagcccgaga acaactacaa gaccaccccc cccgtgctgg actccgacgg ctccttcttc 2820
[7782] ctgtactcca agctgaccgt ggacaagtcc aggtggcagc agggcaacgt gttctcctgc 2880
[7783] tccgtgatgc acgaggccct gcacaaccac tacacccaga agtccctgtc cctgtccccc 2940
[7784] ggcaagtga 2949
[7785] <210> 92
[7786] <211> 2949
[7787] <212> DNA
[7788] <213> 人工序列
[7789] <220>
[7790] <223> hDAO-Fc-Hepmut5
[7791] <400> 92
[7792] atgccggccc tgggctgggc cgtggctgcc atcctgatgc tgcagacggc catggcggag 60
[7793] ccctccccgg ggactctgcc caggaaggca ggggtgtttt cagacctaag caaccaagag 120
[7794] ctgaaggcag tgcacagctt cctctggtcc aagaaggagc tgaggctgca gccctccagt 180
[7795] accaccacca tggccaagaa caccgtgttt ctcatcgaga tgctgctgcc caagaagtac 240
[7796] catgtgctga ggtttctgga taaaggtgaa aggcatcctg tgcgggaagc ccgtgccgtc 300
[7797] atcttctttg gtgaccagga gcatcccaat gtcaccgagt ttgctgtggg gcccctgcca 360
[7798] gggccctgct acatgcgagc actgtccccc aggcctgggt accagtcctc ctgggcatcg 420
[7799] aggcccatct ccacagcaga gtatgccctc ctctaccaca ccctgcagga agccaccaag 480
[7800] cccctgcatc agttcttcct caataccaca ggcttctcat tccaagactg ccatgacaga 540
[7801] tgcctggcct tcaccgatgt ggcccccccgg ggtgtggctt ctggccagcg ccgcagttgg 600
[7802] cttatcatac agcgctatgt agaaggctac tttctgcacc ccactgggct ggagctcctc 660
[7803] gtggatcatg ggagcacaga tgctgggcac tgggccgtgg agcaggtgtg gtacaacggg 720
[7804] aagttctatg ggagcccaga ggaactggct cggaagtatg cagatggaga ggtggacgtg 780
[7805] gtggtcctgg aggacccgct gcctgggggc aaggggcatg acagcacaga ggagccgccc 840
[7806] ctcttctcct cccacaagcc ccgcggggac ttccccagcc ccatccatgt gagcggcccc 900
[7807] cgcttggtcc agccccacgg ccctcgcttc aggctggagg gcaacgctgt gctctacggc 960
[7808] ggctggagct ttgccttccg gctgcgctcc tcctccgggc tgcaggtcct gaacgtgcac 1020
[7809] ttcggcggag agcgcattgc ctatgaggtc agcgtgcaag aggcagtggc gctgtatgga 1080
[7810] ggacacacac ctgcaggcat gcagaccaag tacctcgatg tcggctgggg cctgggcagc 1140
[7811] gtcactcatg agttagcccc cggcatcgac tgcccggaga ccgccacctt cctggacact 1200

[7812] ttccactact atgatgccga tgacccggtc cattatcccc gagccctctg cctctttgaa 1260
[7813] atgcccacag gggtgcccct tcggcggcac tttaattcca actttaaagg tggcttcaac 1320
[7814] ttctatgcgg ggctgaaggg ccaggtgctg gtgctgcgga caacttcaac tgtctacaat 1380
[7815] tatgattaca tttgggactt tatcttctac cccaacgggg tgatggaggc caagatgcat 1440
[7816] gccactggct acgtccacgc caccttctac acccccgagg ggctgcgcca cggcactcgc 1500
[7817] ctgcacaccc acctgattgg caacatacac actcacttgg tgcactaccg cgtagacctg 1560
[7818] gatgtggcag gcaccaagaa cagcttccag acactgcaga tgaagctaga aaacatcacc 1620
[7819] aacccctgga gcccaagaca ccgcgtggtc cagccaactc tggagcagac gcagtactcc 1680
[7820] tgggagcgcc aggcggcctt ccgcttcaaa acgaagctgc ccacgtacct gctctttacc 1740
[7821] agcccccagg agaacccctg gggccacaag cgcagctacc gcctgcagat ccactccatg 1800
[7822] gccgaccagg tgctgccccc aggctggcag gaggagcagg ccatcacctg ggcaaggtac 1860
[7823] cccctggcag tgaccaagta ccgggagtcg gagctgtgca gcagcagcat ctaccaccag 1920
[7824] aacgacccct ggcacccgcc cgtggtcttt gagcagtttc ttcacaacaa cgagaacatt 1980
[7825] gaaaatgagg acctggtggc ctgggtgacg gtgggcttcc tgcacatccc ccactcagag 2040
[7826] gacattccca acacagccac acctgggaac tccgtgggct tcctgctccg gccattcaac 2100
[7827] ttcttcccag aggacccctc cctggcatcc agagacactg tgatcgtgtg gcctcgggac 2160
[7828] aacggcccca actacgtcca gcgctggatc cctgaggaca gggactgctc gatgcctccc 2220
[7829] ccttttagct acaatgggac ctatagacct gtggagccca agtccgccga caagacccac 2280
[7830] acctgccccc cctgccccgc ccccccgtg gccggcccct ccgtgttcct gttccccccc 2340
[7831] aagcccaagg acaccctgat gatctccagg acccccgagg tgacctgcgt ggtggtggac 2400
[7832] gtgtcccacg aggaccccga ggtgaagttc aactggtacg tggacggcgt ggaggtgcac 2460
[7833] aacgccaaga ccaagcccag ggaggagcag tacaactcca cctacagggt ggtgtccgtg 2520
[7834] ctgaccgtgc tgcaccagga ctggctgaac ggcaaggagt acaagtgcaa ggtgtccaac 2580
[7835] aagggcctgc cctcctccat cgagaagacc atctccaagg ccaagggcca gcccagggag 2640
[7836] ccccaggtgt acaccctgcc cccctccagg gaggagatga ccaagaacca ggtgtccctg 2700
[7837] acctgcctgg tgaagggctt ctacccctcc gacatcgccg tggagtggga gtccaacggc 2760
[7838] cagcccgaga acaactacaa gaccaccccc cccgtgctgg actccgacgg ctccttcttc 2820
[7839] ctgtactcca agctgaccgt ggacaagtcc aggtggcagc agggcaacgt gttctcctgc 2880
[7840] tccgtgatgc acgaggccct gcacaaccac tacacccaga agtccctgtc cctgtccccc 2940
[7841] ggcaagtga 2949
[7842] <210> 93
[7843] <211> 2949
[7844] <212> DNA
[7845] <213> 人工序列
[7846] <220>
[7847] <223> hDAO-Fc-Hepmut6
[7848] <400> 93
[7849] atgccggccc tgggctgggc cgtggctgcc atcctgatgc tgcagacggc catggcggag 60
[7850] ccctccccgg ggactctgcc caggaaggca ggggtgtttt cagacctaag caaccaagag 120
[7851] ctgaaggcag tgcacagctt cctctggtcc aagaaggagc tgaggctgca gccctccagt 180
[7852] accaccacca tggccaagaa caccgtgttt ctcatcgaga tgctgctgcc caagaagtac 240
[7853] catgtgctga ggtttctgga taaaggtgaa aggcatcctg tgcgggaagc ccgtgccgtc 300

[7854] atcttctttg gtgaccagga gcatcccaat gtcaccgagt ttgctgtggg gcccctgcca 360
[7855] gggccctgct acatgcgagc actgtccccc aggcctgggt accagtcctc ctgggcatcg 420
[7856] aggcccatct ccacagcaga gtatgccctc ctctaccaca ccctgcagga agccaccaag 480
[7857] cccctgcatc agttcttcct caataccaca ggcttctcat tccaagactg ccatgacaga 540
[7858] tgcctggcct tcaccgatgt ggcccccccgg ggtgtggctt ctggccagcg ccgcagttgg 600
[7859] cttatcatac agcgctatgt agaaggctac tttctgcacc ccactgggct ggagctcctc 660
[7860] gtggatcatg ggagcacaga tgctgggcac tgggccgtgg agcaggtgtg gtacaacggg 720
[7861] aagttctatg ggagcccaga ggaactggct cggaagtatg cagatggaga ggtggacgtg 780
[7862] gtggtcctgg aggacccgct gcctgggggc aaggggcatg acagcacaga ggagccgccc 840
[7863] ctcttctcct cccacaagcc ccgcggggac ttccccagcc ccatccatgt gagcggcccc 900
[7864] cgcttggtcc agccccacgg ccctcgcttc aggctggagg gcaacgctgt gctctacggc 960
[7865] ggctggagct ttgccttccg gctgcgctcc tcctccgggc tgcaggtcct gaacgtgcac 1020
[7866] ttcggcggag agcgcattgc ctatgaggtc agcgtgcaag aggcagtggc gctgtatgga 1080
[7867] ggacacacac ctgcaggcat gcagaccaag tacctcgatg tcggctgggg cctgggcagc 1140
[7868] gtcactcatg agttagcccc cggcatcgac tgcccggaga ccgccacctt cctggacact 1200
[7869] ttccactact atgatgccga tgacccggtc cattatcccc gagccctctg cctctttgaa 1260
[7870] atgcccacag gggtgcccct tcggcggcac tttaattcca actttaaagg tggcttcaac 1320
[7871] ttctatgcgg ggctgaaggg ccaggtgctg gtgctgcgga caacttcaac tgtctacaat 1380
[7872] tatgattaca tttgggactt tatcttctac cccaacgggg tgatggaggc caagatgcat 1440
[7873] gccactggct acgtccacgc caccttctac acccccgagg ggctgcgcca cggcactcgc 1500
[7874] ctgcacaccc acctgattgg caacatacac actcacttgg tgcactaccg cgtagacctg 1560
[7875] gatgtggcag gcaccaagaa cagcttccag acactgcaga tgaagctaga aaacatcacc 1620
[7876] aacccctgga gcccaagaca ccgcgtggtc cagccaactc tggagcagac gcagtactcc 1680
[7877] tgggagcgcc aggcggcctt ccgcttcgga cagacgctgc ccaagtacct gctctttacc 1740
[7878] agcccccagg agaacccctg gggccacaag cgcagctacc gcctgcagat ccactccatg 1800
[7879] gccgaccagg tgctgccccc aggctggcag gaggagcagg ccatcacctg ggcaaggtac 1860
[7880] cccctggcag tgaccaagta ccgggagtcg gagctgtgca gcagcagcat ctaccaccag 1920
[7881] aacgacccct ggcacccgcc cgtggtcttt gagcagtttc ttcacaacaa cgagaacatt 1980
[7882] gaaaatgagg acctggtggc ctgggtgacg gtgggcttcc tgcacatccc ccactcagag 2040
[7883] gacattccca acacagccac acctgggaac tccgtgggct tcctgctccg gccattcaac 2100
[7884] ttcttcccag aggacccctc cctggcatcc agagacactg tgatcgtgtg gcctcgggac 2160
[7885] aacggcccca actacgtcca gcgctggatc cctgaggaca gggactgctc gatgcctccc 2220
[7886] ccttttagct acaatgggac ctatagacct gtggagccca agtccgccga caagacccac 2280
[7887] acctgccccc cctgccccgc ccccccccgtg gccggcccct ccgtgttcct gttccccccc 2340
[7888] aagcccaagg acaccctgat gatctccagg acccccgagg tgacctgcgt ggtggtggac 2400
[7889] gtgtcccacg aggaccccga ggtgaagttc aactggtacg tggacggcgt ggaggtgcac 2460
[7890] aacgccaaga ccaagcccag ggaggagcag tacaactcca cctacagggt ggtgtccgtg 2520
[7891] ctgaccgtgc tgcaccagga ctggctgaac ggcaaggagt acaagtgcaa ggtgtccaac 2580
[7892] aagggcctgc cctcctccat cgagaagacc atctccaagg ccaagggcca gcccagggag 2640
[7893] ccccaggtgt acaccctgcc ccctccagg gaggagatga ccaagaacca ggtgtccctg 2700
[7894] acctgcctgg tgaagggctt ctacccctcc gacatcgccg tggagtggga gtccaacggc 2760
[7895] cagcccgaga acaactacaa gaccaccccc cccgtgctgg actccgacgg ctccttcttc 2820

[7896] ctgtactcca agctgaccgt ggacaagtcc aggtggcagc agggcaacgt gttctcctgc 2880
[7897] tccgtgatgc acgaggccct gcacaaccac tacacccaga agtccctgtc cctgtccccc 2940
[7898] ggcaagtga 2949
[7899] <210> 94
[7900] <211> 2949
[7901] <212> DNA
[7902] <213> 人工序列
[7903] <220>
[7904] <223> hDAO-Fc-Hepmut7
[7905] <400> 94
[7906] atgccggccc tgggctgggc cgtggctgcc atcctgatgc tgcagacggc catggcggag 60
[7907] ccctccccgg ggactctgcc caggaaggca ggggtgtttt cagacctaag caaccaagag 120
[7908] ctgaaggcag tgcacagctt cctctggtcc aagaaggagc tgaggctgca gccctccagt 180
[7909] accaccacca tggccaagaa caccgtgttt ctcatcgaga tgctgctgcc caagaagtac 240
[7910] catgtgctga ggtttctgga taaaggtgaa aggcatcctg tgcgggaagc ccgtgccgtc 300
[7911] atcttctttg gtgaccagga gcatcccaat gtcaccgagt ttgctgtggg gcccctgcca 360
[7912] gggccctgct acatgcgagc actgtccccc aggcctgggt accagtcctc ctgggcatcg 420
[7913] aggcccatct ccacagcaga gtatgccctc ctctaccaca ccctgcagga agccaccaag 480
[7914] cccctgcatc agttcttcct caataccaca ggcttctcat tccaagactg ccatgacaga 540
[7915] tgcctggcct tcaccgatgt ggcccccccgg ggtgtggctt ctggccagcg ccgcagttgg 600
[7916] cttatcatac agcgctatgt agaaggctac tttctgcacc ccactgggct ggagctcctc 660
[7917] gtggatcatg ggagcacaga tgctgggcac tgggccgtgg agcaggtgtg gtacaacggg 720
[7918] aagttctatg ggagcccaga ggaactggct cggaagtatg cagatggaga ggtggacgtg 780
[7919] gtggtcctgg aggacccgct gcctgggggc aaggggcatg acagcacaga ggagccgccc 840
[7920] ctcttctcct cccacaagcc ccgcggggac ttccccagcc ccatccatgt gagcggcccc 900
[7921] cgcttggtcc agccccacgg ccctcgcttc aggctggagg gcaacgctgt gctctacggc 960
[7922] ggctggagct ttgccttccg gctgcgctcc tcctccgggc tgcaggtcct gaacgtgcac 1020
[7923] ttcggcggag agcgcattgc ctatgaggtc agcgtgcaag aggcagtggc gctgtatgga 1080
[7924] ggacacacac ctgcaggcat gcagaccaag tacctcgatg tcggctgggg cctgggcagc 1140
[7925] gtcactcatg agttagcccc cggcatcgac tgcccggaga ccgccacctt cctggacact 1200
[7926] ttccactact atgatgccga tgacccggtc cattatcccc gagccctctg cctctttgaa 1260
[7927] atgcccacag gggtgcccct tcggcggcac tttaattcca actttaaagg tggcttcaac 1320
[7928] ttctatgcgg ggctgaaggg ccaggtgctg gtgctgcgga caacttcaac tgtctacaat 1380
[7929] tatgattaca tttgggactt tatcttctac cccaacgggg tgatggaggc caagatgcat 1440
[7930] gccactggct acgtccacgc caccttctac acccccgagg ggctgcgcca cggcactcgc 1500
[7931] ctgcacaccc acctgattgg caacatacac actcacttgg tgcactaccg cgtagacctg 1560
[7932] gatgtggcag gcaccaagaa cagcttccag acactgcaga tgaagctaga aaacatcacc 1620
[7933] aacccctgga gcccaagaca ccgcgtggtc cagccaactc tggagcagac gcagtactcc 1680
[7934] tgggagcgcc aggcggcctt cagcttcaaa aggaagctgc ccacgtacct gctctttacc 1740
[7935] agcccccagg agaacccctg gggccacaag cgcagctacc gcctgcagat ccactccatg 1800
[7936] gccgaccagg tgctgccccc aggctggcag gaggagcagg ccatcacctg ggcaaggtac 1860
[7937] cccctggcag tgaccaagta ccgggagtcg gagctgtgca gcagcagcat ctaccaccag 1920

[7938] aacgacccct ggcacccgcc cgtggtcttt gagcagtttc ttcacaacaa cgagaacatt 1980
[7939] gaaaatgagg acctggtggc ctgggtgacg gtgggcttcc tgcacatccc ccactcagag 2040
[7940] gacattccca acacagccac acctgggaac tccgtgggct tcctgctccg gccattcaac 2100
[7941] ttcttcccag aggacccctc cctggcatcc agagacactg tgatcgtgtg gcctcgggac 2160
[7942] aacggcccca actacgtcca gcgctggatc cctgaggaca gggactgctc gatgcctccc 2220
[7943] ccttttagct acaatgggac ctatagacct gtggagccca agtccgccga caagacccac 2280
[7944] acctgccccc cctgccccgc ccccccgtg gccggcccct ccgtgttcct gttccccccc 2340
[7945] aagcccaagg acaccctgat gatctccagg acccccgagg tgacctgcgt ggtggtggac 2400
[7946] gtgtcccacg aggaccccga ggtgaagttc aactggtacg tggacggcgt ggaggtgcac 2460
[7947] aacgccaaga ccaagcccag ggaggagcag tacaactcca cctacagggt ggtgtccgtg 2520
[7948] ctgaccgtgc tgcaccagga ctggctgaac ggcaaggagt acaagtgcaa ggtgtccaac 2580
[7949] aagggcctgc cctcctccat cgagaagacc atctccaagg ccaagggcca gcccagggag 2640
[7950] ccccaggtgt acaccctgcc cccctccagg gaggagatga ccaagaacca ggtgtccctg 2700
[7951] acctgcctgg tgaagggctt ctacccctcc gacatcgccg tggagtggga gtccaacggc 2760
[7952] cagcccgaga acaactacaa gaccaccccc cccgtgctgg actccgacgg ctccttcttc 2820
[7953] ctgtactcca agctgaccgt ggacaagtcc aggtggcagc agggcaacgt gttctcctgc 2880
[7954] tccgtgatgc acgaggccct gcacaaccac tacacccaga agtccctgtc cctgtccccc 2940
[7955] ggcaagtga 2949
[7956] <210> 95
[7957] <211> 2949
[7958] <212> DNA
[7959] <213> 人工序列
[7960] <220>
[7961] <223> hDAO-Fc-Cysmut
[7962] <400> 95
[7963] atgccggccc tgggctgggc cgtggctgcc atcctgatgc tgcagacggc catggcggag 60
[7964] ccctccccgg ggactctgcc caggaaggca ggggtgtttt cagacctaag caaccaagag 120
[7965] ctgaaggcag tgcacagctt cctctggtcc aagaaggagc tgaggctgca gccctccagt 180
[7966] accaccacca tggccaagaa caccgtgttt ctcatcgaga tgctgctgcc caagaagtac 240
[7967] catgtgctga ggtttctgga taaaggtgaa aggcatcctg tgcgggaagc ccgtgccgtc 300
[7968] atcttctttg gtgaccagga gcatcccaat gtcaccgagt ttgctgtggg gcccctgcca 360
[7969] gggcccgcct acatgcgagc actgtccccc aggcctgggt accagtcctc ctgggcatcg 420
[7970] aggcccatct ccacagcaga gtatgccctc ctctaccaca ccctgcagga agccaccaag 480
[7971] cccctgcatc agttcttcct caataccaca ggcttctcat tccaagactg ccatgacaga 540
[7972] tgcctggcct tcaccgatgt ggcccccccgg ggtgtggctt ctggccagcg ccgcagttgg 600
[7973] cttatcatac agcgctatgt agaaggctac tttctgcacc ccactgggct ggagctcctc 660
[7974] gtggatcatg ggagcacaga tgctgggcac tgggccgtgg agcaggtgtg gtacaacggg 720
[7975] aagttctatg ggagcccaga ggaactggct cggaagtatg cagatggaga ggtggacgtg 780
[7976] gtggtcctgg aggacccgct gcctgggggc aaggggcatg acagcacaga ggagccgccc 840
[7977] ctcttctcct cccacaagcc ccgcggggac ttccccagcc ccatccatgt gagcggcccc 900
[7978] cgcttggtcc agccccacgg ccctcgcttc aggctggagg gcaacgctgt gctctacggc 960
[7979] ggctggagct ttgccttccg gctgcgctcc tcctccgggc tgcaggtcct gaacgtgcac 1020

[7980] ttcggcggag agcgcattgc ctatgaggtc agcgtgcaag aggcagtggc gctgtatgga 1080
[7981] ggacacacac ctgcaggcat gcagaccaag tacctcgatg tcggctgggg cctgggcagc 1140
[7982] gtcactcatg agttagcccc cggcatcgac tgcccggaga ccgccacctt cctggacact 1200
[7983] ttccactact atgatgccga tgacccggtc cattatcccc gagccctctg cctctttgaa 1260
[7984] atgcccacag gggtgcccct tcggcggcac tttaattcca actttaaagg tggcttcaac 1320
[7985] ttctatgcgg ggctgaaggg ccaggtgctg gtgctgcgga caacttcaac tgtctacaat 1380
[7986] tatgattaca tttgggactt tatcttctac cccaacgggg tgatggaggc caagatgcat 1440
[7987] gccactggct acgtccacgc caccttctac acccccgagg ggctgcgcca cggcactcgc 1500
[7988] ctgcacaccc acctgattgg caacatacac actcacttgg tgcactaccg cgtagacctg 1560
[7989] gatgtggcag gcaccaagaa cagcttccag acactgcaga tgaagctaga aaacatcacc 1620
[7990] aacccctgga gcccaagaca ccgcgtggtc cagccaactc tggagcagac gcagtactcc 1680
[7991] tgggagcgcc aggcggcctt ccgcttcaaa aggaagctgc ccaagtacct gctctttacc 1740
[7992] agcccccagg agaacccctg gggccacaag cgcagctacc gcctgcagat ccactccatg 1800
[7993] gccgaccagg tgctgccccc aggctggcag gaggagcagg ccatcacctg ggcaaggtac 1860
[7994] cccctggcag tgaccaagta ccgggagtcg gagctgtgca gcagcagcat ctaccaccag 1920
[7995] aacgacccct ggcacccgcc cgtggtcttt gagcagtttc ttcacaacaa cgagaacatt 1980
[7996] gaaaatgagg acctggtggc ctgggtgacg gtgggcttcc tgcacatccc ccactcagag 2040
[7997] gacattccca acacagccac acctgggaac tccgtgggct tcctgctccg gccattcaac 2100
[7998] ttcttcccag aggacccctc cctggcatcc agagacactg tgatcgtgtg gcctcgggac 2160
[7999] aacggcccca actacgtcca gcgctggatc cctgaggaca gggactgctc gatgcctccc 2220
[8000] ccttttagct acaatgggac ctatagacct gtggagccca agtccgccga caagacccac 2280
[8001] acctgccccc cctgccccgc ccccccgtg gccggcccct ccgtgttcct gttccccccc 2340
[8002] aagcccaagg acaccctgat gatctccagg acccccgagg tgacctgcgt ggtggtggac 2400
[8003] gtgtcccacg aggaccccga ggtgaagttc aactggtacg tggacggcgt ggaggtgcac 2460
[8004] aacgccaaga ccaagcccag ggaggagcag tacaactcca cctacagggt ggtgtccgtg 2520
[8005] ctgaccgtgc tgcaccagga ctggctgaac ggcaaggagt acaagtgcaa ggtgtccaac 2580
[8006] aagggcctgc cctcctccat cgagaagacc atctccaagg ccaagggcca gcccagggag 2640
[8007] ccccaggtgt acaccctgcc cccctccagg gaggagatga ccaagaacca ggtgtccctg 2700
[8008] acctgcctgg tgaagggctt ctacccctcc gacatcgccg tggagtggga gtccaacggc 2760
[8009] cagcccgaga acaactacaa gaccaccccc cccgtgctgg actccgacgg ctccttcttc 2820
[8010] ctgtactcca agctgaccgt ggacaagtcc aggtggcagc agggcaacgt gttctcctgc 2880
[8011] tccgtgatgc acgaggccct gcacaaccac tacacccaga agtccctgtc cctgtccccc 2940
[8012] ggcaagtga 2949
[8013] <210> 96
[8014] <211> 2949
[8015] <212> DNA
[8016] <213> 人工序列
[8017] <220>
[8018] <223> hDAO-Fc-Hepmut1-Cysmut
[8019] <400> 96
[8020] atgccggccc tgggctgggc cgtggctgcc atcctgatgc tgcagacggc catggcggag 60
[8021] ccctccccgg ggactctgcc caggaaggca ggggtgtttt cagacctaag caaccaagag 120

[8022] ctgaaggcag tgcacagctt cctctggtcc aagaaggagc tgaggctgca gccctccagt 180
[8023] accaccacca tggccaagaa caccgtgttt ctcatcgaga tgctgctgcc caagaagtac 240
[8024] catgtgctga ggtttctgga taaaggtgaa aggcatcctg tgcgggaagc ccgtgccgtc 300
[8025] atcttctttg gtgaccagga gcatcccaat gtcaccgagt ttgctgtggg gcccctgcca 360
[8026] gggcccgcct acatgcgagc actgtccccc aggcctgggt accagtcctc ctgggcatcg 420
[8027] aggcccatct ccacagcaga gtatgccctc ctctaccaca ccctgcagga agccaccaag 480
[8028] cccctgcatc agttcttcct caataccaca ggcttctcat tccaagactg ccatgacaga 540
[8029] tgcctggcct tcaccgatgt ggcccccccgg ggtgtggctt ctggccagcg ccgcagttgg 600
[8030] cttatcatac agcgctatgt agaaggctac tttctgcacc ccactgggct ggagctcctc 660
[8031] gtggatcatg ggagcacaga tgctgggcac tgggccgtgg agcaggtgtg gtacaacggg 720
[8032] aagttctatg ggagcccaga ggaactggct cggaagtatg cagatggaga ggtggacgtg 780
[8033] gtggtcctgg aggacccgct gcctgggggc aaggggcatg acagcacaga ggagccgccc 840
[8034] ctcttctcct cccacaagcc ccgcggggac ttccccagcc ccatccatgt gagcggcccc 900
[8035] cgcttggtcc agccccacgg ccctcgcttc aggctggagg gcaacgctgt gctctacggc 960
[8036] ggctggagct ttgccttccg gctgcgctcc tcctccgggc tgcaggtcct gaacgtgcac 1020
[8037] ttcggcggag agcgcattgc ctatgaggtc agcgtgcaag aggcagtggc gctgtatgga 1080
[8038] ggacacacac ctgcaggcat gcagaccaag tacctcgatg tcggctgggg cctgggcagc 1140
[8039] gtcactcatg agttagcccc cggcatcgac tgcccggaga ccgccacctt cctggacact 1200
[8040] ttccactact atgatgccga tgacccggtc cattatcccc gagccctctg cctctttgaa 1260
[8041] atgcccacag gggtgcccct tcggcggcac tttaattcca actttaaagg tggcttcaac 1320
[8042] ttctatgcgg ggctgaaggg ccaggtgctg gtgctgcgga caacttcaac tgtctacaat 1380
[8043] tatgattaca tttgggactt tatcttctac cccaacgggg tgatggaggc caagatgcat 1440
[8044] gccactggct acgtccacgc caccttctac acccccgagg ggctgcgcca cggcactcgc 1500
[8045] ctgcacaccc acctgattgg caacatacac actcacttgg tgcactaccg cgtagacctg 1560
[8046] gatgtggcag gcaccaagaa cagcttccag acactgcaga tgaagctaga aaacatcacc 1620
[8047] aacccctgga gcccaagaca ccgcgtggtc cagccaactc tggagcagac gcagtactcc 1680
[8048] tgggagcgcc aggcggcctt cagcttcaaa aggaagctgc ccaagtacct gctctttacc 1740
[8049] agcccccagg agaacccctg gggccacaag cgcagctacc gcctgcagat ccactccatg 1800
[8050] gccgaccagg tgctgccccc aggctggcag gaggagcagg ccatcacctg ggcaaggtac 1860
[8051] cccctggcag tgaccaagta ccgggagtcg gagctgtgca gcagcagcat ctaccaccag 1920
[8052] aacgacccct ggcacccgcc cgtggtcttt gagcagtttc ttcacaacaa cgagaacatt 1980
[8053] gaaaatgagg acctggtggc ctgggtgacg gtgggcttcc tgcacatccc ccactcagag 2040
[8054] gacattccca acacagccac acctgggaac tccgtgggct tcctgctccg gccattcaac 2100
[8055] ttcttcccag aggacccctc cctggcatcc agagacactg tgatcgtgtg gcctcgggac 2160
[8056] aacggcccca actacgtcca gcgctggatc cctgaggaca gggactgctc gatgcctccc 2220
[8057] ccttttagct acaatgggac ctatagacct gtggagccca agtccgccga caagacccac 2280
[8058] acctgccccc cctgccccgc ccccccgtg gccggcccct ccgtgttcct gttccccccc 2340
[8059] aagcccaagg acaccctgat gatctccagg acccccgagg tgacctgcgt ggtggtggac 2400
[8060] gtgtcccacg aggaccccga ggtgaagttc aactggtacg tggacggcgt ggaggtgcac 2460
[8061] aacgccaaga ccaagcccag ggaggagcag tacaactcca cctacagggt ggtgtccgtg 2520
[8062] ctgaccgtgc tgcaccagga ctggctgaac ggcaaggagt acaagtgcaa ggtgtccaac 2580
[8063] aagggcctgc cctcctccat cgagaagacc atctccaagg ccaagggcca gcccagggag 2640

[8064] ccccaggtgt acaccctgcc cccctccagg gaggagatga ccaagaacca ggtgtccctg 2700
[8065] acctgcctgg tgaagggctt ctacccctcc gacatcgccg tggagtggga gtccaacggc 2760
[8066] cagcccgaga acaactacaa gaccaccccc cccgtgctgg actccgacgg ctccttcttc 2820
[8067] ctgtactcca agctgaccgt ggacaagtcc aggtggcagc agggcaacgt gttctcctgc 2880
[8068] tccgtgatgc acgaggccct gcacaaccac tacacccaga agtccctgtc cctgtccccc 2940
[8069] ggcaagtga 2949
[8070] <210> 97
[8071] <211> 2949
[8072] <212> DNA
[8073] <213> 人工序列
[8074] <220>
[8075] <223> hDAO-Fc-Hepmut2-Cysmut
[8076] <400> 97
[8077] atgccggccc tgggctgggc cgtggctgcc atcctgatgc tgcagacggc catggcggag 60
[8078] ccctccccgg ggactctgcc caggaaggca ggggtgtttt cagacctaag caaccaagag 120
[8079] ctgaaggcag tgcacagctt cctctggtcc aagaaggagc tgaggctgca gccctccagt 180
[8080] accaccacca tggccaagaa caccgtgttt ctcatcgaga tgctgctgcc caagaagtac 240
[8081] catgtgctga ggtttctgga taaaggtgaa aggcatcctg tgcgggaagc ccgtgccgtc 300
[8082] atcttctttg gtgaccagga gcatcccaat gtcaccgagt ttgctgtggg gcccctgcca 360
[8083] gggcccgcct acatgcgagc actgtccccc aggcctgggt accagtcctc ctgggcatcg 420
[8084] aggcccatct ccacagcaga gtatgccctc ctctaccaca ccctgcagga agccaccaag 480
[8085] cccctgcatc agttcttcct caataccaca ggcttctcat tccaagactg ccatgacaga 540
[8086] tgcctggcct tcaccgatgt ggcccccccgg ggtgtggctt ctggccagcg ccgcagttgg 600
[8087] cttatcatac agcgctatgt agaaggctac tttctgcacc ccactgggct ggagctcctc 660
[8088] gtggatcatg ggagcacaga tgctgggcac tgggccgtgg agcaggtgtg gtacaacggg 720
[8089] aagttctatg ggagcccaga ggaactggct cggaagtatg cagatggaga ggtggacgtg 780
[8090] gtggtcctgg aggacccgct gcctgggggc aaggggcatg acagcacaga ggagccgccc 840
[8091] ctcttctcct cccacaagcc ccgcggggac ttccccagcc ccatccatgt gagcggcccc 900
[8092] cgcttggtcc agccccacgg ccctcgcttc aggctggagg gcaacgctgt gctctacggc 960
[8093] ggctggagct ttgccttccg gctgcgctcc tcctccgggc tgcaggtcct gaacgtgcac 1020
[8094] ttcggcggag agcgcattgc ctatgaggtc agcgtgcaag aggcagtggc gctgtatgga 1080
[8095] ggacacacac ctgcaggcat gcagaccaag tacctcgatg tcggctgggg cctgggcagc 1140
[8096] gtcactcatg agttagcccc cggcatcgac tgcccggaga ccgccacctt cctggacact 1200
[8097] ttccactact atgatgccga tgacccggtc cattatcccc gagccctctg cctctttgaa 1260
[8098] atgcccacag gggtgcccct tcggcggcac tttaattcca actttaaagg tggcttcaac 1320
[8099] ttctatgcgg ggctgaaggg ccaggtgctg gtgctgcgga caacttcaac tgtctacaat 1380
[8100] tatgattaca tttgggactt tatcttctac cccaacgggg tgatggaggc caagatgcat 1440
[8101] gccactggct acgtccacgc caccttctac acccccgagg ggctgcgcca cggcactcgc 1500
[8102] ctgcacaccc acctgattgg caacatacac actcacttgg tgcactaccg cgtagacctg 1560
[8103] gatgtggcag gcaccaagaa cagcttccag acactgcaga tgaagctaga aaacatcacc 1620
[8104] aacccctgga gcccaagaca ccgcgtggtc cagccaactc tggagcagac gcagtactcc 1680
[8105] tgggagcgcc aggcggcctt ccgcttcaaa aggaagctgc ccacgtacct gctctttacc 1740

[8106] agcccccagg agaacccctg gggccacaag cgcagctacc gcctgcagat ccactccatg 1800
[8107] gccgaccagg tgctgccccc aggctggcag gaggagcagg ccatcacctg ggcaaggtac 1860
[8108] cccctggcag tgaccaagta ccgggagtcg gagctgtgca gcagcagcat ctaccaccag 1920
[8109] aacgacccct ggcacccgcc cgtggtcttt gagcagtttc ttcacaacaa cgagaacatt 1980
[8110] gaaaatgagg acctggtggc ctgggtgacg gtgggcttcc tgcacatccc ccactcagag 2040
[8111] gacattccca acacagccac acctgggaac tccgtgggct tcctgctccg gccattcaac 2100
[8112] ttcttcccag aggacccctc cctggcatcc agagacactg tgatcgtgtg gcctcgggac 2160
[8113] aacggcccca actacgtcca gcgctggatc cctgaggaca gggactgctc gatgcctccc 2220
[8114] ccttttagct acaatgggac ctatagacct gtggagccca agtccgccga caagacccac 2280
[8115] acctgccccc cctgccccgc ccccccgtg gccggcccct ccgtgttcct gttccccccc 2340
[8116] aagcccaagg acaccctgat gatctccagg acccccgagg tgacctgcgt ggtggtggac 2400
[8117] gtgtcccacg aggaccccga ggtgaagttc aactggtacg tggacggcgt ggaggtgcac 2460
[8118] aacgccaaga ccaagcccag ggaggagcag tacaactcca cctacagggt ggtgtccgtg 2520
[8119] ctgaccgtgc tgcaccagga ctggctgaac ggcaaggagt acaagtgcaa ggtgtccaac 2580
[8120] aagggcctgc cctcctccat cgagaagacc atctccaagg ccaagggcca gcccagggag 2640
[8121] ccccaggtgt acaccctgcc cccctccagg gaggagatga ccaagaacca ggtgtccctg 2700
[8122] acctgcctgg tgaagggctt ctacccctcc gacatcgccg tggagtggga gtccaacggc 2760
[8123] cagcccgaga acaactacaa gaccaccccc cccgtgctgg actccgacgg ctccttcttc 2820
[8124] ctgtactcca agctgaccgt ggacaagtcc aggtggcagc agggcaacgt gttctcctgc 2880
[8125] tccgtgatgc acgaggccct gcacaaccac tacacccaga agtccctgtc cctgtccccc 2940
[8126] ggcaagtga 2949
[8127] <210> 98
[8128] <211> 2949
[8129] <212> DNA
[8130] <213> 人工序列
[8131] <220>
[8132] <223> hDAO-Fc-Hepmut3-Cysmut
[8133] <400> 98
[8134] atgccggccc tgggctgggc cgtggctgcc atcctgatgc tgcagacggc catggcggag 60
[8135] ccctccccgg ggactctgcc caggaaggca ggggtgtttt cagacctaag caaccaagag 120
[8136] ctgaaggcag tgcacagctt cctctggtcc aagaaggagc tgaggctgca gccctccagt 180
[8137] accaccacca tggccaagaa caccgtgttt ctcatcgaga tgctgctgcc caagaagtac 240
[8138] catgtgctga ggtttctgga taaaggtgaa aggcatcctg tgcgggaagc ccgtgccgtc 300
[8139] atcttctttg gtgaccagga gcatcccaat gtcaccgagt ttgctgtggg gcccctgcca 360
[8140] gggcccgcct acatgcgagc actgtccccc aggcctgggt accagtcctc ctgggcatcg 420
[8141] aggcccatct ccacagcaga gtatgccctc ctctaccaca ccctgcagga agccaccaag 480
[8142] cccctgcatc agttcttcct caataccaca ggcttctcat tccaagactg ccatgacaga 540
[8143] tgcctggcct tcaccgatgt ggcccccccgg ggtgtggctt ctggccagcg ccgcagttgg 600
[8144] cttatcatac agcgctatgt agaaggctac tttctgcacc ccactgggct ggagctcctc 660
[8145] gtggatcatg ggagcacaga tgctgggcac tgggccgtgg agcaggtgtg gtacaacggg 720
[8146] aagttctatg ggagcccaga ggaactggct cggaagtatg cagatggaga ggtggacgtg 780
[8147] gtggtcctgg aggacccgct gcctgggggc aaggggcatg acagcacaga ggagccgccc 840

[8148] ctcttctcct cccacaagcc ccgcggggac ttccccagcc ccatccatgt gagcggcccc 900
[8149] cgcttggtcc agccccacgg ccctcgcttc aggctggagg gcaacgctgt gctctacggc 960
[8150] ggctggagct ttgccttccg gctgcgctcc tcctccgggc tgcaggtcct gaacgtgcac 1020
[8151] ttcggcggag agcgcattgc ctatgaggtc agcgtgcaag aggcagtggc gctgtatgga 1080
[8152] ggacacacac ctgcaggcat gcagaccaag tacctcgatg tcggctgggg cctgggcagc 1140
[8153] gtcactcatg agttagcccc cggcatcgac tgcccggaga ccgccacctt cctggacact 1200
[8154] ttccactact atgatgccga tgacccggtc cattatcccc gagccctctg cctctttgaa 1260
[8155] atgcccacag gggtgcccct tcggcggcac tttaattcca actttaaagg tggcttcaac 1320
[8156] ttctatgcgg ggctgaaggg ccaggtgctg gtgctgcgga caacttcaac tgtctacaat 1380
[8157] tatgattaca tttgggactt tatcttctac cccaacgggg tgatggaggc caagatgcat 1440
[8158] gccactggct acgtccacgc caccttctac acccccgagg ggctgcgcca cggcactcgc 1500
[8159] ctgcacaccc acctgattgg caacatacac actcacttgg tgcactaccg cgtagacctg 1560
[8160] gatgtggcag gcaccaagaa cagcttccag acactgcaga tgaagctaga aaacatcacc 1620
[8161] aacccctgga gcccaagaca ccgcgtggtc cagccaactc tggagcagac gcagtactcc 1680
[8162] tgggagcgcc aggcggcctt ccgcttcaaa acgaagctgc ccaagtacct gctctttacc 1740
[8163] agcccccagg agaacccctg gggccacaag cgcagctacc gcctgcagat ccactccatg 1800
[8164] gccgaccagg tgctgccccc aggctggcag gaggagcagg ccatcacctg ggcaaggtac 1860
[8165] cccctggcag tgaccaagta ccgggagtcg gagctgtgca gcagcagcat ctaccaccag 1920
[8166] aacgacccct ggcacccgcc cgtggtcttt gagcagtttc ttcacaacaa cgagaacatt 1980
[8167] gaaaatgagg acctggtggc ctgggtgacg gtgggcttcc tgcacatccc ccactcagag 2040
[8168] gacattccca acacagccac acctgggaac tccgtgggct tcctgctccg gccattcaac 2100
[8169] ttcttcccag aggacccctc cctggcatcc agagacactg tgatcgtgtg gcctcgggac 2160
[8170] aacggcccca actacgtcca gcgctggatc cctgaggaca gggactgctc gatgcctccc 2220
[8171] ccttttagct acaatgggac ctatagacct gtggagccca agtccgccga caagacccac 2280
[8172] acctgccccc cctgccccgc ccccccgtg gccggccct ccgtgttcct gttccccccc 2340
[8173] aagcccaagg acaccctgat gatctccagg acccccgagg tgacctgcgt ggtggtggac 2400
[8174] gtgtcccacg aggaccccga ggtgaagttc aactggtacg tggacggcgt ggaggtgcac 2460
[8175] aacgccaaga ccaagcccag ggaggagcag tacaactcca cctacagggt ggtgtccgtg 2520
[8176] ctgaccgtgc tgcaccagga ctggctgaac ggcaaggagt acaagtgcaa ggtgtccaac 2580
[8177] aagggcctgc cctcctccat cgagaagacc atctccaagg ccaagggcca gcccagggag 2640
[8178] ccccaggtgt acaccctgcc cccctccagg gaggagatga ccaagaacca ggtgtccctg 2700
[8179] acctgcctgg tgaagggctt ctacccctcc gacatcgccg tggagtggga gtccaacggc 2760
[8180] cagcccgaga acaactacaa gaccaccccc cccgtgctgg actccgacgg ctccttcttc 2820
[8181] ctgtactcca agctgaccgt ggacaagtcc aggtggcagc agggcaacgt gttctcctgc 2880
[8182] tccgtgatgc acgaggccct gcacaaccac tacacccaga agtccctgtc cctgtccccc 2940
[8183] ggcaagtga 2949
[8184] <210> 99
[8185] <211> 2949
[8186] <212> DNA
[8187] <213> 人工序列
[8188] <220>
[8189] <223> hDAO-Fc-Hepmut4-Cysmut

[8190] <400> 99

[8191] atgccggccc tgggctgggc cgtggctgcc atcctgatgc tgcagacggc catggcggag 60

[8192] ccctccccgg ggactctgcc caggaaggca ggggtgtttt cagacctaag caaccaagag 120

[8193] ctgaaggcag tgcacagctt cctctggtcc aagaaggagc tgaggctgca gccctccagt 180

[8194] accaccacca tggccaagaa caccgtgttt ctcatcgaga tgctgctgcc caagaagtac 240

[8195] catgtgctga ggtttctgga taaaggtgaa aggcatcctg tgcgggaagc ccgtgccgtc 300

[8196] atcttctttg gtgaccagga gcatcccaat gtcaccgagt ttgctgtggg gcccctgcca 360

[8197] gggcccgcct acatgcgagc actgtccccc aggcctgggt accagtcctc ctgggcatcg 420

[8198] aggcccatct ccacagcaga gtatgccctc ctctaccaca ccctgcagga agccaccaag 480

[8199] cccctgcatc agttcttcct caataccaca ggcttctcat tccaagactg ccatgacaga 540

[8200] tgcctggcct tcaccgatgt ggcccccccgg ggtgtggctt ctggccagcg ccgcagttgg 600

[8201] cttatcatac agcgctatgt agaaggctac tttctgcacc ccactgggct ggagctcctc 660

[8202] gtggatcatg ggagcacaga tgctgggcac tgggccgtgg agcaggtgtg gtacaacggg 720

[8203] aagttctatg ggagcccaga ggaactggct cggaagtatg cagatggaga ggtggacgtg 780

[8204] gtggtcctgg aggacccgct gcctgggggc aaggggcatg acagcacaga ggagccgccc 840

[8205] ctcttctcct cccacaagcc ccgcggggac ttccccagcc ccatccatgt gagcggcccc 900

[8206] cgcttggtcc agccccacgg ccctcgcttc aggctggagg gcaacgctgt gctctacggc 960

[8207] ggctggagct ttgccttccg gctgcgctcc tcctccgggc tgcaggtcct gaacgtgcac 1020

[8208] ttcggcggag agcgcattgc ctatgaggtc agcgtgcaag aggcagtggc gctgtatgga 1080

[8209] ggacacacac ctgcaggcat gcagaccaag tacctcgatg tcggctgggg cctgggcagc 1140

[8210] gtcactcatg agttagcccc cggcatcgac tgcccggaga ccgccacctt cctggacact 1200

[8211] ttccactact atgatgccga tgacccggtc cattatcccc gagccctctg cctctttgaa 1260

[8212] atgcccacag gggtgcccct tcggcggcac tttaattcca actttaaagg tggcttcaac 1320

[8213] ttctatgcgg ggctgaaggg ccaggtgctg gtgctgcgga caacttcaac tgtctacaat 1380

[8214] tatgattaca tttgggactt tatcttctac cccaacgggg tgatggaggc caagatgcat 1440

[8215] gccactggct acgtccacgc caccttctac acccccgagg ggctgcgcca cggcactcgc 1500

[8216] ctgcacaccc acctgattgg caacatacac actcacttgg tgcactaccg cgtagacctg 1560

[8217] gatgtggcag gcaccaagaa cagcttccag acactgcaga tgaagctaga aaacatcacc 1620

[8218] aacccctgga gcccaagaca ccgcgtggtc cagccaactc tggagcagac gcagtactcc 1680

[8219] tgggagcgcc aggcggcctt cagcttcaaa acgaagctgc ccaagtacct gctctttacc 1740

[8220] agcccccagg agaacccctg gggccacaag cgcagctacc gcctgcagat ccactccatg 1800

[8221] gccgaccagg tgctgccccc aggctggcag gaggagcagg ccatcacctg ggcaaggtac 1860

[8222] cccctggcag tgaccaagta ccgggagtcg gagctgtgca gcagcagcat ctaccaccag 1920

[8223] aacgacccct ggcacccgcc cgtggtcttt gagcagtttc ttcacaacaa cgagaacatt 1980

[8224] gaaaatgagg acctggtggc ctgggtgacg gtgggcttcc tgcacatccc ccactcagag 2040

[8225] gacattccca acacagccac acctgggaac tccgtgggct tcctgctccg gccattcaac 2100

[8226] ttcttcccag aggacccctc cctggcatcc agagacactg tgatcgtgtg gcctcgggac 2160

[8227] aacggcccca actacgtcca gcgctggatc cctgaggaca gggactgctc gatgcctccc 2220

[8228] ccttttagct acaatgggac ctatagacct gtggagccca agtccgccga caagacccac 2280

[8229] acctgccccc cctgccccgc ccccccccgtg gccggcccct ccgtgttcct gttcccccccc 2340

[8230] aagcccaagg acaccctgat gatctccagg acccccgagg tgacctgcgt ggtggtggac 2400

[8231] gtgtcccacg aggaccccga ggtgaagttc aactggtacg tggacggcgt ggaggtgcac 2460

[8232] aacgccaaga ccaagcccag ggaggagcag tacaactcca cctacagggt ggtgtccgtg 2520
[8233] ctgaccgtgc tgcaccagga ctggctgaac ggcaaggagt acaagtgcaa ggtgtccaac 2580
[8234] aagggcctgc cctcctccat cgagaagacc atctccaagg ccaagggcca gcccagggag 2640
[8235] ccccaggtgt acaccctgcc cccctccagg gaggagatga ccaagaacca ggtgtccctg 2700
[8236] acctgcctgg tgaagggctt ctacccctcc gacatcgccg tggagtggga gtccaacggc 2760
[8237] cagcccgaga acaactacaa gaccaccccc cccgtgctgg actccgacgg ctccttcttc 2820
[8238] ctgtactcca agctgaccgt ggacaagtcc aggtggcagc agggcaacgt gttctcctgc 2880
[8239] tccgtgatgc acgaggccct gcacaaccac tacacccaga agtccctgtc cctgtccccc 2940
[8240] ggcaagtga 2949
[8241] <210> 100
[8242] <211> 2949
[8243] <212> DNA
[8244] <213> 人工序列
[8245] <220>
[8246] <223> hDAO-Fc-Hepmut5-Cysmut
[8247] <400> 100
[8248] atgccggccc tgggctgggc cgtggctgcc atcctgatgc tgcagacggc catggcggag 60
[8249] ccctccccgg ggactctgcc caggaaggca ggggtgtttt cagacctaag caaccaagag 120
[8250] ctgaaggcag tgcacagctt cctctggtcc aagaaggagc tgaggctgca gccctccagt 180
[8251] accaccacca tggccaagaa caccgtgttt ctcatcgaga tgctgctgcc caagaagtac 240
[8252] catgtgctga ggtttctgga taaaggtgaa aggcatcctg tgcgggaagc ccgtgccgtc 300
[8253] atcttctttg gtgaccagga gcatcccaat gtcaccgagt ttgctgtggg gcccctgcca 360
[8254] gggcccgcct acatgcgagc actgtccccc aggcctgggt accagtcctc ctgggcatcg 420
[8255] aggcccatct ccacagcaga gtatgccctc ctctaccaca ccctgcagga agccaccaag 480
[8256] cccctgcatc agttcttcct caataccaca ggcttctcat tccaagactg ccatgacaga 540
[8257] tgcctggcct tcaccgatgt ggcccccccgg ggtgtggctt ctggccagcg ccgcagttgg 600
[8258] cttatcatac agcgctatgt agaaggctac tttctgcacc ccactgggct ggagctcctc 660
[8259] gtggatcatg ggagcacaga tgctgggcac tgggccgtgg agcaggtgtg gtacaacggg 720
[8260] aagttctatg ggagcccaga ggaactggct cggaagtatg cagatggaga ggtggacgtg 780
[8261] gtggtcctgg aggacccgct gcctgggggc aaggggcatg acagcacaga ggagccgccc 840
[8262] ctcttctcct cccacaagcc ccgcggggac ttccccagcc ccatccatgt gagcggcccc 900
[8263] cgcttggtcc agccccacgg ccctcgcttc aggctggagg gcaacgctgt gctctacggc 960
[8264] ggctggagct ttgccttccg gctgcgctcc tcctccgggc tgcaggtcct gaacgtgcac 1020
[8265] ttcggcggag agcgcattgc ctatgaggtc agcgtgcaag aggcagtggc gctgtatgga 1080
[8266] ggacacacac ctgcaggcat gcagaccaag tacctcgatg tcggctgggg cctgggcagc 1140
[8267] gtcactcatg agttagcccc cggcatcgac tgcccggaga ccgccacctt cctggacact 1200
[8268] ttccactact atgatgccga tgacccggtc cattatcccc gagccctctg cctctttgaa 1260
[8269] atgcccacag gggtgcccct tcggcggcac tttaattcca actttaaagg tggcttcaac 1320
[8270] ttctatgcgg ggctgaaggg ccaggtgctg gtgctgcgga caacttcaac tgtctacaat 1380
[8271] tatgattaca tttgggactt tatcttctac cccaacgggg tgatggaggc caagatgcat 1440
[8272] gccactggct acgtccacgc caccttctac acccccgagg ggctgcgcca cggcactcgc 1500
[8273] ctgcacaccc acctgattgg caacatacac actcacttgg tgcactaccg cgtagacctg 1560

[8274] gatgtggcag gcaccaagaa cagcttccag acactgcaga tgaagctaga aaacatcacc 1620
[8275] aacccctgga gcccaagaca ccgcgtggtc cagccaactc tggagcagac gcagtactcc 1680
[8276] tgggagcgcc aggcggcctt ccgcttcaaa acgaagctgc ccacgtacct gctctttacc 1740
[8277] agcccccagg agaacccctg gggccacaag cgcagctacc gcctgcagat ccactccatg 1800
[8278] gccgaccagg tgctgccccc aggctggcag gaggagcagg ccatcacctg ggcaaggtac 1860
[8279] cccctggcag tgaccaagta ccgggagtcg gagctgtgca gcagcagcat ctaccaccag 1920
[8280] aacgacccct ggcacccgcc cgtggtcttt gagcagtttc ttcacaacaa cgagaacatt 1980
[8281] gaaaatgagg acctggtggc ctgggtgacg gtgggcttcc tgcacatccc ccactcagag 2040
[8282] gacattccca acacagccac acctgggaac tccgtgggct tcctgctccg gccattcaac 2100
[8283] ttcttcccag aggacccctc cctggcatcc agagacactg tgatcgtgtg gcctcgggac 2160
[8284] aacggcccca actacgtcca gcgctggatc cctgaggaca gggactgctc gatgcctccc 2220
[8285] ccttttagct acaatgggac ctatagacct gtggagccca agtccgccga caagacccac 2280
[8286] acctgccccc cctgccccgc ccccccgtg gccggcccct ccgtgttcct gttccccccc 2340
[8287] aagcccaagg acaccctgat gatctccagg acccccgagg tgacctgcgt ggtggtggac 2400
[8288] gtgtcccacg aggaccccga ggtgaagttc aactggtacg tggacggcgt ggaggtgcac 2460
[8289] aacgccaaga ccaagcccag ggaggagcag tacaactcca cctacagggt ggtgtccgtg 2520
[8290] ctgaccgtgc tgcaccagga ctggctgaac ggcaaggagt acaagtgcaa ggtgtccaac 2580
[8291] aagggcctgc cctcctccat cgagaagacc atctccaagg ccaagggcca gcccagggag 2640
[8292] ccccaggtgt acaccctgcc cccctccagg gaggagatga ccaagaacca ggtgtccctg 2700
[8293] acctgcctgg tgaagggctt ctacccctcc gacatcgccg tggagtggga gtccaacggc 2760
[8294] cagcccgaga acaactacaa gaccaccccc cccgtgctgg actccgacgg ctccttcttc 2820
[8295] ctgtactcca agctgaccgt ggacaagtcc aggtggcagc agggcaacgt gttctcctgc 2880
[8296] tccgtgatgc acgaggccct gcacaaccac tacacccaga agtccctgtc cctgtccccc 2940
[8297] ggcaagtga 2949
[8298] <210> 101
[8299] <211> 2949
[8300] <212> DNA
[8301] <213> 人工序列
[8302] <220>
[8303] <223> hDAO-Fc-Hepmut6-Cysmut
[8304] <400> 101
[8305] atgccggccc tgggctgggc cgtggctgcc atcctgatgc tgcagacggc catggcggag 60
[8306] ccctccccgg ggactctgcc caggaaggca ggggtgtttt cagacctaag caaccaagag 120
[8307] ctgaaggcag tgcacagctt cctctggtcc aagaaggagc tgaggctgca gccctccagt 180
[8308] accaccacca tggccaagaa caccgtgttt ctcatcgaga tgctgctgcc caagaagtac 240
[8309] catgtgctga ggtttctgga taaaggtgaa aggcatcctg tgcgggaagc ccgtgccgtc 300
[8310] atcttctttg gtgaccagga gcatcccaat gtcaccgagt ttgctgtggg gcccctgcca 360
[8311] gggcccgcct acatgcgagc actgtccccc aggcctgggt accagtcctc ctgggcatcg 420
[8312] aggcccatct ccacagcaga gtatgccctc ctctaccaca ccctgcagga agccaccaag 480
[8313] cccctgcatc agttcttcct caataccaca ggcttctcat tccaagactg ccatgacaga 540
[8314] tgcctggcct tcaccgatgt ggcccccccgg ggtgtggctt ctggccagcg ccgcagttgg 600
[8315] cttatcatac agcgctatgt agaaggctac tttctgcacc ccactgggct ggagctcctc 660

[8316] gtggatcatg ggagcacaga tgctgggcac tgggccgtgg agcaggtgtg gtacaacggg 720
[8317] aagttctatg ggagcccaga ggaactggct cggaagtatg cagatggaga ggtggacgtg 780
[8318] gtggtcctgg aggacccgct gcctgggggc aaggggcatg acagcacaga ggagccgccc 840
[8319] ctcttctcct cccacaagcc ccgcggggac ttccccagcc ccatccatgt gagcggcccc 900
[8320] cgcttggtcc agccccacgg ccctcgcttc aggctggagg gcaacgctgt gctctacggc 960
[8321] ggctggagct ttgccttccg gctgcgctcc tcctccgggc tgcaggtcct gaacgtgcac 1020
[8322] ttcggcggag agcgcattgc ctatgaggtc agcgtgcaag aggcagtggc gctgtatgga 1080
[8323] ggacacacac ctgcaggcat gcagaccaag tacctcgatg tcggctgggg cctgggcagc 1140
[8324] gtcactcatg agttagcccc cggcatcgac tgcccggaga ccgccacctt cctggacact 1200
[8325] ttccactact atgatgccga tgacccggtc cattatcccc gagccctctg cctctttgaa 1260
[8326] atgcccacag gggtgcccct tcggcggcac tttaattcca actttaaagg tggcttcaac 1320
[8327] ttctatgcgg ggctgaaggg ccaggtgctg gtgctgcgga caacttcaac tgtctacaat 1380
[8328] tatgattaca tttgggactt tatcttctac cccaacgggg tgatggaggc caagatgcat 1440
[8329] gccactggct acgtccacgc caccttctac acccccgagg ggctgcgcca cggcactcgc 1500
[8330] ctgcacaccc acctgattgg caacatacac actcacttgg tgcactaccg cgtagacctg 1560
[8331] gatgtggcag gcaccaagaa cagcttccag acactgcaga tgaagctaga aaacatcacc 1620
[8332] aacccctgga gcccaagaca ccgcgtggtc cagccaactc tggagcagac gcagtactcc 1680
[8333] tgggagcgcc aggcggcctt ccgcttcgga cagacgctgc ccaagtacct gctctttacc 1740
[8334] agcccccagg agaacccctg gggccacaag cgcagctacc gcctgcagat ccactccatg 1800
[8335] gccgaccagg tgctgccccc aggctggcag gaggagcagg ccatcacctg ggcaaggtac 1860
[8336] cccctggcag tgaccaagta ccgggagtcg gagctgtgca gcagcagcat ctaccaccag 1920
[8337] aacgacccct ggcacccgcc cgtggtcttt gagcagtttc ttcacaacaa cgagaacatt 1980
[8338] gaaaatgagg acctggtggc ctgggtgacg gtgggcttcc tgcacatccc ccactcagag 2040
[8339] gacattccca acacagccac acctgggaac tccgtgggct tcctgctccg gccattcaac 2100
[8340] ttcttcccag aggacccctc cctggcatcc agagacactg tgatcgtgtg gcctcgggac 2160
[8341] aacggcccca actacgtcca gcgctggatc cctgaggaca gggactgctc gatgcctccc 2220
[8342] ccttttagct acaatgggac ctatagacct gtggagccca agtccgccga caagacccac 2280
[8343] acctgccccc cctgccccgc ccccccgtg gccggcccct ccgtgttcct gttccccccc 2340
[8344] aagcccaagg acaccctgat gatctccagg acccccgagg tgacctgcgt ggtggtggac 2400
[8345] gtgtcccacg aggaccccga ggtgaagttc aactggtacg tggacggcgt ggaggtgcac 2460
[8346] aacgccaaga ccaagcccag ggaggagcag tacaactcca cctacagggt ggtgtccgtg 2520
[8347] ctgaccgtgc tgcaccagga ctggctgaac ggcaaggagt acaagtgcaa ggtgtccaac 2580
[8348] aagggcctgc cctcctccat cgagaagacc atctccaagg ccaagggcca gcccagggag 2640
[8349] ccccaggtgt acaccctgcc cccctccagg gaggagatga ccaagaacca ggtgtccctg 2700
[8350] acctgcctgg tgaagggctt ctacccctcc gacatcgccg tggagtggga gtccaacggc 2760
[8351] cagcccgaga acaactacaa gaccaccccc cccgtgctgg actccgacgg ctccttcttc 2820
[8352] ctgtactcca agctgaccgt ggacaagtcc aggtggcagc agggcaacgt gttctcctgc 2880
[8353] tccgtgatgc acgaggccct gcacaaccac tacacccaga agtccctgtc cctgtccccc 2940
[8354] ggcaagtga 2949
[8355] <210> 102
[8356] <211> 2949
[8357] <212> DNA

[8358] <213> 人工序列

[8359] <220>

[8360] <223> hDAO-Fc-Hepmut7-Cysmut

[8361] <400> 102

[8362] atgccggccc tgggctgggc cgtggctgcc atcctgatgc tgcagacggc catggcggag 60

[8363] ccctccccgg ggactctgcc caggaaggca ggggtgtttt cagacctaag caaccaagag 120

[8364] ctgaaggcag tgcacagctt cctctggtcc aagaaggagc tgaggctgca gccctccagt 180

[8365] accaccacca tggccaagaa caccgtgttt ctcatcgaga tgctgctgcc caagaagtac 240

[8366] catgtgctga ggtttctgga taaaggtgaa aggcatcctg tgcgggaagc ccgtgccgtc 300

[8367] atcttctttg gtgaccagga gcatcccaat gtcaccgagt ttgctgtggg gcccctgcca 360

[8368] gggcccgcct acatgcgagc actgtccccc aggcctgggt accagtcctc ctgggcatcg 420

[8369] aggcccatct ccacagcaga gtatgccctc ctctaccaca ccctgcagga agccaccaag 480

[8370] cccctgcatc agttcttcct caataccaca ggcttctcat tccaagactg ccatgacaga 540

[8371] tgcctggcct tcaccgatgt ggcccccccgg ggtgtggctt ctggccagcg ccgcagttgg 600

[8372] cttatcatac agcgctatgt agaaggctac tttctgcacc ccactgggct ggagctcctc 660

[8373] gtggatcatg ggagcacaga tgctgggcac tgggccgtgg agcaggtgtg gtacaacggg 720

[8374] aagttctatg ggagcccaga ggaactggct cggaagtatg cagatggaga ggtggacgtg 780

[8375] gtggtcctgg aggacccgct gcctgggggc aaggggcatg acagcacaga ggagccgccc 840

[8376] ctcttctcct cccacaagcc ccgcggggac ttccccagcc ccatccatgt gagcggcccc 900

[8377] cgcttggtcc agccccacgg ccctcgcttc aggctggagg gcaacgctgt gctctacggc 960

[8378] ggctggagct ttgccttccg gctgcgctcc tcctccgggc tgcaggtcct gaacgtgcac 1020

[8379] ttcggcggag agcgcattgc ctatgaggtc agcgtgcaag aggcagtggc gctgtatgga 1080

[8380] ggacacacac ctgcaggcat gcagaccaag tacctcgatg tcggctgggg cctgggcagc 1140

[8381] gtcactcatg agttagcccc cggcatcgac tgcccggaga ccgccacctt cctggacact 1200

[8382] ttccactact atgatgccga tgacccggtc cattatcccc gagccctctg cctctttgaa 1260

[8383] atgcccacag gggtgcccct tcggcggcac tttaattcca actttaaagg tggcttcaac 1320

[8384] ttctatgcgg ggctgaaggg ccaggtgctg gtgctgcgga caacttcaac tgtctacaat 1380

[8385] tatgattaca tttgggactt tatcttctac cccaacgggg tgatggaggc caagatgcat 1440

[8386] gccactggct acgtccacgc caccttctac acccccgagg ggctgcgcca cggcactcgc 1500

[8387] ctgcacaccc acctgattgg caacatacac actcacttgg tgcactaccg cgtagacctg 1560

[8388] gatgtggcag gcaccaagaa cagcttccag acactgcaga tgaagctaga aaacatcacc 1620

[8389] aacccctgga gcccaagaca ccgcgtggtc cagccaactc tggagcagac gcagtactcc 1680

[8390] tgggagcgcc aggcggcctt cagcttcaaa aggaagctgc ccacgtacct gctctttacc 1740

[8391] agcccccagg agaacccctg gggccacaag cgcagctacc gcctgcagat ccactccatg 1800

[8392] gccgaccagg tgctgccccc aggctggcag gaggagcagg ccatcacctg ggcaaggtac 1860

[8393] cccctggcag tgaccaagta ccgggagtcg gagctgtgca gcagcagcat ctaccaccag 1920

[8394] aacgacccct ggcacccgcc cgtggtcttt gagcagtttc ttcacaacaa cgagaacatt 1980

[8395] gaaaatgagg acctggtggc ctgggtgacg gtgggcttcc tgcacatccc ccactcagag 2040

[8396] gacattccca acacagccac acctgggaac tccgtgggct tcctgctccg gccattcaac 2100

[8397] ttcttcccag aggacccctc cctggcatcc agagacactg tgatcgtgtg gcctcgggac 2160

[8398] aacggcccca actacgtcca gcgctggatc cctgaggaca gggactgctc gatgcctccc 2220

[8399] ccttttagct acaatgggac ctatagacct gtggagccca agtccgccga caagacccac 2280

[8400] acctgccccc cctgccccgc ccccccgtg gccggcccct ccgtgttcct gttccccccc 2340
[8401] aagcccaagg acaccctgat gatctccagg acccccgagg tgacctgcgt ggtggtggac 2400
[8402] gtgtcccacg aggaccccga ggtgaagttc aactggtacg tggacggcgt ggaggtgcac 2460
[8403] aacgccaaga ccaagcccag ggaggagcag tacaactcca cctacagggt ggtgtccgtg 2520
[8404] ctgaccgtgc tgcaccagga ctggctgaac ggcaaggagt acaagtgcaa ggtgtccaac 2580
[8405] aagggcctgc cctcctccat cgagaagacc atctccaagg ccaagggcca gcccagggag 2640
[8406] ccccaggtgt acaccctgcc cccctccagg gaggagatga ccaagaacca ggtgtccctg 2700
[8407] acctgcctgg tgaagggctt ctacccctcc gacatcgccg tggagtggga gtccaacggc 2760
[8408] cagcccgaga acaactacaa gaccaccccc cccgtgctgg actccgacgg ctccttcttc 2820
[8409] ctgtactcca agctgaccgt ggacaagtcc aggtggcagc agggcaacgt gttctcctgc 2880
[8410] tccgtgatgc acgaggccct gcacaaccac tacacccaga agtccctgtc cctgtccccc 2940
[8411] ggcaagtga 2949
[8412] <210> 103
[8413] <211> 585
[8414] <212> PRT
[8415] <213> 智人
[8416] <400> 103
[8417] Asp Ala His Lys Ser Glu Val Ala His Arg Phe Lys Asp Leu Gly Glu
[8418] 1 5 10 15
[8419] Glu Asn Phe Lys Ala Leu Val Leu Ile Ala Phe Ala Gln Tyr Leu Gln
[8420] 20 25 30
[8421] Gln Cys Pro Phe Glu Asp His Val Lys Leu Val Asn Glu Val Thr Glu
[8422] 35 40 45
[8423] Phe Ala Lys Thr Cys Val Ala Asp Glu Ser Ala Glu Asn Cys Asp Lys
[8424] 50 55 60
[8425] Ser Leu His Thr Leu Phe Gly Asp Lys Leu Cys Thr Val Ala Thr Leu
[8426] 65 70 75 80
[8427] Arg Glu Thr Tyr Gly Glu Met Ala Asp Cys Cys Ala Lys Gln Glu Pro
[8428] 85 90 95
[8429] Glu Arg Asn Glu Cys Phe Leu Gln His Lys Asp Asp Asn Pro Asn Leu
[8430] 100 105 110
[8431] Pro Arg Leu Val Arg Pro Glu Val Asp Val Met Cys Thr Ala Phe His
[8432] 115 120 125
[8433] Asp Asn Glu Glu Thr Phe Leu Lys Lys Tyr Leu Tyr Glu Ile Ala Arg
[8434] 130 135 140
[8435] Arg His Pro Tyr Phe Tyr Ala Pro Glu Leu Leu Phe Phe Ala Lys Arg
[8436] 145 150 155 160
[8437] Tyr Lys Ala Ala Phe Thr Glu Cys Cys Gln Ala Ala Asp Lys Ala Ala
[8438] 165 170 175
[8439] Cys Leu Leu Pro Lys Leu Asp Glu Leu Arg Asp Glu Gly Lys Ala Ser
[8440] 180 185 190
[8441] Ser Ala Lys Gln Arg Leu Lys Cys Ala Ser Leu Gln Lys Phe Gly Glu

[8442] 195 200 205

[8443] Arg Ala Phe Lys Ala Trp Ala Val Ala Arg Leu Ser Gln Arg Phe Pro

[8444] 210 215 220

[8445] Lys Ala Glu Phe Ala Glu Val Ser Lys Leu Val Thr Asp Leu Thr Lys

[8446] 225 230 235 240

[8447] Val His Thr Glu Cys Cys His Gly Asp Leu Leu Glu Cys Ala Asp Asp

[8448] 245 250 255

[8449] Arg Ala Asp Leu Ala Lys Tyr Ile Cys Glu Asn Gln Asp Ser Ile Ser

[8450] 260 265 270

[8451] Ser Lys Leu Lys Glu Cys Cys Glu Lys Pro Leu Leu Glu Lys Ser His

[8452] 275 280 285

[8453] Cys Ile Ala Glu Val Glu Asn Asp Glu Met Pro Ala Asp Leu Pro Ser

[8454] 290 295 300

[8455] Leu Ala Ala Asp Phe Val Glu Ser Lys Asp Val Cys Lys Asn Tyr Ala

[8456] 305 310 315 320

[8457] Glu Ala Lys Asp Val Phe Leu Gly Met Phe Leu Tyr Glu Tyr Ala Arg

[8458] 325 330 335

[8459] Arg His Pro Asp Tyr Ser Val Val Leu Leu Leu Arg Leu Ala Lys Thr

[8460] 340 345 350

[8461] Tyr Glu Thr Thr Leu Glu Lys Cys Cys Ala Ala Ala Asp Pro His Glu

[8462] 355 360 365

[8463] Cys Tyr Ala Lys Val Phe Asp Glu Phe Lys Pro Leu Val Glu Glu Pro

[8464] 370 375 380

[8465] Gln Asn Leu Ile Lys Gln Asn Cys Glu Leu Phe Glu Gln Leu Gly Glu

[8466] 385 390 395 400

[8467] Tyr Lys Phe Gln Asn Ala Leu Leu Val Arg Tyr Thr Lys Lys Val Pro

[8468] 405 410 415

[8469] Gln Val Ser Thr Pro Thr Leu Val Glu Val Ser Arg Asn Leu Gly Lys

[8470] 420 425 430

[8471] Val Gly Ser Lys Cys Cys Lys His Pro Glu Ala Lys Arg Met Pro Cys

[8472] 435 440 445

[8473] Ala Glu Asp Tyr Leu Ser Val Val Leu Asn Gln Leu Cys Val Leu His

[8474] 450 455 460

[8475] Glu Lys Thr Pro Val Ser Asp Arg Val Thr Lys Cys Cys Thr Glu Ser

[8476] 465 470 475 480

[8477] Leu Val Asn Arg Arg Pro Cys Phe Ser Ala Leu Glu Val Asp Glu Thr

[8478] 485 490 495

[8479] Tyr Val Pro Lys Glu Phe Asn Ala Glu Thr Phe Thr Phe His Ala Asp

[8480] 500 505 510

[8481] Ile Cys Thr Leu Ser Glu Lys Glu Arg Gln Ile Lys Lys Gln Thr Ala

[8482] 515 520 525

[8483] Leu Val Glu Leu Val Lys His Lys Pro Lys Ala Thr Lys Glu Gln Leu

[8484] 530 535 540
[8485] Lys Ala Val Met Asp Asp Phe Ala Ala Phe Val Glu Lys Cys Cys Lys
[8486] 545 550 555 560
[8487] Ala Asp Asp Lys Glu Thr Cys Phe Ala Glu Glu Gly Lys Lys Leu Val
[8488] 565 570 575
[8489] Ala Ala Ser Gln Ala Ala Leu Gly Leu
[8490] 580 585
[8491] <210> 104
[8492] <211> 21
[8493] <212> DNA
[8494] <213> 人工序列
[8495] <220>
[8496] <223> 正向引物
[8497] <400> 104
[8498] cagaccacag gcttctcatt c 21
[8499] <210> 105
[8500] <211> 18
[8501] <212> DNA
[8502] <213> 人工序列
[8503] <220>
[8504] <223> 反向引物
[8505] <400> 105
[8506] gaggaagaac tgatgcag 18
[8507] <210> 106
[8508] <211> 751
[8509] <212> PRT
[8510] <213> 人工序列
[8511] <220>
[8512] <223> hDAO-Hepmut4 Asn168Gln
[8513] <400> 106
[8514] Met Pro Ala Leu Gly Trp Ala Val Ala Ala Ile Leu Met Leu Gln Thr
[8515] 1 5 10 15
[8516] Ala Met Ala Glu Pro Ser Pro Gly Thr Leu Pro Arg Lys Ala Gly Val
[8517] 20 25 30
[8518] Phe Ser Asp Leu Ser Asn Gln Glu Leu Lys Ala Val His Ser Phe Leu
[8519] 35 40 45
[8520] Trp Ser Lys Lys Glu Leu Arg Leu Gln Pro Ser Ser Thr Thr Thr Met
[8521] 50 55 60
[8522] Ala Lys Asn Thr Val Phe Leu Ile Glu Met Leu Leu Pro Lys Lys Tyr
[8523] 65 70 75 80
[8524] His Val Leu Arg Phe Leu Asp Lys Gly Glu Arg His Pro Val Arg Glu
[8525] 85 90 95

[8526] Ala Arg Ala Val Ile Phe Phe Gly Asp Gln Glu His Pro Asn Val Thr
[8527] 100 105 110
[8528] Glu Phe Ala Val Gly Pro Leu Pro Gly Pro Cys Tyr Met Arg Ala Leu
[8529] 115 120 125
[8530] Ser Pro Arg Pro Gly Tyr Gln Ser Ser Trp Ala Ser Arg Pro Ile Ser
[8531] 130 135 140
[8532] Thr Ala Glu Tyr Ala Leu Leu Tyr His Thr Leu Gln Glu Ala Thr Lys
[8533] 145 150 155 160
[8534] Pro Leu His Gln Phe Phe Leu Gln Thr Thr Gly Phe Ser Phe Gln Asp
[8535] 165 170 175
[8536] Cys His Asp Arg Cys Leu Ala Phe Thr Asp Val Ala Pro Arg Gly Val
[8537] 180 185 190
[8538] Ala Ser Gly Gln Arg Arg Ser Trp Leu Ile Ile Gln Arg Tyr Val Glu
[8539] 195 200 205
[8540] Gly Tyr Phe Leu His Pro Thr Gly Leu Glu Leu Leu Val Asp His Gly
[8541] 210 215 220
[8542] Ser Thr Asp Ala Gly His Trp Ala Val Glu Gln Val Trp Tyr Asn Gly
[8543] 225 230 235 240
[8544] Lys Phe Tyr Gly Ser Pro Glu Glu Leu Ala Arg Lys Tyr Ala Asp Gly
[8545] 245 250 255
[8546] Glu Val Asp Val Val Val Leu Glu Asp Pro Leu Pro Gly Gly Lys Gly
[8547] 260 265 270
[8548] His Asp Ser Thr Glu Glu Pro Pro Leu Phe Ser Ser His Lys Pro Arg
[8549] 275 280 285
[8550] Gly Asp Phe Pro Ser Pro Ile His Val Ser Gly Pro Arg Leu Val Gln
[8551] 290 295 300
[8552] Pro His Gly Pro Arg Phe Arg Leu Glu Gly Asn Ala Val Leu Tyr Gly
[8553] 305 310 315 320
[8554] Gly Trp Ser Phe Ala Phe Arg Leu Arg Ser Ser Ser Gly Leu Gln Val
[8555] 325 330 335
[8556] Leu Asn Val His Phe Gly Gly Glu Arg Ile Ala Tyr Glu Val Ser Val
[8557] 340 345 350
[8558] Gln Glu Ala Val Ala Leu Tyr Gly Gly His Thr Pro Ala Gly Met Gln
[8559] 355 360 365
[8560] Thr Lys Tyr Leu Asp Val Gly Trp Gly Leu Gly Ser Val Thr His Glu
[8561] 370 375 380
[8562] Leu Ala Pro Gly Ile Asp Cys Pro Glu Thr Ala Thr Phe Leu Asp Thr
[8563] 385 390 395 400
[8564] Phe His Tyr Tyr Asp Ala Asp Asp Pro Val His Tyr Pro Arg Ala Leu
[8565] 405 410 415
[8566] Cys Leu Phe Glu Met Pro Thr Gly Val Pro Leu Arg Arg His Phe Asn
[8567] 420 425 430

[8568] Ser Asn Phe Lys Gly Gly Phe Asn Phe Tyr Ala Gly Leu Lys Gly Gln
[8569] 435 440 445
[8570] Val Leu Val Leu Arg Thr Thr Ser Thr Val Tyr Asn Tyr Asp Tyr Ile
[8571] 450 455 460
[8572] Trp Asp Phe Ile Phe Tyr Pro Asn Gly Val Met Glu Ala Lys Met His
[8573] 465 470 475 480
[8574] Ala Thr Gly Tyr Val His Ala Thr Phe Tyr Thr Pro Glu Gly Leu Arg
[8575] 485 490 495
[8576] His Gly Thr Arg Leu His Thr His Leu Ile Gly Asn Ile His Thr His
[8577] 500 505 510
[8578] Leu Val His Tyr Arg Val Asp Leu Asp Val Ala Gly Thr Lys Asn Ser
[8579] 515 520 525
[8580] Phe Gln Thr Leu Gln Met Lys Leu Glu Asn Ile Thr Asn Pro Trp Ser
[8581] 530 535 540
[8582] Pro Arg His Arg Val Val Gln Pro Thr Leu Glu Gln Thr Gln Tyr Ser
[8583] 545 550 555 560
[8584] Trp Glu Arg Gln Ala Ala Phe Ser Phe Lys Thr Lys Leu Pro Lys Tyr
[8585] 565 570 575
[8586] Leu Leu Phe Thr Ser Pro Gln Glu Asn Pro Trp Gly His Lys Arg Ser
[8587] 580 585 590
[8588] Tyr Arg Leu Gln Ile His Ser Met Ala Asp Gln Val Leu Pro Pro Gly
[8589] 595 600 605
[8590] Trp Gln Glu Glu Gln Ala Ile Thr Trp Ala Arg Tyr Pro Leu Ala Val
[8591] 610 615 620
[8592] Thr Lys Tyr Arg Glu Ser Glu Leu Cys Ser Ser Ser Ile Tyr His Gln
[8593] 625 630 635 640
[8594] Asn Asp Pro Trp His Pro Pro Val Val Phe Glu Gln Phe Leu His Asn
[8595] 645 650 655
[8596] Asn Glu Asn Ile Glu Asn Glu Asp Leu Val Ala Trp Val Thr Val Gly
[8597] 660 665 670
[8598] Phe Leu His Ile Pro His Ser Glu Asp Ile Pro Asn Thr Ala Thr Pro
[8599] 675 680 685
[8600] Gly Asn Ser Val Gly Phe Leu Leu Arg Pro Phe Asn Phe Phe Pro Glu
[8601] 690 695 700
[8602] Asp Pro Ser Leu Ala Ser Arg Asp Thr Val Ile Val Trp Pro Arg Asp
[8603] 705 710 715 720
[8604] Asn Gly Pro Asn Tyr Val Gln Arg Trp Ile Pro Glu Asp Arg Asp Cys
[8605] 725 730 735
[8606] Ser Met Pro Pro Pro Phe Ser Tyr Asn Gly Thr Tyr Arg Pro Val
[8607] 740 745 750

hDAO-野生型

MPALGWAVAAILMLQTAMAEPSPGTLPRKAGVFSDLSNQELKAVHSFLWSKKELRLQPSSTTTMAKNT
VFLIEMLLPKKYHVLRFLDKGERHPVREARAVIFFGDQEHPNVTEFAVGPLPGPCYMRALSPRPGYQSS
WASRPISTAEYALLYHTLQEATKPLHQFFL**N**TTGFSFQDCHDRCLAFTDVAPRGVASGQRRSWLIIQRY
VEGYFLHPTGLELLVDHGSTDAGHWAVEQVWYNGKFYGSPEELARKYADGEVDVVVLEDPLPGGKGH
DSTEEPPLFSSHKPRGDFPSPIHVSGPRLVQPHGPRFRLEGNAVLYGGWSFAFRLRSSSGLQVLNVHF
GGERIAYEVSVQEAVALYGGHTPAGMQTKYLDVGWGLGSVTHELAPGIDCPETATFLDTFHYYDADDP
VHYPRALCLFEMPTGVPLRRHFNSNFKGGFNFYAGLKGQVLVLRTTSTVYNYDYIWDFIFYPNGVMEAK
MHATGYVHATFYTPEGLRHGTRLHTHLIGNIHTHLVHYRVDLDVAGTKNSFQTLQMKLENITNPWSPRH
RVVQPTLEQTQYSWERQAAFRFKRKLPKYLLFTSPQENPWGHKRSYRLQIHSMADQVLPPGWQEEQA
ITWARYPLAVTKYRESELCSSSIYHQNDPWHPPVVFEQFLHNNENIENEDLVAWVTVGFLHIPHSEDIPN
TATPGNSVGFLLRPFNFFPEDPSLASRDTVIVWPRDNGPNYVQRWIPEDRDCSMPPPFSYNGTYRPV
(SEQ ID NO:1)

hDAO-Hepmut1

MPALGWAVAAILMLQTAMAEPSPGTLPRKAGVFSDLSNQELKAVHSFLWSKKELRLQPSSTTTMAKNT
VFLIEMLLPKKYHVLRFLDKGERHPVREARAVIFFGDQEHPNVTEFAVGPLPGPCYMRALSPRPGYQSS
WASRPISTAEYALLYHTLQEATKPLHQFFLNTTGFSFQDCHDRCLAFTDVAPRGVASGQRRSWLIIQRY
VEGYFLHPTGLELLVDHGSTDAGHWAVEQVWYNGKFYGSPEELARKYADGEVDVVVLEDPLPGGKGH
DSTEEPPLFSSHKPRGDFPSPIHVSGPRLVQPHGPRFRLEGNAVLYGGWSFAFRLRSSSGLQVLNVHF
GGERIAYEVSVQEAVALYGGHTPAGMQTKYLDVGWGLGSVTHELAPGIDCPETATFLDTFHYYDADDP
VHYPRALCLFEMPTGVPLRRHFNSNFKGGFNFYAGLKGQVLVLRTTSTVYNYDYIWDFIFYPNGVMEAK
MHATGYVHATFYTPEGLRHGTRLHTHLIGNIHTHLVHYRVDLDVAGTKNSFQTLQMKLENITNPWSPRH
RVVQPTLEQTQYSWERQAAF**S**FKRKLPKYLLFTSPQENPWGHKRSYRLQIHSMADQVLPPGWQEEQA
ITWARYPLAVTKYRESELCSSSIYHQNDPWHPPVVFEQFLHNNENIENEDLVAWVTVGFLHIPHSEDIPN
TATPGNSVGFLLRPFNFFPEDPSLASRDTVIVWPRDNGPNYVQRWIPEDRDCSMPPPFSYNGTYRPV
(SEQ ID NO:2)

hDAO-Hepmut2

MPALGWAVAAILMLQTAMAEPSPGTLPRKAGVFSDLSNQELKAVHSFLWSKKELRLQPSSTTTMAKNT
VFLIEMLLPKKYHVLRFLDKGERHPVREARAVIFFGDQEHPNVTEFAVGPLPGPCYMRALSPRPGYQSS
WASRPISTAEYALLYHTLQEATKPLHQFFLNTTGFSFQDCHDRCLAFTDVAPRGVASGQRRSWLIIQRY
VEGYFLHPTGLELLVDHGSTDAGHWAVEQVWYNGKFYGSPEELARKYADGEVDVVVLEDPLPGGKGH
DSTEEPPLFSSHKPRGDFPSPIHVSGPRLVQPHGPRFRLEGNAVLYGGWSFAFRLRSSSGLQVLNVHF
GGERIAYEVSVQEAVALYGGHTPAGMQTKYLDVGWGLGSVTHELAPGIDCPETATFLDTFHYYDADDP
VHYPRALCLFEMPTGVPLRRHFNSNFKGGFNFYAGLKGQVLVLRTTSTVYNYDYIWDFIFYPNGVMEAK
MHATGYVHATFYTPEGLRHGTRLHTHLIGNIHTHLVHYRVDLDVAGTKNSFQTLQMKLENITNPWSPRH
RVVQPTLEQTQYSWERQAAFRFKRKLP**T**YLLFTSPQENPWGHKRSYRLQIHSMADQVLPPGWQEEQA
ITWARYPLAVTKYRESELCSSSIYHQNDPWHPPVVFEQFLHNNENIENEDLVAWVTVGFLHIPHSEDIPN
TATPGNSVGFLLRPFNFFPEDPSLASRDTVIVWPRDNGPNYVQRWIPEDRDCSMPPPFSYNGTYRPV
(SEQ ID NO:3)

hDAO-Hepmut3

MPALGWAVAAILMLQTAMAEPSPGTLPRKAGVFSDLSNQELKAVHSFLWSKKELRLQPSSTTTMAKNT
VFLIEMLLPKKYHVLRFLDKGERHPVREARAVIFFGDQEHPNVTEFAVGPLPGPCYMRALSPRPGYQSS
WASRPISTAEYALLYHTLQEATKPLHQFFLNTTGFSFQDCHDRCLAFTDVAPRGVASGQRRSWLIIQRY
VEGYFLHPTGLELLVDHGSTDAGHWAVEQVWYNGKFYGSPEELARKYADGEVDVVVLEDPLPGGKGH
DSTEEPPLFSSHKPRGDFPSPIHVSGPRLVQPHGPRFRLEGNAVLYGGWSFAFRLRSSSGLQVLNVHF
GGERIAYEVSVQEAVALYGGHTPAGMQTKYLDVGWGLGSVTHELAPGIDCPETATFLDTFHYYDADDP
VHYPRALCLFEMPTGVPLRRHFNSNFKGGFNFYAGLKGQVLVLRTTSTVYNYDYIWDFIFYPNGVMEAK
MHATGYVHATFYTPEGLRHGTRLHTHLIGNIHTHLVHYRVDLDVAGTKNSFQTLQMKLENITNPWSPRH
RVVQPTLEQTQYSWERQAAFRF**K**T**K**LPKYLLFTSPQENPWGHKRSYRLQIHSMADQVLPPGWQEEQA
ITWARYPLAVTKYRESELCSSSIYHQNDPWHPPVVFEQFLHNNENIENEDLVAWVTVGFLHIPHSEDIPN
TATPGNSVGFLLRPFNFFPEDPSLASRDTVIVWPRDNGPNYVQRWIPEDRDCSMPPPFSYNGTYRPV
(SEQ ID NO:4)

图1

hDAO-Hepmut4

MPALGWAVAAILMLQTAMAEPSPGTLPRKAGVFSDLSNQELKAVHSFLWSKKELRLQPSSTTTMAKNT
VFLIEMLLPKKYHVLRFLDKGERHPVREARAVIFFGDQEHPNVTEFAVGPLPGPCYMRALSPRPGYQSS
WASRPISTAEYALLYHTLQEATKPLHQFFLNTTGFSFQDCHDRCLAFTDVAPRGVASGQRRSWLIIQRY
VEGYFLHPTGLELLVDHGSTDAGHWAVEQVWYNGKFYGSPEELARKYADGEVDVVVLEDPLPGGKGH
DSTEEPPLFSSHKPRGDFPSPIHVSGPRLVQPHGPRFRLEGNAVLYGGWSFAFRLRSSSGLQVLNVHF
GGERIAYEVSVQEAVALYGGHTPAGMQTKYLDVGWGLGSVTHELAPGIDCPETATFLDTFHYYDADDP
VHYPRALCLFEMPTGVPLRRHFNSNFKGGFNFYAGLKGQVLVLRTTSTVYNYDYIWDFIFYPNGVMEAK
MHATGYVHATFYTPEGLRHGTRLHTHLIGNIHTHLVHYRVDLDVAGTKNSFQTLQMKLENITNPWSPRH
RVVQPTLEQTQYSWERQAAFSFKTKLPKYLLFTSPQENPWGHKRSYRLQIHSMADQVLPPGWQEEQAI
TWARYPLAVTKYRESELCSSSIYHQNDPWHPPVVFEQFLHNNENIENEDLVAWVTVGFLHIPHSEDIPN
TATPGNSVGFLLRPFNFFPEDPSLASRDTVIVWPRDNGPNYVQRWIPEDRDCSMPPPFSYNGTYRPV
(SEQ ID NO:5)

hDAO-Hepmut5

MPALGWAVAAILMLQTAMAEPSPGTLPRKAGVFSDLSNQELKAVHSFLWSKKELRLQPSSTTTMAKNT
VFLIEMLLPKKYHVLRFLDKGERHPVREARAVIFFGDQEHPNVTEFAVGPLPGPCYMRALSPRPGYQSS
WASRPISTAEYALLYHTLQEATKPLHQFFLNTTGFSFQDCHDRCLAFTDVAPRGVASGQRRSWLIIQRY
VEGYFLHPTGLELLVDHGSTDAGHWAVEQVWYNGKFYGSPEELARKYADGEVDVVVLEDPLPGGKGH
DSTEEPPLFSSHKPRGDFPSPIHVSGPRLVQPHGPRFRLEGNAVLYGGWSFAFRLRSSSGLQVLNVHF
GGERIAYEVSVQEAVALYGGHTPAGMQTKYLDVGWGLGSVTHELAPGIDCPETATFLDTFHYYDADDP
VHYPRALCLFEMPTGVPLRRHFNSNFKGGFNFYAGLKGQVLVLRTTSTVYNYDYIWDFIFYPNGVMEAK
MHATGYVHATFYTPEGLRHGTRLHTHLIGNIHTHLVHYRVDLDVAGTKNSFQTLQMKLENITNPWSPRH
RVVQPTLEQTQYSWERQAAFRFKTKLPTYLLFTSPQENPWGHKRSYRLQIHSMADQVLPPGWQEEQAI
TWARYPLAVTKYRESELCSSSIYHQNDPWHPPVVFEQFLHNNENIENEDLVAWVTVGFLHIPHSEDIPN
TATPGNSVGFLLRPFNFFPEDPSLASRDTVIVWPRDNGPNYVQRWIPEDRDCSMPPPFSYNGTYRPV
(SEQ ID NO:6)

hDAO-Hepmut6

MPALGWAVAAILMLQTAMAEPSPGTLPRKAGVFSDLSNQELKAVHSFLWSKKELRLQPSSTTTMAKNT
VFLIEMLLPKKYHVLRFLDKGERHPVREARAVIFFGDQEHPNVTEFAVGPLPGPCYMRALSPRPGYQSS
WASRPISTAEYALLYHTLQEATKPLHQFFLNTTGFSFQDCHDRCLAFTDVAPRGVASGQRRSWLIIQRY
VEGYFLHPTGLELLVDHGSTDAGHWAVEQVWYNGKFYGSPEELARKYADGEVDVVVLEDPLPGGKGH
DSTEEPPLFSSHKPRGDFPSPIHVSGPRLVQPHGPRFRLEGNAVLYGGWSFAFRLRSSSGLQVLNVHF
GGERIAYEVSVQEAVALYGGHTPAGMQTKYLDVGWGLGSVTHELAPGIDCPETATFLDTFHYYDADDP
VHYPRALCLFEMPTGVPLRRHFNSNFKGGFNFYAGLKGQVLVLRTTSTVYNYDYIWDFIFYPNGVMEAK
MHATGYVHATFYTPEGLRHGTRLHTHLIGNIHTHLVHYRVDLDVAGTKNSFQTLQMKLENITNPWSPRH
RVVQPTLEQTQYSWERQAAFRFGQTLPKYLLFTSPQENPWGHKRSYRLQIHSMADQVLPPGWQEEQA
ITWARYPLAVTKYRESELCSSSIYHQNDPWHPPVVFEQFLHNNENIENEDLVAWVTVGFLHIPHSEDIPN
TATPGNSVGFLLRPFNFFPEDPSLASRDTVIVWPRDNGPNYVQRWIPEDRDCSMPPPFSYNGTYRPV
(SEQ ID NO:7)

hDAO-Hepmut7

MPALGWAVAAILMLQTAMAEPSPGTLPRKAGVFSDLSNQELKAVHSFLWSKKELRLQPSSTTTMAKNT
VFLIEMLLPKKYHVLRFLDKGERHPVREARAVIFFGDQEHPNVTEFAVGPLPGPCYMRALSPRPGYQSS
WASRPISTAEYALLYHTLQEATKPLHQFFLNTTGFSFQDCHDRCLAFTDVAPRGVASGQRRSWLIIQRY
VEGYFLHPTGLELLVDHGSTDAGHWAVEQVWYNGKFYGSPEELARKYADGEVDVVVLEDPLPGGKGH
DSTEEPPLFSSHKPRGDFPSPIHVSGPRLVQPHGPRFRLEGNAVLYGGWSFAFRLRSSSGLQVLNVHF
GGERIAYEVSVQEAVALYGGHTPAGMQTKYLDVGWGLGSVTHELAPGIDCPETATFLDTFHYYDADDP
VHYPRALCLFEMPTGVPLRRHFNSNFKGGFNFYAGLKGQVLVLRTTSTVYNYDYIWDFIFYPNGVMEAK
MHATGYVHATFYTPEGLRHGTRLHTHLIGNIHTHLVHYRVDLDVAGTKNSFQTLQMKLENITNPWSPRH
RVVQPTLEQTQYSWERQAAFSFKRKLPTYLLFTSPQENPWGHKRSYRLQIHSMADQVLPPGWQEEQA
ITWARYPLAVTKYRESELCSSSIYHQNDPWHPPVVFEQFLHNNENIENEDLVAWVTVGFLHIPHSEDIPN
TATPGNSVGFLLRPFNFFPEDPSLASRDTVIVWPRDNGPNYVQRWIPEDRDCSMPPPFSYNGTYRPV
(SEQ ID NO:8)

图1续

hDAO-Cysmut

MPALGWAVAAILMLQTAMAEPSPGTLPRKAGVFSDLSNQELKAVHSFLWSKKELRLQPSSTTTMAKNT
VFLIEMLLPKKYHVLRFLDKGERHPVREARAVIFFGDQEHPNVTEFAVGPLPGPAYMRALSPRPGYQSS
WASRPISTAEYALLYHTLQEATKPLHQFFLNTTGFSFQDCHDRCLAFTDVAPRGVASGQRRSWLIIQRY
VEGYFLHPTGLELLVDHGSTDAGHWAVEQVWYNGKFYGSPEELARKYADGEVDVVVLEDPLPGGKGH
DSTEEPPLFSSHKPRGDFPSPIHVSGPRLVQPHGPRFRLEGNAVLYGGWSFAFRLRSSSGLQVLNVHF
GGERIAYEVSVQEAVALYGGHTPAGMQTKYLDVGWGLGSVTHELAPGIDCPETATFLDTFHYYDADDP
VHYPRALCLFEMPTGVPLRRHFNSNFKGGFNFYAGLKGQVLVLRTTSTVYNYDYIWDFIFYPNGVMEAK
MHATGYVHATFYTPEGLRHGTRLHTHLIGNIHTHLVHYRVDLDVAGTKNSFQTLQMKLENITNPWSPRH
RVVQPTLEQTQYSWERQAAFRFKRKLPKYLLFTSPQENPWGHKRSYRLQIHSMADQVLPPGWQEEQA
ITWARYPLAVTKYRESELCSSSIYHQNDPWHPPVVFEQFLHNNENIENEDLVAWVTVGFLHIPHSEDIPN
TATPGNSVGFLLRPFNFFPEDPSLASRDTVIVWPRDNGPNYVQRWIPEDRDCSMPPPFSYNGTYRPV
(SEQ ID NO:9)

hDAO-Hepmut1-Cysmut

MPALGWAVAAILMLQTAMAEPSPGTLPRKAGVFSDLSNQELKAVHSFLWSKKELRLQPSSTTTMAKNT
VFLIEMLLPKKYHVLRFLDKGERHPVREARAVIFFGDQEHPNVTEFAVGPLPGPAYMRALSPRPGYQSS
WASRPISTAEYALLYHTLQEATKPLHQFFLNTTGFSFQDCHDRCLAFTDVAPRGVASGQRRSWLIIQRY
VEGYFLHPTGLELLVDHGSTDAGHWAVEQVWYNGKFYGSPEELARKYADGEVDVVVLEDPLPGGKGH
DSTEEPPLFSSHKPRGDFPSPIHVSGPRLVQPHGPRFRLEGNAVLYGGWSFAFRLRSSSGLQVLNVHF
GGERIAYEVSVQEAVALYGGHTPAGMQTKYLDVGWGLGSVTHELAPGIDCPETATFLDTFHYYDADDP
VHYPRALCLFEMPTGVPLRRHFNSNFKGGFNFYAGLKGQVLVLRTTSTVYNYDYIWDFIFYPNGVMEAK
MHATGYVHATFYTPEGLRHGTRLHTHLIGNIHTHLVHYRVDLDVAGTKNSFQTLQMKLENITNPWSPRH
RVVQPTLEQTQYSWERQAAFSFKRKLPKYLLFTSPQENPWGHKRSYRLQIHSMADQVLPPGWQEEQA
ITWARYPLAVTKYRESELCSSSIYHQNDPWHPPVVFEQFLHNNENIENEDLVAWVTVGFLHIPHSEDIPN
TATPGNSVGFLLRPFNFFPEDPSLASRDTVIVWPRDNGPNYVQRWIPEDRDCSMPPPFSYNGTYRPV
(SEQ ID NO:10)

hDAO-Hepmut2-Cysmut

MPALGWAVAAILMLQTAMAEPSPGTLPRKAGVFSDLSNQELKAVHSFLWSKKELRLQPSSTTTMAKNT
VFLIEMLLPKKYHVLRFLDKGERHPVREARAVIFFGDQEHPNVTEFAVGPLPGPAYMRALSPRPGYQSS
WASRPISTAEYALLYHTLQEATKPLHQFFLNTTGFSFQDCHDRCLAFTDVAPRGVASGQRRSWLIIQRY
VEGYFLHPTGLELLVDHGSTDAGHWAVEQVWYNGKFYGSPEELARKYADGEVDVVVLEDPLPGGKGH
DSTEEPPLFSSHKPRGDFPSPIHVSGPRLVQPHGPRFRLEGNAVLYGGWSFAFRLRSSSGLQVLNVHF
GGERIAYEVSVQEAVALYGGHTPAGMQTKYLDVGWGLGSVTHELAPGIDCPETATFLDTFHYYDADDP
VHYPRALCLFEMPTGVPLRRHFNSNFKGGFNFYAGLKGQVLVLRTTSTVYNYDYIWDFIFYPNGVMEAK
MHATGYVHATFYTPEGLRHGTRLHTHLIGNIHTHLVHYRVDLDVAGTKNSFQTLQMKLENITNPWSPRH
RVVQPTLEQTQYSWERQAAFRFKRKLPTYLLFTSPQENPWGHKRSYRLQIHSMADQVLPPGWQEEQA
ITWARYPLAVTKYRESELCSSSIYHQNDPWHPPVVFEQFLHNNENIENEDLVAWVTVGFLHIPHSEDIPN
TATPGNSVGFLLRPFNFFPEDPSLASRDTVIVWPRDNGPNYVQRWIPEDRDCSMPPPFSYNGTYRPV
(SEQ ID NO:11)

hDAO-Hepmut3-Cysmut

MPALGWAVAAILMLQTAMAEPSPGTLPRKAGVFSDLSNQELKAVHSFLWSKKELRLQPSSTTTMAKNT
VFLIEMLLPKKYHVLRFLDKGERHPVREARAVIFFGDQEHPNVTEFAVGPLPGPAYMRALSPRPGYQSS
WASRPISTAEYALLYHTLQEATKPLHQFFLNTTGFSFQDCHDRCLAFTDVAPRGVASGQRRSWLIIQRY
VEGYFLHPTGLELLVDHGSTDAGHWAVEQVWYNGKFYGSPEELARKYADGEVDVVVLEDPLPGGKGH
DSTEEPPLFSSHKPRGDFPSPIHVSGPRLVQPHGPRFRLEGNAVLYGGWSFAFRLRSSSGLQVLNVHF
GGERIAYEVSVQEAVALYGGHTPAGMQTKYLDVGWGLGSVTHELAPGIDCPETATFLDTFHYYDADDP
VHYPRALCLFEMPTGVPLRRHFNSNFKGGFNFYAGLKGQVLVLRTTSTVYNYDYIWDFIFYPNGVMEAK
MHATGYVHATFYTPEGLRHGTRLHTHLIGNIHTHLVHYRVDLDVAGTKNSFQTLQMKLENITNPWSPRH
RVVQPTLEQTQYSWERQAAFRFKTKLPKYLLFTSPQENPWGHKRSYRLQIHSMADQVLPPGWQEEQA
ITWARYPLAVTKYRESELCSSSIYHQNDPWHPPVVFEQFLHNNENIENEDLVAWVTVGFLHIPHSEDIPN
TATPGNSVGFLLRPFNFFPEDPSLASRDTVIVWPRDNGPNYVQRWIPEDRDCSMPPPFSYNGTYRPV
(SEQ ID NO:12)

图1续

hDAO-Hepmut4-Cysmut

MPALGWAVAAILMLQTAMAEPSPGTLPRKAGVFSDLSNQELKAVHSFLWSKKELRLQPSSTTTMAKNT
VFLIEMLLPKKYHVLRFLDKGERHPVREARAVIFFGDQEHPNVTEFAVGPLPGP**A**YMRALSPRPGYQSS
WASRPISTAEYALLYHTLQEATKPLHQFFLNTTGFSFQDCHDRCLAFTDVAPRGVASGQRRSWLIIQRY
VEGYFLHPTGLELLVDHGSTDAGHWAVEQVWYNGKFYGSPEELARKYADGEVDVVVLEDPLPGGKGH
DSTEEPPLFSSHKPRGDFPSPIHVSGPRLVQPHGPRFRLEGNAVLYGGWSFAFRLRSSSGLQVLNVHF
GGERIAYEVSVQEAVALYGGHTPAGMQTKYLDVGWGLGSVTHELAPGIDCPETATFLDTFHYYDADDP
VHYPRALCLFEMPTGVPLRRHFNSNFKGGFNFYAGLKGQVLVLRTTSTVYNYDYIWDFIFYPNGVMEAK
MHATGYVHATFYTPEGLRHGTRLHTHLIGNIHTHLVHYRVDLDVAGTKNSFQTLQMKLENITNPWSPRH
RVVQPTLEQTQYSWERQAAF**S**FK**T**KLPKYLLFTSPQENPWGHKRSYRLQIHSMADQVLPPGWQEEQAI
TWARYPLAVTKYRESELCSSSIYHQNDPWHPPVVFEQFLHNNENIENEDLVAWVTVGFLHIPHSEDIPN
TATPGNSVGFLLRPFNFFPEDPSLASRDTVIVWPRDNGPNYVQRWIPEDRDCSMPPPFSYNGTYRPV
(SEQ ID NO:13)

hDAO-Hepmut5-Cysmut

MPALGWAVAAILMLQTAMAEPSPGTLPRKAGVFSDLSNQELKAVHSFLWSKKELRLQPSSTTTMAKNT
VFLIEMLLPKKYHVLRFLDKGERHPVREARAVIFFGDQEHPNVTEFAVGPLPGP**A**YMRALSPRPGYQSS
WASRPISTAEYALLYHTLQEATKPLHQFFLNTTGFSFQDCHDRCLAFTDVAPRGVASGQRRSWLIIQRY
VEGYFLHPTGLELLVDHGSTDAGHWAVEQVWYNGKFYGSPEELARKYADGEVDVVVLEDPLPGGKGH
DSTEEPPLFSSHKPRGDFPSPIHVSGPRLVQPHGPRFRLEGNAVLYGGWSFAFRLRSSSGLQVLNVHF
GGERIAYEVSVQEAVALYGGHTPAGMQTKYLDVGWGLGSVTHELAPGIDCPETATFLDTFHYYDADDP
VHYPRALCLFEMPTGVPLRRHFNSNFKGGFNFYAGLKGQVLVLRTTSTVYNYDYIWDFIFYPNGVMEAK
MHATGYVHATFYTPEGLRHGTRLHTHLIGNIHTHLVHYRVDLDVAGTKNSFQTLQMKLENITNPWSPRH
RVVQPTLEQTQYSWERQAAFRF**K**T**K**LP**T**YLLFTSPQENPWGHKRSYRLQIHSMADQVLPPGWQEEQAI
TWARYPLAVTKYRESELCSSSIYHQNDPWHPPVVFEQFLHNNENIENEDLVAWVTVGFLHIPHSEDIPN
TATPGNSVGF**L**LRPFNFFPEDPSLASRDTVIVWPRDNGPNYVQRWIPEDRDCSMPPPFSYNGTYRPV
(SEQ ID NO:14)

hDAO-Hepmut6-Cysmut

MPALGWAVAAILMLQTAMAEPSPGTLPRKAGVFSDLSNQELKAVHSFLWSKKELRLQPSSTTTMAKNT
VFLIEMLLPKKYHVLRFLDKGERHPVREARAVIFFGDQEHPNVTEFAVGPLPGP**A**YMRALSPRPGYQSS
WASRPISTAEYALLYHTLQEATKPLHQFFLNTTGFSFQDCHDRCLAFTDVAPRGVASGQRRSWLIIQRY
VEGYFLHPTGLELLVDHGSTDAGHWAVEQVWYNGKFYGSPEELARKYADGEVDVVVLEDPLPGGKGH
DSTEEPPLFSSHKPRGDFPSPIHVSGPRLVQPHGPRFRLEGNAVLYGGWSFAFRLRSSSGLQVLNVHF
GGERIAYEVSVQEAVALYGGHTPAGMQTKYLDVGWGLGSVTHELAPGIDCPETATFLDTFHYYDADDP
VHYPRALCLFEMPTGVPLRRHFNSNFKGGFNFYAGLKGQVLVLRTTSTVYNYDYIWDFIFYPNGVMEAK
MHATGYVHATFYTPEGLRHGTRLHTHLIGNIHTHLVHYRVDLDVAGTKNSFQTLQMKLENITNPWSPRH
RVVQPTLEQTQYSWERQAAFRF**GQT**LPKYLLFTSPQENPWGHKRSYRLQIHSMADQVLPPGWQEEQA
ITWARYPLAVTKYRESELCSSSIYHQNDPWHPPVVFEQFLHNNENIENEDLVAWVTVGFLHIPHSEDIPN
TATPGNSVGFLLRPFNFFPEDPSLASRDTVIVWPRDNGPNYVQRWIPEDRDCSMPPPFSYNGTYRPV
(SEQ ID NO:15)

hDAO-Hepmut7-Cysmut

MPALGWAVAAILMLQTAMAEPSPGTLPRKAGVFSDLSNQELKAVHSFLWSKKELRLQPSSTTTMAKNT
VFLIEMLLPKKYHVLRFLDKGERHPVREARAVIFFGDQEHPNVTEFAVGPLPGP**A**YMRALSPRPGYQSS
WASRPISTAEYALLYHTLQEATKPLHQFFLNTTGFSFQDCHDRCLAFTDVAPRGVASGQRRSWLIIQRY
VEGYFLHPTGLELLVDHGSTDAGHWAVEQVWYNGKFYGSPEELARKYADGEVDVVVLEDPLPGGKGH
DSTEEPPLFSSHKPRGDFPSPIHVSGPRLVQPHGPRFRLEGNAVLYGGWSFAFRLRSSSGLQVLNVHF
GGERIAYEVSVQEAVALYGGHTPAGMQTKYLDVGWGLGSVTHELAPGIDCPETATFLDTFHYYDADDP
VHYPRALCLFEMPTGVPLRRHFNSNFKGGFNFYAGLKGQVLVLRTTSTVYNYDYIWDFIFYPNGVMEAK
MHATGYVHATFYTPEGLRHGTRLHTHLIGNIHTHLVHYRVDLDVAGTKNSFQTLQMKLENITNPWSPRH
RVVQPTLEQTQYSWERQAAF**S**FKRKLP**T**YLLFTSPQENPWGHKRSYRLQIHSMADQVLPPGWQEEQA
ITWARYPLAVTKYRESELCSSSIYHQNDPWHPPVVFEQFLHNNENIENEDLVAWVTVGFLHIPHSEDIPN
TATPGNSVGFLLRPFNFFPEDPSLASRDTVIVWPRDNGPNYVQRWIPEDRDCSMPPPFSYNGTYRPV
(SEQ ID NO:16)

图1续

hDAO-野生型

atgccggccctgggctgggccgtggctgccatcctgatgctgcagacggccatggcggagccctccccggggactctgcccaggaa
ggcaggggtgttttcagacctaagcaaccaagagctgaaggcagtgcacagcttcctctggtccaagaaggagctgaggctgcagccctccagt
accaccaccatggccaagaacaccgtgtttctcatcgagatgctgctgcccaagaagtaccatgtgctgaggtttctggataaaggtgaaaggcat
cctgtgcgggaagcccgtgccgtcatcttctttggtgaccaggagcatcccaatgtcaccgagtttgctgtggggcccctgccagggccctgctaca
tgcgagcactgtccccaggcctgggtaccagtcctcctgggcatcgaggcccatctccacagcagagtatgccctcctctaccacaccctgcag
gaagccaccaagcccctgcatcagttcttcctcaataccacaggcttctcattccaagactgccatgacagatgcctggccttcaccgatgtggccc
cccggggtgtggcttctggccagcgccgcagttggcttatcatacagcgctatgtagaaggctactttctgcaccccactgggctggagctcctcgtg
gatcatgggagcacagatgctgggcactgggccgtggagcaggtgtggtacaacgggaagttctatgggagcccagaggaactggctcggaa
gtatgcagatggagaggtggacgtggtggtcctggaggacccgctgcctgggggcaaggggcatgacagcacagaggagccgcccctcttctc
ctcccacaagccccgcggggacttccccagccccatccatgtgagcggccccgcttggtccagccccacggccctcgcttcaggctggaggg
caacgctgtgctctacggcggctggagctttgccttccggctgcgctcctcctccgggctgcaggtcctgaacgtgcacttcggcggagagcgcatt
gcctatgaggtcagcgtgcaagaggcagtggcgctgtatggaggacacacacctgcaggcatgcagaccaagtacctcgatgtcggctggggc
ctgggcagcgtcactcatgagttagccccggcatcgactgcccggagacgccacctttcctggacactttccactactatgatgccgatgacccg
gtccattatccccgagccctctgcctctttgaaatgcccacaggggtgcccttcggcggcactttaattccaactttaaaggtggcttcaacttctatg
cggggctgaagggccaggtgctggtgctgcggacaacttcaactgtctacaattatgattacatttgggactttatcttctaccccaacggggtgatg
gaggccaagatgcatgccactggctacgtccacgccacctttctacacccccgaggggctgcgccacggcactcgcctgcacacccacctgattg
gcaacatacacactcacttggtgcactaccgcgtagacctggatgtggcaggcaccaagaacagcttccagacactgcagatgaagctagaaa
acatcaccaaccccctggagcccaagacaccgcgtggtccagccaactctggagcagacgcagtactcctgggagcgccaggcggccttccgc
ttcaaaaggaagctgcccaagtacctgctctttaccagcccccaggagaaccctggggccacaagcgcagctaccgcctgcagatccactcc
atggccgaccaggtgctgcccccaggctggcaggaggagcaggccatcacctgggcaaggtacccccctggcagtgaccaagtaccgggagt
cggagctgtgcagcagcagcatctaccaccagaacgacccctggcacccgcccgtggtctttgagcagtttcttcacaacaacgagaacattga
aaatgaggacctggtggcctgggtgacggtgggcttcctgcacatccccccactcagaggacattcccaacacagccacacctgggaactccgtg
ggcttcctgctccggccattcaacttcttcccagaggacccctccctggcatccagagacactgtgatcgtgtggcctcgggacaacggccccaac
tacgtccagcgctggatccctgaggacagggactgctcgatgcctccccctttagctacaatgggacctatagacctgtgtga (SEQ ID NO:17)

hDAO-Hepmut1

atgccggccctgggctgggccgtggctgccatcctgatgctgcagacggccatggcggagccctccccggggactctgcccaggaa
ggcaggggtgttttcagacctaagcaaccaagagctgaaggcagtgcacagcttcctctggtccaagaaggagctgaggctgcagccctccagt
accaccaccatggccaagaacaccgtgtttctcatcgagatgctgctgcccaagaagtaccatgtgctgaggtttctggataaaggtgaaaggcat
cctgtgcgggaagcccgtgccgtcatcttctttggtgaccaggagcatcccaatgtcaccgagtttgctgtggggcccctgccagggccctgctaca
tgcgagcactgtccccaggcctgggtaccagtcctcctgggcatcgaggcccatctccacagcagagtatgccctcctctaccacaccctgcag
gaagccaccaagcccctgcatcagttcttcctcaataccacaggcttctcattccaagactgccatgacagatgcctggccttcaccgatgtggccc
cccggggtgtggcttctggccagcgccgcagttggcttatcatacagcgctatgtagaaggctactttctgcaccccactgggctggagctcctcgtg
gatcatgggagcacagatgctgggcactgggccgtggagcaggtgtggtacaacgggaagttctatgggagcccagaggaactggctcggaa
gtatgcagatggagaggtggacgtggtggtcctggaggacccgctgcctgggggcaaggggcatgacagcacagaggagccgcccctcttctc
ctcccacaagccccgcggggacttccccagccccatccatgtgagcggccccgcttggtccagccccacggccctcgcttcaggctggaggg
caacgctgtgctctacggcggctggagctttgccttccggctgcgctcctcctccgggctgcaggtcctgaacgtgcacttcggcggagagcgcatt
gcctatgaggtcagcgtgcaagaggcagtggcgctgtatggaggacacacacctgcaggcatgcagaccaagtacctcgatgtcggctggggc
ctgggcagcgtcactcatgagttagccccggcatcgactgcccggagacgccacctttcctggacactttccactactatgatgccgatgacccg
gtccattatccccgagccctctgcctctttgaaatgcccacaggggtgcccttcggcggcactttaattccaactttaaaggtggcttcaacttctatg
cggggctgaagggccaggtgctggtgctgcggacaacttcaactgtctacaattatgattacatttgggactttatcttctaccccaacggggtgatg
gaggccaagatgcatgccactggctacgtccacgccacctttctacacccccgaggggctgcgccacggcactcgcctgcacacccacctgattg
gcaacatacacactcacttggtgcactaccgcgtagacctggatgtggcaggcaccaagaacagcttccagacactgcagatgaagctagaaa
acatcaccaaccccctggagcccaagacaccgcgtggtccagccaactctggagcagacgcagtactcctgggagcgccaggcggccttc**ag**
cttcaaaaggaagctgcccaagtacctgctctttaccagcccccaggagaaccctggggccacaagcgcagctaccgcctgcagatccactc
catggccgaccaggtgctgcccccaggctggcaggaggagcaggccatcacctgggcaaggtacccccctggcagtgaccaagtaccgggag
tcggagctgtgcagcagcagcatctaccaccagaacgacccctggcacccgcccgtggtctttgagcagtttcttcacaacaacgagaacattga
aaatgaggacctggtggcctgggtgacggtgggcttcctgcacatccccccactcagaggacattcccaacacagccacacctgggaactccgtg
ggcttcctgctccggccattcaacttcttcccagaggacccctccctggcatccagagacactgtgatcgtgtggcctcgggacaacggccccaac
tacgtccagcgctggatccctgaggacagggactgctcgatgcctccccctttagctacaatgggacctatagacctgtgtga (SEQ ID NO:18)

图1续

hDAO-Hepmut2

atgccggccctgggctgggccgtggctgccatcctgatgctgcagacggccatggcggagccctccccggggactctgcccaggaa
ggcaggggtgttttcagacctaagcaaccaagagctgaaggcagtgcacagcttcctctggtccaagaaggagctgaggctgcagccctccagt
accaccaccatggccaagaacaccgtgtttctcatcgagatgctgctgcccaagaagtaccatgtgctgaggtttctggataaaggtgaaaggcat
cctgtgcgggaagcccgtgccgtcatcttctttggtgaccaggagcatcccaatgtcaccgagtttgctgtggggcccctgccagggccctgctaca
tgcgagcactgtcccccaggcctgggtaccagtcctcctgggcatcgaggcccatctccacagcagagtatgccctcctctaccacaccctgcag
gaagccaccaagcccctgcatcagttcttcctcaataccacaggcttctcattccaagactgccatgacagatgcctggccttcaccgatgtggccc
cccggggtgtggcttctggccagcgccgcagttggcttatcatacagcgctatgtagaaggctactttctgcaccccactgggctggagctcctcgtg
gatcatgggagcacagatgctgggcactgggccgtggagcaggtgtggtacaacgggaagttctatgggagcccagaggaactggctcggaa
gtatgcagatggagaggtggacgtggtggtcctggaggacccgctgcctgggggcaaggggcatgacagcacagaggagccgcccctcttctc
ctcccacaagccccgcggggacttccccagccccatccatgtgagcggcccccgcttggtccagccccacggccctcgcttcaggctggaggg
caacgctgtgctctacggcggctggagctttgccttccggctgcgctcctcctccgggctgcaggtcctgaacgtgcacttcggcggagagcgcatt
gcctatgaggtcagcgtgcaagaggcagtggcgctgtatggaggacacacacctgcaggcatgcagaccaagtacctcgatgtcggctggggc
ctgggcagcgtcactcatgagttagcccccggcatcgactgcccggagaccgccaccttcctggacactttccactactatgatgccgatgacccg
gtccattatccccgagccctctgcctctttgaaatgcccacaggggtgcccccttcggcggcactttaattccaactttaaaggtggcttcaacttctatg
cggggctgaagggccaggtgctggtgctgcggacaacttcaactgtctacaattatgattacatttgggactttatcttctaccccaacggggtgatg
gaggccaagatgcatgccactggctacgtccacgccacccttctacacccccgaggggctgcgccacggcactcgcctgcacacccacctgattg
gcaacatacacactcacttggtgcactaccgcgtagacctggatgtggcaggcaccaagaacagcttccagacactgcagatgaagctagaaa
acatcaccaacccctggagcccaagacaccgcgtggtccagccaactctggagcagacgcagtactcctgggagcgccaggcggccttccgc
ttcaaaaggaagctgccc**acgt**acctgctctttaccagccccaggagaaccctggggccacaagcgcagctaccgcctgcagatccactcc
atggccgaccaggtgctgccccaggctggcaggaggagcaggccatcacctgggcaaggtacccccctggcagtgaccaagtaccgggagt
cggagctgtgcagcagcagcatctaccaccagaacgacccctggcacccgcccgtggtctttgagcagtttcttcacaacaacgagaacattga
aaatgaggacctggtggcctgggtgacggtgggcttcctgcacatccccactcagaggacattcccaacacagccacacctgggaactccgtg
ggcttcctgctccggccattcaacttcttcccagaggaccctccctggcatccagagacactgtgatcgtgtggcctcgggacaacggccccaac
tacgtccagcgctggatccctgaggacagggactgctcgatgcctcccccttttagctacaatgggacctatagacctgtgtga (SEQ ID NO:19)

hDAO-Hepmut3

atgccggccctgggctgggccgtggctgccatcctgatgctgcagacggccatggcggagccctccccggggactctgcccaggaa
ggcaggggtgttttcagacctaagcaaccaagagctgaaggcagtgcacagcttcctctggtccaagaaggagctgaggctgcagccctccagt
accaccaccatggccaagaacaccgtgtttctcatcgagatgctgctgcccaagaagtaccatgtgctgaggtttctggataaaggtgaaaggcat
cctgtgcgggaagcccgtgccgtcatcttctttggtgaccaggagcatcccaatgtcaccgagtttgctgtggggcccctgccagggccctgctaca
tgcgagcactgtcccccaggcctgggtaccagtcctcctgggcatcgaggcccatctccacagcagagtatgccctcctctaccacaccctgcag
gaagccaccaagcccctgcatcagttcttcctcaataccacaggcttctcattccaagactgccatgacagatgcctggccttcaccgatgtggccc
cccggggtgtggcttctggccagcgccgcagttggcttatcatacagcgctatgtagaaggctactttctgcaccccactgggctggagctcctcgtg
gatcatgggagcacagatgctgggcactgggccgtggagcaggtgtggtacaacgggaagttctatgggagcccagaggaactggctcggaa
gtatgcagatggagaggtggacgtggtggtcctggaggacccgctgcctgggggcaaggggcatgacagcacagaggagccgcccctcttctc
ctcccacaagccccgcggggacttccccagccccatccatgtgagcggcccccgcttggtccagccccacggccctcgcttcaggctggaggg
caacgctgtgctctacggcggctggagctttgccttccggctgcgctcctcctccgggctgcaggtcctgaacgtgcacttcggcggagagcgcatt
gcctatgaggtcagcgtgcaagaggcagtggcgctgtatggaggacacacacctgcaggcatgcagaccaagtacctcgatgtcggctggggc
ctgggcagcgtcactcatgagttagcccccggcatcgactgcccggagaccgccaccttcctggacactttccactactatgatgccgatgacccg
gtccattatccccgagccctctgcctctttgaaatgcccacaggggtgcccccttcggcggcactttaattccaactttaaaggtggcttcaacttctatg
cggggctgaagggccaggtgctggtgctgcggacaacttcaactgtctacaattatgattacatttgggactttatcttctaccccaacggggtgatg
gaggccaagatgcatgccactggctacgtccacgccacccttctacacccccgaggggctgcgccacggcactcgcctgcacacccacctgattg
gcaacatacacactcacttggtgcactaccgcgtagacctggatgtggcaggcaccaagaacagcttccagacactgcagatgaagctagaaa
acatcaccaacccctggagcccaagacaccgcgtggtccagccaactctggagcagacgcagtactcctgggagcgccaggcggccttccgc
ttcaaa**acg**aagctgcccaagtacctgctctttaccagccccaggagaaccctggggccacaagcgcagctaccgcctgcagatccactcc
atggccgaccaggtgctgccccaggctggcaggaggagcaggccatcacctgggcaaggtacccccctggcagtgaccaagtaccgggagt
cggagctgtgcagcagcagcatctaccaccagaacgacccctggcacccgcccgtggtctttgagcagtttcttcacaacaacgagaacattga
aaatgaggacctggtggcctgggtgacggtgggcttcctgcacatccccactcagaggacattcccaacacagccacacctgggaactccgtg
ggcttcctgctccggccattcaacttcttcccagaggaccctccctggcatccagagacactgtgatcgtgtggcctcgggacaacggccccaac
tacgtccagcgctggatccctgaggacagggactgctcgatgcctcccccttttagctacaatgggacctatagacctgtgtga (SEQ ID NO:20)

图1续

hDAO-Hepmut4

atgccggccctgggctgggccgtggctgccatcctgatgctgcagacggccatggcggagccctccccggggactctgcccaggaa
ggcaggggtgttttcagacctaagcaaccaagagctgaaggcagtgcacagcttcctctggtccaagaaggagctgaggctgcagccctccagt
accaccaccatggccaagaacaccgtgtttctcatcgagatgctgctgcccaagaagtaccatgtgctgaggtttctggataaaggtgaaaggcat
cctgtgcgggaagcccgtgccgtcatcttctttggtgaccaggagcatcccaatgtcaccgagtttgctgtggggcccctgccagggccctgctaca
tgcgagcactgtcccccaggcctgggtaccagtcctcctgggcatcgaggcccatctccacagcagagtatgccctcctctaccacaccctgcag
gaagccaccaagcccctgcatcagttcttcctcaataccacaggcttctcattccaagactgccatgacagatgcctggccttcaccgatgtggccc
cccggggtgtggcttctggccagcgccgcagttggcttatcatacagcgctatgtagaaggctactttctgcaccccactgggctggagctcctcgtg
gatcatgggagcacagatgctgggcactgggccgtggagcaggtgtggtacaacgggaagttctatgggagcccagaggaactggctcggaa
gtatgcagatggagaggtggacgtggtggtcctggaggacccgctgcctgggggcaaggggcatgacagcacagaggagccgcccctcttctc
ctcccacaagccccgcggggacttccccagccccatccatgtgagcggcccccgcttggtccagccccacggccctcgcttcaggctggaggg
caacgctgtgctctacggcggctggagctttgccttccggctgcgctcctcctccgggctgcaggtcctgaacgtgcacttcggcggagagcgcatt
gcctatgaggtcagcgtgcaagaggcagtggcgctgtatggaggacacacacctgcaggcatgcagaccaagtacctcgatgtcggctggggc
ctgggcagcgtcactcatgagttagcccccggcatcgactgcccggagaccgccaccttcctggacactttccactactatgatgccgatgacccg
gtccattatccccgagccctctgcctctttgaaatgcccacaggggtgccccttcggcggcactttaattccaactttaaaggtggcttcaacttctatg
cggggctgaagggccaggtgctggtgctgcggacaacttcaactgtctacaattatgattacatttgggactttatcttctaccccaacggggtgatg
gaggccaagatgcatgccactggctacgtccacgccaccttctacacccccgaggggctgcgccacggcactcgcctgcacacccacctgattg
gcaacatacacactcacttggtgcactaccgcgtagacctggatgtggcaggcaccaagaacagcttccagacactgcagatgaagctagaaa
acatcaccaaccccctggagcccaagacaccgcgtggtccagccaactctggagcagacgcagtactcctgggagcgccaggcggccttc**ag**
cttcaaa**acg**aagctgcccaagtacctgctctttaccagcccccaggagaaccccctggggccacaagcgcagctaccgcctgcagatccactc
catggccgaccaggtgctgcccccaggctggcaggaggagcaggccatcacctgggcaaggtacccccctggcagtgaccaagtaccgggag
tcggagctgtgcagcagcagcatctaccaccagaacgacccctggcacccgcccgtggtctttgagcagtttcttcacaacaacgagaacattga
aaatgaggacctggtggcctgggtgacggtgggcttcctgcacatccccactcagaggacattcccaacacagccacacctgggaactccgtg
ggcttcctgctccggccattcaacttcttcccagaggacccctccctggcatccagagacactgtgatcgtgtggcctcgggacaacggccccaac
tacgtccagcgctggatccctgaggacagggactgctcgatgcctccccctttagctacaatgggacctatagacctgtgtga (SEQ ID NO:21)

hDAO-Hepmut5

atgccggccctgggctgggccgtggctgccatcctgatgctgcagacggccatggcggagccctccccggggactctgcccaggaa
ggcaggggtgttttcagacctaagcaaccaagagctgaaggcagtgcacagcttcctctggtccaagaaggagctgaggctgcagccctccagt
accaccaccatggccaagaacaccgtgtttctcatcgagatgctgctgcccaagaagtaccatgtgctgaggtttctggataaaggtgaaaggcat
cctgtgcgggaagcccgtgccgtcatcttctttggtgaccaggagcatcccaatgtcaccgagtttgctgtggggcccctgccagggccctgctaca
tgcgagcactgtcccccaggcctgggtaccagtcctcctgggcatcgaggcccatctccacagcagagtatgccctcctctaccacaccctgcag
gaagccaccaagcccctgcatcagttcttcctcaataccacaggcttctcattccaagactgccatgacagatgcctggccttcaccgatgtggccc
cccggggtgtggcttctggccagcgccgcagttggcttatcatacagcgctatgtagaaggctactttctgcaccccactgggctggagctcctcgtg
gatcatgggagcacagatgctgggcactgggccgtggagcaggtgtggtacaacgggaagttctatgggagcccagaggaactggctcggaa
gtatgcagatggagaggtggacgtggtggtcctggaggacccgctgcctgggggcaaggggcatgacagcacagaggagccgcccctcttctc
ctcccacaagccccgcggggacttccccagccccatccatgtgagcggcccccgcttggtccagccccacggccctcgcttcaggctggaggg
caacgctgtgctctacggcggctggagctttgccttccggctgcgctcctcctccgggctgcaggtcctgaacgtgcacttcggcggagagcgcatt
gcctatgaggtcagcgtgcaagaggcagtggcgctgtatggaggacacacacctgcaggcatgcagaccaagtacctcgatgtcggctggggc
ctgggcagcgtcactcatgagttagcccccggcatcgactgcccggagaccgccaccttcctggacactttccactactatgatgccgatgacccg
gtccattatccccgagccctctgcctctttgaaatgcccacaggggtgccccttcggcggcactttaattccaactttaaaggtggcttcaacttctatg
cggggctgaagggccaggtgctggtgctgcggacaacttcaactgtctacaattatgattacatttgggactttatcttctaccccaacggggtgatg
gaggccaagatgcatgccactggctacgtccacgccaccttctacacccccgaggggctgcgccacggcactcgcctgcacacccacctgattg
gcaacatacacactcacttggtgcactaccgcgtagacctggatgtggcaggcaccaagaacagcttccagacactgcagatgaagctagaaa
acatcaccaaccccctggagcccaagacaccgcgtggtccagccaactctggagcagacgcagtactcctgggagcgccaggcggccttccgc
ttcaaa**acg**aagctgccc**acg**tacctgctctttaccagcccccaggagaaccccctggggccacaagcgcagctaccgcctgcagatccactcc
atggccgaccaggtgctgcccccaggctggcaggaggagcaggccatcacctgggcaaggtacccccctggcagtgaccaagtaccgggagt
cggagctgtgcagcagcagcatctaccaccagaacgacccctggcacccgcccgtggtctttgagcagtttcttcacaacaacgagaacattga
aaatgaggacctggtggcctgggtgacggtgggcttcctgcacatccccactcagaggacattcccaacacagccacacctgggaactccgtg
ggcttcctgctccggccattcaacttcttcccagaggacccctccctggcatccagagacactgtgatcgtgtggcctcgggacaacggccccaac
tacgtccagcgctggatccctgaggacagggactgctcgatgcctccccctttagctacaatgggacctatagacctgtgtga (SEQ ID NO:22)

图1续

hDAO-Hepmut6

atgccggccctgggctgggccgtggctgccatcctgatgctgcagacggccatggcggagccctccccggggactctgcccaggaa
ggcaggggtgttttcagacctaagcaaccaagagctgaaggcagtgcacagcttcctctggtccaagaaggagctgaggctgcagccctccagt
accaccaccatggccaagaacaccgtgtttctcatcgagatgctgctgcccaagaagtaccatgtgctgaggtttctggataaaggtgaaaggcat
cctgtgcgggaagcccgtgccgtcatcttctttggtgaccaggagcatcccaatgtcaccgagtttgctgtggggcccctgccagggccctgctaca
tgcgagcactgtcccccaggcctgggtaccagtcctcctgggcatcgaggcccatctccacagcagagtatgccctcctctaccacaccctgcag
gaagccaccaagcccctgcatcagttcttcctcaataccacaggcttctcattccaagactgccatgacagatgcctggccttcaccgatgtggccc
ccggggtgtggcttctggccagcgccgcagttggcttatcatacagcgctatgtagaaggctactttctgcaccccactgggctggagctcctcgtg
gatcatgggagcacagatgctgggcactgggccgtggagcaggtgtggtacaacgggaagttctatgggagcccagaggaactggctcggaa
gtatgcagatggagaggtggacgtggtggtcctggaggacccgctgcctgggggcaaggggcatgacagcacagaggagccgcccctcttctc
ctcccacaagccccgcggggacttccccagccccatccatgtgagcggcccccgcttggtccagccccacggccctcgcttcaggctggaggg
caacgctgtgctctacggcggctggagctttgccttccggctgcgctcctcctccgggctgcaggtcctgaacgtgcacttcggcggagagcgcatt
gcctatgaggtcagcgtgcaagaggcagtggcgctgtatggaggacacacacctgcaggcatgcagaccaagtacctcgatgtcggctggggc
ctgggcagcgtcactcatgagttagccccggcatcgactgcccggagaccgccaccttcctggacactttccactactatgatgccgatgacccg
gtccattatccccgagccctctgcctctttgaaatgcccacaggggtgccccttcggcggcactttaattccaactttaaaggtggcttcaacttctatg
cggggctgaagggccaggtgctggtgctgcggacaacttcaactgtctacaattatgattacatttgggactttatcttctaccccaacggggtgatg
gaggccaagatgcatgccactggctacgtccacgccacccttctacacccccgaggggctgcgccacggcactcgcctgcacacccacctgattg
gcaacatacacactcacttggtgcactaccgcgtagacctggatgtggcaggcaccaagaacagcttccagacactgcagatgaagctagaaa
acatcaccaaccccctggagcccaagacaccgcgtggtccagccaactctggagcagacgcagtactcctgggagcgccaggcggccttccgc
ttc**ggacagacg**ctgcccaagtacctgctctttaccagccccaggagaaccccctggggccacaagcgcagctaccgcctgcagatccactcc
atggccgaccaggtgctgccccaggctggcaggaggagcaggccatcacctgggcaaggtacccccctggcagtgaccaagtaccgggagt
cggagctgtgcagcagcagcatctaccaccagaacgaccccctggcacccgcccgtggtctttgagcagtttcttcacaacaacgagaacattga
aaatgaggacctggtggcctgggtgacggtgggcttcctgcacatccccactcagaggacattcccaacacagccacacctgggaactccgtg
ggcttcctgctccggccattcaacttcttcccagaggaccccctccctggcatccagagacactgtgatcgtgtggcctcgggacaacggccccaac
tacgtccagcgctggatccctgaggacagggactgctcgatgcctccccctttagctacaatgggacctatagacctgtgtga (SEQ ID NO:23)

hDAO-Hepmut7

atgccggccctgggctgggccgtggctgccatcctgatgctgcagacggccatggcggagccctccccggggactctgcccaggaa
ggcaggggtgttttcagacctaagcaaccaagagctgaaggcagtgcacagcttcctctggtccaagaaggagctgaggctgcagccctccagt
accaccaccatggccaagaacaccgtgtttctcatcgagatgctgctgcccaagaagtaccatgtgctgaggtttctggataaaggtgaaaggcat
cctgtgcgggaagcccgtgccgtcatcttctttggtgaccaggagcatcccaatgtcaccgagtttgctgtggggcccctgccagggccctgctaca
tgcgagcactgtcccccaggcctgggtaccagtcctcctgggcatcgaggcccatctccacagcagagtatgccctcctctaccacaccctgcag
gaagccaccaagcccctgcatcagttcttcctcaataccacaggcttctcattccaagactgccatgacagatgcctggccttcaccgatgtggccc
ccggggtgtggcttctggccagcgccgcagttggcttatcatacagcgctatgtagaaggctactttctgcaccccactgggctggagctcctcgtg
gatcatgggagcacagatgctgggcactgggccgtggagcaggtgtggtacaacgggaagttctatgggagcccagaggaactggctcggaa
gtatgcagatggagaggtggacgtggtggtcctggaggacccgctgcctgggggcaaggggcatgacagcacagaggagccgcccctcttctc
ctcccacaagccccgcggggacttccccagccccatccatgtgagcggcccccgcttggtccagccccacggccctcgcttcaggctggaggg
caacgctgtgctctacggcggctggagctttgccttccggctgcgctcctcctccgggctgcaggtcctgaacgtgcacttcggcggagagcgcatt
gcctatgaggtcagcgtgcaagaggcagtggcgctgtatggaggacacacacctgcaggcatgcagaccaagtacctcgatgtcggctggggc
ctgggcagcgtcactcatgagttagccccggcatcgactgcccggagaccgccaccttcctggacactttccactactatgatgccgatgacccg
gtccattatccccgagccctctgcctctttgaaatgcccacaggggtgccccttcggcggcactttaattccaactttaaaggtggcttcaacttctatg
cggggctgaagggccaggtgctggtgctgcggacaacttcaactgtctacaattatgattacatttgggactttatcttctaccccaacggggtgatg
gaggccaagatgcatgccactggctacgtccacgccacccttctacacccccgaggggctgcgccacggcactcgcctgcacacccacctgattg
gcaacatacacactcacttggtgcactaccgcgtagacctggatgtggcaggcaccaagaacagcttccagacactgcagatgaagctagaaa
acatcaccaaccccctggagcccaagacaccgcgtggtccagccaactctggagcagacgcagtactcctgggagcgccaggcggccttc**ag**
cttcaaaaggaagctgccc**acg**tacctgctctttaccagccccaggagaaccccctggggccacaagcgcagctaccgcctgcagatccactc
catggccgaccaggtgctgccccaggctggcaggaggagcaggccatcacctgggcaaggtacccccctggcagtgaccaagtaccgggag
tcggagctgtgcagcagcagcatctaccaccagaacgaccccctggcacccgcccgtggtctttgagcagtttcttcacaacaacgagaacattga
aaatgaggacctggtggcctgggtgacggtgggcttcctgcacatccccactcagaggacattcccaacacagccacacctgggaactccgtg
ggcttcctgctccggccattcaacttcttcccagaggaccccctccctggcatccagagacactgtgatcgtgtggcctcgggacaacggccccaac
tacgtccagcgctggatccctgaggacagggactgctcgatgcctccccctttagctacaatgggacctatagacctgtgtga (SEQ ID NO:24)

图1续

hDAO-Cysmut

atgccggccctgggctgggccgtggctgccatcctgatgctgcagacggccatggcggagccctccccggggactctgcccaggaa
ggcaggggtgttttcagacctaagcaaccaagagctgaaggcagtgcacagcttcctctggtccaagaaggagctgaggctgcagccctccagt
accaccaccatggccaagaacaccgtgtttctcatcgagatgctgctgcccaagaagtaccatgtgctgaggtttctggataaaggtgaaaggcat
cctgtgcgggaagcccgtgccgtcatcttctttggtgaccaggagcatcccaatgtcaccgagtttgctgtggggcccctgccagggccc**gcc**tac
atgcgagcactgtcccccaggcctgggtaccagtcctcctgggcatcgaggcccatctccacagcagagtatgccctcctctaccacaccctgca
ggaagccaccaagcccctgcatcagttcttcctcaataccacaggcttctcattccaagactgccatgacagatgcctggccttcaccgatgtggcc
ccccggggtgtggcttctggccagcgccgcagttggcttatcatacagcgctatgtagaaggctactttctgcaccccactgggctggagctcctcgt
ggatcatgggagcacagatgctgggcactgggccgtggagcaggtgtggtacaacgggaagttctatgggagcccagaggaactggctcgga
agtatgcagatggagaggtggacgtggtggtcctggaggacccgctgcctgggggcaaggggcatgacagcacagaggagccgcccctcttc
tcctcccacaagccccgcggggacttccccagccccatccatgtgagcggcccccgcttggtccagccccacggccctcgcttcaggctggagg
gcaacgctgtgctctacggcggctggagctttgccttccggctgcgctcctcctccgggctgcaggtcctgaacgtgcacttcggcggagagcgca
ttgcctatgaggtcagcgtgcaagaggcagtggcgctgtatggaggacacacacctgcaggcatgcagaccaagtacctcgatgtcggctggg
gcctgggcagcgtcactcatgagttagccccggcatcgactgcccggagaccgccaccttcctggacactttccactactatgatgccgatgacc
cggtccattatccccgagccctctgcctctttgaaatgcccacaggggtgcccctcggcggcactttaattccaactttaaaggtggcttcaacttcta
tgcggggctgaagggccaggtgctggtgctgcggacaacttcaactgtctacaattatgattacatttgggactttatcttctaccccaacggggtgat
ggaggccaagatgcatgccactggctacgtccacgccaccttctacacccccgaggggctgcgccacggcactcgcctgcacacccacctgatt
ggcaacatacacactcacttggtgcactaccgcgtagacctggatgtggcaggcaccaagaacagcttccagacactgcagatgaagctagaa
aacatcaccaaccccctggagcccaagacaccgcgtggtccagccaactctggagcagacgcagtactcctgggagcgccaggcggccttccg
cttcaaaaggaagctgcccaagtacctgctctttaccagcccccaggagaaccccctggggccacaagcgcagctaccgcctgcagatccactc
catggccgaccaggtgctgcccccaggctggcaggaggagcaggccatcacctgggcaaggtacccccctggcagtgaccaagtaccgggag
tcggagctgtgcagcagcagcatctaccaccagaacgacccctggcacccgcccgtggtctttgagcagtttcttcacaacaacgagaacattga
aaatgaggacctggtggcctgggtgacggtgggcttcctgcacatcccccactcagaggacattcccaacacagccacacctgggaactccgtg
ggcttcctgctccggccattcaacttcttcccagaggacccctccctggcatccagagacactgtgatcgtgtggcctcgggacaacggccccaac
tacgtccagcgctggatccctgaggacagggactgctcgatgcctccccctttagctacaatgggacctatagacctgtgtga (SEQ ID NO:25)

hDAO-Hepmut1-Cysmut

atgccggccctgggctgggccgtggctgccatcctgatgctgcagacggccatggcggagccctccccggggactctgcccaggaa
ggcaggggtgttttcagacctaagcaaccaagagctgaaggcagtgcacagcttcctctggtccaagaaggagctgaggctgcagccctccagt
accaccaccatggccaagaacaccgtgtttctcatcgagatgctgctgcccaagaagtaccatgtgctgaggtttctggataaaggtgaaaggcat
cctgtgcgggaagcccgtgccgtcatcttctttggtgaccaggagcatcccaatgtcaccgagtttgctgtggggcccctgccagggccc**gcc**tac
atgcgagcactgtcccccaggcctgggtaccagtcctcctgggcatcgaggcccatctccacagcagagtatgccctcctctaccacaccctgca
ggaagccaccaagcccctgcatcagttcttcctcaataccacaggcttctcattccaagactgccatgacagatgcctggccttcaccgatgtggcc
ccccggggtgtggcttctggccagcgccgcagttggcttatcatacagcgctatgtagaaggctactttctgcaccccactgggctggagctcctcgt
ggatcatgggagcacagatgctgggcactgggccgtggagcaggtgtggtacaacgggaagttctatgggagcccagaggaactggctcgga
agtatgcagatggagaggtggacgtggtggtcctggaggacccgctgcctgggggcaaggggcatgacagcacagaggagccgcccctcttc
tcctcccacaagccccgcggggacttccccagccccatccatgtgagcggcccccgcttggtccagccccacggccctcgcttcaggctggagg
gcaacgctgtgctctacggcggctggagctttgccttccggctgcgctcctcctccgggctgcaggtcctgaacgtgcacttcggcggagagcgca
ttgcctatgaggtcagcgtgcaagaggcagtggcgctgtatggaggacacacacctgcaggcatgcagaccaagtacctcgatgtcggctggg
gcctgggcagcgtcactcatgagttagccccggcatcgactgcccggagaccgccaccttcctggacactttccactactatgatgccgatgacc
cggtccattatccccgagccctctgcctctttgaaatgcccacaggggtgcccctcggcggcactttaattccaactttaaaggtggcttcaacttcta
tgcggggctgaagggccaggtgctggtgctgcggacaacttcaactgtctacaattatgattacatttgggactttatcttctaccccaacggggtgat
ggaggccaagatgcatgccactggctacgtccacgccaccttctacacccccgaggggctgcgccacggcactcgcctgcacacccacctgatt
ggcaacatacacactcacttggtgcactaccgcgtagacctggatgtggcaggcaccaagaacagcttccagacactgcagatgaagctagaa
aacatcaccaaccccctggagcccaagacaccgcgtggtccagccaactctggagcagacgcagtactcctgggagcgccaggcggccttc**a**
gcttcaaaaggaagctgcccaagtacctgctctttaccagcccccaggagaaccccctggggccacaagcgcagctaccgcctgcagatccact
ccatggccgaccaggtgctgcccccaggctggcaggaggagcaggccatcacctgggcaaggtacccccctggcagtgaccaagtaccggga
gtcggagctgtgcagcagcagcatctaccaccagaacgacccctggcacccgcccgtggtctttgagcagtttcttcacaacaacgagaacattg
aaaatgaggacctggtggcctgggtgacggtgggcttcctgcacatcccccactcagaggacattcccaacacagccacacctgggaactccgt
gggcttcctgctccggccattcaacttcttcccagaggacccctccctggcatccagagacactgtgatcgtgtggcctcgggacaacggccccaa
ctacgtccagcgctggatccctgaggacagggactgctcgatgcctccccctttagctacaatgggacctatagacctgtgtga (SEQ ID NO:26)

图1续

hDAO-Hepmut2-Cysmut

atgccggccctgggctgggccgtggctgccatcctgatgctgcagacggccatggcggagccctccccggggactctgcccaggaa
ggcaggggtgttttcagacctaagcaaccaagagctgaaggcagtgcacagcttcctctggtccaagaaggagctgaggctgcagccctccagt
accaccaccatggccaagaacaccgtgtttctcatcgagatgctgctgcccaagaagtaccatgtgctgaggtttctggataaaggtgaaaggcat
cctgtgcgggaagcccgtgccgtcatcttctttggtgaccaggagcatcccaatgtcaccgagtttgctgtggggcccctgccagggccc**gcc**tac
atgcgagcactgtcccccaggcctgggtaccagtcctcctgggcatcgaggcccatctccacagcagagtatgccctcctctaccacaccctgca
ggaagccaccaagcccctgcatcagttcttcctcaataccacaggcttctcattccaagactgccatgacagatgcctggccttcaccgatgtggcc
ccccggggtgtggcttctggccagcgccgcagttggcttatcatacagcgctatgtagaaggctactttctgcaccccactgggctggagctcctcgt
ggatcatgggagcacagatgctgggcactgggccgtggagcaggtgtggtacaacgggaagttctatgggagcccagaggaactggctcgga
agtatgcagatggagaggtggacgtggtggtcctggaggacccgctgcctgggggcaaggggcatgacagcacagaggagccgcccctcttc
tcctcccacaagcccccgcggggacttccccagccccatccatgtgagcggcccccgcttggtccagccccacggccctcgcttcaggctggagg
gcaacgctgtgctctacggcggctggagctttgccttccggctgcgctcctcctccgggctgcaggtcctgaacgtgcacttcggcggagagcgca
ttgcctatgaggtcagcgtgcaagaggcagtggcgctgtatggaggacacacacctgcaggcatgcagaccaagtacctcgatgtcggctggg
gcctgggcagcgtcactcatgagttagccccggcatcgactgcccggagaccgccaccttcctggacactttccactactatgatgccgatgacc
cggtccattatccccgagccctctgcctctttgaaatgcccacaggggtgcccttcggcggcactttaattccaacttttaaaggtggcttcaacttcta
tgcggggctgaagggccaggtgctggtgctgcggacaacttcaactgtctacaattatgattacatttgggactttatcttctaccccaacggggtgat
ggaggccaagatgcatgccactggctacgtccacgccaccttctacacccccgaggggctgcgccacggcactcgcctgcacacccacctgatt
ggcaacatacacactcacttggtgcactaccgcgtagacctggatgtggcaggcaccaagaacagcttccagacactgcagatgaagctagaa
aacatcaccaacccctggagcccaagacaccgcgtggtccagccaactctggagcagacgcagtactcctgggagcgccaggcggccttccg
cttcaaaagg**acg**tacctgctctttaccagccccaggagaaccctggggccacaagcgcagctaccgcctgcagatccactc
catggccgaccaggtgctgcccccaggctggcaggaggagcaggccatcacctgggcaaggtacccctggcagtgaccaagtaccgggag
tcggagctgtgcagcagcagcatctaccaccagaacgacccctggcacccgcccgtggtctttgagcagtttcttcacaacaacgagaacattga
aaatgaggacctggtggcctgggtgacggtgggcttcctgcacatccccactcagaggacattcccaacacagccacacctgggaactccgtg
ggcttcctgctccggccattcaacttcttcccagaggaccctccctggcatccagagacactgtgatcgtgtggcctcgggacaacggccccaac
tacgtccagcgctggatccctgaggacagggactgctcgatgcctcccccttttagctacaatgggacctatagacctgtgtga (SEQ ID NO:27)

hDAO-Hepmut3-Cysmut

atgccggccctgggctgggccgtggctgccatcctgatgctgcagacggccatggcggagccctccccggggactctgcccaggaa
ggcaggggtgttttcagacctaagcaaccaagagctgaaggcagtgcacagcttcctctggtccaagaaggagctgaggctgcagccctccagt
accaccaccatggccaagaacaccgtgtttctcatcgagatgctgctgcccaagaagtaccatgtgctgaggtttctggataaaggtgaaaggcat
cctgtgcgggaagcccgtgccgtcatcttctttggtgaccaggagcatcccaatgtcaccgagtttgctgtggggcccctgccagggccc**gcc**tac
atgcgagcactgtcccccaggcctgggtaccagtcctcctgggcatcgaggcccatctccacagcagagtatgccctcctctaccacaccctgca
ggaagccaccaagcccctgcatcagttcttcctcaataccacaggcttctcattccaagactgccatgacagatgcctggccttcaccgatgtggcc
ccccggggtgtggcttctggccagcgccgcagttggcttatcatacagcgctatgtagaaggctactttctgcaccccactgggctggagctcctcgt
ggatcatgggagcacagatgctgggcactgggccgtggagcaggtgtggtacaacgggaagttctatgggagcccagaggaactggctcgga
agtatgcagatggagaggtggacgtggtggtcctggaggacccgctgcctgggggcaaggggcatgacagcacagaggagccgcccctcttc
tcctcccacaagcccccgcggggacttccccagccccatccatgtgagcggcccccgcttggtccagccccacggccctcgcttcaggctggagg
gcaacgctgtgctctacggcggctggagctttgccttccggctgcgctcctcctccgggctgcaggtcctgaacgtgcacttcggcggagagcgca
ttgcctatgaggtcagcgtgcaagaggcagtggcgctgtatggaggacacacacctgcaggcatgcagaccaagtacctcgatgtcggctggg
gcctgggcagcgtcactcatgagttagccccggcatcgactgcccggagaccgccaccttcctggacactttccactactatgatgccgatgacc
cggtccattatccccgagccctctgcctctttgaaatgcccacaggggtgcccttcggcggcactttaattccaacttttaaaggtggcttcaacttcta
tgcggggctgaagggccaggtgctggtgctgcggacaacttcaactgtctacaattatgattacatttgggactttatcttctaccccaacggggtgat
ggaggccaagatgcatgccactggctacgtccacgccaccttctacacccccgaggggctgcgccacggcactcgcctgcacacccacctgatt
ggcaacatacacactcacttggtgcactaccgcgtagacctggatgtggcaggcaccaagaacagcttccagacactgcagatgaagctagaa
aacatcaccaacccctggagcccaagacaccgcgtggtccagccaactctggagcagacgcagtactcctgggagcgccaggcggccttccg
cttcaaa**acg**aagctgcccaagtacctgctctttaccagccccaggagaaccctggggccacaagcgcagctaccgcctgcagatccactc
catggccgaccaggtgctgcccccaggctggcaggaggagcaggccatcacctgggcaaggtacccctggcagtgaccaagtaccgggag
tcggagctgtgcagcagcagcatctaccaccagaacgacccctggcacccgcccgtggtctttgagcagtttcttcacaacaacgagaacattga
aaatgaggacctggtggcctgggtgacggtgggcttcctgcacatccccactcagaggacattcccaacacagccacacctgggaactccgtg
ggcttcctgctccggccattcaacttcttcccagaggaccctccctggcatccagagacactgtgatcgtgtggcctcgggacaacggccccaac
tacgtccagcgctggatccctgaggacagggactgctcgatgcctcccccttttagctacaatgggacctatagacctgtgtga (SEQ ID NO:28)

图1续

hDAO-Hepmut4-Cysmut

atgccggccctgggctgggccgtggctgccatcctgatgctgcagacggccatggcggagccctccccggggactctgcccaggaa
ggcaggggtgttttcagacctaagcaaccaagagctgaaggcagtgcacagcttcctctggtccaagaaggagctgaggctgcagccctccagt
accaccaccatggccaagaacaccgtgtttctcatcgagatgctgctgcccaagaagtaccatgtgctgaggtttctggataaaggtgaaaggcat
cctgtgcgggaagcccgtgccgtcatcttctttggtgaccaggagcatcccaatgtcaccgagtttgctgtggggcccctgccagggccc**gcc**tac
atgcgagcactgtcccccaggcctgggtaccagtcctcctgggcatcgaggcccatctccacagcagagtatgccctcctctaccacaccctgca
ggaagccaccaagcccctgcatcagttcttcctcaataccacaggcttctcattccaagactgccatgacagatgcctggccttcaccgatgtggcc
ccccggggtgtggcttctggccagcgccgcagttggcttatcatacagcgctatgtagaaggctactttctgcaccccactgggctggagctcctcgt
ggatcatgggagcacagatgctgggcactgggccgtggagcaggtgtggtacaacgggaagttctatgggagcccagaggaactggctcgga
agtatgcagatggagaggtggacgtggtggtcctggaggacccgctgcctgggggcaaggggcatgacagcacagaggagccgccctcttc
tcctcccacaagccccgcggggacttccccagccccatccatgtgagcggcccccgcttggtccagccccacggccctcgcttcaggctggagg
gcaacgctgtgctctacggcggctggagctttgccttccggctgcgctcctcctccgggctgcaggtcctgaacgtgcacttcggcggagagcgca
ttgcctatgaggtcagcgtgcaagaggcagtggcgctgtatggaggacacacacctgcaggcatgcagaccaagtacctcgatgtcggctggg
gcctgggcagcgtcactcatgagttagccccggcatcgactgcccggagaccgccaccttcctggacactttccactactatgatgccgatgacc
cggtccattatccccgagccctctgcctctttgaaatgcccacaggggtgccccttcggcggcactttaattccaactttaaaggtggcttcaacttcta
tgcggggctgaagggccaggtgctggtgctgcggacaacttcaactgtctacaattatgattacatttgggactttatcttctaccccaacggggtgat
ggaggccaagatgcatgccactggctacgtccacgccaccttctacaccccgaggggctgcgccacggcactcgcctgcacacccacctgatt
ggcaacatacacactcacttggtgcactaccgcgtagacctggatgtggcaggcaccaagaacagcttccagacactgcagatgaagctagaa
aacatcaccaaccccctggagcccaagacaccgcgtggtccagccaactctggagcagacgcagtactcctgggagcgccaggcggccttc**a**
gcttcaaa**acg**aagctgcccaagtacctgctctttaccagcccccaggagaaccccctggggccacaagcgcagctaccgcctgcagatccact
ccatggccgaccaggtgctgcccccaggctggcaggaggagcaggccatcacctgggcaaggtacccccctggcagtgaccaagtaccggga
gtcggagctgtgcagcagcagcatctaccaccagaacgacccctggcacccgcccgtggtctttgagcagtttcttcacaacaacgagaacattg
aaaatgaggacctggtggcctgggtgacggtgggcttcctgcacatcccccactcagaggacattcccaacacagccacacctgggaactccgt
gggcttcctgctccggccattcaacttcttcccagaggacccctccctggcatccagagacactgtgatcgtgtggcctcgggacaacggccccaa
ctacgtccagcgctggatccctgaggacagggactgctcgatgcctcccccttttagctacaatgggacctatagacctgtgtga (SEQ ID
NO:29)

hDAO-Hepmut5-Cysmut

atgccggccctgggctgggccgtggctgccatcctgatgctgcagacggccatggcggagccctccccggggactctgcccaggaa
ggcaggggtgttttcagacctaagcaaccaagagctgaaggcagtgcacagcttcctctggtccaagaaggagctgaggctgcagccctccagt
accaccaccatggccaagaacaccgtgtttctcatcgagatgctgctgcccaagaagtaccatgtgctgaggtttctggataaaggtgaaaggcat
cctgtgcgggaagcccgtgccgtcatcttctttggtgaccaggagcatcccaatgtcaccgagtttgctgtggggcccctgccagggccc**gcc**tac
atgcgagcactgtcccccaggcctgggtaccagtcctcctgggcatcgaggcccatctccacagcagagtatgccctcctctaccacaccctgca
ggaagccaccaagcccctgcatcagttcttcctcaataccacaggcttctcattccaagactgccatgacagatgcctggccttcaccgatgtggcc
ccccggggtgtggcttctggccagcgccgcagttggcttatcatacagcgctatgtagaaggctactttctgcaccccactgggctggagctcctcgt
ggatcatgggagcacagatgctgggcactgggccgtggagcaggtgtggtacaacgggaagttctatgggagcccagaggaactggctcgga
agtatgcagatggagaggtggacgtggtggtcctggaggacccgctgcctgggggcaaggggcatgacagcacagaggagccgccctcttc
tcctcccacaagccccgcggggacttccccagccccatccatgtgagcggcccccgcttggtccagccccacggccctcgcttcaggctggagg
gcaacgctgtgctctacggcggctggagctttgccttccggctgcgctcctcctccgggctgcaggtcctgaacgtgcacttcggcggagagcgca
ttgcctatgaggtcagcgtgcaagaggcagtggcgctgtatggaggacacacacctgcaggcatgcagaccaagtacctcgatgtcggctggg
gcctgggcagcgtcactcatgagttagccccggcatcgactgcccggagaccgccaccttcctggacactttccactactatgatgccgatgacc
cggtccattatccccgagccctctgcctctttgaaatgcccacaggggtgccccttcggcggcactttaattccaactttaaaggtggcttcaacttcta
tgcggggctgaagggccaggtgctggtgctgcggacaacttcaactgtctacaattatgattacatttgggactttatcttctaccccaacggggtgat
ggaggccaagatgcatgccactggctacgtccacgccaccttctacaccccgaggggctgcgccacggcactcgcctgcacacccacctgatt
ggcaacatacacactcacttggtgcactaccgcgtagacctggatgtggcaggcaccaagaacagcttccagacactgcagatgaagctagaa
aacatcaccaaccccctggagcccaagacaccgcgtggtccagccaactctggagcagacgcagtactcctgggagcgccaggcggccttccg
cttcaaa**acg**aagctgccc**acg**tacctgctctttaccagcccccaggagaaccccctggggccacaagcgcagctaccgcctgcagatccactc
catggccgaccaggtgctgcccccaggctggcaggaggagcaggccatcacctgggcaaggtacccccctggcagtgaccaagtaccgggag
tcggagctgtgcagcagcagcatctaccaccagaacgacccctggcacccgcccgtggtctttgagcagtttcttcacaacaacgagaacattga
aaatgaggacctggtggcctgggtgacggtgggcttcctgcacatcccccactcagaggacattcccaacacagccacacctgggaactccgtg
ggcttcctgctccggccattcaacttcttcccagaggacccctccctggcatccagagacactgtgatcgtgtggcctcgggacaacggccccaac
tacgtccagcgctggatccctgaggacagggactgctcgatgcctcccccttttagctacaatgggacctatagacctgtgtga (SEQ ID
NO:30)

图1续

hDAO-Hepmut6-Cysmut

atgccggccctgggctgggccgtggctgccatcctgatgctgcagacggccatggcggagccctccccggggactctgcccaggaa
ggcaggggtgttttcagacctaagcaaccaagagctgaaggcagtgcacagcttcctctggtccaagaaggagctgaggctgcagccctccagt
accaccaccatggccaagaacaccgtgtttctcatcgagatgctgctgcccaagaagtaccatgtgctgaggtttctggataaaggtgaaaggcat
cctgtgcgggaagcccgtgccgtcatcttctttggtgaccaggagcatcccaatgtcaccgagtttgctgtggggcccctgccagggcccgcctac
atgcgagcactgtcccccaggcctgggtaccagtcctcctgggcatcgaggcccatctccacagcagagtatgccctcctctaccacaccctgca
ggaagccaccaagcccctgcatcagttcttcctcaataccacaggcttctcattccaagactgccatgacagatgcctggccttcaccgatgtggcc
ccccggggtgtggcttctggccagcgccgcagttggcttatcatacagcgctatgtagaaggctactttctgcaccccactgggctggagctcctcgt
ggatcatgggagcacagatgctgggcactgggccgtggagcaggtgtggtacaacgggaagttctatgggagcccagaggaactggctcgga
agtatgcagatggagaggtggacgtggtggtcctggaggacccgctgcctgggggcaaggggcatgacagcacagaggagccgccctcttc
tcctcccacaagcccccgcggggacttccccagccccatccatgtgagcggccccgcttggtccagccccacggccctcgcttcaggctggagg
gcaacgctgtgctctacggcggctggagctttgccttccggctgcgctcctcctccgggctgcaggtcctgaacgtgcacttcggcggagagcgca
ttgcctatgaggtcagcgtgcaagaggcagtggcgctgtatggaggacacacacctgcaggcatgcagaccaagtacctcgatgtcggctggg
gcctgggcagcgtcactcatgagttagccccggcatcgactgcccggagaccgccaccttcctggacactttccactactatgatgccgatgacc
cggtccattatccccgagccctctgcctctttgaaatgcccacaggggtgccccttcggcggcactttaattccaactttaaaggtggcttcaacttcta
tgcggggctgaagggccaggtgctggtgctgcggacaacttcaactgtctacaattatgattacatttgggactttatcttctaccccaacggggtgat
ggaggccaagatgcatgccactggctacgtccacgccacctttctacaccccgaggggctgcgccacggcactcgcctgcacacccacctgatt
ggcaacatacacactcacttggtgcactaccgcgtagacctggatgtggcaggcaccaagaacagcttccagacactgcagatgaagctagaa
aacatcaccaaccccctggagcccaagacaccgcgtggtccagccaactctggagcagacgcagtactcctgggagcgccaggcggccttccg
cttcggacagacgctgcccaagtacctgctctttaccagccccaggagaaccccctggggccacaagcgcagctaccgcctgcagatccactc
catggccgaccaggtgctgcccccaggctggcaggaggagcaggccatcacctgggcaaggtacccccctggcagtgaccaagtaccgggag
tcggagctgtgcagcagcagcatctaccaccagaacgacccctggcacccgcccgtggtctttgagcagtttcttcacaacaacgagaacattga
aaatgaggacctggtggcctgggtgacggtgggcttcctgcacatcccccactcagaggacattcccaacacagccacacctgggaactccgtg
ggcttcctgctccggccattcaacttcttcccagaggacccctccctggcatccagagacactgtgatcgtgtggcctcgggacaacggccccaac
tacgtccagcgctggatccctgaggacagggactgctcgatgcctcccccttttagctacaatgggacctatagacctgtgtga (SEQ ID NO:31)

hDAO-Hepmut7-Cysmut

atgccggccctgggctgggccgtggctgccatcctgatgctgcagacggccatggcggagccctccccggggactctgcccaggaa
ggcaggggtgttttcagacctaagcaaccaagagctgaaggcagtgcacagcttcctctggtccaagaaggagctgaggctgcagccctccagt
accaccaccatggccaagaacaccgtgtttctcatcgagatgctgctgcccaagaagtaccatgtgctgaggtttctggataaaggtgaaaggcat
cctgtgcgggaagcccgtgccgtcatcttctttggtgaccaggagcatcccaatgtcaccgagtttgctgtggggcccctgccagggcccgcctac
atgcgagcactgtcccccaggcctgggtaccagtcctcctgggcatcgaggcccatctccacagcagagtatgccctcctctaccacaccctgca
ggaagccaccaagcccctgcatcagttcttcctcaataccacaggcttctcattccaagactgccatgacagatgcctggccttcaccgatgtggcc
ccccggggtgtggcttctggccagcgccgcagttggcttatcatacagcgctatgtagaaggctactttctgcaccccactgggctggagctcctcgt
ggatcatgggagcacagatgctgggcactgggccgtggagcaggtgtggtacaacgggaagttctatgggagcccagaggaactggctcgga
agtatgcagatggagaggtggacgtggtggtcctggaggacccgctgcctgggggcaaggggcatgacagcacagaggagccgccctcttc
tcctcccacaagcccccgcggggacttccccagccccatccatgtgagcggccccgcttggtccagccccacggccctcgcttcaggctggagg
gcaacgctgtgctctacggcggctggagctttgccttccggctgcgctcctcctccgggctgcaggtcctgaacgtgcacttcggcggagagcgca
ttgcctatgaggtcagcgtgcaagaggcagtggcgctgtatggaggacacacacctgcaggcatgcagaccaagtacctcgatgtcggctggg
gcctgggcagcgtcactcatgagttagccccggcatcgactgcccggagaccgccaccttcctggacactttccactactatgatgccgatgacc
cggtccattatccccgagccctctgcctctttgaaatgcccacaggggtgccccttcggcggcactttaattccaactttaaaggtggcttcaacttcta
tgcggggctgaagggccaggtgctggtgctgcggacaacttcaactgtctacaattatgattacatttgggactttatcttctaccccaacggggtgat
ggaggccaagatgcatgccactggctacgtccacgccacctttctacaccccgaggggctgcgccacggcactcgcctgcacacccacctgatt
ggcaacatacacactcacttggtgcactaccgcgtagacctggatgtggcaggcaccaagaacagcttccagacactgcagatgaagctagaa
aacatcaccaaccccctggagcccaagacaccgcgtggtccagccaactctggagcagacgcagtactcctgggagcgccaggcggccttca
gcttcaaaaggaagctgcccacgtacctgctctttaccagccccaggagaaccccctggggccacaagcgcagctaccgcctgcagatccact
ccatggccgaccaggtgctgcccccaggctggcaggaggagcaggccatcacctgggcaaggtacccccctggcagtgaccaagtaccggga
gtcggagctgtgcagcagcagcatctaccaccagaacgacccctggcacccgcccgtggtctttgagcagtttcttcacaacaacgagaacattg
aaaatgaggacctggtggcctgggtgacggtgggcttcctgcacatcccccactcagaggacattcccaacacagccacacctgggaactccgt
gggcttcctgctccggccattcaacttcttcccagaggacccctccctggcatccagagacactgtgatcgtgtggcctcgggacaacggccccaa
ctacgtccagcgctggatccctgaggacagggactgctcgatgcctcccccttttagctacaatgggacctatagacctgtgtga (SEQ ID NO:32)

图1续

Fc-hDAO

MPALGWAVAAILMLQTAMA***ECPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVK FNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKG QPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYS KLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK***EPKSADKTHT**EPSPGTLPRKAGVFSDLS NQELKAVHSFLWSKKELRLQPSSTTTMAKNTVFLIEMLLPKKYHVLRFLDKGERHPVREARAVIFFGDQ EHPNVTEFAVGPLPGPCYMRALSPRPGYQSSWASRPISTAEYALLYHTLQEATKPLHQFFLNTTGFSFQ DCHDRCLAFTDVAPRGVASGQRRSWLIIQRYVEGYFLHPTGLELLVDHGSTDAGHWAVEQVWYNGKF YGSPEELARKYADGEVDVVVLEDPLPGGKGHDSTEEPPLFSSHKPRGDFPSPIHVSGPRLVQPHGPRF RLEGNAVLYGGWSFAFRLRSSSGLQVLNVHFGGERIAYEVSVQEAVALYGGHTPAGMQTKYLDVGWG LGSVTHELAPGIDCPETATFLDTFHYYDADDPVHYPRALCLFEMPTGVPLRRHFNSNFKGGFNFYAGLK GQVLVLRTTSTVYNYDYIWDFIFYPNGVMEAKMHATGYVHATFYTPEGLRHGTRLHTHLIGNIHTHLVHY RVDLDVAGTKNSFQTLQMKLENITNPWSPRHRVVQPTLEQTQYSWERQAAFRFKRKLPKYLLFTSPQE NPWGHKRSYRLQIHSMADQVLPPGWQEEQAITWARYPLAVTKYRESELCSSSIYHQNDPWHPPVVFE QFLHNNENIENEDLVAWVTVGFLHIPHSEDIPNTATPGNSVGFLLRPFNFFPEDPSLASRDTVIVWPRDN GPNYVQRWIPEDRDCSMPPPFSYNGTYRPV (SEQ ID NO:39)

Fc-hDAO-Hepmut1

MPALGWAVAAILMLQTAMA***ECPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVK FNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKG QPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYS KLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK***EPKSADKTHT**EPSPGTLPRKAGVFSDLS NQELKAVHSFLWSKKELRLQPSSTTTMAKNTVFLIEMLLPKKYHVLRFLDKGERHPVREARAVIFFGDQ EHPNVTEFAVGPLPGPCYMRALSPRPGYQSSWASRPISTAEYALLYHTLQEATKPLHQFFLNTTGFSFQ DCHDRCLAFTDVAPRGVASGQRRSWLIIQRYVEGYFLHPTGLELLVDHGSTDAGHWAVEQVWYNGKF YGSPEELARKYADGEVDVVVLEDPLPGGKGHDSTEEPPLFSSHKPRGDFPSPIHVSGPRLVQPHGPRF RLEGNAVLYGGWSFAFRLRSSSGLQVLNVHFGGERIAYEVSVQEAVALYGGHTPAGMQTKYLDVGWG LGSVTHELAPGIDCPETATFLDTFHYYDADDPVHYPRALCLFEMPTGVPLRRHFNSNFKGGFNFYAGLK GQVLVLRTTSTVYNYDYIWDFIFYPNGVMEAKMHATGYVHATFYTPEGLRHGTRLHTHLIGNIHTHLVHY RVDLDVAGTKNSFQTLQMKLENITNPWSPRHRVVQPTLEQTQYSWERQAAF**S**FKRKLPKYLLFTSPQE NPWGHKRSYRLQIHSMADQVLPPGWQEEQAITWARYPLAVTKYRESELCSSSIYHQNDPWHPPVVFE QFLHNNENIENEDLVAWVTVGFLHIPHSEDIPNTATPGNSVGFLLRPFNFFPEDPSLASRDTVIVWPRDN GPNYVQRWIPEDRDCSMPPPFSYNGTYRPV (SEQ ID NO:40)

Fc-hDAO-Hepmut2

MPALGWAVAAILMLQTAMA***ECPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVK FNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKG QPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYS KLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK***EPKSADKTHT**EPSPGTLPRKAGVFSDLS NQELKAVHSFLWSKKELRLQPSSTTTMAKNTVFLIEMLLPKKYHVLRFLDKGERHPVREARAVIFFGDQ EHPNVTEFAVGPLPGPCYMRALSPRPGYQSSWASRPISTAEYALLYHTLQEATKPLHQFFLNTTGFSFQ DCHDRCLAFTDVAPRGVASGQRRSWLIIQRYVEGYFLHPTGLELLVDHGSTDAGHWAVEQVWYNGKF YGSPEELARKYADGEVDVVVLEDPLPGGKGHDSTEEPPLFSSHKPRGDFPSPIHVSGPRLVQPHGPRF RLEGNAVLYGGWSFAFRLRSSSGLQVLNVHFGGERIAYEVSVQEAVALYGGHTPAGMQTKYLDVGWG LGSVTHELAPGIDCPETATFLDTFHYYDADDPVHYPRALCLFEMPTGVPLRRHFNSNFKGGFNFYAGLK GQVLVLRTTSTVYNYDYIWDFIFYPNGVMEAKMHATGYVHATFYTPEGLRHGTRLHTHLIGNIHTHLVHY RVDLDVAGTKNSFQTLQMKLENITNPWSPRHRVVQPTLEQTQYSWERQAAFRFKRKLP**T**YLLFTSPQE NPWGHKRSYRLQIHSMADQVLPPGWQEEQAITWARYPLAVTKYRESELCSSSIYHQNDPWHPPVVFE QFLHNNENIENEDLVAWVTVGFLHIPHSEDIPNTATPGNSVGFLLRPFNFFPEDPSLASRDTVIVWPRDN GPNYVQRWIPEDRDCSMPPPFSYNGTYRPV (SEQ ID NO:41)

图1续

Fc-hDAO-Hepmut3

MPALGWAVAAILMLQTAMA***ECPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVK FNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKG QPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYS KLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK*** EPKSADKTHT EPSPGTLPRKAGVFSDLS NQELKAVHSFLWSKKELRLQPSSTTTMAKNTVFLIEMLLPKKYHVLRFLDKGERHPVREARAVIFFGDQ EHPNVTEFAVGPLPGPCYMRALSPRPGYQSSWASRPISTAEYALLYHTLQEATKPLHQFFLNTTGFSFQ DCHDRCLAFTDVAPRGVASGQRRSWLIIQRYVEGYFLHPTGLELLVDHGSTDAGHWAVEQVWYNGKF YGSPEELARKYADGEVDVVVLEDPLPGGKGHDSTEEPPLFSSHKPRGDFPSPIHVSGPRLVQPHGPRF RLEGNAVLYGGWSFAFRLRSSSGLQVLNVHFGGERIAYEVSVQEAVALYGGHTPAGMQTKYLDVGWG LGSVTHELAPGIDCPETATFLDTFHYYDADDPVHYPRALCLFEMPTGVPLRRHFNSNFKGGFNFYAGLK GQVLVLRTTSTVYNYDYIWDFIFYPNGVMEAKMHATGYVHATFYTPEGLRHGTRLHTHLIGNIHTHLVHY RVDLDVAGTKNSFQTLQMKLENITNPWSPRHRVVQPTLEQTQYSWERQAAFRFK**T**KLPKYLLFTSPQE NPWGHKRSYRLQIHSMADQVLPPGWQEEQAITWARYPLAVTKYRESELCSSSIYHQNDPWHPPVVFE QFLHNNENIENEDLVAWVTVGFLHIPHSEDIPNTATPGNSVGFLLRPFNFFPEDPSLASRDTVIVWPRDN GPNYVQRWIPEDRDCSMPPPFSYNGTYRPV (SEQ ID NO:42)

Fc-hDAO-Hepmut4

MPALGWAVAAILMLQTAMA***ECPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVK FNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKG QPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYS KLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK*** EPKSADKTHT EPSPGTLPRKAGVFSDLS NQELKAVHSFLWSKKELRLQPSSTTTMAKNTVFLIEMLLPKKYHVLRFLDKGERHPVREARAVIFFGDQ EHPNVTEFAVGPLPGPCYMRALSPRPGYQSSWASRPISTAEYALLYHTLQEATKPLHQFFLNTTGFSFQ DCHDRCLAFTDVAPRGVASGQRRSWLIIQRYVEGYFLHPTGLELLVDHGSTDAGHWAVEQVWYNGKF YGSPEELARKYADGEVDVVVLEDPLPGGKGHDSTEEPPLFSSHKPRGDFPSPIHVSGPRLVQPHGPRF RLEGNAVLYGGWSFAFRLRSSSGLQVLNVHFGGERIAYEVSVQEAVALYGGHTPAGMQTKYLDVGWG LGSVTHELAPGIDCPETATFLDTFHYYDADDPVHYPRALCLFEMPTGVPLRRHFNSNFKGGFNFYAGLK GQVLVLRTTSTVYNYDYIWDFIFYPNGVMEAKMHATGYVHATFYTPEGLRHGTRLHTHLIGNIHTHLVHY RVDLDVAGTKNSFQTLQMKLENITNPWSPRHRVVQPTLEQTQYSWERQAAF**S**FK**T**KLPKYLLFTSPQE NPWGHKRSYRLQIHSMADQVLPPGWQEEQAITWARYPLAVTKYRESELCSSSIYHQNDPWHPPVVFE QFLHNNENIENEDLVAWVTVGFLHIPHSEDIPNTATPGNSVGFLLRPFNFFPEDPSLASRDTVIVWPRDN GPNYVQRWIPEDRDCSMPPPFSYNGTYRPV (SEQ ID NO:43)

Fc-hDAO-Hepmut5

MPALGWAVAAILMLQTAMA***ECPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVK FNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKG QPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYS KLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK*** EPKSADKTHT EPSPGTLPRKAGVFSDLS NQELKAVHSFLWSKKELRLQPSSTTTMAKNTVFLIEMLLPKKYHVLRFLDKGERHPVREARAVIFFGDQ EHPNVTEFAVGPLPGPCYMRALSPRPGYQSSWASRPISTAEYALLYHTLQEATKPLHQFFLNTTGFSFQ DCHDRCLAFTDVAPRGVASGQRRSWLIIQRYVEGYFLHPTGLELLVDHGSTDAGHWAVEQVWYNGKF YGSPEELARKYADGEVDVVVLEDPLPGGKGHDSTEEPPLFSSHKPRGDFPSPIHVSGPRLVQPHGPRF RLEGNAVLYGGWSFAFRLRSSSGLQVLNVHFGGERIAYEVSVQEAVALYGGHTPAGMQTKYLDVGWG LGSVTHELAPGIDCPETATFLDTFHYYDADDPVHYPRALCLFEMPTGVPLRRHFNSNFKGGFNFYAGLK GQVLVLRTTSTVYNYDYIWDFIFYPNGVMEAKMHATGYVHATFYTPEGLRHGTRLHTHLIGNIHTHLVHY RVDLDVAGTKNSFQTLQMKLENITNPWSPRHRVVQPTLEQTQYSWERQAAFRFK**T**KLP**T**YLLFTSPQE NPWGHKRSYRLQIHSMADQVLPPGWQEEQAITWARYPLAVTKYRESELCSSSIYHQNDPWHPPVVFE QFLHNNENIENEDLVAWVTVGFLHIPHSEDIPNTATPGNSVGFLLRPFNFFPEDPSLASRDTVIVWPRDN GPNYVQRWIPEDRDCSMPPPFSYNGTYRPV (SEQ ID NO:44)

图1续

Fc-hDAO-Hepmut6

MPALGWAVAAILMLQTAMA***ECPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVK FNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKG QPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYS KLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK*** EPKSADKTHT EPSPGTLPRKAGVFSDLS NQELKAVHSFLWSKKELRLQPSSTTTMAKNTVFLIEMLLPKKYHVLRFLDKGERHPVREARAVIFFGDQ EHPNVTEFAVGPLPGPCYMRALSPRPGYQSSWASRPISTAEYALLYHTLQEATKPLHQFFLNTTGFSFQ DCHDRCLAFTDVAPRGVASGQRRSWLIIQRYVEGYFLHPTGLELLVDHGSTDAGHWAVEQVWYNGKF YGSPEELARKYADGEVDVVVLEDPLPGGKGHDSTEEPPLFSSHKPRGDFPSPIHVSGPRLVQPHGPRF RLEGNAVLYGGWSFAFRLRSSSGLQVLNVHFGGERIAYEVSVQEAVALYGGHTPAGMQTKYLDVGWG LGSVTHELAPGIDCPETATFLDTFHYYDADDPVHYPRALCLFEMPTGVPLRRHFNSNFKGGFNFYAGLK GQVLVLRTTSTVYNYDYIWDFIFYPNGVMEAKMHATGYVHATFYTPEGLRHGTRLHTHLIGNIHTHLVHY RVDLDVAGTKNSFQTLQMKLENITNPWSPRHRVVQPTLEQTQYSWERQAAFRF**GQT**LPKYLLFTSPQE NPWGHKRSYRLQIHSMADQVLPPGWQEEQAITWARYPLAVTKYRESELCSSSIYHQNDPWHPPVVFE QFLHNNENIENEDLVAWVTVGFLHIPHSEDIPNTATPGNSVGFLLRPFNFFPEDPSLASRDTVIVWPRDN GPNYVQRWIPEDRDCSMPPPFSYNGTYRPV (SEQ ID NO:45)

Fc-hDAO-Hepmut7

MPALGWAVAAILMLQTAMA***ECPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVK FNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKG QPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYS KLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK*** EPKSADKTHT EPSPGTLPRKAGVFSDLS NQELKAVHSFLWSKKELRLQPSSTTTMAKNTVFLIEMLLPKKYHVLRFLDKGERHPVREARAVIFFGDQ EHPNVTEFAVGPLPGPCYMRALSPRPGYQSSWASRPISTAEYALLYHTLQEATKPLHQFFLNTTGFSFQ DCHDRCLAFTDVAPRGVASGQRRSWLIIQRYVEGYFLHPTGLELLVDHGSTDAGHWAVEQVWYNGKF YGSPEELARKYADGEVDVVVLEDPLPGGKGHDSTEEPPLFSSHKPRGDFPSPIHVSGPRLVQPHGPRF RLEGNAVLYGGWSFAFRLRSSSGLQVLNVHFGGERIAYEVSVQEAVALYGGHTPAGMQTKYLDVGWG LGSVTHELAPGIDCPETATFLDTFHYYDADDPVHYPRALCLFEMPTGVPLRRHFNSNFKGGFNFYAGLK GQVLVLRTTSTVYNYDYIWDFIFYPNGVMEAKMHATGYVHATFYTPEGLRHGTRLHTHLIGNIHTHLVHY RVDLDVAGTKNSFQTLQMKLENITNPWSPRHRVVQPTLEQTQYSWERQAAF**S**FKRKLP**T**YLLFTSPQE NPWGHKRSYRLQIHSMADQVLPPGWQEEQAITWARYPLAVTKYRESELCSSSIYHQNDPWHPPVVFE QFLHNNENIENEDLVAWVTVGFLHIPHSEDIPNTATPGNSVGFLLRPFNFFPEDPSLASRDTVIVWPRDN GPNYVQRWIPEDRDCSMPPPFSYNGTYRPV (SEQ ID NO:46)

Fc-hDAO-Cysmut

MPALGWAVAAILMLQTAMA***ECPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHE DPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTI SKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGS FFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK*** EPKSADKTHT EPSPGTLPRKAGV FSDLSNQELKAVHSFLWSKKELRLQPSSTTTMAKNTVFLIEMLLPKKYHVLRFLDKGERHPVREARAVIF FGDQEHPNVTEFAVGPLPGP**A**YMRALSPRPGYQSSWASRPISTAEYALLYHTLQEATKPLHQFFLNTT GFSFQDCHDRCLAFTDVAPRGVASGQRRSWLIIQRYVEGYFLHPTGLELLVDHGSTDAGHWAVEQVW YNGKFYGSPEELARKYADGEVDVVVLEDPLPGGKGHDSTEEPPLFSSHKPRGDFPSPIHVSGPRLVQP HGPRFRLEGNAVLYGGWSFAFRLRSSSGLQVLNVHFGGERIAYEVSVQEAVALYGGHTPAGMQTKYL DVGWGLGSVTHELAPGIDCPETATFLDTFHYYDADDPVHYPRALCLFEMPTGVPLRRHFNSNFKGGFN FYAGLKGQVLVLRTTSTVYNYDYIWDFIFYPNGVMEAKMHATGYVHATFYTPEGLRHGTRLHTHLIGNIH THLVHYRVDLDVAGTKNSFQTLQMKLENITNPWSPRHRVVQPTLEQTQYSWERQAAFRFKRKLPKYLL FTSPQENPWGHKRSYRLQIHSMADQVLPPGWQEEQAITWARYPLAVTKYRESELCSSSIYHQNDPWH PPVVFEQFLHNNENIENEDLVAWVTVGFLHIPHSEDIPNTATPGNSVGFLLRPFNFFPEDPSLASRDTVIV WPRDNGPNYVQRWIPEDRDCSMPPPFSYNGTYRPV (SEQ ID NO:47)

图1续

Fc-hDAO-Hepmut1-Cysmut

MPALGWAVAAILMLQTAMA*ECPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVK FNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKG QPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYS KLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK*EPKSADKTHT EPSPGTLPRKAGVFSDLS NQELKAVHSFLWSKKELRLQPSSTTTMAKNTVFLIEMLLPKKYHVLRFLDKGERHPVREARAVIFFGDQ EHPNVTEFAVGPLPGP**A**YMRALSPRPGYQSSWASRPISTAEYALLYHTLQEATKPLHQFFLNTTGFSFQ DCHDRCLAFTDVAPRGVASGQRRSWLIIQRYVEGYFLHPTGLELLVDHGSTDAGHWAVEQVWYNGKF YGSPEELARKYADGEVDVVVLEDPLPGGKGHDSTEEPPLFSSHKPRGDFPSPIHVSGPRLVQPHGPRF RLEGNAVLYGGWSFAFRLRSSSGLQVLNVHFGGERIAYEVSVQEAVALYGGHTPAGMQTKYLDVGWG LGSVTHELAPGIDCPETATFLDTFHYYDADDPVHYPRALCLFEMPTGVPLRRHFNSNFKGGFNFYAGLK GQVLVLRTTSTVYNYDYIWDFIFYPNGVMEAKMHATGYVHATFYTPEGLRHGTRLHTHLIGNIHTHLVHY RVDLDVAGTKNSFQTLQMKLENITNPWSPRHRVVQPTLEQTQYSWERQAAF**S**FKRKLPKYLLFTSPQE NPWGHKRSYRLQIHSMADQVLPPGWQEEQAITWARYPLAVTKYRESELCSSSIYHQNDPWHPPVVFE QFLHNNENIENEDLVAWVTVGFLHIPHSEDIPNTATPGNSVGFLLRPFNFFPEDPSLASRDTVIVWPRDN GPNYVQRWIPEDRDCSMPPPFSYNGTYRPV (SEQ ID NO:48)

Fc-hDAO-Hepmut2-Cysmut

MPALGWAVAAILMLQTAMA*ECPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVK FNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKG QPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYS KLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK*EPKSADKTHT EPSPGTLPRKAGVFSDLS NQELKAVHSFLWSKKELRLQPSSTTTMAKNTVFLIEMLLPKKYHVLRFLDKGERHPVREARAVIFFGDQ EHPNVTEFAVGPLPGP**A**YMRALSPRPGYQSSWASRPISTAEYALLYHTLQEATKPLHQFFLNTTGFSFQ DCHDRCLAFTDVAPRGVASGQRRSWLIIQRYVEGYFLHPTGLELLVDHGSTDAGHWAVEQVWYNGKF YGSPEELARKYADGEVDVVVLEDPLPGGKGHDSTEEPPLFSSHKPRGDFPSPIHVSGPRLVQPHGPRF RLEGNAVLYGGWSFAFRLRSSSGLQVLNVHFGGERIAYEVSVQEAVALYGGHTPAGMQTKYLDVGWG LGSVTHELAPGIDCPETATFLDTFHYYDADDPVHYPRALCLFEMPTGVPLRRHFNSNFKGGFNFYAGLK GQVLVLRTTSTVYNYDYIWDFIFYPNGVMEAKMHATGYVHATFYTPEGLRHGTRLHTHLIGNIHTHLVHY RVDLDVAGTKNSFQTLQMKLENITNPWSPRHRVVQPTLEQTQYSWERQAAFRFKRKLP**T**YLLFTSPQE NPWGHKRSYRLQIHSMADQVLPPGWQEEQAITWARYPLAVTKYRESELCSSSIYHQNDPWHPPVVFE QFLHNNENIENEDLVAWVTVGFLHIPHSEDIPNTATPGNSVGFLLRPFNFFPEDPSLASRDTVIVWPRDN GPNYVQRWIPEDRDCSMPPPFSYNGTYRPV (SEQ ID NO:49)

Fc-hDAO-Hepmut3-Cysmut

MPALGWAVAAILMLQTAMA*ECPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVK FNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKG QPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYS KLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK*EPKSADKTHT EPSPGTLPRKAGVFSDLS NQELKAVHSFLWSKKELRLQPSSTTTMAKNTVFLIEMLLPKKYHVLRFLDKGERHPVREARAVIFFGDQ EHPNVTEFAVGPLPGP**A**YMRALSPRPGYQSSWASRPISTAEYALLYHTLQEATKPLHQFFLNTTGFSFQ DCHDRCLAFTDVAPRGVASGQRRSWLIIQRYVEGYFLHPTGLELLVDHGSTDAGHWAVEQVWYNGKF YGSPEELARKYADGEVDVVVLEDPLPGGKGHDSTEEPPLFSSHKPRGDFPSPIHVSGPRLVQPHGPRF RLEGNAVLYGGWSFAFRLRSSSGLQVLNVHFGGERIAYEVSVQEAVALYGGHTPAGMQTKYLDVGWG LGSVTHELAPGIDCPETATFLDTFHYYDADDPVHYPRALCLFEMPTGVPLRRHFNSNFKGGFNFYAGLK GQVLVLRTTSTVYNYDYIWDFIFYPNGVMEAKMHATGYVHATFYTPEGLRHGTRLHTHLIGNIHTHLVHY RVDLDVAGTKNSFQTLQMKLENITNPWSPRHRVVQPTLEQTQYSWERQAAFRFK**T**KLPKYLLFTSPQE NPWGHKRSYRLQIHSMADQVLPPGWQEEQAITWARYPLAVTKYRESELCSSSIYHQNDPWHPPVVFE QFLHNNENIENEDLVAWVTVGFLHIPHSEDIPNTATPGNSVGFLLRPFNFFPEDPSLASRDTVIVWPRDN GPNYVQRWIPEDRDCSMPPPFSYNGTYRPV (SEQ ID NO:50)

图1续

Fc-hDAO-Hepmut4-Cysmut

MPALGWAVAAILMLQTAMA***ECPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVK FNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKG QPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYS KLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK*** EPKSADKTHT EPSPGTLPRKAGVFSDLS NQELKAVHSFLWSKKELRLQPSSTTTMAKNTVFLIEMLLPKKYHVLRFLDKGERHPVREARAVIFFGDQ EHPNVTEFAVGPLPGP**A**YMRALSPRPGYQSSWASRPISTAEYALLYHTLQEATKPLHQFFLNTTGFSFQ DCHDRCLAFTDVAPRGVASGQRRSWLIIQRYVEGYFLHPTGLELLVDHGSTDAGHWAVEQVWYNGKF YGSPEELARKYADGEVDVVVLEDPLPGGKGHDSTEEPPLFSSHKPRGDFPSPIHVSGPRLVQPHGPRF RLEGNAVLYGGWSFAFRLRSSSGLQVLNVHFGGERIAYEVSVQEAVALYGGHTPAGMQTKYLDVGWG LGSVTHELAPGIDCPETATFLDTFHYYDADDPVHYPRALCLFEMPTGVPLRRHFNSNFKGGFNFYAGLK GQVLVLRTTSTVYNYDYIWDFIFYPNGVMEAKMHATGYVHATFYTPEGLRHGTRLHTHLIGNIHTHLVHY RVDLDVAGTKNSFQTLQMKLENITNPWSPRHRVVQPTLEQTQYSWERQAAF**S**FK**T**KLPKYLLFTSPQE NPWGHKRSYRLQIHSMADQVLPPGWQEEQAITWARYPLAVTKYRESELCSSSIYHQNDPWHPPVVFE QFLHNNENIENEDLVAWVTVGFLHIPHSEDIPNTATPGNSVGFLLRPFNFFPEDPSLASRDTVIVWPRDN GPNYVQRWIPEDRDCSMPPPFSYNGTYRPV (SEQ ID NO:51)

Fc-hDAO-Hepmut5-Cysmut

MPALGWAVAAILMLQTAMA***ECPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVK FNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKG QPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYS KLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK*** EPKSADKTHT EPSPGTLPRKAGVFSDLS NQELKAVHSFLWSKKELRLQPSSTTTMAKNTVFLIEMLLPKKYHVLRFLDKGERHPVREARAVIFFGDQ EHPNVTEFAVGPLPGP**A**YMRALSPRPGYQSSWASRPISTAEYALLYHTLQEATKPLHQFFLNTTGFSFQ DCHDRCLAFTDVAPRGVASGQRRSWLIIQRYVEGYFLHPTGLELLVDHGSTDAGHWAVEQVWYNGKF YGSPEELARKYADGEVDVVVLEDPLPGGKGHDSTEEPPLFSSHKPRGDFPSPIHVSGPRLVQPHGPRF RLEGNAVLYGGWSFAFRLRSSSGLQVLNVHFGGERIAYEVSVQEAVALYGGHTPAGMQTKYLDVGWG LGSVTHELAPGIDCPETATFLDTFHYYDADDPVHYPRALCLFEMPTGVPLRRHFNSNFKGGFNFYAGLK GQVLVLRTTSTVYNYDYIWDFIFYPNGVMEAKMHATGYVHATFYTPEGLRHGTRLHTHLIGNIHTHLVHY RVDLDVAGTKNSFQTLQMKLENITNPWSPRHRVVQPTLEQTQYSWERQAAFRFK**T**KLP**T**YLLFTSPQE NPWGHKRSYRLQIHSMADQVLPPGWQEEQAITWARYPLAVTKYRESELCSSSIYHQNDPWHPPVVFE QFLHNNENIENEDLVAWVTVGFLHIPHSEDIPNTATPGNSVGFLLRPFNFFPEDPSLASRDTVIVWPRDN GPNYVQRWIPEDRDCSMPPPFSYNGTYRPV (SEQ ID NO:52)

Fc-hDAO-Hepmut6-Cysmut

MPALGWAVAAILMLQTAMA***ECPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVK FNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKG QPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYS KLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK*** EPKSADKTHT EPSPGTLPRKAGVFSDLS NQELKAVHSFLWSKKELRLQPSSTTTMAKNTVFLIEMLLPKKYHVLRFLDKGERHPVREARAVIFFGDQ EHPNVTEFAVGPLPGP**A**YMRALSPRPGYQSSWASRPISTAEYALLYHTLQEATKPLHQFFLNTTGFSFQ DCHDRCLAFTDVAPRGVASGQRRSWLIIQRYVEGYFLHPTGLELLVDHGSTDAGHWAVEQVWYNGKF YGSPEELARKYADGEVDVVVLEDPLPGGKGHDSTEEPPLFSSHKPRGDFPSPIHVSGPRLVQPHGPRF RLEGNAVLYGGWSFAFRLRSSSGLQVLNVHFGGERIAYEVSVQEAVALYGGHTPAGMQTKYLDVGWG LGSVTHELAPGIDCPETATFLDTFHYYDADDPVHYPRALCLFEMPTGVPLRRHFNSNFKGGFNFYAGLK GQVLVLRTTSTVYNYDYIWDFIFYPNGVMEAKMHATGYVHATFYTPEGLRHGTRLHTHLIGNIHTHLVHY RVDLDVAGTKNSFQTLQMKLENITNPWSPRHRVVQPTLEQTQYSWERQAAFRF**GQT**LPKYLLFTSPQE NPWGHKRSYRLQIHSMADQVLPPGWQEEQAITWARYPLAVTKYRESELCSSSIYHQNDPWHPPVVFE QFLHNNENIENEDLVAWVTVGFLHIPHSEDIPNTATPGNSVGFLLRPFNFFPEDPSLASRDTVIVWPRDN GPNYVQRWIPEDRDCSMPPPFSYNGTYRPV (SEQ ID NO:53)

图1续

Fc-hDAO-Hepmut7-Cysmut

MPALGWAVAAILMLQTAMA***ECPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVK FNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKG QPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYS KLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK*** EPKSADKTHT EPSPGTLPRKAGVFSDLS NQELKAVHSFLWSKKELRLQPSSTTTMAKNTVFLIEMLLPKKYHVLRFLDKGERHPVREARAVIFFGDQ EHPNVTEFAVGPLPGP**A**YMRALSPRPGYQSSWASRPISTAEYALLYHTLQEATKPLHQFFLNTTGFSFQ DCHDRCLAFTDVAPRGVASGQRRSWLIIQRYVEGYFLHPTGLELLVDHGSTDAGHWAVEQVWYNGKF YGSPEELARKYADGEVDVVVLEDPLPGGKGHDSTEEPPLFSSHKPRGDFPSPIHVSGPRLVQPHGPRF RLEGNAVLYGGWSFAFRLRSSSGLQVLNVHFGGERIAYEVSVQEAVALYGGHTPAGMQTKYLDVGWG LGSVTHELAPGIDCPETATFLDTFHYYDADDPVHYPRALCLFEMPTGVPLRRHFNSNFKGGFNFYAGLK GQVLVLRTTSTVYNYDYIWDFIFYPNGVMEAKMHATGYVHATFYTPEGLRHGTRLHTHLIGNIHTHLVHY RVDLDVAGTKNSFQTLQMKLENITNPWSPRHRVVQPTLEQTQYSWERQAAF**S**FKRKLP**T**YLLFTSPQE NPWGHKRSYRLQIHSMADQVLPPGWQEEQAITWARYPLAVTKYRESELCSSSIYHQNDPWHPPVVFE QFLHNNENIENEDLVAWVTVGFLHIPHSEDIPNTATPGNSVGFLLRPFNFFPEDPSLASRDTVIVWPRDN GPNYVQRWIPEDRDCSMPPPFSYNGTYRPV (SEQ ID NO:54)

hDAO-Fc

MPALGWAVAAILMLQTAMAEPSPGTLPRKAGVFSDLSNQELKAVHSFLWSKKELRLQPSSTTTMAKNT VFLIEMLLPKKYHVLRFLDKGERHPVREARAVIFFGDQEHPNVTEFAVGPLPGPCYMRALSPRPGYQSS WASRPISTAEYALLYHTLQEATKPLHQFFLNTTGFSFQDCHDRCLAFTDVAPRGVASGQRRSWLIIQRY VEGYFLHPTGLELLVDHGSTDAGHWAVEQVWYNGKFYGSPEELARKYADGEVDVVVLEDPLPGGKGH DSTEEPPLFSSHKPRGDFPSPIHVSGPRLVQPHGPRFRLEGNAVLYGGWSFAFRLRSSSGLQVLNVHF GGERIAYEVSVQEAVALYGGHTPAGMQTKYLDVGWGLGSVTHELAPGIDCPETATFLDTFHYYDADDP VHYPRALCLFEMPTGVPLRRHFNSNFKGGFNFYAGLKGQVLVLRTTSTVYNYDYIWDFIFYPNGVMEAK MHATGYVHATFYTPEGLRHGTRLHTHLIGNIHTHLVHYRVDLDVAGTKNSFQTLQMKLENITNPWSPRH RVVQPTLEQTQYSWERQAAFRFKRKLPKYLLFTSPQENPWGHKRSYRLQIHSMADQVLPPGWQEEQA ITWARYPLAVTKYRESELCSSSIYHQNDPWHPPVVFEQFLHNNENIENEDLVAWVTVGFLHIPHSEDIPN TATPGNSVGFLLRPFNFFPEDPSLASRDTVIVWPRDNGPNYVQRWIPEDRDCSMPPPFSYNGTYRPV***E PKSADKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEV HNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTL PPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQ QGNVFSCSVMHEALHNHYTQKSLSLSPGK*** (SEQ ID NO:55)

hDAO-Fc-Hepmut1

MPALGWAVAAILMLQTAMAEPSPGTLPRKAGVFSDLSNQELKAVHSFLWSKKELRLQPSSTTTMAKNT VFLIEMLLPKKYHVLRFLDKGERHPVREARAVIFFGDQEHPNVTEFAVGPLPGPCYMRALSPRPGYQSS WASRPISTAEYALLYHTLQEATKPLHQFFLNTTGFSFQDCHDRCLAFTDVAPRGVASGQRRSWLIIQRY VEGYFLHPTGLELLVDHGSTDAGHWAVEQVWYNGKFYGSPEELARKYADGEVDVVVLEDPLPGGKGH DSTEEPPLFSSHKPRGDFPSPIHVSGPRLVQPHGPRFRLEGNAVLYGGWSFAFRLRSSSGLQVLNVHF GGERIAYEVSVQEAVALYGGHTPAGMQTKYLDVGWGLGSVTHELAPGIDCPETATFLDTFHYYDADDP VHYPRALCLFEMPTGVPLRRHFNSNFKGGFNFYAGLKGQVLVLRTTSTVYNYDYIWDFIFYPNGVMEAK MHATGYVHATFYTPEGLRHGTRLHTHLIGNIHTHLVHYRVDLDVAGTKNSFQTLQMKLENITNPWSPRH RVVQPTLEQTQYSWERQAAF**S**FKRKLPKYLLFTSPQENPWGHKRSYRLQIHSMADQVLPPGWQEEQA ITWARYPLAVTKYRESELCSSSIYHQNDPWHPPVVFEQFLHNNENIENEDLVAWVTVGFLHIPHSEDIPN TATPGNSVGFLLRPFNFFPEDPSLASRDTVIVWPRDNGPNYVQRWIPEDRDCSMPPPFSYNGTYRPV***E PKSADKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEV HNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTL PPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQ QGNVFSCSVMHEALHNHYTQKSLSLSPGK*** (SEQ ID NO:56)

图1续

hDAO-Fc-Hepmut2

MPALGWAVAAILMLQTAMAEPSPGTLPRKAGVFSDLSNQELKAVHSFLWSKKELRLQPSSTTTMAKNT
VFLIEMLLPKKYHVLRFLDKGERHPVREARAVIFFGDQEHPNVTEFAVGPLPGPCYMRALSPRPGYQSS
WASRPISTAEYALLYHTLQEATKPLHQFFLNTTGFSFQDCHDRCLAFTDVAPRGVASGQRRSWLIIQRY
VEGYFLHPTGLELLVDHGSTDAGHWAVEQVWYNGKFYGSPEELARKYADGEVDVVVLEDPLPGGKGH
DSTEEPPLFSSHKPRGDFPSPIHVSGPRLVQPHGPRFRLEGNAVLYGGWSFAFRLRSSSGLQVLNVHF
GGERIAYEVSVQEAVALYGGHTPAGMQTKYLDVGWGLGSVTHELAPGIDCPETATFLDTFHYYDADDP
VHYPRALCLFEMPTGVPLRRHFNSNFKGGFNFYAGLKGQVLVLRTTSTVYNYDYIWDFIFYPNGVMEAK
MHATGYVHATFYTPEGLRHGTRLHTHLIGNIHTHLVHYRVDLDVAGTKNSFQTLQMKLENITNPWSPRH
RVVQPTLEQTQYSWERQAAFRFKRKLPTYLLFTSPQENPWGHKRSYRLQIHSMADQVLPPGWQEEQA
ITWARYPLAVTKYRESELCSSSIYHQNDPWHPPVVFEQFLHNNENIENEDLVAWVTVGFLHIPHSEDIPN
TATPGNSVGFLLRPFNFFPEDPSLASRDTVIVWPRDNGPNYVQRWIPEDRDCSMPPPFSYNGTYRPV***E***
PKSADKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEV
HNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTL
PPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQ
QGNVFSCSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO:57)

hDAO-Fc-Hepmut3

MPALGWAVAAILMLQTAMAEPSPGTLPRKAGVFSDLSNQELKAVHSFLWSKKELRLQPSSTTTMAKNT
VFLIEMLLPKKYHVLRFLDKGERHPVREARAVIFFGDQEHPNVTEFAVGPLPGPCYMRALSPRPGYQSS
WASRPISTAEYALLYHTLQEATKPLHQFFLNTTGFSFQDCHDRCLAFTDVAPRGVASGQRRSWLIIQRY
VEGYFLHPTGLELLVDHGSTDAGHWAVEQVWYNGKFYGSPEELARKYADGEVDVVVLEDPLPGGKGH
DSTEEPPLFSSHKPRGDFPSPIHVSGPRLVQPHGPRFRLEGNAVLYGGWSFAFRLRSSSGLQVLNVHF
GGERIAYEVSVQEAVALYGGHTPAGMQTKYLDVGWGLGSVTHELAPGIDCPETATFLDTFHYYDADDP
VHYPRALCLFEMPTGVPLRRHFNSNFKGGFNFYAGLKGQVLVLRTTSTVYNYDYIWDFIFYPNGVMEAK
MHATGYVHATFYTPEGLRHGTRLHTHLIGNIHTHLVHYRVDLDVAGTKNSFQTLQMKLENITNPWSPRH
RVVQPTLEQTQYSWERQAAFRFK**T**KLPKYLLFTSPQENPWGHKRSYRLQIHSMADQVLPPGWQEEQA
ITWARYPLAVTKYRESELCSSSIYHQNDPWHPPVVFEQFLHNNENIENEDLVAWVTVGFLHIPHSEDIPN
TATPGNSVGFLLRPFNFFPEDPSLASRDTVIVWPRDNGPNYVQRWIPEDRDCSMPPPFSYNGTYRPV***E***
PKSADKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEV
HNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTL
PPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQ
QGNVFSCSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO:58)

hDAO-Fc-Hepmut4

MPALGWAVAAILMLQTAMAEPSPGTLPRKAGVFSDLSNQELKAVHSFLWSKKELRLQPSSTTTMAKNT
VFLIEMLLPKKYHVLRFLDKGERHPVREARAVIFFGDQEHPNVTEFAVGPLPGPCYMRALSPRPGYQSS
WASRPISTAEYALLYHTLQEATKPLHQFFLNTTGFSFQDCHDRCLAFTDVAPRGVASGQRRSWLIIQRY
VEGYFLHPTGLELLVDHGSTDAGHWAVEQVWYNGKFYGSPEELARKYADGEVDVVVLEDPLPGGKGH
DSTEEPPLFSSHKPRGDFPSPIHVSGPRLVQPHGPRFRLEGNAVLYGGWSFAFRLRSSSGLQVLNVHF
GGERIAYEVSVQEAVALYGGHTPAGMQTKYLDVGWGLGSVTHELAPGIDCPETATFLDTFHYYDADDP
VHYPRALCLFEMPTGVPLRRHFNSNFKGGFNFYAGLKGQVLVLRTTSTVYNYDYIWDFIFYPNGVMEAK
MHATGYVHATFYTPEGLRHGTRLHTHLIGNIHTHLVHYRVDLDVAGTKNSFQTLQMKLENITNPWSPRH
RVVQPTLEQTQYSWERQAAF**S**FK**T**KLPKYLLFTSPQENPWGHKRSYRLQIHSMADQVLPPGWQEEQAI
TWARYPLAVTKYRESELCSSSIYHQNDPWHPPVVFEQFLHNNENIENEDLVAWVTVGFLHIPHSEDIPN
TATPGNSVGFLLRPFNFFPEDPSLASRDTVIVWPRDNGPNYVQRWIPEDRDCSMPPPFSYNGTYRPV***E***
PKSADKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEV
HNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTL
PPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQ
QGNVFSCSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO:59)

图1续

hDAO-Fc-Hepmut5

MPALGWAVAAILMLQTAMAEPSPGTLPRKAGVFSDLSNQELKAVHSFLWSKKELRLQPSSTTTMAKNT
VFLIEMLLPKKYHVLRFLDKGERHPVREARAVIFFGDQEHPNVTEFAVGPLPGPCYMRALSPRPGYQSS
WASRPISTAEYALLYHTLQEATKPLHQFFLNTTGFSFQDCHDRCLAFTDVAPRGVASGQRRSWLIIQRY
VEGYFLHPTGLELLVDHGSTDAGHWAVEQVWYNGKFYGSPEELARKYADGEVDVVVLEDPLPGGKGH
DSTEEPPLFSSHKPRGDFPSPIHVSGPRLVQPHGPRFRLEGNAVLYGGWSFAFRLRSSSGLQVLNVHF
GGERIAYEVSVQEAVALYGGHTPAGMQTKYLDVGWGLGSVTHELAPGIDCPETATFLDTFHYYDADDP
VHYPRALCLFEMPTGVPLRRHFNSNFKGGFNFYAGLKGQVLVLRTTSTVYNYDYIWDFIFYPNGVMEAK
MHATGYVHATFYTPEGLRHGTRLHTHLIGNIHTHLVHYRVDLDVAGTKNSFQTLQMKLENITNPWSPRH
RVVQPTLEQTQYSWERQAAFRF**KT**KLP**T**YLLFTSPQENPWGHKRSYRLQIHSMADQVLPPGWQEEQAI
TWARYPLAVTKYRESELCSSSIYHQNDPWHPPVVFEQFLHNNENIENEDLVAWVTVGFLHIPHSEDIPN
TATPGNSVGFLLRPFNFFPEDPSLASRDTVIVWPRDNGPNYVQRWIPEDRDCSMPPPFSYNGTYRPV***E***
PKSADKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEV
HNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTL
PPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQ
QGNVFSCSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO:60)

hDAO-Fc-Hepmut6

MPALGWAVAAILMLQTAMAEPSPGTLPRKAGVFSDLSNQELKAVHSFLWSKKELRLQPSSTTTMAKNT
VFLIEMLLPKKYHVLRFLDKGERHPVREARAVIFFGDQEHPNVTEFAVGPLPGPCYMRALSPRPGYQSS
WASRPISTAEYALLYHTLQEATKPLHQFFLNTTGFSFQDCHDRCLAFTDVAPRGVASGQRRSWLIIQRY
VEGYFLHPTGLELLVDHGSTDAGHWAVEQVWYNGKFYGSPEELARKYADGEVDVVVLEDPLPGGKGH
DSTEEPPLFSSHKPRGDFPSPIHVSGPRLVQPHGPRFRLEGNAVLYGGWSFAFRLRSSSGLQVLNVHF
GGERIAYEVSVQEAVALYGGHTPAGMQTKYLDVGWGLGSVTHELAPGIDCPETATFLDTFHYYDADDP
VHYPRALCLFEMPTGVPLRRHFNSNFKGGFNFYAGLKGQVLVLRTTSTVYNYDYIWDFIFYPNGVMEAK
MHATGYVHATFYTPEGLRHGTRLHTHLIGNIHTHLVHYRVDLDVAGTKNSFQTLQMKLENITNPWSPRH
RVVQPTLEQTQYSWERQAAFRF**GQT**LPKYLLFTSPQENPWGHKRSYRLQIHSMADQVLPPGWQEEQA
ITWARYPLAVTKYRESELCSSSIYHQNDPWHPPVVFEQFLHNNENIENEDLVAWVTVGFLHIPHSEDIPN
TATPGNSVGFLLRPFNFFPEDPSLASRDTVIVWPRDNGPNYVQRWIPEDRDCSMPPPFSYNGTYRPV***E***
PKSADKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEV
HNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTL
PPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQ
QGNVFSCSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO:61)

hDAO-Fc-Hepmut7

MPALGWAVAAILMLQTAMAEPSPGTLPRKAGVFSDLSNQELKAVHSFLWSKKELRLQPSSTTTMAKNT
VFLIEMLLPKKYHVLRFLDKGERHPVREARAVIFFGDQEHPNVTEFAVGPLPGPCYMRALSPRPGYQSS
WASRPISTAEYALLYHTLQEATKPLHQFFLNTTGFSFQDCHDRCLAFTDVAPRGVASGQRRSWLIIQRY
VEGYFLHPTGLELLVDHGSTDAGHWAVEQVWYNGKFYGSPEELARKYADGEVDVVVLEDPLPGGKGH
DSTEEPPLFSSHKPRGDFPSPIHVSGPRLVQPHGPRFRLEGNAVLYGGWSFAFRLRSSSGLQVLNVHF
GGERIAYEVSVQEAVALYGGHTPAGMQTKYLDVGWGLGSVTHELAPGIDCPETATFLDTFHYYDADDP
VHYPRALCLFEMPTGVPLRRHFNSNFKGGFNFYAGLKGQVLVLRTTSTVYNYDYIWDFIFYPNGVMEAK
MHATGYVHATFYTPEGLRHGTRLHTHLIGNIHTHLVHYRVDLDVAGTKNSFQTLQMKLENITNPWSPRH
RVVQPTLEQTQYSWERQAAF**S**FKRKLP**T**YLLFTSPQENPWGHKRSYRLQIHSMADQVLPPGWQEEQA
ITWARYPLAVTKYRESELCSSSIYHQNDPWHPPVVFEQFLHNNENIENEDLVAWVTVGFLHIPHSEDIPN
TATPGNSVGFLLRPFNFFPEDPSLASRDTVIVWPRDNGPNYVQRWIPEDRDCSMPPPFSYNGTYRPV***E***
PKSADKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEV
HNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTL
PPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQ
QGNVFSCSVMHEALHNHYTQKSLSLSPGK(SEQ ID NO:62)

图1续

hDAO-Fc-Cysmut

MPALGWAVAAILMLQTAMAEPSPGTLPRKAGVFSDLSNQELKAVHSFLWSKKELRLQPSSTTTMAKNT
VFLIEMLLPKKYHVLRFLDKGERHPVREARAVIFFGDQEHPNVTEFAVGPLPGP**A**YMRALSPRPGYQSS
WASRPISTAEYALLYHTLQEATKPLHQFFLNTTGFSFQDCHDRCLAFTDVAPRGVASGQRRSWLIIQRY
VEGYFLHPTGLELLVDHGSTDAGHWAVEQVWYNGKFYGSPEELARKYADGEVDVVVLEDPLPGGKGH
DSTEEPPLFSSHKPRGDFPSPIHVSGPRLVQPHGPRFRLEGNAVLYGGWSFAFRLRSSSGLQVLNVHF
GGERIAYEVSVQEAVALYGGHTPAGMQTKYLDVGWGLGSVTHELAPGIDCPETATFLDTFHYYDADDP
VHYPRALCLFEMPTGVPLRRHFNSNFKGGFNFYAGLKGQVLVLRTTSTVYNYDYIWDFIFYPNGVMEAK
MHATGYVHATFYTPEGLRHGTRLHTHLIGNIHTHLVHYRVDLDVAGTKNSFQTLQMKLENITNPWSPRH
RVVQPTLEQTQYSWERQAAFRFKRKLPKYLLFTSPQENPWGHKRSYRLQIHSMADQVLPPGWQEEQA
ITWARYPLAVTKYRESELCSSSIYHQNDPWHPPVVFEQFLHNNENIENEDLVAWVTVGFLHIPHSEDIPN
TATPGNSVGFLLRPFNFFPEDPSLASRDTVIVWPRDNGPNYVQRWIPEDRDCSMPPPFSYNGTYRPV***E***
PKSADKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEV
HNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTL
PPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQ
QGNVFSCSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO:63)

hDAO-Fc-Hepmut1-Cysmut

MPALGWAVAAILMLQTAMAEPSPGTLPRKAGVFSDLSNQELKAVHSFLWSKKELRLQPSSTTTMAKNT
VFLIEMLLPKKYHVLRFLDKGERHPVREARAVIFFGDQEHPNVTEFAVGPLPGP**A**YMRALSPRPGYQSS
WASRPISTAEYALLYHTLQEATKPLHQFFLNTTGFSFQDCHDRCLAFTDVAPRGVASGQRRSWLIIQRY
VEGYFLHPTGLELLVDHGSTDAGHWAVEQVWYNGKFYGSPEELARKYADGEVDVVVLEDPLPGGKGH
DSTEEPPLFSSHKPRGDFPSPIHVSGPRLVQPHGPRFRLEGNAVLYGGWSFAFRLRSSSGLQVLNVHF
GGERIAYEVSVQEAVALYGGHTPAGMQTKYLDVGWGLGSVTHELAPGIDCPETATFLDTFHYYDADDP
VHYPRALCLFEMPTGVPLRRHFNSNFKGGFNFYAGLKGQVLVLRTTSTVYNYDYIWDFIFYPNGVMEAK
MHATGYVHATFYTPEGLRHGTRLHTHLIGNIHTHLVHYRVDLDVAGTKNSFQTLQMKLENITNPWSPRH
RVVQPTLEQTQYSWERQAAF**S**FKRKLPKYLLFTSPQENPWGHKRSYRLQIHSMADQVLPPGWQEEQA
ITWARYPLAVTKYRESELCSSSIYHQNDPWHPPVVFEQFLHNNENIENEDLVAWVTVGFLHIPHSEDIPN
TATPGNSVGFLLRPFNFFPEDPSLASRDTVIVWPRDNGPNYVQRWIPEDRDCSMPPPFSYNGTYRPV***E***
PKSADKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEV
HNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTL
PPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQ
QGNVFSCSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO:64)

hDAO-Fc-Hepmut2-Cysmut

MPALGWAVAAILMLQTAMAEPSPGTLPRKAGVFSDLSNQELKAVHSFLWSKKELRLQPSSTTTMAKNT
VFLIEMLLPKKYHVLRFLDKGERHPVREARAVIFFGDQEHPNVTEFAVGPLPGP**A**YMRALSPRPGYQSS
WASRPISTAEYALLYHTLQEATKPLHQFFLNTTGFSFQDCHDRCLAFTDVAPRGVASGQRRSWLIIQRY
VEGYFLHPTGLELLVDHGSTDAGHWAVEQVWYNGKFYGSPEELARKYADGEVDVVVLEDPLPGGKGH
DSTEEPPLFSSHKPRGDFPSPIHVSGPRLVQPHGPRFRLEGNAVLYGGWSFAFRLRSSSGLQVLNVHF
GGERIAYEVSVQEAVALYGGHTPAGMQTKYLDVGWGLGSVTHELAPGIDCPETATFLDTFHYYDADDP
VHYPRALCLFEMPTGVPLRRHFNSNFKGGFNFYAGLKGQVLVLRTTSTVYNYDYIWDFIFYPNGVMEAK
MHATGYVHATFYTPEGLRHGTRLHTHLIGNIHTHLVHYRVDLDVAGTKNSFQTLQMKLENITNPWSPRH
RVVQPTLEQTQYSWERQAAFRFKRKLP**T**YLLFTSPQENPWGHKRSYRLQIHSMADQVLPPGWQEEQA
ITWARYPLAVTKYRESELCSSSIYHQNDPWHPPVVFEQFLHNNENIENEDLVAWVTVGFLHIPHSEDIPN
TATPGNSVGFLLRPFNFFPEDPSLASRDTVIVWPRDNGPNYVQRWIPEDRDCSMPPPFSYNGTYRPV***E***
PKSADKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEV
HNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTL
PPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQ
QGNVFSCSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO:65)

图1续

hDAO-Fc-Hepmut3-Cysmut

MPALGWAVAAILMLQTAMAEPSPGTLPRKAGVFSDLSNQELKAVHSFLWSKKELRLQPSSTTTMAKNT
VFLIEMLLPKKYHVLRFLDKGERHPVREARAVIFFGDQEHPNVTEFAVGPLPGP**A**YMRALSPRPGYQSS
WASRPISTAEYALLYHTLQEATKPLHQFFLNTTGFSFQDCHDRCLAFTDVAPRGVASGQRRSWLIIQRY
VEGYFLHPTGLELLVDHGSTDAGHWAVEQVWYNGKFYGSPEELARKYADGEVDVVVLEDPLPGGKGH
DSTEEPPLFSSHKPRGDFPSPIHVSGPRLVQPHGPRFRLEGNAVLYGGWSFAFRLRSSSGLQVLNVHF
GGERIAYEVSVQEAVALYGGHTPAGMQTKYLDVGWGLGSVTHELAPGIDCPETATFLDTFHYYDADDP
VHYPRALCLFEMPTGVPLRRHFNSNFKGGFNFYAGLKGQVLVLRTTSTVYNYDYIWDFIFYPNGVMEAK
MHATGYVHATFYTPEGLRHGTRLHTHLIGNIHTHLVHYRVDLDVAGTKNSFQTLQMKLENITNPWSPRH
RVVQPTLEQTQYSWERQAAFRFK**T**KLPKYLLFTSPQENPWGHKRSYRLQIHSMADQVLPPGWQEEQA
ITWARYPLAVTKYRESELCSSSIYHQNDPWHPPVVFEQFLHNNENIENEDLVAWVTVGFLHIPHSEDIPN
TATPGNSVGFLLRPFNFFPEDPSLASRDTVIVWPRDNGPNYVQRWIPEDRDCSMPPPFSYNGTYRPV***E***
PKSADKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEV
HNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTL
PPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQ
QGNVFSCSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO:66)

hDAO-Fc-Hepmut4-Cysmut

MPALGWAVAAILMLQTAMAEPSPGTLPRKAGVFSDLSNQELKAVHSFLWSKKELRLQPSSTTTMAKNT
VFLIEMLLPKKYHVLRFLDKGERHPVREARAVIFFGDQEHPNVTEFAVGPLPGP**A**YMRALSPRPGYQSS
WASRPISTAEYALLYHTLQEATKPLHQFFLNTTGFSFQDCHDRCLAFTDVAPRGVASGQRRSWLIIQRY
VEGYFLHPTGLELLVDHGSTDAGHWAVEQVWYNGKFYGSPEELARKYADGEVDVVVLEDPLPGGKGH
DSTEEPPLFSSHKPRGDFPSPIHVSGPRLVQPHGPRFRLEGNAVLYGGWSFAFRLRSSSGLQVLNVHF
GGERIAYEVSVQEAVALYGGHTPAGMQTKYLDVGWGLGSVTHELAPGIDCPETATFLDTFHYYDADDP
VHYPRALCLFEMPTGVPLRRHFNSNFKGGFNFYAGLKGQVLVLRTTSTVYNYDYIWDFIFYPNGVMEAK
MHATGYVHATFYTPEGLRHGTRLHTHLIGNIHTHLVHYRVDLDVAGTKNSFQTLQMKLENITNPWSPRH
RVVQPTLEQTQYSWERQAAF**S**FK**T**KLPKYLLFTSPQENPWGHKRSYRLQIHSMADQVLPPGWQEEQAI
TWARYPLAVTKYRESELCSSSIYHQNDPWHPPVVFEQFLHNNENIENEDLVAWVTVGFLHIPHSEDIPN
TATPGNSVGFLLRPFNFFPEDPSLASRDTVIVWPRDNGPNYVQRWIPEDRDCSMPPPFSYNGTYRPV***E***
PKSADKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEV
HNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTL
PPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQ
QGNVFSCSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO:67)

hDAO-Fc-Hepmut5-Cysmut

MPALGWAVAAILMLQTAMAEPSPGTLPRKAGVFSDLSNQELKAVHSFLWSKKELRLQPSSTTTMAKNT
VFLIEMLLPKKYHVLRFLDKGERHPVREARAVIFFGDQEHPNVTEFAVGPLPGP**A**YMRALSPRPGYQSS
WASRPISTAEYALLYHTLQEATKPLHQFFLNTTGFSFQDCHDRCLAFTDVAPRGVASGQRRSWLIIQRY
VEGYFLHPTGLELLVDHGSTDAGHWAVEQVWYNGKFYGSPEELARKYADGEVDVVVLEDPLPGGKGH
DSTEEPPLFSSHKPRGDFPSPIHVSGPRLVQPHGPRFRLEGNAVLYGGWSFAFRLRSSSGLQVLNVHF
GGERIAYEVSVQEAVALYGGHTPAGMQTKYLDVGWGLGSVTHELAPGIDCPETATFLDTFHYYDADDP
VHYPRALCLFEMPTGVPLRRHFNSNFKGGFNFYAGLKGQVLVLRTTSTVYNYDYIWDFIFYPNGVMEAK
MHATGYVHATFYTPEGLRHGTRLHTHLIGNIHTHLVHYRVDLDVAGTKNSFQTLQMKLENITNPWSPRH
RVVQPTLEQTQYSWERQAAFRFK**T**KLP**T**YLLFTSPQENPWGHKRSYRLQIHSMADQVLPPGWQEEQAI
TWARYPLAVTKYRESELCSSSIYHQNDPWHPPVVFEQFLHNNENIENEDLVAWVTVGFLHIPHSEDIPN
TATPGNSVGFLLRPFNFFPEDPSLASRDTVIVWPRDNGPNYVQRWIPEDRDCSMPPPFSYNGTYRPV***E***
PKSADKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEV
HNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTL
PPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQ
QGNVFSCSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO:68)

图1续

hDAO-Fc-Hepmut6-Cysmut

MPALGWAVAAILMLQTAMAEPSPGTLPRKAGVFSDLSNQELKAVHSFLWSKKELRLQPSSTTTMAKNT
VFLIEMLLPKKYHVLRFLDKGERHPVREARAVIFFGDQEHPNVTEFAVGPLPGP**A**YMRALSPRPGYQSS
WASRPISTAEYALLYHTLQEATKPLHQFFLNTTGFSFQDCHDRCLAFTDVAPRGVASGQRRSWLIIQRY
VEGYFLHPTGLELLVDHGSTDAGHWAVEQVWYNGKFYGSPEELARKYADGEVDVVVLEDPLPGGKGH
DSTEEPPLFSSHKPRGDFPSPIHVSGPRLVQPHGPRFRLEGNAVLYGGWSFAFRLRSSSGLQVLNVHF
GGERIAYEVSVQEAVALYGGHTPAGMQTKYLDVGWGLGSVTHELAPGIDCPETATFLDTFHYYDADDP
VHYPRALCLFEMPTGVPLRRHFNSNFKGGFNFYAGLKGQVLVLRTTSTVYNYDYIWDFIFYPNGVMEAK
MHATGYVHATFYTPEGLRHGTRLHTHLIGNIHTHLVHYRVDLDVAGTKNSFQTLQMKLENITNPWSPRH
RVVQPTLEQTQYSWERQAAFRF**GQT**LPKYLLFTSPQENPWGHKRSYRLQIHSMADQVLPPGWQEEQA
ITWARYPLAVTKYRESELCSSSIYHQNDPWHPPVVFEQFLHNNENIENEDLVAWVTVGFLHIPHSEDIPN
TATPGNSVGFLLRPFNFFPEDPSLASRDTVIVWPRDNGPNYVQRWIPEDRDCSMPPPFSYNGTYRPV
EPKSADKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEV
HNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTL
PPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQ
QGNVFSCSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO:69)

hDAO-Fc-Hepmut7-Cysmut

MPALGWAVAAILMLQTAMAEPSPGTLPRKAGVFSDLSNQELKAVHSFLWSKKELRLQPSSTTTMAKNT
VFLIEMLLPKKYHVLRFLDKGERHPVREARAVIFFGDQEHPNVTEFAVGPLPGP**A**YMRALSPRPGYQSS
WASRPISTAEYALLYHTLQEATKPLHQFFLNTTGFSFQDCHDRCLAFTDVAPRGVASGQRRSWLIIQRY
VEGYFLHPTGLELLVDHGSTDAGHWAVEQVWYNGKFYGSPEELARKYADGEVDVVVLEDPLPGGKGH
DSTEEPPLFSSHKPRGDFPSPIHVSGPRLVQPHGPRFRLEGNAVLYGGWSFAFRLRSSSGLQVLNVHF
GGERIAYEVSVQEAVALYGGHTPAGMQTKYLDVGWGLGSVTHELAPGIDCPETATFLDTFHYYDADDP
VHYPRALCLFEMPTGVPLRRHFNSNFKGGFNFYAGLKGQVLVLRTTSTVYNYDYIWDFIFYPNGVMEAK
MHATGYVHATFYTPEGLRHGTRLHTHLIGNIHTHLVHYRVDLDVAGTKNSFQTLQMKLENITNPWSPRH
RVVQPTLEQTQYSWERQAAF**S**FKRKLP**T**YLLFTSPQENPWGHKRSYRLQIHSMADQVLPPGWQEEQA
ITWARYPLAVTKYRESELCSSSIYHQNDPWHPPVVFEQFLHNNENIENEDLVAWVTVGFLHIPHSEDIPN
TATPGNSVGFLLRPFNFFPEDPSLASRDTVIVWPRDNGPNYVQRWIPEDRDCSMPPPFSYNGTYRPV***E***
PKSADKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEV
HNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTL
PPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQ
QGNVFSCSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO:70)

Fc-hDAO

ATGCCGGCCCTGGGCTGGGCCGTGGCTGCCATCCTGATGCTGCAGACGGCCATGGCG***GA***
GTGCCCCCCCCTGCCCCGCCCCCCCCGTGGCCGGCCCCTCCGTGTTCCTGTTCCCCCCCAAGCCC
AAGGACACCCTGATGATCTCCAGGACCCCCGAGGTGACCTGCGTGGTGGTGGACGTGTCCCACG
AGGACCCCGAGGTGAAGTTCAACTGGTACGTGGACGGCGTGGAGGTGCACAACGCCAAGACCA
AGCCCAGGGAGGAGCAGTACAACTCCACCTACAGGGTGGTGTCCGTGCTGACCGTGCTGCACC
AGGACTGGCTGAACGGCAAGGAGTACAAGTGCAAGGTGTCCAACAAGGGCCTGCCCTCCTCCAT
CGAGAAGACCATCTCCAAGGCCAAGGGCCAGCCCAGGGAGCCCCAGGTGTACACCCTGCCCCCC
CTCCAGGGAGGAGATGACCAAGAACCAGGTGTCCCTGACCTGCCTGGTGAAGGGCTTCTACCCC
TCCGACATCGCCGTGGAGTGGGAGTCCAACGGCCAGCCCGAGAACAACTACAAGACCACCCCC
CCCGTGCTGGACTCCGACGGCTCCTTCTTCCTGTACTCCAAGCTGACCGTGGACAAGTCCAGGT
GGCAGCAGGGCAACGTGTTCTCCTGCTCCGTGATGCACGAGGCCCTGCACAACCACTACACCCA
GAAGTCCCTGTCCCTGTCCCCCGGCAAGGAGCCCAAGTCCGCCGACAAGACCCACACCGAGCC
CTCCCCGGGGACTCTGCCCAGGAAGGCAGGGGTGTTTTCAGACCTAAGCAACCAAGAGCTGAAGG
CAGTGCACAGCTTCCTCTGGTCCAAGAAGGAGCTGAGGCTGCAGCCCTCCAGTACCACCACCATG
GCCAAGAACACCGTGTTTCTCATCGAGATGCTGCTGCCCAAGAAGTACCATGTGCTGAGGTTTCTG
GATAAAGGTGAAAGGCATCCTGTGCGGGAAGCCCGTGCCGTCATCTTCTTTGGTGACCAGGAGCA
TCCCAATGTCACCGAGTTTGCTGTGGGGCCCCTGCCAGGCCCCTGCTACATGCGAGCACTGTCCC
CCAGGCCTGGGTACCAGTCCTCCTGGGCATCGAGGCCCATCTCCACAGCAGAGTATGCCCTCCTC
TACCACACCCTGCAGGAAGCCACCAAGCCCCTGCATCAGTTCTTCCTCAATACCACAGGCTTCTCA
TTCCAAGACTGCCATGACAGATGCCTGGCCTTCACCGATGTGGCCCCCCGGGGTGTGGCTTCTGG
CCAGCGCCGCAGTTGGCTTATCATACAGCGCTATGTAGAAGGCTACTTTCTGCACCCCACTGGGCT
GGAGCTCCTCGTGGATCATGGGAGCACAGATGCTGGGCACTGGGCCGTGGAGCAGGTGTGGTAC
AACGGGAAGTTCTATGGGAGCCCAGAGGAACTGGCTCGGAAGTATGCAGATGGAGAGGTGGACGT

图1续

GGTGGTCCTGGAGGACCCGCTGCCTGGGGGCAAGGGGCATGACAGCACAGAGGAGCCGCCCCT
CTTCTCCTCCCACAAGCCCCGCGGGGACTTCCCCAGCCCCATCCATGTGAGCGGCCCCCGCTTGG
TCCAGCCCCACGGCCCTCGCTTCAGGCTGGAGGGCAACGCTGTGCTCTACGGCGGCTGGAGCTT
TGCCTTCCGGCTGCGCTCCTCCTCCGGGCTGCAGGTCCTGAACGTGCACTTCGGCGGAGAGCGC
ATTGCCTATGAGGTCAGCGTGCAAGAGGCAGTGGCGCTGTATGGAGGACACACACCTGCAGGCAT
GCAGACCAAGTACCTCGATGTCGGCTGGGGCCTGGGCAGCGTCACTCATGAGTTAGCCCCCGGC
ATCGACTGCCCGGAGACCGCCACCTTCCTGGACACTTTCCACTACTATGATGCCGATGACCCGGTC
CATTATCCCCGAGCCCTCTGCCTCTTTGAAATGCCCACAGGGGTGCCCCTTCGGCGGCACTTTAAT
TCCAACTTTAAAGGTGGCTTCAACTTCTATGCGGGGCTGAAGGGCCAGGTGCTGGTGCTGCGGAC
AACTTCAACTGTCTACAATTATGATTACATTTGGGACTTTATCTTCTACCCCAACGGGGTGATGGAG
GCCAAGATGCATGCCACTGGCTACGTCCACGCCACCTTCTACACCCCCGAGGGGCTGCGCCACG
GCACTCGCCTGCACACCCACCTGATTGGCAACATACACACTCACTTGGTGCACTACCGCGTAGACC
TGGATGTGGCAGGCACCAAGAACAGCTTCCAGACACTGCAGATGAAGCTAGAAAACATCACCAACC
CCTGGAGCCCAAGACACCGCGTGGTCCAGCCAACTCTGGAGCAGACGCAGTACTCCTGGGAGCG
CCAGGCGGCCTTCCGCTTCAAAAGGAAGCTGCCCAAGTACCTGCTCTTTACCAGCCCCCAGGAGA
ACCCCTGGGGCCACAAGCGCAGCTACCGCCTGCAGATCCACTCCATGGCCGACCAGGTGCTGCC
CCCAGGCTGGCAGGAGGAGCAGGCCATCACCTGGGCAAGGTACCCCCTGGCAGTGACCAAGTAC
CGGGAGTCGGAGCTGTGCAGCAGCAGCATCTACCACCAGAACGACCCCTGGCACCCGCCCGTGG
TCTTTGAGCAGTTTCTTCACAACAACGAGAACATTGAAAATGAGGACCTGGTGGCCTGGGTGACGG
TGGGCTTCCTGCACATCCCCCACTCAGAGGACATTCCCAACACAGCCACACCTGGGAACTCCGTG
GGCTTCCTGCTCCGGCCATTCAACTTCTTCCCAGAGGACCCCTCCCTGGCATCCAGAGACACTGTG
ATCGTGTGGCCTCGGGACAACGGCCCCAACTACGTCCAGCGCTGGATCCCTGAGGACAGGGACT
GCTCGATGCCTCCCCCTTTTAGCTACAATGGGACCTATAGACCTGTGTGA (SEQ ID NO:71)

Fc-hDAO-Hepmut1

ATGCCGGCCCTGGGCTGGGCCGTGGCTGCCATCCTGATGCTGCAGACGGCCATGGCG***GA***
GTGCCCCCCCCTGCCCCGCCCCCCCCGTGGCCGGCCCCTCCGTGTTCCTGTTCCCCCCCAAGCCC
AAGGACACCCTGATGATCTCCAGGACCCCCGAGGTGACCTGCGTGGTGGTGGACGTGTCCCACG
AGGACCCCGAGGTGAAGTTCAACTGGTACGTGGACGGCGTGGAGGTGCACAACGCCAAGACCA
AGCCCAGGGAGGAGCAGTACAACTCCACCTACAGGGTGGTGTCCGTGCTGACCGTGCTGCACC
AGGACTGGCTGAACGGCAAGGAGTACAAGTGCAAGGTGTCCAACAAGGGCCTGCCCTCCTCCAT
CGAGAAGACCATCTCCAAGGCCAAGGGCCAGCCCAGGGAGCCCCAGGTGTACACCCTGCCCCC
CTCCAGGGAGGAGATGACCAAGAACCAGGTGTCCCTGACCTGCCTGGTGAAGGGCTTCTACCCC
TCCGACATCGCCGTGGAGTGGGAGTCCAACGGCCAGCCCGAGAACAACTACAAGACCACCCCC
CCCGTGCTGGACTCCGACGGCTCCTTCTTCCTGTACTCCAAGCTGACCGTGGACAAGTCCAGGT
GGCAGCAGGGCAACGTGTTCTCCTGCTCCGTGATGCACGAGGCCCTGCACAACCACTACACCCA
GAAGTCCCTGTCCCTGTCCCCCGGCAAGGAGCCCAAGTCCGCCGACAAGACCCACACCGAGCC
CTCCCCGGGGACTCTGCCCAGGAAGGCAGGGGTGTTTTCAGACCTAAGCAACCAAGAGCTGAAGG
CAGTGCACAGCTTCCTCTGGTCCAAGAAGGAGCTGAGGCTGCAGCCCTCCAGTACCACCACCATG
GCCAAGAACACCGTGTTTCTCATCGAGATGCTGCTGCCCAAGAAGTACCATGTGCTGAGGTTTCTG
GATAAAGGTGAAAGGCATCCTGTGCGGGAAGCCCGTGCCGTCATCTTCTTTGGTGACCAGGAGCA
TCCCAATGTCACCGAGTTTGCTGTGGGGCCCCTGCCAGGCCCCTGCTACATGCGAGCACTGTCCC
CCAGGCCTGGGTACCAGTCCTCCTGGGCATCGAGGCCCATCTCCACAGCAGAGTATGCCCTCCTC
TACCACACCCTGCAGGAAGCCACCAAGCCCCTGCATCAGTTCTTCCTCAATACCACAGGCTTCTCA
TTCCAAGACTGCCATGACAGATGCCTGGCCTTCACCGATGTGGCCCCCCGGGGTGTGGCTTCTGG
CCAGCGCCGCAGTTGGCTTATCATACAGCGCTATGTAGAAGGCTACTTTCTGCACCCCACTGGGCT
GGAGCTCCTCGTGGATCATGGGAGCACAGATGCTGGGCACTGGGCCGTGGAGCAGGTGTGGTAC
AACGGGAAGTTCTATGGGAGCCCAGAGGAACTGGCTCGGAAGTATGCAGATGGAGAGGTGGACGT
GGTGGTCCTGGAGGACCCGCTGCCTGGGGGCAAGGGGCATGACAGCACAGAGGAGCCGCCCCT
CTTCTCCTCCCACAAGCCCCGCGGGGACTTCCCCAGCCCCATCCATGTGAGCGGCCCCCGCTTGG
TCCAGCCCCACGGCCCTCGCTTCAGGCTGGAGGGCAACGCTGTGCTCTACGGCGGCTGGAGCTT
TGCCTTCCGGCTGCGCTCCTCCTCCGGGCTGCAGGTCCTGAACGTGCACTTCGGCGGAGAGCGC
ATTGCCTATGAGGTCAGCGTGCAAGAGGCAGTGGCGCTGTATGGAGGACACACACCTGCAGGCAT
GCAGACCAAGTACCTCGATGTCGGCTGGGGCCTGGGCAGCGTCACTCATGAGTTAGCCCCCGGC
ATCGACTGCCCGGAGACCGCCACCTTCCTGGACACTTTCCACTACTATGATGCCGATGACCCGGTC
CATTATCCCCGAGCCCTCTGCCTCTTTGAAATGCCCACAGGGGTGCCCCTTCGGCGGCACTTTAAT
TCCAACTTTAAAGGTGGCTTCAACTTCTATGCGGGGCTGAAGGGCCAGGTGCTGGTGCTGCGGAC
AACTTCAACTGTCTACAATTATGATTACATTTGGGACTTTATCTTCTACCCCAACGGGGTGATGGAG
GCCAAGATGCATGCCACTGGCTACGTCCACGCCACCTTCTACACCCCCGAGGGGCTGCGCCACG
GCACTCGCCTGCACACCCACCTGATTGGCAACATACACACTCACTTGGTGCACTACCGCGTAGACC

图1续

TGGATGTGGCAGGCACCAAGAACAGCTTCCAGACACTGCAGATGAAGCTAGAAAACATCACCAACC
CCTGGAGCCCAAGACACCGCGTGGTCCAGCCAACTCTGGAGCAGACGCAGTACTCCTGGGAGCG
CCAGGCGGCCTTC**AGC**TTCAAAAGGAAGCTGCCCAAGTACCTGCTCTTTACCAGCCCCCAGGAGA
ACCCCTGGGGCCACAAGCGCAGCTACCGCCTGCAGATCCACTCCATGGCCGACCAGGTGCTGCC
CCCAGGCTGGCAGGAGGAGCAGGCCATCACCTGGGCAAGGTACCCCCTGGCAGTGACCAAGTAC
CGGGAGTCGGAGCTGTGCAGCAGCAGCATCTACCACCAGAACGACCCCTGGCACCCGCCCGTGG
TCTTTGAGCAGTTTCTTCACAACAACGAGAACATTGAAAATGAGGACCTGGTGGCCTGGGTGACGG
TGGGCTTCCTGCACATCCCCCACTCAGAGGACATTCCCAACACAGCCACACCTGGGAACTCCGTG
GGCTTCCTGCTCCGGCCATTCAACTTCTTCCCAGAGGACCCCTCCCTGGCATCCAGAGACACTGTG
ATCGTGTGGCCTCGGGACAACGGCCCCAACTACGTCCAGCGCTGGATCCCTGAGGACAGGGACT
GCTCGATGCCTCCCCCTTTTAGCTACAATGGGACCTATAGACCTGTGTGA (SEQ ID NO:72)

Fc-hDAO-Hepmut2

ATGCCGGCCCTGGGCTGGGCCGTGGCTGCCATCCTGATGCTGCAGACGGCCATGGCG***GA***
GTGCCCCCCCTGCCCCGCCCCCCCCGTGGCCGGCCCCTCCGTGTTCCTGTTCCCCCCCAAGCCC
AAGGACACCCTGATGATCTCCAGGACCCCCGAGGTGACCTGCGTGGTGGTGGACGTGTCCCACG
AGGACCCCGAGGTGAAGTTCAACTGGTACGTGGACGGCGTGGAGGTGCACAACGCCAAGACCA
AGCCCAGGGAGGAGCAGTACAACTCCACCTACAGGGTGGTGTCCGTGCTGACCGTGCTGCACC
AGGACTGGCTGAACGGCAAGGAGTACAAGTGCAAGGTGTCCAACAAGGGCCTGCCCTCCTCCAT
CGAGAAGACCATCTCCAAGGCCAAGGGCCAGCCCAGGGAGCCCCAGGTGTACACCCTGCCCCC
CTCCAGGGAGGAGATGACCAAGAACCAGGTGTCCCTGACCTGCCTGGTGAAGGGCTTCTACCCC
TCCGACATCGCCGTGGAGTGGGAGTCCAACGGCCAGCCCGAGAACAACTACAAGACCACCCCC
CCCGTGCTGGACTCCGACGGCTCCTTCTTCCTGTACTCCAAGCTGACCGTGGACAAGTCCAGGT
GGCAGCAGGGCAACGTGTTCTCCTGCTCCGTGATGCACGAGGCCCTGCACAACCACTACACCCA
GAAGTCCCTGTCCCTGTCCCCCGGCAAGGAGCCCAAGTCCGCCGACAAGACCCACACCGAGCC
CTCCCCGGGGACTCTGCCCAGGAAGGCAGGGGTGTTTTCAGACCTAAGCAACCAAGAGCTGAAGG
CAGTGCACAGCTTCCTCTGGTCCAAGAAGGAGCTGAGGCTGCAGCCCTCCAGTACCACCACCATG
GCCAAGAACACCGTGTTTCTCATCGAGATGCTGCTGCCCAAGAAGTACCATGTGCTGAGGTTTCTG
GATAAAGGTGAAAGGCATCCTGTGCGGGAAGCCCGTGCCGTCATCTTCTTTGGTGACCAGGAGCA
TCCCAATGTCACCGAGTTTGCTGTGGGGCCCCTGCCAGGCCCCTGCTACATGCGAGCACTGTCCC
CCAGGCCTGGGTACCAGTCCTCCTGGGCATCGAGGCCCATCTCCACAGCAGAGTATGCCCTCCTC
TACCACACCCTGCAGGAAGCCACCAAGCCCCTGCATCAGTTCTTCCTCAATACCACAGGCTTCTCA
TTCCAAGACTGCCATGACAGATGCCTGGCCTTCACCGATGTGGCCCCCCGGGGTGTGGCTTCTGG
CCAGCGCCGCAGTTGGCTTATCATACAGCGCTATGTAGAAGGCTACTTTCTGCACCCCACTGGGCT
GGAGCTCCTCGTGGATCATGGGAGCACAGATGCTGGGCACTGGGCCGTGGAGCAGGTGTGGTAC
AACGGGAAGTTCTATGGGAGCCCAGAGGAACTGGCTCGGAAGTATGCAGATGGAGAGGTGGACGT
GGTGGTCCTGGAGGACCCGCTGCCTGGGGGCAAGGGGCATGACAGCACAGAGGAGCCGCCCCT
CTTCTCCTCCCACAAGCCCCGCGGGGACTTCCCCAGCCCCATCCATGTGAGCGGCCCCCGCTTGG
TCCAGCCCCACGGCCCTCGCTTCAGGCTGGAGGGCAACGCTGTGCTCTACGGCGGCTGGAGCTT
TGCCTTCCGGCTGCGCTCCTCCTCCGGGCTGCAGGTCCTGAACGTGCACTTCGGCGGAGAGCGC
ATTGCCTATGAGGTCAGCGTGCAAGAGGCAGTGGCGCTGTATGGAGGACACACACCTGCAGGCAT
GCAGACCAAGTACCTCGATGTCGGCTGGGGCCTGGGCAGCGTCACTCATGAGTTAGCCCCCGGC
ATCGACTGCCCGGAGACCGCCACCTTCCTGGACACTTTCCACTACTATGATGCCGATGACCCGGTC
CATTATCCCCGAGCCCTCTGCCTCTTTGAAATGCCCACAGGGGTGCCCCTTCGGCGGCACTTTAAT
TCCAACTTTAAAGGTGGCTTCAACTTCTATGCGGGGCTGAAGGGCCAGGTGCTGGTGCTGCGGAC
AACTTCAACTGTCTACAATTATGATTACATTTGGGACTTTATCTTCTACCCCAACGGGGTGATGGAG
GCCAAGATGCATGCCACTGGCTACGTCCACGCCACCTTCTACACCCCCGAGGGGCTGCGCCACG
GCACTCGCCTGCACACCCACCTGATTGGCAACATACACACTCACTTGGTGCACTACCGCGTAGACC
TGGATGTGGCAGGCACCAAGAACAGCTTCCAGACACTGCAGATGAAGCTAGAAAACATCACCAACC
CCTGGAGCCCAAGACACCGCGTGGTCCAGCCAACTCTGGAGCAGACGCAGTACTCCTGGGAGCG
CCAGGCGGCCTTCCGCTTCAAAAGGAAGCTGCCC**ACG**TACCTGCTCTTTACCAGCCCCCAGGAGA
ACCCCTGGGGCCACAAGCGCAGCTACCGCCTGCAGATCCACTCCATGGCCGACCAGGTGCTGCC
CCCAGGCTGGCAGGAGGAGCAGGCCATCACCTGGGCAAGGTACCCCCTGGCAGTGACCAAGTAC
CGGGAGTCGGAGCTGTGCAGCAGCAGCATCTACCACCAGAACGACCCCTGGCACCCGCCCGTGG
TCTTTGAGCAGTTTCTTCACAACAACGAGAACATTGAAAATGAGGACCTGGTGGCCTGGGTGACGG
TGGGCTTCCTGCACATCCCCCACTCAGAGGACATTCCCAACACAGCCACACCTGGGAACTCCGTG
GGCTTCCTGCTCCGGCCATTCAACTTCTTCCCAGAGGACCCCTCCCTGGCATCCAGAGACACTGTG
ATCGTGTGGCCTCGGGACAACGGCCCCAACTACGTCCAGCGCTGGATCCCTGAGGACAGGGACT

图1续

Fc-hDAO-Hepmut3

ATGCCGGCCCTGGGCTGGGCCGTGGCTGCCATCCTGATGCTGCAGACGGCCATGGCG***GA***
GTGCCCCCCCCTGCCCCGCCCCCCCCGTGGCCGGCCCCTCCGTGTTCCTGTTCCCCCCCAAGCCC
AAGGACACCCTGATGATCTCCAGGACCCCCGAGGTGACCTGCGTGGTGGTGGACGTGTCCCACG
AGGACCCCGAGGTGAAGTTCAACTGGTACGTGGACGGCGTGGAGGTGCACAACGCCAAGACCA
AGCCCAGGGAGGAGCAGTACAACTCCACCTACAGGGTGGTGTCCGTGCTGACCGTGCTGCACC
AGGACTGGCTGAACGGCAAGGAGTACAAGTGCAAGGTGTCCAACAAGGGCCTGCCCTCCTCCAT
CGAGAAGACCATCTCCAAGGCCAAGGGCCAGCCCAGGGAGCCCCAGGTGTACACCCTGCCCCC
CTCCAGGGAGGAGATGACCAAGAACCAGGTGTCCCTGACCTGCCTGGTGAAGGGCTTCTACCCC
TCCGACATCGCCGTGGAGTGGGAGTCCAACGGCCAGCCCGAGAACAACTACAAGACCACCCCC
CCCGTGCTGGACTCCGACGGCTCCTTCTTCCTGTACTCCAAGCTGACCGTGGACAAGTCCAGGT
GGCAGCAGGGCAACGTGTTCTCCTGCTCCGTGATGCACGAGGCCCTGCACAACCACTACACCCA
GAAGTCCCTGTCCCTGTCCCCCGGCAAGGAGCCCAAGTCCGCCGACAAGACCCACACCGAGCC
CTCCCCGGGGACTCTGCCCAGGAAGGCAGGGGTGTTTTCAGACCTAAGCAACCAAGAGCTGAAGG
CAGTGCACAGCTTCCTCTGGTCCAAGAAGGAGCTGAGGCTGCAGCCCTCCAGTACCACCACCATG
GCCAAGAACACCGTGTTTCTCATCGAGATGCTGCTGCCCAAGAAGTACCATGTGCTGAGGTTTCTG
GATAAAGGTGAAAGGCATCCTGTGCGGGAAGCCCGTGCCGTCATCTTCTTTGGTGACCAGGAGCA
TCCCAATGTCACCGAGTTTGCTGTGGGGCCCCTGCCAGGCCCCTGCTACATGCGAGCACTGTCCC
CCAGGCCTGGGTACCAGTCCTCCTGGGCATCGAGGCCCATCTCCACAGCAGAGTATGCCCTCCTC
TACCACACCCTGCAGGAAGCCACCAAGCCCCTGCATCAGTTCTTCCTCAATACCACAGGCTTCTCA
TTCCAAGACTGCCATGACAGATGCCTGGCCTTCACCGATGTGGCCCCCCGGGGTGTGGCTTCTGG
CCAGCGCCGCAGTTGGCTTATCATACAGCGCTATGTAGAAGGCTACTTTCTGCACCCCACTGGGCT
GGAGCTCCTCGTGGATCATGGGAGCACAGATGCTGGGCACTGGGCCGTGGAGCAGGTGTGGTAC
AACGGGAAGTTCTATGGGAGCCCAGAGGAACTGGCTCGGAAGTATGCAGATGGAGAGGTGGACGT
GGTGGTCCTGGAGGACCCGCTGCCTGGGGGCAAGGGGCATGACAGCACAGAGGAGCCGCCCCT
CTTCTCCTCCCACAAGCCCCGCGGGGACTTCCCCAGCCCCATCCATGTGAGCGGCCCCCGCTTGG
TCCAGCCCCACGGCCCTCGCTTCAGGCTGGAGGGCAACGCTGTGCTCTACGGCGGCTGGAGCTT
TGCCTTCCGGCTGCGCTCCTCCTCCGGGCTGCAGGTCCTGAACGTGCACTTCGGCGGAGAGCGC
ATTGCCTATGAGGTCAGCGTGCAAGAGGCAGTGGCGCTGTATGGAGGACACACACCTGCAGGCAT
GCAGACCAAGTACCTCGATGTCGGCTGGGGCCTGGGCAGCGTCACTCATGAGTTAGCCCCCGGC
ATCGACTGCCCGGAGACCGCCACCTTCCTGGACACTTTCCACTACTATGATGCCGATGACCCGGTC
CATTATCCCCGAGCCCTCTGCCTCTTTGAAATGCCCACAGGGGTGCCCCTTCGGCGGCACTTTAAT
TCCAACTTTAAAGGTGGCTTCAACTTCTATGCGGGGCTGAAGGGCCAGGTGCTGGTGCTGCGGAC
AACTTCAACTGTCTACAATTATGATTACATTTGGGACTTTATCTTCTACCCCAACGGGGTGATGGAG
GCCAAGATGCATGCCACTGGCTACGTCCACGCCACCTTCTACACCCCCGAGGGGCTGCGCCACG
GCACTCGCCTGCACACCCACCTGATTGGCAACATACACACTCACTTGGTGCACTACCGCGTAGACC
TGGATGTGGCAGGCACCAAGAACAGCTTCCAGACACTGCAGATGAAGCTAGAAAACATCACCAACC
CCTGGAGCCCAAGACACCGCGTGGTCCAGCCAACTCTGGAGCAGACGCAGTACTCCTGGGAGCG
CCAGGCGGCCTTCCGCTTCAAA**ACG**AAGCTGCCCAAGTACCTGCTCTTTACCAGCCCCCAGGAGA
ACCCCTGGGGCCACAAGCGCAGCTACCGCCTGCAGATCCACTCCATGGCCGACCAGGTGCTGCC
CCCAGGCTGGCAGGAGGAGCAGGCCATCACCTGGGCAAGGTACCCCCTGGCAGTGACCAAGTAC
CGGGAGTCGGAGCTGTGCAGCAGCAGCATCTACCACCAGAACGACCCCTGGCACCCGCCCGTGG
TCTTTGAGCAGTTTCTTCACAACAACGAGAACATTGAAAATGAGGACCTGGTGGCCTGGGTGACGG
TGGGCTTCCTGCACATCCCCCACTCAGAGGACATTCCCAACACAGCCACACCTGGGAACTCCGTG
GGCTTCCTGCTCCGGCCATTCAACTTCTTCCCAGAGGACCCCTCCCTGGCATCCAGAGACACTGTG
ATCGTGTGGCCTCGGGACAACGGCCCCAACTACGTCCAGCGCTGGATCCCTGAGGACAGGGACT
GCTCGATGCCTCCCCCTTTTAGCTACAATGGGACCTATAGACCTGTGTGA (SEQ ID NO:74)

Fc-hDAO-Hepmut4

ATGCCGGCCCTGGGCTGGGCCGTGGCTGCCATCCTGATGCTGCAGACGGCCATGGCG***GA***
GTGCCCCCCCCTGCCCCGCCCCCCCCCGTGGCCGGCCCCTCCGTGTTCCTGTTCCCCCCCAAGCCC
AAGGACACCCTGATGATCTCCAGGACCCCCGAGGTGACCTGCGTGGTGGTGGACGTGTCCCACG
AGGACCCCGAGGTGAAGTTCAACTGGTACGTGGACGGCGTGGAGGTGCACAACGCCAAGACCA
AGCCCAGGGAGGAGCAGTACAACTCCACCTACAGGGTGGTGTCCGTGCTGACCGTGCTGCACC
AGGACTGGCTGAACGGCAAGGAGTACAAGTGCAAGGTGTCCAACAAGGGCCTGCCCTCCTCCAT
CGAGAAGACCATCTCCAAGGCCAAGGGCCAGCCCAGGGAGCCCCAGGTGTACACCCTGCCCCC
CTCCAGGGAGGAGATGACCAAGAACCAGGTGTCCCTGACCTGCCTGGTGAAGGGCTTCTACCCC
TCCGACATCGCCGTGGAGTGGGAGTCCAACGGCCAGCCCGAGAACAACTACAAGACCACCCCC

图1续

CCCGTGCTGGACTCCGACGGCTCCTTCTTCCTGTACTCCAAGCTGACCGTGGACAAGTCCAGGT
GGCAGCAGGGCAACGTGTTCTCCTGCTCCGTGATGCACGAGGCCCTGCACAACCACTACACCCA
GAAGTCCCTGTCCCTGTCCCCCGGCAAGGAGCCCAAGTCCGCCGACAAGACCCACACCGAGCC
CTCCCCGGGGACTCTGCCCAGGAAGGCAGGGGTGTTTTCAGACCTAAGCAACCAAGAGCTGAAGG
CAGTGCACAGCTTCCTCTGGTCCAAGAAGGAGCTGAGGCTGCAGCCCTCCAGTACCACCACCATG
GCCAAGAACACCGTGTTTCTCATCGAGATGCTGCTGCCCAAGAAGTACCATGTGCTGAGGTTTCTG
GATAAAGGTGAAAGGCATCCTGTGCGGGAAGCCCGTGCCGTCATCTTCTTTGGTGACCAGGAGCA
TCCCAATGTCACCGAGTTTGCTGTGGGGCCCCTGCCAGGCCCCTGCTACATGCGAGCACTGTCCC
CCAGGCCTGGGTACCAGTCCTCCTGGGCATCGAGGCCCATCTCCACAGCAGAGTATGCCCTCCTC
TACCACACCCTGCAGGAAGCCACCAAGCCCCTGCATCAGTTCTTCCTCAATACCACAGGCTTCTCA
TTCCAAGACTGCCATGACAGATGCCTGGCCTTCACCGATGTGGCCCCCCGGGGTGTGGCTTCTGG
CCAGCGCCGCAGTTGGCTTATCATACAGCGCTATGTAGAAGGCTACTTTCTGCACCCCACTGGGCT
GGAGCTCCTCGTGGATCATGGGAGCACAGATGCTGGGCACTGGGCCGTGGAGCAGGTGTGGTAC
AACGGGAAGTTCTATGGGAGCCCAGAGGAACTGGCTCGGAAGTATGCAGATGGAGAGGTGGACGT
GGTGGTCCTGGAGGACCCGCTGCCTGGGGGCAAGGGGCATGACAGCACAGAGGAGCCGCCCCT
CTTCTCCTCCCACAAGCCCCGCGGGGACTTCCCCAGCCCCATCCATGTGAGCGGCCCCCGCTTGG
TCCAGCCCCACGGCCCTCGCTTCAGGCTGGAGGGCAACGCTGTGCTCTACGGCGGCTGGAGCTT
TGCCTTCCGGCTGCGCTCCTCCTCCGGGCTGCAGGTCCTGAACGTGCACTTCGGCGGAGAGCGC
ATTGCCTATGAGGTCAGCGTGCAAGAGGCAGTGGCGCTGTATGGAGGACACACACCTGCAGGCAT
GCAGACCAAGTACCTCGATGTCGGCTGGGGCCTGGGCAGCGTCACTCATGAGTTAGCCCCCGGC
ATCGACTGCCCGGAGACCGCCACCTTCCTGGACACTTTCCACTACTATGATGCCGATGACCCGGTC
CATTATCCCCGAGCCCTCTGCCTCTTTGAAATGCCCACAGGGGTGCCCCTTCGGCGGCACTTTAAT
TCCAACTTTAAAGGTGGCTTCAACTTCTATGCGGGGCTGAAGGGCCAGGTGCTGGTGCTGCGGAC
AACTTCAACTGTCTACAATTATGATTACATTTGGGACTTTATCTTCTACCCCAACGGGGTGATGGAG
GCCAAGATGCATGCCACTGGCTACGTCCACGCCACCTTCTACACCCCCGAGGGGCTGCGCCACG
GCACTCGCCTGCACACCCACCTGATTGGCAACATACACACTCACTTGGTGCACTACCGCGTAGACC
TGGATGTGGCAGGCACCAAGAACAGCTTCCAGACACTGCAGATGAAGCTAGAAAACATCACCAACC
CCTGGAGCCCAAGACACCGCGTGGTCCAGCCAACTCTGGAGCAGACGCAGTACTCCTGGGAGCG
CCAGGCGGCCTTC**AGC**TTCAAA**ACG**AAGCTGCCCAAGTACCTGCTCTTTACCAGCCCCCAGGAGA
ACCCCTGGGGCCACAAGCGCAGCTACCGCCTGCAGATCCACTCCATGGCCGACCAGGTGCTGCC
CCCAGGCTGGCAGGAGGAGCAGGCCATCACCTGGGCAAGGTACCCCCTGGCAGTGACCAAGTAC
CGGGAGTCGGAGCTGTGCAGCAGCAGCATCTACCACCAGAACGACCCCTGGCACCCGCCCGTGG
TCTTTGAGCAGTTTCTTCACAACAACGAGAACATTGAAAATGAGGACCTGGTGGCCTGGGTGACGG
TGGGCTTCCTGCACATCCCCCACTCAGAGGACATTCCCAACACAGCCACACCTGGGAACTCCGTG
GGCTTCCTGCTCCGGCCATTCAACTTCTTCCCAGAGGACCCCTCCCTGGCATCCAGAGACACTGTG
ATCGTGTGGCCTCGGGACAACGGCCCCAACTACGTCCAGCGCTGGATCCCTGAGGACAGGGACT
GCTCGATGCCTCCCCCTTTTAGCTACAATGGGACCTATAGACCTGTGTGA (SEQ ID NO:75)

Fc-hDAO-Hepmut5

ATGCCGGCCCTGGGCTGGGCCGTGGCTGCCATCCTGATGCTGCAGACGGCCATGGCG***GA***
GTGCCCCCCCCTGCCCCGCCCCCCCCCGTGGCCGGCCCCTCCGTGTTCCTGTTCCCCCCCAAGCCC
AAGGACACCCTGATGATCTCCAGGACCCCCGAGGTGACCTGCGTGGTGGTGGACGTGTCCCACG
AGGACCCCGAGGTGAAGTTCAACTGGTACGTGGACGGCGTGGAGGTGCACAACGCCAAGACCA
AGCCCAGGGAGGAGCAGTACAACTCCACCTACAGGGTGGTGTCCGTGCTGACCGTGCTGCACC
AGGACTGGCTGAACGGCAAGGAGTACAAGTGCAAGGTGTCCAACAAGGGCCTGCCCTCCTCCAT
CGAGAAGACCATCTCCAAGGCCAAGGGCCAGCCCAGGGAGCCCCAGGTGTACACCCTGCCCCCC
CTCCAGGGAGGAGATGACCAAGAACCAGGTGTCCCTGACCTGCCTGGTGAAGGGCTTCTACCCC
TCCGACATCGCCGTGGAGTGGGAGTCCAACGGCCAGCCCGAGAACAACTACAAGACCACCCCC
CCCGTGCTGGACTCCGACGGCTCCTTCTTCCTGTACTCCAAGCTGACCGTGGACAAGTCCAGGT
GGCAGCAGGGCAACGTGTTCTCCTGCTCCGTGATGCACGAGGCCCTGCACAACCACTACACCCA
GAAGTCCCTGTCCCTGTCCCCCGGCAAGGAGCCCAAGTCCGCCGACAAGACCCACACCGAGCC
CTCCCCGGGGACTCTGCCCAGGAAGGCAGGGGTGTTTTCAGACCTAAGCAACCAAGAGCTGAAGG
CAGTGCACAGCTTCCTCTGGTCCAAGAAGGAGCTGAGGCTGCAGCCCTCCAGTACCACCACCATG
GCCAAGAACACCGTGTTTCTCATCGAGATGCTGCTGCCCAAGAAGTACCATGTGCTGAGGTTTCTG
GATAAAGGTGAAAGGCATCCTGTGCGGGAAGCCCGTGCCGTCATCTTCTTTGGTGACCAGGAGCA
TCCCAATGTCACCGAGTTTGCTGTGGGGCCCCTGCCAGGCCCCTGCTACATGCGAGCACTGTCCC
CCAGGCCTGGGTACCAGTCCTCCTGGGCATCGAGGCCCATCTCCACAGCAGAGTATGCCCTCCTC
TACCACACCCTGCAGGAAGCCACCAAGCCCCTGCATCAGTTCTTCCTCAATACCACAGGCTTCTCA

图1续

TTCCAAGACTGCCATGACAGATGCCTGGCCTTCACCGATGTGGCCCCCCGGGGTGTGGCTTCTGG
CCAGCGCCGCAGTTGGCTTATCATACAGCGCTATGTAGAAGGCTACTTTCTGCACCCCACTGGGCT
GGAGCTCCTCGTGGATCATGGGAGCACAGATGCTGGGCACTGGGCCGTGGAGCAGGTGTGGTAC
AACGGGAAGTTCTATGGGAGCCCAGAGGAACTGGCTCGGAAGTATGCAGATGGAGAGGTGGACGT
GGTGGTCCTGGAGGACCCGCTGCCTGGGGGCAAGGGGCATGACAGCACAGAGGAGCCGCCCCT
CTTCTCCTCCCACAAGCCCCGCGGGGACTTCCCCAGCCCCATCCATGTGAGCGGCCCCCGCTTGG
TCCAGCCCCACGGCCCTCGCTTCAGGCTGGAGGGCAACGCTGTGCTCTACGGCGGCTGGAGCTT
TGCCTTCCGGCTGCGCTCCTCCTCCGGGCTGCAGGTCCTGAACGTGCACTTCGGCGGAGAGCGC
ATTGCCTATGAGGTCAGCGTGCAAGAGGCAGTGGCGCTGTATGGAGGACACACACCTGCAGGCAT
GCAGACCAAGTACCTCGATGTCGGCTGGGGCCTGGGCAGCGTCACTCATGAGTTAGCCCCCGGC
ATCGACTGCCCGGAGACCGCCACCTTCCTGGACACTTTCCACTACTATGATGCCGATGACCCGGTC
CATTATCCCCGAGCCCTCTGCCTCTTTGAAATGCCCACAGGGGTGCCCCTTCGGCGGCACTTTAAT
TCCAACTTTAAAGGTGGCTTCAACTTCTATGCGGGGCTGAAGGGCCAGGTGCTGGTGCTGCGGAC
AACTTCAACTGTCTACAATTATGATTACATTTGGGACTTTATCTTCTACCCCAACGGGGTGATGGAG
GCCAAGATGCATGCCACTGGCTACGTCCACGCCACCTTCTACACCCCCGAGGGGCTGCGCCACG
GCACTCGCCTGCACACCCACCTGATTGGCAACATACACACTCACTTGGTGCACTACCGCGTAGACC
TGGATGTGGCAGGCACCAAGAACAGCTTCCAGACACTGCAGATGAAGCTAGAAAACATCACCAACC
CCTGGAGCCCAAGACACCGCGTGGTCCAGCCAACTCTGGAGCAGACGCAGTACTCCTGGGAGCG
CCAGGCGGCCTTCCGCTTCAAA**ACG**AAGCTGCCC**ACG**TACCTGCTCTTTACCAGCCCCCAGGAGA
ACCCCTGGGGCCACAAGCGCAGCTACCGCCTGCAGATCCACTCCATGGCCGACCAGGTGCTGCC
CCCAGGCTGGCAGGAGGAGCAGGCCATCACCTGGGCAAGGTACCCCCTGGCAGTGACCAAGTAC
CGGGAGTCGGAGCTGTGCAGCAGCAGCATCTACCACCAGAACGACCCCTGGCACCCGCCCGTGG
TCTTTGAGCAGTTTCTTCACAACAACGAGAACATTGAAAATGAGGACCTGGTGGCCTGGGTGACGG
TGGGCTTCCTGCACATCCCCCACTCAGAGGACATTCCCAACACAGCCACACCTGGGAACTCCGTG
GGCTTCCTGCTCCGGCCATTCAACTTCTTCCCAGAGGACCCCTCCCTGGCATCCAGAGACACTGTG
ATCGTGTGGCCTCGGGACAACGGCCCCAACTACGTCCAGCGCTGGATCCCTGAGGACAGGGACT
GCTCGATGCCTCCCCCTTTTAGCTACAATGGGACCTATAGACCTGTGTGA (SEQ ID NO:76)

Fc-hDAO-Hepmut6

ATGCCGGCCCTGGGCTGGGCCGTGGCTGCCATCCTGATGCTGCAGACGGCCATGGCG***GA***
GTGCCCCCCCTGCCCCGCCCCCCCCGTGGCCGGCCCCTCCGTGTTCCTGTTCCCCCCCAAGCCC
AAGGACACCCTGATGATCTCCAGGACCCCCGAGGTGACCTGCGTGGTGGTGGACGTGTCCCACG
AGGACCCCGAGGTGAAGTTCAACTGGTACGTGGACGGCGTGGAGGTGCACAACGCCAAGACCA
AGCCCAGGGAGGAGCAGTACAACTCCACCTACAGGGTGGTGTCCGTGCTGACCGTGCTGCACC
AGGACTGGCTGAACGGCAAGGAGTACAAGTGCAAGGTGTCCAACAAGGGCCTGCCCTCCTCCAT
CGAGAAGACCATCTCCAAGGCCAAGGGCCAGCCCAGGGAGCCCCAGGTGTACACCCTGCCCCC
CTCCAGGGAGGAGATGACCAAGAACCAGGTGTCCCTGACCTGCCTGGTGAAGGGCTTCTACCCC
TCCGACATCGCCGTGGAGTGGGAGTCCAACGGCCAGCCCGAGAACAACTACAAGACCACCCCC
CCCGTGCTGGACTCCGACGGCTCCTTCTTCCTGTACTCCAAGCTGACCGTGGACAAGTCCAGGT
GGCAGCAGGGCAACGTGTTCTCCTGCTCCGTGATGCACGAGGCCCTGCACAACCACTACACCCA
GAAGTCCCTGTCCCTGTCCCCCGGCAAGGAGCCCAAGTCCGCCGACAAGACCCACACCGAGCC
CTCCCCGGGGACTCTGCCCAGGAAGGCAGGGGTGTTTTCAGACCTAAGCAACCAAGAGCTGAAGG
CAGTGCACAGCTTCCTCTGGTCCAAGAAGGAGCTGAGGCTGCAGCCCTCCAGTACCACCACCATG
GCCAAGAACACCGTGTTTCTCATCGAGATGCTGCTGCCCAAGAAGTACCATGTGCTGAGGTTTCTG
GATAAAGGTGAAAGGCATCCTGTGCGGGAAGCCCGTGCCGTCATCTTCTTTGGTGACCAGGAGCA
TCCCAATGTCACCGAGTTTGCTGTGGGGCCCCTGCCAGGCCCCTGCTACATGCGAGCACTGTCCC
CCAGGCCTGGGTACCAGTCCTCCTGGGCATCGAGGCCCATCTCCACAGCAGAGTATGCCCTCCTC
TACCACACCCTGCAGGAAGCCACCAAGCCCCTGCATCAGTTCTTCCTCAATACCACAGGCTTCTCA
TTCCAAGACTGCCATGACAGATGCCTGGCCTTCACCGATGTGGCCCCCCGGGGTGTGGCTTCTGG
CCAGCGCCGCAGTTGGCTTATCATACAGCGCTATGTAGAAGGCTACTTTCTGCACCCCACTGGGCT
GGAGCTCCTCGTGGATCATGGGAGCACAGATGCTGGGCACTGGGCCGTGGAGCAGGTGTGGTAC
AACGGGAAGTTCTATGGGAGCCCAGAGGAACTGGCTCGGAAGTATGCAGATGGAGAGGTGGACGT
GGTGGTCCTGGAGGACCCGCTGCCTGGGGGCAAGGGGCATGACAGCACAGAGGAGCCGCCCCT
CTTCTCCTCCCACAAGCCCCGCGGGGACTTCCCCAGCCCCATCCATGTGAGCGGCCCCCGCTTGG
TCCAGCCCCACGGCCCTCGCTTCAGGCTGGAGGGCAACGCTGTGCTCTACGGCGGCTGGAGCTT
TGCCTTCCGGCTGCGCTCCTCCTCCGGGCTGCAGGTCCTGAACGTGCACTTCGGCGGAGAGCGC
ATTGCCTATGAGGTCAGCGTGCAAGAGGCAGTGGCGCTGTATGGAGGACACACACCTGCAGGCAT
GCAGACCAAGTACCTCGATGTCGGCTGGGGCCTGGGCAGCGTCACTCATGAGTTAGCCCCCGGC

图1续

ATCGACTGCCCGGAGACCGCCACCTTCCTGGACACTTTCCACTACTATGATGCCGATGACCCGGTC
CATTATCCCCGAGCCCTCTGCCTCTTTGAAATGCCCACAGGGGTGCCCCTTCGGCGGCACTTTAAT
TCCAACTTTAAAGGTGGCTTCAACTTCTATGCGGGGCTGAAGGGCCAGGTGCTGGTGCTGCGGAC
AACTTCAACTGTCTACAATTATGATTACATTTGGGACTTTATCTTCTACCCCAACGGGGTGATGGAG
GCCAAGATGCATGCCACTGGCTACGTCCACGCCACCTTCTACACCCCCGAGGGGCTGCGCCACG
GCACTCGCCTGCACACCCACCTGATTGGCAACATACACACTCACTTGGTGCACTACCGCGTAGACC
TGGATGTGGCAGGCACCAAGAACAGCTTCCAGACACTGCAGATGAAGCTAGAAAACATCACCAACC
CCTGGAGCCCAAGACACCGCGTGGTCCAGCCAACTCTGGAGCAGACGCAGTACTCCTGGGAGCG
CCAGGCGGCCTTCCGCTTC**GGACAGACG**CTGCCCAAGTACCTGCTCTTTACCAGCCCCCAGGAGA
ACCCCTGGGGCCACAAGCGCAGCTACCGCCTGCAGATCCACTCCATGGCCGACCAGGTGCTGCC
CCCAGGCTGGCAGGAGGAGCAGGCCATCACCTGGGCAAGGTACCCCCTGGCAGTGACCAAGTAC
CGGGAGTCGGAGCTGTGCAGCAGCAGCATCTACCACCAGAACGACCCCTGGCACCCGCCCGTGG
TCTTTGAGCAGTTTCTTCACAACAACGAGAACATTGAAAATGAGGACCTGGTGGCCTGGGTGACGG
TGGGCTTCCTGCACATCCCCCACTCAGAGGACATTCCCAACACAGCCACACCTGGGAACTCCGTG
GGCTTCCTGCTCCGGCCATTCAACTTCTTCCCAGAGGACCCCTCCCTGGCATCCAGAGACACTGTG
ATCGTGTGGCCTCGGGACAACGGCCCCAACTACGTCCAGCGCTGGATCCCTGAGGACAGGGACT
GCTCGATGCCTCCCCCTTTTAGCTACAATGGGACCTATAGACCTGTGTGA (SEQ ID NO:77)

Fc-hDAO-Hepmut7

ATGCCGGCCCTGGGCTGGGCCGTGGCTGCCATCCTGATGCTGCAGACGGCCATGGCG***GA***
GTGCCCCCCCCTGCCCCGCCCCCCCCGTGGCCGGCCCCTCCGTGTTCCTGTTCCCCCCCAAGCCC
AAGGACACCCTGATGATCTCCAGGACCCCCGAGGTGACCTGCGTGGTGGTGGACGTGTCCCACG
AGGACCCCGAGGTGAAGTTCAACTGGTACGTGGACGGCGTGGAGGTGCACAACGCCAAGACCA
AGCCCAGGGAGGAGCAGTACAACTCCACCTACAGGGTGGTGTCCGTGCTGACCGTGCTGCACC
AGGACTGGCTGAACGGCAAGGAGTACAAGTGCAAGGTGTCCAACAAGGGCCTGCCCTCCTCCAT
CGAGAAGACCATCTCCAAGGCCAAGGGCCAGCCCAGGGAGCCCCAGGTGTACACCCTGCCCCC
CTCCAGGGAGGAGATGACCAAGAACCAGGTGTCCCTGACCTGCCTGGTGAAGGGCTTCTACCCC
TCCGACATCGCCGTGGAGTGGGAGTCCAACGGCCAGCCCGAGAACAACTACAAGACCACCCCC
CCCGTGCTGGACTCCGACGGCTCCTTCTTCCTGTACTCCAAGCTGACCGTGGACAAGTCCAGGT
GGCAGCAGGGCAACGTGTTCTCCTGCTCCGTGATGCACGAGGCCCTGCACAACCACTACACCCA
GAAGTCCCTGTCCCTGTCCCCCGGCAAGGAGCCCAAGTCCGCCGACAAGACCCACACCGAGCC
CTCCCCGGGGACTCTGCCCAGGAAGGCAGGGGTGTTTTCAGACCTAAGCAACCAAGAGCTGAAGG
CAGTGCACAGCTTCCTCTGGTCCAAGAAGGAGCTGAGGCTGCAGCCCTCCAGTACCACCACCATG
GCCAAGAACACCGTGTTTCTCATCGAGATGCTGCTGCCCAAGAAGTACCATGTGCTGAGGTTTCTG
GATAAAGGTGAAAGGCATCCTGTGCGGGAAGCCCGTGCCGTCATCTTCTTTGGTGACCAGGAGCA
TCCCAATGTCACCGAGTTTGCTGTGGGGCCCCTGCCAGGCCCCTGCTACATGCGAGCACTGTCCC
CCAGGCCTGGGTACCAGTCCTCCTGGGCATCGAGGCCCATCTCCACAGCAGAGTATGCCCTCCTC
TACCACACCCTGCAGGAAGCCACCAAGCCCCTGCATCAGTTCTTCCTCAATACCACAGGCTTCTCA
TTCCAAGACTGCCATGACAGATGCCTGGCCTTCACCGATGTGGCCCCCCGGGGTGTGGCTTCTGG
CCAGCGCCGCAGTTGGCTTATCATACAGCGCTATGTAGAAGGCTACTTTCTGCACCCCACTGGGCT
GGAGCTCCTCGTGGATCATGGGAGCACAGATGCTGGGCACTGGGCCGTGGAGCAGGTGTGGTAC
AACGGGAAGTTCTATGGGAGCCCAGAGGAACTGGCTCGGAAGTATGCAGATGGAGAGGTGGACGT
GGTGGTCCTGGAGGACCCGCTGCCTGGGGGCAAGGGGCATGACAGCACAGAGGAGCCGCCCCT
CTTCTCCTCCCACAAGCCCCGCGGGGACTTCCCCAGCCCCATCCATGTGAGCGGCCCCCGCTTGG
TCCAGCCCCACGGCCCTCGCTTCAGGCTGGAGGGCAACGCTGTGCTCTACGGCGGCTGGAGCTT
TGCCTTCCGGCTGCGCTCCTCCTCCGGGCTGCAGGTCCTGAACGTGCACTTCGGCGGAGAGCGC
ATTGCCTATGAGGTCAGCGTGCAAGAGGCAGTGGCGCTGTATGGAGGACACACACCTGCAGGCAT
GCAGACCAAGTACCTCGATGTCGGCTGGGGCCTGGGCAGCGTCACTCATGAGTTAGCCCCCGGC
ATCGACTGCCCGGAGACCGCCACCTTCCTGGACACTTTCCACTACTATGATGCCGATGACCCGGTC
CATTATCCCCGAGCCCTCTGCCTCTTTGAAATGCCCACAGGGGTGCCCCTTCGGCGGCACTTTAAT
TCCAACTTTAAAGGTGGCTTCAACTTCTATGCGGGGCTGAAGGGCCAGGTGCTGGTGCTGCGGAC
AACTTCAACTGTCTACAATTATGATTACATTTGGGACTTTATCTTCTACCCCAACGGGGTGATGGAG
GCCAAGATGCATGCCACTGGCTACGTCCACGCCACCTTCTACACCCCCGAGGGGCTGCGCCACG
GCACTCGCCTGCACACCCACCTGATTGGCAACATACACACTCACTTGGTGCACTACCGCGTAGACC
TGGATGTGGCAGGCACCAAGAACAGCTTCCAGACACTGCAGATGAAGCTAGAAAACATCACCAACC
CCTGGAGCCCAAGACACCGCGTGGTCCAGCCAACTCTGGAGCAGACGCAGTACTCCTGGGAGCG
CCAGGCGGCCTTC**AGC**TTCAAAAGGAAGCTGCCC**ACG**TACCTGCTCTTTACCAGCCCCCAGGAGA
ACCCCTGGGGCCACAAGCGCAGCTACCGCCTGCAGATCCACTCCATGGCCGACCAGGTGCTGCC
CCCAGGCTGGCAGGAGGAGCAGGCCATCACCTGGGCAAGGTACCCCCTGGCAGTGACCAAGTAC

图1续

CGGGAGTCGGAGCTGTGCAGCAGCAGCATCTACCACCAGAACGACCCCTGGCACCCGCCCGTGG
TCTTTGAGCAGTTTCTTCACAACAACGAGAACATTGAAAATGAGGACCTGGTGGCCTGGGTGACGG
TGGGCTTCCTGCACATCCCCCACTCAGAGGACATTCCCAACACAGCCACACCTGGGAACTCCGTG
GGCTTCCTGCTCCGGCCATTCAACTTCTTCCCAGAGGACCCCTCCCTGGCATCCAGAGACACTGTG
ATCGTGTGGCCTCGGGACAACGGCCCCAACTACGTCCAGCGCTGGATCCCTGAGGACAGGGACT
GCTCGATGCCTCCCCCTTTTAGCTACAATGGGACCTATAGACCTGTGTGA (SEQ ID NO:78)

Fc-hDAO-Cysmut

ATGCCGGCCCTGGGCTGGGCCGTGGCTGCCATCCTGATGCTGCAGACGGCCATGGCG***GA***
GTGCCCCCCCCTGCCCCGCCCCCCCCGTGGCCGGCCCCTCCGTGTTCCTGTTCCCCCCCAAGCCC
AAGGACACCCTGATGATCTCCAGGACCCCCGAGGTGACCTGCGTGGTGGTGGACGTGTCCCACG
AGGACCCCGAGGTGAAGTTCAACTGGTACGTGGACGGCGTGGAGGTGCACAACGCCAAGACCA
AGCCCAGGGAGGAGCAGTACAACTCCACCTACAGGGTGGTGTCCGTGCTGACCGTGCTGCACC
AGGACTGGCTGAACGGCAAGGAGTACAAGTGCAAGGTGTCCAACAAGGGCCTGCCCTCCTCCAT
CGAGAAGACCATCTCCAAGGCCAAGGGCCAGCCCAGGGAGCCCCAGGTGTACACCCTGCCCCC
CTCCAGGGAGGAGATGACCAAGAACCAGGTGTCCCTGACCTGCCTGGTGAAGGGCTTCTACCCC
TCCGACATCGCCGTGGAGTGGGAGTCCAACGGCCAGCCCGAGAACAACTACAAGACCACCCCC
CCCGTGCTGGACTCCGACGGCTCCTTCTTCCTGTACTCCAAGCTGACCGTGGACAAGTCCAGGT
GGCAGCAGGGCAACGTGTTCTCCTGCTCCGTGATGCACGAGGCCCTGCACAACCACTACACCCA
GAAGTCCCTGTCCCTGTCCCCCGGCAAGGAGCCCAAGTCCGCCGACAAGACCCACACCGAGCC
CTCCCCGGGGACTCTGCCCAGGAAGGCAGGGGTGTTTTCAGACCTAAGCAACCAAGAGCTGAAGG
CAGTGCACAGCTTCCTCTGGTCCAAGAAGGAGCTGAGGCTGCAGCCCTCCAGTACCACCACCATG
GCCAAGAACACCGTGTTTCTCATCGAGATGCTGCTGCCCAAGAAGTACCATGTGCTGAGGTTTCTG
GATAAAGGTGAAAGGCATCCTGTGCGGGAAGCCCGTGCCGTCATCTTCTTTGGTGACCAGGAGCA
TCCCAATGTCACCGAGTTTGCTGTGGGGCCCCTGCCAGGCCCC**GCC**TACATGCGAGCACTGTCCC
CCAGGCCTGGGTACCAGTCCTCCTGGGCATCGAGGCCCATCTCCACAGCAGAGTATGCCCTCCTC
TACCACACCCTGCAGGAAGCCACCAAGCCCCTGCATCAGTTCTTCCTCAATACCACAGGCTTCTCA
TTCCAAGACTGCCATGACAGATGCCTGGCCTTCACCGATGTGGCCCCCCGGGGTGTGGCTTCTGG
CCAGCGCCGCAGTTGGCTTATCATACAGCGCTATGTAGAAGGCTACTTTCTGCACCCCACTGGGCT
GGAGCTCCTCGTGGATCATGGGAGCACAGATGCTGGGCACTGGGCCGTGGAGCAGGTGTGGTAC
AACGGGAAGTTCTATGGGAGCCCAGAGGAACTGGCTCGGAAGTATGCAGATGGAGAGGTGGACGT
GGTGGTCCTGGAGGACCCGCTGCCTGGGGGCAAGGGGCATGACAGCACAGAGGAGCCGCCCCT
CTTCTCCTCCCACAAGCCCCGCGGGGACTTCCCCAGCCCCATCCATGTGAGCGGCCCCCGCTTGG
TCCAGCCCCACGGCCCTCGCTTCAGGCTGGAGGGCAACGCTGTGCTCTACGGCGGCTGGAGCTT
TGCCTTCCGGCTGCGCTCCTCCTCCGGGCTGCAGGTCCTGAACGTGCACTTCGGCGGAGAGCGC
ATTGCCTATGAGGTCAGCGTGCAAGAGGCAGTGGCGCTGTATGGAGGACACACACCTGCAGGCAT
GCAGACCAAGTACCTCGATGTCGGCTGGGGCCTGGGCAGCGTCACTCATGAGTTAGCCCCCGGC
ATCGACTGCCCGGAGACCGCCACCTTCCTGGACACTTTCCACTACTATGATGCCGATGACCCGGTC
CATTATCCCCGAGCCCTCTGCCTCTTTGAAATGCCCACAGGGGTGCCCCTTCGGCGGCACTTTAAT
TCCAACTTTAAAGGTGGCTTCAACTTCTATGCGGGGCTGAAGGGCCAGGTGCTGGTGCTGCGGAC
AACTTCAACTGTCTACAATTATGATTACATTTGGGACTTTATCTTCTACCCCAACGGGGTGATGGAG
GCCAAGATGCATGCCACTGGCTACGTCCACGCCACCTTCTACACCCCCGAGGGGCTGCGCCACG
GCACTCGCCTGCACACCCACCTGATTGGCAACATACACACTCACTTGGTGCACTACCGCGTAGACC
TGGATGTGGCAGGCACCAAGAACAGCTTCCAGACACTGCAGATGAAGCTAGAAAACATCACCAACC
CCTGGAGCCCAAGACACCGCGTGGTCCAGCCAACTCTGGAGCAGACGCAGTACTCCTGGGAGCG
CCAGGCGGCCTTCCGCTTCAAAAGGAAGCTGCCCAAGTACCTGCTCTTTACCAGCCCCCAGGAGA
ACCCCTGGGGCCACAAGCGCAGCTACCGCCTGCAGATCCACTCCATGGCCGACCAGGTGCTGCC
CCCAGGCTGGCAGGAGGAGCAGGCCATCACCTGGGCAAGGTACCCCCTGGCAGTGACCAAGTAC
CGGGAGTCGGAGCTGTGCAGCAGCAGCATCTACCACCAGAACGACCCCTGGCACCCGCCCGTGG
TCTTTGAGCAGTTTCTTCACAACAACGAGAACATTGAAAATGAGGACCTGGTGGCCTGGGTGACGG
TGGGCTTCCTGCACATCCCCCACTCAGAGGACATTCCCAACACAGCCACACCTGGGAACTCCGTG
GGCTTCCTGCTCCGGCCATTCAACTTCTTCCCAGAGGACCCCTCCCTGGCATCCAGAGACACTGTG
ATCGTGTGGCCTCGGGACAACGGCCCCAACTACGTCCAGCGCTGGATCCCTGAGGACAGGGACT
GCTCGATGCCTCCCCCTTTTAGCTACAATGGGACCTATAGACCTGTGTGA (SEQ ID NO:79)

图1续

Fc-hDAO-Hepmut1-Cysmut

ATGCCGGCCCTGGGCTGGGCCGTGGCTGCCATCCTGATGCTGCAGACGGCCATGGCG***GA***
GTGCCCCCCCCTGCCCCGCCCCCCCCCGTGGCCGGCCCCTCCGTGTTCCTGTTCCCCCCCAAGCCC
AAGGACACCCTGATGATCTCCAGGACCCCCGAGGTGACCTGCGTGGTGGTGGACGTGTCCCACG
AGGACCCCGAGGTGAAGTTCAACTGGTACGTGGACGGCGTGGAGGTGCACAACGCCAAGACCA
AGCCCAGGGAGGAGCAGTACAACTCCACCTACAGGGTGGTGTCCGTGCTGACCGTGCTGCACC
AGGACTGGCTGAACGGCAAGGAGTACAAGTGCAAGGTGTCCAACAAGGGCCTGCCCTCCTCCAT
CGAGAAGACCATCTCCAAGGCCAAGGGCCAGCCCAGGGAGCCCCAGGTGTACACCCTGCCCCC
CTCCAGGGAGGAGATGACCAAGAACCAGGTGTCCCTGACCTGCCTGGTGAAGGGCTTCTACCCC
TCCGACATCGCCGTGGAGTGGGAGTCCAACGGCCAGCCCGAGAACAACTACAAGACCACCCCC
CCCGTGCTGGACTCCGACGGCTCCTTCTTCCTGTACTCCAAGCTGACCGTGGACAAGTCCAGGT
GGCAGCAGGGCAACGTGTTCTCCTGCTCCGTGATGCACGAGGCCCTGCACAACCACTACACCCA
GAAGTCCCTGTCCCTGTCCCCCGGCAAGGAGCCCAAGTCCGCCGACAAGACCCACACCGAGCC
CTCCCCGGGGACTCTGCCCAGGAAGGCAGGGGTGTTTTCAGACCTAAGCAACCAAGAGCTGAAGG
CAGTGCACAGCTTCCTCTGGTCCAAGAAGGAGCTGAGGCTGCAGCCCTCCAGTACCACCACCATG
GCCAAGAACACCGTGTTTCTCATCGAGATGCTGCTGCCCAAGAAGTACCATGTGCTGAGGTTTCTG
GATAAAGGTGAAAGGCATCCTGTGCGGGAAGCCCGTGCCGTCATCTTCTTTGGTGACCAGGAGCA
TCCCAATGTCACCGAGTTTGCTGTGGGGCCCCTGCCAGGCCCC**GCC**TACATGCGAGCACTGTCCC
CCAGGCCTGGGTACCAGTCCTCCTGGGCATCGAGGCCCATCTCCACAGCAGAGTATGCCCTCCTC
TACCACACCCTGCAGGAAGCCACCAAGCCCCTGCATCAGTTCTTCCTCAATACCACAGGCTTCTCA
TTCCAAGACTGCCATGACAGATGCCTGGCCTTCACCGATGTGGCCCCCCGGGGTGTGGCTTCTGG
CCAGCGCCGCAGTTGGCTTATCATACAGCGCTATGTAGAAGGCTACTTTCTGCACCCCACTGGGCT
GGAGCTCCTCGTGGATCATGGGAGCACAGATGCTGGGCACTGGGCCGTGGAGCAGGTGTGGTAC
AACGGGAAGTTCTATGGGAGCCCAGAGGAACTGGCTCGGAAGTATGCAGATGGAGAGGTGGACGT
GGTGGTCCTGGAGGACCCGCTGCCTGGGGGCAAGGGGCATGACAGCACAGAGGAGCCGCCCCT
CTTCTCCTCCCACAAGCCCCGCGGGGACTTCCCCAGCCCCATCCATGTGAGCGGCCCCCGCTTGG
TCCAGCCCCACGGCCCTCGCTTCAGGCTGGAGGGCAACGCTGTGCTCTACGGCGGCTGGAGCTT
TGCCTTCCGGCTGCGCTCCTCCTCCGGGCTGCAGGTCCTGAACGTGCACTTCGGCGGAGAGCGC
ATTGCCTATGAGGTCAGCGTGCAAGAGGCAGTGGCGCTGTATGGAGGACACACACCTGCAGGCAT
GCAGACCAAGTACCTCGATGTCGGCTGGGGCCTGGGCAGCGTCACTCATGAGTTAGCCCCCGGC
ATCGACTGCCCGGAGACCGCCACCTTCCTGGACACTTTCCACTACTATGATGCCGATGACCCGGTC
CATTATCCCCGAGCCCTCTGCCTCTTTGAAATGCCCACAGGGGTGCCCCTTCGGCGGCACTTTAAT
TCCAACTTTAAAGGTGGCTTCAACTTCTATGCGGGGCTGAAGGGCCAGGTGCTGGTGCTGCGGAC
AACTTCAACTGTCTACAATTATGATTACATTTGGGACTTTATCTTCTACCCCAACGGGGTGATGGAG
GCCAAGATGCATGCCACTGGCTACGTCCACGCCACCTTCTACACCCCCGAGGGGCTGCGCCACG
GCACTCGCCTGCACACCCACCTGATTGGCAACATACACACTCACTTGGTGCACTACCGCGTAGACC
TGGATGTGGCAGGCACCAAGAACAGCTTCCAGACACTGCAGATGAAGCTAGAAAACATCACCAACC
CCTGGAGCCCAAGACACCGCGTGGTCCAGCCAACTCTGGAGCAGACGCAGTACTCCTGGGAGCG
CCAGGCGGCCTTC**AGC**TTCAAAAGGAAGCTGCCCAAGTACCTGCTCTTTACCAGCCCCCAGGAGA
ACCCCTGGGGCCACAAGCGCAGCTACCGCCTGCAGATCCACTCCATGGCCGACCAGGTGCTGCC
CCCAGGCTGGCAGGAGGAGCAGGCCATCACCTGGGCAAGGTACCCCCTGGCAGTGACCAAGTAC
CGGGAGTCGGAGCTGTGCAGCAGCAGCATCTACCACCAGAACGACCCCTGGCACCCGCCCGTGG
TCTTTGAGCAGTTTCTTCACAACAACGAGAACATTGAAAATGAGGACCTGGTGGCCTGGGTGACGG
TGGGCTTCCTGCACATCCCCCACTCAGAGGACATTCCCAACACAGCCACACCTGGGAACTCCGTG
GGCTTCCTGCTCCGGCCATTCAACTTCTTCCCAGAGGACCCCTCCCTGGCATCCAGAGACACTGTG
ATCGTGTGGCCTCGGGACAACGGCCCCAACTACGTCCAGCGCTGGATCCCTGAGGACAGGGACT
GCTCGATGCCTCCCCCTTTTAGCTACAATGGGACCTATAGACCTGTGTGA (SEQ ID NO:80)

Fc-hDAO-Hepmut2-Cysmut

ATGCCGGCCCTGGGCTGGGCCGTGGCTGCCATCCTGATGCTGCAGACGGCCATGGCG***GA***
GTGCCCCCCCCTGCCCCGCCCCCCCCCGTGGCCGGCCCCTCCGTGTTCCTGTTCCCCCCCAAGCCC
AAGGACACCCTGATGATCTCCAGGACCCCCGAGGTGACCTGCGTGGTGGTGGACGTGTCCCACG
AGGACCCCGAGGTGAAGTTCAACTGGTACGTGGACGGCGTGGAGGTGCACAACGCCAAGACCA
AGCCCAGGGAGGAGCAGTACAACTCCACCTACAGGGTGGTGTCCGTGCTGACCGTGCTGCACC
AGGACTGGCTGAACGGCAAGGAGTACAAGTGCAAGGTGTCCAACAAGGGCCTGCCCTCCTCCAT
CGAGAAGACCATCTCCAAGGCCAAGGGCCAGCCCAGGGAGCCCCAGGTGTACACCCTGCCCCC
CTCCAGGGAGGAGATGACCAAGAACCAGGTGTCCCTGACCTGCCTGGTGAAGGGCTTCTACCCC
TCCGACATCGCCGTGGAGTGGGAGTCCAACGGCCAGCCCGAGAACAACTACAAGACCACCCCC

图1续

CCCGTGCTGGACTCCGACGGCTCCTTCTTCCTGTACTCCAAGCTGACCGTGGACAAGTCCAGGT
GGCAGCAGGGCAACGTGTTCTCCTGCTCCGTGATGCACGAGGCCCTGCACAACCACTACACCCA
GAAGTCCCTGTCCCTGTCCCCCGGCAAGGAGCCCAAGTCCGCCGACAAGACCCACACCGAGCC
CTCCCCGGGGACTCTGCCCAGGAAGGCAGGGGTGTTTTCAGACCTAAGCAACCAAGAGCTGAAGG
CAGTGCACAGCTTCCTCTGGTCCAAGAAGGAGCTGAGGCTGCAGCCCTCCAGTACCACCACCATG
GCCAAGAACACCGTGTTTCTCATCGAGATGCTGCTGCCCAAGAAGTACCATGTGCTGAGGTTTCTG
GATAAAGGTGAAAGGCATCCTGTGCGGGAAGCCCGTGCCGTCATCTTCTTTGGTGACCAGGAGCA
TCCCAATGTCACCGAGTTTGCTGTGGGGCCCCTGCCAGGCCCC**GCC**TACATGCGAGCACTGTCCC
CCAGGCCTGGGTACCAGTCCTCCTGGGCATCGAGGCCCATCTCCACAGCAGAGTATGCCCTCCTC
TACCACACCCTGCAGGAAGCCACCAAGCCCCTGCATCAGTTCTTCCTCAATACCACAGGCTTCTCA
TTCCAAGACTGCCATGACAGATGCCTGGCCTTCACCGATGTGGCCCCCCGGGGTGTGGCTTCTGG
CCAGCGCCGCAGTTGGCTTATCATACAGCGCTATGTAGAAGGCTACTTTCTGCACCCCACTGGGCT
GGAGCTCCTCGTGGATCATGGGAGCACAGATGCTGGGCACTGGGCCGTGGAGCAGGTGTGGTAC
AACGGGAAGTTCTATGGGAGCCCAGAGGAACTGGCTCGGAAGTATGCAGATGGAGAGGTGGACGT
GGTGGTCCTGGAGGACCCGCTGCCTGGGGGCAAGGGGCATGACAGCACAGAGGAGCCGCCCCT
CTTCTCCTCCCACAAGCCCCGCGGGGACTTCCCCAGCCCCATCCATGTGAGCGGCCCCCGCTTGG
TCCAGCCCCACGGCCCTCGCTTCAGGCTGGAGGGCAACGCTGTGCTCTACGGCGGCTGGAGCTT
TGCCTTCCGGCTGCGCTCCTCCTCCGGGCTGCAGGTCCTGAACGTGCACTTCGGCGGAGAGCGC
ATTGCCTATGAGGTCAGCGTGCAAGAGGCAGTGGCGCTGTATGGAGGACACACACCTGCAGGCAT
GCAGACCAAGTACCTCGATGTCGGCTGGGGCCTGGGCAGCGTCACTCATGAGTTAGCCCCCGGC
ATCGACTGCCCGGAGACCGCCACCTTCCTGGACACTTTCCACTACTATGATGCCGATGACCCGGTC
CATTATCCCCGAGCCCTCTGCCTCTTTGAAATGCCCACAGGGGTGCCCCTTCGGCGGCACTTTAAT
TCCAACTTTAAAGGTGGCTTCAACTTCTATGCGGGGCTGAAGGGCCAGGTGCTGGTGCTGCGGAC
AACTTCAACTGTCTACAATTATGATTACATTTGGGACTTTATCTTCTACCCCAACGGGGTGATGGAG
GCCAAGATGCATGCCACTGGCTACGTCCACGCCACCTTCTACACCCCCGAGGGGCTGCGCCACG
GCACTCGCCTGCACACCCACCTGATTGGCAACATACACACTCACTTGGTGCACTACCGCGTAGACC
TGGATGTGGCAGGCACCAAGAACAGCTTCCAGACACTGCAGATGAAGCTAGAAAACATCACCAACC
CCTGGAGCCCAAGACACCGCGTGGTCCAGCCAACTCTGGAGCAGACGCAGTACTCCTGGGAGCG
CCAGGCGGCCTTCCGCTTCAAAAGGAAGCTGCCC**ACG**TACCTGCTCTTTACCAGCCCCCAGGAGA
ACCCCTGGGGCCACAAGCGCAGCTACCGCCTGCAGATCCACTCCATGGCCGACCAGGTGCTGCC
CCCAGGCTGGCAGGAGGAGCAGGCCATCACCTGGGCAAGGTACCCCCTGGCAGTGACCAAGTAC
CGGGAGTCGGAGCTGTGCAGCAGCAGCATCTACCACCAGAACGACCCCTGGCACCCGCCCGTGG
TCTTTGAGCAGTTTCTTCACAACAACGAGAACATTGAAAATGAGGACCTGGTGGCCTGGGTGACGG
TGGGCTTCCTGCACATCCCCCACTCAGAGGACATTCCCAACACAGCCACACCTGGGAACTCCGTG
GGCTTCCTGCTCCGGCCATTCAACTTCTTCCCAGAGGACCCCTCCCTGGCATCCAGAGACACTGTG
ATCGTGTGGCCTCGGGACAACGGCCCCAACTACGTCCAGCGCTGGATCCCTGAGGACAGGGACT
GCTCGATGCCTCCCCCTTTTAGCTACAATGGGACCTATAGACCTGTGTGA (SEQ ID NO:81)

Fc-hDAO-Hepmut3-Cysmut

ATGCCGGCCCTGGGCTGGGCCGTGGCTGCCATCCTGATGCTGCAGACGGCCATGGCG***GA***
GTGCCCCCCCCTGCCCCGCCCCCCCCGTGGCCGGCCCCTCCGTGTTCCTGTTCCCCCCCAAGCCC
AAGGACACCCTGATGATCTCCAGGACCCCCGAGGTGACCTGCGTGGTGGTGGACGTGTCCCACG
AGGACCCCGAGGTGAAGTTCAACTGGTACGTGGACGGCGTGGAGGTGCACAACGCCAAGACCA
AGCCCAGGGAGGAGCAGTACAACTCCACCTACAGGGTGGTGTCCGTGCTGACCGTGCTGCACC
AGGACTGGCTGAACGGCAAGGAGTACAAGTGCAAGGTGTCCAACAAGGGCCTGCCCTCCTCCAT
CGAGAAGACCATCTCCAAGGCCAAGGGCCAGCCCAGGGAGCCCCAGGTGTACACCCTGCCCCC
CTCCAGGGAGGAGATGACCAAGAACCAGGTGTCCCTGACCTGCCTGGTGAAGGGCTTCTACCCC
TCCGACATCGCCGTGGAGTGGGAGTCCAACGGCCAGCCCGAGAACAACTACAAGACCACCCCC
CCCGTGCTGGACTCCGACGGCTCCTTCTTCCTGTACTCCAAGCTGACCGTGGACAAGTCCAGGT
GGCAGCAGGGCAACGTGTTCTCCTGCTCCGTGATGCACGAGGCCCTGCACAACCACTACACCCA
GAAGTCCCTGTCCCTGTCCCCCGGCAAGGAGCCCAAGTCCGCCGACAAGACCCACACCGAGCC
CTCCCCGGGGACTCTGCCCAGGAAGGCAGGGGTGTTTTCAGACCTAAGCAACCAAGAGCTGAAGG
CAGTGCACAGCTTCCTCTGGTCCAAGAAGGAGCTGAGGCTGCAGCCCTCCAGTACCACCACCATG
GCCAAGAACACCGTGTTTCTCATCGAGATGCTGCTGCCCAAGAAGTACCATGTGCTGAGGTTTCTG
GATAAAGGTGAAAGGCATCCTGTGCGGGAAGCCCGTGCCGTCATCTTCTTTGGTGACCAGGAGCA
TCCCAATGTCACCGAGTTTGCTGTGGGGCCCCTGCCAGGCCCC**GCC**TACATGCGAGCACTGTCCC
CCAGGCCTGGGTACCAGTCCTCCTGGGCATCGAGGCCCATCTCCACAGCAGAGTATGCCCTCCTC
TACCACACCCTGCAGGAAGCCACCAAGCCCCTGCATCAGTTCTTCCTCAATACCACAGGCTTCTCA
TTCCAAGACTGCCATGACAGATGCCTGGCCTTCACCGATGTGGCCCCCCGGGGTGTGGCTTCTGG

图1续

CCAGCGCCGCAGTTGGCTTATCATACAGCGCTATGTAGAAGGCTACTTTCTGCACCCCACTGGGCT
GGAGCTCCTCGTGGATCATGGGAGCACAGATGCTGGGCACTGGGCCGTGGAGCAGGTGTGGTAC
AACGGGAAGTTCTATGGGAGCCCAGAGGAACTGGCTCGGAAGTATGCAGATGGAGAGGTGGACGT
GGTGGTCCTGGAGGACCCGCTGCCTGGGGGCAAGGGGCATGACAGCACAGAGGAGCCGCCCCT
CTTCTCCTCCCACAAGCCCCGCGGGGACTTCCCCAGCCCCATCCATGTGAGCGGCCCCCGCTTGG
TCCAGCCCCACGGCCCTCGCTTCAGGCTGGAGGGCAACGCTGTGCTCTACGGCGGCTGGAGCTT
TGCCTTCCGGCTGCGCTCCTCCTCCGGGCTGCAGGTCCTGAACGTGCACTTCGGCGGAGAGCGC
ATTGCCTATGAGGTCAGCGTGCAAGAGGCAGTGGCGCTGTATGGAGGACACACACCTGCAGGCAT
GCAGACCAAGTACCTCGATGTCGGCTGGGGCCTGGGCAGCGTCACTCATGAGTTAGCCCCCGGC
ATCGACTGCCCGGAGACCGCCACCTTCCTGGACACTTTCCACTACTATGATGCCGATGACCCGGTC
CATTATCCCCGAGCCCTCTGCCTCTTTGAAATGCCCACAGGGGTGCCCCTTCGGCGGCACTTTAAT
TCCAACTTTAAAGGTGGCTTCAACTTCTATGCGGGGCTGAAGGGCCAGGTGCTGGTGCTGCGGAC
AACTTCAACTGTCTACAATTATGATTACATTTGGGACTTTATCTTCTACCCCAACGGGGTGATGGAG
GCCAAGATGCATGCCACTGGCTACGTCCACGCCACCTTCTACACCCCCGAGGGGCTGCGCCACG
GCACTCGCCTGCACACCCACCTGATTGGCAACATACACACTCACTTGGTGCACTACCGCGTAGACC
TGGATGTGGCAGGCACCAAGAACAGCTTCCAGACACTGCAGATGAAGCTAGAAAACATCACCAACC
CCTGGAGCCCAAGACACCGCGTGGTCCAGCCAACTCTGGAGCAGACGCAGTACTCCTGGGAGCG
CCAGGCGGCCTTCCGCTTCAAA**ACG**AAGCTGCCCAAGTACCTGCTCTTTACCAGCCCCCAGGAGA
ACCCCTGGGGCCACAAGCGCAGCTACCGCCTGCAGATCCACTCCATGGCCGACCAGGTGCTGCC
CCCAGGCTGGCAGGAGGAGCAGGCCATCACCTGGGCAAGGTACCCCCTGGCAGTGACCAAGTAC
CGGGAGTCGGAGCTGTGCAGCAGCAGCATCTACCACCAGAACGACCCCTGGCACCCGCCCGTGG
TCTTTGAGCAGTTTCTTCACAACAACGAGAACATTGAAAATGAGGACCTGGTGGCCTGGGTGACGG
TGGGCTTCCTGCACATCCCCCACTCAGAGGACATTCCCAACACAGCCACACCTGGGAACTCCGTG
GGCTTCCTGCTCCGGCCATTCAACTTCTTCCCAGAGGACCCCTCCCTGGCATCCAGAGACACTGTG
ATCGTGTGGCCTCGGGACAACGGCCCCAACTACGTCCAGCGCTGGATCCCTGAGGACAGGGACT
GCTCGATGCCTCCCCCTTTTAGCTACAATGGGACCTATAGACCTGTGTGA ((SEQ ID NO:82)

Fc-hDAO-Hepmut4-Cysmut

ATGCCGGCCCTGGGCTGGGCCGTGGCTGCCATCCTGATGCTGCAGACGGCCATGGCG***GA***
GTGCCCCCCCCTGCCCCGCCCCCCCCGTGGCCGGCCCCTCCGTGTTCCTGTTCCCCCCCAAGCCC
AAGGACACCCTGATGATCTCCAGGACCCCCGAGGTGACCTGCGTGGTGGTGGACGTGTCCCACG
AGGACCCCGAGGTGAAGTTCAACTGGTACGTGGACGGCGTGGAGGTGCACAACGCCAAGACCA
AGCCCAGGGAGGAGCAGTACAACTCCACCTACAGGGTGGTGTCCGTGCTGACCGTGCTGCACC
AGGACTGGCTGAACGGCAAGGAGTACAAGTGCAAGGTGTCCAACAAGGGCCTGCCCTCCTCCAT
CGAGAAGACCATCTCCAAGGCCAAGGGCCAGCCCAGGGAGCCCCAGGTGTACACCCTGCCCCCC
CTCCAGGGAGGAGATGACCAAGAACCAGGTGTCCCTGACCTGCCTGGTGAAGGGCTTCTACCCC
TCCGACATCGCCGTGGAGTGGGAGTCCAACGGCCAGCCCGAGAACAACTACAAGACCACCCCC
CCCGTGCTGGACTCCGACGGCTCCTTCTTCCTGTACTCCAAGCTGACCGTGGACAAGTCCAGGT
GGCAGCAGGGCAACGTGTTCTCCTGCTCCGTGATGCACGAGGCCCTGCACAACCACTACACCCA
GAAGTCCCTGTCCCTGTCCCCCGGCAAGGAGCCCAAGTCCGCCGACAAGACCCACACCGAGCC
CTCCCCGGGGACTCTGCCCAGGAAGGCAGGGGTGTTTTCAGACCTAAGCAACCAAGAGCTGAAGG
CAGTGCACAGCTTCCTCTGGTCCAAGAAGGAGCTGAGGCTGCAGCCCTCCAGTACCACCACCATG
GCCAAGAACACCGTGTTTCTCATCGAGATGCTGCTGCCCAAGAAGTACCATGTGCTGAGGTTTCTG
GATAAAGGTGAAAGGCATCCTGTGCGGGAAGCCCGTGCCGTCATCTTCTTTGGTGACCAGGAGCA
TCCCAATGTCACCGAGTTTGCTGTGGGGCCCCTGCCAGGCCCC**GCC**TACATGCGAGCACTGTCCC
CCAGGCCTGGGTACCAGTCCTCCTGGGCATCGAGGCCCATCTCCACAGCAGAGTATGCCCTCCTC
TACCACACCCTGCAGGAAGCCACCAAGCCCCTGCATCAGTTCTTCCTCAATACCACAGGCTTCTCA
TTCCAAGACTGCCATGACAGATGCCTGGCCTTCACCGATGTGGCCCCCCGGGGTGTGGCTTCTGG
CCAGCGCCGCAGTTGGCTTATCATACAGCGCTATGTAGAAGGCTACTTTCTGCACCCCACTGGGCT
GGAGCTCCTCGTGGATCATGGGAGCACAGATGCTGGGCACTGGGCCGTGGAGCAGGTGTGGTAC
AACGGGAAGTTCTATGGGAGCCCAGAGGAACTGGCTCGGAAGTATGCAGATGGAGAGGTGGACGT
GGTGGTCCTGGAGGACCCGCTGCCTGGGGGCAAGGGGCATGACAGCACAGAGGAGCCGCCCCT
CTTCTCCTCCCACAAGCCCCGCGGGGACTTCCCCAGCCCCATCCATGTGAGCGGCCCCCGCTTGG
TCCAGCCCCACGGCCCTCGCTTCAGGCTGGAGGGCAACGCTGTGCTCTACGGCGGCTGGAGCTT
TGCCTTCCGGCTGCGCTCCTCCTCCGGGCTGCAGGTCCTGAACGTGCACTTCGGCGGAGAGCGC
ATTGCCTATGAGGTCAGCGTGCAAGAGGCAGTGGCGCTGTATGGAGGACACACACCTGCAGGCAT
GCAGACCAAGTACCTCGATGTCGGCTGGGGCCTGGGCAGCGTCACTCATGAGTTAGCCCCCGGC

图1续

TCCAACTTTAAAGGTGGCTTCAACTTCTATGCGGGGCTGAAGGGCCAGGTGCTGGTGCTGCGGAC
AACTTCAACTGTCTACAATTATGATTACATTTGGGACTTTATCTTCTACCCCAACGGGGTGATGGAG
GCCAAGATGCATGCCACTGGCTACGTCCACGCCACCTTCTACACCCCCGAGGGGCTGCGCCACG
GCACTCGCCTGCACACCCACCTGATTGGCAACATACACACTCACTTGGTGCACTACCGCGTAGACC
TGGATGTGGCAGGCACCAAGAACAGCTTCCAGACACTGCAGATGAAGCTAGAAAACATCACCAACC
CCTGGAGCCCAAGACACCGCGTGGTCCAGCCAACTCTGGAGCAGACGCAGTACTCCTGGGAGCG
CCAGGCGGCCTTC**AGC**TTCAAA**ACG**AAGCTGCCCAAGTACCTGCTCTTTACCAGCCCCCAGGAGA
ACCCCTGGGGCCACAAGCGCAGCTACCGCCTGCAGATCCACTCCATGGCCGACCAGGTGCTGCC
CCCAGGCTGGCAGGAGGAGCAGGCCATCACCTGGGCAAGGTACCCCCTGGCAGTGACCAAGTAC
CGGGAGTCGGAGCTGTGCAGCAGCAGCATCTACCACCAGAACGACCCCTGGCACCCGCCCGTGG
TCTTTGAGCAGTTTCTTCACAACAACGAGAACATTGAAAATGAGGACCTGGTGGCCTGGGTGACGG
TGGGCTTCCTGCACATCCCCCACTCAGAGGACATTCCCAACACAGCCACACCTGGGAACTCCGTG
GGCTTCCTGCTCCGGCCATTCAACTTCTTCCCAGAGGACCCCTCCCTGGCATCCAGAGACACTGTG
ATCGTGTGGCCTCGGGACAACGGCCCCAACTACGTCCAGCGCTGGATCCCTGAGGACAGGGACT
GCTCGATGCCTCCCCCTTTTAGCTACAATGGGACCTATAGACCTGTGTGA ((SEQ ID NO:83)

Fc-hDAO-Hepmut5-Cysmut

ATGCCGGCCCTGGGCTGGGCCGTGGCTGCCATCCTGATGCTGCAGACGGCCATGGCG***GA***
GTGCCCCCCCCTGCCCCGCCCCCCCCGTGGCCGGCCCCTCCGTGTTCCTGTTCCCCCCCAAGCCC
AAGGACACCCTGATGATCTCCAGGACCCCCGAGGTGACCTGCGTGGTGGTGGACGTGTCCCACG
AGGACCCCGAGGTGAAGTTCAACTGGTACGTGGACGGCGTGGAGGTGCACAACGCCAAGACCA
AGCCCAGGGAGGAGCAGTACAACTCCACCTACAGGGTGGTGTCCGTGCTGACCGTGCTGCACC
AGGACTGGCTGAACGGCAAGGAGTACAAGTGCAAGGTGTCCAACAAGGGCCTGCCCTCCTCCAT
CGAGAAGACCATCTCCAAGGCCAAGGGCCAGCCCAGGGAGCCCCAGGTGTACACCCTGCCCCCC
CTCCAGGGAGGAGATGACCAAGAACCAGGTGTCCCTGACCTGCCTGGTGAAGGGCTTCTACCCC
TCCGACATCGCCGTGGAGTGGGAGTCCAACGGCCAGCCCGAGAACAACTACAAGACCACCCCC
CCCGTGCTGGACTCCGACGGCTCCTTCTTCCTGTACTCCAAGCTGACCGTGGACAAGTCCAGGT
GGCAGCAGGGCAACGTGTTCTCCTGCTCCGTGATGCACGAGGCCCTGCACAACCACTACACCCA
GAAGTCCCTGTCCCTGTCCCCCGGCAAGGAGCCCAAGTCCGCCGACAAGACCCACACCGAGCC
CTCCCCGGGGACTCTGCCCAGGAAGGCAGGGGTGTTTTCAGACCTAAGCAACCAAGAGCTGAAGG
CAGTGCACAGCTTCCTCTGGTCCAAGAAGGAGCTGAGGCTGCAGCCCTCCAGTACCACCACCATG
GCCAAGAACACCGTGTTTCTCATCGAGATGCTGCTGCCCAAGAAGTACCATGTGCTGAGGTTTCTG
GATAAAGGTGAAAGGCATCCTGTGCGGGAAGCCCGTGCCGTCATCTTCTTTGGTGACCAGGAGCA
TCCCAATGTCACCGAGTTTGCTGTGGGGCCCCTGCCAGGCCCC**GCC**TACATGCGAGCACTGTCCC
CCAGGCCTGGGTACCAGTCCTCCTGGGCATCGAGGCCCATCTCCACAGCAGAGTATGCCCTCCTC
TACCACACCCTGCAGGAAGCCACCAAGCCCCTGCATCAGTTCTTCCTCAATACCACAGGCTTCTCA
TTCCAAGACTGCCATGACAGATGCCTGGCCTTCACCGATGTGGCCCCCCGGGGTGTGGCTTCTGG
CCAGCGCCGCAGTTGGCTTATCATACAGCGCTATGTAGAAGGCTACTTTCTGCACCCCACTGGGCT
GGAGCTCCTCGTGGATCATGGGAGCACAGATGCTGGGCACTGGGCCGTGGAGCAGGTGTGGTAC
AACGGGAAGTTCTATGGGAGCCCAGAGGAACTGGCTCGGAAGTATGCAGATGGAGAGGTGGACGT
GGTGGTCCTGGAGGACCCGCTGCCTGGGGGCAAGGGGCATGACAGCACAGAGGAGCCGCCCCT
CTTCTCCTCCCACAAGCCCCGCGGGGACTTCCCCAGCCCCATCCATGTGAGCGGCCCCCGCTTGG
TCCAGCCCCACGGCCCTCGCTTCAGGCTGGAGGGCAACGCTGTGCTCTACGGCGGCTGGAGCTT
TGCCTTCCGGCTGCGCTCCTCCTCCGGGCTGCAGGTCCTGAACGTGCACTTCGGCGGAGAGCGC
ATTGCCTATGAGGTCAGCGTGCAAGAGGCAGTGGCGCTGTATGGAGGACACACACCTGCAGGCAT
GCAGACCAAGTACCTCGATGTCGGCTGGGGCCTGGGCAGCGTCACTCATGAGTTAGCCCCCGGC
ATCGACTGCCCGGAGACCGCCACCTTCCTGGACACTTTCCACTACTATGATGCCGATGACCCGGTC
CATTATCCCCGAGCCCTCTGCCTCTTTGAAATGCCCACAGGGGTGCCCCTTCGGCGGCACTTTAAT
TCCAACTTTAAAGGTGGCTTCAACTTCTATGCGGGGCTGAAGGGCCAGGTGCTGGTGCTGCGGAC
AACTTCAACTGTCTACAATTATGATTACATTTGGGACTTTATCTTCTACCCCAACGGGGTGATGGAG
GCCAAGATGCATGCCACTGGCTACGTCCACGCCACCTTCTACACCCCCGAGGGGCTGCGCCACG
GCACTCGCCTGCACACCCACCTGATTGGCAACATACACACTCACTTGGTGCACTACCGCGTAGACC
TGGATGTGGCAGGCACCAAGAACAGCTTCCAGACACTGCAGATGAAGCTAGAAAACATCACCAACC
CCTGGAGCCCAAGACACCGCGTGGTCCAGCCAACTCTGGAGCAGACGCAGTACTCCTGGGAGCG
CCAGGCGGCCTTCCGCTTCAAA**ACG**AAGCTGCCC**ACG**TACCTGCTCTTTACCAGCCCCCAGGAGA
ACCCCTGGGGCCACAAGCGCAGCTACCGCCTGCAGATCCACTCCATGGCCGACCAGGTGCTGCC
CCCAGGCTGGCAGGAGGAGCAGGCCATCACCTGGGCAAGGTACCCCCTGGCAGTGACCAAGTAC
CGGGAGTCGGAGCTGTGCAGCAGCAGCATCTACCACCAGAACGACCCCTGGCACCCGCCCGTGG
TCTTTGAGCAGTTTCTTCACAACAACGAGAACATTGAAAATGAGGACCTGGTGGCCTGGGTGACGG

图1续

TGGGCTTCCTGCACATCCCCCACTCAGAGGACATTCCCAACACAGCCACACCTGGGAACTCCGTG
GGCTTCCTGCTCCGGCCATTCAACTTCTTCCCAGAGGACCCCTCCCTGGCATCCAGAGACACTGTG
ATCGTGTGGCCTCGGGACAACGGCCCCAACTACGTCCAGCGCTGGATCCCTGAGGACAGGGACT
GCTCGATGCCTCCCCCTTTTAGCTACAATGGGACCTATAGACCTGTGTGA (SEQ ID NO:84)

Fc-hDAO-Hepmut6-Cysmut

ATGCCGGCCCTGGGCTGGGCCGTGGCTGCCATCCTGATGCTGCAGACGGCCATGGCG***GA***
GTGCCCCCCCCTGCCCCGCCCCCCCCCGTGGCCGGCCCCTCCGTGTTCCTGTTCCCCCCCAAGCCC
AAGGACACCCTGATGATCTCCAGGACCCCCGAGGTGACCTGCGTGGTGGTGGACGTGTCCCACG
AGGACCCCGAGGTGAAGTTCAACTGGTACGTGGACGGCGTGGAGGTGCACAACGCCAAGACCA
AGCCCAGGGAGGAGCAGTACAACTCCACCTACAGGGTGGTGTCCGTGCTGACCGTGCTGCACC
AGGACTGGCTGAACGGCAAGGAGTACAAGTGCAAGGTGTCCAACAAGGGCCTGCCCTCCTCCAT
CGAGAAGACCATCTCCAAGGCCAAGGGCCAGCCCAGGGAGCCCCAGGTGTACACCCTGCCCCC
CTCCAGGGAGGAGATGACCAAGAACCAGGTGTCCCTGACCTGCCTGGTGAAGGGCTTCTACCCC
TCCGACATCGCCGTGGAGTGGGAGTCCAACGGCCAGCCCGAGAACAACTACAAGACCACCCCC
CCCGTGCTGGACTCCGACGGCTCCTTCTTCCTGTACTCCAAGCTGACCGTGGACAAGTCCAGGT
GGCAGCAGGGCAACGTGTTCTCCTGCTCCGTGATGCACGAGGCCCTGCACAACCACTACACCCA
GAAGTCCCTGTCCCTGTCCCCCGGCAAGGAGCCCAAGTCCGCCGACAAGACCCACACCGAGCC
CTCCCCGGGGACTCTGCCCAGGAAGGCAGGGGTGTTTTCAGACCTAAGCAACCAAGAGCTGAAGG
CAGTGCACAGCTTCCTCTGGTCCAAGAAGGAGCTGAGGCTGCAGCCCTCCAGTACCACCACCATG
GCCAAGAACACCGTGTTTCTCATCGAGATGCTGCTGCCCAAGAAGTACCATGTGCTGAGGTTTCTG
GATAAAGGTGAAAGGCATCCTGTGCGGGAAGCCCGTGCCGTCATCTTCTTTGGTGACCAGGAGCA
TCCCAATGTCACCGAGTTTGCTGTGGGGCCCCTGCCAGGCCCC**GCC**TACATGCGAGCACTGTCCC
CCAGGCCTGGGTACCAGTCCTCCTGGGCATCGAGGCCCATCTCCACAGCAGAGTATGCCCTCCTC
TACCACACCCTGCAGGAAGCCACCAAGCCCCTGCATCAGTTCTTCCTCAATACCACAGGCTTCTCA
TTCCAAGACTGCCATGACAGATGCCTGGCCTTCACCGATGTGGCCCCCCGGGGGTGTGGCTTCTGG
CCAGCGCCGCAGTTGGCTTATCATACAGCGCTATGTAGAAGGCTACTTTCTGCACCCCACTGGGCT
GGAGCTCCTCGTGGATCATGGGAGCACAGATGCTGGGCACTGGGCCGTGGAGCAGGTGTGGTAC
AACGGGAAGTTCTATGGGAGCCCAGAGGAACTGGCTCGGAAGTATGCAGATGGAGAGGTGGACGT
GGTGGTCCTGGAGGACCCGCTGCCTGGGGGCAAGGGGCATGACAGCACAGAGGAGCCGCCCCT
CTTCTCCTCCCACAAGCCCCGCGGGGACTTCCCCAGCCCCATCCATGTGAGCGGCCCCCGCTTGG
TCCAGCCCCACGGCCCTCGCTTCAGGCTGGAGGGCAACGCTGTGCTCTACGGCGGCTGGAGCTT
TGCCTTCCGGCTGCGCTCCTCCTCCGGGCTGCAGGTCCTGAACGTGCACTTCGGCGGAGAGCGC
ATTGCCTATGAGGTCAGCGTGCAAGAGGCAGTGGCGCTGTATGGAGGACACACACCTGCAGGCAT
GCAGACCAAGTACCTCGATGTCGGCTGGGGCCTGGGCAGCGTCACTCATGAGTTAGCCCCCGGC
ATCGACTGCCCGGAGACCGCCACCTTCCTGGACACTTTCCACTACTATGATGCCGATGACCCGGTC
CATTATCCCCGAGCCCTCTGCCTCTTTGAAATGCCCACAGGGGTGCCCCTTCGGCGGCACTTTAAT
TCCAACTTTAAAGGTGGCTTCAACTTCTATGCGGGGCTGAAGGGCCAGGTGCTGGTGCTGCGGAC
AACTTCAACTGTCTACAATTATGATTACATTTGGGACTTTATCTTCTACCCCAACGGGGTGATGGAG
GCCAAGATGCATGCCACTGGCTACGTCCACGCCACCTTCTACACCCCCGAGGGGCTGCGCCACG
GCACTCGCCTGCACACCCACCTGATTGGCAACATACACACTCACTTGGTGCACTACCGCGTAGACC
TGGATGTGGCAGGCACCAAGAACAGCTTCCAGACACTGCAGATGAAGCTAGAAAACATCACCAACC
CCTGGAGCCCAAGACACCGCGTGGTCCAGCCAACTCTGGAGCAGACGCAGTACTCCTGGGAGCG
CCAGGCGGCCTTCCGCTTC**GGACAGACG**CTGCCCAAGTACCTGCTCTTTACCAGCCCCCAGGAGA
ACCCCTGGGGCCACAAGCGCAGCTACCGCCTGCAGATCCACTCCATGGCCGACCAGGTGCTGCC
CCCAGGCTGGCAGGAGGAGCAGGCCATCACCTGGGCAAGGTACCCCCTGGCAGTGACCAAGTAC
CGGGAGTCGGAGCTGTGCAGCAGCAGCATCTACCACCAGAACGACCCCTGGCACCCGCCCGTGG
TCTTTGAGCAGTTTCTTCACAACAACGAGAACATTGAAAATGAGGACCTGGTGGCCTGGGTGACGG
TGGGCTTCCTGCACATCCCCCACTCAGAGGACATTCCCAACACAGCCACACCTGGGAACTCCGTG
GGCTTCCTGCTCCGGCCATTCAACTTCTTCCCAGAGGACCCCTCCCTGGCATCCAGAGACACTGTG
ATCGTGTGGCCTCGGGACAACGGCCCCAACTACGTCCAGCGCTGGATCCCTGAGGACAGGGACT
GCTCGATGCCTCCCCCTTTTAGCTACAATGGGACCTATAGACCTGTGTGA (SEQ ID NO:85)

Fc-hDAO-Hepmut7-Cysmut

ATGCCGGCCCTGGGCTGGGCCGTGGCTGCCATCCTGATGCTGCAGACGGCCATGGCG***GA***
GTGCCCCCCCCTGCCCCGCCCCCCCCCGTGGCCGGCCCCTCCGTGTTCCTGTTCCCCCCCAAGCCC
AAGGACACCCTGATGATCTCCAGGACCCCCGAGGTGACCTGCGTGGTGGTGGACGTGTCCCACG

AGGACCCCGAGGTGAAGTTCAACTGGTACGTGGACGGCGTGGAGGTGCACAACGCCAAGACCA
AGCCCAGGGAGGAGCAGTACAACTCCACCTACAGGGTGGTGTCCGTGCTGACCGTGCTGCACC
AGGACTGGCTGAACGGCAAGGAGTACAAGTGCAAGGTGTCCAACAAGGGCCTGCCCTCCTCCAT
CGAGAAGACCATCTCCAAGGCCAAGGGCCAGCCCAGGGAGCCCCAGGTGTACACCCTGCCCCC
CTCCAGGGAGGAGATGACCAAGAACCAGGTGTCCCTGACCTGCCTGGTGAAGGGCTTCTACCCC
TCCGACATCGCCGTGGAGTGGGAGTCCAACGGCCAGCCCGAGAACAACTACAAGACCACCCCC
CCCGTGCTGGACTCCGACGGCTCCTTCTTCCTGTACTCCAAGCTGACCGTGGACAAGTCCAGGT
GGCAGCAGGGCAACGTGTTCTCCTGCTCCGTGATGCACGAGGCCCTGCACAACCACTACACCCA
GAAGTCCCTGTCCCTGTCCCCCGGCAAGGAGCCCAAGTCCGCCGACAAGACCCACACCGAGCC
CTCCCCGGGGACTCTGCCCAGGAAGGCAGGGGTGTTTTCAGACCTAAGCAACCAAGAGCTGAAGG
CAGTGCACAGCTTCCTCTGGTCCAAGAAGGAGCTGAGGCTGCAGCCCTCCAGTACCACCACCATG
GCCAAGAACACCGTGTTTCTCATCGAGATGCTGCTGCCCAAGAAGTACCATGTGCTGAGGTTTCTG
GATAAAGGTGAAAGGCATCCTGTGCGGGAAGCCCGTGCCGTCATCTTCTTTGGTGACCAGGAGCA
TCCCAATGTCACCGAGTTTGCTGTGGGGCCCCTGCCAGGCCCC**GCC**TACATGCGAGCACTGTCCC
CCAGGCCTGGGTACCAGTCCTCCTGGGCATCGAGGCCCATCTCCACAGCAGAGTATGCCCTCCTC
TACCACACCCTGCAGGAAGCCACCAAGCCCCTGCATCAGTTCTTCCTCAATACCACAGGCTTCTCA
TTCCAAGACTGCCATGACAGATGCCTGGCCTTCACCGATGTGGCCCCCCGGGGTGTGGCTTCTGG
CCAGCGCCGCAGTTGGCTTATCATACAGCGCTATGTAGAAGGCTACTTTCTGCACCCCACTGGGCT
GGAGCTCCTCGTGGATCATGGGAGCACAGATGCTGGGCACTGGGCCGTGGAGCAGGTGTGGTAC
AACGGGAAGTTCTATGGGAGCCCAGAGGAACTGGCTCGGAAGTATGCAGATGGAGAGGTGGACGT
GGTGGTCCTGGAGGACCCGCTGCCTGGGGGCAAGGGGCATGACAGCACAGAGGAGCCGCCCCT
CTTCTCCTCCCACAAGCCCCGCGGGGACTTCCCCAGCCCCATCCATGTGAGCGGCCCCCGCTTGG
TCCAGCCCCACGGCCCTCGCTTCAGGCTGGAGGGCAACGCTGTGCTCTACGGCGGCTGGAGCTT
TGCCTTCCGGCTGCGCTCCTCCTCCGGGCTGCAGGTCCTGAACGTGCACTTCGGCGGAGAGCGC
ATTGCCTATGAGGTCAGCGTGCAAGAGGCAGTGGCGCTGTATGGAGGACACACACCTGCAGGCAT
GCAGACCAAGTACCTCGATGTCGGCTGGGGCCTGGGCAGCGTCACTCATGAGTTAGCCCCCGGC
ATCGACTGCCCGGAGACCGCCACCTTCCTGGACACTTTCCACTACTATGATGCCGATGACCCGGTC
CATTATCCCCGAGCCCTCTGCCTCTTTGAAATGCCCACAGGGGTGCCCCTTCGGCGGCACTTTAAT
TCCAACTTTAAAGGTGGCTTCAACTTCTATGCGGGGCTGAAGGGCCAGGTGCTGGTGCTGCGGAC
AACTTCAACTGTCTACAATTATGATTACATTTGGGACTTTATCTTCTACCCCAACGGGGTGATGGAG
GCCAAGATGCATGCCACTGGCTACGTCCACGCCACCTTCTACACCCCCGAGGGGCTGCGCCACG
GCACTCGCCTGCACACCCACCTGATTGGCAACATACACACTCACTTGGTGCACTACCGCGTAGACC
TGGATGTGGCAGGCACCAAGAACAGCTTCCAGACACTGCAGATGAAGCTAGAAAACATCACCAACC
CCTGGAGCCCAAGACACCGCGTGGTCCAGCCAACTCTGGAGCAGACGCAGTACTCCTGGGAGCG
CCAGGCGGCCTTC**AGC**TTCAAAAGGAAGCTGCCC**ACG**TACCTGCTCTTTACCAGCCCCCAGGAGA
ACCCCTGGGGCCACAAGCGCAGCTACCGCCTGCAGATCCACTCCATGGCCGACCAGGTGCTGCC
CCCAGGCTGGCAGGAGGAGCAGGCCATCACCTGGGCAAGGTACCCCCTGGCAGTGACCAAGTAC
CGGGAGTCGGAGCTGTGCAGCAGCAGCATCTACCACCAGAACGACCCCTGGCACCCGCCCGTGG
TCTTTGAGCAGTTTCTTCACAACAACGAGAACATTGAAAATGAGGACCTGGTGGCCTGGGTGACGG
TGGGCTTCCTGCACATCCCCCACTCAGAGGACATTCCCAACACAGCCACACCTGGGAACTCCGTG
GGCTTCCTGCTCCGGCCATTCAACTTCTTCCCAGAGGACCCCTCCCTGGCATCCAGAGACACTGTG
ATCGTGTGGCCTCGGGACAACGGCCCCAACTACGTCCAGCGCTGGATCCCTGAGGACAGGGACT
GCTCGATGCCTCCCCCTTTTAGCTACAATGGGACCTATAGACCTGTGTGA (SEQ ID NO:86)

hDAO-Fc

ATGCCGGCCCTGGGCTGGGCCGTGGCTGCCATCCTGATGCTGCAGACGGCCATGGCGGA
GCCCTCCCCGGGGACTCTGCCCAGGAAGGCAGGGGTGTTTTCAGACCTAAGCAACCAAGAGCTGA
AGGCAGTGCACAGCTTCCTCTGGTCCAAGAAGGAGCTGAGGCTGCAGCCCTCCAGTACCACCACC
ATGGCCAAGAACACCGTGTTTCTCATCGAGATGCTGCTGCCCAAGAAGTACCATGTGCTGAGGTTT
CTGGATAAAGGTGAAAGGCATCCTGTGCGGGAAGCCCGTGCCGTCATCTTCTTTGGTGACCAGGA
GCATCCCAATGTCACCGAGTTTGCTGTGGGGCCCCTGCCAGGGCCCTGCTACATGCGAGCACTGT
CCCCCAGGCCTGGGTACCAGTCCTCCTGGGCATCGAGGCCCATCTCCACAGCAGAGTATGCCCTC
CTCTACCACACCCTGCAGGAAGCCACCAAGCCCCTGCATCAGTTCTTCCTCAATACCACAGGCTTC
TCATTCCAAGACTGCCATGACAGATGCCTGGCCTTCACCGATGTGGCCCCCCGGGGTGTGGCTTC
TGGCCAGCGCCGCAGTTGGCTTATCATACAGCGCTATGTAGAAGGCTACTTTCTGCACCCCACTGG
GCTGGAGCTCCTCGTGGATCATGGGAGCACAGATGCTGGGCACTGGGCCGTGGAGCAGGTGTGG
TACAACGGGAAGTTCTATGGGAGCCCAGAGGAACTGGCTCGGAAGTATGCAGATGGAGAGGTGGA
CGTGGTGGTCCTGGAGGACCCGCTGCCTGGGGGCAAGGGGCATGACAGCACAGAGGAGCCGCC
CCTCTTCTCCTCCCACAAGCCCCGCGGGGACTTCCCCAGCCCCATCCATGTGAGCGGCCCCCGCT

图1续

TGGTCCAGCCCCACGGCCCTCGCTTCAGGCTGGAGGGCAACGCTGTGCTCTACGGCGGCTGGAG
CTTTGCCTTCCGGCTGCGCTCCTCCTCCGGGCTGCAGGTCCTGAACGTGCACTTCGGCGGAGAGC
GCATTGCCTATGAGGTCAGCGTGCAAGAGGCAGTGGCGCTGTATGGAGGACACACACCTGCAGGC
ATGCAGACCAAGTACCTCGATGTCGGCTGGGGCCTGGGCAGCGTCACTCATGAGTTAGCCCCCGG
CATCGACTGCCCGGAGACCGCCACCTTCCTGGACACTTTCCACTACTATGATGCCGATGACCCGGT
CCATTATCCCCGAGCCCTCTGCCTCTTTGAAATGCCCACAGGGGTGCCCCTTCGGCGGCACTTTAA
TTCCAACTTTAAAGGTGGCTTCAACTTCTATGCGGGGCTGAAGGGCCAGGTGCTGGTGCTGCGGA
CAACTTCAACTGTCTACAATTATGATTACATTTGGGACTTTATCTTCTACCCCAACGGGGTGATGGA
GGCCAAGATGCATGCCACTGGCTACGTCCACGCCACCTTCTACACCCCCGAGGGGCTGCGCCAC
GGCACTCGCCTGCACACCCACCTGATTGGCAACATACACACTCACTTGGTGCACTACCGCGTAGAC
CTGGATGTGGCAGGCACCAAGAACAGCTTCCAGACACTGCAGATGAAGCTAGAAAACATCACCAAC
CCCTGGAGCCCAAGACACCGCGTGGTCCAGCCAACTCTGGAGCAGACGCAGTACTCCTGGGAGC
GCCAGGCGGCCTTCCGCTTCAAAAGGAAGCTGCCCAAGTACCTGCTCTTTACCAGCCCCCAGGAG
AACCCCTGGGGCCACAAGCGCAGCTACCGCCTGCAGATCCACTCCATGGCCGACCAGGTGCTGC
CCCCAGGCTGGCAGGAGGAGCAGGCCATCACCTGGGCAAGGTACCCCCTGGCAGTGACCAAGTA
CCGGGAGTCGGAGCTGTGCAGCAGCAGCATCTACCACCAGAACGACCCCTGGCACCCGCCCGTG
GTCTTTGAGCAGTTTCTTCACAACAACGAGAACATTGAAAATGAGGACCTGGTGGCCTGGGTGACG
GTGGGCTTCCTGCACATCCCCCACTCAGAGGACATTCCCAACACAGCCACACCTGGGAACTCCGT
GGGCTTCCTGCTCCGGCCATTCAACTTCTTCCCAGAGGACCCCTCCCTGGCATCCAGAGACACTGT
GATCGTGTGGCCTCGGGACAACGGCCCCAACTACGTCCAGCGCTGGATCCCTGAGGACAGGGAC
TGCTCGATGCCTCCCCCTTTTAGCTACAATGGGACCTATAGACCTGTG***GAGCCCAAGTCCGCCGA***
CAAGACCCACACCTGCCCCCCCTGCCCCGCCCCCCCCGTGGCCGGCCCCTCCGTGTTCCTGTTC
CCCCCCAAGCCCAAGGACACCCTGATGATCTCCAGGACCCCCGAGGTGACCTGCGTGGTGGTG
GACGTGTCCCACGAGGACCCCGAGGTGAAGTTCAACTGGTACGTGGACGGCGTGGAGGTGCAC
AACGCCAAGACCAAGCCCAGGGAGGAGCAGTACAACTCCACCTACAGGGTGGTGTCCGTGCTG
ACCGTGCTGCACCAGGACTGGCTGAACGGCAAGGAGTACAAGTGCAAGGTGTCCAACAAGGGC
CTGCCCTCCTCCATCGAGAAGACCATCTCCAAGGCCAAGGGCCAGCCCAGGGAGCCCCAGGTG
TACACCCTGCCCCCCTCCAGGGAGGAGATGACCAAGAACCAGGTGTCCCTGACCTGCCTGGTGA
AGGGCTTCTACCCCTCCGACATCGCCGTGGAGTGGGAGTCCAACGGCCAGCCCGAGAACAACT
ACAAGACCACCCCCCCCGTGCTGGACTCCGACGGCTCCTTCTTCCTGTACTCCAAGCTGACCGT
GGACAAGTCCAGGTGGCAGCAGGGCAACGTGTTCTCCTGCTCCGTGATGCACGAGGCCCTGCAC
AACCACTACACCCAGAAGTCCCTGTCCCTGTCCCCCGGCAAGTGA(SEQ ID NO:87)

hDAO-Fc-Hepmut1

ATGCCGGCCCTGGGCTGGGCCGTGGCTGCCATCCTGATGCTGCAGACGGCCATGGCGGA
GCCCTCCCCGGGGACTCTGCCCAGGAAGGCAGGGGTGTTTTCAGACCTAAGCAACCAAGAGCTGA
AGGCAGTGCACAGCTTCCTCTGGTCCAAGAAGGAGCTGAGGCTGCAGCCCTCCAGTACCACCACC
ATGGCCAAGAACACCGTGTTTCTCATCGAGATGCTGCTGCCCAAGAAGTACCATGTGCTGAGGTTT
CTGGATAAAGGTGAAAGGCATCCTGTGCGGGAAGCCCGTGCCGTCATCTTCTTTGGTGACCAGGA
GCATCCCAATGTCACCGAGTTTGCTGTGGGGCCCCTGCCAGGGCCCTGCTACATGCGAGCACTGT
CCCCCAGGCCTGGGTACCAGTCCTCCTGGGCATCGAGGCCCATCTCCACAGCAGAGTATGCCCTC
CTCTACCACACCCTGCAGGAAGCCACCAAGCCCCTGCATCAGTTCTTCCTCAATACCACAGGCTTC
TCATTCCAAGACTGCCATGACAGATGCCTGGCCTTCACCGATGTGGCCCCCCGGGGTGTGGCTTC
TGGCCAGCGCCGCAGTTGGCTTATCATACAGCGCTATGTAGAAGGCTACTTTCTGCACCCCACTGG
GCTGGAGCTCCTCGTGGATCATGGGAGCACAGATGCTGGGCACTGGGCCGTGGAGCAGGTGTGG
TACAACGGGAAGTTCTATGGGAGCCCAGAGGAACTGGCTCGGAAGTATGCAGATGGAGAGGTGGA
CGTGGTGGTCCTGGAGGACCCGCTGCCTGGGGGCAAGGGGCATGACAGCACAGAGGAGCCGCC
CCTCTTCTCCTCCCACAAGCCCCGCGGGGACTTCCCCAGCCCCATCCATGTGAGCGGCCCCCGCT
TGGTCCAGCCCCACGGCCCTCGCTTCAGGCTGGAGGGCAACGCTGTGCTCTACGGCGGCTGGAG
CTTTGCCTTCCGGCTGCGCTCCTCCTCCGGGCTGCAGGTCCTGAACGTGCACTTCGGCGGAGAGC
GCATTGCCTATGAGGTCAGCGTGCAAGAGGCAGTGGCGCTGTATGGAGGACACACACCTGCAGGC
ATGCAGACCAAGTACCTCGATGTCGGCTGGGGCCTGGGCAGCGTCACTCATGAGTTAGCCCCCGG
CATCGACTGCCCGGAGACCGCCACCTTCCTGGACACTTTCCACTACTATGATGCCGATGACCCGGT
CCATTATCCCCGAGCCCTCTGCCTCTTTGAAATGCCCACAGGGGTGCCCCTTCGGCGGCACTTTAA
TTCCAACTTTAAAGGTGGCTTCAACTTCTATGCGGGGCTGAAGGGCCAGGTGCTGGTGCTGCGGA
CAACTTCAACTGTCTACAATTATGATTACATTTGGGACTTTATCTTCTACCCCAACGGGGTGATGGA
GGCCAAGATGCATGCCACTGGCTACGTCCACGCCACCTTCTACACCCCCGAGGGGCTGCGCCAC
GGCACTCGCCTGCACACCCACCTGATTGGCAACATACACACTCACTTGGTGCACTACCGCGTAGAC
CTGGATGTGGCAGGCACCAAGAACAGCTTCCAGACACTGCAGATGAAGCTAGAAAACATCACCAAC

图1续

CCCTGGAGCCCAAGACACCGCGTGGTCCAGCCAACTCTGGAGCAGACGCAGTACTCCTGGGAGC
GCCAGGCGGCCTTC**AGC**TTCAAAAGGAAGCTGCCCAAGTACCTGCTCTTTACCAGCCCCCAGGAG
AACCCCTGGGGCCACAAGCGCAGCTACCGCCTGCAGATCCACTCCATGGCCGACCAGGTGCTGC
CCCCAGGCTGGCAGGAGGAGCAGGCCATCACCTGGGCAAGGTACCCCCTGGCAGTGACCAAGTA
CCGGGAGTCGGAGCTGTGCAGCAGCAGCATCTACCACCAGAACGACCCCTGGCACCCGCCCGTG
GTCTTTGAGCAGTTTCTTCACAACAACGAGAACATTGAAAATGAGGACCTGGTGGCCTGGGTGACG
GTGGGCTTCCTGCACATCCCCCACTCAGAGGACATTCCCAACACAGCCACACCTGGGAACTCCGT
GGGCTTCCTGCTCCGGCCATTCAACTTCTTCCCAGAGGACCCCTCCCTGGCATCCAGAGACACTGT
GATCGTGTGGCCTCGGGACAACGGCCCCAACTACGTCCAGCGCTGGATCCCTGAGGACAGGGAC
TGCTCGATGCCTCCCCCTTTTAGCTACAATGGGACCTATAGACCTGTG**GAGCCCAAGTCCGCCGA**
CAAGACCCACACCTGCCCCCCCTGCCCCGCCCCCCCCGTGGCCGGCCCCTCCGTGTTCCTGTTC
CCCCCCAAGCCCAAGGACACCCTGATGATCTCCAGGACCCCCGAGGTGACCTGCGTGGTGGTG
GACGTGTCCCACGAGGACCCCGAGGTGAAGTTCAACTGGTACGTGGACGGCGTGGAGGTGCAC
AACGCCAAGACCAAGCCCAGGGAGGAGCAGTACAACTCCACCTACAGGGTGGTGTCCGTGCTG
ACCGTGCTGCACCAGGACTGGCTGAACGGCAAGGAGTACAAGTGCAAGGTGTCCAACAAGGGC
CTGCCCTCCTCCATCGAGAAGACCATCTCCAAGGCCAAGGGCCAGCCCAGGGAGCCCCAGGTG
TACACCCTGCCCCCCTCCAGGGAGGAGATGACCAAGAACCAGGTGTCCCTGACCTGCCTGGTGA
AGGGCTTCTACCCCTCCGACATCGCCGTGGAGTGGGAGTCCAACGGCCAGCCCGAGAACAACT
ACAAGACCACCCCCCCCGTGCTGGACTCCGACGGCTCCTTCTTCCTGTACTCCAAGCTGACCGT
GGACAAGTCCAGGTGGCAGCAGGGCAACGTGTTCTCCTGCTCCGTGATGCACGAGGCCCTGCAC
AACCACTACACCCAGAAGTCCCTGTCCCTGTCCCCCGGCAAGTGA(SEQ ID NO:88)

hDAO-Fc-Hepmut2

ATGCCGGCCCTGGGCTGGGCCGTGGCTGCCATCCTGATGCTGCAGACGGCCATGGCGGA
GCCCTCCCCGGGGACTCTGCCCAGGAAGGCAGGGGTGTTTTCAGACCTAAGCAACCAAGAGCTGA
AGGCAGTGCACAGCTTCCTCTGGTCCAAGAAGGAGCTGAGGCTGCAGCCCTCCAGTACCACCACC
ATGGCCAAGAACACCGTGTTTCTCATCGAGATGCTGCTGCCCAAGAAGTACCATGTGCTGAGGTTT
CTGGATAAAGGTGAAAGGCATCCTGTGCGGGAAGCCCGTGCCGTCATCTTCTTTGGTGACCAGGA
GCATCCCAATGTCACCGAGTTTGCTGTGGGGCCCCTGCCAGGGCCCTGCTACATGCGAGCACTGT
CCCCCAGGCCTGGGTACCAGTCCTCCTGGGCATCGAGGCCCATCTCCACAGCAGAGTATGCCCTC
CTCTACCACACCCTGCAGGAAGCCACCAAGCCCCTGCATCAGTTCTTCCTCAATACCACAGGCTTC
TCATTCCAAGACTGCCATGACAGATGCCTGGCCTTCACCGATGTGGCCCCCCGGGGTGTGGCTTC
TGGCCAGCGCCGCAGTTGGCTTATCATACAGCGCTATGTAGAAGGCTACTTTCTGCACCCCACTGG
GCTGGAGCTCCTCGTGGATCATGGGAGCACAGATGCTGGGCACTGGGCCGTGGAGCAGGTGTGG
TACAACGGGAAGTTCTATGGGAGCCCAGAGGAACTGGCTCGGAAGTATGCAGATGGAGAGGTGGA
CGTGGTGGTCCTGGAGGACCCGCTGCCTGGGGGCAAGGGGCATGACAGCACAGAGGAGCCGCC
CCTCTTCTCCTCCCACAAGCCCCGCGGGGACTTCCCCAGCCCCATCCATGTGAGCGGCCCCCGCT
TGGTCCAGCCCCACGGCCCTCGCTTCAGGCTGGAGGGCAACGCTGTGCTCTACGGCGGCTGGAG
CTTTGCCTTCCGGCTGCGCTCCTCCTCCGGGCTGCAGGTCCTGAACGTGCACTTCGGCGGAGAGC
GCATTGCCTATGAGGTCAGCGTGCAAGAGGCAGTGGCGCTGTATGGAGGACACACACCTGCAGGC
ATGCAGACCAAGTACCTCGATGTCGGCTGGGGCCTGGGCAGCGTCACTCATGAGTTAGCCCCCGG
CATCGACTGCCCGGAGACCGCCACCTTCCTGGACACTTTCCACTACTATGATGCCGATGACCCGGT
CCATTATCCCCGAGCCCTCTGCCTCTTTGAAATGCCCACAGGGGTGCCCCTTCGGCGGCACTTTAA
TTCCAACTTTAAAGGTGGCTTCAACTTCTATGCGGGGCTGAAGGGCCAGGTGCTGGTGCTGCGGA
CAACTTCAACTGTCTACAATTATGATTACATTTGGGACTTTATCTTCTACCCCAACGGGGTGATGGA
GGCCAAGATGCATGCCACTGGCTACGTCCACGCCACCTTCTACACCCCCGAGGGGCTGCGCCAC
GGCACTCGCCTGCACACCCACCTGATTGGCAACATACACACTCACTTGGTGCACTACCGCGTAGAC
CTGGATGTGGCAGGCACCAAGAACAGCTTCCAGACACTGCAGATGAAGCTAGAAAACATCACCAAC
CCCTGGAGCCCAAGACACCGCGTGGTCCAGCCAACTCTGGAGCAGACGCAGTACTCCTGGGAGC
GCCAGGCGGCCTTCCGCTTCAAAAGGAAGCTGCCC**ACG**TACCTGCTCTTTACCAGCCCCCAGGAG
AACCCCTGGGGCCACAAGCGCAGCTACCGCCTGCAGATCCACTCCATGGCCGACCAGGTGCTGC
CCCCAGGCTGGCAGGAGGAGCAGGCCATCACCTGGGCAAGGTACCCCCTGGCAGTGACCAAGTA
CCGGGAGTCGGAGCTGTGCAGCAGCAGCATCTACCACCAGAACGACCCCTGGCACCCGCCCGTG
GTCTTTGAGCAGTTTCTTCACAACAACGAGAACATTGAAAATGAGGACCTGGTGGCCTGGGTGACG
GTGGGCTTCCTGCACATCCCCCACTCAGAGGACATTCCCAACACAGCCACACCTGGGAACTCCGT
GGGCTTCCTGCTCCGGCCATTCAACTTCTTCCCAGAGGACCCCTCCCTGGCATCCAGAGACACTGT
GATCGTGTGGCCTCGGGACAACGGCCCCAACTACGTCCAGCGCTGGATCCCTGAGGACAGGGAC
TGCTCGATGCCTCCCCCTTTTAGCTACAATGGGACCTATAGACCTGTG**GAGCCCAAGTCCGCCGA**
CAAGACCCACACCTGCCCCCCCCTGCCCCGCCCCCCCCCGTGGCCGGCCCCTCCGTGTTCCTGTTC

图1续

CCCCCCAAGCCCAAGGACACCCTGATGATCTCCAGGACCCCCGAGGTGACCTGCGTGGTGGTG
GACGTGTCCCACGAGGACCCCGAGGTGAAGTTCAACTGGTACGTGGACGGCGTGGAGGTGCAC
AACGCCAAGACCAAGCCCAGGGAGGAGCAGTACAACTCCACCTACAGGGTGGTGTCCGTGCTG
ACCGTGCTGCACCAGGACTGGCTGAACGGCAAGGAGTACAAGTGCAAGGTGTCCAACAAGGGC
CTGCCCTCCTCCATCGAGAAGACCATCTCCAAGGCCAAGGGCCAGCCCAGGGAGCCCCAGGTG
TACACCCTGCCCCCCTCCAGGGAGGAGATGACCAAGAACCAGGTGTCCCTGACCTGCCTGGTGA
AGGGCTTCTACCCCTCCGACATCGCCGTGGAGTGGGAGTCCAACGGCCAGCCCGAGAACAACT
ACAAGACCACCCCCCCCGTGCTGGACTCCGACGGCTCCTTCTTCCTGTACTCCAAGCTGACCGT
GGACAAGTCCAGGTGGCAGCAGGGCAACGTGTTCTCCTGCTCCGTGATGCACGAGGCCCTGCAC
AACCACTACACCCAGAAGTCCCTGTCCCTGTCCCCCGGCAAGTGA(SEQ ID NO:89)

hDAO-Fc-Hepmut3

ATGCCGGCCCTGGGCTGGGCCGTGGCTGCCATCCTGATGCTGCAGACGGCCATGGCGGA
GCCCTCCCCGGGGACTCTGCCCAGGAAGGCAGGGGTGTTTTCAGACCTAAGCAACCAAGAGCTGA
AGGCAGTGCACAGCTTCCTCTGGTCCAAGAAGGAGCTGAGGCTGCAGCCCTCCAGTACCACCACC
ATGGCCAAGAACACCGTGTTTCTCATCGAGATGCTGCTGCCCAAGAAGTACCATGTGCTGAGGTTT
CTGGATAAAGGTGAAAGGCATCCTGTGCGGGAAGCCCGTGCCGTCATCTTCTTTGGTGACCAGGA
GCATCCCAATGTCACCGAGTTTGCTGTGGGGCCCCTGCCAGGGCCCTGCTACATGCGAGCACTGT
CCCCCAGGCCTGGGTACCAGTCCTCCTGGGCATCGAGGCCCATCTCCACAGCAGAGTATGCCCTC
CTCTACCACACCCTGCAGGAAGCCACCAAGCCCCTGCATCAGTTCTTCCTCAATACCACAGGCTTC
TCATTCCAAGACTGCCATGACAGATGCCTGGCCTTCACCGATGTGGCCCCCCGGGGTGTGGCTTC
TGGCCAGCGCCGCAGTTGGCTTATCATACAGCGCTATGTAGAAGGCTACTTTCTGCACCCCACTGG
GCTGGAGCTCCTCGTGGATCATGGGAGCACAGATGCTGGGCACTGGGCCGTGGAGCAGGTGTGG
TACAACGGGAAGTTCTATGGGAGCCCAGAGGAACTGGCTCGGAAGTATGCAGATGGAGAGGTGGA
CGTGGTGGTCCTGGAGGACCCGCTGCCTGGGGGCAAGGGGCATGACAGCACAGAGGAGCCGCC
CCTCTTCTCCTCCCACAAGCCCCGCGGGGACTTCCCCAGCCCCATCCATGTGAGCGGCCCCCGCT
TGGTCCAGCCCCACGGCCCTCGCTTCAGGCTGGAGGGCAACGCTGTGCTCTACGGCGGCTGGAG
CTTTGCCTTCCGGCTGCGCTCCTCCTCCGGGCTGCAGGTCCTGAACGTGCACTTCGGCGGAGAGC
GCATTGCCTATGAGGTCAGCGTGCAAGAGGCAGTGGCGCTGTATGGAGGACACACACCTGCAGGC
ATGCAGACCAAGTACCTCGATGTCGGCTGGGGCCTGGGCAGCGTCACTCATGAGTTAGCCCCCGG
CATCGACTGCCCGGAGACCGCCACCTTCCTGGACACTTTCCACTACTATGATGCCGATGACCCGGT
CCATTATCCCCGAGCCCTCTGCCTCTTTGAAATGCCCACAGGGGTGCCCCTTCGGCGGCACTTTAA
TTCCAACTTTAAAGGTGGCTTCAACTTCTATGCGGGGCTGAAGGGCCAGGTGCTGGTGCTGCGGA
CAACTTCAACTGTCTACAATTATGATTACATTTGGGACTTTATCTTCTACCCCAACGGGGTGATGGA
GGCCAAGATGCATGCCACTGGCTACGTCCACGCCACCTTCTACACCCCCGAGGGGCTGCGCCAC
GGCACTCGCCTGCACACCCACCTGATTGGCAACATACACACTCACTTGGTGCACTACCGCGTAGAC
CTGGATGTGGCAGGCACCAAGAACAGCTTCCAGACACTGCAGATGAAGCTAGAAAACATCACCAAC
CCCTGGAGCCCAAGACACCGCGTGGTCCAGCCAACTCTGGAGCAGACGCAGTACTCCTGGGAGC
GCCAGGCGGCCTTCCGCTTCAAA**ACG**AAGCTGCCCAAGTACCTGCTCTTTACCAGCCCCCAGGAG
AACCCCTGGGGCCACAAGCGCAGCTACCGCCTGCAGATCCACTCCATGGCCGACCAGGTGCTGC
CCCCAGGCTGGCAGGAGGAGCAGGCCATCACCTGGGCAAGGTACCCCCTGGCAGTGACCAAGTA
CCGGGAGTCGGAGCTGTGCAGCAGCAGCATCTACCACCAGAACGACCCCTGGCACCCGCCCGTG
GTCTTTGAGCAGTTTCTTCACAACAACGAGAACATTGAAAATGAGGACCTGGTGGCCTGGGTGACG
GTGGGCTTCCTGCACATCCCCCACTCAGAGGACATTCCCAACACAGCCACACCTGGGAACTCCGT
GGGCTTCCTGCTCCGGCCATTCAACTTCTTCCCAGAGGACCCCTCCCTGGCATCCAGAGACACTGT
GATCGTGTGGCCTCGGGACAACGGCCCCAACTACGTCCAGCGCTGGATCCCTGAGGACAGGGAC
TGCTCGATGCCTCCCCCTTTTAGCTACAATGGGACCTATAGACCTGTG***GAGCCCAAGTCCGCCGA***
CAAGACCCACACCTGCCCCCCCCTGCCCCGCCCCCCCCCGTGGCCGGCCCCTCCGTGTTCCTGTTC
CCCCCCAAGCCCAAGGACACCCTGATGATCTCCAGGACCCCCGAGGTGACCTGCGTGGTGGTG
GACGTGTCCCACGAGGACCCCGAGGTGAAGTTCAACTGGTACGTGGACGGCGTGGAGGTGCAC
AACGCCAAGACCAAGCCCAGGGAGGAGCAGTACAACTCCACCTACAGGGTGGTGTCCGTGCTG
ACCGTGCTGCACCAGGACTGGCTGAACGGCAAGGAGTACAAGTGCAAGGTGTCCAACAAGGGC
CTGCCCTCCTCCATCGAGAAGACCATCTCCAAGGCCAAGGGCCAGCCCAGGGAGCCCCAGGTG
TACACCCTGCCCCCCTCCAGGGAGGAGATGACCAAGAACCAGGTGTCCCTGACCTGCCTGGTGA
AGGGCTTCTACCCCTCCGACATCGCCGTGGAGTGGGAGTCCAACGGCCAGCCCGAGAACAACT
ACAAGACCACCCCCCCCGTGCTGGACTCCGACGGCTCCTTCTTCCTGTACTCCAAGCTGACCGT
GGACAAGTCCAGGTGGCAGCAGGGCAACGTGTTCTCCTGCTCCGTGATGCACGAGGCCCTGCAC
AACCACTACACCCAGAAGTCCCTGTCCCTGTCCCCCGGCAAGTGA (SEQ ID NO:90)

图1续

hDAO-Fc-Hepmut4

ATGCCGGCCCTGGGCTGGGCCGTGGCTGCCATCCTGATGCTGCAGACGGCCATGGCGGA
GCCCTCCCCGGGGACTCTGCCCAGGAAGGCAGGGGTGTTTTCAGACCTAAGCAACCAAGAGCTGA
AGGCAGTGCACAGCTTCCTCTGGTCCAAGAAGGAGCTGAGGCTGCAGCCCTCCAGTACCACCACC
ATGGCCAAGAACACCGTGTTTCTCATCGAGATGCTGCTGCCCAAGAAGTACCATGTGCTGAGGTTT
CTGGATAAAGGTGAAAGGCATCCTGTGCGGGAAGCCCGTGCCGTCATCTTCTTTGGTGACCAGGA
GCATCCCAATGTCACCGAGTTTGCTGTGGGGCCCCTGCCAGGGCCCTGCTACATGCGAGCACTGT
CCCCCAGGCCTGGGTACCAGTCCTCCTGGGCATCGAGGCCCATCTCCACAGCAGAGTATGCCCTC
CTCTACCACACCCTGCAGGAAGCCACCAAGCCCCTGCATCAGTTCTTCCTCAATACCACAGGCTTC
TCATTCCAAGACTGCCATGACAGATGCCTGGCCTTCACCGATGTGGCCCCCCGGGGTGTGGCTTC
TGGCCAGCGCCGCAGTTGGCTTATCATACAGCGCTATGTAGAAGGCTACTTTCTGCACCCCACTGG
GCTGGAGCTCCTCGTGGATCATGGGAGCACAGATGCTGGGCACTGGGCCGTGGAGCAGGTGTGG
TACAACGGGAAGTTCTATGGGAGCCCAGAGGAACTGGCTCGGAAGTATGCAGATGGAGAGGTGGA
CGTGGTGGTCCTGGAGGACCCGCTGCCTGGGGGCAAGGGGCATGACAGCACAGAGGAGCCGCC
CCTCTTCTCCTCCCACAAGCCCCGCGGGGACTTCCCCAGCCCCATCCATGTGAGCGGCCCCCGCT
TGGTCCAGCCCCACGGCCCTCGCTTCAGGCTGGAGGGCAACGCTGTGCTCTACGGCGGCTGGAG
CTTTGCCTTCCGGCTGCGCTCCTCCTCCGGGCTGCAGGTCCTGAACGTGCACTTCGGCGGAGAGC
GCATTGCCTATGAGGTCAGCGTGCAAGAGGCAGTGGCGCTGTATGGAGGACACACACCTGCAGGC
ATGCAGACCAAGTACCTCGATGTCGGCTGGGGCCTGGGCAGCGTCACTCATGAGTTAGCCCCCGG
CATCGACTGCCCGGAGACCGCCACCTTCCTGGACACTTTCCACTACTATGATGCCGATGACCCGGT
CCATTATCCCCGAGCCCTCTGCCTCTTTGAAATGCCCACAGGGGTGCCCCTTCGGCGGCACTTTAA
TTCCAACTTTAAAGGTGGCTTCAACTTCTATGCGGGGCTGAAGGGCCAGGTGCTGGTGCTGCGGA
CAACTTCAACTGTCTACAATTATGATTACATTTGGGACTTTATCTTCTACCCCAACGGGGTGATGGA
GGCCAAGATGCATGCCACTGGCTACGTCCACGCCACCTTCTACACCCCCGAGGGGCTGCGCCAC
GGCACTCGCCTGCACACCCACCTGATTGGCAACATACACACTCACTTGGTGCACTACCGCGTAGAC
CTGGATGTGGCAGGCACCAAGAACAGCTTCCAGACACTGCAGATGAAGCTAGAAAACATCACCAAC
CCCTGGAGCCCAAGACACCGCGTGGTCCAGCCAACTCTGGAGCAGACGCAGTACTCCTGGGAGC
GCCAGGCGGCCTTC**AGC**TTCAAA**ACG**AAGCTGCCCAAGTACCTGCTCTTTACCAGCCCCCAGGAG
AACCCCTGGGGCCACAAGCGCAGCTACCGCCTGCAGATCCACTCCATGGCCGACCAGGTGCTGC
CCCCAGGCTGGCAGGAGGAGCAGGCCATCACCTGGGCAAGGTACCCCCTGGCAGTGACCAAGTA
CCGGGAGTCGGAGCTGTGCAGCAGCAGCATCTACCACCAGAACGACCCCTGGCACCCGCCCGTG
GTCTTTGAGCAGTTTCTTCACAACAACGAGAACATTGAAAATGAGGACCTGGTGGCCTGGGTGACG
GTGGGCTTCCTGCACATCCCCCACTCAGAGGACATTCCCAACACAGCCACACCTGGGAACTCCGT
GGGCTTCCTGCTCCGGCCATTCAACTTCTTCCCAGAGGACCCCTCCCTGGCATCCAGAGACACTGT
GATCGTGTGGCCTCGGGACAACGGCCCCAACTACGTCCAGCGCTGGATCCCTGAGGACAGGGAC
TGCTCGATGCCTCCCCCTTTTAGCTACAATGGGACCTATAGACCTGTG***GAGCCCAAGTCCGCCGA***
CAAGACCCACACCTGCCCCCCCTGCCCCGCCCCCCCCGTGGCCGGCCCCTCCGTGTTCCTGTTC
CCCCCCAAGCCCAAGGACACCCTGATGATCTCCAGGACCCCCGAGGTGACCTGCGTGGTGGTG
GACGTGTCCCACGAGGACCCCGAGGTGAAGTTCAACTGGTACGTGGACGGCGTGGAGGTGCAC
AACGCCAAGACCAAGCCCAGGGAGGAGCAGTACAACTCCACCTACAGGGTGGTGTCCGTGCTG
ACCGTGCTGCACCAGGACTGGCTGAACGGCAAGGAGTACAAGTGCAAGGTGTCCAACAAGGGC
CTGCCCTCCTCCATCGAGAAGACCATCTCCAAGGCCAAGGGCCAGCCCAGGGAGCCCCAGGTG
TACACCCTGCCCCCCTCCAGGGAGGAGATGACCAAGAACCAGGTGTCCCTGACCTGCCTGGTGA
AGGGCTTCTACCCCTCCGACATCGCCGTGGAGTGGGAGTCCAACGGCCAGCCCGAGAACAACT
ACAAGACCACCCCCCCCGTGCTGGACTCCGACGGCTCCTTCTTCCTGTACTCCAAGCTGACCGT
GGACAAGTCCAGGTGGCAGCAGGGCAACGTGTTCTCCTGCTCCGTGATGCACGAGGCCCTGCAC
AACCACTACACCCAGAAGTCCCTGTCCCTGTCCCCCGGCAAGTGA (SEQ ID NO:91)

hDAO-Fc-Hepmut5

ATGCCGGCCCTGGGCTGGGCCGTGGCTGCCATCCTGATGCTGCAGACGGCCATGGCGGA
GCCCTCCCCGGGGACTCTGCCCAGGAAGGCAGGGGTGTTTTCAGACCTAAGCAACCAAGAGCTGA
AGGCAGTGCACAGCTTCCTCTGGTCCAAGAAGGAGCTGAGGCTGCAGCCCTCCAGTACCACCACC
ATGGCCAAGAACACCGTGTTTCTCATCGAGATGCTGCTGCCCAAGAAGTACCATGTGCTGAGGTTT
CTGGATAAAGGTGAAAGGCATCCTGTGCGGGAAGCCCGTGCCGTCATCTTCTTTGGTGACCAGGA
GCATCCCAATGTCACCGAGTTTGCTGTGGGGCCCCTGCCAGGGCCCTGCTACATGCGAGCACTGT
CCCCCAGGCCTGGGTACCAGTCCTCCTGGGCATCGAGGCCCATCTCCACAGCAGAGTATGCCCTC
CTCTACCACACCCTGCAGGAAGCCACCAAGCCCCTGCATCAGTTCTTCCTCAATACCACAGGCTTC
TCATTCCAAGACTGCCATGACAGATGCCTGGCCTTCACCGATGTGGCCCCCCGGGGTGTGGCTTC

图1续

TGGCCAGCGCCGCAGTTGGCTTATCATACAGCGCTATGTAGAAGGCTACTTTCTGCACCCCACTGG
GCTGGAGCTCCTCGTGGATCATGGGAGCACAGATGCTGGGCACTGGGCCGTGGAGCAGGTGTGG
TACAACGGGAAGTTCTATGGGAGCCCAGAGGAACTGGCTCGGAAGTATGCAGATGGAGAGGTGGA
CGTGGTGGTCCTGGAGGACCCGCTGCCTGGGGGCAAGGGGCATGACAGCACAGAGGAGCCGCC
CCTCTTCTCCTCCCACAAGCCCCGCGGGGACTTCCCCAGCCCCATCCATGTGAGCGGCCCCCGCT
TGGTCCAGCCCCACGGCCCTCGCTTCAGGCTGGAGGGCAACGCTGTGCTCTACGGCGGCTGGAG
CTTTGCCTTCCGGCTGCGCTCCTCCTCCGGGCTGCAGGTCCTGAACGTGCACTTCGGCGGAGAGC
GCATTGCCTATGAGGTCAGCGTGCAAGAGGCAGTGGCGCTGTATGGAGGACACACACCTGCAGGC
ATGCAGACCAAGTACCTCGATGTCGGCTGGGGCCTGGGCAGCGTCACTCATGAGTTAGCCCCCGG
CATCGACTGCCCGGAGACCGCCACCTTCCTGGACACTTTCCACTACTATGATGCCGATGACCCGGT
CCATTATCCCCGAGCCCTCTGCCTCTTTGAAATGCCCACAGGGGTGCCCCTTCGGCGGCACTTTAA
TTCCAACTTTAAAGGTGGCTTCAACTTCTATGCGGGGCTGAAGGGCCAGGTGCTGGTGCTGCGGA
CAACTTCAACTGTCTACAATTATGATTACATTTGGGACTTTATCTTCTACCCCAACGGGGTGATGGA
GGCCAAGATGCATGCCACTGGCTACGTCCACGCCACCTTCTACACCCCCGAGGGGCTGCGCCAC
GGCACTCGCCTGCACACCCACCTGATTGGCAACATACACACTCACTTGGTGCACTACCGCGTAGAC
CTGGATGTGGCAGGCACCAAGAACAGCTTCCAGACACTGCAGATGAAGCTAGAAAACATCACCAAC
CCCTGGAGCCCAAGACACCGCGTGGTCCAGCCAACTCTGGAGCAGACGCAGTACTCCTGGGAGC
GCCAGGCGGCCTTCCGCTTCAAA**ACG**AAGCTGCCC**ACG**TACCTGCTCTTTACCAGCCCCCAGGAG
AACCCCTGGGGCCACAAGCGCAGCTACCGCCTGCAGATCCACTCCATGGCCGACCAGGTGCTGC
CCCCAGGCTGGCAGGAGGAGCAGGCCATCACCTGGGCAAGGTACCCCCTGGCAGTGACCAAGTA
CCGGGAGTCGGAGCTGTGCAGCAGCAGCATCTACCACCAGAACGACCCCTGGCACCCGCCCGTG
GTCTTTGAGCAGTTTCTTCACAACAACGAGAACATTGAAAATGAGGACCTGGTGGCCTGGGTGACG
GTGGGCTTCCTGCACATCCCCCACTCAGAGGACATTCCCAACACAGCCACACCTGGGAACTCCGT
GGGCTTCCTGCTCCGGCCATTCAACTTCTTCCCAGAGGACCCCTCCCTGGCATCCAGAGACACTGT
GATCGTGTGGCCTCGGGACAACGGCCCCAACTACGTCCAGCGCTGGATCCCTGAGGACAGGGAC
TGCTCGATGCCTCCCCCTTTTAGCTACAATGGGACCTATAGACCTGTG***GAGCCCAAGTCCGCCGA***
CAAGACCCACACCTGCCCCCCCTGCCCCGCCCCCCCCGTGGCCGGCCCCTCCGTGTTCCTGTTC
CCCCCCAAGCCCAAGGACACCCTGATGATCTCCAGGACCCCCGAGGTGACCTGCGTGGTGGTG
GACGTGTCCCACGAGGACCCCGAGGTGAAGTTCAACTGGTACGTGGACGGCGTGGAGGTGCAC
AACGCCAAGACCAAGCCCAGGGAGGAGCAGTACAACTCCACCTACAGGGTGGTGTCCGTGCTG
ACCGTGCTGCACCAGGACTGGCTGAACGGCAAGGAGTACAAGTGCAAGGTGTCCAACAAGGGC
CTGCCCTCCTCCATCGAGAAGACCATCTCCAAGGCCAAGGGCCAGCCCAGGGAGCCCCAGGTG
TACACCCTGCCCCCCTCCAGGGAGGAGATGACCAAGAACCAGGTGTCCCTGACCTGCCTGGTGA
AGGGCTTCTACCCCTCCGACATCGCCGTGGAGTGGGAGTCCAACGGCCAGCCCGAGAACAACT
ACAAGACCACCCCCCCCGTGCTGGACTCCGACGGCTCCTTCTTCCTGTACTCCAAGCTGACCGT
GGACAAGTCCAGGTGGCAGCAGGGCAACGTGTTCTCCTGCTCCGTGATGCACGAGGCCCTGCAC
AACCACTACACCCAGAAGTCCCTGTCCCTGTCCCCCGGCAAGTGA (SEQ ID NO:92)

hDAO-Fc-Hepmut6

ATGCCGGCCCTGGGCTGGGCCGTGGCTGCCATCCTGATGCTGCAGACGGCCATGGCGGA
GCCCTCCCCGGGGACTCTGCCCAGGAAGGCAGGGGTGTTTTCAGACCTAAGCAACCAAGAGCTGA
AGGCAGTGCACAGCTTCCTCTGGTCCAAGAAGGAGCTGAGGCTGCAGCCCTCCAGTACCACCACC
ATGGCCAAGAACACCGTGTTTCTCATCGAGATGCTGCTGCCCAAGAAGTACCATGTGCTGAGGTTT
CTGGATAAAGGTGAAAGGCATCCTGTGCGGGAAGCCCGTGCCGTCATCTTCTTTGGTGACCAGGA
GCATCCCAATGTCACCGAGTTTGCTGTGGGGCCCCTGCCAGGGCCCTGCTACATGCGAGCACTGT
CCCCCAGGCCTGGGTACCAGTCCTCCTGGGCATCGAGGCCCATCTCCACAGCAGAGTATGCCCTC
CTCTACCACACCCTGCAGGAAGCCACCAAGCCCCTGCATCAGTTCTTCCTCAATACCACAGGCTTC
TCATTCCAAGACTGCCATGACAGATGCCTGGCCTTCACCGATGTGGCCCCCCGGGGTGTGGCTTC
TGGCCAGCGCCGCAGTTGGCTTATCATACAGCGCTATGTAGAAGGCTACTTTCTGCACCCCACTGG
GCTGGAGCTCCTCGTGGATCATGGGAGCACAGATGCTGGGCACTGGGCCGTGGAGCAGGTGTGG
TACAACGGGAAGTTCTATGGGAGCCCAGAGGAACTGGCTCGGAAGTATGCAGATGGAGAGGTGGA
CGTGGTGGTCCTGGAGGACCCGCTGCCTGGGGGCAAGGGGCATGACAGCACAGAGGAGCCGCC
CCTCTTCTCCTCCCACAAGCCCCGCGGGGACTTCCCCAGCCCCATCCATGTGAGCGGCCCCCGCT
TGGTCCAGCCCCACGGCCCTCGCTTCAGGCTGGAGGGCAACGCTGTGCTCTACGGCGGCTGGAG
CTTTGCCTTCCGGCTGCGCTCCTCCTCCGGGCTGCAGGTCCTGAACGTGCACTTCGGCGGAGAGC
GCATTGCCTATGAGGTCAGCGTGCAAGAGGCAGTGGCGCTGTATGGAGGACACACACCTGCAGGC
ATGCAGACCAAGTACCTCGATGTCGGCTGGGGCCTGGGCAGCGTCACTCATGAGTTAGCCCCCGG
CATCGACTGCCCGGAGACCGCCACCTTCCTGGACACTTTCCACTACTATGATGCCGATGACCCGGT
CCATTATCCCCGAGCCCTCTGCCTCTTTGAAATGCCCACAGGGGTGCCCCTTCGGCGGCACTTTAA

图1续

TTCCAACTTTAAAGGTGGCTTCAACTTCTATGCGGGGCTGAAGGGCCAGGTGCTGGTGCTGCGGA
CAACTTCAACTGTCTACAATTATGATTACATTTGGGACTTTATCTTCTACCCCAACGGGGTGATGGA
GGCCAAGATGCATGCCACTGGCTACGTCCACGCCACCTTCTACACCCCCGAGGGGCTGCGCCAC
GGCACTCGCCTGCACACCCACCTGATTGGCAACATACACACTCACTTGGTGCACTACCGCGTAGAC
CTGGATGTGGCAGGCACCAAGAACAGCTTCCAGACACTGCAGATGAAGCTAGAAAACATCACCAAC
CCCTGGAGCCCAAGACACCGCGTGGTCCAGCCAACTCTGGAGCAGACGCAGTACTCCTGGGAGC
GCCAGGCGGCCTTCCGCTTC**GGACAGACG**CTGCCCAAGTACCTGCTCTTTACCAGCCCCCAGGA
GAACCCCTGGGGCCACAAGCGCAGCTACCGCCTGCAGATCCACTCCATGGCCGACCAGGTGCTG
CCCCCAGGCTGGCAGGAGGAGCAGGCCATCACCTGGGCAAGGTACCCCCTGGCAGTGACCAAGT
ACCGGGAGTCGGAGCTGTGCAGCAGCAGCATCTACCACCAGAACGACCCCTGGCACCCGCCCGT
GGTCTTTGAGCAGTTTCTTCACAACAACGAGAACATTGAAAATGAGGACCTGGTGGCCTGGGTGAC
GGTGGGCTTCCTGCACATCCCCCACTCAGAGGACATTCCCAACACAGCCACACCTGGGAACTCCG
TGGGCTTCCTGCTCCGGCCATTCAACTTCTTCCCAGAGGACCCCTCCCTGGCATCCAGAGACACTG
TGATCGTGTGGCCTCGGGACAACGGCCCCAACTACGTCCAGCGCTGGATCCCTGAGGACAGGGA
CTGCTCGATGCCTCCCCCTTTTAGCTACAATGGGACCTATAGACCTGTG***GAGCCCAAGTCCGCCG***
ACAAGACCCACACCTGCCCCCCCTGCCCCGCCCCCCCCGTGGCCGGCCCCTCCGTGTTCCTGTT
CCCCCCCAAGCCCAAGGACACCCTGATGATCTCCAGGACCCCCGAGGTGACCTGCGTGGTGGT
GGACGTGTCCCACGAGGACCCCGAGGTGAAGTTCAACTGGTACGTGGACGGCGTGGAGGTGCA
CAACGCCAAGACCAAGCCCAGGGAGGAGCAGTACAACTCCACCTACAGGGTGGTGTCCGTGCT
GACCGTGCTGCACCAGGACTGGCTGAACGGCAAGGAGTACAAGTGCAAGGTGTCCAACAAGGG
CCTGCCCTCCTCCATCGAGAAGACCATCTCCAAGGCCAAGGGCCAGCCCAGGGAGCCCCAGGT
GTACACCCTGCCCCCCTCCAGGGAGGAGATGACCAAGAACCAGGTGTCCCTGACCTGCCTGGTG
AAGGGCTTCTACCCCTCCGACATCGCCGTGGAGTGGGAGTCCAACGGCCAGCCCGAGAACAAC
TACAAGACCACCCCCCCCGTGCTGGACTCCGACGGCTCCTTCTTCCTGTACTCCAAGCTGACCGT
GGACAAGTCCAGGTGGCAGCAGGGCAACGTGTTCTCCTGCTCCGTGATGCACGAGGCCCTGCAC
AACCACTACACCCAGAAGTCCCTGTCCCTGTCCCCCGGCAAGTGA (SEQ ID NO:93)

hDAO-Fc-Hepmut7

ATGCCGGCCCTGGGCTGGGCCGTGGCTGCCATCCTGATGCTGCAGACGGCCATGGCGGA
GCCCTCCCCGGGGACTCTGCCCAGGAAGGCAGGGGTGTTTTCAGACCTAAGCAACCAAGAGCTGA
AGGCAGTGCACAGCTTCCTCTGGTCCAAGAAGGAGCTGAGGCTGCAGCCCTCCAGTACCACCACC
ATGGCCAAGAACACCGTGTTTCTCATCGAGATGCTGCTGCCCAAGAAGTACCATGTGCTGAGGTTT
CTGGATAAAGGTGAAAGGCATCCTGTGCGGGAAGCCCGTGCCGTCATCTTCTTTGGTGACCAGGA
GCATCCCAATGTCACCGAGTTTGCTGTGGGGCCCCTGCCAGGGCCCTGCTACATGCGAGCACTGT
CCCCCAGGCCTGGGTACCAGTCCTCCTGGGCATCGAGGCCCATCTCCACAGCAGAGTATGCCCTC
CTCTACCACACCCTGCAGGAAGCCACCAAGCCCCTGCATCAGTTCTTCCTCAATACCACAGGCTTC
TCATTCCAAGACTGCCATGACAGATGCCTGGCCTTCACCGATGTGGCCCCCCGGGGTGTGGCTTC
TGGCCAGCGCCGCAGTTGGCTTATCATACAGCGCTATGTAGAAGGCTACTTTCTGCACCCCACTGG
GCTGGAGCTCCTCGTGGATCATGGGAGCACAGATGCTGGGCACTGGGCCGTGGAGCAGGTGTGG
TACAACGGGAAGTTCTATGGGAGCCCAGAGGAACTGGCTCGGAAGTATGCAGATGGAGAGGTGGA
CGTGGTGGTCCTGGAGGACCCGCTGCCTGGGGGCAAGGGGCATGACAGCACAGAGGAGCCGCC
CCTCTTCTCCTCCCACAAGCCCCGCGGGGACTTCCCCAGCCCCATCCATGTGAGCGGCCCCCGCT
TGGTCCAGCCCCACGGCCCTCGCTTCAGGCTGGAGGGCAACGCTGTGCTCTACGGCGGCTGGAG
CTTTGCCTTCCGGCTGCGCTCCTCCTCCGGGCTGCAGGTCCTGAACGTGCACTTCGGCGGAGAGC
GCATTGCCTATGAGGTCAGCGTGCAAGAGGCAGTGGCGCTGTATGGAGGACACACACCTGCAGGC
ATGCAGACCAAGTACCTCGATGTCGGCTGGGGCCTGGGCAGCGTCACTCATGAGTTAGCCCCCGG
CATCGACTGCCCGGAGACCGCCACCTTCCTGGACACTTTCCACTACTATGATGCCGATGACCCGGT
CCATTATCCCCGAGCCCTCTGCCTCTTTGAAATGCCCACAGGGGTGCCCCTTCGGCGGCACTTTAA
TTCCAACTTTAAAGGTGGCTTCAACTTCTATGCGGGGCTGAAGGGCCAGGTGCTGGTGCTGCGGA
CAACTTCAACTGTCTACAATTATGATTACATTTGGGACTTTATCTTCTACCCCAACGGGGTGATGGA
GGCCAAGATGCATGCCACTGGCTACGTCCACGCCACCTTCTACACCCCCGAGGGGCTGCGCCAC
GGCACTCGCCTGCACACCCACCTGATTGGCAACATACACACTCACTTGGTGCACTACCGCGTAGAC
CTGGATGTGGCAGGCACCAAGAACAGCTTCCAGACACTGCAGATGAAGCTAGAAAACATCACCAAC
CCCTGGAGCCCAAGACACCGCGTGGTCCAGCCAACTCTGGAGCAGACGCAGTACTCCTGGGAGC
GCCAGGCGGCCTTC**AGC**TTCAAAAGGAAGCTGCCC**ACG**TACCTGCTCTTTACCAGCCCCCAGGAG
AACCCCTGGGGCCACAAGCGCAGCTACCGCCTGCAGATCCACTCCATGGCCGACCAGGTGCTGC
CCCCAGGCTGGCAGGAGGAGCAGGCCATCACCTGGGCAAGGTACCCCCTGGCAGTGACCAAGTA
CCGGGAGTCGGAGCTGTGCAGCAGCAGCATCTACCACCAGAACGACCCCTGGCACCCGCCCGTG

图1续

GTCTTTGAGCAGTTTCTTCACAACAACGAGAACATTGAAAATGAGGACCTGGTGGCCTGGGTGACG
GTGGGCTTCCTGCACATCCCCCACTCAGAGGACATTCCCAACACAGCCACACCTGGGAACTCCGT
GGGCTTCCTGCTCCGGCCATTCAACTTCTTCCCAGAGGACCCCTCCCTGGCATCCAGAGACACTGT
GATCGTGTGGCCTCGGGACAACGGCCCCAACTACGTCCAGCGCTGGATCCCTGAGGACAGGGAC
TGCTCGATGCCTCCCCCTTTTAGCTACAATGGGACCTATAGACCTGTG***GAGCCCAAGTCCGCCGA***
CAAGACCCACACCTGCCCCCCCCTGCCCCGCCCCCCCCGTGGCCGGCCCCTCCGTGTTCCTGTTC
CCCCCCAAGCCCAAGGACACCCTGATGATCTCCAGGACCCCCGAGGTGACCTGCGTGGTGGTG
GACGTGTCCCACGAGGACCCCGAGGTGAAGTTCAACTGGTACGTGGACGGCGTGGAGGTGCAC
AACGCCAAGACCAAGCCCAGGGAGGAGCAGTACAACTCCACCTACAGGGTGGTGTCCGTGCTG
ACCGTGCTGCACCAGGACTGGCTGAACGGCAAGGAGTACAAGTGCAAGGTGTCCAACAAGGGC
CTGCCCTCCTCCATCGAGAAGACCATCTCCAAGGCCAAGGGCCAGCCCAGGGAGCCCCAGGTG
TACACCCTGCCCCCCTCCAGGGAGGAGATGACCAAGAACCAGGTGTCCCTGACCTGCCTGGTGA
AGGGCTTCTACCCCTCCGACATCGCCGTGGAGTGGGAGTCCAACGGCCAGCCCGAGAACAACT
ACAAGACCACCCCCCCCGTGCTGGACTCCGACGGCTCCTTCTTCCTGTACTCCAAGCTGACCGT
GGACAAGTCCAGGTGGCAGCAGGGCAACGTGTTCTCCTGCTCCGTGATGCACGAGGCCCTGCAC
AACCACTACACCCAGAAGTCCCTGTCCCTGTCCCCCGGCAAGTGA (SEQ ID NO:94)

hDAO-Fc-Cysmut

ATGCCGGCCCTGGGCTGGGCCGTGGCTGCCATCCTGATGCTGCAGACGGCCATGGCGGA
GCCCTCCCCGGGGACTCTGCCCAGGAAGGCAGGGGTGTTTTCAGACCTAAGCAACCAAGAGCTGA
AGGCAGTGCACAGCTTCCTCTGGTCCAAGAAGGAGCTGAGGCTGCAGCCCTCCAGTACCACCACC
ATGGCCAAGAACACCGTGTTTCTCATCGAGATGCTGCTGCCCAAGAAGTACCATGTGCTGAGGTTT
CTGGATAAAGGTGAAAGGCATCCTGTGCGGGAAGCCCGTGCCGTCATCTTCTTTGGTGACCAGGA
GCATCCCAATGTCACCGAGTTTGCTGTGGGGCCCCTGCCAGGGCCC**GCC**TACATGCGAGCACTGT
CCCCCAGGCCTGGGTACCAGTCCTCCTGGGCATCGAGGCCCATCTCCACAGCAGAGTATGCCCTC
CTCTACCACACCCTGCAGGAAGCCACCAAGCCCCTGCATCAGTTCTTCCTCAATACCACAGGCTTC
TCATTCCAAGACTGCCATGACAGATGCCTGGCCTTCACCGATGTGGCCCCCCGGGGTGTGGCTTC
TGGCCAGCGCCGCAGTTGGCTTATCATACAGCGCTATGTAGAAGGCTACTTTCTGCACCCCACTGG
GCTGGAGCTCCTCGTGGATCATGGGAGCACAGATGCTGGGCACTGGGCCGTGGAGCAGGTGTGG
TACAACGGGAAGTTCTATGGGAGCCCAGAGGAACTGGCTCGGAAGTATGCAGATGGAGAGGTGGA
CGTGGTGGTCCTGGAGGACCCGCTGCCTGGGGGCAAGGGGCATGACAGCACAGAGGAGCCGCC
CCTCTTCTCCTCCCACAAGCCCCGCGGGGACTTCCCCAGCCCCATCCATGTGAGCGGCCCCCGCT
TGGTCCAGCCCCACGGCCCTCGCTTCAGGCTGGAGGGCAACGCTGTGCTCTACGGCGGCTGGAG
CTTTGCCTTCCGGCTGCGCTCCTCCTCCGGGCTGCAGGTCCTGAACGTGCACTTCGGCGGAGAGC
GCATTGCCTATGAGGTCAGCGTGCAAGAGGCAGTGGCGCTGTATGGAGGACACACACCTGCAGGC
ATGCAGACCAAGTACCTCGATGTCGGCTGGGGCCTGGGCAGCGTCACTCATGAGTTAGCCCCCGG
CATCGACTGCCCGGAGACCGCCACCTTCCTGGACACTTTCCACTACTATGATGCCGATGACCCGGT
CCATTATCCCCGAGCCCTCTGCCTCTTTGAAATGCCCACAGGGGTGCCCCTTCGGCGGCACTTTAA
TTCCAACTTTAAAGGTGGCTTCAACTTCTATGCGGGGCTGAAGGGCCAGGTGCTGGTGCTGCGGA
CAACTTCAACTGTCTACAATTATGATTACATTTGGGACTTTATCTTCTACCCCAACGGGGTGATGGA
GGCCAAGATGCATGCCACTGGCTACGTCCACGCCACCTTCTACACCCCCGAGGGGCTGCGCCAC
GGCACTCGCCTGCACACCCACCTGATTGGCAACATACACACTCACTTGGTGCACTACCGCGTAGAC
CTGGATGTGGCAGGCACCAAGAACAGCTTCCAGACACTGCAGATGAAGCTAGAAAACATCACCAAC
CCCTGGAGCCCAAGACACCGCGTGGTCCAGCCAACTCTGGAGCAGACGCAGTACTCCTGGGAGC
GCCAGGCGGCCTTCCGCTTCAAAAGGAAGCTGCCCAAGTACCTGCTCTTTACCAGCCCCCAGGAG
AACCCCTGGGGCCACAAGCGCAGCTACCGCCTGCAGATCCACTCCATGGCCGACCAGGTGCTGC
CCCCAGGCTGGCAGGAGGAGCAGGCCATCACCTGGGCAAGGTACCCCCTGGCAGTGACCAAGTA
CCGGGAGTCGGAGCTGTGCAGCAGCAGCATCTACCACCAGAACGACCCCTGGCACCCGCCCGTG
GTCTTTGAGCAGTTTCTTCACAACAACGAGAACATTGAAAATGAGGACCTGGTGGCCTGGGTGACG
GTGGGCTTCCTGCACATCCCCCACTCAGAGGACATTCCCAACACAGCCACACCTGGGAACTCCGT
GGGCTTCCTGCTCCGGCCATTCAACTTCTTCCCAGAGGACCCCTCCCTGGCATCCAGAGACACTGT
GATCGTGTGGCCTCGGGACAACGGCCCCAACTACGTCCAGCGCTGGATCCCTGAGGACAGGGAC
TGCTCGATGCCTCCCCCTTTTAGCTACAATGGGACCTATAGACCTGTG***GAGCCCAAGTCCGCCGA***
CAAGACCCACACCTGCCCCCCCCTGCCCCGCCCCCCCCCGTGGCCGGCCCCTCCGTGTTCCTGTTC
CCCCCCAAGCCCAAGGACACCCTGATGATCTCCAGGACCCCCGAGGTGACCTGCGTGGTGGTG
GACGTGTCCCACGAGGACCCCGAGGTGAAGTTCAACTGGTACGTGGACGGCGTGGAGGTGCAC
AACGCCAAGACCAAGCCCAGGGAGGAGCAGTACAACTCCACCTACAGGGTGGTGTCCGTGCTG
ACCGTGCTGCACCAGGACTGGCTGAACGGCAAGGAGTACAAGTGCAAGGTGTCCAACAAGGGC
CTGCCCTCCTCCATCGAGAAGACCATCTCCAAGGCCAAGGGCCAGCCCAGGGAGCCCCAGGTG

图1续

TACACCCTGCCCCCCTCCAGGGAGGAGATGACCAAGAACCAGGTGTCCCTGACCTGCCTGGTGA
AGGGCTTCTACCCCTCCGACATCGCCGTGGAGTGGGAGTCCAACGGCCAGCCCGAGAACAACT
ACAAGACCACCCCCCCCGTGCTGGACTCCGACGGCTCCTTCTTCCTGTACTCCAAGCTGACCGT
GGACAAGTCCAGGTGGCAGCAGGGCAACGTGTTCTCCTGCTCCGTGATGCACGAGGCCCTGCAC
AACCACTACACCCAGAAGTCCCTGTCCCTGTCCCCCGGCAAGTGA(SEQ ID NO:95)

hDAO-Fc-Hepmut1-Cysmut

ATGCCGGCCCTGGGCTGGGCCGTGGCTGCCATCCTGATGCTGCAGACGGCCATGGCGGA
GCCCTCCCCGGGGACTCTGCCCAGGAAGGCAGGGGTGTTTTCAGACCTAAGCAACCAAGAGCTGA
AGGCAGTGCACAGCTTCCTCTGGTCCAAGAAGGAGCTGAGGCTGCAGCCCTCCAGTACCACCACC
ATGGCCAAGAACACCGTGTTTCTCATCGAGATGCTGCTGCCCAAGAAGTACCATGTGCTGAGGTTT
CTGGATAAAGGTGAAAGGCATCCTGTGCGGGAAGCCCGTGCCGTCATCTTCTTTGGTGACCAGGA
GCATCCCAATGTCACCGAGTTTGCTGTGGGGCCCCTGCCAGGGCCC**GCC**TACATGCGAGCACTGT
CCCCCAGGCCTGGGTACCAGTCCTCCTGGGCATCGAGGCCCATCTCCACAGCAGAGTATGCCCTC
CTCTACCACACCCTGCAGGAAGCCACCAAGCCCCTGCATCAGTTCTTCCTCAATACCACAGGCTTC
TCATTCCAAGACTGCCATGACAGATGCCTGGCCTTCACCGATGTGGCCCCCCGGGGTGTGGCTTC
TGGCCAGCGCCGCAGTTGGCTTATCATACAGCGCTATGTAGAAGGCTACTTTCTGCACCCCACTGG
GCTGGAGCTCCTCGTGGATCATGGGAGCACAGATGCTGGGCACTGGGCCGTGGAGCAGGTGTGG
TACAACGGGAAGTTCTATGGGAGCCCAGAGGAACTGGCTCGGAAGTATGCAGATGGAGAGGTGGA
CGTGGTGGTCCTGGAGGACCCGCTGCCTGGGGGCAAGGGGCATGACAGCACAGAGGAGCCGCC
CCTCTTCTCCTCCCACAAGCCCCGCGGGGACTTCCCCAGCCCCATCCATGTGAGCGGCCCCCGCT
TGGTCCAGCCCCACGGCCCTCGCTTCAGGCTGGAGGGCAACGCTGTGCTCTACGGCGGCTGGAG
CTTTGCCTTCCGGCTGCGCTCCTCCTCCGGGCTGCAGGTCCTGAACGTGCACTTCGGCGGAGAGC
GCATTGCCTATGAGGTCAGCGTGCAAGAGGCAGTGGCGCTGTATGGAGGACACACACCTGCAGGC
ATGCAGACCAAGTACCTCGATGTCGGCTGGGGCCTGGGCAGCGTCACTCATGAGTTAGCCCCCGG
CATCGACTGCCCGGAGACCGCCACCTTCCTGGACACTTTCCACTACTATGATGCCGATGACCCGGT
CCATTATCCCCGAGCCCTCTGCCTCTTTGAAATGCCCACAGGGGTGCCCCTTCGGCGGCACTTTAA
TTCCAACTTTAAAGGTGGCTTCAACTTCTATGCGGGGCTGAAGGGCCAGGTGCTGGTGCTGCGGA
CAACTTCAACTGTCTACAATTATGATTACATTTGGGACTTTATCTTCTACCCCAACGGGGTGATGGA
GGCCAAGATGCATGCCACTGGCTACGTCCACGCCACCTTCTACACCCCCGAGGGGCTGCGCCAC
GGCACTCGCCTGCACACCCACCTGATTGGCAACATACACACTCACTTGGTGCACTACCGCGTAGAC
CTGGATGTGGCAGGCACCAAGAACAGCTTCCAGACACTGCAGATGAAGCTAGAAAACATCACCAAC
CCCTGGAGCCCAAGACACCGCGTGGTCCAGCCAACTCTGGAGCAGACGCAGTACTCCTGGGAGC
GCCAGGCGGCCTTC**AGC**TTCAAAAGGAAGCTGCCCAAGTACCTGCTCTTTACCAGCCCCCAGGAG
AACCCCTGGGGCCACAAGCGCAGCTACCGCCTGCAGATCCACTCCATGGCCGACCAGGTGCTGC
CCCCAGGCTGGCAGGAGGAGCAGGCCATCACCTGGGCAAGGTACCCCCTGGCAGTGACCAAGTA
CCGGGAGTCGGAGCTGTGCAGCAGCAGCATCTACCACCAGAACGACCCCTGGCACCCGCCCGTG
GTCTTTGAGCAGTTTCTTCACAACAACGAGAACATTGAAAATGAGGACCTGGTGGCCTGGGTGACG
GTGGGCTTCCTGCACATCCCCCACTCAGAGGACATTCCCAACACAGCCACACCTGGGAACTCCGT
GGGCTTCCTGCTCCGGCCATTCAACTTCTTCCCAGAGGACCCCTCCCTGGCATCCAGAGACACTGT
GATCGTGTGGCCTCGGGACAACGGCCCCAACTACGTCCAGCGCTGGATCCCTGAGGACAGGGAC
TGCTCGATGCCTCCCCCTTTTAGCTACAATGGGACCTATAGACCTGTG***GAGCCCAAGTCCGCCGA***
CAAGACCCACACCTGCCCCCCCCTGCCCCGCCCCCCCCGTGGCCGGCCCCTCCGTGTTCCTGTTC
CCCCCCAAGCCCAAGGACACCCTGATGATCTCCAGGACCCCCGAGGTGACCTGCGTGGTGGTG
GACGTGTCCCACGAGGACCCCGAGGTGAAGTTCAACTGGTACGTGGACGGCGTGGAGGTGCAC
AACGCCAAGACCAAGCCCAGGGAGGAGCAGTACAACTCCACCTACAGGGTGGTGTCCGTGCTG
ACCGTGCTGCACCAGGACTGGCTGAACGGCAAGGAGTACAAGTGCAAGGTGTCCAACAAGGGC
CTGCCCTCCTCCATCGAGAAGACCATCTCCAAGGCCAAGGGCCAGCCCAGGGAGCCCCAGGTG
TACACCCTGCCCCCCTCCAGGGAGGAGATGACCAAGAACCAGGTGTCCCTGACCTGCCTGGTGA
AGGGCTTCTACCCCTCCGACATCGCCGTGGAGTGGGAGTCCAACGGCCAGCCCGAGAACAACT
ACAAGACCACCCCCCCCCGTGCTGGACTCCGACGGCTCCTTCTTCCTGTACTCCAAGCTGACCGT
GGACAAGTCCAGGTGGCAGCAGGGCAACGTGTTCTCCTGCTCCGTGATGCACGAGGCCCTGCAC
AACCACTACACCCAGAAGTCCCTGTCCCTGTCCCCCGGCAAGTGA (SEQ ID NO:96)

图1续

hDAO-Fc-Hepmut2-Cysmut

ATGCCGGCCCTGGGCTGGGCCGTGGCTGCCATCCTGATGCTGCAGACGGCCATGGCGGA
GCCCTCCCCGGGGACTCTGCCCAGGAAGGCAGGGGTGTTTTCAGACCTAAGCAACCAAGAGCTGA
AGGCAGTGCACAGCTTCCTCTGGTCCAAGAAGGAGCTGAGGCTGCAGCCCTCCAGTACCACCACC
ATGGCCAAGAACACCGTGTTTCTCATCGAGATGCTGCTGCCCAAGAAGTACCATGTGCTGAGGTTT
CTGGATAAAGGTGAAAGGCATCCTGTGCGGGAAGCCCGTGCCGTCATCTTCTTTGGTGACCAGGA
GCATCCCAATGTCACCGAGTTTGCTGTGGGGCCCCTGCCAGGGCCC**GCC**TACATGCGAGCACTGT
CCCCCAGGCCTGGGTACCAGTCCTCCTGGGCATCGAGGCCCATCTCCACAGCAGAGTATGCCCTC
CTCTACCACACCCTGCAGGAAGCCACCAAGCCCCTGCATCAGTTCTTCCTCAATACCACAGGCTTC
TCATTCCAAGACTGCCATGACAGATGCCTGGCCTTCACCGATGTGGCCCCCCGGGGTGTGGCTTC
TGGCCAGCGCCGCAGTTGGCTTATCATACAGCGCTATGTAGAAGGCTACTTTCTGCACCCCACTGG
GCTGGAGCTCCTCGTGGATCATGGGAGCACAGATGCTGGGCACTGGGCCGTGGAGCAGGTGTGG
TACAACGGGAAGTTCTATGGGAGCCCAGAGGAACTGGCTCGGAAGTATGCAGATGGAGAGGTGGA
CGTGGTGGTCCTGGAGGACCCGCTGCCTGGGGGCAAGGGGCATGACAGCACAGAGGAGCCGCC
CCTCTTCTCCTCCCACAAGCCCCGCGGGGACTTCCCCAGCCCCATCCATGTGAGCGGCCCCCGCT
TGGTCCAGCCCCACGGCCCTCGCTTCAGGCTGGAGGGCAACGCTGTGCTCTACGGCGGCTGGAG
CTTTGCCTTCCGGCTGCGCTCCTCCTCCGGGCTGCAGGTCCTGAACGTGCACTTCGGCGGAGAGC
GCATTGCCTATGAGGTCAGCGTGCAAGAGGCAGTGGCGCTGTATGGAGGACACACACCTGCAGGC
ATGCAGACCAAGTACCTCGATGTCGGCTGGGGCCTGGGCAGCGTCACTCATGAGTTAGCCCCCGG
CATCGACTGCCCGGAGACCGCCACCTTCCTGGACACTTTCCACTACTATGATGCCGATGACCCGGT
CCATTATCCCCGAGCCCTCTGCCTCTTTGAAATGCCCACAGGGGTGCCCCTTCGGCGGCACTTTAA
TTCCAACTTTAAAGGTGGCTTCAACTTCTATGCGGGGCTGAAGGGCCAGGTGCTGGTGCTGCGGA
CAACTTCAACTGTCTACAATTATGATTACATTTGGGACTTTATCTTCTACCCCAACGGGGTGATGGA
GGCCAAGATGCATGCCACTGGCTACGTCCACGCCACCTTCTACACCCCCGAGGGGCTGCGCCAC
GGCACTCGCCTGCACACCCACCTGATTGGCAACATACACACTCACTTGGTGCACTACCGCGTAGAC
CTGGATGTGGCAGGCACCAAGAACAGCTTCCAGACACTGCAGATGAAGCTAGAAAACATCACCAAC
CCCTGGAGCCCAAGACACCGCGTGGTCCAGCCAACTCTGGAGCAGACGCAGTACTCCTGGGAGC
GCCAGGCGGCCTTCCGCTTCAAAAGGAAGCTGCCC**ACG**TACCTGCTCTTTACCAGCCCCCAGGAG
AACCCCTGGGGCCACAAGCGCAGCTACCGCCTGCAGATCCACTCCATGGCCGACCAGGTGCTGC
CCCCAGGCTGGCAGGAGGAGCAGGCCATCACCTGGGCAAGGTACCCCCTGGCAGTGACCAAGTA
CCGGGAGTCGGAGCTGTGCAGCAGCAGCATCTACCACCAGAACGACCCCTGGCACCCGCCCGTG
GTCTTTGAGCAGTTTCTTCACAACAACGAGAACATTGAAAATGAGGACCTGGTGGCCTGGGTGACG
GTGGGCTTCCTGCACATCCCCCACTCAGAGGACATTCCCAACACAGCCACACCTGGGAACTCCGT
GGGCTTCCTGCTCCGGCCATTCAACTTCTTCCCAGAGGACCCCTCCCTGGCATCCAGAGACACTGT
GATCGTGTGGCCTCGGGACAACGGCCCCAACTACGTCCAGCGCTGGATCCCTGAGGACAGGGAC
TGCTCGATGCCTCCCCCTTTTAGCTACAATGGGACCTATAGACCTGTG***GAGCCCAAGTCCGCCGA***
CAAGACCCACACCTGCCCCCCCCTGCCCCGCCCCCCCCCGTGGCCGGCCCCTCCGTGTTCCTGTTC
CCCCCCAAGCCCAAGGACACCCTGATGATCTCCAGGACCCCCGAGGTGACCTGCGTGGTGGTG
GACGTGTCCCACGAGGACCCCGAGGTGAAGTTCAACTGGTACGTGGACGGCGTGGAGGTGCAC
AACGCCAAGACCAAGCCCAGGGAGGAGCAGTACAACTCCACCTACAGGGTGGTGTCCGTGCTG
ACCGTGCTGCACCAGGACTGGCTGAACGGCAAGGAGTACAAGTGCAAGGTGTCCAACAAGGGC
CTGCCCTCCTCCATCGAGAAGACCATCTCCAAGGCCAAGGGCCAGCCCAGGGAGCCCCAGGTG
TACACCCTGCCCCCCTCCAGGGAGGAGATGACCAAGAACCAGGTGTCCCTGACCTGCCTGGTGA
AGGGCTTCTACCCCTCCGACATCGCCGTGGAGTGGGAGTCCAACGGCCAGCCCGAGAACAACT
ACAAGACCACCCCCCCCGTGCTGGACTCCGACGGCTCCTTCTTCCTGTACTCCAAGCTGACCGT
GGACAAGTCCAGGTGGCAGCAGGGCAACGTGTTCTCCTGCTCCGTGATGCACGAGGCCCTGCAC
AACCACTACACCCAGAAGTCCCTGTCCCTGTCCCCCGGCAAGTGA (SEQ ID NO:97)

hDAO-Fc-Hepmut3-Cysmut

ATGCCGGCCCTGGGCTGGGCCGTGGCTGCCATCCTGATGCTGCAGACGGCCATGGCGGA
GCCCTCCCCGGGGACTCTGCCCAGGAAGGCAGGGGTGTTTTCAGACCTAAGCAACCAAGAGCTGA
AGGCAGTGCACAGCTTCCTCTGGTCCAAGAAGGAGCTGAGGCTGCAGCCCTCCAGTACCACCACC
ATGGCCAAGAACACCGTGTTTCTCATCGAGATGCTGCTGCCCAAGAAGTACCATGTGCTGAGGTTT
CTGGATAAAGGTGAAAGGCATCCTGTGCGGGAAGCCCGTGCCGTCATCTTCTTTGGTGACCAGGA
GCATCCCAATGTCACCGAGTTTGCTGTGGGGCCCCTGCCAGGGCCC**GCC**TACATGCGAGCACTGT
CCCCCAGGCCTGGGTACCAGTCCTCCTGGGCATCGAGGCCCATCTCCACAGCAGAGTATGCCCTC
CTCTACCACACCCTGCAGGAAGCCACCAAGCCCCTGCATCAGTTCTTCCTCAATACCACAGGCTTC
TCATTCCAAGACTGCCATGACAGATGCCTGGCCTTCACCGATGTGGCCCCCCGGGGTGTGGCTTC

图1续

TGGCCAGCGCCGCAGTTGGCTTATCATACAGCGCTATGTAGAAGGCTACTTTCTGCACCCCACTGG
GCTGGAGCTCCTCGTGGATCATGGGAGCACAGATGCTGGGCACTGGGCCGTGGAGCAGGTGTGG
TACAACGGGAAGTTCTATGGGAGCCCAGAGGAACTGGCTCGGAAGTATGCAGATGGAGAGGTGGA
CGTGGTGGTCCTGGAGGACCCGCTGCCTGGGGGCAAGGGGCATGACAGCACAGAGGAGCCGCC
CCTCTTCTCCTCCCACAAGCCCCGCGGGGACTTCCCCAGCCCCATCCATGTGAGCGGCCCCCGCT
TGGTCCAGCCCCACGGCCCTCGCTTCAGGCTGGAGGGCAACGCTGTGCTCTACGGCGGCTGGAG
CTTTGCCTTCCGGCTGCGCTCCTCCTCCGGGCTGCAGGTCCTGAACGTGCACTTCGGCGGAGAGC
GCATTGCCTATGAGGTCAGCGTGCAAGAGGCAGTGGCGCTGTATGGAGGACACACACCTGCAGGC
ATGCAGACCAAGTACCTCGATGTCGGCTGGGGCCTGGGCAGCGTCACTCATGAGTTAGCCCCCGG
CATCGACTGCCCGGAGACCGCCACCTTCCTGGACACTTTCCACTACTATGATGCCGATGACCCGGT
CCATTATCCCCGAGCCCTCTGCCTCTTTGAAATGCCCACAGGGGTGCCCCTTCGGCGGCACTTTAA
TTCCAACTTTAAAGGTGGCTTCAACTTCTATGCGGGGCTGAAGGGCCAGGTGCTGGTGCTGCGGA
CAACTTCAACTGTCTACAATTATGATTACATTTGGGACTTTATCTTCTACCCCAACGGGGTGATGGA
GGCCAAGATGCATGCCACTGGCTACGTCCACGCCACCTTCTACACCCCCGAGGGGCTGCGCCAC
GGCACTCGCCTGCACACCCACCTGATTGGCAACATACACACTCACTTGGTGCACTACCGCGTAGAC
CTGGATGTGGCAGGCACCAAGAACAGCTTCCAGACACTGCAGATGAAGCTAGAAAACATCACCAAC
CCCTGGAGCCCAAGACACCGCGTGGTCCAGCCAACTCTGGAGCAGACGCAGTACTCCTGGGAGC
GCCAGGCGGCCTTCCGCTTCAAA**ACG**AAGCTGCCCAAGTACCTGCTCTTTACCAGCCCCCAGGAG
AACCCCTGGGGCCACAAGCGCAGCTACCGCCTGCAGATCCACTCCATGGCCGACCAGGTGCTGC
CCCCAGGCTGGCAGGAGGAGCAGGCCATCACCTGGGCAAGGTACCCCCTGGCAGTGACCAAGTA
CCGGGAGTCGGAGCTGTGCAGCAGCAGCATCTACCACCAGAACGACCCCTGGCACCCGCCCGTG
GTCTTTGAGCAGTTTCTTCACAACAACGAGAACATTGAAAATGAGGACCTGGTGGCCTGGGTGACG
GTGGGCTTCCTGCACATCCCCCACTCAGAGGACATTCCCAACACAGCCACACCTGGGAACTCCGT
GGGCTTCCTGCTCCGGCCATTCAACTTCTTCCCAGAGGACCCCTCCCTGGCATCCAGAGACACTGT
GATCGTGTGGCCTCGGGACAACGGCCCCAACTACGTCCAGCGCTGGATCCCTGAGGACAGGGAC
TGCTCGATGCCTCCCCCTTTTAGCTACAATGGGACCTATAGACCTGTG***GAGCCCAAGTCCGCCGA***
CAAGACCCACACCTGCCCCCCCCTGCCCCGCCCCCCCCCGTGGCCGGCCCCTCCGTGTTCCTGTTC
CCCCCCAAGCCCAAGGACACCCTGATGATCTCCAGGACCCCCGAGGTGACCTGCGTGGTGGTG
GACGTGTCCCACGAGGACCCCGAGGTGAAGTTCAACTGGTACGTGGACGGCGTGGAGGTGCAC
AACGCCAAGACCAAGCCCAGGGAGGAGCAGTACAACTCCACCTACAGGGTGGTGTCCGTGCTG
ACCGTGCTGCACCAGGACTGGCTGAACGGCAAGGAGTACAAGTGCAAGGTGTCCAACAAGGGC
CTGCCCTCCTCCATCGAGAAGACCATCTCCAAGGCCAAGGGCCAGCCCAGGGAGCCCCAGGTG
TACACCCTGCCCCCCTCCAGGGAGGAGATGACCAAGAACCAGGTGTCCCTGACCTGCCTGGTGA
AGGGCTTCTACCCCTCCGACATCGCCGTGGAGTGGGAGTCCAACGGCCAGCCCGAGAACAACT
ACAAGACCACCCCCCCCGTGCTGGACTCCGACGGCTCCTTCTTCCTGTACTCCAAGCTGACCGT
GGACAAGTCCAGGTGGCAGCAGGGCAACGTGTTCTCCTGCTCCGTGATGCACGAGGCCCTGCAC
AACCACTACACCCAGAAGTCCCTGTCCCTGTCCCCCGGCAAGTGA(SEQ ID NO:98)

hDAO-Fc-Hepmut4-Cysmut

ATGCCGGCCCTGGGCTGGGCCGTGGCTGCCATCCTGATGCTGCAGACGGCCATGGCGGA
GCCCTCCCCGGGGACTCTGCCCAGGAAGGCAGGGGTGTTTTCAGACCTAAGCAACCAAGAGCTGA
AGGCAGTGCACAGCTTCCTCTGGTCCAAGAAGGAGCTGAGGCTGCAGCCCTCCAGTACCACCACC
ATGGCCAAGAACACCGTGTTTCTCATCGAGATGCTGCTGCCCAAGAAGTACCATGTGCTGAGGTTT
CTGGATAAAGGTGAAAGGCATCCTGTGCGGGAAGCCCGTGCCGTCATCTTCTTTGGTGACCAGGA
GCATCCCAATGTCACCGAGTTTGCTGTGGGGCCCCTGCCAGGGCCC**GCC**TACATGCGAGCACTGT
CCCCCAGGCCTGGGTACCAGTCCTCCTGGGCATCGAGGCCCATCTCCACAGCAGAGTATGCCCTC
CTCTACCACACCCTGCAGGAAGCCACCAAGCCCCTGCATCAGTTCTTCCTCAATACCACAGGCTTC
TCATTCCAAGACTGCCATGACAGATGCCTGGCCTTCACCGATGTGGCCCCCCGGGGTGTGGCTTC
TGGCCAGCGCCGCAGTTGGCTTATCATACAGCGCTATGTAGAAGGCTACTTTCTGCACCCCACTGG
GCTGGAGCTCCTCGTGGATCATGGGAGCACAGATGCTGGGCACTGGGCCGTGGAGCAGGTGTGG
TACAACGGGAAGTTCTATGGGAGCCCAGAGGAACTGGCTCGGAAGTATGCAGATGGAGAGGTGGA
CGTGGTGGTCCTGGAGGACCCGCTGCCTGGGGGCAAGGGGCATGACAGCACAGAGGAGCCGCC
CCTCTTCTCCTCCCACAAGCCCCGCGGGGACTTCCCCAGCCCCATCCATGTGAGCGGCCCCCGCT
TGGTCCAGCCCCACGGCCCTCGCTTCAGGCTGGAGGGCAACGCTGTGCTCTACGGCGGCTGGAG
CTTTGCCTTCCGGCTGCGCTCCTCCTCCGGGCTGCAGGTCCTGAACGTGCACTTCGGCGGAGAGC
GCATTGCCTATGAGGTCAGCGTGCAAGAGGCAGTGGCGCTGTATGGAGGACACACACCTGCAGGC
ATGCAGACCAAGTACCTCGATGTCGGCTGGGGCCTGGGCAGCGTCACTCATGAGTTAGCCCCCGG
CATCGACTGCCCGGAGACCGCCACCTTCCTGGACACTTTCCACTACTATGATGCCGATGACCCGGT
CCATTATCCCCGAGCCCTCTGCCTCTTTGAAATGCCCACAGGGGTGCCCCTTCGGCGGCACTTTAA

图1续

TTCCAACTTTAAAGGTGGCTTCAACTTCTATGCGGGGCTGAAGGGCCAGGTGCTGGTGCTGCGGA
CAACTTCAACTGTCTACAATTATGATTACATTTGGGACTTTATCTTCTACCCCAACGGGGTGATGGA
GGCCAAGATGCATGCCACTGGCTACGTCCACGCCACCTTCTACACCCCCGAGGGGCTGCGCCAC
GGCACTCGCCTGCACACCCACCTGATTGGCAACATACACACTCACTTGGTGCACTACCGCGTAGAC
CTGGATGTGGCAGGCACCAAGAACAGCTTCCAGACACTGCAGATGAAGCTAGAAAACATCACCAAC
CCCTGGAGCCCAAGACACCGCGTGGTCCAGCCAACTCTGGAGCAGACGCAGTACTCCTGGGAGC
GCCAGGCGGCCTTC**AGC**TTCAAA**ACG**AAGCTGCCCAAGTACCTGCTCTTTACCAGCCCCCAGGAG
AACCCCTGGGGCCACAAGCGCAGCTACCGCCTGCAGATCCACTCCATGGCCGACCAGGTGCTGC
CCCCAGGCTGGCAGGAGGAGCAGGCCATCACCTGGGCAAGGTACCCCCTGGCAGTGACCAAGTA
CCGGGAGTCGGAGCTGTGCAGCAGCAGCATCTACCACCAGAACGACCCCTGGCACCCGCCCGTG
GTCTTTGAGCAGTTTCTTCACAACAACGAGAACATTGAAAATGAGGACCTGGTGGCCTGGGTGACG
GTGGGCTTCCTGCACATCCCCCACTCAGAGGACATTCCCAACACAGCCACACCTGGGAACTCCGT
GGGCTTCCTGCTCCGGCCATTCAACTTCTTCCCAGAGGACCCCTCCCTGGCATCCAGAGACACTGT
GATCGTGTGGCCTCGGGACAACGGCCCCAACTACGTCCAGCGCTGGATCCCTGAGGACAGGGAC
TGCTCGATGCCTCCCCCTTTTAGCTACAATGGGACCTATAGACCTGTG***GAGCCCAAGTCCGCCGA***
CAAGACCCACACCTGCCCCCCCTGCCCCGCCCCCCCCGTGGCCGGCCCCTCCGTGTTCCTGTTC
CCCCCCAAGCCCAAGGACACCCTGATGATCTCCAGGACCCCCGAGGTGACCTGCGTGGTGGTG
GACGTGTCCCACGAGGACCCCGAGGTGAAGTTCAACTGGTACGTGGACGGCGTGGAGGTGCAC
AACGCCAAGACCAAGCCCAGGGAGGAGCAGTACAACTCCACCTACAGGGTGGTGTCCGTGCTG
ACCGTGCTGCACCAGGACTGGCTGAACGGCAAGGAGTACAAGTGCAAGGTGTCCAACAAGGGC
CTGCCCTCCTCCATCGAGAAGACCATCTCCAAGGCCAAGGGCCAGCCCAGGGAGCCCCAGGTG
TACACCCTGCCCCCCTCCAGGGAGGAGATGACCAAGAACCAGGTGTCCCTGACCTGCCTGGTGA
AGGGCTTCTACCCCTCCGACATCGCCGTGGAGTGGGAGTCCAACGGCCAGCCCGAGAACAACT
ACAAGACCACCCCCCCCGTGCTGGACTCCGACGGCTCCTTCTTCCTGTACTCCAAGCTGACCGT
GGACAAGTCCAGGTGGCAGCAGGGCAACGTGTTCTCCTGCTCCGTGATGCACGAGGCCCTGCAC
AACCACTACACCCAGAAGTCCCTGTCCCTGTCCCCCGGCAAGTGA (SEQ ID NO:99)

hDAO-Fc-Hepmut5-Cysmut

ATGCCGGCCCTGGGCTGGGCCGTGGCTGCCATCCTGATGCTGCAGACGGCCATGGCGGA
GCCCTCCCCGGGGACTCTGCCCAGGAAGGCAGGGGTGTTTTCAGACCTAAGCAACCAAGAGCTGA
AGGCAGTGCACAGCTTCCTCTGGTCCAAGAAGGAGCTGAGGCTGCAGCCCTCCAGTACCACCACC
ATGGCCAAGAACACCGTGTTTCTCATCGAGATGCTGCTGCCCAAGAAGTACCATGTGCTGAGGTTT
CTGGATAAAGGTGAAAGGCATCCTGTGCGGGAAGCCCGTGCCGTCATCTTCTTTGGTGACCAGGA
GCATCCCAATGTCACCGAGTTTGCTGTGGGGCCCCTGCCAGGGCCC**GCC**TACATGCGAGCACTGT
CCCCCAGGCCTGGGTACCAGTCCTCCTGGGCATCGAGGCCCATCTCCACAGCAGAGTATGCCCTC
CTCTACCACACCCTGCAGGAAGCCACCAAGCCCCTGCATCAGTTCTTCCTCAATACCACAGGCTTC
TCATTCCAAGACTGCCATGACAGATGCCTGGCCTTCACCGATGTGGCCCCCCGGGGTGTGGCTTC
TGGCCAGCGCCGCAGTTGGCTTATCATACAGCGCTATGTAGAAGGCTACTTTCTGCACCCCACTGG
GCTGGAGCTCCTCGTGGATCATGGGAGCACAGATGCTGGGCACTGGGCCGTGGAGCAGGTGTGG
TACAACGGGAAGTTCTATGGGAGCCCAGAGGAACTGGCTCGGAAGTATGCAGATGGAGAGGTGGA
CGTGGTGGTCCTGGAGGACCCGCTGCCTGGGGGCAAGGGGCATGACAGCACAGAGGAGCCGCC
CCTCTTCTCCTCCCACAAGCCCCGCGGGGACTTCCCCAGCCCCATCCATGTGAGCGGCCCCCGCT
TGGTCCAGCCCCACGGCCCTCGCTTCAGGCTGGAGGGCAACGCTGTGCTCTACGGCGGCTGGAG
CTTTGCCTTCCGGCTGCGCTCCTCCTCCGGGCTGCAGGTCCTGAACGTGCACTTCGGCGGAGAGC
GCATTGCCTATGAGGTCAGCGTGCAAGAGGCAGTGGCGCTGTATGGAGGACACACACCTGCAGGC
ATGCAGACCAAGTACCTCGATGTCGGCTGGGGCCTGGGCAGCGTCACTCATGAGTTAGCCCCCGG
CATCGACTGCCCGGAGACCGCCACCTTCCTGGACACTTTCCACTACTATGATGCCGATGACCCGGT
CCATTATCCCCGAGCCCTCTGCCTCTTTGAAATGCCCACAGGGGTGCCCCTTCGGCGGCACTTTAA
TTCCAACTTTAAAGGTGGCTTCAACTTCTATGCGGGGCTGAAGGGCCAGGTGCTGGTGCTGCGGA
CAACTTCAACTGTCTACAATTATGATTACATTTGGGACTTTATCTTCTACCCCAACGGGGTGATGGA
GGCCAAGATGCATGCCACTGGCTACGTCCACGCCACCTTCTACACCCCCGAGGGGCTGCGCCAC
GGCACTCGCCTGCACACCCACCTGATTGGCAACATACACACTCACTTGGTGCACTACCGCGTAGAC
CTGGATGTGGCAGGCACCAAGAACAGCTTCCAGACACTGCAGATGAAGCTAGAAAACATCACCAAC
CCCTGGAGCCCAAGACACCGCGTGGTCCAGCCAACTCTGGAGCAGACGCAGTACTCCTGGGAGC
GCCAGGCGGCCTTCCGCTTCAAA**ACG**AAGCTGCCC**ACG**TACCTGCTCTTTACCAGCCCCCAGGAG
AACCCCTGGGGCCACAAGCGCAGCTACCGCCTGCAGATCCACTCCATGGCCGACCAGGTGCTGC
CCCCAGGCTGGCAGGAGGAGCAGGCCATCACCTGGGCAAGGTACCCCCTGGCAGTGACCAAGTA
CCGGGAGTCGGAGCTGTGCAGCAGCAGCATCTACCACCAGAACGACCCCTGGCACCCGCCCGTG
GTCTTTGAGCAGTTTCTTCACAACAACGAGAACATTGAAAATGAGGACCTGGTGGCCTGGGTGACG

图1续

GTGGGCTTCCTGCACATCCCCCACTCAGAGGACATTCCCAACACAGCCACACCTGGGAACTCCGT
GGGCTTCCTGCTCCGGCCATTCAACTTCTTCCCAGAGGACCCCTCCCTGGCATCCAGAGACACTGT
GATCGTGTGGCCTCGGGACAACGGCCCCAACTACGTCCAGCGCTGGATCCCTGAGGACAGGGAC
TGCTCGATGCCTCCCCCTTTTAGCTACAATGGGACCTATAGACCTGTG***GAGCCCAAGTCCGCCGA***
CAAGACCCACACCTGCCCCCCCTGCCCCGCCCCCCCCGTGGCCGGCCCCTCCGTGTTCCTGTTC
CCCCCCAAGCCCAAGGACACCCTGATGATCTCCAGGACCCCCGAGGTGACCTGCGTGGTGGTG
GACGTGTCCCACGAGGACCCCGAGGTGAAGTTCAACTGGTACGTGGACGGCGTGGAGGTGCAC
AACGCCAAGACCAAGCCCAGGGAGGAGCAGTACAACTCCACCTACAGGGTGGTGTCCGTGCTG
ACCGTGCTGCACCAGGACTGGCTGAACGGCAAGGAGTACAAGTGCAAGGTGTCCAACAAGGGC
CTGCCCTCCTCCATCGAGAAGACCATCTCCAAGGCCAAGGGCCAGCCCAGGGAGCCCCAGGTG
TACACCCTGCCCCCCTCCAGGGAGGAGATGACCAAGAACCAGGTGTCCCTGACCTGCCTGGTGA
AGGGCTTCTACCCCTCCGACATCGCCGTGGAGTGGGAGTCCAACGGCCAGCCCGAGAACAACT
ACAAGACCACCCCCCCCGTGCTGGACTCCGACGGCTCCTTCTTCCTGTACTCCAAGCTGACCGT
GGACAAGTCCAGGTGGCAGCAGGGCAACGTGTTCTCCTGCTCCGTGATGCACGAGGCCCTGCAC
AACCACTACACCCAGAAGTCCCTGTCCCTGTCCCCCGGCAAGTGA (SEQ ID NO:100)

hDAO-Fc-Hepmut6-Cysmut

ATGCCGGCCCTGGGCTGGGCCGTGGCTGCCATCCTGATGCTGCAGACGGCCATGGCGGA
GCCCTCCCCGGGGACTCTGCCCAGGAAGGCAGGGGTGTTTTCAGACCTAAGCAACCAAGAGCTGA
AGGCAGTGCACAGCTTCCTCTGGTCCAAGAAGGAGCTGAGGCTGCAGCCCTCCAGTACCACCACC
ATGGCCAAGAACACCGTGTTTCTCATCGAGATGCTGCTGCCCAAGAAGTACCATGTGCTGAGGTTT
CTGGATAAAGGTGAAAGGCATCCTGTGCGGGAAGCCCGTGCCGTCATCTTCTTTGGTGACCAGGA
GCATCCCAATGTCACCGAGTTTGCTGTGGGGCCCCTGCCAGGGCCC**GCC**TACATGCGAGCACTGT
CCCCCAGGCCTGGGTACCAGTCCTCCTGGGCATCGAGGCCCATCTCCACAGCAGAGTATGCCCTC
CTCTACCACACCCTGCAGGAAGCCACCAAGCCCCTGCATCAGTTCTTCCTCAATACCACAGGCTTC
TCATTCCAAGACTGCCATGACAGATGCCTGGCCTTCACCGATGTGGCCCCCCGGGGTGTGGCTTC
TGGCCAGCGCCGCAGTTGGCTTATCATACAGCGCTATGTAGAAGGCTACTTTCTGCACCCCACTGG
GCTGGAGCTCCTCGTGGATCATGGGAGCACAGATGCTGGGCACTGGGCCGTGGAGCAGGTGTGG
TACAACGGGAAGTTCTATGGGAGCCCAGAGGAACTGGCTCGGAAGTATGCAGATGGAGAGGTGGA
CGTGGTGGTCCTGGAGGACCCGCTGCCTGGGGGCAAGGGGCATGACAGCACAGAGGAGCCGCC
CCTCTTCTCCTCCCACAAGCCCCGCGGGGACTTCCCCAGCCCCATCCATGTGAGCGGCCCCCGCT
TGGTCCAGCCCCACGGCCCTCGCTTCAGGCTGGAGGGCAACGCTGTGCTCTACGGCGGCTGGAG
CTTTGCCTTCCGGCTGCGCTCCTCCTCCGGGCTGCAGGTCCTGAACGTGCACTTCGGCGGAGAGC
GCATTGCCTATGAGGTCAGCGTGCAAGAGGCAGTGGCGCTGTATGGAGGACACACACCTGCAGGC
ATGCAGACCAAGTACCTCGATGTCGGCTGGGGCCTGGGCAGCGTCACTCATGAGTTAGCCCCCGG
CATCGACTGCCCGGAGACCGCCACCTTCCTGGACACTTTCCACTACTATGATGCCGATGACCCGGT
CCATTATCCCCGAGCCCTCTGCCTCTTTGAAATGCCCACAGGGGTGCCCCTTCGGCGGCACTTTAA
TTCCAACTTTAAAGGTGGCTTCAACTTCTATGCGGGGCTGAAGGGCCAGGTGCTGGTGCTGCGGA
CAACTTCAACTGTCTACAATTATGATTACATTTGGGACTTTATCTTCTACCCCAACGGGGTGATGGA
GGCCAAGATGCATGCCACTGGCTACGTCCACGCCACCTTCTACACCCCCGAGGGGCTGCGCCAC
GGCACTCGCCTGCACACCCACCTGATTGGCAACATACACACTCACTTGGTGCACTACCGCGTAGAC
CTGGATGTGGCAGGCACCAAGAACAGCTTCCAGACACTGCAGATGAAGCTAGAAAACATCACCAAC
CCCTGGAGCCCAAGACACCGCGTGGTCCAGCCAACTCTGGAGCAGACGCAGTACTCCTGGGAGC
GCCAGGCGGCCTTCCGCTTC**GGACAGACG**CTGCCCAAGTACCTGCTCTTTACCAGCCCCCAGGA
GAACCCCTGGGGCCACAAGCGCAGCTACCGCCTGCAGATCCACTCCATGGCCGACCAGGTGCTG
CCCCCAGGCTGGCAGGAGGAGCAGGCCATCACCTGGGCAAGGTACCCCCTGGCAGTGACCAAGT
ACCGGGAGTCGGAGCTGTGCAGCAGCAGCATCTACCACCAGAACGACCCCTGGCACCCGCCCGT
GGTCTTTGAGCAGTTTCTTCACAACAACGAGAACATTGAAAATGAGGACCTGGTGGCCTGGGTGAC
GGTGGGCTTCCTGCACATCCCCCACTCAGAGGACATTCCCAACACAGCCACACCTGGGAACTCCG
TGGGCTTCCTGCTCCGGCCATTCAACTTCTTCCCAGAGGACCCCTCCCTGGCATCCAGAGACACTG
TGATCGTGTGGCCTCGGGACAACGGCCCCAACTACGTCCAGCGCTGGATCCCTGAGGACAGGGA
CTGCTCGATGCCTCCCCCTTTTAGCTACAATGGGACCTATAGACCTGTG***GAGCCCAAGTCCGCCG***
ACAAGACCCACACCTGCCCCCCCTGCCCCGCCCCCCCCGTGGCCGGCCCCTCCGTGTTCCTGTT
CCCCCCCAAGCCCAAGGACACCCTGATGATCTCCAGGACCCCCGAGGTGACCTGCGTGGTGGT
GGACGTGTCCCACGAGGACCCCGAGGTGAAGTTCAACTGGTACGTGGACGGCGTGGAGGTGCA
CAACGCCAAGACCAAGCCCAGGGAGGAGCAGTACAACTCCACCTACAGGGTGGTGTCCGTGCT
GACCGTGCTGCACCAGGACTGGCTGAACGGCAAGGAGTACAAGTGCAAGGTGTCCAACAAGGG
CCTGCCCTCCTCCATCGAGAAGACCATCTCCAAGGCCAAGGGCCAGCCCAGGGAGCCCCAGGT

图1续

GTACACCCTGCCCCCCTCCAGGGAGGAGATGACCAAGAACCAGGTGTCCCTGACCTGCCTGGT
GAAGGGCTTCTACCCCTCCGACATCGCCGTGGAGTGGGAGTCCAACGGCCAGCCCGAGAACAA
CTACAAGACCACCCCCCCCGTGCTGGACTCCGACGGCTCCTTCTTCCTGTACTCCAAGCTGACCG
TGGACAAGTCCAGGTGGCAGCAGGGCAACGTGTTCTCCTGCTCCGTGATGCACGAGGCCCTGCA
CAACCACTACACCCAGAAGTCCCTGTCCCTGTCCCCCGGCAAGTGA (SEQ ID NO:101)

hDAO-Fc-Hepmut7-Cysmut

ATGCCGGCCCTGGGCTGGGCCGTGGCTGCCATCCTGATGCTGCAGACGGCCATGGCGGA
GCCCTCCCCGGGGACTCTGCCCAGGAAGGCAGGGGTGTTTTCAGACCTAAGCAACCAAGAGCTGA
AGGCAGTGCACAGCTTCCTCTGGTCCAAGAAGGAGCTGAGGCTGCAGCCCTCCAGTACCACCACC
ATGGCCAAGAACACCGTGTTTCTCATCGAGATGCTGCTGCCCAAGAAGTACCATGTGCTGAGGTTT
CTGGATAAAGGTGAAAGGCATCCTGTGCGGGAAGCCCGTGCCGTCATCTTCTTTGGTGACCAGGA
GCATCCCAATGTCACCGAGTTTGCTGTGGGGCCCCTGCCAGGGCCC**GCC**TACATGCGAGCACTGT
CCCCCAGGCCTGGGTACCAGTCCTCCTGGGCATCGAGGCCCATCTCCACAGCAGAGTATGCCCTC
CTCTACCACACCCTGCAGGAAGCCACCAAGCCCCTGCATCAGTTCTTCCTCAATACCACAGGCTTC
TCATTCCAAGACTGCCATGACAGATGCCTGGCCTTCACCGATGTGGCCCCCCGGGGTGTGGCTTC
TGGCCAGCGCCGCAGTTGGCTTATCATACAGCGCTATGTAGAAGGCTACTTTCTGCACCCCACTGG
GCTGGAGCTCCTCGTGGATCATGGGAGCACAGATGCTGGGCACTGGGCCGTGGAGCAGGTGTGG
TACAACGGGAAGTTCTATGGGAGCCCAGAGGAACTGGCTCGGAAGTATGCAGATGGAGAGGTGGA
CGTGGTGGTCCTGGAGGACCCGCTGCCTGGGGGCAAGGGGCATGACAGCACAGAGGAGCCGCC
CCTCTTCTCCTCCCACAAGCCCCGCGGGGACTTCCCCAGCCCCATCCATGTGAGCGGCCCCCGCT
TGGTCCAGCCCCACGGCCCTCGCTTCAGGCTGGAGGGCAACGCTGTGCTCTACGGCGGCTGGAG
CTTTGCCTTCCGGCTGCGCTCCTCCTCCGGGCTGCAGGTCCTGAACGTGCACTTCGGCGGAGAGC
GCATTGCCTATGAGGTCAGCGTGCAAGAGGCAGTGGCGCTGTATGGAGGACACACACCTGCAGGC
ATGCAGACCAAGTACCTCGATGTCGGCTGGGGCCTGGGCAGCGTCACTCATGAGTTAGCCCCCGG
CATCGACTGCCCGGAGACCGCCACCTTCCTGGACACTTTCCACTACTATGATGCCGATGACCCGGT
CCATTATCCCCGAGCCCTCTGCCTCTTTGAAATGCCCACAGGGGTGCCCCTTCGGCGGCACTTTAA
TTCCAACTTTAAAGGTGGCTTCAACTTCTATGCGGGGCTGAAGGGCCAGGTGCTGGTGCTGCGGA
CAACTTCAACTGTCTACAATTATGATTACATTTGGGACTTTATCTTCTACCCCAACGGGGTGATGGA
GGCCAAGATGCATGCCACTGGCTACGTCCACGCCACCTTCTACACCCCCGAGGGGCTGCGCCAC
GGCACTCGCCTGCACACCCACCTGATTGGCAACATACACACTCACTTGGTGCACTACCGCGTAGAC
CTGGATGTGGCAGGCACCAAGAACAGCTTCCAGACACTGCAGATGAAGCTAGAAAACATCACCAAC
CCCTGGAGCCCAAGACACCGCGTGGTCCAGCCAACTCTGGAGCAGACGCAGTACTCCTGGGAGC
GCCAGGCGGCCTTC**AGC**TTCAAAAGGAAGCTGCCC**ACG**TACCTGCTCTTTACCAGCCCCCAGGAG
AACCCCTGGGGCCACAAGCGCAGCTACCGCCTGCAGATCCACTCCATGGCCGACCAGGTGCTGC
CCCCAGGCTGGCAGGAGGAGCAGGCCATCACCTGGGCAAGGTACCCCCTGGCAGTGACCAAGTA
CCGGGAGTCGGAGCTGTGCAGCAGCAGCATCTACCACCAGAACGACCCCTGGCACCCGCCCGTG
GTCTTTGAGCAGTTTCTTCACAACAACGAGAACATTGAAAATGAGGACCTGGTGGCCTGGGTGACG
GTGGGCTTCCTGCACATCCCCCACTCAGAGGACATTCCCAACACAGCCACACCTGGGAACTCCGT
GGGCTTCCTGCTCCGGCCATTCAACTTCTTCCCAGAGGACCCCTCCCTGGCATCCAGAGACACTGT
GATCGTGTGGCCTCGGGACAACGGCCCCAACTACGTCCAGCGCTGGATCCCTGAGGACAGGGAC
TGCTCGATGCCTCCCCCTTTTAGCTACAATGGGACCTATAGACCTGTG***GAGCCCAAGTCCGCCGA***
CAAGACCCACACCTGCCCCCCCCTGCCCCGCCCCCCCCGTGGCCGGCCCCTCCGTGTTCCTGTTC
CCCCCCAAGCCCAAGGACACCCTGATGATCTCCAGGACCCCCGAGGTGACCTGCGTGGTGGTG
GACGTGTCCCACGAGGACCCCGAGGTGAAGTTCAACTGGTACGTGGACGGCGTGGAGGTGCAC
AACGCCAAGACCAAGCCCAGGGAGGAGCAGTACAACTCCACCTACAGGGTGGTGTCCGTGCTG
ACCGTGCTGCACCAGGACTGGCTGAACGGCAAGGAGTACAAGTGCAAGGTGTCCAACAAGGGC
CTGCCCTCCTCCATCGAGAAGACCATCTCCAAGGCCAAGGGCCAGCCCAGGGAGCCCCAGGTG
TACACCCTGCCCCCCTCCAGGGAGGAGATGACCAAGAACCAGGTGTCCCTGACCTGCCTGGTGA
AGGGCTTCTACCCCTCCGACATCGCCGTGGAGTGGGAGTCCAACGGCCAGCCCGAGAACAACT
ACAAGACCACCCCCCCCGTGCTGGACTCCGACGGCTCCTTCTTCCTGTACTCCAAGCTGACCGT
GGACAAGTCCAGGTGGCAGCAGGGCAACGTGTTCTCCTGCTCCGTGATGCACGAGGCCCTGCAC
AACCACTACACCCAGAAGTCCCTGTCCCTGTCCCCCGGCAAGTGA (SEQ ID NO:102)

图1续

人血清白蛋白（HSA），野生型序列

DAHKSEVAHRFKDLGEENFKALVLIAFAQYLQQCPFEDHVKLVNEVTEFAKTCVADESAENCDKSLHTL
FGDKLCTVATLRETYGEMADCCAKQEPERNECFLQHKDDNPNLPRLVRPEVDVMCTAFHDNEETFLKK
YLYEIARRHPYFYAPELLFFAKRYKAAFTECCQAADKAACLLPKLDELRDEGKASSAKQRLKCASLQKF
GERAFKAWAVARLSQRFPKAEFAEVSKLVTDLTKVHTECCHGDLLECADDRADLAKYICENQDSISSKL
KECCEKPLLEKSHCIAEVENDEMPADLPSLAADFVESKDVCKNYAEAKDVFLGMFLYEYARRHPDYSVV
LLLRLAKTYETTLEKCCAAADPHECYAKVFDEFKPLVEEPQNLIKQNCELFEQLGEYKFQNALLVRYTKK
VPQVSTPTLVEVSRNLGKVGSKCCKHPEAKRMPCAEDYLSVVLNQLCVLHEKTPVSDRVTKCCTESLV
NRRPCFSALEVDETYVPKEFNAETFTFHADICTLSEKERQIKKQTALVELVKHKPKATKEQLKAVMDDFA
AFVEKCCKADDKETCFAEEGKKLVAASQAALGL (SEQ ID NO:103)

hDAO-Hepmut4 Asn168Gln

MPALGWAVAAILMLQTAMAEPSPGTLPRKAGVFSDLSNQELKAVHSFLWSKKELRLQPSSTTTMAKNT
VFLIEMLLPKKYHVLRFLDKGERHPVREARAVIFFGDQEHPNVTEFAVGPLPGPCYMRALSPRPGYQSS
WASRPISTAEYALLYHTLQEATKPLHQFFLQTTGFSFQDCHDRCLAFTDVAPRGVASGQRRSWLIIQRY
VEGYFLHPTGLELLVDHGSTDAGHWAVEQVWYNGKFYGSPEELARKYADGEVDVVVLEDPLPGGKGH
DSTEEPPLFSSHKPRGDFPSPIHVSGPRLVQPHGPRFRLEGNAVLYGGWSFAFRLRSSSGLQVLNVHF
GGERIAYEVSVQEAVALYGGHTPAGMQTKYLDVGWGLGSVTHELAPGIDCPETATFLDTFHYYDADDP
VHYPRALCLFEMPTGVPLRRHFNSNFKGGFNFYAGLKGQVLVLRTTSTVYNYDYIWDFIFYPNGVMEAK
MHATGYVHATFYTPEGLRHGTRLHTHLIGNIHTHLVHYRVDLDVAGTKNSFQTLQMKLENITNPWSPRH
RVVQPTLEQTQYSWERQAAFSFKTKLPKYLLFTSPQENPWGHKRSYRLQIHSMADQVLPPGWQEEQAI
TWARYPLAVTKYRESELCSSSIYHQNDPWHPPVVFEQFLHNNENIENEDLVAWVTVGFLHIPHSEDIPN
TATPGNSVGFLLRPFNFFPEDPSLASRDTVIVWPRDNGPNYVQRWIPEDRDCSMPPPFSYNGTYRPV
(SEQ ID NO:106)

图1续

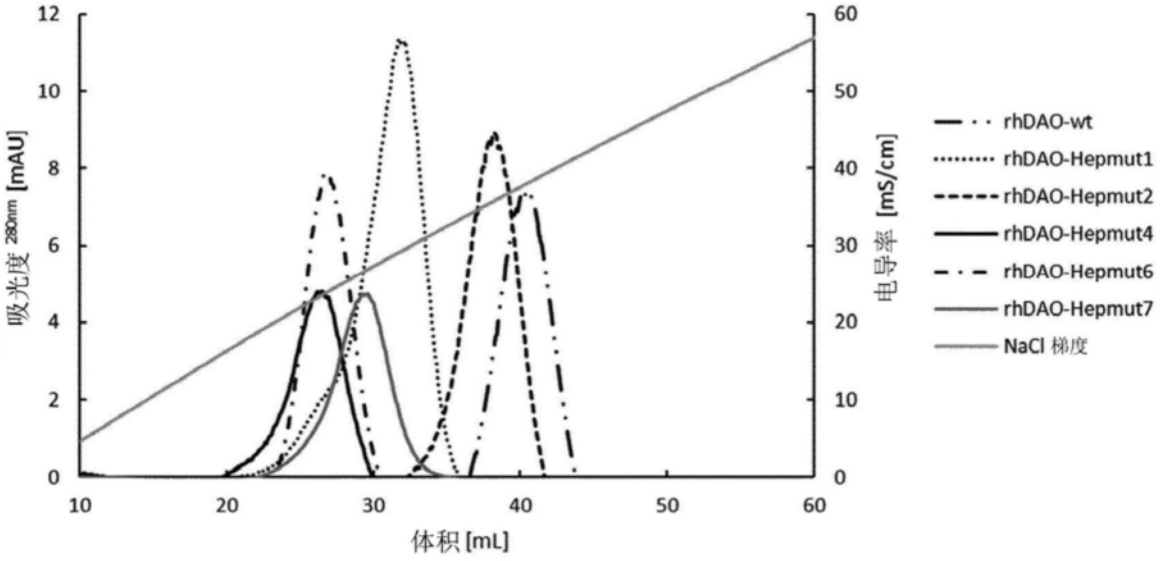


图2

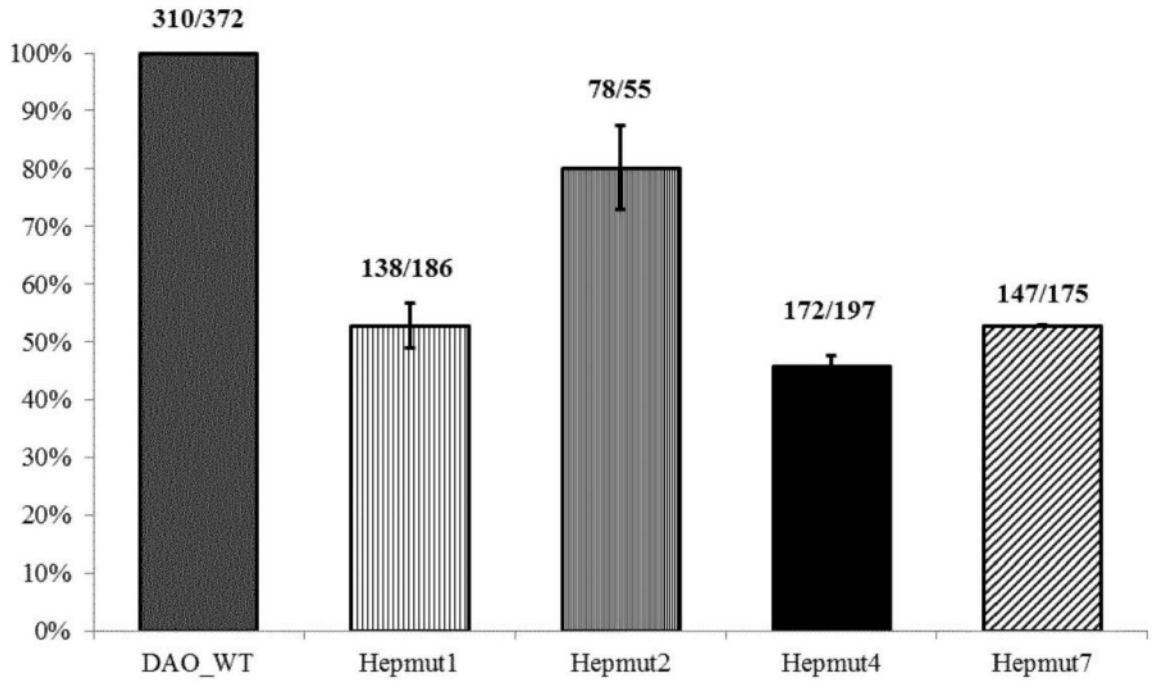

310/372
78/55
138/186
172/197
147/175
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
DAO_WT
Hepmut1
Hepmut2
Hepmut4
Hepmut7

图3

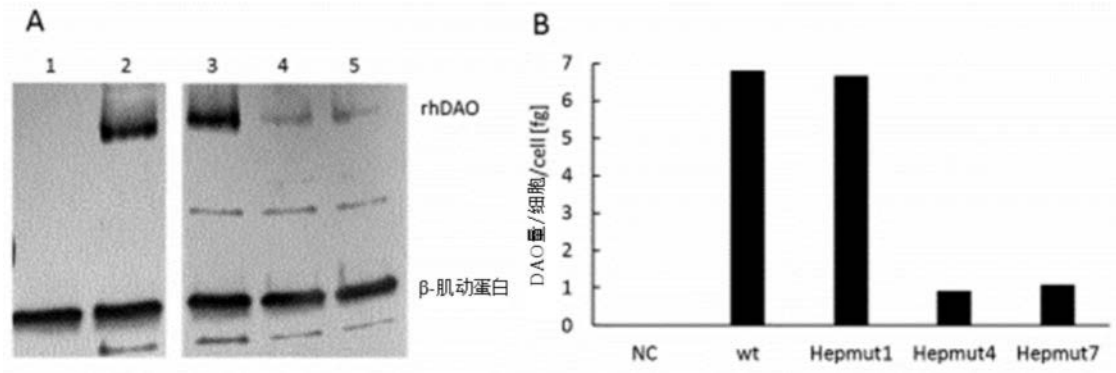

A
1
2
3
4
5
rhDAO
β-肌动蛋白
B
DAO量/细胞/cell [fg]
7
6
5
4
3
2
1
0
NC
wt
Hepmut1
Hepmut4
Hepmut7

图4

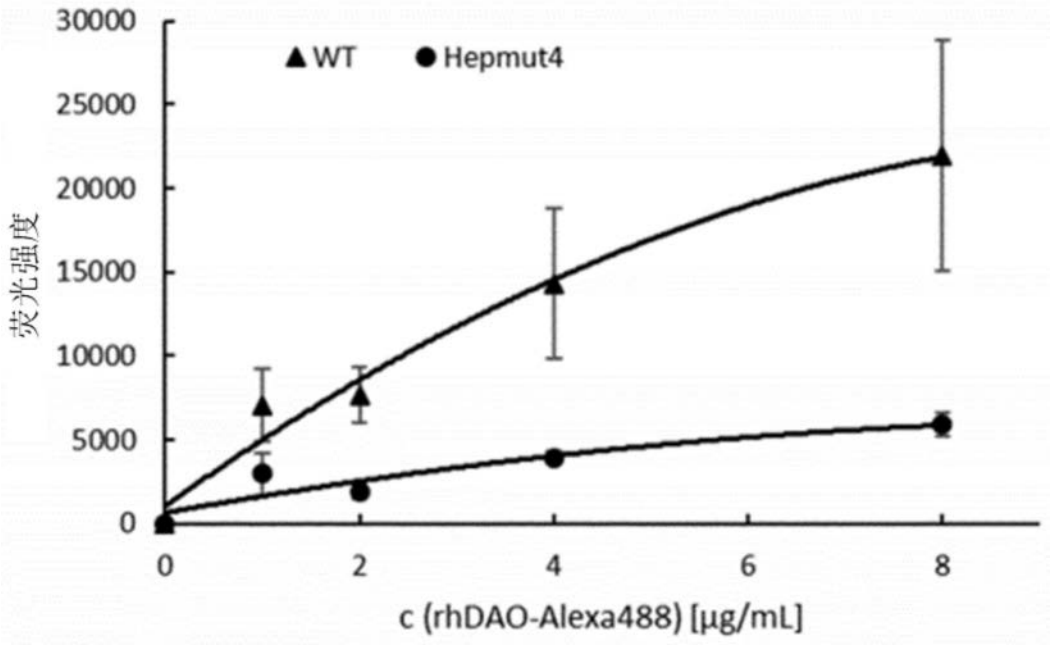

30000
25000
20000
15000
10000
5000
0
荧光强度
▲WT
●Hepmut4
0
2
4
6
8
c (rhDAO-Alexa488) [μg/mL]

图5

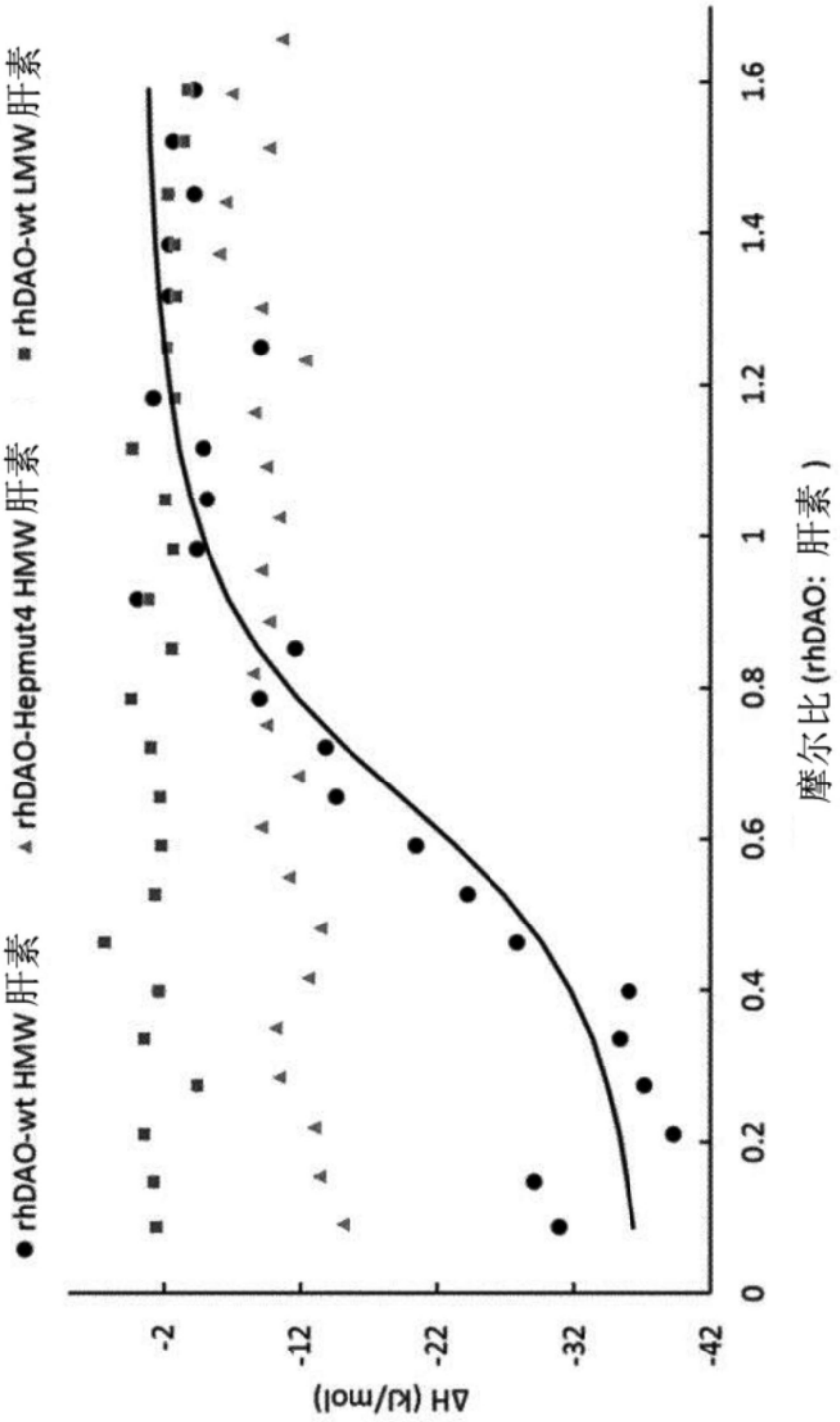

● rhDAO-wt HMW 肝素
▲ rhDAO-Hepmut4 HMW 肝素
■ rhDAO-wt LMW 肝素
ΔH (kJ/mol)
-2
-12
-22
-32
-42
0
0.2
0.4
0.6
0.8
1
1.2
1.4
1.6
摩尔比 (rhDAO: 肝素)

图6

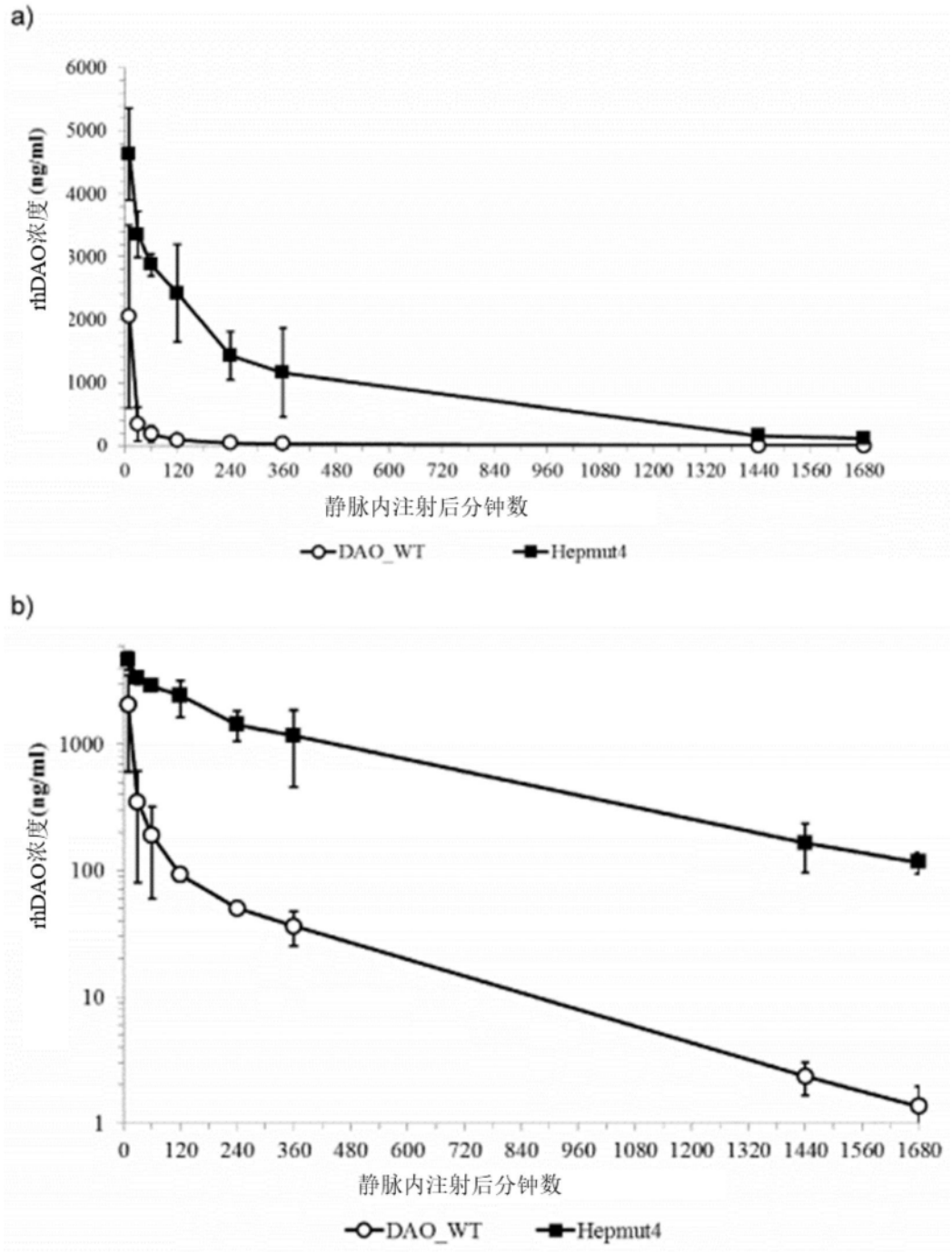

a)
rhDAO浓度 (ng/ml)
6000
5000
4000
3000
2000
1000
0
0 120 240 360 480 600 720 840 960 1080 1200 1320 1440 1560 1680
静脉内注射后分钟数
DAO_WT
Hepmut4
b)
rhDAO浓度(ng/ml)
1000
100
10
1
0 120 240 360 480 600 720 840 960 1080 1200 1320 1440 1560 1680
静脉内注射后分钟数
DAO_WT
Hepmut4

图7

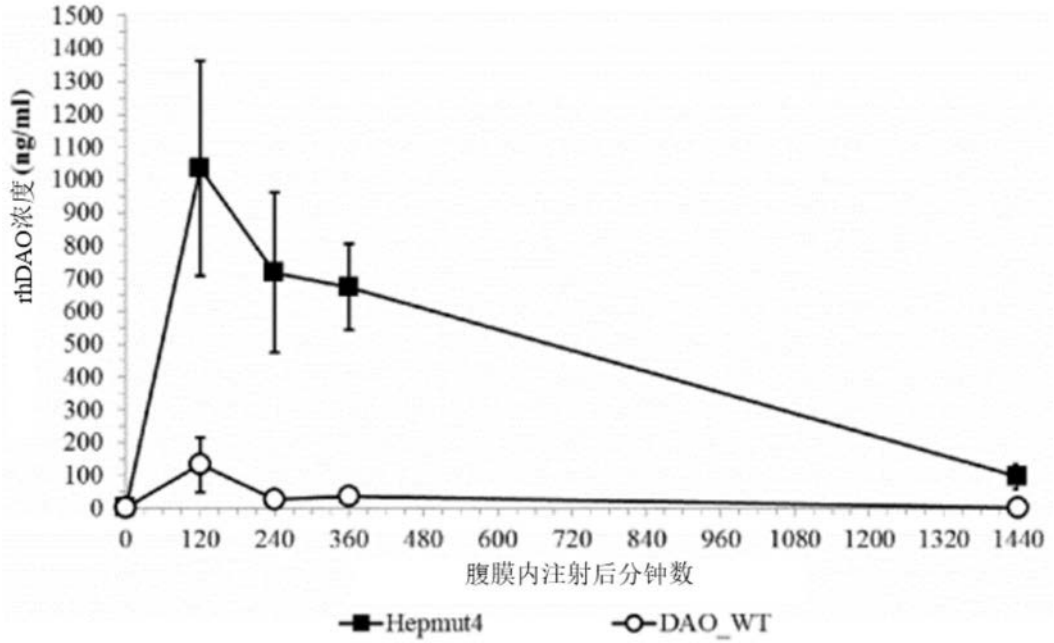

rhDAO浓度(ng/ml)
1500
1400
1300
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
0 120 240 360 480 600 720 840 960 1080 1200 1320 1440
腹膜内注射后分钟数
Hepmut4
DAO_WT

图8

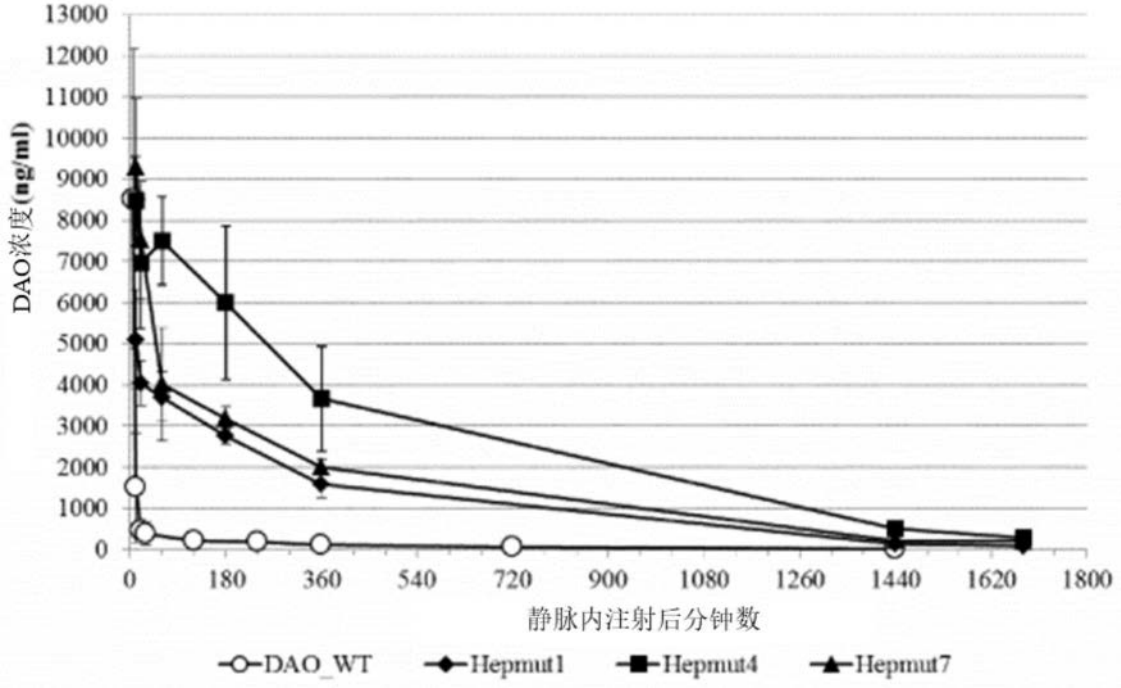

DAO浓度(ng/ml)
13000
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
0 180 360 540 720 900 1080 1260 1440 1620 1800
静脉内注射后分钟数
DAO_WT
Hepmut1
Hepmut4
Hepmut7

图9

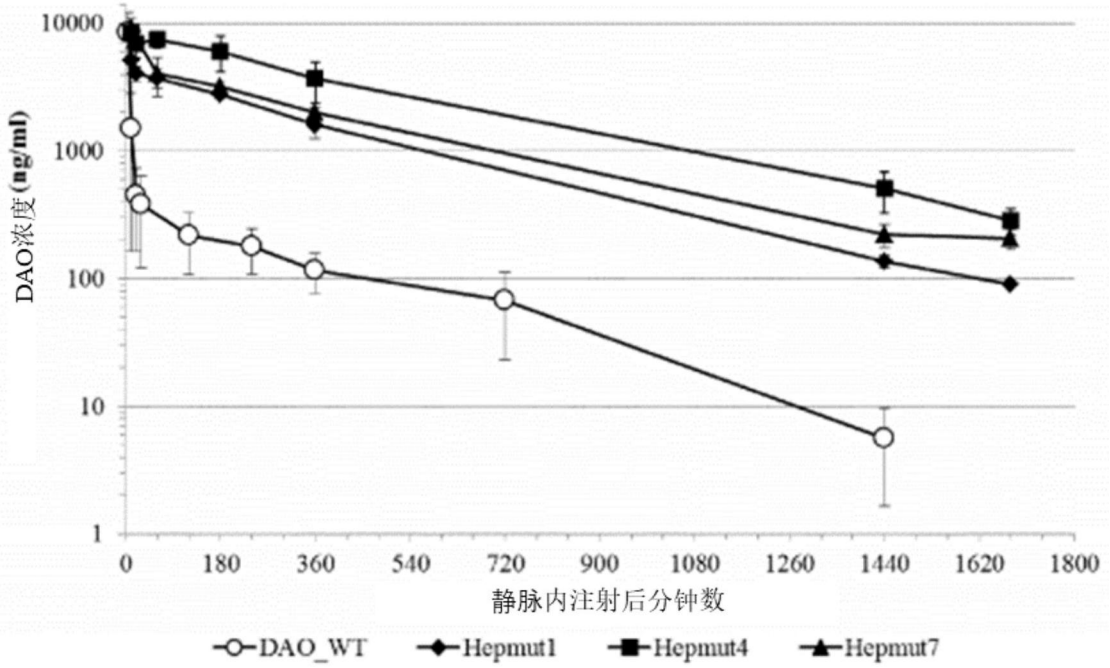

10000
1000
100
10
1
DAO浓度(ng/ml)
0
180
360
540
720
900
1080
1260
1440
1620
1800
静脉内注射后分钟数
DAO_WT
Hepmut1
Hepmut4
Hepmut7

图10

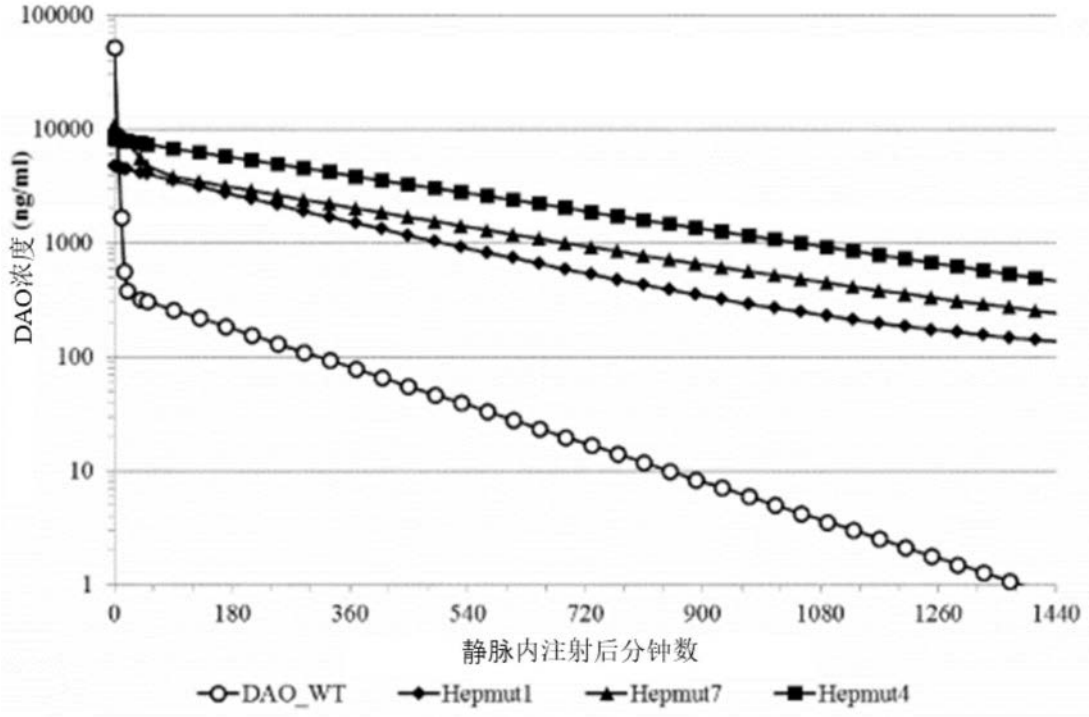

100000
10000
1000
100
10
1
DAO浓度 (ng/ml)
0
180
360
540
720
900
1080
1260
1440
静脉内注射后分钟数
DAO_WT
Hepmut1
Hepmut7
Hepmut4

图11

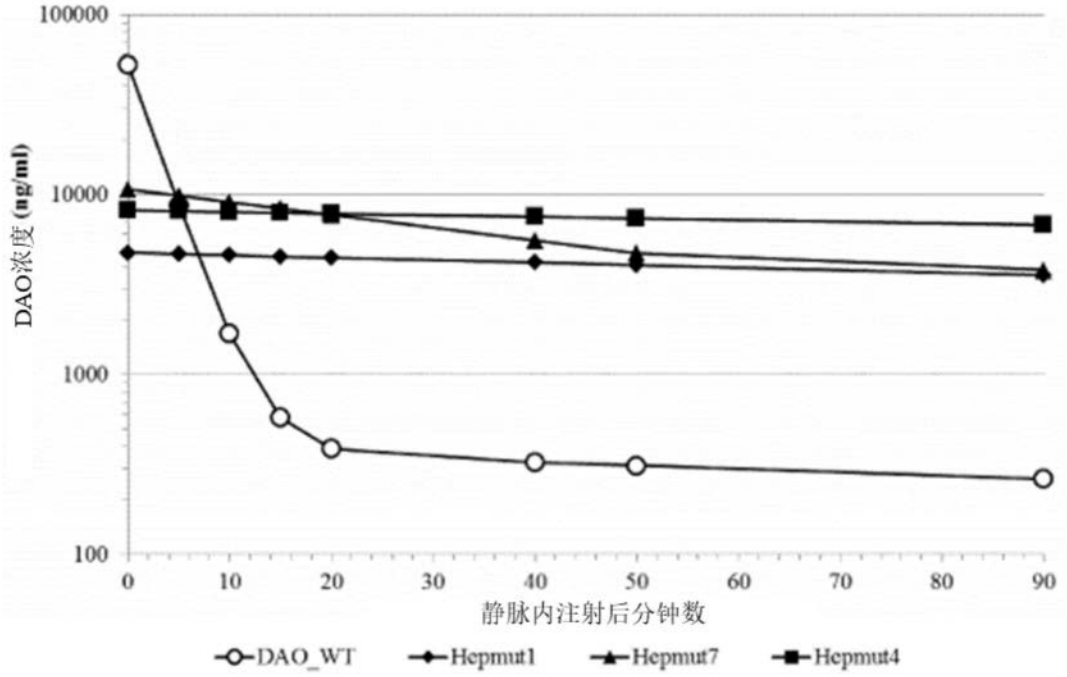

100000
10000
1000
100
DAO浓度(ng/ml)
0
10
20
30
40
50
60
70
80
90
静脉内注射后分钟数
DAO_WT
Hepmut1
Hepmut7
Hepmut4

图12

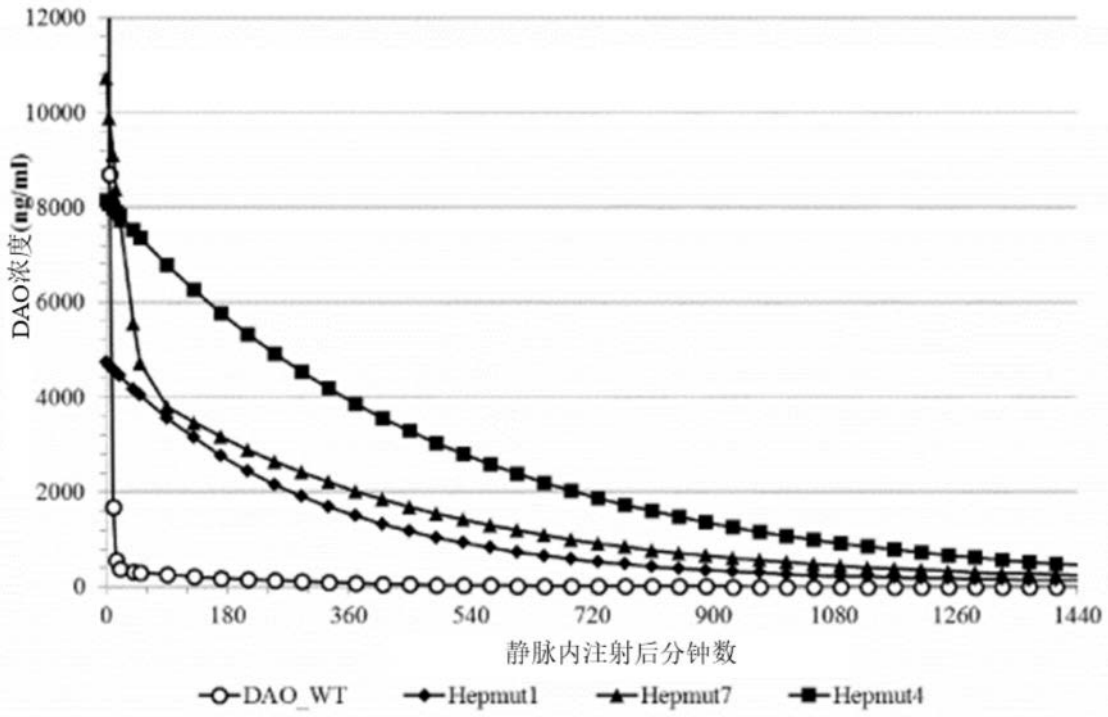

12000
10000
8000
6000
4000
2000
0
DAO浓度(ng/ml)
0
180
360
540
720
900
1080
1260
1440
静脉内注射后分钟数
DAO_WT
Hepmut1
Hepmut7
Hepmut4

图13

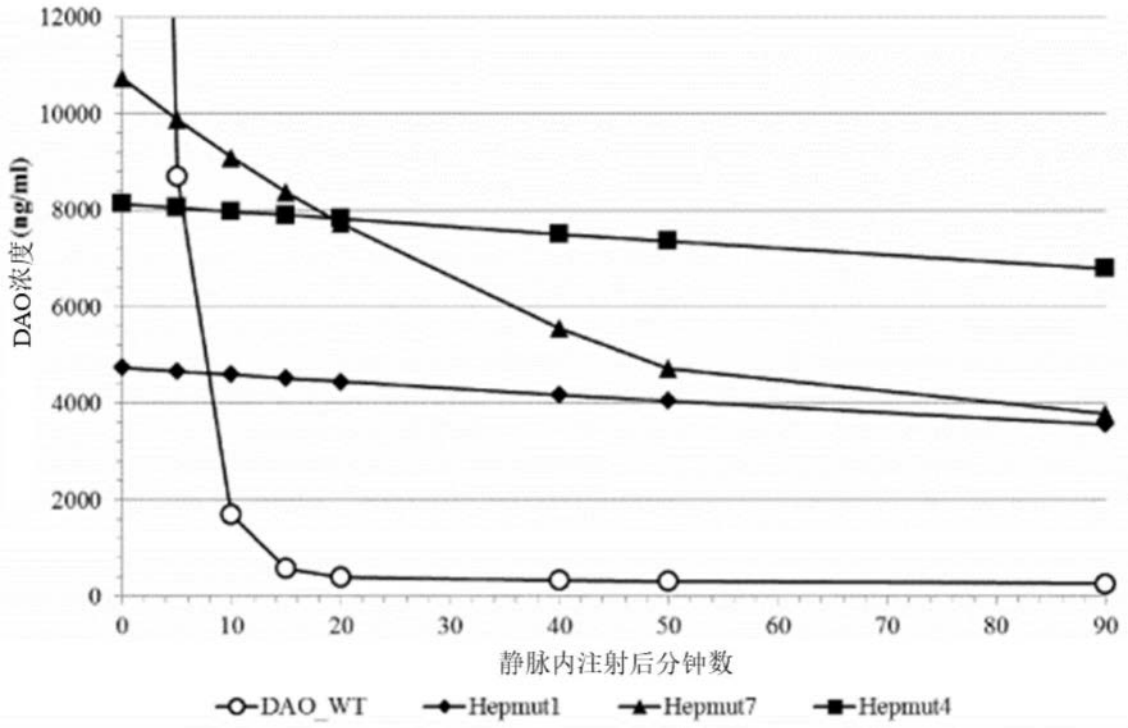

12000
10000
8000
6000
4000
2000
0
DAO浓度(ng/ml)
0
10
20
30
40
50
60
70
80
90
静脉内注射后分钟数
DAO_WT
Hepmut1
Hepmut7
Hepmut4

图14

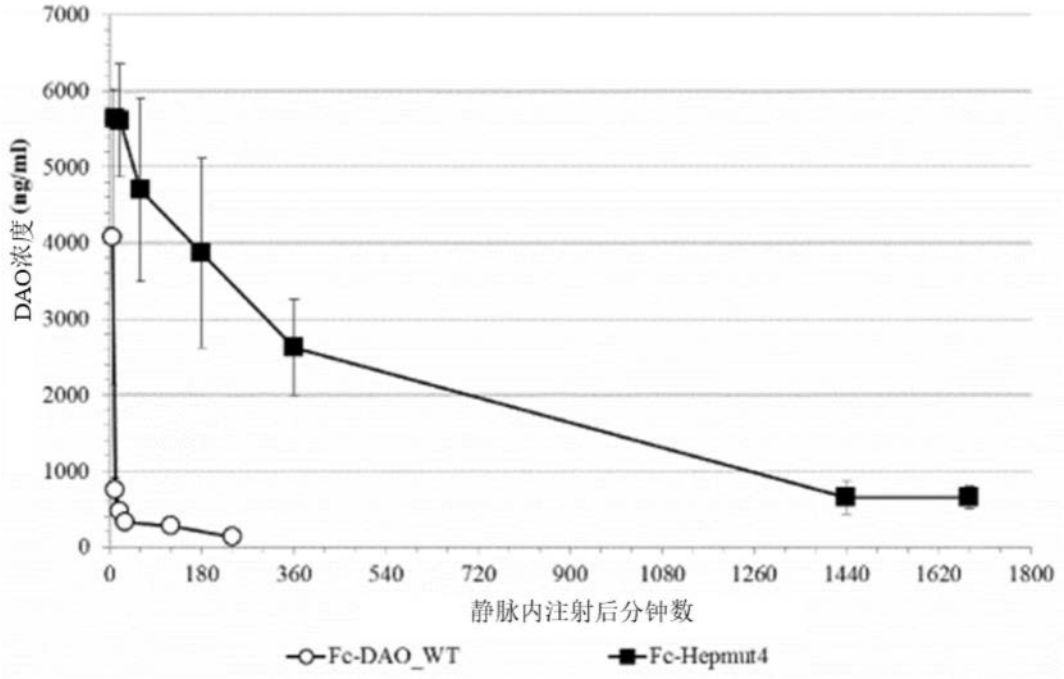

7000
6000
5000
4000
3000
2000
1000
0
DAO浓度 (ng/ml)
0
180
360
540
720
900
1080
1260
1440
1620
1800
静脉内注射后分钟数
Fc-DAO_WT
Fc-Hepmut4

图15

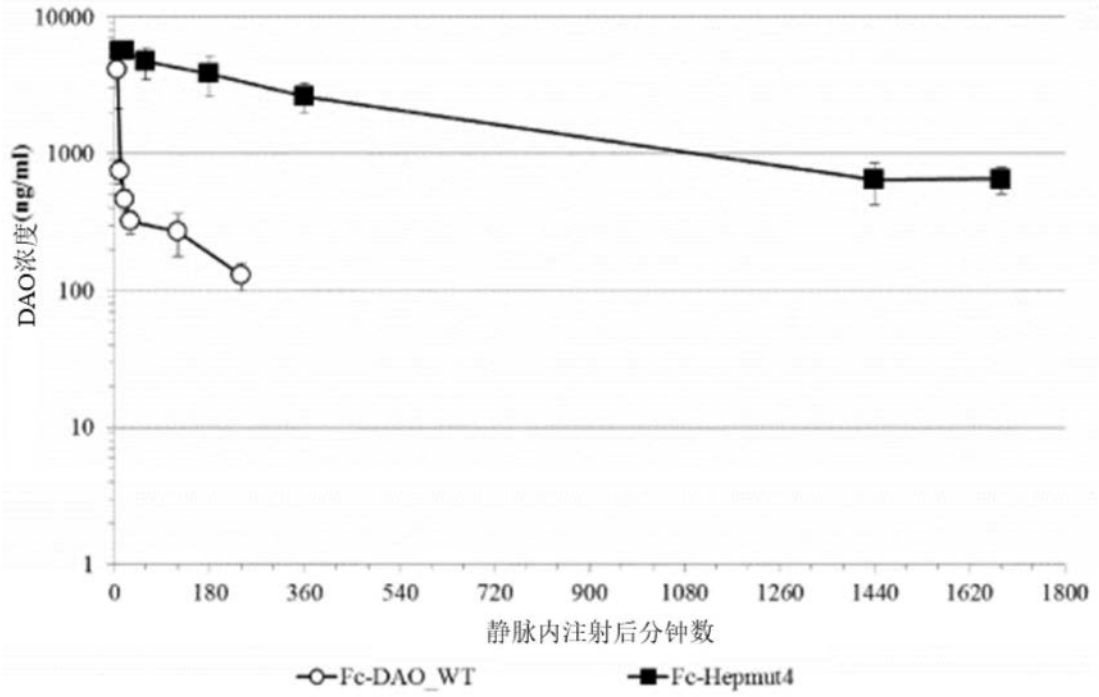

10000
1000
100
10
1
DAO浓度(ng/ml)
0
180
360
540
720
900
1080
1260
1440
1620
1800
静脉内注射后分钟数
Fc-DAO_WT
Fc-Hepmut4

图16

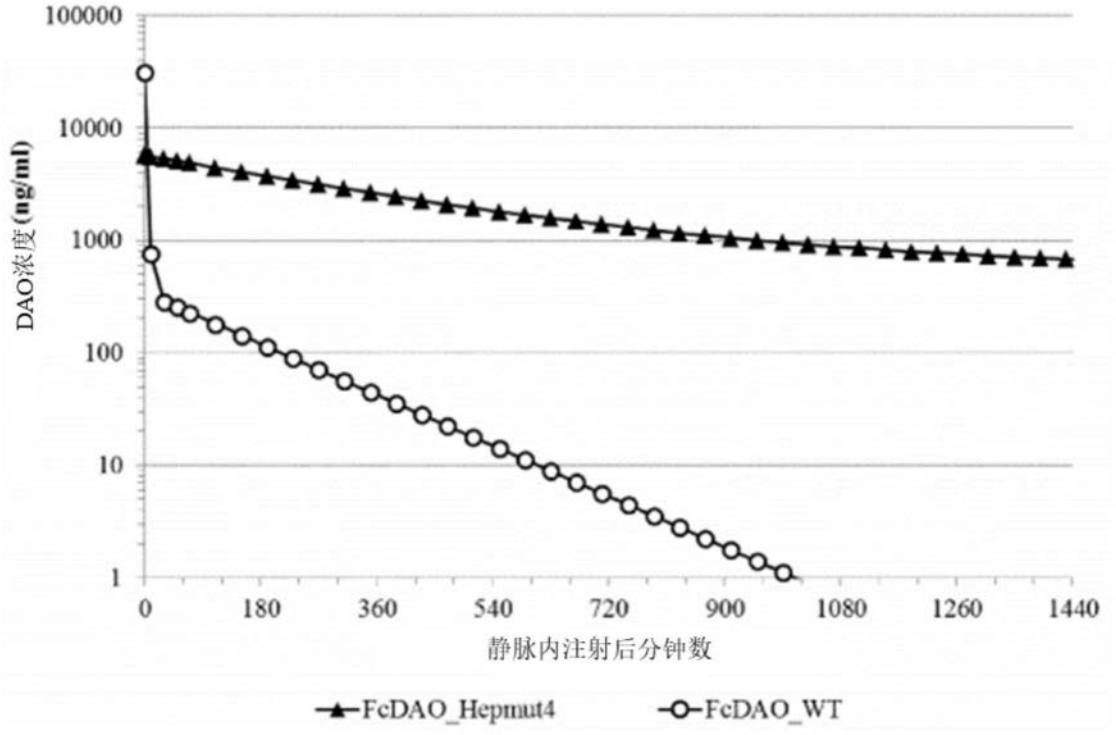

100000
10000
1000
100
10
1
DAO浓度 (ng/ml)
0
180
360
540
720
900
1080
1260
1440
静脉内注射后分钟数
FcDAO_Hepmut4
FcDAO_WT

图17

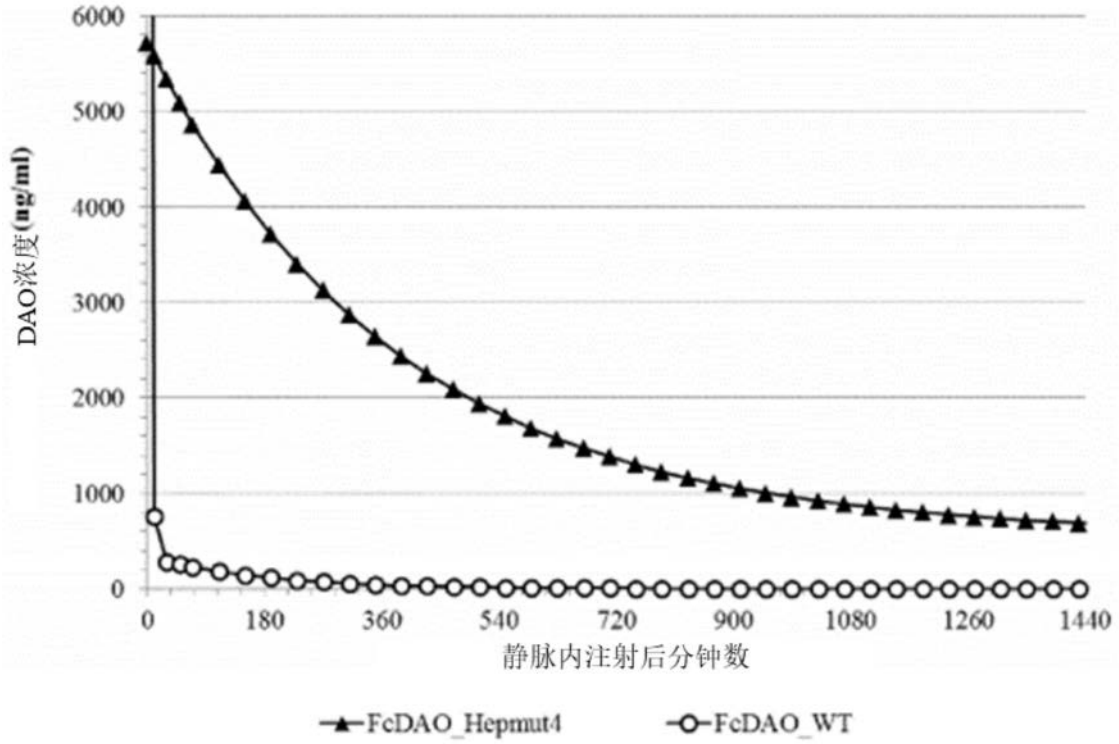

6000
5000
4000
3000
2000
1000
0
DAO浓度(ng/ml)
0
180
360
540
720
900
1080
1260
1440
静脉内注射后分钟数
FcDAO_Hepmut4
FcDAO_WT

图18

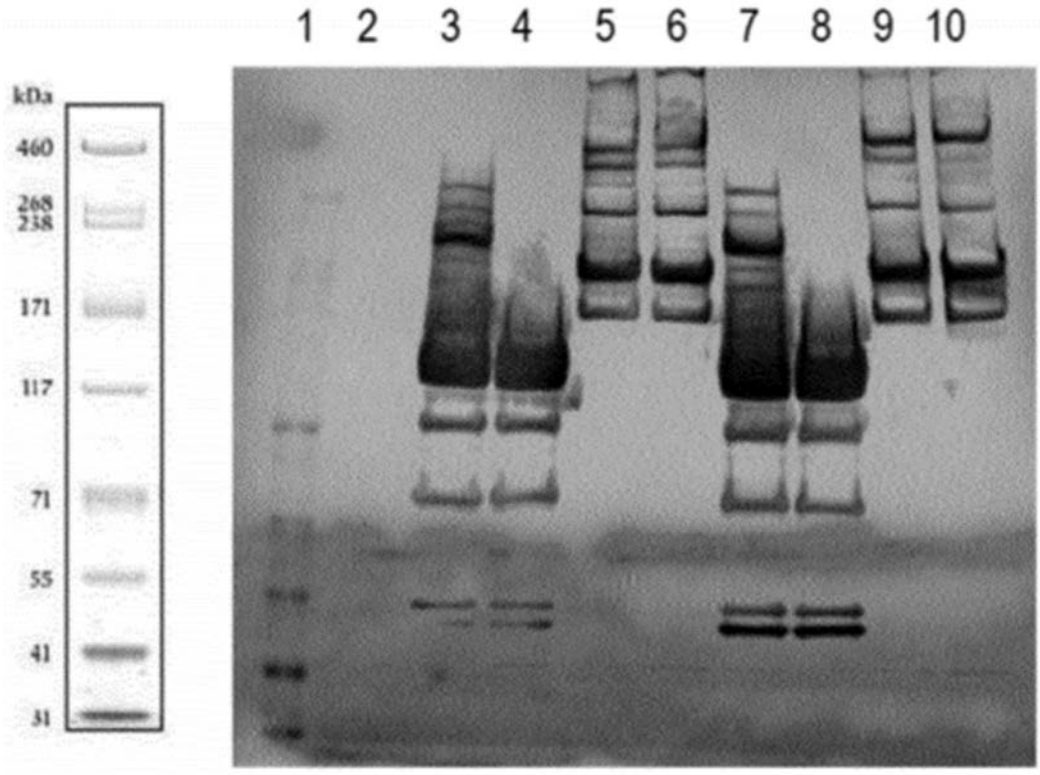

1 2 3 4 5 6 7 8 9 10
kDa
460
268
238
171
117
71
55
41
31

图19

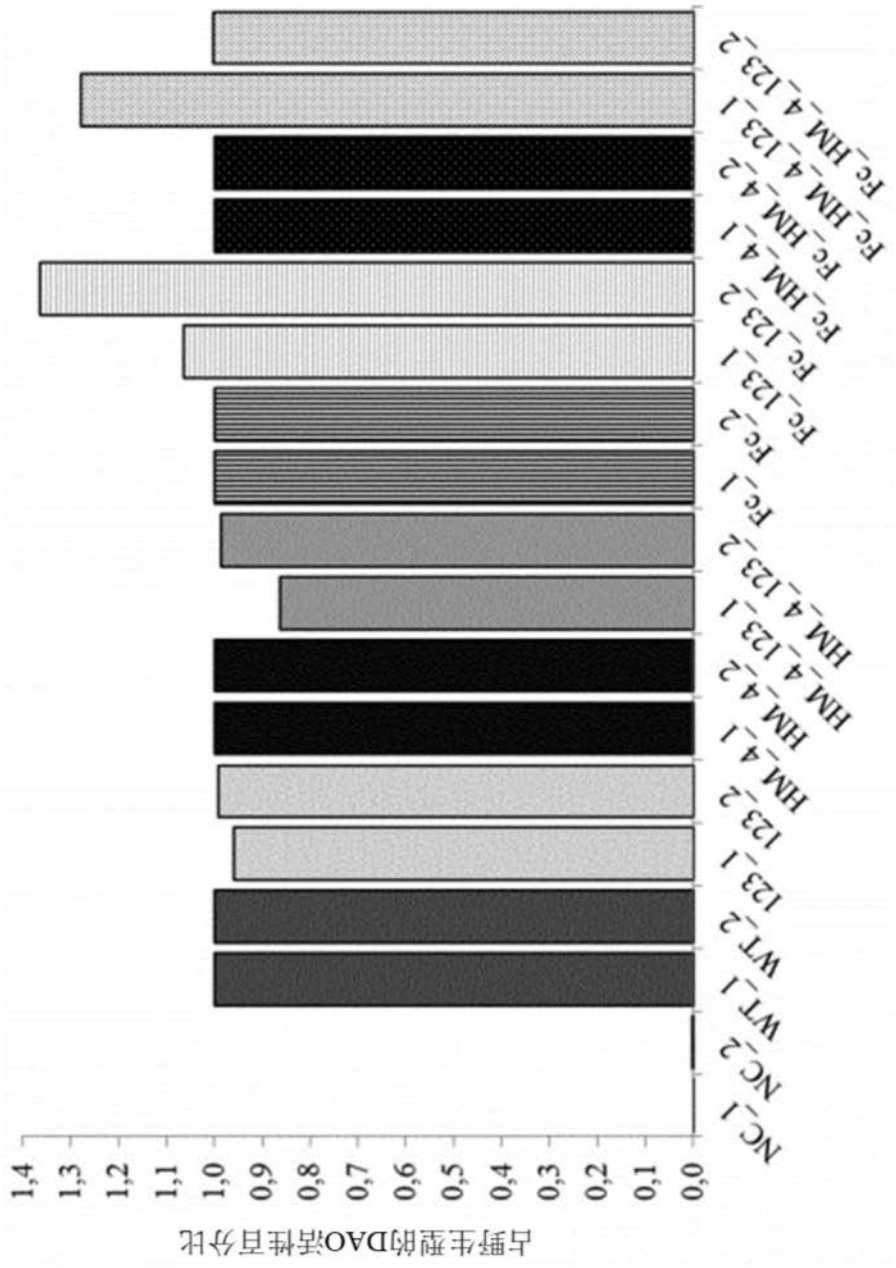

NC_1
NC_2
WT_1
WT_2
123_1
123_2
HM_4_1
HM_4_2
HM_4_123_1
HM_4_123_2
Fc_1
Fc_2
Fc_123_1
Fc_123_2
Fc_HM_4_1
Fc_HM_4_2
Fc_HM_4_123_1
Fc_HM_4_123_2
1,4
1,3
1,2
1,1
1,0
0,9
0,8
0,7
0,6
0,5
0,4
0,3
0,2
0,1
0,0
占野生型的DAO活性百分比

图20