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(54) 发明名称

用于基因组编辑的多核苷酸、组合物及方法

(57) 摘要

本发明提供用于基因编辑的组合物及方法。在一些实施例中,提供一种编码Cas9的多核苷酸,其可提供改良的编辑效率、降低的免疫原性或其它益处中的一种或多种。

1. 一种mRNA,其包含的开放阅读框架区为SEQ ID NO:111,113-119,146和148-154中的任一项所示的序列,其中所述开放阅读框架编码RNA引导的DNA结合剂。

2. 如权利要求1所述的mRNA,其中所述mRNA包含SEQ ID NO:32、34、36、38、41或75至77中的任一项的序列的5'UTR。

3. 如权利要求1所述的mRNA,其中所述mRNA包含SEQ ID NO:33、35、37、39或40中的任一项的序列的3'UTR。

4. 如权利要求1所述的mRNA,其中所述mRNA包含SEQ ID NO:32、34、36、38、41或75至77中的任一项的序列的5'UTR,和SEQ ID NO:33、35、37、39或40中的任一项的序列的3'UTR。

5. 如权利要求4所述的mRNA,其中所述mRNA包含来自同一来源的5'UTR及3'UTR。

6. 如权利要求1-4中任一项所述的mRNA,其包含选自Cap0、Cap1及Cap2的5'帽结构。

7. 如权利要求1-4中任一项所述的mRNA,其中所述RNA引导的DNA结合剂是Cas9裂解酶。

8. 如权利要求1-4中任一项所述的mRNA,其中所述mRNA包含的ORF区为SEQ ID NO:111的序列。

9. 如权利要求1-4中任一项所述的mRNA,其中所述RNA引导的DNA结合剂是Cas9切口酶。

10. 如权利要求1-4中任一项所述的mRNA,其中所述mRNA包含的ORF区为SEQ ID NO:114的序列。

11. 如权利要求1至4中任一项所述的mRNA,其中所述RNA引导的DNA结合剂包含dCas9 DNA结合域。

12. 如权利要求1-4中任一项所述的mRNA,其中所述mRNA包含的ORF区为SEQ ID NO:117的序列。

13. 如权利要求1-4中任一项所述的mRNA,其中所述mRNA包含编码SEQ ID NO:3、6、8或186-196中任一项所示的氨基酸序列的核酸序列。

14. 如权利要求1-4中任一项所述的mRNA,其中所述RNA引导的DNA结合剂进一步包含异源功能域。

15. 如权利要求14所述的mRNA,其中所述异源功能域为FokI核酸酶。

16. 如权利要求14所述的mRNA,其中所述异源功能域为转录调节域。

17. 如权利要求1-4中任一项所述的mRNA,其中至少10%的尿苷被经修饰的尿苷取代。

18. 如权利要求17所述的mRNA,其中所述经修饰的尿苷为N1-甲基-假尿苷、假尿苷、5-甲氧基尿苷或5-碘尿苷中的一种或多种。

19. 如权利要求17所述的mRNA,其中所述经修饰的尿苷为N1-甲基-假尿苷或5-甲氧基尿苷中的一种或两种。

20. 如权利要求17所述的mRNA,其中所述经修饰的尿苷为N1-甲基-假尿苷。

21. 如权利要求17所述的mRNA,其中所述经修饰的尿苷为5-甲氧基尿苷。

22. 如权利要求17所述的mRNA,其中15%至45%的所述尿苷被经修饰的尿苷取代。

23. 如权利要求17所述的mRNA,其中至少20%或至少30%的所述尿苷被经修饰的尿苷取代。

24. 如权利要求23所述的mRNA,其中至少80%或至少90%的所述尿苷被经修饰的尿苷取代。

25. 如权利要求24所述的mRNA,其中100%的尿苷被经修饰的尿苷取代。

26. 如权利要求1-4中任一项所述的mRNA,其中所述mRNA为SEQ ID NO:177所示的序列。
27. 一种表达构建体,其包含以可操作方式连接编码如权利要求1-26中任一项所述的mRNA的序列的启动子。
28. 一种质粒,其包含如权利要求27所述的表达构建体。
29. 一种宿主细胞,其包含如权利要求27所述的表达构建体或如权利要求28所述的质粒。
30. 一种制备mRNA的方法,该方法包含使如权利要求27所述的表达构建体或如权利要求28所述的质粒与RNA聚合酶在容许进行所述mRNA的转录的条件下接触,其中在体外进行所述接触步骤。
31. 一种组合物,其包含如权利要求1至26中任一项所述的mRNA及至少一种引导RNA。
32. 一种脂质纳米颗粒,其包含如权利要求1至26中任一项所述的mRNA。
33. 一种医药组合物,其包含如权利要求1至26中任一项所述的mRNA及医药学上可接受的载体。
34. 如权利要求32所述的脂质纳米颗粒或如权利要求33所述的医药组合物,其进一步包含至少一种引导RNA。
35. 如权利要求31-34中任一项所述的组合物或脂质纳米颗粒或医药组合物,其中至少一种引导RNA靶向TTR。
36. 一种如权利要求1至27或31至35中任一项所述的mRNA、表达构建体、组合物、脂质纳米颗粒或医药组合物的用途,其用于制造用于基因组编辑或修饰靶基因的药剂。
37. 如权利要求36所述的用途,其中所述靶基因的基因组编辑或修饰是在肝脏细胞中进行。
38. 如权利要求37所述的用途,其中所述肝脏细胞为肝细胞。
39. 如权利要求36至38中任一项所述的用途,其中所述靶基因的基因组编辑或修饰是在体内进行。
40. 如权利要求36至38中任一项所述的用途,其中所述靶基因的基因组编辑或修饰是在经分离或培养的细胞中进行。

用于基因组编辑的多核苷酸、组合物及方法

[0001] 本申请要求基于2017年9月29日提出的美国临时申请第62/556,144号的优先权,且其全部内容以引用方式并入。

[0002] 本申请含有以ASCII格式电子提交的序列列表且其全部内容以引用方式并入本文中。于2018年9月28日创建的该ASCII拷贝命名为2018-09-28_01155-0020-00PCT_ST25.txt且大小为963,200个字节。

技术领域

[0003] 本发明是关于用于基因组编辑的多核苷酸、组合物及方法,该基因组编辑涉及RNA引导的DNA结合剂,诸如CRISPR-Cas系统及其亚基。

背景技术

[0004] RNA引导的DNA结合剂,诸如CRISPR-Cas系统可用于进行靶基因组编辑,包括在真核细胞中及活体内。已显示此类编辑能够不活化某些有害等位基因或校正某些有害点突变。该结合剂可通过提供编码的mRNA来原位表达。然而,现有方法提供的编辑效率可能要比所需编辑效率低或可能具有非所期望的免疫原性,例如可能会引起细胞介素含量的升高为非所期望的。

[0005] 因此,需要经改良的用于基因组编辑的多核苷酸、组合物及方法。本发明旨在提供用于基因组编辑的组合物及方法,其提供一或多种益处,诸如经改良的编辑效率或经降低的免疫原性(例如施用后经降低的细胞介素的升高量)中的至少一者;或至少为公众提供一种有用选择。在一些实施例中,提供一种编码RNA引导的DNA结合剂的多核苷酸,其中其密码子使用、非编码序列(例如UTR)、异源域(例如NLS)及/或核苷酸含量中的一项或多项以本文所揭示的方式与现有多核苷酸不同。已发现此类特征可提供诸如上文所述的益处。在一些实施例中,经改良的编辑效率出现在哺乳动物的器官或细胞型,诸如肝脏或肝细胞中或对其具有特异性。

[0006] 发明详述

[0007] 实施例1为一种包含编码RNA引导的DNA结合剂的开放阅读框架的mRNA,其中该开放阅读框架的尿苷含量在其最小尿苷含量至最小尿苷含量的150%范围内。

[0008] 实施例2为一种包含编码RNA引导的DNA结合剂的开放阅读框架的mRNA,其中该开放阅读框架的尿苷二核苷酸含量在其最小尿苷二核苷酸含量至最小尿苷二核苷酸含量的150%范围内。

[0009] 实施例3为一种包含编码RNA引导的DNA结合剂的开放阅读框架的mRNA,其中该开放阅读框架的腺嘌呤含量在其最小腺嘌呤含量至最小腺嘌呤含量的150%范围内。

[0010] 实施例4为一种包含编码RNA引导的DNA结合剂的开放阅读框架的mRNA,其中该开放阅读框架的腺嘌呤二核苷酸含量在其最小腺嘌呤二核苷酸含量至最小腺嘌呤二核苷酸含量的150%范围内。

[0011] 实施例5为一种包含与SEQ ID NO:1、4、7、9、10、11、12、14、15、17、18、20、21、23、

24、26、27、29、30、50、52、54、65、66、或107-175任一项具有至少90%的一致性的序列的mRNA,其中该mRNA包含编码RNA引导的DNA结合剂的开放阅读框架。

[0012] 实施例6为一种包含编码RNA引导的DNA结合剂的开放阅读框架的mRNA,其中该开放阅读框架与SEQ ID NO:1、4、7、9、10、11、12、14、15、17、18、20、21、23、24、26、27、29、30、50、52、54、65、66、或107-175以下任一项在至少其前30、50、70、100、150、200、250或300个核苷酸上具有至少90%的一致性。

[0013] 实施例7为如前述技术方案中任一项的mRNA,其中开放阅读框架由一组密码子组成,其中至少75%的密码子为(i)表1、表2或表3中所列的密码子或(ii)一组表4中所列的密码子。

[0014] 实施例8为一种编码RNA引导的DNA结合剂的mRNA,其包含编码RNA引导的DNA结合剂的开放阅读框架,其中开放阅读框架由一组密码子组成,其中至少75%的密码子为表1、表2、表3中所列的密码子或(ii)一组表4中所列的密码子。

[0015] 实施例9为如技术方案7或8的mRNA,其中开放阅读框架由一组密码子组成,其中至少75%的密码子为表4中低U1组的密码子。

[0016] 实施例10为如技术方案7或8的mRNA,其中开放阅读框架由一组密码子组成,其中至少75%的密码子为表4中低A组的密码子。

[0017] 实施例11为如技术方案7或8的mRNA,其中开放阅读框架由一组密码子组成,其中至少75%的密码子为表4中低A/U组的密码子。

[0018] 实施例12为如技术方案7或8的mRNA,其中开放阅读框架由一组密码子组成,其中至少75%的密码子为表4中长半衰期组的密码子。

[0019] 实施例13为如技术方案7至12中任一项的mRNA,其中至少80%、85%、90%、95%、98%、99%或100%的密码子为(i)表1、表2或表3中所列的密码子或(ii)一组表4中所列的密码子。

[0020] 实施例14为如技术方案1至5或7至13中任一项的mRNA,其中开放阅读框架与SEQ ID NO:1、4、7、9、10、11、12、14、15、17、18、20、21、23、24、26、27、29、30、50、52、54、65、66、或107-175任一项在至少其前30、50、70、100、150、200、250或300个核苷酸上具有至少90%的一致性。

[0021] 实施例15为如前述技术方案中任一项的mRNA,其中开放阅读框架与SEQ ID NO:1、4、7、9、10、11、12、14、15、17、18、20、21、23、24、26、27、29、30、50、52、54、65、66、或107-175任一项在至少其序列之前10%、12%、15%、20%、25%、30%或35%上具有至少90%的一致性。

[0022] 实施例16为如技术方案1至4或6至15中任一项的mRNA,其中该mRNA包含与SEQ ID NO:1、4、7、9、10、11、12、14、15、17、18、20、21、23、24、26、27、29、30、50、52、54、65、66、或107-175任一项有至少90%的一致性的序列。

[0023] 实施例17为如前述技术方案中任一项的mRNA,其中开放阅读框架的尿苷二核苷酸含量在其最小尿苷二核苷酸含量至最小尿苷二核苷酸含量的101%、102%、103%、105%、110%、115%、120%、125%、130%、135%、140%、145%或150%范围内。

[0024] 实施例18为如前述技术方案中任一项的mRNA,其中开放阅读框架的尿苷含量在其最小尿苷含量至最小尿苷含量的101%、102%、103%、105%、110%、115%、120%、125%、

130%、135%、140%、145%或150%范围内。

[0025] 实施例19为如前述技术方案中任一项的mRNA,其中开放阅读框架的腺嘌呤含量在其最小腺嘌呤含量至最小腺嘌呤含量的101%、102%、103%、105%、110%、115%、120%、125%、130%、135%、140%、145%或150%范围内。

[0026] 实施例20为如前述技术方案中任一项的mRNA,其中开放阅读框架的腺嘌呤二核苷酸含量在其最小腺嘌呤二核苷酸含量至最小腺嘌呤二核苷酸含量的101%、102%、103%、105%、110%、115%、120%、125%、130%、135%、140%、145%或150%范围内。

[0027] 实施例21为如前述技术方案中任一项的mRNA,其包含与SEQ ID NO:32、34、36、38、41或75—77中的任一项有至少90%的一致性的5'UTR。

[0028] 实施例22为如前述技术方案中任一项的mRNA,其包含与SEQ ID NO:33、35、37、39或40中的任一项有至少90%的一致性的3'UTR。

[0029] 实施例23为如技术方案21或22的mRNA,其中mRNA包含来自同一起来源的5'UTR及3'UTR。

[0030] 实施例24为如前述技术方案中任一项的mRNA,其包含选自Cap0、Cap1及Cap2的5'帽结构。

[0031] 实施例25为如前述技术方案中任一项的mRNA,其中开放阅读框架具有提高哺乳动物中的mRNA转译的密码子。

[0032] 实施例26为如技术方案25的mRNA,其中开放阅读框架具有提高哺乳动物的特定器官中的mRNA转译的密码子。

[0033] 实施例27为如技术方案26的mRNA,其中器官为肝脏。

[0034] 实施例28为如技术方案25至27中任一项的mRNA,其中哺乳动物为人类。

[0035] 实施例29为如技术方案25至28中任一项的mRNA,其中相对于包含具有由SEQ ID NO:5组成的序列的ORF的mRNA的转译,密码子提高哺乳动物中的mRNA的转译。

[0036] 实施例30为如前述技术方案中任一项的mRNA,其中当以医药组合物形式向哺乳动物施用该mRNA时,哺乳动物展现出比施用包含具有大于150%最小尿苷含量的编码Cas9核酸酶的ORF的mRNA的哺乳动物低至少5倍的细胞介素反应。

[0037] 实施例31为如技术方案30的mRNA,其中包含具有大于150%最小尿苷含量的编码Cas9核酸酶的ORF的mRNA具有由SEQ ID NO:5组成的序列。

[0038] 实施例32为如前述技术方案中任一项的mRNA,其中RNA引导的DNA结合剂具有双股核酸内切酶活性。

[0039] 实施例33为如技术方案32的mRNA,其中RNA引导的DNA结合剂包含Cas裂解酶。

[0040] 实施例34为如前述技术方案中任一项的mRNA,其中RNA引导的DNA结合剂具有切口酶活性。

[0041] 实施例35为如技术方案34的mRNA,其中RNA引导的DNA结合剂包含Cas切口酶。

[0042] 实施例36为如技术方案1至31中任一项的mRNA,其中RNA引导的DNA结合剂包含dCas DNA结合域。

[0043] 实施例37为如技术方案33或35至36中任一项的mRNA,其中Cas裂解酶、Cas切口酶或dCas DNA结合域为Cas9裂解酶、Cas9切口酶、或dCas9 DNA结合域。

[0044] 实施例38为如前述技术方案中任一项的mRNA,其中经编码的RNA引导的DNA结合剂

包含核定位信号(NLS)。

[0045] 实施例39为如技术方案38的mRNA,其中NLS连接于RNA引导的DNA结合剂的C端。

[0046] 实施例40为如技术方案38的mRNA,其中NLS连接于RNA引导的DNA结合剂的N端。

[0047] 实施例41为如技术方案38至40中任一项的mRNA,其中NLS包含与SEQ ID NO:78-91中的任一项具有至少80%、85%、90%或95%的一致性的序列。

[0048] 实施例42为如技术方案38至40中任一项的mRNA,其中NLS包含SEQ ID NO:78—91中的任一项的序列。

[0049] 实施例43为如技术方案38至42中任一项的mRNA,其中NLS由与SEQ ID NO:92-104中的任一项的序列具有至少80%、85%、90%、95%、98%或100%的一致性的序列编码。

[0050] 实施例44为如技术方案37至43中任一项的mRNA,其中该mRNA包含与SEQ ID NO:4、7或9有至少90%的一致性的序列。

[0051] 实施例45为如技术方案37至43中任一项的mRNA,其中该mRNA包含与SEQ ID NO:4、7或9有至少95%的一致性的序列。

[0052] 实施例46为如技术方案37至43中任一项的mRNA,其中该mRNA包含与SEQ ID NO:4、7或9有至少98%的一致性的序列。

[0053] 实施例47为如技术方案37至43中任一项的mRNA,其中该mRNA包含与SEQ ID NO:4、7或9有100%一致性的序列。

[0054] 实施例48为如技术方案37至43中任一项的mRNA,其中该mRNA包含与SEQ ID NO:111、114或117有至少90%的一致性的序列。

[0055] 实施例49为如技术方案37至43中任一项的mRNA,其中该mRNA包含与SEQ ID NO:111、114或117有至少95%的一致性的序列。

[0056] 实施例50为如技术方案37至43中任一项的mRNA,其中该mRNA包含与SEQ ID NO:111、114或117有至少98%的一致性的序列。

[0057] 实施例51为如技术方案37至43中任一项的mRNA,其中该mRNA包含与SEQ ID NO:112、122或125有100%一致性的序列。

[0058] 实施例52为如技术方案37至43中任一项的mRNA,其中该mRNA包含与SEQ ID NO:112、122或125有至少90%的一致性的序列。

[0059] 实施例53为如技术方案37至43中任一项的mRNA,其中该mRNA包含与SEQ ID NO:112、122或125有至少95%的一致性的序列。

[0060] 实施例54为如技术方案37至43中任一项的mRNA,其中该mRNA包含与SEQ ID NO:10、11、12、14、15、17、18、20、21、23、24、26、27、29、30、50、52、54、65、66、或107—175有至少90%的一致性的序列。

[0061] 实施例55为如技术方案37至43中任一项的mRNA,其中该mRNA包含与SEQ ID NO:10、11、12、14、15、17、18、20、21、23、24、26、27、29、30、50、52、54、65、66、或107-175有至少95%的一致性的序列。

[0062] 实施例56为如技术方案37至43中任一项的mRNA,其中该mRNA包含与SEQ ID NO:10、11、12、14、15、17、18、20、21、23、24、26、27、29、30、50、52、54、65、66、或107-175有至少98%的一致性的序列。

[0063] 实施例57为如技术方案37至43中任一项的mRNA,其中该mRNA包含与SEQ ID NO:

10、11、12、14、15、17、18、20、21、23、24、26、27、29、30、50、52、54、65、66、或107-175有100%一致性的序列。

[0064] 实施例58为如技术方案37至57中任一项的mRNA,其中该mRNA编码包含SEQ ID NO: 3、6、8或186-196的氨基酸序列的多肽。

[0065] 实施例59为如前述技术方案中任一项的mRNA,其中RNA引导的DNA结合剂进一步包含异源功能域。

[0066] 实施例60为如技术方案59的mRNA,其中异源功能域为FokI核酸酶。

[0067] 实施例61为如技术方案59的mRNA,其中异源功能域为转录调节域。

[0068] 实施例62为如前述技术方案中任一项的mRNA,其中当以包含脂质纳米颗粒的医药组合物形式向哺乳动物施用有效量的mRNA以及靶向哺乳动物的TTR基因的引导RNA时,在得自哺乳动物肝细胞的至少50%基因组DNA中的TTR基因座处形成插入缺失标记(indel)。

[0069] 实施例63为如前述技术方案中任一项的mRNA,其中当以包含脂质纳米颗粒的医药组合物形式向哺乳动物施用有效量的mRNA以及靶向哺乳动物的TTR基因的引导RNA时,哺乳动物的血清中的TTR的浓度降低至少50%。

[0070] 实施例64为如前述技术方案中任一项的mRNA,其中至少10%的尿苷被经修饰的尿苷取代。

[0071] 实施例65为如技术方案64的mRNA,其中经修饰的尿苷为N1-甲基-假尿苷、假尿苷、5-甲氧基尿苷或5-碘尿苷中的一种或多种。

[0072] 实施例66为如技术方案64的mRNA,其中经修饰的尿苷为N1-甲基-假尿苷或5-甲氧基尿苷中的一种或两种。

[0073] 实施例67为如技术方案64的mRNA,其中经修饰的尿苷为N1-甲基-假尿苷。

[0074] 实施例68为如技术方案64的mRNA,其中经修饰的尿苷为5-甲氧基尿苷。

[0075] 实施例69为如技术方案64至68中任一项的mRNA,其中15%至45%的尿苷被经修饰的尿苷取代。

[0076] 实施例70为如技术方案64至68中任一项的mRNA,其中至少20%或至少30%的尿苷被经修饰的尿苷取代。

[0077] 实施例71为如技术方案70的mRNA,其中至少80%或至少90%的尿苷被经修饰的尿苷取代。

[0078] 实施例72为如技术方案70的mRNA,其中100%的尿苷被经修饰的尿苷取代。

[0079] 实施例73为如技术方案64至72中任一项的mRNA,其中当以包含脂质纳米颗粒的医药组合物形式向哺乳动物施用有效量的mRNA以及靶向哺乳动物的TTR基因的引导RNA时,在得自哺乳动物肝细胞的至少70%或至少90%基因组DNA中的TTR基因座处形成插入缺失标记(indel)。

[0080] 实施例74为如技术方案64至73中任一项的mRNA,其中当以包含脂质纳米颗粒的医药组合物形式向哺乳动物施用mRNA以及靶向哺乳动物的TTR基因的引导RNA时,哺乳动物的血清中的TTR的浓度降低至少70%或至少90%。

[0081] 实施例75为如技术方案62、63、71或72的mRNA,其中动物为小鼠且引导RNA具有由SEQ ID NO:42组成的序列。

[0082] 实施例76为如技术方案62、63、71或72的mRNA,其中动物为大鼠且引导RNA具有由

SEQ ID NO:69组成的序列。

[0083] 实施例77为如前述技术方案中任一项的mRNA,其中该mRNA包含与SEQ ID NO:43、44、51、53、55-61或176-185中的任一项有至少90%的一致性的序列。

[0084] 实施例78为如前述技术方案中任一项的mRNA,其中该mRNA包含与SEQ ID NO:43、44、51、53、55-61或176-185中的任一项有至少95%的一致性的序列。

[0085] 实施例79为如前述技术方案中任一项的mRNA,其中该mRNA包含与SEQ ID NO:43、44、51、53、55-61或176-185中的任一项有至少98%的一致性的序列。

[0086] 实施例80为如前述技术方案中任一项的mRNA,其中该mRNA包含与SEQ ID NO:43、44、51、53、55-61或176-185中的任一项有至少99%的一致性的序列。

[0087] 实施例81为如前述技术方案中任一项的mRNA,其中该mRNA包含与SEQ ID NO:43、44、51、53、55-61或176-185中的任一项有100%一致性的序列。

[0088] 实施例82为一种表达构建体,其包含以可操作方式连接编码如前述技术方案中任一项的mRNA的序列的启动子。

[0089] 实施例83为一种包含如技术方案82的表达构建体的质粒。

[0090] 实施例84为一种包含如技术方案82的表达构建体或如技术方案83的质粒的宿主细胞。

[0091] 实施例85为一种制备mRNA的方法,该方法包含使如技术方案82的表达构建体或如技术方案83的质粒与核糖核酸聚合酶在容许进行mRNA的转录的条件下接触。

[0092] 实施例86为如技术方案85的方法,其中活体外进行接触步骤。

[0093] 实施例87为一种组合物,其包含如技术方案1至81中任一项的mRNA及至少一种引导RNA。

[0094] 实施例88为一种脂质纳米颗粒,其包含如技术方案1至81中任一项的mRNA。

[0095] 实施例89为一种医药组合物,其包含如技术方案1至81中任一项的mRNA及医药学上可接受的载体。

[0096] 实施例90为如技术方案88的脂质纳米颗粒或如技术方案89的医药组合物,其进一步包含至少一种引导RNA。

[0097] 实施例91为如技术方案87至90中任一项的组合物或脂质纳米颗粒,其中至少一种引导RNA靶向TTR。

[0098] 实施例92为一种基因组编辑或修饰靶基因的方法,其包含使细胞与如技术方案1至83或87至91中任一项的mRNA、表达构建体、组合物或脂质纳米颗粒接触。

[0099] 实施例93为如技术方案1至83或87至91中任一项的mRNA、表达构建体、组合物或脂质纳米颗粒的用途,其用于基因组编辑或修饰靶基因。

[0100] 实施例94为如技术方案1至83或87至91中任一项的mRNA、表达构建体、组合物或脂质纳米颗粒的用途,其用于制造用于基因组编辑或修饰靶基因的药剂。

[0101] 实施例95为如技术方案92至94中任一项的方法或用途,其中基因组编辑或修饰靶基因在肝脏细胞中进行。

[0102] 实施例96为如技术方案95的方法或用途,其中肝脏细胞为肝细胞。

[0103] 实施例97为如技术方案92至96中任一项的方法或用途,其中基因组编辑或修饰靶基因在活体内进行。

[0104] 实施例98为如技术方案92至97中任一项的方法或用途,其中基因组编辑或修饰靶基因在经分离或经培养的细胞中进行。

[0105] 所揭示的序列的简要说明

[0106]

SEQ ID NO	描述
1	使用表3中所列的最小尿苷密码子的胸苷类似物的Cas9的DNA编码序列, 其具有起始和终止密码子
2	使用通常在人类中高度表达的密码子的Cas9的DNA编码序列
3	具有一个核定位信号(1×NLS)作为C端7个氨基酸的Cas9的氨基酸序列
4	使用如表3中所列的最小尿苷密码子的Cas9 mRNA ORF, 其具有具有起始和终止密码子
5	使用通常在人类中高度表达的密码子的Cas9 mRNA ORF, 其具有具有起始和终止密码子
6	具有1×NLS作为C端7个氨基酸的Cas9切口酶的氨基酸序列
7	使用如表3中所列的最小尿苷密码子编码SEQ ID NO: 6的, 具有起始和终止密码子的Cas9切口酶mRNA ORF
8	具有1×NLS作为C端7个氨基酸的dCas9的氨基酸序列
9	使用如表3中所列的最小尿苷密码子编码SEQ ID NO: 8的, 具有起始和终止密码子的dCas9 mRNA ORF
10	使用如表3中所列的最小尿苷密码子的Cas9 mRNA编码序列(无起始或终止密码子; 适于包括在融合蛋白质编码序列中)
11	使用如表3中所列的最小尿苷密码子的Cas9切口酶mRNA编码序列(无起始或终止密码子; 适于包括在融合蛋白质编码序列中)
12	使用如表3中所列的最小尿苷密码子的dCas9 mRNA编码序列(无起始或终止密码子; 适于包括在融合蛋白质编码序列中)
13	Cas9 (无NLS)的氨基酸序列
14	使用如表3中所列的最小尿苷密码子编码SEQ ID NO: 13的, 具有起始和终止密码子的Cas9 mRNA ORF
15	使用如表3中所列的最小尿苷密码子编码SEQ ID NO: 13的Cas9编码序列(无起始或终止密码子; 适于包括在融合蛋白质编码序列中)

[0107]

16	Cas9切口酶(无NLS)的氨基酸序列
17	使用如表3中所列的最小尿苷密码子编码SEQ ID NO: 16的, 具有起始和终止密码子的Cas9切口酶mRNA ORF
18	使用如表3中所列的最小尿苷密码子编码SEQ ID NO: 16的Cas9切口酶编码序列(无起始或终止密码子; 适于包括在融合蛋白质编码序列中)
19	dCas9 (无NLS)的氨基酸序列
20	使用如表3中所列的最小尿苷密码子编码SEQ ID NO: 13的, 具有起始和终止密码子的dCas9 mRNA ORF
21	使用如表3中所列的最小尿苷密码子编码SEQ ID NO: 13的dCas9编码序列(无起始或终止密码子; 适于包括在融合蛋白质编码序列中)
22	具有两个核定位信号(2×NLS)作为C端氨基酸的Cas9的氨基酸序列
23	使用如表3中所列的最小尿苷密码子编码SEQ ID NO: 13的, 具有起始和终止密码子的Cas9 mRNA ORF
24	使用如表3中所列的最小尿苷密码子编码SEQ ID NO: 13的Cas9编码序列(无起始或终止密码子; 适于包括在融合蛋白质编码序列中)
25	具有两个核定位信号作为C端氨基酸的Cas9切口酶的氨基酸序列
26	使用如表3中所列的最小尿苷密码子编码SEQ ID NO: 16的, 具有起始和终止密码子的Cas9切口酶mRNA ORF
27	使用如表3中所列的最小尿苷密码子编码SEQ ID NO: 16的Cas9切口酶编码序列(无起始或终止密码子; 适于包括在融合蛋白质编码序列中)
28	具有两个核定位信号作为C端氨基酸的dCas9的氨基酸序列
29	使用如表3中所列的最小尿苷密码子编码SEQ ID NO: 13的, 具有起始和终止密码子的dCas9 mRNA ORF

[0108]

30	使用如表3中所列的最小尿苷密码子编码SEQ ID NO: 13的dCas9编码序列(无起始或终止密码子;适于包括在融合蛋白质编码序列中)
31	T7启动子
32	人类 β -血球蛋白 5' UTR
33	人类 β -血球蛋白 3' UTR
34	人类 α -血球蛋白5' UTR
35	人类 α -血球蛋白3' UTR
36	有爪蟾 β -血球蛋白5' UTR
37	有爪蟾 β -血球蛋白 3' UTR
38	牛生长激素5' UTR
39	牛生长激素3' UTR
40	小家鼠血红蛋白 α , 成年链1 (Hba-a1), 3' UTR
41	HSD17B4 5' UTR
42	靶向小鼠TTR 基因的G282单一引导RNA
43	具有HSD的5' UTR、对应于SEQ ID NO: 4的ORF、Kozak序列及ALB的3' UTR的Cas9转录物
44	具有HSD的5' UTR、对应于SEQ ID NO: 4的ORF及ALB的3' UTR的Cas9转录物
45	具有19.36% U含量的替代Cas9 ORF
46	具有HSD的5' UTR、对应于SEQ ID NO: 45的ORF、Kozak序列及ALB的3' UTR的Cas9转录物
47	具有HSD的5' UTR、对应于SEQ ID NO: 45的ORF及ALB的3' UTR的Cas9转录物
48	包含使用通常在人类中高度表达的密码子的Cas9 ORF的Cas9转录物
49	包含Kozak序列以及使用通常在人类中高度表达的密码子的Cas9 ORF的Cas9转录物
50	剪接接点经移除; 具有12.75% U含量的Cas9 ORF

[0109]

51	具有HSD的5' UTR、对应于SEQ ID NO: 50的ORF、Kozak序列及ALB的3' UTR的Cas9转录物
52	具有一般经常用于人类中的最小尿苷密码子；具有12.75% U含量的Cas9 ORF
53	具有HSD的5' UTR、对应于SEQ ID NO: 52的ORF、Kozak序列及ALB的3' UTR的Cas9转录物
54	具有一般不经常用于人类中的最小尿苷密码子；具有12.75% U含量的Cas9 ORF
55	具有HSD的5' UTR、对应于SEQ ID NO: 54的ORF、Kozak序列及ALB的3' UTR的Cas9转录物
56	具有AGG作为供与CleanCap™一起使用之前三个核苷酸、HSD的5' UTR、对应于SEQ ID NO: 4的ORF、Kozak序列及ALB的3' UTR的Cas9转录物
57	具有来自CMV的5' UTR、对应于SEQ ID NO: 4的ORF、Kozak序列及ALB的3' UTR的Cas9转录物
58	具有来自HBB的5' UTR、对应于SEQ ID NO: 4的ORF、Kozak序列及HBB的3' UTR的Cas9转录物
59	具有来自XBG的5' UTR、对应于SEQ ID NO: 4的ORF、Kozak序列及XBG的3' UTR的Cas9转录物
60	具有AGG作为供与CleanCap™一起使用之前三个核苷酸、来自XBG的5' UTR、对应于SEQ ID NO: 4的ORF、Kozak序列及XBG的3' UTR的Cas9转录物
61	具有AGG作为供与CleanCap™一起使用之前三个核苷酸、来自HSD的5' UTR、对应于SEQ ID NO: 4的ORF、Kozak序列及ALB的3' UTR的Cas9转录物
62	30/30/39 聚-A序列
63	聚A 100序列
64	靶向小鼠TTR 基因的G209单一引导RNA
65	使用如表3中所列的最小尿苷密码子编码脑膜炎双球菌Cas9的,

[0110]

	具有起始和终止密码子的ORF
66	使用如表3中所列的最小尿苷密码子编码脑膜炎双球菌Cas9的ORF (无起始或终止密码子; 适于包括在融合蛋白质编码序列中)
67	包含SEQ ID NO: 65 (编码脑膜炎双球菌Cas9)的转录物
68	脑膜炎双球菌Cas9的氨基酸序列
69	靶向大鼠TTR 基因的G390单一引导RNA
70	靶向食蟹猕猴TTR 基因的G502单一引导RNA
71	靶向食蟹猕猴TTR 基因的G509单一引导RNA
72	靶向大鼠TTR 基因的G534 单一引导RNA
73	eGFP的DNA编码序列
74	经修饰的 sgRNA模式
75	CMV-1 5' UTR
76	CMV-2 5' UTR
77	CMV-3 5' UTR
78	SV40 NLS
79	示例性NLS 1
80	示例性NLS 2
81	示例性NLS 3
82	示例性NLS 4
83	示例性NLS 5
84	示例性NLS 6
85	示例性NLS 7
86	示例性NLS 8
87	示例性NLS 9
88	示例性NLS 10
89	示例性NLS 11
90	替代SV40 NLS
91	核质蛋白NLS
92	SV40 NLS的示例性编码序列
93	NLS1的示例性编码序列

[0111]

94	NLS2的示例性编码序列
95	NLS3的示例性编码序列
96	NLS4的示例性编码序列
97	NLS5的示例性编码序列
98	NLS6的示例性编码序列
99	NLS7的示例性编码序列
100	NLS8的示例性编码序列
101	NLS9的示例性编码序列
102	NLS10的示例性编码序列
103	NLS11的示例性编码序列
104	替代SV40 NLS的示例性编码序列
105	示例性Kozak序列
107	使用表4的长半衰期密码子, 具有起始及终止密码子的Cas9 ORF
108	使用表4的富含U的密码子, 具有起始及终止密码子的Cas9 ORF
109	使用表4的低G密码子, 具有起始及终止密码子的Cas9 ORF
110	使用表4的低C密码子, 具有起始及终止密码子的Cas9 ORF
111	使用表4的低A密码子, 具有起始及终止密码子的Cas9 ORF
112	使用表4的低A/U密码子, 具有起始及终止密码子的Cas9 ORF
113	使用表4的低A密码子, 具有两个C端NLS序列及起始及终止密码子的Cas9 ORF
114	使用表4的低A密码子, 具有起始及终止密码子的Cas9切口酶ORF
115	使用表4的低A密码子, 具有起始及终止密码子且无NLS的Cas9切口酶ORF
116	使用表4的低A密码子, 具有两个C端NLS序列及起始及终止密码子的Cas9切口酶ORF
117	使用表4的低A密码子, 具有起始及终止密码子的dCas9 ORF
118	使用表4的低A密码子, 具有起始及终止密码子且无NLS的dCas9 ORF

[0112]

119	使用表4的低A密码子, 具有两个C端NLS序列及起始及终止密码子的dCas9 ORF
120	使用表4的低A/U密码子, 具有两个C端NLS序列及起始及终止密码子的Cas9 ORF
121	使用表4的低A/U密码子, 具有起始及终止密码子且无NLS的Cas9 ORF
122	使用表4的低A/U密码子, 具有起始及终止密码子的Cas9切口酶ORF
123	使用表4的低A/U密码子, 具有两个C端NLS序列及起始及终止密码子的Cas9切口酶ORF
124	使用表4的低A/U密码子, 具有起始及终止密码子且无NLS的Cas9切口酶ORF
125	使用表4的低A/U密码子, 具有起始及终止密码子的dCas9 ORF
126	使用表4的低A/U密码子, 具有两个C端NLS序列及起始及终止密码子的dCas9 ORF
127	使用表4的低A/U密码子, 具有起始及终止密码子且无NLS的dCas9 ORF
128	使用表4的低A密码子, 具有起始及终止密码子的Nme Cas9 ORF
129	使用表4的低A/U密码子, 具有起始及终止密码子的Nme Cas9 ORF
130	具有NLS1的Cas9的开放阅读框架, 其具有起始及终止密码子
131	具有NLS2的Cas9的开放阅读框架, 其具有起始及终止密码子
132	具有NLS3的Cas9的开放阅读框架, 其具有起始及终止密码子
133	具有NLS4的Cas9的开放阅读框架, 其具有起始及终止密码子
134	具有NLS5的Cas9的开放阅读框架, 其具有起始及终止密码子
135	具有NLS6的Cas9的开放阅读框架, 其具有起始及终止密码子
136	具有NLS7的Cas9的开放阅读框架, 其具有起始及终止密码子
137	具有NLS8的Cas9的开放阅读框架, 其具有起始及终止密码子
138	具有NLS9的Cas9的开放阅读框架, 其具有起始及终止密码子
139	具有NLS10的Cas9的开放阅读框架, 其具有起始及终止密码子

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140	具有NLS11的Cas9的开放阅读框架, 其具有起始及终止密码子
141	使用通常在人类中高度表达的密码子的Cas9 ORF (无起始或终止密码子; 适于包括在融合蛋白质编码序列中)
142	使用表4的长半衰期密码子的Cas9 ORF (无起始或终止密码子; 适于包括在融合蛋白质编码序列中)
143	使用表4的富含U的密码子的Cas9 ORF (无起始或终止密码子; 适于包括在融合蛋白质编码序列中)
144	使用表4的低G密码子的Cas9 ORF (无起始或终止密码子; 适于包括在融合蛋白质编码序列中)
145	使用表4的低C密码子的Cas9 ORF (无起始或终止密码子; 适于包括在融合蛋白质编码序列中)
146	使用表4的低A密码子的Cas9 ORF (无起始或终止密码子; 适于包括在融合蛋白质编码序列中)
147	使用表4的低A/U密码子的Cas9 ORF (无起始或终止密码子; 适于包括在融合蛋白质编码序列中)
148	使用表4的低A密码子, 具有两个C端NLS序列的Cas9 ORF (无起始或终止密码子; 适于包括在融合蛋白质编码序列中)
149	使用表4的低A密码子的Cas9切口酶ORF (无起始或终止密码子; 适于包括在融合蛋白质编码序列中)
150	使用表4的低A密码子的Cas9切口酶ORF (无NLS且无起始或终止密码子; 适于包括在融合蛋白质编码序列中)
151	使用表4的低A密码子, 具有两个C端NLS序列的Cas9切口酶ORF (无起始或终止密码子; 适于包括在融合蛋白质编码序列中)
152	使用表4的低A密码子的dCas9 ORF (无起始或终止密码子; 适于包括在融合蛋白质编码序列中)
153	使用表4的低A密码子的dCas9 ORF (无NLS且无起始或终止密码子; 适于包括在融合蛋白质编码序列中)
154	使用表4的低A密码子, 具有两个C端NLS序列的dCas9 ORF (无起始或终止密码子; 适于包括在融合蛋白质编码序列中)

[0114]

155	使用表4的低A/U密码子, 具有两个C端NLS序列的Cas9 ORF (无起始或终止密码子; 适于包括在融合蛋白质编码序列中)
156	使用表4的低A/U密码子的Cas9 ORF (无NLS且无起始或终止密码子; 适于包括在融合蛋白质编码序列中)
157	使用表4的低A/U密码子的Cas9切口酶ORF (无起始或终止密码子; 适于包括在融合蛋白质编码序列中)
158	使用表4的低A/U密码子, 具有两个C端NLS序列的Cas9切口酶ORF (无起始或终止密码子; 适于包括在融合蛋白质编码序列中)
159	使用表4的低A/U密码子的Cas9切口酶ORF (无NLS且无起始或终止密码子; 适于包括在融合蛋白质编码序列中)
160	使用表4的低A/U密码子的dCas9 ORF (无起始或终止密码子; 适于包括在融合蛋白质编码序列中)
161	使用表4的低A/U密码子, 具有两个C端NLS序列的dCas9 ORF (无起始或终止密码子; 适于包括在融合蛋白质编码序列中)
162	使用表4的低A/U密码子的dCas9 ORF (无NLS且无起始或终止密码子; 适于包括在融合蛋白质编码序列中)
163	使用表4的低A密码子的Nme Cas9 ORF (无起始或终止密码子; 适于包括在融合蛋白质编码序列中)
164	使用表4的低A/U密码子的Nme Cas9 ORF (无起始或终止密码子; 适于包括在融合蛋白质编码序列中)
165	具有NLS1的Cas9的开放阅读框架(无起始或终止密码子; 适于包括在融合蛋白质编码序列中)
166	具有NLS2的Cas9的开放阅读框架(无起始或终止密码子; 适于包括在融合蛋白质编码序列中)
167	具有NLS3的Cas9的开放阅读框架(无起始或终止密码子; 适于包括在融合蛋白质编码序列中)
168	具有NLS4的Cas9的开放阅读框架(无起始或终止密码子; 适于包括在融合蛋白质编码序列中)
169	具有NLS5的Cas9的开放阅读框架(无起始或终止密码子; 适于包

[0115]

	括在融合蛋白质编码序列中)
170	具有NLS6的Cas9的开放阅读框架(无起始或终止密码子; 适于包括在融合蛋白质编码序列中)
171	具有NLS7的Cas9的开放阅读框架(无起始或终止密码子; 适于包括在融合蛋白质编码序列中)
172	具有NLS8的Cas9的开放阅读框架(无起始或终止密码子; 适于包括在融合蛋白质编码序列中)
173	具有NLS9的Cas9的开放阅读框架(无起始或终止密码子; 适于包括在融合蛋白质编码序列中)
174	具有NLS10的Cas9的开放阅读框架(无起始或终止密码子; 适于包括在融合蛋白质编码序列中)
175	具有NLS11的Cas9的开放阅读框架(无起始或终止密码子; 适于包括在融合蛋白质编码序列中)
176	具有XBG UTR及含有表4的低U 1密码子的Cas9 ORF的mRNA转录物
177	具有XBG UTR及含有表4的低A密码子的Cas9 ORF的mRNA转录物
178	具有XBG UTR及含有表4的低U/A密码子的Cas9 ORF的mRNA转录物
179	具有编码带有HiBiT标记标签的Cas9的ORF、HSD 5' UTR及人类ALB 3' UTR的mRNA转录物
180	具有编码带有HiBiT标签的Cas9的ORF、CMV-1 5' UTR及人类ALB 3' UTR的mRNA转录物
181	具有编码带有HiBiT标签的Cas9的ORF、CMV-2 5' UTR及人类ALB 3' UTR的mRNA转录物
182	具有编码带有HiBiT标签的Cas9的ORF、CMV-3 5' UTR及人类ALB 3' UTR的mRNA转录物
183	具有编码带有HiBiT标签的Cas9的ORF、HBA 5' UTR及人类ALB 3' UTR的mRNA转录物

[0116]	184	具有编码带有HiBiT标签的Cas9的ORF、HBB 5' UTR及人类ALB 3' UTR的mRNA转录物
	185	具有编码带有HiBiT标签的Cas9的ORF、XBG 5' UTR及人类ALB 3' UTR的mRNA转录物
	186	具有NLS1的Cas9的氨基酸序列
	187	具有NLS2的Cas9的氨基酸序列
	188	具有NLS3的Cas9的氨基酸序列
	189	具有NLS4的Cas9的氨基酸序列
	190	具有NLS5的Cas9的氨基酸序列
	191	具有NLS6的Cas9的氨基酸序列
	192	具有NLS7的Cas9的氨基酸序列
	193	具有NLS8的Cas9的氨基酸序列
	194	具有NLS9的Cas9的氨基酸序列
	195	具有NLS10的Cas9的氨基酸序列
	196	具有NLS11的Cas9的氨基酸序列
	197	靶向TTR的G506引导RNA
	198	靶向TTR的G510引导RNA

[0117] 对于序列本身,参见下文序列列表。转录物序列一般包括GGG作为供与ARCA一起使用之前三个核苷酸,或包括AGG作为供与CleanCap™一起使用之前三个核苷酸。因此,可对前三个核苷酸进行修饰以供与其它加帽结构方法,诸如牛痘加帽结构酶一起使用。启动子及聚-A序列不包括于转录物序列中。启动子,诸如T7启动子(SEQ ID NO:31)及聚-A序列,诸如SEQ ID NO:62或63可在5'及3'端处分别附接于所揭示的转录物序列。大多数核苷酸序列以DNA形式提供,但可通过将Ts变成Us而容易转化成RNA。

[0118] 附图简述

[0119] 图1A至图1D显示以0.5或1mg/kg (mpk) 施用PBS或脂质纳米颗粒(LNP) 调配物LNP417至LNP421后的IFN α 、IL-6、TNF α 及MCP-1的含量。

[0120] 图2A至图2B显示以0.5或1mpk施用PBS或LNP调配物LNP417至LNP421后的血清TTR含量及肝脏编辑百分比。

[0121] 图3显示由Cas9 DNA构建体进行的转录的活体外转录(IVT)产量。用未经修饰的尿苷-5'-三磷酸(UTP)或单独的(横轴上,0)、用与指定比例的5-甲氧基UTP混合(横轴上,20至80)的或与100%5-甲氧基UTP混合(100)的N1-甲基-假UTP进行转录。对于各组的三个条形图,左侧条形图使用N1-甲基-假UTP及/或5-甲氧基UTP及SEQ ID NO:2;中间的条形图使用未经修饰的UTP及/或5-甲氧基UTP及SEQ ID NO:2;且右侧条形图使用未经修饰的UTP及/或5-甲氧基UTP及SEQ ID NO:1。

[0122] 图4显示根据Cas9(SEQ ID NO:2)及经最佳化的Cas9(SEQ ID NO:1)DNA构建体的

活体外转录 (IVT) 结果的mRNA的纯度。由SEQ ID NO:2的Cas9序列用未经修饰的尿苷-5'-三磷酸 (UTP) (正方形) 或用单独 (0) 的或与指定比例的5-甲氧基UTP混合 (20至80) 的或与100%5-甲氧基UTP混合 (100) 的N1-甲基-假UTP (黑色圆形) 进行转录。由SEQ ID NO:1的Cas9序列 (浅色圆形) 用未经修饰的UTP (0) 或与指定比例的5-甲氧基UTP混合 (20至80) 或与100%5-甲氧基UTP混合 (100) 的未经修饰的UTP进行转录。各编码序列包括一个核定位信号。

[0123] 图5A至图5D显示抗dsRNA抗体墨点分析法结果。结果是伴随双股RNA对照 (A)、在UTP及/或5-甲氧基UTP存在下转录的Cas9 (B)、在UTP及/或5-甲氧基UTP存在下转录的包含SEQ ID NO:4的Cas9 mRNA序列 (C) 及在N1-甲基-假UTP及/或5-甲氧基UTP存在下转录的Cas9 (D) 而产生。图 (B) 至图 (D) 是用含有0%至100%5-甲氧基UTP及100%至0%UTP或N1-甲基UTP进行。

[0124] 图6A及图6B显示用Cas9 mRNA处理的神经母细胞瘤2A细胞 (Neuro 2A cell) 中的mRNA的活体外编辑效率,其呈现为编辑百分比 (A) 或编辑EC50 (B)。评定增加Cas9 mRNA中5-甲氧基-UTP的浓度的影响。由SEQ ID NO:2的Cas9序列用N1-甲基-假UTP (A中的左组;B中的深色圆形) 或用单独 (0) 的或与指定比例的5-甲氧基UTP混合 (20至80) 或与100%5-甲氧基UTP混合 (100) 的未经修饰的尿苷-5'-三磷酸 (UTP) (A中的中间组;B中的正方形) 进行转录。由SEQ ID NO:1的Cas9序列 (A中的右组;B中的浅色圆形) 用未经修饰的UTP (0) 或与指定比例的5-甲氧基UTP混合 (20至80) 或与100%5-甲氧基UTP混合 (100) 的未经修饰的UTP进行转录。各编码序列包括一个核定位信号。

[0125] 图7A至图7D展示LNP调配物LNP720至LNP724给药后4小时时的血清细胞介素含量。图7A中的星号指示至少一个独立测量小于侦测极限。

[0126] 图8A及图8B展示用LNP调配物LNP720至LNP724给药后7天时的血清TTR含量 (A) 及肝脏中的TTR编辑百分比 (B)。图8A中的星号指示至少一个独立测量小于侦测极限。

[0127] 图9显示以1mpk用LNP调配物LNP720至LNP724给药后7天时的脾脏中的TTR编辑百分比。

[0128] 图10显示使用LNP调配物LNP720至LNP724及LNP685的初级小鼠肝细胞 (PMH) 中的TTR编辑百分比。

[0129] 图11A及图11B显示投配包含Cas9 mRNA的调配物之后的血清TTR含量,在该Cas9 mRNA中,ORF具有SEQ ID NO:5或4的序列。TTR数据呈现为血清含量 (A) 或相对于经TSS处理的动物中的TTR含量的百分比 (B)。

[0130] 图12显示以5mpk或2mpk投配包含Cas9 mRNA的调配物之后的肝脏中的TTR编辑百分比,在该Cas9 mRNA中,ORF具有SEQ ID NO:5或4的序列。

[0131] 图13A至图13E显示投配指定LNP调配物之后的血清TTR含量及肝脏中的TTR编辑百分比。

[0132] 图14显示用0.3、1、3或10ng LNP815-821、823或824处理的初级小鼠肝细胞 (PMH) 中的TTR编辑百分比。

[0133] 图15A至图15B显示以指定引导物:Cas9比率及量投配合有Cas9 mRNA的LNP调配物之后的血清TTR含量,在该Cas9 mRNA中,ORF具有SEQ ID NO:5或4的序列。

[0134] 图16A至图16B显示以指定引导物:Cas9比率及量投配合有Cas9 mRNA的LNP调配物

之后的肝脏中的TTR编辑百分比,在该Cas9 mRNA中,ORF具有SEQ ID NO:5或4的序列。

[0135] 图17A至图17B显示以指定引导物:Cas9比率及量投配含有Cas9 mRNA的LNP调配物之后的脾脏中的TTR编辑百分比,在该Cas9 mRNA中,ORF具有SEQ ID NO:5或4的序列。

[0136] 图18显示针对以指定引导物:Cas9比率投配含有Cas9 mRNA的LNP调配物之后的肝脏中的Cas9表达的蛋白质印迹法,在该Cas9 mRNA中,ORF具有SEQ ID NO:5或4的序列。

[0137] 图19A至图19B显示以指定量投配指定LNP调配物之后的血清TTR含量。

[0138] 图20显示以指定量投配指定LNP调配物之后的肝脏中的TTR编辑百分比。

[0139] 图21A至图21C显示以指定量投配指定LNP调配物之后的肝脏编辑含量(A)及血清TTR(B以 $\mu\text{g}/\text{ml}$ 为单位;C呈TSS对照的百分比形式)。

[0140] 图22A至22D显示以指定比率及量投配LNP调配物之后的血清TTR及编辑结果。

[0141] 图23显示用Cas9 mRNA处理之后的Hep2G细胞中的Cas9蛋白质表达,在该Cas9 mRNA中,ORF具有指定SEQ ID NO的序列。

[0142] 图24显示以指定浓度用Cas9 mRNA处理之后的Hep2G细胞中的编辑百分比,在该Cas9 mRNA中,ORF具有指定SEQ ID NO的序列。

[0143] 图25显示投配具有Cas9 mRNA的LNP调配物之后的肝脏中的Cas9表达,在该Cas9 mRNA中,ORF具有指定SEQ ID NO的序列。

[0144] 图26显示投配具有Cas9 mRNA的LNP调配物之后的TTR基因座处的活体内编辑结果,在该Cas9 mRNA中,ORF具有指定SEQ ID NO的序列。

[0145] 图27A至图27B显示投配具有Cas9 mRNA的LNP调配物之后的血清TTR(A)及血清TTR(TSS%) (B),在该Cas9 mRNA中,ORF具有指定SEQ ID NO的序列。

[0146] 图28显示以指定量投配具有Cas9 mRNA的LNP调配物之后的活体内肝脏编辑,在该Cas9 mRNA中,ORF具有指定SEQ ID NO的序列。

[0147] 图29A至图29B显示以指定量投配具有Cas9 mRNA的LNP调配物之后的血清TTR含量(A)及血清TTR(TSS%) (B),在该Cas9 mRNA中,ORF具有指定SEQ ID NO的序列。

[0148] 图30A至图30B显示投配具有Cas9 mRNA的LNP调配物之后的血清TTR含量(A)及肝脏中的编辑%(B),在该Cas9 mRNA中,转录物具有指定SEQ ID NO的序列。

[0149] 图31显示以指定剂量投配经mRNA调配的LNP之后的肝脏中的TTR编辑百分比,该mRNA具有指定帽结构及转录物序列。

[0150] 图32显示以指定剂量投配经mRNA调配的LNP之后的血清TTR含量,该mRNA具有指定帽结构及转录物序列。

[0151] 图33显示投配经编码Cas9的mRNA调配的LNP之后的肝脏中的TTR编辑百分比,在该mRNA中,ORF具有指定SEQ ID NO的序列,包括如所指示的NLS。

[0152] 图34A至图34B显示投配经编码Cas9的mRNA调配的LNP之后的血清TTR含量(A)及血清TTR(TSS%) (B),在该mRNA中,ORF具有指定SEQ ID NO的序列,包括如所指示的NLS。

[0153] 图35显示投配经编码Cas9且包括不同类别及活性含量的NLS序列的mRNA调配的LNP之后的NLS活性与编辑效率的相关性。

[0154] 图36显示HepG2细胞中来自具有指定序列及如所指示的5'UTR的mRNA转录物的Cas9蛋白质的表达水平。

[0155] 实施方式

[0156] 现将详细参考本发明的某些实施例,其实例在附图中加以说明。尽管本发明将结合所说明的实施例描述,但应理解其并不意欲将本发明限于这些实施例。相反,本发明意欲涵盖所有替代方案、修改及等效物,其可如所附权利要求所限定包括在本发明内。

[0157] 在详细描述本发明教导内容之前,应理解,本发明不限于特定组合物或方法步骤,因而可加以改变。应注意,除非上下文另外明确规定,否则如本说明书及所附权利要求中所用,单数形式“一(a/an)”及“该(the)”包括复数个所指物。因此,例如,提及“结合物”包括复数个结合物且提及“细胞”包括复数个细胞及其类似者。

[0158] 数值范围包括界定该范围的数字。考虑到有效数字及与测量相关的误差,测量及可测量值应理解为大致的。此外,“包含(comprise/comprises/comprising)”、“含有(contain/contains/containing)”及“包括(include/includes/including)”的使用并不意欲为限制性的。应理解,前述一般描述及详细描述仅为示例性及解释性的且并不限制教导内容。

[0159] 术语“约”或“大约”意谓如由一般熟习此项技术者所测定的特定值的可接受的误差,其在某种程度上视如何测量或测定该值、或变化程度不会实质上影响所述标的物的特性(例如在10%、5%、2%或1%内)而定。因此,除非有相反指示,否则以下说明书及所附权利要求中所阐述的数值参数为可视设法获得的所需特性而变化的近似值。至少,且不试图将均等论的应用限于权利要求的范畴,各数值参数至少应根据所报导的有效数字的数目且通过应用普通舍入技术来解释。

[0160] 除非以上说明书中具体指出,否则本说明书中叙述“包含”各种组分的实施例亦设想为“由所述组分组成”或“基本上由所述组分组成”;本说明书中叙述“由各种组分组成”的实施例亦设想为“包含”所述组分或“基本上由所述组分组成”;且本说明书中叙述“基本上由各种组分组成”的实施例亦设想为“由所述组分组成”或“包含”所述组分(此互换性并不适用于此等术语在权利要求中的使用)。

[0161] 本文所用的章节标题仅出于组织目的而不应解释为以任何方式限制所需标的物。在以引用的方式并入的任何文献与本说明书的表述内容(包括(但不限于)定义)相矛盾的情况下,以本说明书的表述内容为准。虽然本教导内容是与多个实施例结合描述,但并不意欲将本教导内容限制于该实施例。相反,如熟习此项技术者将了解,本教导内容涵盖各种替代方案、修改及等效物。

[0162] A. 定义

[0163] 除非另外说明,否则如本文所用的以下术语及片语意欲具有以下含义:

[0164] 如本文所用,术语“或其组合”是指在该术语前面所列项的所有排列及组合。例如,“A、B、C或其组合”意欲包括以下中的至少一者:A、B、C、AB、AC、BC或ABC,且若在特定情况下顺序为重要的,则亦包括BA、CA、CB、ACB、CBA、BCA、BAC或CAB。继续此实例,明确地包括含有一或多个项或条项的重复的组合,诸如BB、AAA、AAB、BBC、AAABCCCC、CBBAAB、CABABB等。熟习此项技术者应理解,除非另外自上下文显而易见,否则通常不存在对任何组合中的项目或术语数目的限制。

[0165] 如本文所用,术语“试剂盒”是指相关组分,诸如一或多种多核苷酸或组合物及一或多种相关材料,诸如递送装置(例如注射器)、溶剂、溶液、缓冲剂、说明书或干燥剂的封装组。

[0166] 除非本文另有规定,否则“或”是依包括性意义使用,即,等效于“及/或”。

[0167] “多核苷酸”及“核酸”在本文中用于指代包含核苷或具有沿主链连接在一起的含氮杂环碱基或碱基类似物的核苷类似物的多聚化合物,其包括习知RNA、DNA、混合RNA-DNA及其类似物的聚合物。核酸“主链”可由多个键组成,其包括糖-磷酸二酯键、肽-核酸键(“肽核酸”或PNA;PCT第W0 95/32305号)、硫代磷酸酯键、磷酸甲酯键或其组合中的一种或多种。核酸的糖部分可为核糖、脱氧核糖或具有取代,例如2'甲氧基或2'卤基取代的类似化合物。含氮碱基可为习知碱基(A、G、C、T、U);其类似物(例如经修饰的尿苷,诸如5-甲氧基尿苷、假尿苷或N1-甲基假尿苷或其它);肌核苷;嘌呤或嘧啶的衍生物(例如N⁴-甲基脱氧鸟苷、脱氮或氮杂嘌呤、脱氮或氮杂嘧啶、在5或6位处具有取代基的嘧啶碱基(例如5-甲基胞嘧啶)、在2、6或8位处具有取代基的嘌呤碱基、2-氨基-6-甲氨基嘌呤、0⁶-甲基鸟嘌呤、4-硫基-嘧啶、4-氨基-嘧啶、4-二甲基胍-嘧啶及0⁴-烷基-嘧啶;美国专利第5,378,825号及PCT第W0 93/13121号)。对于一般论述,参见The Biochemistry of the Nucleic Acids 5-36, Adams等人编,第11版,1992。核酸可包括一或多个“无碱基”残基,其中主链不包括针对聚合物位置的含氮碱基(美国专利第5,585,481号)。核酸可仅包含习知RNA或DNA糖、碱基及键,或可包括习知组分及取代两者(例如具有2'甲氧基键的习知碱基或含有习知碱基及一或多个碱基类似物两者的聚合物)。核酸包括“锁核酸”(LNA),一种含有一或多种LNA核苷酸单体的类似物,该单体具有模拟糖构象的锁定于RNA中的双环呋喃糖单元,其会增强对互补RNA及DNA序列的杂交亲和性(Vester及Wengel,2004,Biochemistry 43(42):13233-41)。RNA及DNA具有不同糖部分且可通过在RNA中存在尿嘧啶或其类似物及在DNA中存在胸腺嘧啶或其类似物而有所不同。

[0168] “经修饰的尿苷”在本文中用于指代除胸苷外的具有与尿苷相同的氢键受体且与尿苷存在一或多种结构性差异的核苷。在一些实施例中,经修饰的尿苷为经取代的尿苷,即其中一或多个非质子取代(例如烷氧基,诸如甲氧基)代替质子的尿苷。在一些实施例中,经修饰的尿苷为假尿苷。在一些实施例中,经修饰的尿苷为经取代的假尿苷,即其中一或多个非质子取代(例如烷基,诸如甲基)代替质子的假尿苷。在一些实施例中,经修饰的尿苷为经取代的尿苷、假尿苷或经取代的假尿苷中的任一个。

[0169] 如本文所用,“尿苷位置”是指多核苷酸中由尿苷或经修饰的尿苷占据的位置。因此,例如,其中“100%的尿苷位置为经修饰的尿苷”的多核苷酸在相同序列的习知RNA(其中所有碱基均为标准A、U、C或G碱基)中应为尿苷的每个位置处均含有经修饰的尿苷。除非另外指明,否则本发明中或附随本发明的序列表(sequence table/sequence listing)的多核苷酸序列中的U可为尿苷或经修饰的尿苷。

[0170] 如本文所用,若第一序列与第二序列的比对显示整个第二序列的X%或大于X%的位置与第一序列相匹配,则该第一序列视为“包含与第二序列具有至少X%一致性的序列”。例如,序列AAGA包含与序列AAG具有100%一致性的序列,因为与第二序列的全部三个位置均出现匹配,所以比对结果为100%一致性。RNA与DNA之间的差异(通常而言,尿苷更换为胸苷或反之亦然)及核苷类似物(诸如经修饰的尿苷)的存在不会造成多核苷酸之间一致性或互补性的差异,只要相关核苷酸(诸如胸苷、尿苷或经修饰的尿苷)具有相同互补序列(例如针对胸苷、尿苷或经修饰的尿苷均为腺苷;另一实例为胞嘧啶及5-甲基胞嘧啶,这两者均以鸟苷作为互补序列)即可。因此,例如,序列5'-AXG(其中X为任何经修饰的尿苷,诸如假尿

昔、N1-甲基假尿昔或5-甲氧基尿昔)视为与AUG具有100%一致性,因为两者与同一序列(5'-CAU)完全互补。比对算法实例为Smith-Waterman及Needleman-Wunsch算法,其是此项技术中熟知者。熟习此项技术者应理解选择何种算法及参数设置才适合于所要比对的一对指定序列;对于具有一般类似长度及预期氨基酸有>50%一致性或核苷酸有>75%一致性的序列而言,由EBI于www.ebi.ac.uk网站服务器提供的Needleman-Wunsch算法接口的具有默认设置的Needleman-Wunsch算法通常为合适的。

[0171] “mRNA”在本文中用于指代非DNA且包含可转译成多肽的开放阅读框架的多核苷酸(即可作为由核糖体及氨基酰化tRNA进行转译的底物)。mRNA可包含包括核糖残基或其类似物,例如2'-甲氧基核糖残基的磷酸酯-糖主链。在一些实施例中,mRNA磷酸酯-糖主链的糖基本上由核糖残基、2'-甲氧基核糖残基或其组合组成。通常而言,mRNA不含大量胸苷残基(例如0个残基或小于30、20、10、5、4、3或2个胸苷残基;或小于10%、9%、8%、7%、6%、5%、4%、3%、2%、1%、0.5%、0.2%或0.1%的胸苷含量)。mRNA可在其一些或全部尿苷位置处含有经修饰的尿苷。

[0172] 如本文所用,“RNA引导的DNA结合剂”意谓具有RNA及DNA结合活性的多肽或多肽复合物,或此类复合物的DNA结合亚基,其中DNA结合活性具有序列特异性且视RNA的序列而定。示例性RNA引导的DNA结合剂包括Cas裂解酶/切口酶及其不活化形式(“dCas DNA结合剂”)。如本文所用,“Cas核酸酶”亦称作“Cas蛋白质”,其涵盖Cas裂解酶、Cas切口酶及dCas DNA结合剂。Cas裂解酶/切口酶及dCas DNA结合剂包括III型CRISPR系统的Csm或Cmr复合物、其Cas10、Csm1或Cmr2亚基、I型CRISPR系统的级联复合物、其Cas3亚基及2类Cas核酸酶。如本文所用,“2类Cas核酸酶”为具有经RNA引导的DNA结合活性的单链多肽,诸如Cas9核酸酶或Cpf1核酸酶。2类Cas核酸酶包括2类Cas裂解酶及2类Cas切口酶(例如H840A、D10A或N863A变异体),其进一步具有经RNA引导的DNA裂解酶或切口酶活性,及2类dCas DNA结合剂,其中裂解酶/切口酶活性未活化。2类Cas核酸酶包括例如Cas9、Cpf1、C2c1、C2c2、C2c3、HF Cas9(例如N497A、R661A、Q695A、Q926A变异体)、HypaCas9(例如N692A、M694A、Q695A、H698A变异体)、eSPCas9(1.0)(例如K810A、K1003A、R1060A变异体)及eSPCas9(1.1)(例如K848A、K1003A、R1060A变异体)蛋白质及其变体。Cpf1蛋白质(Zetsche等人,Cell,163:1-13(2015))与Cas9同源且含有类RuvC核酸酶域。Zetsche的Cpf1序列以全文引用的方式并入。参见例如Zetsche,表S1及表S3。“Cas9”涵盖Spy Cas9、本文中所列的Cas9的变异体及其等效物。参见例如,Makarova等人,Nat Rev Microbiol,13(11):722-36(2015);Shmakov等人,Molecular Cell,60:385-397(2015)。

[0173] 如本文所用,给定开放阅读框架(ORF)的“最小尿苷含量”为以下的ORF的尿苷含量:(a)每个位置处使用最小尿苷密码子及(b)编码与给定ORF相同的氨基酸序列。给定氨基酸的最小尿苷密码子为具有最少尿苷的密码子(通常0或1个,除了苯丙氨酸的密码子外,其中最小尿苷密码子具有2个尿苷)。出于评估最小尿苷含量的目的,经修饰的尿苷残基视为等效于尿苷。

[0174] 如本文所用,给定开放阅读框架(ORF)的“最小尿苷二核苷酸含量”为以下的ORF的最低可能的尿苷二核苷酸(UU)含量:(a)在每个位置处使用最小尿苷密码子(如上文所述)及(b)编码与给定ORF相同的氨基酸序列。尿苷二核苷酸(UU)含量在绝对意义上可表示为ORF中的UU二核苷酸的计数或基于比率,表示为尿苷二核苷酸的尿苷所占据的位置的百

分比(例如,AUUUAU的尿苷二核苷酸含量为40%,因为尿苷二核苷酸的尿苷占据了5个位置中的2个)。出于评估最小尿苷二核苷酸含量的目的,经修饰的尿苷残基视为等效于尿苷。

[0175] 如本文所用,给定开放阅读框架(ORF)的“最小腺嘌呤含量”为以下的ORF的腺嘌呤含量:(a)每个位置处使用最小腺嘌呤密码子及(b)编码与给定ORF相同的氨基酸序列。给定氨基酸的最小腺嘌呤密码子为具有最少腺嘌呤的密码子(通常0或1个,除了赖氨酸及天冬酰胺的密码子外,其中最小腺嘌呤密码子具有2个腺嘌呤)。出于评估最小腺嘌呤含量的目的,经修饰的腺嘌呤残基视为等效于腺嘌呤。

[0176] 如本文所用,给定开放阅读框架(ORF)的“最小腺嘌呤二核苷酸含量”为以下的ORF的最低可能的腺嘌呤二核苷酸(AA)含量:(a)在每个位置处使用最小腺嘌呤密码子(如上文所述)及(b)编码与给定ORF相同的氨基酸序列。腺嘌呤二核苷酸(AA)含量在绝对意义上可表示为ORF中的AA二核苷酸的计数或基于比率,表示为腺嘌呤二核苷酸的腺嘌呤所占位置的百分比(例如,UAAUA的腺嘌呤二核苷酸含量为40%,因为腺嘌呤二核苷酸的腺嘌呤占据了5个位置中的2个)。出于评估最小腺嘌呤二核苷酸含量的目的,经修饰的腺嘌呤残基视为等效于腺嘌呤。

[0177] “引导RNA”、“gRNA”及“引导物”在本文中互换使用来指代crRNA(也称为CRISPR RNA)或crRNA与trRNA(也称为tracrRNA)的组合任一个。crRNA及trRNA可以单一RNA分子(单引导RNA,sgRNA)或以两个独立RNA分子(双引导RNA,dgRNA)形式缔合。“引导RNA”或“gRNA”是指各类型。trRNA可为天然存在的序列或与天然存在的序列相比具有修饰或变化的trRNA序列。

[0178] 如本文所用,“引导序列”是指引导RNA中与靶序列互补且通过由RNA引导的DNA结合剂将引导RNA导引至靶序列以供结合或修饰(例如裂解)的序列。“引导序列”也可称为“靶序列”或“间隔序列”。引导序列的长度可为20个碱基对,例如在化脓链球菌(*Streptococcus pyogenes*) (即Spy Cas9)及相关Cas9同源物/直是同源物的情况下。较短或较长序列亦可用作引导物,例如长度为15-、16-、17-、18-、19-、21-、22-、23-、24-或25-个核苷酸。在一些实施例中,靶序列处于例如基因中或染色体上,且与引导序列互补。在一些实施例中,引导序列与其相应靶序列之间的互补性或一致性的程度可为约75%、80%、85%、90%、95%、96%、97%、98%、99%或100%。在一些实施例中,引导序列与标靶区可为100%互补或一致的。在其它实施例中,引导序列与标靶区可含有至少一个错配。例如,引导序列及靶序列可含有1、2、3或4个错配,其中靶序列的总长度为至少17、18、19、20或更多个碱基对。在一些实施例中,引导序列及标靶区可含有1至4个错配,其中引导序列包含至少17、18、19、20或更多个核苷酸。在一些实施例中,引导序列及标靶区可含有1、2、3或4个错配,其中引导序列包含20个核苷酸。

[0179] 针对Cas蛋白质的靶序列包括基因组DNA的正股及负股两者(即给定序列及该序列的反向互补序列),因为Cas蛋白质的核酸底物为双股核酸。因此,在论述引导序列“与靶序列互补”的情况下,应理解,引导序列可导引引导RNA结合至靶序列的反向互补序列。因此,在一些实施例中,在引导序列结合靶序列的反向互补序列的情况下,引导序列与靶序列(例如不包括PAM的靶序列)的某些核苷酸相同,不同的处在于引导序列中U取代T。

[0180] 如本文所用,“插入缺失标记(indel)”是指由多个核苷酸组成的插入/缺失突变,该核苷酸在核酸中的双股断裂(DSB)位点处进行插入或缺失。

[0181] 如本文所用,“基因减弱(knockdown)”是指特定基因产物(例如蛋白质、mRNA或两者)的表达降低。可通过侦测由组织或细胞群(例如在血清或细胞培养基中)分泌的蛋白质或通过侦测来自相关组织或细胞群的蛋白质的总细胞量来测量蛋白质的基因减弱。用于测量mRNA的基因减弱的方法为已知的,且包括对自相关组织或细胞群分离的mRNA进行测序。在一些实施例中,“基因减弱”可指代特定基因产物表达有一些损失,例如经转录的mRNA的量下降或由细胞群(包括活体内细胞群,诸如这些出现在组织中者)表达或分泌的蛋白质的量下降。

[0182] 如本文所用,“基因剔除”是指丧失细胞中特定蛋白质的表达。可通过侦测由组织或细胞群(例如在血清或细胞培养基中)分泌的蛋白质的量或通过侦测组织或细胞群中蛋白质的总细胞量来测量基因剔除。在一些实施例中,本发明方法在一或多种细胞(例如在细胞群,包括活体内细胞群,诸如这些出现在组织中者)“基因剔除”靶蛋白。在一些实施例中,基因剔除并非例如通过插入缺失标记(indel)导致形成突变靶蛋白,而是细胞中完全丧失靶蛋白的表达。

[0183] 如本文所用,“核糖核蛋白”(RNP)或“RNP复合物”是指引导RNA以及RNA引导的DNA结合剂,诸如Cas裂解酶、切口酶或dCas DNA结合剂(例如Cas9)。在一些实施例中,引导RNA将RNA引导的DNA结合剂,诸如Cas9导引至靶序列,且该引导RNA与靶序列杂交且该结合剂结合于靶序列;在结合剂为裂解酶或切口酶的情况下,结合之后进行裂解或切口。

[0184] 如本文所用,“靶序列”是指靶基因中与gRNA的引导序列互补的核酸序列。靶序列与引导序列的相互作用导引RNA引导的DNA结合剂结合,且在靶序列中潜在地链裂或裂解(视试剂活性而定)。

[0185] 如本文所用,“治疗”是指用于个体的疾病或病症的治疗剂的任何施用或施用,且包括抑制疾病、遏制其发展、缓解疾病的一或多种症状、治愈疾病或预防疾病的一或多种症状的复发。

[0186] B. 示例性多核苷酸及组合物

[0187] 1. 具有低尿苷含量的mRNA及ORF

[0188] 在一些实施例中,提供一种编码包含开放阅读框架(ORF)的RNA引导的DNA结合剂的mRNA,该ORF的尿苷含量在其最小尿苷含量至其最小尿苷含量的约150%范围内。在一些实施例中,ORF的尿苷含量小于或等于其最小尿苷含量的约145%、140%、135%、130%、125%、120%、115%、110%、105%、104%、103%、102%或101%。在一些实施例中,提供一种编码包含开放阅读框架(ORF)的RNA引导的DNA结合剂的mRNA,该ORF的尿苷含量等于其最小尿苷含量。在一些实施例中,提供一种编码包含开放阅读框架(ORF)的RNA引导的DNA结合剂的mRNA,该ORF的尿苷含量小于或等于其最小尿苷含量的约150%。在一些实施例中,提供一种编码包含开放阅读框架(ORF)的RNA引导的DNA结合剂的mRNA,该ORF的尿苷含量小于或等于其最小尿苷含量的约145%。在一些实施例中,提供一种编码包含开放阅读框架(ORF)的RNA引导的DNA结合剂的mRNA,该ORF的尿苷含量小于或等于其最小尿苷含量的约140%。在一些实施例中,提供一种编码包含开放阅读框架(ORF)的RNA引导的DNA结合剂的mRNA,该ORF的尿苷含量小于或等于其最小尿苷含量的约135%。在一些实施例中,提供一种编码包含开放阅读框架(ORF)的RNA引导的DNA结合剂的mRNA,该ORF的尿苷含量小于或等于其最小尿苷含量的约130%。在一些实施例中,提供一种编码包含开放阅读框架(ORF)的RNA引导的

DNA结合剂的mRNA,该ORF的尿苷含量小于或等于其最小尿苷含量的约125%。在一些实施例中,提供一种编码包含开放阅读框架(ORF)的RNA引导的DNA结合剂的mRNA,该ORF的尿苷含量小于或等于其最小尿苷含量的约120%。在一些实施例中,提供一种编码包含开放阅读框架(ORF)的RNA引导的DNA结合剂的mRNA,该ORF的尿苷含量小于或等于其最小尿苷含量的约115%。在一些实施例中,提供一种编码包含开放阅读框架(ORF)的RNA引导的DNA结合剂的mRNA,该ORF的尿苷含量小于或等于其最小尿苷含量的约110%。在一些实施例中,提供一种编码包含开放阅读框架(ORF)的RNA引导的DNA结合剂的mRNA,该ORF的尿苷含量小于或等于其最小尿苷含量的约105%。在一些实施例中,提供一种编码包含开放阅读框架(ORF)的RNA引导的DNA结合剂的mRNA,该ORF的尿苷含量小于或等于其最小尿苷含量的约104%。在一些实施例中,提供一种编码包含开放阅读框架(ORF)的RNA引导的DNA结合剂的mRNA,该ORF的尿苷含量小于或等于其最小尿苷含量的约103%。在一些实施例中,提供一种编码包含开放阅读框架(ORF)的RNA引导的DNA结合剂的mRNA,该ORF的尿苷含量小于或等于其最小尿苷含量的约102%。在一些实施例中,提供一种编码包含开放阅读框架(ORF)的RNA引导的DNA结合剂的mRNA,该ORF的尿苷含量小于或等于其最小尿苷含量的约101%。

[0189] 在一些实施例中,提供一种编码包含开放阅读框架(ORF)的RNA引导的DNA结合剂的mRNA,该ORF的尿苷二核苷酸含量在其最小尿苷二核苷酸含量至其最小尿苷二核苷酸含量的200%范围内。在一些实施例中,ORF的尿苷二核苷酸含量小于或等于其最小尿苷二核苷酸含量的约195%、190%、185%、180%、175%、170%、165%、160%、155%、150%、145%、140%、135%、130%、125%、120%、115%、110%、105%、104%、103%、102%或101%。在一些实施例中,提供一种编码包含开放阅读框架(ORF)的RNA引导的DNA结合剂的mRNA,该ORF的尿苷二核苷酸含量等于其最小尿苷二核苷酸含量。在一些实施例中,提供一种编码包含开放阅读框架(ORF)的RNA引导的DNA结合剂的mRNA,该ORF的尿苷二核苷酸含量小于或等于其最小尿苷二核苷酸含量的约200%。在一些实施例中,提供一种编码包含开放阅读框架(ORF)的RNA引导的DNA结合剂的mRNA,该ORF的尿苷二核苷酸含量小于或等于其最小尿苷二核苷酸含量的约195%。在一些实施例中,提供一种编码包含开放阅读框架(ORF)的RNA引导的DNA结合剂的mRNA,该ORF的尿苷二核苷酸含量小于或等于其最小尿苷二核苷酸含量的约190%。在一些实施例中,提供一种编码包含开放阅读框架(ORF)的RNA引导的DNA结合剂的mRNA,该ORF的尿苷二核苷酸含量小于或等于其最小尿苷二核苷酸含量的约185%。在一些实施例中,提供一种编码包含开放阅读框架(ORF)的RNA引导的DNA结合剂的mRNA,该ORF的尿苷二核苷酸含量小于或等于其最小尿苷二核苷酸含量的约180%。在一些实施例中,提供一种编码包含开放阅读框架(ORF)的RNA引导的DNA结合剂的mRNA,该ORF的尿苷二核苷酸含量小于或等于其最小尿苷二核苷酸含量的约175%。在一些实施例中,提供一种编码包含开放阅读框架(ORF)的RNA引导的DNA结合剂的mRNA,该ORF的尿苷二核苷酸含量小于或等于其最小尿苷二核苷酸含量的约170%。在一些实施例中,提供一种编码包含开放阅读框架(ORF)的RNA引导的DNA结合剂的mRNA,该ORF的尿苷二核苷酸含量小于或等于其最小尿苷二核苷酸含量的约165%。在一些实施例中,提供一种编码包含开放阅读框架(ORF)的RNA引导的DNA结合剂的mRNA,该ORF的尿苷二核苷酸含量小于或等于其最小尿苷二核苷酸含量的约160%。在一些实施例中,提供一种编码包含开放阅读框架(ORF)的RNA引导的DNA结合剂的mRNA,该ORF的尿苷二核苷酸含量小于或等于其最小尿苷二核苷酸含量的约

155%。在一些实施例中,提供一种编码包含开放阅读框架(ORF)的RNA引导的DNA结合剂的mRNA,该ORF的尿苷二核苷酸含量等于其最小尿苷二核苷酸含量。在一些实施例中,提供一种编码包含开放阅读框架(ORF)的RNA引导的DNA结合剂的mRNA,该ORF的尿苷二核苷酸含量小于或等于其最小尿苷二核苷酸含量的约150%。在一些实施例中,提供一种编码包含开放阅读框架(ORF)的RNA引导的DNA结合剂的mRNA,该ORF的尿苷二核苷酸含量小于或等于其最小尿苷二核苷酸含量的约145%。在一些实施例中,提供一种编码包含开放阅读框架(ORF)的RNA引导的DNA结合剂的mRNA,该ORF的尿苷二核苷酸含量小于或等于其最小尿苷二核苷酸含量的约140%。在一些实施例中,提供一种编码包含开放阅读框架(ORF)的RNA引导的DNA结合剂的mRNA,该ORF的尿苷二核苷酸含量小于或等于其最小尿苷二核苷酸含量的约135%。在一些实施例中,提供一种编码包含开放阅读框架(ORF)的RNA引导的DNA结合剂的mRNA,该ORF的尿苷二核苷酸含量小于或等于其最小尿苷二核苷酸含量的约130%。在一些实施例中,提供一种编码包含开放阅读框架(ORF)的RNA引导的DNA结合剂的mRNA,该ORF的尿苷二核苷酸含量小于或等于其最小尿苷二核苷酸含量的约125%。在一些实施例中,提供一种编码包含开放阅读框架(ORF)的RNA引导的DNA结合剂的mRNA,该ORF的尿苷二核苷酸含量小于或等于其最小尿苷二核苷酸含量的约120%。在一些实施例中,提供一种编码包含开放阅读框架(ORF)的RNA引导的DNA结合剂的mRNA,该ORF的尿苷二核苷酸含量小于或等于其最小尿苷二核苷酸含量的约115%。在一些实施例中,提供一种编码包含开放阅读框架(ORF)的RNA引导的DNA结合剂的mRNA,该ORF的尿苷二核苷酸含量小于或等于其最小尿苷二核苷酸含量的约110%。在一些实施例中,提供一种编码包含开放阅读框架(ORF)的RNA引导的DNA结合剂的mRNA,该ORF的尿苷二核苷酸含量小于或等于其最小尿苷二核苷酸含量的约105%。在一些实施例中,提供一种编码包含开放阅读框架(ORF)的RNA引导的DNA结合剂的mRNA,该ORF的尿苷二核苷酸含量小于或等于其最小尿苷二核苷酸含量的约104%。在一些实施例中,提供一种编码包含开放阅读框架(ORF)的RNA引导的DNA结合剂的mRNA,该ORF的尿苷二核苷酸含量小于或等于其最小尿苷二核苷酸含量的约103%。在一些实施例中,提供一种编码包含开放阅读框架(ORF)的RNA引导的DNA结合剂的mRNA,该ORF的尿苷二核苷酸含量小于或等于其最小尿苷二核苷酸含量的约102%。在一些实施例中,提供一种编码包含开放阅读框架(ORF)的RNA引导的DNA结合剂的mRNA,该ORF的尿苷二核苷酸含量小于或等于其最小尿苷二核苷酸含量的约101%。

[0190] 在一些实施例中,提供一种编码包含开放阅读框架(ORF)的RNA引导的DNA结合剂的mRNA,该ORF的尿苷二核苷酸含量在其最小尿苷二核苷酸含量至呈编码与相关mRNA相同的蛋白质的参考序列的最大尿苷二核苷酸含量的90%或低于90%的尿苷二核苷酸含量范围内。在一些实施例中,ORF的尿苷二核苷酸含量小于或等于编码与相关mRNA相同的蛋白质的参考序列的最大尿苷二核苷酸含量的约85%、80%、75%、70%、65%、60%、55%、50%、45%、40%、35%、30%、25%、20%、15%、10%或5%。

[0191] 在一些实施例中,提供一种编码包含开放阅读框架(ORF)的RNA引导的DNA结合剂的mRNA,该ORF的尿苷三核苷酸含量在0个尿苷三核苷酸至1、2、3、4、5、6、7、8、9、10、20、30、40或50个尿苷三核苷酸范围内(其中一连串较长的尿苷计为其内特有三尿苷区段的数目,例如尿苷四核苷酸含有两个尿苷三核苷酸,尿苷五核苷酸含有三个尿苷三核苷酸等)。在一些实施例中,提供一种编码包含开放阅读框架(ORF)的RNA引导的DNA结合剂的mRNA,该ORF

的尿苷三核苷酸含量在0%尿苷三核苷酸至0.1%、0.2%、0.3%、0.4%、0.5%、0.6%、0.7%、0.8%、0.9%、1%、1.5%或2%尿苷三核苷酸范围内,其中尿苷三核苷酸的百分比含量计算为序列中由形成尿苷三核苷酸的一部分(或一连串较长尿苷),以使得序列UUUAAA及UUUUAAAA将各具有50%的尿苷三核苷酸含量的尿苷所占据的位置的百分比。例如,在一些实施例中,ORF的尿苷三核苷酸含量小于或等于2%。例如,在一些实施例中,ORF的尿苷三核苷酸含量小于或等于1.5%。在一些实施例中,ORF的尿苷三核苷酸含量小于或等于1%。在一些实施例中,ORF的尿苷三核苷酸含量小于或等于0.9%。在一些实施例中,ORF的尿苷三核苷酸含量小于或等于0.8%。在一些实施例中,ORF的尿苷三核苷酸含量小于或等于0.7%。在一些实施例中,ORF的尿苷三核苷酸含量小于或等于0.6%。在一些实施例中,ORF的尿苷三核苷酸含量小于或等于0.5%。在一些实施例中,ORF的尿苷三核苷酸含量小于或等于0.4%。在一些实施例中,ORF的尿苷三核苷酸含量小于或等于0.3%。在一些实施例中,ORF的尿苷三核苷酸含量小于或等于0.2%。在一些实施例中,ORF的尿苷三核苷酸含量小于或等于0.1%。在一些实施例中,提供一种编码包含开放阅读框架(ORF)的RNA引导的DNA结合剂的mRNA,该ORF不含尿苷三核苷酸。

[0192] 在一些实施例中,提供一种编码包含开放阅读框架(ORF)的RNA引导的DNA结合剂的mRNA,该ORF的尿苷三核苷酸含量在其最小尿苷三核苷酸含量至呈编码与相关mRNA相同的蛋白质的参考序列的最大尿苷三核苷酸含量的90%或低于90%的尿苷三核苷酸含量范围内。在一些实施例中,ORF的尿苷三核苷酸含量小于或等于编码与相关mRNA相同的蛋白质的参考序列的最大尿苷三核苷酸含量的约85%、80%、75%、70%、65%、60%、55%、50%、45%、40%、35%、30%、25%、20%、15%、10%或5%。

[0193] 在一些实施例中,提供一种编码包含开放阅读框架(ORF)的RNA引导的DNA结合剂的mRNA,该ORF具有极少核苷酸均聚物,例如重复的相同核苷酸的串。例如,在一些实施例中,当自表1中所列的密码子选择最小尿苷密码子时,通过选择降低核苷酸均聚物的数量及长度的最小尿苷密码子(例如,对于丙氨酸,选择GCA代替GCC;或对于甘氨酸,选择GGA代替GGG;或对于赖氨酸,选择AAG代替AAA)来构筑mRNA。

[0194] 可例如通过在ORF的足够多的一部分中使用最小尿苷密码子来降低给定ORF的尿苷含量或尿苷二核苷酸含量或尿苷三核苷酸含量。例如,可通过将氨基酸转化成密码子而将RNA引导的DNA结合剂的氨基酸序列转译回ORF序列,其中ORF中的一些或全部使用以下所示的示例性最小尿苷密码子。在一些实施例中,ORF中至少约50%、55%、60%、65%、70%、75%、80%、85%、90%、95%、98%、99%或100%的密码子为表1中所列的密码子。

[0195] 表1. 示例性最小尿苷密码子

	氨基酸	最小尿苷密码子	
[0196]	A	丙氨酸	GCA或GCC或GCG
	G	甘氨酸	GGA或GGC或GGG
	V	缬氨酸	GUC或GUA或GUG
	D	天冬氨酸	GAC
	E	谷氨酸	GAA或GAG
	I	异亮氨酸	AUC或AUA
	T	苏氨酸	ACA或ACC或ACG
	N	天冬酰胺	AAC
	K	赖氨酸	AAG或AAA
	[0197]	S	丝氨酸
R		精氨酸	AGA或AGG
L		亮氨酸	CUG或CUA或CUC
P		脯氨酸	CCG或CCA或CCC
H		组氨酸	CAC
Q		谷氨酰胺	CAG或CAA
F		苯丙氨酸	UUC
Y		酪氨酸	UAC
C		半胱氨酸	UGC
W		色氨酸	UGG
M	甲硫氨酸	AUG	

[0198] 在一些实施例中,提供一种编码包含开放阅读框架(ORF)的RNA引导的DNA结合剂的mRNA,该ORF由其中至少约75%、80%、85%、90%、95%、98%、99%或100%的密码子为表1中所列的密码子的一组密码子组成。

[0199] 2. 具有低腺嘌呤含量的mRNA及ORF

[0200] 在一些实施例中,提供一种编码包含开放阅读框架(ORF)的RNA引导的DNA结合剂的mRNA,该ORF的腺嘌呤含量在其最小腺嘌呤含量至其最大腺嘌呤含量的约150%范围内。在一些实施例中,ORF的腺嘌呤含量小于或等于其最小腺嘌呤含量的约145%、140%、135%、130%、125%、120%、115%、110%、105%、104%、103%、102%或101%。在一些实施例中,提供一种编码包含开放阅读框架(ORF)的RNA引导的DNA结合剂的mRNA,该ORF的腺嘌

呤含量等于其最小腺嘌呤含量。在一些实施例中,提供一种编码包含开放阅读框架(ORF)的RNA引导的DNA结合剂的mRNA,该ORF的腺嘌呤含量小于或等于其最小腺嘌呤含量的约150%。在一些实施例中,提供一种编码包含开放阅读框架(ORF)的RNA引导的DNA结合剂的mRNA,该ORF的腺嘌呤含量小于或等于其最小腺嘌呤含量的约145%。在一些实施例中,提供一种编码包含开放阅读框架(ORF)的RNA引导的DNA结合剂的mRNA,该ORF的腺嘌呤含量小于或等于其最小腺嘌呤含量的约140%。在一些实施例中,提供一种编码包含开放阅读框架(ORF)的RNA引导的DNA结合剂的mRNA,该ORF的腺嘌呤含量小于或等于其最小腺嘌呤含量的约135%。在一些实施例中,提供一种编码包含开放阅读框架(ORF)的RNA引导的DNA结合剂的mRNA,该ORF的腺嘌呤含量小于或等于其最小腺嘌呤含量的约130%。在一些实施例中,提供一种编码包含开放阅读框架(ORF)的RNA引导的DNA结合剂的mRNA,该ORF的腺嘌呤含量小于或等于其最小腺嘌呤含量的约125%。在一些实施例中,提供一种编码包含开放阅读框架(ORF)的RNA引导的DNA结合剂的mRNA,该ORF的腺嘌呤含量小于或等于其最小腺嘌呤含量的约120%。在一些实施例中,提供一种编码包含开放阅读框架(ORF)的RNA引导的DNA结合剂的mRNA,该ORF的腺嘌呤含量小于或等于其最小腺嘌呤含量的约115%。在一些实施例中,提供一种编码包含开放阅读框架(ORF)的RNA引导的DNA结合剂的mRNA,该ORF的腺嘌呤含量小于或等于其最小腺嘌呤含量的约110%。在一些实施例中,提供一种编码包含开放阅读框架(ORF)的RNA引导的DNA结合剂的mRNA,该ORF的腺嘌呤含量小于或等于其最小腺嘌呤含量的约105%。在一些实施例中,提供一种编码包含开放阅读框架(ORF)的RNA引导的DNA结合剂的mRNA,该ORF的腺嘌呤含量小于或等于其最小腺嘌呤含量的约104%。在一些实施例中,提供一种编码包含开放阅读框架(ORF)的RNA引导的DNA结合剂的mRNA,该ORF的腺嘌呤含量小于或等于其最小腺嘌呤含量的约103%。在一些实施例中,提供一种编码包含开放阅读框架(ORF)的RNA引导的DNA结合剂的mRNA,该ORF的腺嘌呤含量小于或等于其最小腺嘌呤含量的约102%。在一些实施例中,提供一种编码包含开放阅读框架(ORF)的RNA引导的DNA结合剂的mRNA,该ORF的腺嘌呤含量小于或等于其最小腺嘌呤含量的约101%。

[0201] 在一些实施例中,提供一种编码包含开放阅读框架(ORF)的RNA引导的DNA结合剂的mRNA,该ORF的腺嘌呤二核苷酸含量在其最小腺嘌呤二核苷酸含量至其最小腺嘌呤二核苷酸含量的200%范围内。在一些实施例中,ORF的腺嘌呤二核苷酸含量小于或等于其最小腺嘌呤二核苷酸含量的约195%、190%、185%、180%、175%、170%、165%、160%、155%、150%、145%、140%、135%、130%、125%、120%、115%、110%、105%、104%、103%、102%或101%。在一些实施例中,提供一种编码包含开放阅读框架(ORF)的RNA引导的DNA结合剂的mRNA,该ORF的腺嘌呤二核苷酸含量等于最小腺嘌呤二核苷酸含量。在一些实施例中,提供一种编码包含开放阅读框架(ORF)的RNA引导的DNA结合剂的mRNA,该ORF的腺嘌呤二核苷酸含量小于或等于其最小腺嘌呤二核苷酸含量的约200%。在一些实施例中,提供一种编码包含开放阅读框架(ORF)的RNA引导的DNA结合剂的mRNA,该ORF的腺嘌呤二核苷酸含量小于或等于其最小腺嘌呤二核苷酸含量的约195%。在一些实施例中,提供一种编码包含开放阅读框架(ORF)的RNA引导的DNA结合剂的mRNA,该ORF的腺嘌呤二核苷酸含量小于或等于其最小腺嘌呤二核苷酸含量的约190%。在一些实施例中,提供一种编码包含开放阅读框架(ORF)的RNA引导的DNA结合剂的mRNA,该ORF的腺嘌呤二核苷酸含量小于或等于其最小腺嘌呤二核苷酸含量的约185%。在一些实施例中,提供一种编码包含开放阅读框架(ORF)的RNA

[0202] 在一些实施例中,提供一种编码包含开放阅读框架(ORF)的RNA引导的DNA结合剂的mRNA,该ORF的腺嘌呤二核苷酸含量在其最小腺嘌呤二核苷酸含量至呈编码与相关mRNA相同的蛋白质的参考序列的最大腺嘌呤二核苷酸含量的90%或低于90%的腺嘌呤二核苷酸含量范围内。在一些实施例中,ORF的腺嘌呤二核苷酸含量小于或等于编码与相关mRNA相同的蛋白质的参考序列的最大腺嘌呤二核苷酸含量约85%、80%、75%、70%、65%、60%、55%、50%、45%、40%、35%、30%、25%、20%、15%、10%或5%。

[0203] 在一些实施例中,提供一种编码包含开放阅读框架(ORF)的RNA引导的DNA结合剂的mRNA,该ORF的腺嘌呤三核苷酸含量在0个腺嘌呤三核苷酸至1、2、3、4、5、6、7、8、9、10、20、30、40或50个腺嘌呤三核苷酸范围内(其中一连串较长的腺嘌呤计为其内特有三腺嘌呤区段的数目,例如腺嘌呤四核苷酸含有两个腺嘌呤三核苷酸,腺嘌呤五核苷酸含有三个腺嘌呤三核苷酸等)。在一些实施例中,提供一种编码包含开放阅读框架(ORF)的RNA引导的DNA结合剂的mRNA,该ORF的腺嘌呤三核苷酸含量在0%腺嘌呤三核苷酸至0.1%、0.2%、0.3%、0.4%、0.5%、0.6%、0.7%、0.8%、0.9%、1%、1.5%或2%腺嘌呤三核苷酸范围内,其中腺嘌呤三核苷酸的百分比含量计算为序列中由形成腺嘌呤三核苷酸的一部分(或一连串较长腺嘌呤),以使得序列UUUAAA及UUUUAAA将各具有50%的腺嘌呤三核苷酸含量的腺嘌呤所占的位置的百分比。例如,在一些实施例中,ORF的腺嘌呤三核苷酸含量小于或等于2%。例如,在一些实施例中,ORF的腺嘌呤三核苷酸含量小于或等于1.5%。在一些实施例中,ORF的腺嘌呤三核苷酸含量小于或等于1%。在一些实施例中,ORF的腺嘌呤三核苷酸含量小于或等于0.9%。在一些实施例中,ORF的腺嘌呤三核苷酸含量小于或等于0.8%。在一些实施例中,ORF的腺嘌呤三核苷酸含量小于或等于0.7%。在一些实施例中,ORF的腺嘌呤三核苷酸含量小于或等于0.6%。在一些实施例中,ORF的腺嘌呤三核苷酸含量小于或等于0.5%。在一些实施例中,ORF的腺嘌呤三核苷酸含量小于或等于0.4%。在一些实施例中,ORF的腺嘌呤三核苷酸含量小于或等于0.3%。在一些实施例中,ORF的腺嘌呤三核苷酸含量小于或等于0.2%。在一些实施例中,ORF的腺嘌呤三核苷酸含量小于或等于0.1%。在一些实施例中,提供一种编码包含开放阅读框架(ORF)的RNA引导的DNA结合剂的mRNA,该ORF不含腺嘌呤三核苷酸。

[0204] 在一些实施例中,提供一种编码包含开放阅读框架(ORF)的RNA引导的DNA结合剂的mRNA,该ORF具有极少核苷酸均聚物,例如重复的相同核苷酸的串。例如,在一些实施例中,当自表1中所列的密码子选择最小腺嘌呤密码子时,通过选择降低核苷酸均聚物的数量及长度的最小腺嘌呤密码子(例如,对于丙氨酸,选择GCA代替GCC;或对于甘氨酸,选择GGA代替GGG;或对于赖氨酸,选择AAG代替AAA)来构筑mRNA。

[0205] 在一些实施例中,提供一种编码包含开放阅读框架(ORF)的RNA引导的DNA结合剂的mRNA,该ORF的腺嘌呤三核苷酸含量在其最小腺嘌呤三核苷酸含量至呈编码与相关mRNA相同的蛋白质的参考序列的最大腺嘌呤三核苷酸含量的90%或低于90%的腺嘌呤三核苷酸含量范围内。在一些实施例中,ORF的腺嘌呤三核苷酸含量小于或等于编码与相关mRNA相同的蛋白质的参考序列的最大腺嘌呤三核苷酸含量的约85%、80%、75%、70%、65%、60%、55%、50%、45%、40%、35%、30%、25%、20%、15%、10%或5%。

[0206] 可例如通过在ORF的足够多的一部分中使用最小腺嘌呤密码子来降低给定ORF的腺嘌呤含量或腺嘌呤二核苷酸含量或腺嘌呤三核苷酸含量。例如,可通过将氨基酸转化成

密码子而将RNA引导的DNA结合剂的氨基酸序列转译回ORF序列,其中ORF中的一些或全部使用以下所示的示例性最小腺嘌呤密码子。在一些实施例中,ORF中至少约50%、55%、60%、65%、70%、75%、80%、85%、90%、95%、98%、99%或100%的密码子为表2中所列的密码子。

[0207] 表2. 示例性最小腺嘌呤密码子

	氨基酸	最小腺嘌呤密码子
A	丙氨酸	GCU或GCC或GCG
G	甘氨酸	GGU或GGC或GGG
V	缬氨酸	GUC或GUU或GUG
D	天冬氨酸	GAC或GAU
E	谷氨酸	GAG
I	异亮氨酸	AUC或AUU
T	苏氨酸	ACU或ACC或ACG
N	天冬酰胺	AAC或AAU
K	赖氨酸	AAG
S	丝氨酸	UCU或UCC或UCG
R	精氨酸	CGU或CGC或CGG
L	亮氨酸	CUG或CUC或CUU
P	脯氨酸	CCG或CCU或CCC
H	组氨酸	CAC或CAU
Q	谷氨酰胺	CAG
F	苯丙氨酸	UUC或UUU

[0208]

[0209]

Y	酪氨酸	UAC或UAU
C	半胱氨酸	UGC或UGU
W	色氨酸	UGG
M	甲硫氨酸	AUG

[0210] 在一些实施例中,提供一种编码包含开放阅读框架(ORF)的RNA引导的DNA结合剂的mRNA,该ORF由其中至少约75%、80%、85%、90%、95%、98%、99%或100%的密码子为表2中所列的密码子的一组密码子组成。

[0211] 3. 具有低腺嘌呤及低尿苷含量的mRNA及ORF

[0212] 就可行性而言,上文关于低腺嘌呤含量所述的任一特征可与上文关于低尿苷含量所述的任一特征组合。例如,可提供一种编码包含开放阅读框架(ORF)的RNA引导的DNA结合剂的mRNA,该ORF的尿苷含量在其最小尿苷含量至其最小尿苷含量的约150%范围内(例如ORF的尿苷含量小于或等于其最小尿苷含量的约145%、140%、135%、130%、125%、120%、115%、110%、105%、104%、103%、102%或101%),且该ORF的腺嘌呤含量在其最小腺嘌呤含量至其最小腺嘌呤含量的约150%范围内(例如小于或等于其最小腺嘌呤含量的约145%、140%、135%、130%、125%、120%、115%、110%、105%、104%、103%、102%或101%)。对于尿苷及腺嘌呤二核苷酸亦如此。同样,ORF中的尿苷核苷酸及腺嘌呤二核苷酸的含量可如上文所阐述。同样,ORF中的尿苷二核苷酸及腺嘌呤核苷酸的含量可如上文所阐述。

[0213] 可例如通过在ORF的足够多的一部分中使用最小尿苷及腺嘌呤密码子来降低给定ORF的尿苷及腺嘌呤核苷酸及/或二核苷酸含量。例如,可通过将氨基酸转化成密码子而将RNA引导的DNA结合剂的氨基酸序列转译回ORF序列,其中ORF中的一些或全部使用以下所示的示例性最小尿苷及腺嘌呤密码子。在一些实施例中,ORF中至少约50%、55%、60%、65%、70%、75%、80%、85%、90%、95%、98%、99%或100%的密码子为表3中所列的密码子。

[0214] 表3. 示例性最小尿苷及腺嘌呤密码子

[0215]

	氨基酸	最小尿苷密码子
A	丙氨酸	GCC或GCG
G	甘氨酸	GGC或GGG
V	缬氨酸	GUC或GUG
D	天冬氨酸	GAC
E	谷氨酸	GAG
I	异亮氨酸	AUC
T	苏氨酸	ACC或ACG
N	天冬酰胺	AAC
K	赖氨酸	AAG
S	丝氨酸	AGC或UCC或UCG
R	精氨酸	CGC或CGG
L	亮氨酸	CUG或CUC
P	脯氨酸	CCG或CCC
H	组氨酸	CAC
Q	谷氨酰胺	CAG
F	苯丙氨酸	UUC
Y	酪氨酸	UAC
C	半胱氨酸	UGC
W	色氨酸	UGG
M	甲硫氨酸	AUG

[0216] 在一些实施例中,提供一种编码包含开放阅读框架(ORF)的RNA引导的DNA结合剂的mRNA,该ORF由其中至少约75%、80%、85%、90%、95%、98%、99%或100%的密码子为表

3中所列的密码子的一组密码子组成。如表3中可看出,三个所列丝氨酸密码子中的每一个含有一个A或一个U。在一些实施例中,对于丝氨酸,通过使用AGC密码子来优先化进行尿苷最小化。在一些实施例中,对于丝氨酸,通过使用UCC及/或UCG密码子优先化进行腺嘌呤最小化。

[0217] 4.提高转译及/或对应于高度表达的tRNA的密码子;示例性密码子组

[0218] 在一些实施例中,mRNA包含具有增加哺乳动物,诸如人类中的转译的密码子的ORF。在其它实施例中,mRNA包含具有增加哺乳动物,例如人类的器官,诸如肝脏中的转译的密码子的ORF。在其它实施例中,mRNA包含具有增加哺乳动物,例如人类的细胞型,诸如肝细胞中的转译的密码子的ORF。哺乳动物中;哺乳动物(人类)的细胞型、器官中;人类器官等中的转译的提高可相对于ORF的野生型序列转译程度或相对于以下ORF进行测定:该ORF具有与ORF所源自的生物体或在一定氨基酸含量下含有最类似ORF的生物体,诸如化脓链球菌、金黄色葡萄球菌(*S.aureus*)或另一原核生物(当情况可能为来源于原核生物的Cas核酸酶,诸如来自下文所述的其它原核生物的Cas核酸酶时)的密码子分布相匹配的密码子分布。可替代地,在一些实施例中,哺乳动物中;哺乳动物(人类)的细胞型、器官中;人类器官等中的Cas9序列转译的提高是相对于具有SEQ ID NO:5,同时所有其它方面(包括任何适用点突变、异源域及其类似者)相同的序列的ORF的转译进行测定。适用于提高人类,包括人类肝脏及人类肝细胞中的表达的密码子可为对应于人类肝脏/肝细胞中高度表达的tRNA的密码子,其论述于Dittmar KA, *PLoS Genetics* 2(12):e221(2006)中。在一些实施例中,ORF中至少约75%、80%、85%、90%、95%、96%、97%、98%、99%或100%的密码子为对应于哺乳动物,诸如人类中的高度表达的tRNA(例如针对各氨基酸的表达最高的tRNA)的密码子。在一些实施例中,ORF中至少75%、80%、85%、90%、95%、96%、97%、98%、99%或100%的密码子为对应于哺乳动物器官,诸如人类器官中的高度表达的tRNA(例如针对各氨基酸的表达最高的tRNA)的密码子。在一些实施例中,ORF中至少75%、80%、85%、90%、95%、96%、97%、98%、99%或100%的密码子为对应于哺乳动物肝脏,诸如人类肝脏中的高度表达的tRNA(例如针对各氨基酸的表达最高的tRNA)的密码子。在一些实施例中,ORF中至少75%、80%、85%、90%、95%、96%、97%、98%、99%或100%的密码子为对应于哺乳动物肝细胞,诸如人类肝细胞中的高度表达的tRNA(例如针对各氨基酸的表达最高的tRNA)的密码子。

[0219] 可替代地,通常可使用对应于生物体(例如人类)中的高度表达的tRNA的密码子。

[0220] 前述密码子选择方法中的任一个与上文所示的最小尿苷及/或腺嘌呤密码子可例如通过以下进行组合:以表1、表2或表3的密码子开始,且随后在可利用多于一种选择的情况下,使用对应于一般生物体(例如人类)中,或相关器官或细胞型,诸如肝脏或肝细胞(例如人类肝脏或人类肝细胞)中的较高度表达的tRNA的密码子。

[0221] 在一些实施例中,ORF中至少75%、80%、85%、90%、95%、96%、97%、98%、99%或100%的密码子为来自表4中所示的密码子组(例如低U1、低A或低A/U密码子组)的密码子。低U1、低G、低C、低A及低A/U组中的密码子使用将所指定的核苷酸减至最小的密码子,同时在可利用多于一种选择的情况下,亦使用对应于高度表达的tRNA的密码子。在一些实施例中,ORF中至少75%、80%、85%、90%、95%、96%、97%、98%、99%或100%的密码子为来自表4中所示的低U1密码子组的密码子。在一些实施例中,ORF中至少75%、80%、85%、90%、95%、96%、97%、98%、99%或100%的密码子为来自表4中所示的低A密码子组的密

码子。在一些实施例中,ORF中至少75%、80%、85%、90%、95%、96%、97%、98%、99%或100%的密码子为来自表4中所示的低A/U密码子组的密码子。

[0222] 表4. 示例性密码子组.

氨基酸	低U 1	低U 2	高U	低G	低C	低A	低A/U	长半衰期
Gly	GGC	GGG	GGT	GGC	GGA	GGC	GGC	GGT
Glu	GAG	GAA	GAA	GAA	GAG	GAG	GAG	GAA
Asp	GAC	GAC	GAT	GAC	GAT	GAC	GAC	GAC
Val	GTG	GTA	GTT	GTC	GTG	GTG	GTG	GTC
Ala	GCC	GCG	GCT	GCC	GCT	GCC	GCC	GCC
Arg	AGA	CGA	CGT	AGA	AGA	CGG	CGG	AGA
Ser	AGC	AGC	TCT	TCC	AGT	TCC	AGC	TCT
Lys	AAG	AAA	AAA	AAA	AAG	AAG	AAG	AAG
Asn	AAC	AAC	AAT	AAC	AAT	AAC	AAC	AAC
Met	ATG	ATG	ATG	ATG	AGT	ATG	ATG	ATG
Ile	ATC	ATA	ATT	ATC	ATT	ATC	ATC	ATC
Thr	ACC	ACG	ACT	ACC	ACA	ACC	ACC	ACC
Trp	TGG	TGG	TGG	TGG	TGG	TGG	TGG	TGG
Cys	TGC	TGC	TGT	TGC	TGT	TGC	TGC	TGC
Tyr	TAC	TAC	TAT	TAC	TAT	TAC	TAC	TAC
Leu	CTG	CTA	TTA	CTC	TTG	CTG	CTG	TTG
Phe	TTC	TTC	TTT	TTC	TTT	TTC	TTC	TTC
Gln	CAG	CAA	CAA	CAA	CAG	CAG	CAG	CAA
His	CAC	CAC	CAT	CAC	CAT	CAC	CAC	CAC

[0225] 5. 经编码的RNA引导的DNA结合剂

[0226] 在一些实施例中, RNA引导的DNA结合剂为2类Cas核酸酶。在一些实施例中, RNA引导的DNA结合剂具有裂解酶活性, 其亦可称作双股核酸内切酶活性。在一些实施例中, RNA引导的DNA结合剂包含Cas核酸酶, 诸如2类Cas核酸酶(其可为例如第II型、第V型或第VI型Cas核酸酶)。2类Cas核酸酶包括例如Cas9、Cpf1、C2c1、C2c2及C2c3蛋白质及其修饰形式。Cas9核酸酶的实例包括化脓链球菌、金黄色葡萄球菌及其它原核生物(参见例如下一段落中的清单)的II型CRISPR系统的那些及其经修饰(例如经工程改造或突变型)形式。参见例如, US2016/0312198 A1; US 2016/0312199 A1。Cas核酸酶的其他实例包括III型CRISPR系统的Csm或Cmr复合物或其Cas10、Csm1或Cmr2亚基; 及I型CRISPR系统的级联复合物或其Cas3亚基。在一些实施例中, Cas核酸酶可来自第IIA型、第IIB型或第IIC型系统。对于不同CRISPR系统及Cas核酸酶的论述, 参见例如Makarova等人NAT. REV. MICROBIOL. 9: 467-477 (2011); Makarova等人, NAT. REV. MICROBIOL. 13: 722-36 (2015); Shmakov等人, MOLECULAR CELL, 60: 385-397 (2015)。

[0227] 可衍生出Cas核酸酶的非限制性示例性物种包括化脓链球菌(*Streptococcus pyogenes*)、嗜热链球菌(*Streptococcus thermophilus*)、链球菌属(*Streptococcus sp.*)、

金黄色葡萄球菌 (*Staphylococcus aureus*)、无害李氏菌 (*Listeria innocua*)、加氏乳杆菌 (*Lactobacillus gasseri*)、新凶手弗朗西斯氏菌 (*Francisella novicida*)、产琥珀酸沃廉菌 (*Wolinella succinogenes*)、华德萨特菌 (*Sutterella wadsworthensis*)、 γ -变形菌 (*Gammaproteobacterium*)、脑膜炎双球菌 (*Neisseria meningitidis*)、空肠弯曲杆菌 (*Campylobacter jejuni*)、多杀性巴氏杆菌 (*Pasteurella multocida*)、产琥珀酸丝状杆菌 (*Fibrobacter succinogene*)、深红红螺菌 (*Rhodospirillum rubrum*)、达松维尔拟诺卡氏菌 (*Nocardiopsis dassonvillei*)、始旋链霉菌 (*Streptomyces pristinaespiralis*)、产绿色链霉菌 (*Streptomyces viridochromogenes*)、玫瑰链孢囊菌 (*Streptosporangium roseum*)、酸热脂环杆菌 (*Alicyclobacillus acidocaldarius*)、假蕈状芽孢杆菌 (*Bacillus pseudomycoides*)、砷还原芽孢杆菌 (*Bacillus selenitireducens*)、西伯利亚微小杆菌 (*Exiguobacterium sibiricum*)、戴白氏乳杆菌 (*Lactobacillus delbrueckii*)、唾液乳杆菌 (*Lactobacillus salivarius*)、布氏乳杆菌 (*Lactobacillus buchneri*)、齿垢密螺旋体 (*Treponema denticola*)、海洋微颤菌 (*Microscilla marina*)、伯克霍尔德里氏细菌 (*Burkholderiales bacterium*)、食萘极单胞菌 (*Polaromonas naphthalenivorans*)、极单胞菌属 (*Polaromonas sp.*)、瓦氏鳄球藻 (*Crocospaera watsonii*)、蓝丝菌属 (*Cyanothece sp.*)、绿脓微囊藻 (*Microcystis aeruginosa*)、聚球藻属 (*Synechococcus sp.*)、阿拉伯糖醋杆菌 (*Acetohalobium arabaticum*)、丹氏制氨菌 (*Ammonifex degensii*)、热解纤维素菌 (*Caldicelulosiruptor beccsii*)、金矿菌候选种 (*Candidatus Desulforudis*)、肉毒梭菌 (*Clostridium botulinum*)、艰难梭菌 (*Clostridium difficile*)、大芬戈尔德菌 (*Fingoldia magna*)、嗜热盐碱厌氧菌 (*Natranaerobius thermophilus*)、热丙酸盐暗色厌氧香肠状菌 (*Pelotomaculum thermopropionicum*)、喜温嗜酸硫杆菌 (*Acidithiobacillus caldus*)、氧化亚铁嗜酸硫杆菌 (*Acidithiobacillus ferrooxidans*)、酒色异着色菌 (*Allochromatium yinosum*)、海杆菌属 (*Marinobacter sp.*)、嗜盐亚硝化球菌 (*Nitrosococcus halophilus*)、瓦氏亚硝化球菌 (*Nitrosococcus watsoni*)、游海假交替单胞菌 (*Pseudoalteromonas haloplanktis*)、消旋纤线杆菌 (*Ktedonobacter racemifer*)、调查甲烷盐菌 (*Methanohalobium evesrigatum*)、多变念珠藻 (*Anabaena variabilis*)、泡沫节球藻 (*Nodularia spumigena*)、念珠藻属 (*Nostoc sp.*)、极大节旋藻 (*Arthrospira maxima*)、钝顶节旋藻 (*Arthrospira platensis*)、节旋藻属 (*Arthrospira sp.*)、鞘丝藻属 (*Lyngbya sp.*)、原型微鞘藻 (*Microcoleus chthonoplastes*)、颤藻属 (*Oscillatoria sp.*)、运动石袍菌 (*Petrotoga mobilis*)、非洲高热杆菌 (*Thermosiphon africanus*)、巴氏链球菌 (*Streptococcus pasteurianus*)、灰色奈瑟菌 (*Neisseria cinerea*)、红嘴鸥曲杆菌 (*Campylobacter lari*)、食清洁剂细小棒菌 (*Parvibaculum lavamentivorans*)、白喉棒状杆菌 (*Corynebacterium diphtheria*)、氨基酸球菌属 (*Acidaminococcus sp.*)、毛螺科菌 ND2006 (*Lachnospiraceae bacterium ND2006*) 及海洋藻青菌 (*Acaryochloris marina*)。

[0228] 在一些实施例中,Cas核酸酶为来自化脓链球菌 (*Streptococcus pyogenes*) 的 Cas9核酸酶。在一些实施例中,Cas核酸酶为来自嗜热链球菌的 Cas9核酸酶。在一些实施例中,Cas核酸酶为来自脑膜炎双球菌的 Cas9核酸酶。在一些实施例中,Cas核酸酶为来自金黄色葡萄球菌的 Cas9核酸酶。在一些实施例中,Cas核酸酶为来自新凶手弗朗西斯氏菌的 Cpf1核酸酶。在一些实施例中,Cas核酸酶为来自氨基酸球菌属的 Cpf1核酸酶。在一些实施例中,

Cas核酸酶为来自毛螺科菌ND2006的Cpf1核酸酶。在其它实施例中,Cas核酸酶为来自以下的Cpf1核酸酶:土拉文氏杆菌(*Francisella tularensis*)、毛螺科菌、瘤胃溶纤维丁酸弧菌(*Butyrivibrio proteoclasticus*)、佩氏细菌(*Peregrinibacteria bacterium*)、帕库氏菌(*Parcubacteria bacterium*)、史密斯氏菌(*Smithella*)、氨基酸球菌属、白蚁甲烷支原体菌候选种(*Candidatus Methanoplasma termitum*)、挑剔真杆菌(*Eubacterium eligens*)、牛眼莫拉菌(*Moraxella bovoculi*)、稻田钩端螺旋体(*Leptospira inadai*)、狗口腔卟啉单胞菌(*Porphyromonas crevioricanis*)、解糖豚普雷沃菌(*Prevotella disiens*)或猕猴卟啉单胞菌(*Porphyromonas macacae*)。在某些实施例中,Cas核酸酶为来自氨基酸球菌或毛螺科菌的Cpf1核酸酶。

[0229] 野生型Cas9具有两个核酸酶域:RuvC及HNH。RuvC域裂解非靶DNA股,且HNH域裂解靶DNA股。在一些实施例中,Cas9核酸酶包含多于一个RuvC域及/或多于一个HNH域。在一些实施例中,Cas9核酸酶为野生型Cas9。在一些实施例中,Cas9能够诱导靶DNA中的双股断裂。在某些实施例中,Cas核酸酶可裂解dsDNA,其可裂解dsDNA的一个股,或其可不具有DNA裂解酶或切口酶活性。一个示例性Cas9氨基酸序列提供呈SEQ ID NO:3形式。一个包括起始及终止密码子的示例性Cas9 mRNA ORF序列提供呈SEQ ID NO:4形式。一个适于包括在融合蛋白质中的示例性Cas9 mRNA编码序列提供呈SEQ ID NO:10形式。

[0230] 在一些实施例中,使用嵌合Cas核酸酶,其中该蛋白质的一个域或区经不同蛋白质的一部分置换。在一些实施例中,Cas核酸酶域可经来自诸如FokI的不同核酸酶的域置换。在一些实施例中,Cas核酸酶可为经修饰的核酸酶。

[0231] 在其它实施例中,Cas核酸酶可来自I型CRISPR/Cas系统。在一些实施例中,Cas核酸酶可为I型CRISPR/Cas系统的级联复合物的组分。在一些实施例中,Cas核酸酶可为Cas3蛋白质。在一些实施例中,Cas核酸酶可来自III型CRISPR/Cas系统。在一些实施例中,Cas核酸酶可具有RNA裂解活性。

[0232] 在一些实施例中,RNA引导的DNA结合剂具有单股切口酶活性,即可切割一个DNA股以产生单股断裂,亦称为“切口(nick)”。在一些实施例中,RNA引导的DNA结合剂包含Cas切口酶。切口酶为引起dsDNA中出现切口,即,切割一个股但不切割DNA双螺旋的另一股的酶。在一些实施例中,Cas切口酶为其中例如通过催化域的一或多种变化(例如点突变),使核酸内切酶活性位点不活化的Cas核酸酶的形式(例如上文所论述的Cas核酸酶)。参见例如关于Cas切口酶及示例性催化域变化的论述的美国专利第8,889,356号。在一些实施例中,Cas切口酶,诸如Cas9切口酶具有不活化的RuvC或HNH域。一个示例性Cas9切口酶氨基酸序列提供呈SEQ ID NO:6形式。一个包括起始及终止密码子的示例性Cas9切口酶mRNA ORF序列提供呈SEQ ID NO:7形式。一个适于包括在融合蛋白质中的示例性Cas9切口酶mRNA编码序列提供呈SEQ ID NO:11形式。

[0233] 在一些实施例中,RNA引导的DNA结合剂经修饰而仅含有一个功能核酸酶域。例如,该结合剂蛋白质可经修饰以使得核酸酶域中的一者经突变或完全或部分缺失以降低其核酸裂解活性。在一些实施例中,使用具有活性降低的RuvC域的切口酶。在一些实施例中,使用具有非活性RuvC域的切口酶。在一些实施例中,使用具有活性降低的HNH域的切口酶。在一些实施例中,使用具有非活性HNH域的切口酶。

[0234] 在一些实施例中,Cas蛋白质核酸酶域中的保守氨基酸经取代以降低或改变核酸

酶活性。在一些实施例中,Cas核酸酶可在RuvC或类RuvC核酸酶域中包含氨基酸取代。RuvC或类RuvC核酸酶域中的示例性氨基酸取代包括D10A(基于化脓链球菌Cas9蛋白质)。参见例如,Zetsche等人(2015)Cell Oct 22;163(3):759-771。在一些实施例中,Cas核酸酶可在HNH或类HNH核酸酶域中包含氨基酸取代。HNH或类HNH核酸酶域中的示例性氨基酸取代包括E762A、H840A、N863A、H983A及D986A(基于化脓链球菌Cas9蛋白质)。参见例如,Zetsche等人(2015)。其它示例性氨基酸取代包括D917A、E1006A及D1255A(基于新凶手弗朗西斯氏菌U112Cpf1(FnCpf1)序列(UniProtKB-A0Q7Q2(CPF1_FRATN))。

[0235] 在一些实施例中,将与一对分别与靶序列的有义股及反义股互补的引导RNA组合提供编码切口酶的mRNA。在此实施例中,引导RNA将切口酶导引至靶序列且通过在靶序列的相对股上产生切口而引入DSB(即双切口)。在一些实施例中,使用双重切口可提高特异性及减少脱靶效应。在一些实施例中,连同靶向DNA的相对股的两个独立引导RNA使用切口酶以在靶DNA中产生双重切口。在一些实施例中,连同经选择以非常接近的两个独立引导RNA使用切口酶以在靶DNA中产生双重切口。

[0236] 在一些实施例中,RNA引导的DNA结合剂缺乏裂解酶及切口酶活性。在一些实施例中,RNA引导的DNA结合剂包含dCas DNA结合多肽。dCas多肽具有DNA结合活性,而基本上缺乏催化(裂解酶/切口酶)活性。在一些实施例中,dCas多肽为dCas9多肽。在一些实施例中,缺乏裂解酶及切口酶活性的RNA引导的DNA结合剂或dCas DNA结合多肽为其中例如通过催化域的一或多种变化(例如点突变),使核酸内切酶活性位点不活化的Cas核酸酶的形式(例如上文所论述的Cas核酸酶)。参见例如US 2014/0186958 A1;US 2015/0166980 A1。示例性dCas9氨基酸序列提供呈SEQ ID NO:8形式。一个包括起始及终止密码子的示例性dCas9 mRNA ORF序列提供呈SEQ ID NO:9形式。一个适于包括在融合蛋白质中的示例性dCas9 mRNA编码序列提供呈SEQ ID NO:12形式。

[0237] 6. 异源功能域;核定位信号

[0238] 在一些实施例中,RNA引导的DNA结合剂包含一或多个异源功能域(例如为或包含融合多肽)。

[0239] 在一些实施例中,异源功能域可促进将RNA引导的DNA结合剂输送至细胞核中。例如,异源功能域可为核定位信号(NLS)。在一些实施例中,RNA引导的DNA结合剂可与1至10个NLS融合。在一些实施例中,RNA引导的DNA结合剂可与1至5个NLS融合。在一些实施例中,RNA引导的DNA结合剂可与一个NLS融合。在使用一个NLS的情况下,NLS可连接在RNA引导的DNA结合剂序列的N端或C端处。在一些实施例中,RNA引导的DNA结合剂可C端融合至至少一个NLS。NLS亦可插入RNA引导的DNA结合剂序列内。在其它实施例中,RNA引导的DNA结合剂可与多于一个NLS融合。在一些实施例中,RNA引导的DNA结合剂可与2、3、4或5个NLS融合。在一些实施例中,RNA引导的DNA结合剂可与两个NLS融合。在某些情况下,两个NLS可相同(例如两个SV40 NLS)或不同。在一些实施例中,RNA引导的DNA结合剂与连接在羧基末端处的两个SV40NLS序列融合。在一些实施例中,RNA引导的DNA结合剂可与两个NLS融合,一个NLS连接在N端处且一个连接在C端处。在一些实施例中,RNA引导的DNA结合剂可与3个NLS融合。在一些实施例中,RNA引导的DNA结合剂可不与NLS融合。在一些实施例中,NLS可为单联(monopartite)序列,诸如SV40 NLS、PKKKRKV(SEQ ID NO:78)或PKKKRRV(SEQ ID NO:90)。在一些实施例中,NLS可为双联序列,诸如核质蛋白的NLS、KRPAATKKAGQAKKKK(SEQ ID NO:

91)。在一些实施例中,NLS序列可包含LAAKRSRTT (SEQ ID NO:79)、QAAKRSRTT (SEQ ID NO:80)、PAPAKRERTT (SEQ ID NO:81)、QAAKRPRTT (SEQ ID NO:82)、RAAKRPRTT (SEQ ID NO:83)、AAAKRSWSMAA (SEQ ID NO:84)、AAAKRVWSMAF (SEQ ID NO:85)、AAAKRSWSMAF (SEQ ID NO:86)、AAAKRKYFAA (SEQ ID NO:87)、RAAKRKAF (SEQ ID NO:88)或RAAKRKYFAV (SEQ ID NO:89)。在一具体实施例中,单一PKKKRKV (SEQ ID NO:78) NLS可连接在RNA引导的DNA结合剂的C端处。一或多个连接子视情况包括在融合位点处。在一些实施例中,根据前述实施例中任一个的一或多个NLS与一或多个额外异源功能域,诸如下文所述的异源功能域中的任一个组合存在于RNA引导的DNA结合剂中。

[0240] 在一些实施例中,异源功能域可能能够调整RNA引导的DNA结合剂的胞内半衰期。在一些实施例中,RNA引导的DNA结合剂的半衰期可得到提高。在一些实施例中,RNA引导的DNA结合剂的半衰期可得到降低。在一些实施例中,异源功能域可能能够增加RNA引导的DNA结合剂的稳定性。在一些实施例中,异源功能域可能能够降低RNA引导的DNA结合剂的稳定性。在一些实施例中,异源功能域可作为蛋白质降解的信号肽。在一些实施例中,蛋白质降解可由蛋白水解酶,诸如蛋白酶体、溶酶体蛋白酶或钙蛋白酶蛋白酶介导。在一些实施例中,异源功能域可包含PEST序列。在一些实施例中,RNA引导的DNA结合剂可通过添加泛素或多泛素链来修饰。在一些实施例中,泛素可为类泛素蛋白质(UBL)。类泛素蛋白质的非限制性实例包括小类泛素修饰因子(SUMO)、泛素交叉反应蛋白(UCRP,亦称为干扰素刺激基因-15 (ISG15))、泛素相关修饰因子-1 (URM1)、神经元-前驱体-细胞表达的发育下调蛋白-8 (NEDD8,在酿酒酵母(*S.cerevisiae*)中亦称作Rub1)、人类白血球抗原F相关(FAT10)、自噬-8(ATG8)及自噬-12(ATG12)、Fau类泛素蛋白(FUB1)、膜锚定UBL(MUB)、泛素折叠修饰因子-1(UFM1)及类泛素蛋白-5(UBL5)。

[0241] 在一些实施例中,异源功能域可为标记域。标记域的非限制性实例包括荧光蛋白质、纯化标签、抗原决定基标签及报导基因序列。在一些实施例中,标记域可为荧光蛋白质。适合荧光蛋白质的非限制实例包括绿色荧光蛋白质(例如,GFP、GFP-2、tagGFP、turboGFP、sfGFP、EGFP、祖母绿(Emerald)、Azami绿(Azami Green)、单体Azami绿(Monomeric Azami Green)、CopGFP、AceGFP、ZsGreen1)、黄色荧光蛋白质(例如,YFP、EYFP、Citrine、Venus、YPet、PhiYFP、ZsYellow1)、蓝色荧光蛋白质(例如,EBFP、EBFP2、Azurite、mKalamal、GFPuv、蓝宝石色(Sapphire)、T-蓝宝石色(T-sapphire))、强化型蓝荧光蛋白质(例如,ECFP、Cerulean、CyPet、AmCyan1、Midoriishi强化型蓝(Midoriishi-Cyan))、红色荧光蛋白质(mKate、mKate2、mPlum、DsRed单体、mCherry、mRFP1、DsRed-Express、DsRed2、DsRed-单体、HcRed串色(HcRed-Tandem)、HcRed1、AsRed2、eqFP611、mRaspberry、mStrawberry、Jred)及橙色荧光蛋白质(mOrange、mKO、Kusabira橙色(Kusabira-Orange)、单体Kusabira橙色(Monomeric Kusabira-Orange)、mTangerine、tdTomato)或任何其它适合荧光蛋白质。在其它实施例中,标记域可为纯化标签及/或抗原决定基标签。非限制性的示例性标签包括谷胱甘肽-S-转移酶(glutathione-S-transferase,GST)、壳质结合蛋白(CBP)、麦芽糖结合蛋白(MBP)、硫氧还蛋白(thioredoxin,TRX)、聚(NANP)、串联亲和纯化(tandem affinity purification,TAP)标签、myc、AcV5、AU1、AU5、E、ECS、E2、FLAG、HA、nus、Saftag 1、Saftag 3、Strep、SBP、Glu-Glu、HSV、KT3、S、S1、T7、V5、VSV-G、6×His、8×His、生物素羧基载体蛋白质(BCCP)、聚His及调钙蛋白。非限制性的示例性报导基因包括谷胱甘肽-S-转移酶(GST)、

辣根过氧化物酶 (HRP)、氯霉素乙酰基转移酶 (CAT)、 β -半乳糖苷酶、 β -葡萄糖苷酸酶、荧光素酶或荧光蛋白质。

[0242] 在其它实施例中,异源功能域可将RNA引导的DNA结合剂靶向至特定细胞器、细胞型、组织或器官。在一些实施例中,异源功能域可将RNA引导的DNA结合剂靶向至线粒体。

[0243] 在其它实施例中,异源功能域可为效应子域。当RNA引导的DNA结合剂导引至其靶序列时,例如当Cas核酸酶通过gRNA导引至靶序列时,效应子域可修饰或影响靶序列。在一些实施例中,效应子域可选自核酸结合域、核酸酶域(例如非Cas核酸酶域)、表观遗传修饰域、转录活化域或转录抑制子域。在一些实施例中,异源功能域为核酸酶,诸如FokI核酸酶。参见例如美国专利第9,023,649号。在一些实施例中,异源功能域为转录活化因子或抑制子。参见例如Qi等人,“Repurposing CRISPR as an RNA-guided platform for sequence-specific control of gene expression”,*Cell* 152:1173-83(2013);Perez-Pinera等人,“RNA-guided gene activation by CRISPR-Cas9-based transcription factors”,*Nat.Methods*10:973-6(2013);Mali等人,“CAS9transcriptional activators for target specificity screening and paired nickases for cooperative genome engineering”,*Nat.Biotechnol.*31:833-8(2013);Gilbert等人,“CRISPR-mediated modular RNA-guided regulation of transcription in eukaryotes”,*Cell* 154:442-51(2013)。因此,RNA引导的DNA结合剂基本上变成可使用引导RNA导引以结合所需靶序列的转录因子。在某些实施例中,DNA修饰域为甲基化域,诸如去甲基化或甲基转移酶域。在某些实施例中,效应子域为DNA修饰域,诸如碱基编辑域。在特定实施例中,DNA修饰域为将特异性修饰引入DNA中的核酸编辑域,诸如脱氨酶域。参见例如WO 2015/089406;US 2016/0304846.WO 2015/089406及US 2016/0304846中所述的核酸编辑域、脱氨酶域及Cas9变体是以引用的方式并入本文中。

[0244] 7.UTR;Kozak序列

[0245] 在一些实施例中,mRNA包含至少一个来自羟基类固醇17- β 脱氢酶4(HSD17B4或HSD)的UTR,例如来自HSD的5'UTR。在一些实施例中,mRNA包含至少一个来自血球蛋白mRNA,例如人类 α 血球蛋白(HBA)mRNA、人类 β 血球蛋白(HBB)mRNA或有爪蟾 β 血球蛋白(XBG)mRNA的UTR。在一些实施例中,mRNA包含来自血球蛋白mRNA,诸如HBA、HBB或XBG的5'UTR、3'UTR、或5'与3'UTR。在一些实施例中,mRNA包含来自牛生长激素、细胞巨大病毒(CMV)、小鼠Hba-a1、HSD、白蛋白基因、HBA、HBB或XBG的5'UTR。在一些实施例中,mRNA包含来自牛生长激素、细胞巨大病毒(CMV)、小鼠Hba-a1、HSD、白蛋白基因、HBA、HBB或XBG的3'UTR。在一些实施例中,mRNA包含来自牛生长激素、细胞巨大病毒、小鼠Hba-a1、HSD、白蛋白基因、HBA、HBB、XBG、热休克蛋白90(Hsp90)、甘油醛3-磷酸脱氢酶(GAPDH)、 β -肌动蛋白、 α -微管蛋白、肿瘤蛋白质(p53)或表皮生长因子受体(EGFR)的5'与3'UTR。

[0246] 在一些实施例中,mRNA包含来自同一来源(例如组成型表达的mRNA,诸如肌动蛋白、白蛋白或血球蛋白(HBA、HBB或XBG))的5'及3'UTR。

[0247] 在一些实施例中,本文所揭示的mRNA包含与SEQ ID NO:32、34、36、38或41中的任一项有至少90%的一致性的5'UTR。在一些实施例中,本文所揭示的mRNA包含与SEQ ID NO:33、35、37、39或40中的任一项有至少90%的一致性的3'UTR。在一些实施例中,前述一致性程度中的任一项为至少95%、至少98%、至少99%或100%。在一些实施例中,本文所揭示的

mRNA包含具有SEQ ID NO:32、34、36、38或41中的任一项目的序列的5'UTR。在一些实施例中,本文所揭示的mRNA包含具有SEQ ID NO:33、35、37、39或40中的任一项目的序列的3'UTR。

[0248] 在一些实施例中,mRNA不包含5'UTR,例如在5'帽结构与起始密码子之间不存在额外核苷酸。在一些实施例中,mRNA在5'帽结构与起始密码子之间包含Kozak序列(下文所述),但不具有任何额外5'UTR。在一些实施例中,mRNA不包含3'UTR,例如在终止密码子与聚-A尾之间不存在额外核苷酸。

[0249] 在一些实施例中,mRNA包含Kozak序列。Kozak序列可影响转译起始及由mRNA转译的多肽的总产量。Kozak序列包括可作为起始密码子的甲硫氨酸密码子。最小Kozak序列为NNNRUGN,其中以下至少一项成立:第一个N为A或G且第二个N为G。在核苷酸序列中,R意指嘌呤(A或G)。在一些实施例中,Kozak序列为RNNRUGN、NNNRUGG、RNNRUGG、RNNAUGN、NNNAUGG或RNNAUGG。在一些实施例中,Kozak序列为具有零错配或呈小写字母形式的位置有至多一或两个错配的rccRUGg。在一些实施例中,Kozak序列为具有零错配或呈小写字母形式的位置有至多一或两个错配的rccAUGg。在一些实施例中,Kozak序列为具有零错配或呈小写字母形式的位置有至多一个、两个或三个错配的gccRccAUGG(SEQ ID NO:105的第4核苷酸至第13核苷酸)。在一些实施例中,Kozak序列为具有零错配或呈小写字母形式的位置有至多一个、二个、三个或四个错配的gccAccAUG。在一些实施例中,Kozak序列为GCCACCAUG。在一些实施例中,Kozak序列为具有零错配或呈小写字母形式的位置有至多一个、二个、三个或四个错配的gccgccRccAUGG(SEQ ID NO:105)。

[0250] 8. 示例性序列

[0251] 在一些实施例中,mRNA包含编码RNA引导的DNA结合剂的ORF,其中该ORF包含与SEQ ID NO:1、4、7、9、10、11、12、14、15、17、18、20、21、23、24、26、27、29、30、50、52、54、65、66或107-175中的任一项有至少90%的一致性的序列。在一些实施例中,mRNA包含编码RNA引导的DNA结合剂的ORF,其中该RNA引导的DNA结合剂包含与SEQ ID NO:3、6、8、13、16、19、22、25、28、68或186-196中的任一项有至少90%的一致性的氨基酸序列:,其中ORF的尿苷含量在其最小尿苷含量至最小尿苷含量的150%范围内,及/或其尿苷二核苷酸含量在其最小尿苷二核苷酸含量至最小尿苷二核苷酸含量的150%范围内。在一些实施例中,mRNA包含编码RNA引导的DNA结合剂的ORF,其中该RNA引导的DNA结合剂包含与SEQ ID NO:3、6、8、13、16、19、22、25、28、68或186—196中的任一项有至少90%的一致性的氨基酸序列:,其中ORF的腺嘌呤含量在其最小腺嘌呤含量至最小腺嘌呤含量的150%范围内,及/或其腺嘌呤二核苷酸含量在其最小腺嘌呤二核苷酸含量至最小腺嘌呤二核苷酸含量的150%范围内。在一些此类实施例中,腺嘌呤含量及尿苷核苷酸含量两者均小于或等于其相应最小值的150%。在一些实施例中,腺嘌呤含量及尿苷二核苷酸含量两者均小于或等于其相应最小值的150%。在一些实施例中,mRNA包含与SEQ ID NO:43、44、51、53、55-61或67中的任一项有至少90%的一致性的序列,其中该序列包含编码RNA引导的DNA结合剂的ORF。在一些实施例中,mRNA包含与SEQ ID NO:43、44、51、53、55-61或67中的任一项有至少90%的一致性的序列,其中该序列包含编码RNA引导的DNA结合剂的ORF,其中省去SEQ ID NO:43、44、51、53、55-61或67的前三个核苷酸。在一些实施例中,前述一致性程度中的任一项为至少95%、至少98%、至少99%或100%。

[0252] 在一些实施例中,mRNA包含编码RNA引导的DNA结合剂的ORF,其中该ORF与SEQ ID

NO:1、4、7、9、10、11、12、14、15、17、18、20、21、23、24、26、27、29、30、50、52、54、65、66或107-175中的任一项在至少其前30、50、70、100、150、200、250或300个核苷酸上有至少90%的一致性。前30、50、70、100、150、200、250或300个核苷酸是自起始密码子(典型地,ATG)的第一个核苷酸开始测量,以使得A为第1核苷酸,T为第2核苷酸等。在一些实施例中,开放阅读框架与SEQ ID NO:1、4、7、9、10、11、12、14、15、17、18、20、21、23、24、26、27、29、30、50、52、54、65、66或107-175中的任一项在至少其序列之前10%、12%、15%、20%、25%、30%或35%上具有至少90%的一致性。ORF的序列的长度为自起始密码子开始至终止密码子结束的核苷酸的数目,且其序列之前10%、12%、15%、20%、25%、30%或35%对应于自起始密码子的第一个核苷酸开始,构成总序列的长度的指定百分比的核苷酸的数目。

[0253] 在一些实施例中,包含编码RNA引导的DNA结合剂的ORF的mRNA包含与SEQ ID NO:43具有至少90%的一致性的序列,视情况地,其中SEQ ID NO:43的ORF(即SEQ ID NO:4)由SEQ ID NO:7、9、10、11、12、14、15、17、18、20、21、23、24、26、27、29、30、50、52、54、65、66或107-175中的任一项替代的ORF取代。

[0254] 在一些实施例中,包含编码RNA引导的DNA结合剂的ORF的mRNA包含与SEQ ID NO:44具有至少90%的一致性的序列,视情况地,其中SEQ ID NO:44的ORF(即SEQ ID NO:4)由SEQ ID NO:7、9、10、11、12、14、15、17、18、20、21、23、24、26、27、29、30、50、52、54、65、66或107-175中的任一项替代的ORF取代。

[0255] 在一些实施例中,包含编码RNA引导的DNA结合剂的ORF的mRNA包含与SEQ ID NO:56具有至少90%的一致性的序列,视情况地,其中SEQ ID NO:56的ORF(即SEQ ID NO:4)由SEQ ID NO:7、9、10、11、12、14、15、17、18、20、21、23、24、26、27、29、30、50、52、54、65、66或107-175中的任一项替代的ORF取代。

[0256] 在一些实施例中,包含编码RNA引导的DNA结合剂的ORF的mRNA包含与SEQ ID NO:57具有至少90%的一致性的序列,视情况地,其中SEQ ID NO:57的ORF(即SEQ ID NO:4)由SEQ ID NO:7、9、10、11、12、14、15、17、18、20、21、23、24、26、27、29、30、50、52、54、65、66或107-175中的任一项替代的ORF取代。

[0257] 在一些实施例中,包含编码RNA引导的DNA结合剂的ORF的mRNA包含与SEQ ID NO:58具有至少90%的一致性的序列,视情况地,其中SEQ ID NO:58的ORF(即SEQ ID NO:4)由SEQ ID NO:7、9、10、11、12、14、15、17、18、20、21、23、24、26、27、29、30、50、52、54、65、66或107-175中的任一项替代的ORF取代。

[0258] 在一些实施例中,包含编码RNA引导的DNA结合剂的ORF的mRNA包含与SEQ ID NO:59具有至少90%的一致性的序列,视情况地,其中SEQ ID NO:59的ORF(即SEQ ID NO:4)由SEQ ID NO:7、9、10、11、12、14、15、17、18、20、21、23、24、26、27、29、30、50、52、54、65、66或107-175中的任一项替代的ORF取代。

[0259] 在一些实施例中,包含编码RNA引导的DNA结合剂的ORF的mRNA包含与SEQ ID NO:60具有至少90%的一致性的序列,视情况地,其中SEQ ID NO:60的ORF(即SEQ ID NO:4)由SEQ ID NO:7、9、10、11、12、14、15、17、18、20、21、23、24、26、27、29、30、50、52、54、65、66或107-175中的任一项替代的ORF取代。

[0260] 在一些实施例中,包含编码RNA引导的DNA结合剂的ORF的mRNA包含与SEQ ID NO:61具有至少90%的一致性的序列,视情况地,其中SEQ ID NO:61的ORF(即SEQ ID NO:4)由

SEQ ID NO:7、9、10、11、12、14、15、17、18、20、21、23、24、26、27、29、30、50、52、54、65、66或107-175中的任一项替代的ORF取代。

[0261] 在一些实施例中,包含编码RNA引导的DNA结合剂的ORF的mRNA包含与SEQ ID NO:176具有至少90%的一致性的序列,视情况地,其中SEQ ID NO:176的ORF由SEQ ID NO:4、7、9、10、11、12、14、15、17、18、20、21、23、24、26、27、29、30、50、52、54、65、66或107—175中的任一项替代的ORF取代。

[0262] 在一些实施例中,包含编码RNA引导的DNA结合剂的ORF的mRNA包含与SEQ ID NO:177具有至少90%的一致性的序列,视情况地,其中SEQ ID NO:177的ORF由SEQ ID NO:4、7、9、10、11、12、14、15、17、18、20、21、23、24、26、27、29、30、50、52、54、65、66或107—175中的任一项替代的ORF取代。

[0263] 在一些实施例中,包含编码RNA引导的DNA结合剂的ORF的mRNA包含与SEQ ID NO:178具有至少90%的一致性的序列,视情况地,其中SEQ ID NO:178的ORF由SEQ ID NO:4、7、9、10、11、12、14、15、17、18、20、21、23、24、26、27、29、30、50、52、54、65、66或107-175中的任一项替代的ORF取代。

[0264] 在一些实施例中,包含编码RNA引导的DNA结合剂的ORF的mRNA包含与SEQ ID NO:179具有至少90%的一致性的序列,视情况地,其中SEQ ID NO:179的ORF由SEQ ID NO:4、7、9、10、11、12、14、15、17、18、20、21、23、24、26、27、29、30、50、52、54、65、66或107-175中的任一项替代的ORF取代。

[0265] 在一些实施例中,包含编码RNA引导的DNA结合剂的ORF的mRNA包含与SEQ ID NO:180具有至少90%的一致性的序列,视情况地,其中SEQ ID NO:180的ORF由SEQ ID NO:4、7、9、10、11、12、14、15、17、18、20、21、23、24、26、27、29、30、50、52、54、65、66或107-175中的任一项替代的ORF取代。

[0266] 在一些实施例中,包含编码RNA引导的DNA结合剂的ORF的mRNA包含与SEQ ID NO:181具有至少90%的一致性的序列,视情况地,其中SEQ ID NO:181的ORF由SEQ ID NO:4、7、9、10、11、12、14、15、17、18、20、21、23、24、26、27、29、30、50、52、54、65、66或107-175中的任一项替代的ORF取代。

[0267] 在一些实施例中,包含编码RNA引导的DNA结合剂的ORF的mRNA包含与SEQ ID NO:182具有至少90%的一致性的序列,视情况地,其中SEQ ID NO:182的ORF由SEQ ID NO:4、7、9、10、11、12、14、15、17、18、20、21、23、24、26、27、29、30、50、52、54、65、66或107-175中的任一项替代的ORF取代。

[0268] 在一些实施例中,包含编码RNA引导的DNA结合剂的ORF的mRNA包含与SEQ ID NO:183具有至少90%的一致性的序列,视情况地,其中SEQ ID NO:183的ORF由SEQ ID NO:4、7、9、10、11、12、14、15、17、18、20、21、23、24、26、27、29、30、50、52、54、65、66或107-175中的任一项替代的ORF取代:。

[0269] 在一些实施例中,包含编码RNA引导的DNA结合剂的ORF的mRNA包含与SEQ ID NO:184具有至少90%的一致性的序列,视情况地,其中SEQ ID NO:184的ORF由SEQ ID NO:4、7、9、10、11、12、14、15、17、18、20、21、23、24、26、27、29、30、50、52、54、65、66或107-175中的任一项替代的ORF取代。

[0270] 在一些实施例中,包含编码RNA引导的DNA结合剂的ORF的mRNA包含与SEQ ID NO:

185具有至少90%的一致性的序列,视情况地,其中SEQ ID NO:185的ORF由SEQ ID NO:4、7、9、10、11、12、14、15、17、18、20、21、23、24、26、27、29、30、50、52、54、65、66或107-175中的任一项替代的ORF取代。

[0271] 在一些实施例中,与SEQ ID NO 43、44、56-61或176-185的任选地经取代的序列的一致性程度为至少95%。在一些实施例中,与SEQ ID NO 43、44、56-61或176-185的任选地经取代的序列的一致性程度为至少98%。在一些实施例中,与SEQ ID NO 43、44、56-61或176-185的任选地经取代的序列的一致性程度为至少99%。在一些实施例中,与SEQ ID NO 43、44、56-61或176-185的任选地经取代的序列的一致性程度为100%。

[0272] 9. 聚-A尾

[0273] 在一些实施例中,mRNA进一步包含聚-A尾。在一些情况下,聚-A尾在聚-A尾中的一或多个位置处经一或多个非腺嘌呤核苷酸“锚”中断。聚-A尾可包含至少8个连续腺嘌呤核苷酸,且亦包含一或多个非腺嘌呤核苷酸。如本文所用,“非腺嘌呤核苷酸”是指不包含腺嘌呤的任何天然或非天然核苷酸。鸟嘌呤、胸腺嘧啶及胞嘧啶核苷酸为示例性非腺嘌呤核苷酸。因此,本文所述的mRNA上的聚-A尾可包含位于3'至编码RNA引导的DNA结合剂或相关序列的核苷酸的连续腺嘌呤核苷酸。在一些情况下,mRNA上的聚-A尾包含位于3'至编码RNA引导的DNA结合剂或相关序列的核苷酸的非连续腺嘌呤核苷酸,其中非腺嘌呤核苷酸以规则或不规则间隔中断腺嘌呤核苷酸。

[0274] 在一些实施例中,聚-A尾编码于用于活体外转录mRNA的质粒中且变成转录物的一部分。编码于质粒中的聚-A序列,即聚-A序列中的连续腺嘌呤核苷酸的数目可能并不精确,例如质粒中的100聚-A序列可能不会在经转录的mRNA中产生恰好100聚-A序列。在一些实施例中,聚-A尾未编码于质粒中,且通过PCR加尾或酶加尾,例如使用大肠杆菌聚(A)聚合酶来添加。

[0275] 在一些实施例中,一或多个非腺嘌呤核苷酸定位成中断连续腺嘌呤核苷酸,以使得聚(A)结合蛋白可结合于连续腺嘌呤核苷酸的一段。在一些实施例中,一或多个非腺嘌呤核苷酸位于至少8、9、10、11或12个连续腺嘌呤核苷酸之后。在一些实施例中,一或多个非腺嘌呤核苷酸位于至少8至50个连续腺嘌呤核苷酸之后。在一些实施例中,一或多个非腺嘌呤核苷酸位于至少8至100个连续腺嘌呤核苷酸之后。在一些实施例中,非腺嘌呤核苷酸在一个、两个、三个、四个、五个、六个或七个腺嘌呤核苷酸之后且之后为至少8个连续腺嘌呤核苷酸。

[0276] 本发明的聚-A尾可包含一个以下顺序:连续腺嘌呤核苷酸,继之以一或多个非腺嘌呤核苷酸,视情况继之以额外腺嘌呤核苷酸。

[0277] 在一些实施例中,聚-A尾包含或含有一个非腺嘌呤核苷酸或2至10个非腺嘌呤核苷酸的一个连续段。在一些实施例中,非腺嘌呤核苷酸位于至少8、9、10、11或12个连续腺嘌呤核苷酸之后。在一些情况下,一或多个非腺嘌呤核苷酸位于至少8至50个连续腺嘌呤核苷酸之后。在一些实施例中,一或多个非腺嘌呤核苷酸位于至少8、9、10、11、12、13、14、15、16、17、18、19、20、21、22、23、24、25、26、27、28、29、30、31、32、33、34、35、36、37、38、39、40、41、42、43、44、45、46、47、48、49或50个连续腺嘌呤核苷酸之后。

[0278] 在一些实施例中,非腺嘌呤核苷酸为鸟嘌呤、胞嘧啶或胸腺嘧啶。在一些情况下,非腺嘌呤核苷酸为鸟嘌呤核苷酸。在一些实施例中,非腺嘌呤核苷酸为胞嘧啶核苷酸。在一

些实施例中,非腺嘌呤核苷酸为胸腺嘧啶核苷酸。在其中存在多于一个非腺嘌呤核苷酸的一些情况下,非腺嘌呤核苷酸可选自:a) 鸟嘌呤及胸腺嘧啶核苷酸;b) 鸟嘌呤及胞嘧啶核苷酸;c) 胸腺嘧啶及胞嘧啶核苷酸;或d) 鸟嘌呤、胸腺嘧啶及胞嘧啶核苷酸。包含非腺嘌呤核苷酸的示例性聚-A尾提供呈SEQ ID NO:62形式。

[0279] 10. 经修饰的核苷酸

[0280] 在一些实施例中,mRNA在一些或所有尿苷位置处包含经修饰的尿苷。在一些实施例中,经修饰的尿苷为在5位处,例如用卤素或C1-C3烷氧基修饰的尿苷。在一些实施例中,经修饰的尿苷为在1位处,例如用C1-C3烷基修饰的假尿苷。经修饰的尿苷可为,例如假尿苷、N1-甲基-假尿苷、5-甲氧基尿苷、5-碘尿苷或其组合。在一些实施例中,经修饰的尿苷为5-甲氧基尿苷。在一些实施例中,经修饰的尿苷为5-碘尿苷。在一些实施例中,经修饰的尿苷为假尿苷。在一些实施例中,经修饰的尿苷为N1-甲基-假尿苷。在一些实施例中,经修饰的尿苷为假尿苷及N1-甲基-假尿苷的组合。在一些实施例中,经修饰的尿苷为假尿苷及5-甲氧基尿苷的组合。在一些实施例中,经修饰的尿苷为N1-甲基假尿苷及5-甲氧基尿苷的组合。在一些实施例中,经修饰的尿苷为5-碘尿苷及N1-甲基-假尿苷的组合。在一些实施例中,经修饰的尿苷为假尿苷及5-碘尿苷的组合。在一些实施例中,经修饰的尿苷为5-碘尿苷及5-甲氧基尿苷的组合。

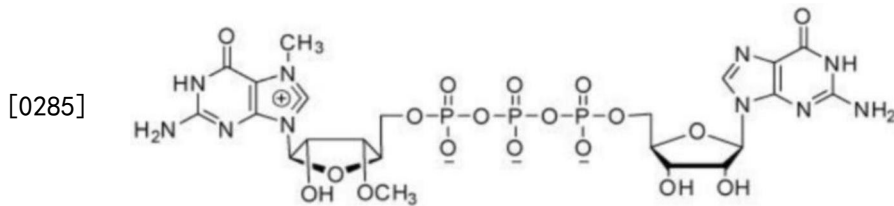
[0281] 在一些实施例中,根据本发明的mRNA中至少10%、15%、20%、25%、30%、35%、40%、45%、50%、55%、60%、65%、70%、75%、80%、85%、90%、95%、98%、99%或100%的尿苷位置为经修饰的尿苷。在一些实施例中,根据本发明的mRNA中10%至25%、15%至25%、25%至35%、35%至45%、45%至55%、55%至65%、65%至75%、75%至85%、85%至95%或90%至100%的尿苷位置为经修饰的尿苷,例如5-甲氧基尿苷、5-碘尿苷、N1-甲基假尿苷、假尿苷或其组合。在一些实施例中,根据本发明的mRNA中10%至25%、15%至25%、25%至35%、35%至45%、45%至55%、55%至65%、65%至75%、75%至85%、85%至95%或90%至100%的尿苷位置为5-甲氧基尿苷。在一些实施例中,根据本发明的mRNA中10%至25%、15%至25%、25%至35%、35%至45%、45%至55%、55%至65%、65%至75%、75%至85%、85%至95%或90%至100%的尿苷位置为假尿苷。在一些实施例中,根据本发明的mRNA中10%至25%、15%至25%、25%至35%、35%至45%、45%至55%、55%至65%、65%至75%、75%至85%、85%至95%或90%至100%的尿苷位置为N1-甲基假尿苷。在一些实施例中,根据本发明的mRNA中10%至25%、15%至25%、25%至35%、35%至45%、45%至55%、55%至65%、65%至75%、75%至85%、85%至95%或90%至100%的尿苷位置为5-碘尿苷。在一些实施例中,根据本发明的mRNA中10%至25%、15%至25%、25%至35%、35%至45%、45%至55%、55%至65%、65%至75%、75%至85%、85%至95%或90%至100%的尿苷位置为5-甲氧基尿苷,且其余者为N1-甲基假尿苷。在一些实施例中,根据本发明的mRNA中10%至25%、15%至25%、25%至35%、35%至45%、45%至55%、55%至65%、65%至75%、75%至85%、85%至95%或90%至100%的尿苷位置为5-碘尿苷,且其余者为N1-甲基假尿苷。

[0282] 11. 5'帽结构

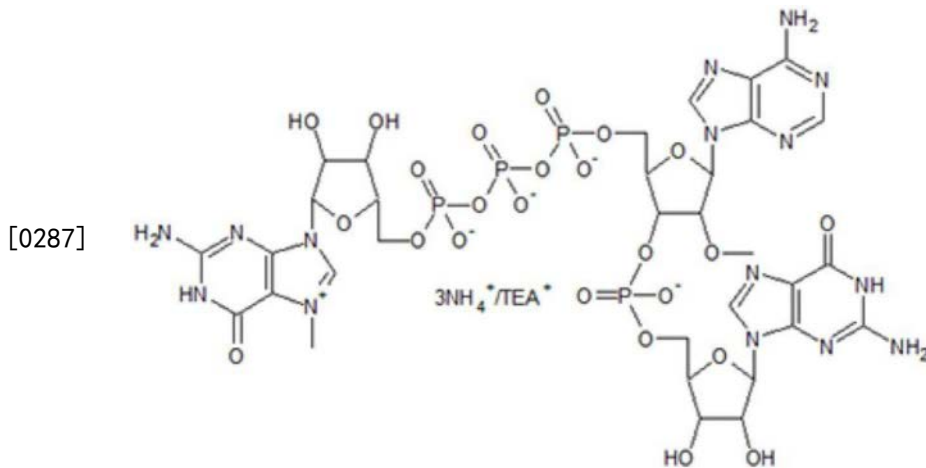
[0283] 在一些实施例中,本文所揭示的mRNA包含5'帽结构,诸如Cap0、Cap1或Cap2。5'帽结构通常为经由5'-三磷酸连接至mRNA的5'至3'链的第一个核苷酸,即第一个帽结构近端

核苷酸的5'位的7-甲基鸟嘌呤核糖核苷酸(其可经进一步修饰,如下文例如关于ARCA所论述)。在Cap0中,mRNA的第一及第二帽结构近端核苷酸的核糖两者均包含2'-羟基。在Cap1中,mRNA的第一及第二转录核苷酸的核糖分别包含2'-甲氧基及2'-羟基。在Cap2中,mRNA的第一及第二帽结构近端核苷酸的核糖两者均包含2'-甲氧基。参见例如Katibah等人(2014) Proc Natl Acad Sci USA 111(33):12025-30;Abbas等人(2017) Proc Natl Acad Sci USA 114(11):E2106-E2115。大多数内源高等真核生物mRNA,包括哺乳动物mRNA(诸如人类mRNA)包含Cap1或Cap2。归因于通过先天免疫系统的组分,诸如IFIT-1及IFIT-5识别为“非自体(non-self)”,Cap0及与Cap1及Cap2不同的其它帽结构在哺乳动物,诸如人类中可呈免疫原性,其可导致细胞介素,包括I型干扰素含量升高。先天免疫系统的组分,诸如IFIT-1及IFIT-5亦可与eIF4E竞争结合具有除Cap1或Cap2外的帽结构的mRNA,此可能会抑制mRNA的转译。

[0284] 帽结构可以共转录方式包括在内。例如,ARCA(抗反向帽结构类似物;Thermo Fisher Scientific目录号AM8045)为包含连接至鸟嘌呤核糖核苷酸的5'位的7-甲基鸟嘌呤3'-甲氧基-5'-三磷酸的帽结构类似物,其可在一开始时活体外并入转录物中。ARCA产生Cap0帽结构,其中第一个帽结构近端核苷酸的2'位为羟基。参见例如,Stepinski等人(2001)“Synthesis and properties of mRNAs containing the novel ‘anti-reverse’ cap analogs 7-methyl (3'-O-methyl)GpppG and 7-methyl (3'-deoxy)GpppG”,RNA 7:1486-1495。ARCA结构显示如下。



[0286] CleanCap™ AG (m7G (5')ppp (5') (2'OMeA) pG;TriLink Biotechnologies目录号N-7113)或CleanCap™ GG (m7G (5')ppp (5') (2'OMeG) pG;TriLink Biotechnologies目录号N-7133)可用于以共转录方式提供Cap1结构。CleanCap™ AG及CleanCap™ GG的3'-O-甲基化形式亦可分别以目录号N-7413及N-7433购自TriLink Biotechnologies。CleanCap™ AG结构显示如下。CleanCap™结构在本文中有时会使用上文所列的目录号的最后三个数字来指代(例如对于TriLink Biotechnologies目录号N-7113,使用“CleanCap™ 113”指代)。



[0288] 可替代地,可以转录后方式将帽结构添加至RNA。例如,牛痘加帽结构酶可在市面上购得(New England Biolabs目录号M2080S),且具有由其D1亚基提供的RNA三磷酸酶及鸟苷酰基转移酶活性及由其D12亚基提供的鸟嘌呤甲基转移酶活性。因此,在S-腺苷甲硫氨酸及GTP存在下,可将7-甲基鸟嘌呤添加至RNA,以产生Cap0。参见例如Guo, P.及Moss, B. (1990) Proc. Natl. Acad. Sci. USA 87, 4023-4027; Mao, X.及Shuman, S. (1994) J. Biol. Chem. 269, 24472-24479。对于帽结构及加帽结构方法的其它论述,参见例如W02017/053297及Ishikawa等人, Nucl. Acids. Symp. Ser. (2009) 第53期, 129-130。

[0289] 12. 引导RNA

[0290] 在一些实施例中,与本文所揭示的mRNA组合来提供至少一个引导RNA。在一些实施例中,引导RNA提供呈与mRNA分离的分子。在一些实施例中,引导RNA提供呈本文所揭示的mRNA的一部分,诸如UTR的一部分。在一些实施例中,至少一个引导RNA靶向TTR。

[0291] 在一些实施例中,引导RNA包含经修饰的sgRNA。在一些实施例中,sgRNA包含SEQ ID NO:74中所示出的修饰模式,其中N为任何天然或非天然核苷酸,且其中全部N'均包含引导序列。例如,SEQ ID NO:74涵盖在本文中,其中N'经本文所揭示的引导序列中的任一者置换。尽管N'经引导物的核苷酸取代,但修饰仍如SEQ ID NO:74中所示。即,尽管引导的核苷酸置换“N'”,但前三个核苷酸仍为经2'OMe修饰的,且在第一核苷酸与第二核苷酸、第二核苷酸与第三核苷酸及第三核苷酸与第四核苷酸之间存在硫代磷酸酯键。

[0292] 13. 脂质;调配物;递送

[0293] 在一些实施例中,将本文所述的单独或伴有一或多个引导RNA的mRNA调配于脂质纳米颗粒中或经由该脂质纳米颗粒施用;参见例如2017年3月30日申请的要求2016年3月30日申请的U.S.S.N.62/315,602的优先权,且标题为“CRISPR/CAS组分的脂质纳米颗粒调配物(LIPID NANOPARTICLE FORMULATIONS FOR CRISPR/CAS COMPONENTS)”的PCT/US2017/024973,该文献的内容以全文引用的方式并入本文中。可利用熟习此项技术者已知的能够将核苷酸递送至个体的任何脂质纳米颗粒(LNP)来施用本文所述的RNA,在一些实施例中,该RNA伴有一或多个引导RNA。在一些实施例中,将本文所述的单独或伴有一或多个引导RNA的mRNA调配于脂质体、纳米颗粒、胞外体或微囊泡中或经由脂质体、纳米颗粒、胞外体或微囊泡施用。乳液、微胞及悬浮液可为用于局部及/或表面递送的适合组合物。

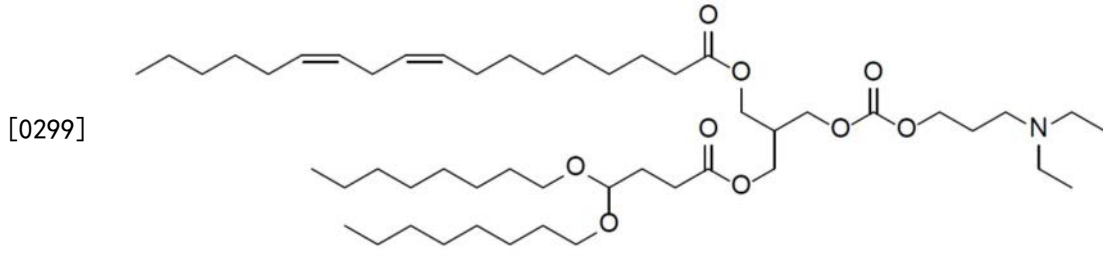
[0294] 本文揭示RNA的LNP调配物,包括CRISPR/Cas载荷(CRISPR/Cas cargo)的多个实施例。此类LNP调配物可包括(i) CCD脂质,诸如胺脂质、(ii) 中性脂质、(iii) 辅助脂质及(iv) 隐形脂质,诸如PEG脂质。LNP调配物的一些实施例包括“胺脂质”以及辅助脂质、中性脂质及隐形脂质,诸如PEG脂质。“脂质纳米颗粒”意谓包含通过分子间力彼此物理缔合的复数个(即多于一个)脂质分子的粒子。

[0295] CCD脂质

[0296] 用于将CRISPR/Cas mRNA及引导RNA组分递送至肝脏细胞的脂质组合物包含CCD脂质。

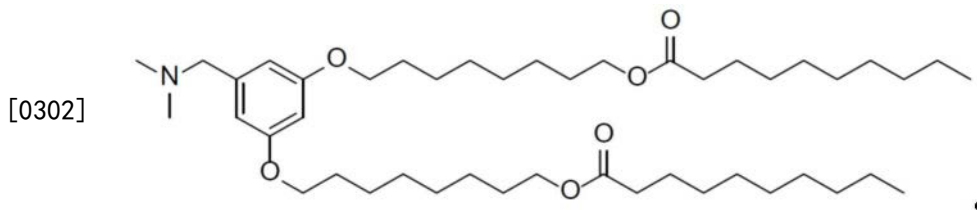
[0297] 在一些实施例中,CCD脂质为脂质A,其为十八-9,12-二烯酸(9Z,12Z)-3-((4,4-双(辛氧基)丁酰基)氧基)-2-(((3-(二乙胺基)丙氧基)羰基)氧基)甲基)丙酯,亦称作(9Z,12Z)-十八-9,12-二烯酸3-((4,4-双(辛氧基)丁酰基)氧基)-2-(((3-(二乙胺基)丙氧基)羰基)氧基)甲基)丙酯。

[0298] 脂质A可描绘为:



[0300] 可根据W02015/095340(例如第84-86页)合成脂质A。

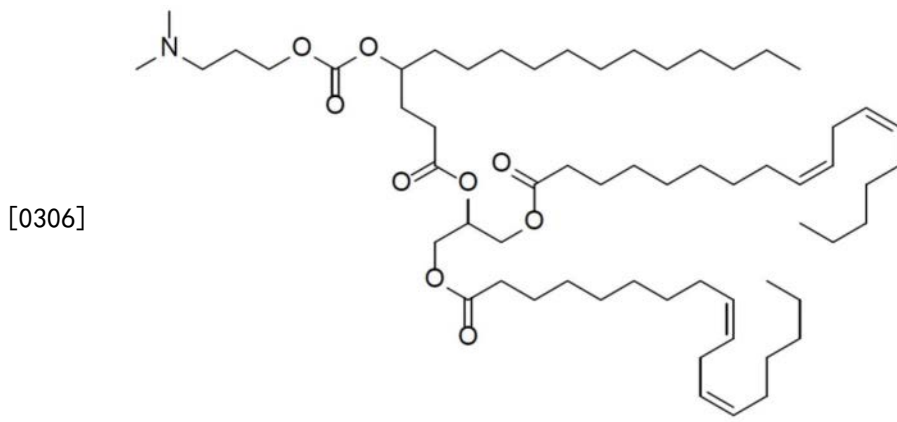
[0301] 在一些实施例中,CCD脂质为脂质B,其为((5-((二甲胺基)甲基)-1,3-伸苯基)双(氧基))双(辛烷-8,1-二基)双(癸酸酯),亦称作((5-((二甲胺基)甲基)-1,3-伸苯基)双(氧基))双(辛烷-8,1-二基)双(癸酸酯)。脂质B可描绘为:



[0303] 可根据W02014/136086(例如第107-109页)合成脂质B。

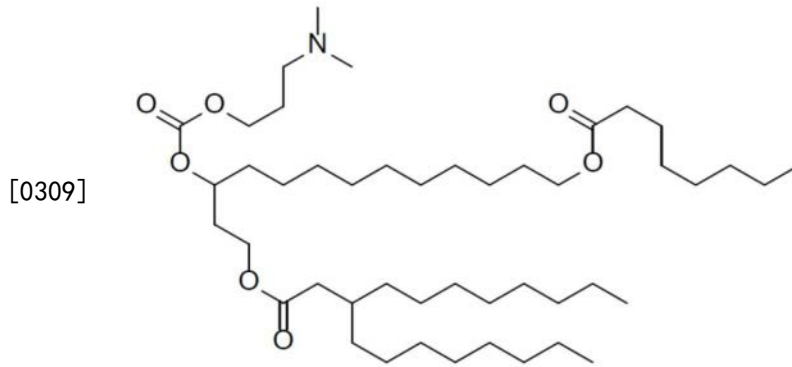
[0304] 在一些实施例中,CCD脂质为脂质C,其为2-((4-(((3-(二甲胺基)丙氧基)羰基)氧基)十六酰基)氧基)丙烷-1,3-二基(9Z,9'Z,12Z,12'Z)-双(十八-9,12-二烯酸酯)。

[0305] 脂质C可描绘为:



[0307] 在一些实施例中,CCD脂质为脂质D,其为3-辛基十一烷酸3-(((3-(二甲胺基)丙氧基)羰基)氧基)-13-(辛酰氧基)十三酯。

[0308] 脂质D可描绘为:



[0310] 可根据W02015/095340合成脂质C及脂质D。

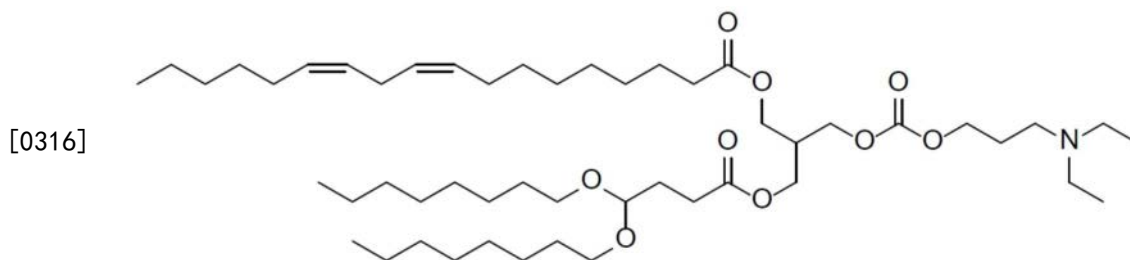
[0311] CCD脂质亦可为脂质A、脂质B、脂质C或脂质D的等效物。在某些实施例中,CCD脂质为脂质A的等效物、脂质B的等效物、脂质C的等效物或脂质D的等效物。

[0312] 胺脂质

[0313] 在一些实施例中,用于生物活性剂的递送的LNP组合物包含“胺脂质”,其定义为脂质A或其等效物,包括脂质A的缩醛类似物。

[0314] 在一些实施例中,胺脂质为脂质A,其为十八-9,12-二烯酸(9Z,12Z)-3-((4,4-双(辛氧基)丁酰基)氧基)-2-(((3-(二乙胺基)丙氧基)羰基)氧基)甲基)丙酯,亦称作(9Z,12Z)-十八-9,12-二烯酸3-((4,4-双(辛氧基)丁酰基)氧基)-2-(((3-(二乙胺基)丙氧基)羰基)氧基)甲基)丙酯。

[0315] 脂质A可描绘为:



[0317] 可根据W02015/095340(例如第84-86页)合成脂质A。在某些实施例中,胺脂质为脂质A的等效物。

[0318] 在某些实施例中,胺脂质为脂质A的类似物。在某些实施例中,脂质A类似物为脂质A的缩醛类似物。在特定LNP组合物中,缩醛类似物为C4-C12缩醛类似物。在一些实施例中,缩醛类似物为C5-C12缩醛类似物。在其它实施例中,缩醛类似物为C5-C10缩醛类似物。在其它实施例中,缩醛类似物是选自C4、C5、C6、C7、C9、C10、C11及C12缩醛类似物。

[0319] 适用于本文所述的LNP中的胺脂质可活体内生物降解。胺脂质具有低毒性(例如以大于或等于10mg/kg的量在动物模型中得到耐受而不具有不良作用)。在某些实施例中,包含胺脂质的LNP包括其中会在8、10、12、24或48小时或3、4、5、6、7或10天内自血浆清除至少75%的胺脂质的LNP。在某些实施例中,包含胺脂质的LNP包括其中会在8、10、12、24或48小时或3、4、5、6、7或10天内自血浆清除至少50%的mRNA或gRNA的LNP。在某些实施例中,包含胺脂质的LNP包括其中例如通过测量脂质(例如,胺脂质)、RNA(例如mRNA)或其它组分,会在8、10、12、24或48小时或3、4、5、6、7或10天内自血浆清除至少50%的LNP的LNP。在某些实施例中,测量LNP的经脂质囊封组分对游离脂质组分、RNA组分或核酸组分。

[0320] 脂质清除率可如文献中所述来测量。参见Maier, M.A. 等人 *Biodegradable Lipids Enabling Rapidly Eliminated Lipid Nanoparticles for Systemic Delivery of RNAi Therapeutics*. *Mol. Ther.* 2013, 21 (8), 1570-78 (“Maier”)。例如, 在Maier中, 以0.3mg/kg通过静脉内快速注射经由外侧尾部静脉向六至八周龄雄性C57BL/6小鼠施用含有靶向荧光素酶的siRNA的LNP-siRNA系统。在给药后0.083、0.25、0.5、1、2、4、8、24、48、96及168小时收集血液、肝脏及脾脏样本。在收集组织之前向小鼠灌注生理盐水且处理血液样本以获得血浆。处理且通过LC-MS分析所有样本。此外, Maier描述了一种用于评定施用LNP-siRNA调配物之后的毒性的程序。例如, 以0、1、3、5及10mg/kg (5只动物/组) 经由单一静脉内快速注射以5mL/kg的剂量体积向雄性史泊格-多利大鼠 (Sprague-Dawley rat) 施用靶向荧光素酶的siRNA。在24小时之后, 由清醒的动物的颈静脉获得约1mL血液且分离血清。在给药后72小时, 将所有动物安乐死以用于尸体剖检。进行临床症状、体重、血清化学、器官重量及组织病理学的评定。尽管Maier描述了用于评定siRNA-LNP调配物的方法, 但此等方法亦可适用于评定本发明的LNP组合物的投药的清除率、药物动力学及毒性。

[0321] 胺脂质引起增加的清除速率。在一些实施例中, 清除速率为脂质清除速率, 例如自血液、血清或血浆清除胺脂质的速率。在一些实施例中, 清除速率为RNA清除速率, 例如自血液、血清或血浆清除mRNA或gRNA的速率。在一些实施例中, 清除速率为自血液、血清或血浆清除LNP的速率。在一些实施例中, 清除速率为自组织, 诸如肝脏组织或脾脏组织清除LNP的速率。在某些实施例中, 清除速率的高速率会产生不具有显著不良作用的安全分布。胺脂质减少循环中及组织中的LNP积聚。在一些实施例中, 循环中及组织中的LNP积聚减少会产生不具有显著不良作用的安全分布。

[0322] 可视本发明的胺脂质所处的培养基的pH而定, 对该胺脂质进行电离。例如, 在弱酸性培养基中, 胺脂质可经质子化且因此带有正电荷。相反地, 在弱碱性培养基中, 诸如其中pH为大约7.35的血液中, 胺脂质可不经质子化且因此不带电荷。在一些实施例中, 可在至少约9的pH下对本发明的胺脂质进行质子化。在一些实施例中, 可在至少约10的pH下对本发明的胺脂质进行质子化。

[0323] 胺脂质带有电荷的能力与其固有pKa有关。例如, 本发明的胺脂质可各自独立地具有在约5.8至约6.2范围内的pKa。例如, 本发明的胺脂质可各自独立地具有在约5.8至约6.5范围内的pKa。当已发现, pKa在约5.1至约7.4范围内的阳离子型脂质对将载荷活体内递送至例如肝脏为有效的时, 此可为有利的。此外, 已发现, pKa在约5.3至约6.4范围内的阳离子型脂质对活体内递送至例如肿瘤为有效的。参见例如W02014/136086。

[0324] 其它脂质

[0325] 适用于本发明的脂质组合物中的“中性脂质”包括例如多种中性、不带电荷或两性离子型脂质。适用于本发明中的中性磷脂的实例包括 (但不限于) 5-十七基苯-1,3-二醇 (间苯二酚)、二软脂酰基磷脂酰胆碱 (DPPC)、二硬脂酰基磷脂酰胆碱 (DSPC)、磷酸胆碱 (DOPC)、二肉豆蔻酰基磷脂酰胆碱 (DMPC)、磷脂酰胆碱 (PLPC)、1,2-二硬脂酰基-sn-甘油-3-磷酸胆碱 (DAPC)、磷脂酰乙醇胺 (PE)、卵磷脂酰胆碱 (EPC)、二月桂酰基磷脂酰胆碱 (DLPC)、1-肉豆蔻酰基-2-软脂酰基磷脂酰胆碱 (MPPC)、1-软脂酰基-2-肉豆蔻酰基磷脂酰胆碱 (PMPC)、1-软脂酰基-2-硬脂酰基磷脂酰胆碱 (PSPC)、1,2-二花生酰基-sn-甘油-3-磷酸胆碱 (DBPC)、1-硬脂酰基-2-软脂酰基磷脂酰胆碱 (SPPC)、1,2-二十碳烯酰基-sn-甘油-3-磷酸胆碱

(DEPC)、软脂酰油酰基磷脂酰胆碱(POPC)、溶血磷脂酰基胆碱、二油酰基磷脂酰乙醇胺(DOPE)、二亚油酰基磷脂酰胆碱二硬脂酰基磷脂酰乙醇胺(DSPE)、二肉豆蔻酰基磷脂酰乙醇胺(DMPE)、二软脂酰基磷脂酰乙醇胺(DPPE)、软脂酰油酰基磷脂酰乙醇胺(POPE)、溶血磷脂酰乙醇胺及其组合。在一个实施例中,中性磷脂可选自由以下组成的群:二硬脂酰基磷脂酰胆碱(DSPC)及二肉豆蔻酰基磷脂酰乙醇胺(DMPE)。在另一实施例中,中性磷脂可为二硬脂酰基磷脂酰胆碱(DSPC)。

[0326] “辅助脂质”包括类固醇、固醇及烷基间苯二酚。适用于本发明中的辅助脂质包括(但不限于)胆固醇、5-十七基间苯二酚及胆固醇半丁二酸酯。在一个实施例中,辅助脂质可为胆固醇。在一个实施例中,辅助脂质可为胆固醇半丁二酸酯。

[0327] “隐形脂质”为改变纳米颗粒可在活体内(例如血液中)存在的时长的脂质。隐形脂质可通过例如减少粒子聚集且控制粒度辅助调配过程。本文中所用的隐形脂质可调节LNP的药物动力学特性。适用于本发明中的隐形脂质包括(但不限于)具有连接至脂质部分的亲水性头基的隐形脂质。适用于本发明脂质组合物的隐形脂质及关于此类脂质的生物化学的信息可见于Romberg等人, *Pharmaceutical Research*, 第25卷, 第1期, 2008, 第55-71页及Hoekstra等人, *Biochimica et Biophysica Acta* 1660(2004) 41-52。额外适合PEG脂质揭示于例如WO 2006/007712中。

[0328] 在一个实施例中,隐形脂质的亲水性头基包含选自基于PEG的聚合物的聚合物部分。隐形脂质可包含脂质部分。在一些实施例中,隐形脂质为PEG脂质。

[0329] 在一个实施例中,隐形脂质包含选自基于以下的聚合物的聚合物部分:PEG(有时称作聚(环氧乙烷))、聚(恶唑啉)、聚(乙烯醇)、聚(甘油)、聚(N-乙基吡咯啉酮)、聚氨基酸及聚[N-(2-羟丙基)甲基丙烯酰胺]。

[0330] 在一个实施例中,PEG脂质包含基于PEG(有时称作聚(环氧乙烷))的聚合物部分。

[0331] PEG脂质进一步包含脂质部分。在一些实施例中,脂质部分可源自二酰基甘油或二酰基甘油酰胺(diacylglycamide),包括包含二烷基甘油基或二烷基甘油酰胺基的那些,该基团具有独立地包含约C4至约C40饱和或不饱和碳原子的烷基链长,其中该链可包含一或多个官能基,诸如酰胺基或酯基。在一些实施例中,烷基链长度包含约C10至C20。二烷基甘油或二烷基甘油酰胺基可进一步包含一或多个经取代的烷基。链长可为对称或不对称的。

[0332] 除非另外指明,否则如本文所用,术语“PEG”意指任何聚乙二醇或其它聚伸烷醚聚合物。在一个实施例中,PEG为乙二醇或环氧乙烷的视情况经取代的直链或分支链聚合物。在一个实施例中,PEG为未经取代的。在一个实施例中,PEG经例如一或多个烷基、烷氧基、酰基、羟基、或芳基取代。在一个实施例中,该术语包括PEG共聚物,诸如PEG-聚胺基甲酸酯或PEG-聚丙烯(参见例如J.Milton Harris, *Poly(ethylene glycol) chemistry: biotechnical and biomedical applications*(1992));在另一实施例中,该术语不包括PEG共聚物。在一个实施例中,PEG的分子量为约130至约50,000,在一子实施例中,约150至约30,000,在一子实施例中,约150至约20,000,在一子实施例中,约150至约15,000,在一子实施例中,约150至约10,000,在一子实施例中,约150至约6,000,在一子实施例中,约150至约5,000,在一子实施例中,约150至约4,000,在一子实施例中,约150至约3,000,在一子实施例中,约300至约3,000,在一子实施例中,约1,000至约3,000且在一子实施例中,约1,500至约2,500。

[0333] 在某些实施例中,PEG(例如与脂质部分或脂质,诸如隐形脂质结合)、为“PEG-2K”,亦称为“PEG2000”,其具有约2,000道尔顿的平均分子量。PEG-2K在本文中由下式(I)表示,其中n为45,意谓经数量平均化的聚合度包含约45个亚基。然而,亦可使用此项技术中已知的其它PEG实施例,包括例如其中经数量平均化的聚合度包含约23个亚基(n=23)及/或68个亚基(n=68)的那些。在一些实施例中,n可在约30至约60范围内。在一些实施例中,n可在约35至约55范围内。在一些实施例中,n可在约40至约50范围内。在一些实施例中,n可在约42至约48范围内。在一些实施例中,n可为45。在一些实施例中,R可选自H、经取代的烷基及未经取代的烷基。在一些实施例中,R可为未经取代的烷基。在一些实施例中,R可为甲基。

[0334] 在本文中描述的任一实施例中,PEG脂质可选自PEG-二月桂酰甘油、PEG-二肉豆蔻酰甘油(PEG-DMG)(目录号GM-020,来自日本东京的NOF)、PEG-二软脂酰甘油、PEG-二硬脂酰甘油(PEG-DSPE)(目录号DSPE-020CN,日本东京的NOF)、PEG-二月桂酰甘油酰胺、PEG-二肉豆蔻酰甘油酰胺、PEG-二软脂酰甘油酰胺、及PEG-二硬脂酰甘油酰胺、PEG-胆固醇(1-[8'-(胆甾-5-烯-3[β]-氧基)甲酰胺基-3',6'-二氧杂辛烷]胺甲酰基-[ω]-甲基-聚(乙二醇)、PEG-DMB(3,4-双十四氧基苯甲基-[ω]-甲基-聚(乙二醇)醚)、1,2-二肉豆蔻酰基-sn-甘油-3-磷酸乙醇胺-N-[甲氧基(聚乙二醇)-2000](PEG2k-DMG)(目录号880150P,来自美国亚拉巴马州阿拉巴斯特(Alabaster,Alabama,USA)的Avanti Polar Lipids)、1,2-二硬脂酰基-sn-甘油-3-磷酸乙醇胺-N-[甲氧基(聚乙二醇)-2000](PEG2k-DSPE)(目录号880120C,来自美国亚拉巴马州阿拉巴斯特的Avanti Polar Lipids)、1,2-二硬脂酰基-sn-甘油,甲氧基聚乙二醇(PEG2k-DSG;GS-020,日本东京的NOF)、聚(乙二醇)-2000-二甲基丙烯酸酯(PEG2k-DMA)、及1,2-二硬脂氧基丙基-3-胺-N-[甲氧基(聚乙二醇)-2000](PEG2k-DSA)。在一个实施例中,PEG脂质可为PEG2k-DMG。在一些实施例中,PEG脂质可为PEG2k-DSG。在一个实施例中,PEG脂质可为PEG2k-DSPE。在一个实施例中,PEG脂质可为PEG2k-DMA。在一个实施例中,PEG脂质可为PEG2k-C-DMA。在一个实施例中,PEG脂质可为化合物S027,其揭示于WO2016/010840(第[00240]至[00244]段)中。在一个实施例中,PEG脂质可为PEG2k-DSA。在一个实施例中,PEG脂质可为PEG2k-C11。在一些实施例中,PEG脂质可为PEG2k-C14。在一些实施例中,PEG脂质可为PEG2k-C16。在一些实施例中,PEG脂质可为PEG2k-C18。

[0335] LNP可含有(i)用于囊封及用于核内体逃逸(endosomal escape)的胺脂质、(ii)用于稳定的中性脂质、(iii)亦用于稳定的辅助脂质及(iv)隐形脂质,诸如PEG脂质。

[0336] 在一些实施例中,LNP组合物可包含RNA组分,其包括以下中的一种或多种:RNA引导的DNA结合剂、Cas核酸酶mRNA、2类Cas核酸酶mRNA、Cas9 mRNA及gRNA。在一些实施例中,LNP组合物可包括2类Cas核酸酶及gRNA作为RNA组分。在某些实施例中,LNP组合物可包含RNA组分、胺脂质、辅助脂质、中性脂质及隐形脂质。在某些LNP组合物中,辅助脂质为胆固醇。在其它组合物中,中性脂质为DSPC。在其它实施例中,隐形脂质为PEG2k-DMG或PEG2k-C11。在某些实施例中,LNP组合物包含脂质A或脂质A的等效物;辅助脂质;中性脂质;隐形脂质;及引导RNA。在某些组合物中,胺脂质为脂质A。在某些组合物中,胺脂质为脂质A或其缩醛类似物;辅助脂质为胆固醇;中性脂质为DSPC且隐形脂质为PEG2k-DMG。

[0337] 在某些实施例中,根据调配物中脂质组分的相应摩尔比描述脂质组合物。本发明的实施例提供根据调配物中脂质组分的相应摩尔比描述的脂质组合物。在一个实施例中,胺脂质的mol%可为约30mol%至约60mol%。在一个实施例中,胺脂质的mol%可为约

40mol%至约60mol%。在一个实施例中,胺脂质的mol%可为约45mol%至约60mol%。在一个实施例中,胺脂质的mol%可为约50mol%至约60mol%。在一个实施例中,胺脂质的mol%可为约55mol%至约60mol%。在一个实施例中,胺脂质的mol%可为约50mol%至约55mol%。在一个实施例中,胺脂质的mol%可为约50mol%。在一个实施例中,胺脂质的mol%可为约55mol%。在一些实施例中,LNP批料的胺脂质mol%将为目标mol%的 $\pm 30\%$ 、 $\pm 25\%$ 、 $\pm 20\%$ 、 $\pm 15\%$ 、 $\pm 10\%$ 、 $\pm 5\%$ 或 $\pm 2.5\%$ 。在一些实施例中,LNP批料的胺脂质mol%将为目标mol%的 $\pm 4\text{mol}\%$ 、 $\pm 3\text{mol}\%$ 、 $\pm 2\text{mol}\%$ 、 $\pm 1.5\text{mol}\%$ 、 $\pm 1\text{mol}\%$ 、 $\pm 0.5\text{mol}\%$ 或 $\pm 0.25\text{mol}\%$ 。所有mol%数均以LNP组合物的脂质组分的一定分率给定。在某些实施例中,胺脂质mol%的LNP批次间变化率将低于15%、低于10%或小于5%。

[0338] 在一个实施例中,中性脂质的mol%可为约5mol%至约15mol%。在一个实施例中,中性脂质的mol%可为约7mol%至约12mol%。在一个实施例中,中性脂质的mol%可为约9mol%。在一些实施例中,LNP批料的中性脂质mol%将为目标中性脂质mol%的 $\pm 30\%$ 、 $\pm 25\%$ 、 $\pm 20\%$ 、 $\pm 15\%$ 、 $\pm 10\%$ 、 $\pm 5\%$ 或 $\pm 2.5\%$ 。在某些实施例中,LNP批次间变化率将低于15%、低于10%或小于5%。

[0339] 在一个实施例中,辅助脂质的mol%可为约20mol%至约60mol%。在一个实施例中,辅助脂质的mol%可为约25mol%至约55mol%。在一个实施例中,辅助脂质的mol%可为约25mol%至约50mol%。在一个实施例中,辅助脂质的mol%可为约25mol%至约40mol%。在一个实施例中,辅助脂质的mol%可为约30mol%至约50mol%。在一个实施例中,辅助脂质的mol%可为约30mol%至约40mol%。在一个实施例中,基于胺脂质、中性脂质及PEG脂质浓度而调整辅助脂质的mol%以使脂质组分达100mol%。在一些实施例中,LNP批料的辅助脂质mol%将为目标mol%的 $\pm 30\%$ 、 $\pm 25\%$ 、 $\pm 20\%$ 、 $\pm 15\%$ 、 $\pm 10\%$ 、 $\pm 5\%$ 或 $\pm 2.5\%$ 。在某些实施例中,LNP批次间变化率将低于15%、低于10%或小于5%。

[0340] 在一个实施例中,PEG脂质的mol%可为约1mol%至约10mol%。在一个实施例中,PEG脂质的mol%可为约2mol%至约10mol%。在一个实施例中,PEG脂质的mol%可为约2mol%至约8mol%。在一个实施例中,PEG脂质的mol%可为约2mol%至约4mol%。在一个实施例中,PEG脂质的mol%可为约2.5mol%至约4mol%。在一个实施例中,PEG脂质的mol%可为约3mol%。在一个实施例中,PEG脂质的mol%可为约2.5mol%。在一些实施例中,LNP批料的PEG脂质mol%将为目标PEG脂质mol%的 $\pm 30\%$ 、 $\pm 25\%$ 、 $\pm 20\%$ 、 $\pm 15\%$ 、 $\pm 10\%$ 、 $\pm 5\%$ 或 $\pm 2.5\%$ 。在某些实施例中,LNP批次间变化率将低于15%、低于10%或小于5%。

[0341] 在某些实施例中,载荷包括编码RNA引导的DNA结合剂(例如Cas核酸酶、2类Cas核酸酶或Cas9)的mRNA,及gRNA或编码gRNA的核酸,或mRNA及gRNA的组合。在一个实施例中,LNP组合物可包含脂质A或其等效物。在一些方面中,胺脂质为脂质A。在一些方面中,胺脂质为脂质A等效物,例如脂质A的类似物。在某些方面中,胺脂质为脂质A的缩醛类似物。在各种实施例中,LNP组合物包含胺脂质、中性脂质、辅助脂质及PEG脂质。在某些实施例中,辅助脂质为胆固醇。在某些实施例中,中性脂质为DSPC。在特定实施例中,PEG脂质为PEG2k-DMG。在一些实施例中,LNP组合物可包含脂质A、辅助脂质、中性脂质及PEG脂质。在一些实施例中,LNP组合物包含胺脂质、DSPC、胆固醇及PEG脂质。在一些实施例中,LNP组合物包含PEG脂质,该脂质包含DMG。在某些实施例中,胺脂质选自脂质A,及脂质A的等效物,包括脂质A的缩醛类似物。在其它实施例中,LNP组合物包含脂质A、胆固醇、DSPC及PEG2k-DMG。

[0342] 本发明的实施例亦提供根据待囊封的核酸的胺脂质的带正电胺基(N)与带负电磷酸基团(P)之间的摩尔比描述的脂质组合物。此可由方程式N/P数学表示。在一些实施例中,LNP组合物可包含脂质组分,其包含胺脂质、辅助脂质、中性脂质及隐形脂质;及核酸组分,其中N/P比为约3至10。在一些实施例中,LNP组合物可包含脂质组分,其包含胺脂质、辅助脂质、中性脂质及隐形脂质;及RNA组分,其中N/P比为约3至10。在一个实施例中,N/P比可为约5至7。在一个实施例中,N/P比可为约4.5至8。在一个实施例中,N/P比可为约6。在一个实施例中,N/P比可为 6 ± 1 。在一个实施例中,N/P比可为 6 ± 0.5 。在一些实施例中,N/P比将为目标N/P比的 $\pm 30\%$ 、 $\pm 25\%$ 、 $\pm 20\%$ 、 $\pm 15\%$ 、 $\pm 10\%$ 、 $\pm 5\%$ 或 $\pm 2.5\%$ 。在某些实施例中,LNP批次间变化率将低于15%、低于10%或小于5%。

[0343] 在一些实施例中,RNA组分可包含mRNA,诸如本文所揭示的mRNA,例如编码Cas核酸酶的mRNA。在一个实施例中,RNA组分可包含Cas9 mRNA。在一些包含编码Cas核酸酶的mRNA的组合物中,LNP进一步包含gRNA核酸,诸如gRNA。在一些实施例中,RNA组分包含Cas核酸酶mRNA及gRNA。在某些实施例中,RNA组分包含2类Cas核酸酶mRNA及gRNA。

[0344] 在某些实施例中,LNP组合物可包含编码Cas核酸酶(诸如2类Cas核酸酶)的mRNA、胺脂质、辅助脂质、中性脂质及PEG脂质。在某些包含编码Cas核酸酶(诸如2类Cas核酸酶)的mRNA的LNP组合物中,辅助脂质为胆固醇。在其它包含编码Cas核酸酶(诸如2类Cas核酸酶)的mRNA的组合物中,中性脂质为DSPC。在其它包含编码Cas核酸酶(诸如2类Cas核酸酶)的mRNA的实施例中,PEG脂质为PEG2k-DMG或PEG2k-C11。在包含编码Cas核酸酶(诸如2类Cas核酸酶)的mRNA的特定组合物中,胺脂质选自脂质A及其等效物,诸如脂质A的缩醛类似物。

[0345] 在一些实施例中,LNP组合物可包含gRNA。在某些实施例中,LNP组合物可包含胺脂质、gRNA、辅助脂质、中性脂质及PEG脂质。在某些包含gRNA的LNP组合物中,辅助脂质为胆固醇。在某些包含gRNA的组合物中,中性脂质为DSPC。在其它包含gRNA的实施例中,PEG脂质为PEG2k-DMG或PEG2k-C11。在某些实施例中,胺脂质选自脂质A及其等效物,诸如脂质A的缩醛类似物。

[0346] 在一个实施例中,LNP组合物可包含sgRNA。在一个实施例中,LNP组合物可包含Cas9 sgRNA。在一个实施例中,LNP组合物可包含Cpf1 sgRNA。在某些包含sgRNA的组合物中,LNP包括胺脂质、辅助脂质、中性脂质及PEG脂质。在某些包含sgRNA的组合物中,辅助脂质为胆固醇。在其它包含sgRNA的组合物中,中性脂质为DSPC。在其它包含sgRNA的实施例中,PEG脂质为PEG2k-DMG或PEG2k-C11。在某些实施例中,胺脂质选自脂质A及其等效物,诸如脂质A的缩醛类似物。

[0347] 在某些实施例中,LNP组合物包含本文所揭示的mRNA,例如编码Cas核酸酶的mRNA,及gRNA,其可为sgRNA。在一个实施例中,LNP组合物可包含胺脂质、编码Cas核酸酶的mRNA、gRNA、辅助脂质、中性脂质及PEG脂质。在某些包含编码Cas核酸酶的mRNA及gRNA的组合物中,辅助脂质为胆固醇。在某些包含编码Cas核酸酶的mRNA及gRNA的组合物中,中性脂质为DSPC。在其它包含编码Cas核酸酶的mRNA及gRNA的实施例中,PEG脂质为PEG2k-DMG或PEG2k-C11。在某些实施例中,胺脂质选自脂质A及其等效物,诸如脂质A的缩醛类似物。

[0348] 在某些实施例中,LNP组合物包括Cas核酸酶mRNA,诸如2类Cas mRNA,及至少一个gRNA。在某些实施例中,LNP组合物包括比率为约25:1至约1:25的gRNA与Cas核酸酶mRNA,诸如2类Cas核酸酶mRNA。在某些实施例中,LNP调配物包括比率为约10:1至约1:10的gRNA与

Cas核酸酶mRNA, 诸如2类Cas核酸酶mRNA。在某些实施例中,LNP调配物包括比率为约8:1至约1:8的gRNA与Cas核酸酶mRNA, 诸如2类Cas核酸酶mRNA。如本文中所测量, 比率是以重量计。在一些实施例中,LNP调配物包括比率为约5:1至约1:5的gRNA与Cas核酸酶mRNA, 诸如2类Cas mRNA。在一些实施例中, 比率范围为约3:1至1:3、约2:1至1:2、约5:1至1:2、约5:1至1:1、约3:1至1:2、约3:1至1:1、约3:1、约2:1至1:1。在一些实施例中,gRNA与mRNA的比为约3:1或约2:1。在一些实施例中,gRNA与Cas核酸酶mRNA, 诸如2类Cas核酸酶的比为约1:1。比率可为约25:1、10:1、5:1、3:1、1:1、1:3、1:5、1:10或1:25。

[0349] 本文中所揭示的LNP组合物可包括模板核酸。模板核酸可经编码Cas核酸酶的mRNA, 诸如2类Cas核酸酶mRNA共调配。在一些实施例中, 模板核酸可经引导RNA共调配。在一些实施例中, 模板核酸可经编码Cas核酸酶的mRNA及引导RNA两者共调配。在一些实施例中, 模板核酸可经编码Cas核酸酶的mRNA及引导RNA分开调配。模板核酸可与LNP组合物一起或与其分开递送。在一些实施例中, 模板核酸可为单股或双股的, 其视所需修复机制而定。模板可具有与靶DNA或与邻近于靶DNA的序列同源的区域。

[0350] 本文所述的LNP及LNP调配物中的任一者适用于递送单独或与一或多个引导RNA一起的编码RNA引导的DNA结合剂, 诸如Cas核酸酶的mRNA。在一些实施例中, 涵盖一种包含以下的LNP组合物: RNA组分及脂质组分, 其中脂质组分包含胺脂质、中性脂质、辅助脂质及隐形脂质; 且其中N/P比为约1至10。

[0351] 在一些情况下, 脂质组分包含脂质A或其缩醛类似物、胆固醇、DSPC及PEG-DMG; 且其中N/P比为约1至10。在一些实施例中, 脂质组分包含: 约40至60mol%胺脂质; 约5至15mol%中性脂质; 及约1.5%至10mol%PEG脂质, 其中脂质组分的其余部分为辅助脂质, 且其中LNP组合物的N/P比为约3至10。在一些实施例中, 脂质组分包含: 约50至60mol%胺脂质; 约8至10mol%中性脂质; 及约2.5%至4mol%PEG脂质, 其中脂质组分的其余部分为辅助脂质, 且其中LNP组合物的N/P比为约3至8。在一些情况下, 脂质组分包含: 约50至60mol%胺脂质; 约5至15mol%DSPC; 及约2.5%至4mol%PEG脂质, 其中脂质组分的其余部分为胆固醇, 且其中LNP组合物的N/P比为约3至8。在一些情况下, 脂质组分包含: 48至53mol%脂质A; 约8至10mol%DSPC; 及约1.5%至10mol%PEG脂质, 其中脂质组分的其余部分为胆固醇, 且其中LNP组合物的N/P比为3至8±0.2。

[0352] 在一些实施例中,LNP是通过混合RNA水溶液与有机溶剂基脂质溶液, 例如100%乙醇而形成。适合溶液或溶剂包括或可含有: 水、PBS、Tris缓冲液、NaCl、柠檬酸盐缓冲液、乙醇、氯仿、二乙醚、环己烷、四氢呋喃、甲醇、异丙醇。可将医药学上可接受的缓冲液用于例如LNP的活体内投药。在某些实施例中, 缓冲液用于将包含LNP的组合物的pH维持处于或高于pH 6.5。在某些实施例中, 缓冲液用于将包含LNP的组合物的pH维持处于或高于pH 7.0。在某些实施例中, 组合物的pH在约7.2至约7.7范围内。在其它实施例中, 组合物的pH在约7.3至约7.7范围内或约7.4至约7.6范围内。在其它实施例中, 组合物的pH为约7.2、7.3、7.4、7.5、7.6或7.7。组合物的pH可用微型pH探针进行测量。在某些实施例中, 组合物中包括低温保护剂。低温保护剂的非限制性实例包括蔗糖、海藻糖、甘油、DMSO及乙二醇。示例性组合物可包括至多10%低温保护剂, 诸如蔗糖。在某些实施例中,LNP组合物可包括约1%、2%、3%、4%、5%、6%、7%、8%、9%或10%低温保护剂。在某些实施例中,LNP组合物可包括约1%、2%、3%、4%、5%、6%、7%、8%、9%或10%蔗糖。在一些实施例中,LNP组合物可包括

缓冲液。在一些实施例中,缓冲液可包含磷酸酯缓冲液(PBS)、Tris缓冲液、柠檬酸盐缓冲液及其混合物。在某些示例性实施例中,缓冲液包含NaCl。在某些实施例中,省去NaCl。NaCl的示例性量可在约20mM至约45mM范围内。NaCl的示例性量可在约40mM至约50mM范围内。在一些实施例中,NaCl的量为约45mM。在一些实施例中,缓冲液为Tris缓冲液。Tris的示例性量可在约20mM至约60mM范围内。Tris的示例性量可在约40mM至约60mM范围内。在一些实施例中,Tris的量为约50mM。在一些实施例中,缓冲液包含NaCl及Tris。LNP组合物的某些示例性实施例含有5%蔗糖及45mM NaCl的Tris缓冲液。在其它示例性实施例中,组合物含有呈约5%w/v的量的蔗糖、约45mM NaCl及pH 7.5下的约50mM Tris。盐、缓冲液及低温保护剂量可有所变化以使总体调配物的重量莫耳渗透浓度得到维持。例如,最终重量莫耳渗透浓度可维持低于450mOsm/L。在其它实施例中,重量莫耳渗透浓度在350与250mOsm/L之间。某些实施例的最终重量莫耳渗透浓度为300+/-20mOsm/L。

[0353] 在一些实施例中,使用微流混合、T型混合或交错混合。在某些方面中,流动速率、接头大小、接头几何结构、接头形状、管径、溶液及/或RNA及脂质浓度可有所变化。LNP或LNP组合物可例如经由渗析、切向流过滤或层析得到浓缩或纯化。LNP可以例如悬浮液、乳液或冻干粉末形式储存。在一些实施例中,LNP组合物储存于2至8°C下,在某些方面中,LNP组合物储存于室温下。在其它实施例中,冷冻储存,例如在-20°C或-80°C下储存LNP组合物。在其它实施例中,将LNP组合物储存于约0°C至约-80°C范围内的温度下。可在使用之前例如在冰上,在4°C下、在室温下或在25°C下融化冷冻LNP组合物。可将冷冻LNP组合物维持在不同温度下,例如在冰上,在4°C下、在室温下、在25°C下或在37°C下。

[0354] 在一些实施例中,LNP组合物具有大于约80%的囊封率。在一些实施例中,LNP组合物的粒度小于约120nm。在一些实施例中,LNP组合物的pdi小于约0.2。在一些实施例中,存在此等特征中的至少两者。在一些实施例中,存在此等三个特征中的每一者。用于测定此等参数的分析方法论述于下文通用试剂及方法章节中。

[0355] 在一些实施例中,与本文所揭示的mRNA缔合的LNP供用于制备药剂。

[0356] 电致孔为递送载荷的熟知手段,且任何电致孔方法可用于递送本文所揭示的gRNA中的任一者。在一些实施例中,电致孔可用于递送本文所揭示的mRNA及一或多个引导RNA。

[0357] 在一些实施例中,提供一种用于将本文所揭示的mRNA递送至离体细胞的方法,其中mRNA与LNP缔合或不与LNP缔合。在一些实施例中,mRNA/LNP或mRNA亦与一或多个引导RNA缔合。

[0358] 在一些实施例中,当以医药组合物形式向哺乳动物施用本文所揭示的mRNA时,该哺乳动物展现出比施用最小尿苷含量大于150%的编码Cas9核酸酶的mRNA的哺乳动物要低至少1.5、2、2.5、3、3.5、4、4.5、5、5.5、6、7、7.5、8、8.5、9、9.5或10倍的细胞介素反应。可如实例中所述测定细胞介素反应。细胞介素反应之间的差异可以一组细胞介素,诸如以下细胞介素中的至少一种、两种、三种或四种的平均变化的形式来测量:IFN α 、IL-6、TNF α 及MCP-1。在一些实施例中,当以医药组合物形式向哺乳动物施用本文所揭示的mRNA时,该哺乳动物展现出比施用具有编码Cas9核酸酶的ORF的mRNA的哺乳动物要低至少1.5、2、2.5、3、3.5、4、4.5、5、5.5、6、7、7.5、8、8.5、9、9.5或10倍的细胞介素反应,其中ORF的序列由SEQ ID NO:5组成。在一些实施例中,具有由SEQ ID NO:5组成的序列的ORF中的尿苷为未经修饰的。据通常理解,除mRNA外的比较组合物的特征应保持恒定,包括剂量,且剂量应处于适当范

围,诸如0.1至5mpk或本文所述的其它范围内(例如,如mRNA功效的测定章节所论述)。

[0359] 在一些实施例中,编码引导RNA的核苷酸序列可位于相同载体、转录物或包含编码RNA引导的DNA结合剂的核苷酸序列的mRNA上。在一些实施例中,引导RNA的表达及RNA引导的DNA结合剂的表达可通过其自身对应启动子来驱动。在一些实施例中,引导RNA的表达可由驱动RNA引导的DNA结合剂的表达的相同启动子来驱动。在一些实施例中,引导RNA及编码RNA引导的DNA结合剂的ORF可包含于单一转录物中。例如,引导RNA可处于RNA引导的DNA结合剂转录物的非转译区(UTR)中。在一些实施例中,引导RNA可处于RNA引导的DNA结合剂转录物的5'UTR中。在一些实施例中,引导RNA可处于RNA引导的DNA结合剂转录物的3'UTR中。在一些实施例中,RNA引导的DNA结合剂转录物的胞内半衰期可通过将引导RNA包含在该转录物的3'UTR中且藉此缩短其3'UTR的长度而减小。在其它实施例中,引导RNA可处于RNA引导的DNA结合剂转录物的内含子中。在一些实施例中,可在引导RNA所处的内含子处添加适合剪接位点以使得自转录物恰当地剪接掉引导RNA。在一些实施例中,相同载体上紧邻的RNA引导的DNA结合剂及引导RNA的表达可促进较高效形成RNA引导的DNA结合剂与引导RNA的核糖核蛋白复合物。

[0360] 在一些实施例中,提供一种包含本发明的mRNA的医药调配物。在一些实施例中,提供一种包含至少一种脂质,例如包含本发明的mRNA的LNP的医药调配物。可使用适用于递送RNA的任何LNP,诸如上文所述的LNP;其它示例性LNP描述于3月30,2017日申请的PCT/US2017/024973中。医药调配物可进一步包含医药学上可接受的载体,例如水或缓冲液。医药调配物可进一步包含一或多种医药学上可接受的赋形剂,诸如稳定剂、防腐剂、膨化剂或其类似者。医药调配物可进一步包含一或多种医药学上可接受的盐,诸如氯化钠。在一些实施例中,医药调配物经调配以用于静脉内施用。在一些实施例中,医药调配物经调配以用于递送至肝循环中。

[0361] C.mRNA功效的测定

[0362] 在一些实施例中,当与RNP的其它组分,例如至少一个gRNA,诸如靶向TTR的gRNA一起表达时,测定mRNA的功效。

[0363] 具有裂解酶活性的RNA引导的DNA结合剂可引起DNA中发生双股断裂。非同源末端连接(NHEJ)为一种以下方法,通过该方法,DNA中的双股断裂(DSB)经由重新连接断裂末端而得到修补,其可能会产生呈插入/缺失(插入缺失标记(indel))突变形式的错误。在重新连接末端之前,DSB的DNA末端常常会经历酶处理,其引起在一或两个股处添加或移除核苷酸。重新连接之前的此等添加或移除引起DNA序列中NHEJ修复位点处存在插入或缺失(插入缺失标记(indel))突变。归因于插入缺失标记(indel)的多种突变会改变阅读框架或过早地引入终止密码子,且因此产生非功能性蛋白质。

[0364] 在一些实施例中,基于活体外模型而测定编码核酸酶的mRNA的功效。在一些实施例中,活体外模型为HEK293细胞。在一些实施例中,活体外模型为HUH7人类肝癌细胞。在一些实施例中,活体外模型为初级肝细胞,诸如初级人类或小鼠肝细胞。

[0365] 在一些实施例中,通过TTR的编辑百分比测量RNA的功效。用于测定编辑百分比的示例性程序在以下实例中给出。在一些实施例中,将TTR的编辑百分比与当mRNA包含具有未经修饰的尿苷的SEQ ID NO:5的ORF且所有其它者为相同的时所获得的编辑百分比进行比较。

[0366] 在一些实施例中,使用施用包含mRNA及靶向TTR的gRNA,例如SEQ ID NO:42的LNP后的小鼠中的血清TTR浓度来测定mRNA的功效。在一些实施例中,使用施用包含mRNA及靶向TTR的gRNA,例如SEQ ID NO:69的LNP后的大鼠中的血清TTR浓度来测定mRNA的功效。血清TTR浓度可以绝对术语或以相对于假处理对照的基因减弱%来表示。在一些实施例中,使用施用包含mRNA及靶向TTR的gRNA,例如SEQ ID NO:42的LNP后的小鼠中的肝脏中的编辑百分比来测定mRNA的功效。在一些实施例中,有效量能够达成血清TTR的至少50的编辑%或50的基因减弱%。示例性有效量在0.1至10mg/kg (mpk),例如0.1至0.3mpk、0.3至0.5mpk、0.5至1mpk、1至2mpk、2至3mpk、3至5mpk、5至10mpk范围内,或为0.1、0.2、0.3、0.5、1、2、3、5、或10mpk。

[0367] 在一些实施例中,侦测基因编辑事件,诸如靶DNA中的插入/缺失(“插入缺失标记(indel)”)突变的形成及同源定向修复(HDR)事件会利用伴随加标签的引物且分离加标签的扩增产物的线性扩增(后文称为“LAM-PCR”或“线性扩增(LA)”法)。

[0368] 在一些实施例中,该方法包含自己已经诱导而具有双股断裂(DSB)且视情况地,已具有HDR模板以修复DSB的细胞分离细胞DNA;用加标签的引物进行至少一轮DNA的线性扩增;分离包含标签的线性扩增产物,藉此舍弃用非加标签的引物扩增的任何扩增产物;视情况进一步扩增分离产物;且分析线性扩增产物或经进一步扩增的产物以测定靶DNA中是否存在编辑事件,诸如双股断裂、插入、缺失或HDR模板序列。在一些情况下,编辑事件可经定量。如本文所用(包括在HDR及非HDR编辑事件,诸如插入缺失标记(indel)的情形下),定量及其类似者包括侦测总体中编辑事件的次数及/或类型。

[0369] 在一些实施例中,仅进行一轮线性扩增。

[0370] 在一些情况下,加标签的引物包含分子条形码。在一些实施例中,加标签的引物包含分子条形码,且仅进行一轮线性扩增。

[0371] 在一些实施例中,分析步骤包含对线性扩增产物或经进一步扩增的产物进行测序。测序可包含熟习此项技术者已知的任何方法,包括次世代测序(next generation sequencing)及将线性扩增产物或经进一步扩增的产物克隆于质粒中且对质粒或质粒的一部分进行测序。在其它方面中,分析步骤包含对线性扩增产物或经进一步扩增的产物进行数字PCR(dPCR)或液滴式数字PCR(ddPCR)。在其它情况下,分析步骤包含使线性扩增产物或经进一步扩增的产物与经设计以鉴别包含HDR模板序列的DNA的核酸探针接触,且侦测已结合至线性扩增产物或经进一步扩增的产物的探针。在一些实施例中,该方法进一步包含测定靶DNA中HDR模板的位置。

[0372] 在某些实施例中,该方法进一步包含测定靶DNA中插入位点的序列,其中插入位点为HDR模板并入靶DNA中所处的位置,且其中插入位点可包括部分靶DNA序列及部分HDR模板序列。

[0373] 在一些实施例中,使用加标签的引物的靶DNA的线性扩增进行1至50轮、1至60轮、1至70轮、1至80轮、1至90轮或1至100轮。

[0374] 在一些实施例中,使用加标签的引物的靶DNA的线性扩增包含分离DNA双螺旋体的变性步骤、使引物结合的黏接步骤及延伸步骤。在一些实施例中,线性扩增为等温的(不需要温度变化)。在一些实施例中,等温线性扩增为环介导等温扩增(LAMP)、股置换扩增(SDA)、解螺旋酶依赖性扩增或切口酶扩增反应。

[0375] 在一些实施例中,加标签的引物黏接至与期望编辑事件位置,例如插入、缺失或模板插入位点相距至少50、至少60、至少70、至少80、至少90、至少100、至少110、至少120、至少130、至少140、至少150、至少160、至少170、至少180、至少190、至少200、至少210、至少220、至少230、至少240、至少250、至少260、至少270、至少280、至少290、至少300、至少1,000、至少5,000或至少10,000个核苷酸的靶DNA。

[0376] 在一些实施例中,加标签的引物包含分子条形码。在一些实施例中,分子条形码包含与靶DNA不互补的序列。在一些实施例中,分子条形码包含6、8、10或12个核苷酸。

[0377] 在一些实施例中,引物上的标签为生物素、抗生蛋白链菌素、地高辛(digoxigenin)、DNA序列或荧光异硫氰酸盐(FITC)。

[0378] 在一些实施例中,使用对引物上的标签具有特异性的捕捉试剂分离线性扩增产物。在一些实施例中,捕捉试剂处于珠粒、固体载体、基质或管柱上。在一些实施例中,分离步骤包含使线性扩增产物与对引物上的标签具有特异性的捕捉试剂接触。在一些实施例中,捕捉试剂为生物素、抗生蛋白链菌素、地高辛、DNA序列或荧光异硫氰酸盐(FITC)。

[0379] 在一些实施例中,标签为生物素且捕捉试剂为抗生蛋白链菌素。在一些实施例中,标签为抗生蛋白链菌素且捕捉试剂为生物素。在一些实施例中,标签处于引物的5'端、引物的3'端上或处于引物内部。在一些实施例中,在分离步骤之后移除标签及/或捕捉试剂。在一些实施例中,不移除标签及/或捕捉试剂,且在标签及/或捕捉试剂存在下进行进一步扩增及分析步骤。

[0380] 在一些实施例中,进一步扩增为非线性的。在一些实施例中,进一步扩增为数字PCR、qPCR或RT-PCR。在一些实施例中,测序为次世代测序(NGS)。

[0381] 在一些实施例中,靶DNA为基因组或线粒体。在一些实施例中,靶DNA为原核或真核细胞的基因组DNA。在一些实施例中,靶DNA为哺乳动物DNA。靶DNA可来自非分裂细胞或分裂细胞。在一些实施例中,靶DNA可来自初级细胞。在一些实施例中,靶DNA来自复制细胞。

[0382] 在一些情况下,在线性扩增之前剪切细胞DNA。在一些实施例中,经剪切的DNA的平均尺寸在0.5kb与20kb之间。在一些情况下,细胞DNA经剪切而呈0.5、0.75、1.0、1.25、1.5、1.75、2.0、2.25、2.5、2.75、3.0、3.25、3.5、3.75、4.0、4.25、4.5、4.75、5.0、5.25、5.5、5.75、6.0、6.25、6.5、6.75、7.0、7.25、7.5、7.75、8.0、8.25、8.5、8.75、9.0、9.25、9.5、9.75、10.0、10.25、10.5、10.75、11.0、11.25、11.5、11.75、12.0、12.25、12.5、12.75、13.0、13.25、13.5、13.75、14.0、14.25、14.5、14.75、15.0、15.25、15.5、15.75、16.0、16.25、16.5、16.75、17.0、17.25、17.5、17.75、18.0、18.25、18.5、18.75、19.0、19.25、19.5、19.75或20.0kb的平均尺寸。在一些情况下,细胞DNA经剪切而呈约1.5kb的平均尺寸。

[0383] D. 示例性用途、方法及治疗

[0384] 在一些实施例中,mRNA、LNP或医药组合物供用于基因组编辑,例如编辑靶基因中。在一些实施例中,mRNA、LNP或医药组合物供用于修饰靶基因,例如改变其序列或后生状态(epigenetic status)中。在一些实施例中,mRNA、LNP或医药组合物供用于在靶基因中诱导双股断裂(DSB)中。在一些实施例中,mRNA、LNP或医药组合物供用于在靶基因中诱导插入缺失标记(indel)中。在一些实施例中,提供本文所揭示的mRNA、LNP或医药组合物的用途,其用于制备用于基因组编辑,例如编辑靶基因的药剂。在一些实施例中,提供本文所揭示的mRNA、LNP或医药组合物的用途,其用于制备用于修饰靶基因,例如改变其序列或后生状态

的药剂。在一些实施例中,提供本文所揭示的mRNA、LNP或医药组合物的用途,其用于制备用于在靶基因中诱导双股断裂(DSB)的药剂。在一些实施例中,提供本文所揭示的mRNA、LNP或医药组合物的用途,其用于制备用于在靶基因中诱导插入缺失标记(indel)的药剂。在一些实施例中,靶基因处于个体,诸如哺乳动物,诸如人类中。在一些实施例中,靶基因处于器官,诸如肝脏,诸如哺乳动物肝脏,诸如人类肝脏中。在一些实施例中,靶基因处于肝脏细胞,诸如哺乳动物肝脏细胞,诸如人类肝脏细胞中。在一些实施例中,靶基因处于肝细胞,诸如哺乳动物肝细胞,诸如人类肝细胞中。在一些实施例中,肝脏细胞或肝细胞处于原位。在一些实施例中,肝脏细胞或肝细胞分离于例如培养物中,诸如原代培养物中。亦提供对应于本文所揭示的用途的方法,其包含向个体施用本文所揭示的mRNA、LNP或医药组合物或使细胞,诸如上文所述的细胞与本文所揭示的mRNA、LNP或医药组合物接触。

[0385] 在一些实施例中,mRNA、LNP或医药组合物供用于疗法中或治疗疾病,例如与TTR相关的淀粉样变性(ATTR)中。在一些实施例中,提供本文所揭示的mRNA(例如以本文所提供的组合物形式)的用途,其用于制备例如用于治疗患有与TTR相关的淀粉样变性(ATTR)的个体的药剂。

[0386] 在一些实施例中,出于上文关于生物体、器官或原位细胞所论述的用途中的任一者静脉内施用mRNA、LNP或医药组合物。在一些实施例中,以在0.01至10mg/kg(mpk),例如0.01至0.1mpk、0.1至0.3mpk、0.3至0.5mpk、0.5至1mpk、1至2mpk、2至3mpk、3至5mpk、5至10mpk范围内或0.1、0.2、0.3、0.5、1、2、3、5或10mpk的剂量施用mRNA、LNP或医药组合物。

[0387] 在涉及个体之前述实施例中的任一者中,个体可为哺乳动物。在涉及个体之前述实施例中的任一者中,个体可为人类。在涉及个体之前述实施例中的任一者中,个体可为牛、猪、猴、绵羊、狗、猫、鱼或家禽。

[0388] 在一些实施例中,静脉内施用本文所揭示的mRNA、LNP或医药组合物或将其用于静脉内投药。在一些实施例中,将引导RNA、组合物及调配物施用至肝循环中或用于肝循环中的投药。

[0389] 在一些实施例中,单次施用本文所揭示的mRNA、LNP或医药组合物足以使靶基因产物的表达发生基因减弱。在一些实施例中,单次施用本文所揭示的mRNA、LNP或医药组合物足以使靶基因产物的表达发生基因剔除。在其它实施例中,不止一次施用本文所揭示的mRNA、LNP或医药组合物对于使编辑、修饰、插入缺失标记(indel)形成、DSB形成或其类似者经由累积效应达至最大可为有益的。

[0390] 在一些实施例中,会在递送之后1年、2年、3年、4年、5年或10年看到本文所揭示的mRNA、LNP或医药组合物的治疗功效。

[0391] 在一些实施例中,治疗会减缓或中断疾病进展。

[0392] 在一些实施例中,治疗会引起器官功能或器官,诸如肝脏的疾病的症状得到改善、稳定或减缓其变化。

[0393] 在一些实施例中,通过增加个体的存活时间来测量治疗功效。

[0394] E. 示例性DNA分子、载体、表达构建体、宿主细胞及制造方法

[0395] 在某些实施例中,本发明提供一种DNA分子,其包含编码mRNA中的任一者的序列,该mRNA编码本文所述的RNA引导的DNA结合剂。在一些实施例中,除了RNA引导的DNA结合剂序列之外,DNA分子进一步包含不编码RNA引导的DNA结合剂的核酸。不编码RNA引导的DNA结

合剂的核酸包括(但不限于)启动子、强化子、调节序列及编码引导RNA的核酸。

[0396] 在一些实施例中,DNA分子进一步包含编码crRNA、trRNA或crRNA及trRNA的核苷酸序列。在一些实施例中,编码crRNA、trRNA或crRNA及trRNA的核苷酸序列包含或由以下组成:通过来自天然存在的CRISPR/Cas系统的重复序列的全部或部分侧接的引导序列。包含或由crRNA、trRNA或crRNA及trRNA组成的核酸可进一步构成载体序列,其中该载体序列包含或由以下组成:不会与crRNA、trRNA或crRNA及trRNA一起经天然发现的核酸。在一些实施例中,crRNA及trRNA由一个载体中的非连续核酸编码。在其它实施例中,crRNA及trRNA可由连续核酸编码。在一些实施例中,crRNA及trRNA由单一核酸的相对股编码。在其它实施例中,crRNA及trRNA由单一核酸的相同股编码。

[0397] 在一些实施例中,DNA分子进一步包含以可操作方式连接编码mRNA中的任一者的序列的启动子,该mRNA编码本文所述的RNA引导的DNA结合剂。在一些实施例中,DNA分子为适用于在哺乳动物细胞,例如人类细胞或小鼠细胞,诸如人类肝细胞或啮齿动物(例如小鼠)肝细胞中表达的构建体。在一些实施例中,DNA分子为适用于在哺乳动物器官,例如人类肝脏或啮齿动物(例如小鼠)肝脏的细胞中表达的构建体。在一些实施例中,DNA分子为质粒或游离基因组。在一些实施例中,DNA分子包含于宿主细胞,诸如细菌或经培养的真核细胞中。示例性细菌包括变形菌门,诸如大肠杆菌。示例性经培养的真核细胞包括初级肝细胞,包括啮齿动物(例如小鼠)或人源的肝细胞;肝细胞细胞株,包括啮齿动物(例如小鼠)或人源的肝细胞;人类细胞株;啮齿动物(例如小鼠)细胞株;CHO细胞;微生物真菌,诸如裂殖或出芽酵母,例如酵母菌,诸如酿酒酵母;及昆虫细胞。

[0398] 在一些实施例中,提供一种制造本文所揭示的mRNA的方法。在一些实施例中,此类方法包含使本文所述的DNA分子与核糖核酸聚合酶在容许转录的条件下接触。在一些实施例中,活体外,例如在无细胞系统中进行接触。在一些实施例中,核糖核酸聚合酶为噬菌体源的核糖核酸聚合酶,诸如T7核糖核酸聚合酶。在一些实施例中,提供包括至少一种如上文所论述的经修饰的核苷酸的NTP。在一些实施例中,NTP包括至少一种如上文所论述的经修饰的核苷酸且不包含UTP。

[0399] 在一些实施例中,单独或与一或多个引导RNA一起的本文所揭示的mRNA可包含在一或多个载体的载体系统中或通过其递送。在一些实施例中,载体中的一种或多种或所有载体可为DNA载体。在一些实施例中,载体中的一种或多种或所有载体可为RNA载体。在一些实施例中,载体中的一种或多种或所有载体可为环状的。在一些实施例中,载体中的一种或多种或所有载体可为线性的。在一些实施例中,载体中的一种或多种或所有载体可包封在脂质纳米颗粒、脂质体、非脂质纳米颗粒或病毒衣壳中。非限制性示例性载体包括质粒、噬菌粒、黏质粒、人工染色体、袖珍染色体、转座子、病毒载体及表达载体。

[0400] 非限制性示例性病毒载体包括腺相关病毒(AAV)载体、慢病毒载体、腺病毒载体、辅助依赖型腺病毒载体(HDA)、单纯疱疹病毒(HSV-1)载体、噬菌体T4、杆状病毒载体及反转录病毒载体。在一些实施例中,病毒载体可为AAV载体。在其它实施例中,病毒载体可为慢病毒载体。在一些实施例中,慢病毒可为非整合性的。在一些实施例中,病毒载体可为腺病毒载体。在一些实施例中,腺病毒可为高克隆容量或“无肠(gutless)”腺病毒,其中除5'及3'倒转末端重复序列(ITR)及包装信号('I')之外的所有病毒编码区自病毒中删除以增加其包装容量。在又其它实施例中,病毒载体可为HSV-1载体。在一些实施例中,HSV-1类载体

为辅助依赖型,且在其它实施例中,其为非辅助依赖型。例如,仅保留包装序列的扩增子载体需要具有结构性组分的辅助病毒用于包装,而移除非必需病毒功能的缺失30kb的HSV-1载体不需要辅助病毒。在其它实施例中,病毒载体可为噬菌体T4。在一些实施例中,当清空病毒头时,噬菌体T4可能能够包装任何线性或环状DNA或RNA分子。在其它实施例中,病毒载体可为杆状病毒载体。在又其它实施例中,病毒载体可为反转录病毒载体。在使用具有较小克隆容量的AAV或慢病毒载体的实施例中,可能需要使用多于一个载体以递送如本文所揭示的载体系统的全部组分。例如,一个AAV载体可含有编码Cas蛋白的序列,而第二AAV载体可含有一或多个引导序列。

[0401] 在一些实施例中,载体可能能够驱动细胞中一或多个编码序列,诸如本文所揭示的mRNA的编码序列的表达。在一些实施例中,细胞可为原核细胞,诸如细菌细胞。在一些实施例中,细胞可为真核细胞,诸如酵母、植物、昆虫或哺乳动物细胞。在一些实施例中,真核细胞可为哺乳动物细胞。在一些实施例中,真核细胞可为啮齿动物细胞。在一些实施例中,真核细胞可为人类细胞。驱动不同类型细胞中的表达的适合启动子为此项技术中已知的。在一些实施例中,启动子可为野生型。在其它实施例中,启动子可经修饰以供较高效或较有效表达。在又其它实施例中,启动子可经截短但仍保留其功能。例如,启动子可具有正常尺寸或适用于将载体适当包装于病毒中的减小的尺寸。

[0402] 在一些实施例中,载体系统可包含一个编码RNA引导的DNA结合剂的核苷酸序列的复本。在其它实施例中,载体系统可包含多于一个编码RNA引导的DNA结合剂的核苷酸序列的复本。在一些实施例中,编码RNA引导的DNA结合剂的核苷酸序列可以可操作方式连接至少一个转录或转译控制序列。在一些实施例中,编码核酸酶的核苷酸序列可以可操作方式连接至少一个启动子。

[0403] 在一些实施例中,启动子可为组成性、诱导性或组织特异性的。在一些实施例中,启动子可为组成性启动子。非限制性示例性的组成性启动子包括细胞巨大病毒即刻早期启动子(CMV)、猴病毒(SV40)启动子、腺病毒主要晚期启动子(MLP)、劳斯肉瘤病毒(RSV)启动子、小鼠乳腺肿瘤病毒(MMTV)启动子、磷酸甘油酸激酶(PGK)启动子、延长因子- α (EF1a)启动子、泛素启动子、肌动蛋白启动子、微管蛋白启动子、免疫球蛋白启动子、其功能性片段或前述中的任一者的组合。在一些实施例中,启动子可为CMV启动子。在一些实施例中,启动子可为经截短的CMV启动子。在其它实施例中,启动子可为EF1a启动子。在一些实施例中,启动子可为诱导性启动子。非限制性示例性的诱导性启动子包括可通过热休克、光、化学物质、肽、金属、类固醇、抗生素或醇诱导的诱导性启动子。在一些实施例中,诱导性启动子可为具有低基础(非经诱导)表达程度的诱导性启动子,诸如Tet-On[®]启动子(Clontech)。

[0404] 在一些实施例中,启动子可为组织特异性启动子,例如对肝脏中的表达具有特异性的启动子。

[0405] 载体可进一步包含编码至少一个引导RNA的核苷酸序列。在一些实施例中,载体包含一个引导RNA的复本。在其它实施例中,载体包含多于一个引导RNA的复本。在具有多于一个引导RNA的实施例中,引导RNA可不同以使其靶向不同靶序列,或可相同以便其靶向相同靶序列。在其中载体包含多于一个引导RNA的一些实施例中,各引导RNA可具有其它不同特性,诸如在与RNA引导的DNA结合剂的核糖核蛋白复合物中的活性或稳定性。在一些实施例中,编码引导RNA的核苷酸序列可以可操作方式连接至少一个转录或转译控制序列,诸如

启动子、3'UTR或5'UTR。在一个实施例中,启动子可为tRNA启动子,例如tRNA^{Lys3},或tRNA嵌合体。参见Mefferd等人,RNA.201521:1683-9;Scherer等人,Nucleic Acids Res.2007 35:2620-2628。在一些实施例中,启动子可通过RNA聚合酶III(Pol III)识别。Pol III启动子的非限制性实例包括U6及H1启动子。在一些实施例中,编码引导RNA的核苷酸序列可以可操作方式连接小鼠或人类U6启动子。在其它实施例中,编码引导RNA的核苷酸序列可以可操作方式连接小鼠或人类H1启动子。在具有多于一个引导RNA的实施例中,用于驱动表达的启动子可相同或不同。在一些实施例中,编码引导RNA的crRNA的核苷酸及编码引导RNA的trRNA的核苷酸可提供于相同载体上。在一些实施例中,编码crRNA的核苷酸及编码trRNA的核苷酸可通过同一启动子驱动。在一些实施例中,crRNA及trRNA可转录为单一转录物。例如,crRNA及trRNA可由单一转录物进行处理以形成双分子引导RNA。或者,crRNA及trRNA可转录为单分子引导RNA。在其它实施例中,crRNA及trRNA可通过其处于相同载体上的相应启动子来驱动。在又其它实施例中,crRNA及trRNA可通过不同载体编码。

[0406] 在一些实施例中,组合物包含载体系统,其中该系统包含多于一个载体。在一些实施例中,载体系统可包含一个单一载体。在其它实施例中,载体系统可包含两个载体。在其它实施例中,载体系统可包含三个载体。当将不同引导RNA用于多任务(multiplexing)时或当使用引导RNA的多个复本时,载体系统可包含多于三个载体。

[0407] 在一些实施例中,载体系统可包含诱导性启动子以仅在其递送至靶细胞之后开始表达。非限制性示例性的诱导性启动子包括可通过热休克、光、化学物质、肽、金属、类固醇、抗生素或醇诱导的诱导性启动子。在一些实施例中,诱导性启动子可为具有低基础(非经诱导)表达程度的诱导性启动子,诸如Tet-On[®]启动子(Clontech)。

[0408] 在其它实施例中,载体系统可包含组织特异性启动子以仅在其递送至特定组织之后开始表达。

[0409] 实例

[0410] 提供以下实例以说明某些所揭示的实施例且不应理解为以任何方式限制本发明的范畴。

[0411] 通用试剂及方法.除非另外指明,否则通过活体外转录(IVT)使用线性化质粒DNA模板及T7核糖核酸聚合酶来合成mRNA。转录通常由以下来进行:包含T7启动子的构建体;本文所揭示的转录物序列,诸如SEQ ID NO:43(其包含SEQ ID NO:1且编码SEQ ID NO:4的RNA ORF)或SEQ ID NO:48(其包含SEQ ID NO:2且编码SEQ ID NO:5的RNA ORF)及编码于质粒中的聚-A尾(SEQ ID NO:63)。其中测试多个UTR的实验使用相似构建体,不同的处在于使用转录物序列,诸如SEQ ID NO:58及SEQ ID NO:59。通过与XbaI利用以下条件在37°C下培育2小时来线性化含有T7启动子及100nt聚(A/T)区的质粒DNA:200ng/ μ L质粒、2U/ μ L XbaI(NEB)及1 \times 反应缓冲液。通过在65°C下加热反应20分钟来灭活XbaI。使用二氧化硅最大自旋管柱(Epoch Life Sciences)自酶及缓冲盐纯化线性化质粒且通过琼脂糖凝胶加以分析以证实线性化。用于产生经Cas9修饰的mRNA的IVT反应物在37°C下在以下条件下培育4小时:50ng/ μ L线性化质粒;2mM的GTP、ATP、CTP及UTP(或若指示,代替CTP或UTP的经修饰的三磷酸核苷酸(例如N1-甲基假UTP(Trilink))中的每一者;10mM ARCA(Trilink);5U/ μ L T7 RNA聚合酶(NEB);1U/ μ L鼠类RNA酶抑制剂(NEB);0.004U/ μ L无机大肠杆菌焦磷酸酶(NEB);及1 \times 反应缓冲液。在4小时培育之后,添加TURBO脱氧核糖核酸酶(ThermoFisher)至0.01U/ μ L的最终

浓度,且再培育反应物30分钟以移除DNA模板。使用MegaClear转录清除试剂盒根据制造商方案(ThermoFisher)自酶及核苷酸纯化Cas9 mRNA。经由沉淀方案(在一些情况下,其继之以基于HPLC的纯化)来纯化mRNA。简言之,在DNA酶消化之后,通过添加 $0.21 \times$ 体积的7.5M LiCl溶液且加以混合来沉淀mRNA,且通过离心来集结经沉淀的mRNA。移除上清液后,将mRNA复水。使用乙酸铵及乙醇再次沉淀mRNA。将5M乙酸铵连同 $2 \times$ 体积的100% EtOH一起添加至mRNA溶液中,使最终浓度为2M。混合溶液且在 -20°C 下将其培育15分钟。再次通过离心集结经沉淀的mRNA,移除上清液且将mRNA复水。使用乙酸钠及乙醇沉淀mRNA作为最终步骤。将 $1/10$ 体积的3M乙酸钠(pH 5.5)连同 $2 \times$ 体积的100% EtOH一起添加至溶液中。混合溶液且在 -20°C 下将其培育15分钟。再次通过离心集结经沉淀的mRNA,移除上清液,用70%低温乙醇洗涤集结粒且使其风干。将mRNA复水。对于经HPLC纯化的mRNA,在LiCl沉淀及复水之后,通过RP-IP HPLC纯化mRNA(参见例如Kariko等人Nucleic Acids Research, 2011,第39卷,第21期e142)。合并选择用于汇集的溶离份且通过如上文所述的乙酸钠/乙醇沉淀来去盐。

[0412] 对于所有方法,通过测量260nm处的吸光度(Nanodrop)测定转录物浓度,且通过利用Bioanalyzer(Agilent)进行毛细电泳法来分析转录物。

[0413] 除非另外指明,否则用来自Charles River Laboratories的CD-1雌性小鼠及史泊格-多利大鼠进行活体内编辑实验。除非另外指明,否则小鼠中的血清TTR含量的分析如下进行。收集血液且如所指示地分离血清。

[0414] 在适用实例中指明的情况下,亦测量经处理的小鼠中的细胞介素诱导。对于此分析,通过尾静脉切口收集大约50至 $100\mu\text{L}$ 血液用于血清细胞介素测量。使血液在室温下凝结持续大约2小时,且随后在 $1000 \times g$ 下离心10分钟,随后收集血清。测量IL-6、TNF- α 、IFN- α 及MCP-1的基于Luminex的磁珠多任务分析(Affymetrix ProcartaPlus,目录号Exp040-00000-801)用于收集样本中的细胞介素分析。如制造商方案中所指导地制备试剂盒试剂及标准品。使用所提供的样本稀释剂对小鼠血清进行4倍稀释,且将 $50\mu\text{L}$ 添加至含有经 $50\mu\text{L}$ 稀释抗体涂布的磁珠的孔中。将板在室温下培育2小时且随后加以洗涤。稀释生物素抗体($50\mu\text{L}$)添加至珠粒且在室温下培育1小时。再次洗涤珠粒,之后将 $50\mu\text{L}$ 稀释抗生素蛋白链菌素-PE添加至各孔中,接着培育30分钟。再次洗涤珠粒且随后悬浮于 $100\mu\text{L}$ 洗涤缓冲液中且在Bio-Plex 200仪器(Bio-Rad)上读取。使用Bioplex Manager 6.1版分析软件包,通过使用五参数逻辑曲线拟合脱离标准曲线计算的细胞介素浓度分析数据。

[0415] 除非另外指明,否则使用未经修饰的ATP、GTP、CTP及UTP。除非另外指明,否则所有mRNA均编码有一个核定位信号。

[0416] 通过使用Precision Nanosystems NanoAssemblr™ Benchtop仪器,根据制造商方案,将脂质及RNA溶液微流混合或错流混合而形成LNP,如下文所述。除非另外指明,否则LNP含有45%脂质A、9%DSPC、44%胆固醇及2%PEG2k-DMG及4.5的N:P比。

[0417] LNP调配-NanoAssemblr

[0418] 通常,以不同脂质组分摩尔比将脂质纳米颗粒组分溶解于100%乙醇中。将RNA载荷溶解于25mM柠檬酸盐、100mM NaCl(pH 5.0)中,产生大约 0.45mg/mL 的RNA载荷浓度。用约4.5或约6的脂质胺与RNA磷酸(N:P)摩尔比,及以重量计呈1:1的mRNA与gRNA的比调配LNP。

[0419] 通过使用Precision Nanosystems NanoAssemblr™ Benchtop仪器,根据制造商的方案,将脂质及RNA溶液微流混合而形成LNP。使用差分流动速率在混合期间维持水相与有

机溶剂的2:1比率。混合之后,收集LNP,在水中稀释(大约1:1v/v),在室温下保持1小时,且进一步用水稀释(大约1:1v/v),之后进行最终缓冲液更换。用PD-10去盐管柱(GE)来完成将最终缓冲液更换为50mM Tris、45mM NaCl、5% (w/v) 蔗糖,pH 7.5(TSS)。必要时,用Amicon 100kDa离心过滤器(Millipore)通过离心浓缩调配物。所得混合物随后使用0.2 μ m无菌过滤器过滤。在进一步使用之前,将最终LNP储存于-80 $^{\circ}$ C下。

[0420] LNP调配-错流

[0421] 对于使用错流技术制备的LNP,通过脂质的乙醇溶液与两个体积的RNA溶液及一个体积的水进行撞击喷流混合来形成LNP。经由混合十字管使脂质的乙醇溶液与两个体积的RNA溶液混合。经由沿线T形管将第四水流与十字管的引出流混合(参见W02016010840图2.)。将LNP在室温下保持1小时且进一步用水稀释(大约1:1v/v)。使用切向流过滤在平板滤筒(Sartorius,100kD MWC0)上浓缩经稀释的LNP,且随后通过透滤,将其缓冲液更换为50mM Tris、45mM NaCl、5% (w/v) 蔗糖,pH 7.5(TSS)。可替代地,用PD-10去盐管柱(GE)来完成将最终缓冲液更换为TSS。必要时,用Amicon 100kDa离心过滤器(Millipore)通过离心浓缩调配物。所得混合物随后使用0.2 μ m无菌过滤器过滤。在进一步使用之前,将最终LNP储存于4 $^{\circ}$ C或-80 $^{\circ}$ C下。

[0422] 调配物分析

[0423] 使用动态光散射(“DLS”)表征本发明的LNP的多分散性指数(“pdi”)及尺寸。DLS测量由将样本置于光源下而产生的光的散射。如根据DLS测量所测定,PDI表示总体中(平均粒度周围)粒度的分布,其中完全均一总体的PDI为零。平均粒径及多分散性是通过动态光散射(DLS)使用Malvern Zetasizer仪器来测量。在通过DLS测量之前,在PBS中将LNP样本稀释30 \times 。连同数目平均直径及pdi一起报导Z-平均直径,其为平均粒径的基于强度的量度。Malvern Zetasizer仪器亦用于测量LNP的 ζ 电位。测量之前,将样本在0.1 \times PBS,pH 7.4中以1:17(50 μ L于800 μ L中)稀释。

[0424] 使用基于荧光的分析(**Ribogreen[®]**, ThermoFisher Scientific)来测定总RNA浓度及游离RNA。囊封效率计算为(总RNA-游离RNA)/总RNA。用含有0.2% Triton-X 100的1 \times TE缓冲液以适当方式稀释LNP样本以测定总RNA或用1 \times TE缓冲液稀释以测定游离RNA。通过利用用于制得调配物的起始RNA溶液制备标准曲线,且稀释于1 \times TE缓冲液+/-0.2% Triton-X 100中。随后将经稀释的**RiboGreen[®]**染料(根据制造商的说明书)添加至标准品及样本中的每一者中,且使其在不存在光下在室温下培育大约10分钟。使用SpectraMax M5微量盘式读取器(Molecular Devices),伴随分别设定成488nm、515nm及525nm的激发、自动截止及发射波长来读取样本。根据合适标准曲线测定总RNA及游离RNA。

[0425] 囊封效率计算为(总RNA-游离RNA)/总RNA。可使用相同程序测定基于DNA的载荷组分的囊封效率。对于单股DNA,可使用Oligreen染料,且对于双股DNA,可使用Picogreen染料。

[0426] 典型地,当制备LNP时,囊封效率>80%,粒度<120nm且pdi为<0.2。

[0427] LNP活体内递送

[0428] 除非另外指出,否则各研究中使用在6至10周龄范围内的CD-1雌性小鼠。对动物称重且根据体重分组以基于组平均体重制备投配溶液。经由侧尾静脉以每只动物0.2mL(每公

斤体重大约10mL)的体积投配LNP。在给药后大约6小时观测动物副作用。在投药后二十四小时测量体重,且动物通过在异氟烷麻醉下经由心脏穿刺放血而在各个时间点安乐死。将血液收集至血清分离管中或含有用于如本文所述的血浆的缓冲柠檬酸钠的管中。对于涉及活体内编辑的研究,自来自各动物的中叶或三个独立叶片(例如右中、左中及左外侧叶片)收集肝脏组织用于DNA提取及分析。

[0429] 针对肝脏编辑通过次世代测序(NGS)及血清TTR含量(资料未示)测量小鼠群组。

[0430] 甲状腺素转运蛋白(TTR)ELISA分析

[0431] 收集血液且如所指示地分离血清。使用小鼠前白蛋白(甲状腺素转运蛋白)ELISA试剂盒(Aviva Systems Biology,目录号OKIA00111)测定总小鼠TTR血清含量。根据制造商方案,使用大鼠特异性ELISA试剂盒(Aviva Systems Biology目录号OKIA00159)来测量大鼠TTR血清含量。简言之,用试剂盒样本稀释剂将血清连续稀释至最终稀释度为10,000倍。随后将此稀释样本添加至ELISA板且随后根据指示进行分析。

[0432] NGS测序

[0433] 简言之,为了定量地测定基因组中靶位置处的编辑效率,分离基因组DNA且利用深度测序鉴别存在通过基因编辑造成的插入及缺失。

[0434] 在靶位点(例如TTR)周围设计PCR引物,且扩增相关基因组区。引物序列提供于下文中。根据制造商的方案(Illumina)进行额外PCR以对于测序添加所需化学性质。在Illumina MiSeq仪器上对扩增子测序。在消除具有低质量评分的读段之后,将读段与人类参考基因组(例如hg38)进行比对。将含有读段的所得档案映像至参考基因组(BAM档案),其中选择与相关目标区重迭的读段且计算野生型读段的数目相对于含有插入、取代或缺失的读段的数目。

[0435] 编辑百分比(例如“编辑效率”或“编辑%”)定义为具有插入或缺失的序列读段的总数相比于包括野生型的序列读段的总数。

[0436] 1.具有经修饰的核苷酸的Cas9 mRNA的活体内表征

[0437] 用不同的如下表5中所示的经修饰的核苷酸内含物制备包含如SEQ ID NO:5中所阐述的ORF的mRNA。将mRNA与靶向甲状腺素转运蛋白基因(TTR)的引导RNA(G282;SEQ ID NO:42)合并并且并入至LNP中。未经修饰的胞苷用于所有LNP中,除了LNP420。

[0438] 表5.用于活体内研究的LNP417至LNP421

LNP	Cas9 SEQ ID NO	经修饰的核苷酸
LNP417	5	N1-甲基-假尿苷
LNP418	5	无
[0439] LNP419	5	假尿苷
LNP420	5	假尿苷及5-甲基胞苷
LNP421	5	60% N1-甲基-假尿苷(40%未经修饰的尿苷)

[0440] 以0.5mg/kg (mpk) 或1mpk剂量向小鼠施用LNP417至LNP421。给药后4小时 (hpd) 测量细胞介素 (IFN α 、IL-6、TNF α 及MCP-1) 诱导。结果示于图1A至图1D中。

[0441] 在投药之后7天进行尸体剖检时,收集血清及肝脏分别用于血清TTR测量及编辑功效的分析。结果示于图2A至图2B中。

[0442] 观测到,使用假尿苷及5-甲基CTP几乎完全消除细胞介素诱导。使用呈60% (LNP421) 或100% (LNP417) 的N1-甲基假尿苷亦会引起比未经修饰的Cas9 mRNA要少的细胞介素诱导,且60%N1-甲基假尿苷下的减少程度与100%类似。

[0443] 所有经修饰的Cas9构建体在降低血清TTR方面有相似效应,且可能归因于增加的稳定性,其比未经修饰的构建体更有效。根据肝脏编辑数据,使用假尿苷及N1-甲基假尿苷的构建体同样有效。具有假尿苷及5-甲基胞苷的构建体的效应明显要比用单独假尿苷的构建体低。具有60%N1-甲基假尿苷的构建体的效应可能要比具有100%N1-甲基假尿苷的构建体略低。

[0444] 2. 编码Cas9的经修饰的mRNA的研发及活体外表征

[0445] Cas9序列 (SEQ ID NO:1) 经设计以改善肝脏表达且将尿苷减至最少。基于具有最少可能的尿苷含量及肝脏中对应tRNA的最大表达来选择密码子。对于肝脏tRNA表达,参见 Dittmar KA, PLoS Genetics 2 (12):e221 (2006)。降低Cas9 mRNA的尿苷含量意欲降低对mRNA的先天性免疫反应及/或提供其它益处。表6显示基于tRNA含量的最佳肝脏密码子及具有最少可能数目的尿苷的密码子。最小尿苷密码子与最佳肝脏密码子不同的情况呈粗斜体形式。表格亦显示化脓链球菌Cas9的氨基酸序列 (SEQ ID NO:3) 中的各氨基酸的数目。

[0446] 表6:密码子最佳化参数

[0447]

	氨基酸	最佳肝脏密码子	最小尿苷密码子	Cas9 频率
A	丙氨酸	GCA	GCA	73
G	甘氨酸	GGA	GGA	73
V	缬氨酸	GTC	GTC	74
D	天冬氨酸	GAT	GAC	100
E	谷氨酸	GAA	GAA	111
I	异亮氨酸	ATC	ATC	93
T	苏氨酸	ACA	ACA	66
N	天冬酰胺	AAC	AAC	70
K	赖氨酸	AAG	AAG	155

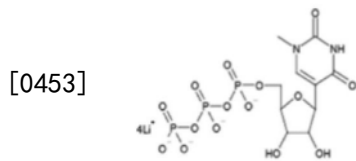
[0448]	S	丝氨酸	TCG	<i>AGC</i>	79
	R	精氨酸	AGA	AGA	79
	L	亮氨酸	CTG	CTG	148
	P	脯氨酸	CCG	CCG	36
	H	组氨酸	CAC	CAC	32
	Q	谷氨酰胺	CAG	CAG	52
	F	苯丙氨酸	TTC	TTC	64
	Y	酪氨酸	TAC	TAC	55
	C	半胱氨酸	TGC	TGC	2
	W	色氨酸	TGG	TGG	7
	M	甲硫氨酸	ATG	ATG	22

[0449] 在天冬氨酸及丝氨酸的情况下,对应于表达最高的tRNA的肝脏密码子包含胸苷,其将在对应mRNA中转录为尿苷。针对天冬氨酸及丝氨酸选择最小尿苷密码子(分别为GAC及AGC)。Cas9 ORF序列呈4140nt长,含有528个U(12.8%尿苷含量),且在ORF中避免具有3个或更多于3个连续尿苷的任何连接。序列中存在63种UU二核苷酸的情况(126/4140=3%尿苷二核苷酸含量)。SEQ ID NO:2提供含有19.6%尿苷作为RNA ORF的替代Cas9序列。

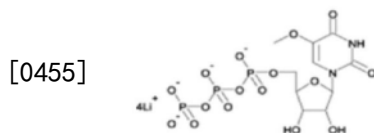
[0450] SEQ ID NO:3提供由SEQ ID NO:1及SEQ ID NO:2两者编码的Cas9的氨基酸序列作为未改变经编码的氨基酸序列的Cas9 ORF的新型设计。SEQ ID NO:4为SEQ ID NO:1的ORF的RNA形式。SEQ ID NO:5为SEQ ID NO:2的ORF的RNA形式。

[0451] 亦评估经修饰的核苷酸的作用。用于转录Cas9转录的经修饰的UTP包括N1-甲基-假UTP及5-甲氧基-UTP。

[0452] N1-甲基-假UTP的结构为:



[0454] 5-甲氧基-UTP的结构为:



[0456] 针对包含SEQ ID NO:4及SEQ ID NO:5的ORF的mRNA,测定活体外转录 (IVT) 产量。两者均编码核定位信号 (NLS)。在未经修饰的UTP或N1-甲基-假UTP任一者存在下,转录包含SEQ ID NO:5的序列。在未经修饰的UTP存在下,转录包含SEQ ID NO:4的序列。亦在渐增的5-甲氧基-UTP百分比下进行IVT,如图3的X轴上所示,其显示以分光光度法测定的此等构建

体中的每一者的产量。

[0457] 此等结果显示,当mRNA的5-甲氧基尿苷含量增加时,产量略微降低,但mRNA产量在所有条件下为可接受的。因此,可针对两个Cas9序列,经由所测试的条件产生具有可接受产量的Cas9 mRNA。

[0458] 使用曲线下面积(AUC)分析法,依利用Agilent Bioanalyzer 2100获得的mRNA毛细电泳法(CE)迹线,计算活体外转录的mRNA的纯度(图4)。使用未经修饰的UTP所生成SEQ ID NO:5Cas9 mRNA的纯度通常会随5-甲氧基-UTP取代增加而提高,而用N1-甲基-假UTP制得的相同构建体则受增加的5-甲氧基-UTP取代的影响较小。

[0459] 用未经修饰的UTP制得的SEQ ID NO:4Cas9似乎相对不受5-甲氧基-UTP取代的影响,在0%与20%之间的5-甲氧基-UTP取代度下,略微提高纯度。

[0460] 不同mRNA的免疫原性的评估法是采用墨点分析法,使用抗dsRNA抗体作为双股(ds)mRNA特征的量度,其是潜在免疫原性的指标(图5A至图5D)。图5B及图5D使用包含SEQ ID NO:5的Cas9 mRNA序列且图5C使用包含SEQ ID NO:4的Cas9 mRNA序列。对于使用未经修饰的UTP所生成的构建体(图5B至图5C),随着5-甲氧基-UTP含量增加,双股型通常会明显降低。使用N1-甲基-假UTP所生成的mRNA(图5D)显示与抗dsRNA抗体的结合性下降,但与抗体的结合性亦呈现随5-甲氧基-UTP含量增加而降低。

[0461] 随后由mRNA与靶向甲状腺素转运蛋白(TTR)的引导序列(G209;SEQ ID NO:64)一起转染至Neuro 2A细胞中,且测量编辑百分比,于活体外评估编辑效率。

[0462] 如图6A中所示,评估由包含具有N1-甲基-假UTP及2个核定位序列及HA标签的SEQ ID NO:2的构建体转录的Cas9 mRNA(由最左边括号指示的群组)、由包含具有UTP及2个核定位序列及HA标签转录的SEQ ID NO:2的构建体转录的Cas9 mRNA(通过中间括号指示的组)及由包含具有UTP的SEQ ID NO:1的构建体转录的Cas9 mRNA(由最右边括号指示的群组)。对于各组,针对呈如X轴上所指示的0%至100%的增加量的5-甲氧基-UTP的转录来评定0.1ng至100ng的mRNA的不同浓度。未处理细胞未显示可测量的编辑。图6B显示表示为EC50值(ng)的编辑效率数据。

[0463] 转录期间增加的5-甲氧基-UTP含量呈现对两个SEQ ID NO:5条件下的编辑效率具有不利作用,亦含有N1-甲基-假UTP的转录物要比含UTP的转录物稳健(例如在60%及80% 5-甲氧基-UTP下)。相比之下,包含SEQ ID NO:4的Cas9 mRNA序列的编辑效率对增加的5-甲氧基-UTP含量显示很小(若存在)效应。因此,根据此系统,包含SEQ ID NO:4mRNA的Cas9 mRNA序列可伴随至多100% 5-甲氧基-尿苷提供与含有未经修饰的尿苷的形式类似的编辑效率。

[0464] 3. 编码Cas9的mRNA的活体内表征

[0465] 评估包含SEQ ID NO:4的Cas9 mRNA序列对包含SEQ ID NO:5的Cas9 mRNA序列的活体内功效及在未经修饰的UTP、N1-甲基-假UTP、40% 5-甲氧基-UTP+60% 未经修饰的UTP或100% 5-甲氧基-UTP存在下包含SEQ ID NO:4的Cas9 mRNA序列的转录的效应。表7提供关于此等活体内研究组的信息。以脂质纳米颗粒(LNP)调配物形式施用各mRNA。

[0466] 表7. 用于活体内研究的LNP720至LNP724

[0467]	LNP	Cas9 ORF SEQ ID NO	经修饰的核苷酸
	LNP720	5	N1-甲基-假尿苷
[0468]	LNP721	4	N1-甲基-假尿苷
	LNP722	4	未经修饰
	LNP723	4	40% 5-甲氧基尿苷/60%未经修饰
	LNP724	4	5-甲氧基尿苷

[0469] 活体内研究设计如下。CD-1雌性小鼠是来自Charles River(每组n=5)。以每公斤1mg (mpk) 或0.5mpk连同针对甲状腺素转运蛋白 (TTR) 的单一引导RNA (SEQ ID NO:42) 一起对动物进行静脉内 (i.v.) 投配。在给药后4小时 (hpd) 针对MCP-1、IL-6、IFN- α 及TNF- α 的细胞介素分析对接受1mpk剂量的动物进行抽血。24hpd时针对总体健康对动物加以评定。在给药后7天进行尸体剖检,同时针对血清TTR分析收集血液,且针对次世代测序 (NGS) 编辑分析收集肝脏。

[0470] 4hpd时收集来自以1mpk投配的动物的血清,且制备血清且根据制造商说明书运作 **ProcartaPlex**[®] 小鼠4丛分析 (Thermo Fisher)。针对MCP-1、IL-6、IFN- α 及TNF- α 的血清含量的结果展现于图7A至图7D中。此等结果表明,用经修饰的UTP制备的包含SEQ ID NO:4的Cas9 mRNA序列 (LNP721、LNP723或LNP724) 显示相对较低含量的细胞介素产量。

[0471] 亦在给药后7天评定血清中的TTR含量,如图8A及表8中所示。TSS(即5%蔗糖、45mM NaCl、50mM Tris (pH 7.5)) 样本指示未进行LNP处理的TTR含量。所有LNP调配物均描述于表7中。

[0472] 表8:投配LNP720至LNP724之后的血清TTR含量的结果

LNP	Cas9 ORF SEQ ID NO	经修饰的核苷酸	TTR (μ g/ml) , 0.5 mpk	TTR (μ g/ml) , 1 mpk
TSS	不适用	不适用	1019.0	
[0473] LNP720	5	N1-甲基-假尿苷	559.4	287.2
LNP721	4	N1-甲基-假尿苷	160.1	35.3
LNP722	4	未经修饰	483.4	247.0
LNP723	4	40% 5-甲氧基尿苷/	525.8	170.1
[0474]		60%未经修饰		
LNP724	4	5-甲氧基尿苷	774.0	505.4

[0475] 表9及图8B提供关于如由次世代测序 (NGS) 测量的肝脏中TTR的编辑百分比的结果。

[0476] 表9:呈投配LNP720至LNP724之后的肝脏中TTR的编辑百分比的结果

LNP	Cas9 SEQ ID NO	经修饰的核苷酸	编辑%, 0.5 mpk	编辑%, 1 mpk
TSS	不适用	不适用	0.16	
LNP720	5	N1-甲基-假尿苷	34.9	50.3
[0477] LNP721	4	N1-甲基-假尿苷	63.3	74.8
LNP722	4	未经修饰	43.6	53.7
LNP723	4	40% 5-甲氧基尿苷/ 60%未经修饰	31.8	63.2
LNP724	4	5-甲氧基尿苷	15.9	35.2

[0478] 与TSS对照样本相比,包含Cas9的所有LNP均显示血清TTR含量降低及高于基线的编辑。在比较均用N1-甲基-假UTP转录的标准Cas9 mRNA (SEQ ID NO:5, LNP720) 与包含SEQ ID NO:4mRNA的Cas9 mRNA序列 (SEQ ID NO:4, LNP721) 时,包含SEQ ID NO:4的Cas9 mRNA序列显示经改良的活性(较低TTR及较高编辑%)。对于包含SEQ ID NO:4的Cas9 mRNA序列,活性在N1-甲基-假UTP情况下为最高的,且伴随40%5-甲氧基-UTP+60%未经修饰的UTP的转录(LNP723)产生的活性要比100%5-甲氧基-UTP (LNP724) 高。

[0479] 作为脱靶效应的量度,亦测量用1mpk上文所述的LNP调配物投配的动物的脾脏中的编辑,如图7及表10中所示。对于所有LNP调配物,无论在Cas9或经最佳化的Cas9下,均在肝脏中看到大于20倍的较高编辑(图6A)。

[0480] 表10:关于投配1mpk包含sgRNA及不同Cas9的LNP之后的脾脏中的TTR的编辑百分比的结果

LNP	Cas9 SEQ ID NO	经修饰的核苷酸	编辑%, 1 mpk
TSS	不适用	不适用	0.1
LNP720	5	N1-甲基-假尿苷	0.66
[0481] LNP721	4	N1-甲基-假尿苷	2.42
LNP722	4	未经修饰	0.68
LNP723	4	40% 5-甲氧基尿苷/ 60%未经修饰	1.12
LNP724	4	5-甲氧基尿苷	0.34

[0482] 4. 编码Cas9的mRNA在初级小鼠肝细胞中的功效的表征

[0483] 活体外评估不同LNP在初级小鼠肝细胞 (PMH) 中的功效。

[0484] 在100ng下,表5中所述的所有LNP均支持TTR的编辑,如图10中所示。如所预期,未处理的细胞未显示可测量的TTR的编辑。

[0485] 表11显示基于图10中展现的资料计算的各LNP的EC50值。

[0486] 表11:针对PMH中TTR的基因编辑的经估算的EC50值 (ng)

	LNP	EC50
	LNP720	45.65
	LNP721	23.04
[0487]	LNP722	54.00
	LNP723	52.40
	LNP724	164.1
	LNP685	59.88

[0488] 5. 含Cas9 mRNA的LNP在大鼠中的活体内表征

[0489] 在大鼠中评估包含SEQ ID NO:4的Cas9 mRNA序列对包含SEQ ID NO:5的Cas9 mRNA序列的活体内功效。表12提供关于此等活体内研究组的信息。标准Cas9 mRNA是指SEQ ID NO:5,而缺乏U(U-dep)的mRNA是指SEQ ID NO:4。各mRNA是以脂质纳米颗粒 (LNP) 调配物形式施用。

[0490] LNP716(标准Cas9)及LNP738(缺乏U)LNP调配物的详情显示于表12中。

[0491] 表12:LNP调配物表征

	LNP ID	RNA 制备及方法	N:P	RNA 浓度 (mg/mL)	囊封率(%)	粒度(nm)	粒子 PDI
[0492]	716	柠檬酸盐 -NaCl ; X-flow_TFF	4.5	2.00	98	88.42	0.056
	738	柠檬酸盐 -NaCl ; X-flow_TFF	4.5	2.22	97	92.80	0.044

[0493] PDI=多分散性指数

[0494] N:P=N:P比,如上文所述

[0495] 如先前所述测量血清TTR。

[0496] 在大鼠中在2mpk及5mpk的剂量下将具有SEQ ID NO:5的ORF的Cas9 mRNA与具有SEQ ID NO:4的ORF的Cas9 mRNA(图11A至图11B)进行比较,如图11A及表13中所示。此等资料表明,在2mpk及5mpk两者下,与SEQ ID NO:5的Cas9 ORF相比,SEQ ID NO:4的Cas9 ORF引起血清TTR较显著降低。图11B及表13展示呈相对于经TSS处理的对照的值的百分比形式的此等结果。5mpk剂量的U-dep Cas9 LNP引起血清TTR含量降低大于90%。

[0497] 表13:用LNP716及LNP738 Cas9调配物投配之后的血清TTR含量

[0498]	LNP	Cas9	剂量(MPK)	血清TTR ($\mu\text{g/ml}$)	血清TTR (KD%)
	TSS	-	-	1954.40	-
[0499]	716	标准	5	950.36	51.37
			2	1474.58	24.55
	738	U-Dep	5	153.30	92.16
			2	824.93	57.79

[0500] KD% = 与TSS样本的平均血清浓度相比的基因减弱%

[0501] 图10及表14显示用LNP716 (标准) 及LNP738 (U-dep) 调配物以2mpk及5mpk投配之后的TTR的肝脏编辑。尽管TSS显示可忽略的编辑, 但LNP716及LNP738调配物两者均引起TTR的肝脏编辑。在比较调配物中, 包含U缺乏的LNP738调配物引起的编辑为包含标准Cas9的LNP716调配物的两倍。

[0502] 表14: 用缺乏U及标准Cas9调配物投配之后的TTR的肝脏编辑

	LNP	Cas9	剂量(MPK)	肝脏编辑(%)
	TSS	-	-	0.10
[0503]	716	标准	5	32.14
			2	8.04
	738	U-Dep	5	66.02
			2	31.60

[0504] 此等数据表明, 缺乏U的Cas9 mRNA显著地改良肝脏中TTR的编辑程度。

[0505] 6. 具有不同UTR的mRNA的表征

[0506] 将如表15中所指示的具有UTR及+/-血球凝集素 (HA) 标签的编码Cas9的mRNA与靶向TTR的引导RNA (G282; SEQ ID NO: 42) 调配为LNP。使用Nano Assemblr™组配LNP, 其含有45%脂质A、9%DSPC、44%胆固醇及2%PEG2k-DMG, 且使用Amicon PD 10过滤器纯化, 且以0.5mg/ml的浓度 (LNP浓度) 使用。以0.5或1.0mpk静脉内投配CD-1雌性小鼠 (每组n=5)。在给药后7天, 将动物处死, 收集血液及肝脏, 且测量血清TTR及肝脏编辑。

[0507] 表15. LNP662至LNP669 mRNA描述及血清TTR及肝脏编辑分析的结果

[0508]	LNP	mRNA描述	剂 量	血 清 TTR	血 清 TTR	肝 脏 编 辑
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		(mpk)	(平均 μg /mL)	(平均 KD%)	(%)
TSS	-	-	944.52		0.06
LNP662	ORF: SEQ ID NO: 5; 无HA标签	1	729.56	22.76	20.08
		0.5	988.75	-4.68	8.26
LNP663	ORF: 具有HA标签的 SEQ ID NO: 45	1	488.62	48.27	39.12
		0.5	842.88	10.76	20.18
LNP664	ORF: 具有HA标签; HBA UTR的SEQ ID NO: 45	1	628.35	33.47	32.68
		0.5	1087.10	-15.10	14.68
LNP665	ORF: 具有HA标签; HBB UTR的SEQ ID NO: 45	1	524.43	44.48	42.70
		0.5	797.37	15.58	18.72
LNP666	ORF: 具有HA标签; XBG UTR的SEQ ID NO: 45	1	233.46	75.28	54.28
		0.5	1011.22	-7.06	17.96
LNP667	ORF: SEQ ID NO: 4; 无HA标签	1	197.58	79.08	58.64
		0.5	689.24	27.03	31.26
LNP668	ORF: SEQ ID NO: 4; 无HA标签; 未经修饰 的NTP	1	622.42	34.10	34.44
		0.5	811.94	14.04	21.30
LNP669	ORF: SEQ ID NO: 5; 无HA标签; 未经修饰 的NTP	1	1050.68	-11.24	9.82
		0.5	1189.70	-25.96	4.04

[0510] 除非另外指明, 否则mRNA中的UTR为HSD/A1b。HBA: 人类 α 血球蛋白; HBB: 人类 β 血球蛋白 (HBB); XBG: 爪蟾 β 血球蛋白 (XBG)。除非另外指明, 否则mRNA含有100% N1-甲基假尿苷代替尿苷。

[0511] 图13A至图13E显示血清TTR (在图13A中显示为 $\mu\text{g}/\text{ml}$, 且在图13B中显示为TSS的%); 所有LNP662至LNP669的肝脏编辑 (图13C); 其中仅UTR变化的LNP663至LNP666的肝脏编辑 (图13D); 及其中仅mRNA序列及UTP修饰变化的LNP662及LNP667至LNP669的肝脏编辑 (图13E)。

[0512] 人类白蛋白、人类 α 血球蛋白、人类 β 血球蛋白及爪蟾 β 血球蛋白UTR大致同样有效; 人类 α 血球蛋白的值可略微较低但并不明确差值是否明显。

[0513] 含有较少尿苷的SEQ ID NO:4的ORF增加肝脏中的编辑的量。用N1-甲基假尿苷制得的Cas9 mRNA要比用未经修饰的尿苷制得的Cas9 mRNA有效。

[0514] 7. 使用不同引导物:Cas9比的活体外及活体内编辑

[0515] 将包含根据SEQ ID NO:4或SEQ ID NO:5的ORF的mRNA与靶向TTR的引导RNA以如表16中所示的不同引导物:Cas9 mRNA重量比调配为LNP。通过如上文所指示的IVT合成用代替尿苷三磷酸的N1-甲基假尿苷三磷酸、HSD 5'UTR、人类白蛋白3'UTR及聚-A尾制得Cas9 mRNA。

[0516] 表16. 用于活体外及活体内研究的LNP815至LNP824

[0517]

LNP	Cas9 SEQ ID NO	RNA比 (引导物:Cas9)
LNP815	5	2:1
LNP816	5	1:1
LNP817	5	1:2
LNP818	5	1:4
LNP819	5	1:8
LNP820	4	2:1
LNP821	4	1:1
LNP822	4	1:2
LNP823	4	1:4
LNP824	4	1:8

[0518] 将初级小鼠肝细胞 (PMH) 涂铺于补充有3% 食蟹猕猴血清的培养基中持续24小时, 且随后用表16中所示的0.3、1、3或10ng LNP处理。48小时之后裂解细胞, 且通过NGS测定编辑%。结果显示在图14及表17中。

[0519] 表17. PMH中的活体外编辑

[0520]

LNP	mRNA	引导物:mRNA 比	10 ng	3 ng	1 ng	0.3 ng
LNP815	5	2:1	75.0	41.7	9.3	1.3
LNP816	5	1:1	80.9	51.5	15.5	2.6
LNP817	5	1:2	79.1	49.8	16.3	2.2
LNP819	5	1:8	90.7	67.2	27.8	5.2
LNP820	4	2:1	78.8	44.3	9.8	0.9
LNP821	4	1:1	81.9	49.9	12.3	2.1
LNP823	4	1:4	85.5	58.3	17.8	2.0
LNP824	4	1:8	84.9	47.4	13.1	1.6

[0521] 对于活体内表征, 以0.2、0.5或1mpk向小鼠施用LNP (每组n=5)。在给药后8天, 将动物处死, 收集血液及肝脏以及脾脏, 且测量血清TTR、肝脏编辑及脾脏编辑。血清TTR结果显示在图15A至图15B及表18中。肝脏编辑结果显示在图16A至图16B及表19中。脾脏编辑结

果显示在图17A至图17B及表20中。用媒介剂(转化及储存溶液;“TSS”)投配阴性对照小鼠。使用LNP815至LNP819的实验及使用LNP820至LNP824的实验运作独立对照。

[0522] 表18. 用LNP815至LNP824投配之后的血清TTR含量

LNP	引导物:Cas9比	剂 量 (mpk)	血 清 TTR ($\mu\text{g/mL}$)	血 清 TTR (KD%)
TSS			974.23	-
LNP815	2:1	1	300.32	69.17
		0.5	539.37	44.64
		0.2	800.85	17.80
LNP816	1:1	1	183.61	81.15
		0.5	466.63	52.10
		0.2	859.05	11.82
LNP817	1:2	1	117.86	87.90
		0.5	487.26	49.99
		0.2	715.35	26.57
LNP818	1:4	1	168.44	82.71
		0.5	428.89	55.98
		0.2	935.14	4.01

LNP819	1:8	1	323.87	72.29
		0.5	664.80	31.76
		0.2	1039.66	-6.72
TSS			1104.27	-
LNP820	2:1	1	38.12	96.55
		0.5	122.59	88.90
		0.2	358.88	67.50
LNP821	1:1	1	38.53	96.51
		0.5	190.30	82.77
		0.2	501.05	54.63
LNP822	1:2	1	25.76	97.67
		0.5	123.34	88.83
		0.2	520.73	52.84
LNP823	1:4	1	28.00	97.46
		0.5	98.99	91.04
		0.2	529.35	52.06
LNP824	1:8	1	93.65	91.52
		0.5	174.43	84.20
		0.2	731.43	33.76

[0525] KD%提供相对于TSS对照的TTR含量的基因减弱%。

[0526] 表19. 用LNP815至LNP824投配之后的肝脏编辑

[0527]

LNP	引导物:Cas9比	剂 量 (MPK)	编辑%
TSS			0.78
LNP815	2:1	1	57.52
		0.5	38.76
		0.2	12.28
LNP816	1:1	1	63.46
		0.5	40.26
		0.2	14.12
LNP817	1:2	1	68.18
		0.5	38.38
		0.2	17.58
LNP818	1:4	1	61.8
		0.5	41.58
		0.2	9.44
LNP819	1:8	1	55.88
		0.5	31.26

[0528]

		0.2	6.4
TSS			0.22
LNP820	2:1	1	67
		0.5	69.58
		0.2	48.78
LNP821	1:1	1	75.82
		0.5	64.02
		0.2	41.2
LNP822	1:2	1	73.26
		0.5	69.74
		0.2	44.16
LNP823	1:4	1	75.48
		0.5	66.7
		0.2	38.7
LNP824	1:8	1	69.14
		0.5	63.16
		0.2	20.78

[0529] LNP820至LNP824通常产生大于或约等于相同比率下的其LNP815至LNP819对应物的肝脏编辑结果。LNP820至LNP824在0.5及1mpk下测试的比率范围内及0.2mpk下2:1至1:4

的比率下显示恒定效能。

[0530] 表20. 用LNP815至LNP824投配之后的脾脏编辑

LNP	引导物:Cas9比	剂 量 (MPK)	编辑%
TSS			0.12
LNP815	2:1	1	0.6
		0.5	0.62
		0.2	0.28
LNP816	1:1	1	0.74
		0.5	1
		0.2	0.28
LNP817	1:2	1	0.74
		0.5	0.58
		0.2	0.22
LNP818	1:4	1	1.22
		0.5	0.44
		0.2	0.3
LNP819	1:8	1	0.9
		0.5	0.64
		0.2	0.36
TSS			0.225
LNP820	2:1	1	0.83
		0.5	0.825
		0.2	0.525
LNP821	1:1	1	1.425
		0.5	0.9
		0.2	0.425
LNP822	1:2	1	1.85
		0.5	0.625
		0.2	1.74
LNP823	1:4	1	1.475
		0.5	0.8
		0.2	0.32
LNP824	1:8	1	1.14
		0.5	1.34
		0.2	0.56

[0533] 用各调配物以3mpk投配额外小鼠组 (n=2), 且在6hpd处死以用于测定肝脏中的蛋白质表达。来自用3mpk 1:1及1:4比率调配物 (LNP816、LNP818、LNP821及LNP823) 处理的小鼠的肝脏蛋白质的蛋白质印迹法展示在图18中。针对蛋白质印迹法的初级Ab为呈1:5,000

的Immunoprecise™兔抗Cas9,且二级Ab为呈1:12,500的Dylight™山羊抗兔。Cas9蛋白质表达在使用具有SEQ ID NO:4的ORF的mRNA的LNP中明显较高。

[0534] 8. 经修饰的核苷酸的影响的表征

[0535] 将编码Cas9且含有如表21中所指示的经修饰的核苷酸的mRNA与靶向TTR的引导RNA(G282;SEQ ID NO:42)调配为LNP。LNP1034含有自Trilink Biotechnologies有限责任公司市售获得的Cas9 mRNA且包括CleanCap™(其中7-甲基鸟嘌呤帽结构之后的第一核苷酸经2'-O-甲基化的Cap1结构)。LNP1027至LNP1033含有包含根据SEQ ID NO:4的ORF的mRNA及ARCA(抗反向帽结构类似物)Cap0。使用Nano Assemblr™组配LNP,其含有45%脂质A、9% DSPC、44%胆固醇及2%PEG2k-DMG,使用Amicon PD10过滤器纯化,且悬浮于TSS缓冲液中。LNP中的N:P(氮与磷酸)比为4.5且调配物的RNA浓度为0.4mg/ml。以0.1或0.3mpk静脉内投配CD-1雌性小鼠(每组n=5)。在给药后7天,将动物处死,收集血液及肝脏,且测量血清TTR及肝脏编辑。

[0536] 表21. 用于活体内研究的LNP1027至LNP1034

LNP ID	Cas9 ORF	帽结构	经修饰的核苷酸
LNP1027	SEQ ID NO: 4	ARCA	N1-甲基-假尿苷
LNP1028	SEQ ID NO: 4	ARCA	25% 5-碘尿苷
LNP1029	SEQ ID NO: 4	ARCA	50% 5-碘尿苷
[0537] LNP1030	SEQ ID NO: 4	ARCA	25% 5-碘胞苷
LNP1031	SEQ ID NO: 4	ARCA	25% 5-碘尿苷及25% 5-碘胞苷
LNP1032	SEQ ID NO: 4	ARCA	假尿苷
LNP1033	SEQ ID NO: 4	ARCA	假尿苷及5-甲基胞苷
LNP1034	Trilink Cas9 mRNA	CleanCap™	5-甲氧基尿苷

[0538] 对于其中列出经修饰的尿苷及/或胞苷核苷酸呈25%或50%的LNP,尿苷及/或胞苷的剩余部分分别为未经修饰的。

[0539] 血清TTR结果展示于图19A至图19B(血清TTR结果分别以μg/mL及TSS对照的%表示);图20(肝脏编辑);及表22中。

[0540] 表22. LNP1027至LNP1034的血清TTR及肝脏编辑结果

LNP ID	剂量 (mpk)	经修饰的核 苷酸	血清 TTR ($\mu\text{g/mL}$)	血清 TTR (KD%)	平均编辑%
[0541] TSS	-		1438.43 8	-	0.20
LNP1027	0.3	N1-甲基-假	381.474	73.48	51.08
	0.1	尿苷	979.404	31.91	15.76
LNP 1028	0.3	25% 5-碘尿	311.738	78.33	54.96
	0.1	苷	758.41	47.28	18.82
LNP1029	0.3	50% 5-碘尿	714.748	50.31	31.94
	0.1	苷	1034.69	28.07	8.26
LNP1030	0.3	25% 5-碘胞	676.164	52.99	26.28
	0.1	苷	973.836	32.30	6.58
[0542] LNP1031	0.3	25% 5-碘尿	546.946	61.98	30.30
	0.1	苷及25% 5- 碘胞苷	969.92	32.57	6.12
LNP1032	0.3	假尿苷	448.582	68.81	42.68
	0.1		947.602	34.12	9.60
LNP1033	0.3	假尿苷及5-	979.284	31.92	11.36
	0.1	甲基胞苷	1031.33	28.30	2.22
LNP1034	0.3	5-甲氧基尿	1133.82 6	21.18	4.82
	0.1	苷	1339.30 4	6.89	0.78

[0543] LNP1027的含N1-甲基假尿苷的mRNA具有比LNP1032的含假尿苷的mRNA略微较高的编辑效率。含有假尿苷及5-甲基胞嘧啶核苷两者的mRNA (LNP1033) 的效能显著降低。含有25% 5-碘尿苷的mRNA显示与含N1-甲基假尿苷的mRNA相等的编辑效率。在50% 5-碘尿苷下, 效能有所降低。来自Trilink的5-甲氧基尿苷mRNA显示较低活性。

[0544] 9. 大鼠中具有不同UTR的mRNA的影响的表征

[0545] 此研究评估经ARCA加帽结构的具有HBB (人类 β -血球蛋白) 5'及3'UTR; XBG (爪蟾 β -血球蛋白) 5'及3'UTR; 或具有人类HSD17B4 (HSD) 5'UTR及白蛋白 (ALB) 3'UTR的Cas9 mRNA在

大鼠中的活体内功效。

[0546] 使用上文所述的错流方法制备含有在LNP中呈1:1摩尔比的靶向大鼠TTR基因的引导RNA(G534;SEQ ID NO:72)及Cas9 mRNA的调配物且将其在VivaFlow™ 50膜上过滤。LNP含有呈45:9:43:3摩尔比的阳离子型脂质(脂质A)、胆固醇、DSPC及PEG2k-DMG且具有6.0的N:P比。以1mpk及0.3mpk投配调配物。所有大鼠均为来自Charles River的史泊格多利雌性,每组n=5。尸体剖检(给药后7天)时,针对TTR分析收集血清且针对编辑分析收集肝脏。在LNP1058中,mRNA含有HBB UTR。在LNP1059中,mRNA含有XBG UTR。在LNP1060中,mRNA分别含有HSD及ALB 5'及3'UTR。在所有情况下,mRNA编码序列是根据SEQ ID NO:4。

[0547] 肝脏编辑及血清TTR结果展示于图21A至图21C及表23中。

[0548] 表23. 大鼠中使用LNP1058至LNP1060的肝脏编辑及血清TTR结果。

LNP	UTR	剂 量 (mpk)	肝 脏 编 辑 (%)	血 清 TTR (µg/ml)	血 清 TTR (KD %)
TSS			0.0	1366.9	
[0549] 1058	HBB (3'及5')	1	66.3	84.4	93.8
		0.3	27.6	881.1	35.5
1059	XBG (3'及5')	1	69.1	63.0	95.4
		0.3	31.6	748.7	45.2
1060	HSD (5') 及 ALB (3')	1	62.6	115.6	91.5
		0.3	20.9	896.0	34.4

[0550] 结果表明,LNP1058至LNP1060中所有经测试的mRNA均能够支持编辑。伴随LNP1059中含有XBG UTR的mRNA看到最高编辑程度及血清TTR的最显著降低。

[0551] 10. RNA载荷:mRNA及gRNA共调配

[0552] 此研究评估不同gRNA与mRNA比在小鼠中的活体内功效。通过如实例1中所指示的IVT合成用代替尿苷三磷酸的N1-甲基假尿苷三磷酸来制得经CleanCap™加帽结构的具有SEQ ID NO:4的ORF、HSD 5'UTR、人类白蛋白3'UTR、Kozak序列及聚-A尾的Cas9 mRNA。

[0553] 由所述mRNA及如实例2中所述的sg282(SEQ ID NO:42;G282)与脂质A、胆固醇、DSPC及PEG2k-DMG以55:33:9:3摩尔比且以6的N:P比制备LNP调配物。调配物的gRNA:Cas9 mRNA重量比如表24中所示。

[0554] 表24. LNP1110至LNP1116的表征。

LNP ID	RNA浓度 (mg/mL)	EE (%)	粒度(nm)	粒子PDI	数量平均 (nm)
1110	0.92	99	69.52	0.022	56.47
1111	0.86	97	76.65	0.065	57.36
[0555] 1112	0.90	99	76.58	0.036	63.11
1113	0.97	99	76.60	0.071	58.92
1114	1.05	99	76.34	0.018	62.82
1115	0.65	99	82.64	0.018	66.63
1116	0.75	100	82.01	0.039	65.05

[0556] 对于活体内表征,以每公斤0.1mg总RNA(引导RNA毫克数+mRNA毫克数)向小鼠施用

以上LNP (每组n=5)。在给药后7至9天,将动物处死,收集血液及肝脏,且如上文所述测量血清TTR及肝脏编辑。血清TTR及肝脏编辑结果展示于图22A及图22B中。用TSS媒剂投配阴性对照小鼠。

[0557] 此外,以每公斤0.05mg mRNA的恒定mRNA剂量,同时将gRNA剂量自0.06mg/kg变为0.4mg/kg来向小鼠施用以上LNP (每组n=5)。在给药后7至9天,将动物处死,收集血液及肝脏,且测量血清TTR及肝脏编辑。血清TTR及肝脏编辑结果展示于图22C及图22D中。用TSS媒剂投配阴性对照小鼠。

[0558] 11. 密码子方案的表征

[0559] 设计使用不同密码子方案的Cas9序列以针对经改良的蛋白质表达进行测试。各序列经设计以使用独特密码子组编码SEQ ID No:3的Cas9氨基酸。在各开放阅读框架序列中,使用单一密码子编码各氨基酸。基于密码子在基于NCBI-GenBank Flat File Release 160.0 (Nakamura等人 (2000) Nucl. Acids Res. 28, 292; Benson等人 (2006) Nucleic Acids Res. 34 (数据库期), D16-20) 的智人中的整个蛋白质编码基因中的出现频率及特定核苷酸在密码子中的丰度来改变序列。基于Table 4中所示的密码子方案,构筑编码SEQ ID NO:3的Cas9蛋白质的七个不同Cas9开放阅读框架 (SEQ ID NO:52、SEQ ID NO:54及SEQ ID NO:108至SEQ ID NO:112)。将此等并入至亦含有HSD 5'UTR (SEQ ID NO:41)、白蛋白3'UTR、T7启动子及聚A尾的构建体中。含有白蛋白3'UTR及聚A尾的示例性序列为SEQ ID NO:53,其中3'UTR及聚A尾在HSD 5'UTR及SEQ ID NO:52的ORF之后。使用如由Presnyak及同事 (2015) 所述的基于用于改良的mRNA半衰期的最佳密码子的密码子流程编码SEQ ID NO:3的Cas9蛋白质的以类似方式构成的构建体 (SEQ ID NO:107, 使用表4的长半衰期密码子组) 亦包括于此等评估中。

[0560] 通过IVT产生各构建体的信使RNA。用800ng各Cas9 mRNA使用Lipofectamine™ MessengerMAX™转染剂 (ThermoFisher) 转染HepG2细胞。转染后六小时,通过冻融裂解细胞且通过离心清除。通过ELISA分析测定Cas9蛋白质含量。简言之,通过二辛可宁酸 (蛋白) 含量测定法测定总蛋白质浓度。根据制造商方案使用Cas9小鼠抗体 (Origene, 目录号CF811179) 作为捕捉抗体且使用Cas9 (7A9-3A3) 小鼠mAb (Cell Signaling Technology, 目录号14697) 作为侦测抗体来制备MSD GOLD 96孔抗生蛋白链菌素SECTOR板 (Meso Scale Diagnostics, 目录号L15SA-1)。在具有无EDTA的1×Halt™蛋白酶抑制剂混合液 (ThermoFisher, 目录号78437) 的稀释剂39中的呈0、0.12、0.49、1.95、7.81、31.25、125及500ng/mL的Cas9蛋白质用作校正标准。使用Meso Quickplex SQ120仪器 (Meso Scale Discovery) 读取ELISA板且用Discovery Workbench 4.0软件包 (Meso Scale Discovery) 分析资料。

[0561] 通过将mRNA以及靶向甲状腺素转运蛋白 (TTR) 的引导物 (G502; SEQ ID NO:70) 转染于HepG2细胞中且测量编辑百分比来活体外评定编辑效率。在3ng至100ng的mRNA浓度下评定包含表25中所指示的SEQ ID No的Cas9 mRNA。未处理细胞未显示可测量的编辑。图23至图24及表25显示不同密码子组对Cas9蛋白质表达及活体外编辑的影响。

[0562] 表25. 具有不同密码子组的ORF的活体外编辑及表达。

ORF (密码子组)	每毫克总蛋白质的Cas9 纳克数	每毫克总蛋白质的Cas9 纳克数标准 差	编辑 % (经转染 的 30 ng mRNA)	编辑标准 差
SEQ ID No: 50 (表6最小 尿苷密码子, 剪接接点经 移除)	10.99	1.04	35.6	2.11
SEQ ID No: 107 (表4长 半衰期)	18.78	2.83	36.5	3.27
SEQ ID No: 52 (表4低U 1)	31.23	4.47	22.2	2.83
[0563] SEQ ID No: 54 (表4低U 2)	1.54	0.16	14.7	0.40
SEQ ID No: 108 (表4高 U)	1.41	0.12	14.0	2.95
SEQ ID No: 109 (表4低 G)	4.95	0.70	19.6	2.29
SEQ ID No: 110 (表4低 C)	2.26	0.16	23.1	4.07
SEQ ID No: 111 (表4低 A)	74.62	15.53	41.3	3.56
SEQ ID No: 112 (表4低 A/U)	77.32	10.60	34.8	7.32
SEQ ID No: 4 (表6最小 尿苷密码子)	17.16	1.54	34.7	1.15

[0564] 为了测定密码子方案的活体内有效性,当使用表4中所述的密码子方案自编码Cas9的mRNA活体内表达时,测量Cas9蛋白质表达。将如表26中所指示的信使RNA与靶向TTR的引导RNA(G282;SEQ ID NO:42)调配为LNP。使用错程序组配LNP,且其含有分别呈50:38:9:3摩尔比的50%脂质A、9%DSPC、38%胆固醇及3%PEG2k-DMG,且具有6.0的N:P比。使用Amicon PD-10过滤器(GE Healthcare)纯化LNP,且以0.32mg/ml的浓度(LNP浓度)使用。以1mpk静脉内投配CD-1雌性小鼠(每组n=5)。在给药后3小时,将动物处死,收集肝脏且测量肝脏中的Cas9表达。使用上文所述的Meso Scale Discovery ELISA分析测量肝脏中的Cas9蛋白质表达。通过珠粒研磨机在具有1×Complete蛋白酶抑制剂片剂(Roche,目录号11836170001)的RIPA缓冲液(Boston Bioproducts BP-115)中将大约40mg肝脏组织均质化。图25及表26显示肝脏中的Cas9表达结果。低A及low A/U密码子方案(SEQ ID NO:111及SEQ ID NO:112的ORF)的mRNA显示所测试的ORF的最高Cas9表达。阴性对照及SEQ ID NO:54

的ORF的Cas9蛋白质表达小于定量下限 (LLOQ)。

[0565] 表26

ORF	平均Cas9(每公克肝脏的纳克数)	标准差
TSS	<LLOQ	0.0
SEQ ID No:4	1644	1172
SEQ ID NO:52	1562	951
SEQ ID NO:54	<LLOQ	0.0
SEQ ID NO:111	2630	730
SEQ ID NO:112	2134	362

[0567] 为了测定密码子方案的活体内有效性,自使用不同密码子方案的编码Cas9的mRNA活体内测量基因组编辑。将如表27中所指示的信使RNA与靶向TTR的引导RNA(G282;SEQ ID NO:42)调配为LNP。使用错流程序组配LNP,且其含有分别呈50:38:9:3摩尔比的50%脂质A、9%DSPC、38%胆固醇及3%PEG2k-DMG,且具有6.0的N:P比。使用Amicon PD-10过滤器(GE Healthcare)纯化LNP,且以0.05mg/ml的浓度(LNP浓度)使用。以0.1mpk静脉内投配CD-1雌性小鼠(每组n=5,不同的处在于用SEQ ID NO:52处理的组,n=4)。在给药后6天,将动物处死,收集血液及肝脏,且测量血清TTR及肝脏编辑。表27及图26显示活体内编辑结果。表27及图27A至图27B显示血清TTR含量。

[0568] 表27

ORF	平均编辑%	编辑标准差	血清TTR(μg/ml)	血清TTR标准差	n
TSS	0.06	0.05	856	68	5
SEQ ID No: 4	40.96	8.41	329	143	5
SEQ ID No: 107	44.28	11.45	255	97	5
SEQ ID No: 52	60.10	8.07	143	78	4
SEQ ID No: 54	1.50	0.66	822	161	5
SEQ ID No: 108	0.74	0.36	914	182	5
SEQ ID No: 111	57.26	4.15	216	62	5
SEQ ID No: 112	61.44	4.50	100	79	5

[0570] 为了测定不同mRNA浓度下的密码子方案的功效,进行活体内剂量反应实验。将如表28中所指示的信使RNA与靶向TTR的引导RNA(G282;SEQ ID NO:42)调配为LNP。使用错流方法组配LNP且其含有50%脂质A、9%DSPC、38%胆固醇及3%PEG2k-DMG。使用Amicon PD-10过滤器(GE Healthcare)纯化LNP,且以0.7mg/ml的浓度(LNP浓度)使用。以0.03、0.1或0.3mpk静脉内投配CD-1雌性小鼠(每组n=5)。在给药后7天,将动物处死,收集血液及肝脏,且测量血清TTR及肝脏编辑。表28及图28显示活体内编辑结果。表28及图29A至图29B显示血清TTR含量。

[0571] 表28

ORF	剂量 (mpk)	肝脏编 辑(%)	血清TTR ($\mu\text{g/mL}$)	血清TTR (KD%)
TSS	不 适 用	0.1	576.8	0.0
[0572] SEQ ID No: 4	0.3	51.3	165.6	71.3
	0.1	17.3	540.7	6.3
	0.03	1.9	761.4	-32.0
SEQ ID No: 52	0.3	57.0	100.8	82.5
	0.1	29.6	336.1	41.7
	0.03	5.0	636.4	-10.3
SEQ ID NO: 111	0.3	59.4	93.8	83.7
	0.1	30.6	373.5	35.2
	0.03	5.9	559.6	3.0
SEQ ID	0.3	60.6	92.0	87.2
[0573] NO: 112	0.1	25.5	397.5	31.1
	0.03	7.8	555.3	3.7

[0574] 为了测定具有不同UTR的密码子方案的有效性,在施用编码Cas9的mRNA后活体内测量基因组编辑。将如表29中所指示的信使RNA与靶向TTR的引导RNA(G282;SEQ ID NO:42)调配为LNP。使用错程序组配LNP,且其含有分别呈50:38:9:3摩尔比的50%脂质A、9% DSPC、38%胆固醇及3%PEG2k-DMG,且具有6.0的N:P比。使用Amicon PD-10过滤器(GE Healthcare)纯化LNP,且以0.05mg/ml的浓度(LNP浓度)使用。以0.1mpk静脉内投配CD-1雌性小鼠(每组n=5;针对SEQ ID NO:43编辑,n=4)。在给药后6天,将动物处死,收集血液及肝脏,且测量血清TTR及肝脏编辑。表29及图30A至图30B显示活体内编辑(B)及血清TTR结果(A)。

[0575] 表29

mRNA构建体	编辑%	标准差	血清TTR($\mu\text{g/ml}$)	标准差
TSS	0	0	1274	214
SEQ ID No:43	28	4	630	152
SEQ ID No:176	35	8	482	138
SEQ ID No:177	37	9	316	143
SEQ ID No:178	42	6	524	192

[0577] 12. 加帽结构的影响的表征

[0578] 将编码Cas9且含有如表30中所指示的帽结构、UTR及聚A尾的mRNA与靶向TTR的引导RNA(G282;SEQ ID NO:42)调配为LNP。使用错程序组配LNP,其含有分别呈50:38:9:3摩尔比的50%脂质A、9% DSPC、38%胆固醇及3%PEG2k-DMG,且具有6.0的N:P比。使用Amicon PD-10过滤器(GE Healthcare)纯化LNP,且以0.06mg/ml的浓度(LNP浓度)使用。以0.1或0.3mpk静脉内投配CD-1雌性小鼠(每组n=5)。在给药后7天,将动物处死,收集血液及肝脏,

且测量血清TTR及肝脏编辑。

[0579] 图31及表30显示0.1mpk剂量下,具有Cap 1的mRNA具有比具有Cap 0的mRNA高约10%的平均编辑。在0.3mpk剂量下,具有XBG UTR的mRNA具有比具有HSD UTR的mRNA略微较高的平均编辑,除酶cap 0外。血清TTR结果显示于图32(血清TTR结果分别以 $\mu\text{g}/\text{mL}$ 及TSS对照的%表示);图31(肝脏编辑);及表30中。

[0580] 表30. 针对活体内加帽结构研究的血清TTR及肝脏编辑结果

[0581]

mRNA 构建体	帽结构类型	帽结构	5' UTR	剂量	平均编辑 (%)	标准差
SEQ ID No. 43	Cap 0	ARCA	HSD	0.1 mpk	21.76	11.61
SEQ ID No. 59	Cap 0	ARCA	XBG	0.1 mpk	22.9	5.53
SEQ ID No. 59	Cap 0	酶Cap 0	XBG	0.1 mpk	17.98	7.04
SEQ ID No. 59	Cap 1	酶Cap 1	XBG	0.1 mpk	31.03	6.4
SEQ ID No. 60	Cap 1	Clean Cap 113	XBG	0.1 mpk	31.08	8.67
SEQ ID No. 60	Cap 1	Clean Cap 413	XBG	0.1 mpk	32.78	2.05
SEQ ID No. 43	Cap 0	ARCA	HSD	0.3 mpk	52.28	5.14
SEQ ID No. 59	Cap 0	ARCA	XBG	0.3 mpk	59.56	4.57
SEQ ID No. 59	Cap 0	酶Cap 0	XBG	0.3 mpk	54.93	10.22
SEQ ID No. 59	Cap 1	酶Cap 1	XBG	0.3 mpk	63.2	0.28
SEQ ID No. 60	Cap 1	Clean Cap 113	XBG	0.3 mpk	61.28	4.76
SEQ ID No. 60	Cap 1	Clean Cap 413	XBG	0.3 mpk	60.56	3.97

[0582] 13. 核定位信号的表征

[0583] 设计且测试使用若干核定位信号(NLS)的Cas9序列以测定功效。十一种不同强度的非典型NLS是选自由Kosugi等人(2009) Journal of Biological Chemistry, 284(1), 478-485所鉴别的NLS, 如表31中所示。将此等氨基酸序列添加至Cas9氨基酸序列(SEQ ID NO:13)的羧基端。对照序列编码SEQ ID No.4。

[0584] 表31

[0585]

NLS名称	NLS氨基酸序列	NLS编码序列(CDS)	SEQ ID No (NLS 氨基酸, NLS CDS, ORF CDS)
SV40	PKKKRKV	CCGAAGAAGAAGAGAAA GGTC	78, 92, 4
NLS1	LAAKRSRTT	CTGGCAGCAAAGAGAAGC AGAACAACA	79, 93, 130
NLS2	QAAKRSRTT	CAGGCAGCAAAGAGAAG CAGAACAACA	80, 94, 131
NLS3	PAPAKRERTT	CCGGCACCGGCAAAGAGA GAAAGAACAACA	81, 95, 132
NLS4	QAAKRPRTT	CAGGCAGCAAAGAGACCG AGAACAACA	82, 96, 133
NLS5	RAAKRPRTT	AGAGCAGCAAAGAGACC GAGAACAACA	83, 97, 134
NLS6	AAAKRSWSM AA	GCAGCAGCAAAGAGAAG CTGG AGCATGGCAGCA	84, 98, 135
NLS7	AAAKRVWSM AF	GCAGCAGCAAAGAGAGTC TGGAGCATGGCATTTC	85, 99, 136
NLS8	AAAKRSWSM AF	GCAGCAGCAAAGAGAAG CTGGAGCATGGCATTTC	86, 100, 137
NLS9	AAAKRKYFAA	GCAGCAGCAAAGAGAAA GTACTTCGCAGCA	87, 101, 138
NLS10	RAAKRKAFAA	AGAGCAGCAAAGAGAAA GGCATTTCGCAGCA	88, 102, 139
NLS11	RAAKRKYFAV	AGAGCAGCAAAGAGAAA GTACTTCGCAGTC	89, 103, 140

[0586] 将具有如表31中所指示的NLS的编码Cas9的mRNA与与靶向TTR的引导RNA (G282; SEQ ID NO:42) 调配为LNP。使用错程序组配LNP,且其含有分别呈50:38:9:3摩尔比的50%脂质A、9%DSPC、38%胆固醇及3%PEG2k-DMG,且具有6.0的N:P比。使用Amicon PD-10过滤器 (GE Healthcare) 纯化LNP,且以0.07mg/ml的浓度 (LNP浓度) 使用。以0.1mpk静脉内投配CD-1雌性小鼠 (每组n=5)。在给药后7天,将动物处死,收集血液及肝脏,且测量血清TTR及肝脏编辑。结果展示在表32及图33中。对于对应于表32中列出的NLS的SEQ ID NO,参见表31。

[0587] 表32-伴随不同核定位信号的肝脏编辑

NLS	NLS 类别	NLS 强度	0.1 MPK 编辑%	STDEV
SV40	不适用	不适用	14.67	4.17
NLS1	2	3	3.76	1.61
NLS2	2	4	5.86	1.69
NLS3	2	5	2.50	1.82
NLS4	2	6	27.38	11.98
NLS5	2	9	27.80	2.37
NLS6	3	1	2.20	0.82
NLS7	3	6	7.90	0.42
NLS8	3	10	25.52	15.75
NLS9	4	2	3.26	1.65
NLS10	4	5	0.23	0.04
NLS11	4	8	21.02	4.9

[0589] NLS5显示相比于SV40 NLS的统计学上显著的增加(单向ANOVA, $p=0.006$)。NLS4及NLS8各展现与SV40 NLS相比编辑增加的可能趋势,但在此实验中差距在统计学上并不显著。图34A至图34B显示施用核定位信号变异体后的血清TTR含量。Kosugi等人(2009)(见上文),针对核定位程度的NLS的评级活性(表32中的“NLS强度”),其中10为完全在核内,且1为弥漫在整个细胞中。如此文献中评级的NLS活性与编辑效率正相关,如图35中所示。

[0590] 14. UTR的影响的活体外表征

[0591] 表33及图36显示来自具有不同5'UTR的转录物的Cas9表达。所有构建体均使用3'人类白蛋白UTR。通过IVT产生各构建体的信使RNA。使用线性化质粒产生SEQ ID No:179的信使RNA,且使用PCR产物作为模板生成所有其它者。用100ng各Cas9 mRNA及25nM最终浓度的靶向甲状腺素转运蛋白(TTR)的引导物(G502; SEQ ID NO:70)使用LipofectamineTM MessengerMAXTM转染剂(ThermoFisher)转染HepG2细胞。转染后六小时通过Nano-Glo[®] HiBiT裂解分析(Promega)裂解细胞。通过使用Nano-Glo[®] Nano-Glo HiBiT胞外侦测系统(Promega, 目录号N2420)测定Cas9蛋白质含量。表33及图36显示来自具有不同5'UTR的转录物的Cas9表达。

[0592] 表33: Cas9表达

mRNA 构建体 SEQ ID NO	5' UTR	分子 Cas9 (10 ⁷)	标准差(10 ⁷)
179	HSD	447	61
180	CMV-1	723	39
[0593] 181	CMV-2	672	158
182	CMV-3	662	117
183	HBA	488	101
184	HBB	595	124
185	XBG	813	62

[0594] 15. 至非人类灵长类动物的LNP递送

[0595] 用如上文所述使用X-flow/TFF方法制备的LNP调配物进行三项研究。特定莫耳量及载荷提供于表34至表36中。含有Cas9 mRNA及引导RNA (gRNA) 的各调配物具有以重量计1:1的mRNA:gRNA比。在表格中指示LNP的剂量(以mg/kg为单位,总RNA含量)、给药途径及动物是否接受地塞米松的预处理。对于接受地塞米松(Dex)预处理的动物,在施用LNP或媒介之前1小时通过IV快速注射以2mg/kg施用Dex。

[0596] 对于血液化学分析,针对所测量的各因素在如表格中所指示的时间对动物进行抽血。在处理前及处理后的NHP中测量细胞介素诱导。自受约束的清醒动物的外周静脉将最少0.5mL的全血收集于4mL血清分离管中。在室温下使血液结块最少30分钟,之后以2000×g离心15分钟。将血清等分于2个120μL聚丙烯微管中,且在分析之前各储存于-60℃至-86℃下。使用来自Meso Scale Discovery (MSD)的非人类灵长类动物U-Plex细胞介素定制试剂盒来加以分析。分析中包括以下参数:INF-g、IL-1b、IL-2、IL-4、IL-6、IL-8、IL-10、IL-12p40、MCP-1及TNF-α,其中聚焦于IL-6及MCP-1。如制造商方案中所指导地制备试剂盒试剂及标准品。以纯形式使用NHP血清。将板运作于MSD Sector成像仪6000,伴随用MSD Discovery work bench软件版本4012进行分析。

[0597] 在处理前及处理后动物中通过酶免疫分析测量补体含量。自受约束的清醒动物的外周静脉将0.5mL体积的全血收集于0.5mL k₂EDTA管中。以2000×g离心血液15分钟。将血浆等分于2个120μL聚丙烯微管中,且在分析之前各储存于-60℃至-86℃下。使用Quidel MicroVue Complement Plus EIA试剂盒(C3a-Cat号A031)或(Bb-Cat号A027)来加以分析。如制造商方案中所指导地制备试剂盒试剂及标准品。将板运作于450nm下的光密度下的MSD Sector成像仪6000上。使用4参数曲线拟合分析结果。

[0598] 细胞介素诱导及补体活化的数据提供于下表中。“BLQ”意谓小于定量限值。

[0599] 表34,研究1

处理组	分子比(分别呈脂质A、胆固醇、DSPC及PEG2k-DMG)	N:P	载荷	样本大小(n)	途径	剂量程度, 总RNA含量 (mg/kg)	Dex
(1) TSS (媒剂)	不适用	不适用	不适用	3	IV输注	不适用	否
[0600] (2) LNP699 G502	45/44/9/2	4.5	Cas9 mRNA (SEQ ID NO:48); G000502	3	IV输注	3	否
(3) LNP688 G506	45/44/9/2	4.5	Cas9 mRNA (SEQ ID NO:48); G000506	3	IV输注	3	否
(4) LNP689 G509	45/44/9/2	4.5	Cas9 mRNA (SEQ ID	3	IV输注	3	否
			NO:48); G000509				
[0601] (5) LNP690 G510	45/44/9/2	4.5	Cas9 mRNA (SEQ ID NO:48); G000510	3	IV输注	3	否

[0602] 表35, 研究2

[0603]

处理组	分子比(分别呈脂质A、胆固醇、DSPC 及 PEG2k-DMG)	N:P	载荷	样本大小 (n)	途径	剂量程度, 总RNA含量 (mg/kg)	Dex
(1) TSS (媒剂)	不适用	不适用		1	IV 快速注射	不适用	是
(2) TSS (媒剂)	不适用	不适用		1	IV 快速注射	不适用	否
(3) LNP898 G502	45/44/9/2	4.5	Cas9 mRNA (SEQ ID NO:48) ; G00050 2	1	IV 输注	3	是
(4) LNP898 G502	45/44/9/2	4.5	Cas9 mRNA (SEQ ID	1	IV 输	3	否

[0604]

			NO:48) ; G00050 2		注		
(5) LNP897 G502	45/43/9/3	4.5	Cas9 mRNA (SEQ ID NO:48) ; G00050 2	1	IV 快 速 注 射	3	是
(6) LNP897 G502	45/43/9/3	4.5	Cas9 mRNA (SEQ ID NO:48) ; G00050 2	1	IV 快 速 注 射	3	否
(7) LNP897 G502	45/43/9/3	4.5	Cas9 mRNA (SEQ ID NO:48) ; G00050 2	1	IV 输 注	3	是
(8) LNP897 G502	45/43/9/3	4.5	Cas9 mRNA (SEQ ID NO:48) ; G00050 2	1	IV 输 注	3	否
(9) LNP916 GFP	45/43/9/3	4.5	eGFP mRNA (SEQ ID NO:73)	1	IV 输 注	6	是
(10) LNP916 GFP	45/43/9/3	4.5	eGFP mRNA (SEQ ID NO:73)	1	IV 输 注	6	否

[0605] 表36,研究3

[0606]

处理组	分子比(分别呈脂质A、胆固醇、DSPC及PEG2k-DMG)	N:P	载荷	样本大小(n)	途径	剂量程度, 总RNA含量(mg/kg)	De x
(1) TSS	不适用	不适用	不适用	3	IV快速注射	不适用	否
(2) LNP102 1 G502	50/38/9/3	6	Cas9 mRNA (SEQ ID NO:43); G000502	3	IV快速注射	1	否
(3) LNP102 1 G502	50/38/9/4	6	Cas9 mRNA (SEQ ID NO:43); G000502	1	IV快速注射	1	是
(4) LNP102 2 G502	55/33/9/3	6	Cas9 mRNA (SEQ ID NO:43); G000502	3	IV快速注射	1	否
(5) LNP102 3 G502	45/43/9/3	4.5	Cas9 mRNA (SEQ ID NO:43); G000502	3	IV快速注射	3	否
(6) LNP102 4 G509	50/38/9/3	6	Cas9 mRNA (SEQ ID NO:43); G000509	3	IV快速注射	1	否
(7) LNP102 4 G509	50/38/9/4	6	Cas9 mRNA (SEQ ID NO:43); G000509	1	IV快速注射	1	是
(8) LNP102 5 G509	55/33/9/3	6	Cas9 mRNA (SEQ ID NO:43);	3	IV快速注	1	否

			G000509		射		
[0607]	(9) LNP102 1 G502	50/38/9/3	6	Cas9 mRNA (SEQ ID NO:43); G000502	1	IV快 速注 射	3 否
	(10) LNP102 2 G502	50/38/9/3	6	Cas9 mRNA (SEQ ID NO:43); G000502	1	IV快 速注 射	3 否

[0608] 表37. 根据研究1的IL-6测量

[0609]	处理组	采血前	6小时	24小时
	(1) TSS (媒剂)	5.71±2.70	29.1±20.37	7.05±3.49
	(2) LNP699G502	9.73±8.34	1296.41±664.71	5.43±7.68
	(3) LNP688G506	16.83±4.08	1749.47±1727.22	38.57±39.39
	(4) LNP689G509	18.11±11.51	1353.49±766.66	32.42±18.40
	(5) LNP690G510	13.95±1.85	11838±17161.74	90.07±96.02

[0610] 表38. 根据研究1的MCP-1测量

[0611]	处理组	采血前	6小时	24小时
	(1) TSS (媒剂)	810.49±178.27	1351.16±397.31	745.25±56.49
	(2) LNP699G502	842.31±350.65	19298.49±11981.14	2092.89±171.21
	(3) LNP688G506	1190.79±383.64	13500.17±12691.60	1414.71±422.43
	(4) LNP689G509	838.63±284.42	14427.7±8715.48	1590±813.23
	(5) LNP690G510	785.32±108.97	52557.24±48034.68	6319.77±983.37

[0612] 表39. 根据研究1的补体C3a测量

[0613]	处理组	采血前	6小时	第7天
	(1) TSS (媒剂)	23.9±11.95	25.51±14.79	30.67±18.36
	(2) LNP699 G502	32.36±11.29	94.33±58.45	38.50±12.69
	(3) LNP688 G506	22.30±1.73	127.00±22.34	37.80±6.86
	(4) LNP689 G509	35.83±21.94	174.00±44.51	50.83±21.92
	(5) LNP690 G510	36.30±8.21	163.00±40.60	42.50±12.44

[0614] 表40. 根据研究1的补体bb测量

	处理组	04-bb	采血前	6小时	第7天
[0615]	(1) TSS (媒剂)	对照	1.53±0.19	3.37±2.13	1.43±0.71
	(2) LNP699 G502	G502	1.45±0.39	9.01±5.28	1.57±0.54
	(3) LNP688 G506	G506	1.45±0.78	11.78±2.33	1.78±0.84
[0616]	(4) LNP689 G509	G509	1.95±0.99	15.73±2.23	2.83±0.88
	(5) LNP690 G510	G510	2.12±0.44	13.57±1.23	2.21±0.72

[0617] 表41. 根据研究2的IL-6测量

处理组	采血前	90分钟	6小时	24小时	第7天
(1) TSS (媒介)	1.77	11.46	4.2	2.76	3.01
(2) TSS (媒介)	5.23	18.11	20.36	13.2	6.36
(3) LNP898G502	2.02	1305.75	1138.22	383.32	16.02
(4) LNP898G502	2.34	37.19	91.59	14.11	3.07
(5) LNP897G502	2.1	55.79	6.89	2.26	2.01
(6) LNP897G502	6.8	10.1	44.72	5.4	2.01
(7) LNP897G502	1.97	44.87	32.61	2.97	1.11
(8) LNP897G502	3.14	37.68	73.41	8.58	2.22
(9) LNP916GFP	1.6	BLQ	95.32	27.58	BLQ
(10) LNP916GFP	2.43	BLQ	883.01	66.71	BLQ

[0619] 表42. 根据研究2的MCP-1测量

处理组	采血前	90分钟	6小时	24小时	第7天
(1) TSS (媒介)	312.12	197.24	145.36	177.02	403.82
(2) TSS (媒介)	232.44	175.08	187.72	136.64	325.69
(3) LNP898 G502	249.1	2183.5	1814.64	1887.41	372.38
(4) LNP898 G502	349.51	430.49	5635.55	953.05	236.6
(5) LNP897 G502	492.3	989.98	409.08	302.97	506.82
(6) LNP897 G502	283.79	225.1	1141.08	484.59	259.46
(7) LNP897 G502	223.16	349.79	398.57	172.67	287.09
(8) LNP897 G502	584.42	853.51	3880.81	1588.46	692.99
(9) LNP916 GFP	325.84	BLQ	1189.97	2279.82	BLQ
(10) LNP916 GFP	175.47	BLQ	3284.16	2023.53	BLQ

[0621] 表43. 根据研究2的补体C3a测量

处理组	采血前	90分钟	6小时	24小时	第7天
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[0622]

[0623]	(1) TSS (媒介)	0.087	0.096	0.048	0.033	0.038
	(2) TSS (媒介)	0.369	0.311	0.146	0.1	0.106
	(3) LNP898 G502	0.087	0.953	0.647	0.277	0.065
	(4) LNP898 G502	0.099	0.262	0.123	0.049	0.044
	(5) LNP897 G502	0.067	0.479	0.209	0.036	0.036
	(6) LNP897 G502	0.141	0.433	0.34	0.11	0.074
	(7) LNP897 G502	0.1	0.345	0.396	0.096	0.127
	(8) LNP897 G502	0.261	0.458	0.409	0.244	0.313
	(9) LNP916 GFP	0.149	BLQ	0.714	0.382	BLQ
	(10) LNP916 GFP	0.117	BLQ	0.752	0.723	BLQ

[0624] 表44. 根据研究2的补体bb测量

[0625]	处理组	采血前	90分钟	6小时	24小时	第7天
	(1) TSS (媒介)	0.087	0.096	0.048	0.033	0.038
	(2) TSS (媒介)	0.369	0.311	0.146	0.1	0.106
	(3) LNP898G502	0.087	0.953	0.647	0.277	0.065
	(4) LNP898G502	0.099	0.262	0.123	0.049	0.044
	(5) LNP897G502	0.067	0.479	0.209	0.036	0.036
	(6) LNP897G502	0.141	0.433	0.34	0.11	0.074
	(7) LNP897G502	0.1	0.345	0.396	0.096	0.127
	(8) LNP897G502	0.261	0.458	0.409	0.244	0.313
	(9) LNP916GFP	0.149	BLQ	0.714	0.382	BLQ
	(10) LNP916GFP	0.117	BLQ	0.752	0.723	BLQ

[0626] 表45. 根据研究3的IL-6测量

[0627]	处理组	采血前	90分钟	6小时	24小时	第7天
	(1) TSS	1.89±0.97	2.56±1.41	0.90±0.71	BLQ	0.08
	(2) LNP1021G502	210±0.35	7.44±5.16	6.94±8.45	1.07±1.11	1.76±0.98
	(3) LNP1021G502	0.79	2.96	4.25	0.67	0.27
	(4) LNP1022G502	1.54±1.32	20.42±31.60	13.94±10.10	0.98±0.41	2.04±0.65
	(5) LNP1023G502	2.92±1.68	6.28±7.18	6.06±2.31	3.62±4.68	2.00±1.21
	(6) LNP1024G509	1.43±0.62	2.64±1.92	7.72±11.96	0.45±0.19	0.88±0.79
	(7) LNP1024G509	1.35±0.74	2.64±2.35	1.71±0.41	0.36±0.58	0.51±0.32
	(8) LNP1025G509	1.64	2.68	25.65	0.58	2.00
	(9) LNP1021G502	0.56	6.15	28.80	0.85	0.61
	(10) LNP1022G502	1.76	8.66	2907.86	11.26	1.72

[0628] 表46. 根据研究2的MCP-1测量

[0629]	处理组	采血前	90分钟	6小时	24小时	第7天
	(1) TSS	204.01±46.39	197.62±19.54	310.84±45.87	179.07±20.77	234.61±71.79

[0630]	(2) LNP1021 G502	303.67±36.37	337.63±195.18	755.20±581.45	339.75±206.20	214.82±40.81
	(3) LNP1021 G502	229.30	358.10	3182.00	413.56	178.30
	(4) LNP1022 G502	393.63±187.81	467.72±221.61	1852.94±2199.66	497.12±412.30	382.19±67.27
	(5) LNP1023 G502	213.72±8.85	196.18±62.81	1722.18±1413.90	197.83±74.01	156.16±18.87
	(6) LNP1024 G509	237.76±96.36	210.37±95.17	468.53±250.42	22.32±69.06	141.20±71.90
	(7) LNP1024 G509	207.36	183.07	1885.66	235.70	163.11
	(8) LNP1025 G509	259.57±112.98	299.21±304.89	1193.10±974.04	258.82±88.53	219.86±219.86
	(9) LNP1021 G502	199.29	286.04	2001.23	197.57	196.44
	(10) LNP1022 G502	305.81	970.65	7039.06	8379.05	203.47

[0631] 表47. 根据研究3的补体C3a测量

处理组	采血前	90分钟	6小时	24小时	第7天
(1) TSS	42.47±10.30	55.40±13.58	29.30±14.46	41.70±23.65	27.43±12.43
(2) LNP1021 G502	34.37±0.50	86.50±3.66	90.07±4.85	56.60±2.25	32.53±0.93
(3) LNP1021 G502	34.30	128.00	93.30	33.40	28.20
(4) LNP1022 G502	41.55±13.51	151.37±109.98	82.00±31.82	45.57±18.58	32.77±6.45
(5) LNP1023 G502	31.67±3.19	74.40±22.08	74.13±48.61	33.83±9.75	27.70±8.05

[0633]	(6) LNP1024 G509	56.60±25.61	100.37±77.95	74.73±70.15	55.20±48.34	49.97±39.94
	(7) LNP1024 G509	33.80	33.90	33.70	26.10	20.90
	(8) LNP1025 G509	39.90±13.01	75.73±1.38	46.13±30.56	25.00±3.80	23.90±7.18
	(9) LNP1021 G502	34	85.70	133.00	62.00	25.50
	(10) LNP1022 G502	29.8	68.10	113.00	71.70	23.30

[0634] 表48. 根据研究3的补体bb测量

[0635]	处理组	采血前	90分钟	6小时	24小时	第7天
	(1) TSS	1.46±0.70	2.18±0.78	1.96±0.64	0.945±0.15	1.34±0.50
	(2) LNP1021 G502	1.77±0.60	6.51±3.66	11.00±4.85	3.59±2.25	2.07±0.93
	(3) LNP1021 G502	1.24	2.90	11.50	2.97	1.24
	(4) LNP1022 G502	1.52±0.34	5.67±2.28	10.2±3.36	3.66±1.68	1.84±0.24
	(5) LNP1023 G502	1.65±0.94	4.4±1	7.68±4.67	2.64±1.18	2.08±1.32
	(6) LNP1024 G509	1.61±0.13	4.52±1.81	4.50±3.22	1.63±0.84	1.63±0.32
	(7) LNP1024 G509	0.96	2.99	2.64	1.13	1.07
	(8) LNP1025 G509	1.37±0.17	4.9±4.51	3.79±3.84	1.66±1.43	1.35±0.44
	(9) LNP1021 G502	1.41	5.67	11.50	4.64	1.38
	(10) LNP1022 G502	1.28	5.22	14.10	5.64	1.87

[0636] 16. 小鼠肝脏中不同mRNA的Cas9表达的比较

[0637] 在施用编码Cas9的不同mRNA后活体内测量Cas9表达。将如表49中所指示的信使RNA与靶向小鼠TTR基因的小鼠sgRNA (1:2的sgRNA:mRNA重量比) 调配为LNP。使用错流程序组配具有50%脂质A、9% DSPC、38%胆固醇及3% PEG2k-DMG及6.0的N:P比的LNP。使用Sartocon Slice 200 (Sartorius) 纯化LNP, 且以1.53mg/ml的浓度 (RNA浓度) 使用。针对如上文所述的RNA的平均粒径、多分散性 (pdi)、总RNA含量及囊封效率分析LNP调配物 (数据未示)。

[0638] 以0.3mpk静脉内投配CD-1雌性小鼠 (每组n=5)。在给药后1小时、3小时及6小时, 将动物处死, 收集肝脏组织, 且如实例11中所述通过MSD ELISA测量Cas9蛋白质含量。表49显示Cas9蛋白质含量。在各时间点, 在用SEQ ID NO:177处理的动物中检测到比用SEQ ID NO:43处理的动物要多的Cas9蛋白质。

[0639] 表49

mRNA	时间点(小时)	每公克肝脏的 Cas9纳克数	标准差	样本大小(n)
TSS		0	28	5
SEQ ID NO: 43	1	429	164	5
SEQ ID NO: 177	1	1872	907	5
SEQ ID NO: 43	3	1167	814	5
SEQ ID NO: 177	3	2233	929	5
SEQ ID NO: 43	6	535	297	5
SEQ ID NO: 177	6	1663	443	5

[0641] 17. 不同mRNA的剂量反应的比较

[0642] 比较编码Cas9的不同mRNA的活体内剂量反应曲线。用SEQ ID No.43及SEQ ID No.177的mRNA及sg502 (SEQ ID NO:70;G502) 制备LNP调配物,如实例16中所述进行调配。将脂质纳米颗粒组分溶解于100%乙醇中,其中脂质组分摩尔比为50/9/38/3 (LP01/DSPC/胆固醇/PEG-DMG)。以约6的脂质胺与RNA磷酸(N:P)摩尔比及以重量计1:2的gRNA与mRNA比调配LNP。针对如上文所述的RNA的平均粒径、多分散性(pdi)、总RNA含量及囊封效率分析LNP调配物(数据未示)。

[0643] 对于活体内表征,以每公斤(每组n=5)0.03、0.1或0.3mg总RNA(引导RNA毫克数+mRNA毫克数)静脉内投配CD-1雌性小鼠(每组n=5)。在给药后七天,将动物处死,收集血液及肝脏,且如实例1中所述测量血清TTR及肝脏编辑。用TSS媒剂投配阴性对照动物。编辑数据提供于下表50中。对于SEQ ID NO:43,提供平均8项活体内实验,各伴随5只动物。对于SEQ ID NO:177,提供活体内实验的平均值,各剂量下伴随5只动物。在各剂量下,用SEQ ID NO:177处理的动物中的编辑%要高于用SEQ ID NO:43处理的动物。

[0644] 表50

mRNA	编辑%		
	0.3 mg/kg剂量 平均值 (范围)	0.1 mg/kg 平均值 (范围)	0.03 mg/kg 平均值 (范围)
SEQ ID NO: 43	65.8% (62.2-71.2%)	40.6% (29.2-55.6%)	11.4% (6.2-20.1%)
SEQ ID NO: 177	71.2%	58.9%	29.3%

[0646] 序列表

[0647] 以下序列表提供本文所揭示的序列的清单。应理解,若关于RNA提及DNA序列(包含Ts),则Ts应由Us替代(其可视情况而为经修饰或未经修饰的),且反之亦然。

[0648]

描述	序列	SEQ ID No.
Cas9 DNA 编码序列2	ATGGACAAGAAGTACAGCATCGGACTGGACATCGGAACAAACAGCGTCGGATGGG CAGTCATCACAGACGAATACAAGGTCCCGAGCAAGAAAGTTCAAGGTCCTGGGAAA CCAGACAGACACAGCATCAAGAAGAACCTGATCGGAGCACTGCTGTTTCGACAGC GGAGAAAACAGCAGAAAGCAACAAGACTGAAGAGAACAGCAAGAAGAAGATACAC AAGAAGAAAGAACAGAATCTGCTACCTGCAGGAAATCTTCAGCAACGAAATGGCA AAGGTGACGACAGCTTCTCCACAGACTGGAAGAAAGCTTCTGGTCAAGAAAG ACAAGAAGCACGAAAGACACCCGATCTTCGAAAACATCGTCGACGAAGTCGCATA CCACGAAAAGTACCCGACAATCTACCACCTGAGAAAAGAGCTGGTCAACAGCACA GACAAGGCAGACCTGAGACTGATCTACCTGGCACTGGCACACATGATCAAGTTCA GAGGACACTTCTGATCGAAGGAGACCTGAACCCGGACAACAGCGACGTCGACAA GCTGTTTCATCCAGCTGGTCCAGACATACAACCAGCTGTTCAAGAAAACCCGATCA ACGCAAGCGGAGTCGACGCAAAAGGCAATCTGAGCGCAAGACTGAGCAAGAGCA GAAGACTGGAAAACCTGATCGCACAGCTGCCGGGAGAAAAGAAGAACGGACTGT TCGGAAACCTGATCGCACTGAGCCTGGGACTGACACCGAACTTCAAGAGCAACTT CGACCTGGCAGAAAGACGCAAGACTGCAGCTGAGCAAGGACACATACGACGACGA CCTGGACAACCTGCTGGCACAGATCGGAGACCAGTACGCAGACCTGTTCTGGCA GCAAAGAACCTGAGCGACGCAATCTGCTGAGCGACATCTGAGAGTCAACACAG AAATCACAAGGCACCGCTGAGCGCAAGCATGATCAAGAGATACGACGAACACCA CCAGGACCTGACACTGCTGAAGGCACTGGTCAAGACAGCAGCTGCCGGAAAAGTAC AAGGAAATCTTCTTCGACCAGAGCAAGAACGGATACGCAGGATACATCGACGGAG GACAAGCCAGGAAGAATTCTACAAGTTCATCAAGCCGATCTGGAAAAGATGGA CGGAACAGAAAGAACTGCTGGTCAAGCTGAACAGAGAAAGACCTGCTGAGAAA GAGAACATTGACAACCGGAAGCATCCCGCACCAGATCCACTGGGAGAACTGCAC GCAATCTGAGAAGACAGGAAGACTTCTACCCGTTCTGAAGGACAACAGAGAAA AGATCGAAAAGATCCTGACATTCAGAATCCCGTACTACGTCGGACCGCTGGCAAGA GGAAAACAGCAGATTCGCATGGATGACAAGAAAAGAGCGAAGAAAACAATCACACCT GGAATTCGAAGAAGTCGTCGACAAGGGAGCAAGCGCACAGAGCTTCATCGAAA GAATGACAACTTCGACAAGAACCTGCCGAACGAAAAGGTCTGCCGAAGCACA GCCTGCTGTACGAATACTTACAGTCTACAACGAACTGACAAAGGTCAAGTACGTC ACAGAAGGAATGAGAAAGCCGGCATTCTGAGCGGAGAACAGAAGAAGCAATC GTCGACCTGCTGTTCAAGACAAAACAGAAAAGGTACAGTCAAGCAGCTGAAGGAA GACTACTTCAAGAAGATCGAATGCTTCGACAGCGTCGAAATCAGCGGAGTCGAAG ACAGATTCAACGCAAGCCTGGGAACATACCACGACCTGCTGAAGATCATCAAGGA CAAGGACTTCTGGACAACGAAGAAAACGAAGACATCTGGAAGACATCGTCTCTG AACTGACACTGTTCAAGACAGAGAAATGATCGAAGAAAAGACTGAAGACATACG CACACCTGTTTCGACGACAAGGTCATGAAGCAGCTGAAGAGAAGAAGATACACAGG ATGGGGAAGACTGAGCAGAAAAGCTGATCAACGGAATCAGAGACAAGCAGAGCGG AAAGACAATCCTGGACTTCTGAAGAGCGACGGATTTCGAAAACAGAAACTTCATG CAGTGATCCACGACGACAGCCTGACATTCGAAGGAAGACATCCAGAAGGCACAGG TCAGCGGACAGGGAGACAGCCTGCACGAACACATCGCAAACCTGGCAGGAAGCC CGGCAATCAAGAAGGGAATCCTGCAGACAGTCAAGGTGTCGACGAACTGGTCAA GGTATGGGAAGACACAAGCCGAAAACATCGTTCATCGAAATGGCAAGAGAAAAC CAGACAACACAGAAGGGACAGAAGAACAGCAGAGAAAAGAAATGAAGAGAATCGA AGAAGGAATCAAGGAACCTGGGAAGCCAGATCCTGAAGGAACACCCGGTCGAAAA CACACAGCTGCAGAACGAAAAGCTGTACCTGTACTACCTGCAGAACGGAAGAGAC ATGTACGTCGACCAGGAACTGGACATCAACAGACTGAGCGACTACGACGTCGACC ACATCGTCCCGCAGAGCTTCTGAAGGACGACAGCATCGACAACAAGGTCTGAC AAGAAGCGACAAGAACAGAGGAAAGAGCGACAACGTCCCGAGCGAAGAAGTCGT CAAGAAGATGAAGAACTACTGGAGACAGCTGCTGAACGCAAAGCTGATCACACAG AGAAAGTTCGACAACCTGACAAAGGCAGAGAGAGGAGGACTGAGCGAACTGGAC AAGGCAGGATTCATCAAGAGACAGCTGGTCAAAACAAGACAGATCACAAAGCAG TCGCACAGATCCTGGACAGCAGAATGAACACAAAAGTACGACGAAAACGACAAGCT GATCAGAGAAGTCAAGGTTCATCACACTGAAGAGCAAGCTGGTCAAGCACTTCAGA AAGGACTTCCAGTTCTACAAGGTCAAGAGAAATCAACAATACCACCACGCACACG ACGCATACCTGAACGCAGTCGTCGGAACAGCACTGATCAAGAAGTACCCGAAGCT	1

[0649]

	<p>GGAAAGCGAATTCGTCTACGGAGACTACAAGGTCTACGACGTCAGAAAGATGATC GCAAAGAGCGAACAGGAAATCGGAAAGGCAACAGCAAAGTACTTCTTCTACAGCA ACATCATGAACTTCTTCAAGACAGAAATCACACTGGCAAACGGAGAAATCAGAAA GAGACCCTGTATCGAAACAAACGGAGAAACAGGAGAAATCGTCTGGGACAAGGG AAGAGACTTCGCAACAGTCAGAAAGGTCTGAGCATGCCGCAGGTCAACATCGTC AAGAAGACAGAAGTCCAGACAGGAGGATTACGCAAGGAAAGCATCTGCCGAAAG AGAAACAGCGACAAGCTGATCGCAAGAAAGAAGGACTGGGACCCGAAGAAGTAC GGAGGATTTCGACAGCCCCGACAGTCGCATACAGCGTCTGGTCTGCGCAAAGTCTG AAAAGGGAAAGAGCAAGAAGCTGAAGAGCGTCAAGGAACTGCTGGGAATCACAA TCATGGAAAGAAGCAGCTTCGAAAAGAACCCGATCGACTTCTTGGAAAGCAAAGGG ATACAAGGAAGTCAAGAAGGACCTGATCATCAAGCTGCCGAAGTACAGCCTGTTC GAACTGGAAAACGGAAGAAAGAGAATGCTGGCAAGCGCAGGAGAAGTGCAGAAG GGAAACGAACTGGCACTGCCGAGCAAGTACGTCAACTTCTGTACCTGGCAAGCC ACTACGAAAAGCTGAAGGGAAAGCCCGAAGACAACGAAACAGAAAGCAGCTGTTCG TCGAAACAGCACAAAGCACTACCTGGACGAAATCATCGAACAGATCAGCAATTCAG CAAGAGAGTCATCCTGGCAGACGCAAACTGGACAAGGTCTGAGCGCATAACAAC AAGCACAGAGACAAGCCGATCAGAGAACAGGCAGAAAACATCATCCACCTGTTCA CACTGACAAAACCTGGGAGCACCGGCAGCATTCAAGTACTTCGACACAACAATCGA CAGAAAAGAGATACAAAGCACAAAGGAAGTCTGGACGCAACACTGATCCACCAG AGCATCACAGGACTGTACGAAACAAGAATCGACCTGAGCCAGCTGGGAGGAGACG GAGGAGGAAGCCGAAGAAGAAGAGAAAGGTCTAG</p>	
<p>Cas9 DNA 编码序列1</p>	<p>ATGGATAAGAAGTACTCAATCGGGCTGGATATCGGAACTAATCCGTGGGTTGGGC AGTGATCACGGATGAATACAAAGTGCCGTCCAAGAAGTTCAGGTCCTGGGGAAC ACCGATAGACACAGCATCAAGAAAATCTCATCGGAGCCCTGCTGTTTACTCCGG CGAAACCGCAGAAAGCGACCCGGCTCAAACGTACCGCGAGGGCAGCTACACCCGG CGGAAGAATCGCATCTGCTATCTGCAAGAGATCTTTTCGAAACGAAATGGCAAAGGT CGACGACAGCTTCTTCCACCGCCTGGAAGAATCTTCTGTTGGAGGAGGACAAG AAGCATGAACGGCATCTATCTTTGGAAACATCGTCGACGAAGTGGCGTACCACGA AAAGTACCCGACCATCTACCATCTGCCGGAAGAAGTTGGTTGACTCAACTGACAAGG CCGACCTCAGATTGATCTACTTGGCCCTCGCCATATGATCAAATTCGGCGGACACT TCCTGATCGAAGGCGATCTGAACCTGATAACTCCGACGTGGATAAGCTTTTCATT AACTGGTGCAGACCTACAACCACTGTTGCAAGAAAACCAATCAATGCTAGCGG CGTCGATGCCAAGGCCATCCTGTCCGCCCGGCTGTCGAAGTCGCGCGCTCGAAA ACCTGATCGACAGCTGCCGGGAGAGAAAAAGAACGGACTTTTCGGCAACTTGAT CGCTCTCTACTGGGACTCACTCCCAATTTCAAGTCCAATTTTGACCTGGCCGAGG ACGCGAAGCTGCAACTCTCAAAGGACACCTACGACGACGACTTGGACAATTTGCT GGCACAATTTGGCGATCAGTACGCGGATCTGTTCTTGGCGTAAGAACCTTTCGG ACGCAATCTTGCTGTCCGATATCCTGCGCGTGAACACCGAAATAACCAAAGCGCCG CTTAGCGCTCGATGATTAAGCGGTACGACGAGCATACCAGGATCTCACGCTGCT CAAAGCGCTCGTGAGACAGCAACTGCCTGAAAAGTACAAGGAGATCTTCTTCGAC CAGTCCAAGAATGGGTACGCAGGGTACATCGATGGAGGCGTAGCCAGGAAGAGT TCTATAAGTTCATCAAGCCAATCCTGGAAAAGATGGACGGAACCGAAGAACTGCTG GTCAAGCTGAACAGGGAGGATCTGCTCCGGAACAGAGAACCCTTGACAACGGAT CCATTCCCCACCAGATCCATCTGGGTGAGCTGCACGCCATCTGCGGCGCCAGGAG GACTTTTACCCATTCTCAAGGACAACCGGGAAAAGATCGAGAAAATTTGACGTT CCGATCCCCTGATTACGTGGGCCACTGGCGCGCGGCAATTCGCGCTTCGCGTGA TGACTAGAAAATCAGAGGAAACCATCACTCCTTGGAAATTCGAGGAAGTTGTGGAT AAGGGAGCTTCGGCACAAAGCTTCATCGAACGAATGACCAACTTCGACAAGAATC TCCAAAACGAGAAGGTGCTTCTAAGCACAGCCTCCTTACGAATACTTCACTGTC TACAACGAACTGACTAAAGTGAATACGTTACTGAAGGAATGAGGAAGCCGGCCT TTCTGTCCGGAGAACAGAAGAAAGCAATTGTGATCTGCTGTTCAAGACCAACCG CAAGGTGACCGTCAAGCAGCTTAAAGAGGACTACTTCAAGAAGATCGAGTGTTC GACTCAGTGAAATCAGCGGGGTGGAGGACAGATTCAACGCTTCGCTGGGAACCT ATCATGATCTCTGAAGATCATCAAGGACAAGGACTTCTTGACAACGAGGAGAAC GAGGACATCCTGGAAGATATCGTCTGACCTTGACCTTTTCGAGGATCGCGAGAT GATCGAGGAGAGGCTTAAAGACTACGCTCATCTCTTCGACGATAAGGTGATGAAAC AACTCAAGCGCCGCCGTACTGTTGGGGCCGCTCTCCCGAAGCTGATCAA CGGTATTCGCGATAAACAGAGCGGTAAAACCTATCTGGATTTCTCAAATCGGATGG CTTCGCTAATCGTAACTTCATGCAATTGATCCACGACGACAGCCTGACCTTTAAGGA GGACATCCAAAAAGCACAAGTGTCCGGACAGGGAGACTCACTCCATGAACACATC GCGAATCTGGCCGGTTCGCCGGGATTAAGAAGGGAATTCGAAAACGTGGAAGG TGGTGACGAGCTGGTGAAGGTATGGGACGGCACAAACCGGAGAATATCGTGA TGAAATGGCCCAGAAAACAGACTACCCAGAAGGGCCAGAAAACCTCCCGCA AAGGATGAAGCGGATCGAAGAAGGAATCAAGGAGCTGGGCAGCGAGTCTGAA AGAGCACCCGGTGGAAAACACGCAGCTGCAGAACGAGAAGCTCTACCTGTACTAT TTGCAAAATGGACGGGACATGTACGTGGACCAAGAGCTGGACATCAATCGGTTGTC TGATTACGACGTGGACCACATCGTTCCACAGTCTTCTGAAAGGATGACTCGATCGA</p>	<p>2</p>

[0650]

	<p>TAACAAGGTGTTGACTCGCAGCGACAAGAACAGAGGGAAGTCAGATAATGTGCCA TCGGAGGAGGTCGTGAAGAAGATGAAGAATTACTGGCGGCAGCTCCTGAATGCGA AGCTGATTACCCAGAGAAAGTTTGACAATCTACTAAAGCCGAGCGCGCGGACT CTCAGAGCTGGATAAGGCTGGATTATCAAACGGCAGCTGGTTCGAGACTCGGCAG ATTACCAAGCACGTGGCGCAGATCTTGGACTCCCGCATGAACACTAAATACGACGA GAACGATAAGCTCATCCGGGAAGTGAAGGTGATTACCTGAAAAGCAAACCTTGTGT CGGACTTTCGGAAGGACTTTTCAGTTTTACAAAGTGAGAGAAATCAACAACTACCAT CACGCGCATGACGCATACCTCAACGCTGTGGTTCGGTACCGCCCTGATCAAAAAGTA CCCTAAACTTGAATCGGAGTTTGTGTACGGAGACTACAAGGTCTACGACGTGAGGA AGATGATAGCCAAGTCCGAACAGGAAATCGGGAAAGCAACTGCGAAATACTTCTTT TACTCAAACATCATGAACTTTTTCAAGACTGAAATTACGCTGGCCAATGGAGAAAT CAGGAAGAGGCCACTGATCGAAACTAACGGAGAAACGGGCGAAATCGTGTGGGA CAAGGGCAGGGACTTCGCAACTGTTTCGCAAAAGTGCTCTCTATGCCGCAAGTCAATA TTGTGAAGAAAACCGAAGTGCAAACCGGCGGATTTTCAAAGGAATCGATCCTCCC AAAGAGAAATAGCGACAAGCTCATTGCACGCAAGAAAGACTGGGACCCGAAGAA GTACGGAGGATTTCGATTCGCCGACTGTGCATACTCCGTCTCTGTTGGTGGCCAAGG TGGAGAAGGGAAAGAGCAAAAAGCTCAAATCCGTCAAAGAGCTGCTGGGGATTAC CATCATGGAACGATCCTCGTTCGAGAAGAACCCGATTGATTTCTCGAGGCGAAGG GTTACAAGGAGGTGAAGAAGGATCTGATCATCAAACCTCCCAAGTACTCACTGTTT GAACTGGAAAATGGTCGGAAGCGCATGCTGGCTTCGGCCGAGAACTCCAAAAAG GAAATGAGCTGGCCTTGCTTAGCAAGTACGTCAACTTCTCTATCTTGCTTCGCACT ACGAAAACTCAAAGGGTCAACCGAAGATAACGAACAGAAGCAGCTTTTCGTGGA GCAGCACAAGCATTATCTGGATGAAATCATCGAACAATCTCCGAGTTTTCAAAGC GCGTGATCTTCGCCGACGCCAACCTCGACAAAGTCTGTCCGCCATAAATAAGCAT AGAGATAAGCCGATCAGAGAACAGGCCGAGAACATTATCCACTTGTTCACCCTGAC TAACCTGGGAGCCCCAGCCGCTTCAAGTACTTCGATACTACTATCGATCGAAAA GATACACGTCCACCAAGGAAGTTCTGGACGCGACCCTGATCCACCAAGCATCACT GGACTTACGAAACTAGGATCGATCTGTGCGAAGTGGGTGGCGATGGCGGTGGATC TCGAAAAAGAAGAGAAAGGTGTAATGA</p>	
<p>Cas9 氨基 酸序列</p>	<p>MDKKYSIGLDIGTNSVGVAVITDEYKVPSSKFKVLGNTDRHSIKKNLIGALLFDSGET AEATRLKRTARRRYTRRKNRICYLQEIFSNEMAKVDDSFHRLSEESFLVEEDKKHERHP IFGNIVDEVAYHEKYPTIYHLRKKLV DSTDKADLRLIYLALAHMIKFRGHFLIEGDLNP DNSVDVKLFIQLVQTYNQLFEEENPINASGVDAKAILSARLSKSRLENLIAQLPGEKKN GLFGNLIALSLGLTPNFKSNFDLAEADAKLQLSKDTYDDLDLNLQAIGDQYADLFLAA KNLSDAILLSDILRVNTEITKAPLSASMIKRYDEHHQDLTLKALVRQQLPEKYKEIFFD QSKNGYAGYIDGGASQEEFYKFIKPILEKMDGTEELVKNLNRDLRQRTFDNGSIPH QIHLGELHAILRRQEDFYFPLKDNREKIEKILTRIPYVYVPLARGNSRFAMTRKSEET ITPWNFEVVDKGGASQSFIERMTNFDKLPNEKVLPHKSLLYEYFTVYNELTKVKYV TEGMRKPAFLSGEQKKAIVDLLFKTNRKVTVKQLKEDYFKKIECFDSVEISGVEDRFN ASLQTYHDLKIIKDKDFLDNEENEDILEDIVLTLTLFEDREMIEERLKYAHLFDDKV MKQLKRRRYTGWRLSRKLLINGIRDKQSGKTILDFLKSDFANRNFMQILKHDDSLTFK EDIQKAQVSGQDLSLHEHIANLAGSPAIKK GILQTVKVVDELVKVMGRHKPENIVIE ARENQTTQKQKNSRERMKRIEIEGKELGSQILKEHPVENTQLQNEKLYLYLQNGRD MYVDQELDINRLSDYVDHIVPQSFLKDDSIDNKVLRSDKNRKGSDNVPSEEVVKK MKNYWRQLLNAKLITQRKFDNLTKAERGGLELTKAGFIKQVETVQITKHVAQILD SRMNTKYDENDKLIREVKVITLKSCLVSDFRKDFQFYKVINNYHHAHDAYLNAV GTALIKKYPKLESEFVYGDYK VYDVRKMIKSEQEI GKATAYFFYSNIMNFFKTEITL ANGEIRKRP LIETNGETGEIVWDKGRDFATVRKVL SMPQVNVKKTVEVQTGGFSKESIL PKRNSDKLIARKKDWDPKKYGGFDSPTVAYSVLV VAKVEKGKSKLKS VKELLGITIM ERSSFENPIDFLEAKGYKEVKDLIHKLPKYSLFELENGRKRMLASAGELQKGNELAL PSKYVNFYLA SHYEKLGSPEDNEQQLFVEQHKHYLDEIIEQISEFSKRVLADANL DKVLSAYNKHRDKPIREQAENIIHLFTLNLGAPAAFYFDTTIDRKRYTSTKEVL DAT LIHQSI TGLYETRIDLSQLGGDGGGSPKKKRKV</p>	<p>3</p>
<p>Cas9 mRNA 开 放阅读框 架(ORF) 2</p>	<p>AUGGACAAGAAGUACAGCAUCGGACUGGACAUCGGAACAAACAGCGUCGGAUG GGCAGUCAUCACAGACGAAUACAAGGUCCGAGCAAGAAGUUCAAGGUCCUGG GAAACACAGACAGACACAGCAUCAAGAAGAACCUGAUCGGAGACUCUGUGUUC GACAGCGGAGAAAACAGCAGAAGCAACAAGACUGAAGAGAACAGCAAGAAGAAG AUACACAAGAAGAAAAGAACAGAAUCUGCUACCUGCAGGAAAUCUUCAGCAACG AAAUGGCAAAGGUCGACGACAGCUUCUUCACAGACUGGAAGAAAGCUUCCUG GUCGAAGAAGACAAGAAGCAGCAAGACACCCGAUCUUCGGAACAUUCGUCGA CGAAGUCGAUACCACGAAAAGUACCCGACAUCUACCACCUAGAGAAAGAAAGC UGGUCGACAGCACAGACAAGGACAGACCUAGAGACUGAUCUACCUGGACUAGGCA CACAUGAUCAAGUUCAGAGGACACUUCUGAUCGAAGGAGACCUAGAACCCGGA CAACAGCGACGUCGACAAGCUGUUAUCCAGCUGGUCAGACAUAACAACAGCU GUUCGAAGAAAACCCGAUCAACGCAAGCGGAGUCGACGCAAGGCAAUCCUGA</p>	<p>4</p>

[0651]

	<p>GCGCAAGACUGAGCAAGAGCAGAAGACUGGAAAACCGAUCGCACAGCUGCCG GGAGAAAAGAAGAACGGACUGUUCGGAAAACCGAUCGCACAGCCUGGGACU GACACCGAACUUC AAGAGCAACUUCGACCUGGCAGAAGACGCAAAGCUGCAGC UGAGCAAGGACACAUACGACGACGACCUGGACAACCGUGGCACAGAUCCGGA GACCAGUACGCAGACCUGUUCUGGCAGCAAAGAACCUGAGCGACGCAAUCCUG CUGAGCGCAUCCUGAGAGUCAACACAGAAAUCACAAAAGGCACCGCUGAGCGC AAGCAUGAUC AAGAGAUACGACGAAACCACCAGGACCUGACACUGCUGAAGG CACUGGUCAGACAGCAGCUGCCGGAAAAAGUACAAGGAAAUCUUCUUCGACCAG AGCAAGAACGGAUACGCAGGAUACAUCGACGGAGGAGCAAGCCAGGAAGAUAU CUACAAGUUC AUC AAGCCG AUCCUGGAAAAGAUUGGACGGAAACAGAAGAACUCG UGGUAAGCUGAACAGAGAAGACCUGCUGAGAAAAGCAGAGAACAUCGACAAC GGAAGCAUCCCGCACCAGAUCACCUGGGAGAACUGCAGCAGCAAUCCUGAGAAGA CAGGAAGACUUCUACCCGUUCUGAAGGACAACAGAGAAAAGAUCCGAAAAGAU CCUGACAUCAGAAUCCCGUACUACGUCGGACCUGGCAAGAGGAAAACAGCA GAUUCGCAUUGG AUGACAAGAAAGAGCGAAGAAAACAUCACACCCUGGAAUCU GAAGAAGUCGUCGACAAGGGAGCAAGCGCACAGAGCUUCAUCGAAAGAAUGAC AAACUUCGACAAGAACCCUGCCGAACGAAAAGGUCCUGCCGAAGCACAGCCUGCU GUACGAUAUCUACAGUCUACAACGAACUGACAAAAGGUCAAGUACGUCACAG UACGAAUUGAGAAAAGCCGGCAUUCUGAGCGGAGAACAGAAGAAGGCAUCCUG GACCUGCUGUUC AAGACAAAACAGAAAAGGUCACAGUCAAGCAGCUGAAGGAAGA CUACUUC AAGAAGAU CGAAUGCUUCGACAGCGUCGAAAUCAGCGGAGUCGAA ACAGAUUCAACGCAAGCCUGGGAACAUAACACGACCUGCUGAAGAUCAUCAAG GACAAGGACUUCUGGACAACGAAGAAAACGAAGACAUCUGGAAGACAUCCUG CCUGACACUGACACUGUUCGAAGACAGAGAAAUGAUCGAAAGAACUGAAGGA CAUACGCACACCUGUUCGACGACAAGGUCAUGAAGCAGCUGAAGAGAAGAAGA UACACAGGAUGGGGAAGACUGAGCAGAAAAGCUGAUAACGGAAUCAGAGACAA GCAGAGCGGAAAGACAAUCCUGGACUUCUGAAGAGCGACGGAUUCGCAAAACA GAAACUUC AUGCAGCUGAUCCACGACGACAGCCUGACAUUCAAGGAAGACAUC CAGAAGGCACAGGUCAGCGGACAGGGAGACAGCCUGCACGAACACAUCGCAAA CCUGGCAGGAAGCCCGCAAUCAAGAAGGGAAUCCUGCAGACAGUCAAGGUCG UCGACGAACUGGUC AAGGUCAUGGGAAAGACACAAGCCGAAAACAUCGUCAU GAAAUGGCAAGAGAAAACCAGACAACACAGAAGGGACAGAAGAACAGCAGAGA AAGAAUGAAGAGAAUUCGAAGAAAGGAAUCAAAGGAACUUGGGAAGCCAGAUCCUGA AGGAACACCCGGUCGAAAAACACAGCUGCAGAACGAAAAGCUGUACCCUGUAC UACCUGCAGAACGGAAAGAGACAUGUACGUCGACCAGGAACUGGACAUCAACAG ACUGAGCGACUACGACGUCGACCACAUCGUCCCGCAGAGCUUCUGAAGGACGA CAGCAUCGACAACAAGGUCCUGACAAGAAGCGACAAGAACAGGAAAGAGGAGCG ACAACGUCCGAGCGAAGAAGUCGUAAGAAGAUGAAGAACUACUGGAGACAG CUGCUGAACGCAAAGCUGAUCACACAGAGAAAAGUUCGACAACCCUGACAAAGGC AGAGAGAGGAGGACUGAGCGAACUGGACAAGGCAGGAUUCAUCAAGAGACAGC UGGUCGAAACAAGACAGAUCAAAAGCAGCUGCAGCAGAUCCUGGACAGCAGA AUGAACACAAGUACGACGAAAACGACAAGCUGAUCAGAGAAGUCAAAGGUCAU CACACUGAAGAGCAAGCUGGUCAGCGACUUCAGAAAGGACUUCAGUUCUACA AGGUCAGAGAAAUCAACAACUACCACCACGCACACGCAUACCCUGAACGCAG UCGUCGGAACAGCACUGAUC AAGAAGUACCCGAAGCUGGAAAAGC GAAUUCGUC UACGGAGACUACAAGGUUCACGACGUCAGAAAAGAUUGAUCGAAAGCAAGCA GGAAAUCGAAAAGGCAACAGCAAAGUACUUCUUCUACAGCAACAUCAUGAACU UCUUC AAGACAGAAAUCACACUGGCAAACGGAGAAAUCAGAAAGAGACCUCG AUCGAAAACAACGGAGAAACAGGAGAAAUCGUCUGGGACAAGGGAAAGAGACU CGAACAGUCAGAAAAGGUCCUGAGCAUGCCCGAGGUAACAUCGUAAGAAAGA CAGAAGUCCAGACAGGAGGAUUCAGCAAGGAAAGCAUCCUGCCGAAGAGAAAC AGCGACAAGCUGAUCGCAAGAAAAGGACUGGGACCCGAAGAAGUACGGAGG AUUCGACAGCCGACAGUCGCAUACAGCGUCCUGGUCGUCGCAAAAGGUCGAAA AGGGAAAGAGCAAGAAGCUGAAGAGCGUCAAGGAACUGCUGGGAAUCACAUC AUGGAAAAGAGCAGCUUCGAAAAGAACCCGAUCGACUUCGGAAGCAAAGGG AUACAAGGAAGUCAAGAAGGACCUGAUCAUCAAGCUGCCGAAGUACAGCCUGU UCGAACUGGAAAACGGAAAGAGAAUGCUGGCAAGCGCAGGAGAACUGCAG AAGGGAAACGAACUGGCACUGCCGAGCAAGUACGUAACUUCUGUACCCUGGC AAGCCACUACGAAAAGCUGAAGGGAAAGCCCGAAGACAACGAACAGAAGCAGC UGUUCGUCGAACAGCACAAAGCACUACCUGGACGAAAUCAUCGAAACAGAUACG GAAUUCAGCAAGAGAGUCAUCCUGGCAGACGCAAACCCUGGACAAGGUCCUGAG CGAUACAACAAGCACAGAGACAAGCCGAUCAGAGAACAGGCAGAAAACAUCA UCCACCUGUUCACACUGACAAAACCCUGGGAGCACC GGCAAGUUCAGUACUUCG ACACAACAUCGACAGAAAAGAGAUACAACAAGCACAAAGGAAGUCCUGGACGCA ACACUGAUCCACCAGAGCAUCACAGGACUGUACGAAAACAAGAAUCGACCUGAG CCAGCUGGGAGGAGACGGAGGAGGAAAGCCGAAAGAAGAAGAGAAAGGUCUAG</p>	
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[0652]

<p>Cas9 mRNA ORF 1</p>	<p>AUGGAUAAGAAGUACUCAAUCGGGCGUGGAUAUCGGAACUAAUUCGGUGGGUUG GGCAGUGAUCACGGGAUGAAUACAAAAGUGCCGUCCAAGAAGUUAAGGUCCUGG GGAACACCGAUAGACACAGCAUCAAGAAAAAUCUCAUCGGAGCCUCUGUGUUU GACUCCGGCGAAACCGCAGAAAGCGACCCGGCUCAAACGUACCGCGAGGGCGACGC UACACCCGGCGGAAGAAUCGCAUCUGCUAUCUGCAAGAGAUCUUUUCGAACGA AAUGGCAAAGGUCGACGACAGCUUCUUCACCGCCUGGAAGAAUCUUUCUGG UGGAGGAGGACAAGAAGCAUGAACGGCAUCCUAUCUUUGGAAACAUCGUCGAC GAAGUGGGCUACCGAAAAGUACCCGACCAUCUACCAUCUGCGGAAGAAGUU GGUUGACUCAACUGACAAGGCCGACCUCAGAUUGAUCUACUUGGCCUCGCCCCA UAUGAUCAAUUCGGGACACUCCUGAUCGAAGGCGAUCUGAACCCUGAU ACUCCGACGUGGAUAAGCUUUUCAUUAACUGGUGCAGACCUACAACCAACUG UUCGAAGAAAACCAAUCAAUGCUAGCGGGCUGCAUGCCAAGGCCAUCCUGUCC GCCCGGCGUGCGAAGUCGCGGGCGCCUCGAAAACCGAUCGACAGCUGCCGGGA GAGAAAAAGAACGGACUUUUCGGCAACUUGAUCGCUCUCACUGGGACUCAC UCCCAAUUUCAAGUCCAAUUUUGACCUGGCCGAGGACGCGAAGCUGCAACUC AAAGGACACCUACGACGACGACUUGGACAAUUUGCUGGCACAAAUUGGCGAUC AGUACGCGGAUCUGUCCUUGCCGCUAAGAACCUUUCGGACGCAAUUCUGUG UCCGAUAUCCUGCGCGUGAACACCGAAAUAACCAAAGCGCCGCUUAGCGCCUCG AUGAUUAAGCGGUACGACGAGCAUACCAGGAUCUCACGCUCGCUCAAAGCGCU CGUGAGACAGCAACUGCCUGAAAAGUACAAGGAGAUUCUUCGACCAAGUCCA AGAAUGGGUACGCAGGGUACAUCGAUGGAGGCGCUAGCCAGGAAGAGUUCUAU AAGUUAUCAAGCCAAUCCUGGAAAAGAUUGGACGGAACCGAAGAACUGCUGGU CAAGCUGAACAGGGAGGAUCUGCUCGGAAAACAGAGAACCUUUGACAACGGAU CCAUUCACCAAGAUCCUUGGGGUGAGCUGCAGCACAUCUUGGACCAACUAGC AGGACUUUUACCAUUCUCAAGGACAACCGGGAAAAGAUUCGAGAAAAUUCUG ACGUUCGCAUCCGUAUUACGUGGGCCACUGGCAGCGGCAAUUCGCGCUUC GCGUGGAUGACUAGAAAUCAGAGGAAACCAUCACUCCUUGGAAUUUCGAGGA AGUUUGGGAUAAGGGAGCUUCGGCACAAGCUUCAUCGAACGAUUGACCAACU UCGACAAGAAUCUCCAAACGAGAAGGUGCUUCCUAAAGCACAGCCUCCUUACG AAUACUUCACUGUCUACAACGAACUGACUAAAGUGAAAUACGUUACUGAAGGA AUGAGGAAGCCGGCCUUUCUGUCCGGAGAACAGAAGAAAGCAAUUGUCGAUCU GCUUUAAGACCAACCGCAAGGUGACCGUCAAGCAGCUUAAAGAGGACUACU UCAAGAAGAUUCGAGUUGUUCGACUCAGUGGAAAUCAGCGGGGUGGAGGACAGA UUCAACGCUUCGUGGGAACCUAUCAUUGAUCUCCUGAAGAUCAUCAAGGACAA GGACUUCUUGACACGAGGAGAACGAGGACAUCUUGGAAGAUUCGUCUCUGA CCUUGACCCUUUCGAGGAUCGCGAGAUUGAUCGAGGAGAGGCUUAAAGACCUAC GCUCAUCUUCGACGUAUAGGUAUGAAACAACUCAAGCGCCGCGGUAACU GGUUGGGGCGCCUCUCCCGCAAGCUGAUCACGGUAUUCGCGAUAACACAGAG CGGUAAAAACUAUCCUGGAUUUCCUCAAAUCGGAUUGGUUCGCUAAUCGUAACU UCAUGCAAUUGAUCCACGACGACAGCCUGACCUUUAAGGAGGACUCCAAAAA GCACAAGUGUCCGGACAGGGAGACUCACUCCAUGAACACAUCGCGAAUUCGGCC GGUUCGCGGCGAUUAAAGAAAGGAAUUCUGCAAACUUGAAGGUGGUCGACGA GCUGGUAAGGUAUGGGACGGCACAACCGGAGAAUUCGUGAUUGAAUUGG CCCGAGAAAACAGACUACCCAGAAAGGGCCAGAAAAACUCCCGCGAAAAGGAUG AAGCGGAUCGAAGAAGGAUCAAAGGAGCUGGGCAGCCAGAUCCUGAAAGAGCA CCCGUGGAAAACACGACGUCGAGAACGAGAAGCUCUACCUUUGUUAUUUGC AAAAUGGACGGGACAUUGACGUGGACCAAGAGCUGGACAUCAAUCGGUUGUCU GAUUACGACGUGGACCACUUCGUUCCACAGUCCUUCUGAAGGAUGACUCGAU CGAUAAACAAGGUGUUGACUCGACGCGACAAGAACAGAGGGAAAGUCAGAUAAUG UGCCAUCGGAGGAGGUCGUGAAGAAGAUUGAAAUUACUGGCGGCAGCUCUCCG AAUGCGAAGCUGAUUACCCAGAGAAAAGUUUGACAACUCACUAAAAGCCGAGCG CGGCGGACUCUCAGAGCUGGAUAAAGGCUUGAUUCAUCAACGGCAGCUGGUCG AGACUCGGCAGAUUACCAAGCACGUGGCGCAGAUUCUGGACUCCGCAUGAAC ACUAAAUACGACGAGAACGAUAAGCUCUACCGGGAAGUGAAGGUGAUUACCCU GAAAAGCAAACUUGUGUCGGACUUUCGGAAGGACUUUCAGUUUUACAAGUGA GAGAAAUCAACAACUACCAUCACGCGCAUGACGCAUACCUCAACGCUGUGGUCG GUACCGCCUGAUCAAAAAGUACCCUAAACUUGAAUCGGAGUUUUGUGUACGGA GACUACAAGGUCUACGACGUGAGGAAAGAUUGAUAGCCAAGUCCGAACAGGAAU CGGGAAGCAACUGCGAAAUACUUCUUUACUCAAAACUACUGAACUUUUUCA AGACUGAAAUACGCUUGGCAAUGGAGAAAUCAGGAAGAGGCCACUGAUCGAA ACUAACGGAGAAACGGGCGAAAUCGUGUGGACAAGGGCAGGGACUUCGCAAC UGUUCGCAAAGUGCUCUCUAUGCCGCAAGUCAAUUUGUGAAGAAAACCGAAG UGCAAACCGGCGGAUUUUCAAAGGAAUCGAUCCUCCAAAGAGAAAUAGCGAC AAGCUAUUGCACGCAAGAAAGACUGGGACCCGAAAGAUACGGAGAUUCG UUCGCCGACUGUCGAUACUCCGUCUUGGUGGCAAGGUGGAGAAAGGAA AGAGCAAAAAGCUCAAAUCGUCAAAAGAGCUGCUGGGGAUUACCAUCAUGGAA CGAUCCUGUUCGAGAAGAACCCGAUUUGAUUUCUUGGAGGCGAAGGGUUACAA</p>	<p>5</p>
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[0653]

	<p>GGAGGUGAAGAAGGAUCUGAUCUCAAACUCCCCAAGUACUCACUGUUCGAAC UGGAAAAUGGUCGGAAGCGCAUGCUGGCUUCGGCCGGAAGAACUCCAAAAAGGA AAUGAGCUGGCCUUGCCUAGCAAGUACGUCUAAUCCUCUUAUCUUGCUUCGCAC UACGAAAAACUCAAGGGUCACCGGAAGAUAAACGAACAGAAGCAGCUUUUCGU GGAGCAGCACAAGCAUUAUCUGGAGUAAAUAUCGAACAAAUCUCCGAGUUUU CAAAGCGCGUGAUCCUCGCGGACGCCAACCCUCGACAAAAGUCCUGCGGCUACA AUAAGCAUAGAGAUAAAGCCGAUCAGAGAACAGGCCGAGAACAUAUCCACUUG UUCACCCUGACUACCUGGGAGCCCCAGCCGCCUUAAGUACUUCGAUACUACU AUCGAUCGCAAAAGAUACACGUCCACCAAGGAAGUUCUGGACGCGACCCUGAU CCACCAAAGCAUCACUGGACUCUACGAAACUAGGAUCGAUCUUCGCGACUGG GUGGCGAUGGCGGUGGAUCUCCGAAAAAGAGAAAGGUGUAUAUGA</p>	
<p>Cas9 切口 酶 (D10A) 氨基酸序 列</p>	<p>MDDKYSIGLAIGTNSVGVAVITDEYKVPSSKFKVLGNTDRHSIKKNLIGALLFDSGET AEATRLKRTARRRYTRRKNRICYLQEIFSNEMAKVDDSFHRLSEESFLVEEDKKHERHP IFGNIVDEVAYHEKYPTIYHLRKKLV DSTKADLRLLIYLALAHMIKFRGHFLIEGDLNP DNSDVDKLFIQLVQTYNQLFEENPINASGVDAKAILSARLSKSRRLLENLIAQLPGEKKN GLFGNLIALSLGLTPNFKSNFDLAEDAKLQLSKD TYDDDLNLLAQIGDQYADLFLAA KNLSDAILLSDILRVNTEITKAPLSASMIKRYDEHHQDLTLLKALVRQQLPEKYKEIFFD QSKNGYAGYIDGGASQE EYFKIPKILEKMDGTEELVKNREDLLRKRQRTFDNGSIPH QIHLGELHAILRRQEDFYPLKDNREKIEKILTRIPYYVGPLARGNSRFVWMTSEET ITPWNFEEVVDK GASAQSFIERMTNFDKNLPNEKVLPHSLLYEYFTVYNELTKVKYV TEGMRKPAFLSGEQKAIVDLLFKTNRKVTVKQLKEDYFKKIECFDSVEISGVEDRFN ASLGTYHDLKIIKDKDFLDNEENEDILEDIVLTLTLFEDREMIEERLKYAHLFDDKV MKQLKRRRYTGWGRLSRKLINGIRDKQSGKTILDFLKSDFANRNFMLIHDDSLTFK EDIQKAQVSGQDSLHEHIANLAGSPAIKK GILQTVKVVDELVKVMGRHKPENVIEM ARENQTTQKGGKNSRERMKRIE EGIKELGSQILKEHPVENTQLQNEKLYLYLQNGRD MYVDQELDIRLSYD VDVHIVPQSFLKDDSIDNKVLT RSDKNRKGSDNVPSEEVVK MKNYWRQLLNAKLITQRKFDNLTKAERGGLSELDKAGFIKRLVETROITKHVAQLD SRMNTKYDENDKLIREVKVITLKS LVSDFRKFDFQYK VREINNYHHAHDAYLNAV GTALIKKYPKLESEFVYGDYK VYDVRKMIAKSEQEIGKATAKYFFYSNIMNFFKTEITL ANGEIRKRPLIETNGETGEIVWDKGRDFATVRKVL SMPQVNIKKTEVQTGGFSKESIL PKRNSDKLIARKKDWDPK KYGGFDSPTVAYSVLV VAKVEKGKSKKLSVKELLGITIM ERSSFENPIDFLEAKGYKEVKKDLI IKLPKYSLFEL ENGRKRMLASAGELQKGNELAL PSKYVNFLYLASHYEKLGSPEDNEQK QLFVEQHKHYLDEIIEQISEFSKRVLADANL DKVLSAYNKHRDKPIREQAENIHLFTLNLGAPA AFKYFDTTIDRKRYTSTKEVLDAT LIHQSI TGLYETRIDLSQLGGDGGGSPKKKRKV</p>	<p>6</p>
<p>Cas9 切口 酶 (D10A) mRNA ORF</p>	<p>AUGGACAAGAAGUACAGCAUCGGACUGGCAAUCGGAACAAACAGCGUCGGAUG GGCAGUCAUCACAGACGAAUACAAGGUCCCAGCAAGAAGUUCAAGGUCCUGG GAAACACAGACAGACACAGCAUCAAGAAGAACCUGAUCGGAGCACUGCUGUUC GACAGCGGAGAAAACAGCAGAAGCAACAAGACUGAAGAGAACAGCAAGAAGAAG AUACACAAGAAGAAAGAACAGAAUCUGCUACCUGCAGGAAAUCUUCAGCAACG AAAUGGCAAAGGUCGACGACAGCUUCUUCACAGACUGGAAGAAGAUCCUG GUCGAAGAAGACAAGAAGCACGAAAGACACCCGAUCUUCGGAACAUUCGUCGA CGAAGUCGCAUACCACGAAAAGUACCCGACAAUCUACCACCUAGAAAAGAAGC UGGUCGACAGCACAGACAAGGCAGACCUGAGACUGAUCUACCUGGCACUGGCA CACAUGAUCAGUUCAGAGGACACUUCUGAUCGAAGGAGACCUGAACCCGGA CAACAGCGACGUCGACAAGCUGUUAUCCAGCUGGUCCAGACAUAACAACAGCU GUUCGAAGAAAACCCGAUCAACGCAAGCGGAGUCGACGCAAAGGCAAUCCUGA GCGCAAGACUGAGCAAGAGCAGAAGACUGGAAAACCUAGUACGACAGCUGGCC GGAGAAAAGAAGAACGGACUGUUCGGAACCUAGUACGACUGAGCCUGGGACU GACACCGAACUUAAGAGCAACUUCGACCUGGCAGAAGACGCAAAGCAGC UGAGCAAGGACACAUACGACGACGACCUGGACAACCUGCUGGCACAGAUCCGGA GACCAGUACGCAGACCUGUUCCUGGCAGCAAAGAACCUGAGCGACGCAAUCCUG CUGAGCGCAUCCUGAGAGUCAACACAGAAAUCACAAAGGCACCGCUGAGCGC AAGCAUGAUC AAGAGAUACGACGAACACCACCAGGACCUGACACUGCUGAAGG CACUGGUCAGACAGCAGCUGCCGGAAGUAACAAGGAAAUCUUCUUCGACCA AGCAAGAACGGAUACGCAGGAUACAUCGACGGAGGAGCAAGCCAGGAAGAAU CUACAAGUUCAUCAAGCCGAUCCUGGAAAAGAUUGGACGGAACAGAAGAACUGC UGGUCAAGCUGAACAGAGAAGACCUGCUGAGAAAAGCAGAGAACAUCGACAAC GGAAGCAUCCCGACCAAGAUCCACCUGGGAGAACUGCAGCAAUCCUGGAGAAGA CAGGAAGACUUCUACCCGUUCUGAAGGACAACAGAGAAAAGAUUCGAAAAGAU CCUGACAUUCAGAAUCCGUACUACGUCGACCGCUGGCAAGAGGAAAACAGCA GAUUCGCAUGGAUGACAAGAAAGAGCGAAGAAAACAACACCCUGGAACUUC GAAGAAGUCGUCGACAAGGGAGCAAGCGCACAGAGCUUCAUCGAAAAGAAUGAC AAACUUCGACAAGAACCUGCCGAACGAAAAGGUCCUGCCGAAGCACAGCCUGCU GUACGAAUACUUCACAGUCUACAACGAACUGACAAAGGUCAGUACGUCACAG AAGGAAUGAGAAAAGCCGCAUUCUUCGACGGAGAACAAGAAGAAGGCAAUCGUC</p>	<p>7</p>

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	<p>GACCUGCUGUUAAGACAAACAGAAAGGUCACAGUCAAGCAGCUGAAGGAAGA CUACUUCAAGAAGAUUCGAAUGCUUCGACAGCGUCGAAAUCAGCGGAGUCGAAAG ACAGAUUCAACGCAAGCCUGGGAACAUACCACGACCUGCUGAAGAUCAUCAAG GACAAGGACUUCUGGACAACGAAGAAAACGAAGACAUCUGGGAAGACAUUCGU CCUGACACUGACACUGUUCGAAGACAGAGAAAUGAUCGAAGAAAGACUGAAGA CAUACGCACACCUUGUUCGACGACAAGGUCAUGAAGCAGCUGAAGAGAAAGAA UACACAGGAUUGGGGAAGACUGAGCAGAAAAGCUGAUAACGGAAUCAGAGACAA GCAGAGCGGAAAGACAAUCCUGGACUUCUGAAGAGCGACGGAUUCGCAAAAC GAAACUUCUAGCAGCUGAUCCACGACGACAGCCUGACAUUCAAGGAAGACAUC CAGAAGGCACAGGUCAGCGGACAGGGAGACAGCCUGCAGCAGAAACAUUCGAAA CCUGGCAGGAAGCCCGCAAUCAAGAAGGGAAUCCUGCAGACAGUCAAGGUCG UCGACGAACUGGUAAGGUCAUGGGAAAGACACAAGCCGGAAAACAUCGUCUUC GAAAUGGCAAGAGAAAACAGACAACACAGAAGGGACAGAAGAAGCAGCAGAGA AAGAAUGAAGAGAAUCGAAGAAGGAUCAAGGAACUGGGAAGCCAGAUCUGA AGGAACACCCGUCGAAAACACACAGCUGCAGAACGAAAAGCUGGAGACUAC UACCUGCAGAACGGAAAGAGACAUGUACGUCGACCAGGAACUGGACAUCAACAG ACUGAGCGACUACGACGUCGACCACAUCGUCCCGCAGAGCUUCUGAAGGACGA CAGCAUCGACAACAAGGUCCUGACAAGAAGCGACAAGAACAGAGGAAAAGAGCG ACAACGUCCGAGCGAAGAGUCGUAAGAAGAUAGAAGAAUCUAGGAGACAG CUGCUGAACGCAAAGCUGAUCACACAGAGAAAAGUUCGACAACCGACAAAAGGC AGAGAGAGGAGGACUGAGCGAACUGGACAAGGCAGGAUUCAUCAAGAGACAGC UGGUCGAAAACAAGACAGAUCAAAAAGCAGCUGCAGCAGAUCCUGGACAGCAGA AUGAACACAAAGUACGACGAAAACGACAAGCUGAUCAGAGAAGUCAAGGUCUAC CACACUGAAGAGCAAGCUGGUCAGCGACUUCAGAAAAGGACUUCAGUUAACA AGGUCAGAGAAAUCAACAACUACCACCACGCACACGACGCAUACCUGAACGCAG UCGUCGGAACAGCACUGAUCAGAAGUACCCGAAGCUGGAAAAGCGAAUUCGUC UACGGAGACUACAAGGUCUACGACGUCAGAAAAGAUAGUUCGCAAAGAGCGAAAC GGAAAUCGGAAGGCAACAGCAAGUACUUCUUCUACAGCAACAUCAUGAACU UCUUCAAGACAGAAAUCACACUGGCAAACGGAGAAAUCAGAAAGAGACCGCUG AUCGAAACAAACGGAGAAACAGGAGAAAUCGUCUGGGACAAGGGAAGAGACUU CGAACAGUCAGAAAGGUCCUGAGCAUGCCGCAGGUAACAUUCGUAAGAAAGA CAGAAGUCCAGACAGGAGGAUUCAGCAAGGAAAAGCAUCCUGCCGAAGAGAAAC AGCGACAAGCUGAUCGCAAGAAAAGAGGACUUGGGACCCGAAGAAGUACGGAGG AUUCGACAGCCCGACAGUCGAUACAGCGUCCUGGUCGUCGCAAAGGUCGAAA AGGGAAAGAGCAAGAAGCUGAAGAGCGUCAAGGAACUGCUGGGAAUCACAAUC AUGGAAAGAAGCAGCUUCGAAAAGAACCCGAUCGACUUCUGGAAGCAAAGGG AUACAAGGAAGUCAAGAAGGACCUGAUCAUCAAGCUGCCGAAGUACAGCCUGU UCGAACUGGAAAACGGAAAGAAAGAGAAUGCUGGCAAGCGCAGGAGAACUGCAG AAGGGAAACGAACUGGCACUGCCGAGCAAGUACGUAACUUCUGUACCUUGGC AAGCCACUACGAAAAGCUGAAGGGAAAGCCCGGAAGACAACGAACAGAAGCAGC UGUUCGUCGAACAGCACAAGCACUACCUGGACGAAAUCAUCGAACAGCAUCAGC GAAUUCAGCAAGAGAGUCAUCCUGGCAGACGCAAACCUUGGACAAGGUUCGAG CGCAUACAACAAGCACAGAGACAAGCCGAUCAGAGAACAGGCAGAAAACAUCA UCCACUGUUCACACUGACAAAACCUUGGGAGCACCAGCAUUAAGUACUUCG ACACAACAUCGACAGAAAAGAGAUACAACAAGCACAAGGAAGUCCUGGACGCA ACACUGAUCCACAGAGCAUCACAGGACUGUACGAAAACAAGAAUACGACUGAG CCAGCUGGGAGGAGACGGAGGAGGAAGCCGAAGAAGAAGAGAAAAGGUCUAG</p>	
<p>dCas9 (D10A H840A) 氨 基酸序列</p>	<p>MDKKYSIGLAIGTNSVGVAVITDEYKVPSSKFKVLGNTDRHSIKKNLIGALLFDSGET AEATRLKRTARRRYTRRKNRICYLQEIFSNEMAKVDDSFHRLLESFLVEEDKKHERHP IFGNIVDEVAYHEKYPTIYHLRKKLVDSTDKADLRLIYLALAHMIKFRGHFLIEGDLNP DNSVDKLFIQLVQTYNQLFEENPINASGVDAKAILSARLSKSRRENLIQAQLPGEKKN GLFGNLIALSLGLTPNFKSNFDLAEDAQLQLSKDQYDDDLNLLAQIGDQYADLFLAA KNLSDAILLSDILRVNTEITKAPLSASMIKRYDEHHQDLTLLKALVRQQLPEKYKEIFFD QSKNGYAGYIDGGASQEEFYKFIKPILEKMDGTEELLVKNREDLLRQRTFDNGSIPH QIHLGELHAILRRQEDFYFPLKDNREKIEKILTRIPYYVGPLARGNSRFVWMTKSEET ITPWNFEVVDKGASAQSFIERMTNFDKNLPNEKVLPHSLLYEYFTVYNELTKVKYV TEGMRKPAFLSGEQKKAIVDLLFKTNRKVTVKQLKEDYFKKIECFDSVEISGVEDRFN ASLGTYHDLKIIKDKDFLDNEENEDILEDIVLTLTLFEDREMIEERLKYAHLFDDKV MKQLKRRRYTGWRLSRKLINGIRDKQSGKTILDFLKSDFANRNFMLIHDDSLTFK EDIQKAQVSGGDSLHEHIANLAGSPAIKKGILQTVKVVDELVKVMGRHKPENIVIE ARENQTTQKQKNSRERMKRIEIKELGSQILKEHPVENTQLQNEKLYLYLQNGRD MYVDQELDINRLSDYDVAIVPQSFLKDDSIDNKVLTRSDKNRGSNDVNPSEEVVKK MKNYWRQLNAKLITQRKFDNLTKAERGGSELKAGFIKRLVETRQITKHVAQILD SRMNTKYDENDKLIREVKVITLKSGLVDFRKFDFQYKVIKREINNYHHAMDAYLNAV GTALIKYPKLESEFYGDYKYYDVRKMIKSEQEI GKATAKYFFYSNIMNFFKTEITL ANGEIRKPLIETNGETGEIVWDKGRDFATVRKVLVSMQVNVKKEVQTTGGFSKESIL PKRNSDKLIARKKDWDPKKYGGFDSPTVAYSVLVVAKEVGKSKKLSVKELGITIM</p>	<p>8</p>

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	<p>ERSSFENPIDFLEAKGYKEVKKDLIILPKYSLFELENGRKRMLASAGELQKGNELAL PSKYVNFYLAHYEKLKGSPEDEQKQLFVEQHKHYLDEIIEQISEFSKRVILADANL DKVLSAYNKHDRDKPIREQAENIHLFTLTNLGAPAAFYFDTTIDRKRYTSTKEVLDT LIHQSIITGLYETRIDLSQLGGDGGGSPKKKRKV</p>	
<p>dCas9 (D10A H840A) mRNA ORF</p>	<p>AUGGACAAGAAGUACAGCAUCGGACUGGCAAUCGGAACAACAGCGUCGGAUG GGCAGUCAUCACAGACGAAUACAAGGUCCCAGCAAGAAGUUCAAGGUCCUGG GAAACACAGACAGACACAGCAUCAAGAAGAACCUGAUCGGAGCACUGCUGUUC GACAGCGGAGAAAACAGCAGAAGCAACAAGACUGAAGAGAACAGCAAGAAGAAG AUACACAAGAAGAAAGAACAGAAUCUGCUACCUGCAGGAAAUCUUCAGCAACG AAAUGGCAAAGGUCGACGACAGCUUCUCCACAGACUGGAAGAAAGCUUCCUG GUCGAAGAAGACAAGAAGCACGAAAAGACACCCGAUCUUCGGAAAACUUCGUCGA CGAAGUCGCAUACCACGAAAAGUACCCGACAAUCUACCACCUAGAAAAGAAGC UGGUCGACAGCACAGACAAGGCAGACCUAGAGACUGAUCUACCUGGCACUGGCA CACAUCAAGUUCAGAGGACACUCCUGAUCGAAGGAGACCUGAACCCGGA CAACAGCGACGUCGACAAGCUGUUAUCCAGCUGGUCCAGACAUACAACCAGCU GUUCGAAGAAAACCCGAUCAACGCAAGCGGAGUCGACGCAAAGGCAAUCCUGA GCGCAAGACUGAGCAAGAGCAGAAGACUGGAAAACCUAGUCGCACAGCUGCCG GGAGAAAAGAAGAACGGACUGUUCGGAAAACCUAGUCGCACUGAGCCUGGGACU GACACCGAACUUCAGAGCAACUUCGACCUUGGAGAAGACGCAAAGCUGCAGC UGAGCAAGGACACAUACGACGACGACCUAGGACAACCUUGCUGGACAGAUCCGGA GACCAGUACGCAGACCUGUUCCUGGCAGCAAAGAACCUGAGCGACGCAAUCCUG CUGAGCGCAUCCUGAGAGUCAACACAGAAAUCACAAAGGCACCGCUGAGCGC AAGCAUGAUCAGAGAUACGACGAACACCACCAGGACCUAGACUUCUGGAAGC CACUGGUCAGACAGCAGCUGCCGAAAAGUACAAGGAAAUCUUCUCCAGCAGC AGCAAGAACGGAUACGCAGGAUACAUCGACGAGGAGCAAGCCAGGAAGAUAU CUACAAGUUCUUCAGCCGAUCCUGGAAAAGAUUGGACGGAACAGAAAGACUGC UGGUAAGCUGAACAGAGAAGACCUUGCUGAGAAAAGCAGAGAACAUCGACAAC GGAAGCAUCCCGCACAGAUCCACCUGGGAGAACUGCAGCAAUCCUGGAGAAGA CAGGAAGACUUCUACCCGCUUCCUGAAGGACAACAGAGAAAAGAUUCGAAAAGU CCUGACAUCAGAAUCCGUAUCUACGUCGGACCGCUGGCAAGAGGAAAACAGCA GAUUCGCAUUGGAUGACAAGAAAGAGCGAAGAAAACAUCACACCGUGGAACUUC GAAGAAGUCGUCGACAAGGGAGCAAGCGCACAGAGCUUCAUCGAAAAGAAUGAC AAACUUCGACAAGAACCUGCCGAACGAAAAGGUCCUGCCGAAGCAGCAGCUGCU GUACGAAUACUUCACAGUCUACAACGAACUGACAAAGGUCAAGUACGUCACAG AAGGAAUGAGAAAAGCCGGCAUUCUUGAGCGGAGAACAGAAAGGCAAUCCUGC GACCUGCUGUUCAGACAAAACAGAAAAGGUCACAGUCAAGCAGCUGAAGGAAGA CUACUUCAGAAGAUUCGAAUGCUUCGACAGCGUCGAAAUCAGCGGAGUCGAAAG ACAGAUUCAACGCAAGCCUGGGAACAUAACCACGACCUUGCUGAUAUCAAG GACAAGGACUUCUGGACAACGAAGAAAACGAAGACAUCUGGAAGACAUCGU CCUGACACUGACACUGUUCGAAGACAGAGAAAUGAUCGAAGAAAAGACUGAAGA CAUACGCACACCUUGUUCGACGACAAGGUCAUGAAGCAGCUGAAGAGAGAAGA UACACAGGAUUGGGGAAGACUGAGCAGAAAAGCUUGAUAACCGGAAUACAGACAA GCAGAGCGGAAAGACAAUCCUGGACUUCUGAAGAGCGACGGAUUCGCAAACA GAAACUUCUAGCAGCUGAUCCACGACGACAGCCUGACAUCUUCAGGAAGACAUC CAGAAGGCACAGGUCAGCGGACAGGGAGACAGCCUGCACGAACAUCGCAAAA CCUGGCAGGAAGCCCGCAAUCAAGAAGGGAAUCCUGCAGACAGUCAAGGUUCG UCGACGAACUGGUAAGGUCAUUGGGAAGACACAAGCCGAAAACUUCGUAUC GAAAUGGCAAGAGAAAACCAGACAACACAGAAAGGACAGAAAGAACAGCAGAGA AAGAAUGAAGAGAAUUCGAAGAAGGAUUCAGGAACUGGGAAGCCAGAUCCUGA AGGAACACCCGGUCGAAAACACACAGCUGCAGAACGAAAAGCUGUACCUUGUAC UACCUGCAGAACGGAAGAGACAUGUACGUCGACACAGGAACUGGACAUCAACAG ACUGAGCGACUACGACGUCGACGCAAUCGUCCCGCAGAGCUUCCUGAAGGACGA CAGCAUCGACAACAAGGUCCUGACAAGAAGCGACAAGAACAGAGGAAAAGAGCG ACAACGUCCGAGCGAAGAAGUCGUCAAGAAGAUGAAGAACUACUGGAGACAG CUGCUGAACGCAAAGCUGAUCACACAGAGAAAAGUUCGACAACCUAGACAAGGC AGAGAGAGGAGGACUGAGCGAACUGGACAAGGCAGGAUUCAUACAAGAGACAGC UGGUCGAAAACAAGACAGAUACAAGACAGCUCGACAGAUCCUGGACAGCAGA AUGAACACAAAGUACGACGAAAACGACAAGCUGAUCAGAGAAGUCAAGGUCAU CACACUGAAGAGCAAGCUGGUCAGCGACUUCAGAAAAGGACUUCAGUUCUACA AGGUCAGAGAAAUCAACAACUACCACACGACACGACGCAUCCUGAAGCAGCAG UCGUCGGAACAGCACUGAUCAGAAGUACCCGAAGCUGGAAAGCGAAUUCGUC UACGGAGACUACAAGGUUCACGACGUCAGAAAAGAUUGAUCGAAAAGAGCGAACA GGAAAUCGAAAAGGCAACGCAAAAGUACUUCUUCUACAGCAACAUCUAGAUC UCUUCAAAGACAGAAAUCACACUUGGCAAAACGAGAAAUCAGAAAAGAGACCGCUG AUCGAAAACAACGGAGAAAACAGGAGAAAUCGUCUGGGAACAAGGGAAGAGACUUC CGAACAGUCAGAAAAGGUCCUGAGCAUGCCCGAGGUCAACUUCGUAAGAAGA CAGAAGUCCAGACAGGAGGAUUCAGCAAGGAAAAGCAUCCUGCCGAAGAGAAAAC</p>	<p>9</p>

	<p>AGCGACAAGCUGAUCGCAAGAAAGAAGGACUGGGACCCGAAGAAGUACGGAGG AUUCGACAGCCCGACAGUCGCAUACAGCGUCCUGGUCGUCGCAAAGGUCGAAA AGGGAAAGAGCAAGAAGCUGAAGAGCGUCAAGGAACUGCUGGGAAUCACAAUC AUGGAAAGAAGCAGCUUCGAAAAGAACCCGAUCGACUUCUGGAAGCAAAGGG AUACAAGGAAGUCAAGAAGGACCUGAUCAUCAAGCUGCCGAAGUACAGCCUGU UCGAACUGGAAAACGGAAGAAAGAGAAUGCUGGCAAGCGCAGGAGAACUCGAG AAGGGAAACGAACUGGCACUGCCGAGCAAGUACGUCAACUUCUGUACCUGGC AAGCCACUACGAAAAGCUGAAGGGGAAGCCCGAAGACAACGAACAGAAGCAGC UGUUCGUCGAACAGCACAAGCACUACCUGGACGAAAUCAUCGAACAGAUACAGC GAAUUCAGCAAGAGAGUCAUCCUGGCAGACGCAAACCCUGGACAAGGUCCUGAG CGCAUACAACAAGCACAGAGACAAGCCGAUCAGAGAACAGGCAGAAAAUCA UCCACUGUUCACACUGACAAACCCUGGGAGCACCAGCAGCAUUAAGUACUUCG ACACAACAUCGACAGAAAAGAGAUACACAAGCACAAGGAAGUCCUGGACGCA ACACUGAUCCACCAGAGCAUCACAGGACUGACGAAACAAGAAUUCGACCGUAG CCAGCUGGGAGGAGACGGAGGAGGAAGCCCGAAGAAGAAGAGAAAAGGUCUAG</p>	
<p>Cas9 裸编 码序列</p>	<p>GACAAGAAGUACAGCAUCGGACUGGACAUCGGAACAAACAGCGUCGGAUGGGC AGUCAUCACAGACGAAUACAAGGUCCCGAGCAAGAAGUUAAGGUCCUGGGAA ACACAGACAGACACAGCAUCAAGAAGAACCUGAUCGGAGCACUGCUGUUCGAC AGCGGAGAAACAGCAGAAGCAACAAGACUGAAGAGAACAGCAAGAAGAAGUA CACAAGAAGAAGAAACAGAAUCUGCUACCUGCAGGAAAUCUUCAGCAAGAAA UGGCAAAGGUCGACGACAGCUUCUCCACAGACUGGAAGAAAGCUUCUGGUC GAAGAAGACAAGAAGCACGAAAGACACCCGAUCUUCGGAACAUCGUCGACGA AGUUCGCAUACCACGAAAAGUACCCGACAACUACACCUCUGAGAAAAGAACUGG UCGACAGCACAGCAAGGCAGACCUGAGACUGAUCUACCUGGCACAGCAACA UGAUCAGUUCAGAGGACACUUCUGAUCGAAGGAGACCUGAACCCGGACAAC AGCGACGUCGACAAGCUGUUAUCCAGCUGGUCCAGACAUACACCAGCUGUUC GAAGAAAACCCGAUCAACGCAAGCGGAGUCGACGCAAAGGCAAUCCUGAGCGC AAGACUGAGCAAGAGCAGAAGACUGGAAAACCCUGAUCGCACAGCUGCCGGGAG AAAAGAAGAACGGACUGUUCGGAAACCCUGAUCGCACUAGCCUGGGACUGACA CCGAACUUCAGAGCAACUUCGACCCUGGCAGAAGACGCAAAGCUGCAGCUGAG CAAGGACACAUACGACGACGACCUGGACAACCUGCUGGCACAGAUCCGGAGACCA GUACGCAGACCUGUUCUGGCAGCAAAGAACCUGAGCGACGCAAUCCUGCUGA GCGACAUCUGAGAGUAACACAGAAAUCACAAGGGCACCCUGGAAACUCCGAAG AUGAUCAGAGAUACGACGAAACACCACCAGGACCUGACACUGCUGAAGGCACU GGUCAGACAGCAGCUGCCGGAAAAGUACAAGGAAAUCUUCUUCGACCAGAGCA AGAACGGAUACGCAGGAUCAUCGACGAGGAGCAAGCCAGGAAGAUAUUCUAC AAGUUAUCAAGCCGAUCCUGGAAAAGAUUGGACGGAACAGAAGAAGCUGCUGU CAAGCUGAACAGAGAAGACCUGCUGAGAAAAGCAGAGAACAUAUCGACAAACGGAA GCAUCCCGCACCAGAUCCACCUGGGAGAACUGCAGCACAACUCCUGAGAAGACAGG AAGACUUCUACCCGUUCUGAAGGACAACAGAGAAAAGAUUCGAAAAGAUCCUG ACAUUCAGAAUCCCGUACUACGUCGGACCCUGGCAAGAGGAAACAGCAGAUU CGCAUGGAUGACAAGAAAGAGCGAAGAAAACAUAACACCUGGAAACUUCGAAG AAGUCGUCGACAAGGGAGCAAGCGCACAGAGCUUCAUCGAAAGAAUGACAAAC UUCGACAAGAACCUGCCGAACGAAAAGGUCCUGCCGAAGCACAGCCUGCUGUAC GAAUACUUCACAGUCUACAACGAACUGACAAAGGUCAAGUACGUCACAGAAGG AAUGAGAAAAGCCGGCAUUCUGAGCGGAGAACAGAAGAAGGCAAUUCGUCGAGC UGCUGUUAAGACAAAACAGAAAAGGUCACAGUCAAGCAGCUGAAGGAAGCAUAC UUCAAGAAGAUUCGAAUGCUUCGACAGCGUCGAAAUCAGCGGAGUCGAAGACAG AUUCAACGCAAGCCUGGGAACAUAACCACGACCUGCUGAAGAUCAUCAAGGACA AGGACUUCUGGACAACGAAGAAAACGAAGACAUCUCCUGGAAGACAUCGUCCUG ACACUGACACUGUUCGAAGACAGAGAAAUGAUCGAAGAAAAGACUGAAGACAU CGCACACCUGUUCGACGACAAGGUCAUGAAGCAGCUGAAGAGAAGAAGAUACA CAGGAUUGGGGAAGACUGAGCAGAAAAGCUGAUAACGGAAUCAGAGACAAGCAG AGCGGAAAGACAACUCCUGGACUUCUGAAGAGCGACGGAUUCGCAAACAGAAA CUUCAUGCAGCUGAUCCACGACGACAGCCUGACAUAUUAAGGAAGACAUCACAGA AGGCACAGGUCAGCGGACAGGGAGACAGCCUGCACGAACACAUCCGAAAACCCUG GCAGGAAGCCCGCAAUCAAGAAGGGAUCCUGCAGACAGUCAAGGUCGUCGGA CGAACUGGUAAGGUCAUGGGAAGACACAAGCCGGAAAACAUCGUAUCGAAA UGGCAAGAGAAAACAGACAACACAGAAGGGACAGAAGAAGCAGAGAGAAAGA AUGAAGAGAAUUCGAAGAAGGAAUCAAGGAACUGGGAAGCCAGAUCCUGAAGGA ACACCCGGUCGAAAACACACAGCUGCAGAACGAAAAGCUGUACCUUGUACUACCU GCAGAACGGAAGAGACUAGUACGUCGACCAGGAACUGGACAUAACAGACUGA GCGACUACGACGUCGACCACAUCGUCCCGCAGAGCUUCCUGAAGGACGACAGCA UCGACAACAAGGUCCUGACAAGAAGCGACAAGAACAGAGGAAAGAGCGACAAC GUCCCGAGCGAAGAAGUCGUAAGAAGAUAGAAGAACUACUGGAGACAGCUCU GAACGCAAAGCUGAUCACACAGAGAAAGUUCGACAACCUGACAAAGGCAGAGA GAGGAGGACUGAGCGAACUGGACAAGGCAGGAUUAUCAAGAGACAGCUGGUC</p>	<p>10</p>

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	<p>GAAACAAGACAGAUCACAAAGCACGUCGCACAGAUCUGGACAGCAGAAUGAA CACAAAGUACGACGAAAACGACAAGCUGAUCAGAGAAGUCAAGGUCAUCACAC UGAAGAGCAAGCUGGUCAGCGACUUCAGAAAAGGACUUCAGUUCUACAAGGUC AGAGAAAUCAACAACUACCACCACGCACACGACGCAUACCUGAACGCAGUCGUC GGAACAGCACUGAUCAGAAGUACCCGAAGCUGGAAAGCGAAUUCGUCUACGG AGACUACAAGGUUCACGACGUCAGAAAAGAUAGUUCGCAAAGAGCGAACAGGAAA UCGGAAAGGCAACAGCAAAGUACUUCUUCUACAGCAACAUCGAACUUCUUC AAGACAGAAAUCACACUGGCAAACGGAGAAAUCAGAAAAGAGACCGCUGAUCGA AACAAACGGAGAAACAGGAGAAAUCGUCUGGGACAAGGGAAGAGACUUCGCAA CAGUCAGAAAAGGUCCUGAGCAUGCCGACGGUCAACAUCGUCUACAAGAACAGAA GUCCAGACAGGAGGAUUCAGCAAGGAAAAGCAUCCUGCCGAAGAGAAAACAGCGA CAAGCUGAUCGCAAGAAAGAAAGGACUGGGACCCGAAGAAGUACGGAGGAUUCG ACAGCCCGACAGUCGCAUACAGCGUCCUGGUCGUCGCAAAGGUCGAAAAGGGA AAGAGCAAGAAGCUGAAGAGCGUCAAGGAACUGCUGGGAAUCACAAUCAUGGA AAGAAGCAGCUUCGAAAAGAACCCGUAUCGACUUCUGGAAAGCAAAGGGAUACA AGGAAGUCAAGAAGGACCUGAUCAUCAAGCUGCCGAAGUACAGCCUGUUCGAA CUGGAAAACGGAAAGAAAGAGAAUGCUGGCAAGCGCAGGAGAACUGCAGAAGGG AAACGAACUGGCACUGCCGAGCAAGUACGUCUACUUCUGUACCUUGGCAAGCCCA CUACGAAAAGCUGAAGGGAAGCCCGAAGACAACGAACAGAAGCAGAGCUUCG UCGAACAGCACAAAGCACUACCUGGACGAAAUCAUCGAACAGAUACAGCGAAUUC AGCAAGAGAGUCAUCCUGGCAGACGCAAACCUUGGACAAGGUCCUGAGCGCAUA CAACAAGCACAGAGACAAGCCGAUCAGAGAACAGGCAGAAAACAUCUCCACC UGUUCACACUGACAAACCUUGGAGCACCCGGCAGCAUUCAGUACUUCGACACA ACAAUCGACAGAAAGAGAUACACAAGCACAAAGGAAGUCCUGGACGCAACACU GAUCCACCAGAGCAUCACAGGACUGUACGAAACAAGAAUCGACCUGAGCCAGC UGGGAGGAGACGGAGGAGGAAGCCGAAGAAGAAGAGAAAAGGUC</p>	
<p>Cas9 切口 酶裸编码 序列</p> <p>[0657]</p>	<p>GACAAGAAGUACAGCAUCGGACUGGCAAUCGGAACAAACAGCGUCGGUAGGGC AGUCAUCACAGACGAAUACAAGGUCCCGAGCAAGAAGUUAAGGUCCUGGGAA ACACAGACAGACAGCAUCAAGAAGAACCUGAUCGGAGCAGCUGCUGUUCGAC AGCGGAGAAACAGCAGAAGCAACAAGACUGAAGAGAACAGCAAGAAGAAGAU CACAAGAAGAAAGAACAGAAUCUGCUACCUGCAGGAAAUCUUCAGCAACGAAA UGGCAAAGGUCGACGACAGCUUCUCCACAGACUGGAAGAAAGCUUCUGGUC GAAGAAGACAAGAAGCACGAAAGACACCCGAUCUUCGGAACAUCGUCGACGAG AGUCGCAUACCACGAAAAGUACCCGACAAUCUACCACCUGAGAAAAGAGCUGG UCGACAGCACAGACAAGGCAGACCUGAGACUGAUCUACCUGGCACUGGCACACA UGAUCAGUUCAGAGGACACUUCUGAUCGAAGGAGACCUGAACCCGGACAAC AGCGACGUCGACAAGCUGUUCUACUCCAGCUGGUCAGACAUACAACACGUGUUC GAAGAAAACCCGAUCAACGCAAGCGGAGUCGACGCAAAGGCAAUUCUGAGCGC AAGACUGAGCAAGAGCAGAAGACUGGAAAACCUGAUCGCACAGCUGCCGGGAG AAAAGAAGAACGGACUGUUCGGAACCUGAUCGCACUGAGCCUGGGACUGACA CCGAACUUCAGAGCAACUUCGACCUGGACAGAACGCAAGCUGCAGCUGAG CAAGGACACAUACGACGACGACCUUGGACAACCUUGCUGGACAGAUCCGAGACCA GUACGCAGACCUGUUCUGGACGAAAAGAACCUGAGCGACGCAAUCCUGCUGA GCGACAUCCUGAGAGUCAACACAGAAAUCACAAAGGCACCGCUGAGCGCAAGC AUGAUCAGAGAUACGACGAAACACCACCAGGACCUGACACUGCUGAAGGCACU GGUCAGACAGCAGCUGCCGAAAAGUACAAGGAAAUUCUUCUCCAGCAGCA AGAACGGAUACGCAGGAUACAUCGACGAGGAGCAAGCCAGGAAGAUAUUCUAC AAGUUCAUCAAGCCGAUCCUGGAAAAGAUUGGACGGAACAGAAGAACUGCUGGU CAAGCUGAACAGAGAAGACCUGCUGAGAAAAGCAGAGAACAUCGACAACGGAA GCAUCCCGCACAGAUCCACCUGGAGAACUGCAGCACAUCUGAGAGAAGACAGG AAGACUUCUACCCGUUCUGAAGGACAACAGAGAAAAGAUCCGAAAAGAUCCUG ACAUCAGAAUCCCGUACUACGUCGGACCGCUGGCAAGAGGAAACAGCAGAUU CGAUGGAUGACAAGAAAGAGCGAAGAAACAUCACACCGUGGAACUUCGAAG AAGUCGUCGACAAGGGAGCAAGCGCACAGAGCUUCAUCGAAAGAAUGACAAC UUCGACAAGAACCUGCCGAACGAAAAGGUCCUGCCGAAGCACAGCCUGCUGUAC GAUACUUCACAGUCUACAACGAACUGACAAAGGUACAAGUACGUCACAGAAAG AAUGAGAAAGCCGGCAUUCUGAGCGGAGAACAGAAGAAGGCAUUCGUCGACC UGCUGUUCAGACAAACAGAAAGGUCACAGUCAAGCAGCUGAAGGAAGACUAC UUCAAGAAGAUCCGAAUGCUUCGACAGCGUCGAAAUCAGCGGAGUCGAAGACAG AUUCAACGCAAGCCUGGGAACAUAACCACGACCUGCUGAAGAUCAUCAAGGACA AGGACUUCUGGACAACGAAGAAAACGAAGACAUCUGGAAGACAUCGUCCUG ACACUGACACUGUUCGAAGACAGAGAAAUGAUCGAAGAAAGACUGAAGACAUA CGCACACCUGUUCGACGACAAGGUCAUGAAGCAGCUGAAGAGAAGAAGAUACA CAGGAUGGGGAAGACUGAGCAGAAAAGCUGAUAACCGGAAUCAGAGACAAGCAG AGCGAAAAGACAUCUCCUGGACUUCUGAAGAGCGACGGAUUCGCAACAGAAA CUUCAUGCAGCUGAUCCAGCAGCAGCCUGACAUCUUCAGGAAGACAUCACAGA AGGCACAGGUCAGCGGACAGGGAGACAGCCUGCACGAACACAUCGCAAACCUUG</p>	<p>11</p>

[0658]

	<p>GCAGGAAGCCCGGCAAUCAAGAAGGGAAUCCUGCAGACAGUCAAGGUCGUCGA CGAACUGGUC AAGGUC AUGCAGGAAAGACACAAGCCGGAAAACAUCGUC AUCGAAA UGGCAAGAGAAAAC CAGACAACACAGAAGGGACAGAAGAACAGCAGAGAAAAGA AUGAAGAGAAUCGAAAGAAAGGAAUC AAGGAACUGGGAAAGCCAGAUCUGAAGGA ACACCCGGUCGAAAACACACAGCUCGAGAACGAAAAGCUGUACCUUACUACCU GCAGAACGGAAAGAGACAU GUACGUCGACCAGGAACUGGACAUCAACAGACUGA GCGACUACGACGUCGACCACAUCGUCCCGCAGAGCUUCCUGAAGGACGACAGCA UCGACAACAAGGUCCUGACAAGAAGCGACAAGAACAGAGGAAAAGAGCGAC AAC GUCCCGAGCGAAGAAGUCGUC AAGAAGAUGAAGAACUACUGGAGACAGCUCGU AAGACGAAAUCACACAGAGAAAAGUUCGACAACCCUGACAAGGACAGCAGCUGA GAGGAGGACUGAGCGAACUGGACAAGGCAGGAUUAUCAAGAGACAGCUGGUC GAAACAAGACAGAUCAAAAGCAGUCGCACAGAUCUGGACAGCAGAAUGAA CACAAAGUACGACGAAAACGACAAGCUGAUCAGAGAAGUCAAGGUC AUCACAC UGAAGAGCAAGCUGGUCAGCGACUUCAGAAAAGGACUUCAGUUCUACAAGGUC AGGAAAUCAACAACUACCACCACGACACGACGCAUACCUAGAACGACAGCUC GGAACAGCACUGAUC AAGAAGUACCCGAAGCUGGAAAAGCGAAUUCGUCUACGG AGACUACAAGGUCUACGACGUCAGAAAAGAU GAUCGAAAAGAGCGAACAGGAAA UCGAAAAGGCAACAGCAAAGUACUUCUUCUACAGCAACAUCAUGAACUUCUUC AAGACAGAAAUCACACUGGCAAACCGGAGAAAUCAGAAAAGAGACCCGUGAUCGA AACAAACGGAGAAAACAGGAGAAAUCGUCUGGGACAAGGGAAGAGACUUCGCAA CAGUCAGAAAAGGUCCUGAGCAUGCCCGCAGGUAACAUCGUC AAGAAGACAGAA GUCCAGACAGGAGGAUUCAGCAAAGGAAAGCAUCCUGCCGAAGAGAAAACAGCGA CAAGCUGAUCGCAAGAAAAGAGGACUGGGACCCGAAGAAGUACGGAGGAUUCG ACAGCCCGACAGUCGAUACAGCGUCCUGGUCGUCGCAAGGUCGAAAAGGUCGAAA AAGAGCAAGAAGCUGAAGAGCGUCAAGGAACUGCUGGGAAUCACAAUCAUGGA AAGAAGCAGCUUCGAAAAGAACCCGACUUCGACUUCUGGAAGCAAAGGGAUACA AGGAAGUCAAGAAGGACCUGAUC AUC AAGCUGCCGAAGUACAGCCUGUUCGAA CUGGAAAACGGAAAGAAAAGAGAAUGCUGGCAAAGCGCAGGAGAACUGCAGAAGGG AAACGAACUGGCACUGCCGAGCAAGUACGUC AACUUCUGUACCUUGGCAAGCCA CUACGAAAAGCUGAAGGGAAGCCCGGAAGACAACGAACAGAAGCAGCUGUUCG UCGAACAGCAC AAGCACUACCUUGGACGAAAUCAUCGAACAGAUACGCGAAUUC AGCAAGAGAGUCAUCCUGGCAGACGCAAACCCUGGACAAGGUCCUGAGCGCAUA CAACAAGCACAGAGACAAGCCGAUCAGAGAACAGGCAGAAAACAUCAUCCACC UGUUCACACUGACAAAACCUUGGAGCACCGGCAGCAUUC AAGUACUUCGACACA ACAAUCGACAGAAAGAGAUACACAAGCACAAAGGAAGUCCUGGACGCAACACU GAUCCACCAGAGCAUCACAGGACUGUACGAAAACAAGAAUCGACCUUGAGCCAGC UGGAGGAGAGCGGAGGAGGAAGCCGAAGAAGAAGAGAAAAGGUC</p>	
dCas9 裸编 码序列	<p>GACAAGAAGUACAGCAUCGGACUGGCAAUCGGAACAAACAGCGUCGGAUGGGC AGUCAUCACAGACGAAUACAAGGUCCCGAGCAAGAAGUUAAGGUCCUGGGAA ACACAGACAGACACAGCAUCAAGAAGAACCUGAUCGGAGCACUGCUGUUCGAC AGCGGAGAAACAGCAGAAGCAACAAGACUGAAGAGAAACAGCAAGAAGAAGAU ACAAGAAGAAAGAACAGAAUCUGCUACCUAGCAGGAAAUCUUCAGCAACGAA UGGCAAAGGUCGACGACAGCUUCUCCACAGACUGGAAGAAAGCUUCUGGUC GAAGAAGACAAGAAGCACGAAAGACACCCGAUCUUCGGAACAUCGUCGACGA AGUCGCAUACCCAGAAAAGUACCCGACAAUCUACCCACUGAGAAAAGAGCUGG UCGACAGCACAGACAAGGCAGACCUGAGACUGAUCUACCUUGGCACUGGCACACA UGAUC AAGUUCAGAGGACACUUCUUGAUCGAAGGAGACCUGAACCCGGACAAC AGCGACGUCGACAAGCUGUUAUCAGCUGGUCAGACAUACAACCAGCUGUUC GAAGAAAACCCGAUCAACGCAAGCGGAGUCGACGCAAAGGCAAUCCUGAGCGC AAGACUGAGCAAGAGCAGAAGACUGGAAAACCUGAUCGCACAGCUGCCGGGAG AAAAGAAGAACGGACUGUUCGGAACCUGAUCGCACUGAGCCUGGGACUGACA CCGAACUUC AAGAGCAACUUCGACCUUGGCAGAAAGACGCAAAGCUGCAGCUGAG CAAGGACACAUACGACGACGACCUUGGACAACCUUGCUGGCACAGAUCCGAGACCA GUACGCAGACCUGUUCUGGCAGCAAAGAACCUGAGCGACGCAAUCCUGCUGA GCGCAUCCUGAGAGUCAACACAGAAAUCACAAAGGCACCGCUGAGCGCAAGC AUGAUC AAGAGAUACGACGAAACACCACAGGACCUGACACUGCUGAAGGCACU GGUCAGACAGCAGCUGCCGAAAAGUACAAGGAAAUCUUCUUCGACCAGAGCA AGAACGGAUACGCAGGAUCAUCGACGAGGAGCAAGCCAGGAAGAAUUCUAC AAGUUC AUC AAGCCGAUCCUGGAAAAGAUUGGACGGAACAGAAGAACUGCUGGU CAAGCUGAACAGAGAAGACCUGCUGAGAAAAGCAGAGAACAUCGACAACGGAA GCAUCCCGCACAGAUCCACCUUGGAGAACUGCACGCAAUCCUGAGAAGACAGG AAGACUUCUACCCGUUCUGAAGGACAACAGAGAAAAGAUCCGAAAAGAUCCUG ACAUUCAGAAUCCCGUACUACGUCGACCGCUGGCAAGAGGAAAACAGCAGAU CGAUGGAGACAAGAAAAGAGCGAAGAAAACAACACCCGUGGAACUUCGAAAG AAGCUGCAGCAAAGGGAGCAAAGCGCACAGAGCUUCAUCGAAAAGAAUGCAAAC UUCGACAAGAACCUGCCGAACGAAAAGGUCCUGCCGAAGCACAGCCUGCUGUAC GAAUACUUCACAGUCUACAACGAACUGACAAAAGGUCAAGUACGUCACAGAAGG</p>	12

[0659]

	AAUGAGAAAGCCGGCAUUCUGAGCGGAGAACAGAAGAAGGCAUUCGUCGACC UGCUGUUCAAGACAAACAGAAAGGUCACAGUCAAGCAGCUGAAGGAAGACUAC UUCAAGAAGAUCGAAUGCUUCGACGCGUCGAAAUCAGCGGAGUCGAAGACAG AUUCAACGCAAGCCUGGGAAACAUACCACGACCGUCUGAAGAUAUCAAGGACA AGGACUUCUGGACAACGAAGAAAACGAAGACAUCUGGAAGACAUCGUCCUG ACACUGACACUGUUCGAAGACAGAGAAAUGAUCGAAAGAAAGACUGAAGACAUA CGCACACCGUUCGACGACAAGGUCAUGAAGCAGCUGAAGAGAAGAAGAUACA CAGGAUGGGGAAGACUGAGCAGAAAGCUGAUAACGGAAUCAGAGACAAGCAG AGCGGAAAGACAAUCCUGGACUCCUGAAGAGCGGACGGAUUCGCAAACAGAAA CUUCAUGCAGCUGAUCCACGACGACAGCCUGACAUUCAAGGAAGACAUCGAGA AGGCACAGGUCAGCGGACAGGGAGACAGCCUGCACGAACACAUCGAAAACCG GCAGGAAGCCCGCAAUCAAGAAGGGAAUCCUGCAGACAGUCAAGGUCGUCGA CGAACUGGUCAAGGUCAUGGGAAGACACAAGCCGGAAAACAUCGUCUACGAAA UGGCAAGAGAAAACCAGACAACACAGAAGGGACAGAAGAACAGCAGAGAAAAGA AUGAAGAGAAUUCGAAGAAGGAAUUCAGGAACUGGGAAGCCAGAUCCUGAAGGA ACACCCGGUCGAAAACACACAGCUGCAGAACGAAAAGCUGUACCGUACUACCU GCAGAACGGAAGAGACUAGUACGUCGACCAGGAACUGGACAUAACAGACUGA GCGACUACGACGUCGACGCAAUCGUCCCGCAGAGCUUCCUGAAGGACGACAGCA UCGACAACAAGGUCCUGACAAGAAGCGACAAGAACAGAGGAAAGAGCCAGCAAC GUCCCGAGCGAAGAAGUCGUCAAGAAGAUGAAGAACUACUGGAGACAGCUGCU GAACGCAAAGCUGAUCACACAGAGAAAAGUUCGACAACCGACAAAGGCAGAGA GAGGAGGACUGAGCGAACUGGACAAGGCAGGAUUAUCAAGAGACAGCUGGUC GAAACAAGACAGAUACAAAAGCAGCUGCAGACAGAUCCUGGACAGCAGAAUUGAA CACAAAGUACGACGAAAACGACAAGCUGAUCAGAGAAGUCAAGGUAUCACAC UGAAGAGCAAGCUGGUCAGCGACUUCAGAAAAGGACUUCAGUUCUACAAGGUC AGAGAAAUCAACAACUACCACCACGACACGACGCAUACCGAAGCAGCAGUCGUC GGAACAGCACUGAUAAGAAGUACCCGAAGCUGGAAAGCGAAUUCGUCUACGG AGACUACAAGGUCUACGACGUCAGAAAAGAUUGAUCGAAAGAGCGAACAGGAAA UCGGAAGGCAACAGCAAAGUACUUCUUCUACAGCAACAUAUGAACUUCUUC AAGACAGAAAUCACACUGGCAAACGGAGAAAUCAGAAAGAGACCCGUGAUCGA AACAAACGGAGAAACAGGAGAAAUCGUCUGGGACAAGGGAAGAGACUUCGCAA CAGUCAGAAAGGUCCUGAGCAUGCCGACAGGUAACAUCGUAAGAAGACAGAA GUCCAGACAGGAGGUAUCAGCAAGGAAAGCAUCCUGCCGAAAGGAAACAGCGA CAAGCUGAUCGCAAGAAAGAGGACUGGGACCCGAAAGUACGGAGGAUUCG ACAGCCGACAGUCGCAUACAGCGUCCUGGUCGUCGCAAAGGUCGAAAAGGGGA AAGAGCAAGAAGCUGAAGAGCGUCAAGGAACUGCUGGGAAUCACAAUCAUGGA AAGAAGCAGCUUCGAAAAGAACCCGACUCCUGGAAAGCAAGGAAAGGAAUACA AGGAAGUCAAGAAGGACCGUAUCAUAAGCUGCCGAAAGUACAGCCUGUUCGAA CUGGAAAACGGAAGAAAGAGAAUAGCUGGCAAGCGCAGGAGAACUGCAGAAGGG AAACGAACUGGCACUGCCGAGCAAGUACGUAACUUCUGUACCGCAAGCCA CUACGAAAAGCUGAAGGGAAGCCCGAAAGACAACGAACAGAAGCAGCUGUUCG UCGAACAGCACAAAGCAUACCGGACGAAAUAUCGAACAGAUACAGCGAAUUC AGCAAGAGAGUCAUCCUGGACAGCGCAAACCGGACAAGGUCCUGAGCGCAUA CAACAAGCACAGAGACAAGCCGACUAGAGAACAGGCAGAAAACUACUCCACC UGUUCACACUGACAAACCGGGAGCACCGGCAGCAUUCAGUACUUCGACACA ACAUCGACAGAAAGAGAUACAACAAGCACAAGGAAGUCCUGGACGCAACU GAUCCACCAGAGCAUCACAGGACUGUACGAAAACAAGAAUCGACCUGAGCCAGC UGGGAGGAGACGGAGGAGGAAGCCGAAAGAAGAAGAGAAAAGGUC	
Cas9 (无 NLS)的氨 基酸序列	MDKKYSIGLDIGTNSVGVAVITDEYKVPSSKFKVLGNTDRHSIKKNLIGALLFDSGET AEATRLKRTARRRYTRRKNRICYLQEIFSNEMAKVDDSFHRLLESFLVEEDKKHERHP IFGNIVDEVAYHEKYPTIYHLRKKLVDSTDKADLRLIYLALAHMIKFRGHFLIEGDLNP DNSDVKLFIQLVQTYNQLFEENPINASGVDAKAILSARLSKSRLENLIAQLPGEKKN GLFGNLIALSLGLTPNFKSNFDLAEDAQLQSKDQYDDDLNLLAQIGDQYADLFLAA KNLSDAILLSDILRVNTEITKAPLSASMIKRYDEHHQDLTLLKALVRQQLPEKYKEIFFD QSKNGYAGYIDGGASQEEFYKFIKPILEKMDGTEELVKNREDLLRQRFTDNGSIPH QIHLGELHAILRRQEDFYPLKDNREKIEKILTRIPYYVGLARGNSRFAWMTRKSEET ITPWNFEVVDKGSASQSFIERMTNFDKNLPNEKVLPHSLLYEYFTVYNELTKVKYV TEGMRKPAFLSGEQKKAIVDLLFKTNRKVTVKQLKEDYFKKIECFDSVEISGVEDRFN ASLGTYHDLKIIKDKDFLDNEENEDILEDIVLTTLFEDREMIEERLKYAHLFDDKV MKQLKRRRYTGWRLSRKLLINGIRDKQSGKTILDFLKSDFANRNFMLIHDDSLTFK EDIQKAQVSGQDLSLHEHIANLAGSPAIKKILQTVKVVDELVKVMGRHKPENIVIE ARENQTTQKQKNSRERMKRIEIGIKELGSQILKEHPVENTQLQNEKLYLYLQNGRD MYVDQELDIRLSYDVIDHVPQSFLKDDSIDNKVLTSDKNRSGSDNPVSEEVVKK MKNYWRQLLNAKLITQRKFDNLTKAERGGLELSDKAGFIKRLVETRQITKHVAQILD SRMNTKYDENDKLIREVKVITLKSLLVDFRKFDFQYKVRINNYHHAHDVLANVV GTALIKKYPKLESEFVYGDYKVDVRKMIKSEQEI GKATAKYFFYSNIMNFFKTEITL ANGEIRKPLIETNGETGEIVWDKGRDFATVRKVLSMPQVNIKKTEVQTGGFSKESIL	13

	PKRNSDKLIARKKDWDPKKYGGFDSPTVAYSVLVAKVEKGKSKKLKSVKELLGITIM ERSSFENPIDFLEAKGYKEVKKDLIILKPKYSLFELENGRKRMLASAGELQKGNELAL PSKYVNFYLAHYEKLKGSPEDEQKQLFVEQHKHYLDEIIEQISEFSKRVLADANL DKVLSAYNKHHRDKPIREQAENIHLFTLTNLGAPAAFKYFDTTIDRKRYTSTKEVLDAT LIHQITGLYETRIDLSQLGGD	
使用如表3中所列的最小尿苷密码子编码SEQ ID NO: 13的, 具有起始和终止密码子的Cas9 mRNA ORF	AUGGACAAGAAGUACAGCAUCGGACUGGACAUCGGAACAAACAGCGUCGGAUG GGCAGUCAUCACAGACGAAUACAAGGUCCGAGCAAGAAGUUCAAGGUCCUGG GAAACACAGACAGACACAGCAUCAAGAAGAACCUGAUCGGAGCACUCUGUUC GACAGCGGAGAAAACAGCAGAAGCAACAAGACUGAAGAGAACAGCAAGAAGAAG AUACACAAGAAGAAAAGAACAGAAUCUGCUACCUGCAGGAAAUCUUCAGCAACG AAAUGGCAAAGGUCGACGACAGCUUCUCCACAGACUGGAAGAAAAGCUUCUG GUCGAAGAAGACAAGAAGCACGAAAAGACACCCGAUCUUCGGAACAUCGUCGA CGAAGUCGCAUACCACGAAAAGUACCCGACAAUCUACCACCUAGAAAAGAACG UGGUCGACAGCACAGACAAGGCAGACCUGAGACUGAUCUACCUGGCACUGGCA CACAUGAUCAAAGUUCAGAGGACACUCCUGAUCGAAGGAGACCUGAACCCGGA CAACAGCGACGUCGACAAGCUGUUAUCCAGCUGGUCCAGACAUAACAACCAGCU GUUCGAAGAAAACCCGAUCAACGCAAGCGGAGUCGACGCAAAGGCAUCCUGA GCGCAAGACUGAGCAAGAGCAGAAGACUGGAAAACCUAUCGCACAGCUGCCG GGAGAAAAGAAGAACGGACUGUUCGAAAACCUAUCGCACUGACCCUGGGACU GACACCGAACUUAAGAGCAACUUCGACCUCCGAGAACGCAAGACGAAAAGAGC UGAGCAAGGACACAUACGACGACGACCUGGACAACCUGCUGGCACAGAUCCGA GACCAGUACGCAGACCUGUUCUGGCAGCAAAGAACCUGAGCGACGCAAUCCUG CUGAGCGACAUCUGAGAGUCAACACAGAAAUCACAAAGGCACCCGUCGAGCGC AAGCAUGAUCAAAGAGAUACGACGAAACACCACAGGACCUGACUUCGAAAGG CACUGGUCAGACAGCAGCUGCCGAAAAGUACAAGGAAAUCUUCUUCGACCAG AGCAAGAACCGAUACGCAGGAUCAUCGACGGAGGAGCAAGCCAGGAAGAAUU CUACAAGUUCAUCAAGCCGAUCCUGGAAAAGAUGGACGGAACAGAAGAACUGC UGGUAAGCUGAACAGAGAAGACCUGCUGAGAAAAGCAGAGAACAUCGACAAAG GGAAGCAUCCCGACCAAGAUCCACCUGGGAGAACUGCACGCAAUCCUGAAGAAG CAGGAAGACUUCUACCCGUUCUGAAGGACAACAGAGAAAAGAUCCGAAAAGAU CCUGACAUUCAGAAUCCCGUACUACGUCGACCCGUCGCAAGAGGAAAACAGCA GAUUCGCAUGGAUGACAAGAAAGAGCGAAGAAAACAACACCCUGGAACUUC GAAGAAGUCGUCGACAAGGAGCAAGCGCACAGAGCUUCAUCGAAAAGAAUGAC AAACUUCGACAAGAACCUGCCGAACGAAAAGGUCCUGCCGAAGCACAGCCUGCU GUACGAUACUUCACAGUCUACAACGAACUGACAAAGGUCAAGUACGUCACAG AAGGAAUGAGAAAGCCGGCAUCCUGAGCGGAGAACAGAAAGGCAAUCCGUC GACCUGCUUUCAGACAACAGAAAAGGUCACAGUCAAGCAGCAAGGAAAGGAA CUACUUCAGAAAGAUUCGAAUGCUUCGACAGCGUCGAAAUCAGCGGAGGAAAG ACAGAUUCAACGCAAGCCUGGAAACAUACCACGACCUGCUGAAGAUCAUCAAG GACAAGGACUUCUGGACAACGAAGAAAACGAAGACAUCUGGAAGACAUUCGU CCUGACACUGACACUGUUCGAAGACAGAGAAAUGAUCGAAGAAGACUGAAGA CAUACGCACACCUGUUCGACGACAAGGUCAUGAAGCAGCUGAAGAGAAAGAA UACACAGGAUGGGGAAGACUGAGCAGAAAAGCUGAUCAAACGGAUUCAGAGACAA GCAGAGCGGAAAGACAACUCCUGGACUCCUGAAGAGCGACGGAUUCGCAACA GAAACUUCUAGCAGCUGAUCCACGACGACAGCCUGACAUCUUCAGGAAGACAUC CAGAAGGCACAGGUCAGCGGACAGGGAGACAGCCUGCACGAACACAUCCGAAA CCUGGCAGGAAGCCCGCAAUCAAGAAGGAAUCCUGCAGACAGUCAAGGAAAGC UCGACGAACUGGUCAAGGUCAUGGGAAGACACAAGCCGAAAACAUCGUCUUC GAAAUGGCAAGAGAAAACAGACAACACAGAAGGGACAGAAGAACAGCAGAGA AAGAAUGAAGAGAAUCGAAGAAGGAUUCAGGAACUGGGAAGCCAGAUCCUGA AGGAACACCCCGUCCGAAAACACACAGCUGCAGAACGAAAAGCUUACCUAGUAC UACCUGCAGAACGGAAGAGACAUGUACGUCGACCAGGAACUGGACAUCAACAG ACUGAGCGACUACGACGUCGACCACAUCGUCCCGCAGAGCUUCUGAAGGACGA CAGCAUCGACAACAAGGUCCUGACAAGAAGCGACAAGAACAGAGGAAAAGAGCG ACAACGUCCGAGCGAAGAAGUCGUCAAGAAGAUGAAGAACUACUGGAGACAG CUGCUAACGCAAAGCUGAUCACACAGAGAAAGUUCGACAACCUGACAAAAGGC AGAGAGAGGAGGACUGAGCGAACUGGACAAGGCAGGAUUCAUCAAGAGACAGC UGGUCGAAAACAAGACAGAUCAAAAAGCAGCUCGACAGAUCCUGGACAGCAGA AUGAACACAAGUACGACGAAAACGACAAGCUGAUCAGAGAAGUCAAAGGUCAU CACACUGAAGAGCAAGCUGGUCAGCGACUUCAGAAAAGGACUCCAGUUCUACA AGGUCAGAGAAAUCAACAACUACCACCACGCACACGACGCAUACCUGAACGCAG UCGUCGGAACAGCACUGAUCAGAAGUACCCGAAGCUGGAAAGCGAAUUCGUC UACGGAGACUACAAGGUUCUACGACGUCAGAAAAGAUCAUCGAAAAGAGCGAAC GAAAUCGGAAGGCAACAGCAAAGUACUUCUUCUACAGCAACAUCUAUGAACU UCUUCAGACAGAAAUCACACUGGCAAACGGAAGAAUCAGAAAAGAGACCCGUC AUCGAAAACAACGGAGAAAACAGGAGAAAUCGUCUGGGACAAGGGAAGAGACU CGAACAGUCAGAAAAGGUCCUGAGCAUGCCGAGGUAACAUCGUCAAGAAGA	14

[0660]

[0661]

	<p>CAGAAGUCCAGACAGGAGGAUUCAGCAAGGAAAGCAUCCUGCCGAAGAGAAAC AGCGACAAGCUGAUCGCAAGAAAAGAGACUGGGACCCGAAGAAGUACGGAGG AUUCGACAGCCCAGAGUCGCAUACAGCGUCCUGGUCGUCGCAAAGGUCGAAA AGGGAAAGAGCAAGAAGCUGAAGAGCGUCAAGGAACUCGUGGGAAUCACAAUC AUGGAAAGAAGCAGCUUCGAAAAGAACCCGAUCGACUUCUGGAAGCAAAGGG AUACAAGGAAGUCAAGAAGGACCUGAUCAUCAAGCUGCCGAAGUACAGCCUGU UCGAACUGGAAAACGGAAGAAAGAGAAUGCUGGCAAGCGCAGGAGAACUCGAG AAGGGAAACGAACUGGCACUGCCGAGCAAGUACGUCAACUUCUGUACCUGGC AAGCCACUACGAAAAGCUGAAGGGGAAGCCCGGAAGACAACGAACAGAAGCAGC UGUUCGUCGAACAGCACAAGCACUACCUUGGACGAAAUCAUCGAACAGAUACAG GAAUUCAGCAAGAGAGUCAUCCUGGACAGCGCAAACCUUGGACAAGGUCCUGAG CGCAUACAACAAGCACAGAGACAAGCCGAUCAGAGAACAGGCAGAAAACAUCA UCCACCGUUCACACUGACAAACCUGGGAGCACCCGGCAGCAUUAAGUACUUCG ACACAACAUCGACAGAAAAGAGAUACACAAGCACAAAGGAAGUCCUGGACGCA ACACUGAUCCACAGAGCAUCACAGGACUGUACGAAAACAAGAAUCGACCUAG CCAGCUGGGAGGAGACUAG</p>	
<p>使用如表3 中所列的 最小尿苷 密码子编 码SEQ ID NO: 13的 Cas9 编码 序列(无起 始或终止 密码子;适 于包括在 融合蛋白 质编码序 列中)</p>	<p>GACAAGAAGUACAGCAUCGGACUUGGACUUCGGAACAAACAGCGUCGGAUGGGC AGUCAUCACAGACGAAUACAAGGUCCCGAGCAAGAAGUUAAGGUCCUGGGAA ACACAGACAGACACAGCAUCAAGAAGAACCUGAUCGGAGCACUGCUUUCGAC AGCGGAGAAAACAGCAGAAGCAACAGACUGAAGAGAACAGCAAGAAGAAGAU CACAAGAAGAAGAACAGAAUCUGCUACCUGCAGGAAAUCUUCAGCAACGAAA UGGCAAAGGUCGACGACAGCUUCUCCACAGACUGGAAGAAAGCUUCUGGUC GAAGAAGACAAGAAGCACGAAAGACACCCGAUCUUCGGAACAUCGUCGACGA GUACGCAUACCCGAAAAGUACCCGACAUCUACCACUGAGAAAAGGCAUCCUGG UCGACAGCACAGACAAGGCAGACCUGAGACUGAUCUACCUGGCACUGGCACACA UGAUCUAGUUCAGAGGACAUUCUGAUCGAAGGAGACCUGAACCCGGACAAC AGCGACGUCGACAAGCUGUUAUCCAGCUGGUCAGACAUACAACCAGCUGUUC GAAGAAAACCCGAUCAACGCAAGCGGAGUCGACGCAAAGGCAUCCUGAGCGC AAGACUGAGCAAGAGCAGAAGACUUGGAAAACCUGAUCGCACAGCUGCCGGAG AAAAGAAGAACGGACUGUUCGGAACCUGAUCGCACUGAGCCUGGGACUGACA CCGAACUUC AAGAGCAACUUCGACCUUGGACAGAAAGACGCAAAGCUGCAGCUGAG CAAGGACACAUACGACGACGACCUGGACAACCUGCUGGCACAGAUCCGGAACCA GUACGACAGACCUGUUCUGGACGCAAAGAACCUGAGCGACGCAUCCUGGUGA GCGCAUCCUGAGAGUCAACACAGAAAUCACAAAGGCACCGCUGAGCGCAAGC AUGAUCUAGAGAUACGACGAACACCAGGACCUGACACUGCUGAAGGCACU GGUCAGACAGCAGCUGCCGGAAAAGUACAAGGAAAUCUUCUUCGACAGGACGA AGAACGGAUACGCAGGAUACAUCGACGGAGGAGCAAGCCAGGAAGAUAUCUAC AAGUUCUACAAGCCGAUCCUGGAAAAGAUUGGACGGAACAGAAAGAAUCGUGGU CAAGCUGAACAGAGAAGACCUGCUGAGAAAAGCAGAGAACAUCGACAACGGAA GCAUCCCGACCCAGAUCCACCUUGGGAGAACUGCACGCAAUCCUGAGAAGACAGG AAGACUUCUACCCGUUCUGAAGGACAACAGAGAAAAGAUCCGAAAAGAUCCUG ACAUUCAGAAUCCCGUACUACGUCGACCCGUGGCAAGAGGAAACAGCAGAUU CGCAUGGAUGACAAGAAAGAGCGAAGAAAACAUCACACCGUGGAACUUCGAAG AAGUCGUCGACAAGGGAGCAAGCGCACAGAGCUUCAUCGAAAGAAUGACAAC UUCGACAAGAACCUGCCGAACGAAAAGGUCCUGCCGAAGCACAGCCUCGUGUAC GAAUACUUCACAGUCUACAACGAACUGACAAAAGGUCAAGUACGUCACAGAAAG AAUGAGAAAGCCGGCAUUCUGAGCGGAGAGAACAAGAAGGCAUUCGUCGACC UGCUGUUC AAGACAAACAGAAAGGUCACAGUCAAGCAGCUGAAGGAAGACUAC UUCAAGAAGAUUCGAAUGCUUCGACAGCGUCGAAAUCAGCGGAGUCGAAGACAG AUUCAACGCAAGCCUGGGAACAUAACCACGACCUGCUGAAGAUCAUCAAGGACA AGGACUUCUGGACAACGAAGAAAACGAAGACAUCCUGGAAGACAUCGUCCUG ACACUGACACUGUUCGAAGACAGAGAAAUGAUCGAAGAAAGACUGAAGACAU CGCACACCUUGUUCGACGACAAGGUCAUGAAGCAGCUGAAGAGAAGAAGAUACA CAGGAUGGGGAAGACUGAGCAGAAAAGCUGAUC AACGGAAUCAGAGACAAGCAG AGCGGAAAGACAAUCCUGGACUUCUGAAGAGCGACGGAUUCGCAAACAGAAA CUUCAUGCAGCUGAUCCACGACACGCCUGACAUUCAAGGAAGACAUCAGAGA AGGCACAGGUCAGCGGACAGGGAGACGCCUGCACGAACACAUCGCAAACCU GCAGGAAGCCCGCAAUCAAGAAGGGAAUCCUGCAGACAGUCAAGGUUCGUCGA CGAACUGGUCAAGGUCAUGGGAAGACACAAGCCGGAAAACAUCGUCUUCGAAA UGGCAAGAGAAAACCAGACAACACAGAAAGGACAGAAGAACAGCAGAGAAAAGA AUGAAGAGAAUCGAAGAAGGAUACAAGGAACUGGGAAGCCAGAUCCUGAAGGA ACACCCGUCGAAAACACACAGCUGCAGAACGAAAAGCUGUACCUGUACUACCU GCAGAACGGAAGAGACAUUGUACGUCGACCAGGAACUGGACAUACAACAGACUGA GCGACUACGACGUCGACCACAUCGCCGACAGCUCUCCUGAAGGACGACAGCA UCGACAACAAGGUCCUGACAAGAAAGCGACAAGAACAGAGGAAAAGCGCACAA GUCCCGAGCGAAGAAGUCGUCUACAAGAAUGAAGAACUACUGGAGACAGCUGCU GAACGCAAAGCUGAUCACACAGAGAAAAGUUCGACAACCUGACAAAGGCAGAGA</p>	<p>15</p>

[0662]

	<p>GAGGAGGACUGAGCGAACUGGACAAGGCAGGAUUAUCAAGAGACAGCUGGUC GAAACAAGACAGAUCAAAAGCACGUCGACAGAUCCUGGACAGCAGAAUGAA CACAAAGUACGACGAAAACGACAAGCUGAUCAGAGAAGUCAAGGUCAUCACAC UGAAGAGCAAGCUGGUCAGCGACUUCAGAAAAGGACUCCAGUUCUACAAGGUC AGAGAAAUCAACAACUACCACCACGCACACGCAUACCUGAACCGACAGUCGUC GGAACAGCACUGAUCAAGAAGUACCCGAAGCUGGAAAGCGAAUUCGUCUACGG AGACUACAAGGUCUACGACGUCAGAAAAGAUAGUCGAAAGAGCGAACAGGAAA UCGGAAAGGCAACAGCAAAGUACUUCUUCUACAGCAACAUAUGAACUUCUUC AAGACAGAAAUCACACUGGCAAAACGGAGAAAUCAGAAAAGAGACCGCUGAUCGA AACAAACGGAGAAAACAGGAGAAAUCGUCUGGGACAAGGGAAGAGACUUCGCAA CAGUCAGAAAGGUCCUGAGCAUGCCGACAGGUCAACAUCGUAAGAAGACAGAA GUCCAGACAGGAGGAUUCAGCAAGGAAAGCAUCCUGCCGAAGAGAAACAGCGA CAAGCUGAUCGCAAGAAAGAAAGGACUUGGGACCCGAAGAAGUACGGAGGAUUCG ACAGCCCGACAGUCGCAUACAGCGUCCUGGUCGUCGCAAAGGUCGAAAAGGGA AAGAGCAAGAAGCUGAAGAGCGUCAAGGAACUGCUGGGAAUACAAUCAUGGA AAGAAGCAGCUUCGAAAAGAACCCGAUCGACUUCUGGAAGCAAAGGGAUACA AGGAAGUCAAGAAGGACCUGAUCAUCAAGCUGCCGAAGUACAGCCUGUUCGAA CUGGAAAACGGAAGAAAGAGAUGCUGGCAAGCGCAGGAGAACUGCAGAAGGG AAACGAACUGGCACUGCCGAGCAAGUACGUAACUCCUGUACCCUGGCAAGGCA CUACGAAAAGCUGAAGGGAAGCCCGGAAGACAACGAACAGAAGCAGCUGUUCG UCGAACAGCACAAGCACUACCUGGACGAAAUCAUCGAACAGAUACAGCGAAUUC AGCAAGAGAGUCAUCCUGGACAGCGCAAACCUGGACAAGGUCCUGAGCGCAUA CAACAAGCACAGAGACAAGCCGAUCAGAGAACAGGCAGAAAACAUAUCCACC UGUUCACACUGACAACCUGGGAGCACCGGCAGCAUUAAGUACUUCGACACA ACAUUCGACAGAAAGAGAUACACAAGCACAAAAGGAAGUCCUGGACGCAACACU GAUCCACCAGAGCAUCACAGGACUGUACGAAACAAGAAUCGACCUGAGCCAGC UGGGAGGAGAC</p>	
<p>Cas9 切口 酶(无NLS) 的氨基酸 序列</p>	<p>MDKKYSIGLAIGTNSVGVAVITDEYKVPSSKFKVLGNTDRHSIKKNLIGALLFDSGET AEATRLKRTARRRYTRRNRCYLQEIFSNEMAKVDDSFHRLLESFLVEEDKKHERHP IFGNIVDEVAYHEKYPTIYHLRKKLVDSTDKADLRLIYLALAHMIKFRGHFLIEGDLNP DNSVDVKLFIQLVQTYNQLFEENPINASGVDAKAILSARLSKSRLENLIAQLPGEKKN GLFGNLIALSLGLTPNFKSNFDLAEDAQLQSKDTYDDLDNLLAQIGDQYADLFLAA KNLSDAILLSDILRVNTEITKAPLSASMIKRYDEHHQDLTLLKALVRQQLPEKYKEIFFD QSKNGYAGYIDGGASQEEFYKFIKPILEKMDGTEELLVKLNREDLLRQRTFDNGSIPH QIHLGELHAILRRQEDFYFPLKDNREKIEKILTRIPYYVGPLARGNSRFAWMTRKSEET ITPWNFEVVVDKGASAQSFIERMTNFDKNLPNEKVLPHKSLLYEYFTVYNELTKVKYV TEGMRKPAFLSGEQKKAIVDLLFKTNRKVTVKQLKEDYFKKIECFDSVEISGVDFRHN ASLGTYHDLKIKDKDFLDNEENEDILEDIVLTLTLFEDREMIERLKYAHLFDDKV MKQLKRRRYTGWRLSRKLINGIRDKQSGKTILDFLKSDGFANRNFMLIHDDSLTFK EDIQAQVSGGDSLHEHIANLAGSPAIKKILQTVKVVDELVKVMGRHKPENIVIEM ARENTTQKQKNSRERMKRIEIKELGSQILKEHPVENTQLQNEKLYLYLQNGRD MYVDQELDINRLSDYDVDHIVPQSFLKDDSIDNKVLTRSDKNRKGKSDNVPSEEVVKK MKNYWRQLLNAKLITQRKFDNLTKAERGGLELSELDKAGFIKRLVETRQITKHVAQILD SRMNTKYDENDKLIREVKVITLKSCLVSDFRKDFQFYKVINNYHHHAHDAYLNAV GTALIKKYPKLESEFVYGDYKVDYRVMIAKSEQIEGKATAKYFFYSNIMNFFKTEITL ANGEIRKRPLIETNGETGEIVWDKGRDFATVRKVLVSMQVNIKKTEVQTGGFSKESIL PKRNSDKLIARKKDWDPKYGGFDSPTVAYSVLVVAKVEKGSKKLSVKELLGITIM ERSSFENPIDFLEAKGYKEVKKDLIILPKYSLFELENGRKRMLASAGELQKGNELAL PSKYVNFYLAHYEKLKSPEDNEQKQLFVEQHKHYLDEIIEQISEFSKRVLADANL DKVLSAYNKHRDKPIREQAENIIHLFTLNLGAPAAFKYFDTTIDRKRYTSTKEVLDT LIHQSIITGLYETRIDLSQLGGD</p>	<p>16</p>
<p>使用如表3 中所列的 最小尿苷 密码子编 码SEQ ID NO: 16的, 具有起始 和终止密 码子的 Cas9 切口</p>	<p>AUGGACAAGAAGUACAGCAUCGGACUGGCAAUCGGAACAAACAGCGUCGGAUG GGCAGUCAUCACAGACGAAUACAAGGUCCGAGCAAGAAGUUAAGGUCCUGG GAAACACAGACAGACAGCAUCAAGAAGAACCUGAUCGGAGCAGUCUGUUC GACAGCGGAGAAAACAGCAGAAGCAACAAGACUGAAGAGAACAGCAAGAAGAAG AUACACAAGAAGAAAAGAACAGAAUCUGCUACCUGCAGGAAAUUCUACGCAACG AAAUGGCAAAGGUCGACGACAGCUUCUCCACAGACUGGAAGAAAGCUUCCUG GUCGAAGAAGACAAGAAGCACGAAAGACACCCGAUCUUCGGAACAUUCGUCGA CGAAGUCGCAUACCACGAAAAGUACCCGACAAUCUACCACCUGAGAAAAGAAAGC UGGUCGACAGCACAGACAAGGCAGACCUGAGACUGAUCUACCUGGCAACUGGCA CACAUGAUCAAGUUCAGAGGACACUCCUGAUCGAAGGAGACCUGAACCCGGA CAACAGCGACGUCGACAAGCUGUUAUCCAGCUGGUCCAGACAUACAACCAGCU GUUCGAAGAAAACCCGAUCAACGCAAGCGGAGUCGACGCAAAGGCAAUCCUGA GCGCAAGACUGAGCAAGAGCAGAAGACUGGAAAACCUAUCGCACAGCUGCCG GGAGAAAAGAAGAACGGACUGUUCGGAACCUAUCGACACUAGCCUGGGACU GACACCGAACUUAAGAGCAACUUCGACCUGGCAGAAGACGCAAAGCUGCAGC UGAGCAAGGACACAUACGACGACGACCUGGACAACCUGCUGGCACAGAUCCGA</p>	<p>17</p>

[0663]

<p>酶 mRNA ORF</p>	<p>GACCAGUACGCAGACCUUGUUCUGGCGAGCAAAGAACCUGAGCGACGCAAUCCUG CUGAGCGCAUCCUGAGAGUCAACACAGAAAUCACAAAGGCACCGCUGAGCGC AAGCAUGAUAAGAGAUACGACGAAACCACCAGGACCUGACACUGCUAAGG CACUGGUCAGACAGCAGCUGCCGGAAAAAGUACAAGGAAAUUCUUCUUGACCAG AGCAAGAACGGAUACGCAGGAUACAUCGACGGAGGAGCAAGCCAGGAAGAAU CUACAAGUUCUACAAGCCGUAUCCUGGAAAAAGAUUGGACGGAACAGAAGAUCG UGGUCAAGCUGAACAGAGAAGACCUGCUGAGAAAAGCAGAGAACAUCGACAAC GGAAGCAUCCCGCACCAGAUCCACCUGGGAGAUCGACGCAAUCCUGAGAAGA CAGGAAGACUUCUACCCGUUCCUGAAGGACAACAGAGAAAAGAUUGGAAACGAA CCUGACAUUCAGAAUCCCGUAUCUACGUCGACCGCUGGCAAGAGAAACAGCA GAUUCGCAUGGAUGACAAGAAAGAGCGAAGAAAACAUCACACCGUGGAACUUC GAAGAAGUCGUCGACAAGGGAGCAAGCGCACAGAGCUUCAUCGAAAGAAUGAC AAACUUCGACAAGAACCUGCCGAACGAAAAGGUCCUGCCGAAGCAGCCUGCU GUACGAAUACUUCACAGUCUACAACGAACUGACAAAGGUCAAGUACGUCACAG AAGGAAUGAGAAAAGCCGGCAUUCUUGAGCGGAGAACAAGAAGAAGCAUUCGUC GACCUGCUUUAAGACAAAACAGAAAAGGUCACAGUCAAGCAGCUGAAGGAAGA CUACUUAAGAAGAUUGAAUGCUUUCGACAGCGUCGAAAUCAGCGGAGUCGAAAG ACAGAUUCAACGCAAGCCUGGGAACAUAACCACGACCUGCUGAAGAUCAUCAAG GACAAGGACUUCUGGACAACGAAGAAAACGAAGACAUCUCCUGGAAGACAUCGU CCUGACACUGACACUGUUCGAAGACAGAGAAAUGAUUGAAGAAAGACUGAAGA CAUACGCACACCUUGUUCGACGACAAGGUCAUGAAGCAGCUGAAGAGAAAGA UACACAGGAUUGGGAAAGACUGAGCAGAAAAGCUGAUCAACGGAAUCAGAGACAA GCAGAGCGGAAAGACAACUCCUGGACUUCUGAAGAGCGACGGAUUCGCAAAACA GAAACUUAUGCAGUGAUCCACGACGACAGCCUGACAUUCGAAAGAAAGCAGC CAGAAGGCACAGGUCAGCGGACAGGGAGACAGCCUGCACGAACACAUCGCAAA CCUGGCAGGAAGCCGGCAAUCAAGAAGGGAAUCCUGCAGACAGUCAAGGUCG UCGACGAACUGGUCAAGGUCAUGGGAAGACACAAGCCGGAAAACAUCGUCAU GAAAUGGCAAGAGAAAACCAGACAACACAGAAGGGACAGAAGAACAGCAGAGA AAGAAUGAAGAGAAUCGAAGAAGGAAUCAAGGAACUGGGAAGCCAGAUCCUGA AGGAACACCCGGUCGAAAACACACAGCUGCAGAACGAAAAGCUGUACCUGUAC UACCGCAGAACGGAAAGAGACAUGUACGUCGACCAGGAACUGGACAUCAACAG ACUGAGCGACUACGACGUCGACCACAUCGUCCCGCAGAGCUUCUGAAGGACGA CAGCAUCGACAACAAGGUCCUGACAAGAAGCGACAAGAACAGAGAAAGAGCG ACAACGUCCCGAGCGAAGAAGUCGUCAAGAAGAUGAAGAACUACUGGAGACAG CUGCUGAACGCAAAGCUGAUACACAGAGAAAAGUUCGACAACCUAGCAAAGGC AGAGAGAGGAGGACUGAGCGAACUGGACAAGGCAGGAUUCAUCAAGAGACAGC UGGUCGAAACAAGACAGAUACAAGCAGCUCGACAGAUCCUGGACAGCAGAGA AUGAACACAAAGUACGACGAAAAACGACAAGCUGAUCAAGAGAAGUCAAGGUCAU CACACUGAAGAGCAAGCUGGUCAGCGACUUCAGAAAGGACUCCAGUUCUACA AGGUCAGAGAAAUCAACAACUACCACCACGCACAGCAGCAUACCUUGAACGCA UCGUCGGAACAGCACUGAUCAAGAAGUACCCGAAGCUGGAAAGCGAAUUCGUC UACGGAGACUACAAGGUUCUACGACGUCAGAAAAGAUAGUUCGCAAAAGCGAAC GGAAAUCGGAAAGGCAACAGCAAAGUACUUCUUCUACAGCAACAUCAUUGAACU UCUUAAGACAGAAAUCACACUGGCAAACGGAGAAAUCAGAAAGAGACCUGC AUCGAAACAACGGAGAAAACAGGAGAAAUCGUCUGGGACAAGGGAAAGAGACUU CGCAACAGUCAGAAAGGUCCUGAGCAUGCCCGCAGGUAACAUCUGGAAAGAGGA CAGAAGUCCAGACAGGAGGAUUCAGCAAGGAAAAGCAUCCUGCCGAAGAGAAAC AGCGACAAGCUGAUCGCAAGAAAAGAGACUGGGACCCGAAGAAGUACGGAGG AUUCGACAGCCGACAGUCGAUACAGCGUCCUGGUCGUCGCAAAAGGUCGAAA AGGGAAAGAGCAAGAAGCUGAAGAGCGUCAAGGAACUGCUGGGAUUCACAUC AUGGAAAGAAGCAGCUUCGAAAAGAACCCGAUCGACUUCUCCUGGAAGCAAAGGG AUACAAGGAAGUCAAGAAGGACCUGAUCAUCAAGCUGCCGAAGUACAGCCUGU UCGAACUGGAAAACGGAAAGAGAAUGCUUGGCAAGCGCAGGAGAACUGCAG AAGGGAAACGAACUGGCACUGCCGAGCAAGUACGUCAACUUCUUGUACCUUGGC AAGCCACUACGAAAAGCUGAAGGGAAAGCCCGAAGACAACGAACAGAGAAGCAG UGUUCGUCGAACAGCACAAGCACUACCUGGACGAAAUCAUCGAACAGAUACAGC GAAUUCAGCAAGAGAGUCAUCCUGGACAGCGCAAACCUGGACAAGGUCCUGAG CGAUACAACAAGCACAGAGACAAGCCGAUCAGAGAACAGGCAGAAAACAUCA UCCACCUGUUCACACUGACAAAACCUGGGAGCACCCGGCAGCAUUCAGUACUUCG ACACAACAUCGACAGAAAAGAGAUACAACAAGCACAAAGGAAGUCCUGGACGCA ACACUGAUCCACCAGAGCAUCACAGGACUGUACGAAACAAGAUCGACCUGAG CCAGCUGGGAGGAGACUAG</p>	
<p>使用如表3 中所列的 最小尿苷</p>	<p>GACAAGAAGUACAGCAUCGGACUGGCAAUCGGAACAAACAGCGUCGGAUUGGGC AGUCAUCACAGACGAAUACAAGGUCCCGAGCAAGAAGUUAAGGUCCUGGGAA ACACAGACAGACACAGAUCAAGAAGAACCUGAUCGGAGACACUGCUUUCGAC AGCGGAGAAACAGCAGAAGCAACAAGACUGAAGAGAACAGCAAGAAGAAGAU CACAAGAAGAAGAAACAGAAUCUGCUACCUGCAGGAAAUCUUCAGCAACGAAA</p>	<p>18</p>

<p>密码子编 码SEQ ID NO: 16的 Cas9切口 酶编码序 列(无起始 或终止密 码子;适于 包括在融 合蛋白质 编码序列 中)</p>	<p>UGGCAAAGGUCGACGACAGCUUCUCCACAGACUGGAAGAAAGCUUCCUGGUC GAAGAAGACAAGAAGCACGAAAGACACCCGAUCUUCGGAAACAUCGUCGACGA AGUCGCAUACCACGAAAAGUACCCGACAAUCUACCACCUGAGAAAGAACUGG UCGACAGCACAGACAAGGCAGACCUGAGACUGAUCUACCUGGCACUGGCACACA AUGAUAAGUUCAGAGGACACUCCUGAUCGAAGGAGACCUGAACCCGGACAAC AGCGACGUCGACAAGCUGUUCUCCAGCUGGUCAGACAUACAACCCAGCUGUUC GAAGAAAACCCGAUCAACGCAAGCGGAGUCGACGCAAAGGCAAUCCUGAGCGC AAGACUGAGCAAGAGCAGAAGACUGGAAAACCUGAUCGCACAGCUGCCGGGAG AAAAGAAGAACGGACUGUUCGGAAAACCUGAUCGCACUGAGCCUGGGACUGACA CCGAACUUC AAGAGCAACUUCGACCUGGCAGAGACGCAAAGCUGCAGAGACG CAAGGACACAUACGACGACGACCUGGACAACCCUGCUGGCACAGAUCCGAGACCA GUACGCAGACCUGUUCUGGCAGCAAAGAACCUGAGCGACGCAAUCCUGCUGA GCGCAUCCUGAGAGUCAACACAGAAAUCACAAAGGCACCCGUGAGCGCAAAGC AUGAUAAGAGAUACGACGAACACCACCAGGACCUGACACUGCUGAAGGCACU GGUCAGACAGCAGCUGCCGAAAAGUACAAGGAAAUCUUCUCCAGCAGAGACG AGAACGGAUACGCAGGAUACAUCGACGAGGAGCAAGCCAGGAAGAUAUUCUAC AAGUUAUCAAGCCGAUCCUGGAAAAGAUUGGACGGAACAGAAAGCUGCUGGU CAAGCUGAACAGAGAAGACCUGCUGAGAAAAGCAGAGAACAUCGACAACGGAA GCAUCCCGCACAGAUCCACCUGGGAGAACUGCACGCAAUCCUGAAGAAAGAGG AAGACUUCUACCCGUUCCUGAAGGACAACAGAGAAAAGAUCCGAAAAGAUCCUG ACAUUCAGAAUCCCGUACUACGUCGGACCCGUGGCAAGAGGAAACAGCAGAUU CGAUUGGAUGACAAGAAAGAGCGAAGAAAACAUCACACCCUGGAACUUCGAAAG AAGUCGUCGACAAGGGAGCAAGCGCACAGAGCUUCAUCGAAAGAAUGACAAC UUCGACAAGAACCUGCCGAAACGAAAAGGUCCUGCCGAAAGCAGCAGGCUUAC GAAUACUUCACAGUCUACAACGAACUGACAAAGGUCAAGUACGUCACAGAAAGG AAUGAGAAAGCCGGCAUUCUUGAGCGGAGAAACAGAAAGAGGCAAUCGUCGACC UGCUGUUAAGACAAACAGAAAAGGUCACAGUCAAGCAGCUGAAGGAAGACUAC UUCAAGAAGAUCCGAUUGCUUCGACAGCGUCGAAAUCAGCGGAGUCGAAAGCAG AUUCAACGCAAGCCUGGGAACAUACCACGACCUGCUGAAGAUCAUCAAGGACA AGGACUCCUGGACAACGAAGAAAACGAAGACAUCUGGAAGACAUCGUCCUG ACACUGACACUGUUCGAAGACAGAGAAAUGAUCGAAGAAAGACUGAAGACAU CGCACACCUGUUCGACGACAAGGUCAUGAAGCAGCUGAAGAGAAGAAGAUACA CAGGAUUGGGAAAGACUGAGCAGGAAAGCUGAUCAACGGAAUCAGAGACAAGCAG AGCGGAAAGACAACUCCUGGACUUCUGAAGAGCGACGGAUUCGCAAACAGAAA CUUCAUGCAGCUGAUCCACGACGACAGCCUGACAUUCAAGGAAGACAUCAGAA AGGCACAGGUCAGCGGACAGGGAGACAGCCUGCACGAACACAUCGCAAAACCCUG GCAGGAAGCCCGCAAUCAAGAAGGGAAUCCUGCAGACAGUCAAGGUCGUCG CGAACUGGUCAAGGUCAUGGGAAGACACAAGCCGAAAACAUCGUCUACGAAA UGGCAAGAGAAAACCAGACAACACAGAAGGGACAGAAGAACAGCAGAGAAAGA AUGAAGAGAAUCCGAAGAAGGAUUAAGGAACUGGGAAAGCCAGAUCCUGAAGGA ACACCCGGUCGAAAACACACAGCUGCAGAACGAAAAGCUGUACCUUGUACUACCU GCAGAACGGAAAGAGACAUUGUACGUCGACCAGGAACUGGACAUCAACAGACUG GCGACUACGACGUCGACCACAUCGUCCCGCAGAGCUUCUGAAGGACGACAGCA UCGACAACAAGGUCCUGACAAGAAGCGACAAGAACAGAGGAAAGAGCGACAAAC GUCCCGAGCGAAGAAGUCGUAAGAAGAUGAAGAACUACUGGAGACAGCUGCU GAACGCAAAGCUGAUCACACAGAGAAAAGUUCGACAACCCUGACAAAGCGAGAA GAGGAGGACUGAGCGAACUGGACAAGGCAGGAUUAUCAAGAGACAGCUGGGUC GAAACAAGACAGAUCAAAAGCAGUCGCACAGAUCUGGACAGCAGAAUGAA CACAAAGUACGACGAAAACGACAAGCUGAUCAGAGAAGUCAAGGUCAUCACAC UGAAGAGCAAGCUGGUCAGCGACUUCAGAAAAGGACUUCAGUUCUACAAGGUC AGAGAAAUCAACAACUACCACCACGCACACGACGCAUACCUGAACGCAGCUGC GGAACAGCACUGAUCAAGAAGUACCCGAAGCUGGAAAGCGAAUUCGUCUACGG AGACUACAAGGUCUACGACGUCAGAAAAGAUUGAUCGAAAAGAGCGAACAGGAAA UCGGAAGGCAACAGCAAAGUACUUCUUCUACAGCAACAUCGAACUUCUUC AAGACAGAAAUCACACUGGCAAACCGGAGAAAUCAGAAAAGAGACCCGUGAUCGA AACAACGGAGAAAACAGGAGAAAUCGUCUGGGACAAGGGAAGAGACUUCGCAA CAGUCAGAAAGGUCCUGAGCAUGCCGACAGGUAACAUCGUAAGAAGACAGAA GUCCAGACAGGAGGAUUCAGCAAAGGAAAGCAUCCUGCCGAAAGAGAAACAGCG CAAGCUGAUCGCAAGAAAAGAGGACUGGGACCCGAAAGAAGUACGGAGGAUUCG ACAGCCCGACAGUCGCAUACAGCGUCCUGGUCGUCGCAAAGGUCGAAAAGGGGA AAGAGCAAGAAGCUGAAGAGCGUCAAGGAACUGCUGGGAAUCACAUCAUUGGA AAGAAGCAGCUUCGAAAAGAACCCGAUCGACUUCUGGAAGCAAAGGGAUACA AGGAAGUCAAGAAGGACCUGAUCAUCAAGCUGCCGAAAGUACAGCCUGUUCGAA CUGGAAAACGGAAAGAAAAGAGAAUGCUGGCAAGCGCAGGAGAACUCGAGAAGGG AAACGAACUGGCACUGCCGAGCAAAGUACGUAACUUCUGUACUCCUGGCAAGGCA CUACGAAAAGCUGAAGGGAAGCCGGAAGACAACGAACAGAAGCAGCUGUUCG UCGAACAGCACAAAGCACUACCUGGACGAAAUCAUCGAACAGAUACGCGAAUUC</p>	
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[0665]

	<p>AGCAAGAGAGUCAUCCUGGCAGACGCAAACCUGGACAAGGUCCUGAGCGCAUA CAACAAGCACAGAGACAAGCCGAUCAGAGAACAGGCAGAAAACAUCAUCCACC UGUUCACACUGACAAAACCUGGGAGCACCAGCAUUCAGUACUUCGACACA ACAAUCGACAGAAAGAGAUACACAAGCACAAGGAAGUCCUGGACGCAACACU GAUCCACCAGAGCAUCACAGGACUGUACGAAAACAAGAAUCGACCUGAGCCAGC UGGGAGGAGAC</p>	
<p>dCas9 (无 NLS)的氨 基酸序列</p>	<p>MDKKYSIGLAIGTNSVGAVITDEYKVPSPKFKVLGNTDRHSIKKNLIGALLFDSGET AEATRLKRTARRRYTRRNKRICYLQEIFSNEMAKVDDSFHRLSEESFLVEEDKHERHP IFGNIVDEVAYHEKYPTIYHLRKKLVDSTDKADLRLLIYLALAHMIKFRGHFLIEGDLNP DNSDVDKLFIQLVQTYNQLFEEFNINASGVDAKAILSARLSKSRRLLENLIAQLPGEKKN GLFGNLIALLSLGLTPNFKSNFDLAEDAKLQLSKDTYDDDLNLLAQIGDQYADLFLAA KNLSDAILLSDILRVNTEITKAPLSASMIKRYDEHHQDLTLLKALVRQQLPEKYKEIFFD QSKNGYAGYIDGGASQEEFYKFIKPILEKMDGTEELLVKLNREDLLRQRTFDNGSIPH QIHLGELHAILRRQEDFYFPLKDNREKIEKILTRIPYVYVPLARGNSRFAMTRKSEET ITPWNFEVVDKGAQAQSFIERMTNFDKLNLPNEKVLPHSLLYEYFTVYNELTKVKYV TEGMRKPAFLSGEQKKAIVDLLFKTNRKVTVKQLKEDYFKKIECFDSVEISGVEDRFN ASLGTYHDLLKIIKDKDFLDNEENEDILEDIVLTLTLFEDREMIEERLKYAHLFDDKV MKQLKRRRYTGWGRLSRKLINGIRDKQSGKTLDFLKSDFANRNFMLIHDDSLTFK EDIQKAQVSGQDSLHEHIANLAGSPAIKKILQTVKVVDELVKVMGRHKPENIVEM ARENQTTQKQKNSRMRKRIEIGIKELGSQILKEHPVENTQLQNEKLYLYLQNGRD MYVDQELDINRLSDYDVAIVPQSFLKDDSIDNKVLRSDKNRGSNDNPSEEVVKK MKNYWRQLLNAKLITQRKFDNLTKAERGGLSELDKAGFIKRLVETROITKHVAQILD SRMNTKYDENDKLIREVKVITLKSCLVSDFRKDFQFYKREINNYHHAHDAYLNAV GTALIKKYPKLESEFYGDYKVVYDVRKMIKSEIQAQKATAKYFFYSNMNFFKTEITL ANGEIRKRPLIETNGETGEIVWDKGRDFATVRKVLVSMQVNVKKEVQTGGFSKESIL PKRNSDKLIARKKDWDPKKYGGFDSPTVAYSVLVVAKEKGSKLLKSVKELLGITIM ERSSEFKNPIDFLEAKGYKEVKKDLIILPKYSLFELENRKRMLASAGELQKGNELAL PSKYVNFYLLASHYEKLKSPEDNEQKQLFVEQHKHYLDEIIEQISEFSKRVLADANL DKVLSAYNKHRDKPIREQAENIHLFTLTNLGAPAAFKYFDTTIDRKYRSTSTKEVL LIHQSIITGLYETRIDLSQLGGD</p>	<p>19</p>
<p>使用如表3 中所列的 最小尿苷 密码子编 码SEQ ID NO: 19的, 具有起始 和终止密 码子的 dCas9 mRNA ORF</p>	<p>AUGGACAAGAAGUACAGCAUCGGACUGGCAAUCGGAACAAACAGCGUCGGAUG GGCAGUCAUCACAGACGAAUACAAGGUCCGAGCAAGAAGUUCAGGUCCUGG GAAACACAGACAGACACAGCAUCAAGAAGAACCUGAUCGGAGCAGCUGCUUUC GACAGCGGAGAAAACAGCAGAAGCAACAAGACUGAAGAGAACAGCAAGAAGAAG AUACACAAGAAGAAAAGAACAGAAUCUGCUACCUGCAGGAAAUCUUCAGCAACG AAAUGGCAAAGGUCGACGACAGCUUCUUCACAGACUGGAAGAAAGCUUCCUG GUCGAAGAAGACAAGAAGCACGAAAAGACACCCGAUCUUCGGAACAUUCGUCGA CGAAGUCGCAUACCCAGAAAAGUACCCGACAAUCUACCCUUCGAGAAAAGAAC UGGUCGACAGCACAGACAAGGCAGACCUGAGACUGAUCUACCCUGGCACUGGCA CACAUGAUCUACAGUUCAGAGGACACUUCUGAUCGAAGGAGACCUGAACCCGGA CAACAGCGACGUCGACAAGCUGUUAUCCAGCUGGUCAGACAUAACAACCAGCU GUUCGAAAGAAAACCCGAUCAACGCAAGCGGAGUCGACGCAAAGGCAAUUCUGA GCGCAAGACUGAGCAAGAGCAGAAGACUGGAAAACCUGAUCGCACAGCUGCCG GGAGAAAAGAAGAACGGACUGUUCGGAACCUGAUCGCACUGAGCCUGGGACU GACACCGAACUUCAGAGCAACUUCGACUCCUGGACAGGAGACGCAAAGCUGCAGC UGAGCAAGGACACAUACGACGACGACCUGGACAACCUGCUGGCACAGAAUCGGA GACCAGUACGACGACCUUUCUUCGAGCAAAGAACCUGAGCGCAAUUCUUCG CUGAGCGCAUCCUGAGAGUCAACACAGAAAUCACAAAGGCACCCGUGAGCGC AAGCAUGAUCUACAGAUACGACGAAACACCACCAGGACCUGACACUGCUGAAGG CACUGGUCAGACAGCAGCUGCCGAAAAGUACAAGGAAAUCUUCUUCGACCAG AGCAAGAACCGAUACGACGAGAUACAUCGACGAGGAGCAAGCCAGGAAGAUAU CUACAAGUUCUACAAGCCGAUCCUGGAAAAGAUGGACGGAACAGAAGAACUGC UGGUCUACGUAACAGAGAAGACCUGCUGAGAAAAGCAGAGAACAUCGACAAC GGAAGCAUCCCGACCAAGAUCCACCUGGAGAACUGCAGCAAUUCUGAGAAGA CAGGAAGACUUCUACCCGUUCUGAAGGACAACAGAGAAAAGAUCAAGAAAAGAU CCUGACAUUCAGAAUCCCGUACUACGUCGACCGCUGGCAAGAGGAAACAGCA GAUUCGCAUGGAUGACAAGAAAGAGCGAAGAAAACAUCACACCGUGGAACUUC GAAGAAGUCGUCGACAAGGGAGCAAGCGCACAGAGCUUCAUCGAAAGAAUGAC AAACUUCGACAAGAACCUGCCGAACGAAAAGGUCCUGCCGAAGCACAGCCUGCU GUACGAAUACUUCACAGUCUACAACGAACUGACAAGGUCAAGUACGUCACAG AAGGAAUGAGAAAGCCGGCAUUCUUCGAGCGGAGAAACAGAAAGGCAUUCGUC GACCUGCUGUUAAGACAAACAGAAAGGUCACAGUCAAGCAGCUGAAGGAAGA CUACUUCAGAAAGAUUCGAAUGCUUCGACAGCGUCGAAUUCAGCGGAGUCGAA ACAGAUUCAACGCAAGCCUGGAAACAUACCACGACCUGCUGAAGAUCAUCAAG GACAAGGACUUCUGGACAACGAAAGAAAACGAAGACAUCUUCGGAAGACUUCG CCUGACACUGACACUGUUCGAAAGACAGAGAAAUGAUCGAAAGAAAGACUGAAGA CAUACGCACACCUGUUCGACGACAAGGUCAUGAAGCAGCUGAAGAGAAAGA</p>	<p>20</p>

[0666]

	<p>UACACAGGAUGGGGAAGACUGAGCAGAAAAGCUGAUCAACGGAAUCAGAGACAA GCAGAGCGGAAAGACAAUCCUGGACUUCUGAAGAGCGACGGAUUCGCAAAACA GAAACUUAUGCAGCUGAUCCACGACGACAGCCUGACAUUAAGGAAGACAUC CAGAAGGCACAGGUCAGCGGACAGGGAGACAGCCUGCAGCAACACAUCGCAAAA CCUGGCAGGAAGCCCGGCAAUCAAGAAGGGAAUCCUGCAGACAGUCAAGGUCCG UCGACGAACUGGUCAAGGUCAUUGGGAAAGACACAAGCCGGAAAACAUCGUCAUC GAAAUGGCAAGAGAAAACCAGACAACACAGAAGGGACAGAAGAACAGCAGAGA AAGAAUGAAGAGAAUUCGAAGAAGGAAUCAAGGAACUGGGGAAAGCCAGAUCCUGA AGGAACACCCGGUCGAAAACACACAGCUGCAGAACGAAAAGCUGUACCCUGUAC UACCGCAGAACGGAAAGAGACAUGUACGUCGACCAGGAACUGGACAUCACACAG ACUGAGCGACUACGACGUCGACGCAAUUCGUCCCGCAGAGCUUCUGAAGGACGA CAGCAUCGACAACAAGGUCCUGACAAGAAGCGACAAGAACAGAGGAAAGAGCG ACAACGUCCGAGCGAAGAAGUCGUCAAGAAGAUGAAGAACUACUGGAGACAG CUGCUGAACGCAAAGCUGAUCACACAGAGAAAAGUUCGACAACCCUGACAAGGC AGAGAGAGGAGGACUGAGCGAACUGGACAAGGCAGGAUUAUCAAGAGACAGC UGGUCGAAACAAGACAGAUCAACAAGCAGCUGCAGACAGAUCCUGGACAGCAGA AUGAACACAAAGUACGACGAAAACGACAAGCUGAUCAGAGAAGUACAAGGUCAU CACACUGAAGAGCAAGCUGGUCAGCGACUUCAGAAAAGGACUUCAGUUCUACA AGGUCAGAGAAAUCAACAACUACCACCACGACACGACGCAUACCCUGAAGCAG UCGUCGGAACAGCACUGAUCAAGAAGUACCCGAAGCUGGAAAGCGAAUUCGUC UACGGAGACUACAAGGUCUACGACGUCAGAAAAGAUCAUCGCAAAGAGCGAACA GGAAUUCGGAAGGCAACAGCAAAAGUACUUCUUCUACAGCAACAUCUAGAUCU UCUUAAGACAGAAAUCACACUGGCAAAACGGAGAAAUCAGAAAAGAGACCCGUC AUCGAAAACAACGGAGAAAACAGGAGAAAUCGUCUGGCAAAAGGAAAGAGACU CGCAACAGUCAGAAAAGGUCCUGAGCAUGCCCGCAGGUACAACUAGUCAAGAAGA CAGAAGUCCAGACAGGAGGAUUCAGCAAGGAAAGCAUCCUGCCGAAGAGAAAAC AGCGACAAGCUGAUCGCAAGAAAAGGAGCUGGGACCCGAAGAAGUACGGAGG AUUCGACAGCCGACAGUCGCAUACAGCUGCCUGGUCGUCGCAAAAGGUCGAAA AGGGAAAGAGCAAGAAGCUGAAGAGCGUCAAGGAACUGCUGGGAAUCACAUC AUGGAAAGAAGCAGCUUCGAAAAGAACCCGUAUCGACUUCUGGAAGCAAAGGG AUACAAGGAAGUCAAGAAGGACCUCAUCAUCAAGCUGCCGAAGUACAGCCUGU UCGAACUGGAAAACGGAAAGAAAGAGAAUUCGUGGCAAGCGCAGGAGAACUCGAG AAGGGAAACGAACUGGCACUGCCGAGCAAGUACGUCAACUUCUGUACCCUGGC AAGCCACUACGAAAAGCUGAAGGGAAAGCCCGGAAGACAACGAACAGAAGCAGC UGUUCGUCGAACAGCACAAGCACUACCCUGGACGAAAUCAUCGAAACAGAUACAGC GAAUUCAGCAAGAGAGUCAUCCUGGCAGACGCAAACCUUGGACAAGGUCCUGAG CGAUACAACAAGCACAGAGACAAGCCGAUCAGAGAACAGGCAGAAAACAUCA UCCACCUGUUCACACUGACAACCCUGGGAGCACCCGGCAGCAUUAAGUACUUCG ACACAACAUCGACAGAAAAGAGAUACAACAAGCACAAGGAAGUCCUGGACGCA ACACUGAUCCACCAGAGCAUACAGGACUGUACGAAAACAAGAAUCGACCUGAG CCAGCUGGGAGGAGACUAG</p>	
<p>使用如表3 中所列的 最小尿苷 密码子编 码SEQ ID NO: 19的 dCas9编码 序列(无起 始或终止 密码子;适 于包括在 融合蛋白 质编码序 列中)</p>	<p>GACAAGAAGUACAGCAUCGGACUUGGCAAUUCGGAACAAACAGCGUCGGAUGGGC AGUCAUCACAGACGAAUACAAGGUCCCGAGCAAGAAGUUAAGGUCCUGGGAA ACACAGACAGACACAGCAUCAAGAAGAACCUGAUCGGAGCACUGCUGUUCGAC AGCGGAGAAAACAGCAGAAGCAACAAGACUGAAGAGAAACAGCAAGAAGAAGAU CACAAGAAGAAAGAACAGAAUCUGCUACCCUGCAGGAAAUCUUCAGCAACGAAA UGGCAAAGGUCGACGACGACUUCUUCACAGACUGGAAAGAAAGCUUCUGGUC GAAGAAGACAAGAAGCACGAAAAGACACCCGAUCUUCGGAACAUCGUCGACGA AGUCGCAUACCACGAAAAGUACCCGACAUCUACCCACUGAGAAAAGAGCUGG UCGACAGCACAGACAAGGCAGACCUGAGACUGAUCUACCCUGGCACUGGCACACA UGAUCAAAGUUCAGAGGACACUUCUUCGUAUCGAAGGAGACCUGAACCCGGACAAC AGCGACGUCGACAAGCUGUUAUCCAGCUGGUCCAGACAUACAACCAGCUGUUC GAAGAAAACCCGAUCAACGCAAGCGGAGUCGACGCAAAGGCAUUCUGAGCGC AAGACUGAGCAAGAGCAGAAGACUGGAAAACCUGAUCGCACAGCUGCCGGGAG AAAAGAAGAACGGACUGUUCGGAACCUGAUCGCACUGAGCCUGGGACUGACA CCGAACUUAAGAGCAACUUCGACUUGGCAAGAGCAGCAAGAGCAGCAAGCUGAG CAAGGACACAUACGACGACGACCUUGGACAACCUGCUGGCACAGAUCCUGGAGACCA GUACGCAGACCUGUUCUGGACGAAAGAACCUGAGCGACGCAUCCUGCUGA GCGCAUCCUGAGAGUCAACACAGAAAUCACAAAGGCACCCGUCGAGCGCAAGC AUGAUCAAAGAGAUACGACGAAACACCACCAGGACCUGACACUGCUGAAGGACU GGUCAGACAGCAGCUGCCGGAAAAGUACAAGGAAAUCUUCUUCGACCAGAGCA AGAACCGAUACGCAGGAUACAUCGACGGAGGAGCAAGCCAGGAAGAUAUCUAC AAGUUAUCAAGCCGAUCCUGGAAAAGAUUGGACGGAACAGAAGAACUUCUGGU CAAGCUGAACAGAGAAGACCUGCUGAGAAAAGCAGAGAACAUCGACAACCGGAA GCAUCCCGACCAAGAACUCCUGGGAGAACUGCAGCAAUCCUGGAGACAGG AAGACUUCUACCCGUUCUGAAGGACAACAGAGAAAAGAUUCGAAAAGAUCCUG ACAUCAGAAUCCGUACUACGUCGGACCCGUGGCAAGAGGAAAACAGCAGAUU</p>	<p>21</p>

[0667]

	<p>CGCAUGGAUGACAAGAAAGAGCGAAGAAACAUAUCACACCGUGGAACUUCGAAG AAGUCGUCGACAAGGGAGCAAGCGCACAGAGCUUCAUCGAAAAGAAUGACAAAC UUCGACAAGAACCUGCCGAACGAAAAGGUCCUGCCGAAGCACAGCCUGCUGUAC GAAUACUUCACAGUCUACAACGAACUGACAAAGGUCAAGUACGUCACAGAAAG AAUGAGAAAAGCCGGCAUUCUGAGCGGAGAACAGAAGAAGGCAUUCGUCGACC UGCUGUUAAGACAAAACAGAAAGGUACACAGUCAAGCAGCUGAAGGAAAGACUAC UUCAAGAAGAUUCGAAUGCUUCGACAGCGUCGAAAUCAGCGGAGUCGAAGACAG AUUCAACGCAAGCCUGGGAACAUACCACGACCUGCUGAAGAUCAUCAAGGACA AGGACUUCUGGACAACGAAGAAAACGAAGACAUCUCCUGGAAGACAUCGUCCUG ACACUGACACUGUUCGAAGACAGAGAAAUGAUCGAAGAAAAGACUGAAGACUA CGCACACCGUUCGACGACAAGGUCAUGAAGCAGCUGAAGAGAAGAAGAUACA CAGGAUGGGGAAGACUGAGCAGAAAAGCUGAUAACGGAAUCAGAGACAAGCAG AGCGGAAAAGACAAUCCUGGACUUCUGAAGAGCGACGGAUUCGCAAAACAGAAA CUUCAUGCAGCUGAUCCACGACGACAGCCUGACAUAAGGAAGACAUCCAGA AGGCACAGGUCAGCGGACAGGGAGACAGCCUGCAGCAACACAUCGCAAAACCUG GCAGGAAGCCCGCAAUCAAGAAGGGAUCCUGCAGACAGUCAAGGUCGUCGA CGAACUGGUCAAAGGUCUUGGGAAGACACAAGCCGGAAAACAUCGUCUUCGAAA UGGCAAGAGAAAACCAGACAACACAGAAGGGACAGAAGAAGCAGCAGAGAAAAGA AUGAAGAGAAUUCGAAGAAGGAAUCAAGGAACUUGGGAAGCCAGAUCCUGAAGGA ACACCCGGUCGAAAACACACAGCUGCAGAACGAAAAGCUGUACCUGUACUACCU GCAGAACCGGAAGAGACAUGUACGUCGACCAGGAACUGGACAUAACAGACUGA GCGACUACGACGUCGACGCAAUCGUCCCGCAGAGCUUCUGAAGGACGACAGCA UCGACAACAAGGUCCUGACAAGAAGCGACAAGAACAGAGGAAAGAGCGACAAC GUCCGAGCGAAGAAGUGUCAAGAAGAUAGAAGAACUACUGGAGACUUCGAAUCU GAACGCAAAGCUGAUCACACAGAGAAAAGUUCGACAACCUGACAAGGCGAGAGA GAGGAGGACUGAGCGAACUGGACAAGGCAGGAUUAUCAAGAGACAGCUGGUC GAAACAAGACAGAUACAAGCAGCUCGACAGAUCCUGGACAGCAGAAUUGAA CACAAGUACGACGAAAACGACAAGCUGAUCAGAGAAGUCAAGGUCUACAC UGAAGAGCAAGCUGGUCAGCGACUUCAGAAAAGGACUUCAGUUCUACAAGGUC AGAGAAAUCAACAACUACCACCACGCACACGACGCAUACCUGAACGCAGUCGUC GGAACAGCACUGAUCAGAAGUACCCGAAGCUGGAAAAGCGAAUUCGUCUACGG AGACUACAAGGUCUACGACGUCAGAAAAGAUAGUUCGCAAAGAGCGAACAGGAAA UCGGAAGGCAACAGCAAAGUACUUCUUCUACAGCAACAUCUAGAACUUCU AAGACAGAAAUCACACUGGCAAAACGAGAAAUCAGAAAAGAGACCGCUGAUCGA AACAAACGGAGAAACAGGAGAAAUCGUCUGGGACAAGGGAAAGAGACUUCGCAA CAGUCAGAAAAGGUCCUGAGCAUCCCGCAGGUAACAUCGUAAGAAGACAGAA GUCCAGACAGGAGGAUUCAGCAAGGAAAGCAUCCUGCCGAAGAGAAAACAGCGA CAAGCUGAUCGCAAGAAAAGGACUGGGACCCGAAGAAGUACGGAGGAUUCG ACAGCCCGACAGUCGCAUACAGCGUCCUGGUCGUCGCAAAGGUCGAAAAGGGA AAGAGCAAGAAGCUGAAGAGCGUCAAGGAACUUCGUGGGAUUCACAUAUGGA AAGAAGCAGCUUCGAAAAGAACCCGAUCGACUUCUGGAAGCAAAGGGAUACA AGGAAGUCAAGAAGGACUGAUCAUCAAGCUGCCGAAGUACAGCCUGUUCGAA CUGGAAAACGGAAGAAAGAGAAUGCUGGCAAGCGCAGGAGAACUGCAGAAGGG AAACGAACUGGCACUGCCGAGCAAGUACGUAACUUCUGUACCUGGCAAGCCA CUACGAAAAGCUGAAGGGAAGCCCGAAGACAACGAACAGAAGCAGCUGUUCG UCGAACAGCACAAAGCAUACCUGGACGAAAUAUCGAACAGAUACAGGAAUUC AGCAAGAGAGUCAUCCUGGACAGCAGCAAAACCUGGACAAGGUCCUGAGCGCAUA CAACAAGCACAGAGACAAGCCGAUCAGAGAACAGGCAGAAAACAUAUCCACC UGUUCACACUGACAAACCGGGAGCACCGGCAGCAUUCAGUACUUCGACACA ACAAUCGACAGAAAGAGAUACAAGCACAAGGAAGUCCUGGACGCAACACU GAUCCACCAGAGCAUCACAGGACUGUACGAAAACAAGAAUCGACCUGAGCCAGC UGGGAGGAGACGGAGGAGGAAGC</p>	
<p>具有两个核定位信号作为C端氨基酸的Cas9的氨基酸序列</p>	<p>MDKKYSIGLDIGTNSVGVAVITDEYKVPKFKVLGNTDRHSIKKNLIGALLFDSGET AEATRLKRTARRRYTRRKNRICYLQEIFSNEMAKVDDSFHRLSEESFLVEEDKKHERHP IFGNVDEVAYHEKYPTIYHLRKKLVDSTDKADLRLIYLALAHMIKFRGHFLIEGDLNP DNSDVKLFIQLVQTYNQLFEENPINASGVDAKAILSARLSKSRLENLIAQLPGEKKN GLFGLNLIASLGLTPNFKSNFDLAEDAKLQLSKDHYDDDLNLLAQIGDQYADLFLAA KNLSDAILLSDILRVNTEITKAPLSASMIKRYDEHHQDLTLLKALVRQQLPEKYKEIFFD QSKNGYAGYIDGGASQEEFYKFIKPILEKMDGTEELLVKLNREDLLRKQRTFDNGSIPH QIHLGELHAILRRQEDFYPLKDNREKIEKILTRIPYYVGLARGNSRFAMTRKSEET ITPWNFEVVDKGSASAQSFIERMNFKNLPNEKVLPHKSLLYEYFTVYNELTKVKYV TEGMRKPAFLSGEQKKAIVDLLFKTNRKVTVKQLKEDYFKKIECFDSVEISGVEDRFN ASLGTYHDLKIIKDKDFLDNEENEDILEDIVLTTLFEDREMIEERLKYAHLFDDKV MKQLKRRRYTGWRLSRKLINGIRDKQSGKTILDFLKSDFANRNFMRQLIHDDSLTFK EDIQKAQVSGQDSLHEHIANLAGSPAIKKGILQTVKVVDELVKVMGRHKPENVIEM ARENQTTQKGQKNSRERMKRIEELGKELGSQILKEHPVENTQLQNEKLYLYLQNGRD MYVDQELDINRLSDYDVDHIVPQSFLKDDSIDNKVLTRSDKNRGSNDNPSEEVVKK</p>	<p>22</p>

[0668]

	<p>MKNYWRQLLNAKLITQRKFDNLTKAERGLSELDKAGFIKQRLVETRQITKHVAQILD SRMNTKYDENDKLIREVKVITLKSGLVSDFRKDFQFYKVRINNYHHHAHDAYLNAV GTALIKKYPKLESEFVYGDYK VYDVRKMIKSEQEIGKATAKYFFYSNIMNFFKTEITL ANGEIRKRPLIETNGETGEIVWDKGRDFATVRKVL SMPQVNIVKKTEVQTGGFSKESIL PKRNSDKLIARKKDWDPKKYGGFDSPTVAYSVLVVAKEVGKSKLKS VKELLGITIM ERSSEFNPIDFLEAKGYKEVKKDLIILPKYSLFELENGRKRMLASAGELQKGNELAL PSKYVNFLYLASHYEKLGSPEDNEQKQLFVEQHKHYLDEIIEQISEFSKRVLADANL DKVLSAYNKHRDKPIREQAENIIHLFTLNLGAPAFKYFDTTIDRKRYTSTKEVLDAT LIHSITGLYETRIDLSQLGGD GSGSPKKKRKVDGSPKKKRKVDSG</p>	
<p>使用如表3中所列的最小尿苷密码子编码SEQ ID NO: 22的, 具有起始和终止密码子的 Cas9 mRNA ORF</p>	<p>AUGGACAAGAAGUACAGCAUCGGACUGGACAUCGGAACAACAGCGUCGGAUG GGCAGUCAUCACAGACGAAUACAAGGUCCCGAGCAAGAAGUUCAAGGUCCUGG GAAACACAGACAGACACAGCAUCAAGAAGAACCUGAUCGGAGCACUGCUGUUC GACAGCGGAGAAAACAGCAGAAGCAACAAGACUGAAGAGAACAGCAAGAAGAAG AUACACAAGAAGAAAAGAACAGAAUCUGCUACCUGCAGGAAAUCUUCAGCAACG AAAUGGCAAAGGUCGACGACAGCUUCUUCACAGACUGGAAGAAGAAAGCUCCUG GUCGAAGAAGACAAGAAGCACGAAAGACACCCGAUCUUCGGAACAUCGUCGCA CGAAGUCGCAUACCACGAAAAGUACCCGACAAUCUACCACUGAGAAAAGAAGC UGGUCGACAGCACAGACAAGGCAGACCUGAGACUGAUCUACCUGGCACUGGCA CACAUCAAGUUCAGAGGACACUCCUGAUCGAAAGAGACCUCCGAAACCCGGA CAACAGCGACGUCGACAAGCUGUUAUCCAGCUGGUCCAGACAUAACAACAGCU GUUCGAAGAAAACCCGAUCAACGCAAGCGGAGUCGACGCAAAAGGCAAUCCUGA GCGCAAGACUGAGCAAGAGCAGAAGACUGGAAAACCCUGAUCGCACAGUCGCCG GGAGAAAAGAAGAACCGACUGUUCGGAACCCUGAUCGCACUGAGCCUGGGACU GACACCGAACUUAAGAGCAACUUCGACCUGGCAGAGAAGACGCAAAAGCAGC UGAGCAAGGACACAUACGACGACGACCUGGACAACCCUGCUGGCACAGAUCCGA GACCAGUACGCAGACCUGUUCUGGCAGCAAAGAACCUGAGCGACGCAAUCCUG CUGAGCGCAUCCUGAGAGUCAACACAGAAAUCACAAAGGCACCGCUGAGCGC AAGCAUGAUCAAGAGAUACGACGAAACACCCAGGACCUGACUCUGUAGAAAGG CACUGGUCAGACAGCAGCUGCCGAAAAGUACAAGGAAUUCUUCGACACAG AGCAAGAACGGAUACGCAGGAUACAUCGACGGAGGAGCAAGCCAGGAAGAAUU CUACAAGUUCAUCAAGCCGAUCCUGGAAAAGAUGGACGGAACAGAAAGACUCC UGGUCAGGUAACGAGAGAAGACCUGCUGAGAAAAGCAGAGAACAUCGACAAC GGAAAGAUCCCGCAACAGAUCCACCUGGGAGAACUGCAGCAAUCCUGAAGAAG CAGGAAGACUUCUACCCGUUCUGAAGGACAACAGAGAAAAGAUUCGAAAAGAU CCUGACAUUCAGAAUCCCGUACUACGUCGACCGCUGGCAAGAGGAAAACAGCA GAUUCGCAUGGAUGACAAGAAAGAGCGAAGAAAACAUCACACCGUGGAACUUC GAAGAAGUCGUCGACAAGGGAGCAAGCGCACAGAGCUUCUUCGAAAAGAAUGAC AAACUUCGACAAGAACCCUGCCGAACGAAAAGGUCCUGCCGAAGCAGAAAGUCCU GUACGAAUACUUCACAGUCUACAACGAACUGACAAGGUCAAGUACGUCACAG AAGGAAUGAGAAAAGCCGGCAUUCUGAGCGGAGAAACAGAAAGAGGCAUUCGUC GACCUGCUGUUCAGCAAAACAGAAAAGGUCACAGUCAAGCAGCUGAAGGAAGA CUACUUCAGAAAGAUUCGAAUGCUUCGACAGCGUCGAAAUCAGCGGAGUAGGAA ACAGAUUCAACGCAAGCCUGGAAACAUACCACGACCUGCUGAAGAUCAUCAAG GACAAGGACUUCUGGACAACGAAAGAAAACGAAAGCAUCCUGGAAGACAUCCGU CCUGACACUGACACUGUUCGAAGACAGAGAAAUGAUCGAAAGAAAGACUGAAGA CAUACGCACACCCUGUUCGACGACAAGGUCUUGAAGCAGCUGAAGAGAGAAGA UACACAGGAUGGGGAAAGACUGAGCAGAAAAGCUUGAUAACCGGAUUCAGAGCAA GCAGAGCGGAAAGACAAUCCUGGACUUCUGAAGAGCGACGGAUUCGCAAACA GAAACUUCAGUCAGCUGAUCCACGACGACAGCCUGACAUUCAGGAAGACAUUC CAGAAGGCACAGGUCAGCGGACAGGGAGACAGCCUGCACGAACACAUCGCAAAA CCUGGCAGGAAGCCCGCAAUCAAGAAGGGAUUCUGCAGACAGUCAAGGUCG UCGACGAACUGGUAAGGUAUGGGAAGACACAAGCCGAAAACAUCGUCAUC GAAAUGGCAAGAGAAAACCAGACAACACAGAAAGGGACAGAAAGAACAGCAGAGA AAGAAUGAAGAGAAUUCGAAGAAGGAAUCAAGGAACUGGGAAGCCAGAUCUGA AGGAACACCCGGUCGAAAACACACAGCUGCAGAACGAAAAGCUGUACCUUGUAC UACCUGCAGAACGGAAAGAGACAUUGUACGUCGACCAGGAACUGGACAUCAACAG ACUGAGCGACUACGACGUCGACCACAUUCGUCCCGCAGAGCUUCUGAAGGACGA CAGCAUCGACAACAAGGUCCUGACAAAGAAGCGACAAGAACAGAGGAAAGAGCG ACAACGUCCGAGCGAAGAAUGUCGUAAGAAGAUAGAACUACUGGAGACAG CUGCUGAACGCAAAGCUGAUACACACAGAGAAAAGUUCGACAACCUUGACAAGGC AGAGAGAGGAGGACUGAGCGAACUGGACAAGGCAGGAUUCAUCAAGAGACAGC UGGUCGAAAACAAGACAGAUACAAGACGACGUCGCACAGAUCCUGGACAGCAGA AUGAACACAAAGUACGACGAAAACGACAAGCUGAUCAGAGAAAGUCAAGGUCAU CACACUGAAGAGCAAGCUGGUCAGCGACUUCAGAAAGGACUCCAGUUCUUCAC AGGUCAGAGAAAUAACAACUACCACACGACACGACGCAUCCUGAACGACGAG UCGUCGGAACAGCAGCUGAUCAGAAGUACCCGAAGCUGGAAAGCGAAUUCGUC UACGGAGACUACAAGGUUCUACGACGUCAGAAAAGAUUGAUCGAAAAGAGCGAAC</p>	<p>23</p>

[0669]

	<p>GGAAUUCGAAAGGCAACAGCAAAGUACUUCUUCUACAGCAACAUCAUGAACU UCUUCAAGACAGAAAUCACACUGGCAAACGGAGAAAUCAGAAAGAGACCGCUG AUCGAAACAAACGGAGAAACAGGAGAAAUCGUCUGGGACAAGGGAAGAGACUU CGAACAGUCAGAAAAGGUCCUGAGCAUGCCGAGGUAACAUUGUCAAGGAAGA CAGAAGUCCAGACAGGAGGAUUCAGCAAGGAAAAGCAUCCUGCCGAAGAGAAAC AGCGACAAGCUGAUCGCAAGAAAAGAAAGGACUGGGACCCGAAGAAGUACGGAGG AUUCGACAGCCCAGACAGUCGCAUACAGCGUCCUGGUCGUCGCAAAGGUCGAAA AGGGAAAGAGCAAGAAGCUGAAGAGCGUCAAGGAACUGCUGGGAAUCACAAUC AUGGAAAGAAGCAGCUUCGAAAAGAACCCGAUCGACUUCUGGAAGCAAAGGG AUACAAGGAAGUCAAGAAGGACCUGAUCAUCAAGCUGCCGAAGUACAGCGU UCGAACUGGAAAACGGAAAGAAAGAGAAUGCUGGCAAGCGCAGGAGAACUGCAG AAGGGAAACGAACUGGCACUGCCGAGCAAGUACGUAACUUCUGUACCUUGGC AAGCCACUACGAAAAGCUGAAGGGAAAGCCCGGAAGACAACGAACAGAAAGCAGC UGUUCGUCGAACAGCACAAGCACUACCUUGGACGAAAUCAUCGAACAGAUACAGC GAAUUCAGCAAGAGAGUCAUCCUGGCAGACGCAAACCUUGGACAAGGUCCUGAG CGCAUACAACAAGCACAGAGACAAGCCGAUCAGAGAACAGGCAGAAAACAUCA UCCACCUUUCACACUGACAACCCUGGGAGCACCCGGCAGCAUUAAGUACUUCG ACACAACAUCGACAGAAAAGAGAUACACAAGCACAAGGAAGUCCUGGACGCA ACACUGAUCCACAGAGCAUCACAGGACUGUACGAAACAAGAAUCGACCUUGAG CCAGCUGGGAGGAGACGGAAAGCGGAAGCCCGAAGAAGAAGAGAAAAGGUCGACG GAAGCCCGAAGAAGAAGAGAAAAGGUCGACAGCGGAUAG</p>	
<p>使用如表3 中所列的 最小尿苷 密码子编 码SEQ ID NO: 23的 Cas9 编码 序列(无起 始或终止 密码子;适 于包括在 融合蛋白 质编码序 列中)</p>	<p>GACAAGAAGUACAGCAUCGGACUGGACAUCGGAACAAACAGCGUCGGAUGGGC AGUCAUCACAGACGAAUACAAGGUCCCGAGCAAGAAGUUCAAGGUCCUGGGAA ACACAGACAGACACAGCAUCAAGAAGAACCUGAUCGGAGCACUGUGUUCGAC AGCGGAGAAACAGCAGAAGCAACAAGACUGAAGAGAACAGCAAGAAGAAGAU CACAAGAAGAAAGAACAGAAUCUGCUACCUUGCAGGAAAUCUUCAGCAACGAAA UGGCAAAGGUCGACGACAGCUUCUCCACAGACUGGAAGAAAGCUUCUCCUGGUC GAAGAAGACAAGAAGCACGAAAGACACCCGAUCUUCGGAACAUCGUCGACGCA AGUCGCAUACCCAGAAAAGUACCCGACAAUCUACCCUUGAGAAAAGAGCUGG UCGACAGCACAGACAAGGCAGACCUUGAGACUGAUCUACCUUGGCACUGGCACACA UGAUCAAGUUCAGAGGACACUUCUGAUCGAAGGAGACCUGAACCCGGACAAC AGCGACGUCGACAAGCUGUUAUCCAGCUGGUCAGACAUAACAACACGUCGUC GAAGAAAACCCGAUCCACGAAAGUACCCGACAAUCUACCCUUGAGAAAAGAGCUG AAGACUGAGCAAGAGCAGAAGACUGGAAAACCUGAUCGCACAGCUGCCGGGAG AAAAGAAGAACCGACUGUUCGGAACCUUGAUCGCACUGAGCCUGGGACUGACA CCGAACUUCAGAGCAACUUCGACCUUGGCAGAAAGACGCAAGCUGCAGCUGAG CAAGGACACAUACGACGACGACCUUGGACAACCUUGCUGGCACAGAUCCGGACCA GUACGCAAGACCUUGUUCUUGGACGAAAGAACCUGAGCGACGCAUCCUGCUGA GCGACAUCUGAGAGUCAACACAGAAAUCACAAAGGCACCCGUGAGCGCAAGC AUGAUCAAGAGAUACGACGAACACCACCAGGACCUGACACUGCUGAAGGCACU GGUCAGACAGCAGCUGCCGAAAAGUACAAGGAAAUCUUCUUCGACCAAGCA AGAACGGAUACGCAAGGAUACAUCGACGAGGAGCAAGCCAGGAAGAUAUCUAC AAGUUAUCAAGCCGAUCCUGGAAAAGAUGGACGGAACAGAAGAACUGCUGGU CAAGCUGAACAGAGAAGACCUUGCUGAGAAAAGCAGAGAACAUCGACAACGGAA GCAUCCCGCACCAAGAUCCUUGGAGAACUGCACGCAAUCCUGAGAAGACAGG AAGACUUCUACCCGUUCUGAAGGACAACAGAGAAAAGAUCGAAAAGACUCCUG ACAUUCAGAAUCCCGUACUACGUCGGAACCGCUGGCAAGAGGAAACAGCAU CGAUGGAUGACAAGAAAGAGCGAAGAAAACAUCACACCGUGGAACUUCGAAG AAGUCGUCGACAAGGGAGCAAGCGCACAGAGCUUCAUCGAAAGAAUGACAAC UUCGACAAGAACCUGCCGAACGAAAAGGUCCUGCCGAAGCACAGCCUGCUGUAC GAUUAUCACAGUCUACAACGAACUGACAAGGUUCAAGUACGUCACAGAAAG AAUGAGAAAGCCGGCAUUCUUGAGCGGAGAACAGAAGAAGGCAUUCGUCGACC UGCUGUUAAGACAAACAGAAAGGUCACAGUCAAGCAGCUGAAGGAAGACUAC UUCAAGAAGAUUGAUGCUUCGACAGCGUCGAAAUCAGCGGAGUCGAAGACAG AUUCAACGCAAGCCUGGGAACAUAACCACGACCUUGCUGAAGAUCAUCAAGGACA AGGACUUCUUGGACAACGAAGAAAACGAAGACAUCUUGGAAGACAUCGUCU ACACUGACACUGUUCGAAGACAGAGAAAUGAUCGAAGAAAGACUGAAGACAU CGCACACCUUGUUCGACGACAAGGUCAUGAAGCAGCUGAAGAGAAAGAUACA CAGGAUGGGGAAGACUGAGCAGAAAAGCUGAUAACGGAAUCAGAGACAAGCAG AGCGGAAAAGACAUCUUGGACUUCUUGAAGAGCGACGGAUUCGCAAAACAGAAA CUUCAUGCAGCUGAUCCACGACGACAGCCUGACAUCUUCAGGAAGACAUCACAG AGGCACAGGUCAGCGGACAGGGAGACAGCCUGCACGAACACAUCCGAAACCU GCAGGAAGCCCGCAAUCAAGAAGGGAAUCCUGCAGACAGUCAAGGUCGUCGCA GCAACUGGUCAAGGUCAUGGGAAAGACACAAGCCGGAAAACAUCGUAUCGAAA UGGCAAGAGAAAACAGACAACACAGAAAGGACAGAAGAACAGCAGAGAAAAG AUGAAGAGAAUCGAAGAAGGAUACAAGGAACUGGGAAGCCAGAUCCUGAAGGA ACACCCGGUCGAAAACACACAGCUGCAGAACGAAAAGCUGUACCUUGUACUACCU</p>	<p>24</p>

[0670]

	<p>GCAGAACGGAAGAGACAUGUACGUCGACCAGGAACUGGACAUCAACAGACUGA GCGACUACGACGUCGACCACAUCGUCCCGCAGAGCUUCCUGAAGGACGACAGCA UCGACAACAAGGUCCUGACAAGAAGCGACAAGAACAGAGGAAAGAGCGACAAC GUCCCGAGCGAAGAGUCGUGAAGAAUGAUGAAGAACUACUGGAGACAGCUGCU GAACGCAAAGCUGAUCACACAGAGAAAGUUCGACAACCCUGACAAAGGCAGAGA GAGGAGGACUGAGCGAAACUGGACAAGGCAGGAUUAUCAAGAGACAGCUGGUC GAAACAAGACAGAUACAAAAGCAGCUGCGACAGAUCCUGGACAGCAGAAUGAA CACAAAGUACGACGAAAACGACAAGCUGAUCAGAGAAGUCAAGGUAUCACAC UGAAGAGCAAGCUGGUCAGCGACUUCAGAAAAGGACUUCAGUUCUACAAGGUC AGAGAAUUAACAACUACCACCACGACACGACGCAUACCUGAACGACGAGUCGUC GGAACAGCACUGAUCAAGAAGUACCCGAAGCUGGAAAGCGAAUUCGUCUACGG AGACUACAAGGUCUACGACGUCAGAAAGAUGAUCGCAAAGAGCGAACAGGAAA UCGGAAGGCAACAGCAAAGUACUUCUUCUACAGCAACAUCAUGAACUUCUUC AAGACAGAAUACACACUGGCAAACCGGAGAAAUCAGAAAAGACCUCUGACGAA AACAAACGGAGAAAACAGGAGAAAUCGUCUGGGACAAGGGAAGAGACUUCGCAA CAGUCAGAAAGGUCCUGAGCAUGCCGAGGUAACAUCGUAAGAAGACAGAA GUCCAGACAGGAGGAUUCAGCAAGGAAAGCAUCCUGCCGAAGAGAAACAGCGA CAAGCUGAUCGCAAGAAAGAAGGACUGGGACCCGAAGAAGUACGGAGGAUUCG ACGCCCGACAGUCGAUACAGCGUCCUGGUCGUCGCAAAGGUCGAAAAGGGA AAGAGCAAGAAGCUGAAGAGCGUCAAGGAACUGCUGGGAAUCACAAUCAUGGA AAGAAGCAGCUUCGAAAAGAACCUGAUCGACUUCUGGAAGCAAAGGGAUACA AGGAAGUCAAGAAGGACCUGAUCAUCAAGCUGCCGAAGUACAGCCUGUUCGAA CUGGAAAACGGAAGAAAGAGAUGCUGGCAAGCGCAGGAGAACUCGAGAAGGG AAACGAACUGGCACUGCCGAGCAAGUACGUAACUUCUGUACCUAGGCAAGCCA CUACGAAAAGCUGAAGGGAAGCCCGAAAGACAACGAACAGAAGCAGCUGUUCG UCGAACAGCACAAAGCACUACCUGGACGAAAUCAUCGAACAGAUACGCGAAUUC AGCAAGAGAGUCAUCCUGGACAGCAGCAAACCUGGACAAGGUCUGAGCGCAUA CAACAAGCACAGAGACAAGCCGAUCAGAGAACAGGCAGAAAACUACCCACC UGUUCACACUGACAAACCUGGAGCACCAGCAGCAUUCAGUACUUCGACACA ACAAUCGACAGAAAGAGAUACACAAGCACAAAAGGAAGUCCUGGACGCAACACU GAUCCACCAGAGCAUCACAGGACUGUACGAAAACAAGAAUCGACCUGAGCCAGC UGGGAGGAGACGGAAGCGGAAAGCCCGAAGAAAGAAAGAAAGGUCGACGGAAGC CCGAAGAAGAAGAGAAAGGUCGACAGCGGA</p>	
<p>具有两个核定位信号作为C端氨基酸的Cas9切口酶的氨基酸序列</p>	<p>MDKKYSIGLAIGTNSVGWAVITDEYKVPSSKFKVLGNTDRHSIKKNLIGALLFDSGET AEATRLKRTARRRYTRRKNRICYLQEIFSNEMAKVDDSFHRLLEESFLVEEDKHERHP IFGNIVDEVAYHEKYPTIYHLRKKLVDSTDKADLRLIYLALAHMIKFRGHFLIEGDLNP DNSDVKLFIQLVQTYNQLFEENPINASGVDAKAILSARLSKSRLENLIAQLPGEKKN GLFGNLIALSLGLTPNFKSNFDLAEDAKLQLSKDTYDDDLNLLAQIGDQYADLFLAA KNLSDAILLSDILRVNTEITKAPLSASMIKRYDEHHQDLTLLKALVRQQLPEKYKEIFFD QSKNGYAGYIDGGASQEFYKFIKPILEKMDGTEELVVLNREDLLRQRTFDNGSIPH QIHLGELHAILRRQEDFYFPLKDNREKIEKILTRIPYVGPLARGNSRFAMTRKSEET ITPWNFEVVDKGSASAQSFIERMTNFDKLPNEKVLPHSLLYEYFTVYNELTKVKYV TEGMRKPAFLSGEQKKAIVDLLFKTNRKVTVKQLKEDYFKKIECFDSVEISGVEDRFN ASLGTYHDLLKIIKDKDFLDNEENEDILEDIVLTLTLFEDREMIEERLKYAHLFDDKV MKQLKRRRYTGWRLSRKLINGIRDKQSGKTILDFLKSDFANRNFMLIHDDSLTFK EDIQKAQVSGQDSLHEHIANLAGSPAIKKILQTVKVVDELVKVMGRHKPENIVNIE ARENQTTQKGQKNSRERMKRIEIGIKELGSQILKEHPVENTQLQNEKLYLYLQNGRD MYVDQELDINRLSDYVDHIVPQSFLKDDSIDNKVLRSDKNRGSNDNPSEEVVKK MKNYWRQLLNAKLITQRKFDNLTKAERGGLSELDKAGFIKRLVETRQITKHVAQILD SRMNTKYDENDKLIREVKVITLKSCLVSDFRKDFQFYKREINNYHHAHDAYLNAV GTALIKKYPKLESEFVYGDYKVDVRKMIKSEIQEIGKATAKYFFYSNIMNFFKTEITL ANGEIRKRPLIETNGETGEIVWDKGRDFATVRKVLVSMQVNVKKTQVQGGFSKESIL PKRNSDKLIARKKDWDPKKYGGFDSPTVAYSVLVVAKEKGSKLLKSVKELLGITIM ERSSEFKNPIDFLEAKGYKEVKKDLIILPKYSLFELENRGRMLASAGELQKGNELAL PSKYVNFYLLASHYEKLGKSPEDNEQKQLFVEQHKHYLDEIIEQISEFSKRVLADANL DKVLSAYNKHDKPIREQAENIHLFTLTNLGAPAFKYFDTTIDRKYRSTKEVLDAT LIHQITGLYETRIDLSQLGGDGSPPKRRKVDGSPKRRKVDG</p>	<p>25</p>
<p>使用如表3中所列的最小尿昔密码子编码SEQ ID NO: 25的,</p>	<p>AUGGACAAGAAGUACAGCAUCGGACUGGCAAUCGGAACAAACAGCGUCGGAUG GGCAGUCAUCACAGACGAAUACAAGGUCCCGAGCAAGAAGUUAAGGUCCUGG GAAACACAGACAGACACAGCAUCAAGAAGAACCUGAUCGGAGCACUGCUGUUC GACAGCGGAGAAACAGCAGAAGCAACAAGACUGAAGAGAACAGCAAGAAGAAG AUACACAAGAAGAAAGAACAAGAAUCUGCUACCUGCAGGAAAUCUUCAGCAACG AAAUGGCAAAGGUCGACGACAGCUUCUUCACAGACUGGAAAGAAAGCUUCCUG GUCGAAGAAGACAAGAAGCACGAAAAGACACCCGAUCUUCGGAACAAUCGUCGA CGAAGUCGCAUACCACGAAAAGUACCCGACAACUACCAUCCUGAAGAAAAGAGC UGGUCGACAGCACAGACAAGGCAGACCUGAGACUGAUCUACCUGGCACUGGCA CACAUGAUCAAAGUUCAGAGGACACUUCUGAUCGAAGGAGACCUGAACCCGGA</p>	<p>26</p>

<p>具有起始和终止密码子的 Cas9 切口酶 mRNA ORF</p>	<p>CAACAGCGACGUCGACAAGCUGUUAUCCAGCUGGUCCAGACAUAACAACAGCU GUUCGAAGAAAACCCGAUCAACGCAAGCGGAGUCGACGCAAAGGCAAUCCUGA GCGCAAGACUGAGCAAGAGCAGAAGACUGGAAAACCUGAUCGCACAGCUGCCG GGAGAAAAGAAGAACGGACUGUUCGGAAAACCUGAUCGCACUGAGCCUGGGACU GACACCGAACUUAAGAGCAACUUCGACCUGGCAGAAGACGCAAAGCUGCAGC UGAGCAAGGACACAUACGACGACGACCUUGGACAACCUUGCUGGCACAGAUCCGGA GACCAGUACGCAGACCUGUUCUGGCAGCAAAGAACCUGAGCGACGCAAUCCUG CUGAGCGCAUCCUGAGAGUCAACACAGAAAUCACAAAGGCACCGCUGAGCGC AAGCAUGAUCAAGAGAUACGACGAAACCACCAGGACCUGACACUGCUGAAGG CACUGGUCAGACAGCAGCUGCCGGAAAAGUACAAGGAAAUCUUCUUCGACCA AGCAAGAACGGAUACGCAGGAUACAUCGACGGAGGAGCAAGCCAGGAAGAAUU CUACAAGUUAUCAAGCCGAUCCUGGAAAAGAUGGACGGAACAGAAGAACUGC UGGUAAGCUGAACAGAGAAGACCUGCUGAGAAAAGCAGAGAACAUCGACAAC GGAAGCAUCCCGCACCAGAUCCACCUGGGAGAACUGCAGCAAUCCUGAGAAGA CAGGAAGACUUCUACCCGUAUCUACGUCGGACCUGGCAAGAGGAAAACAGCA CCUGACAUCAGAAUCCCGUAUCUACGUCGGACCUGGCAAGAGGAAAACAGCA GAUUCGCAUGGAUGACAAGAAAGAGCGAAGAAAACAUCACACCCUGGAACUUC GAAGAAGUCGUCGACAAGGGAGCAAGCGCACAGAGCUUAUCGAAAAGAAUGAC AAACUUCGACAAGAACCUGCCGAACGAAAAGGUCCUGCCGAAGCACAGCCUGCU GUACGAUACUUCACAGUCUACAACGAACUGACAAAGGUCAAGUACGUCACAG AAGGAAUGAGAAAGCCGGCAUUCUGAGCGGAGAACAGAAGAAGGCAAUCGUC GACCUGCUGUUC AAGACAAAACAGAAAAGGUCACAGUCAAGCAGCUGAAGGAAAG CUACUUC AAGAAGAU CGAAUGCUUCGACAGCGUCGAAAUCAGCGGAGUCGAAAG ACAGAUUCAACGCAAGCCUGGGAAACAUAACCACGACCUGUGAAGACUAGCAAG GACAAGGACUUCUGGACAACGAAGAAAACGAAGACAUCUUGGAAGACAUCGU CCUGACACUGACACUGUUCGAAGACAGAGAAAUGAUCGAAGAAAAGACUGAAGA CAUACGCACACCUGUUCGACGACAAGGUCAUGAAGCAGCUGAAGAGAAGAAGA UACACAGGAUGGGGAAGACUUGAGCAGAAAAGCUGAUACAACGGAAUCAGAGACA GCAGAGCGGAAAGACA AUCCUGGACUUCUGAAGAGCGACGGAUUCGCAAACA GAAACUUC AUGCAGCUGAUCCACGACGACAGCCUGACA UUCAAGGAAGACAUC CAGAAGGCACAGGUCAGCGGACAGGGAGACAGCCUGCACGAACACAUCGCAAA CCUGGCAGGAAGCCCGCAAUCAAGAAGGGAAUCCUGCAGACAGUCAAGGUCG UCGACGAACUGGUC AAGGUCAUGGGAAGACACAAGCCGGAAAACUUCGUAUC GAAAUGGCAAGAGAAAACAGACAACACAGAAGGGACAGAAGAACAGCAGAGA AAGAAUGAAGAGAAUUCGAAGAAGGAAUC AAGGAAUCUGGGAAGCCAGAUCCUGA AGGAACACCCGGUCGAAAACACACAGCUGCAGAACGAAAAGCUGUACCUUAC UACUCGAGAACGGAAAGAGACAUGUACGUCGACCAGGAACUGGACAUCACAG ACUGAGCGACUACGACGUCGACCACAUCGUCCCGCAGAGCUUCUGAAGGACGA CAGCAUCGACAACAAGGUCCUGACAAGAAGCGACAAGAACAGAGGAAAGAGCG ACAACGUCCGAGCGAAGAAGUCGUCAAGAAGAUGAAGAACUACUGGAGACAG CUGCUGAACGCAAAGCUGAUACACAGAGAAAAGUUCGACAACCUGACA AAAGGC AGAGAGAGGAGGACUGAGCGAACUGGACAAGGCAGGAUUAUCAAGAGAGACAG UGGUCGAAAACAAGACAGAUCACAAAGCACGUCGACAGAUCCUGGACAGCAGA AUGAACACAAAGUACGACGAAAACGACAAGCUGAUCAAGAGAAGUCAAGGUCAU CACACUGAAGAGCAAGCUGGUCAGCGACUUCAGAAAAGGACUUCAGUUCUACA AGGUCAGAGAAAUCAACAACUACCACCACGCACACGACGCAUCCUGAAGGACGAG UCGUCGGAACAGCACUGAUCAAGAAGUACCCGAAGCUGGAAAAGCGAAUUCGUC UACGGAGACUACAAGGUCUACGACGUCAGAAAAGAU GAUCGCAAAGAGCGAACA GGAAUUCGAAAAGGCAACAGCAAAGUACUUCUUCUACAGCAACAUCAUGAACU UCUUC AAGACAGAAAUCACACUGGCAAAACGGAGAAAUCAGAAAGAGACC CGCUG AUCGAAAACAAACGGAGAAAACAGGAGAAAUCGUCUGGGACAAGGGAAGAGACUU CGCAACAGUCAGAAAAGGUCCUGAGCAUGCCCGCAGGUCAACAUCGUAAGAAGA CAGAAGUCCAGACAGGAGGAUUCAGCAAGGAAAAGCAUCCUGCCGAAGAGAAAC AGCGACAAGCUGAUUCGCAAGAAAAGGACUGGGACCCGAAGAAGUACGGAGG AUUCGACAGCCCGACAGUCGCAUACAGCGUCCUGGUCGUCGCAAAAGGUCGAAA AGGGAAAGAGCAAGAAGCUGAAGAGCGUCAAGGAACUGCUGGGAUUCACAAUC AUGGAAAGAAGCAGCUUCGAAAAGAACCCGAUCGACUUCUGGAAGCAAAGGG AUACAAGGAAGUCAAGAAGGACCUGAUCAUCAAGCUGCCGAAGUACAGCCUGU UCGAACUGGAAAACGGAAAGAAAGAGAAUGCUGGCAAGCGCAGGAGAACUGCAG AAGGGAAACGAACUGGCACUGCCGAGCAAGUACGUCAACUUCUGUACCUUGGC AAGCCACUACGAAAAGCUGAAGGGAAAGCCCGGAAGACAACGAACAGAAGCAGC UGUUCGUCGAACAGCACAAAGCACUACCUGGACGAAAUCAUCGAACAGAUACAGC GAAUUCAGCAAGAGAGUCAUCCUGGCAGACGCAAACCUUGACAAGGUCCUGAG CGAUACAACAAGCACAGAGACAAGCCGAUCAGAGAACAGGCAGAAAACAUCA UCCACCUGUUCACACUGACAAAACCUUGGGAGCACCCGGCAGCAUUAAGAUCUUCG ACACAACAUCGACAGAAAAGAUACAACAAGCACAAAGGAAGUCCUGGACGCA ACACUGAUCCACCAGAGCAUACAGGACUGUACGAAAACAAGAAUCGACCUGAG</p>	
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<p>使用如表3中所列的最小尿苷密码子编码SEQ ID NO: 25的Cas9切口酶编码序列(无起始或终止密码子;适于包括在融合蛋白质编码序列中)</p>	<pre>CCAGCUGGGAGGACGGAAGCGGAAGCCGAAAGAAGAAGAGAAAAGGUCGACG GAAGCCCGAAGAAGAAGAGAAAAGGUCGACAGCGGAUAG GACAAGAAGUACAGCAUCGACUGGCAAUCGGAACAAACAGCGUCGGAUUGGGC AGUCAUCACAGACGAAUACAAGGUCCCGAGCAAGAAGUUCAAGGUCCUGGGAA ACACAGACAGACACAGCAUCAAGAAGAACCUGAUCGGAGCACUGCGUUCGAC AGCGGAGAAAACAGCAGAAGCAACAAGACUGAAGAGAACAGCAAGAAGAAGUA CACAAGAAGAAGAACAGAAUCUGCUACCUGCAGGAAAUCUUCAGCAACGAAA UGGCAAAGGUCGACGACAGCUUCUCCACAGACUGGAAGAAAGCUUCCUGGUC GAAGAAGACAAGAAGCAGAAAGACACCCGAUCUUCGGAACAUUCGUCGACGA AGUCGCAUACCACGAAAAGUACCCGACAAUCUACCACCUGAGAAAGAAGCUGG UCGACAGCACAGACAAGGCAGACCUGAGACUGAUCUACCUGGCACUGGCACACA UGAUCAAGUUCAGAGGACACUUCUGAUCGAAGGAGACCUGAACCCGGACAAC AGCGACGUCGACAAAGCUGUUAUCCAGCUGGUCCAGACAUACACCAGCUGUUC GAAGAAAACCCGAUCAACGCAAGCGGAGUCGACGCAAAGGCAAUCCUGAGCGC AAGACUGAGCAAGAGCAAGACACUUGGAAAACCUGAUCGCACAGCUGCCGGAG AAAAGAAGAACGGACUGUUCGGAACCUGAUCGCACUGAGCCUGGGACUGACA CCGAACUUC AAGAGCAACUUCGACCUGGCAGAAGACGCAAAGCUGCAGCUGAG CAAGGACACAUACGACGACGACCUGGACAACCUGCUGGCACAGAUCGGAGACCA UJACGACACCUGUUCUGGCAGAAAGAACCUGAGCGACGCAAUCCUGAGCA GCGACAUCCUGAGAGUCAACACAGAAAUCACAAAGGCACCGCUGGACGCAAGC AUGAUCAAGAGAUACGACGAACACCACCAGGACCUGACACUGCUGAAGGCACU GGUCAGACAGCAGCUGCCGAAAAGUACAAGGAAAUCUUCUUCGACCAGAGCA AGAACGGAUACGCAGGAUCAUCGACGGAGGAGCAAGCCAGGAAGAUAUCUAC AAGUUAUCAAGCCGAUCCUGGAAAAGAUUGGACGGAACAGAAGAACCUGCUGGU CAAGCUGAACAGAGAAGACCUGCUGAGAAAAGCAGAGAACAUCGACAACGGAA GCAUCCCGCACAGAUCCACCUGGGAGAUCGACGCAAUCCUGAGAGAAGACAGG AAGACUUCUACCCGUUCUGAAGGACAACAGAGAAAAGAUUCGAAAAGAUCUUC ACAUUCAGAAUCCCGUACUACGUCGGACCCUGGCAAGAGGAAACAGCAGCAAU CGAUUGGAUGACAAGAAAGAGCGAAGAAAACAUCACACCCGUGGAACUUCGAA AAGUCGUCGACAAGGGAGCAAGCGCACAGAGCUUCAUCGAAAGAAGACAAAAC UUCGACAAGAACCUGCCGAACGAAAAGGUCCUGCCGAAGCACGCCUCGUGUAC GAAUACUUCACAGUCUACAACGAACUGACAAAAGGUCAAGUACGUCACAGAAGG AAUGAGAAAAGCCGGCAUCCUGAGCGGAGAACAAGAAAGGAAUCCUGCUGACC UGCUGUUAAGACAAAACAGAAAAGGUCACAGUCAAGCAGCUGAAGGAAGACUAC UUCAAGAAGAUUGAAUGCUUCGACAGCGUCGAAAUCAGCGGAGUCGAAGACAG AUUCAACGCAAGCCUGGGAACAUACCACGACCUGCUGAAGAUAUCAAAAGGACA AGGACUUCUGGACAACGAAGAAAACGAAGACAUCCUGGAAAGACAUUCGUCCUG ACACUGACACUGUUCGAAAGACAGAGAAAUGAUCGAAGAAGAAAGACUAGACAU CGCACACCUGUUCGACGACAAGGUCAUGAAGCAGCUGAAGAGAAGAAGAUACA CAGGAUUGGGAAAGACUGAGCAGAAAAGCUGAUAACGGAAUCAGAGACAAGCAG AGCGGAAAGACAACUCCUGGACUUCUGAAGAGCGACGGAUUCGCAAACAGAAA AUUCAUGCAGCUGAUCCACGACGACAGCCUGACAUUCAAGGAAGACGAGAA AGGCACAGGUCAGCGGACAGGGAGACGCCUGCACGAACACAUCGCAAACCUG GCAGGAAGCCCGCAAUCAAGAAGGGAAUCCUGCAGACAGUCAAGGUCUGCGA CGAACUGGUAAGGUCAUGGGAAGACACAAGCCGGAAAACAUCGUCUUCGAAA UGGCAAGAGAAAACAGACAACACAGAAGGGACAGAAGAACAGCAGAGAAAAGA AUGAAGAGAAUUCGAAGAAGGAAUCAAGGAAUCUGGGAAGCCAGAUCCGAAAG ACACCCGGUCGAAAACACACAGCUGCAGAACGAAAAGCUGUACCUUACUACCU GCAGAACGGAAGAGACAUUACGUCGACCAGGAACUGGACAUACAACAGACUGA GCGACUACGACGUCGACCACAUCGUCCCGCAGAGCUUCCUGAAGGACGACAGCA UCGACAACAAGGUCCUGACAAGAAGCGACAAGAACAGAGGAAAAGAGCGACAAC GUCCCGAGCGAAGAAGUCGUCACAAGAAGUAGAAGAACAUCUGGAGACAGCUGCU GAACGCAAAGCUGAUCACACAGAGAAAAGUUCGACAACCUGACAAAGGCAGAGA GAGGAGGACUGAGCGAACUGGACAAGGCAGGAUUAUCAAGAGACAGCUGGUC GAAACAAGACAGAUACAAAAGCACGUCGCACAGAUCCUGGACAGCAGAAUGAA CACAAAGUACGACGAAAACGACAAGCUGAUCAGAGAAGUCAAGGUCAUCACAC UGAAGAGCAAGCUGGUCAGCGACUUCAGAAAAGGACUUCAGUUCUACAAGGUC AGAGAAAUCAACAACUACCACCACGCACACGACGCAUACCUGAACGACAGUCGUC GGAACAGCACUGAUCAAGAAGUACCCGAAGCUGGAAAAGCGAAUUCGUCUACGG AGACUACAAGGUCUACGACGUCAGAAAAGAUAGUUCGAAAAGAGCGAACAGGAAA UCGGAAGGCAACAGCAAAAGUACUUCUUCUACAGCAACAUCAUGAACUUCUUC AAGACAGAAAUCACACUGGCAAACGGAGAAAUCAGAAAAGAGACCCGUGAUCGA AACAAACGGAGAAACAGGAGAAAUCGUCUGGGACAAGGGAAGAGACUUCGCAA CAGUCAGAAAAGGUCCUGAGCAUGCCGACAGUACAACUUCGUAAGAAGACAGAA GUCCAGACAGGAGAAUUCAGCAAGGAAAAGCAUCCUGCCGAAGAAACAGCGA CAAGCUGAUCGCAAGAAAAGGACUGGGACCCGAAGAAGUACGGAGGAUUCG ACAGCCCGACAGUCGCAUACAGCGUCCUGGUCGUCGCAAAGGUCGAAAAGGGA</pre>	<p>27</p>
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[0673]

	<p>AAGAGCAAGAAGCUGAAGAGCGUCAAGGAACUGCUGGGAAUCACAAUCAUGGA AAGAAGCAGCUUCGAAAAGAACCCGAUCGACUCCUGGAAGCAAAGGGAUACA AGGAAGUCAAGAAGGACCUGAUCAUCAAGCUGCCGAAGUACAGCCUGUUCGAA CUGGAAAACGGAAAGAAAGAGAAUGCUGGCAAGCGCAGGAGAACUGCAGAAGGG AAACGAACUGGCACUGCCGAGCAAGUACGUAACUCCUGUACCUGGCAAGCCCA CUACGAAAAGCUGAAGGGAAAGCCCGAAAGACAACGAACAGAAGCAGCUGUUCG UCGAACAGCACAAAGCACUACCUGGACGAAAUCAUCGAACAGAUACAGCGAAUUC AGCAAGAGAGUCAUCCUGGACAGCGCAAACCUGGACAAGGUCCUGAGCGCAUA CAACAAGCACAGAGACAAGCCGAUCAGAGAACAGGCAGAAAACAUCAUCCACC UGUUCACACUGACAAACCUGGGAGCACCGGCAGCAUUAAGUACUUCGACACA ACAAUCGACAGAAAGAGAUACACAAGCACAAAGGAAGUCCUGGACGCAACACU GAUCCACCAGAGCAUCACAGGACUGUACGAAACAAGAAUCGACCUGAGCCAGC UGGGAGGAGAC GGAAGCGGAAGCCCGAAGAAGAAGAGAAAAGGUCCGACGGAAGCCCGAAGAAGAA GAGAAAAGGUCCGACAGCGGA</p>	
<p>具有两个核定位信号作为C端氨基酸的dCas9的氨基酸序列</p>	<p>MDKKYSIGLAIGTNSVGWAVITDEYKVPSSKFKVLGNTDRHSIKKNLIGALLFDSGET AEATRLKRTARRRYTRRNRCYQLQEIFSNEMAKVDDSFHRLSEESFLVEEDKHERHP IFGNIVDEVAYHEKYPTIYHLRKKLVDSTDKADLRLLIYLAALAHMIKFRGHFLIEGDLNP DNSDVKLFIQLVQTYNQLFEENPINASGVDAKAILSARLSKSRRENLIQPLGKKN GLFGNLIASLGLTPNFKSNFLAEDAKLQLSKDTYDDDLNLLAQIGDQYADLFLAA KNLSDAILLSDILRVNTEITKAPLSASMIKRYDEHHQDLTLLKALVRQQLPEKYKEIFFD QKNGYAGYIDGGASQEFYKFIKPILEKMDGTEELVYKLNREDLLRQRTFDNGSIPH QIHLGELHAILRRQEDFYFPLKDNREKIEKILTFRIPYYVGPLARGNSRFAMTRKSEET ITPWNFEEVVDKGAASQSFIERMTNFDKLPNEKVLPHSLLYEYFTVYNELTKVYV TEGMRKPAFLSGEQKKAIVDLLFKTNRKVTVKQLKEDYFKKIECFDSVEISGVEDRFN ASLGTYHDLLKIKDKDFLDNEENEDILEDIVLTLTLFEDREMIEERLKYAHLFDDKV MKQLKRRRYTGWGRLSRKLINGIRDKQSGKTILDFLKSDFANRNFMLIHDDSLTFK EDIQKAQVSGGDSLHEHIANLAGSPAIAKKGILQTVKVVDELVKVMGRHKPENIVEM ARENQTTQKGGKNSRMRKRIEIGIKELGSQILKEHPVENTQLQNEKLYLYLQNGRD MYVDQELDINRLSDYDVAIVPQSFLKDDSIDNKVLRSDKNRKGSDNVPSEEVKK MKNYWRQLLNAKLITQRKFDNLTKAERGGLSELDKAGFIKRLVETROITKHVAQILD SRMNTKYDENDKLIREVKVITLKSCLVSDFRKDFQFYKREINNYHHAHDAYLNAV GTALIKKYPKLESEFVYGDYKVVYDVRKMIKSEIQAATAKYFFYSNMNFFKTEITL ANGEIRKRPLIETNGETGEIVWDKGRDFATVRKVLVSMQVNVKKTVEVQTGGFSKESIL PKRNSDKLIARKKDWDPKKYGGFDSPTVAYSVLVVAKEKGSKLLKSVKELLGITIM ERSSEFKNPIDFLEAKGYKEVKKDLIKLPKYSLFELENGRKRMLASAGELQKGNELAL PSKYVNFYLAHYEKLKSPEDNEQKQLFVEQHKHYLDEIIEQISEFSKRVLADANL DKVLSAYNKHARDKPIREQAENIHLFTLTNLGAPAAFKYFDTTIDRKRYTSTKEVLDT LIHQSTGLYETRIDLSQLGGDGSGPSKPKKRVKVDGSPKPKKRVDSG</p>	<p>28</p>
<p>使用如表3中所列的最小尿苷密码子编码SEQ ID NO: 28的, 具有起始和终止密码子的dCas9 mRNA ORF</p>	<p>AUGGACAAGAAGUACAGCAUCGGACUGGCAAUCGGAACAAACAGCGUCGGAUG GGCAGUCAUCACAGACGAAUACAAGGUCCGAGCAAGAAGUUCGAAAGGUCCUGG GAAACACAGACAGACACAGCAUCAAGAAGAACCUGAUCGGAGCAGCUGCUGUUC GACAGCGGAGAAACAGCAGAAGCAACAAGACUGAAGAGAACAGCAAGAAGAAG AUACACAAGAAGAAAGAACAGAAUCUGCUACCUGCAGGAAAUCUUCAGCAACG AAAUGGCAAAGGUCGACGACAGCUUCUUCACAGACUGGAAGAAAGCUUCCUG GUCGAAGAAGACAAGAAGCACGAAAAGACACCCGAUCUUCGGAACAAUCGUCGA CGAAGUCGCAUACCACGAAAAGUACCCGACAAUCUACCACUGAGGAAAGAACGC UGGUCGACAGCACAGACAAGGCAGACCUGAGACUGAUCUACCUGGCACUGGCA CACAUGAUCAGUUCAGAGGACACUCCUGAUCGAAGGAGACCUGAACCCGGA CAACAGCGACGUCGACAAGCUGUUAUCCAGCUGGUCCAGACAUAACAACAGCU GUUCGAAGAAAACCCGAUCAACGCAAGCGGAGUCGACGCAAAGGCAAUCCUGA GCGCAAGACUGAGCAAGAGCAGAAGACUGGAAAACCUGAUCGCACAGCUGCCG GGAGAAAAGAAGAACGGACUGUUCGGAACCUGAUCGCACUGAGCCUGGGACU GACACCGAACUUCAGAGCAACUUCGACCUCCGAGAAAGACGCAAAGCUGCAGC UGAGCAAGGACACAUACGACGACGACCUGGACAACCUGCUGGCACAGAUCCGGA GACCAGUACGACAGCCUGUUCUGGACGAAAGAACCUGAGCGACGCAAUCCUG CUGAGCGACAUCUGAGAGUCAACACAGAAAUCACAAAGGCACCGCUGAGCGC AAGCAUGAUCAGAGAUACGACGAAACACCACCAGGACCUGACACUGCUGAAGG CACUGGUCAGACAGCAGCUGCCGAAAAGUACAAGGAAAUCUUCUUCGACAGCAG AGCAAGAACGGAUACGACAGGAUCAUCGACGAGGAGCAAGCCAGGAAGAAU CUACAAGUUCAUCAAGCCGAUCCUGGAAAAGAUGGACGGAACAGAAGAACUGC UGGUAAGCUGAACAGAGAAGACCUGCUGAGAAAAGCAGAGAACAUCGACAAC GGAAGCAUCCGACAGAGAUCCACCUGGGAGAACUGCAGCAAUCCUGAGAAGA CAGGAAGACUUCUACCCGUUCUGAAGGACAACAGAGAAAAGAUCCGAAAAGAU CCUGACAUUCAGAAUCCCGUACUACGUCGACCGCUGGCAAGGAAACAGCA GAUUCGCAUGGAUGACAAGAAAGAGCGAAGAAACAUCACACCGUGGAACUUC GAAGAAGUCGUCGACAAGGGAGCAAGCGCACAGAGCUUCAUCGAAAGAAUGAC</p>	<p>29</p>

[0674]

	AAACUUCGACAAGAACCUGCCGAACGAAAAGGUCCUGCCGAAGCACAGCCUGCU GUACGAUACUUCACAGUCUACAACGAACUGACAAAGGUCAAGUACGUCACAG AAGGAAUGAGAAAGCCGGCAUUCUUGAGCGGAGAACAGAAGAAGGCAAUCGUC GACCUUGCUGUUCACAGACAAACAGAAAAGGUCACAGUCAAGCAGCUGAAGGAAAG CUACUUCACAGAAGAUUCGAAUGCUUCGACAGCGUCGAAAUCAGCGGAGUCGAA ACAGAUUCAACGCAAGCCUGGGAAACAUACCACGACCUGCUGAAGAUCAUCAAG GACAAGGACUUCUUGGACAACGAAGAAAACGAAGACAUCUUGGAAGACAUCGU CCUGACACUGACACUGUUCGAAGACAGAGAAAUGAUCGAAGAAAAGACUGAAGA CAUACGCACACCUGUUCGACGACAAGGUCAUGAAGCAGCUGAAGAGAAGAAGA UACACAGGAUUGGGGAAGACUGAGCAGAAAAGCUGAUCAACGGAAUCAGAGACAA GCAGAGCGGAAAGACAUCUUGGACUUCUGAAGAGCGACGGAUUCGCAAAACA GAAACUUCACAGCUGAUCCACGACGACAGCCUGACAUUCAGGAAGACAUC CAGAAGGCACAGGUCAGCGGACAGGGAGACAGCCUGCACGAACACAUCGCAAA CCUGGCAGGAAGCCCAGCAUCAAGAAGGGAAUCCUGCAGACAGUCAAGGUCG UCGACGAACUGGUCACAGGUCUUGGGAAAGACACAAGCCGAAAACAUUCGUAUC GAAAUGGCAAGAGAAAACCAGACAACACAGAAGGGACAGAAGAACAGCAGAGA AAGAAUGAAGAGAAUUCGAAGAAGGAAUCAGGAACUGGGAAAGCCAGAUCUGA AGGAACACCCGGUCGAAAACACACAGCUGCAGAACGAAAAGCUGUACUCCUGUAC UACCGGAGAACGGAAAGAGACAUGUACGUCGACCAGGAACUGGACUACCAAG ACUGAGCGACUACGACGUCGACGCAAUUCGUCCCGCAGAGCUUCUGAAGGACGA CAGCAUCGACAACAAGGUCCUGACAAGAAGCGACAAGAACAGAGGAAAGAGCG ACAACGUCCGAGCGAAGAAGUCGUCAAGAAGAUGAAGAACUACUGGAGACAG CUGCUGAACGCAAAGCUGAUACACAGAGAAAAGUUCGACAACCUGACAAAAGGC AGAGAGAGGAGGACUGAGCGAACUGGACAAGGCAGGAUUAUCAAGAGACAGC UGGUCGAAACAAGACAGAUACAAAAGCAGUCGACAGAUCCUGGACAGCAGA AUGAACACAAAGUACGACGAAAACGACAAGCUGAUCAGAGAAGUACAAGGUCAU CACACUGAAGAGCAAGCUGGUCAGCGACUUCAGAAAAGGACUUCAGUUCUACA AGGUCAGAGAAAUCAACAACUACCACCACGACACGACGCAUACCUAGAACGCGAG UCGUCGGAACAGCACUGAUCAAGAAGUACCCGAAGCUGGAAAGCGAAUUCGUC UACGGAGACUACAAGGUCUACGACGUCAGAAAAGAUCAUCGCAAAGAGCGAACA GGAAUUCGAAAGGCAACAGCAAAGUACUUCUUCUACAGCAACAUCAUGAACU UCUUCACAGAGAAAUCACACUGGCAAAACGGAGAAAUCAGAAAGAGACCAGCUG AUCGAAAACAACGGAGAAAACAGGAGAAAUCGUCUGGGACAAGGGAAGAGACUU CGCAACAGUCAGAAAAGGUCCUGAGCAUGCCCGCAGGUAACAUCGUAAGAAGA CAGAAGUCCAGACAGGAGGAUUCAGCAAGGAAAGCAUCCUGCCGAAGAGAAAAC AGCGACAAGCUGAUCGCAAGAAAAGGACUGGGACCCGAAGAAGUACGGAGG AUUCGACAGCCGACAGUCGCAUACAGCGUCCUGGUCGUCGCAAAGGUCGAAA AGGGAAAGAGCAAGAAGCUGAAGAGCGUCAAGGAACUGCUGGGAAUCACAAUC AUGGAAAGAAGCAGCUUCGAAAAGAACCCGAUCGACUUCUUGGAAGCAAAGGG AUACAAGGAAGUCAAGAAGGACCUCAUCAUCAAGCUGCCGAAGUACAGCCUGU UCGAACUGGAAAACGGAAAGAAAGAGAAUGCUGGCAAGCGCAGGAGAACUCGAG AAGGAAACGAAACUGGCAUCGCCGAGCAAGUACGUAACUUCUUCGUAACUGGC AAGCCACUACGAAAAGCUGAAGGGAAAGCCGGAAGACAACGAACAGAAGCAGC UGUUCGUCGAACAGCACAAAGCACUACCUGGACGAAAUCAUCGAACAGAUACAGC GAAUUCAGCAAGAGAGUCAUCCUGGACAGCAGCAAAACCUUGGACAAGGUCCUGAG CGAUACAACAAGCACAGAGACAAGCCGAUCAGAGAACAGGCAGAAACAUCA UCCACCUUUCACACUGACAAAACCUUGGGAGCACCCGGCAGCAUUAAGAUAUCG ACACAACAUCGACAGAAAAGAGAUACAACAAGCACAAAGGAAGUCCUGGACGCA ACACUGAUCCACCAGAGCAUCACAGGACUGUACGAAAACAAGAAUCGACCUGAG CCAGCUGGGAGGAGAC GGAAGCGGAAGCCCAGAAAGAAAGAGAAAAGGUCGACGGAAGCCCAGAAAGAA GAGAAAGGUCGACAGCGGAUAG	
使用如表3 中所列的 最小尿苷 密码子编 码SEQ ID NO: 28的 dCas9编码 序列(无起 始或终止 密码子;适	GACAAGAAGUACAGCAUCGGACUGGCAAUUCGGAACAAACAGCGUCGGAUUGGGC AGUCAUCACAGACGAAUACAAGGUCCCGAGCAAGAAGUUCAGGUCCUGGGAA ACACAGACAGACACAGCAUCAAGAAGAACCUGAUCGGAGCACUUCGUGUUCGAC AGCGGAGAAAACAGCAGAAGCAACAAGACUGAAGAGAACAGCAAGAAGAAGAU CACAAGAAGAAGAACAGAAUUCGCUACCUGCAGGAAAUCUUCAGCAACGAAA UGGCAAAGGUCGACGACAGCUUCUCCACAGACUGGAAGAAAAGCUUCUUGGUC GAAGAAGACAAGAAGCACGAAAAGACACCCGAUCUUCGGAACAUCGUCGACGA AGUCGCAUACCAGAAAAGUACCCGACAAUCUACCACUGAGAAAAGAAAGCUGG UCGACAGCACAGACAAGGCAGACCUGAGACUGAUCUACCUGGCACUGGCACACA UGAUCAAAGUUCAGAGGACAUUCUUGAUCGAAGGAGACCUGAACCCGGACAAC AGCGACGUCGACAAGCUGUUAUCCAGCUGGUCCAGACAUACAACCAGCUGUUC GAAGAAAACCCGAUCAACGCAAGCGGAGUCGACGCAAAGGCAAUCCUGAGCGC AAGACUGAGCAAGAGCAGCAAGACUUGGAAAACCUGAUCGCACAGCUGCCGGAG AAAAGAAGAACGGACUGUUCGGAACCUGAUCGCACUGAGCCUGGGACUGACA CCGAACUUCAAAGAGCAACUUCGACCUGGCAGAAGACGCAAAGCUGCAGCUGAG	30

[0675]

<p>于包括在融合蛋白质编码序列中)</p>	<p>CAAGGACACAUACGACGACGACCUGGACAACCUGCUGGCACAGAUCGGAGACCA GUACGCAGACCUGUUCUGGCAGCAAAGAACCUGAGCGACGCAAUCCUGCUGA GCGACAUCCUGAGAGUCAACACAGAAAUCACAAAGGCACCGCUGAGCGCAAGC AUGAUCAAGAGAUACGACGAAACACCACCAGGACCUGACACUGCUGAAAGGCACU GGUCAGACAGCAGCUGCCGGAAAAGUACAAGGAAAUCUUCUUCGACCAGAGCA AGAACGGAUACGCAGGAUACAUCGACGAGGAGCAAGCCAGGAAGAAUUCUAC AAGUUAUCAAGCCGAUCCUGGAAAAGAUUGGACGGAACAGAAGAACUUCUGGU CAAGCUGAACAGAGAAGACCUGCUGAGAAAAGCAGAGAACAUCGACAACGGAA GCAUCCCGCACCAGAUCCACCUGGGAGAUCGACGCAAUCCUGAGAAGACAGG AAGACUUCUACCCGUUCUGAAGGACAACAGAGAAAAGAUUCGAAAAGAUCCUG ACAUUCAGAAUCCCGUACUACGUCGGACCGCUGGCAAGAGGAAACAGCAGAUU CGAUGGAUGACAAGAAAGAGCGAAGAAAACAUCACACCGUGGAACUUCGAAG AAGUCGUCGACAAGGGAGCAAGCGCACAGAGCUUAUCGAAAGAAUGACAAC UUCGACAAGAACCUGCCGAACGAAAAGGUCCUGCCGAAGCACAGCCUGCUGUAC GAAUACUUCACAGUCUACAACGAACUGACAAGGUACAAGUACGUCACAGAAAG AAUGAGAAAGCCGGCAUUCUGAGCGGAGAACAGAAGAAGGCAUUCGUCGACC UGCUGUUAAGACAAACAGAAAGGUCACAGUCAAGCAGCUGAAGGAAGACUAC UUCAAGAAGAUUGCUUCGACAGCGUCGAAAUCAGCGGAGUCGAAGACAG AUUCAACGCAAGCCUGGGAACUACCACGACCUGCUGAAGAUAUCAAGGACA AGGACUUCUGGACAACGAAGAAAACGAAGACAUCUGGAAGACAUCGUCCUG ACACUGACACUGUUCGAAGACAGAGAAAUGAUCGAAGAAAGACUGAAGACAU CGCACACCUGUUCGACGACAAGGUCAUGAAGCAGCUGAAGAGAAGAAGAUACA CAGGAUGGGGAAGACUGAGCAGAAAAGCUGAUCAACGGAAUCAGAGACAAGCAG AGCGGAAAGACAUCUCCUGGACUUCUGAAGAGCGACGGAAUUCGUAACGAAA CUUCAUGCAGCUGAUCCACGACGACAGCCUGACAUCUUAAGGAAGACAUCAG AGGCACAGGUCAGCGGACAGGGAGACAGCCUGCACGAACACUCCGAAACCUG GCAGGAAGCCCGCAAUCAAGAAGGGAAUCCUGCAGACAGUCAAGGUCGUCGA CGAACUGGUAAGGUCUUGGGAAGACACAAGCCGGAAAACAUCGUAUCGAAA UGGCAAGAGAAAACAGACAACACAGAAAGGACAGAAAGAACAGCAGAGAAAAG AUGAAGAGAAUCGAAGAAGGAUACAAGGAACUGGGAAGCCAGAUCCUGAAGGA ACACCCGGUCGAAAACACACAGCUGCAGAACGAAAAGCUGUACCUUGUACUACCU GCAGAACGGAAGAGACAUGUACGUCGACCAGGAACUGGACAUCAACAGACUGA GCGACUACGACGUCGACGCAAUUCGUCCCGCAGAGCUUCUGAAGAGCAGACGA UCGACAACAAGGUCCUGACAAGAAGCGACAAGAACAGAGGAAAGAGCGACAAC GUCCCGAGCGAAGAGUCGUAAGAAGAUUAAGAAUCUACUGGAGACAGCUGCU GAACGCAAAGCUGAUCACACAGAGAAAAGUUCGACAACCUGACAAAGGCAGAGA GAGGAGACUGAGCGAACUGGACAAGGCAGGAUUAUCAAGAGACAGCUGGUC GAAACAAGACAGAUACAAGCAGCAGCAGAUCCUGGACAGCAGAAUUGAA CACAAAGUACGACGAAAACGACAAGCUGAUCAGAGAAGUCAAGGUCAUCACAC UGAAGAGCAAGCUGGUCAGCGACUUCAGAAAAGGACUUCAGUUCUACAAGGUC AGAGAAAUCAACAACUACCACCACGACACGCAUACCUGAACGACGUCGUC GGAACAGCAGUACAAGAGUACCCGAAGCUGGAAAGCGAAUUCGUCUACGG AGACUACAAGGUCUACGACGUCAGAAAAGAUAGUACGCAAAGAGCGAACAGGAAA UCGGAAGGCAACAGCAAAGUACUUCUUCUACAGCAACAUCUAGAACUUCUUC AAGACAGAAUACACUUGGCAAACCGGAGAAAUCAGAAAGAGACCGCUGAUCGA AACAAACGGAGAAAACAGGAGAAAUCGUCUGGGACAAGGGAAGAGACUUCGCAA CAGUCAGAAAGGUCCUGAGCAUGCCGACAGGUAACAUCGUCUACAAGAGACAGAA GUCCAGACAGGAGGAUUCAGCAAGGAAAGCAUCCUGCCGAAGAGAAACAGCGA CAAGCUGAUCGCAAGAAAGAAAGGACUGGGACCCGAAGAAGUACGGAGGAUUCG ACAGCCCGACAGUCGCAUACAGCGUCCUGGUCGUCGCAAAGGUCGAAAAGGGA AAGAGCAAGAAGCUGAAGAGCGUCAAGGAACUGCUGGGAAUCAACAUCUUGGA AAGAAGCAGCUUCGAAAAGAACCCGAUCGACUUCUUGGAAGCAAAGGGAUACA AGGAAGUCAAGAAGGACCUGAUCAUCAAGCUGCCGAAGUACAGCCUGUUCGAA CUGGAAAACGGAAGAAAGAGAUGCUGGCAAGCGCAGGAGAACUGCAGAAGGG AAACGAACUGGCACUGCCGAGCAAGUACGUAACUUCUUGUACUGGCAAGGCAAGCA CUACGAAAAGCUGAAGGGAAAGCCCGAAAGACAACGAACAGAAGCAGCUGUUCG UCGAACAGCACAAGCACUACCUGGACGAAAUCAUCGAACAGAUACAGCGAAUUC AGCAAGAGAGUCAUCCUGGACAGCGCAAACCUGGACAAGGUCCUGAGCGCAUA CAACAAGCACAGAGACAAGCCGAUCAGAGAACAGGCAGAAAACAUCAUCCACC UGUUCACACUGACAACCCUGGGAGCACCCGGCAGCAUUAAGUACUUCGACACA ACAAUCGACAGAAAGAGAUACACAAGCACAAAAGGAAGUCCUGGACGCAACACU GAUCCACCAGAGCAUCACAGGACUGUACGAAACAAGAAUCGACCUGAGCCAGC UGGGAGGAGAC GGAAGCGGAAGCCCGAAGAAGAAGAGAAAAGGUCGACGGAAGCCCGAAGAAGAA GAGAAAGGUCCAGCGGA</p>	
<p>T7启动子</p>	<p>TAATACGACTCACTATA</p>	<p>31</p>

[0676]

人类β-血球蛋白5' UTR	ACATTTGCTTCTGACACAACCTGTGTTCACTAGCAACCTCAAACAGACACC	32
人类β-血球蛋白3' UTR	GCTCGCTTTCTTGCTGTCCAATTTCTATTAAGGTTCCCTTTGTTCCCTAAGTCCAACCTACTAAACTGGGGGATATTATGAAGGGCCTTGAGCATCTGGATTCTGCCTAATAAAAAACATTTATTTTCATTGC	33
人类α-血球蛋白5' UTR	CATAAACCTGGCGCGCTCGCGGCCCGGCACTCTTCTGGTCCCCACAGACTCAGAGAGAACCACC	34
人类α-血球蛋白3' UTR	GCTGGAGCCTCGGTGGCCATGCTTCTTGCCCTTGGGCCTCCCCCAGCCCTCCTCCCCTTCTGCACCCGTACCCCGTGGTCTTTGAATAAAGTCTGAGTGGGCGGC	35
有爪蟾β-血球蛋白5' UTR	AAGCTCAGAATAAACGCTCAACTTTGGCC	36
有爪蟾β-血球蛋白3' UTR	ACCAGCCTCAAGAACACCCGAATGGAGTCTCTAAGCTACATAATACCAACTTACACTTTACAAAATGTTGTCACCCAAAATGTAGCCATTCGTATCTGCTCCTAATAAAAAAGAAAGTTTCTTCACATTCT	37
牛生长激素5' UTR	CAGGGTCCTGTGGACAGCTCACCAGCT	38
牛生长激素3' UTR	TTGCCAGCCATCTGTTGTTTGGCCCTCCCCGTGCCTTCTTGACCCTGGAAGGTGCACCTCCCCTGTCTTTCTAATAAAAATGAGGAAATTGCATCGCA	39
小家鼠血红蛋白α, 成年链1 (Hba-1), 3' UTR	GCTGCCTTCTGCGGGGCTTGCCCTTCTGGCCATGCCCTTCTTCTCCCTTGACCTGTACCTCTTGGTCTTTGAATAAAGCCTGAGTAGGAAG	40
HSD17B4 5' UTR	TCCCGCAGTCGGCGTCCAGCGGCTCTGCTTGTTCGTGTGTGTGTCGTTGCAGGCCTTATTC	41
靶向TTR的G282引导RNA	mU*mU*mA*CAGCCACGUCUACAGCAGUUUUAGAmGmCmUmAmGmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmUmGmCmU*mU*mU*mU	42
具有HSD的5' UTR、对应于SEQ ID NO: 4的ORF、Kozak序列及ALB的3' UTR的Cas9转录物	GGGTCCCGCAGTCGGCGTCCAGCGGCTCTGCTTGTTCGTGTGTGTGTCGTTGCAGGCCTTATTTCGGATCCGCCACCATGGACAAGAAGTACAGCATCGGACTGGACATCGGAACAAACAGCGTCGGATGGGCAGTCATCACAGACGAATACAAGGTCCCAGCAAGAAGTTCAAGGTCCTGGGAAACACAGACAGACACAGCATCAAGAAGAACCCTGATCGGAGCACTGCTGTCGACAGCGGAGAAACAGCAGAAGCAACAAGACTGAAGAGAACAGCAAGAAGAAGATACACAAGAAGAAAAGAACAAGAATCTGCTACCTGCAGGAAATCTCAGCAACGAAATGGCAAAGGTCGACGACAGCTTCTTCCACAGACTGGAAGAAAAGCTTCTGGTCAAGAAAGACAAGAAGCAGCAAGACACCCGATCTTCGGAACATCGTCGACGAAGTCGCATACCACGAAAAGTACCCGACAATCTACCACCTGAGAAAAGAAGCTGGTCGACAGCACAGACAAGGCAGACCTGAGACTGATCTACCTGGCACTGCACACATGATCAAGTTCAGAGGACACTTCTGATCGAAGGAGACCTGAACCCGGAACAACAGCGACGTCGACAAGCTGTTTATCCAGCTGGTCCAGACATACAACCAGCTGTTCGAAGAAAACCCGATCAACGCAAGCGGAGTCGACGCAAGGCAATCCTGAGCGCAAGACTGAGCAAGAGCAGAAGACTGGAAAACCTGATCGCACAGCTGCCGGGAGAAAAGAAGAACGGACTGTTTCGAAAACCTGATCGCACTGAGCCTGGGACTGACACCGAACTTCAAGAGCAACTTCGACCTGGCAGAAGACGCAAGCTGCAGCTGAGCAAGGACACATACGACGACGACCTGGACAACCTGCTGGCACAGATCGGAGACCAGTACGCAGACCTGTTCTGCGAGCAAAGAACCTGAGCGACGCAATCCTGCTGAGCGACAT	43

[0677]

	<p>CCTGAGAGTCAACACAGAAATCACAAAGGCACCGCTGAGCGCAAGCATGATCAAG AGATACGACGAAACACCACCAGGACCTGACACTGCTGAAGGCACTGGTCAGACAGC AGCTGCCGAAAAGTACAAGGAAATCTTCTTCCGACCAGAGCAAGAACGGATACGC AGGATACATCGACGGAGGAGCAAGCCAGGAAGAATTCTACAAGTTCATCAAGCCG ATCCTGGAAAAGATGGACGGAAACAGAAGAAGCTGCTGGTCAAGCTGAACAGAGAA GACCTGCTGAGAAAAGCAGAGAAACATTGACAACCGAAAGCATCCCGCACAGATCC ACCTGGGAGAACTGCACGCAATCCTGAGAAGACAGGAAGACTTCTACCCGTTTCT GAAGGACAACAGAGAAAAGATCGAAAAGATCCTGACATTCAGAATCCCGTACTAC GTCGGACCGCTGGCAAGAGGAAAACAGCAGATTCGCATGGATGACAAGAAAAGAGC GAAGAAACAATCACACCGTGGAACTTCGAAGAAGTCTGACGACAAGGGAGCAGC GCACAGAGCTTCATCGAAAAGATGACAAAACCTTCGACAAGAACCTGCCGAACGAAA AGGTCCTGCCGAAGCACAGCCTGCTGTACGAATACTTCACAGTCTACAACGAACTG ACAAAGGTCAAGTACGTCACAGAAGGAATGAGAAAAGCCGGCATTCTTGAGCGGAG AACAGAAGAAGGCAATCGTCGACCTGCTGTTCAAGACAAAACAGAAAAGGTACAGT CAAGCAGCTGAAGGAAGACTACTTCAAGAAGATCGAATGCTTCGACAGCGTCGAA ATCAGCGGAGTCGAAGACAGATTCAACGCAAGCCTGGGAACATAACCAGACCTGC TGAAGATCATCAAGGACAAGGACTTCTTGACAACGAAGAAAACGAAGACATCCT GGAAGACATCGTCTGACACTGACACTGTTCTGAAGACAGAGAAATGATCGAAGAA GACTGAAGACATACGCACACCTGTTCTGACGACAAGGTCATGAAGCAGTCAAGGTG GAAGAAGATACACAGGATGGGGAAGACTGAGCAGAAAAGCTGATCAACGGAAATCA GAGACAAGCAGAGCGGAAAGACAATCCTGGACTTCTGAAGAGCGACGGATTTCG AAACAGAAAACCTCATGCAGCTGATCCACGACGACAGCCTGACATTCAGGAAGAC ATCCAGAAGGCACAGGTGACGGGACAGGGAGACAGCCTGCACGAACACATCGCA AACCTGGCAGGAAGCCCGGCAATCAAGAAGGGAATCTGACAGACAGTCAAGGTTCG TCGACGAACTGGTCAAGGTTCATGGGAAGACACAAGCCGGAAAACATCGTTCATCGA AATGGCAAGAGAAAACAGACAACACAGAAGGGACAGAAGAAGCAGCAGAGAAA GAATGAAGAGAATCGAAGAAGGAATCAAGGAACTGGGAAGCCAGATCCTGAAGG AACACCCGGTCGAAAACACACAGCTGCAGAACGAAAAGCTGTACTCTGACTACTCT GCAGAACGGAAGAGACATGTACGTCGACCAGGAACTGGACATCAACAGACTGAGC GACTACGACGTCGACCACATCGTCCCGCAGAGCTTCTGAAGGACGACAGCATCG ACAACAAGGTCTGACAAGAAGCGACAAGAACAGAGGAAAGAGCGACAACGTCC CGAGCGAAGAAGTCTGTAAGAAGATGAAGAATACTGGAGACAGCTGCTGAACG CAAAGCTGATCACACAGAGAAAGTTTCGACAACCTGACAAAAGGCAGAGAGAGGAG GACTGAGCGAACTGGACAAGGCAGGATTCATCAAGAGACAGCTGGTTCGAAAACA GACAGATCAAAAAGCACGTCGCACAGATCCTGGACAGCAGAATGAACACAAAAGTA CGACGAAAACGACAAGCTGATCAGAGAAGTCAAGGTTCATCACACTGAAGAGCAA CTGGTCAGCGACTTCAGAAAAGGACTTCCAGTTCTACAAGGTCAGAGAAAATCAAC AACTACCACCACGCACACGACGCATACCTGAACGCAGTCGTCGGAACAGCACTGA TCAAGAAGTACCCGAAGCTGGAAAGCGAATTCGTCTACGGAGACTACAAGGTCTA CGACGTCAGAAAAGATGATCGCAAAGAGCGAACAGGAAATCGGAAAAGGCAACAGC AAAGTACTTCTTCTACAGCAACATCATGAACCTTCTTCAAGACAGAAATCACACTGG CAAACGGAGAAAATCAGAAAAGAGACCCGCTGATCGAAAACAAAACGGAGAAAACAGGAG AAATCGTCTGGGACAAGGGAAGAGACTTCGCAACAGTCAGAAAAGGTCTGAGCAT GCCCGAGGTCAACATCGTCAAGAAGACAGAAGTCCAGACAGGAGGATTACAGCAA GGAAAGCATCCTGCCGAAGAGAAAACAGCGACAAGCTGATCGCAAGAAAAGAAAGGA TGGGACCCGAAAGAAGTACGGAGGATTTCGACAGCCCGACAGTTCGATACAGGTC CTGGTCTGCAAAAGGTTCGAAAAGGGAAGAGCAAGAAGCTGAAGAGCGTCAAG GAACTGCTGGGAATCACAAATCATGGAAAAGAGCAGCTTCGAAAAGAACCCGATCG ACTTCTGGAAGCAAAGGGATACAAGGAAGTCAAGAAGGACCTGATCATCAAGCT GCCGAAGTACAGCCTGTTTCAACTGGAAAACGGAAGAAAAGAGAATGCTGGCAAG CGCAGGAGAAGTGCAGAAGGGAAAACGAACTGGCACTGCCGAGCAAGTACGTCAA TTCTCTGTACTTGGCAAGCCACTACGAAAAGCTGAAGGGAAGCCCGGAAGACAAC GAACAGAAGCAGCTGTTCTGTCGAACAGCACAAGCACTACCTGGACGAAATCATCG AACAGATCAGCGAATTCAGCAAGAGAGTTCATCCTGGCAGACGCAAACTGGACAA GGTCTGAGCGCATAACAAGCACAGAGACAAGCCGATCAGAGAACAGGCAAGCAGC AAACATCATCCACCTGTTCAACTGACAAAACCTGGGAGCACCAGGAGCATTCAAGT ACTTCGACACAACAATCGACAGAAAGAGATACACAAGCACAAAAGGAAGTCTGGA CGAACACTGATCCACCAGAGCATCACAGGACTGTACGAAAACAAGAATCGACCTG AGCCAGCTGGGAGGAGACGGAGGAGGAAGCCGAAAGAAGAAGAGAAAAGGTCTA GCTAGCCATCACATTTAAAAGCATCTCAGCCTACCATGAGAATAAGAGAAAAGAAA TGAAGATCAATAGCTTATTCATCTCTTTTTCTTTTTCTGTTGGTGTAAAAGCCAACCCC TGCTAAAAAACATAAATTTCTTAAATCATTTGCCTCTTTTCTGTGCTTCAATTA TAAAAATGAAAAGAACCTCGAG</p>	
<p>具有HSD 的 5'</p>	<p>GGGTCCCGCAGTCGGCGTCCAGCGGCTCTGCTTGTTCGTGTGTGTGCTGTCAGG CCTTATTCGGATCCATGGACAAGAAGTACAGCATCGGACTGGACATCGGAACAAAC AGCGTCCGATGGGAGTTCATCACAGACGAATACAAGGTCCCGAGCAAGAAGTTCA AGGTCCTGGGAAAACAGACAGACACAGCATCAAGAAGAAGCTGATCGGAGCACT</p>	<p>44</p>

<p>UTR, 对应于SEQ ID NO: 4 的 ORF 及 ALB 的 3' UTR 的 Cas9 转录物</p>	<p>GCTGTTTCGACAGCGGAGAAACAGCAGAAGCAACAAGACTGAAGAGAACAGCAAG AAGAAGATACACAAGAAGAAAAGAACAGAATCTGCTACCTGCAGGAAATCTTCAGC AACGAAATGGCAAAGGTCGACGACAGCTTCTTCCACAGACTGGAAGAAAGCTTCC TGGTCGAAAGAGACAAGAAGCAGCAAGAACACCCGATCTTCGAAACATCGTCGA CGAAGTCGCATACCACGAAAAGTACCCGACAATCTACCACCTGAGAAAAGACTG GTCGACAGCACAGACAAGGCAGACCTGAGACTGATCTACCTGGCAGACACA TGATCAAGTTTCAGAGGACACTTCTGATCGAAGGAGACCTGAACCCGGACAACAG CGACGTCGACAAGCTGTTTACCTCAGCTGGTCCAGACATACAACCAGCTGTTTCGAAG AAAACCCGATCAACGCAAGCGGAGTCGACGCAAAAGGCAATCTGAGCGCAAGACT GAGCAAGAGCAGAAGACTGGAACCTGATCGCACAGCTGCCGGGAGAAAAGAA GAACGGACTGTTTCGAAACCTGATCGCACTGAGCCTGGGACTGACACCGAACTTC AAGAGCAACTTCGACCTGGCAGAAGACGCAAAAGCTGACGCTGAGCAAGGACACA TACGACGACGACCTGGACAACCTGCTGGCACAGATCGGAGACCAGTACGCAGACC TGTTCTGGCAGCAAAGAACCTGAGCGACGCAATCTGCTGAGCGACATCCTGAG AGTCAACACAGAAATCACAAAGGCACCGCTGAGCGCAAGCATGATCAAGAGATAC GACGAACACCACCAGGACCTGACACTGCTGAAGGCACTGGTCAGACAGCAGCTGC CGGAAAAGTACAAGGAAATCTTCTTCGACCAGAGCAAGAACGGATACGCAGGATA CATCGACGGAGGAGCAAGCCAGGAAGAATTCTACAAGTTTCAAGCCGATCCTG GAAAAGATGGACGGAACAGAGAAGAACTGCTGGTCAAGCTGAACAGAGAAGACCTG CTGAGAAAAGCAGAGAACATTTCGACAACGGAAGCATCCCACCAGATCCACCTGG GAGAACTGCACGCAATCCTGAGAAGACAGGAAGACTTCTACCCGTTCTGAAAGGA CAACAGAGAAAAGATCGAAAAGATCCTGACATTGAGAATCCCGTACTACGTCGGAC CGCTGGCAAGAGGAAAACAGCAGATTCGCATGGATGACAAGAAAGAGCGAAGAAA CAATCACACCGTGGAACTTCGAGAAGTCTGTCGACAAGGGAGCAAGCGACAGA GCTTCATCGAAAAGATGACAACTTCGACAAGAACCTGCCGAACGAAAAGGTCCT GCCGAAGCACAGCTGCTGTACGAATACTTCACAGTCTACAACGAACTGACAAAAG GTCAAGTACGTACAGAAAGGAATGAGAAAGCCGGCATTCTGAGCGGAGAAACAGA AGAAGGCAATCGTGCACCTGCTGTTCAAGACAACAGAAAAGGTCACAGTCAAGCA GCTGAAGGAAGACTACTTCAAGAAGATCGAATGCTTCGACAGCGTCGAAATCAGC GGAGTCGAAGACAGATTCAACGCAAGCTGGGAACATACCACGACCTGCTGAAGA TCATCAAGGACAAGGACTTCTGGACAACGAAGAAAACGAAGACATCCTGGAAGA CATCGTCTGACACTGACACTGTTTCGAAAGACAGAGAAATGATCGAAGAAAAGACTG AAGACATACGCACACCTGTTTCGACGACAAGGTCATGAAGCAGCTGAAGAGAAGAA GATACACAGGATGGGGAAGACTGAGCAGAAAAGCTGATCAACGGAATCAGAGACAA GCAGAGCGGAAAGACAATCCTGGACTTCTGAAGAGCGACGGATTTCGAAAACAGA AACTTCATGCAGCTGATCCACGACGACAGCCTGACATTCAAGGAAGACATCCAGA AGGCACAGGTCACGGGACAGGGAGACAGCCTGCACGAAACATCGAAAACCTGG CAGGAAGCCCAGCAATCAAGAAGGGAATCTGACAGAGTCAAGGTCGTCGACGA ACTGGTCAAGGTCATGGGAAGACACAAGCCGAAAACATCGTCATCGAAATGGCA AGAGAAAACCAGACAACACAGAAGGGACAGAAGAACAGCAGAGAAAAGAAATGAA GAGAATCGAAGAAGGAATCAAGGAAGCTGGGAAGCCAGATCCTGAAGGAACACCC GGTCGAAAACACACAGCTGCAGAACGAAAAGCTGTACTGTACTACTGCAAGAAC GGAAGAGACATGTACGTCGACCAGGAAGTGGACATCAACAGACTGAGCGACTACG ACGTCGACACATCGTCCGACAGACTTCTGAAAGGACGACAGCATCGACAACAA GGTCTGACAAGAAGCGACAAGAACAGAGGAAAGAGCGACAACGTTCCCGAGCGA AGAAGTCGTCAAGAAGATGAAGAAGTACTGGAGACAGCTGCTGAAGCAAGTCA GATCACACAGAGAAAAGTTTCGACAACCTGACAAAAGGCAGAGAGAGGAGGACTGAG CGAACTGGACAAGGCAGGATTCATCAAGAGACAGCTGGTCGAAACAAGACAGATC ACAAAGCAGTCGCACAGATCCTGGACAGCAGAATGAACACAAAGTACGACGAA AACGACAAGCTGATCAGAGAAGTCAAGGTCATCACACTGAAGAGCAAGCTGGTCA CGACTTCAGAAAAGGACTTCCAGTTCTACAAGGTCAGAGAAATCAACAACACTACCA CCACGCACACGACGCATACCTGAACGCAAGTCTGCGGAACAGCACTGATCAAGAAG TACCCGAAGCTGGAAAGCGAATTCGTTCTACGGAGACTACAAGGTCTACGACGTC GAAAGATGATCGAAAAGGCGAAGCAGGAAATCGGAAAGGCAACAGCAAAAGTACT TCTTCTACAGCAACATCATGAACCTTCTCAAGACAGAAATCACACTGGCAACCGGA GAAATCAGAAAAGAGACCCTGATCGAAAACAAACGGAGAAAACAGGAGAAATCGTC TGGGACAAGGGAAGAGACTTTCGCAACAGTCAGAAAAGGTCCTGAGCATGCCGACG GTCAACATCGTCAAGAAGACAGAAGTCCAGACAGGAGGATTACGCAAGGAAAAGC ATCCTGCCGAAGAGAAAACAGCGACAAGCTGATCGCAAGAAAAGGAAAGGACTGGGAC CCGAAGAAGTACGGAGGATTTCGACAGCCGACAGTCCGATACAGCGTCTGGTTCG TCGCAAAAGGTCGAAAAGGAAAAGGCAAGAAGCTGAAGAGCGTCAAGGAACTGC TGGGAATCACAATCATGGAAAGAAGCAGCTTCGAAAAGAACCCGATCGACTTCT GGAAGCAAAAGGATAACAAGGAAGTCAAGAAGGACCTGATCATCAAGCTGCCGAA GTACAGCTGTTTCGAACTGGAAAACGGAAGAAAAGAGAATGCTGGCAAGCGCAGG AGAAGTGCAGAAGGGAACGAACTGGCACTGCCGAGCAAGTACGTCAACTTCTGT TACCTGGCAAGCCACTACGAAAAGCTGAAGGGAAGCCCGGAAGACAACGAACAG AAGCAGCTGTTCTGTCGAACAGCACAAGCACTACCTGGACGAAATCATCGAACAGA</p>	
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	<p>TCAGCGAATTCAGCAAGAGAGTCATCCTGGCAGACGCAAACCTGGACAAGGTCCT GAGCGCATAACAACAAGCACAGAGACAAGCCGATCAGAGAACAGGCAGAAAACAT CATCCACCTGTTTACACTGACAAAACCTGGGAGCACCGGCAGCATTCAAGTACTTCG ACACAACAATCGACAGAAAAGAGATACACAAGCACAAAAGGAAGTCTGGACGCAA CACTGATCCACCAGAGCATCACAGGACTGTACGAAACAAGAATCGACCTGAGCCA GCTGGGAGGAGACGGAGGAGGAAGCCCGAAGAAAGAAAGAGAAAAGGTCTAGCTAGC CATCACATTTAAAAGCATCTCAGCCTACCATGAGAATAAGAGAAAAGAAAATGAAGA TCAATAGCTTATTCATCTCTTTTCTTTTCTGTTGGTGTAAAGCCAACACCTGTCTA AAAAACATAAAATTTCTTTAATCATTTTGCCTCTTTTCTCTGTGCTTCAATTAATAAAA AATGGAAAAGAACCTCGAG</p>	
<p>具有 19.36% U 含量的替 代 Cas9 ORF</p>	<p>ATGGATAAGAAGTACTCGATCGGGCTGGATATCGGAACTAATTCCGTGGGTGGGC AGTGATCACGGATGAATACAAAAGTGCCTCCAAGAAGTTCAAGGTCTGGGGAAC ACCGATAGACACAGCATCAAGAAGAAATCTCATCGGAGCCCTGCTGTTGACTCCGG CGAAACCGCAGAAGCGACCCGGCTCAAACGTACCCGCGAGGGCAGCCTACACCCGG GGACGACAGCTTCTTCCACCGCCTGGAAGAATCTTTCCTGGTGGAGGAGGACAAG AAGCATGAACGGCATCTATCTTTGAAAACATCGTGGACGAAGTGGCGTACCACGA AAAGTACCCGACCATCTACCATCTGCGGAAGAAGTTGGTTGACTCAACTGACAAGG CCGACCTCAGATTGATCTACTTGGCCCTCGCCATATGATCAAATTCGCGGACACT TCCTGATCGAAGGCGATCTGAACCCTGATAACTCCGACGTGGATAAGCTGTTCTTTC AACTGGTGCAGACCTACAACCAACTGTTTGAAGAAAACCAATCAATGCCAGCGG CGTGCATGCCAAGGCCATCTGTCCGCCCGGCTGTGCAAGTCCGCGGCCCTCGAAA ACCTGATCGACAGCTGCCGGGAGAGAAGAAGAACGGACTTTTCGGCAACTTTGAT CGTCTCTCACTGGGACTCACTCCCAATTTCAAGTCCAATTTGACCTGGCCGAGG ACGCGAAGCTGCAACTCTCAAAGGACACCTACGACGACGACTTGGACAATTTGCT GGCACAATTTGGCGATCAGTACCGGGATCTGTTCTTCCGCTAAGAACCTTTCCG ACGCAATCTTGCTGTCCGATATCTGCGCGTGAACACCGAAATAACCAAGCGCCG CTTAGCGCTCGATGATTAAGCGGTACGACGAGCATCACAGGATCTCACGCTGCT CAAAGCGCTCGTGAGACGCAACTGCCTGAAAAGTACAAGGAGATTTTCTTCCGAC CAGTCCAAGAATGGGTACGCAGGGTACATCGATGGAGGCCAGCCAGGAAGAGT TCTATAAGTTCATCAAGCCAATCTTGGAAAAGATGGACGGAACCGAAGAACTGCTG GTCAAGCTGAACAGGGAGGATCTGCTCCGAAAACAGAGAACCTTTGACAACGGAA GCATTCACACCAGATCTTGGGTGAGCTGCACGCCATCTTGCGGCCAGGAG GACTTTTACCCATTCTCAAGGACAACCGGGAAAAGATCGAGAAAATTTCTGACGTT CCGCATCCCGTATTACGTGGGCCACTGGCGCGCGGCAATTCGCGCTTCGCGTGG TGACTAGAAAATCAGAGGAAACCATCACTCCTTGGAAATTTGAGGAAGTTGTGGAT AAGGAGCTTCGGCACAATCTTCATCGAACGAATGACCAACTTCGACAAGAATCT CCCAAACGAGAAGGTGCTTCCATAAGCACAGCCTCCTTTACGAATACTTCACTGTCT ACAACGAACTGACTAAAGTGAATACGTTACTGAAGGAATGAGGAAGCCGGCCTT TCTGAGCGGAGAACAGAAAGAAAGCGATTGTCGATCTGCTGTTCAAGACCAACCGC AAGGTGACCGTCAAGCAGCTTAAAGAGGACTACTTCAAGAAGATCGAGTGTTTCCG ACTCAGTGGAAATCAGCGGAGTGGAGGACAGATTCAACGCTTTCGCTGGAACTA TCATGATCTCCTGAAGATCATCAAGGACAAGGACTTCTTGGACAACGAGGAGAACG AGGACATCCTGGAAGATATCGTCTGACCTTGACCCTTTTCGAGGATCGCGAGATG ATCGAGGAGAGGCTTAAGACCTACGCTCATCTTTCGACGATAAGGTGATGAAACA ACTCAAGCGCCCGGTACACTGGTTGGGGCCCGCTTCCCGCAAGTCTGATCAAC GGTATTTCGCGATAAACAGAGCGGTAATAACTATCCTGGATTTCCTCAAATCGGATGG TTCGCTAATCGTAACTTCATGCAGTTGATCCACGACGACGCCTGACCTTTAAGGA GGACATCCAGAAAGCACAAAGTGAAGCGGACAGGGAGACTCACTCCATGAACACATC GCGAATCTGGCCGTTCCGCCGGGATTAAGAAGGGAATCCTGCAAACGTGTAAGG TGGTGGACGAGCTGGTGAAGTTCATGGGACGGCACAAAACCGGAGAATATCGTGAT TGAAATGGCCCAGAAAACAGACTACCCAGAAGGGCCAGAAGAAGTCCCGCGA AAGGATGAAGCGGATCGAAGAAGGAATCAAGGAGCTGGGCAGCCAGATCCTGAA AGAGCACCCGGTGAAAAACACGACGCTGCAGAACGAGAAGCTCTACCTGTAAT TTGCAAAATGGACGGGACATGTACGTGGACCAAGAGCTGGACATCAATCGGTTGTC TGATTACGACGTGGACCACATCGTTCACAGTCTTTTCTGAAGGATGACTCCATCGA TAACAAGGTGTTGACTCGCAGCGACAAGAACAGAGGGAAAGTCAGATAATGTGCCA TCGGAGGAGGTCTGTGAAGAAGATGAAGAATTACTGGCGGCAGCTCCTGAATGCCA AGCTGATTACCCAGAGAAAGTTTGAACAATCTCACTAAAGCCGAGCGCGCCGGACT CTCAGAGCTGGATAAGGCTGGATTATCAAAACGGCAGCTGGTTCGAGACTCGGCAG ATTACCAAGCACGTGGCGCAGATCCTGGACTCCCGCATGAACACTAAAATACGACGA GAACGATAAGCTCATCCGGGAAGTGAAGGTGATTACCCTGAAAAGCAAACCTGTGT CGGACTTTTCGGAAGGACTTTTCAAGTTTACAAAGTGAGAGAAATCAACAACACTAC CACGCGCATGACGCATACCTCAACGCTGTGGTCCGACACCGCCCTGATCAAGTAAGTA CCCTAAACTTGAATCGGAGTTTGTGTACGGAGACTACAAGGTCTACGACGTGAGGA AGATGATAGCCAAGTCCGAACAGGAAATCGGGAAAGCAACTGCGAAATACTTCTTT TACTCAAACATCATGAACTTCTTCAAGACTGAAATTACGCTGGCCAATGGAGAAAT</p>	<p>45</p>

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	<p>CAGGAAGAGGCCACTGATCGAAACTAACGGAGAAACGGGCAAAATCGTGTGGGA CAAGGGCAGGGACTTCGCAACTGTTGCGAAAAGTGTCTCTATGCCGCAAGTCAATA TTGTGAAGAAAACCGAAGTGCAAACCGGCGGATTTTCAAAGGAATCGATCCTCCC AAAGAGAAATAGCGCAAGCTCATTGCACGCAAGAAAGACTGGGACCCGAAAGAA GTACGGAGGATTTCGATTCCGGGACTGTCGCATACTCCGTCCTCGTGGTGGCCAAGG TGGAGAAGGGAAAGAGCAAGAGCTCAAATCCGTCAAAGAGCTGGGGGATTAC CATCATGGAACGATCCTCGTTTCGAGAAGAACCCGATTGATTTCTGGAGGCGAAGG GTTACAAGGAGGTGAAGAAGGATCTGATCATCAAACCTGCCCAAGTACTACTGTTT GAACTGGAAAATGGTCGGAAGCGCATGCTGGCTTCGGCCGAGAACTCCAGAAAAG GAAATGAGCTGGCCTTGCCTAGCAAGTACGTCAACTTCTCTATCTTGGCTTCGCAT ACGAGAAAACCAAAGGGTACCAGGAAAGATAACGAACAGAAAGCAGCTTTTCTGTTGGA GCAGACAAGCATTATCTGGATGAAATCATCGAACAAATCTCCGAGTTTCAAAGC GCGTGATCCTCGCCGACGCCAACCTCGACAAAGTCTGTCCGGCCTACATAAGCAT AGAGATAAGCCGATCAGAGAACAGGCCGAGAACATTATCCACTTGTCCACCTGAC TAACCTGGGAGCTCCAGCCGCTTCAAAGTACTTCGATACTACTATCGACCCGAAAA GATACACGTCCACCAAGGAAGTTCTGGACGCGACCCTGATCCACCAAGCATCACT GGACTTACGAAACTAGGATCGATCTGTCGACGCTGGGTGGCGATGGTGGCGGTGG ATCCTACCCATACGACGTGCCTGACTACGCCTCCGGAGGTGGTGGCCCCAAGAAGA AACGGAAAGGTGTGATAG</p>	
<p>具有 HSD 的 5' UTR、对应 于 SEQ ID NO: 45 的 ORF、 Kozak 序列 及 ALB 的 3' UTR 的 Cas9 转 录物</p>	<p>GGGTCCCGCAGTCGGCGTCCAGCGGCTCTGCTTGTTCGTGTGTGTGTCGTTGCAGG CCTTATTCGGATCTGCCACCATGGATAAGAAGTACTCGATCGGGCTGGATATCGGAA CTAATTCCTGGGTGGGCAAGTATCACGGATGAATACAAAGTGCCGTCCAAGAAG TTCAAGGTCCTGGGGAACACCGATAGACACAGCATCAAGAAGAATCTCATCGGAG CCCTGCTGTTTACTCCGGCGAAAACCGCAGAAGCGACCCGGCTCAAACGTACCCG GAGGCGACGCTACACCCGGCGGAAGAATCGCATCTGCTATCTGCAAGAAATCTTTT CGAACGAAATGGCAAAGGTGGACGACAGCTTCTTCCACCGCTTGGAAAGATCTTT CCTGGTGGAGGAGGACAAGAAGCATGAACGGCATCCTATCTTTGGAACATCGTG GACGAAGTGGCGTACCACGAAAAGTACCCGACCATCTACCATCTCGGAAAGAAAT TGTTGACTCAACTGACAAGGCCGACCTCAGATTGATCTACTTGGCCCTCGCCATA TGATCAAATTCGCGGACACTTCTGTATCGAAGGCGATCTGAACCCTGATAACTCC GACGTGGATAAGCTGTTCACTCAACTGGTGACAGCTTACAACCAACTGTTTCGAAGA AAACCAATCAATGCCAGCGCGCTGATGCCAAGGCCATCCTGTCCGCCCGGCTGT CGAAGTCCGGCGCCTCGAAAACCTGATCGCACAGCTGCCGGGAGAGAAGAAGA ACGGACTTTTCGGCAACTTGATCGCTCTCTACTGGGACTCACTCCCAATTTCAAGT CCAATTTGACCTGGCCGAGGACGCGAAGCTGCAACTCTCAAAGGACACCTACGA CGACGACTTGGAACAATTTGCTGGCACAATTTGGCGATCAGTACGCGGATCTGTTC TTGCCGTAAGAACCCTTTCGGACGCAATCTGTCTGTCGATATCCTGCGCGTGAACA CCGAAATAACCAAGCGCCGCTTAGCGCCTCGATGATTAAGCGGTACGACGAGCAT CACCAGGATCTCACGCTGCTCAAAGCGCTCGTGAGACAGCAACTGCCTGAAAAGT ACAAGGAGATTTTCTCGACCAAGTCCAAGAATGGGTACGACAGGGTACATCGATGGA GGCGCCAGCCAGGAAGAGTTCTATAAGTTCATCAAGCCAATCCTGGAAAAGATGGA CGAAACCGAAGAACTGCTGGTCAAGCTGAACAGGGAGGATCTGCTCCGCAACAG AGAACCTTTGACAACGGAAGCATTCCACACCAGATCCATCTGGGTGAGCTGCACGC CATCTGCGGCGCCAGGAGGACTTTTACCCATTCTCAAGGACAACCGGGAAAAGA TCGAGAAAATTTGACGTTCCGATCCCCTATTACGTGGGCCACTGGCGCGCGGG AATTCGCGCTTCGCGTGGATGACTAGAAAATCAGAGGAAACCATCACTCCTTGGAA TTTCGAGGAAGTTGTGGATAAGGGAGCTTCGGCACAAATCCTTCACTGAACCAATGA CCAATTCGACAAGAATCTCCAAACGAGAAGGTGCTTCTTAAGCACAGCCTCCTT TACGAATACTTCACTGTCTACAACGAACTGACTAAAGTGAATAACGTTACTGAAGG AATGAGGAAGCCGGCCTTTCTGAGCGGAGAACAAGAAGAAAGCGATTGTGATCTG CTGTTCAAGACCAACCGCAAGGTGACCGTCAAGCAGCTTAAAGAGGACTACTTCA AGAAGATCGAGTGTTCGACTCAGTGGAAATCAGCGGAGTGGAGGACAGATTCAA CGTTTCGCTGGGAACCTATCATGATCTCCTGAAGATCATCAAGGACAAGGACTTCC TTGACAACGAGGAGAACGAGGACATCCTGGAAGATATCGTCTGACCTTGACCCTT TTCGAGGATCGCGAGATGATCGAGGAGAGGCTTAAAGACTACGCTCATCTCTTCA CGATAAGGTATGAAACAACCTCAAAGCGCCGCTACACTGGTTGGGGCCGCTCT CCCGCAAGCTGATCAACGGTATTTCGCGATAAACAGAGCGGTAACACTATCCTGGAT TTCTCAAATCGGATGGCTTCGCTAATCGTAACTTCAATGACGTTGATCCACGACGAC AGCCTGACCTTTAAGGAGGACATCCAGAAAAGCACAAGTGAGCGGACAGGGAGAC TCACTCCATGAACACATCGCAATCTGGCCGGTTCGCGGCGATTAAAGAAGGGAAT CCTGCAAACTGTGAAGGTGGTGGACGAGCTGGTGAAGGTGATGGGACGGCACAAA CCGGAGAATATCGTGATTGAAATGGCCCGAGAAAACCAGACTACCCAGAAGGGCC AGAAGAACTCCCGCAAAGGATGAAGCGGATCGAAGAAGGAATCAAGGAGCTGG GCAGCCAGATCCTGAAAGAGCACCCGGTGGAAAACACGCAGCTGCAGAACGAGA AGCTTACCTGACTATTTGCAAAAATGGACGGGACATGTACGTGGACAAGAGCTG GACATCAATCGGTTGTCTGATTACGACGTGGACCACATCGTTCCACAGTCTTTCTG AAGGATGACTCCATCGATAACAAGGTGTTGACTCGCAGCGACAAGAACAGAGGGA</p>	<p>46</p>

	<p>AGTCAGATAATGTGCCATCGGAGGAGGTCGTGAAGAAGATGAAGAATTACTGGCG GCAGCTCCTGAATGCGAAGCTGATTACCCAGAGAAAAGTTTGACAATCTCACTAAAG CCGAGCGCGGCGGACTCTCAGAGCTGGATAAGGCTGGATTCATCAAACGGCAGCT GGTCCGAGACTCGGCAGATTACCAAGCACGTGGCGCAGATCCTGGACTCCCGCATG AACACTAAATACGACGAGAACGATAAGCTCATCCGGGAAGTGAAGGTGATTACCCCT GAAAAGCAAACCTTGTGTGCGACTTTCGGAAGGACTTTCAGTTTTACAAAAGTGAGA GAAATCAACAACCTACCATCACGCGCATGACGCATACCTCAACGCTGTGGTCCGGCAC CGCCCTGATCAAGAAGTACCCTAAACTTGAATCGGAGTTTGTGTACGGAGACTACA AGGTCTACGACGTGAGGAAGATGATAGCCAAGTCCGAACAGGAAATCGGGAAAGC AACTGCGAAATACTTCTTTTACTCAAACATCATGAACTTCTTCAAGACTGAAATTAC GCTGGCCAAATGGAGAAATCAGGAAGAGGGCCACTGATCGAAACTAACGGAGAAACG GGCGAAATCGTGTGGGACAAGGGCAGGGACTTCGCAACTGTTCCGAAAAGTGCTCT CTATGCCGCAAGTCAATATTGTGAAGAAAACCGAAGTGCAAACCGCGGATTTTCA AAGGAATCGATCCTCCCAAAGAGAAAATAGCGACAAGCTCATTGCACGCAAGAAAAG ACTGGGACCCGAAAGATACGGAGGATTTCGATTTCGCCGACTGTGCATACCTCCGTC CTCGTGGTGGCCAAGGTGGAGAAGGGAAAGAGCAAGAAGCTCAAATCCGTCAAA GAGCTGTGGGGATTACCATCATGGAACGATCCTCGTTCGAGAAGAACCCGATTGA TTTTCTGGAGGGCAAGGGTTACAAGGAGGTGAAGAAGGATCTGATCATCAAACCTG CCCAAGTACTACTGTTGAACTGGAAAATGGTCGGAAGCGCATGCTGGCTTCGGC CGGAGAACTCCAGAAAAGAAAATGAGCTGGCCTTGCCTAGCAAGTACGTCAACTTC CTCTATCTTGTCTCGCACTACGAGAACTCAAAGGGTCCACCGAAGATAACGAACA GAAGCAGCTTTTCTGTGGAGCAGCAAGCATTATCTGGATGAAATCATCGAACAAA TCTCCGAGTTTTCAAAGCGCGTGATCCTCGCCGACGCCAACCTCGACAAAAGTCTGT TCGGCTACAATAAGCATAGAGATAAGCCGATCAGAGAACAGGCCGAGAACTTAT CCACTTGTTCACCCTGACTAACCTGGGAGCTCCAGCCGCTTCAAGTACTTTCGATA CTACTATCGACCGCAAAAGATACACGTCCACCAAGGAAGTTCTGGACGCGACCTG ATCCACCAAAGCATCACTGGACTCTACGAACTAGGATCGATCTGTGCGAGCTGGG TGCGGATGGTGGCGGTGGATCCTACCATACGACGTGCCTGACTACGCACTCCGGAG GTGGTGGCCCAAGAAGAAAACGGAAGGTGTGATAGCTAGCCATCACATTTAAAAG CATCTCAGCCTACCATGAGAATAAGAGAAAAGAAAATGAAGATCAATAGCTTATTTCAT CTCTTTTTCTTTTCGTTGGTGTAAAGCCAACACCTGTCTAAAAAACATAAATTC TTTAATCATTTTGCCTCTTTCTCTGTGCTTCAATTAATAAAAAATGGAAAGAACCTC GAG</p>		
[0681]	<p>具有 HSD 的 5' UTR, 对应 于 SEQ ID NO: 45 的 ORF 及 ALB 的 3' UTR 的 Cas9 转录 物</p>	<p>GGGTCCCGCAGTCGGCGTCCAGCGGCTCTGCTTGTTCGTGTGTGTGTCGTTGCAGG CCTTATTCGGATCTATGGATAAGAAGTACTCGATCGGGCTGGATATCGGAACTAATTC CGTGGGTTGGGCAAGTATCAGGATGAATACAAAGTGCCGTCGAAGAAGTTCAAG GTCCTGGGGAACCCGATAGACACAGCATCAAGAAGAATCTCATCGGACCCCTGCT TTTTGACTCCGGCGAAACCGCAGAAAGCGACCCGGCTCAAACGTACCAGGAGGCGA CGCTACACCCGGCGGAAGAATCGCATCTGCTATCTGCAAGAAATCTTTTCGAACGA AATGGCAAAAGGTGGACGACAGCTTCTTCCACCGCCTGGAAGAATCTTCTGTTGG AGGAGGACAAGAAGCATGAACGGCATCTATCTTTGGAAAACATCGTGGACGAAAGT GGCGTACCACGAAAAGTACCCGACCATCTACCATCTGCGGAAGAAGTTGGTTGACT CAACTGACAAGGCCGACCTCAGATTGATCTACTTGGCCCTCGCCATATGATCAAAT TCCGCGGACACTTCTGATCGAAGGGCATCTGAACCTGATAACTCCGACGTGGAT AAGCTGTTCACTTCACTGGTGCAGACCTACAACCAACTGTTTCGAAGAAAACCCAAT CAATGCCAGCGGCTCGATGCCAAGGCCATCCTGTCCGCCGCTGTCGAAGTTCGC GGCGCCTCGAAAACCTGATCGCACAGCTGCCGGGAGAGAAGAAGAACGGACTTTT CGGCAACTTGATCGCTCTCTCACTGGGACTCACTCCCAATTTCAAGTCCAATTTTGA CCTGGCCGAGGACGCGAAGCTGCAACTCTCAAAGGACACCTACGACGACGACTTG GACAATTTGCTGGCACAATTTGGCGATCAGTACGCGGATCTGTTCTTGGCCGCTAA GAACCTTTCGGACGCAATCTTGTGTCGATATCCTGCGCGTGAACACCCGAAATAA CCAAAGCGCCGCTTAGCGCCTCGATGATTAAGCGGTACGACGAGCATCACCAGGAT CTCACGTGCTCAAAGCGCTCGTGAGACAGCAACTGCCTGAAAAGTACAAGGAGA TTTTCTTCGACCAGTCCAAGAATGGGTACGACGGGTACATCGATGGAGGCGCCAGC CAGGAAGAGTTCTATAAGTTCATCAAGCCAATCCTGGAAAAGATGGACGGAACCG AAGAAGTGTGGTCAAGCTGAACAGGGAGGATCTGCTCCGCAACAGAGAACCTT TGACAACGGAAGCATTCCACACCAGATCCATCTGGGTGAGCTGCACGCCATCTTGC GGCGCCAGGAGGACTTTTACCCATTCTCAAGGACAACCGGGAAAAGATCGAGAA AATTTGACGTTCCGCATCCCGTATTACGTGGGCCCACTGGCGCGCGGCAATTCGCG CTTCGCGTGGATGACTAGAAAATCAGAGGAAACCATCACTCCTTGGAAATTCGAGG AAGTTGTGGATAAGGGAGCTTCGGCACAATCCTTCATCGAACGAATGACCAACTTC GACAAGAATCTCCAAACGAGAAGGTGCTTCTAAGCACAGCTCCTTACGAATA CTTCACTGTCTACAACGAACTGACTAAAGTGAATAACGTTACTGAAGGAATGAGGA AGCCGGCCTTTCTGAGCGGAGAACAGAAGAAAGCGATTGTGCTGCTGCTGTTCAA GACCAACCGCAAGGTGACCGTCAAGCAGCTTAAAGAGGACTACTTCAAGAAGATC GAGTGTTCGACTCAGTGGAATCAGCGGAGTGGAGGACAGATTCAACGCTTCGC TGGAACCTATCATGATCTCCTGAAGATCATCAAGGACAAGGACTTCTTGACAAAC</p>	47

[0682]

	<p>GAGGAGAACGAGGACATCTGGAAGATATCGTCCTGACCTTGACCCTTTTCGAGGA TCGCGAGATGATCGAGGAGAGGCTTAAAGACCTACGCTCATCTCTTCGACGATAAGG TCATGAAACAACCTCAAGCGCCGCCGTACACTGGTTGGGGCCGCCTCTCCCGCAA GCTGATCAACGGTATTTCGCGATAAACAGAGCGGTAAAACCTATCTGGATTCTCAA ATCGGATGGCTTCGCTAATCGTAACTTCATGCAGTTGATCCACGACGACAGCTGAC CTTTAAGGAGGACATCCAGAAAAGCACAAGTGAGCGGACAGGGGAGACTCACTCCAT GAACACATCGGAATCTGGCCGGTTCGCCGGCGATTAAGAAGGGAATCCTGCAAA CTGTGAAGGTGGTGGACGAGCTGGTGAAGTTCATGGGACGGCACAAACCGGAGA ATATCGTGATTGAAATGGCCCGAGAAAACAGACTACCCAGAAGGGCCAGAAGAA CTCCCGCAAAGGATGAAGCGGATCGAAGAAGGAATCAAGGAGCTGGGCGAGCA GATCCTGAAAAGAGCACCCGGTGGAAAACACGCAGCTGCAGAACGAGAAGCTCTAC CTGTACTATTTGCAAAATGGACGGGACATGTACGTGGACCAAGAGCTGGACATCAA TCGGTTGTCTGATTACGACGTGGACCACATCGTTCCACAGTCTTTCTGAAAGGATG ACTCCATCGATAACAAGGTGTTGACTCGCAGCGACAAGAACAGAGGGAAGTCCAGA TAATGTGCCATCGGAGGAGGTCTGTGAAGAAGATGAAGAATTACTGGCGGCGAGCTCC TGAATGCGAAGCTGATTACCCAGAGAAAAGTTTGACAATCTCACTAAAGCCGAGCGC GGCGGACTCTCAGAGCTGGATAAGGCTGGATTCAATCAACGGCAGCTGGTTCGAGA CTCGGCAGATTACCAAGCACGTGGCGCAGATCTGGACTCCCGCATGAACACTAAA TACGACGAGAACGATAAGCTCATCCGGGAAGTGAAGGTGATTACCCTGAAAAGCA AACTTGTGTCGGACTTTTCGGAAGGACTTTTCAGTTTACAAAAGTGAGAGAAATCAAC AACTACCATCACGCGCATGACGCATACCTCAACGCTGTGGTCGGCACCCGCCCTGAT CAAGAAGTACCCTAACTTGAATCGGAGTTTGTGTACGGAGACTACAAAGTCTACG ACGTGAGGAAGATGATAGCCAAGTCCGAACAGGAAATCGGGAAGCAACTGCGA AATACTCTTTTACTCAAACATCATGAACTTCTTCAAGACTGAAATTAAGTCTGGCCA ATGGAGAAATCAGGAAGAGGGCCACTGATCGAAACTAACGGAGAAAACGGGCGAAAT CGTGTGGGACAAGGGCAGGGACTTCGCAACTGTTTCGAAAAGTGTCTCTATGCCG CAAGTCAATATTGTGAAGAAAACCGAAGTGCAACCGGCGGATTTTCAAAGGAAT CGATCTCCCAAAGAGAAAATAGCGACAAGCTCATTGCACGCAAGAAAAGACTGGGA CCCGAAGAAGTACGGAGGATTCGATTGCGCGACTGTCGCATACTCCGTCCTCGTGG TGGCCAAGGTGGAGAAGGGAAGAGCAAGAAGCTCAAATCCGTCAAAGAGCTGC TGGGGATTACCATCATGGAACGATCCTCGTTCGAGAAGAACCCGATTGATTCTCTGG AGGCGAAGGGTTACAAGGAGGTGAAGAAGGATCTGATCATCAAATGCCAAAGTA CTCACTGTTTCAACTGGAAAATGGTTCGGAAGCGCATGCTGGCTTCGGCCGGAGAA CTCCAGAAAAGGAAATGAGCTGGCCTTGCTAGCAAGTACGTCAACTTCTCTATCT TGCTTCGCACTACGAGAACTCAAAGGGTCAACCGAAGATAACGAACAGAAAGCAG CTTTTCGTTGGAGCAGCACAAAGCATTATCTGGATGAAATCATCGAACAATCTCCGA GTTTTCAAAGCGCGTGATCCTCGCCGACGCCAACCTCGACAAAAGTCTGTCCGGCT ACAATAAGCATAGAGATAAGCCGATCAGAGAACAGGCCGAGAACATTATCCACTTG TTCACCTGACTAACCTGGGAGCTCCAGCCGCCTTCAAGTACTTCGATACTACTATC GACCGCAAAAGATACACGTCCACCAAGGAAGTTCTGGACGCGACCCTGATCCACC AAAGCATCACTGGACTCTACGAACTAGGATCGATCTGTCGCAGCTGGGTGGCGAT GGTGGCGGTGGATCCTACCATACGACGTGCCTGACTACGCCCTCCGGAGGTGGTGG CCCCAAGAAGAAACGGAAGGTGTGATAGCTAGCCATCACATTTAAAAGCATCTCAG CCTACCATGAGAATAAGAGAAAAGAAAATGAAGATCAATAGCTTATCATCTCTTTTT TTTTTCTGTTGGTGAAGGCAACACCCTGTCTAAAAAACATAAATTTCTTTATCA TTTTGCCTCTTTCTCTGTGCTTCAATTAATAAAAAAATGGAAAGAACCTCGAG</p>	
<p>包含使用 通常在人 类中高度 表达的密 码子的 Cas9 ORF 的 Cas9 转 录物</p>	<p>GGGTCCCGCAGTCGGCGTCCAGCGGCTCTGCTTGTCTGTGTGTGTCGTTGCAGG CCTTATTCGGATCCATGCCTAAGAAAAAGCGGAAGGTTCGACGGGGATAAGAAGTAC TCAATCGGGCTGGATATCGGAACATAATCCGTGGGTTGGGCGAGTGATCACGGATGA ATACAAAAGTCCCGTCCAAGAAGTTCAAGGTCTGGGGAACACCGATAGACACAGC ATCAAGAAAAATCTCATCGGAGCCCTGCTGTTTGAATCCGCGCAAACCGCAGAAG CGACCCGGCTCAAACGTACCGCGAGGCGACGCTACACCCGGCGGAAGAATCGCAT CTGCTATCTGCAAGAGATCTTTTCGAAACGAAATGGCAAAGGTTCGACGACAGCTTCT TCCACCGCTGGAAGAATCTTCTGTTGGAGGAGGACAAGAAGCATGAACGGCA TCCTATCTTTGGAACATCGTCGACGAAAGTGGCGTACCACGAAAAGTACCCGACCA TCTACCATCTGCGGAAGAAAGTTGGTTGACTCAACTGACAAGGCCGACCTCAGATTG ATCTACTTGGCCCTCGCCATATGATCAAATCCGCGGACACTTCTGATCGAAGGC GATCTGAACCCTGATAACTCCGACGTGGATAAGCTTTTCAATTCAACTGGTGCAGACC TACAACCAACTGTTTCAAGAAAACCAATCAATGCTAGCGGGCTCGATGCCAAGGC CATCCTGTCCGCCCGGCTGTGCAAGTCCGCGGCGCCTCGAAAACCTGATCGCACAGC TGCCGGGAGAGAAAAAGAACGGAATTTTCGGCAACTTGATCGCTCTCTCACTGGG ACTACTCCCAATTTCAAGTCAATTTGACCTGGCCGAGGACGCGAAGCTGCAAC TCTCAAAGGACACCTACGACGACGACTTGGACAATTTGCTGGCACAAATTTGGCGAT CAGTACGCGGATCTGTTCTTCCCGCTAAGAACCTTTTCGGACGCAATCTTGTCTCC GATCTCGCGGTGAACACCGAAAATAACCAAAGCGCCGCTTAGCGCCTCGATGAT TAAGCGGTACGACGAGCATCACAGGATCTCACGTGCTCAAAGCGCTCGTGAGA CAGCAACTGCCTGAAAAGTACAAGGAGATCTTCTTCGACCAGTCCAAGAATGGT</p>	<p>48</p>

[0683]

	<p>ACGCAGGGTACATCGATGGAGGCGCTAGCCAGGAAGAGTTCATAAGTTCATCAAG CCAATCCTGGAAAAGATGGACGGAAACCGAAGAACTGCTGGTCAAGCTGAACAGGG AGGATCTGCTCCGGAAACAGAGAACCTTTGACAACGGATCCATTCCCCACGATC CATCTGGGTGAGCTGCACGCCATCTTGCGGCGCCAGGAGGACTTTTACCCATTCTC CAAGGACAACCGGGAAAAGATCGAGAAAATTCTGACGTTCCGCATCCCGTATTACG TGGGCCACTGGCGCGCGGAATTCGCGCTTCGCGTGGATGACTAGAAAATCAGA GGAAACCATCACTCCTTGAATTTGAGGAAGTTGTGGATAAGGGAGCTTCGGCAC AAAGCTTCATCGAACGAATGACCAACTTCGACAAGAATCTCCCAAACGAGAAAGGT GCTTCCTAAGCACAGCCTCCTTTACGAATACTTCACTGTCTACAACGAAGTACTAA AGTAAAATACGTTACTGAAGGAATGAGGAAGCCGGCCTTCTGTCCGGAGAACAG AAGAAAGCAATTGTGCATCTGCTGTTCAAGACCAACCGCAAGGTGACCGTCAAGC AGCTTAAAGAGGACTACTTCAAGAAGATCGAGTGTTCGACTCAGTGGAAATCAGC GGGGTGGAGGACAGATTCAACGCTTCGCTGGGAACCTATCATGATCTCTGAAGAT CATCAAGGACAAGGACTTCCCTTGACAACGAGGAGAACGAGGACATCTGGAAGAT ATCGCTGACCTTGACCTTTTCGAGGATCGCGAGATGATCGAGGAGAGGCTTAA GACCTACGCTCATCTCTTCGACGATAAGGTTCATGAAACAACCTCAAGCGCCCGGT ACACTGGTTGGGGCCGCCTTCCCCGAAGCTGATCAACGGTATTTCGCGATAAACAG AGCGGTAATAACTATCCTGGATTTCCCTCAAATCGGATGGCTTCGCTAATCGTAACTTC ATGCAATTGATCCACGACGACGCTGACCTTAAAGGAGACATCCAAAAAGCAC AAGTGTCCGGACAGGGAGACTCACTCCATGAACACATCGCGAATCTGGCCGGTTC GCCGGCGATTAAGAAGGGAATTCTGCAAACTGTGAAGGTGGTCGACGAGCTGGTG AAGGTCATGGGACGGCACAACCGGAGAATATCGTGATTGAAATGGCCCCGAGAAA ACCAGACTACCCAGAAGGGCCAGAAAACTCCCGGAAAAGGATGAAGCGGATCG AAGAAGGAATCAAGGAGCTGGCGAGCCAGATCCTGAAAGAGCACCCGGTGGAAA ACACGCAGCTGCAGAACGAGAAGCTTACTGTACTATTTGCAAAATGGACGGGA CATGTACGTGGACCAAGAGCTGGACATCAATCGGTTGTCTGATTACGACGTGGACC ACATCGTTCCACAGTCTTTCTGAAGGATGACTCGATCGATAACAAGGTGTTGACT CGCAGCGACAAGAACAGAGGGAAGTCAGATAATGTCCATCGGAGGAGGTCGTGA AGAAGATGAAGAATTAAGGCGCAGCTCCTGAATGCGAAGCTGATTACCCAGAG AAAGTTTGACAATCTCACTAAAGCCGAGCGCGGGGACTCTCAGAGCTGGATAAG GCTGGATTCATCAAACGGCAGCTGGTCGAGACTCGGCAGATTACCAAGCAGTGG CGCAGATCTTGACTCCCGCATGAACACTAAATACGACGAGAACGATAAGCTCATC CGGAAAGTGAAGGTGATTACCCTGAAAAGCAAACCTGTGTCCGACTTTCGAAAG ACTTTCAGTTTTACAAAGTGAGAGAAATCAACAACCTACCATCACGCGCATGACGCA TACCTCAACGCTGTGGTCCGTACCGCCCTGATCAAAAAGTACCTAAACTTGAATC GGAGTTTGTGTACGGAGACTACAAGGTCTACGACGTGAGGAAGATGATAGCCAAAG TCGGAACAGGAAATCGGAAAGCAACTGCGAAATACTTCTTTACTCAAACATCAT GAACTTTTTCAAGACTGAAATTACGCTGGCCAATGGAGAAATCAGGAAAGAGGCCA CTGATCGAAACTAACGGAGAAACGGGCGAAATCGTGTGGGACAAGGGCAGGGAC TTCCCAACTGTTCCGAAAAGTCTCTATGCCGCAAGTCAATATTGTGAAGAAAAC CGAAGTGCAAACCGCGGATTTTCAAAGGAATCGATCCTCCCAAAGGAAATAGC GACAAGCTCATTGCACGCAAGAAAGACTGGGACCCGAAGAAGTACGGAGGATTTCG ATTCGCCGACTGTCGCATACTCCGTCTCGTGGTGGCCAAAGGTGGAGAAGGGAAA GAGCAAAAAGCTCAAATCCGTCAAAGAGCTGCTGGGGATTACCATCATGGAACGAT CCTCGTTTCGAGAAGAACCCGATTGATTTCTCGAGGCGAAGGGTTACAAGGAGGT GAAGAAGGATCTGATCATCAAACCTCCCAAGTACTCACTGTTCTGAACTGGAAAATG GTCGGAAGCGCATGCTGGCTTCGGCCGAGAACTCCAAAAAGGAAATGAGCTGGC CTTGCTAGCAAGTACGTCAACTTCTCTATCTTGTTCGCACTACGAAAAACTCAA AGGGTCACCGGAAGATAACGAACGAAAGCAGCTTTTCGTGGAGCAGCACAAGCAT TATCTGGATGAAATCATCGAACAAATCTCCGAGTTTTCAAAGCGCGTATCCTCGCC GACGCCAACCTCGACAAAAGTCTGTCCGCTACAATAAGCATAGAGATAAGCCGAT CAGAGAACAGGCCGAGAACATTATCCACTTGTTCACCCTGACTAACCTGGGAGCCC CAGCCGCTTCAAGTACTTCGATACTACTATCGATCGCAAAAAGATACACGTCCACCA AGGAAGTTCTGGACGCGACCCTGATCCACCAAAGCATCACTGGACTCTACGAAACT AGGATCGATCTGTCGAGCTGGGTGGCGATTGATAGTCTAGCCATCACATTTAAAAG CATCTCAGCCTACCATGAGAATAAGAGAAAAGAAAATGAAGATCAATAGCTTATTCAT CTCTTTTCTTTTCGTTGGTGTAAAGCCAACACCCTGTCTAAAAAACATAAATTTT TTAATCATTTTGCCTTTTTCTGTGCTTCAATTAATAAAAAATGGAAAGAACCTC GAG</p>	
<p>Cas9 包含 Kozak序列 以及使用 通常在人 类中高度</p>	<p>GGGTCCCGCAGTCGGCGTCCAGCGGCTCTGCTTGTTCGTGTGTGTGCTTGCAGG CCTTATTCGGATCCGCCACCATGCCATAAGAAAAAGCGGAAGGTTCGACGGGGATAAG AAGTACTCAATCGGGCTGGATATCGGAACTAATTCCGTGGGTTGGGCAGTGATCAC GGATGAATACAAAGTGCCGTCCAAGAAGTTCAAGGTCTGGGGAACACCGATAGA CACAGCATCAAGAAAAATCTCATCGGAGCCCTGCTTTTACTCCGGCGAAACCGC AGAAGCGACCCGGCTCAAACGTACCAGGAGGCGACGCTACACCCGGCGGAAGAT CGCATCTGCTATCTGCAAGAGATCTTTTCAACGAAATGGCAAAGGTTCGACGACAG CTTCTCCACCCGCTGGAAGAATCTTCTGTTGGTGGAGGAGGACAAGAAGCATGAA</p>	<p>49</p>

<p>表达的密码子的 Cas9 ORF 的 Cas9 转录物</p>	<p>CGGCATCCTATCTTTGAAACATCGTCGACGAAAGTGGCGTACCACGAAAAGTACCC GACCATCTACCATCTGCGGAAGAAAGTTGGTTGACTCAACTGACAAGGCCGACCTCA GATTGATCTACTTGGCCCTCGCCATATGATCAAATTCGCGGACACTTCTGATCG AAGGCGATCTGAACCCTGATAACTCCGACGTGGATAAGCTTTTCATTCAACTGGTG CAGACCTACAACCAACTGTTGAAAGAAAACCAATCAATGCTAGCGGCGTCGATGC CAAGGCCATCTGTCCGCCCGGCTGTCGAAAGTCCGCGCGCTCGAAAACCTGATCG CACAGCTGCCGGGAGAGAAAAGAACGGACTTTTCGGCAACTTGATCGCTCTCTC ACTGGGACTCACTCCCAATTTCAAGTCCAATTTTGACCTGGCCGAGGACGCGAAGC TGCAACTCTCAAAGGACACCTACGACGACGACTTGGACAATTTGCTGGCACAAAT GGCGATCAGTACGCGGATCTGTTCCCTTGCCGTAAGAACCTTTCGGACGCAATCTT GCTGTCCGATATCTGCGCGTGAACACCGAAATAACCAAAGCGCCGTTAGCGCCT CGATGATTAAGCGGTACGACGAGCATACCAGGATCTCACGCTGCTCAAAGCGCTC GTGAGACAGCAACTGCCTGAAAAGTACAAGGAGATCTTCTTCGACCAGTCCAAGA ATGGGTACGCAGGGTACATCGATGGAGGCGTAGCCAGGAAGAGTTCTATAAGTTC ATCAAGCCAATCTGGAAAAGATGGACGGAACCGAAGAAGTCTGGTCAAGTGA ACAGGGAGGATCTGCTCCGGAACAGAGAACCTTTGACAACGGATCCATTCCCCA CCAGATCCATCTGGGTGAGCTGCACGCCATCTTGCGGCGCCAGGAGACTTTTACC CATTCTCAAGGACAACCGGAAAAGATCGAGAAAATTTGACGTTCCGCATCCCG TATTACGTGGGCCACTGGCGCGCGCAATTCGCGCTTCGCGTGGATGACTAGAAA ATCAGAGGAAACCATCACTCCTTGAATTTTCGAGGAAGTTGTGGATAAGGGAGCTT CGGCACAAAGCTTCATCGAACGAATGACCAACTTCGACAAGAATCTCCCAAACGA GAAGGTGCTTCTAAGCACAGCTCCTTTACGAATACTTCACTGTCTACACGAAC TGACTAAAGTGAATACTGTTACTGAAGGAATGAGGAAGCCGGCCTTTCTGTCCGGA GAACAGAAGAAAGCAATTGTCGATCTGCTGTTCAAGACCAACCGCAAGGTGACCG TCAAGCAGCTTAAAGAGGACTACTTCAAGAAGATCGAGTGTTCGACTCAGTGA AATCAGCGGGGTGGAGGACAGATTCAACGCTTCGCTGGGAACCTATCATGATCTCC TGAAGATCATCAAGGACAAGGACTTCTTGACAACGAGGAGAACGAGGACATCCT GGAAGATATCGTCTGACCTTGACCCTTTTCGAGGATCGCGAGATGATCGAGGAGA GGCTTAAAGCTACGCTCATCTCTTCGACGATAAGGTCATGAAAACACTCAAGCGC CGCCGGTACACTGGTTGGGGCCGCTCTCCCGAAGCTGATCAACGGTATTTCGCGA TAAACAGAGCGGTA AAAACTATCCTGGATTCTCAAATCGGATGGCTTCGTAATCG TACTTCATGCAATTGATCCACGACGACAGCCTGACCTTTAAGGAGGACATCCAAA AAGCACAAGTGTCCGGACAGGGAGACTACTCCATGAACACATCGCAAGTCTGGC CGGTTCCGCGGCGATTAAGAAGGGAATTCTGCAAACTGTGAAGGTGGTTCGACGAG CTGGTGAAGGTCATGGGACGGCACAAACCGGAGAATATCGTGATTGAAATGGCCC GAGAAAACAGACTACCCAGAAGGGCCAGAAAAACTCCCGGAAAAGGATGAAGC GGATCGAAGAAGGAATCAAGGAGCTGGGCAGCCAGATCTGAAAGAGCACCCGGT GGAAAACACGCAGCTGCAGAACGAGAAGCTCTACCTGTACTATTTGCAAAATGGA CGGGACATGTACGTGGACCAAGAGCTGGACATCAATCGGTTGTCTGATTACGACGT GGACCACATCGTTCCACAGTCTTTCTGAAGGATGACTCGATCGATAACAAGGTGT TGACTCGCAGCGACAAGAACAGAGGGAAAGTCAGATAATGTGCCATCGGAGGAGGT CGTGAAGAAGATGAAGAATTACTGGCGGCAAGTCTGAAATGCGAAGCTGATTACCC AGAGAAAGTTTGACAATCTCACTAAAGCCGAGCGCGGGGACTCTCAGAGCTGGA TAAGGCTGGATTATCAAACGGCAGCTGGTCGAGACTCGGCAGATTACCAAGCAG TGCGCAGATCTTGGACTCCCGCATGAACACTAAATACGACGAGAACGATAAGCTC ATCCGGAAAGTGAAGGTGATTACCCTGAAAAGCAAACCTTGTGTCGGATTTCGGA AGGACTTTCAGTTTACAAGTGAGAGAAATCAACAACACTACCATCACGCGCATGAC GCATACCTCAACGCTGTGGTCCGTACCGCCTGATCAAAAAGTACCCTAAACTTGA ATCGGAGTTTGTGTACGGAGACTACAAGGTCTACGACGTGAGGAAGATGATAGCCA AGTCCGAACAGGAAATCGGGAAAGCAACTGCGAAATACTTCTTTACTCAAAACATC ATGAACTTTTTCAAGACTGAAATTACGCTGGCCAATGGAGAAAATCAGGAAGAGGCC ACTGATCGAAAATAACGGAGAAACGGGCGAAATCGTGTGGGACAAGGGCAGGGA CTTCGCAACTGTTCGCAAAAGTCTCTATGCCGCAAGTCAATATTGTGAAGAAAA CCGAAGTGCAAAACCGGCGGATTTTCAAAGGAATCGATCTCCCAAAGAGAAATAG CGACAAGCTCATTGCACGCAAGAAAAGACTGGGACCCGAAGAAGTACGGAGATT GATTCCGCGACTGTGCGATACTCCGCTCCTCGTGGTGGCCAAGGTGGAGAAGGGAA AGAGCAAAAAGCTCAAATCCGTCAAAGAGCTGCTGGGGATTACCATCATGGAACG ATCCTCGTTTCGAGAAGAACCAGATTGATTCTCGAGGCGAAGGGTTACAAGGAGG TGAAGAAGGATCTGATCATCAAACCTCCCAAGTACTCACTGTTGCAACTGGAAAAT GGTCGGAAGCGCATGCTGGCTTCGGCCGGAGAACTCCAAAAAGGAAATGAGCTGG CCTTGCTAGCAAGTACGTCAACTTCTCTATCTTGTCTGCGACTACGAAAACTCA AAGGGTACCAGGAAAGATAACGAACAGAAGCAGCTTTTCGTGGAGCAGACAAGCA TTATCTGGATGAAATCATCGAACAAATCTCCGAGTTTTCAAAGCGCGTATCTCCG CGACGCCAACCTCGACAAAAGTCTGTCGGCTACAATAAGCATAGAGATAAGCCGA TCAGAGAACAGGCCGAGAACATTATCCACTTGTTCACCCTGACTAACCTGGGAGCC CCAGCCGCTTCAAGTACTTCGATACTACTATCGATCGAAAAGATAACGCTCCACC AAGGAAGTTCTGGACGCGACCCTGATCCACCAAAGCATCACTGGACTTACGAAA</p>
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[0684]

	<p>CTAGGATCGATCTGTCGACGCTGGGTGGCGATTGATAGTCTAGCCATCACATTTAAA AGCATCTCAGCCTACCATGAGAATAAGAGAAAAGAAAATGAAGATCAATAGCTTATT CATCTCTTTTTCTTTTTCTGTTGGTGAAAGCCAACACCCTGTCTAAAAAACATAAAT TTCTTTAATCATTTCCTCTTTCTCTGTGCTTCAATTAATAAAAAATGGAAAGAAC CTCGAG</p>	
<p>剪接点 经移除;具 有 12.75% U 含量的 Cas9 ORF</p>	<p>ATGGACAAGAAGTACAGCATCGGACTGGACATCGGAACAAACAGCGTCGGATGGG CAGTCATCACAGACGAATACAAGGTCCCAGCAAGAAGTTCAAGGTCTGGGAAA CACAGACAGACACAGCATCAAGAAGAACCCTGATCGGAGCACTGCTGTTCCAGACG GGAGAAACAGCAGAAGCAACAAGACTGAAGAGAACAGCAAGAAGAAGATACAC AAGAAGAAAGAACAAGAATCTGCTACCTGCAGGAAATCTCAGCAACGAAATGGCA AAGGTCGACGACAGCTTCTTCCACcggCTGGAAGAAAAGCTTCTGGTCCGAAGAAGA CAAGAAGCACGAAAGACACCCGATCTTCGGAAACATCGTCGACGAAGTCGCATAC CACGAAAAGTACCCGACAATCTACCACCTGAGAAAAGAAGCTGGTCCAGACGACAG ACAAGGCAGACCTGAGACTGATCTACCTGGCACTGGCACACATGATCAAGTTTCA AGGACACTTCTGATCGAAGGAGACCTGAACCCGGACAACAGCGACGTCGACAAG CTGTTTATCCAGCTGGTCCAGACATACAACCAGCTGTTTCAAGAAAACCCGATCAA CGAAGCGGAGTCGACGCAAAAGGCAATCCTGAGCGCAAGACTGAGCAAGAGCAG AAGACTGGAAAACCTGATCGCACAGCTGCCGGGAGAAAAGAAGAACGGACTGTT CGGAAACCTGATCGCACTGAGCTGGGACTGACACCGAACTTCAAGAGCAACTTC GACCTGGCAGAAGACGCAAAAGCTGCAGCTGAGCAAGGACACATACGACAGCAG CTGGACAACCTGCTGGCACAGATCGGAGACCAGTACGCAGACCTGTTCTGGCAG CAAAGAACCTGAGCGACGCAATCCTGCTGAGCGACATCCTGAGAGTCAACACAGA AATCACAAGGCACCGCTGAGCGCAAGCATGATCAAGAGATACGACGAACACCAC CAGGACCTGACACTGCTGAAGGCACTGGTTCAGACAGCAGCTGCCGGAAGTACA AGGAAATCTTCTCGACCAGAGCAAGAACGGATACGCAGGATACATCGACGGAGG AGCAAGCCAGGAAGAATTCTACAAGTTCATCAAGCCGATCCTGGAAAAGATGGAC GGAACAGAAGAAGTCTGGTCAAGCTGAACAGAGAAGACCTGCTGAGAAAAGCAG AGAACATTCGACAACGGAAGCATCCCACCAGATCCACCTGGGAGCAACTGCACG CAATCCTGAGAAGACAGGAAGACTTCTACCCGTTCTGAAGGACAACAAGAAAA GATCGAAAAGATCCTGACATTCAGAATCCCGTACTACGTCGGACCGCTGGCAAGAG GAAACAGCAGATTCGCATGGATGACAAGAAAAGAGCGAAGAAAACAATCACACCGTG GAACTTCGAAGAAGTCGTCGACAAGGGAGCAAGCGCACAGAGCTTTCATCGAAAAG AATGACAAACTTCGACAAGAACCCTGCCGAACGAAAAGGTTCTGCCGAAGCAGC CTGCTGTACGAATACTTACAGTCTACAACGAACTGACAAAGGTCAAGTACGTCAC AGAAGGAATGAGAAAAGCCGGCATTCTGAGCGGAGAACAGAAGAAGGCAATCGT CGACCTGCTGTTCAAGACAAACAGAAAAGGTCAAGTCAAGCAGCTGAAGGAAGA TACTTCAAGAAGATCGAATGCTTTCGACAGCGTCGAAATCAGCGGATCGAAGAC AGATTC AACGCAAGCCTGGGAACATACCACGACCTGCTGAAGATCATCAAGGACA AGGACTTCTGGACAACGAAGAAAACGAAGACATCCTGGAAGACATCGTCTGAC ACTGACACTGTTTGAAGACAGAGAAATGATCGAAGAAAAGACTGAAGACATACGCA CACCTGTTGACGACAAGGTATGAAGCAGCTGAAGAGAAGAAGATACACAGGAT GGGAAAGACTGAGCAGAAAAGCTGATCAACGGAATCAGAGACAAGCAGAGCGGAA AGACAATCCTGGACTTCTGAAAGAGCGACGGATTTCGAAAACAGAAACTTTCATGCA GCTGATCCACGACGACAGCCTGACATTCAAGGAAGACATCCAGAAGGCACAGGTC AGCGGACAGGGAGACAGCCTGCACGAACACATCGAAAACCTGGCAGGAAGCCCG GCAATCAAGAAGGGAATCCTGCAGACAGTCAAGGTCTGACGAACTGGTCAAGG TCATGGGAAGACACAAGCCGGAAAACATCGTATCGAAAATGGCAAGAGAAGAACCA GACAACACAGAAGGGACAGAAGAACAGCAGAGAAAAGAAATGAAGAGAATCGAAG AAGGAATCAAGGAAGTGGGAAGCCAGATCCTGAAGGAACACCCGGTCCGAAAACA CACAGCTGCAGAACGAAAAGCTGTACCTGTACTACCTGCAaAACGGAAGAGACAT GTACGTCGACCAGGAAGTGGACATCAACAGACTGAGCGACTACGACGTCGACCAC ATCGTCCCGCAGAGCTTCTGAAAGGACGACAGCATCGACAACAAGGTCTTGACAA GAAGCGACAAGAACAGAGGAAAGAGCGACAACGTCGCCGAGCGAAGAAGTCGTCA AGAAGATGAAGAACTACTGGAGACAGCTGCTGAACGCAAAAGCTGATCACACAGAG AAAGTTCGACAACCTGACAAAAGGCAGAGAGAGGAGGACTGAGCGAACTGGACAA GGCAGGATTCATCAAGAGACAGCTGGTTCGAAAACAAGACAGATCAAAAAGCACGTC GCACAGATCCTGGACAGCAGAATGAACACAAGTACGACGAAAACGACAAGCTGA TCAGAGAAGTCAAGGTATCACACTGAAGAGCAAGCTGGTCAGCGACTTCAGAAA GGACTTCCAGTTCTACAAGGTTCAGAGAAATCAACAATAACCACACGACACGAC GCATACCTGAACGCAGTCTCGGAAACAGCACTGATCAAGAAGTACCCGAAAGCTGG AAAGCGAATTCGTCTACGGAGACTACAAGGTCTACGACGTCAGAAAAGATGATCGC AAAGAGCGAACAGGAAATCGGAAAGGCAACAGCAAAGTACTTCTTACAGCAAC ATCATGAACTTCTTCAAGACAGAAATCACACTGGCAAAACGGAGAAATCAGAAAAG GACCGCTGATCGAAAACAAAGGAGAAACAGGAGAAATCGTCTGGCAAGGGGAA GAGACTTCGCAACAGTCAAAAAGGTCTGAGCATGCCGCAAGTCAACATCGTCAA GAAGACAGAAGTCCAGACAGGAGGATTCAGCAAGGAAAAGCATCCTGCCGAAAGAG AAACAGCGACAAGCTGATCGCAAGAAAAGGACTGGGACCCGAAAGAAGTACGG</p>	<p>50</p>

[0685]

	<p>AGGATTCGACAGCCCACAGTCGCATACAGCGTCTGGTCGTCGCAAAGGTCGAA AAGGGAAAGAGCAAGAAGCTGAAGAGCGTCAAGGAACTGCTGGGAATCACAATC ATGGAAAGAAGCAGCTTCGAAAAGAACCCGATCGACTTCTGGAAGCAAAGGGAT ACAAGGAAGTCAAGAAGGACCTGATCATCAAGCTGCCGAAGTACAGCCTGTTTCCA ACTGGAAAACGGAAGAAAAGAGAATGCTGGCAAAGCGCAGGAGAAGTGCAGAAAGGG AAACGAACTGGCACTGCCGAGCAAGTACGTCAACTTCTGTACTGGCAAGCCAC TACGAAAAGCTGAAGGGAAGCCCGGAAGACAACGAACAGAAGCAGCTGTTCTGTC GAACAGCACAAGCACTACCTGGACGAAATCATCGAACAGATCAGCGAATTCAGCA AGAGAGTATCCTGGCAGACGCAAACCTGGACAAGGTCCTGAGCGCATACAACAA GCACAGAGACAAGCCGATCAGAGAACAGGCAGAAAACATCATCCACCTGTTTACA CTGACAAACCTGGGAGCACCAGGACAGATTCAAGTACTTGCACACAACAATCGACA GAAAGAGATACAAAGCACAAGGAAGTCTGGACGCAACACTGATCCACCAGA GCATCACAGGACTGTACGAAACAAGAAATCGACCTGAGCCAGCTGGGAGGAGACGG AGGAGGAAGCCGAAGAAGAAGAGAAAAGGTCTAG</p>	
<p>具有 HSD 的 5' UTR、对应 于 SEQ ID NO: 50 的 ORF、 Kozak 序列 及 ALB 的 3' UTR 的 Cas9 转 录物</p>	<p>GGGTCCCAGTCGGCGTCCAGCGGCTCTGCTTGTCTGTGTGTGTCGTTGCAGG CCTTATTTCGGATCCGCCACCATGGACAAGAAGTACAGCATCGGACTGGACATCGGA ACAAACAGCGTCGGATGGGCAGTCAACAGACGAATACAAGGTCCCAGCAAGA AGTTCAAGGTCCTGGGAAACACAGACAGACACAGCATCAAGAAGAACCTGATCGG AGCACTGCTGTTTCGACAGCGGAGAAACAGCAGAAGCAACAAGACTGAAGAGAAAC AGCAAGAAGAAGATACACAAGAAGAAAAGAACAGAATCTGTACTCTGACGAAATC TTCAGCAACGAAATGGCAAAGGTCGACGACAGCTTCTTCCAC_{egg}CTGGAAGAAAG CTTCTGTGTCGAAGAAGACAAGAAGCAGAAAGACACCCGATCTTCGAAAACATC GTCGACGAAGTCGCATACCACGAAAAGTACCCGACAATCTACCACCTGAGAAAAGA AGCTGGTCGACAGCACAGACAAGGCAGACCTGAGACTGATCTACTGCTGACTGGC ACACATGATCAAGTTCAGAGGACACTTCTGATCGAAGGAGACCTGAACCCGGAC AACAGCGACGTCGACAAGCTGTTTATCCAGCTGGTCCAGACATACAACCAGCTGTT CGAAGAAAACCCGATCAACGCAAGCGGAGTCGACGCAAAGGCAATCTGAGCGC AAGACTGAGCAAGAGCAGAAGACTGGAAAACCTGATCGCACAGCTGCCGGGAGA AAAGAAGAACGGACTGTTTCGAAAACCTGATCGACTGAGCCTGGGACTGACACCG AACTTCAAGAGCAACTTCGACCTGGCAGAAGACGCAAAGCTGCAGCTGAGCAAG GACACATACGACGACGACCTGGACAACTGCTGGCACAGATCGGAGACCAGTACG CAGACCTGTTCTGGCAGCAAAGAACCTGAGCGACGCAATCCTGTGAGCGACAT CCTGAGAGTCAACACAGAAATCACAAAGGCCACCGCTGAGCGCAAGCATGATCAAG AGATACGACGAACACCACCAGGACCTGACACTGCTGAAGGCACTGGTCAGACAGC AGCTGCCGAAAAGTACAAGGAAATCTTCTTCGACCAGAGCAAGAACGGATACGC AGGATACATCGACGGAGGAGCAAGCCAGGAAGAATTCTACAAGTTCATCAAGCCG ATCCTGGAAAAGATGGACGGAACAGAAGAAGTCTGCTGATCAAGTCAAGCAGAGAA GACCTGCTGAGAAAAGCAGAGAAACATTTCGACAACGGAAGCATCCCGACACAGATCC ACCTGGGAGAACTGCACGCAATCTGAGAAGACAGGAAGACTTCTACCCGTTCTCCT GAAGGACAACAGAGAAAAGATCGAAAAGATCTGACATTCAGAATCCCGTACTAC GTCGGACCGCTGGCAAGAGGAAAACAGCAGATTGCGATGGATGACAAGAAAAGAGC GAAGAAAACAATCACACCTGGAACCTCGAAGAAGTCTGACGCAAGGGAGCAAGC GCACAGAGCTTCATCGAAAAGATGACAAACTTCGACAAGAACCTGCCGAACGAAA AGGTCTGCCGAAGCACAGCCTGCTGTACGAATACTTCACAGTCTACAACGAACTG ACAAAGGTCAAGTACGTACAGAAGGAATGAGAAAAGCCGGCATTCTGAGCGGAG AACAGAAGAAGGCAATCGTCGACCTGCTGTTCAAGACAACAGAAAAGTCAAGT CAAGCAGCTGAAGGAAGACTTCAAGAAAGATCGAATGCTTCGACAGCTCAAGGTCGAA ATCAGCGGAGTCGAAGACAGATTCAACGCAAGCCTGGGAACATACCACGACCTGC TGAAGATCATCAAGGACAAGGACTTCTGGACAACGAAGAAAACGAAGACATCCT GGAAGACATCGTCTGACACTGACACTGTTTCAAGACAGAGAAATGATCGAAGAA AGACTGAAGACATACGCACACCTGTTTCGACGACAAGGTCATGAAGCAGCTGAAGA GAAGAAGATACACAGGATGGGGAAGACTGAGCAGAAAAGCTGATCAACGGAATCA GAGACAAGCAGAGCGGAAAAGACAATCCTGGACTTCTGAAGAGCGACGGATTTCGC AAACAGAAACTTCATGCAGCTGATCCACGACGACAGCCTGACATTCAGGAAGAC ATCCAGAAGGCACAGGTCAGCGGACAGGGAGACAGCCTGCACGAACACATCGCA AACCTGGCAGGAAGCCCGCAATCAAGAAGGGAACTCTGCAGACAGTCAAGGTCG TCGACGAACTGGTCAAGGTCATGGGAAGACACAAGCCGAAAACATCGTCATCGA AATGGCAAGAGAAAACAGACAACACAGAAGGGACAGAAGAAGCAGAGAGAAA GAATGAAGAGAATCGAAGAAGGAATCAAGGAAGTGGGAAGCCAGATCCTGAAGG AACACCCGGTCGAAAACACACAGCTGCAGAAGCAGAAAAGCTGTACTCTACTACCT GCAaAACGGAAGAGACATGTACGTGACCGAGGAAGTGGACATCAACAGACTGAGC GACTACGACGTGACACATCGTCCCGCAGAGCTTCTGAAGGACGACAGCATCG ACAACAAGGTCCTGACAAGAAGCGACAAGAACAGAGGAAAGAGCGACAACGTCC CGAGCGAAGAAGTCTCAAGAAGATGAAGAAGTACTGGAGACAGCTGCTGAACG CAAAGCTGATCACACAGAGAAAAGTTCGACAACCTGACAAAAGGCAGAGAGAGGAG GACTGAGCGAACTGGACAAGGCAGGATTATCAAGAGACAGCTGGTGCAAAACA GACAGATCAAAAACGACGTGACAGATCCTGGACAGCAGAATGAACACAAAAGTA</p>	<p>51</p>

[0686]

[0687]

	<p>CGACGAAAACGACAAGCTGATCAGAGAAGTCAAGGTCATCACAAGGAGCAA GCTGGTCAGCGACTTCAGAAAGGACTTCCAGTTCTACAAGGTCAGAGAAATCAAC AACTACCACCACGCACACGACGCATACCTGAACGCAGTCTGCGGAACAGCACTGA TCAAGAAGTACCCGAAGCTGGAAAGCGAATTCGTCTACGGAGACTACAAGGTCTA CGACGTCAGAAAGATGATCGCAAAGAGCGAACAGGAAATCGGAAAGGCAACAGC AAAGTACTTCTTACAGCAACATCATGAACCTTCTCAAGACAGAAATCACACTGG CAAACGGAGAAATCAGAAAGAGACCGCTGATCGAAAACAAACGGAGAAACAGGAG AAATCGTCTGGGACAAGGGAAGAGACTTCGCAACAGTCAGAAAAGGTCTGAGCAT GCCGCAGGTCAACATCGTCAAGAAGACAGAAGTCCAGACAGGAGGATTTCAGCAA GGAAAGCATCCTGCCGAAGAGAAACAGCGACAAGCTGATCGCAAGAAAGAAAGGA CTGGGACCCGAAGAAGTACGGAGGATTTCGACAGCCCGACAGTCGCATACAGCGTC CTGGTCTGTCGAAAAGGTCGAAAAGGGAAAGAGCAAGAAGCTGAAGAGCGTCAAG GAACTGCTGGGAATCACAATCATGGAAAAGAGCAGCTTCGAAAAAGAACCCGATCG ACTTCTGGAAGCAAAGGGATAACAAGGAAGTCAAGAAGGACCTGATCATCAAGCT GCCGAAGTACAGCCTGTTGCAACTGGAAAACGGAAAGAAAGAGAATGCTGGCAAG CGCAGGAGAAGTGCAGAAGGGAAACGAACTGGCACTGCCGAGCAAGTACGTCAA CTTCTGTACCTGGCAAGCCACTACGAAAAGCTGAAGGGAAGCCCGGAAGACAAC GAACAGAAGCAGCTGTTTCGTGCAACAGCACAAGCAACTACCTGGACGAAATCATCG AACAGATCAGCGAATTCAGCAAGAGAGTTCATCTGCGCAGACGCAACCTGGCAA GGTCTGAGCGCATACAACAAGCACAGAGACAAGCCGATCAGAGAACAGGCAGA AAACATCATCCACCTGTTTACACTGACAAACCTGGGAGCACCGGCAGCATTCAAGT ACTTCGACACAACAATCGACAGAAAGAGATACACAAGCACAAAGGAAAGTCTGGGA CGCAACTGATCCACCAGAGCATCACAGGACTGTACGAAAACAAGAATCGACCTG AGCCAGCTGGGAGGAGAGCGGAGGAGGAAGCCCGAAGAAGAAGAGAAAGGTTA GCTAGCCATCACATTTAAAAGCATCTCAGCCTACCATGAGAATAAGAGAAAGAAAA TGAAGATCAATAGCTTATTTCATCTCTTTTCTTTTCTGTTGGTGTAAAGCCAACACCC TGTTCTAAAAAACATAAATTTCTTTAATCATTTTGCCTCTTTTCTCTGTGCTTCAATTA TAAAAAATGGAAAGAACCTCGAG</p>	
<p>具有一般 经常用于 人类中的 最小尿苷 密码子;具 有 12.75% U 含量的 Cas9 ORF</p>	<p>ATGGACAAGAAGTACAGCATCGGCCTGGACATCGGCACCAACAGCGTGGGCTGGG CCGTGATCACCGACGAGTACAAGGTGCCAGCAAGAAGTTCAAGGTGCTGGGCAA CACCGACAGACACAGCATCAAGAAGAACCTGATCGGCGCCCTGCTGTTTCGACAGC GGCGAGACCGCCGAGGCCACCAGACTGAAGAGAACCGCCAGAAGAAGATACACC AGAAGAAAGAACAGAACTGCTACCTGCAAGGAGATCTTCAGCAACGAGATGGCCA AGGTGGACGACAGCTTCTTCCACAGACTGGAGGAGAGCTTCTGTTGGAGGAGGA CAAGAAGCAGGAGAGACACCCCATCTTCGGCAACATCGTGGACGAGGTGGCCTAC CACGAGAAGTACCCACCATCTACCACCTGAGAAAAGAAGCTGGTGGACAGCACCG ACAAGGCCGACCTGAGACTGATCTACCTGGCCCTGGCCCATGATCAAGTTTCAGA GGCCACTTCTGATCGAGGGCGACTGAACCCCGACAACAGCGAGCTGGACAAGC TGTTTCATCCAGCTGGTGCAGACCTACAACCAGCTGTTTCGAGGAGAACCCCATCAAC GCCAGCGGCGTGGACGCCAAGGCCATCTGAGCGCCAGACTGAGCAAGAGCAGA AGACTGGAGAACCTGATCGCCAGCTGCCCGGCGAGAAGAAGAACGGCCTGTTTCG GCAACCTGATCGCCCTGAGCCTGGGCCTGACCCCAACTTCAAGAGCAACTTCGA CCTGGCCGAGGACGCCAAGCTGCAGCTGAGCAAGGACACCTACGACGACGACCTG GACAACCTGCTGGCCAGATCGGCGACCAGTACGCCGACCTGTTCTGCGCCGCA AGAACCTGAGCGACGCCATCTGCTGAGCGACATCTGAGAGTGAACACCCGAGAT CACCAAGGCCCCCTGAGCGCCAGCATGATCAAGAGATACGACGAGCACCACCATG GACCTGACCCTGCTGAAGGCCCTGGTGAAGACAGCAGCTGCCCGAGAGTACAAGG AGATCTTCTTCGACCAGAGCAAGAACGGCTACGCCGGCTACATCGACGGCGGCGC CAGCCAGGAGGAGTTCTACAAGTTCATCAAGCCATCCTGGAGAAGATGGACGGC ACCGAGGAGCTGCTGGTGAAGCTGAACAGAGAGGACCTGCTGAGAAAAGCAGAGA ACCTTCGACAACGGCAGCATCCCCACCAGATCCACCTGGGCGAGCTGCACGCCAT CCTGAGAAGACAGGAGGACTTCTACCCTTCTGAAAGGACAACAGAGAGAAGATC GAGAAGATCCTGACCTTCAGAATCCCCTACTACGTGGGCCCCCTGGCCAGAGGCAA CAGCAGATTCGCTGGATGACCAGAAAGAGCGAGGAGACCATACCCCTGGAAC TTCGAGGAGGTGGTGGACAAGGGCGCCAGCGCCAGAGCTTTCATCGAGAGAATGA CCAATTTCGACAAGAACCTGCCCAACGAGAAAGGTGCTGCCAAGCACAGCTGCT GTACGAGTACTTACCCTGTACAACGAGCTGACCAAGGTGAAGTACGTGACCGAG GGCATGAGAAAGCCCGCCTTCTGAGCGGCGAGCAGAAGAAGGCCATCGTGGACC TGCTGTTCAAGACCAACAGAAAGGTGACCGTGAAGCAGCTGAAGGAGGACTACTT CAAGAAGATCGAGTGCTTCGACAGCGTGGAGATCAGCGGCGTGGAGGACAGATT AACGCCAGCCTGGGCACCTACCACGACCTGCTGAAGATCATCAAGGACAAGGACT TCCTGGACAACGAGGAGAACGAGGACATCCTGGAGGACATCGTGTGACCCTGAC CCTGTTTCGAGGACAGAGAGATGATCGAGGAGAGACTGAAGACCTACGCCACCTG TTCGACGACAAGGTGATGAAGCAGCTGAAGAGAAGAAGATACACCGCTGGGGC AGACTGAGCAGAAAGCTGATCAACGGCATCAGAGACAAGCAGAGCGGCAAGACC ATCCTGGACTTCTGAAAGAGCGACGGCTTCGCCAACAGAACTTCATGCAGCTGAT CCACGACGACAGCCTGACCTTCAAGGAGGACATCCAGAAGGCCAGGTGAGCGGC</p>	<p>52</p>

[0688]

	<p>CAGGGCGACAGCCTGCACGAGCACATCGCCAACCTGGCCGGCAGCCCCGCCATCA AGAAGGGCATCCTGCAGACCGTGAAGGTGGTGGACGAGCTGGTGAAGGTGATGGG CAGACACAAGCCCGAGAACATCGTGATCGAGATGGCCAGAGAGAACCAGACCACC CAGAAGGGCCAGAAGAACAGCAGAGAGAGAATGAAGAGAATCGAGGAGGGGCATC AAGGAGCTGGGCAGCCAGATCCTGAAGGAGCACCCCCGTGGAGAACCACCCAGCTG CAGAACGAGAAGCTGTACTCTACTACTCGCAGAACGGCAGAGACATGTACGTGG ACCAGGAGCTGGACATCAACAGACTGAGCGACTACGACGTGGACCACATCGTGCC CCAGAGCTTCTGAAGGACGACAGCATCGACAACAAGGTGCTGACCAGAAGCGAC AAGAACAGAGGCAAGAGCGACAACGTGCCAGCGAGGAGGTGGTGAAGAAGATG AAGAACTACTGGAGACAGCTGCTGAACGCCAAGCTGATCACCCAGAGAAAAGTTCG ACAACCTGACCAAGGCCGAGAGAGGGCGCCTGAGCGAGCTGGACAAGGCCGGCT TCATCAAGAGACAGCTGGTGGAGACCAGACAGATCACCAGACGTGGCCAGAT CCTGGACAGCAGAATGAACACCAAGTACGACGAGAACGACAAGCTGATCAGAGA GGTGAAGGTGATCACCCCTGAAGAGCAAGCTGGTGAAGCGACTTCAGAAAAGGACTTC CAGTTCTACAAGGTGAGAGAGATCAACAACCTACCACCAGCCACAGCCAGCTTAC TGAACGCCGTGGTGGGCACCGCCCTGATCAAGAAGTACCCCAAGCTGGAGAGCGA GTTCTGTACGCGACTACAAGGTGTACGACGTGAGAAAAGTATCGCCAAGAGC GAGCAGGAGATCGGCAAGGCCACCGCCAAGTACTTCTTACAGCAACATCATGAA CTTCTTCAAGACCGAGATCACCCCTGGCCAACGGCGAGATCAGAAAAGAGACCCTC ATCGAGACCAACGGCGAGACCGGGCGAGATCGTGTGGGACAAGGGCAGAGACTTC GCCACCGTGAGAAAAGGTGCTGAGCATGCCCCAGGTGAACATCGTGAAGAAGACCG AGGTGCAGACCGCGGCTTCAGCAAGGAGAGCATCTGCCAAAGAGAAAACAGCG ACAAGCTGATGCCAGAAAAGGACTGGGACCCCAAGAAGTACGGCGGCTTCG ACAGCCCCACCGTGGCTACAGCGTGTGGTGGTGGCCAAGGTGGAGAAAGGGCAA GAGCAAGAAGCTGAAGAGCGTGAAGGAGCTGCTGGGCATCACCATCATGGAGAGA AGCAGCTTCGAGAAGAACCCCATCGACTTCTGGAGGCCAAGGGCTACAAGGAGG TGAAGAAGGACCTGATCATCAAGCTGCCAAGTACAGCCTGTTTCGAGCTGGAGAA CGGCAGAAAAGAGAATGTGGCCAGCGCCGGCGAGCTGCAGAAAAGGGCAACGGACT GGCCCTGCCAGCAAGTACGTGAACCTTCTGTACTTGGCCAGCCACTACGAGAAG CTGAAGGGCAGCCCCGAGGACAACGAGCAGAAGCAGCTGTTCTGTGGAGCAGCAC AAGCACTACCTGGACGAGATCATCGAGCAGATCAGCGAGTTCAGCAAGAGAGTGA TCCTGGCCGACGCCAACCTGGACAAGGTGCTGAGCGCCTACAACAAGCACAGAGA CAAGCCCATCAGAGAGCAGGCCGAGAACATCATCCACCTGTTTACCCTGACCAAC CTGGGCGCCCCCGCCCTTCAAGTACTTCGACACCACCATCGACAGAAAAGAGATA CACCAGCACAAGGAGGTGCTGGACGCCACCCTGATCCACCAGAGCATCACCGGC CTGTACGAGACCAGAATCGACCTGAGCCAGCTGGGCGGGCAGCGCGGGCAGCC CCAAGAAGAAGAGAAAAGGTGTGA</p>	
<p>具有 HSD 的 5' UTR, 对应 于 SEQ ID NO: 52 的 ORF、 Kozak 序列 及 ALB 的 3' UTR 的 Cas9 转 录物</p>	<p>GGGTCCCGCAGTCGGCGTCCAGCGGCTCTGCTTGTTCGTGTGTGTGTCGTTGCAGG CCTTATTCGGATCCGCCACCATGGACAAGAAGTACAGCATCGGCCTGGACATCGGC ACCAACAGCGTGGGCTGGGCCGTGATCACCGACGAGTACAAGGTGCCAGCAAGA AGTTCAAGGTGCTGGGCAACACCGACAGACACAGCATCAAGAAGAACCCTGATCGG CGCCCTGCTGTTTCGACAGCGGGCAGAGACCGCCGAGGCCACCAGACTGAAGAGAAC GCCAGAAGAAGATACACCAGAAGAAGAACAAGAAATCTGCTACCTGCAGGAGATCT TCAGCAACGAGATGGCCAAGGTGGACGACAGCTTCTTCCACAGACTGGAGGAGAG CTTCTGTGGAGGAGGACAAGAAGCAGAGAGACACCCCATCTTCGGCAACATC GTGGACGAGGTGGCTACCAGAGAAGTACCCACCATCTACCACCTGAGAAAAGA AGTGGTGGACAGCACCGACAAGGCCGACCTGAGACTGATCTACCTGGCCCTGGC CCACATGATCAAGTTCAGAGGCCACTTCTGATCGAGGGCGACCTGAACCCCGACA ACAGCGACGTGGACAAGCTGTTTATCCAGCTGGTGCAGACCTACAACCAGCTGTT CGAGGAGAACCCATCAACGCCAGCGGCGTGGACGCCAAGGCCATCTGAGCGCC AGACTGAGCAAGAGCAGAAGACTGGAGAACCTGATCGCCAGCTGCCCGGCGAG AAGAAGAACGGCTGTTTCGGCAACCTGATCGCCCTGAGCCTGGGCCTGACCCCCA ACTTCAAGAGCAACTTCGACCTGGCCGAGGACGCCAAGCTGCAGCTGAGCAAGGA CACCTACGACGACGACCTGGACAACCTGCTGGCCAGATCGGGCAGCAAGTACGCC GACCTGTTCTGGCCGCAAGAACCTGAGCGACGCCATCCTGCTGAGCGACATCCT GAGAGTGAACACCGAGATCAACCAAGGCCCCCTGAGCGCCAGCATGATCAAGAGA TACGACGAGCACACCAGGACCTGACCCTGCTGAAGGCCCTGGTGAAGACAGCAGC TGCCCGAGAAGTACAAGGAGATCTTCTCGACCAGAGCAAGAACGGCTACGCCGG CTACATCGACGGCGGGCCAGCCAGGAGGATCTACAAGTTCATCAAGCCCATCC TGGAGAAGATGGACGGCACCCAGGAGCTGCTGGTGAAGCTGAACAGAGAGAGGACC TGCTGAGAAAAGCAGAGAACCTTCGACAACGGCAGCATCCCCACCAGATCCACCT GGGCGAGCTGCACGCCATCCTGAGAAGACAGGAGGACTTCTACCCCTTCTGAAAG GACAACAGAGAGAAGATCGAGAAGATCCTGACCTTCAAGATCCCCTACTACGTGG GCCCTGGCCAGAGGCAACAGCAGATTCGCTGGATGACCAGAAAAGCAGCGAGGA GACCATCACCCCTGGAACCTTCGAGGAGGTGGTGGACAAGGGCGCCAGCGCCAG AGCTTATCGAGAGAATGACCAACTTCGACAAGAACCTGCCAACGAGAAGGTGC TGCCAAAGCACAGCCTGCTGTACGAGTACTTACCCTGTACAACGAGCTGACCAA</p>	<p>53</p>

[0689]

	<p>GGTGAAGTACGTGACCGAGGGCATGAGAAAGCCGCCTTCCTGAGCGGCGAGCAG AAGAAGGCCATCGTGGACCTGCTGTTCAAGACCAACAGAAAGGTGACCGTGAAGC AGCTGAAGGAGGACTACTTCAAGAAGATCGAGTGCTTCGACAGCGTGGAGATCAG CGGCGTGGAGGACAGATTCAACGCCAGCCTGGGCACCTACCACGACCTGCTGAAG ATCATCAAGGACAAGGACTTCTGGACAACGAGGAGAACGAGGACATCCTGGAGG ACATCGTGTGACCCGTACCCCTGTTTCGAGGACAGAGAGATGATCGAGGAGAGACT GAAGACCTACGCCACCTGTTTCGACGACAAGGTGATGAAGCAGCTGAAGAGAAGA AGATACACCGGCTGGGGCAGACTGAGCAGAAAAGCTGATCAACGCCATCAGAGACA AGCAGAGCGGCAAGACCATCCTGGACTTCTGAAGAGCGACGGCTTCGCCAACAG AAACTTCATGCAGCTGATCCACGACGACAGCCTGACCTTCAAGGAGGACATCCAG AAGGCCAGGTGAGCGGCCAGGGCGACAGCCTGCACGAGCACATCGCCAACCTG GCCGGCAGCCCGCCATCAAGAAGGGCATCCTGCAGACCGTGAAGGTGGTGGACG AGCTGGTGAAGGTGATGGGCAGACACAAGCCCGAGAACATCGTATCGAGATGGC CAGAGAGAACCAGACCACCCAGAAGGGCCAGAAGAAGCAGCAGAGAGAGAATGA AGAGAATCGAGGAGGGCATCAAGGAGCTGGGCAGCCAGATCCTGAAGGAGCACC CCGTGGAGAACACCAGCTGCAGAACGAGAAGCTGTACCTGTACTACCTGCAGAA CGGCAGAGACATGTACGTGGACCAGGAGCTGGACATCAACAGACTGAGCGACTAC GACGTGGACCACATCGTGCCCCAGAGCTTCTGAAGGACGACAGCATCGACAACA AGGTGCTGACCAGAAGCGACAAGAACAGAGGCAAGAGCGACACCTGCCCAGCG AGGAGGTGGTGAAGAAGATGAAGAAGTACTGGAGACAGCTGCTGAACGCCAACG TGATCACCCAGAGAAAGTTCGACAACCTGACCAAGGCCGAGAGAGGCCGCTGA GCGAGCTGGACAAGGCCGGCTTCAAGAGACAGCTGGTGGAGACCAGACAGAT CACCAAGCACGTGGCCAGATCCTGGACAGCAGAATGAACACCAAGTACGACGAG AACGACAAGCTGATCAGAGAGGTGAAGGTGATCACCTGAAGAGCAAGTGGTGA GCGACTTCAGAAAAGACTTCCAGTTCTACAAGGTGAGAGAGATCAACAACACTACCA CCACGCCACGACGCCTACCTGAACGCCGTGGTGGGCACCGCCTGATCAAGAA TACCCCAAGCTGGAGAGCGAGTTCGTGTACGGCGACTACAAGGTGTACGACGTGA GAAAGATGATCGCCAAGAGCGAGCAGGAGATCGGCAAGGCCACCGCAAGTACTT CTTCTACAGCAACATCATGAACCTTCTCAAGACCGAGATCACCTGGCCAACGGCG AGATCAGAAAGAGACCCCTGATCGAGACCAACGGCGAGACCGGCGAGATCGTGTG GGACAAGGGCAGAGACTTCGCCACCGTGAGAAAGGTGCTGAGCATGCCCCAGGTG AACATCGTGAAGAAGACCGAGGTGCAGACCGCGGCTTCAGCAAGGAGACATCC TGCCCAAGAGAAAACAGCGACAAGCTGATCGCCAGAAAAGAAAGACTGGGACCCCA AGAAGTACGGCGGCTTCGACAGCCCCACCGTGGCCTACAGCGTGTGGTGGTGGC CAAGGTGGAGAAGGGCAAGAGCAAGAAGCTGAAGAGCGTGAAGGAGCTGTGGG CATCACCATCATGGAGAGAAGCAGCTTCGAGAAGAACCCCATCGACTTCTCTGGAG GCCAAGGGTACAAGGAGGTGAAGAAGGACCTGATCATCAAGCTGCCAAGTACAG GCCTGTTTCGAGCTGGAGAACGGCAGAAAAGAGAATGCTGGCCAGCGCCGGCGAGCT GCAGAAGGGCAACGAGCTGGCCCTGCCAGCAAGTACGTGAACCTCCTGTACCTG GCCAGCCACTACGAGAAGCTGAAGGGCAGCCCCGAGGACAACGAGCAGAAGCAG CTGTTCTGTGGAGCAGCACAAGCACTACCTGGACGAGATCATCGAGCAGATCAGCG AGTTCAGCAAGAGAGTGTATCCTGGCCGACGCCAACCTGGACAAGGTGCTGAGCGC CTACAACAAGCACAGAGACAAGCCCATCAGAGAGCAGGCCGAGAATCATCCAC CTGTTACCCTGACCAACCTGGGGCAGCCCCGCGCCTTCAAGTACTTCGACACCAC CATCGACAGAAAAGAGATACACCAGCACAAGGAGGTGCTGGACGCCACCCTGATC CACCAGAGCATACCGGCCTGTACGAGACCAGAATCGACCTGAGCGAAGTGGCG GCGACGGCGGGCGGACGCCCCAAGAAGAAGAGAAAAGGTGTGACTAGCCATCACATT TAAAAGCATCTCAGCCTACCATGAGAATAAGAGAAAAGAAAATGAAGATCAATAGCT TATTCATCTCTTTTCTTTTCTGTTGGTGTAAAGCCAACACCCTGTCTAAAAACATA AATTTCTTTAATCATTTTGCCCTCTTTTCTCTGTGCTTCAATTAATAAAAAATGAAAAG AACCTCGAG</p>	
<p>具有一般不经常用于人类中的最小尿苷密码子; 具有 12.75% U 含量的 Cas9 ORF</p>	<p>ATGGACAAAAAATACAGCATAGGGCTAGACATAGGGACGAAACAGCGTAGGGTGGG CGGTAATAACGGACGAATACAAAGTACCGAGCAAAAAATTCAAAAGTACTAGGGAA CACGGACCACACAGCATAAAAAAAACCTAATAGGGGGCGTACTATTTCGACAGC GGGAAAACGGCGGAAGCGACGCGACTAAAACGAACGGCGCGACGACGATACAG CGACGAAAAAACCGAATATGTACTACTACAAGAAATATTCAGCAACGAAATGGCGAA AGTAGACGACAGCTTCTTCCACCGACTAGAAGAAAGCTTCTAGTAGAAGAAGAC AAAAACACGAACGACACCCGATATTCGGGAACATAGTAGACGAAGTAGCGTACC ACGAAAAATACCCGACGATATACCCTACGAAAAAACTAGTAGACAGCACGGGA CAAAGCGGACCTACGACTAATATACCTAGCGCTAGCGCACATGATAAAAATCCGAG GGCACTTCTAATAGAAGGGGACCTAAACCCGGACAACAGCGACGTAGACAAACT ATTCATACAACTAGTACAAACGTACAACCAACTATTTCGAAGAAAACCCGATAAACG CGAGCGGGGTAGACGCGAAAGCGATACTAAGCGCGCGACTAAGCAAAAAGCCGAC GACTAGAAAACCTAATAGCGCAACTACCGGGGAAAAAAAACCGGGCTATTCGG GAACCTAATAGCGCTAAGCCTAGGGCTAACGCCGAACCTTCAAAAAGCAACTTCGACC TAGCGGAAGACGCGAAACTACAACCTAAGCAAGACACGTACGACGACGACCTAGA CAACCTACTAGCGCAATAGGGGACCAATACGCGGACCTATTCTAGCGGGCGAAAA</p>	<p>54</p>

[0690]

	<p>ACCTAAGCGACGCGATACTACTAAGCGACATACTACGAGTAAACACGGAAATAACG AAAGCGCCGCTAAGCGCGAGCATGATAAAACGATACGACGAAACACCACCAAGACC TAACGCTACTAAAAGCGCTAGTACGACAACAACCTACCGGAAAAATACAAAAGAAATA TTCTTCGACCAAAGCAAAAACGGGTACGCGGGGTACATAGACGGGGGGGCGAGCC AAGAAGAATTCTACAAATTCATAAAACCGATACTAGAAAAAATGGACGGGACGGA AGAACTACTAGTAAACTAAACCGGAGAAAGACCTACTACGAAAAACAACGAACGTTT GACAACGGGAGCATAACCGACCAAATACACCTAGGGGAACTACACGCGATACTACG ACGACAAGAAGACTTCTACCCGTTCTAAAAGACAACCGAGAAAAATAGAAAAA ATACTAACGTTCCGAATACCGTACTACGTAGGGCCGCTAGCGCGAGGGAACAGCCG ATTTCGGTGGATGACGCGAAAAAGCGAAGAAACGATAACGCCGTGGAACCTCGAA GAAGTAGTAGACAAAAGGGGCGAGCGCGCAAAGCTTCATAGAACGAATGACGAACT TCGACAAAAACCTACCGAACGAAAAAGTACTACCGAAACACAGCCTACTATACGA ATACTTCACGGTATAACAACGAACTAACGAAAGTAAATACGTAACGGAAGGGATGC GAAAACCGGCGTTCTAAGCGGGGAACAAAAAAGCGATAGTAGACCTACTATT CAAAACGAACCGAAAAGTAAACGTTAAACAACCTAAAAAGAAAGACTACTTCAAAAA AATAGAATGCTTCGACAGCGTAGAAATAAGCGGGGTAGAAGACCGATTCAACGCG AGCCTAGGGACGTACCACGACCTACTAAAAATAATAAAAGACAAAGACTTCTTAGA CAACGAAGAAAACGAAGACATACTAGAAGACATAGTACTAACGCTAACGCTATTTCG AAGACCGAGAAATGATAGAAAGAACGACTAAAAACGTACGCGCACCTATTTCAGCA CAAAGTAATGAAAACAATAAAACGACGACGATACACGGGGTGGGGGCGACTAAGC CGAAAACATAAAACGGGATACGAGACAAAACAAAGCGGGAAAACGATACTAGACT TCCTAAAAAGCGACGGGTTCGCGAACCGGAACTTCATGCAACTAATACACGACGA CAGCCTAACGTTCAAAGAAGACATACAAAAAGCGCAAGTAAGCGGGCAAGGGGA CAGCCTACCGAACACATAGCGAACCTAGCGGGGAGCCCGCGGATAAAAAAAGGG ATACTACAAAACGGTAAAAGTAGTAGACGAACTAGTAAAAAGTAATGGGGCGACACA AACCGGAAAACATAGTAATAGA AATGGCGCGAGAAAACCAAACGACGCAAAAAAG GGCAAAAAACAGCCGAGAACGAATGAAACGAATAGAAGAAGGGATAAAAAGAAC TAGGGAGCCAATACTAAAAGAACACCCGGTAGAAAACACGCAACTACAAAAACGA AAAACCTACCTATACTACCTACAAAACGGGCGAGACATGTACGTAGACCAAGAAC TAGACATAAACCGACTAAGCGACTACGACGTAGACCACATAGTACCGCAAAGCTTC CTAAAAGACGACAGCATAGACAACAAAGTACTAACCGGAAGCGACAAAAACCGA GGGAAAAGCGACAACGTACCGAGCGAAGAAGTAGTAAAAAATGAAAAACTAC TGGCGAACTACTAAAACGCGAACTAATAACGCAACGAAAATTCGACAACCTAA CGAAAGCGGAACGAGGGGGGCTAAGCGAACTAGACAAAAGCGGGGTTCAAAAAAC GACAACCTAGTAGAAAACGCGACAAAATAACGAAACACGTAGCGCAATACTAGACAG CCGAATGAACACGAAATACGACGAAAACGACAAAATAACGAGAAAGTAAAAGTA ATAACGCTAAAAGCAAACCTAGTAAGCGACTTCCGAAAAGACTTCAATTCTACAA AGTACGAGAAAATAAAACAACCTACCACGCGCACGACGCGTACCTAACGCGGGTA GTAGGGACGGCGCTAATAAAAAAATACCCGAAACTAGAAAAGCGAATTCGTATACGG GGACTACAAAGTATACGACGTACGAAAAATGATAGCGAAAAGCGAACAAGAAATA GGGAAAGCGACGGCGAAATACTTCTTCTACAGCAACATAATGAACCTTCTTCAAAC GGAAATAACGCTAGCGAACCGGGGAAATACGAAAACGACCGCTAATAAGAACGAAC GGGGAACGGGGGAAATAGTATGGGACAAAAGGGCGAGACTTCGCGACGGTACGA AAAGTACTAAGCATGCCGCAAGTAAACATAGTAAAAAAAACGGAAGTACAAACGG GGGGTTTACGCAAAAGAAAGCATACTACCGAAAACGAAACAGCGACAAAATAATAGC GCGAAAAAAGACTGGGACCCGAAAAAATACGGGGGGTTCGACAGCCCGGT AGCGTACAGCGTACTAGTAGTAGCGAAAAGTAGAAAAAGGGAAAAGCAAAAAACTA AAAAGCGTAAAAGAACTACTAGGGATAACGATAATGGAACGAAGCAGCTTCGAAA AAAACCCGATAGACTTCCTAGAAGCGAAAAGGGTACAAAGAAAGTAAAAAAGACCT AATAATAAACTACCGAAATACAGCCTATTGAACTAGAAAACGGGCGAAAACGAA TGCTAGCGAGCGCGGGGAACTACAAAAGGGAAACGAACTAGCGTACCGGAGCA AATACGTAACCTTCTTATACCTAGCGAGCCACTACGAAAAACTAAAAGGGAGCCCG GAAGACAACGAACAAAAACAATACTATTCTGTAAGAACAACACAAACACTACCTAGACG AAATAATAGAACAATAAGCGAATTCAGCAAACGAGTAATACTAGCGGACGCGAAC CTAGACAAAGTACTAAGCGCGTACAACAACACCGAGACAAACCGATACGAGAAC AAGCGGAAAACATAATACCTATTACGCTAACGAACCTAGGGGCGCCGGCGGCG TTCAAATACTTCGACACGACGATAGACCGAAAACGATACACGAGCACGAAAAGAA TACTAGACGCGACGCTAATACACCAAAGCATAACGGGGTATACGAAAACGCGAATA GACCTAAGCCAACCTAGGGGGGGACGGGGGGGGAGCCGAAAAAACAACGAAAA GTATGA</p>	
<p>具有 HSD 的 5' UTR, 对应 于 SEQ ID</p>	<p>GGGTCCCGCAGTCGGCGTCCAGCGGCTCTGCTTGTTCGTGTGTGTGTCGTTGCAGG CCTTATTCGGATCCGCCACCATGGACAAAAAATACAGCATAGGGCTAGACATAGGG ACGAACAGCGTAGGGTGGGCGGTAATAACGGACGAATACAAAGTACCGAGCAAAA AATTCAAAGTACTAGGGAACACGGACCGACACAGCATAAAAAAACAATAATAGG GGCGTACTATTTCGACAGCGGGGAAACGGCGGAAGCGACGCGACTAAAAACGAACG GCGGACGACGATACACGCGACGAAAAACCGAATATGCTACCTACAAGAAATATT CAGCAACGAAATGGCGAAAAGTAGACGACAGCTTCTTCCACCGACTAGAAGAAAGC</p>	<p>55</p>

<p>NO: 54 的 ORF 、 Kozak序列及 ALB 的 3' UTR 的 Cas9 转录物</p>	<pre> TTCCTAGTAGAAGAAGACAAAAACACGAACGACACCCGATATTCGGGAACATAGT AGACGAAGTAGCGTACCACGAAAAATACCCGACGATATACCACCTACGAAAAAAA CTAGTAGACAGCACGGACAAAGCGGACCTACGACTAATATACCTAGCGCTAGCGCA CATGATAAAATTCGAGGGGCACTTCCTAATAGAAGGGGACCTAAACCCGGACAACA GCGACGTAGACAACTATTCATACAACCTAGTACAAAACGTACAACCACTATTTCGAA GAAAAACCCGATAAACCGCGAGCGGGGTAGACGCGAAAAGCGATACTAAGCGCGGAC TAAGCAAAAAGCCGACGACTAGAAAACCTAATAGCGCAACTACCGGGGGAAAAAAA AAACGGGCTATTTCGGGAACCTAATAGCGCTAAGCCTAGGGGCTAACGCCGAACCTCA AAAGCAACTTCGACCTAGCGGAAGACGCGAAAACCTACAACCTAAGCAAAAGACACGTA CGACGACGACCTAGACAACCTACTAGCGCAAATAGGGGACCAATACGCGGACTAT TCCTAGCGGGCAAAAAACCTAAGCGACGCGATACTACTAAGCGACATACTACGAGTA AACACGGAAATAACGAAAGCGCCGCTAAGCGCGAGCATGATAAAACGATACGACG AACACCACCAAGACCTAACGCTACTAAAAGCGCTAGTACGACAACAACCTACCGGA AAAATACAAAAGAAATATTCCTCGACCAAAGCAAAAACGGGTACGCGGGGTACATAG ACGGGGGGCGAGCCAAAGAAGATTCTACAATTCATAAAACCGATACTAGAAAA AATGGACGGGACGGAAGAACTACTAGTAAAACCTAACCGGAGAAGACCTACTACGA AAACAACGAACGTTTCGACAACGGGAGCATACCGCACCAATACACCTAGGGGAAC TACACGCGATACTACGACGACAAGAAGACTTCTACCCGTTCTAAAAGACAACCGA GAAAAAATAGAAAAAATACTAACGTTCCGAATACCGTACTACGTAGGGCCGTAGC GCGAGGGAAACAGCCGATTTCGCGTGGATGACGCGAAAAAGCGAAGAAACGATAAC GCCGTGGAACCTTCGAAGAAGTAGTAGACAAAAGGGGCGAGCGCGCAAAGCTTCATA GAACGAATGACGAACTTCGACAAAAACCTACCGAACGAAAAAGTACTACCGAAAC ACAGCCTACTATACGAATACTTCACGGTATACAACGAACTAACGAAAAGTAAAATACG TAACGGAAGGGGATGCGAAAACCGCGCTTCCTAAGCGGGGAACAAAAAAGCGATG AGTAGACCTACTATTCAAAAACGAAACCGAAAAGTAAACGGTAAAACAACCTAAAAGAA GACTACTTCAAAAAAATAGAATGCTTCGACAGCGTAGAAAATAAGCGGGGTAGAAG ACCGATTCAACGCGAGCCTAGGGACGTACCACGACCTACTAAAATAATAAAAGAC AAAAGACTTCTAGACAACGAAGAAAACGAAAGACATACTAGAAGACATAGTACTAA CGCTAACGCTATTTCGAAGACCGAGAAATGATAGAAGAACGACTAAAACGTACGC GCACCTATTTCGACGACAAAGTAATGAAACAACCTAAAACGACGACGATACACGGGG TGGGGGCGACTAAGCCGAAAACATAAAACGGGATACGAGACAAAACAAAGCGGG AAAACGATACTAGACTTCTAAAAGCGACGGGTTTCGCGAACCGAAACTTCATGC AACTAATACACGACGACGCCTAACGTTCAAAGAAGACATACAAAAGCGAAAGT AAGCGGGCAAGGGGACAGCCTACACGAACACATAGCGAACCTAGCGGGGAGCCC GGCGATAAAAAAGGGGATACTACAACCGGTAAGTAGTAGACGAACTAGTAAAA GTAATGGGGCGACACAAACCGGAAAACATAAGTAATAAGAAATGGCGCGAGAAAAC AAACGACGCAAAAAGGGCAAAAAACAGCCGAGAACGAATGAAACGAATAGAAG AAGGGATAAAAAGAACTAGGGAGCCAAATACTAAAAGAACACCCGGTAGAAAAACAC GCAACTACAAAACGAAAAACTATACCTATACTACCTACAAAACGGGCGAGACATGT ACGTAGACCAAGAAGTAGACATAAACCGACTAAGCGACTACGACGTAGACCACATA GTACCGCAAAAGCTTCTAAAAGACGACAGCATAGACAACAAAGTACTAACGCGAA GCGACAAAAACCGAGGGGAAAAGCGACAACGTACCGAGCGGAAGAAAGTAAAGAAA AAATGAAAACTACTGGCGACAACCTACTAACCGCGAACTAATAACGCAACGAAA ATTCGACAACCTAACGAAAGCGGAACGAGGGGGGCTAAGCGAACTAGACAAAGC GGGGTTCATAAAACGACAACCTAGTAGAAAACGCGACAAATAACGAAACACGTAGCG CAAATACTAGACAGCCGAATGAACACGAAATACGACGAAAACGACAACATAATAC GAGAAGTAAAAGTAATAACGCTAAAAAGCAAACCTAGTAAAGCGACTTCCGAAAAGA CTTCCAATTCTACAAAGTACGAGAAATAAACAACTACCACCACGCGCACGACGCGT ACCTAACCGCGGTAGTAGGGACGGCGCTAATAAAAAAATACCCGAAACTAGAAAAG CGAATTCGTATACGGGGACTACAAAGTATACGACGTACGAAAAATGATAGCGAAAA GCGAACAAAGAAATAGGGAAAGCGACGGCGAAATACTTCTTCTACAGCAACATAAT GAACTTCTTCAAAACGGAAATAACGCTAGCGAACGGGGAAATACGAAAACGACCG CTAATAGAAACGAACGGGGAAACGGGGGAAATAGTATGGGACAAAAGGGCGAGACT TCGCGACGGTACGAAAAGTACTAAGCATGCCGCAAGTAAACATAGTAAAAAAAAC GGAAGTACAAAACGGGGGGGTTTCAGCAAAGAAAGCATACTACCGAAAACGAAACAG CGACAAACTAATAGCGCGAAAAAAAAGACTGGGACCCGAAAAAATACGGGGGGTTC GACAGCCCACGGTAGCGTACAGCTACTAGTAGTAGCGAAAAGTAGAAAAAGGGA AAAGCAAAAAACTAAAAAGCGTAAAAGAACTACTAGGGATAACGATAATGGAACG AAGCAGCTTCGAAAAAAACCCGATAGACTTCTAGAAAGCGAAAAGGGTACAAAGAA GTAAAAAAAGACCTAATAATAAAACTACCGAAATACAGCCTATTTCGAACTAGAAAA CGGGCGAAAACGAATGCTAGCGAGCGCGGGGAACTACAAAAGGGGAACGAACT AGCGCTACCGAGCAAATACGTAACCTTCTATACCTAGCGAGCCACTACGAAAAAC TAAAAGGGAGCCCGGAAGACAACGAACAAAACAACCTATTTCGTAGAACAAACACA AACACTACCTAGACGAAATAATAGAACAATAAGCGAATTCAGCAAAACGAGTAAATA CTAGCGGACGCAACCTAGACAAAGTACTAAGCGCGTACAACAAAACCGGAGACA AACCGATACGAGAACAAGCGGAAAACATAATACACCTATTTCAGCTAACGAACTA GGGGCGCCGGCGGTTCAAATACTTCGACACGACGATAGACCGAAAACGATACA </pre>
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[0691]

	<p>CGAGCACGAAAGAAGTACTAGACGCGACGCTAATACACCAAAGCATAACGGGGCT ATACGAAACCGGAATAGACCTAAGCCAACTAGGGGGGGACGGGGGGGGAGCCC GAAAAAAAAACGAAAAGTATGACTAGCCATCACATTTAAAAGCATCTCAGCCTACC ATGAGAATAAGAGAAAAGAAAATGAAGATCAATAGCTTATTCATCTCTTTTTCTTTTT CGTTGGTGTAAGCCAACACCCTGTCTAAAAAACATAATTTCTTTAATCATTTTGC CTTTTTCTGTGCTTCAATTAATAAAAAATGGAAAAGAACCCTCGAG</p>	
<p>具有 AGG 作为供与 CleanCap^T M一起使用之前三个核苷酸、HSD 的 5' UTR、对应于 SEQ ID NO: 4 的 ORF、Kozak 序列及 ALB 的 3' UTR 的 Cas9 转录物</p>	<p>AGGTCCCGCAGTCGGCGTCCAGCGGCTCTGCTTGTTCGTGTGTGTGTCGTTGCAGG CCTTATTCGGATCCGCCACCATGGACAAGAAGTACAGCATCGGACTGGACATCGGA ACAAACAGCGTCGGATGGGCAGTCATCACAGACGAATACAAGGTCCCAGCAAGA AGTTCAAGGTCCTGGGAAACACAGACAGACACAGCATCAAGAAGAACCCTGATCGG AGCACTGCTGTTTCGACAGCGGAGAAAACAGCAGAAGCAACAAGACTGAAGAGAAC AGCAAGAAGAAGATACACAAGAAGAAGAACAAGAAATCTGCTACCTGCAGGAAATC TTCAGCAACGAAATGGCAAAGGTCGACGACAGCTTCTCCACAGACTGGAAGAAA GCTTCTGCTGCAAGAAGACAAGAAGCACGAAAGACACCCGATCTTCGAAACAT CGTCGACGAAGTCGCATACCACGAAAAGTACCCGACAATCTACCACCTGAGAAAAG AAGCTGGTCGACAGCACAGACAAGGCAGACCTGAGACTGATCTACCTGGCACTGG CACACATGATCAAGTTCAGAGGACACTTCTGATCGAAGGAGACCTGAACCCGGA CAACAGCGACGTCGACAAGCTGTTTATCCAGCTGGTCCAGACATACAACCAGCTGT TCGAAGAAAACCCGATCAACGCAAGCGGAGTCGACGCAAGGCAATCCTGAGCGC AAGACTGAGCAAGAGCAGAAAGACTGGAAAACCTGATCGACAGCTGACCGGGAGA AAAGAAGAACGGACTGTTTCGAAAACCTGATCGCACTGAGCCTGGGACTGACACCG AACTCAAGAGCAACTTCGACCTGGCAGAAGACGCAAGACTGCAGCTGAGCAAG GACACATACGACGACGACCTGGACAACCTGCTGGCACAGATCGGAGACCAGTACG CAGACCTGTTCTGGCAGAAAAGAACCTGAGCGCAATCCTGCTGAGCAGATGATCAAG CCTGAGAGTCAACACAGAAATCACAAAGGCACCGCTGAGCGCAAGCATGATCAAG AGATACGACGAACACCACCAGGACCTGACACTGCTGAAGGCACTGGTCAGACAGC AGTGCCTGGAAAAGTACAAGGAAATCTTCTTCGACCAGACGAAGAACGGATACGC AGGATACATCGACGGAGGAGCAAGCCAGGAAGAATTCTACAAGTTCATCAAGCCG ATCCTGGAAAAGATGGACGGAACAGAGAAGAACTGCTGGTCAAGCTGAACAGAGAA GACCTGCTGAGAAAAGCAGAGAACATTCGACAACGGAAGCATCCCGCACAGATCC ACCTGGGAGAACTGCACGCAATCCTGAGAAGACAGGAAGACTTCTACCCTGTTCT GAAGGACAACAGAGAAAAGATCGAAAAGATCCTGACATTCAGAATCCCGTACTAC GTCCGACCGCTGGCAAGAGGAAACAGCAGATTCGCATGGATGACAAGAAAAGC GAAGAAAACAATCACACCGTGAACCTTCAAGAAGTCTGTCGACAAGGGAGCAAGC GCACAGAGCTTCATCGAAAAGATGACAAACTTCGACAAGAACCTGCCGAACGAAA AGGTCTGCCGAAGCACAGCCTGCTGTACGAATACTTCAAGTCTACAACGAAGT ACAAAGGTCAAGTACGTCACAGAAGGAATGAGAAAAGCCGGCATTCTGAGCGGAG AACAGAAGAAGGCAATCGTCGACCTGCTGTTCAAGACAAAACAGAAAAGGTCACAGT CAAGCAGCTGAAGGAAGACTACTTCAAGAAGATCGAATGCTTCGACAGCGTCGAA ATCAGCGGAGTCGAAGACAGATTAACGCAAGCCTGGGAACATACCACGACCTGC TGAAGATCATCAAGGACAAGGACTTCTGGACAACGAAGAAAACGAAGACATCCT GGAAGACATCGTCTGACACTGACACTGACACTGTTTCAAGACAGAGAAATGATCGAAGAA AGACTGAAGACATACGCACACCTGTTTCGACGACAAGGTCATGAAGCAGCTGAAGA GAAGAAGATACACAGGATGGGGAAGACTGAGCAGAAAAGCTGATCAACGGAATCA GAGACAAGCAGAGCGGAAAAGACAATCCTGGACTTCTGAAGAGCGACGGATTTCG AAACAGAAAACCTCATGCAGCTGATCCACGACGACAGCCTGACATTCAGGAAGAC ATCCAGAAGGCACAGGTCAAGGACAGGGAGACAGCCTGCACGAACACATCGCA AACCTGGCAGGAAGCCCGCAATCAAGAAGGGAATCCTGCAGACAGTCAAGGTG TCGACGAACTGGTCAAGGTCATGGGAAGACACAAGCCGGAACATCGTCATCGA AATGGCAAGAGAAAACAGACAACACAGAAGGGACAGAAGAAGCAGCAGAGAAA GAATGAAGAGAATCGAAGAAGGAATCAAGGAACTGGGAAGCCAGATCCTGAAGG AACACCCGGTCAAAAACACACAGCTGCAGAACGAAAAGCTGTACTGTACTACCT GCAGAACGGAAGAGACATGTACGTCGACCAGGAAGTGGACATCAACAGACTGAGC GACTACGACGTCGACCACATCGTCCCGCAGAGCTTCTGAAGGACGACAGCATCG ACAACAAGGTCTGACAAGAAGCGACAAGAACAGAGGAAAAGAGCGACAACGTCC CGAGCGAAGAAGTCGTCAAGAAAGATGAAGAAGTACTGGAGACAGCTGCTGAACG CAAAGCTGATCACACAGAGAAAGTTCGACAACCTGACAAAGGCAGAGAGAGGAG GACTGAGCGAACTGGACAAGGCAGGATTCATCAAGAGACAGCTGGTCGAAAACAA GACAGATCAAAAACGACGTCGACAGATCCTGGACAGCAGAATGAACACAAAAGTA CGACGAAAACGACAAGCTGATCAGAGAAGTCAAGGTCATCACACTGAAAGGCAA GCTGGTCAGCGACTTCAGAAAGGACTTCCAGTTCTACAAGGTGAGAGAAATCAAC AACTACCACACGACACGACGCATACCTGAACGCAGTCTGTCGGAACAGCACTGA TCAAGAAGTACCCGAAGTGGAAAGCGAATTCGTCTACGGAGACTACAAGGTCTA CGAGTCAGAAAAGATGATCGCAAAGAGCGAACAGGAAATCGGAAAAGGCAACAGC AAAGTACTTCTTACAGCAACATCATGAACCTTCTCAAGACAGAAAATCACACTGG CAAACGGAGAAATCAGAAAAGAGACCGCTGATCGAAAACAACGGAGAAAACAGGAG AAATCGTCTGGGACAAGGGAAGAGACTTCGCAACAGTCAGAAAAGGTCTGAGCAT</p>	<p>56</p>

[0692]

[0693]

	<p>GCCGCAGGTCAACATCGTCAAGAAGACAGAAGTCCAGACAGGAGGATTTCAGCAA GGAAAGCATCCTGCCGAAGAGAAAACAGCGACAAGCTGATCGCAAGAAAGAAAGGA CTGGGACCCGAAGAAGTACGGAGGATTTCGACAGCCCCGACAGTCGCATACAGCGTC CTGGTCTGTCGAAAGGTCGAAAAGGGAAAGAGCAAGAAAGCTGAAGAGCGTCAAG GAACCTGCTGGGAATCACAATCATGGAAAAGAGCAGCTTCGAAAAGAACCCTGATCG ACTTCTGGAAAGCAAAGGGATACAAGGAAGTCAAGAAGGACCTGATCATCAAGCT GCCGAAGTACAGCCTGTTTCCGAAGTGGAAAACGGAAGAAAGAGAATGCTGGCAAG CGCAGGAGAACTGCAGAAGGGAAACGAACTGGCACTGCCGAGCAAGTACGTCAA CTTCTGTACTTGGCAAGCCACTACGAAAAGCTGAAGGGAAAGCCCGGAAGACAAC GAACAGAAGCAGCTGTTTCTGTCGAACAGCACAAGCACTACCTGGACGAAATCATCG AACAGATCAGCGAATTCAGCAAGAGAGTCACTCCTGGCAGACGCAAACTGGACAA GGTCTGAGCGCATAACAACAGCACAGAGACAAGCCGATCAGAGAACAGGCAGA AAACATCATCCACCTGTTTACACTGACAAACCTGGGAGCACCAGGACGATTCAGT ACTTCGACACAACAATCGACAGAAAGAGATACACAAGCACAAGGAAGTCTGGGA CGCAACTGATCCACCAGAGCATCACAGGACTGTACGAAAACAAGAATCGACCTG AGCCAGCTGGGAGGAGACGGAGGAGGAAGCCGAAGAAGAAGAGAAAGGTCTA GCTAGCCATCACATTTAAAAGCATCTCAGCCTACCATGAGAATAAGAGAAAAGAAA TGAAGATCAATAGCTTATTCATCTCTTTTTCTTTTCTTTTCTGTTGGTGTAAAAGCCAAACCCC TGTCTAAAAAACATAAATTTCTTTAATCATTTTGCCTCTTTTCTGTGCTTCAATTA TAAAAATGGAAAAGAACCTCGAG</p>	
<p>具有来自 CMV 的 5' UTR、对应 于SEQ ID NO: 4 的 ORF、 Kozak序列 及 ALB 的 3' UTR 的 Cas9 转 录物</p>	<p>GGGCAGATCGCTGGAGACGCCATCCACGCTGTTTTGACCTCCATAGAAGACACCG GGACCGATCCAGCCTCCGCGGCCGGGAACGGTGCATTGGAACGCGGATTCCCCGT GCCAAGAGTGACTCACCGTCTTTGACACGGCCACCATGGACAAGAAGTACAGCAT CGGACTGGACATCGGAACAACAGCGTCCGATGGGCAGTCATCACAGACGAAATC AAGGTCCCGAGCAAGAAGTTCAAGGTCTGGGAAACACAGACAGACACAGCATC AAGAAGAACCCTGATCGGAGCACTGCTGTTTCCGACAGCGGAGAAACAGCAGAAGCA ACAAGACTGAAGAGAACAGCAAGAAGAAGATACACAAGAAGAAAAGAACAGAATC TGCTACCTGCAGGAAATCTTCAGCAACGAAATGGCAAAGGTCGACAGACGATCTTT CCACAGACTGGAAGAAAGCTTCTGGTTCGAAGAAGACAAGAAGCAGAAAGACA CCCGATCTTCGAAACATCGTCGACGAAGTCCGATACCACGAAAAGTACCCGACAA TCTACCACCTGAGAAAGAAGCTGGTTCGACAGCACAGACAAGGCAGACCTGAGACT GATCTACCTGGCACTGGCACACATGATCAAGTTTCAGAGGACACTTCTGATCGAAG GAGACCTGAACCCGGACAACAGCGACGTCGACAAGCTGTTTATCCAGTGGTCCA GACATAACAACAGCTGTTTGAAGAAAACCCGATCAACGCAAGCGGAGTTCGACGCA AAGGCAATCCTGAGCGCAAGACTGAGCAAGAGCAGAAGACTGGAAAACCTGATC GCACAGCTGCCGGGAGAAAAGAAGAACGGACTGTTTCCGAAAACCTGATCGCACT AGCCTGGGACTGACACCGAATTCAGAGCAACTTCGACCTGGCAGAAAGACGCA AGCTGCAGCTGAGCAAGGACACATACGACGACGACCTGGACAACCTGCTGGCACA GATCGGAGACCAGTACGCAGACCTGTTTCTGGCAGCAAAGAACCCTGAGCGACGCA ATCCTGCTGAGCGACATCCTGAGAGTCAACACAGAAATCACAAGGCACCCGCTGA GCGCAAGCATGATCAAGAGATACGACGAACACCACCAGGACCTGACACTGCTGAA GGCACTGGTCAAGACAGCAGCTGCCGAAAAGTACAAGGAAATCTTCTCGACAG AGCAAGAACGGATACGCAGGATACATCGACGGAGGCAAGCCAGGAAGAATTCT ACAAGTTCATCAAGCCGATCCTGGAAAAGATGGACGGAACAGAAGAACTGCTGGT CAAGCTGAACAGAGAAGACCTGCTGAGAAAGCAGAGAACATTCGACAACGGAAG CATCCGACCCAGATCCACCTGGGAGAACTGCACGCAATCCTGAGAAGACAGGAA GACTTCTACCCGTTCTGAAAGGACAACAGAGAAAAGATCGAAAAGACTCCTGACAT TCAGAATCCCGTACTACGTCGGACCGCTGGCAAGAGGAAAACAGCAGATTCGCATG GATGACAAGAAAGAGCGAAGAAAACAATCACACCGTGGAACTTCGAAGAAGTCGT CGACAAGGGAGCAAGCGCACAGAGCTTCATCGAAAAGATGACAACTTCGACAA GAACCTGCCGAACGAAAAGGTCTGCGGAAGCACAGCCTGCTGTACGAATACTTC ACAGTCTACAACGAACTGACAAAGGTCAAGTACGTCACAGAAGGAATGAGAAAAGC CGGCATTCCTGAGCGGAGAACAGAAGAAGGCAATCGTCGACCTGCTGTTCAAGAC AAACAGAAAGGTACAGTCAAGCAGCTGAAGGAAGACTACTTCAAGAAGATCGA ATGCTTCGACAGCGTCGAAATCAGCGGAGTCAAGACAGATTCAACGCAAGCCTG GGAACATACCACGACCTGCTGAAGATCATCAAGGACAAGGACTTCTGGACAACG AAGAAAACGAAGACATCCTGGAAGACATCGTCTGACACTGACACTGTTTCAAGA CAGAGAAATGATCGAAGAAAGACTGAAGACATACGCACACCTGTTTCGACGACAAG GTCATGAAGCAGCTGAAGAGAAGAAGATACACAGGATGGGGAAGACTGAGCAGA AAGCTGATCAACGGAATCAGAGACAAGCAGAGCGGAAAAGACAATCCTGGACTTCC TGAAGAGCGACGGATTTCGAAACAGAACTTCATGCAGCTGATCCACGACGACAG CCTGACATTCAAGGAAGACATCCAGAAGGCACAGGTCAGCGGACAGGGAGACAG CCTGCACGAAACACATCGCAAACCTGGCAGGAAGCCCGGCAATCAAGAAGGGAATC CTGCAGACAGTCAAGGTCTGTCGACGAACTGGTCAAGGTCATGGAAAGACACAAGC CGGAAAACATCGTCAATGGAAGTGGCAAGAGAAAACAGACAACACAGAAAGGAC AGAAGAACAGCAGAGAAAGAATGAAGAGAATCGAAGAAGGAATCAAGGAAGTGG GAAGCCAGATCCTGAAGGAACACCCGGTTCGAAAACACACAGCTGCAGAACGAAA</p>	<p>57</p>

[0694]

	<p>AGCTGTACCTGTACTACCTGCAGAACGGAAGAGACATGTACGTCGACCAGGAAC GGACATCAACAGACTGAGCGACTACGACGTCGACCACATCGTCCCAGAGCTTC CTGAAGGACGACAGCATCGACAACAAGGTCCTGACAAGAAGCGACAAGAACAGA GGAAAGAGCGACAACGTCCCGAGCGAAGAAGTCGTCAAGAAAGATGAAGAAGTAC TGGAGACAGCTGCTGAACGCAAAGCTGATCACACAGAGAAAAGTTTCGACAACCTGA CAAAGGCAGAGAGAGGAGGACTGAGCGAACTGGACAAGGCAGGATTCATCAAGA GACAGCTGGTCGAAAACAAGACAGATCACAAAAGCAGTCGCACAGATCCTGGACAG CAGAATGAACACAAAAGTACGACGAAAACGACAAGCTGATCAGAGAAGTCAAGGT CATCACACTGAAGAGCAAGCTGGTCAGCGACTTCAGAAAGGACTTCCAGTTCTAC AAGGTCAGAGAAATCAACAACACTACCACCACGACACGACGCATACCTGAACGAG TCGTCCGAAACAGCACTGATCAAGAAGTACCCGAAGCTGGAAAGCGAATTCGTCTA CGGAGACTACAAGGTCTACGACGTCAGAAAAGATGATCGCAAAGAGCGAACAGGAA ATCGGAAAAGGCAACAGCAAAAGTACTTCTTACAGCAACATCATGAACTTCTTCAA GACAGAAATCACACTGGCAAACGGAGAAATCAGAAAAGAGACCCGCTGATCGAAAC AAACGGAGAAAACAGGAGAAATCGTCTGGGACAAGGGAAGAGACTTCGCAACAGT CAGAAAGGTCCTGAGCATGCCGACAGTCAACATCGTCAAGAAGACAGAAGTCCAG ACAGGAGGATTCAGCAAGGAAAGCATCCTGCCGAAGAGAAAACAGCGACAAGCTG ATCGCAAAGAAAAGGACTGGGACCCGAAGAAGTACGGAGGATTCGACAGCCCCG ACAGTCGCATACAGCGTCTGGTCGTCGCAAAGGTCGAAAAGGGAAAAGAGCAAG AAGCTGAAGAGCGTCAAGGAACTGCTGGGAATCACAATCATGGAAAAGAGCAGCT TCGAAAAGAACCCGATCGACTTCTGGAAGCAAAGGGATACAAGGAAGTCAAGAA GGACCTGATCATCAAGCTGCCGAAGTACAGCCTGTTTGAAGTGGAAAACGGAAAG AAGAGAATGCTGGCAAGCGCAGGAGAAGTGCAGAAGGGAAAACGAACTGGCAGT CCGAGCAAAGTACGTCACCTTCTGTACCTGGCAAGCCACTACGAAAAGTGAAGG GAAGCCCGGAAGACAACGAACAGAAAGCAGCTGTTTCGTCGAACAGCACAAGCAGT ACCTGGACGAAATCATCGAACAGATCAGCGAATTCAGCAAGAGAGTCACTCTGGC AGACGCAAACCTGGACAAGGTCCTGAGCGCATAACAAGCAGACAGAGACAAGCC GATCAGAGAACAGGCAGAAAACATCCTCCACTGTTTCACTGACAAAACCTGGGA GCACCCGGCAGCATTCAAGTACTTTCGACACAACAATCGACAGAAAAGAGATACAAA GCACAAAAGGAAGTCTGGACGCAACACTGATCCACCAGAGCATCACAGGACTGTA CGAAAACAAGATCGACTGAGCCAGCTGGGAGGAGACGGAGGAGGAAAGCCCGAA GAAGAAGAGAAAAGGTTAGCTAGCCATCACATTTAAAAAGCATCTCAGCCTACCATG AGAATAAGAGAAAAGAAAATGAAGATCAATAGCTTATTCATCTCTTTTTCTTTCTGT TGGTGTAAAAGCCAACACCCTGTCTAAAAAACATAAATTTCTTTAATCATTTTGCCTC TTTTCTCTGTGCTTCAATTAATAAAAAATGGAAAAGAACCTCGAG</p>	
<p>具有来自 HBB 的 5' UTR, 对应 于SEQ ID NO: 4 的 ORF、 Kozak序列 及 HBB 的 3' UTR 的 Cas9 转 录物</p>	<p>GGGacattgtcttgacacaactgtttcactagcaacctcaaacagacaccggatctgeaccATGGACAAGAAGTA CAGCATCGACTGGACATCGGAACAAACAGCGTCGGATGGGCAGTCAACAGAC GAATACAAGGTCCCAGCAAGAAGTTCAAGGTCCTGGGAAAACACAGACAGACAC AGCATCAAGAAGAACCTGATCGGAGCACTGCTGTTTCGACAGCGGAGAAAACAGCAG AAGCAACAAGACTGAAGAGAACAGCAAGAAGAAGATACACAAGAAAGAAAAGAAC AGAATCTGTACTCTGCAGGAAATCTTCAGCAACGAAATGGCAAAGGTCGACGACA GTTCTTCCACAGACTGGAAAGAAAGCTTCTGGTTCGAAAGAAGACAAGAAGACAGCA AAGACACCCGATCTTCGAAACATCGTCGACGAAGTCGCATACCACGAAAAGTAC CCGACAATCTACCACCTGAGAAAAGAGCTGGTCGACAGCACAGACAAGGCAGACC TGAGACTGATCTACCTGGCACTGGCACACATGATCAAGTTCAGAGGACACTTCTCTG ATCGAAGGAGACCTGAACCCGGACAACAGCGACGTCGACAAGCTGTTTATCCAGC TGGTCCAGACATAACAACAGCTGTTTCGAAGAAAACCCGATCAACGCAAGCGGAGT CGACGCAAAGGCAATCCTGAGCGCAAGACTGAGCAAGAGCAGAAGACTGGAAAA CCTGATCGCACAGCTGCCGGGAGAAAAGAAAGACGGACTGTTTCGAAAACCTGATC GCACTGAGCCTGGGACTGACACCGAACTTCAAGAGCAACTTCGACCTGGCAGAAG ACGAAAAGCTGCAGCTGAGCAAGGACACATACGACGACGACCTGGACAACCTGCT GGCACAGATCGGAGACCAGTACGCAGACCTGTTCTGGCAGCAAAGAACCTGAGC GACGCAATCCTGCTGAGCGACATCCTGAGAGTCAACACAGAAAATCACAAAAGGCAC CGCTGAGCGCAAGCATGATCAAGAGATACGACGAACACCACCAGGACCTGACACT GCTGAAGGCACTGGTCAGACAGCAGCTGCCGAAAAGTACAAGGAAATCTTCTTC GACCAGCAAGAACCGGATACGAGGATACATCGACGGAGGAGCAAGCCAGGAA GAATCTACAAGTTCATCAAGCCGATCCTGGAAAAGATGGACGGAACAGAAGAAC TGCTGGTCAAGCTGAACAGAGAAGACCTGCTGAGAAAAGCAGAGAACATTCGACA ACGGAAGCATCCCGACCCAGATCCACTGGGAGAACTGCACGCAATCCTGAGAAG ACAGGAAGACTTCTACCCTTCTGAAAGGACAACAGAGAAAAGATCGAAAAGATC CTGACATTCAGAATCCGTAACGTCGACCGCTGGCAAGAGGAAAACAGCAGATT CGCATGGATGACAAGAAAGAGCGAAGAAAACAATCACACCGTGGAACTTCGAAGA AGTCTGTCGACAAGGGAGCAAGCGCACAGAGCTTCATCGAAAAGAAATGACAAAATTC GACAAGAACCTGCCGAACGAAAAGGTCCTGCCGAAGCACAGCCTGCTGTACGAAT ACTTCACAGTCTACAACGAACTGACAAAAGGTCAGTACGTCACAGAAAGAAATGAG AAAGCCGGCATTCTGAGCGGAGAACAGAAGAAGGCAATCGTCGACCTGCTGTTT AAGACAAAACAGAAAGGTCACAGTCAAGCAGCTGAAGGAAGACTACTTCAAGAAAG</p>	<p>58</p>

[0695]

	<p>ATCGAATGCTTCGACAGCGTTCGAAATCAGCGGAGTCGAAGACAGATTCAACGCAA GCCTGGGAACATAACCAGCCTGCTGAAGATCATCAAGGACAAGGACTTCTGGA CAACGAAGAAAACGAAGACATCCTGGAAGACATCGTCTGACACTGACACTGTTT GAAGACAGAGAAAATGATCGAAGAAAAGACTGAAGACATACGCACACCTGTTCGACG ACAAGGTCATGAAGCAGCTGAAGAGAAGAAGATACACAGGATGGGGAAGACTGA GCAGAAAAGCTGATCAACCGAATCAGAGACAAGCAGAGCGGAAAAGACAATCCTGG ACTTCTGAAGAGCGACGGATTTCGAAAACAGAACTTCATGCAGCTGATCCACGA CGACAGCCTGCACATTCAGGAAGACATCCAGAAGGCACAGGTCAGCGGACAGGG AGACAGCCTGCACGAACACATCGCAAACCTGGCAGGAAGCCCGGCAATCAAGAA GGGAATCTGCAGACAGTCAAGGTCGTCGACGAACTGGTCAAGGTCATGGGAAGA CACAAGCCGAAAACATCGTCATCGAAATGGCAAGAGAAAACCAGACAACACAG AAGGGACAGAAGAACAGCAGAGAAAAGAAATGAAGAGAATCGAAGAAGGAATCAAG GAACTGGGAAGCCAGATCCTGAAGGAACACCCGGTCGAAAACACACAGCTGCAG AACGAAAAGCTGTACCTGTACTACCTGCAGAACGGAAGAGACATGTACGTCGACC AGGAATGGACATCAACAGACTGAGCGACTACGACGTCGACCACATCGTCCCGCA GAGCTTCTGAAGGACGACAGCATCGACAACAAGGTCCTGACAAGAAGCGACAA GAACAGAGGAAAAGAGCGAACCGTCCCAGCGAAGAAGTCGTCGAAGAAGATGAA GAACTACTGGAGACAGCTGCTGAACGCAAAGCTGATCACACAGAGAAAAGTTTCGAC AACCTGACAAAAGGCAGAGAGAGGAGGACTGAGCGAACTGGACAAGGACAGATT ATCAAGAGACAGCTGGTCGAAAACAAGACAGATCACAAGCACGTCGCACAGATCC TGGACAGCAGAATGAACACAAAAGTACGACGAAAACGACAAGCTGATCAGAGAAG TCAAGGTCATCACACTGAAGAGCAAGCTGGTCAGCGACTTCAGAAAAGGACTTCCA GTTCTACAAGGTCAGAGAAAATCAACAACCTACCACCACGCACACGACGCATACCTG AACGCAGTCGTCGGAAGCGTCAAGGACTGATCAAGAAGTACCCGAAGCTGGAAAGG TCGTCACGGAGACTACAAGGTCACGACGTCAGAAAAGATGATCGCAAAGAGCGA ACAGGAAAATCGGAAAAGGCAACAGCAAAAGTACTTCTTCTACAGCAACATCATGAAC TTCTTCAAGACAGAAATCACACTGGCAAACGGAGAAAATCAGAAAAGAGACCGCTGA TCGAAAACAACCGAGAAAACAGGAGAAAATCGTCTGGGACAAGGGAAGAGACTTCG CAACAGTCAGAAAAGGTCCTGAGCATGCCGACGGTCAACATCGTCGAAGAAGACAGA AGTCCAGACAGGAGGATTACAGCAAGGAAAGCATCCTGCCGAAGAGAAAACAGCGA CAAGCTGATCGAAGAAAAGAGGACTGGGACCCGAAAGTACGGAGGATTTCGA CAGCCCGACAGTCGCATACAGCGTCTGGTCGTCGAAAAGGTCGAAAAGGGAAG AGCAAGAAGCTGAAGAGCGTCAAGGAACCTGCTGGGAATCACAATCATGGAAAGA AGCAGCTTCGAAAAGAACCAGTCGACTTCTGGAAGCAAAGGGATACAAGGAAG TCAAGAAGGACCTGATCATCAAGCTGCCGAAGTACAGCTGTTTCGAAGCTGGAAA CGGAAGAAAAGAGAATGCTGGCAAGCGCAGGAGAACTGCAGAAAGGGAACGAAGT GGCACTGCCGAGCAAGTACGTCAACTTCTGTACTTGGCAAGCCACTCAGAAAAG CTGAAGGGAAGCCCGAAAGACAACGAACGAAGCAGCTGTTCTGTCGAACAGCAC AAGCACTACCTGGACGAAATCATCGAACAGATCAGCGAATTCAGCAAGAGAGTCA TCCTGGCAGACGCAAACCTGGACAAGGTCCTGAGCGCATACAACAAGCACAGAGA CAAGCCGATCAGAGAACAGGCAGAAAACATCATCCACCTGTTACACTGACAAAC CTGGGAGCACCCGGCAGCATTCAAGTACTTCGACACAACAATCGACAGAAAAGAGAT ACACAAGCACAAAAGGAAAGTCTGGACGCAACACTGATCCACCAGAGCATCACAGG ACTGTACGAAAACAAGAATCGACCTGAGCCAGCTGGGAGGAGACGGAGGAGGAAG CCCGAAGAAGAAGAGAAAAGGTTCTAGctagcctccttcttctgtctccaatttctattaaaggttccttcttccct aagtcctaactactaaactggggatattatgaaggccttgagcatctggattctgctaataaaaaacatttatttcatgctcctgag</p>	
<p>具有来自 XBG 的 5' UTR、对应 于SEQ ID NO: 4 的 ORF、 Kozak序列 及 XBG 的 3' UTR 的 Cas9 转 录物</p>	<p>GGGaaagctcagaataaacgctcaacttggcggatctgcccacCATGGACAAGAAGTACAGCATCGGACT GGACATCGGAACAAAACAGCGTCGGATGGGCAGTCATCACAGACGAATACAAGGTC CCGAGCAAGAAGTTCAAGGTCCTGGGAAAACACAGACAGACACAGCATCAAGAAG AACCTGATCGGAGCACTGCTGTTTCGACAGCGGAGAAAACAGCAGAAGCAACAAGA CTGAAGAGAACAGCAAGAAGAAGATACACAAGAAGAAAAGAACAGAATCTGCTAC CTGCAGGAAATCTTCAGCAACGAAATGGCAAAGGTCGACGACAGCTTCTTCCACA GACTGGAAGAAAAGCTTCTGGTCGAAGAAGACAAGAAGCACGAAAAGACACCCGA TCTTCGAAAACATCGTCGACGAAGTCGCATACCACGAAAAGTACCCGACAATCTAC CACCTGAGAAAAGAAGCTGGTCGACAGCACAGACAAGGCAGACCTGAGACTGATCT ACCTGGCACTGGCACACATGATCAAGTTCAGAGGACACTTCTGATCGAAGGAGA CCTGAACCCGGACAACAGCGACGTCGACAAGCTGTTTCATCCAGCTGGTCCAGACA TACAACAGCTGTTTCGAAGAAAACCCGATCAACGCAAGCGGAGTCGACGCAAAGG CAATCCTGAGCGCAAGACTGAGCAAGAGCAGAAGACTGGAAAACCTGATCGACA GCTGCCGGGAGAAAAGAAGAACGGACTGTTTCGAAAACCTGATCGCACTGAGCCTG GGACTGACACCGAACTTCAAGAGCAACTTCGACCTGGCAGAAGACGCAAAGCTGC AGCTGAGCAAGGACACATACGACGACGACTGGACAACCTGCTGGCACAGATCGG AGACCAGTACGACAGCTGTTCTGGCAGCAAAGAACCTGAGCGACGCAATCCTG CTGAGCGACATCCTGAGAGTCAACACAGAAAATCACAAGGCACCGCTGAGCGCAA GCATGATCAAGAGATACGACGAAACACCACCAGGACCTGACACTGTGAAGGCACT GGTCAGACAGCAGCTGCCGAAAAGTACAAGGAAATCTTCTTCGACCAGAGCAAG AACGGATACGACAGGATACATCGACGGAGGAGCAAGCCAGGAAGAATTCTACAAGT</p>	<p>59</p>

[0696]

	<p>TCATCAAGCCGATCCTGGAAAAGATGGACGGAACAGAAGAACTGCTGGTCAAGCT GAACAGAGAAGACCTGCTGAGAAAAGCAGAGAACATTGACAACCGAAGCATCCC GCACCAGATCCACCTGGGAGAACTGCACGCAATCCTGAGAAGACAGGAAGACTTC TACCCGTTCTGAAAGGACAACAGAGAAAAAGATCGAAAAGATCCTGACATTCAGAA TACCCGTACTACGTCGGACCGCTGGCAAGAGGAAACAGCAGATTTCGATGGATGAC AAGAAAAGAGCGAAGAAAACAATCACACCGTGGAACTTCGAAGAAGTCGTCGACAA GGGAGCAAGCGCACAGAGCTTCATCGAAAAGATGACAAAACCTTCGACAAGAACCTG CCGAACGAAAAGGTCTGCCGAAGCACAGCCTGCTGTACGAATACTTCACAGTCTA CAACGAACTGACAAAAGGTCAAGTACGTCCACAGAAGGAATGAGAAAAGCCGGCATT CTGAGCGGAGAACAGAAGAAGGCAATCGTCGACCTGCTGTTCAAGACAAAACAGA AAGGTCACAGTCAAGCAGCTGAAGGAAGACTACTTCAAGAAGATCGAATGCTTCG ACAGCGTCAAGTACAGCGGAGTCAAGACAGATTCAACGCAAGCCTGGGAACATA CCACGACCTGCTGAAGATCATCAAGGACAAGGACTTCTGAGACAACGAAGAAAAC GAAGACATCCTGGAAGACATCGTCTGACACTGACACTGTTTCAAGACAGAGAAA TGATCGAAGAAAAGACTGAAGACATACGCACACCTGTTGACGACAACAGGTCATGAA GCAGCTGAAGAGAAGAAGATACACAGGATGGGGAAGACTGAGCAGAAAAGCTGAT CAACGGAATCAGAGACAAGCAGAGCGGAAAGACAATCCTGGACTTCTGAAGAG CGACGGATTTCGAAAACAGAACTTCATGCAGCTGATCCACGACGACAGCCTGACAT TCAAGGAAGACATCCAGAAGGCACAGGTCAGCGGACAGGGAGACAGCCTGCACG AACACATCGAAAACCTGGCAGGAAGCCCGCAATCAAGAAGGGAATCCTGCAGAC AGTCAAGGTCGTCGACGAACTGGTCAAGGTCATGGGAAGACACAAGCCGAAAA CATCGTCATCGAAATGGCAAGAGAAAACAGACAACACAGAAGGGACAGAAAGAA CAGCAGAGAAAAGAATGAAGAGAATCGAAGAAGGAATCAAGGAACTGGGAAGCCA GATCCTGAAGGAACACCCGGTCGAAAACACACAGCTGCAGAACGAAAAGCTGTAC CTGTACTACCTGCAGAACGGAAGAGACATGTACGTCGACCAGGAACTGGACATCA ACAGACTGAGCGACTACGACGTCGACCACATCGTCCCGCAGAGCTTCTGAAGGA CGACAGCATCGACAACAAGGTCTGACAAGAAGCGACAAGAACAGAGGAAAGAG CGACAACGTCCCAGCGAAGAAAGTCTCAAGAAGATGAAGAAGTCAAGGACTGAGAG GCTGCTGAACGCAAGGCTGATCACACAGAGAAAAGTTCGACAACCTGACAAAAGGCA GAGAGAGGAGGACTGAGCGAACTGGACAAGGCAGGATTCATCAAGAGACAGCTG GTCGAAAACAAGACAGATCACAAGCACGTCGCACAGATCCTGGACAGCAGAATGA ACAAAAGTACGACGAAAACGACAAGCTGATCAGAGAAGTCAAGGTCATCACAT GAAGAGCAAGCTGGTCAGCGACTTCAGAAAAGGACTTCCAGTTCTCAAGGTCAGAA GAAATCAACAACCTACCACACGCACACGACGCATACCTGAACGCAGTCGTCGGAA CAGCACTGATCAAGAAGTACCCGAAGCTGGAAAAGCGAATTCGTTCTACGGAGACTA CAAGGTCTACGACGTCAGAAAAGATGATCGCAAAGAGCGAACAGGAAATCGGAAA GGCAACAGCAAAGTACTTCTTCTACAGCAACATCATGAACTTCTCAAGACAGAAA TCACACTGGCAAACCGAGAAAATCAGAAAAGAGACCCTGATCGAAAACAACCGGAG AAACAGGAGAAATCGTCTGGGACAAGGGAAGAGACTTCGCAACAGTCAGAAAAGG TCCTGAGCATGCCGACGGTCAACATCGTCAAGAAGACAGAAAGTCCAGACAGGAGG ATTCAGCAAGGAAAGCATCCTGCCGAAGAGAAAACAGCGACAAGCTGATCGCAAGA AAGAAGGACTGGGACCCGAAAGAAAGTACGGAGGATTTCGACAGCCCGATCGCAT ACAGCGTCTGGTCTGTCGCAAAGGTCGAAAAGGGAAGAGCAAGAAGCTGAAGA GCGTCAAGGAACTGCTGGGAATCACAATCATGGAAAAGAGCAGCTTCGAAAAGAA CCCGATCGACTTCTGGAAGCAAAGGGATACAAGGAAGTCAAGAAGGACCTGATC ATCAAGCTGCCGAAGTACAGCCTGTTTCGAACTGGAAAACGGAAGAAAGAGAATGC TGGCAAGCGCAGGAGAACTGCAGAAGGGAAAACGAACTGGCACTGCCGAGCAAGT ACGTCAACTTCTGTACTTGGCAAGCCACTACGAAAAGCTGAAGGGAAGCCCGGA AGACAACGAACAGAAGCAGCTGTTCTGTCGAACAGCACAAAGCACTACCTGGACGA AATCATCGAACAGATCAGCGAATTCAGCAAGAGAGTATCCTGGCAGACGCAAAAC CTGGACAAGGTCTGAGCGCATACAACAAGCACAGAGACAAGCCGATCAGAGAAC AGGCAGAAAACATCATCCACCTGTTCACTGACAAAACCTGGGAGCACCCGGCAGC ATTCAAGTACTTCGACACAACAATCGACAGAAAAGAGATACACAAGCACAAAAGGAA GTCCTGGACGCAACACTGATCCACCAGAGCATCACAGGACTGTACGAAAACAAGAA TCGACCTGAGCCAGCTGGGAGGAGACGGAGGAGGAAGCCCGAAGAAGAAAGAGA AAGGTCTAGctagcaccagcctcaagaacaccgaaatggagtctcttaagctacataataccaacttacacaaatgtgtc ccccaaatgtagecattcgtatctgctcctaataaaaaaaagtcttccacattctctcgag</p>	
<p>具有 AGG 作为供与 CleanCap^T M一起使用 之前三个 核苷酸, 来 自 XBG 的</p>	<p>AGGagctcagaataaacgctcaacttggccggatctgccacCATGGACAGAAGTACAGCATCGGACT GGACATCGGAACAAAACAGCGTCGGATGGGCAGTCATCACAGACGAATACAAGGTC CCGAGCAAGAAGTTCAAGTCTGGGAAAACACAGACAGACACAGCATCAAGAAG AACCTGATCGGAGCACTGCTGTTTCGACAGCGGAGAAAACAGCAGAAGCAACAAGA CTGAAGAGAACAGCAAGAAGAAGATACACAAGAAGAAAAGAAAGCAATCTGCTAC CTGCAGGAAATCTTCAGCAACGAAATGGCAAAGGTGACGACAGCTTCTTCCACA GACTGGAAGAAAAGCTTCTGGTCAAGAAGACAAGAAGACGAAAAGCACCCCGA TCTTCGAAAACATCGTCGACGAAAGTGCATACCACGAAAAGTACCCGACAACTTAC CACCTGAGAAAAGAAGCTGGTCGACAGCACAGACAAGGCAGACCTGAGACTGATCT ACCTGGCACTGGCACACATGATCAAGTTCAGAGGACACTTCTGATCGAAGGAGA</p>	<p>60</p>

<p>5' UTR、 对应于 SEQ ID NO: 4 的 ORF、 Kozak序列 及 XBG 的 3' UTR 的 Cas9 转 录物</p>	<p>CCTGAACCCGGACAACAGCGACGTCGACAAGCTGTTTCATCCAGCTGGTCCAGACA TACAACCAGCTGTTTCGAAGAAAACCCGATCAACGCAAGCGGAGTCGACGCAAAGG CAATCCTGAGCGCAAGACTGAGCAAGAGCAGAAGACTGGAAAACCTGATCGCACA GCTGCCGGGAGAAAAGAAGAACGGACTGTTCCGAAAACCTGATCGCACTGAGCCTG GGACTGACACCGAACTTCAAGAGCAACTTCGACCTGGCAGAAGACGCAAAGCTGC AGCTGAGCAAAGGACACATACGACGACGACCTGGACAACCTGCTGGCACAGATCGG AGACCAGTACGACAGCTGTTCTTGGCAGCAAAGAACCTGAGCGACGCAATCCTG CTGAGCGACATCCTGAGAGTCAACACAGAAATCACAAAGGCACCGCTGAGCGCAA GCATGATCAAGAGATACGACGAACACCACCAGGACCTGACACTGCTGAAGGCACT GGTCAGACAGCAGCTGCCGGAAAAGTACAAGGAAATCTTCTTCGACCAGAGCAA AACGGATACGACAGGATACATCGACGGAGGACAAAGCCAGGAAGAATTCTACAAGT TCATCAAGCCGATCCTGAAAAGATGGACGGAACAGAAGAAGTCTGGTCAAGCT GAACAGAGAAGACCTGCTGAGAAAAGCAGAGAACATTCGACAACGGAAAGCATCC GCACCAGATCCACCTGGGAGAACTGCACGCAATCCTGAGAAGACAGGAAGACTTC TACCGTTCTGAAGGACAAACAGAGAAAAGATCGAAAAGATCCTGCATTCAGAA TCCCGTACTACGTCGGACCGCTGGCAAGAGGAAACAGCAGATTTCGCATGGATGAC AAGAAAGAGCGAAGAAACAATCACACCGTGGAACTTCGAAGAAGTCGTCGACAA GGGAGCAAAGCGCACAGAGCTTCATCGAAAAGATGACAAACTTCGACAAGAAGCTG CCGAACGAAAAGGTCCTGCCGAAGCACAGCCTGCTGTACGAATACTCACAGTCA CAACGAACTGACAAAAGTCAAGTACGTCACAGAAGGAATGAGAAAAGCCGGCATT CTGAGCGGAGAACAGAAGAAGGCAATCGTCGACCTGCTGTTCAAGACAAAACAGA AAGGTCACAGTCAAGCAGCTGAAGGAAGACTACTTCAAGAAGATCGAATGCTTCG ACAGCGTCGAAATCAGCGGAGTCAAGACAGATTCAACGCAAGCCTGGGAACATA CCACGACCTGCTGAAGATCAATCAAGGACAAGGACTTCCTGGACAACGAAGAAAAC GAAGACATCCTGGAAGACATCGTCTGACACTGACACTGTTTGAAGACAGAGAAA TGATCGAAGAAAGACTGAAGACATACGCACACCTGTTTCGACGACAAGGTCATGAA GCAGCTGAAGAGAAGAAGATACACAGGATGGGGAAGACTGAGCAGAAAAGCTGAT CAACGGAATCAGAGACAAGCAGAGCGGAAAGACAATCCTGGACTTCCTGAAGAG CGACGGATTGCAAAACAGAACTTCATGACGCTGATCCACGACGACAGCCTGACAT TCAAGGAAGACATCCAGAAGGCACAGGTCAGCGGACAGGGAGACAGCCTGCACG AACACATCGAAAACCTGGCAGGAAGCCCGCAATCAAGAAGGGAATCCTGCAGAC AGTCAAGGTCGTCGACGAACTGGTCAAGGTCATGGGAAGACACAAGCCGGAAAA CATCGTCATCGAAATGGCAAGAGAAAACAGACAACACAGAAGGACAGAAAGAA CAGCAGAGAAAAGAATGAAGAGAATCGAAGAAGGAATCAAGGAACTGGGAAGCCA GATCCTGAAGGAACACCCGGTCGAAAACACACAGCTGCAGAACGAAAAGCTGTAC CTGTACTACCTGCAGAACGGAAGAGACATGTACGTCGACCAGGAACTGGACATCA ACAGACTGAGCGACTACGACGTCGACCATCGTCCCGCAGAGCTTCTTGAAGGA CGACAGCATCGACAACAAGGTCCTGACAAGAAGCGACAAGAACAGAGGAAAAGAG CGACAACGTCCCGAGCGAAGAAGTCGTCAAGAAGATGAAGAAGTACTGGAGACA GCTGTGAACGCAAAAGCTGATCACACAGAGAAAAGTTCGACAACCTGACAAAAGGCA GAGAGAGGAGGACTGAGCGAACTGGACAAGGCAGGATTCATCAAGAGACAGCTG GTCGAAAACAAGACAGATCACAAAAGCAGTCGACACAGATCCTGGACAGCAAGTGA ACACAAGTACGACGAAAACGACAAGCTGATCAGAGAAGTCAAGGTCATCACACT GAAGAGCAAGCTGGTCAAGCAGCTTCCAGAAAGGACTTCCAGTTCTACAAGGTCAGA GAAATCAACAACACTACCACCACGCACACGACGCATACCTGAACGCACTGTCGGAA CAGCACTGATCAAGAAGTACCCGAAGCTGGAAAAGCGAATTCGCTACGCGAATA CAAGGTCACGACGTCAGAAAGATGATCGCAAAGAGCGAACAGGAAATCGGAAA GGCAACAGCAAAGTACTTCTTCTACAGCAACATCATGAATCTTCAAGACAGAAA TCACACTGGCAAACCGGAGAAATCAGAAAAGAGACCGCTGATCGAAAACAAACGGAG AAACAGGAGAAATCGTCTGGGACAAGGGAAGAGACTTCGCAACAGTCAGAAAAGG TCCTGAGCATGCCGACGGTCAACATCGTCAAGAAGACAGAAAGTCCAGACAGGAGG ATTACAGCAAAGGAAAGCATCCTGCCGAAGAGAAAACAGCGACAAGCTGATCGCAAGA AAGAAGGACTGGGACCCGAAGAAGTACGGAGGATTCGACAGCCCAGACTGCGCAT ACAGCGTCTGGTCTGTCGAAAAGGTCGAAAAGGGAAGAGCAAGAAGCTGAAGA GCGTCAAGGAACTGCTGGGAATCACAAATCATGAAAAGAAGCAGCTTCGAAAAGAA CCCGATCGACTTCTGGAAGCAAAGGGATACAAGGAAGTCAAGAAGGACCTGATC ATCAAGCTGCCGAAGTACAGCCTGTTTCAAGTGGAAAACGGAAGAAAAGAGAATGC TGGCAAGCGCAGGAGAACTGCAGAAGGGAAACGAACTGGCACTGCCGAGCAAGT ACGTCAACTTCTGTACTGGCAAGCCACTACGAAAAGCTGAAGGGAAAGCCCGGA AGACAACGAACAGAAGCAGCTGTTCTGTCGAACGACACAAGCACTACCTGGACGA AATCATCGAACAGATCAGCGAATTCAGCAAGAGAGTCATCCTGGCAGACGCAAAAC CTGGACAAGGTCCTGAGCGCATACAACAAGCACAGAGACAAGCCGATCAGAGAAC AGGCAGAAAACATCATCCACCTGTTTCAACTGACAAAACCTGGGAGCACCCGGCAGC ATTCAAGTACTTCGACACAACAATTCGACAGAAAAGAGATACACAAGCAAAAAGGAA GTCCTGGACGCAACACTGATCCACCAGAGCATCACAGGACTGTACGAAAACAAGAA TCGACCTGAGCCAGCTGGGAGGAGACGGAGGAGGAAGCCGAAAGAAGAAGAGA AAGGTCTAGctagcaccagcctcaagaacaccgaatggagtgctcttaagctacataatccaacttacactttacaaaatggtgct</p>
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<p>具有 AGG 作为供与 CleanCap^T M一起使用之前三个核苷酸、来自 HSD 的 5' UTR、对应于 SEQ ID NO: 4 的 ORF、Kozak 序列及 ALB 的 3' UTR 的 Cas9 转录物</p>	<pre> ccccaaatgtagccattcgtatctgctcctaataaaaaaaaagtftctcacattctctcgag AGGTCCCGCAGTCGGCGTCCAGCGGCTCTGCTTGTTCGTGTGTGTGTCGTTGCAGG CCTTATTCGGATCCGCCACCATGGACAAGAGTACAGCATCGGACTGGACATCGGA ACAAACAGCGTCGGATGGGCGATCATCACAGACGAATACAAGGTCCCGAGCAAGA AGTTCAAGGTCCTGGGAAACACAGACAGACACAGCATCAAGAAGAACCTGATCGG AGCACTGCTGTTTCGACAGCGGAGAAACAGCAGAAGCAACAAGACTGAAGAGAAC AGCAAGAAGAAGATACACAAGAAGAAAGAACAGAATCTGCTACCTGCAGGAAATC TTCAGCAACGAAATGGCAAAGGTCGACGACAGCTTCTCCACAGACTGGAAGAAA GCTTCTGTCGAAGAAGACAAGAAGCACGAAAGACACCCGATCTTCGGAAACAT CGTCGACGAAGTCGCATACCACGAAAAGTACCCGACAATCTACCACCTGAGAAA AAGCTGGTCGACAGCACAGACAAGGCAGACCTGAGACTGATCTACCTGGCACTGG CACACATGATCAAGTTCAGAGGACACTTCTGATCGAAGGAGACCTGAACCCGGA CAACAGCGACGTCGACAAGCTGTTTATCCAGCTGGTCCAGACATACAACCAAGCTGT TCGAAGAAAACCCGATCAACGCAAGCGGAGTCGACGCAAAGGCAATCCTGAGCGC AAGACTGAGCAAGAGCAGAAGACTGGAAAACCTGATCGCACAGACTGCCGGGAA AAAGAAGAACGGACTGTTTCGGAAACCTGATCGCACTGAGCCTGGGACTGACACCG AACTTCAAGAGCAACTTCGACCTGGCAGAAGACGCAAAGCTGCAGCTGAGCAAG GACACATACGACGACGACCTGGACAACCTGCTGGCACAGATCGGAGACCAGTACG CAGACCTGTTCTGGCAGCAAAGAACCTGAGCGCAATCTGTGCTAGGCACTAAG CCTGAGAGTCAACACAGAAATCACAAAGGCACCGCTGAGCGCAAGCATGATCAAG AGATACGACGAACACCACCAGGACCTGACACTGCTGAAGGCACTGGTCAGACAGC AGCTGCCGGAAGTACAAGGAAATCTTCTTCGACCAGACGAAGAACGGATACGC AGGATACATCGACGGAGGAGCAAGCCAGGAAGAATTCTACAAGTTCATCAAGCCG ATCCTGGAAAAGATGGACGGAAACAGAGAAGAACTGCTGGTCAAGCTGAACAGAA GACCTGCTGAGAAAAGCAGAGAACATTCGACAACGGAAGCATCCCGCACCAGATCC ACCTGGGAGAACTGCACGCAATCCTGAGAAGACAGGAAGACTTCTACCCGTTCT GAAGGACAACAGAGAAAAGATCGAAAAGATCCTGACATTCAGAATCCCGTACTAC GTCGGACCGCTGGCAAGAGGAAAACAGCAGATTCGCATGGATGACAAGAAAGAGC GAAGAAAACATCACACCTGGAACCTCGAAGAAAGTCGTCGACAAGGGAGCAAGC GCACAGAGCTTCATCGAAAGAATGACAACTTCGACAAGAACCTGCCGAACGAAA AGGTCTGCCGAAGCACAGCCTGTGTACGAATACTTCACAGTCTACAACGAACTG ACAAAGGTCAAGTACGTCACAGAAGGAATGAGAAAAGCCGGCATTCTGAGCCGAG AACAGAAGAAGGCAATCCTGACCTGCTGTTCAAGACAAAACAGAAAAGTCAAGT CAAGCAGCTGAAGGAAGACTACTTCAAGAAGATCGAATGCTTCGACAGCGTCGAA ATCAGCGGAGTCGAAGACAGATTAACGCAAGCCTGGGAACATAACCACGACCTGC TGAAGATCATCAAGGACAAGGACTTCTGGACAACGAAGAAAACGAAGACATCCT GGAAGACATCGTCTGACACTGACACTGTTTCGAAGACAGAGAATGATCGAAGAA AGACTGAAGACATACGCAACCTGTTTCGACGACAAGGTTCATGAAGAGCTGAAGA GAAGAAGATACACAGGATGGGGAAGACTGAGCAGAAAAGCTGATCAACGGAATCA GAGACAAGCAGAGCGGAAAGACAATCCTGGACTTCTGAAGAGCGACGGATTTCGC AAACAGAACTTTCATGCAGCTGATCCACGACGACAGCCTGACATTCGAAGGAAGC ATCCAGAAGGCACAGGTGACGGACAGGGAGACAGCCTGCACGAACACATCGCA AACCTGGCAGGAAGCCCGCAATCAAGAAGGGAATCCTGCAGACAGTCAAGGTGCG TCGACGAACTGGTCAAGGTCATGGGAAGACACAAGCCGAAAACATCGTCATCGA AATGGCAAGAGAAAACAGACAACACAGAAGGGACAGAAGAAGCAGCAGAGAAA GAATGAAGAGAATCGAAGAAGGAATCAAGGAACTGGGAAGCCAGACTCTGAAG AACACCCGGTCGAAAACACACAGCTGCAGAACGAAAAGCTGTACTGTACTACT GCAGAACGGAAGAGACATGTACGTCGACCAGGAACTGGACATCAACAGACTGAGC GACTACGACGTCGACCACATCGTCCCGCAGAGCTTCTGAAGGACGACAGCATCG ACAACAAGTCTGACAAGAAGCGACAAGAACAGAGGAAAGAGCGACAACGTCC CGAGCGAAGAAGTCTGTCAGAAGATGAAGAACTACTGGAGACAGCTGTGTAACG CAAAGCTGATCACACAGAGAAAGTTCGACAACCTGACAAAGGCAGAGAGAGGAG GACTGAGCGAACTGGACAAGGCAGGATTCATCAAGAGACAGCTGGTTCGAAACAA GACAGATCAAAAACGACGTCGCACAGATCCTGGACAGCAGAATGAACACAAAAGTA CGACGAAAACGACAAGCTGATCAGAGAAGTCAAGGTCATCACACTGAAGAGCAA GCTGGTCAGCGACTTCAGAAAGGACTTCCAGTTCTACAAGGTCAGAGAAATCAAC AACTACCACCGCACACGACGCATACCTGAACGCAGTCGTCGGAACAGCACTGA TCAAGAAGTACCCGAAGCTGGAAAGCGAATTCGTCTACGGAGACTACAAGGTCTA CGACGTCAGAAAAGATGATCGCAAAGAGCGAACAGGAAATCGGAAAGGCAACAGC AAAGTACTTCTTACAGCAACATCATGAACTTCTTCAAGACAGAAAATCACACTGG CAAACGGAGAAATCAGAAAAGAGACCGCTGATCGAAAACAAACGGAGAAAACAGGAG AAATCGTCTGGGACAAGGGAAGAGACTTCGCAACAGTCAGAAAAGGTCCTGAGCAT GCCGCAGGTCAACATCGTCAAGAAGACAGAAGTCCAGACAGGAGGATTACAGCAA GGAAAGCATCCTGCCGAAGAGAAAACAGCGACAAGCTGATCGCAAGAAAAGAAAGG CTGGGACCCGAAGAAAGTACGGAGGATTTCGACAGACCCGACAGTCGCATACAGCGTC CTGGTCTGCGAAAAGGTCGAAAAGGGAAAGAGCAAGAAGCTGAAGAGCGTCAAG GAACTGCTGGGAATCACAATCATGGAAAAGAACAGCTTCGAAAAGAACCCGATCG </pre>	<p>61</p>
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	ACTTCTGGAAGCAAAGGGATACAAGGAAGTCAAGAAGGACCTGATCATCAAGCT GCCGAAGTACAGCCTGTTTCTGAACTGGAAAAACGGAAGAAAGAGAATGCTGGCAAAG CGCAGGAGAACTGCAGAAGGGAAACGAACTGGCACTGCGAGCAAGTACGTCAA CTTCTGTACCTGGCAAGCCACTACGAAAAGCTGAAGGGAAAGCCCGGAAGACAAC GAACAGAAGCAGCTGTTCTGTCGAACAGCACAAGCACTACCTGGAGCAATCATCG AACAGATCAGCGAATTCAGCAAGAGAGTTCATCTTGGCAGACGCAAACTGGACAA GGTCTGAGCGCATAACAAGCACAGAGACAAGCCGATCAGAGAACAGGCAGA AAACATCATCCACCTGTTACACTGACAAACCTGGGAGCACCAGGCAGCATCAAGT ACTTCGACACAACAATCGACAGAAAGAGATACACAAGCACAAAGGAAGTCTGGGA CGCAACTGATCCACCAGAGCATCACAGGACTGTACGAAACAAGAATCGACTG AGCCAGCTGGGAGGAGACGGAGGAGAAAGCCCGAAGAAGAAGAGAAAGGTCTA GCTAGCCATCACATTTAAAAGCATCTCAGCCTACCATGAGAATAAGAGAAAGAAAA TGAAGATCAATAGCTTATTCTCTCTTTTCTTTTCTGTTGGTGTAAAACCAACACC TGCTAAAAAACATAAATTTCTTAATCATTTTGCCTCTTTTCTCTGTGCTTCAATTA TAAAAAATGGAAAGAACCCTCGAG	
30/30/39 聚-A序列	AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAGCGAAAAAAAAAAAAAAAAAAAA AAAAAAAAAAAAACCGAA A	62
聚-A 100 序列	AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA	63
G209 引导 RNA	mC*mC*mA*GUCCAGCGAGGCAAAGGGUUUUAGAGCUAGAAAAUAGCAAGUUAAA AUAAGGCUAGUCCGUUAUCAACUUGAAAAAGUGGCACCGAGUCGGUUGCmU*mU *mU*U	64
编码脑膜 炎双球菌 Cas9 的 ORF	ATGGCAGCATTCAAGCCGAACTCGATCAACTACATCCTGGGACTGGACATCGGAAT CGCATCGGTGCGATGGGCAATGGTCTGAAATCGACGAAGAAGAAAACCCGATCAGA CTGATCGACCTGGGAGTCAGAGTCTTCGAAAGAGCAGAAGTCCCGAAGACAGGAG ACTCGCTGGCAATGGCAAGAAGACTGGCAAGATCGGTGAGAAGACTGACAAGAA GAAGAGCACACAGACTGCTGAGAACAAGAAGACTGCTGAAGAGAGAAGGAGTCC TGCAGGCAGCAAACCTTCGACGAAAACGGACTGATCAAGTCGCTGCCGAACACACC GTGGCAGCTGAGAGCAGCAGCACTGGACAGAAAGCTGACACCCGCTGGAATGGTC GGCAGTCTGCTGCACCTGATCAAGCACAGAGGATACCTGTGCGAGAGAAAGAAC GAAGGAGAAACAGCAGACAAGGAACCTGGGAGCACTGCTGAAGGAGATCGAGGA AACGCACACGCACTGCAGACAGGAGACTTCAGAACACCCGGCAGAACTGGCCTG AACAAGTTCGAAAAGGAATCGGGACACATCAGAAACAGAGATCGGACTACTCGC ACACATTCGAGAAAAGGACCTGCAGGCAGAACTGATCTGCTGTTTCGAAAAGCA GAAGGAATTCGAAAACCCGCACGTCTCGGGAGGACTGAAGGAAGGAATCGAAAC ACTGCTGATGACACAGAGACCCGGCACTGTGCGGAGACGCAGTCCAGAAGATGCTG GGCACTGCACATTCTGAACCCGGCAGAACCGAAGGCAGCAAAGAACACATACACA GCAGAAAAGATTCTATCTGGCTGACAAAGCTGAACAACCTGAGAATCCTGGAACAGG GATCGGAAAAGACCCGCTGACAGACACAGAAAGAGCAACACTGATGGACGAACCGT ACAGAAAGTCGAAGCTGACATACGCACAGGCAAGAAAGTCTGCTGGGACTGGAAG ACACAGCATTCCTCAAGGGACTGAGATACGGAAGGACAACGCAGAAAGCATCGAC ACTGATGGAATGAAGGCATACCACGCAATCTCGAGAGCACTGGAAAAGGAAGGA CTGAAGGACAAGAAGTCGCCGCTGAACCTGTCGCCGGAAGTGCAGGACGAAATCG GAACAGCATTCTCGCTGTTCAAGACAGACGAAGACATCACAGGAAGACTGAAGGA CAGAATCCAGCCGGAATCCTGGAAGCACTGCTGAAGCACATCTCGTTCGACAAG TTCGTCCAGATCTCGCTGAAGGCACTGAGAAGAATCGTCCCCTGATGGAACAGG GAAAGAGATACGACGAAGCATGCGCAGAAATCTACGGAGACCACTACGGAAGAA GAACACAGAAGAAAAGATCTACCTGCCGCCGATCCCAGGACGAAATCAGAAAC CCGCTGCTCTGAGAGCACTGTGCGAGGCAAGAAAGGTCATCAACGGAGTCTGTA GAAGATACGGATCGCCGGCAAGAATCCACATCGAAACAGCAAGAGAGATCGGAAA GTCGTTCAAGGACAGAAAAGGAAATCGAAAAGAGACAGGAAGAAAACAGAAAGG ACAGAGAAAAGGCAGCAGCAAAGTTCAGAGAATACTTCCCGAACTTCGTCGGAGA ACCGAAGTCGAAGGACATCCTGAAGCTGAGACTGTACGAACAGCAGCACGGAAA GTGCCCTGACTCGGAAAAGGAAATCAACCTGGGAAGACTGAAAGAAAAGGGATAC GTCGAAATCGACCACGCACTGCCGTTCTCGAGAACATGGGACGACTCGTTCAACA ACAAGGTCCTGGTCTGGGATCGGAAAACAGAAACAAGGGAAACAGACACCGT ACGAATACTTCAACGGAAAGGACAACCTCGAGAGAATGGCAGGAATTCAAGGCAAG AGTCGAAACATCGAGATTCCTCGAGATCGAAGAAGCAGAGAATCCTGCTCAGAAAG TTCGACGAAGACGGATTCAAGGAAAGAAACCTGAACGACACAAGATACGTCAACA GATTCCTGTGCCAGTTCGTCGACAGACAATGAGACTGACAGGAAAGGGAAAGAA GAGAGTTCGATCGAACGGACAGATCACAAACCTGCTGAGAGGATTCTGGGGA CTGAGAAAGGTCAGAGCAGAAAACGACAGACACCACGCACTGGACGCAGTCTGTC GTCGCATGCTCGACAGTCTCAATGCAGCAGAAGATCAAAAGATTCGTGATACAA GGAAATGAACGCATTTCGACGGAAAGACAATCGACAAGGAAACAGGAGAAGTCTCT GCACCAGAAGACACTTCCCGCAGCCGTGGGAATTCTTCGCACAGGAAGTCATG	65

[0699]

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<p>编码脑膜 炎双球菌 Cas9 的 ORF (无起 始或终止 密码子;适 于包括在 融合蛋白 质编码序 列中)</p>	<p>GCAGATTCAAGCCGAATCGATAACTACATCCTGGGACTGGACATCGGAATCGC ATCGGTTCGGATGGCAATGGTTCGAAATCGACGAAGAAGAAAACCCGATCAGACTG ATCGACCTGGGAGTCAGAGTCTTCGAAAAGAGCAGAAGTCCCGAAGACAGGAGACT CGCTGGCAATGGCAAGAAGACTGGCAAGATCGGTGAGAAGACTGACAAGAAGAA GAGCACACAGACTGCTGAGAACAAGAAGACTGCTGAAGAGAGAAGGAGTCCCTGC AGGCAGCAAATTCGACGAAAACGGACTGATCAAGTCGCTGCCGACACACACCTGTG GCAGCTGAGAGCAGCAGCACTGGACAGAAAGCTGACACCGCTGGAATGGTCGGC AGTCTGCTGCACCTGATCAAGCACAGAGGATACCTGTGCGAGAGAAAAGAACGAA GGAGAAACAGCAGACAAGGAACTGGGAGCACTGCTGAAGGGAGTCGAGGAAAC GCACCGCACTGCAGACAGGAGACTTCAGAACACCGGCAGAACTGGCACTGAAC AAGTTCGAAAAGGAATCGGGACACATCAGAAAACAGAGATCGGACTACTCGCACA CATTCTCGAGAAAAGGACCTGCAGGCAGAAGTATCCTGCTGTTTCGAAAAGCAGAA GGAATTCGAAAACCCGCACGTCTCGGGAGGACTGAAGGAAGGAATCGAAAACACTG CTGATGACACAGAGACCCGCACTGTCGGGAGACGCACTCCAGAAGATGCTGGGAC ACTGCACATTCGAACCCGGCAGAACCGAAGGCAGCAAAGAACACATACACAGCAG AAAGATTCATCTGGCTGACAAAAGCTGAACAACCTGAGAATCCTGGAACAGGGATC GGAAAGACCGTGCAGACACAGAAAAGAGCAAACTGATGGACGAACCCGTACAG AAAGTCAAGCTGACATACGCACAGGCAAGAAAAGCTGCTGGGACTGGAAGACAC AGATTCTTCAAGGGACTGAGATACGGAAAGGACAACGCAGAAGATCGCAACTG ATGGAAATGAAGGCATACCACGCAATCTCGAGAGCACTGGAAAAGGAAAGACTGA AGGACAAGAAGTCGCGCTGAACCTGTGCGCGGAACTGCAGGACGAAATCGGAA CAGCATTCTCGCTGTTCAAGACAGACGAAGACATCAGGAAAGACTGAAGGACAG AATCCAGCCGGAATCCTGGAAGCACTGCTGAAGCACATCTCGTTTCGACAAGTTTCG TCCAGATCTCGCTGAAGGCACTGAGAAGAATCGTCCCGCTGATGGAACAGGGAAA GAGATACGACGAAGCATGCGCAGAAATCTACGGAGACCACTACGGAAAAGAAGAAC ACAGAAGAAAAGATCTACCTGCCGCCGATCCCGGCAGACGAAATCAGAAAACCCGG TCGTCTGAGAGCACTGTGCGAGGCAAGAAAAGGTTCATCAACGGAGTGTGTCAGAAG ATACGGATCGCCGGCAAGAATCCACATCGAAACAGCAAGAGAAGTTCGGAAAGTCCG TTCAAGGACAGAAAAGGAAATCGAAAAGAGACAGGAAAGAAAACAGAAAAGGACAG AGAAAAGGCAGCAGCAAAGTTCAGAGAATACTTCCCGAACTTCGTGCGGAGAACCG AAGTCGAAGGACATCCTGAAGCTGAGACTGTACGAACAGCAGCAGCGAAAAGTGCC TGTAATCGGGAAAAGGAAATCAACCTGGGAAGACTGAACGAAAAGGGATACGTGCA AATCGACCACGCATGCCGTTCTCGAGAACATGGGACGACTCGTTCAACAACAAG GTCCTGGTCTGGGATCGGAAAACCAGAACAGGGAAACCAGACACCCGTACGAAT ACTTCAACGGAAAAGGACAACCTCGAGAGAATGGCAGGAATTCAGGCAAGAGTTCG AAACATCGAGATTCGAGATCGAAGAAGCAGAGAATCCTGCTGCAGAAGTTCGA CGAAGACGGATTCAGGAAAAGAACTGAACGACACAAGATACGTCAACAGATTC CTGTGCCAGTTCTGTCGACAGACAAGATGAGACTGACAGGAAAAGGAAAAGAGAGA GTCTTCGCATCGAACGGACAGATCACAACCTGCTGAGAGGATTCTGGGGACTGA GAAAGGTCAGAGCAGAAAACGACAGACACCACGCACTGGACGCACTCGTCTGTCG CATGCTGCAGTTCGCAATGACAGCAGAAGATCACAAGATTGTCAGATAACAAGGA AATGAACGCATTCGACGGAAAAGACAATCGACAAGGAAAACAGGAGAAGTCTGCA CAGAAGACACACTTCCGACAGCCGTGGGAATTCCTGCGACAGGAAAGTTCATGATCA GAGTCTTCGAAAAGCCGGACGGAAGCCGGAATTCGAAGAAGCAGACACACTGG AAAAGCTGAGAACACTGCTGGCAGAAAAGCTGTGTCGAGACCCGGAAGCAGTCC ACGAATACGTCAACCCGTGTTCTGTCGAGAGCACCGAACAGAAAAGATGTCGGG ACAGGGACACATGGAAAACAGTCAAGTCGGCAAAGAGACTGGACGAAGGATGTC GGTCTGAGAGTCCCGCTGACACAGCTGAAGCTGAAGGACCTGGAAAAGATGGTC AACAGAGAAAAGAGAACCAGGCTGTACGAAGCACTGAAGGCAAGACTGGAAGCA</p>	<p>66</p>

[0700]

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<p>Tran 包含 SEQ ID NO: 65 (编 码脑膜炎 双球菌 Cas9)的转 录物</p>	<p>GGGAGACCCAAGCTGGCTAGCGTTTAAACTTAAGCTTGGATCCGCCACCATGGCAG CATTCAAGCCGAATCGATCAACTACATCCTGGGACTGGACATCGGAATCGCATCG GTCGGATGGGCAATGGTCGAAATCGACGAAGAAGAAAACCCGATCAGACTGATCG ACCTGGGAGTCAGAGTCTTCGAAAGAGCAGAAGTCCCGAAGACAGGAGACTCGC TGGAATGGCAAGAAGACTGGCAAGATCGGTTCAGAAAGACTGACAAGAAGAAGAG CACACAGACTGCTGAGAACAAGAAGACTGCTGAAGAGAGAAGGAGTCTGCAGG CAGCAAACTTCGACGAAAACGGACTGATCAAGTCTGCTGCCGAACACACCCGTGGCA GCTGAGAGCAGCAGCAGTGGACAGAAAAGCTGACACCGCTGGAATGGTCGGCAGTC CTGCTGCACCTGATCAAGCACAGAGGATACCTGTGACAGAGAAAAGAACGAAGGAG AAACAGCAGACAAGGAACTGGGAGCAGTGTGAAGGGAGTTCGAGGAAACGCAC ACGCACTGCAGACAGGAGACTTCAGAACACCCGGCAGAACTGGCACTGAACAAGT TCGAAAAGGAATCGGGACACATCAGAAACCAGAGATCGGACTACTCGCACACATT CTCGAGAAAAGGACCTGCAGGCAGAAGTATCCTGCTGTTTCGAAAAGCAGAAGGAA TTCGAAAACCCGCACGTCTCGGGAGGACTGAAGGAAGGAATCGAAACACTGCTGA TGACACAGAGACCCGGCACTGTCCGGAGACGCAAGTCCAGAAGATGCTGGGACACTG CACATTCGAACCCGGCAGAACCGAAGGCAGCAAGAACACATACACAGCAGAAAAG ATTCATCTGGCTGACAAAAGCTGAACAACCTGAGAATCCTGGAACAGGGATCGGAA AGACCGCTGACAGACACAGAAAAGAGCAACACTGATGGACGAACCGTACAGAAAAG TCGAAGCTGACATACGCACAGGCAAGAAAAGCTGCTGGGACTGGAAGACACAGCAT TCTTCAAGGGACTGAGATACGGAAGGACAACGCAGAAGCATCGCACTGATGGA AATGAAGGCATACCACGCAATCTCGAGAGCACTGGAAAAGGAAGGACTGAAGGAC AAGAAGTCGCCGCTGAACCTGTCCGCCGAACTGCAGGACGAAATCGGAACAGCAT TCTCGCTGTTCAAGACAGACGAAGACATCACAGGAAGACTGAAGGACAGAAATCCA GCCGAAATCCTGGAAGCACTGCTGAAGCACATCTCGTTTCGACAAGTTCTGTCAGA TCTCGTGAAGGCACTGAGAAGAATCGTCCCGCTGATGGAACAGGGAAAGAGATA CGACGAAGCATGCGCAGAAAATCTACGGAGACCCTACGGAAAAGAAAGAAAGAGAA AGAAAAGATCTACCTGCCGCCGATCCCGGCAGACGAAATCAGAAAACCCGGTCTGC CTGAGAGCACTGTGCGAGGCAAGAAAAGGTCATCAACGGAGTGTGTCAGAAAGATACG GATCGCCGGCAAGAATCCACATCGAAACAGCAAGAGAAGTCCGAAAGTCTGTTCAA GGACAGAAAAGGAAATCGAAAAGAGACAGGAAGAAAACAGAAAAGGACAGAGAAA AGGCAGCAGCAAAAGTTCAGAGAATACTTCCGAACTTCGTCGGAGAACCAGGATC GAAGGACATCCTGAAGCTGAGACTGTACGAACAGCAGCAGGAAAAGTGCCTGTAC TCGGAAAGGAAATCAACCTGGGAAGACTGAAACGAAAAGGGATACGTCGAAATCG ACCACGCACTGCCGTTCTCGAAGACATGGGACGACTCGTTCAACAACAAGGTCCT GGTCTGGGATCGGAAAACAGAAACAGGAAACAGGAAACAGACCCGATACGAAATTC AACGGAAGGACAACCTCGAGAGAATGGCAGGAATTCAGGCAAGAGTTCGAAACA TCGAGATTCCCAGATCGAAGAAGCAGAGAATCCTGCTGCAGAAAGTTCGACGAAG ACGGATTCAGGAAAAGAAACCTGAACGACACAAGATACGTCAACAGATTCTGTG CCAGTTCGTCGACAGAGAATGAGACTGACAGGAAAAGGAAAGAAGAGAGTCTT CGCATCGAACGGACAGATCACAAACCTGCTGAGAGGATTCGGGGACTGAGAAAAG GTCAGAGCAGAAAACGACAGACACCACGCACTGGACGCAAGTGTGTCGTCGATGCT CGACAGTCGCAATGCAGCAGAAGATCACAAAGATTCGTGATACAAAGGAAATGAA CGCATTCGACGGAAGACAATCGACAAGGAAACAGGAGAAGTCTGCACCAGAA GACACACTTCCCAGCCGTGGGAATCTTTCGACAGGAAGTTCATGATCAGAGTCT TCGGAAAGCCGGACGGAAGCCGGAATTCGAAGAAGCAGACACACTGGAAAAGC TGAGAACACTGCTGGCAGAAAAGCTGTGCTGAGACCGGAAGCAGTCCACGAATA CGTACACCCGCTGTTCTGTCGAGAGCACCAGAACAGAAAAGATGTCGGGACAGGGA CACATGAAAACAGTCAAGTCCGGCAAAGAGACTGGACGAAGGAGTCTCGGTCTGA GAGTCCCCTGACACAGCTGAAGCTGAAGGACCTGGAAAAGATGGTCAACAGAG AAAGAGAACCAGTGTACGAAGCACTGAAGGCAGACTGGAAGCACACAAGG ACGACCCGGCAAAGGCATTCGACGAACCGTTTACAAGTACGACAAGGCAGGAAA CAGAACACAGCAGGTCAAGGCAGTCAAGTCAAGCAGGTCCAGAAGCAGGAGT CTGGGTCAGAAAACCAACGGAATCGCAGACAACGCAACAATGGTTCAGATGAGC GTCTTCGAAAAGGGAGACAAGTACTACTGGTCCCGATCTACTCGTGGCAGGTGCG AAAGGGAATCCTGCCGGACAGAGCAGTCTCCAGGGAAAGGACGAAGAAGACTG</p>	<p>67</p>

[0701]

[0702]

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脑膜炎双 球菌 Cas9 的氨基酸 序列	MAAFKPNINSYILGLDIGIASVWAMVEIDEENPIRLIDLGVRFERAEVPKTGDSL MARRLARSVRRLLRRRAHRLLRRLKREGVLQAANFDENGLIKSLPNTPWQLRAA ALDRKLTPLEWSAVLLHLIKHRGYLSQRKNEGATADKELGALLKGVAGNAHALQTGD FRTPAELALNKFEKESGHIRNQSDYSHTFSRKDLQAEILLFEKQKEFGNPHVSGGLK EGIETLLMTQRPALSGDAVQKMLGHCTFEPAPKAAKNTYTAERFIWLTKLNNLRILE QGSERPLDTERATLMDEPYRKSCLTYAQAARKLLGLEDTAFFKGLRYGKDNAEASTL MEMKAYHAISRALEKEGLKDKKSPLNLSPELQDEIGTAFSLFKTDEEDITGRLDKRIQEI LEALLKHISFDKFVQISLKLRRIVPLMEQKRYDEACAEIYGDHYGKKNTEEKIYLP IPADEIRNPVLRALSQARKVINGVVRRYGSPARIHIETAREVGSFKDRKEIEKROEEN RKDREKAAAKFREYFPNFVGEPKSKDILKRLYEQQHGKCLYSGKEINLGRLEKGY VEIDHALPFSRTWDDSFNNKLVVLGSENNKGNQTPYEYFNGKDNSREWQEFKARVE TSRFRSKQRILLQKFDDEDFKERNLNDTRYVNRFLCQFVADRMRLTGKGRKRFAS NGQITNLLRGFWGLRKVRAENDRHHALDAVVACSTVAMQKITRFVRYKEMNAFD GKTIDKETGEVLHQKTHFPQPWEFFAQEVMIRVFGKPDGKPEFEEADTLKLRLLAE KLSSRPEAVHEYVTPLFVSRAPNRKMSGQGHMETVKSARKLDEGVSVLRVPLTQLKL KDLEKMVNREREPKLYEALKARLEAHKDDPAKAFAPFYKYDKAGNRTQVVKAVRV EQVQKTGVVWRNHNGIADNATMVRVDVFEKGDYLVPIYSWQVAKGILPDRAVVQ GKDEEDWQLIDDSFNFKFSLHPNDLVEVITKKARMFYFASCHRGTGNINIRIHDLDH KIGKNGILEGIGVKTALSFKYQIDELGKEIRPCRLKKRPPVRSGRKRTADGSEFESPKK RKVE	68
G390 引导 RNA	mG*mC*mC*GAGUCUGGAGAGCUGCAGUUUUAGAmGmCmUmAmGmAmAmUm AmGmCAAGUUAUUUUUAAGGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmAm AmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU	69
G502 引导 RNA	mA*mC*mA*CAAAUACCAGUCCAGCGGUUUUAGAmGmCmUmAmGmAmAmAmUm AmGmCAAGUUAUUUUUAAGGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmAm AmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU	70
G509 引导 RNA	mA*mA*mA*GUUCUAGAUGCCGUCCGUUUUAGAmGmCmUmAmGmAmAmAmUm AmGmCAAGUUAUUUUUAAGGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmAm AmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU	71
G534 引导 RNA	mA*mC*mG*CAAAUUCAGUCCAGCGGUUUUAGAmGmCmUmAmGmAmAmAmUm AmGmCAAGUUAUUUUUAAGGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmAm AmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU	72
eGFP 的 DNA 编码 序列	TCGCGCTTTCGGTGATGACGGTGAACCTCTGACACATGCAGCTCCCGGAGAC GGTCACAGCTTGTCTGTAAAGCGGATGCCGGGAGCAGACAAGCCCGTCAGGGCGCG TCAGCGGTGTTGGCGGGTGTGCGGGCTGGCTTAACATATGCGGCATCAGAGCAGAT TGTAAGTGCAGTGCACCATATGCGGTGTGAAATACCGCACAGATGCGTAAGGAGAA AATACCGCATCAGGCGCCATTCGCCATTCAGGCTGCGCAACTGTTGGGAAGGGCGA TCGGTGCGGGCCTCTTCGCTATTACGCCAGCTGGCGAAAGGGGGATGTGCTGCAAG GCGATTAAGTTGGGTAACGCCAGGGTTTTCCAGTCACGACGTTGTAACACGACGG CCAGTGAATTCTAATACGACTACTATAGGGTCCCGCAGTCGGCGTCCAGCGGCTC TGCTTGTTCGTGTGTGTGCTGTTGCAAGCCTTATTCGGATCCATGGTGAAGGGC GAGGAGCTGTTACCGGGGTGGTGCCTATCCTGGTCGAGCTGGACGGCGACGTAA ACGGCCACAAGTTCAGCGTGTCCGGCGAGGGCGAGGGCGATGCCACCTACGGCAA GCTACCCTGAAGTTCATCTGCACCACCGGCAAGCTGCCCGTCCCGTGGCCACCC TCGTGACCACCCTGACCTACGGCGTGCAGTGTTCAGCCGCTACCCCGACCACATG AAGCAGCAGACTTCTTCAAGTCCGCATGCCGAAGGCTACGTCCAGGAGCGCA CCATCTTCTCAAGGACGACGGCAACTACAAGACCCGCGCCGAGGTGAAGTTCGA GGGCGACACCCTGGTGAACCGCATCGAGCTGAAGGGCATCGACTTCAAGGAGGAC GGCAACATCCTGGGGCAACAAGCTGGAGTACAACACTACAACAGCCACAACGTCTAT CATGGCCGACAAGCAGAAGAACGGCATCAAGGTGAACCTCAAGATCCGCCACAAC ATCGAGGACGGCAGCGTGCAGCTCGCCGACCACTACCAGCAGAACACCCCATCG GCGACGGCCCCGTGTGCTGCCGACAACCACTACCTGAGCACCAGTCCGCCCT GAGCAAAGACCCCAACGAGAAGCGGATCACATGGTCTGTGGAGTTCGTGACC GCCGCCGGGATCACTCTCGGCATGACGAGCTGTACAAGTAATAGGAATTATGCAG	73

[0703]

	<p>TCTAGCCATCACATTTAAAGCATCTCAGCCTACCATGAGAATAAGAGAAAAGAAAA TGAAGATCAATAGCTTATTCATCTCTTTTTCTTTTTCTGTTGGTGTAAGCCAAACACCC TGTCTAAAAAACATAAATTTCTTTAATCATTTTGCCTCTTTTCTCTGTGCTTCAATTA TAAAAATGGAAAGAACCTCGAGAAAAAAGAGAAAAAAGAGAAAAAAGAGAAAAA AAAAAAGAAAAAAGAAAAAAGAAAAAAGAAAAAAGAAAAAAGAAAAAAGAAAAA AAAAAAGAAAAAAGAAAAAAGAAAAAAGAAAAAAGAAAAAAGAAAAAAGAAAAA AAAAAAGAAAAAAGAAAAAAGAAAAAAGAAAAAAGAAAAAAGAAAAAAGAAAAA CATGGTCATAGCTGTTTCTGTGTGAAATTTATCCGCTCACAATTCACACAACAT ACGAGCCGGAAGCATAAAGTGTAAAGCCTGGGGTGCCTAATGAGTGAGCTAACTC ACATTAATTGCGTTGCGCTCACTGCCCCTTTCCAGTCGGGAAACCTGTGCGTCC GCTGCTAATGAATCGGCCAACGCGCGGGGAGAGGGCGTTTGCATTTGGGCGCT CTTCCGCTTCTCGCTCACTGACTCGCTGCGCTCGGTCGTTCCGGCTGCGGCGAGCG GTATCAGCTCACTCAAAGCGGTAATACGGTTATCCACAGAATCAGGGGATAACGC AGGAAAGAACATGTGAGCAAAAGGCCAGCAAAAGGCCAGGAACCGTAAAAAGGC CGCGTTGCTGGCGTTTTTCCATAGGCTCCGCCCCCTGACGAGCATCAAAAAATC GACGCTCAAGTCAGAGGTGGCGAAACCCGACAGGACTATAAAGATACCAGGCGTT TCCCCCTGGAAGCTCCCTCGTGCCTCTCTGTTCCGACCCTGCCGTTACCGGATA CCTGTCCGCCTTTCTCCCTTCGGGAAGCGTGGCGCTTTCTCATAGCTACGCTGTAG GTATCTCAGTTCGGTGTAGGTGCTTCCGCTCCAAGCTGGGCTGTGTGCACGAACCC CCGTTACGCCGACCCTGCGCTTATCCGGTAACATATCGTCTTGAGTCCAACCCG TAAGACACGACTTATCGCCACTGGCAGCAGCCACTGGTAACAGGATTAGCAGAGC GAGGTATGTAGGCGGTGCTACAGAGTTCTTGAAGTGGTGGCCTAACTACGGCTACA CTAGAAGAACAGTATTTGGTATCTGCCTCTGCTGAAGCCAGTTACCTTCGGAAAA AGAGTTGGTAGCTCTTGTATCCGGCAAAACAACCACCCTGGTAGCGGTGGTTTTTT TGTTTGAAGCAGCAGATTACGCGCAGAAAAAAGGATCTCAAGAAGATCCTTTGA TCTTTTCTACGGGCTGACGCTCAGTGGAACGAAAACCTCACGTTAAGGGATTTT GTCATGAGATTATCAAAAAGGATCTTACCTAGATCCTTTAAATAAAAATGAAGT TTTAAATCAATCAAAAGTATATATGAGTAACTTGGTCTGACAGTTACCAATGCTTAA TCAGTGAGGCACCTATCTCAGCGATCTGCTTATTTCGTTTCATCCATAGTTGCCGT CCCCGCTGCTGAGATAACTACGATACGGGAGGGCTTACCATCTGGCCCCAGTGCTG CAATGATAACCGCAGACCCACGCTCACCGGCTCCAGATTTATCAGCAATAAACAG CCAGCCGGAAGGGCCGAGCGCAGAAGTGGTCTGCAACTTTATCCGCCTCCATCCA GTCTAATATGTTGCCGGAAGCTAGAGTAAGTAGTTCCAGTTAATAGTTTGGC CAACGTTGTTGCCATTGCTACAGGCATCGTGGTGTGACGCTCGTCTGGTATGGC TTCATTAGCTCCGGTTCCCAACGATCAAGGCGAGTTACATGATCCCCATGTTGTG CAAAAAGCGGTAGCTCCTCCGTCCTCCGATCGTTGTCAGAAAGTAAAGTTGGCCG CAGTGTATCACTCATGGTTATGGCAGCACTGCATAATCTCTTACTGTCATGCCATC CGTAAGATGCTTTTCTGTGACTGGTGAGTACTCAACCAAGTATTCTGAGAATAGTG TATGCGGCGACCGAGTTGCTCTTGCCCGGCCTCAATACGGGATAATACCGGCCAC ATAGCAGAACTTTAAAGTGCTCATCATTGAAAAACGTTCTTCGGGGCGAAAACCTC TCAAGGATCTTACCCTGTTGAGATCCAGTTCGATGTAACCCACTCGTGACCCAA CTGATCTCAGCATCTTTACTTTACCAGCGTTTCTGGGTGAGCAAAAACAGGAA GGCAAAATGCCGAAAAAAGGGAATAAGGGCGACACGGAATGTTGAATACTCAT ACTCTCTCTTTTCAATATTATTGAAGCATTTATCAGGGTTATTGTCTCATGAGCGGAT ACATATTGAATGTATTAGAAAAATAACAAATAGGGGTTCCGCGCACATTTCCCC GAAAAGTGCCACCTGACGTCTAAGAAACCATATTATCATGACATTAACCTATAAAA ATAGCGTATCACGAGGCCCTTTCGTCG</p>	
<p>经修饰的 sgRNA 模 式, 其中N 为编码引 导序列的 核苷酸</p>	<p>mN*mN*mN*NNNNNNNNNNNNNNNNNGUUUAG AmGmCmUmAmGmAmAmUmAmGmCAAGUUAAA AUAAGGCUAGUCCGUUUCAmAmCmUmUmGmAm AmAmAmAmGmUmGmGmCmAmCmGmAmGmUmC mGmGmUmGmCmU*mU*mU*mU</p>	<p>74</p>
<p>CMV-1 5' UTR</p>	<p>CAGATCGCCTGGAGACCCATCCACGCTGTTTTGACCTCCAT</p>	<p>75</p>
<p>CMV-2 5' UTR</p>	<p>AGAAGACACCGGGACCGATCCAGCCTCCGCGGCCGGGAACGG</p>	<p>76</p>
<p>CMV-3 5' UTR</p>	<p>TGCATTGGAACGCGGATTCCCCGTGCCAAGAGTGACTACCG</p>	<p>77</p>
<p>SV40 NLS</p>	<p>PKKKRKV</p>	<p>78</p>
<p>示例性NLS 1</p>	<p>LAAKRSRTT</p>	<p>79</p>
<p>示例性NLS 2</p>	<p>QAAKRSRTT</p>	<p>80</p>

[0704]

示例性NLS 3	PAPAKRERTT	81
示例性NLS 4	QAAKRPRTT	82
示例性NLS 5	RAAKRPRTT	83
示例性NLS 6	AAAKRSWSMAA	84
示例性NLS 7	AAAKRVWSMAF	85
示例性NLS 8	AAAKRSWSMAF	86
示例性NLS 9	AAAKRKYFAA	87
示例性 NLS 10	RAAKRKAFAA	88
示例性 NLS 11	RAAKRKYFAV	89
替代 SV40 NLS	PKKKRRV	90
核质蛋白 NLS	KRPAATKKAGQAKKKK	91
SV40 NLS的示例性编码序列	CCGAAGAAGAAGAGAAAGGTC	92
NLS1的示例性编码序列	CTGGCAGCAAAGAGAAGCAGAACAACA	93
NLS2的示例性编码序列	CAGGCAGCAAAGAGAAGCAGAACAACA	94
NLS3的示例性编码序列	CCGGCACCGCAAAGAGAGAAAGAACAACA	95
NLS4的示例性编码序列	CAGGCAGCAAAGAGACCGAGAACAACA	96
NLS5的示例性编码序列	AGAGCAGCAAAGAGACCGAGAACAACA	97
NLS6的示例性编码序列	GCAGCAGCAAAGAGAAGCTGGAGCATGGCAGCA	98
NLS7的示例性编码序列	GCAGCAGCAAAGAGAGTCTGGAGCATGGCATT	99
NLS8的示例性编码序列	GCAGCAGCAAAGAGAAGCTGGAGCATGGCATT	100
NLS9的示例性编码序列	GCAGCAGCAAAGAGAAAGTACTTCGCAGCA	101
NLS10 的示例性编码序列	AGAGCAGCAAAGAGAAAGGCATTTCGCAGCA	102
NLS11 的示例性编码序列	AGAGCAGCAAAGAGAAAGTACTTCGCAGTC	103
替代 SV40 NLS 的示例	CCGAAGAAGAAGAGAAAGGTC	104

性编码序列		
示例性Kozak序列	gccgccRccAUGG	105
	未使用	106
使用表4的长半衰期密码子, 具有起始及终止密码子的 Cas9 ORF	<p>ATGGACAAGAAGTACTCTATCGGTTTGGACATCGGTACCAACTCTGTGCGTTGGGCCG TCATCACCGACGAATACAAGTCCCATCTAAGAAGTTCAAGGTCTTGGGTAAACCCG ACAGACACTCTATCAAGAAGAAGCTGATCGGTGCCTTGTGTTGCTGACTCTGGTGAAC CGCCGAAGCCACCAGATTGAAGAGAACCGCCAGAAGAAGATACACCAGAAGAAAGA ACAGAATCTGCTACTTGAAGAAATCTTCTTAACGAAATGGCCAAGGTCGACGACT CTTTCTTCCACAGATTGGAAGAATCTTTCTTGGTTCGAAGAAGACAAGAAGCACGAAA GACACCCAATCTTCGGTAACATCGTCGACGAAGTCGCCTACCACGAAAAGTACCCAA CCATCTACCACTTGAGAAAAGAAGTTGGTTCGACTCTACCGACAAGGCCGACTTGAGAT TGATCTACTTGGCCTTGGCCACATGATCAAGTTCAGAGGTCACTTCTTGATCGAAGG TGACTTGAACCCAGACAACCTGACGTCGACAAGTTGTTTATCCAATGGTCCAAAC CTACAACCAATTGTTTGAAGAAAACCCAATCAACGCCTCTGGTGTGACGCCAAGGC CATCTGTCTGCCAGATTGTCTAAGAGCAGAAGATTGGAAAACCTGATCGCCCAATTG CCAGGTGAAAAGAAGAACGGTTTGTTCGGTAACTTGATCGCCTTGTCTTGGGTTTGA CCCCAACTTCAAGTCTAACTTCGACTTGGCCGAAGACGCCAAGTTGCAATTGTCTA AGGACACCTACGACGACGACTTGGACAACCTTGGTGGCCAAATCGGTGACCAATACG CCGACTTGTCTTGGCCGCAAGAAGCTTGTCTGACGCCATCTTGTGTCTGACATCTT GAGAGTCAACACCGAAATCACCAAGGCCCCATTGTCTGCCTCTATGATCAAGAGATAC GACGAACACCACCAAGACTTGACCTTGTGAAGGCCTTGGTCAGACAACAATTGCCA GAAAAGTACAAGGAAATCTTCTGACCAATCTAAGAACGGTTACGCCGTTACATCG ACGGTGGTGCCTCTCAAGAAGAATTCTACAAGTTCATCAAGCCAATCTTGGAAAAGA TGGACGGTACCGAAGAATTGTTGGTCAAGTTGAACAGAGAAGACTTGTGAGAAAAG CAAAGAACCTTCGACAACGGTTCTATCCACACCAAAATCCACTTGGGTGAATTGCAC GCCATCTTGAGAAGACAAGAAGACTTCTACCCATTCTTGAAGGACAACAGAGAAAAG AAAACGAAGACATCTTGAACCTTCAGAATCCATACTACGTCGGTCCATTGGCCAGAGT ACAGCAGATTGCGCTGGATGACCAGAAAGTCTGAAGAAACCATCACCCATGGAAGT TCGAAGAAGTCTGTCGACAAGGGTGCCTTGCCTCAATCTTTCATCGAAAAGATGACCA ACTTCGACAAGAAGTTCGCAAAACGAAAAGGTCTTGGCAAAGCACTTTTGTGTGACG AATACTCACCGTCTACAACGAATTGACCAAGGTCAAGTACGTCACCGAAGGTATGA GAAAGCCAGCCTTCTTGTCTGGTGAACAAAAGAAGGCCATCGTCGACTTGTGTGTC AGACCAACAGAAAGGTCACCGTCAAGCAATTGAAGGAAGACTACTTCAAGAAGATC GAATGCTTCGACTCTGTGCAAAATCTCTGGTGTGGAAGACAGATTCAACGCCTCTTGG GTACCTACCAGACTTGTGAAGATCATCAAGGACAAGGACTTCTTGGACAACGAAG AAAACGAAGACATCTTGAAGACATCGTCTTGAACCTTGAACCTTGTTCGAAGACAG AAATGATCGAAGAAAGATTGAAGACCTACGCCACTTGTTCGACGACAAGGTCATGA AGCAATTGAAGAGAAGAAGATACACCGGTTGGGGTAGATTGAGCAGAAAAGTTGATCA ACGGTATCAGAGACAAGCAATCTGGTAAAGACCATCTTGGACTTCTTGAAGTCTGACG GTTTCGCCAACAGAAACTTCATGCAATTGATCCACGACGACTCTTGGACCTTCAAGGA AGACATCCAAAAGGCCAAGTCTCTGGTCAAGGTGACTCTTTCGACGAACACATCGC CAACTTGGCCGTTCTCCAGCCATCAAGAAGGGTATCTTGCAAAACCGTCAAGGTCGT CGACGAATTGGTCAAGGTCATGGGTAGACACAAGCCAGAAAACATCGTCATCGAAAT GGCCAGAGAAAACCAACCACCAAAAAGGGTCAAAAAGAACAGCAGAGAAAAGAATG AAGAGAATCGAAGAAGGTATCAAGGAATTGGGTTCTCAAATCTTGAAGGAACACCCA GTCGAAAACACCCAATTGCAAAAACGAAAAGTTGTAATTGTACTACTTGCAAAACGGT AGAGACATGTACGTCGACCAAGAATTGGACATCAACAGATTGTCTGACTACGACGTC GACCACATCGTCCACAATCTTTCTTGAAGGACGACTCTATCGACAACAAGGTCTTGA CCAGATCGACAAGAACAGAGGTAAGTCTGACAACGTCCCATCTGAAGAAGTCGTCA AGAAGATGAAGAACTACTGGAGACAATTGTTGAACGCCAAGTTGATCACCCAAAGAA AGTTTCGACAACCTGACCAAGGCCGAAAGAGGTGGTTTGTCTGAATTGGACAAGGCC GGTTTCATCAAGAGACAATTGGTTCGAAACCAGACAAATCACCAAGCACGTCGCCCAA ATCTTGGACAGCAGAATGAACACCAAGTACGACGAAAACGACAAGTTGATCAGAGA AGTCAAGGTCATCACCTTGAAGTCTAAGTTGGTCTCTGACTTCAGAAAAGGACTTCCAA TTCTACAAGGTCAGAGAAATCAACAACCTACCACCACGCCCACGACGCTACTTGAAC GCCGTCGTCGGTACCGCCTTGATCAAGAAGTACCCAAAGTTGGAATCTGAATTCGTCT ACGGTACTACAAGGTCTACGACGTCGAAAAGATGATCGCCAAGTCTGAACAAGAAA TCGGTAAGGCCACCGCCAAGTACTTCTACTCTAACATCATGAACCTTCTCAAGAC CGAAATCACCTTGGCCAACGGTGAATCAGAAAAGAGACCATTGATCGAAAACCAACGG TGAAAACCGGTGAAATCGTCTGGGACAAGGGTAGAGACTTCGCCACCGTCAGAAAAGG TCTTGTCTATGCCACAAGTCAACATCGTCAAGAAGACCGAAGTCCAAACCGGTGGTT TCTCTAAGGAATCTATCTTGCAAAAGAGAACTCTGACAAGTTGATCGCCAGAAAAGA AGGACTGGGACCCAAAAGAAGTACGGTGGTTTCGACTCTCAACCGTCGCCTACTCTG</p>	107

[0705]

	<p>TCTTGGTCGTCGCCAAGGTCGAAAAGGGTAAGTCTAAGAAGTTGAAGTCTGTCAAGG AATTGTTGGGTATCACCATCATGGAAAAGATCTTCTTTCGAAAAAGAACCCAATCGACTT CTTGGAAAGCCAAGGGTTACAAGGAAGTCAAGAAGGACTTGATCATCAAGTTGCCAAA GTACTCTTTGTTCCGAATTGGAAAACGGTAGAAAAGAGAAATGTTGGCCCTCGCCGGTGA ATTGCAAAAAGGGTAACGAATTGGCCTTGCCATCTAAGTACGTCAACTTCTTGTACTTG GCCTCTACTACGAAAAGTTGAAGGGTCTCCAGAAGACAACGAACAAAAGCAATT GTTTCGTCGAACAACAAGCACTACTTGGACGAAATCATCGAACAAATCTCTGAATTC TCTAAGAGAGTCACTTGGCCGACGCCAAGTGGACAAGGCTTGTCTGCCTACAAC AAGCACAGAGACAAGCCAATCAGAGAACAAGCCGAAAACATCATCCACTTGTTCAC CTTGACCAACTTGGGTGCCCCAGCCGCTTCAAGTACTTCGACACCACCATCGACG AAAAGATACACCTCTACCAAGGAAGTCTTGGACGCCACCTTGATCCACCAATCTATC ACCGGTTTGTACGAAACCAGAATCGACTTGTCTCAATTGGGTGGTGACGGTGGTGGT TCTCCAAAAGAAGAAGAGAAAAGGTCTAA</p>	
<p>使用表4的富 含U的密码 子, 具有起始 及终止密码 子的 Cas9 ORF</p>	<p>ATGGATAAAAAATATTCATTGGTTTATGATATTGGTACTAATTCTGTTGGTGGGCTGTT ATTACTGATGAATATAAAGTTCCTTAAAAAATTTAAAGTTTATAGGTAATCTGATCGT CATTCTATTAATAAAAAATTTAATTGGTCTTTATTATTGATTCTGGTGAACCTGCTGAA GCTACTCGTTTAAAACGTACTGCTCGTCGTCGTTATACTCGTCGTAATAATCGTATTTG TTATTACAAGAAATTTTTCTAATGAAATGGCTAAAAGTTGATGATTCTTTTTTTCATCG TTTAGAAGAATCTTTTTAGTTGAAGAAGATAAAAAACATGAACGTCATCCTATTTTTG GTAATATTGTTGATGAAGTTGCTTATCATGAAAAATATCCTACTATTATCATTACGTAA AAAATTAGTTGATTCTACTGATAAAGCTGATTTACGTTTAAATTTATTAGCTTTAGCTCA TATGATTAAATTCGTGGTCATTTTTAATTGAAGGTGATTTAAATCCTGATAATTCTGA TGTTGATAAATTTATTCAATTAGTTCAAACTTATAATCAATTATTTGAAGAAAATCCT ATTAATGCTTCTGGTGTGATGCTAAAAGCTATTTATCTGCTCGTTTATCTAAATCTCGT CGTTTTAGAAAATTTAATTGCTCAATTACCTGGTGAAAAAATAATGTTTATTTGGTAA TTAATTGCTTTATCTTTAGGTTTAACTCCTAATTTTAAATCTAATTTTGATTTAGCTGAA GATGCTAAATTACAATTATCTAAAGATACTTATGATGATGATTTAGATAATTTATAGCTC AAATGGTGATCAATATGCTGATTTATTTTAGCTGCTAAAAATTTATCTGATGCTATTTT ATTATCTGATATTTTACGTGTTAATACTGAAATTACTAAAAGCTCCTTATCTGCTTCTATG ATTAACGTTTATGATGAACATCATCAAGATTTAACTTTATTAATAAGCTTTAGTTTCGTC ACAATTACCTGAAAAATATAAAGAAATTTTTTTGATCAATCTAAAAATGGTTATGCTG GTTATATTGATGGTGGTCTTCTCAAGAAGAATTTTATAAATTTATTAACCTATTTTAG AAAAATGGATGGTACTGAAGAATTATTAGTTAAATTAATCGTGAAGATTTATTACGT AAACAACGTACTTTTGATAATGGTTCTATTCCTCATCAAATTCATTTAGGTGAATACAT GCTATTTTACGTCGTCAGAAGATTTTATCCTTTTTTAAAGATAATCGTGAAAAAAT TGAAAAAATTTAACTTTTCGATTCCTTATATGTTGGTCCCTTAGCTCGTGGTAATTC TCGTTTTGCTTGGATGACTCGTAAATCTGAAGAACTATTACTCCTTGGAAATTTTGAAG AAGTTGTTGATAAAGGTGCTTCTGCTCAATCTTTTATTGAACGTATGACTAATTTTGATA AAAATTTACCTAATGAAAAAGTTTTACCTAAAACATTCTTTATTATATGAATATTTTACTG TTTATAATGAATTAACATAAAGTTAAATATGTTACTGAAGGTATGCGTAAACCTGCTTTTT TATCTGGTGAACAAAAAAGCTATGTTGATTTATTATTTAAACTAATCGTAAAGTT ACTGTTAAACAATTAAGAAGATTTTAAAAAATGAATGTTTGTGATTCGTTGA AATTTCTGGTGTGAAAGATCGTTTTAATGCTTCTTTAGGTACTTATCATGATTTTATAA AATTTAAAGATAAAGATTTTTTAGATAATGAAGAAATGAAGATATTTAGAAGATA TTGTTTAACTTTAACTTTATTGAAAGATCGTGAATGATTGAAGAACGTTTAAAAACT TATGCTCATTATTTGATGATAAAGTTATGAAACAATTAACCGTCTGTTTATACTGGT TGGGGTCGTTTATCTCGTAAATTAATTAATGGTATTCTGTAATAACAATCTGGTAAACT ATTTTAGATTTTTTAAATCTGATGGTTTTGCTAATCGTAAATTTTATGCAATTAATTCATG ATGATCTTTAACTTTTAAAGAAGATATTCAAAAAGCTCAAGTTTCTGGTCAAGGTGAT TCTTACATGAACATATTGCTAATTTAGCTGGTTCTCCTGCTATTAATAAAGGTATTTTA CAAACTGTTAAAGTTGTTGATGAATTAGTTAAAGTTATGGGTGCTCATAAACCTGAAA ATATTGTTATTGAAATGGCTCGTGAATAAATAAATAAATAAATAAATAAATAAATAAATAA TCGTGAACGTATGAAACGTATTGAAGAAGGTATTAAGAATTAGGTTCTCAAATTTTA AAAGAACATCCTGTTGAAAATACATAATTACAAAATGAAAAATATATTATATTATTTA CAAAATGGTCGTGATATGATGTTGATCAAGAATTAGATATTAATCGTTTATCTGATTAT GATGTTGATCATATTGTTCCCTCAATCTTTTTTAAAGATGATTCTATTGATAATAAAGTTT TAACTCGTTCTGATAAAAATCGTGGTAAATCTGATAATGTTCTTCTGAAAGAAGTTGTT AAAAAATGAAAAATATTGGCGTCAATTATAAATGCTAAATTAATTAATCAACGTAA ATTTGATAATTTAACTAAAGCTGAACGTGGTGGTTTTATCTGAATTAGATAAAGCTGGTT TTATTAACGTCAATTAGTTGAACTCGTCAAATTAATAACATGTTGCTCAAATTTTA GATTCGATGAACTAAATATGATGAAAATGATAAATTAATTCGTGAAGTTAAAGTT ATTACTTTAAATCTAAATTAGTTTCTGATTTTCGTAAGATTTTCAATTTTATAAAGTT CGTGAATTAATAATATCATCATGCTCATGATGCTTATTTAAATGCTGTTGTTGGTACT GCTTTAATTAATAAATATCCTAAATTAGAATCTGAATTTGTTTATGGTGATTATAAAGTT TATGATGTTGTAATAATGATTGCTAAATCTGAACAAGAAATTTGGTAAAGCTACTGCTAA ATATTTTTTTTATTCTAATATATGAATTTTTTTTAAACTGAAATTAATTTAGCTAATGGT GAAATTCGTAACGTCCTTAAATTGAAACTAATGGTGAACGTTGGTGAATTTGTTGGG</p>	<p>108</p>

[0706]

	<p>ATAAAGGTCGTGATTTTGTCTACTGTTTCGTAAGTTTTATCTATGCCTCAAGTTAATATTG TTAAAAAACTGAAAGTTCAAACCTGGTGGTTTTTCTAAAAGAATCTATTTTACCTAAACG TAATTCGATAAATTAATTGCTCGTAAAAAAGATTGGGATCCTAAAAAATATGGTGGTT TTGATTCTCTACTGTTTCTTATTCTGTTTTAGTTGTTGCTAAAAGTTGAAAAAGGTAAA TCTAAAAAATAAAAATCTGTAAAGAATTATTAGGTATTACTATTATGGAACGTTCTTCT TTTGAAAAAATCCTATTGATTTTTTAGAAGCTAAAAGTTATAAAGAAGTTAAAAAAG ATTTAATTATTAATTAACCTAAATATTCTTTATTTGAATTAGAAAATGGTCGTAACCGTAT GTTAGCTTCTGCTGGTGAATTACAAAAAGGTAATGAATTAGCTTTACCTTCTAAATATG TTAATTTTTATATTAGCTTCTCATTATGAAAAATTAAGGTTCTCCTGAAAGATAATG AACAAAAACAATTATTTGTTGAACAACATAAACATTATTTAGATGAAATATTGTAACAA ATTTCTGAATTTTCTAAACGTTTATTTTAGCTGATGCTAATTTAGATAAAGTTTTATCT GCTTATAATAAACATCGTGATAAACCTATTCTGTAACAAGCTGAAAATATTATTCATTTA TTTACTTTAACTAATTTAGGTGCTCCTGCTGCTTTTAAATATTTTGATACTACTATTGATC GTAAACGTTATACTTCTACTAAAGAAGTTTTAGATGCTACTTTAATTCATCAATCTATTA CTGGTTTATATGAAACTCGTATTGATTTATCTCAATTAGGTGGTGGTGGTGGTCTC CTAAAAAAAACGTAAGTTTGA</p>	
<p>使用表4的低 G密码子, 具 有起始及终 止密码子的 Cas9 ORF</p>	<p>ATGGACAAAAAATACTCCATCGGCCCTCGACATCGGCACCAACTCCGTCGGCTGGGCC GTCATCACCGACGAATACAAAGTCCCTCCAAAAAATCAAAGTCCCTCGGCAACACC GACGACACTCCATCAAAAAAACCTCATCGGCGCCCTCCTCTTCGACTCCGGCGAA ACCGCGAAGCCACCAGACTCAAAAAGAACCAGGAGAAAGATACACCGAAGAAA AAACAGAATCTGCTACCTCCAAGAAATCTTCTCCAACGAAATGGCCAAAGTCGACGA CTCCTTCTCCACAGACTCGAAGAATCCTTCTCGTCAAGAAGACAAAAACACGA AAGACACCCCATCTTCGGCAACATCGTCGACGAAGTCGCCTACCACGAAAAATACC CACCATCTACCACCTCAGAAAAAATCTGTCGACTCCACCGACAAAGCCGACCTCAG ACTCATCTACCTCGCCCTCGCCACATGATCAAATTCAGAGGCCACTTCTCATCGAA GGCGACCTCAACCCGACAACCTCGACGTCGACAAACTCTTCATCCAACCTCGTCCAA ACCTACAACCACTCTTCGAAGAAAACCCATCAACGCCTCCGGCGTCGACGCCAAA GCCATCCTCTCGCCAGACTCTCAAATCCAGAAGACTCGAAAACCTCATCGCCCAA CTCCCGGCGAAAAAAAACGGCCCTTTCGGCAACCTCATCGCCCTCCTCCCTCGGC CTCACCCCAACTTCAAATCCAACCTTCGACCTCGCCGAAGACGCCAAACTCCAACCT TCCAAAGACACTACGACGACGACCTCGACAACCTCCTCGCCAAATCGGGCGACCAA TAGCCGACCTCTTCTCGCCGCAAAAAACCTCTCCGACGCCATCCTCTCTCCGACA TCCTCAGAGTCAACACCGAAATCACCAAAAGCCCCCTCTCCGCTCCTGATCAAAA GATACGACGAACACCAAGACTCACCCTCCTCAAAGCCCTCGTCAGACAAAC TCCCGAAAAATACAAAGAAATCTTCTCGACCAATCAAAAAACGGCTACGCCGGCT ACATCGACGGCGGCGCCTCCCAAGAAGAATTCTACAAATTCATCAAACCATCCTCGA AAAAATGGACGGCACCGAAGAACTCCTCGTCAAACTCAACAGAGAAGACCTCCTCA GAAAAAAAAGAACCTTCGACAACGGCTCCATCCCCACCAAATCCACTCGGCGAAC TCCACGCCATCCTCAGAAGACAAGAAGACTTCTACCCCTTCTCAAAGACAACAGAG AAAAATCGAAAAATCCTCACCTTCAAGAATCCCTACTACGTCGGCCCCCTCGCCAG AGGCAACTCCAGATTGCTGCTGACCAAGAAATCCGAAGAAACCATCACCCCTG GAACCTCGAAGAAGTCGTGACAAAGGCCTCCGCCCAATCCTCATCGAAAGAAAT GACCAACTTCGACAAAAAATCCTCCCAACGAAAAAGTCTCCCAACACTCCTCCT CTACGAATACTTACCGTCTACAACGAACCTACCAAAAGTCAAATACGTCACCGAAGG CATGAGAAAACCGCCTTCTTCCGGCGAACAAAAAAGCCATCGTCGACCTCCT TTCAAACAACAGAAAAAGTCAACGTTCAAAACTCAAAAGAAGACTACTTCAAAA AAATCGAATGCTTCGACTCCGTCGAAATCTCCGGCGTCGAAGACAGATTCACGCCT CCCTCGGCACCTACCACGACCTCCTCAAAATCATCAAAGACAAAAGACTTCTCGACA ACGAAGAAAACGAAGACATCCTCGAAGACATCGTCTCACCTCACCTCCTCGAAG ACAGAGAAATGATCGAAGAAAAGACTCAAAACCTACGCCACCTCTTCGACGACAAA GTCATGAAACAACCTCAAAAAGAAGAAGATACACCGGCTGGGGCAGACAAACCCGAAAAC ACTCATCAACGGCATCAGAGACAAACAATCCGGCAAAACCATCCTCGACTTCTCAA ATCCGACGGCTTCGCCAACAGAACTTCATGCAACTCATCCACGACGACTCCCTCAC CTTCAAAGAAGACATCAAAAAGCCCAAGTCTCCGGCCAAGGCGACTCCCTCCACG AACACATCGCCAACCTCGCCGGCTCCCCGCCATCAAAAAAGGCATCCTCCAAACCG TCAAAAGTCGTGACGAACCTGTCAAAGTATGGGCAGACACAAACCCGAAAAACATC GTCATCGAAATGGCCAGAGAAAACCAACCAACCAAAAAAGGCCAAAAAAACTCCAG AGAAAGAATGAAAAGAATCGAAGAAGGCATCAAAGAACTCGGCTCCCAAATCCTCA AAGAACACCCCGTCGAAAAACCCAACCTCAAAAACGAAAAACTTACTCTACTACC TCCAAAACGGCAGAGACATGTACGTCGACCAAGAAGTCTGACATCAACAGACTCCTCG ACTACGACGTCGACCACATCGTCCCCAATCCTTCTCAAAGACGACTCCATCGACAA CAAAGTCTCACCAGATCCGACAAAAACAGAGGCAAAATCCGACAACGTCCTCCCTCG AAGAAGTCGTCAAAAAATGAAAAACTACTGGAGCAACTCCTCAACGCCAAACTC ATCACCAAAAGAAAATTCGACAACCTACCAAAGCCGAAAGAGGGCGCCTCTCCGA ACTCGACAAAAGCCGGCTTCATCAAAGACAACCTCGTCGAAACCGACAAATCACC AACACGTCGCCCAATCCTCGACTCCAGAATGAACACCAATACGACGAAAACGACA AACTCATCAGAGAAGTCAAAGTCATCACCTCAAATCCAACCTCGTCTCCGACTTCA</p>	<p>109</p>

[0707]

	<p>GAAAAGACTTCCAATTCTACAAAGTCAGAGAATCAACAACCTACCACCACGCCACG ACGCCTACCTCAACGCCGTCGTGGCACCGCCCTCATCAAAAAATACCCCAAACCTCG AATCCGAATTCGTCTACGGCGACTACAAAGTCTACGACGTGAGAAAAATGATCGCCA AATCCGAACAAGAAATCGGCAAAGCCACCGCCAAATACTTCTTACTCCAACATCAT GAATTTCTTCAAAAACCGAAATCACCTCGCCAACGGCGAAATCAGAAAAAGACCCCT CATCGAAACCAACGGCGAAACCGGCGAAATCGTCTGGGACAAAAGGAGAGACTTCG CCACCGTCAGAAAAGTCTCTCCATGCCCAAGTCAACATCGTCAAAAAAACCGAAG TCCAAACCGGCGGCTTCTCAAAGAATCCATCCTCCCAAAAGAAACTCCGACAAAC TCATCGCCAGAAAAAAGACTGGGACCCCAAAAAATACGGCGGGCTTCGACTCCCCCA CCGTGCCTACTCCGTCTCGTCTGCCAAAGTCGAAAAAGGCAAAATCCAAAAAAC TCAAATCCGTCAAAGAATCCTCGGCATACCATCATGGAAAGATCCTCTTCGAAAA AAACCCCATCGACTTCTCGAAGCCAAAGGCTACAAAGAAGTCAAAAAAGACCTCAT CATCAAATCCCAAAATATCCCTCTTCGAACTCGAAAACGGCAGAAAAAGAATGCT CGCTCCGCGGCGAACTCAAAAAGGCAACGAACTCGCCCTCCCTCCAAATACGT CCTATCCCTTACCTGCCTCCACTACGAAAAACTCAAAGGCTCCCCGAGACAA CGAACAAAAACAACCTTTCGTGCAACAACACAAACTACCTCGACGAAATCATCGA ACAAATCTCCGAATTCCTCAAAGAGTTCATCTCGCCGACGCCAACCTCGACAAAGT CCTCTCCGCTACAACAAACACAGAGACAAACCCATCAGAGAACAAGCCGAAAAACA TCATCCACCTCTTACCCTACCAACCTCGGCGCCCCGCCCTCAAAATCTCGA CACCACATCGACAGAAAAAGATACACCTCCACCAAGAAGTCTCGACGCCACCT CATCCACCAATCCATCACCAGGCTCTACGAAACCAGAATCGACCTCTCCAACCTCGG GGCAGCGGCGGCTCCCAAAAAAAGAAAGTCTGA</p>	
<p>使用表4的低 C密码子，具 有起始及终 止密码子的 Cas9 ORF</p>	<p>ATGGATAAGAAGTATAGTATTGGATTGGATATTGGAACAAATAGTGTGGGATGGGCTGT GATTACAGATGAGTATAAGGTGCCTAGTAAGAAGTTTAAAGTGTGGGAAATACAGAT AGACATAGTATTAAGAAGAATTTGATTGGAGCTTTGTTGTTGATAGTGGAGAGACAG CTGAGGCTACAAGATTGAAGAGAACAGCTAGAAGAAGATATACAAGAAGAAAGAATA GAATTTGTTATTTGCAGGAGATTTTAGTAATGAGATGGCTAAGGTGGATGATAGTTTT TTTCATAGATTGGAGGAGAGTTTTTTGGTGGAGGAGGATAAGAAGCATGAGAGACAT CCTATTTTGGAAATATTGTGGATGAGGTGGCTTATCATGAGAAGTATCTACAATTTAT CATTTGAGAAAAGAAGTTGGTGGATAGTACAGATAAGGCTGATTTGAGATTGATTTATTT GGCTTTGGCTCATATGATTAAGTTTGAAGGACATTTTGGATTGAGGGAGATTTGAATC CTGATAATAGTGATGTGGATAAGTTGTTTATTCAGTTGGTGCAGACATATAATCAGTTG TTTGAGGAGAATCCTATTAATGCTAGTGGAGTGGATGCTAAGGCTATTTGAGTGCTAG ATTGAGTAAGAGTAGAAGATTGGAGAATTTGATTGCTCAGTTGCCTGGAGGAGAAAGAA GAATGGATTGTTTGGAAATTTGATTGCTTTGAGTTTGGGATTGACACCTAATTTAAGA GTAATTTGATTGGCTGAGGATGCTAAGTTGCAGTTGAGTAAGGATACATATGATGAT GATTTGGATAATTTGGCTCAGATTGGAGATCAGTATGCTGATTTGTTTTGGCTGCT AAGAATTTGAGTGATGCTATTTGTTGAGTGATATTTGAGAGTGAATACAGAGATTAC AAAGGCTCCTTTGAGTGCTAGTATGATTAAGAGATATGATGAGCATCATCAGGATTTGA CATTGTTGAAGGCTTTGGTGAGACAGCAGTTGCCTGAGAAGTATAAGGAGATTTTTTT TGATCAGAGTAAGAATGGATATGCTGGATATTTGATGGAGGAGCTAGTCAGGAGGAG TTTTATAAGTTTATTAAGCCTATTTTGGAGAAGATGGATGGAACAGAGGATTTGTTGGT GAAAGTTGAATAGAGAGGATTTGTTGAGAAAAGCAGAGAACATTTGATAATGGAAAGTATT CCTCATCAGATTCATTTGGGAGAGTTGCATGCTATTTTGAAGAAGACAGGAGGATTTTTA TCCTTTTTGAAGGATAATAGAGAGAAGATTGAGAAGATTTTGAATTTAGAAATTCCTT ATTATGTGGGACCTTTGGCTAGAGGAATAAGTATGATTTGCTTGGATGACAAGAAAGAG TGAGGAGACAATTACACCTTGGAAATTTGAGGAGGTGGTGGATAAGGGAGCTAGTGC TCAGAGTTTTATTGAGAGAATGACAAATTTGATAAGAATTTGCCTAATGAGAAGGTG TTGCCTAAGCATAGTTTGTGTATGAGTATTTACAGTGTATAATGAGTTGACAAAGGT GAAGTATGTGACAGAGGGAATGAGAAAGCCTGCTTTTTGAGTGGAGAGCAGAAGA AGGCTATTGTGGATTTGTTGTTAAGACAAATAGAAAGGTGACAGTGAAGCAGTTGA AGGAGGATTTTAAAGAAGATTGAGTGTGTTGATAAGTGGAGATTAGTGGAGTGGGA GGATAGATTTAATGCTAGTTTGGGAACATATCATGATTTGTTGAAGATTATTAAGGATAA GGATTTTTGGATAATGAGGAGAATGAGGATATTTGGAGGATATTGTGTTGACATTGA CATTGTTTGGAGATAGAGAGATGATTGAGGAGAGATTGAAGACATATGCTCATTGTT TGATGATAAGGTGATGAAGCAGTTGAAGAGAAGAAGATACAGGATGGGGAAGATT GAGTAGAAAAGTTGATTAATGGAATTAGAGATAAGCAGAGTGGAAAAGACAATTTGGA TTTTTTGAAGAGTGATGGATTTGCTAATAGAAATTTATGCAGTTGATTCATGATGATAG TTTGACATTTAAGGAGGATATTCAGAAGGCTCAGGTGAGTGGACAGGGAGATAGTTT GCATGAGCATATTGCTAATTTGGCTGGAAAGTCTGCTATTAAGAAGGGAATTTGACAG ACAGTGAAGGTGGTGGATGAGTTGGTGAAGGTGATGGGAAGACATAAGCCTGAGAAT ATTGTGATTGAGATGGCTAGAGAGAATCAGACAACACAGAAGGGACAGAAGAATAGT AGAGAGAGAATGAAGAGAATTGAGGAGGGAATTAAGGAGTTGGGAAGTCAGATTTT GAAGGAGCATCTGTGGAGAATACACAGTTGCAGAATGAGAAGTTGATTTGTATTAT TTGCAGAATGGAAGAGATATGATGTGGATCAGGAGTTGGATATTAATAGATTGAGTGA TTATGATGTGGATCATATTGTGCCTCAGAGTTTTTTGAAGGATGATAAGTATTGATAATAA GGTGTGACAAGAAGTGATAAGAATAGAGGAAAGAGTGATAATGTGCCTAGTGAGGA</p>	<p>110</p>

[0708]

[0709]

	GGTGGTGAAGAAGATGAAGAATTATTGGAGACAGTTGTTGAATGCTAAGTTGATTACA CAGAGAAAAGTTTGATAATTTGACAAAAGGCTGAGAGAGGAGGATTGAGTGAGTTGGAT AAGGCTGGATTATTAAGAGACAGTTGGTGGAGACAAGACAGATTACAAAGCATGTG GCTCAGATTTTGATAGTGAATGAATACAAAGTATGATGAGAATGATAAGTTGATTAG AGAGGTGAAGGTGATTACATTGAAGAGTAAAGTTGGTGAAGTATTTAGAAAAGGATTTT CAGTTTTATAAGGTGAGAGAGATTAATAATTATCATCATGCTCATGATGCTTATTTGAA GCTGTGGTGGGAACAGCTTTGATTAAGAAGTATCCTAAGTTGGAGAGTGAAGTTGTGT ATGGAGATTATAAGGTGTATGATGTGAGAAAGATGATTGCTAAGAGTGAAGCAGGAGAT TGGAAAGGCTACAGCTAAGTATTTTTTTATAGTAATATTGAATTTTTTAAAGACAGA GATTACATTGGCTAATGGAGAGATTAGAAAAGAGACCTTTGATTGAGACAAATGGAGA GACAGGAGAGATTGTGTGGGATAAGGGAAGAGATTTTGGTACAGTGAGAAAGGAGTTT GAGTATGCCTCAGGTGAATATTGTGAAGAAGACAGAGGTGCAGACAGGAGGATTTAG TAAGGAGAGATTTTTGCCTAAGAGAAATAGTGATAAGTTGATTGCTAGAAAAGAAGGAT TGGGATCCTAAGAAGTATGGAGGATTTGATAGTCTACAGTGGCTTATAGTGTGTGGT GGTGGCTAAGGTGGAGAAGGGAAGAGTAAGAAGTTGAAGAGTGTGAAGGAGTTGT TGGGAATTACAATTATGGAGAGAAGTAGTTTTGAGAAGAATCCTATTGATTTTTTGGGA GGCTAAGGGATATAAGGAGGTGAAGAAGGATTTGATTATTAAGTTGCCTAAGTATAGT TTGTTTGAGTTGGAGAATGGAAGAAAGAGAATGTTGGCTAGTGTGAGAGATTGCAG AAGGGAATGAGTTGGCTTTGCCTAGTAAGTATGTGAATTTTTGTATTTGGCTAGTCA TTATGAGAAGTTGAAGGGAAGTCTCGAGGATAATGAGCAGAAAGCAGATTTGTTGTGGA GCAGCATAAGCATTATTTGGATGAGATTATTGAGCAGATTAGTGAAGTTAGTAAGAGA GTGATTTTGGCTGATGCTAATTTGGATAAGGTGTTGAGTGTCTATAATAAGCATAGAGA TAAGCCTATTAGAGAGCAGGCTGAGAATATTATTCAATTTGTTTACATTGACAAATTTGG GAGTCTCTGCTGCTTTAAGTATTTGATACAACAATTGATAGAAAAGATATACAAAGT ACAAAAGGAGGTGTTGGATGCTACATTGATTATCAGAGTATTACAGGATTGTATGAGA CAAGAATTGATTGAGTCAGTTGGGAGGAGATGGAGGAGGAAGTCTAAGAAGAAG AGAAAAGGTGTGA	
使用表4的低 A密码子，具 有起始及终 止密码子的 Cas9 ORF	ATGGACAAGAAGTACTCCATCGGCCTGGACATCGGCACCAACTCCGTGGGCTGGGCC GTGATCACCGACGAGTACAAGGTGCCCTCCAAGAAGTTCAAGGTGCTGGGCAACACC GACCGGCACTCCATCAAGAAGAACCTGATCGGCGCCCTGCTGTTGACTCCGGCGAG ACCGCCGAGGCCACCGGCTGAAGCGGACCGCCCGGCGGCGGTACACCGCGCGAA GAACCGGATCTGCTACCTGCAGGAGATCTTCTCCAACGAGATGGCCAAGGTGGACGA CTCCTTCTTCCACCGGCTGGAGGATCCTTCTGGTGGAGGAGGACAAGAAGCACGA CGGCAACCCCATCTTCGGCAACATCTGTGGACGAGGTGGCCCTACCACGAGAATCC CACCATCTACCACCTGCGGAAGAAGCTGGTGGACTCCACCGACAAGGCCGACCTGCG GCTGATCTACCTGGCCCTGGCCACATGATCAAGTTCGGGGCCACTTCTGATCGAG GGCGACCTGAACCCCGACAACCTCCGACGTGGACAAGCTGTTATCCAGCTGGTGCAG ACCTACAACCAGCTGTTTCGAGGAGAACCCCATCAACGCCTCCGGCGTGGACGCCAAG GCCATCTGTCCGCCCGGCTGTCCAAGTCCCGGCGGCTGGAGAACCTGATCGCCAG CTGCCCGGCGAGAAGAAGAACGGCCTGTTTCGGCAACCTGATCGCCCTGTCCCTGGGC CTGACCCCAACTTCAAGTCCAACCTTCGACCTGGCCGAGGACGCCAAGCTGCAGCTG TCCAAGGACACCTACGACGACGACCTGGACAACCTGCTGGCCAGATCGGCGACCA GTACGCCGACCTGTTCTGGCCGCCAAGAACCTGTCCGACGCCATCTGTGTCCGA CATCTGCGGGTGAACACCGAGATCACCAGGCCCCCTGTCCGCTCCATGATCAA GCGGTACGACGAGCACACCGAGATCACCAGGCCCCCTGTCCGCTCCATGATCAA AGCTGCCCGAGAAGTACAAGGAGATCTTCTTCGACCAGTCCAAGAACGGCTACGCCG GACTCATCGACGGCGGCCTCCAGGAGGAGTTCTACAAGTTTATCAAGCCATCCTG GGAGAAGATGGACGGCACCGAGGAGCTGCTGGTGAAGCTGAACCGGGAGGACCTGC TGCGGAAGCAGCGGACCTTCGACAACGGCTCCATCCCCACCAGATCCACCTGGGCG AGCTGCACGCCATCTGCGGCGGCAGGAGGACTTCTACCCCTTCTGAAGGACAACC GGGAGAAGATCGAGAAGATCTGACCTTCCGGATCCCCTACTACGTGGGCCCTGG CCCGGGCAACTCCCGGTTGCGCTGGATGACCCGGAAGTCCGAGGAGACCATACCC CCTGGAACCTTCGAGGAGGTGGTGGACAAGGGCGCCTCCGCCAGTCTTTCATCGAGC GGATGACCAACTTCGACAAGAACCTGCCAACGAGAAGGTGCTGCCAAGCACTCC CTGCTGTACGAGTACTTACCCTGTACAACGAGCTGACCAAGGTGAAGTACGTGACC GAGGGCATCGGAAGCCGCCTTCTGTTCCGGCGAGCAGAAGAAGGCCATCTGTGGA CCTGCTGTTCAAGACCAACCGGAAGGTGACCGTGAAGCAGCTGAAGGAGGACTACT TCAAGAAGATCGAGTGCTTCGACTCCGTGGAGATCTCCGGCGTGGAGGACCGGTTCA ACGCCTCCCTGGGCACCTACCACGACCTGCTGAAGATCATCAAGGACAAGGACTTCC TGGACAACGAGGAGAACGAGGACATCCTGGAGGACATCGTGTGACCTGACCTGACC TTTCGAGGACCGGAGATGATCGAGGAGCGGCTGAAGACCTACGCCACCTGTTTCGAC GACAAGGTGATGAAGCAGCTGAAGCGGCGGCGGTACACCGGCTGGGGCCGGCTGTC CCGGAAGCTGATCAACGGCATCCGGGACAAGCAGTCCGGCAAGACCATCTGGACTT CCTGAAGTCCGACGGCTTCGCCAACCAGGAACTTCATGCAGCTGATCCACGACGACTC CTGACCTTCAAGGAGGACATCCAGAAGGCCAAGGTGTCCGGCCAGGGCGACTCCCT GCACGAGCAGATCGCAACCTGGCCGGCTCCCCGCCATCAAGAAGGGCATCCTGCA GACCGTGAAGGTGGTGGACGAGCTGGTGAAGGTGATGGGCCGGCACAAGCCCGAGA	111

[0710]

	<p>ACATCGTGATCGAGATGGCCCGGAGAACACAGACCACCCAGAAGGGCCAGAAGAAC TCCCGGGAGCGGATGAAGCGGATCGAGGAGGGCATCAAGGAGCTGGGCTCCAGAT CCTGAAGGAGCACCCCGTGGAGAACACCCAGCTGCAGAACGAGAAGCTGTACCTGT ACTACCTGCAGAACGGCCGGGACATGTACGTGGACCAGGAGCTGGACATCAACCCGGC TGTCCGACTACGACGTGGACCACATCGTGCCCCAGTCCCTTCTGAAGGACGACTCCAT CGACAACAAGGTGCTGACCCGGTCCGACAAGAACCAGGGGCAAGTCCGACAACGTGC CCTCCGAGGAGGTGGTGAAGAAGATGAAGAATACTGGCGGCAGCTGTGAACGCC AAGCTGATCACCCAGCGGAAGTTCGACAACCTGACCAAGGCCGAGCGGGCGGCCCT GTCCGAGCTGGACAAGGCCGGTTCATCAAGCGGCAGCTGGTGGAGACCCGGCAGA TCACCAAGCACGTGGCCAGATCTGGACTCCCGGATGAACACCAAGTACGACGAGA ACGACAAGCTGATCCGGGAGGTGAAGGTGATCAACCTGAAGTCCAAGCTGGTGTCCG ACTTCCGGAAGGACTTCCAGTTCTACAAGGTGCGGGAGATCAACAATACTACCACCG CCCACGACGCCTACCTGAACGCCGTGGTGGGCACCGCCCTGATCAAGAAGTACCCCA AGCTGGAGTCCGAGTTCGTGTACGGCGACTACAAGGTGTACGACGTGCGGAAGATGA TCGCAAGTCCGAGCAGGAGATCGGCAAGGCCACCGCAAGTACTTCTTACTCCA ACATCATGAACCTTCTCAAGACCGAGATCACCTGGCCAACGGCGAGATCCGGAAGC GGCCCCTGATCGAGACCAACGGCGAGACCGGCAGATCGTGTGGGACAAGGGCCGG GACTTCGCCACCGTGGCGAAGGTGCTGTCCATGCCCAAGGTGAACATCGTGAAGAAG ACCGAGGTGCAGACCGCGGCTTCTCCAAGGAGTCCATCTGCCCAAGCGGAACCTCC GACAAGCTGATCGCCGGAAGAAGGACTGGGACCCCAAGAGTACGGCGGCTTCGA CTCCCCACCGTGGCCTACTCCGTGCTGGTGGTGGCCAAGGTGGAGAAGGGCAAGTC CAAGAAGCTGAAGTCCGTGAAGGAGCTGCTGGGCATCACCATATGGAGCGGTCCCTC CTTCGAGAAGAACCCATCGACTTCTGGAGGCCAAGGGCTACAAGGAGGTGAAGA AGGACTGATCATCAAGCTGCCAAGTACTCCCTGTTTCGAGCTGGAGAACGGCCGGGA AGCGGATGCTGGCCTCCGCCGGCGAGCTGCAGAAGGGCAACGAGCTGGCCCTGCC TCCAAGTACGTGAACCTTCTGTACCTGGCCTCCACTACGAGAAGCTGAAGGGCTCC CCCAGGACAACGAGCAGAAGCAGCTGTTCTGTGGAGCAGCACAAGCACTACCTGGA CGAGATCATCGAGCAGATCTCCGAGTTCCTCAAGCGGGTATCCTGGCCGACGCCAA CCTGGACAAGGTGCTGTCCGCCTACAACAAGCACCGGGACAAGCCATCCGGGAGC AGGCCGAGAACATCATCCACCTGTTACCCCTGACCAACCTGGGCGCCCCCGCCGCT TCAAGTACTTCGACACCACATCGACCGGAAGCGGTACACCTCCACCAAGGAGGTGC TGGACGCCACCCGTATCCACAGTCCATCACCGGCCTGTACGAGACCCGGATCGACC TGTCCAGCTGGGCGGCGACGGCGGCTCCCCAAGAAGAAGCGGAAGGTGTGA</p>	
<p>使用表4的低 A/U密码子, 具有起始及 终止密码子 的Cas9 ORF</p>	<p>ATGGACAAGAAGTACAGCATCGGCCTGGACATCGGCACCAACAGCGTGGGCTGGGCC GTGATCACCGACGAGTACAAGGTGCCAGCAAGAAGTTCAAGGTGTGGGCAACAC CGACCGGCACAGCATCAAGAAGAACCTGATCGGCGCCCTGCTGTTTCGACAGCGGCG AGACCGCCGAGGCCACCCGGCTGAAGCGGACCGCCCGGCGGGTACACCCGGCCG AAGAACCAGGATCTGCTACCTGCAGGAGATCTTCAGCAACGAGATGGCAAGGTGGAC GACAGCTTCTTCCACCGGCTGGAGGAGAGCTTCTGTTGGAGGAGGACAAGAAGCA CGAGCGGCACCCCATCTTCGGCAACATCGTGGACGAGGTGGCCTACCACGAGAAGTA CCCCACCATCTACCACCTGCGGAAGAAGCTGGTGGACAGCACCGACAAGGCCGACCT GGGCTGATCTACCTGGCCCTGGCCACATGATCAAGTTCCGGGGCCACTTCTGTATC GGGCGACCTGAACCCCGACAACAGCAGCAGTGGACAAGCTGTTTCATCCCTGGT GCAGACCTACAACAGCTGTTTCGAGGAGAACCCATCAACGCCAGCGGCGTGGACG CCAAGGCCATCTGAGCGCCCGGCTGAGCAAGAGCCGGCGGCTGGAGAACCTGATC CCCCAGCTGCCCGGCGAGAAGAAGAACGGCCTGTTCCGCAACCTGATCGCCCTGAG CCTGGCCCTGACCCCAACTTCAAGAGCAACTTCGACCTGGCCGAGGACCCCAAGCT GCAGCTGAGCAAGGACACCTACGACGACGACCTGGACAACCTGCTGGCCAGATCG GCGACCAGTACGCCGACCTGTTCTGGCCGCAAGAACCTGAGCGACGCCATCCTGC TGAGCGACATCTGCGGGTGAACACCGAGATCACCAAGGCCCCCTGAGCGCCAGCA TGATCAAGCGGTACGACGAGCACCACAGGACCTGACCCTGTGAAGGCCCTGGTGC GGCAGCAGCTGCCGAGAAGTACAAGGAGATCTTCTTCGACCAGAGCAAGAAGCGC TACGCCGGCTACATCGACGGCGGCCAGCCAGGAGGAGTTCTACAAGTTTCATCAAG CCCATCTGGAGAAGATGGACGGCACCGAGGAGCTGCTGGTGAAGTGAACCGGGA GGACCTGCTGCGGAAGCAGCGGACCTTCGACAACGGCAGCATCCCCACCAGATCCA CCTGGGCGAGCTGCACGCCATCTGCGGCGGCAGGAGGACTTCAACCTTCTCTGAA GGACAACCGGGAGAAGATCGAGAAGATCCTGACCTTCCGGATCCCTACTACGTGGG CCCCCTGGCCCGGGCAACAGCCGGTTCGCCTGGATGACCCGGAAGAGCGAGGAGA CCATACCCCCCTGGAACCTTCGAGGAGGTGGTGGACAAGGGCGCCAGCGCCAGAGC TTCATCGAGCGGATGACCAACTTCGACAAGAACCTGCCAACGAGAAGGTGCTGCC AAGCACAGCCTGCTGTACGAGTACTTACCGTGTACAACGAGCTGACCAAGGTGAAG TACGTGACCGAGGGCATGCGGAAGCCGCCTTCTGAGCGGCGAGCAGAAGAAGGC CATCGTGGACCTGCTGTTCAAGACCAACCGGAAGGTGACCGTGAAGCAGCTGAAGG AGGACTACTTCAAGAAGATCGAGTGTTCGACAGCGTGGAGATCAGCGGCGTGGAG GACCGTTCAACGCCAGCTGGCACCTACCACGACCTGTGAAGATCATCAAGGAC AAGGACTTCTGGACAACGAGGAGAACGAGGACATCTGGAGGACATCGTGTGAC CCTGACCCTGTTTCGAGGACCGGGAGATGATCGAGGAGCGGCTGAAGACCTACGCCCA</p>	112

[0711]

	<p>CCTGTTTCGACGACAAGGTGATGAAGCAGCTGAAGCGGCGGCGGTACACCGGCTGGG GCCGGCTGAGCCGGAAGCTGATCAACGGCATCCGGGACAAGCAGAGCGGCAAGACC ATCCTGGACTTCTGAAGAGCGACGGCTTCGCCAACCGGAACTTCATGCAGCTGATC CACGACGACAGCCTGACCTTCAAGGAGGACATCCAGAAGGCCAGGTGAGCGGCCA GGGCGACAGCCTGCACGAGCACATCGCCAACCTGGCCGGCAGCCCCGCATCAAGA AGGGCATCTGCAGACCGTGAAGGTGGTGGACGAGCTGGTGAAGGTGATGGCCGG CACAAGCCCCGAGAATCGTGATCGAGATGGCCGGGAGAACCAGACCACCCAGAA GGGCCAGAAGAACAGCCGGGAGCGGATGAAGCGGATCGAGGAGGGCATCAAGGAG CTGGGCAGCCAGATCCTGAAGGAGCACCCCGTGGAGAACACCCAGCTGCAGAACGA GAAGCTGTACTGTACTACCTGCAGAACGGCCGGACATGTACGTGGACCAGGAGCT GGACATCAACCGGCTGAGCGACTACGACGTGGACCACATCGTGCCCCAGAGTTCCT GAAGGACGACAGCATCGACAACAAGGTGCTGACCCGGAGCGACAAGAACCGGGC AAGAGCGACAACGTGCCAGCGAGGAGGTGGTGAAGAAGATGAAGAACTACTGGCC CGAGCTGCTGAACGCCAAGCTGATCACCCAGCGGAAGTTCGACAACCTGACCAAGG CCGAGCGGGCGGCTGAGCGAGCTGGACAAGGCCGGCTTCATCAAGCGGCAGCTG GTGGAGACCCGGCAGATCACCAAGCACGTGGCCAGATCCTGGACAGCCGGATGAA CACCAAGTACGACGAGAACGACAAGCTGATCCGGGAGGTGAAGGTGATCACCTGA AGAGCAAGCTGGTGAAGGACTTCCGGAAGGACTTCCAGTTTACAAGGTGCGGGAG ATCAACAACCTACCACACGCCACGACGCCTACCTGAACGCCGTGGTGGCAGCCCT CTGATCAAGAAGTACCCAAAGCTGGAGAGCGAGTTCGTGTACGGCGACTACAAGGTG TACGACGTGCGGAAGATGATCGCCAAGAGCGAGCAGGAGATCGGCAAGGCCACCGC CAAGTACTTCTTACAGCAACATCATGAACTTCTTCAAGACCGAGATCACCCCTGGCC AACGGCGAGATCCGGAAGCGGCCCTGATCGAGACCAACGGCGAGACCCGGCAGAT CTGTGGGACAAGGGCCGGACTTCGCCACCGTGGGAAGGTGCTGACATGACCTGCCC AGGTGAACATCGTGAAGAAGACCGAGGTGCAGACCGCGGCTTCAGCAAGGAGAGC ATCCTGCCAAGCGGAACAGCGACAAGCTGATCGCCCGGAAGAAGGACTGGGACCC CAAGAAGTACGGCGGCTTCGACAGCCCCACCGTGGCCTACAGCGTGTGGTGGTGGC CAAGGTGGAGAAGGGCAAGAGCAAGAAGCTGAAGAGCGTGAAGGAGCTGCTGGCC ATCACCATCATGGAGCGGAGCAGTTCGAGAAGAACCCATCGACTTCTGGAGGCC AAGGGCTACAAGGAGGTGAAGAAGGACCTGATCATCAAGCTGCCAAGTACAGCCT GTTTCGAGCTGGAGAACGGCCGGAAGCGGATGCTGGCCAGCGCCGGCGAGCTGCAGA AGGGCAACGAGCTGGCCCTGCCAGCAAGTACGTGAACCTTCTGTACTTGGCCAGCC ACTACGAGAAGCTGAAGGGCAGCCCCGAGGACAACGAGCAGAAGCAGCTGTTCTGTG GAGCAGCACAAGCACTACCTGGACGAGATCATCGAGCAGATCAGCGAGTTCAGCAA GCGGGTATCCTGGCCGACGCCAACCTGGACAAGGTGCTGAGCGCTACAACAAGC ACCGGGACAAGCCATCCGGGAGCAGGCCGAGAATCATCCACCTGTTACCCCTGA CCAACCTGGGCGCCCCGCCCTTCAAGTACTTCGACACCACCATCGACCCGGAAGC GGTACACCAGCACCAAGGAGGTGCTGGACGCCACCTGATCCACCAGAGACTACCCG GCCTGTACGAGACCCGGATCGACCTGAGCCAGCTGGGCGGCGACGGCGGCGGACG CCCAAGAAGAAGCGGAAGGTGTGA</p>	
<p>使用表4的低 A密码子, 具 有两个C端 NLS序列及 起始及终止 密码子的 Cas9 ORF</p>	<p>ATGGACAAGAAGTACTCCATCGGCCTGGACATCGGCACCAACTCCGTGGGCTGGGCC GTGATCACCGACGAGTACAAGGTGCCCTCCAAGAAGTTCAAGGTGCTGGGCAACACC GACCGGCACTCCATCAAGAAGAACCTGATCGGCGCCTGCTGTTTCGACTCCGGCGAG ACCGCCGAGGCCACCCGGCTGAAGCGGACCGCCCGGCGGCGGTACACCCGGCGGAA GAACCGGATCTGCTACCTGCAGGAGATCTTCTCAACGAGATGGCCAAGGTGGACGA CTCCTTCTTCCACCGGCTGGAGGAGTCTTCTGGTGGAGGAGGACAAGAAGCACGA GCGGCACCCATCTTCGGCAACATCGTGGACGAGGTGGCCTACCACGAGAAGTACCC CACCATCTACCACCTGCGGAAGAAGCTGGTGGACTCCACCGACAAGGCCGACCTGCG GCTGATCTACCTGGCCCTGGCCACATGATCAAGTTCGGGGCCACTTCTGATCGAG GGCGACCTGAACCCGACAACCTCCGACGTGGACAAGCTGTTTCATCCAGCTGGTGCAG ACCTACAACAGCTGTTTCGAGGAGAACCCATCAACGCCTCCGGCGTGGACGCCAAG GCCATCTGTCCGCCGGCTGTCCAAGTCCCGGCGGCTGGAGAACCTGATCGCCAG CTGCCCGGCGAGAAGAAGAACGGCCTGTTTCGGCAACCTGATCGCCCTGTCCCTGGGC CTGACCCCAACTTCAAGTCCAACCTTCGACCTGGCCGAGGACGCCAAGCTGCAGCTG TCCAAGGACACCTACGACGACGACCTGGACAACCTGCTGGCCAGATCGGCGACCA GTACGCCGACCTGTTCTGGCCGCAAGAACCTGTCCGACGCCATCCTGTGTCCGA CATCCTGCGGGTGAACACCGAGATCACCAAGGCCCCCTGTCCGCTCCATGATCAA GCGGTACGACGAGCACACCAGGACCTGACCCTGCTGAAGGCCCTGGTGGCGGACG AGCTGCCCGAGAAGTACAAGGAGATCTTCTTCGACCAGTCCAAGAACGGCTACGCCG GCTACATCGACGGCGGCGCCTCCAGGAGGAGTCTACAAGTTCATCAAGCCATCCT GGAGAAGATGGACGGCACCGAGGAGCTGCTGGTGAAGCTGAACCGGAGGACCTGC TGCGGAAGCAGCGGACCTTCGACAACGGCTCCATCCCCACCAGATCCACCTGGGCG AGCTGCACGCCATCCTGCGGCGGCGAGGAGTCTTACCCCTTCTGAAGGACAACC GGGAGAAGATCGAGAAGATCCTGACCTTCCGGATCCCCACTACGTGGGCCCTGG CCCCGGCAACTCCCGTTCGCCTGGATGACCCGGAAGTCCGAGGAGACCATCC CCTGGAACCTTCGAGGAGGTGGTGGACAAGGGCGCCTCCGCCAGTCTTTCATCGAGC GGATGACCAACTTCGACAAGAACCTGCCAACGAGAAGGTGCTGCCAAGCACTCC</p>	<p>113</p>

[0712]

	<p>CTGCTGTACGAGTACTTCACCGTGTACAACGAGCTGACCAAGGTGAAGTACGTGACC GAGGGCATGCGGAAGCCGCTTCCCTGTCCGGCAGCAGAAGAAGGCCATCGTGGA CCTGCTGTTCAAGACCAACCGGAAGGTGACCGTGAAGCAGCTGAAGGAGGACTACT TCAAGAAGATCGAGTGCTTCCGACTCCGTGGAGATCTCCGGCGTGGAGGACCGGTTCA ACGCTCCCTGGGCACCTACCACGACCTGCTGAAGATCATCAAGGACAAGGACTTCC TGGACAACGAGGAGAACGAGGACATCTGGAGGACATCGTGTGACCCGACTG TTCGAGGACCGGGAGATGATCGAGGAGCGGCTGAAGACCTACGCCACCTGTTTCGAC GACAAGGTGATGAAGCAGCTGAAGCGGGCGGCTACACCGGCTGGGGCCGGCTGTC CCGGAAGCTGATCAACGGCATCCGGGACAAGCAGTCCGGCAAGACCATCTGGACTT CCTGAAGTCCGACGGCTTCGCCAACCGGAACCTTCATGCAGCTGATCCACGACGACTC CTCGACTTCAAGGAGGACATCCAGAAGGCCAGGTGTCCGGCCAGGCTCCCTGCAG GCACGAGCACATCGCCAACTGGCCGGCTCCCCGCCATCAAGAAGGGCATCCTGCA GACCGTGAAGGTGGTGGACGAGCTGGTGAAGGTGATGGGCGGGCACAAGCCCGAGA ACATCGTGATCGAGATGGCCCGGAGAACCAGACCACCCAGAAGGGCCAGAAGAAC GACCGGAGCGGATGAAGCGGATCGAGGAGGGCATCAAGGAGCTGGGCTCCAGAT CCTGAAGGAGCACCCCGTGGAGAACACCCAGCTGCAGAACGAGAAGCTGTACTGT ACTACCTGCAGAACGGCCGGGACATGTACGTGGACCAGGAGCTGGACATCAACCGGC TGTCCGACTACGACGTGGACCACATCGTGCCCCAGTCTTCTGAAGGACGACTCCAT CGACAACAAGGTGCTGACCCGGTCCGACAAGAACCAGGGGCAAGTCCGACAACGTGC CTCCGAGGAGGTGGTGAAGAAGATGAAGAATACTGGCGGACAGTCCGAGTCCGAG AAGCTGATCACCCAGCGGAAGTTCGACAACCTGACCAAGGCCGAGCGGGCGGCCCT GTCCGAGCTGGACAAGCCGGCTTCATCAAGCGGCAGCTGGTGGAGACCCGGCAGA TCACCAAGCACGTGGCCAGATCCTGGACTCCCGGATGAACACCAAGTACGACGAGA ACGACAAGCTGATCCGGGAGGTGAAGGTGATCACCTGAAGTCCAAGCTGGTGTCCG ACTTCCGGAAGGACTTCCAGTTCACAAGGTGCGGGAGATCAACAATACTACCACG CCCACGACGCCTACCTGAACGCCGTGGTGGGCACCGCCCTGATCAAGAAGTACCCCA AGCTGGAGTCCGAGTTCGTGTACGGGACTACAAGGTGTACGACGTGCGGAAGATGA TCGCCAAGTCCGAGCAGGAGATCGGCCAAGGCCACCGCCAAGTACTTCTTACTCCA ACATCATGAACCTTCTCAAGACCGAGATCACCTGGCCAACGGCGAGATCCGGAAGC GGCCCTGATCGAGACCAACGGCGAGACCGCGGAGATCGTGTGGGACAAGGGCCGG GACTTCGCCACCGTGCAGGAAGGTGCTGTCCATGCCCAAGTGAACATCGTGAAGAAG ACCGAGGTGCAGACCGGGCGCTTCTCCAAGGAGTCCATCTGCCCAAGCGGAACTCC GACAAGCTGATCGCCCGGAAGAAGGACTGGGACCCCAAGAAGTACGCGCGCTTCGA CTCCCCACCGTGGCTACTCCGTGCTGGTGGTGGCCAAGGTGGAGAAGGGCAAGTC CAAGAAGCTGAAGTCCGTGAAGGAGCTGCTGGGCATCACCATATGGAGCGGTCCCT CTTCGAGAAGAACCCATCGACTTCTGGAGGCCAAGGGGCTACAAGGAGGTGAAGA AGGACCTGATCATCAAGCTGCCAAGTACTCCCTGTTTCGAGCTGGAGAACGGCCGGA AGCGGATGCTGGCTCCGCCGGCGAGCTGCAGAAGGGCAACGAGCTGGCCCTGCC TCCAAGTACGTGAACCTTCTGTACCTGGCCTCCACTACGAGAAGCTGAAGGGCTCC CCCAGGACAACGAGCAGAAGCAGCTGTTTCGTGGAGCAGCACAAGCACTACCTGGA CGAGATATCGAGCAGATCTCCGAGTTCCTCAAGCGGGTGATCTGGCCGACGCCAA CTGGACAAGGTGCTGTCCGCCTACAACAAGCACCGGGACAAGCCCATCCGGGAGC AGGCCGAGAACATCATCCACTGTTACCCTGACCAACCTGGGCGCCCCCGCCGCT TCAAGTACTTCGACACCACATCGACCGGAAGCGGTACACTCCACCAAGGAGGTGC TGGAGCCACCTGATCCACCAGTCCATACCGGCCTGTACGAGACCCGGATCGACC TGTCCAGCTGGGCGGCGACGGCTCCGGCTCCCCAAGAAGAAGCGGAAGGTGGAC GGTCCCCCAAGAAGAAGCGGAAGGTGGACTCCGGCTGA</p>	
<p>使用表4的低 A密码子，具 有起始及终 止密码子的 Cas9 切口酶 ORF</p>	<p>ATGGACAAGAAGTACTCCATCGGCCTGGCCATCGGCACCAACTCCGTGGGCTGGGCC GTGATCACCGACGAGTACAAGGTGCCCTCCAAGAAGTTCAAGGTGCTGGGCAACACC GACCGGCACTCCATCAAGAAGAACCTGATCGGGCCTGCTGTTTCGACTCCGGCGAG ACCGCCGAGGCCACCCGGCTGAAGCGGACCGCCGGCGGCTACACCCGGCGGAA GAACCGGATCTGCTACCTGCAGGAGATCTTCTCCAACGAGATGGCCAAGGTGGACGA CTCCTTCTTCCACCGGCTGGAGGAGTCTTCTGGTGGAGGAGGACAAGAAGCACGA GCGGCACCCATCTTCGGCAACATCGTGGACGAGGTGGCCTACCACGAGAAGTACCC CACCATCTACCACCTGCGGAAGAAGCTGGTGGACTCCACCGACAAGGCCGACCTGCG GCTGATCTACCTGGCCCTGGCCACATGATCAAGTTCGGGGCCACTTCTGATCGAG GGCGACCTGAACCCCGACAACCTCCGACGTGGACAAGCTGTTTCATCCAGCTGGTGCAG ACCTACAACCAGCTGTTTCGAGGAGAACCCATCAACGCCTCCGGCGTGGACGCCAAG GCCATCCTGTCCGCCGGCTGTCCAAGTCCCGGGCGGCTGGAGAACCTGATCGCCAG CTGCCCGGCGAGAAGAAGAACGGCCTGTTTCGGCAACCTGATCGCCCTGTCCCTGGC CTGACCCCAACTTCAAGTCCAACCTTCGACCTGGCCGAGGACGCCAAGCTGCAGCTG TCCAAGGACACCTACGACGACGACCTGGACAACCTGCTGGCCAGATCGGCGACCA GTACGCCGACCTGTTTCCTGGCCGCAAGAACCTGTCCGACGCCATCCTGCTGTCCGA CATCCTGCGGGTGAACACCGAGATCAACAAGGCCCCCTGTCCGCTCCATGATCAA GCGGTACGACGAGCACCAACAGGACTGACCTGCTGAAGGCCCTGGTGGCGGACG AGCTGCCCGAGAAGTACAAGGAGATCTTCTTCGACCAGTCCAAGAACGGCTACGCCG GCTACATCGACGGCGGCGCCTCCAGGAGGATTTACAAAGTTCATCAAGCCATCCT</p>	<p>114</p>

[0713]

	<p>GGAGAAGATGGACGGCACCGAGGAGCTGCTGGTGAAGCTGAACCGGGAGGACCTGC TGCGGAAGCAGCGGACCTTCGACAACGGCTCCATCCCCACCAGATCCACCTGGGCG AGCTGCACGCCATCCTGCGGCGGCAGGAGGACTTCTACCCCTTCTGAAGGACAACC GGGAGAAGATCGAGAAGATCCTGACCTCCGGATCCCCACTACGTGGGCCCTGG CCCGGGGCAACTCCCGGTTTCGCTGGATGACCCGGAAGTCCGAGGAGACCATCACCC CCTGGAACCTCGAGGAGGTGGTGGACAAGGGCGCCTCCGCCAGTCTTCATCGAGC GGATGACCAACTTCGACAAGAACCTGCCAACGAGAAGGTGCTGCCAACGACTCC CTGCTGTACGAGTACTTACCCTGTACAACGAGCTGACCAAGGTGAAGTACGTGACC GAGGGCATGCGGAAGCCCGCTTCTGTCGGCGAGCAGAAGAAGGCCATCGTGGGA CCTGCTGTTCAAGACCAACCGGAAGGTGACCGTGAAGCAGCTGAAGGAGGACTACT TCAAGAAGATCGAGTGTCTTCCGACTCCGTGGAGATCTCCGGCGTGGAGGACCGGTTCA ACGCTCCCTGGGCACCTACCACGACTGCTGAAGATCATCAAGGACAAGGACTTCC TGGACAACGAGGAGAACGAGGACATCCTGGAGGACATCGTGCTGACCTGACCCTG TTCGAGGACCGGGAGATGATCGAGGAGCGGCTGAAGACCTACGCCACCTGTTTCGAC GACAAGGTGATGAAGCAGCTGAAGCGGCGGCGGTACACCGGCTGGGCGCGGCTGTC CCGGAAGCTGATCAACGGCATCCGGGACAAGCAGTCCGGCAAGACCATCCTGGACTT CCTGAAGTCCGACGGCTTCGCCAACCGGAACCTTCATGCAGCTGATCCACGACGACTC CCTGACCTTCAAGGAGGACATCCAGAAGGCCAGGTGTCCGGCCAGGGCGACTCCCT GCACGACACATCGCAACCTGGCCGGCTCCCCGCCATCAAGAAGGGCATCCTGCA GACCGTGAAGGTGGTGGACGAGCTGGTGAAGGTGATGGGCGGCAAGCCCGGAGGA ACATCGTGTGAGATGGCCCGGAGAACCAGACCACCCAGAAGGGCCAGAAGAAC TCCCGGGAGCGGATGAAGCGGATCGAGGAGGGCATCAAGGAGCTGGGCTCCAGAT CCTGAAGGAGCACCCCGTGGAGAACACCCAGCTGCAGAACGAGAAGCTGTACTGT ACTACCTGCAGAACGGCCGGGACATGTACGTGGACCAGGAGCTGGACATCAACCGGC TGTCCGACTACGACGTGGACCACATCGTGCCCCAGTCTTCTGAAGGACGACTCCAT CGACAACAAGGTGCTGACCCGGTCCGACAAGAACCAGGGGCAAGTCCGACAACGTGC CCTCCGAGGAGGTGGTGAAGAAGATGAAGAATACTGGCGGCAGCTGTGAACGCC AAGCTGATCACCCAGCGGAAGTTCGACAACCTGACCAAGGCCGAGCGGGCGGCT GTCCGAGCTGGACAAGGCCGGCTTCAAGCGGCAGCTGGTGGAGACCCCGGAGGA TCACCAAGCACGTGGCCAGATCCTGGACTCCCGGATGAACCAAGTACGACGAGA ACGACAAGCTGATCCGGGAGGTGAAGGTGATCACCTGAAGTCCAAGCTGGTGTCCG ACTTCCGGAAGGACTTCCAGTTCATAAGGTGCGGGAGATCAACAATACTACCACAG CCCACGACGCCACTGAAACGGCTGGTGGGACCCGCCCTGATCAAGAAGTACCCCA AGCTGGAGTCCGAGTTCGTGTACGGCGACTACAAGGTGTACGACGTGCGGAAGATGA TCGCCAAGTCCGAGCAGGAGATCGGCAAGGCCACCGCAAGTACTTCTTACTCCA ACATCATGAACCTTCTCAAGACCGAGATCACCTGGCCAACGGCGAGATCCGGAAGC GGCCCTGATCGAGACCAACGGCGAGACCAGGCGAGATCGTGTGGACAAGGGCCGG TCTCCGCCACCGTGCAGGAAGGTGCTGTCCATGCCCAAGGTGAACACTCGTGAAGAAG ACCGAGGTGCAGACCGCGGCTTCTCCAAGGAGTCCATCCTGCCAAGCGGAACCTCC GACAAGCTGATCGCCCGGAAGAAGGACTGGGACCCCAAGAAGTACGGCGGCTTCGA CTCCCCACCGTGGCCTACTCCGTGCTGGTGGTGGCCAAGGTGGAGAAGGGCAAGTC CAAGAAGCTGAAGTCCGTGAAGGAGCTGCTGGGCATCACCATCATGGAGCGGTCTC CTTCGAGAAGAACCCATCGACTTCTGGAGGCCAAGGGCTACAAGGAGGTGAAGA AGGACCTGATCATCAAGCTGCCAAGTACTCCCTGTTTCGAGCTGGAGAACGGCCGGA AGCGGATGCTGGCTCCGCGGCGAGCTGCAGAAGGGCAACGAGCTGGCCCTGCC TCCAAGTACGTGAACCTTCTGTACTTGGCCTCCACTACGAGAAGCTGAAGGGCTCC CCCAGGACAACGAGCAGAAGCAGCTGTTCTGTGGAGCAGCACAAGACTACCTGGGA CGAGATCATCGAGCAGATCTCCGAGTTCCTCAAGCGGGTATCCTGGCCGACGCCAA CCTGGACAAGGTGTGTCCGCTACAACAAGCACCAGGACCAAGCCATCCGGGAGC AGGCCGAGAATCATCCACCTGTTACCCTGACCAACCTGGGCGCCCCCGCCGCT TCAAGTACTTCGACACCACCATCGACCAGGGAAGCGGTACACCTCCACCAAGGAGGTGC TGGACGCCACCTGATCCACCAGTCCATCACCAGGCTGTACGAGACCCGGATCGACC TGTCCAGCTGGGCGGCGACGGCGGCGCTCCCCAAGAAGAAGCGGAAGGTGTGA</p>	<p>使用表4的低 A密码子,具 有起始及终 止密码子且 无 NLS 的 Cas9 切口酶 ORF</p>	<p>ATGGACAAGAAGTACTCCATCGGCTGGCCATCGGCACCAACTCCGTGGGCTGGGCC GTGATCACCGACGAGTACAAGGTGCCCTCCAAGAAGTTCAAGGTGCTGGGCAACACC GACCGCACTCCATCAAGAAGAACCTGATCGGCGCCCTGTGTTGACTCCGGCGAG ACCGCCGAGGCCACCCGGCTGAAGCGGACCGCCCGGCGGCGGTACACCCGGCGGAA GAACCGGATCTGCTACCTGCAGGAGATCTTCTCAACGAGATGGCCAAGGTGGACGA CTCCTTCTTCCACCGGCTGGAGGAGTCTTCTGGTGGAGGAGGACAAGAAGCAGCA GCGGCACCCATCTTCGGCAACATCGTGGACGAGGTGGCTACCACGAGAAGTACC CACCATCACCACCTGCGGAAGAAGCTGGTGGACTCCACCGACAAGGCCGACCTGCG GCTGATCTACCTGGCCCTGGCCACATGATCAAGTTCGGGGGCCACTTCTGATCGAG GGCGACCTGAACCCGACAACCTCCGACGTGGACAAGCTGTTTCATCCAGCTGGTGCAG ACCTACAACCAGCTGTTTCGAGGAGAACCCATCAACGCCTCCGGCGTGGACGCCAAG GCCATCCTGTCGCCCGGCTGTCCAAGTCCCGGCGGCTGGAGAACCTGATCGCCCA CTGCCCGGCGAGAAGAAGACGGCCTGTTTCGGCAACCTGATCGCCCTGTCCCTGGGC CTGACCCCAACTTCAAGTCCAACCTTCGACCTGGCCGAGGACGCCAAGCTGCAGCTG</p>	115
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[0714]

	<p>TCCAAGGACACCTACGACGACGACCTGGACAACCTGCTGGCCCAGATCGGGCGACCA GTACGCCGACCTGTTTCTGGCCGCCAAGAACCTGTCCGACGCCATCCTGCTGTCCGA CATCCTGCGGGTGAACACCGAGATCACCAAGGCCCCCTGTCCGCTCCATGATCAA GCGGTACGACGAGCACCACAGGACCTGACCTGCTGAAGGCCCTGGTGCGGCAGC AGTGCCCGAGAAGTACAAGGAGATCTTCTTCGACCAGTCCAAGAACGGGTACGCCG GTACATCGACGGCGGCCTCCAGGAGGAGTTCTACAAGTTCATCAAGCCATCCT GGAGAAGATGGACGGCACCGAGGAGCTGCTGGTGAAGCTGAACCGGGAGGACCTGC TGCGGAAGCAGCGGACCTTCGACAACGGCTCCATCCCCACAGATCCACCTGGGCG AGCTGCACGCCATCCTGCGGCGGCAGGAGGACTTACCCCTTCTGAAGGACAACC GGGAGAAGATCGAGAAGATCCTGACCTTCCGGATCCCCTACTACGTGGGCCCTGG CCCGGGCAACTCCCGTTCCGCTGGATGACCCGGAAGTCCGAGGACCATCACCC CCTGGAACCTCGAGGAGGTGGTGGACAAGGGCGCCTCCGCCAGTCTTCATCGAGC GGATGACCAACTTCGACAAGAACCTGCCAACGAGAAGGTGCTGCCAACGACTCC CTGTGTACGAGTACTTACCCTGTACAACGAGCTGACCAAGGTGAAGTACGTGACC GGGATGCGGAAGCCGCTTCCGTGTCGGCGAGCAGAAGAAGGCCATCGTGGGA CCTGCTGTTCAAGACCAACCGGAAGGTGACCGTGAAGCAGCTGAAGGAGGACTACT TCAAGAAGATCGAGTGCTTCGACTCCGTGGAGATCTCCGGCGTGGAGGACCGGTTCA ACGCTCCCTGGGCACCTACCACGACCTGCTGAAGATCATCAAGGACAAGGACTTCC TGGACAACGAGGAGAACGAGGACATCCTGGAGGACATCGTGTGACCTGACCTGACC TTTCGAGGACCGGGAGATGATCGAGGAGCGGCTGAAGACCTACGCCACCTGTTTCGAC GACAAGGTGATGAAGCAGCTGAAGCGGCGGCGGTACACCGGCTGGGGCCGGCTGTC CCGGAAGCTGATCAACGGCATCCGGGAC AAGCAGTCCGGCAAGACCATCCTGGACTT CCTGAAGTCCGACGGCTTCGCCAACCGGAACCTTCATGCAGCTGATCCACGACGACTC CTGACCTTCAAGGAGGACATCCAGAAGGCCAAGGTGTCCGGCCAGGCGATCCCT GCACGAGCACATCGCCAACCTGGCCGGCTCCCCGCCATCAAGAAGGGCATCCTGCA GACCGTGAAGGTGGTGGACGAGCTGGTGAAGGTGATGGGCCGGCACAAGCCCGAGA ACATCGTATCGAGATGGCCGGGAGAACCAGACCACCCAGAAGGGCCAGAAGAAC TCCCGGGAGCGGATGAAGCGGATCGAGGAGGGCATCAAGGAGCTGGGCTCCAGAT CCTGAAGGAGCACCCCGTGGAGAACACCCAGCTGCAGAACGAGAAGCTGATACCTGT ACTACCTGCAGAACGGCCGGGACATGTACGTGGACCAGGAGCTGGACATCAACCGGC TGTCCGACTACGACGTGGACCACATCGTGCCCCAGTCTTCTGAAGGACGACTCCAT CGACAACAAGGTGCTGACCCGGTCCGACAAGAACCAGGGGCAAGTCCGACAACGTGC CCTCCGAGGAGGTGGTGAAGAAGATGAAGAATACTGCGGCGAGCTGAAGACCGC AAGCTGATCACCCAGCGGAAGTTCGACAACCTGACCAAGGCCGAGCGGGCGGCT GTCCGAGCTGGACAAGGCCGGCTTCATCAAGCGGCAGCTGGTGGAGACCCGGCAGA TCACCAAGCACGTGGCCAGATCCTGGACTCCCGGATGAACACCAAGTACGACGAGA ACGACAAGCTGATCCGGGAGGTGAAGGTGATCACCTGAAGTCCAAGCTGGTGTCCG ACTTCCGGAAGGACTTCCAGTTCACAAGGTGCGGGAGATCAACAATACCACACG CCCACGACGCCTACCTGAACGCCGTGGTGGGACCGCCCTGATCAAGAAGTACCCCA AGCTGGAGTCCGAGTTCGTGTACGGCGACTACAAGGTGTACGACGTGCGGAAGATGA TCGCCAAGTCCGAGCAGGAGATCGGCAAGGCCACCGCCAAGTACTTCTTACTCCA ACATCATGAACTTCTCAAGACCGAGATCACCTGGCCAACGGCGAGATCCGGGAAGC GGCCCTGATCGAGACCAACGGCGAGACCGGCGAGATCGTGTGGGACAAGGGCCGG GACTTCGCCACCGTGGGAAGGTGCTGTCCATGCCCAAGGTGAACATCGTGAAGAAG ACCGAGGTGCAGACCGGCGGCTTCTCAAGGAGTCCATCCTGCCAAGCGGAACTCC GACAAGCTGATCGCCGGAAGAAGGACTGGGACCCCAAGAAGTACGGCGGCTTCGA CTCCCCACCGTGGCTACTCCGTGCTGGTGGTGGCCAAGGTGGAGAAGGGCAAGT CAAGAAGCTGAAGTCCGTGAAGGAGCTGCTGGGCATCACCATCATGGAGCGGTCTC CTTCGAGAAGAACCCATCGACTTCTGGAGGCCAAGGGCTACAAGGAGGTGAAGA AGGACCTGATCATCAAGCTGCCAAGTACTCCCTGTTTCGAGCTGGAGAACGGCCGGA AGCGGATGCTGGCTCCGCCGGCGAGCTGCAGAAGGGCAACGAGCTGGCCCTGCC TCCAAGTACGTGAACCTTCTGTACTTGGCCTCCACTACGAGAAGCTGAAGGGCTCC CCCAGGACAACGAGCAGAAGCAGCTGTTCTGTGGAGCAGCACAAGCACTACCTGGA CGAGATATCGAGCAGATTCGAGTTCCTCAAGCGGGTATCCTGGCCGACGCCAA CCTGGACAAGGTGCTGTCCGCCTACAACAAGCACCGGGACAAGCCATCCGGGAGC AGGCCGAGAACATCATCCACCTGTTACCTGACCAACCTGGGCGCCCCCGCCCT TCAAGTACTTCGACACCACATCGACCGGAAGCGGTACACCTCCACCAAGGAGGTGC TGGACGCCACCTGATCCACCAGTCCATACCGGCTGTACGAGACCCGGATCGACC TGTCCAGCTGGGCGGCGACTGA</p>	
<p>使用表4的低 A密码子, 具 有两个C端 NLS序列及 起始及终止</p>	<p>ATGGACAAGAAGTACTCCATCGGCCTGGCCATCGGCACCAACTCCGTGGGCTGGCC GTGATCACCGACGAGTACAAGGTGCCCTCCAAGAAGTTC AAGGTGCTGGGCAACACC GACCGGCACTCCATCAAGAAGAACCTGATCGGCGCCCTGCTGTTTCGACTCCGGCGAG ACCGCCGAGGCCACCCGGCTGAAGCGGACCGCCCGGCGGCTACACCCGGCGGAA GAACCCGATCTGCTACCTGCAGGAGATCTTCTCCAACGAGATGGCCAAGGTGGACGA CTCCTTCTCCACCGGCTGGAGGAGTCTTCCCTGGTGGAGGAGGACAAGAAGCACGA GCGGCACCCATCTTCGGCAACATCGTGGACGAGGTGGCCTACCACGAGAAGTACCC CACCATCTACCACCTGCGGAAGAAGCTGGTGGACTCCACCGACAAGGCCGACCTGCG</p>	<p>116</p>

<p>密码子的 Cas9 切口酶 ORF</p>	<p>GCTGATCTACCTGGCCCTGGCCACATGATCAAGTTCGGGGCCACTTCTGATCGAG GGCGACCTGAACCCGACAACCTCCGACGTGGACAAGCTGTTTCATCCAGCTGGTGCAG ACCTACAACCAGCTGTTTCGAGGAGAACCCCATCAACGCCTCCGGCGTGGACGCCAAG GCCATCCTGTCCGCCCGGCTGTCCAAGTCCCAGCGGCTGGAGAACCTGATGCCCCAG CTGCCCGGCGAGAAGAAGAACGGCCTGTTTCGGCAACCTGATCGCCCTGTCCCTGGGC CTGACCCCAACTTCAAGTCCAACCTTCGACCTGGCCGAGGACGCCAAGCTGCAGCTG TCCAAGGACACCTACGACGACGACCTGGACAACCTGCTGGCCAGATCGGCGACCA GTACGCCGACCTGTTCTGGCCGCCAAGAACCTGTCCGACGCCATCCTGCTGTCCGA CATCCTGCGGGTGAACACCGAGATCAACCAAGGCCCCCTGTCGCTCCATGATCAA GCGGTACGACGAGCACCACAGGACCTGACCTGCTGAAGGCCCTGGTGGCGGAC AGCTGCCCGAGAAGTACAAGGAGATCTTCTCGACCAAGTCCAAGAACGGTACGCCG GCTACATCGACGGCGGCGCCTCCCAGGAGGAGTTCTACAAGTTCATCAAGCCATCCT GGAGAAGATGGACGGCACCGAGGAGCTGCTGGTGAAGCTGAACCGGGAGGACCTGC TGCGGAAGCAGCGGACCTTCGACAACGGCTCCATCCCCACCAGATCCACCTGGGCG AGCTGCACGCCATCCTGCGGCGGACGAGGACTTCTACCCCTTCTGAAGGACAAC GGGAGAAGATCGAGAAGATCCTGACCTTCCGGATCCCCTACTACGTGGGCCCTGG CCCAGGCAACTCCCGTTTCGCTGGATGACCCGGAAGTCCGAGGAGACCATCACCC CCTGGAACCTCGAGGAGGTGGTGGACAAGGGCGCCTCCGCCAGTCCCTTCATCGAGC GGATGACCAACTTCGACAAGAACCTGCCAACGAGAAGGTGCTGCCAAGCACTCC CTGCTGTACGAGTACTTCCAGTGTACAACGAGCTGACCAAGGTGAAGTACGAGC GAGGGCATGCGGAAGCCGCTTCTGTCGGCGAGCAGAAGAAGGCCATCGTGGA CCTGCTGTCAAGACCAACCGGAAGGTGACCGTGAAGCAGCTGAAGGAGGACTACT TCAAGAAGATCGAGTGCTTCGACTCCGTGGAGATCTCCGGCGTGGAGGACCGGTTCA ACGCTCCCTGGGCACCTACCACGACCTGCTGAAGATCATCAAGGACAAGGACTTCC TGGACAACGAGGAGAACGAGGACATCCTGGAGGACATCGTGCTGACCTGACCTG TTCGAGGACCGGAGATGATCGAGGAGCGGCTGAAGACCTACGCCACCTGTTTCGAC GACAAGGTGATGAAGCAGCTGAAGCGGCGGCGGTACACCGGCTGGGGCCGGCTGTC CCGGAAGCTGATCAACGGCATCCGGGACAAGCAGTCCGGCAAGACCATCCTGGACTT CCTGAAGTCCGACGGCTTCGCCAACCGGAACCTTCATGCAGCTGATCCACGACATC CCTGACCTTCAAGGAGGACATCCAGAAGGCCAGGTGTCCGGCCAGGGCGACTCCCT GCACGAGCACATCGCAACCTGGCCGGCTCCCCGCCATCAAGAAGGGCATCCTGCA GACCGTGAAGGTGGTGGACGAGCTGGTGAAGGTGATGGGCGGCAAGCCCGAGA ACATCGTGATCGAGATGGCCGGGAGAACCAGACCACCCAGAAGGGCCAGGAAGAAC TCCCGGGAGCGGATGAAGCGGATCGAGGAGGGCATCAAGGAGCTGGGCTCCAGAT CCTGAAGGAGCACCCGTTGGAGAACACCCAGCTGCAGAACGAGAAGCTGTACCTGT ACTACCTGCAGAACGGCCGGGACATGTACGTGGACAGGAGCTGGACATCAACCGGC TGTCGACTACGACGTGGACCACATCGTGCCTCCAGTCTTCTGAAGGACGACTCCAT GACAACAAGGTGCTGACCCGTTCCGACAAGAACCAGGGGCAAGTCCGACACGCTGC CCTCCGAGGAGGTGGTGAAGAAGATGAAGAATACTGGCGGCAGCTGCTGAACGCC AAGCTGATCACCCAGCGGAAGTTCGACAACCTGACCAAGGCCGAGCGGGCGGCT GTCCGAGCTGGACAAGGCCGGCTTCATCAAGCGGCAGCTGGTGGAGACCCGGCAGA TCACCAAGCACGTGGCCAGATCCTGGACTCCCGGATGAACACCAAGTCCAGGAGAGA ACGACAAGCTGATCCGGGAGGTGAAGGTGATCACCTGAAGTCCAAGCTGGTGTCCG ACTTCCGGAAGGACTTCCAGTTCACAAGGTGCGGGAGATCAACAATACTACCACCG CCCACGACGCCTACCTGAACGCCGTGGTGGGCACCGCCCTGATCAAGAAGTACCCCA AGCTGGAGTCCGAGTTCGTGTACGGCGACTACAAGGTGTACGACGTGCGGAAGATGA TCGCCAAGTCCGAGCAGGAGATCGGCAAGGCCACCGCAAGTACTTCTTACTTCA ACATCATGAACCTTCTCAAGACCGAGATCACCTGGCCAACGGCGAGATCCGGAAGC GGCCCTGATCGAGACCAACGGCGAGACCGGCGAGATCGTGTGGGACAAGGGCCGG GACTTCGCCACCGTGGGAAGGTGCTGTCATGCCCCAGGTGAACATCGTGAAGAAG ACCGAGGTGCAGACCGGCGGCTTCTCCAAGGAGTCCATCCTGCCAAGCGGAACCTC GACAAGCTGATCGCCGGAAGAAGGACTGGGACCCCAAGAAGTACGGCGGCTTCGA CTCCCCACCGTGGCCTACTCCGTGCTGGTGGTGGCCAAGGTGGAGAAGGGCAAGTC CAAGAAGCTGAAGTCCGTGAAGGAGCTGCTGGGCATCACCATATGGAGCGGTCTCT CTTCGAGAAGAACCCATCGACTTCTGGAGGCCAAGGGCTACAAGGAGGTGAAGA AGGACCTGATCATCAAGTGCCTCCCAAGTACTCCCTGTTTCGAGCTGGAGAACGGCCGA AGCGGATGCTGGCTCCGCCGGCGAGCTGCAGAAGGGCAACGAGCTGGCCCTGCC TCCAAGTACGTGAACCTTCTGTACCTGGCCTCCCACTACGAGAAGCTGAAGGGCTCC CCCAGGACAACGAGCAGAAGCAGCTGTTCTGTGGAGCAGCACAAGCACTACCTGGA CGAGATCATCGAGCAGATCTCCGAGTTCCTCAAGCGGGTATCCTGGCCGACGCCAA CCTGGACAAGGTGCTGTCCGCTACAACAAGCACCGGGACAAGCCATCCGGGAGC AGGCCGAGAACATCATCCACTGTTTACCCTGACCAACCTGGGCGCCCCCGCCGCT TCAAGTACTTCGACACCACATCGACCGGAAGCGGTACACCTCCACCAAGGAGGTGC TGGACGCCACCTGATCCACAGTCCATACCGGCTGTACGAGACCCGGATCGAC TGTCCAGCTGGGCGGCGACGGCTCCGGCTCCCCAAGAAGAAGCGGAAGGTGGAC GGCTCCCCAAGAAGAAGCGGAAGGTGGACTCCGGCTGA</p>
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[0715]

<p>使用表4的低A密码子, 具有起始及终止密码子的dCas9 ORF</p>	<p>ATGGACAAGAAGTACTCCATCGGCCTGGCCATCGGCACCAACTCCGTGGGCTGGGCC GTGATCACCGACGAGTACAAGGTGCCCTCCAAGAAGTTCAAGGTGCTGGGCAACACC GACCGGCACTCCATCAAGAAGAACCTGATCGGCGCCCTGCTGTTGACTCCGGCGAG ACCGCCGAGGCCACCCGGCTGAAGCGGACCGCCCGCGCGGTACACCCGGCGGAA GAACCGGATCTGCTACCTGCAGGAGATCTTCTCCAACGAGATGGCCAAGGTGGACGA CTCCTTCTTCCACCGGCTGGAGGAGTCTTCTTGGTGGAGGAGGACAAGAAGCACGA GCGGCACCCCATCTTCGGCAACATCGTGGACGAGGTGGCCTACCACGAGAAGTACCC CACCATCTACCACCTGCGGAAGAAGCTGGTGGACTCCACCGACAAGGCCGACCTGCG GCTGATCTACCTGGCCCTGGCCACATGATCAAGTTCGGGGGCCACTTCTGATCGAG GGCGACCTGAACCCGACAACCTCCGACGTGGACAAGCTGTTTCATCCAGCTGGTGCAG ACCTACAACCAAGCTGTTTCAGGAGAACCCCATCAACGCCTCCGGCGTGGACGCCAAG GCCATCTGTCCGCCCGGCTGTCCAAGTCCCGGCGGCTGGAGAACCTGATCGCCAG CTGCCCGGCGAGAAGAAGAACGGCCTGTTTCGGCAACCTGATCGCCCTGTCCCTGGGC CTGACCCCAACTTCAAGTCCAACCTTCGACCTGGCCGAGGACGCCAAGCTGCAGCTG TCCAAGGACACCTACGACGACGACCTGGACAACTGCTGGCCCAAGATCGGCGACCA GTACGCCGACCTGTTCTGGCCGCCAAGAACCTGTCCGACGCCATCCTGCTGTCCGA CATCTGCGGTGAACACCGAGATCAACAAGGCCCCCTGTCCGCCTCATGATCAA GCGGTACGACGAGCACACCAGGACCTGACCCTGCTGAAGGCCCTGGTGCGGCAGC AGTGTCCCGAGAAGTACAAGGAGATCTTTCGACCAAGTCCAAGAACGGCTACGCCG GCTACATCGACGGCGGCCTCCAGGAGGAGTTTACAAGTTTATCAAGCCATCCCT GGAGAAGATGGACGGCACCGAGGAGCTGCTGGTGAAGCTGAACCGGGAGGACCTGC TGCGGAAGCAGCGGACCTTCGACAACGGCTCCATCCCCACAGATCCACCTGGGCG AGTGCACGCCATCCTGCGGCGGACAGGAGGACTTCTACCCCTTCTGAAGGACAAC GGGAGAAGATCGAGAAGATCCTGACCTTCCGGATCCCTACTACGTGGCCCTGG CCCGGGGCAACTCCCGGTTGCGCTGGATGACCCGGAAGTCCGAGGAGACCATCACCC CCTGGAACCTCGAGGAGGTGGTGGACAAGGGCGCTCCGCCAGTCTTCATCGAGC GGATGACCAACTTCGACAAGAACCTGCCAACGAGAAGGTGCTGCCAAGCACTCC CTGCTGTACGAGTACTTACCCTGTACAACGAGCTGACCAAGGTGAAGTACGTGACC GAGGGCATGCGGAAGCCGCTTCCGTGTCGGCGAGCAGAAGAAGGCCATCGTGGGA CCTGCTGTTCAAGACCAACCGGAAGGTGACCGTGAAGCAGCTGAAGGAGGACTACT TCAAGAAGATCGAGTGCTTCGACTCCGTGGAGATCTCCGGCGTGGAGGACCGGTTCA ACGCCTCCCTGGGCACCTACCACGACCTGCTGAAGATCATCAAGGACAAGGACTTCC TGGACAACGAGGAGAACGAGGACATCTGGAGGACATCGTGTGACCCGACCTGT TTCGAGGACCGGGAGATGATCGAGGAGCGGCTGAAGACCTACGCCACCTGTTTCGAC GACAAGGTGATGAAGCAGCTGAAGCGGCGGCGGTACACCGGCTGGGGCCGGCTGTC CCGGAAGCTGATCAACGGCATCCGGGACAAGCAGTCCGGCAAGACCATCCTGGACTT CCTGAAGTCCGACGGCTTCGCCAACCGGAACCTTTCATGCAGCTGATCCACGACGACT CCTGACCTTCAAGGAGGACATCCAGAAGGCCAAGGTGTCCGGCCAGGGCGACTCCCT GCACGAGCACATCGCCAACCTGGCCGGCTCCCCGCCATCAAGAAGGGCATCCTGCA GACCGTGAAGGTGGTGGACGAGCTGGTGAAGGTGATGGGCCGGCACAAGCCCGAGA ACATCGTGATCGAGATGGCCCGGAGAACCAGACCAACCAGAAGGGCCAGAAGAAG TCCCGGAGCGGATGAAGCGGATCGAGGAGGGCATCAAGGAGCTGGGCTCCAGAT CCTGAAGGAGCACCCCGTGGAGAACACCCAGCTGCAGAACGAGAAGCTGTACCTGT ACTACCTGCAGAACGGCCGGGACATGTACGTGGACCAGGAGCTGGACATCAACCGGC TGTCCGACTACGACGTGGACGCCATCGTGCCCCAGTCTTCTGAAGGACGACTCCAT CGACAACAAGGTGCTGACCCGGTCCGACAAGAACCAGGGGCAAGTCCGACAACGTGC CCTCCGAGGAGGTGGTGAAGAAGATGAAGAAGTACTGGCGGACAGTGTGAACGCC AAGCTGATCACCCAGCGGAAGTTCGACAACCTGACCAAGGCCGAGCGGGCGGCCCT GTCCGAGCTGGACAAGGCCGGCTTTCATCAAGCGGACAGCTGGTGGAGACCCGGCAGA TCACCAAGCACGTGGCCAGATCCTGGACTCCCGGATGAACACCAAGTACGACGAGA ACGACAAGCTGATCCGGGAGGTGAAGGTGATCACCTGAAGTCCAAGCTGGTGTCCG ACTTCCGGAAGGACTTCCAGTTCATAAGGTGCGGGAGATCAACAACCTACCACCAG CCCACGACGCCTACCTGAACGCCGTGGTGGGCACCGCCCTGATCAAGAAGTACCCCA AGCTGGAGTCCGAGTTCGTGTACGGCGACTACAAGGTGTACGACGTGCGGAAGATGA TCGCCAAGTCCGAGCAGGAGATCGGCAAGGCCACCGCCAAGTACTTCTTACTCCA ACATCATGAACCTTCAAGACCGAGATCACCTGGCCAACGGCGAGATCCGGAAGC GGCCCTGATCGAGACCAACGGCGAGACCGGCGAGATCGTGTGGGACAAGGGCCGG GACTTCGCCACCGTGCAGGAAGGTGCTGTCCATGCCCAAGGTGAACATCGTGAAGAAG ACCGAGGTGCAGACCGGCGGCTTCTCCAAGGAGTCCATCCTGCCAAGCGGAACCTCC GACAAGCTGATCGCCCGGAAGAAGGACTGGGACCCCAAGAAGTACGGCGGCTTCGA CTCCCCACCGTGGCCTACTCCGTGCTGGTGGTGGCCAAGGTGGAGAAGGGCAAGTC CAAGAAGCTGAAGTCCGTGAAGGAGCTGCTGGGCATCACCATCATGGAGCGGTCCCT CTTCGAGAAGAACCCATCGACTTCTGGAGGCCAAGGGGCTACAAGGAGGTGAAGA AGGACCTGATCATCAAGCTGCCAAGTACTCCCTGTTTCGAGCTGGAGAACGGCCGGA AGCGGATGCTGGCCTCCGCCGGCAGCTGCAGAAGGGCAACGAGCTGGCCCTGCC TCCAAGTACGTGAACCTTCTGTACTTGGCCTCCACTACGAGAAGCTGAAGGGCTCC CCCAGGACAACGAGCAGAAGCAGCTGTTTCGTGGAGCAGCACAAGCACTACCTGGA</p>	<p>117</p>
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[0716]

	<p>CGAGATCATCGAGCAGATCTCCGAGTTCTCCAAGCGGGTGATCCTGGCCGACGCCAA CCTGGACAAGGTGCTGTCCGCCTACAACAAGCACCGGGACAAGCCATCCGGGAGC AGGCCGAGAATCATCCACCTGTTACCCTGACCAACCTGGGCGCCCCGCCGCT TCAAGTACTTCGACACCACCATCGACCGGAAGCGGTACACCTCCACCAAGGAGGTGC TGGACGCCACCCGTATCCACCAGTCCATCACCGGCCTGTACGAGACCCGGATCGACC TGTCACAGCTGGGCGGCGACGGCGGCTCCCCAAGAAGAAGCGGAAGGTGTGA</p>	
<p>使用表4的低 A密码子，具 有起始及终 止密码子且 无 NLS 的 dCas9 ORF</p>	<p>ATGGACAAGAAGTACTCCATCGGCCCTGGCCATCGGCACCAACTCCGTGGGCTGGGCC GTGATCACCGACGAGTACAAGGTGCCCTCCAAGAAGTTCAAGGTGCTGGGCAACACC GACCGGCACTCCATCAAGAAGAACCTGATCGGCGCCCTGCTGTTGACTCCGGCGAG ACCGCCGAGGCCACCCGGCTGAAGCGGACCGCCGGCGGGGTACACCCGGCGGAA GAACCGGATCTGCTACCTGCAGGAGATCTTCTCCAACGAGATGGCCAAAGTGGACGA CTCCTTCTTCCACCGGCTGGAGGAGTCTTCTGTTGGAGGAGGACAAGAAGCACGA GCGGCACCCATCTTCGGCAACATCGTGGACGAGGTGGCCTACCACGAGAAGTACCC CACCATCTACCACCTGCGGAAGAAGCTGGTGGACTCCACCGACAAGGCCGACCTGCG GCTGATCTACCTGGCCCTGGCCACATGATCAAGTTCCGGGGCCACTTCTGTATCGAG GGGACCTGAACCCCGACAACCTCCGACGTGGACAAGCTGTTATCCAGTGTGACAG ACCTACAACCAGCTGTTCCGAGGAGAACCCATCAACGCCTCCGGCGTGGACGCCAAG GCCATCCTGTCCGCCCGGCTGTCAAGTCCCGGCGGCTGGAGAACCTGATCGCCAG CTGCCCGGCGAGAAGAAGAACGGCCTGTTCCGCAACCTGATCGCCCTGTCCCTGGGC CTGACCCCAACTTCAAGTCCAACCTCGACCTGGCCGAGGACGCCAAGTGCAGCTG TCCAAGGACACCTACGACGACGACCTGGACAACCTGCTGGCCAGATCGGCGACCA GTACGCCGACCTGTTCCCTGGCCGCCAAGAACCTGTCCGACGCCATCCTGCTGTCCGA CATCCTGCGGGTGAACACCGAGATCAACAAGGCCCCCTGTCGCTCCATGATCAA GCGGTACGACGAGCACCACCAGGACCTGACCCTGCTGAAGGCCCTGTGCGCGCAGC AGTGCCCGAGAAGTACAAGGAGATCTTCTCGACCAAGTCCAAGAAGCTGACGCGCG GCTACATCGACGCGGCGCCTCCAGGAGGAGTTCTACAAGTTCATCAAGCCATCCT GGAGAAGATGGACGGCACCGAGGAGCTGCTGGTGAAGCTGAACCGGGAGGACCTGC TGCGGAAGCAGCGGACCTTCGACAACGGCTCCATCCCCACCAGATCCACCTGGGCG AGTGCACGCCATCTGCGGCGGCGAGGAGACTTCTACCCCTTCTGAAGGACAAC GGGAGAAGATCGAGAAGATCCTGACCTTCGGATCCCCTACTACGTGGGCCCCCTGG CCCGGGGCAACTCCCGGTTGCGCTGGATGACCCGGAAGTCCGAGGAGACCATCACC CCTGGAATTCGAGGAGGTGGTGGACAAGGGCGCCTCCGCCAGTCCCTTCATCGAGC GGATGACCAACTTCGACAAGAACCTGCCAACGAGAAGGTGCTGCCAAGCATTCC CTGCTGTACGAGTACTTCCCGTGTACAACGAGCTGACCAAGGTGAAGTACGTTGACC GAGGGCATGCGGAAGCCGCTTCTGTCGGCGAGCAGAAGAAGGCCATCGTGA CCTGCTGTTCAAGACCAACCGGAAGGTGACCGTGAAGCAGCTGAAGGAGGACTACT TCAAGAAGATCGAGTGCTTCGACTCCGTGGAGATCTCCGGCGTGGAGGACCGGTTCA ACGCCTCCCTGGGCACCTACCAGCCTGCTGAAGATCATCAAGGACAAGGACTTCC TGGACAACGAGGAGAACGAGGACATCCTGGAGGACATCGTGCTGACCTGACCCTG TTCGAGGACCGGAGATGATCGAGGAGCGGCTGAAGACCTACGCCACCTGTTCCGAC GACAAGGTGATGAAGCAGCTGAAGCGGCGGCGGTACACCGGCTGGGGCCGGCTGTC CCGGAAGCTGATCAACGGCATCCGGGACAAGCAGTCCGGCAAGACCATCTGGACTT CCTGAAGTCCGACGGCTTCGCCAACCGGAACCTTCATGCAGCTGATCCACGACACTC CCTGACCTTCAAGGAGGACATCCAGAAGGCCAGGTGTCCGGCCAGGGCGACTCCCT GCACGACACATCGCCAACCTGGCCGGCTCCCCGCCATCAAGAAGGGCATCCTGCA GACCGTGAAGGTGGTGGACGAGCTGGTGAAGGTGATGGGCCGGCACAAGCCCGAGA ACATCGTGATCGAGATGGCCCGGGAAGAACAGACCACCCAGAAGGGCCAGGAAGAAC TCCCGGGAGCGGATGAAGCGGATCGAGGAGGGCATCAAGGAGCTGGGCTCCAGAT CCTGAAGGAGCACCCGTGGAGAACACCCAGCTGCAAGACGAGAAGCTGTACTGT ACTACCTGCAAGACGGCCGGGACATGTACGTGGACCAGGAGCTGGACATCAACCGGC TGTCGACTACGACGTGGACGCCATCGTGCCCCAGTCTTCTGAAGGACGACTCCAT TGACAACAAGGTGCTGACCCGGTCCGACAAGAACCAGGGGCAAGTCCGACAACGTGC CCTCCGAGGAGGTGGTGAAGAAGATGAAGAATACTGGCGGCAGCTGCTGAACGCC AAGCTGATCACCCAGCGGAAGTTCGACAACCTGACCAAGGCCGAGCGGGCGGCT GTCCGAGCTGGACAAGGCCGGCTTTCATCAAGCGGCAGCTGGTGGAGACCCGGCAGA TCACCAAGCACGTGGCCAGATCCTGGACTCCCGGATGAACACCAAGTACGACGAGA ACGACAAGCTGATCCGGGAGGTGAAGGTGATCACCTGAAGTCCAAGCTGGTGTCCG ACTTCCGGAAGGACTTCCAGTTCACAAGGTGCGGGAGATCAACAATACTACCACAG CCCACGACGCCTACTGAACGCCGTGGTGGGACCGCCCTGATCAAGAAGTACCCCA AGCTGGAGTCCGAGTTCGTGTACGGCGACTACAAGGTGTACGACGTGCGGAAGATGA TCGCCAAGTCCGAGCAGGAGATCGGCAAGGCCACCGCAAGTACTTCTTACTTCA ACATCATGAACCTTCTCAAGACCGAGATCACCTGGCCAACGGCGAGATCCGGAAGC GGCCCCTGATCGAGACCAACGGCGAGACCGGCGAGATCGTGTGGGACAAGGGCCGG GACTTCGCCACCGTGGCGAAGGTGCTGTCATGCCCCAGGTGAACATCGTGAAGAAG ACCGAGGTGACAGCCGGCGGCTTCTCCAAGGAGTCCATCCTGCCAAGCGGAACCTC GACAAGCTGATCGCCGGAAGAAGGACTGGGACCCCAAGAAGTACGGCGGCTTCGA CTCCCCACCGTGGCCTACTCCGTGCTGGTGGTGGCCAAGGTGGAGAAGGGCAAGTC</p>	<p>118</p>

[0717]

	<p>CAAGAAGCTGAAGTCCGTGAAGGAGCTGCTGGGCATCACCATCATGGAGCGGTCCCTC CTTCGAGAAGAACCCCATCGACTTCTGGAGGCCAAGGGCTACAAGGAGGTGAAGA AGGACCTGATCATCAAGCTGCCAAGTACTCCCTGTTTCGAGCTGGAGAACGGCCGGA AGCGGATGCTGGCTCCGCCGGCGAGCTGCAGAAGGGCAACGAGCTGGCCCTGCC TCCAAGTACGTGAACCTTCTGTACTTGGCCTCCACTACGAGAAGCTGAAGGGCTCC CCCGAGACAACGAGCAGAAGCAGCTGTTCTGTGGAGCAGCACAAGCCTACCTGGA CGAGATCATCGAGCAGATCTCCGAGTTCTCCAAGCGGGTGATCTGGCCGACGCCAA CCTGGACAAGGTGCTGTCCGCTACAACAAGCACCAGGACAAGCCATCCGGGAGC AGGCCGAGAATCATCCACCTGTTACCCTGACCAACCTGGGGCCTCCCGCCGCT TCAAGTACTTCGACACCACCATCGACCGGAAGCGGTACACCTCCACCAAGGAGGTGC TGGACGCCACCCTGATCCACCAAGTCCATCACCAGGCTGTACGAGACCCGGATCGACC TGTCCAGCTGGGCGGCGACTGA</p>	
<p>使用表4的低 A密码子,具 有两个C端 NLS序列及 起始及终止 密码子的 dCas9 ORF</p>	<p>ATGGACAAGAAGTACTCCATCGGCCTGGCCATCGGCACCAACTCCGTGGGCTGGCC GTGATCACCAGCAGGTACAAGGTGCCCTCCAAGAAGTTCAAGGTGCTGGGCAACACC GACCCGCACTCCATCAAGAAGAACCTGATCGGCCTGCTGTTTCGACTCCGGCGAG ACCCTCGAGGCCACCCGGCTGAAGCGGACCGCCCGCGCGGTACACCCGGCGGAA GAACCGGATCTGCTACCTGCAGGAGATCTTCTCCAACGAGATGGCCAAGGTGGACGA CTCCTTCTCCACCCGGCTGGAGGAGTCTTCTGGTGGAGGAGGACAAGAAGCACGA GCGGCACCCATCTTCGGCAACATCGTGGACGAGGTGGCCTACCACGAGAAGTACC CACCATCTACCACCTGCGGAAGAAGCTGGTGGACTCCACCACCAAGGCCGACTCGG GCTGATCTACCTGGCCCTGGCCACATGATCAAGTTCGGGGCCACTTCTGATCGAG GGCGACTGAACCCGACAACCTCCGACGTGGACAAGCTGTTTCATCCAGCTGGTGCAG ACCTACAACCAGCTGTTTCGAGGAGAACCCATCAACGCCTCCGGCGTGGACGCCAAG GCCATCTGTCCGCCGGCTGTCCAAGTCCCGCGGCTGGAGAACCTGATCGCCAG CTCCCGCGGAGAGAAGAAGAACGGCCTGTTTCGGCAACCTGATCGCCTGTCTTGGG CTGACCCCAACTTCAAGTCCAACCTTCGACCTGGCCGAGGACGCCAAGCTGCAGCTG TCCAAGGACACTACGACGACGACCTGGACAACCTGCTGGCCAGATCGGCGACCA GTACGCCGACCTGTTCTGGCCGCAAGAACCTGTCCGACGCCATCTGCTGTCCGA CATCTGCGGGTGAACACCAGATCAACAAGGCCCCCTGTCGCCTCCATGATCAA GCGGTACGACGAGCACCACCAGGACCTGACCCTGCTGAAGGCCCTGGTGGCGGACG AGCTGCCCGAGAAGTACAAGGAGATCTTCTTCGACCAGTCCAAGAACGGCTACGCCG GCTACATCGACGGCGGCGCTCCAGGAGGAGTTCTACAAGTTCATCAAGCCCATCT GGAGAAGATGGACGGCACCGGAGCTGCTGGTGAAGCTGAACGGGAGGACCTGC TGCGGAAGCAGCGGACCTTCGACAACGGCTCCATCCCCACCAGATCCACCTGGGCG AGCTGCACGCCATCTGCGGCGGACGAGGACTTCTACCCCTTCTGAAGGACAACC GGGAGAAGATCGAGAAGATCCTGACCTCCGGATCCCTACTACGTGGGCCCTGG CCCGGGGCAACTCCCGGTTGCTGGATGACCCGGAAGTCCGAGGAGACCATCACC CCTGGAACCTTCGAGGAGGTGGTGGACAAGGGCGCCTCCGCCAGTCTTCATCGAGC GGATGACCAACTTCGACAAGAACCTGCCAACGAGAAGGTGCTGCCAAGCACTCC CTGCTGTACGAGTACTTACCCTGTACAACGAGCTGACCAAGGTGAAGTACGTGACC GAGGGCATGCGGAAGCCGCCTTCTGTCGGCGAGCAGAAGAAGGCCATCGTGGGA CTGCTGTTCAAGACCAACCGGAAGGTGACCGTGAAGCAGCTGAAGGAGGACTACT TCAAGAAGATCGAGTGCTTCGACTCCGTGGAGATCTCCGGCGTGGAGGACCGGTTCA ACGCTCCCTGGGACCTACCACGACCTGCTGAAGATCATCAAGGACAAGGACTTCC TGGACAACGAGGAGAACGAGGACATCCTGGAGGACATCGTGCTGACCTGACCTG TTCGAGGACCGGAGATGATCGAGGAGCGGCTGAAGACCTACGCCACCTGTTTCGAC GACAAGGTGATGAAGCAGCTGAAGCGGCGGCGGTACACCGGCTGGGCGCGGCTGTC CCGGAAGCTGATCAACGGCATCCGGGACAAGCAGTCCGGCAAGACCATCTGGACTT CCTGAAGTCCGACGCTTCGCCAACCGGAACCTTCATGCAGCTGATCCACGACGACTC CCTGACCTTCAAGGAGGACATCCAGAAGGCCAGGTGTCCGGCCAGGGCGACTCCCT GCACGACACATCGCAACCTGGCCGGCTCCCCGCCATCAAGAAGGGCATCTGCA GACCGTGAAGGTGGTGGACGAGCTGGTGAAGGTGATGGCCGGCACAAAGCCCGAGA ACATCGTGATCGAGATGGCCGGGAGAACCAGACCACCCAGAAGGGCCAGAAGAAC TCCCGGGAGCGGATGAAGCGGATCGAGGAGGGCATCAAGGAGCTGGGCTCCAGAT CCTGAAGGAGCACCCGTGGAGAACCCAGCTGCAGAACGAGAAGCTGTACCTGT ACTACCTGCAGAACGGCCGGGACATGACGTGGACCAGGAGCTGGACATCAACCGGC TGTCCGACTACGACGTGGACGCCATCGTGCCCCAGTCTTCTGAAGGACGACTCCAT CGACAACAAGGTGCTGACCCGGTCCGACAAGAACCAGGGGCAAGTCCGACAACGTGC CCTCCGAGGAGGTGGTGAAGAAGATGAAGAATACTGGCGGCGAGCTGCTGAACGCC AAGCTGATCACCCAGCGGAAGTTCGACAACCTGACCAAGGCCGAGCGGGCGGCCT GTCCGAGCTGGACAAGGCCGGCTTCAACAAGCGGACGCTGGTGGAGACCCGGCAGA TCACCAAGCACGTGGCCAGATCCTGGACTCCCGGATGAACACCAAGTACGACGAGA ACGACAAGCTGATCCGGGAGGTGAAGGTGATCACCTGAAGTCCAAGCTGGTGTCCG ACTTCCGGAAGGACTTCAAGTCTACAAGGTGCGGGAGATCAACAATACTACCACCAG CCCACGACCTACCTGAACGCCGTGGTGGGACCCGCCCTGATCAAGAAGTACCCCA AGCTGGAGTCCGAGTTCGTGTACGGCGACTACAAGGTGTACGACGTGCGGAAGATGA TCGCCAAGTCCGACGAGGAGATCGGCAAGGCCACCCCAAGTACTTCTTACTCCA</p>	<p>119</p>

[0718]

	<p>ACATCATGAACTTCTTCAAGACCGAGATCACCTGGCCAACGCGGAGATCCGGAAGC GGCCCCTGATCGAGACCAACGGCGAGACCGCGGAGATCGTGTGGGACAAGGGCCGG GACTTCGCCACCGTGCGGAAGGTGCTGTCCATGCCCCAGGTGAACATCGTGAAGAAG ACCGAGGTGCAGACCGCGGCTTCTCCAAGGAGTCCATCCTGCCAAGCGGAACTCC GACAAGCTGATCGCCCGGAAGAAGGACTGGGACCCCAAGAAGTACGGCGGCTTCGA CTCCCCACCGTGGCTACTCCGTGCTGGTGGTGGCCAAGGTGGAGAAGGGCAAGTC CAAGAAGCTGAAGTCCGTGAAGGAGCTGCTGGGCATCACCATCATGGAGCGGTCTCTC CTTCGAGAAGAACCCATCGACTTCTTGAGGGCCAAGGGCTACAAGGAGGTGAAGA AGGACCTGATCATCAAGTGCCTCAAGTACTCCCTGTTTCGAGCTGGAGAACGGCCGGA AGCGGATGCTGGCTCCGCCGGCGAGCTGCAGAAGGGCAACGAGCTGGCCCTGCC TCCAAGTACGTGAACCTTCTGACTGCTGGCTCCCACTACGAGAAGCTGAAGGGCTCC CCCAGGACAACGAGCAGAAGCAGCTGTTCTGGAGCAGCACAAGCACTACCTGGA CGAGATCATCGAGCAGATCTCCGAGTTCTCCAAGCGGGTGATCCTGGCCGACGCCAA CCTGGACAAGGTGCTGTCCGCCTACAACAAGCACCGGGACAAGCCATCCGGGAGC AGGCCGAGAACATCATCCACCTGTTACCTGACCAACCTGGGCGCCCGCCGCTTCC TCAAGTACTTCGACACCACATCGACCGGAAGCGGTACACCTCCACCAAGGAGGTGC TGGACGCCACCTGATCCACAGTCCATCACCGGCTGTACGAGACCCGGATCGACC TGTCCCAGCTGGGCGGCGACGGCTCCGGCTCCCCCAAGAAGAAGCGGAAGGTGGAC GGTCCCCAAGAAGAAGCGGAAGGTGGACTCCGGCTGA</p>	
<p>使用表4的低 A/U密码子, 具有两个C端 NLS序列及 起始及终止 密码子的 Cas9 ORF</p>	<p>ATGGACAAGAAGTACAGCATCGGCCTGGACATCGGCACCAACAGCGTGGGCTGGGCC GTGATCACCGACGAGTACAAGGTGCCAGCAAGAAGTTCAAGGTGCTGGGCAACAC CGACCGGCACAGCATCAAGAAGAACCTGATCGGCGCCCTGCTGTTCGACAGCGGCG AGACCGCCGAGGGCCACCCGGCTGAAGCGGACCGCCCGGCGGCGGTACACCCGGCGG AAGAACCAGGATCTGCTACCTGCAGGAGATCTTCAGCAACGAGATGGCAAGGTGGAC GACAGCTTCTCCACCGGCTGGAGGAGGCTTCTGGTGGAGGAGGACAAGAAGCA CGAGCGGCACCCCATCTTCGGCAACATCGTGGACGAGGTGGCCTACCACGAGAAGTA CCCCACATCTACCACCTGCGGAAGAAGCTGGTGGACAGCACCGACAAGGCCGACCT GCGGCTGATCTACCTGGCCCTGGCCACATGATCAAGTTCGGGGCCACTTCTGATC GAGGGCGACCTGAACCCGACAACAGCAGCGACGTGGACAAGCTGTTTCATCCAGCTGGT GCAGACCTACAACCAGCTGTTTCGAGGAGAACCCATCAACGCCAGCGGCGTGGACG CCAAGGCCATCCTGAGCGCCCGGCTGAGCAAGAGCCGGCGGCTGGAGAACCTGATC GCCAGCTGCCCGGCGAGAAGAAGAAGCGGCTGTTTCGGCAACCTGATCGCCCTGAG CCTGGGCTGACCCCAACTTCAAGAGCAACTTCGACCTGGCCGAGGACGCCAAGCT GCAGTGAAGCAAGGACCTACGACGACGACCTGGACAACCTGTTGGCCACTGAGCTCG GCGACCAGTACGCCGACCTGTTCTGGCCGCAAGAACCTGAGCGACGCCATCCTGC TGAGCGACATCCTGCGGGTGAACACCGAGATCACCAGGCCCCCTGAGCGCCAGCA TGATCAAGCGGTACGACGAGCACCACCAGGACCTGACCCTGTGAAGGCCCTGGTGC GGACAGCTGCCCGAGAAGTACAAGGAGATCTTCTTCGACCAGAGCAAGAACCGG TACGCCGGCTACATCGACGGCGGCCAGCCAGGAGGAGTTTACAAGTTCATCAAG CCCATCCTGGAGAAGATGGACGGCACCGAGGAGCTGCTGGTGAAGCTGAACCGGGA GGACCTGCTGCGGAAGCAGCGGACCTTCGACAACGGCAGCATCCCCACCAGATCCA CCTGGGCGAGCTGCACGCCACTGCGGCGGCAAGGAGGACTTCAACCCCTTCTGAA GGACAACCGGGAAGATCGAGAAGATCCTGACCTTCCGGATCCCTACTGCGCCAGCTG CCCCCTGGCCCGGGCAACAGCCGGTTCGCTGGATGACCCGGAAGAGCGAGGAGA CCATACCCCTGGAACCTCGAGGAGGTGGTGGACAAGGGCGCCAGCGCCAGAGC TTCATCGAGCGGATGACCAACTTCGACAAGAACCTGCCAACGAGAAGGTGCTGCC AAGCACAGCTGCTGTACGAGTACTTACCCTGTACAACGAGCTGACCAAGGTGAAG TACGTGACCGAGGGCATGCGGAAGCCGCCTTCTGAGCGGCGAGCAGAAGAAGGC CATCGTGGACCTGCTGTTCAAGACCAACCGGAAGGTGACCGTGAAGCAGCTGAAGG AGGACTACTTCAAGAAGATCGAGTGTTCGACAGCGTGGAGATCAGCGGCGTGGAG GACCGGTTCAACGCCAGCTGGGCACCTACCACGACCTGCTGAAGATCATCAAGGAC AAGGACTTCTGGACAACGAGGAGAACGAGGACATCCTGGAGGACATCGTCTGAC CCTGACCCCTGTTGAGGACCGGGAGATGATCGAGGAGCGGCTGAAGACCTACGCCCA CCTGTTGACGACAAGGTGATGAAGCAGCTGAAGCGGCGGCGGTACACCGGCTGGG GCCGGCTGAGCCGGAAGCTGATCAACGGCATCCGGGACAAGCAGAGCGGCAAGACC ATCGGACTTCTGAAGAGCGACGGCTTCGCCAACCAGGAACTTATGACAGTGTGATC CACGACGACAGCCTGACCTTCAAGGAGGACATCCAGAAGGCCAGGTGAGCGGCCA GGGCGACAGCCTGCACGACACATCGCCAACCTGGCCGGCAGCCCCGCATCAAGA AGGGCATCCTGCAGACCGTGAAGGTGGTGGACGAGCTGGTGAAGGTGATGGCCGG CACAAGCCCAGAACATCGTGTGATCGAGATGGCCGGGAGAACCAGACCACCCAGAA GGCCAGAGAACAAGCCGGGAGCGGATGAAGCGGATCGAGGAGGGCATCAAGGAG CTGGGCGACCCAGATCCTGAAGGAGCACCCGCTGGAGAACACCCAGCTGCAGAACGA GAAGCTGTACCTGTACTACCTGCAGAACGGCCGGGACATGTACGTGGACCAGGAGCT GAAGGACGACAGCATCGACAACAAGGTGCTGACCCGAGCGACAAGAACCAGGGG AAGAGCGACAACGTGCCAGCGAGGAGGTGGTGAAGAAGATGAAGAAGTACTGGCG GCAGCTGCTGAACGCCAAGCTGATCACCCAGCGGAAGTTCGACAACCTGACCAAGG</p>	<p>120</p>

[0719]

[0720]

	<p>CCGAGCGGGGCGGCCTGAGCGAGCTGGACAAGGCCGGCTTCATCAAGCGGCAGCTG GTGGAGACCCGGCAGATCACCAAGCACGTGGCCAGATCCTGGACAGCCGGATGAA CACCAAGTACGACGAGAACGACAAGCTGATCCGGGAGGTGAAGGTGATCACCTGA AGAGCAAGCTGGTGAAGGACTTCCGGAAGGACTTCCAGTTTACAAGGTGCGGGAG ATCAACAATAACCACCGCCACGACGCCTACCTGAACGCCGTGGTGGGACCCGCC CTGATCAAGAAGTACCCCAAGCTGGAGAGCGAGTTCTGTGTACGGCGACTACAAGGTG TACGACGTGCGGAAGATGATCGCCAAGAGCGAGCAGGAGATCGGCAAGGCCACCGC CAAGTACTTCTTACAGCAACATCATGAACTTCTCAAGACCGAGATCACCTGGCC AACGGCGAGATCCGGAAGCGGCCCTGATCGAGACCAACGGCGAGACCGGCGAGAT CGTGTGGGACAAGGGCCGGACTTCGCCACCGTGGGAAAGGTGCTGAGCATGCCCC AGGTGAACATCGTGAAGAAGACCGAGGTGCAGACCGCGGCTTACAGCAAGGAGGC ATCCTGCCAAGCGGAACAGCGACAAGCTGATCGCCCGGAAGAAGGACTGGGACCC CAAGAAGTACGGCGGCTTCGACAGCCCCACCGTGGCCTACAGCGTGTGGTGGTGGC CAAGGTGGAGAAGGGCAAGAGCAAGAAGCTGAAGAGCGTGAAGGAGCTGCTGGGC ATCACCATCATGGAGCGGAGCAGCTTCGAGAAGAACCCATCGACTTCTGGAGGCC AAGGGCTACAAGGAGGTGAAGAAGGACCTGATCATCAAGCTGCCCAAGTACAGCCT GTTGAGCTGGAGAACGGCCGGAAGCGGATGCTGGCCAGCGCCGGCGAGCTGCAGA AGGGCAACGAGCTGGCCCTGCCAGCAAGTACGTGAACCTTCTGTACTGGCCAGCC ACTACGAGAAGCTGAAGGGCAGCCCCGAGGACAACGAGCAGAAGCAGCTGTTCTGTG GAGCAGCACAAGCACTACCTGGACGAGATCATCGAGCAGATCAGCGAGTTACAGAA GCGGGTATCCTGGCCGACGCCAACCTGGACAAGGTGCTGAGCGCCTACAACAAGC ACCGGGACAAGCCATCCGGGAGCAGGCCGAGAATCATCCACCTGTTACCCCTGA CCAACCTGGGCGCCCCGCGCCTTCAAGTACTTCGACACCACATCGACCGGAAGC GGTACACCAGCACCAAGGAGGTGCTGGACGCCACCTGATCCACCAGATCACCG GCCTGTACGAGACCCGGATCGACCTGAGCCAGCTGGGCGGCGACGGCAGCGGCAGC CCCAAGAAGAAGCGGAAGGTGGACGGCAGCCCCAAGAAGAAGCGGAAGGTGGACA GCGGCTGA</p>	
<p>使用表4的低 A/U密码子, 具有起始及 终止密码子 且无 NLS 的 Cas9 ORF</p>	<p>ATGGACAAGAAGTACAGCATCGGCCTGGACATCGGCACCAACAGCGTGGGCTGGGC GTGATCACCGACGAGTACAAGGTGCCAGCAAGAAGTTCAAGGTGCTGGGCAACAC CGACCGGCACAGCATCAAGAAGAACCTGATCGGCGCCCTGCTGTTGACAGCGGCG AGACCGCCGAGGCCACCCGGCTGAAGCGGACCGCCCGGCGGCGGTACACCCGGCGG AAGAACCAGGATCTGCTACCTGCGAGGAGATCTTACAGCAACGAGATGGCCAAGGTGGAC GACAGCTTCTCCACCGCTGGAGGAGCTTCTGTTGGAGGAGGACAAGAAGCA CGAGCGGCACCCATCTTCGGCAACATCGTGGACGAGGTGGCCTACCACAGAAGTA CCCCACATCTACCACCTGCGGAAGAAGCTGGTGGACAGCACCGACAAGGCCGACCT GCGGCTGATCTACTGGCCCTGGCCACATGATCAAGTTCCGGGGCCACTTCTGATC GAGGGCGACCTGAACCCGACAACAGCGACGTGGACAAGCTGTTTATCCAGCTGGT GCAGACCTACAACCAAGCTGTTTCGAGGAGAACCCCATCAACGCCAGCGCGTGGACG CCAAGGCCATCTGAGCGCCCGGCTGAGCAAGAGCCGGCGGCTGGAGAACCTGATC GCCAGCTGCCGCGGAGAAGAAGAACGGCCTGTTCCGGCAACCTGATGCCCTGAG CCTGGGCTGACCCCCAACTTCAAGAGCAACTTCGACCTGGCCGAGGACGCCAAGCT GCAGCTGAGCAAGGACACCTACGACGACGACCTGGACAACCTGCTGGCCAGATCG GAGACCAAGTACCGACCTGTTCTGGCCGCAAGAACCTGAGCGGACGCCATCTGTC TGAGCGACATCTGCGGGTGAACACCGAGATCACCAAGGCCCCCTGAGCGCCAGCA TGATCAAGCGGTACGACGAGCACCACCGACCTGACCCTGCTGAAGGCCCTGGTGC GGCAGCAGCTGCCCAGAGAAGTACAAGGAGATCTTCTTCGACCAGAGCAAGAACCGC TACGCGGCTACATCGAGCGGCGCCAGCCAGGAGGAGTTTACAAGTTTACAAG CCCATCTGGAGAAGATGGACGGCACCGAGGAGCTGCTGGTGAAGCTGAACCGGGA GGACCTGCTGCGGAAGCAGCGGACCTTCGACAACGGCAGCATCCCCACCAGATCCA CCTGGGCGAGCTGCACGCCATCTGCGGCGGCGAGGAGACTTACCCCTTCTGAA GGACAACCGGAGAAGATCGAGAAGATCTGACCTTCCGGATCCCCTACTACGTGGG CCCCCTGGCCCGGGGCAACAGCCGGTTCGCTGGATGACCCGGAAGAGCGAGGAGA CCATCACCCCTGGAACCTTCGAGGAGGTGGTGGACAAGGGCGCCAGCGCCAGAGC TTCATCGAGCGGATGACCAACTTCGACAAGAACCTGCCAACGAGAAGGTGCTGCC AAGCACAGCCTGCTGTACGAGTACTTACCCTGTACAACGAGCTGACCAAGGTGAAG TACGTGACCGAGGGCATGCGGAAGCCCGCTTCTGAGCGGCGAGCAGAAGAAGGC CATCGTGGACCTGCTGTTCAAGACCAACCGGAAGGTGACCGTGAAGCAGCTGAAGG AGGACTACTTCAAGAAGATCGAGTGTTCGACAGCGTGGAGATCAGCGGCGTGGAG GACCGGTTCAACGCCAGCCTGGGCACCTACCACGACCTGCTGAAGATCATCAAGGAC AAGGACTTCTGGACAACGAGGAGAACGAGGACATCTGGAGGACATCGTGTGAC CCTGACCCTGTTGAGGACCGGAGATGATCGAGGAGCGGCTGAAGACCTACGCCCA CCTGTTGACGACAAGGTGATGAAGCAGCTGAAGCGGCGGCGGTACACCGGCTGGG GCCGGCTGAGCCGGAAGCTGATCAACGGCATCCGGGACAAGCAGAGCGGCAAGACC ATCCTGGACTTCTGAAGAGCGACGGCTTCGCCAACCGGAACCTTATGCAGCTGATC CACGACGACCGCTGACCTTCAAGGAGGACATCCAGAAGGCCAGGTGAGCGGCCA GGGCGACAGCCTGCACGAGCACATCGCCAACCTGGCCGGCAGCCCCGCCATCAAGA AGGGCATCTGCAGACCGTGAAGGTGGTGGACGAGCTGGTGAAGGTGATGGGCCG</p>	<p>121</p>

[0721]

	<p>CACAAGCCCCGAGAATCGTGATCGAGATGGCCCGGGAGAACCAGACCACCCAGAA GGGCCAGAAGAACAGCCGGGAGCGGATGAAGCGGATCGAGGAGGGCATCAAGGAG CTGGGCAGCCAGATCCTGAAGGAGCACCCCGTGAGAAACACCCAGCTGCAGAACGA GAAGCTGTACCTGTACTACCTGCAGAACCGCCGGGACATGTACCTGGACCAGGAGCT GGACATCAACCGGCTGAGCGACTACGACGTGGACCACATCGTCCCCAGAGCTTCCT GAAGGACGACAGCATCGACAACAAGGTGCTGACCCGGAGCGACAAGAACCAGGGG AAGAGCGACAACGTGCCAGCGAGGAGGTGGTGAAGAAGATGAAGAACTACTGGCG GCAGCTGCTGAACGCCAAGCTGATCACCCAGCGGAAGTTCGACAACCTGACCAAGG CCGAGCGGGGCGGCCCTGAGCGAGCTGGACAAGGCCGGCTTCATCAAGCGGCAGCTG GTGGAGACCCGGCAGATCACCAAGCACGTGGCCAGATCCTGGACAGCCGGATGAA CACCAAGTACGACGAGAACGACAAGCTGATCCGGGAGGTGAAGGTGATCACCTGA AGAGCAAGCTGGTGAAGGACTTCCGGAAGGACTTCCAGTTCTACAAGGTGCGGGAG ATCAACAACCTACCACACGCCACGACGCCTACCTGAACGCCGTGGTGGGCACCGCC CTGATCAAGAAGTACCCCAAGCTGGAGAGCGAGTTCGTGTACGGCGACTACAAGGTG AAGCAGTGCAGGAAAGATGATCGCCAAGAGCGAGCAGGAGATCGGCAAGGCCACCG CAAGTACTTCTTCTACAGCAACATCATGAACCTTCTCAAGACCGAGATCACCCCTGGCC AACGGCGAGATCCGGAAGCGGCCCTGATCGAGACCAACGGCGAGACCGGCAGAT CGTGTGGGACAAGGGCCGGGACTTCGCCACCGTGCAGGAAAGGTGCTGAGCATGCC AGGTGAACATCGTGAAGAAGACCGAGGTGCAGACCGCGGCTTCAGCAAGGAGAGC ATCCTGCCAAGCGGAACAGCGACAAGCTGATCGCCGGAAGAAGGACCGCCAGCC CAAGAAGTACGGCGGCTTCGACAGCCCCACCGTGGCCTACAGCGTGTGGTGGTGGC CAAGGTGGAGAAGGGCAAGAGCAAGAAGCTGAAGAGCGTGAAGGAGCTGTGGGC ATCACCATCATGGAGCGGAGCAGCTTCGAGAAGAACCCATCGACTTCTGGAGGGC AAGGGCTACAAGGAGGTGAAGAAGGACCTGATCATCAAGCTGCCAAGTACAGCT GTTGAGCTGGAGAACCGCCGGAAGCGGATGCTGGCCAGCGCGGCGAGCTGCAGA AGGGCAACGAGCTGGCCCTGCCAGCAAGTACGTGAACCTCCTGTACCTGGCCAGCC ACTACGAGAAGCTGAAGGGCAGCCCCGAGGACAACGAGCAGAAGCAGCTGTTCTGT GAGCAGCACAAGCACTACCTGGACGAGATCATCGAGCAGATCAGCGAGTTCAGCAA GCGGGTATCCTGGCCGACGCCAACCTGGACAAGGTGCTGAGCGCCTACAACAAGC ACCGGGACAAGCCATCCGGGAGCAGGCCGAGAACATCATCCACCTGTTACCCCTGA CCAACCTGGGCGCCCCGCCCTTCAAGTACTTCGACACCACCATCGACCGGAAGC GGTACACCAGCACAAGGAGGTGCTGGACGCCACCTGATCCACCAGAGCATCACCG CGCTGTACGAGACCCGAGTGCATGAGCCAGCTGGGCGGCGACTGA</p>	
<p>使用表4的低 A/U密码子, 具有起始及 终止密码子 的 Cas9 切口 酶ORF</p>	<p>ATGGACAAGAAGTACAGCATCGGCCTGGCCATCGGCACCAACAGCGTGGGCTGGGCC GTGATCACCGACGAGTACAAGGTGCCAGCAAGAAGTTCAAGGTGCTGGGCAACAC CGACCGGCACAGCATCAAGAAGAACCTGATCGCGGCCCTGCTGTTGACAGCGGGC AGACCGCCGAGGCCACCCGGCTGAAGCGGACCGCCCGGCGGGTACACCCGGCGG AAGAACCAGGATCTGTACTTGCAGGAGATCTTCAGCAACGAGATGGCCAAGGTGGAC GACAGCTTCTTCCACCGGCTGGAGGAGAGCTTCTGGTGGAGGAGGACAAGAAGCA CGAGCGGCACCCCATCTTCGGCAACATCGTGGACGAGGTGGCCTACCACGAGAAGTA CCCCACCATCTACCACCTGCGGAAGAAGCTGGTGGACAGCACCGCAAGGCCGACCT GCGGCTGATCTACCTGGCCCTGGCCACATGATCAAGTTCCGGGGCCACTTCTGTATC GGCGCAGCTGAACCCCGACAACAGCGACGTGGACAAGCTGTTTCATCCAGTGGT GCAGACCTACAACCAGCTGTTTCGAGGAGAACCCATCAACGCCAGCGGCGTGGACG CCAAGGCCATCTGAGCGCCCGGCTGAGCAAGAGCCGGCGGCTGGAGAACCCTGATC CCCCAGCTGCCCGGCGAGAAGAAGAACCGGCTGTTCCGCAACCTGATCGCCCTGAG CCTGGCCCTGACCCCCAAGTCAAGAGCAACTTCGACCTGGCCGAGGACGCCAAGCT GCAGCTGAGCAAGGACACCTACGACGACGACCTGGACAACCTGCTGGCCAGATCG GCGACCAGTACGCCGACCTGTTCTGGCCGCAAGAACCTGAGCGACGCCATCCTGC TGAGCGACATCTGCGGGTGAACACCGAGATCACCAAGGCCCCCTGAGCGCCAGCA TGATCAAGCGGTACGACGAGCACCACAGGACCTGACCCTGTGAAGGCCCTGGTGC GGCAGCAGCTGCCCGAGAAGTACAAGGAGATCTTTCGACCAGAGCAAGAAGCGGC TACGCCGGCTACATCGACGGCGGCCAGCCAGGAGGAGTTCTACAAGTTTCATCAAG CCCATCTGGAGAAGATGGACGGCACCGAGGAGCTGCTGGTGAAGCTGAACCGGGA GGACCTGCTGCGGAAGCAGCGGACCTTCGACAACGGCAGCATCCCCACCAGATCCA CCTGGGCGAGCTGCACGCCATCTGCGGCGGACGAGGACTTCAACCTTCTGAA GGACAACCGGGAGAAGATCGAGAAGATCCTGACCTTCGGATCCCTACTACGTGGG CCCCCTGGCCCGGGCAACAGCCGGTTCGCTGGATGACCCGGAAGAGCGAGGAGA CCATACCCCCCTGGAACCTTCGAGGAGGTGGTGGACAAGGGCGCCAGCGCCAGAGC TTCATCGAGCGGATGACCAACTTCGACAAGAACCTGCCAACGAGAAGGTGCTGCC AAGCACGCCTGCTGTACGAGTACTTACCCTGTACAACGAGCTGACCAAGGTGAAG TACGTGACCGAGGGCATGCGGAAGCCGCCTTCTGAGCGGCGAGCAGAAGAAGGC CATCGTGGACCTGCTGTTCAAGACCAACCGGAAGGTGACCGTGAAGCAGCTGAAGG AGGACTACTTCAAGAAGATCGAGTGTTCGACAGCGTGGAGATCAGCGGCGTGGAG GACCGTTCAACGCCAGCTGGGCACCTACCACGACCTGCTGAAGATCATCAAGGAC AAGGACTTCTGGACAACGAGGAGAACGAGGACATCCTGGAGGACATCGTGTGAC CCTGACCCTGTTTCGAGGACCGGGAGATGATCGAGGAGCGGCTGAAGACCTACGCCCA</p>	122

[0722]

	<p>CCTGTTTCGACGACAAGGTGATGAAGCAGCTGAAGCGGGCGGCGGTACACCGGCTGGG GCCGGCTGAGCCGGAAGCTGATCAACGGCATCCGGGACAAGCAGAGCGGCAAGACC ATCCTGGACTTCTGAAGAGCGACGGCTTCGCCAACCGGAACTTCATGCAGCTGATC CACGACGACAGCCTGACCTTCAAGGAGGACATCCAGAAGGCCAGGTGAGCGGCCA GGGCGACAGCCTGCACGAGCACATCGCCAACCTGGCCGGCAGCCCCGCCATCAAGA AGGGCATCTGCAGACCTGTAAGGTGGTGGACGAGCTGGTGAAGGTGATGGGCCGG CACAAGCCCCGAGAATCTGTGATCGAGATGGCCGGGAGAACCAGACCACCCAGAA GGGCCAGAAGAACAGCCGGGAGCGGATGAAGCGGATCGAGGAGGGCATCAAGGAG CTGGGCAGCCAGATCCTGAAGGAGCACCCCTGGAGAACACCCAGCTGCAGAACGA GAAGCTGTACTGTACTACCTGCAGAACGGCCGGACATGTACGTGGACCAGGAGCT GGACATCAACCGGCTGAGCGACTACGACGTGGACCACATCGTGCCCCAGAGTTCCT GAAGGACGACAGCATCGACAACAAGGTGCTGACCCGGAGCGACAAGAACCGGGC AAGAGCGACAACGTGCCAGCGAGGAGGTGGTGAAGAAGATGAAGAACTACTGGCC CGAGCTGCTGAACGCCAAGCTGATCACCCAGCGGAAGTTCGACAACCTGACCAAGG CCGAGCGGGCGGCTGAGCGAGCTGGACAAGGCCGGCTTCATCAAGCGGCAGCTG GTGGAGACCCGGCAGATCACCAAGCAGTGGCCAGATCCTGGACAGCCGGATGAA CACCAAGTACGACGAGAACGACAAGCTGATCCGGGAGGTGAAGGTGATCACCTGA AGAGCAAGCTGGTGAAGGACTTCCGGAAGGACTTCCAGTTTACAAGGTGCGGGAG ATCAACAACCTACCACCGCCACGACGCCTACCTGAACCGCTGGTGGCCAGCCCT CTGATCAAGAAGTACCCCAAGCTGGAGAGCGAGTTCGTGTACGGCGACTACAAGGTG TACGACGTGCGGAAGATGATCGCCAAGAGCGAGCAGGAGATCGGCAAGGCCACCGC CAAGTACTTCTTACAGCAACATCATGAACTTCTTCAAGACCGAGATCACCCCTGGCC AACGGCGAGATCCGGAAGCGGCCCTGATCGAGACCAACGGCGAGACCCGGCAGAT CTGTGGGACAAGGGCCGGACTTCGCCACCGTGGGAAGGTGCTGAGCATGAGCAGCC AGGTGAACATCGTGAAGAAGACCGAGGTGCAGACCGCGGCTTCAGCAAGGAGAGC ATCCTGCCAAGCGGAACAGCGACAAGCTGATCGCCCGGAAGAAGGACTGGGACCC CAAGAAGTACGGCGGCTTCGACAGCCCCACCGTGGCTACAGCGTGTGGTGGTGGC CAAGGTGGAGAAGGGCAAGAGCAAGAAGCTGAAGAGCGTGAAGGAGTGTCTGGCC ATCACCATCATGGAGCGGAGCAGCTTCGAGAAGAACCCCATCGACTTCTGGAGGCC AAGGGCTACAAGGAGGTGAAGAAGGACCTGATCATCAAGCTGCCAAGTACAGCCT GTTTCGAGCTGGAGAACGGCCGGAAGCGGATGCTGGCCAGCGCCGGCGAGCTGCAGA AGGGCAACGAGCTGGCCCTGCCAGCAAGTACGTGAACTTCTGTACTTGGCCAGCC ACTACGAGAAGCTGAAGGGCAGCCCCGAGGACAACGAGCAGAAGCAGCTGTTCTGTG GAGCAGCACAAGCACTACCTGGACGAGATCATCGAGCAGATCAGCGAGTTCAGCAA GCGGGTATCCTGGCCGACGCCAACCTGGACAAGGTGCTGAGCGCTACAACAAGC ACCGGGACAAGCCATCCGGGAGCAGGCCGAGAATCATCCACCTGTTTACCCTGA CCAACCTGGCGCCCCGCCCTTCAAGTACTTCGACACCACCATCGACCCGAGCCGAA GGTACACCAGCACCAAGGAGGTGCTGGACGCCACCTGATCCACCAGACGATCACCCG GCCTGTACGAGACCCGGATCGACCTGAGCCAGCTGGGCGGCGACGGCGGCGGACG CCCAAGAAGAAGCGGAAGGTGTGA</p>	
<p>使用表4的低 A/U密码子, 具有两个C端 NLS序列及 起始及终止 密码子的 Cas9切口酶 ORF</p>	<p>ATGGACAAGAAGTACAGCATCGGCCTGGCCATCGGCACCAACAGCGTGGGCTGGGC GTGATCACCGACGAGTACAAGGTGCCAGCAAGAAGTTCAAGGTGCTGGCAACAC CGACCGGCACAGCATCAAGAAGAACCTGATCGCGGCCCTGCTGTTTCGACAGCGGCG AGACCGCCGAGGCCACCCGGCTGAAGCGGACCGCCCGGCGGCGGTACACCCGGCGG AAGAACCAGGATCTGCTACCTGCAGGAGATCTTACGCAACGAGATGGCCAAGGTGGAC GACAGCTTCTTCCACCGGCTGGAGGAGAGCTTCTGGTGGAGGAGGACAAGAAGCA CGAGCGGCACCCATCTTCGGCAACATCGTGGACGAGGTGGCTACCACGAGAAGTA CCCCACCATCTACCACCTGCGGAAGAAGCTGGTGGACAGCACCCGACAAGGCCGACCT GCGGCTGATCTACCTGGCCCTGGCCACATGATCAAGTTCGGGGCCACTTCTGATC GAGGGCGACCTGAACCCGACAACAGCGACGTGGACAAGCTGTTTATCCAGCTGGT GCAGACCTACAACAGCTGTTTCGAGGAGAACCCATCAACGCCAGCGGCGTGGACG CCAAGGCCATCCTGAGCGCCGGCTGAGCAAGAGCCGGCGGCTGGAGAACCTGATC GCCCAGCTGCCCAGGAGAGAAGAAGACGGCCTGTTTCGGCAACCTGATCGCCCTGAG CCTGGGCCTGACCCCAACTTCAAGAGCAACTTCGACCTGGCCGAGGACGCCAAGCT GCAGCTGAGCAAGGACACCTACGACGACGACCTGGACAACCTGCTGGCCAGATCG GCGACCAAGTACGCGACCTGTTCTGGCCGCAAGAACCTGAGCGACGCCATCCTGC TGAGCGACATCCTGCGGGTGAACACCGAGATCACCAAGGCCCCCTGAGCGCCAGCA TGATCAAGCGGTACGACGAGCACCACCAGGACCTGACCCTGCTGAAGCCCTGGTGC GGCAGCAGCTGCCGAGAAGTACAAGGAGATCTTCTTCGACCAGAGCAAGAACGGC TACGCCGTACATCGACGGCGGCCAGCCAGGAGGAGTTTACAAGTTCAATCAAG CCCATCCTGGAGAAGATGGACGGCACCGAGGAGCTGCTGGTGAAGCTGAACGGGA GGACCTGCTGCGGAAGCAGCGGACCTTCGACAACGGCAGCATCCCCACCAGATCCA CCTGGGCGAGCTGCACGCCATCTGCGGCGGCAGGAGGACTTACCCCTTCTGAA GGACAACCGGGAGAAGATCGAGAAGATCCTGACCTTCCGGATCCCTACTACGTGGG CCCCCTGGCCGGGGCAACAGCCGGTTCGCTGGATGACCCGGAAGAGCGAGGAGA CCATCACCCCTGGAACCTTCGAGGAGGTGGTGGACAAGGGCGCCAGCGCCAGAGC TTCATCGAGCGGATGACCAACTTCGACAAGAACCTGCCAACGAGAAGGTGCTGCC</p>	<p>123</p>

[0723]

	<p>AAGCACAGCCTGCTGTACGAGTACTTACCGTGTACAACGAGCTGACCAAGGTGAAG TACGTGACCGAGGGCATGCGGAAGCCCGCTTCTGAGCGGCGAGCAGAAGAAGGC CATCGTGGACCTGCTGTTCAAGACCAACCGGAAGGTGACCGTGAAGCAGCTGAAGG AGGACTACTTCAAGAAGATCGAGTGTTCGACAGCGTGGAGATCAGCGGCGTGGAG GACCGGTTCAACGCCAGCCTGGGCACCTACCACGACCTGCTGAAGATCATCAAGGAC AAGGACTTCTGGACAACGAGGAGAACGAGGACATCCTGGAGGACATCAAGTGTGAC CCTGACCCCTGTTTCGAGGACCGGGAGATGATCGAGGAGCGGCTGAAGACCTACGCCA CCTGTTGACGACAAGGTGATGAAGCAGCTGAAGCGGCGGCGGTACACCGCTGGG GCCGGTGAAGCGGAAGCTGATCAACGGCATCCGGGACAAGCAGAGCGGCAAGACC ATCCTGGACTTCTGAAGAGCGACGGCTTCGCCAACCAGGAACTTCATGCAGCTGATC CACGACGACAGCCTGACCTTCAAGGAGGACATCCAGAAGGCCAGGTGATCAAGGAG GGGCGACAGCCTGCACGAGCACATCGCCAACCTGGCCGGCAGCCCCGCCATCAAGA AGGGCATCCTGCAGACCGTGAAGGTGGTGGACGAGCTGGTGAAGGTGATGGGCCGG CACAAGCCCCGAGAATCGTGATCGAGATGGCCCGGGAGAACCAGACCACCCAGAA GGGCAGAGAACAGCCGGGAGCGGATGAAGCGGATCGAGGAGGGCATCAAGGAG CTGGGCAGCCAGATCCTGAAGGAGCACCCCGTGGAGAACCAGCTGCAGAACGA GAAGCTGTACCTGTACTACCTGCAGAACGGCCGGGACATGTACGTGGACCAGGAGCT GGACATCAACCGGCTGAGCGACTACGACGTGGACCACATCGTCCCCAGAGCTTCT GAAGGACGACAGCATCGACAACAAGGTGCTGACCCGAGCGACAAGAACCAGGGG AAGAGCGACAACGTGCCAGCGAGGAGGTGGTGAAGAAGATGAAGGTGATCACCTGC GCAGCTGCTGAACGCCAAGCTGATCACCCAGCGGAAGTTCGACAACCTGACCAAGG CCGAGCGGGGCGGCTGAGCGAGCTGGACAAGGCCGGCTTCATCAAGCGGCGAGCTG GTGGAGACCCGGCAGATCACCAAGCAGTGGCCAGATCCTGGACAGCCGGATGAA CACCAAGTACGACGAGAACGACAAGCTGATCCGGGAGGTGAAGGTGATCACCTGA AGAGCAAGCTGGTGAAGCGACTTCCGGAAGGACTTCCAGTTTACAAGGTGCGGGAG ATCAACAACCTACCACCGCCACGACGCTACCTGAACCGGCTGGTGGGCACCGCC CTGATCAAGAAGTACCCCAAGCTGGAGAGCGAGTTCGTGTACGGCGACTACAAGGTG TACGACGTGCGGAAGATGATCGCCAAGAGCGAGCAGGAGATCGGCAAGGCCACCGC CAAGTACTTCTTACAGCAACATCATGAACTTCTTCAAGACCGAGATCACCTGGCC AACGGCGAGATCCGGAAGCGGCCCTGATCGAGACCAACGGCGAGACCGGCGAGAT CGTGTGGGACAAGGGCCGGGACTTCGCCACCGTGCAGGAAGGTGCTGAGCATGCC AGGTGAACATCGTGAAGAAGACCGAGGTGCAGACCCGGCGGCTTCAGCAAGGAGAG ATCTGCCAAGCGGAACAGCAGCAAGCTGATCGCCGGAAGAAGGACTGGGACCC CAAGAAGTACGGCGGCTTCGACAGCCCCACCGTGGCCTACAGCGTGTGGTGGTGGC CAAGGTGGAGAAGGGCAAGAGCAAGAAGCTGAAGAGCGTGAAGGAGCTGCTGGGC ATCACCATCATGGAGCGGAGCAGCTTCGAGAAGAACCCATCGACTTCTGGAGGCC AAGGGCTACAAGGAGGTGAAGAAGGACCTGATCATCAAGCTGCCAAGTACAGCT GTTTCGAGCTGGAGAACCGGCCGGAAGCGGATGCTGGCCAGCGCCGGCGAGCAGA AGGGCAACGAGCTGGCCCTGCCAGCAAGTACGTGAACCTTCTGTACTTGGCCAGCC ACTACGAGAAGCTGAAGGGCAGCCCCGAGGACAACGAGCAGAAGCAGCTGTTCTGT GAGCAGCACAAGCACTACCTGGACGAGATCATCGAGCAGATCAGCGAGTTCAAGCA GCGGGTATCCTGGCCGAGCACAACCTGGACAAGGTGCTGAGCGCTACAACAAGC ACCGGGACAAGCCATCCGGGAGCAGGCCGAGAACATCATCCACCTGTTACCCTGA CCAACCTGGGCGCCCCGCCCTTCAAGTACTTCGACACCACCTGACCCGGAAGC GGTACACCAGCACAAGGAGGTGCTGGACGCCACCTGATCCACCAGAGCATCACCG GCCTGTACGAGACCCGATCGACCTGAGCCAGCTGGGCGGCGACGGCAGCGGCAGC CCCAAGAAGAAGCGGAAGGTGGACGGCAGCCCAAGAAGAAGCGGAAGGTGGACA GCGGCTGA</p>	
<p>使用表4的低 A/U密码子, 具有起始及 终止密码子 且无 NLS 的 Cas9 切口酶 ORF</p>	<p>ATGGACAAGAAGTACAGCATCGGCCTGGcCATCGGCACCAACAGCGTGGGCTGGGCC GTGATCACCGACGAGTACAAGGTGCCAGCAAGAAGTTCAAGGTGCTGGGCAACAC CGACCGGCACAGCATCAAGAAGAACCTGATCGGCGCCCTGCTGTTGACAGCGGGC AGACCCCGAGGCCACCCGGCTGAAGCGGACCGCCGGCGGCGGTACACCCGGCGG AAGAACCAGGATCTGCTACCTGCAGGAGATCTTACGCAACGAGATGGCCAAGGTGGAC GACAGCTTCTTCCACCGGCTGGAGGAGAGCTTCTGGTGGAGGAGGACAAGAAGCA CGAGCGGCACCCATCTTCGGCAACATCGTGGACGAGGTGGCCTACCACGAGAAGTA CCCCACCATCTACCACCTGCGGAAGAAGCTGGTGGACAGCACCGACAAGGCCGACCT GCGGCTGATCTACCTGGCCCTGGCCACATGATCAAGTTCGGGGGCACTTCTGATC GAGGGCGACCTGAACCCGACAACAGCGACGTGGACAAGCTGTTTCATCCAGCTGGT GCAGACCTACAACAGCTGTTTCGAGGAGAACCCATCAACGCCAGCGGCGTGGACG CCAAGGCCATCTGAGCGCCCGGCTGAGCAAGAGCCGGCGGCTGGAGAACCTGATC GCCAGCTGCCCGGCGAGAAGAAGAACGGCCTGTTCCGGCAACCTGATGCCCTGAG CCTGGGCTGACCCCAACTTCAAGAGCAACTTCGACCTGGCCGAGGACGCCAAGCT GCAGCTGAGCAAGGACACCTACGACGACGACCTGGACAACCTGCTGGCCAGATCG GCGACCAGTACGCCGACCTGTTCTGGCCGCAAGAACCTGAGCGACGCCATCCTGC TGAGCGACATCTGCGGGTGAACACCGAGATCACAAGGCCCCCTGAGCGCCAGCA TGATCAAGCGGTACGACGAGCACCACAGGACCTGACCCTGCTGAAGGCCCTGGTGC GGCAGCAGCTGCCGAGAAGTACAAGGAGATCTTCTTCGACCAGAGCAAGAACGGC</p>	<p>124</p>

[0724]

	<p>TACGCCGGCTACATCGACGGCGGCCAGCCAGGAGGAGTTCTACAAGTTCATCAAG CCCATCCTGGAGAAGATGGACGGCACCGAGGAGCTGCTGGTGAAGCTGAACCGGGA GGACCTGCTGCGGAAGCAGCGGACCTTCGACAACGGCAGCATCCCCACCAGATCCA CCTGGGCGAGCTGCACGCCATCTCGCGCGGCAGGAGGACTTCTACCCCTTCTGAA GGACAACCGGGAGAAGATCGAGAAGATCCTGACCTTCCGGATCCCCTACTACGTGGG CCCCTGGCCCGGGCAACAGCCGGTTCGCTGGATGACCCGGAAGAGCGGAGGAGA CCATCACCCCTGGAACCTTCGAGGAGGTGGTGGACAAGGGCGCCAGCGCCAGAGC TTCATCGAGCGGATGACCAACTTCGACAAGAACCTGCCAACGAGAAGGTGCTGCC AAGCACAGCCTGCTGTACGAGTACTTACCGTGTACAACGAGCTGACCAAGGTGAAG TACGTACCGAGGGCATGCGGAAGCCCGCCTTCTGAGCGGCAGCAGAAGAAGGC CATCGTGGACCTGCTGTTCAAGACCAACCGGAAGGTGACCGTGAAGCAGCTGAAGG AGGACTACTTCAAGAAGATCGAGTGTTCGACAGCGTGGAGATCAGCGGCGTGGAG GACCGGTTCAACGCCAGCCTGGGCACCTACCACGACCTGCTGAAGATCATCAAGGAC AAGGACTTCTGGACAACGAGGAGAACGAGGACATCCTGGAGGACATCGTGTGAC CCTGACCCTGTTGAGGACCGGAGATGATCGAGGAGCGGCTGAAGACCTACGCCCA CCTGTTGACGACAAGGTGATGAAGCAGCTGAAGCGGCGGGTACACCGGCTGGG GCCGGCTGAGCCGGAAGTGTATCAACGGCATCCGGGACAAGCAGAGCGGCAAGACC ATCCTGGACTTCTGAAGAGCGACGGCTTCGCCAACCGGAACCTTCATGCAGCTGATC CAGCAGCAGCCTGACCTTCAAGGAGGACATCCAGAAGGCCAGGTGAGCGGCCA GGGCGACAGCCTGCACGAGCATCGCCAACCTGGCCGCGAGCCCGCATCAAGA AGGGCATCCTGCAGACCGTGAAGGTGGTGGACGAGCTGGTGAAGGTGATGGCCGG CACAAGCCCCGAGAATCGTGTATCGAGATGGCCGGGAGAACCAGACCACCCAGAA GGGCCAGAAGAAGCCGGGAGCGGATGAAGCGGATCGAGGAGGGCATCAAGGAG TGGGACAGCCAGATCCTGAAGGAGCACCCCGTGGAGAACCACCCAGCTGCAGAACGA GAAGCTGTACCTGTACTACCTGCAGAACGGCCGGGACATGTACGTGGACCAGGAGCT GGACATCAACCGGCTGAGCGACTACGACGTGGACCACATCGTCCCCAGAGCTTCT GAAGGACGACAGCATCGACAACAAGGTGCTGACCCGAGCGACAAGAACCAGGGGC AAGAGCGACAACGTGCCAGCGAGGAGGTGGTGAAGAAGATGAAGAAGTACTAGCGG GCAGCTGCTGAACGCCAAGCTGATCACCAGCGGAAGTTCGACAACCTGACCAAGG CCGAGCGGGCGGCCCTGAGCGAGCTGGACAAGGCCGGCTTCATCAAGCGCAGCTG GTGGAGACCCGGCAGATCACAAGCAGCTGGCCAGATCCTGGACAGCCGGATGAA CACCAAGTACGACGAGAACGACAAGCTGATCCGGGAGGTGAAGGTGATCACCTGA AGCAAGCTGGTGGAGCTTCCGGAAGGACTTCCAGTTCTACAAGTGCAGGAG ATCAACAAGTACCACACGCCACGACGCCTACCTGAACGCCGTGGTGGGCACCGCC CTGATCAAGAAGTACCCCAAGCTGGAGAGCGAGTTCGTGTACGGCGACTACAAGGTG TACGACGTGCGGAAGATGATCGCCAAGAGCGAGCAGGAGATCGGCAAGGCCACCGC CAAGTACTTCTTCTACAGCAACATCATGAACTTCTTCAAGACCGAGATCACCTGGCC AACGGCGAGATCCGGAAGCGGCCCTGATCGAGACCAACGGCGAGACCCGGCGGAT CGTGTGGGACAAGGGCCGGACTTCGCCACCGTGGCAAGGTGCTGAGCATGCCCC AGGTGAACATCGTGAAGAAGACCGAGGTGCAGACCGCGGCTTCAGCAAGGAGAGC ATCCTGCCAAGCGGAACAGCGACAAGCTGATCGCCCGGAAGAAGGACTGGGAGCC CAAGAAGTACGGCGGCTTCGACAGCCCCACCGTGGCCTACAGCGTGTGGTGGGC CAAGGTGGAGAAGGGCAAGAGCAAGAAGCTGAAGAGCGTGAAGGAGCTGCTGGGC ATCACCATCATGGAGCGGAGCAGCTTCGAGAAGAACCCATCGACTTCTGGAGGCC AAGGGCTACAAGGAGGTGAAGAAGGACCTGATCATCAAGCTGCCAAGTACAGCCT GTTGAGCTGGAGAACGGCCGGAAGCGGATGCTGGCCAGCGCCGGCGAGCTGCAGA AGGGCAACGAGCTGGCCCTGGCCAGCAAGTACGTGAACCTTCTGTACTTGGCCAGCC ACTACGAGAAGCTGAAGGGCAGCCCCGAGGACAACGAGCAGAAGCAGCTGTTCTGTG GAGCAGCACAAGCACTACCTGGACGAGATCATCGAGCAGATCAGCGAGTTCAGCAA GCGGGTATCCTGGCCGACGCCAACCTGGACAAGGTGCTGAGCGCTACAACAAGC ACCGGACAAGCCATCCGGGAGCAGGCCGAGAACATCATCCACCTGTTCAACCCTGA CCAACCTGGGCGCCCCCGCCCTTCAAGTACTTCGACACCACCATCGACCGGAAGC GGTACACCAGCACAAGGAGGTGCTGGACGCCACCTGATCCACCAGAGCATCACCG GCCTGTACGAGACCCGGATCGACCTGAGCCAGCTGGGCGGCGACTGA</p>	
<p>使用表4的低 A/U密码子, 具有起始及 终止密码子 的 dCas9 ORF</p>	<p>ATGGACAAGAAGTACAGCATCGGCCTGGcCATCGGCACCAACAGCGTGGGCTGGGCC GTGATCACCGACGAGTACAAGGTGCCAGCAAGAAGTTCAAGGTGCTGGGCAACAC CGACCGGCACAGCATCAAGAAGAACCTGATCGGCGCCCTGCTGTTTCGACAGCGGCG AGACCGCCGAGGCCACCCGGCTGAAGCGGACCGCCCGGCGGGTACACCCGGCGG AAGAACCAGGATCTGCTACCTGCAGGAGATCTTACGCAACGAGATGGCCAAGGTGGAC GACAGCTTCTTCCACCGGCTGGAGGAGCTTCTGGTGGAGGAGGACAAGAAGCA CGAGCGGCACCCATCTTCGGCAACATCGTGGACGAGGTGGCTACCACGAGAAGTA CCCCACCATCTACCACCTGCGGAAGAAGCTGGTGGACAGCACCGACAAGGCCGACCT GCGGCTGATCTACCTGGCCCTGGCCACATGATCAAGTTCGGGGCCACTTCTGATC GAGGGCGACCTGAACCCGACAACAGCGAGCTGGACAAGCTGTTATCCAGCTGGT GCAGACTACAACCAGCTGTTTCGAGGAGAACCCCATCAACGCCAGCGCGTGGACG CCAAGGCCATCTGAGCGCCCGGCTGAGCAAGAGCCGGCGGCTGGAGAACCCTGATC GCCAGCTGCCCGGCGAGAAGAAGAACGGCCTGTTCCGCAACCTGATCGCCCTGAG</p>	<p>125</p>

[0725]

	<p>CCTGGGCCTGACCCCAACTTCAAGAGCAACTTCGACCTGGCCGAGGACGCCAAGCTGCAGCTGAGCAAGGACACCTACGACGACGACCTGGACAACCTGCTGGCCAGATCGGCGACCAGTACGCCGACCTGTTCTGCGCCGCAAGAACCTGAGCGACGCCATCCTGCTGAGCGACATCCTGCGGGTGAACACCGAGATCACCAGGGCCCCCTGAGCGCCAGCATGATCAAGCGGTACGACGAGCACCAGGACCTGACCCTGCTGAAGGCCCTGGTGC GGACGAGCTGCCGAGAAGTACAAGGAGATCTTCTTCGACCAGAGCAAGAACGGC TACGCCGGCTACATCGACGGCGGCCAGCCAGGAGGAGTTCTACAAGTTCATCAAG CCCATCTGGAGAAGATGGACGGCACCGAGGAGCTGCTGGTGAAGCTGAACCGGGA GGACCTGCTGCGGAAGCAGCGGACCTTCGACAACGGCAGCATCCCCACCAGATCCA CCTGGCGAGCTGCACGCCATCTGCGCGGCAGGAGGACTTCTACCCCTTCCTGAA AAGCAACCGGAGAAGATCGAGAAGATCCTGACCTTCGGATCCCTACTACGCTGGG CCCCCTGGCCCGGGCAACAGCCGGTTCGCTGGATGACCCGGAAGAGCGAGGAGA CCATACCCCTGGAACCTCGAGGAGGTGGTGGACAAGGGCGCCAGCGCCAGAGC TTCATCGAGCGGATGACCAACTTCGACAAGAACCTGCCAACGAGAAGGTGCTGCC AAGCACGCTGCTGTACGAGTACTTACCCTGTACAACGAGCTGACCAAGGTGAAG TACGTGACCGAGGGCATGCGGAAGCCCGCCTTCTGAGCGGCGAGCAGAAGAAGGC CATCGTGGACCTGCTGTTCAAGACCAACCGGAAGGTGACCGTGAAGCAGCTGAAGG AGGACTACTTCAAGAAGATCGAGTGTTCGACAGCGTGGAGATCAGCGGCGTGGAG GACCGGTTCAACGCCAGCTGGGCACCTACCAGCCTGCTGAAGATCATCAAGGAC AAGGACTTCTGGACAACGAGGAGAACGAGGACATCCTGGAGGACATCGCTGAC CCTGACCCCTGTTGAGGACCGGGAGATGATCGAGGAGCGGCTGAAGACCTACGCCA CCTGTTGACGACAAGGTGATGAAGCAGCTGAAGCGGCGGCGGTACACCGCTGGG GCGCGCTGAGCCGGAAGCTGATCAACGGCATCCGGGACAAGCAGAGCGGCAAGACC ATCTGGACTTCTGAAGAGCGACGGCTTCGCAACCGGAACTTCAATGACGCTGAC CACGACGACAGCCTGACCTTCAAGGAGGACATCCAGAAGGCCAGGTGAGCGGCCA GGGCGACAGCCTGCACGACACATCGCAACCTGGCCGGCAGCCCCGCTCAAGA AGGGCATCCTGCAGACCGTGAAGGTGGTGGACGAGCTGGTGAAGGTGATGGCCGG CACAAGCCCGAGAACATCGTGATCGAGATGGCCCGGAGAACCAGACCACCCAGAA GGGCCAGAAGAACAGCCGGGAGCGGATGAAGCGGATCGAGGAGGGCATCAAGGAG CTGGGCAGCCAGATCCTGAAGGAGCACCCCGTGGAGAACACCCAGCTGCAGAACGA GAAGCTGTACCTGTACTACCTGCAGAACGGCCGGGACATGTACGTTGACAGGAGCT GGACATCAACCGGCTGAGCGACTACGACGTGGAC_gCATCGTGCCCCAGAGCTTCTG AAGGACGACAGCATCGACAACAAGGTGCTGACCCGGAGCGACAAGAACCAGGGCA AGAGCGACAACGTGCCAGCGAGGAGGTGGTGAAGAAGATGAAGAATACTGGCGG CAGCTGCTGAACCCAAGCTGATCACCCAGCGGAAGTTCGACAACCTGACCAAGGC CGAGCGGGGCGGCTGAGCGAGCTGGACAAGGCCGGCTTCATCAAGCGGCAGCTGG TGGAGACCCGGCAGATCACAAGCACGTGGCCAGATCCTGGACAGCCGATGAAC ACCAAGTACGACGAGAACGACAAGCTGATCCGGGAGGTGAAGGTGATCACCTGAA GAGCAAGCTGGTGAGCGACTTCCGGAAGGACTTCCAGTTCTACAAGGTGCGGGAGAT CAACAATAACACCACGCCACGACGCTACCTGAACGCCGTGGTGGGCACCGCCCT GATCAAGAAGTACCCCAAGTGGAGAGCGAGTTCGTGTACGGCGACTACAAGGTGTA CGAGCTGCGGAAGATGATCGCCAAGAGCGAGCAGGAGATCGGCAAGCCAGGCCA AGTACTTCTTCTACAGCAACATCATGAACCTTCTTCAAGACCGAGATCACCCCTGGCCAA CGGCGAGATCCGGAAGCGGCCCTGATCGAGACCAACGGCGAGACCGGCGAGATCG TGTGGGACAAGGGCCGGGACTTCGCCACCGTGGCGAAGGTGCTGAGCATGCCCCAG GTGAACATCGTGAAGAAGACCGAGGTGCAGACCGCGGCTTCAGCAAGGAGAGCAT CCTGCCAAAGCGGAACAGCGACAAGCTGATCGCCCGAAGAAGGACTGGACCCCA AGAAGTACGGCGGCTTCGACAGCCCCACCGTGGCCTACAGCGTGTGGTGGTGGCA AAGGTGGAGAAGGGCAAGAGCAAGAAGCTGAAGAGCGTGAAGGAGCTGCTGGGCAT CACCATCATGGAGCGGAGCAGCTTCGAGAAGAACCCCATCGACTTCTGGAGGCCAA GGGCTACAAGGAGGTGAAGAAGGACCTGATCATCAAGCTGCCAAAGTACAGCTGTT CGAGCTGGAGAACGGCCGGAAGCGGATGCTGGCCAGCGCCGGCGAGCTGCAGAAGG GCAACGAGCTGGCCCTGCCAGCAAGTACGTGAACCTTCTGTACCTGGCCAGCCACT ACGAGAAGCTGAAGGGCAGCCCCGAGGACAACGAGCAGAAGCAGCTGTTCTGTGGA GCAGCACAAGCACTACCTGGACGAGATCATCGAGCAGATCAGCGAGTTCAGCAAGCG GGTGATCCTGGCCGACGCCAACCTGGACAAGGTGCTGAGCGCCTACAACAAGCAC GGGACAAGCCCATCCGGGAGCAGGCCGAGAACATCATCCACCTGTTACCCCTGACCA ACCTGGGCGCCCCGCCCTTCAAGTACTTCGACACCACCATCGACCGGAAGCGGT ACACAGCACAAGGAGGTGCTGGACGCCACCTGATCCACCAGAGCATCACCGGC CTGTACGAGACCCGGATCGACCTGAGCCAGCTGGGCGGCACGGCGGCGGCAAGCCC CAAGAAGAAGCGGAAGGTGTGA</p>	
<p>使用表4的低A/U密码子, 具有两个C端NLS序列及</p>	<p>ATGGACAAGAAGTACAGCATCGGCCTGGCCATCGGCACCAACAGCGTGGGCTGGGCCGTGATCACCGACGAGTACAAGGTGCCAGCAAGAAGTTCAAGGTGCTGGGCAACACCGACCGGCACAGCATCAAGAAGAACCTGATCGGCGCCCTGCTGTTGACAGCGGCGAGACCCGAGGCCACCCGGCTGAAGCGGACCCGGCGGCGGTACACCCGGCGG AAGAACCAGGATCTGCTACCTGCAGGAGATCTTACGCAACGAGATGGCCAAGGTGGACGACAGCTTCTCCACCGGCTGGAGGAGAGCTTCTGGTGGAGGAGACAAGAAGCA</p>	<p>126</p>

起始及终止 密码子的 dCas9 ORF	CGAGCGGCACCCCATCTTCGGCAACATCGTGGACGAGGTGGCCTACCACGAGAAGTA CCCCACCATCTACCACCTGCGGAAGAAGCTGGTGGACAGCACCGACAAGGCCGACCT GCGGCTGATCTACTTGGCCCTGGCCACATGATCAAGTTCCGGGGCCACTTCTGATC GAGGGCGACCTGAACCCCGACAACAGCGACGTGGACAAGCTGTTTCATCCAGCTGGT GCAGACCTACAACCAGCTGTTTCGAGGAGAACCCCATCAACGCCAGCGGCGTGGACG CCAAGGCCATCCTGAGCGCCCGGCTGAGCAAGAGCCGGCGGCTGGAGAACCTGATC GCCAGCTGCCCGGCGAGAAGAAGAACGGCCTGTTTCGGCAACCTGATCGCCCTGAG CCTGGGCCTGACCCCAACTTCAAGAGCAACTTCGACCTGGCCGAGGACGCCAAGCT GCAGCTGAGCAAGGACACCTACGACGACGACCTGGACAACCTGCTGGCCAGATCG GCGACCAGTACGCCGACCTGTTCTGGCCGCAAGAACCTGAGCGACGCCACTCTGC TGAGCGACATCCTGCGGGTGAACACCGAGATCACCAAGGCCCCCTGAGCGCCAGCA TGATCAAGCGGTACGACGAGCACCACCAGGACCTGACCCTGCTGAAGGCCCTGGTGC GGCAGCAGCTGCCGAGAAGTACAAGGAGATCTTTCGACCAGAGCAAGAACGGC TACGCCGGCTACATCGACGGCGGCCAGCCAGGAGGAGTTCTACAAGTTTCATCAAG CCCATCCTGGAGAAGATGGACGGCACCGAGGAGCTGCTGGTGAAGCTGAACCGGGA GGACCTGCTGCGGAAGCAGCGGACCTTCGACAACGGCAGCATCCCCACCAGATCCA CCTGGGCGAGCTGCACGCCATCCTGCGGCGGCAGGAGGACTTCTACCCCTTCTGAA GGACAACCGGGAGAAGATCGAGAAGATCCTGACCTTCGGATCCCTACTACGTGGG CCCCTGCCCGGGCAACAGCCGTTTCCTGGATGACCCGGAAGAGCGAGGAGA CCATCACCCCTGGAACCTTCGAGGAGGTGGTGGACAAGGGCGCCAGCCAGGAGC TTCATCGAGCGGATGACCAACTTCGACAAGAACCTGCCAACGAGAAGGTGCTGCC AAGCACAGCCTGCTGTACGAGTACTTCACCGTGTACAACGAGCTGACCAAGGTGAAG TACGTGACCGAGGGCATGCGGAAGCCGCCTTCTGAGCGGCGAGCAGAAGAAGGC CATCGTGGACCTGCTGTTCAAGACCAACCGGAAGGTGACCGTGAAGCTGAAGG AGGACTACTTCAAGAAGATCGAGTGTTCGACAGCGTGGAGATCAGCGGCGTGGAG GACCGGTTCAACGCCAGCCTGGGCACCTACCACGACCTGCTGAAGATCATCAAGGAC AAGGACTTCTGGACAACGAGGAGAACGAGGACATCCTGGAGGACATCGTGTGAC CCTGACCCTGTTTCGAGGACCGGGAGATGATCGAGGAGCGGCTGAAGACCTACGCCA CCTGTTTCGACGACAAGGTGATGAAGCAGCTGAAGCGGCGGCGGTACACCGGCTGG GCCGGCTGAGCCGGAAGCTGATCAACGGCATCCGGGACAAGCAGAGCGGCAAGACC ATCCTGGACTTCTGAAGAGCGACGGCTTCGCCAACCGGAACCTCATGCAGCTGATC CACGACGACAGCCTGACCTTCAAGGAGGACATCCAGAAGGCCAGGTGAGCGGCCA GGCGACAGCCTGCACGACCATCGCCAACCTGGCCGGCAGCCCGCATCAAGA AGGGCATCCTGCAGACCGTGAAGGTGGTGGACGAGCTGGTGAAGGTGATGGCCGG CACAAGCCCAGAACATCGTGATCGAGATGGCCCGGAGAACCAGACCACCCAGAA GGGCCAGAAGAACAGCCGGGAGCGGATGAAGCGGATCGAGGAGGGCATCAAGGAG CTGGCAGCCAGATCCTGAAGGAGCACCCCGTGGAGAACCAGCTGCAGAACGA GAAGCTGTACTTACTACCTGCAGAACCGCCGGGACATGTACTGTGACCGGAGCT GGACATCAACCGGCTGAGCGACTACGACGTGGACGCCATCGTCCCCAGAGCTTCT GAAGGACGACAGCATCGACAACAAGGTGCTGACCCGAGCGACAAGAACCAGGGG AAGAGCGACAACGTGCCAGCGAGGAGGTGGTGAAGAAGATGAAGAAGTACTTGGC CAGCTGCTGAACGCCAAGCTGATCACCCAGCGGAAGTTTCGACAACCTGACCAAG CCGAGCGGGGCGGCTGAGCGAGCTGGACAAGGCCGGCTTCATCAAGCGGCGAGCTG GTGGAGACCCGGCAGATCACCAAGCAGTGGCCAGATCCTGGACAGCCGGATGAA CACCAAGTACGACGAGAACGACAAGCTGATCCGGGAGGTGAAGGTGATCACCTGA AGCAAGCTGGTGAAGGACTTCCGGAAGGACTTCCAGTTTACAAGGTGCGGGAG ATCAACAACCTACCACCACGCCACGACGCTACCTGAACGCCGTGGTGGCAGCC CTGATCAAGAAGTACCCCAAGCTGGAGAGCGAGTTCGTGTACGGCGACTACAAGGTG TACGACGTGCGGAAGATGATCGCCAAGAGCGAGCAGGAGATCGGCAAGGCCACCGC CAAGTACTTCTTACAGCAACATCATGAACCTTCTTCAAGACCGAGATCACCCCTGGC AACGGCGAGATCCGGAAGCGGCCCTGATCGAGACCAACGGCGAGACCGGCGAGAT CGTGTGGGACAAGGGCCGGGACTTCGCCACCGTGCAGGAGGTGCTGAGCATGCC AGGTGAACATCGTGAAGAAGACCGAGGTGCAGACCGGCGGCTTCAGCAAGGAGAGC ATCCTGCCAAGCGGAACAGCGACAAGCTGATCGCCGGAAGAAGGACTGGGACCC CAAGAAGTACGGCGGCTTCGACAGCCCCACCGTGGCCTACAGCGTGTGGTGGTGGC CAAGGTGGAGAAGGGCAAGAGCAAGAAGCTGAAGAGCGTGAAGGAGCTGTGGGC ATCACCATCATGGAGCGGAGCAGCTTCGAGAAGAACCCATCGACTTCTGGAGGCC AAGGGCTACAAGGAGGTGAAGAAGGACCTGATCATCAAGCTGCCAAGTACAGCCT GTTTCGAGCTGGAGAACGGCCGGAAGCGGATGCTGGCCAGCGCCGGCGAGCTGCAGA AGGGCAACGAGCTGGCCCTGCCAGCAAGTACGTGAACCTTCTGTACTTGGCCAGCC ACTACGAGAAGCTGAAGGGCAGCCCCGAGGACAACGAGCAGAAGCAGCTGTTCTGTG GAGCAGCACAAGCACTACCTGGACGAGATCATCGAGCAGATCAGCGAGTTCAGCAA GCGGGTATCCTGGCCGACGCCAACCTGGACAAGGTGCTGAGCGCTACAACAAGC ACCGGGACAAGCCATCCGGGAGCAGCCGAGAACATCATCCACTGTTACCCTGA CCAACCTGGGCGCCCCGCCGCTTCAAGTACTTCGACACCACCATCGACCAGGAGC GGTACACCAGCACCAAGGAGGTGCTGGACGCCACCTGATCCACCAGAGCATCACCG GCCTGTACGAGACCCGGATCGACCTGAGCCAGCTGGGCGGCGACGGCAGCGGACG
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[0726]

	<p>CCCAAGAAGAAGCGGAAGGTGGACGGCAGCCCCAAGAAGAAGCGGAAGGTGGACA GCGGCTGA</p>	
<p>使用表4的低 A/U密码子, 具有起始及 终止密码子 且无 NLS 的 dCas9 ORF</p>	<p>ATGGACAAGAAGTACAGCATCGGCCTGGcCATCGGCACCAACAGCGTGGGCTGGGCC GTGATCACCGACGAGTACAAGGTGCCAGCAAGAAGTTCAAGGTGCTGGGCAACAC CGACCGGCACAGCATCAAGAAGAACCTGATCGGCGCCCTGCTGTTTCGACAGCGGCG AGACCGCCGAGGCCACCCGGCTGAAGCGGACCCCGCGGCGGTACACCCGGCGG AAGAACCAGGATCTGCTACCTGCAGGAGATCTTCAGCAACGAGATGGCCAAGGTGGAC GACAGCTTCTCCACCGGCTGGAGGAGAGCTTCTGTTGGAGGAGGACAAGAAGCA CGAGCGGCACCCCATCTTCGGCAACATCGTGGACGAGGTGGCCTACCACGAGAAGTA CCCCACCATCTACCACCTGCGGAAGAAGCTGGTGGACAGCACCGACAAGGCCGACCT GCGGCTGATCTACCTGGCCCTGGCCACATGATCAAGTTCGGGGCCACTTCTGTATC GAGGGCGACCTGAACCCCGACAACAGCGACGTGGACAAGCTGTTTCATCCAGCTGGT GCAGACCTACAACAGCTGTTTCGAGGAGAACCCCATCAACGCCAGCGGCGTGGACG CCAAGGCCATCTGAGCGCCCGGCTGAGCAAGAGCCGGCGGCTGGAGAACCTGATC GCCCAGTGGCCGCGAGAAGAAGAACGGCCTGTTTCGGCAACCTGATCGCCCTGAG CCTGGGCTGACCCCAACTTCAAGAGCAACTTCGACCTGGCCGAGGAGCCCAAGCT GCAGCTGAGCAAGGACACCTACGACGACGACCTGGACAACCTGCTGGCCAGATCG GCGACCAGTACGCCGACCTGTTCTGGCCGCCAAGAACCTGAGCGACGCCATCCTGC TGAGCGACATCTGCGGGTGAACACCGAGATCACCAGGCCCCCTGAGCGCCAGCA TGATCAAGCGGTACGACGAGCACACCAGGACCTGACCCTGCTGAAGGCTGCTGCC GGCAGCAGCTGCCGAGAAGTACAAGGAGATCTTCTTCGACCAGAGCAAGAACGGC TACGCCGGCTACATCGACGGCGGCCAGCCAGGAGGAGTTCTACAAGTTCATCAAG CCCATCTGGAGAAGATGGACGGCACCGAGGAGCTGCTGGTGAAGCTGAACCGGGA GGACCTGCTCGGAAGCAGCGGACCTTCGACAACGGCAGCATCCCCACCAAGTCCA CCTGGCGAGCTGCACGCCATCTGCGCGCGCAGGAGGACTTCTACCCCTCTCTGAA GGACAACCGGGAGAAGATCGAGAAGATCCTGACCTTCGGATCCCTACTACGTGGG CCCCCTGGCCCGGGGAACAGCCGGTTCGCCTGGATACCCGGAAGAGCGAGGAGA CCATACCCCTGGAACCTTCGAGGAGGTGGTGGACAAGGGCGCCAGCGCCAGAGC TTCATCGAGCGGATGACCAACTTCGACAAGAACCTGCCAACGAGAAGGTGCTGCC AAGCACAGCCTGCTGTACGAGTACTTACCCTGTACAACGAGCTGACCAAGGTGAAG TACGTGACCGAGGGCATGCGGAAGCCGCCTTCTGAGCGGCAGCAGAAGAAGGC CATCGTGGACCTGCTGTTCAAGACCAACCGGAAGGTGACCGTGAAGCAGCTGAAG AGGACTACTCAAGAAGATCGAGTGTCTCGACAGCGTGGAGATCAGCGGCTGAGG GACCGGTTCAACGCCAGCTGGGCACCTACCACGACCTGTGAAGATCATCAAGGAC AAGGACTTCTGGACAACGAGGAGAACGAGGACATCTGGAGGACATCGTGTGAC CCTGACCCTGTTTCGAGGACCGGGAGATGATCGAGGAGCGGCTGAAGACCTACGCCA CCTGTTTCGACGACAAGGTGATGAAGCAGCTGAAGCGGCGGCGGTACACCGGCTGGG GCCGCTGAGCCGGAAGCTGATCAACGGCATCCGGGACAAGCAGAGCGGCAAGACC ATCCTGGACTTCTGAAGAGCGACGGCTTCGCCAACCGGAACCTTCATGCAGCTGATC CACGACGACAGCCTGACCTTCAAGGAGGACATCCAGAAGGCCAGGTGAGCGGCCA GGGCGACAGCCTGCACGAGCACATCGCCAACCTGGCCGGCAGCCCCGCCATCAAGA AGGGCATCTGCAGACCGTGAAGGTGGTGGACGAGCTGGTGAAGGTGATGGGCCGG CACAAGCCCAGAACATCGTATCGAGATGGCCCGGGAGAACCAGACCCAGAA GGGCCAGAAGAACAGCCGGGAGCGGATGAAGCGGATCGAGGAGGGCATCAAGGAG CTGGGCGAGCAGATCCTGAAGGAGCACCCGTTGGAGAACACCCAGCTGCAGAACGA GAAGCTGTACCTGTACTACCTGCAGAACGGCCGGGACATGTACGTGGACCAGGAGCT GGACATCAACCGGCTGAGCGACTACGACGTGGACgCATCGTGCCCAAGCTTCTGT AAGGACGACAGCATCGACAACAAGGTGCTGACCCGGAGCGACAAGAACCAGGGGCA AGAGCGACAACGTGCCAGCGAGGAGGTGGTGAAGAAGATGAAGAATACTGGCGG CAGCTGCTGAACGCCAAGCTGATCACCCAGCGGAAGTTCGACAACCTGACCAAGGC CAGCGGGGCGGCTGAGCGAGCTGGACAAGGCCGGCTTCATCAAGCGCAGCTGG TGGAGACCCGGCAGATCACCAGCACGTGGCCAGATCTGGACAGCCGGATGAAC ACCAAGTACGACGAGAACGACAAGCTGATCCGGGAGGTGAAGGTGATCACCTGAA GAGCAAGCTGGTGAAGGACTTCCGGAAGGACTTCCAGTTCACAAGGTGCGGGAGAT CAACAATAACACACGCCACGACGCCTACCTGAACGCCGTGGTGGGACCCGCCCT GATCAAGAAGTACCCCAAGCTGGAGAGCGAGTTCGTGTACGGCAGTACAAGGTGTA CGACGTGCGGAAGATGATCGCCAAGAGCGAGCAGGAGATCGGCAAGGCCACCGCCA AGTACTTCTTACAGCAACATCATGAACCTTCAAGACCGAGATCACCTGGCCAA CGGCGAGATCCGGAAGCGGCCCTGATCGAGACCAACGGCGAGACCGGCGAGATCG TGTGGGACAAGGGCCGGGACTTCGCCACCGTGGCGAAGGTGCTGAGCATGCCCCAG GTGAACATCGTGAAGAAGACCGAGGTGCAGACCGCGGCTTCAGCAAGGAGAGCAT CCTGCCAAGCGGAACAGCGACAAGCTGATCGCCCGGAAGAAGGACTGGGACCCCA AGAAGTACGGCGGCTTCGACAGCCCCACCGTGGCCTACAGCGTGTGGTGGGCCA AGGTGGAGAAGGGCAAGAGCAAGAAGCTGAAGAGCGTGAAGGAGCTGCTGGGCAT CACCATCGGAGCGGAGCAGCTTCGAGAAGAACCATCGACTTCTGGAGGCCAA GGGCTACAAGGAGGTGAAGAAGGACCTGATCATCAAGCTGCCAAGTACAGCCTGTT CGAGCTGGAGAACGGCCGAAGCGGATGCTGGCCAGCGCCGGCAGCTGCAGAAGG</p>	<p>127</p>

[0727]

	<p>GCAACGAGCTGGCCCTGCCAGCAAGTACGTGAACTTCCTGTACCTGGCCAGCCACT ACGAGAAGCTGAAGGGCAGCCCGAGGACAACGAGCAGAAGCAGCTGTTCTGTGGA GCAGCACAAGCACTACCTGGACGAGATCATCGAGCAGATCAGCGAGTTCAGCAAGCG GGTGATCCTGGCCGACGCCAACCTGGACAAGGTGCTGAGCGCCTACAACAAGCACC GGGACAAGCCCATCCGGGAGCAGGCCGAGAATCATCCACCTGTTACCCTGACCA ACCTGGGCGCCCCGCCCTCAAGTACTTCGACACCACCATCGACCAGCGAAGCGGT ACACCAGCACAAGGAGGTGCTGGACGCCACCCTGATCCACCAGAGCATCACCGGC CTGTACGAGACCCGGATCGACCTGAGCCAGCTGGGCGGGGACTGA</p>	
<p>使用表4的低 A密码子, 具 有起始及终 止密码子的 Nme Cas9 ORF</p>	<p>ATGGCCGCTTCAAGCCCAACTCCATCAACTACATCCTGGGCCTGGACATCGGCATCG CCTCCGTGGGCTGGGCCATGGTGGAGATCGACGAGGAGGAGAACCCCATCCGGCTGA TCGACCTGGGCTGCGGGTGTTCGAGCGGGCCGAGGTGCCAAGACCGGCGACTCC CTGGCCATGGCCGCGGGTGGCCCGTCCGTGCGGCGGCTGACCCGGCGGGG CCACC GGCTGCTGCGGACCCGGCGGCTGCTGAAGCGGGAGGGCGTGTGACGGCCG CCAACCTCGACGAGAACCGGCTGATCAAGTCCCTGCCAACACCCCTGGCAGCTGC Nme Cas9 ORF ACCTGATCAAGCACCAGGCTACCTGTCCAGCGGAAGAACGAGGGCGAGCCGCC GACAAGGAGCTGGGCGCCCTGCTGAAGGGCGTGGCCGGCAACGCCACGCCCTGCA GACCGGCGACTTCCGGACCCCGCGGAGCTGGCCCTGAACAAGTTCGAGAAGGAGT CCGGCCACATCCGGAACAGCGGTCCGACTACTCCACACCTTCTCCGGAAAGGACC TGCAGGCGAGCTGATCCTGCTGTTTCGAGAAGCAGAAGGAGTTCGGCAACCCAC GTGTCCGGCGGCCTGAAGGAGGGCATCGAGACCCTGCTGATGACCCAGCGGCCCGCC CTGTCCGGCGACGCCGTGCAGAAGATGCTGGGCCACTGCACCTTCGAGCCCGCCGAG CCCAAGGCCGCCAAGAACACCTACACCGCCGAGCGGTTTCATCTGGCTGACCAAGCTG AACAACTGCGGATCCTGGAGCAGGGCTCCGAGCGGCCCTGACCGACCCGAGCG GGCACCCCTGATGGACGAGCCCTACCGGAAGTCCAAGCTGACCTACGCCACGGCCCG GAAGCTGCTGGGCTGGAGGACACCGCCTTCTTCAAGGGCCTGCGGTACGGCAAGG ACAACGCCGAGGCCTCACCCCTGATGGAGATGAAGGCCTACCACGCCATCTCCGGG CCCTGGAGAAGGAGGGCCTGAAGGACAAGAAGTCCCCCTGAACCTGTCCCCGAG CTGCAGGACGAGATCGGCACCCCTTCTCCCTGTTCAAGACCAGCAGGACATACC GGCCGGCTGAAGGACCGGATCCAGCCCGAGATCCTGGAGGCCCTGCTGAAGCACATC TCCTTCGACAAGTTCGTGCAGATCTCCCTGAAGGCCTGCGGGCGATCGTGCCCTGA TGGAGCAGGGCAAGCGGTACGACGAGGCCTGCGCCGAGATCTACGGCGACCACTAC GGCAAGAAGAACACCGAGGAGAAGATCTACTGCCCCCATCCCCGCCAGCAGATC CGGAACCCCGTGGTGTGCTGCGGGCCCTGTCCAGGCCGGAAGGTGATCAACCGCGT GGTGCGGCGGTACGGCTCCCCCGCCGGATCCACATCGAGACCGCCGGGAGGTGGG CAAGTCTTCAAGGACCGGAAGGAGATCGAGAAGCGGCAGGAGGAGAACCAGGAA GACCCGGGAGAAGGCCGCCGCCAAGTTCGGGAGTACTTCCCCAACTTCGTGGGCGA GCCCAAGTCCAAGGACATCCTGAAGTGCAGGCTGCGGCTGTACGAGCAGCAGCAGG GCCTGTACTCCGGAAGGAGATCAACCTGGGCGGCTGAACGAGAAGGGCTACGTG GAGATCGACCACGCCCTGCCCTTCTCCCGACCTGGGACGACTCCTTCAACAACAAG GTGCTGGTGTGGGCTCCGAGAACCAGAACAAGGGCAACCAGACCCCTACGAGTA CTTCAACGGCAAGGACAACCTCCCGGAGTGGCAGGAGTTCAAGGCCGGGTGGAGA CTCCCGGTTCCCCCGGTCCAGAAGCAGCGGATCCTGCTGCAGAAGTTCGACGAGG ACGGCTTCAAGGAGCGGAACCTGAACGACACCCGGTACGTGAACCGGTTCTGTGCC AGTTCGTGGCCGACCGGATGCGGCTGACCGGCAAGGGCAAGAAGCGGGTGTTCGCC TCCAACGGCCAGATACCAACCTGCTGCGGGGCTTCTGGGCTGCGGAAGGTGCGG TCCGAGAACGACCGGCACACGCCCTGGACGCCGTTGGTGGTGGCTGCTCCACCT GGCCATGCAGCAGAAGATCACCCGGTTCGTGCGGTACAAGGAGATGAACGCCTTCGA CGGCAAGACCATCGACAAGGAGACCGGCGAGGTGCTGCACCAGAAGACCCACTTCC CCCAGCCCTGGGAGTTCTTCGCCAGGAGGTGATGATCCGGGTGTTCCGGCAAGCCCG ACGGCAAGCCCGAGTTCGAGGAGGCCGACACCCTGGAGAAGCTGCGGACCCCTGCTG GCCGAGAAGCTGTCTCCCGGCCGAGGCCGTGCACGAGTACGTGACCCCTGTTTC GTGTCCCGGGCCCCAACCAGGAGATGTCGGCCAGGGCCACATGGAGACCGTGAA GTCCGCCAAGCGGCTGGACGAGGGCGTGTCCGTGCTGCGGGTGCCCTGACCCAGCT GAAGCTGAAGGACCTGGAGAAGATGGTGAACCGGGAGCGGGAGCCCAAGCTGTACG AGGCCCTGAAGGCCCGGCTGGAGGCCACAAGGACGACCCCGCCAAGGCCCTTCGCC GAGCCCTTACAAGTACGACAAGGCCGGCAACCGGACCCAGCAGGTGAAGGCCGT GCGGGTGGAGCAGGTGCAGAAGACCGGCGTGTGGGTGCGGAACCACAACGGCATCG CCGACAACGCCACCATGGTGCGGGTGGACGTGTTTCGAGAAGGGCGACAAGTACTAC CTGGTGGCCATCTACTCCTGGCAGGTGGCCAAGGGCATCCTGCCCGACCCGGCCGTG GTGAGGGCAAGGACGAGGAGGACTGGCAGCTGATCGACGACTCCTTCAACTTCAA GTTCTCCCTGCACCCCAACGACCTGGTGGAGGTGATCACAAGAAGGCCCGGATGTT CGGCTACTTCGCTCCTGCCACCGGGGACCGGCAACATCAACATCCGGATCCACGA CCTGGACCACAAGATCGGCAAGAACGGCATCCTGGAGGGCATCGGCTGAAGACCG CCGTGCTTCCAGAAGTACCAGATCGACGAGCTGGGCAAGGAGATCCGGCCCTGCC GGCTGAAGAAGCGGCCCCCGTGCAGTCCGGCAAGCGGACCGCCGACGGCTCCGAG TTCGAGTCCCCAAGAAGAAGCGGAAGGTGGAGTGA</p>	<p>128</p>

[0728]

[0729]

<p>使用表4的低A/U密码子, 具有起始及终止密码子的Nme Cas9 ORF</p>	<p>ATGGCCGCCTTCAAGCCCAACAGCATCAACTACATCTGGGCCTGGACATCGGCATCG CCAGCGTGGGCTGGGCCATGGTGGAGATCGACGAGGAGGAGAACCCCATCCGGCTG ATCGACCTGGGCGTGGGGTGTTCGAGCGGGCCGAGGTGCCAAGACCGGCGACAG CCTGGCCATGGCCCGGGCGGTGGCCCGGAGCGTGCGGCGGCTGACCCGGCGGGG CCCACCGGCTGCTGCGGACCCGGCGGCTGCTGAAGCGGGAGGGCGTGTGCAAGCC GCCAACTTCGACGAGAACCGGCTGATCAAGAGCCTGCCAACACCCCTGGCAGCTG CGGGCCGCCGCCCTGGACCGGAAGCTGACCCCTGGAGTGGAGCGCCGTGTGTGCT GCACCTGATCAAGCACCAGGGGCTACCTGAGCCAGCGGAAGAAGGAGGGCGAGACCG CCGACAAGGAGCTGGGCGCCCTGTGAAGGGCGTGGCCGGCAACGCCACGCCCTG CAGACCAGGACTTCCGACCCCGGAGCTGGCCCTGAACAAGTTCGAGAAGGA GAGCGCCACATCCGGAACAGCGGAGCGACTACAGCCACACCTTCAGCCGGGAAGG ACCTGCAGGCCGAGCTGATCCTGTGTTGAGAAGCAGAAGGAGTTCGGCAACCCCG ACGTGAGCGCGGCCCTGAAGGAGGGCATCGAGACCTGCTGATGACCCAGCGGCC GCCCTGAGCGGCGACGCCGTGACAGAAGATGTGGGCCACTGCACCTTCGAGCCCGCC GAGCCCAAGGCCGCCAAGAACACTACACCGCCGAGCGGTTTCATCTGGCTGACCA GCTGAACAACCTGCGGATCCTGGAGCAGGGCAGCGAGCGGCCCTGACCGACACCG AGCGGGCCACCCTGATGGACGAGCCCTACCGGAAGAGCAAGCTGACCTACGCCAG GCCCGGAAGCTGTGGCCTGGAGGACACCGCCTTCTTCAAGGGCCTGCGGTACGGC AAGGACAACGCCAGGCCAGCACCTGATGGAGATGAAGGCCCTACCAGCCATCAG CCGGCCCTGGAGAAGGAGGGCCTGAAGGACAAGAAGAGCCCTGACCGGAGCC CCGAGCTGCAGGACGAGATCGGCACCGCCTTACGCTGTTCAAGACCGACGAGGAC ATCACCGCCGGCTGAAGGACCGGATCCAGCCCGAGATCCTGGAGGCCCTGCTGAAG CACATCAGCTTCGACAAGTTCGTGACATCAGCTGAAGGCCCTGCGGCGGATCGTG CCTGTGATGGAGCAGGGCAAGCGGTACGACGAGGCTGCGCCGAGATCAGCGGCA CCACTACGGCAAGAAGAACACCGAGGAGAAGATCTACCTGCCCCCATCCCGCCGA CGAGATCCGGAACCCCGTGGTGTGCGGGCCCTGAGCCAGGCCCGGAAGGTGATCA ACGGCGTGGTGGCGGTTACGGCAGCCCGCCCGGATCCACATCGAGACCGCCCGGG AGGTGGGCAAGAGCTTCAAGGACCGGAAGGAGATCGAGAAGCGGCAGGAGGAGAA CCGGAAGGACCGGGAGAAGGCCGCCCAAGTTCGGGAGTACTTCCCAACTTCG TGGGCGAGCCCAAGAGCAAGGACATCCTGAAGCTGCGGCTGTACGAGCAGCAGCAC GGCAAGTGCCTGTACAGCGGCAAGGAGATCAACCTGGGCCGGTGAACGAGAAGGG CTACGTGGAGATCGACCAGCCCTGCCCTTACGCCGGACTGGGACGACAGCTTCAA CAACAAGGTGCTGGTGTGGCAGCGAGAACCAGAACAAGGGCAACAGCCCTT ACGAGTACTTCAACGGCAAGGACAACAGCCGGGAGTGGCAGGAGTTCAGGGCCCGG GTGGAGACCAGCCGTTCCCGCGAGCAAGAAGCAGCGGATCCTGCTGACAGAAGTT CGACGAGGACGGCTTCAAGGAGCGGAACCTGAACGACACCCGGTACGTGAACCGGT TCCTGTGCCAGTTCGTGGCCGACCGGATGCGGCTGACCGCAAGGGCAAGAAGCGG GTGTTTCGCCAGCAACGGCCAGATCACCAACTGCTGCGGGGCTTCTGGGGCTGCGG AAGGTGCGGGCCGAGAACGACCGGCACCACGCCCTGGACGCCGTGGTGGTGGCCTG CAGCACCGTGGCCATCGAGCAGAAGATACCCGGTTCGTGCGGTACAAGGAGATGAA CGCCTTCGACGGCAAGACCATCGACAAGGAGACCGGCGAGGTGCTGCACCAGAAGA CCCCTTCCCGAGCCCTGGGAGTTCCTCGCCAGGAGGTGATGATCGGGGTGTTTCG GCAAGCCCGACGGCAAGCCGAGTTCGAGGAGGCGGACACCCTGGAGAAGCTGCGG ACCCTGCTGGCCGAGAAGCTGAGCAGCCGGCCGAGGCCGTGCACGAGTACGTGAC CCCCCTGTTGCTGAGCCGGGCCCCCAACCGGAAGATGAGCGGCCAGGGCCACATGG AGACCGTGAAGAGCGCCAAGCGGCTGGACGAGGGCGTGAAGCGTGTGCGGGTGGCC GTGACCCAGCTGAAGCTGAAGACTGGAGAAGATGGTGAACCGGGGAGCGGAGCC CAAGCTGTACGAGGCCCTGAAGGCCCGGCTGGAGGCCACAAGGACGACCCCGCCA AGGCCTTCGCCGAGCCCTTACAAGTACGACAAGGCCGGCAACCGGACCCAGCAG GTGAAGGCCGTGCGGGTGGAGCAGGTGACAGAAGACCGGCCGTGTGGGTGCGGAACA CAACGGCATCGCCGACAACGCCACCATGGTGCGGGTGGACGTGTTGAGAAGGGCG ACAAGTACTACTGTTGCCATCTACAGCTGGCAGGTGGCCAAGGGCATCTGCCCG ACCGGGCCGTGGTGCAGGGCAAGGACGAGGAGGACTGGCAGCTGATCGACGACAGC TTCAACTTCAAGTTCAGCTGCACCCCAACGACCTGGTGGAGGTGATCACCAGAAG GCCCGGATGTTGCGTACTTCGCCAGCTGCCACCGGGGACCGGCAACATCAACATC CGGATCCAGACCTGGACCAAGAATCGGCAAGAACGGCATCCTGGAGGGCATCGGC GTGAAGACCGCCCTGAGCTTCCAGAAGTACCAGATCGACGAGCTGGGCAAGGAGAT CCGGCCCTGCGGCTGAAGAAGCGGCCCCCGTGCAGGAGCGGAAGCGGACCGCCG ACGGCAGCGAGTTCGAGAGCCCAAGAAGAAGCGGAAGGTGGAGTGA</p>	<p>129</p>
<p>具有NLS1的Cas9的开放阅读框架, 具有起始及终止密码子</p>	<p>ATGGACAAGAAGTACAGCATCGGACTGGACATCGGAACAACAGCGTCGGATGGGC AGTCATCACAGACGAATAAAGGTCCTCGAGCAAGAAGTTCAGGTCCTGGGAAACA CAGACAGACACAGCATCAAGAAGAACCTGATCGGAGCACTGCTGTTTCGACAGCGGA GAAACAGCAGAAGCAACAAGACTGAAGAGAACAGCAAGAAGAAGATACACAAGAA GAAAGAACAGAATCTGCTACCTGCAGGAAATCTTACGCAACGAAATGGCAAAGGTG CAGACAGCTTCCACAGACTGGAAGAAAGTTCCTGGTTCGAGAAGACAAAGAAG CACGAAAGACACCCGATCTTCGAAACATCGTCGACGAAATCGCATACCACGAAAAG TACCCGACAATCTACCACCTGAGAAAGAAGCTGGTCGACAGCACAGACAAGGCAGA</p>	<p>130</p>

[0730]

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CACTGACAAAACCTGGGAGCACCGGCAGCATTCAAGTACTTCGACACAACAATCGAC
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CATCACAGGACTGTACGAAAACAAGAATCGACTGAGCCAGCTGGGAGGAGACGGAG
GAGGAAGCCTGGCAGCAAAGAGAAGCAGAACAACATAG

<p>具有NLS2的 Cas9的开放 阅读框架,其 具有起始及 终止密码子</p>	<p>ATGGACAAGAAGTACAGCATCGGACTGGACATCGGAACAACAGCGTCGGATGGGC AGTCATCACAGACGAATACAAGGTCCTCCGAGCAAGAAGTTCAAGGTCCTGGGAAACA CAGACAGACACAGCATCAAGAAGAACCTGATCGGAGCACTGCTGTTTCGACAGCGGA GAAACAGCAGAAGCAACAAGACTGAAGAGAACAGCAAGAAGAAGATACACAAGAA GAAAGAACAGAATCTGCTACCTGCAGGAAATCTTCAGCAACGAAATGGCAAAGGTCG ACGACAGCTTCTCCACAGACTGGAAAGAAAGCTTCTGGTTCGAAGAAGACAAAGAAG CACGAAAGACACCCGATCTTCGGAACATCGTCGACGAAGTCGCATACCACGAAAAG TACCCGACAATCTACCACCTGAGAAAGAAGCTGGTCGACAGCACAGACAAGGCAGA CCTGAGACTGATCTACCTGGCACTGGCACACATGATCAAGTTCAGAGGACACTTCTGT ATCGAAGGAGACCTGAACCCGGACAACAGCGACGTCGACAAGCTGTTTCATCCAGCT GGTCCAGACATAACAACAGCTGTTTCGAAGAAGAAACCCGATCAACGCAAGCGGAGTCG ACGCAAAGGCAATCCTGAGCGCAAGACTGAGCAAGAGCAGAAGACTGGAAAACCTG ATCGCACAGCTGCCGGGAGAAAAGAAGAACGGACTGTTCCGAAACCTGATCGCACT GAGCCTGGGACTGACACCGAACTTCAAGAGCAACTTCGACCTGGCAGAAGACGCAA AGCTGACGCTGAGCAAGGACACATACGACGACGACCTGGACAACCTGCTGGCACAG ATCGGAGACCAGTACGACAGACCTGTTCTGGCAGCAAAGAACCTGAGCGACGCAATC CTGCTGAGCGACATCTGAGAGTCAACACAGAAATCACAAGGCACCGCTGAGCGC AAGCATGATCAAGAGATACGACGAACACCACAGGACCTGACACTGCTGAAGGCACT GGTCAGACAGCAGCTGCCGAAAAGTACAAGGAAATCTTCTTCGACCAGACAAGA ACGGATACGCAAGGATACATCGACGGAGGAGCAAGCCAGGAAGAATTCTAGAAGTTCA TCAAGCCGATCCTGGAAAAGATGGACGGAACAGAAGAACTGCTGGTCAAGCTGAAC AGAGAAGACCTGCTGAGAAAAGCAGAGAACATTCGACAACGGAAGCATCCCGCACA GATCCACCTGGGAGAAGTGCACGCAATCTGAGAAGACAGGAAGACTTCTACCCGTT CCTGAAGGACAACAGAGAAAAGATCGAAAAGATCCTGACATTCAGAACTCCGATCTA CGTCGGACCGCTGGCAAGAGGAAAACAGCAGATTCGCATGGATGACAAGAAAAGAGCG AAGAAACAATCACACCGTGGAACTTCAAGAAGTCGTCGACAAGGGAGCAAGCGCA CAGAGCTTATCGAAAAGATGACAACTTCGACAAGAACCTGCCGAACGAAAAGGT CCTGCCGAAGCACAGCCTGCTGTACGAATACTTACAGTCTACAACGAACTGACAAA GGTCAAGTACGTCACAGAAAGGAATGAGAAAGCCGGCATTCTGAGCGGAGAACAGA AGAAGGCAATCGTCGACCTGCTGTTCAAGACAAACAGAAAGGTCACAGTCAAGCAG CTGAAGGAAGACTACTTCAAGAAGATCGAATGCTTCGACAGCGTCAAGATCAGCGGA GTCGAAGACAGATTCAACGCAAGCCTGGGAACATACCACGACCTGCTGAAGATCATC AAGGACAAGGACTTCTGGACAACGAAGAAAACGAAGACATCCTGGAAAGCATCGT CCTGACACTGACACTGTTCAAGACAGAGAAATGATCGAAGAAAGACTGAAGACAT ACGCACACCTGTTTCGACGACAAGGTCATGAAGCAGCTGAAGAGAAGAAGATACACA GGATGGGGAAGACTGAGCAGAAAAGCTGATCAACGGAAATCAGAGACAAGCAGAGCGG AAAGACAATCCTGGACTTCTGAAGAGCGACGGATTTCGAAAACAGAAAATTCATGCA GCTGATCCACGACGACAGCCTGACATTCGAAGGAAGACATCCAGAAAGCAAGGTCA GCGGACAGGGAGACAGCCTGCACGAACACATCGCAAACCTGGCAGGAAGCCCGGCA ATCAAGAAGGGAATCCTGCAGACAGTCAAGGTGCTGACGAACTGGTCAAGGTTCATG GAGAAGACACAAGCCGGAAAACATCGTCATCGAAATGGCAAGAGAAAACAGACAAC ACAGAAGGGACAGAAGAACAGCAGAGAGAAAGAATGAAGAGAATCGAAGAAGGAATC AAGGAACTGGGAAGCCAGATCCTGAAGGAACACCCGGTTCGAAAACACACAGCTGCA GAACGAAAAGCTGTACTGTACTACCTGCAGAACGGAAGAGACATGTACGTCGACCA GGAATGGACATCAACAGACTGAGCGACTACGACGTCGACCACATCGTCCCGCAGAG CTTCTGAAGGACGACAGCATCGACAACAAGGTCCTGACAAGAAGCGACAAGAACA CAGAAAAGTACTTCTTACAGCAACATCATGAACCTTCTCAAGACAGAAATCACAC TGGAGACAGCTGCTGAACGCAAAGCTGATCACACAGAGAAAGTTTCGACAACCTGAC AAAGGCAGAGAGAGGAGGACTGAGCGAACTGGACAAGGCAGGATTCATCAAGAGA CAGCTGGTCAAGACAAGACAGATCACAAAGCACGTCGACAGATCCTGGACAGCAG AATGAACACAAAAGTACGACGAAAACGACAAGCTGATCAGAGAAGTCAAGGTTCATCA CACTGAAGAGCAAGCTGGTCAGCGACTTCAGAAAGGACTTCCAGTTCTACAAGGTCA GAGAAATCAACAATACCACCACGCACACGACGCATACCTGAACGACAGTCTCGGAA CAGCACTGATCAAGAAGTACCCGAAGCTGGAAAAGCGAATTCGTCTACGGAGACTACA AGGTCTACGACGTCAGAAAAGATGATCGCAAAGAGCGAACAGGAAATCGAAAAGGCA ACAGCAAAGTACTTCTTACAGCAACATCATGAACCTTCTCAAGACAGAAATCACAC TGGCAAACGGAGAAATCAGAAAAGACCGCTGATCGAAAACAAACGGAGAAAACAGG AGAAATCGTCTGGGACAAGGGAAGAGACTTCGCAACAGTCAAGAAAGGTCCTGAGCA TGCCGACAGTCAACATCGTCAAGAAGACAGAAGTCCAGACAGGAGGATTCAGCAAG GAAAGCATCCTGCCGAAGAGAAAACAGCGACAAGCTGATCGCAAGAAAAGAAAGGACTG GGACCCGAAGAAGTACGGAGGATTCGACAGCCCGACAGTCGCATACAGCGTCTGGT CGTCGCAAAGGTCGAAAAGGGAAGAGCAAGAAGCTGAAGAGCGTCAAGGAACTG CTGGGAATCACAATCATGGAAAAGCAGCTTCGAAAAGAACCCTGATCGACTTCTG GAAGCAAAAGGATACAAGGAAGTCAAGAAGGACCTGATCATCAAGTCCCGAAGTA CAGCCTGTTCAAGTGGAAAACGGAAAGAAAGAGAATGCTGGCAAGCGCAGGAGAAC TGCAGAAGGGAAACGAACTGGCACTGCCGAGCAAGTACGTCAACTTCTGTACTCTGG CAAGCCACTACGAAAAGCTGAAGGGAAGCCCGAAGACAACGAAACAGAAGCAGCT</p>	<p>131</p>
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[0731]

	<p>GTTTCGTCGAACAGCACAAGCACTACCTGGACGAAATCATCGAACAGATCAGCGAATT CAGCAAGAGAGTTCATCCTGGCAGACGCAAACCTGGACAAGGTCCTGAGCGCATAACA ACAAGCACAGAGACAAGCCGATCAGAGAACAGGCAGAAAACATCATCCACCTGTTC ACACTGACAAACCTGGGAGCACCAGGACGATTCAGAGTACTTCGACACAACAATCGAC AGAAAAGAGATACACAAGCACAAGGAAGTCTGGACGCAACACTGATCCACCAGAG CATCACAGGACTGTACGAAAACAAGAATCGACCTGAGCCAGCTGGGAGGAGACGGAG GAGGAAGCCAGGCAGCAAAGAGAAGCAGAACAACATAG</p>	
<p>具有NLS3的 Cas9的开放 阅读框架,其 具有起始及 终止密码子</p>	<p>ATGGACAAGAAGTACAGCATCGGACTGGACATCGGAACAAACAGCGTCGGATGGGC AGTCATCACAGACGAATACAAGGTCCTCCGAGCAAGAAAGTTCAAGGTCCTGGGAAACA CAGACAGACACAGCATCAAGAAGAACCTGATCGGAGCACTGCTGTTTCGACAGCGGA GAAACAGCAGAAGCAACAAGACTGAAGAGAACAGCAAGAAAGAAAGATACACAAGAA GAAAGAACAGAATCTGCTACCTGCAGGAAATCTTCAGCAACGAAATGGCAAAGGTCG ACGACAGCTTCTCCACAGACTGGAAGAAAGCTTCTGGTCAAGAAAGACAAGAAAG CACGAAAGACACCCGATCTTCGGAACATCGTCGACGAAGTCCGATACCACGAAAAG TACCCGACAATCTACCACCTGAGAAAAGAAGCTGGTCGACAGCACAGACAAGGCAG CCTGAGACTGATCTACCTGGCACTGGCACACATGATCAAGTTTCAGAGGACACTTCTCT ATCGAAGGAGACCTGAACCCGGACAACAGCGACGTCGACAAGCTGTTTCATCCAGCT GGTCCAGACATAACAACAGCTGTTCAAGAAAACCCGATCAACGCAAGCGGAGTCCG ACGCAAAGGCAATCCTGAGCGCAAGACTGAGCAAGAGCAGAAGACTGGAAAACCTG ATCGCACAGCTGCCGGGAGAAAAGAAGACCGGACTGTTTCGGAAACCTGATCGCACT GAGCCTGGGACTGACACCGAACTTCAAGAGCAACTTCGACCTGGCAGAAGACGCAA AGCTGCAGCTGAGCAAGGACACATACGACGACGACCTGGACAACCTGCTGGCACAG ATCGGAGACCAGTACGACAGCTGTTCTGGCAGCAAAGAACCTGAGCGACGCAATC CTGCTGAGCGACATCCTGAGAGTCAACACAGAAATCACAAGGCACCCGTCGAGCGC AAGCATGATCAAGAGATACGACGAAACACCAAGGACTGACACTGCTGAAGGACT GGTCAGACAGCAGCTGCCGAAAAGTACAAGGAAATCTTCTTCGACCAGAGCAAGA ACGGATACGCAGGATACATCGACGGAGGAGCAAGCCAGGAAGAATCTACAAGTTCA TCAAGCCGATCCTGGAAAAGATGGACGGAACAGAAGAAGTCTGGTCAAGCTGAAC AGAGAAGACCTGCTGAGAAAAGCAGAGAACATTTCGACAACGGAAGCATCCCGCACA GATCCACCTGGGAGAACTGCACGCAATCCTGAGAAGACAGGAAGACTTCTACCCGTT CCTGAAGGACAACAGAGAAAAGATCGAAAAGATCCTGACATTCAGAATCCCGTACTA CGTCGGACCCGCTGGCAAGAGGAAAACAGCAGATTCGCATGGATGACAAGAAAAGCGC AAGAAAACAATCACACCGTGGAACTTCAAGAAGTCTGTCGACAAGGGAGCAAGCGCA CAGAGCTTCAAGAAAAGTACAAAACCTTTCGACAAGAACCTGCCGAAACGAAAAGGT CCTGCCGAAGCACAGCCTGCTGTACGAATACTTACAGTCTACAACGAACTGACAAA GGTCAAGTACGTACAGAAAGGAATGAGAAAAGCCGGCATTCTGAGCGGAGAACAGA AGAAGGCAATCGTCGACCTGCTGTTCAAGACAACAGAAAAGGTCACAGTCAAGCAG CTGAAGGAAGACTACTTCAAGAAGATCGAATGCTTTCGACAGCGTCCGAAATCAGCGGA GTGCAAGACAGATTCAACGCAAGCCTGGGAACATACCACGACCTGCTGAAGATCATC AAGGACAAGGACTTCTGGACAACGAAGAAAACGAAGACATCCTGGAAGACATCGT CCTGACACTGACACTGTTCAAGACAGAGAAATGATCGAAGAAAAGACTGAAGACAT ACGCACACCTGTTTCGACGACAAGGTCATGAAGCAGCTGAAGAGAAGAAGATACACA GGATGGGGAAGACTGAGCAGAAAAGCTGATCAACGGAAATCAGAGACAAAGCAGAGCGG AAAGACAATCCTGGACTTCTGAAAGAGCGACGGATTTCGAAAACAGAAAACCTCATGCA GCTGATCCACGACGACAGCCTGACATTCAAGGAAGACATCCAGAAGGCACAGGTCA CGGGACAGGGGAGACAGCCTGCACGAACACATCGCAAACCTGGCAGGAAGCCCGGCA ATCAAGAAGGGAATCCTGACAGACAGTCAAGGTCGTCGACGAACTGGTCAAGGTCATG GGAAGACACAAGCCGGAAAACATCGTCATCGAAATGGCAAGAGAAAACAGACAAC ACAGAAGGGACAGAAGAAGCAGCAGAGAAAAGTGAAGAGAATCGAAGAAGGAATC AAGGAACTGGGAAGCCAGATCCTGAAGGAACACCCGGTCCGAAAACACACAGCTGCA GAACGAAAAGCTGTACTGTACTACCTGCAGAACGGAAGAGACATGTACGTCGACCA GGAACCTGGACATCAACAGACTGAGCGACTACGACGTCGACCACATCGTCCCGCAGAG CTTCTGAAAGGACGACAGCATCGACAACAAGGTCCTGACAAGAAGCGACAAGAACA GAGGAAAAGAGCGACAACGTCCTCCGAGCGAAGAAAGTCTGTAAGAAGTGAAGAAGTAC TGGAGACAGCTGCTGAACGCAAAGCTGATCACACAGAGAAAAGTTCGACAACCTGAC AAAGGCAGAGAGAGGAGGACTGAGCGAACTGGACAAGGCAGGATTCATCAAGAGA CAGCTGGTCAAAACAAGACAGATCACAAAGCACGTCGCACAGATCCTGGACAGCAG AATGAACACAAAGTACGACGAAAACGACAAGCTGATCAGAGAAGTCAAGGTCATCA CACTGAAGAGCAAGCTGGTCAAGGACTTCAGAAAGGACTTCCAGTTCTACAAGGTCA GAGAAATCAACAACCTACCACACGACACGACGACATACCTGAACGACGTCGTCGGAA CAGCACTGATCAAGAAGTACCCGAAGCTGGAAAAGCAATTCGTTCTACGGAGACTACA AGGTCTACGACGTCAGAAAAGTATGATCGCAAGAGCGAAGCAGGAAATCGGAAAAGGCA ACAGCAAAGTACTTCTTACAGCAACATCATGAACTTCTTCAAGACAGAAAATCACAC TGGCAAACCGGAGAAATCAGAAAAGAGCCGCTGATCGAAAACAAACGGAGAAAACAGG AGAAATCGTCTGGGACAAGGGAAGAGACTTCGCAACAGTCAAGAAAGGTCAGCA TGCCGAGGTCAACATCGTCAAGAAGACAGAAGTCCAGACAGGAGGATTCAGCAAG GAAAGCATCCTGCCGAAGAGAAAACAGCGACAAGCTGATCGCAAGAAAAGAAGGACTG</p>	<p>132</p>

[0732]

	<p>GGACCCGAAGAAGTACGGAGGATTCGACAGCCCGACAGTCGCATACAGCGTCCTGGT CGTCGCAAAGGTCGAAAAGGGAAAAGAGCAAGAAGCTGAAGAGCGTCAAGGAACTG CTGGGAATCACAATCATGGAAAGAAGCAGCTTCGAAAAGAACCCTGATCGACTTCCTG GAAGCAAAGGGATACAAAGGAAGTCAAGAAGGACCTGATCATCAAGCTGCCGAAAGTA CAGCCTGTTCGAACTGGAAAACGGAAAGAGAATGCTGGCAAGCGCAGGAGAAAC TGCAGAAGGGAAACGAACTGGCACTGCCGAGCAAGTACGTCAACTTCCTGTACTGG CAAGCCACTACGAAAAGCTGAAGGGAAAGCCCGGAAGACAACGAACAGAAGCAGCT GTTTCGTCGAACAGCACAAGCACTACCTGGACGAAATCATCGAACAGATCAGCGAATT CAGCAAGAGAGTCACTCTGGCAGACGCAACCTGGACAAGGTCCTGAGCGCATAACA ACAAGCACAGAGACAAGCCGATCAGAGAACAGGCAGAAAACATCATCCACCTGTTT ACACTGACAAAACCTGGGAGCACCGGCAGCATTCAAGTACTTCGACACAACAATCGAC AGAAAAGATACACAAGCACAAGGAAGTCTGGACGCAACACTGATCCACCAGAG CATCACAGGACTGTACGAAAACAAGAATCGACCTGAGCCAGCTGGGAGGAGACGGAG GAGGAAGCCCGCACCCGGCAAGAGAGAAAAGAAACAACATAG</p>	
<p>具有NLS4的 Cas9的开放 阅读框架,其 具有起始及 终止密码子</p>	<p>ATGGACAAGAAGTACAGCATCGGACTGGACATCGGAACAACAGCGTCGGATGGGC AGTCATCACAGACGAATACAAGGTCCCGAGCAAGAAGTTCAAGGTCCTGGGAAACA CAGACAGACACAGCATCAAGAAGAACCCTGATCGGAGCACTGCTGTTTCGACAGCGGA GAAACAGCAGAAGCAACAAGACTGAAGAGAACAGCAAGAAGAAGATACACAAGAA GAAAGAACAGAATCTGCTACCTGCAGGAAATCTTCAGCAACGAAATGGCAAAGGTCG ACGACAGCTTCTCCACAGACTGGAAGAAAGTCTCTGGTCCGAAAGAGCAACAAGAA CACGAAAAGACACCCGATCTTCGAAACATCGTCGACGAAAGTTCGCATACCACGAAAAG TACCCGACAATCTACCACCTGAGAAAAGAAGCTGGTCGACAGCACAGACAAGGCAGA CCTGAGACTGATCTACCTGGCACTGGCACACATGATCAAGTTCAGAGGACACTTCTCT ATCGAAGGAGACTGAACCCGGACAACAGCGACGTCGACAAGCTGTTTCATCCAGT GGTCCAGACATACAACCAGCTGTTTCGAAAGAAAACCCGATCAACGCAACAGCAGTCG ACGCAAAGGCAATCCTGAGCGCAAGACTGAGCAAGAGCAGAAGACTGGAAAACCTG ATCGCACAGCTGCCGGGAGAAAAGAAGAACGGACTGTTCCGAAACCTGATCGCACT GAGCCTGGGACTGACACCGAACTTCAAGAGCAACTTCGACCTGGCAGAAGACGCAA AGTGCAGCTGAGCAAGGACACATACGACGACGACCTGGACAACCTGCTGGCACAG ATCGGAGACCAGTACGACAGCTGTTCTGGCAGCAAAGAACCCTGAGCGACGCAATC CTGCTGAGCGACATCTGAGAGTCAACACAGAAATCACAAGGCACCGCTGAGCGC AAGCATGATCAAGAGATACGACGAAACACCACCAGGACCTGACACTGCTGAAGGCACT GGTCAGACAGCAGCTGCCGAAAAGTACAAGGAAATCTTCTTCGACCAAGCAAGA ACGGATACGCAAGGATACATCGACGGAGGAGCAAGCCAGGAAGAATTCTACAAGTTCA TCAAGCCGATCCTGGAAAAGATGGACGGAACAGAAGAACTGCTGGTCAAGCTGAAC AGAGAAGACCTGCTGAGAAAAGCAGAGAACATTCGACAACGGAAAGCATCCCGCACA GATCCACCTGGGAGAAGTGCACGCAATCCTGAGAAGACAGGAAGACTTCTACCCGTT CCTGAAGGACAACAGAGAAAAGATCGAAAAGATCCTGACATTCAGAACTCCCGTACTA CGTCGGACCGCTGGCAAGAGGAAAACAGCAGATTCGCATGGATGACAAGAAAAGAGCG AAGAAAACAATCACACCGTGGAACTTCAAGAAGTTCGTCGACAAGGGAGCAAGCGCA CAGAGCTTCAAGAAAAGATGACAAACTTCGACAAGAACCCTGCCGAACGAAAAGGT CCTGCCGAAGCACAGCCTGCTGTACGAATACTTCACAGTCTACAACGAACTGACAAA GGTCAAGTACGTCACAGAAAGCAATGAGAAAAGCCGGCATTCTGAGCGGAGAACAGA AGAAGGCAATCGTCGACCTGCTGTTCAAGACAAACAGAAAAGGTCACAGTCAAGCAG CTGAAGGAAGACTACTTCAAGAAGATCGAATGCTTCGACAGCGTTCGAAATCAGCGGA GTCGAAGACAGATTCAACGCAAGCCTGGGAACATACCACGACCTGCTGAAGATCATC AAGGACAAGGACTTCTGGACAACGAAGAAAACGAAGACATCCTGGAAAGACATCCTG CCTGACACTGACACTGTTTCGAAGACAGAGAAATGATCGAAGAAAAGACTGAAGACAT ACGCACACCTGTTTCGACGACAAGGTCATGAAGCAGCTGAAGAGAAGAAGATACACA GGATGGGGAAAGACTGAGCAGAAAAGCTGATCAACGGAAATCAGAGACAAGCAGAGCGG AAAGACAATCCTGGACTTCTGAAGAGCGACGGATTTCGAAAACAGAAAATTTCATGCA GCTGATCCACGACGACAGCTGACATTCAAGGAAGACATCCAGAAGGCACAGGTCAC GCGGACAGGGAGACAGCCTGCACGAACACATCGCAAACCTGGCAGGAAGCCCGGCA ATCAAGAAGGGAATCCTGCAGACAGTCAAGTTCGTCGACGAACTGGTCAAGGTCATG GGAAGACACAAGCCGGAAAACATCGTCATCGAAATGGCAAGAGAAAACCAGACAAC ACAGAAGGGACAGAAGAACAGCAGAGAAAAGAATGAAGAGAATCGAAGAAGGAATC AAGGAACTGGGAAGCCAGATCCTGAAGGAACACCCGGTTCGAAAACACACAGCTGCA GAACGAAAAGCTGTACTGTACTACCTGCAGAACGGAAGAGACATGTACGTCGACCA GGAATGGACATCAACAGACTGAGCGACTACGACGTCGACCACATCGTCCCGCAGAG CTTCTGAAGGACGACAGCATCGACAACAAGGTCCTGACAAGAAGCGACAAGAACA GAGGAAAAGAGCGACAACGTCGCCGAGCGAAGAAAGTCTCAAGAAGATGAAGAAGTAC TGGAGACAGCTGCTGAACGCAAAGCTGATCACACAGAGAAAAGTTTCGACAACCTGAC AAAGGCAGAGAGAGGAGGACTGAGCGAACTGGACAAGGCAGGATTCATCAAGAGA CAGCTGGTCAAACAAGACAGATCACAAAGCACGTCGCACAGATCCTGGACAGCAG AATGAACACAAGTACGACGAAAACGACAAGCTGATCAGAGAAGTCAAGGTCATCA CACTGAAGAGCAAGCTGGTCAGCGACTTCAGAAAAGGACTTCCAGTTCTACAAGGTC GAGAAATCAACAATACCACCACGCACACGACGATACCTGAACGCAGTCGTCGGAA</p>	<p>133</p>

[0733]

	<p>CAGCACTGATCAAGAAGTACCCGAAGCTGGAAAGCGAATTCGTCTACGGAGACTACA AGGTCTACGACGTCAGAAAAGATGATCGCAAAGAGCGAACAGGAAATCGGAAAGGCA ACAGCAAAGTACTTCTTCTACAGCAACATCATGAACTTCTTCAAGACAGAAATCACAC TGGCAAACGGAGAAATCAGAAAAGAGACCGCTGATCGAAAACAAACGGAGAAACAGG AGAAATCGTCTGGGACAAGGGAAAGAGACTTCGCAACAGTCAGAAAAGGTCCTGAGCA TGCCCGCAGGTCAACATCGTCAAGAAGACAGAAAGTCCAGACAGGAGGATTCAGCAAG GAAAGCATCCTGCCGAAGAGAAAACAGCGACAAGCTGATCGCAAGAAAAGAAAGGACTG GGACCCGAAGAAGTACGGAGGATTCGACAGCCCGACAGTCGCATACAGCGTCTGGT CGTCGCAAAGGTGCAAAAAGGGAAAAGAGCAAGAAAGCTGAAGAGCGTCAAGGAACTG CTGGGAATCACAATCATGGAAGAAGCAGCTTCGAAAAGAACCAGATCGACTTCTCTG GAAGCAAAGGGATACAAAGGAAGTCAAGAAGGACCTGATCATCAAGCTGCCGAAGTA CAGCCTGTTGAACTGGAAAACGGAAAGAGAATGCTGGCAAGCGCAGGAGAAC TGCAGAAGGGAAACGAACTGGCACTGCCGAGCAAGTACGTCAACTTCTGTACCTGG CAAGCCACTACGAAAAGCTGAAGGGAAAGCCCGAAGACAACGAACAGAAGCAGCT GTTTCGTAACAGCAACAAGCACTACCTGGACGAAATCATCGAACAGATCAGCGAAT CAGCAAGAGAGTATCCTGGCAGACGCAACCTGGACAAGGTCCTGAGCGCATAACA ACAAGCACAGAGACAAGCCGATCAGAGAACAGGCAGAAAACATCATCCACCTGTTC ACACTGACAAACCTGGGAGCACCAGCAGCATTCAAGTACTTCGACACAACAATCGAC AGAAAGAGATACACAAGCACAAGGAAGTCTGGACGCAACACTGATCCACCAGAG CATCACAGGACTGTACGAAACAAGAATCGACCTGAGCCAGCTGGGAGGAGACGGAG GAGGAAGCCAGGCAGCAAAGAGACCGAGAACAACATAG</p>
<p>具有NLS5的 Cas9的开放 阅读框架,其 具有起始及 终止密码子</p>	<p>ATGGACAAGAAGTACAGCATCGGACTGGACATCGGAACAACAGCGTCGGATGGGC AGTCATCACAGACGAATACAAGGTCCCGAGCAAGAAAGTTCAAGGTCCTGGGAAACA CAGACAGACACAGCATCAAGAAGAACCTGATCGGAGCACTGCTGTTCCGACAGCGGA GAAAACAGCAGAAGCAACAAGACTGAAGAGAACAGCAAGAAAGAAAGATACACAAGAA GAAAAGAACAGAATCTGCTACCTGCAGGAAATCTTCAGCAACGAAATGGCAAAGGTCCG ACGACAGCTTCTCCACAGACTGGAAGAAAGCTTCTGGTCAAGAAAGACAAGAAAG CACGAAAAGACACCCGATCTTCGAAACATCGTCGACGAAGTCGCATACCACGAAAAG TACCCGACAATCTACCACCTGAGAAAAGAAAGCTGGTCGACAGCACAGACAAGGCAGA CCTGAGACTGATCTACCTGGCACTGGCACACATGATCAAGTTCAGAGGACACTTCTCTG ATCGAAGGAGACCTGAACCCGGACAACAGCGACCTCGACAAGCTGTTTCATCCAGCT GGTCCAGACATAACAACAGCTGTTCCGAAGAAAACCCGATCAACGCAAGCGGAGTCCG ACGCAAAGGCAATCTGAGCGCAAGACTGAGCAAGAGCAGAAAGACTGGAAAACCTG ATCGCACAGCTGCCGGGAGAAAAGAAAGACGGACTGTTCCGAAAACCTGATCCACT GAGCCTGGGACTGACACCGAACTTCAAGAGCAACTTCGACCTGGCAGAAGACGCAA AGCTGCAGCTGAGCAAGGACACATACGACGACGACCTGGACAACCTGCTGGCACAG ATCGGAGACCAGTACGCAGACCTGTTCTGGCAGCAAAGAACCCTGAGCGACGCAATC CTGTGAGCGACATCCTGAGAGTCAACACAGAAAATCACAAGGCACCCGTCAGCGC AAGCATGATCAAGAGATACGACGAACACCACCAGGACCTGACACTGCTGAAGGCACT GGTCAGACAGCAGCTGCCGGAAAAGTACAAGGAAATCTTCTCGACCAGAGCAAGA ACGGATACGCAGGATACATCGACGGAGGAGCAAGCCAGGAAGAATCTACAAGTTCA TCAAGCCGATCCTGGAAAAGATGGACGGAAACAGAAGAAGTCTGGTCAAGTGAAC AGAGAAGACCTGCTGAGAAAAGCAGAGAAACATTTCGACAACGGAAAGCAGCAACCA GATCCACCTGGGAGAACTGCACGCAATCCTGAGAAGACAGGAAGACTTCTACCCGTT CCTGAAGGACAACAGAGAAAAGATCGAAAAGATCCTGACATTCAGAATCCCGTACTA CGTCGGACCGCTGGCAAGAGGAAAACAGCAGATTCGCATGGATGACAAGAAAAGAGCG AAGAAAACAATCACACCGTGGAACTTCAAGAAGTCTGTCGACAAGGGAGCAAGCGCA CAGAGCTTATCGAAAAGAAATGACAAACTTCGACAAGAACCCTGCCGAACGAAAAGGT CCTGCCGAAGCACAGCTGCTGTACGAATACTTCACAGTCTACAACGAACTGACAAA GGTCAAGTACGTACAGAAAGGAATGAGAAAGCCGGCATTCTGAGCGGAGAACAGA AGAAGGCAATCGTCGACCTGCTGTTCAAGACAACAGAAAAGGTCACAGTCAAGCAG CTGAAGGAAGACTACTTCAAGAAGATCGAATGCTTCGACAGCGTCAAGTCAAGGTCATG GTCGAAGACAGATTCAACGCAAGCCTGGGAACATACCACGACCTGCTGAAGATCATC AAGGACAAGGACTTCTGGACAACGAAGAAAACGAAGACATCCTGGAAGACATCGT CCTGACACTGACACTGTTCAAGACAGAGAAATGATCGAAGAAAGACTGAAGACAT ACGCACACCTGTTGACGACAAGGTCATGAAGCAGCTGAAGAGAAGAAGATACACA GGATGGGGAAGACTGAGCAGAAAAGCTGATCAACGGAATCAGAGACAAGCAGAGCGG AAAGACAATCCTGGACTTCTGAAGAGCGACGGATTTCGAAAACAGAAAACCTCATGCA GCTGATCCACGACGACAGCCTGACATTCAAGGAAGACATCCAGAAGGCACAGGTCA CGGGACAGGGAGACAGCCTGCACGAACACATCGAAAACCTGGCAGGAAGCCCGCA ATCAAGAAGGGAATCCTGCAGACAGTCAAGGTCTGTCGACGAACTGGTCAAGGTCATG GGAAGACACAAGCCGGAAAACATCGTCATCGAAATGGCAAGAGAAAACCAGACAAC ACAGAAGGGACAGAAGAAGCAGCAGAGAAAAGAAATGAAGAGAATCGAAGAAGGAATC AAGGAACTGGGAAGCCAGATCCTGAAGGAACACCCGGTCCGAAAACACACAGCTGCA GAAGAAAAGCTGTACCTGTACTACCTGCAGAACGGAAGAGACATGTACCTGCACCA GGAAGTGGACATCAACAGACTGAGCGACTACGACGTCGACCACATCGTCCCGCAGAG CTTCTGAAGGACGACAGCATCGACAACAAGGTCTGACAAGAAGCGACAAGAACA</p>

[0734]

[0735]

	<p>GAGGAAAGAGCGACAACGTCCCAGCGAAGAAGTCGTCAAGAAGATGAAGAAGTAC TGGAGACAGCTGCTGAACGCAAAAGCTGATCACACAGAGAAAAGTTTCACAACCTGAC AAAGGCAGAGAGAGGAGGACTGAGCGAACTGGACAAGGCAGGATTCATCAAGAGA CAGCTGGTCAAACAAAGACAGATCACAAAGCAGCTCGCACAGATCCTGGACAGCAG AATGAACACAAAGTACGACGAAAACGACAAGCTGATCAGAGAAGTCAAGGTCATCA CACTGAAGAGCAAGCTGGTCAAGCAGCTTCCAGTTCAGAAAAGGACTTCCAGTTCACAAGGTC GAGAAATCAACAACCTACCACCACGCACACGACGCATACCTGAACGCAGTCTCGGAA CAGCACTGATCAAGAAGTACCCGAAGCTGGAAAAGCGAATTTCGTCTACGGAGACTACA AGGTCTACGACGTCAAGAAAGATGATCGCAAAAGAGCGAACAGGAAATCGGAAAAGGCA ACAGCAAAAGTACTTCTTCTACAGCAACATCATGAACCTTCTCAAGACAGAAATCACAC TGGCAAACGGAGAAAATCAGAAAAGAGACCGCTGATCGAAAACAAACGGAGAAAACAGG AGAAATCGTCTGGGACAAGGGAAGAGACTTCGCAACAGTCAGAAAAGGTCCTGAGCA TGCCCGAGGTCAACATCGTCAAGAAGACAGAAGTCCAGACAGGAGGATTCAGCAAG GAAAGCATCTGCCGAAGAGAAAACAGCGACAAGCTGATCGCAAGAAAAGAAAGGACTG GGACCCGAAGAAGTACGGAGGATTCGACAGCCGACAGTCGCATACAGCGTCTGGT CGTCGCAAAGGTCGAAAAGGAAAAGAGCAAGAAGCTGAAGAGCGTCAAGGAACTG CTGGGAATCACATCATGGAAAGAAGCAGCTTCGAAAAGAACCCTGACTTCCTG GAAGCAAAGGGATACAAGGAAGTCAAGAAGGACCTGATCATCAAGTCTGCCGAAGTA CAGCCTGTTCAAGTGGAAAACGGAAGAAAGAGAATGCTGGCAAGCGCAGGAGAAC TGCAAGAGGGAACGAACTGGCACTGCCGAGCAAGTACGTCAAACTTCCACTCTGGT CAAGCCACTACGAAAAGCTGAAGGGAAGCCCGGAAGACAACGAACAGAAGCAGCT GTTCTGTCGAAACAGCACAAAGCACTACCTGGACGAAATCATCGAACAGATCAGCGAAT CAGCAAGAGAGTCACTCTGGCAGACGCAAACTGGACAAGGTCCTGAGCGCATAACA ACAAGCACAGAGACAAGCCGATCAGAGAACAGGAGAAAACATCATCCACTCTGTT ACACTGACAAACCTGGGAGCACCAGCAGCATTCAAGTACTTCGACACAACAATCGAC AGAAAAGAGATACACAAGCACAAAGGAAGTCTGGACGCAACTGATCCACCAGAG CATCACAGGACTGTACGAAAACAAGAATCGACCTGAGCCAGCTGGGAGGAGACGGAG GAGGAAGCAGAGCAGCAAAAGAGACCGGAGAACACATAG</p>	
<p>具有NLS6的 Cas9的开放 阅读框架,其 具有起始及 终止密码子</p>	<p>ATGGACAAGAAGTACAGCATCGGACTGGACATCGGAACAAACAGCGTCGGATGGGC AGTCATCACAGACGAATACAAGGTCCCAGCAAGAAGTTCAAGGTCCTGGGAAAACA CAGACAGACACAGCATCAAGAAGAACCTGATCGGAGCACTGCTGTTTCGACAGCGGA GAAACAGCAGAAGCAACAAGACTGAAGAGAACAGCAAGAAGAAAGATACACAAGAA GAAAGAACAGAATCTGCTACTTCAGGAAATCTTCAGCAACGAAATGGCAAAGGTCG ACGACAGCTTCTTCCACAGACTGGAAAGAAAGCTTCTGGTTCGAAAGAGACAAGAAAG CACGAAAAGACACCCGATCTTCGAAACATCGTCGACGAAGTCGCATACCACGAAAAG TACCCGACAATCTACCACCTGAGAAAAGAAAGCTGGTTCGACAGCACAGACAAGGCAGA CCTGAGACTGATCTACCTGGCACTGGCACACATGATCAAGTTCAGAGGACACTTCTG ATCGAAGGAGACCTGAACCCGACAACAGCGACGTCGACAAGCTGTTCTATCCAGT GGTCCAGACATAACAACCAGCTGTTTCGAAGAAAACCCGATCAACGCAAGCGGAGTCG ACGCAAAGGCAATCCTGAGCGCAAGACTGAGCAAGAGCAGAAGACTGGAAAACCTG ATCGCACAGCTGCCGGGAGAAAAGAAAGAACGGACTGTTTCGAAAACCTGATCGCACT GAGCCTGGGACTGACACCGAACTTCAAGAGCAACTTCGACCTGGCAGAAGACGCAAA AGCTGCAGCTGAGCAAGGACACATACGACGACGACTGGACAACCTGTTGGCAGAG ATCGGAGACCAGTACGACAGCTGTTCTGGCAGCAAAGAACCTGAGCGACGCAATC CTGCTGAGCGACATCCTGAGAGTCAACACAGAAAATCACAAAGGCACCGCTGAGCGC AAGCATGATCAAGAGATACGACGAACACCACCAGGACCTGACACTGCTGAAGGCACT GGTCAGACAGCAGCTGCCGAAAAGTACAAGGAAATCTTCTTCGACCAGAGCAAGA ACGGATACGCAGGATACATCGACGGAGGAGCAAGCCAGGAAGAATTCTACAAGTTCA TCAAGCCGATCCTGGAAAAGATGGACGGAACAGAAGAACTGCTGGTCAAGCTGAAC AGAGAAGACCTGCTGAGAAAAGCAGAGAAACATTCGACAACGGAAAGCATCCCGCACA GATCCACCTGGGAGAACTGCACGCAATCCTGAGAAGACAGGAAGACTTCTACCCGTT CCTGAAGGACAACAGAGAAAAGATCGAAAAGATCCTGACATTCAGAATCCCGTACTA CGTCGGACCGCTGGCAAGAGGAAAACAGCAGATTTCGATGGATGACAAGAAAAGAGCG AAGAAAACAATCACACCGTGGAACTTCGAAGAAGTCGTGACAAGGGAGCAAGCGCA CAGAGCTTATCGAAAAGATGACAACTTCGACAAGAACCTGCCGAACGAAAAGGT CCTGCCGAAGCACAGCTGCTGTACGATACTTCACAGTCTACAACGAACTGACAAA GGTCAAGTACGTCACAGAAGGAATGAGAAAGCCGGCATTCTGAGCGGAGAACAGA AGAAGGCAATCGTCGACCTGCTGTTCAAGACAAACAGAAAAGGTCACAGTCAAGCAG CTGAAGGAAGACTACTTCAAGAAGATCGAATGCTTCGACAGCGTCGAAAATCAGCGGA GTCGAAGACAGATTCAACGCAAGCCTGGGAACATACCACGACCTGCTGAAGATCATC AAGGACAAGGACTTCTGGACAACGAAGAAAACGAAGACATCCTGGAAGACATCGT CCTGACACTGACTGTTTCGAAGACAGAGAAATGATCGAAGAAAGACTGAAGACAT ACGCACACCTGTTTCGACGACAAGGTCATGAAGCAGCTGAAGAGAAGAAGATACACA GGATGGGGAAGACTGAGCAGAAAAGCTGATCAACGGAAATCAGAGACAAGCAGAGCGG AAAGACAATCCTGGACTTCTGAAAGAGCAGCGGATTCGCAAAACGAAACTTCATGCA GCTGATCCACGACGACAGCCTGACATTCAAGGAAGACATCCAGAAGGCACAGGTCA GCGGACAGGGAGACAGCCTGCACGAACACATCGCAAACTGGCAGGAAGCCCGGCA</p>	<p>135</p>

[0736]

	<p>ATCAAGAAGGGAATCTGCGACAGTCAAGGTCGTCGACGAACTGGTCAAGGTCATG GGAAGACACAAGCCGGAAAAATCGTCATCGAAATGGCAAGAGAAAACCAGACAAC ACAGAAGGGACAGAAGAACAGCAGAGAAAGAATGAAGAGAATCGAAGAAGGAATC AAGGAACTGGGAAGCCAGATCCTGAAGGAACACCCCGTCGAAAAACACACAGCTGCA GAACGAAAAGCTGTACTGTACTACCTGCAGAACCGGAAGAGACATGTACGTCGACCA GGAACCTGGACATCAACAGACTGAGCGACTACGACGTCGACCACATCGTCCCGCAGAG CTTCTCTGAAGGACGACAGCATCGACAACAAGGTCCTGACAAGAAGCGACAAGAACA GAGGAAAGAGCGACAACGTCCCGAGCGAAGAAGTCGTCGAAGAAGTGAAGAAGTAC TGGAGACAGCTGCTGAACGCAAAAGCTGATCACACAGAGAAAAGTTCGACAACCTGAC AAAGGCAGAGAGAGGAGGACTGAGCGAACTGGACAAGGCAGGATTCATCAAGAGA CAGCTGGTCGAAAACAAGACAGATCACAAAAGCACGTCGCACAGATCCTGGAGACTACA AATGAACACAAGTACGACGAAAACGACAAGCTGATCAGAGAAGTCAAGGTCATCA CACTGAAGAGCAAGCTGGTCAGCGACTTCAGAAAGGACTTCCAGTTCTACAAGGTC GAGAAATCAACAACCTACCACCACGACACGACGCATACCTGAACGCAGTCTCGGAA CAGCACTGATCAAGAAGTACCCGAAGCTGGAAAGCGAATTCGTCTACGGAGACTACA AGGTCTACGACGTCAGAAAAGATGATCGAAAAGAGCGAACAGGAAATCGGAAAAGCA ACAGCAAAGTACTTCTTCTACAGCAACATCATGAACCTTCTCAAGACAGAAATCACAC TGGCAAACGGGAAATCAGAAAAGAGACCGCTGATCGAAAACAAACGGGAAACAGG AGAAATCGTCTGGGACAAGGGAAGAGACTTCGCAACAGTCAGAAAAGGTCCTGAGCA CTGCCGAGGTC AACATCGTCAAGAAGACAGAAAGTCCAGACAGGAGGATTCAGCAAG GAAAGCATCCTGCCAAGAGAAAACAGCGACAAGCTGATCGCAAGAAAAGGAAAGGACTG GGACCCGAAGAAGTACGGAGGATTCGACAGCCCGACAGTCGCATACAGCGTCTGGT CGTCGCAAAGGTCGAAAAAGGAAAAGCAAGAAGCTGAAGAGCGTCAAGGAACTG CTGGGAATCACAATCATGGAAAAGAGCAGCTTCGAAAAGAACCAGATCGACTTCTG GAAGCAAAGGGATACAAGGAAGTCAAGAAGGACCTGATCATCAAGCTGCCGAAGTA CAGCCTGTTGAACTGGAAAACCGAAGAAAGAGAATGCTGGCAAGCGCAGGAGAAC TGCAGAAGGGAAACGAACTGGCACTGCCGAGCAAGTACGTCAACTTCTGTACTCTGG CAAGCCACTACGAAAAGCTGAAGGGAAAGCCCGAAGACAACGAACAGAAGCAGCT GTTCTCGAACAGCACAAAGCACTACCTGGACGAAATCATCGAACAGATCAGCGAATT CAGCAAGAGAGTCACTCTGGCAGACGCAAACCTGGACAAGGTCCTGAGCGCATACA ACAAGCACAGAGACAAGCCGATCAGAGAACAGGCAGAAAACATCATCCACCTGTTC ACACTGACAAACCTGGGAGCACCGGCAGCATTCAAGTACTTCGACACAACAATCGAC AGAAAAGAGATACACAAGCACAAAGGAAGTCTGGACGC AACACTGATCCACAGAG CATCACAGGACTGTACGAAAACAAGAATCGACCTGAGCCAGCTGGGAGGAGACGGAG GAGGAAGCGCAGCAGCAAAGAGAAGCTGGAGCATGGCAGCATAG</p>	
<p>具有NLS7的 Cas9 的开放 阅读框架,其 具有起始及 终止密码子</p>	<p>ATGGACAAGAAGTACAGCATCGGACTGGACATCGGAACAAACAGCGTCGGATGGGC AGTCATCACAGACGAATACAAGTCCCAGCAAGAAGTTCAAGGTCCTGGGAAAACA CAGACAGACACAGCATCAAGAAGAACCTGATCGGAGCACTGCTGTTCCAGACGCGGA GAAAACAGCAGAAGCAACAAGACTGAAGAGAACAGCAAGAAGAAGATACACAAGAA GAAAGAACAGAATCTGCTACCTGCAGGAAATCTTACGCAACGAAATGGCAAAGGTCG ACGACAGCTTCTTCCACAGACTGGAAGAAAAGCTTCTGGTGAAGAAGACAAGAAAG CACGAAAAGACACCCGATCTTCGGAACATCGTCGACGAAAGTGCATACACGAAAAG TACCCGACAATCTACCACCTGAGAAAAGAAAGTGGTCGACAGCACAGACAAGCAGAG CCTGAGACTGATCTACCTGGCACTGGCACACATGATCAAGTTCCAGAGGACACTTCTG ATCGAAGGAGACCTGAACCCGGACAACAGCGACGTCGACAAGCTGTTATCCAGCT GGTCCAGACATAACAACAGCTGTTCCGAAGAAAACCCGATCAACGCAAGCGGAGTCCG ACGCAAAGGCAATCCTGAGCGCAAGACTGAGCAAGAGCAGAAGACTGGAAAACCTG ATCGCACAGCTGCCGGGAGAAAAGAAGAACGGACTGTTCCGAAAACCTGATCGCACT GAGCCTGGGACTGACACCGAACTTCAAGAGCAACTTCGACCTGGCAGAAGACGCAA AGCTGCAGCTGAGCAAGGACACATACGACGACGACCTGGACAACCTGTGGCACAG ATCGGAGACCAGTACGCAGACCTGTTCTGGCAGCAAAGAACCTGAGCGACGCAATC CTGCTGAGCGACATCTGAGAGTCAACACAGAAAATCACAAAGGCACCCGTCGAGCGC AAGCATGATCAAGAGATACGACGAACACCACAGGACCTGACACTGCTGAAGGCACT GGTCAGACAGCAGCTGCCGGAAAAGTACAAGGAAATCTTCTCGACCAGAGCAAGA ACGGATACGCAGGATACATCGACGGAGGCAAGCCAGGAAGAATTCTACAAGTTCA TCAAGCCGATCCTGGAAAAGATGGACGGAAACAGAAGAAGTCTGGTCAAGCTGAAC AGAGAAGACCTGTGAGAAAAGCAGAGAACATTCGACAACGGAAAGCATCCCGCACC GATCCACCTGGGAGAAGTGCACGCAATCCTGAGAAGACAGGAAGACTTCTACCCGTT CCTGAAGGACAACAGAGAAAAGATCGAAAAGATCCTGACATTCAGAATCCCGTACTA CGTCGGACCGCTGGCAAGAGGAAAACAGCAGATTCGATGGATGACAAGAAAAGAGCG AAGAAAACAATCACACCGTGGAACTTCGAAGAAGTCTGTCGACAAGGGAGCAAGCGCA CAGAGCTTCATCGAAAAGATGACAACTTCGACAAGAACCTGCCGAACGAAAAGGT CCTGCCAAGCACAGCCTGCTGTACGAATACTTACAGTCTACAACGAACTGACAAA GGTCAAGTACGTCACAGAAGGAATGAGAAAGCCGGCATTCTGAGCGGAGAACAGA AGAAGGCAATCGTCGACTGTGTTCAAGACAAAACAGAAAAGGTCACAGTCAAGCAG CTGAAGGAAGACTACTTCAAGAAGATCGAATGCTTCGACAGCGTCGAAAATCAGCGGA GTCGAAGACAGATTCAACGCAAGCCTGGGAACATACCACGACCTGCTGAAGATCATC</p>	<p>136</p>

[0737]

	<p>AAGGACAAGGACTTCTTGACAACGAAGAAAACGAAGACATCTGGAAGACATCGT CCTGACACTGACACTGTTTCGAAAGACAGAGAAATGATCGAAGAAAAGACTGAAGACAT ACGCACACCTGTTTCGACGACAAGGTCATGAAGCAGCTGAAGAGAAGAAGATACACA GGATGGGGAAAGACTGAGCAGAAAAGCTGATCAACGGAATCAGAGACAAGCAGAGCGG AAAGACAATCTGGACTTCTGAAGAGCGACGGATTTCGCAAAACAGAAAATTCATGCA GCTGATCCACGACGACAGCCTGACATTCAAGGAAGACATCCAGAAGGCACAGGTCA GCGGACAGGGGAGACAGCCTGCACGAACACATCGCAAACTGGCAGGAAGCCCGGCA ATCAAGAAGGGAATCCTGCAGACAGTCAAGTTCGTCGACGAAGTCAAGGTCATG GGAAAGACACAAGCCGGAAAACATCGTCATCGAAATGGCAAGAGAAAACAGACAAC ACAGAAGGGACAGAAGAAGCAGCAGAGAAAAGAAATGAAGAGAATCAAGAAGGAATC AAGGAAGTGGGAAGCCAGATCTGAAAGGAACACCCCGTTCGAAAAACACAGCTGCA GAACGAAAAGCTGTACTGTACTACCTGCAGAACGGAAGAGACATGTACGTCGACCA GGAACTGGACATCAACAGACTGAGCGACTACGACGTCGACCACATCGTCCCGCAGAG CTTCTGAAGGACGACAGCATCGACAACAAGGTCTGACAAGAAGCGACAAGAACA GAGGAAAGAGCGACAACGTCCCGAGCGAAGAAGTTCGTCGAAGAAGATGAAGAACTAC TGGAGACAGCTGCTGAACGCAAAGCTGATCACACAGAGAAAAGTTCGACAACCTGAC AAAGGCAGAGAGAGGAGGACTGAGCGAACTGGACAAGGCAGGATTTCATCAAGAGA CAGCTGGTTCGAAACAAGACAGATCACAAAGCAGCTCGCACAGATCCTGGACAGCAG AATGAACACAAAAGTACGACGAAAACGACAAGCTGATCAGAGAAGTCAAGGTCATCA CACTGAAGAGCAAGCTGGTTCAGCGACTTCAGAAAGGACTTCCAGTTCACAAAGTCA GAGAAATCAACAATACCACCACGCACACGACGCATACCTGAACGCAGTTCGTCGGAA CAGCACTGATCAAGAAGTACCCGAAGCTGGAAAAGCGAATTCGTCTACGGAGACTACA AGGTCTACGACGTCAGAAAAGTATGATCGAAAAGAGCGAACAGGAAATCGGAAAAGCA ACAGCAAAGTACTTCTTCTACAGCAACATCATGAACTTCTTCAAGACAGAAATCACAC TGGCAAACGGAGAAATCAGAAAAGAGACCGCTGATCGAAAACAAACGGAGAAAACAGG AGAAATCGTCTGGGACAAGGGAAAGAGACTTCGCAACAGTCAGAAAAGGTCCTGAGCA TGCCCGAGGTCAACATCGTCAAGAAGACAGAAGTCCAGACAGGAGGATTCAGCAAG GAAAGCATCTGCCAAGAGAAAACAGCGACAAGCTGATCGCAAGAAAAGAAGGACTG GGACCCGAAGAAGTACGGAGGATTCGACAGCCGACAGTTCGCATACAGCGTCTGGT CGTCGCAAAGGTCGAAAAGGGAAAAGCAAGAAGCTGAAGAGCGTCAAGGAACTG CTGGGAATCACAATCATGGAAAAGCAGCTTCGAAAAGAACCCTGACTTCCTG GAAGCAAAGGGATAACAAGGAAGTCAAGAAGGACCTGATCATCAAGCTGCCGAAGTA AGCCTGTTTCGAACTGGAAAACGGAAAAGAGAATGCTGGCAAGCGCAGGAGAAAC TGCAGAAGGGAAACGAACTGGCACTGCCGAGCAAGTACGTCAACTTCTGTACTCTGG CAAGCCACTACGAAAAGCTGAAGGGAAAGCCCGAAGACAACGAACAGAAGCAGCT GTTTCGTGAAACAGCACAAGCACTACCTGGACGAAATCATCGAACAGATCAGCGAATT CAGCAAGAGAGTCACTCTGGCAGACGCAACCTGGACAAGGTCCTGAGCGCATACA ACAAGCACAGAGACAAGCCGATCAGAGAACAGGCAGAAAACATCATCCACCTGTTTC ACACTGACAAAACCTGGGAGCACCGGCAGCATTCAAGTACTTCGACACAACAATCGAC AGAAAAGATACACAAGCACAAAAGGAAGTCTGGACGCAACACTGATCCACCAGAG CATCACAGGACTGTACGAAAACAAGAATCGACCTGAGCCAGCTGGGAGGAGACGGAG GAGGAAGCGCAGCAGCAAAGAGAGTCTGGAGCATGGCATTCTAG</p>	
<p>具有NLS8的 Cas9 的开放 阅读框架, 其 具有起始及 终止密码子</p>	<p>ATGGACAAGAAGTACAGCATCGGACTGGACATCGGAACAAACAGCGTCGGATGGGC AGTCATCACAGACGAATACAAGTCCCGAGCAAGAAGTTCAAGGTCCTGGGAAAACA CAGACAGACACAGCATCAAGAAGAACCTGATCGGAGCACTGCTGTTTCGACAGCGGA GAAAACAGCAGAAGCAACAAGACTGAAGAGAACAGCAAGAAGAAGATACACAAGAA GAAAGAACAAGAATCTGCTACCTGCAGGAAATCTTCAGCAACGAAATGGCAAAGGTCG ACGACAGCTTCTTCCACAGACTGGAAGAAAGCTTCTGGTTCGAAAGAAGACAAGAAG CACGAAAAGACACCCGATCTTCGAAAACATCGTCGACGAAGTCGCATACCACGAAAAG TACCCGACAATCTACCACCTGAGAAAAGAGCTGGTTCGACAGCACAGACAAGGCAGA CCTGAGACTGATCTACCTGGCACTGGCACACATGATCAAGTTCAGAGGACACTTCTCTG ATCGAAGGAGACCTGAACCCGGACAACAGCGACGTCGACAAGCTGTTTCATCCAGCT GGTCCAGACATAACAACAGCTGTTTCGAAAGAAAACCCGATCAACGCAAGCGGAGTCG ACGCAAAGGCAATCCTGAGCGCAAGACTGAGCAAGAGCAGAAAGACTGGAAAACCTG ATCGCACAGCTGCCGGGAGAAAAGAAGAACGGACTGTTTCGAAAACCTGATCGCACT GAGCCTGGGACTGACACCGAACTTCAAGAGCAACTTCGACCTGGCAGAAAGACGCAA AGCTGCAGCTGAGCAAGGACACATACGACGACGACCTGGACAACCTGCTGGCACAG ATCGGAGACCAGTACGACAGCCTGTTCTGGCAGCAAAGAACCTGAGCGACGCAATC CTGCTGAGCGACATCCTGAGAGTCAACACAGAAATCACAAGGCACCGCTGAGCGC AAGCATGATCAAGAGATACGACGAACACCACAGGACCTGACACTGCTGAAGGCACCT GGTCAGACAGCAGCTGCCGGAAAAGTACAAGGAAATCTTCTTCGACCAGAGCAAGA ACGGATACGCAGGATACATCGACGGAGGCAAGCCAGGAAGAATTCTACAAGTTCA TCAAGCCGATCCTGGAAAAGATGGACGGAACAGAAGAAGTCTGGTCAAGCTGAAC AGAGAAGACCTGCTGAGAAAAGCAGAGAACATTCGACAACGGAAAGCATCCCGCACA GATCCACCTGGGAGAACTGCACGCAATCCTGAGAAAGACAGGAAGACTTCTACCCGTT CCTGAAGGACAACAGAGAAAAGATCGAAAAGATCTGACATTGAGAATCCCGTACTA CGTCGGACCGCTGGCAAGAGGAAAACAGCAGATTTCGCATGGATGACAAGAAAGAGCG</p>	<p>137</p>

[0738]

	<p>AAGAAACAATCACACCGTGGAACTTCGAAGAAGTCGTCGACAAGGGAGCAAGCGCA CAGAGCTTCATCGAAAAGAAATGACAACTTCGACAAGAACCTGCCGAACGAAAAGGT CCTGCCGAAGCACAGCCTGCTGTACGAATACTTCACAGTCTACAACGAACTGACAAA GGTCAAGTACGTACAGAAAGGAATGAGAAAGCCGGCATTCTGAGCGGAGAACAGA AGAAGGCAATCGTCGACCTGCTGTTCAAGACAAAACAGAAAGGTCACAGTCAAGCAG CTGAAGAAGGAACTTCAAGAAGATCGAATGCTTCGACAGCGTCGAAATCAGCGGA GTGCAAGACAGATTCAACGCAAGCCTGGGAACATACCACGACCTGCTGAAGATCATC AAGGACAAGGACTTCTGGACAACGAAGAAAACGAAGACATCTGGAAGACATCGT CCTGACACTGACACTGTTGCAAGACAGAGAAATGATCGAAGAAAGACTGAAGACAT ACGCACACCTGTTGACGACAAGGTCATGAAGCAGCTGAAGAGAAGAAGATACACA GGATGGGGAAGACTGAGCAGAAAGCTGATCAACGGAATCAGAGACAAGCAGAGCGG AAAGACAATCCTGGACTTCTGAAAGAGCGACGGATTTCGCAAAACAGAACTTCATGCA GCTGATCCACGACGACAGCCTGACATTCAAGGAAGACATCCAGAAGGCACAGGTCA GCGGACAGGGAGACAGCCTGCACGAACACATCGCAAACTGGCAGGAAGCCCGGCA ATCAAGAAGGAACTCTGACAGACAGTCAAGGTCGTCGACGAACCTGGTCAAGTCA GGAAGACACAAGCCGGAAAACATCGTTCATCGAAATGGCAAGAGAAAACAGACAAC ACAGAAGGGACAGAAGAAGCAGCAGAGAAAGAAATGAAGAGAATCGAAGAAGGAATC AAGGAACTGGGAAGCCAGATCTGAAAGAACACCCGGTGCAGAAAACACACAGCTGCA GAACGAAAAGCTGTACTGTACTACCTGCAGAACGGAAGAGACATGTACCGTGACCA GGAACTGGACATCAACAGACTGAGCGACTACGACGTCGACACATCGTCCCGCAGAG CTTCTGAAAGGACGACAGCATCGACAACAAGGTCCTGACAAGAAGCGACAAGAACA GAGGAAAAGAGCGACAACGTCCCGAGCGAAGAAGTCGTCGAAGAAGTGAAGAAGTAC TGGAGACAGCTGCTGAACGCAAAGCTGATCACACAGAGAAAAGTTCGACAACCTGAC AAAGGCAGAGAGAGGAGGACTGAGCGAACTGGACAAGGCAGGATTTCAGAAAGA CAGCTGGTCAAACAAGACAGATCACAAAGCACGTCGACAGATCTGGACAGCAG AATGAACACAAAGTACGACGAAAACGACAAGCTGATCAGAGAAGTCAAGGTCATCA CACTGAAGAGCAAGCTGGTCAAGGACTTCAGAAAGGACTTCAGTTCTACAAGGTCA GAGAAATCAACAATAACACCACGCACACGACGACATACCTGAACGACGTCGTCGGAA CAGCACTGATCAAGAAGTACCCGAAGCTGGAAAAGCAATTCGTCACGGAGACTACA AGGTCTACGACGTCAGAAAAGATGATCGCAAAGAGCGAAGCAGGAAATCGGAAAAGCA ACAGCAAAGTACTTCTTACAGCAACATCATGAACTTCTTCAAGACAGAAAATCACAC TGGCAAACGGGAAATCAGAAAAGAGACCGCTGATCGAAAACAAACGGAGAAAACAGG AGAAATCGTCTGGGACAAGGGAAGAGACTTCGCAACAGTCAGAAAAGGTCCTGAGCA TGCCGCAGGTCAACATCGTCAAGAAGACAGAAGTCCAGACAGGAGGATTTCAGCAAG GAAAGCATCCTGCCGAAGAGAAAACAGCGACAAGCTGATCGCAAGAAAAGAAAGGACTG GGACCCGAAGAAGTACGGAGGATTCGACAGCCGACAGTCGACATACAGCGTCTGCTGGT CTGCGCAAAGGTCGAAAAGGAAAAGCAAGAAGCTGAAGAGCGTCAAGGAACTGT CTGGGAATCAACAATCATGGAAGAAGCAGCTTCGAAAAGAACCCTGATCGACTTCTG GAAGCAAAGGGATAACAAGGAAGTCAAGAAGGACCTGATCATCAAGCTGCCGAAGTA CAGCCTGTTGAACTGGAAAACGGAAGAAAAGAGAATGCTGGCAAGCGCAGGAGAAC TGAGAAGGGAAACGAACTGGCACTGCCGAGCAAGTACGTCAACTTCTGTACTCTGG CAAGCCACTACGAAAAGCTGAAGGGAAGCCCGAAGACAACGAACAGAGAAGCAGCT GTTCTGTCGAACAGCACAAGCACTACCTGGACGAAATCATCGAACAGATCAGCGAATT CAGCAAGAGAGTATCCTGGCAGACGCAAACCTGGACAAGGTCCTGAGCGCATAACA ACAAGCAGAGACAAGCCGATCAGAGAACAGGCAGAAAACATCATCCACCTGTTT ACACTGACAAACCTGGGAGCACCGGCAGCATTCAAGTACTTCGACACAACAATCGAC AGAAAAGAGATACACAAGCACAAGGAAGTCTGGACGCAACACTGATCCACAGAG CATCACAGGACTGTACGAAAACAAGAATCGACCTGAGCCAGCTGGGAGGAGACGGAG GAGGAAGCGCAGCAGCAAAGAGAAGCTGGAGCATGGCATTCTAG</p>	
<p>具有NLS9的 Cas9的开放 阅读框架,其 具有起始及 终止密码子</p>	<p>ATGGACAAGAAGTACAGCATCGGACTGGACATCGGAACAAACAGCGTCGGATGGGC AGTTCATCACAGACGAATACAAGTCCCGAGCAAGAAGTTCAAGTCTCTGGGAAAACA CAGACAGACACAGCATCAAGAAGAACCTGATCGGAGCACTGCTGTTGACAGCGGA GAAACAGCAGAAGCAACAAGACTGAAGAGAACAGCAAGAAGAAGATACACAAGAA GAAAGAACAGAATCTGCTACCTGCAGGAAATCTTACGCAACGAAATGGCAAAGGTGC ACGACAGCTTCTTCCACAGACTGGAAGAAAGCTTCTGGTCAAAGAAGACAAGAAG CACGAAAAGACACCCGATCTTCGAAAACATCGTCGACGAAGTCGATACCACGAAAAG TACCCGACAATCTACCACCTGAGAAAAGAGCTGGTTCGACAGCACAGACAAGGCAGA CCTGAGACTGATCTACCTGGCACTGGCACACATGATCAAGTTCAGAGGACACTTCTGT ATCGAAGGAGACCTGAACCCGGACAACAGCGACGTCGACAAGCTGTTATCCAGT GGTCCAGACATAACAACAGCTGTTGCAAGAAAACCCGATCAACGCAAGCGGAGTCTG ACGCAAAGGCAATCCTGAGCGCAAGACTGAGCAAGAGCAGAAAGACTGGAAAACCTG ATCGCACAGCTGCCGGGAGAAAAGAAGAACGGACTGTTGGAACCTGATCGCACT GAGCCTGGGACTGACACCGAACTTCAAGAGCAACTTCGACCTGGCAGAAGACGCAA AGCTGCAGCTGAGCAAGGACACATACGACGACGACCTGGACAACCTGCTGGCACA ATCGGAGACCAGTACGACAGCTGTTCTGGCAGCAAAGAACCCTGAGCGCAATC CTGCTGAGCGACATCTGAGAGTCAACACAGAAATCACAAGGCACCGCTGAGCGC AAGCATGATCAAGAGATACGACGAACACCACAGGACCTGACTGCTGAAGGCACT</p>	<p>138</p>

[0739]

	<p>GGTCAGACAGCAGCTGCCGAAAAGTACAAGGAAATCTTCTTCGACCAAGCAAGA ACGGATACGCAGGATACATCGACGGAGGAGCAAGCCAGGAAGAATTCTACAAGTTCA TCAAGCCGATCCTGGAAAAGATGGACGGAACAGAAGAACTGCTGGTCAAGCTGAAC AGAGAAGACCTGCTGAGAAAAGCAGAGAACATTCGACAAACGGAAGCATCCCGCACCA GATCCACCTGGGAGAAGTGCACGCAATCCTGAGAAGACAGGAAGACTTCTACCCGTT CCTGAAGGACAACAGAGAAAAGATCGAAAAGATCCTGACATTCAGAATCCTCGTACTA CGTCGGACCGCTGGCAAGAGGAAAACAGCAGATTCGCATGGATGACAAGAAAAGAGCG AAGAAAACAATCACACCGTGGAACTTCAAGAAAGTCGTCGACAAGGGAGCAAGCGCA CAGAGCTTCATCGAAAAGATGACAACTTCGACAAGAACCTGCCGAACGAAAAGGT CCTGCCGAAGCACAGCTGCTGTACGAATACTTCACAGTCTACAACGAACTGACAAA GGTCAAGTACGTACAGAAAGGAATGAGAAAAGCCGGCATTCTGAGCGGAGAACAGA AGAAGGCAATCGTCGACCTGCTGTTCAAGACAAAACAGAAAAGGTCACAGTCAAGCAG CTGAAGGAAGACTACTTCAAGAAGATCGAATGCTTCGACAGCGTCGAAAATCAGCGGA GTCGAAGACAGATTCAACGCAAGCCTGGGAACATACCACGACCTGCTGAAGATCATC AAGGACAAGGACTTCTGGACAACGAAAGAAAACGAAGACATCCTGGAAGCAGAGTCA CCTGACACTGACACTGTTGGAAGACAGAGAAATGATCGAAGAAAAGACTGAAGACAT ACGCACACCTGTTGACGACAAGGTCATGAAGCAGCTGAAGAGAAGAAGATACACA GGATGGGGAAAGACTGAGCAGAAAAGCTGATCAACGGAAATCAGAGACAAGCAGAGCGG AAAGACAATCCTGGACTTCTGAAGAGCGACGGATTGCAAAACAGAAAATTCATGCA GCTGATCCACGACGACAGCTGACATTCAAGGAAGACATCCAGAAAGGACAGGATCA GCGGACAGGGAGACAGCCTGCACGAACACATCGCAAACCTGGCAGGAAGCCCGGCA ATCAAGAAGGGAATCCTGCAGACAGTCAAGGTGCTGACGAACTGGTCAAGGTCATG GGAAGACACAAGCCGAAAACATCGTCATCGAAATGGCAAGAGAAAACCAGACAAC CAGAAAGGGACAGAAAGAACAGCAGAGAAAAGAAATGAAGAGAATCGAAGAAAGGAATC AAGGAACTGGGAAGCCAGATCCTGAAGGAACACCCGGTCCGAAAACACACAGCTGCA GAACGAAAAGCTGTACTGTACTACCTGCAGAACGGAAGAGACATGTACGTCGACCA GGAATGGACATCAACAGACTGAGCGACTACGACGTCGACCACATCGTCCCGCAGAG CTTCTGAAGGACGACAGCATCGACAACAAGGTCTGACAAGAAGCGACAAGAACA GAGGAAAAGAGCGACAACCTCCGAGCGAAGAAAGTCGTCAGAAGATGAAGAATAC TGGAGACAGCTGCTGAACGCAAAGCTGATCACACAGAGAAAAGTTGACAACCTGAC AAAGGCAGAGAGAGGAGGACTGAGCGAACTGGACAAGGCAGGATTCATCAAGAGA CAGCTGGTCGAAACAAGACAGATCACAAGCACGTCGCACAGATCCTGGACAGCAG AATGAACACAAAAGTACGACGAAAACGACAAGCTGATCAGAGAAGTCAAGGTCATCA CACTGAAGAGCAAGCTGGTCAGCGACTTCAGAAAGGACTTCCAGTTCTACAAGGTCA GAGAAATCAACAATACCACCACGCACACGACGCATACCTGAACGCAGTCGTCGGAA CAGCACTGATCAAGAAGTACCCGAAGCTGGAAAAGCGAATTCGTCACGGAGACTACA AGGTCTACGACGTCAGAAAAGATGATCGAAAAGAGCGAACAGGAAATCGGAAAAGGCA ACAGCAAAGTACTTCTTCTACAGCAACATCATGAACTTCTTCAAGAACGAAAATCACAC TGGCAAACGGAGAAATCAGAAAAGACCCGCTGATCGAAAACAAACGGAGAAAACAGG AGAAATCGTCTGGGACAAGGGAAAGAGACTTCGCAACAGTCAGAAAAGGTCCTGAGCA TGCCGACAGTCAACATCGTCAAGAAGACAGAAGTCCAGACAGGAGGATTCAGCAAG GAAAGCATCCTGCCGAAGGAAAACAGCGACAAGCTGATCGCAAGAAAAGAAAGACTG GGACCCGAAGAAGTACGGAGGATTCGACAGCCCGACAGTCGCATACAGCGTCTGGT CGTCGCAAAGGTCGAAAAGGAAAAGAGCAAGAAGCTGAAGAGCGTCAAGGAACTG CTGGGAATCACAATCATGGAAAGAAAGCAGCTTCGAAAAGAACCCGATCGACTTCTG GAAGCAAAAGGATACAAGGAAGTCAAGAAGGACCTGATCATCAAGCTGCCGAAGTA CAGCCTGTTGAACTGGAAAACGGAAAGAAAAGAGAATGCTGGCAAGCGCAGGAGAAC TGCAGAAGGGAAACGAACTGGCACTGCCGAGCAAGTACGTCAACTTCTGTACTCTGG CAAGCCACTACGAAAAGCTGAAGGGAAAGCCCGAAAGACAACGAACAGAAAGCAGCT GTTCTGTCGAACAGCACAAGCACTACCTGGACGAAATCATCGAACAGATCAGCGAATT CAGCAAGAGAGTCACTTGGCAGACGCAAACCTGGACAAGGTCTGAGCGCATAACA ACAAGCACAGAGACAAGCCGATCAGAGAACAGGCAGAAAACATCATCCACCTGTTC ACACTGACAAACCTGGGAGCACCGGCAGCATTCAAGTACTTCGACACAACAATCGAC AGAAAAGAGATACACAAGCACAAGGAAGTCTGGACGCAACACTGATCCACCAGAG CATCACAGGACTGTACGAAAACAAGAATCGACTGAGCCAGCTGGGAGGAGACGGAG GAGGAAGCGCAGCAGCAAAGAGAAAAGTACTTCGCAGCATAG</p>	
<p>具有NLS10 的Cas9的开 放阅读框架, 其具有起始 及终止密码 子</p>	<p>ATGGACAAGAAGTACAGCATCGGACTGGACATCGGAACAAACAGCGTCGGATGGGC AGTCATCACAGACGAATACAAGGTCCCGAGCAAGAAGTTCAAGGTCTGGGAAACA CAGACAGACACAGCATCAAGAAGAACCTGATCGGAGCACTGCTGTTGACAGCGGA GAAACAGCAGAAGCAACAAGACTGAAGAGAACAGCAAGAAGAAGATACACAAGAA GAAAAGAACAGAATCTGCTACCTGCAGGAAATCTTCAAGCAACGAAATGGCAAAGGTCG ACGACAGCTTCTTCCACAGACTGGAAGAAAGCTTCTGGTTCGAAAGAAGACAAGAAG CACGAAAAGACACCCGATCTTCGAAAACATCGTCGACGAAAGTCGCATACCACGAAAAG TACCCGACAATCTACCCTGAGAAAAGAGCTGGTTCGACAGCACAGACAAGGCAGA CCTGAGACTGATCTACCTGGCACTGGCACACATGATCAAGTTTCAGAGGACACTTCTG ATCGAAGGAGACCTGAACCCGGACAACAGCGACGTCGACAAGCTGTTTCATCCAGCT GGTCCAGACATACAACCAGCTGTTGCAAGAAAACCCGATCAACGAAGCGGAGTCG</p>	<p>139</p>

[0740]

	ACGCAAAGGCAATCCTGAGCGCAAGACTGAGCAAGAGCAGAAGACTGGAAAACCTG ATCGCACAGCTGCCGGGAGAAAAAGAAGAACGGACTGTTCGGAAAACCTGATCGCACT GAGCCTGGGACTGACACCGAACTTCAAGAGCAACTTCGACCTGGCAGAAGACGCAA AGCTGCAGCTGAGCAAGGACACATACGACGACGACCTGGACAACCTGCTGGCACAG ATCGGAGACCAGTACGCAGACCTGTTCTGGCAGCAAAGAACCTGAGCGACGCAATC CTGCTGAGCGACATCCTGAGAGTCAACACAGAAATCACAAAAGGCACCGCTGAGCGC AAGCATGATCAAGAGATACGACGAACACCACCAGGACCTGACTGCTGAAGGCACT GGTCAGACAGCAGCTGCCGGAAAAGTACAAGGAAATCTTCTCGACCAGAGCAAGA ACGGATACGCAGGATACATCGACGGAGGAGCAAGCCAGGAAGAATTCTACAAGTTCA TCAAGCCGATCCTGGAAAAGATGGACGGAAACAGAAGAACTGCTGGTCAAGCTGAAC AGAGAAGACCTGCTGAGAAAGCAGAGAACATTTCGACAACGGAAAGCACCCTCCGACCA GATCCACCTGGGAGAACTGCACGCAATCCTGAGAAGACAGGAAGACTTCTACCCGTT CCTGAAGGACAACAGAGAAAAGATCGAAAAGATCCTGACATTAGAATCCCGTACTA CGTCCGACCGCTGGCAAGAGGAAAACAGCAGATTTCGCATGGATGACAAGAAAAGAGCG AAGAAACAATCACACCGTGGAACTTCGAAGAAGTTCGTCGACAAGGGAGCAAGCGCA CAGAGCTTATCGAAAAGATGACAAACTTCGACAAGAACCTGCCGAACGAAAAGGT CCTGCCGAAGCACAGCTGCTGTACGAATACTTCACAGTCTACAACGAACTGACAAA GGTCAAGTACGTACAGAAAGGAATGAGAAAGCCGGCATTCTGAGCGGAGAACAGA AGAAGGCAATCGTCGACTGCTGTTCAAGACAAAACAGAAAAGGTCACAGTCAAGCAG CTGAAGGAAGACTACTTCAAGAAGATCGAATGCTTCGACAGCGTCAAGGAGCAGCGGA GTGCAAGACAGATTCAACGCAAGCCTGGGAACATACCACGACCTGCTGAAGATCATC AAGGACAAGGACTTCTGGACAACGAAGAAAACGAAGACATCCTGGAAGACATCGT CCTGACTGACTGTTTGAAGACAGAGAAATGATCGAAGAAAGACTGAAGACAT ACGCACACCTGTTGACGACAAGGTCATGAAGCAGCTGAAGAGAAAGATGATACACA GGATGGGGAAGACTGAGCAGAAAAGCTGATCAACGGAATCAGAGACAAGCAGAGCGG AAAGACAATCCTGGACTTCTGAAGAGCGACGGATTTCGAAAACAGAAACTTCATGCA GCTGATCCACGACGACAGCCTGACATTCAAGGAAGACATCCAGAAGGCACAGGTCA GCGGACAGGGAGACAGCCTGCACGAACACATCGAAAACCTGGCAGGAAGCCCGGCA ATCAAGAAGGGAATCCTGCAGACAGTCAAGGTCTGTCGACGAACCTGGTCAAGGTCATG GGAAGACACAAGCCGGAAAACATCGTCATCGAAATGGCAAGAGAAAACCAGACAAC ACAGAAGGGACAGAAGAACAGCAGAGAAAAGATGAAGAGAATCGAAGAAGGAATC AAGGAAGTGGGAAGCCAGATCCTGAAGGAACACCCGGTTCGAAAACACACAGCTGCA GAACGAAAAGCTGTACTTACTTACTCCTGCAGAACGGAAGAGACATGATCAGTCCGACCA GGAAGTGGACATCAACAGACTGAGCGACTACGACGTCGACCACATCGTCCCGCAGAG CTTCTGAAAGGACGACAGCATCGACAACAGGTCTGACAAGAAGCGACAAGACA GAGGAAAAGAGCGACAACGTCCTCCGAGCGAAGAGTTCGTCAAGAAGATGAAGAACTAC TGGAGACAGCTGCTGAACGCAAAGCTGATCACACAGAGAAAAGTTGACAACTGAC AAAAGGCAGAGAGAGGAGGACTGAGCGAACTGGACAAGGCAGGATTCATCAAGAGA CAGCTGGTCGAAACAAGACAGATCACAAAGCACGTCGACAGATCCTGGACAGCAG AATGAACACAAAGTACGACGAAAACGACAAGCTGATCAGAGAAGTCAAGGTATCA CACTGAAGAGCAAGCTGGTCAGCGACTTCAGAAAGGACTTCCAGTTCTACAAGGTCA GAGAAATCAACAACACTACCACCACGACACACGACGCATACCTGAACGCACTCGGAA CAGCACTGATCAAGAAGTACCCGAAGCTGGAAAAGCGAATTTCGTCACGGAGACTACA AGGTCTACGACGTGAGAAAAGATGATCGAAAAGAGCGAACAGGAAATCGGAAAGGCA ACAGCAAAAGTACTTCTTCTACAGCAACATCATGAACTTCTTCAAGACAGAAATCACAC TGGCAAACGGAGAAATCAGAAAAGAGACCGCTGATCGAAAACAACGGAGAAAACAG AGAAAATCGTCTGGGACAAGGGAAAGAGACTTCGCAACAGTCAGAAAAGTCCGAGCA TGCCCGAGGTCAACATCGTCAAGAAGACAGAAGTCCAGACAGGAGGATTAGCAAG GAAAGCATCCTGCCGAAGAGAAAACAGCGACAAGCTGATCGCAAGAAAAGAAAGGACTG GGACCCGAAGAAGTACGGAGGATTTCGACAGCCCGACAGTTCGCATACAGCGTCTGGT CGTCGAAAAGGTGCAAAAAGGGAAGAGCAAGAAGTGAAGAGCGTCAAGGAAGTCTG CTGGGAATACAATCATGGAAAGAAGCAGCTTCGAAAAGAACCAGATCGACTTCTG GAAGCAAAAGGGATACAAGGAAGTCAAGAAGGACCTGATCATCAAGCTGCCGAAGTA CAGCCTGTTTGAAGTGGAAAACGGAAGAAAGAGAATGCTGGCAAGCGCAGGAGAAC TGCAGAAGGGAAACGAACTGGCACTGCCGAGCAAGTACGTCAACTTCTGTACTCTGG CAAGCCTACGAAAAGCTGAAGGGAAGCCCGAAGACAACGAACAGAAAGCAGCT GTTCTGTCGAACAGCACAAAGCACTACCTGGACGAAATCATCGAACAGATCAGCGAATT CAGCAAGAGAGTATCCTGGCAGACGCAAACCTGGACAAGGTCTGAGCGCATAACA ACAAGCACAGAGACAAGCCGATCAGAGAACAGGCAGAAAACATCATCCACCTGTTC CACTGACAAAACCTGGGAGCACCCGGCAGCATTCAAGTACTTCGACACAACAATCGAC AGAAAAGATACACAAGCACAAAGGAAGTCTGGACGCAACACTGATCCACCAGAG CATCACAGGACTGTACGAAAACAAGAATCGACCTGAGCCAGCTGGGAGGAGACGGAG GAGGAAGCAGAGCAGCAAAGAGAAAAGGCATTTCGACGATAG	
具有 NLS11 的 Cas9 的开	ATGGACAAGAAGTACAGCATCGGACTGGACATCGGAACAACAGCGTCGGATGGGC AGTCATCACAGACGAATACAAGTCCCAGCAAGAAGTTCAAGTCTGGGAAAACA CAGACAGACACAGCATCAAGAAGAACCTGATCGGAGCACTGCTGTTTCGACAGCGGA GAAACAGCAGAAGCAACAAGACTGAAGAGAACAGCAAGAAGAAGATACACAAGAA	140

<p>放阅读框架， 其具有起始 及终止密码 子</p>	<p>GAAAGAACAGAATCTGCTACCTGCAGGAAATCTTCAGCAACGAAATGGCAAAGGTCG ACGACAGCTTCTTCCACAGACTGGAAGAAAAGCTTCTGGTGAAGAAAGACAAGAAAG CACGAAAGACACCCGATCTTCGGAAACATCGTCGACGAAAGTCGCATACCACGAAAAG TACCCGACAATCTACCACCTGAGAAAAGAACTGGTTCGACAGCACAGACAAGGCAGA CCTGAGACTGATCTACCTGGCACTGGCACACATGATCAAGTTTCAGAGGACACTTCTG ATCGAAGGAGACCTGAACCCGGACAACAGCGACGTCGACAAGCTGTTTCATCCAGCT GGTCCAGACATAACAACCAGCTGTTTGAAGAAAACCCGATCAACGCAAGCGGAGTCG ACGCAAAGGCAATCCTGAGCGCAAGACTGAGCAAGAGCAGAAGACTGGAAAACCTG ATCGCACAGCTGCCGGGAGAAAAGAAGAACGGACTGTTTCGAAAACCTGATCGCACT GAGCCTGGGACTGACACCGAACTTCAAGAGCAACTTCGACCTGGCAGAAAGACGCAA AGTGCAGCTGAGCAAGGACACATACGACGACGACCTGGACAACCTGCTGGCACAG ATCGGAGACCAGTACGACAGCCTGTTCTGGCAGCAAAGAACCCTGAGCGACGCAATC CTGCTGAGCGACATCCTGAGAGTCAACACAGAAATCACAAAGGCACCGCTGAGCGC AAGCATGATCAAGAGATACGACGAACACCACCAGGACCTGACTGCTGAAGGCACT GGTCAGACAGCAGCTGCCGGAAGTACAAGGAAATCTTCTTCGACCAGAGCAAGA ACGGATACGCAGGATACATCGACGGAGGACAAAGCCAGGAAGAATTCTACAAGTTCA TCAAGCCGATCCTGGAAAAGATGGACGGAACAGAAGAACTGCTGGTCAAGCTGAAC AGAGAAGACCTGCTGAGAAAAGCAGAGAAACATTCGACAACGGAAAGCATCCCGCACA GATCCACCTGGGAGAACTGCACGCAATCCTGAGAAGACAGGAAGACTTCTACCCGTT CCTGAAGGACAACAGAGAAAAGATCGAAAAGATCCTGACATTCAGAACTCCCGTACTA CGTCCGACCGCTGGCAAGAGGAAAACAGCAGATTTCGATGGATGACAAGAAAAGAGCG AAGAAAACAATCACACCGTGGAACTTCAAGAAAGTCGTCGACAAGGGGAGCAAGCGCA CAGAGCTTATCGAAAAGATGACAACTTCGACAAGAACCCTGCCGAACGAAAAGGT CCTGCCGAAGCACAGCTGCTGTACGAATACTTACAGTCTACAACGAACTGACAAA GGTCAAGTACGTCACAGAAGGAATGAGAAAGCCGGCATTCTGAGCGGAGAACAGA AGAAGGCAATCGTCGACCTGCTGTTCAAGACAAACAGAAAAGGTCACAGTCAAGCAG CTGAAGGAAGACTACTTCAAGAAGATCGAATGCTTCGACAGCGTCGAAATCAGCGGA GTCGAAGACAGATTCAACGCAAGCCTGGGAACATACCACGACCTGCTGAAGATCATC AAGGACAAGGACTTCTGGACAACGAAGAAAACGAAGACATCCTGGAAGACATCGT CCTGACACTGACTGTTTCAAGACAGAGAAATGATCGAAGAAAGACTGAAGACAT ACGCACACCTGTTTCGACGACAAGGTCATGAAGCAGCTGAAGAGAAGAAGATACACA GGATGGGGAAGACTGAGCAGAAAAGCTGATCAACGGAAATCAGAGACAAGCAGAGCGG AAAGACAATCCTGGACTTCTGAAAGAGCGACGGATTTCGAAAACAGAACTTCATGCA GCTGATCCACGACGACAGCCTGACATTCAAGGAAGACATCCAGAAGGCACAGGTCA GCGGACAGGGGAGACAGCCTGCACGAACACATCGCAAACCTGGCAGGAAGCCCGGCA ATCAAGAAGGGAATCCTGCAGACAGTCAAGGTCGTCGACGAACTGGTCAAGGTCATG GCAAGACACAAGCCGGA AAAACATCGTCATCGAAATGGCAAGAGAAAACAGACAAC ACAGAAGGGACAGAGAAGAAGCAGCAGAGAAAAGAAATGAAGAGAATCGAAGAAAGGAAATC AAGGAACTGGGAAGCCAGATCCTGAAGGAACACCCGGTCGAAAACACACAGCTGCA GAACGAAAAGCTGTACCTGTACTACCTGCAGAACGGAAGAGACATGTACGTCGACCA GGAATGGACATCAACAGACTGAGCGACTACGACGTCGACCACATCGTCCCGCAGAG GTTCTGAAAGGACGACAGCATCGACAACAAGGTCCTGACAAGAAGCGACAAGAA GAGGAAAAGAGCGACAACGTCGAGCGAAGAAAGTCGTCGAAGAAGATGAAGAAGTAC TGGAGACAGCTGCTGAACGCAAAGCTGATCACACAGAGAAAAGTTTCGACAACCTGAC AAAGGCAGAGAGAGGAGGACTGAGCGAACTGGACAAGGCAGGATTTCATCAAGAGA CAGTGGTCGAAACAAGACAGATCACAAAGCACGTCGCACAGATCCTGGACAGCAG AATGAACACAAGTACGACGAAAACGACAAGCTGATCAGAGAAGTCAAGGTCATCA CACTGAAGAGCAAGCTGGTCAGCGACTTCAGAAAAGGACTTCCAGTTCTACAAGGTCA GAGAAATCAACAATACCACCACGCACACGACGCATACCTGAACGCAAGTTCGCGAA CAGCACTGATCAAGAAGTACCCGAAGCTGGAAAAGCGAATTCGTTCTACGGAGACTACA AGGTCTACGACGTCAGAAAAGATGATCGAAAAGAGCGAACAGGAAATCGGAAAAGGCA ACAGCAAAAGTACTTCTTCTACAGCAACATCATGAACTTCTTCAAGACAGAAATCACAC TGGCAAACGGAGAAATCAGAAAAGAGACCGCTGATCGAAAACAACGGAGAAAACAGG AGAAATCGTCTGGGACAAGGGAAGAGACTTCGCAACAGTCAGAAAAGGTCCTGAGCA TGCCGACAGTCAACATCGTCAAGAAGACAGAAGTCCAGACAGGAGGATTTCAGCAA GAAAAGCATCCTGCCGAAGAGAAAACAGCGACAAGCTGATCGCAAGAAAAGAAGGACTG GGACCCGAAGAAGTACGGAGGATTTCGACAGCCCGACAGTCGCATACAGCGTCTGGT CGTCGCAAAGGTCGAAAAGGGAAGAGCAAGAAGCTGAAGAGCGTCAAGGAACTG CTGGGAATCACAATCATGGAAAGAAGCAGCTTCGAAAAGAACCCTGATCGACTTCTG GAAGCAAAGGGATACAAGGAAGTCAAGAAGGACCTGATCATCAAGCTGCCGAAGTA CAGCCTGTTTCAAGTGGAAAACGGAAAGAAGAGAATGCTGGCAAGCGCAGGAGAAC TGCAGAAGGGAAACGAACTGGCACTGCCGAGCAAGTACGTCAACTTCTGTACCTGG CAAGCCACTACGAAAAGCTGAAGGGAAAGCCCGAAGACAACGAACAGAAGCAGCT GTTCTGCAACAGCACAAAGCACTACCTGGACGAAATCATGAACAGATCAGCGAATT CAGCAAGAGAGTATCCTGGCAGACGCAAACTGGACAAGGTCCTGAGCGCATAACA ACAAGCACAGAGACAAGCCGATCAGAGAACAGGCAGAAAACATCATCCACCTGTTT ACACTGACAAAACCTGGGAGCACCAGCAGATTCAAGTACTTCGACACAACAATCGAC</p>
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[0741]

	AGAAAAGAGATACACAAGCACAAAGGAAGTCCTGGACGCAACACTGATCCACCAGAG CATCACAGGACTGTACGAAACAAGAATCGACCTGAGCCAGCTGGGAGGAGACGGAG GAGGAAGCAGAGCAGCAAAGAGAAAGTACTTCGCAGTCTAG	
使用通常在 人类中高度 表达的密码 子的 Cas9 ORF (无起始 或终止密码 子; 适于包括 在融合蛋白 质编码序列 中)	CCTAAGAAAAAGCGGAAGGTCGACGGGGATAAGAAAGTACTCAATCGGGCTGGATATC GGAACATAATCCGTGGGTTGGGCAGTGATCACGGATGAATACAAAAGTCCGCTCCAAG AAGTTCAAGTCTCGGGGAACACCGATAGACACAGCATCAAGAAAAATCTCATCGGA GCCCTGCTGTTTACTCCGGGAAACCGCAGAAGCGACCCGGCTCAAAACGTACCCGG AGGCGACGCTACACCCGGCGGAAGAATCGCATCTGCTATCTGCAAGAGATCTTTTCGA ACGAAATGGCAAAGGTCGACGACAGCTTCTTCCACCGCTGGAAGAATCTTTCCTGG TGGAGGAGGACAAGAAGCATGAACGGCATCTATCTTTGGAAACATCGTCGACGAAG TGGCGTACCACGAAAAGTACCCGACCATCTACCATCTGCGGAAGAAGTTGGTTGACT CAACTGACAAGGCCACCTCAGATTGATCTACTTGGCCCTCGCCCATATGATCAAATT CCGCGGACACTTCTGATCGAAGGCGATCTGAACCCTGATAACTCCGACGTGGATAA GCTTTTCATTCAACTGGTGCAGACCTACAACCACTGTTTCAAGAAAACCAATCAAT TGTAGCGGCTCGATGCCAAGGCCATCTGTCCGCGGCTGTGCGAAGTTCGCGGCGC CTCAGAAAACCTGATCGCACAGCTGCCGGGAGAGAAAAAGAACGGACTTTTCGGCAA CTTGATCGCTCTCTCACTGGGACTCACTCCCAATTTCAAGTCCAATTTTGACCTGGCC GAGGACGCGAAGCTGCAACTCTCAAAGGACACCTACGACGACGACTTGGACAATTT GCTGGCACAATTTGGCGATCAGTACGCGGATCTGTTCTTGGCGCTAAGAACCTTTTCG GACGCAATCTTGTGTCCGATATCCCTGCGGTGAACACCGAAATTAACAAAAGCGGCG CTTAGCGCCTCGATGATTAAGCGGTACGACGAGCATCACCAGGATCTCACGCTGCTCA AAGCGCTCGTGAGACAGCAACTGCCTGAAAAGTACAAGGAGATCTTCTTCGACCAGT CCAAGAATGGGTACGACGGGTACATCGATGGAGGCGCTAGCCAGGAAGAGTTCTATA AGTTTCAAGCCAATCTGAAAAGATGGACGGAACCGAAGAAGTGTGTTCAAGCGGCT CTGAACAGGGAGGATCTGCTCCGAAACAGAGAACCTTTGACAACGGATCCATTTCC CACCAGATCCATCTGGGTGAGCTGCACGCCATCTTGGCGGCCAGGAGGACTTTTACC CATTCTCAAGGACAACCGGGAAAAGATCGAGAAAATCTGACGTTCCGCATCCCGT ATTACGTGGGCCACTGGCGCGCGCAATTCGCGCTTCGCGTGGATGACTAGAAAATC AGAGGAAACCATCACTCCTTGGAAATTCGAGGAAGTTTGGATAAGGGAGCTTCGCG ACAAAAGCTTCATCGAACGAATGACCAACTTCGACAAGAATCTCCAAAACGAGAAGGT GCTTCTAAGCACAGCCTCCTTACGAATACTTCACTGTCTACAACGAAGTACTAAA GTGAAATACGTTACTGAAGGAATGAGGAAGCCGGCCTTTCTGTCCGGAGAACAGAAG AAAGCAATTTGATGCTGTGTTCAAGACCAACCGCAAGGTGACCGTCAAGCAGTCT AAAGAGGACTACTTCAAGAAGGTGCTCGACGAGCTGTTTTCGACTCAGTGGAAATCAGCGGGGTG GAGGACAGATTCAACGCTTCGCTGGGAACCTATCATGATCTCCTGAAGATCATCAAGG ACAAGGACTTCTTGAACAACGAGGAGAACGAGGACATCTGGAAGATATCGTCTGTA CCTTGACCCTTTTCGAGGATCGCGAGATGATCGAGGAGAGGCTTAAGACCTACGCTCA TCTTTCGACGATAAGGTATGAAAACAACCTAAGCGCCGCGGTTACACTGTTTGGGG CCGCTCTCCGCAAGCTGATCAACGGTATTCGCGATAAACAGAGCGGTAAAACTATC CTGGATTTCCTCAAATCGGATGGCTTCGCTAATCGTAACTTCATGCAATTGATCCACGA CGACAGCCTGACCTTAAGGAGGACATCAAAAAAGCACAAGTGTCCGGACAGGGAG ACTCACTCCATGAACACATCGCAATCTGGCCGGTTCGCGGCGATTAAGAAGGGAA TTCTGCAAACTGTGAAGGTGGTCGACGAGCTGGTGAAGGTATGGGACGGCACAAA CCGGAGAATATCGTGATTGAAATGGCCCGAGAAAACAGACTACCCAGAAGGGCCAG AAAAACTCCCGCAAAGGATGAAGCGGATCGAAGAAGGAATCAAGGAGCTGGGCAG CCGATCTGAAAGAGCACCCGGTGGAAAACACGCAGCTGCAGAACGAGAAGCTCT ACCTGTACTTTTGCAAAATGGACGGGACATGTACGTGGACCAAGAGCTGACGATCAA TCGGTTGTCTGATTACGACGTGGACCACATCGTTCCACAGTCTTTTCTGAAGGATGAC TCGATCGATAACAAGGTGTTGACTCGCAGCGACAAGAACAGAGGGAAGTCAAGATAAT GTGCCATCGGAGGAGTCTGTAAGAAGATGAAGAATTACTGGCGGCAGCTCCTGAAT CGGAAGCTGATTACCCAGAGAAAAGTTTGAACAATCTACTAAAAGCCGAGCGCGGCGGA CTCTCAGAGCTGGATAAGGCTGGATTCATCAAACGGCAGCTGGTCGAGACTCGGCAG ATTACCAAGCACGTGGCGCAGATCTTGGACTCCCGCATGAACACTAAATACGACGAG AACGATAAGCTCATCCGGGAAGTGAAGGTGATTACCCTGAAAAGCAAACCTTGTGTCTG GACTTTTCCGGAAGGACTTTTCAAGTGTGAGAGAAATCAACAACACTACCATCAC GCGCATGACGATACCTCAACGCTGTGGTCCGTACCGCCCTGATCAAAAAGTACCCTA AACTTGAATCGGAGTTTGTGTACGGAGACTACAAGGTCTACGACGTGAGGAAGATGA TAGCCAAGTCCGAACAGGAAATCGGGAAAGCAACTGCGAAATACTTCTTTTACTCAA ACATCATGAACCTTTTCAAGACTGAAATTACGCTGGCCAATGGAGAAATCAGGAAGA GGCCACTGATCGAAACTAACGGAGAAAACGGGCGAAATCGTGTGGGACAAAGGGCAGG GACTTCGCAACTGTTTCGAAAAGTCTCTATGCCGCAAGTCAATATTGTGAAGAAAA CCGAAGTGCAAACCGGCGGATTTTCAAAGGAATCGATCTCCAAAAGAGAAATAGCG ACAAGCTCATTGCACGCAAGAAAGACTGGGACCCGAAGAAGTACGGAGGATTCGATT CGCCGACTGTGCGATACTCCGTCTCGTGGTGGCCAAGGTGGAGAAGGGAAAGAGC AAAAAGCTCAAATCCGTCAAAGAGCTGCTGGGATTACCATCATGGAAGGATCCTCG TTCGAGAAGAACCAGATTGATTTCTCGAGGCGAAGGGTTACAAGGAGGTGAAGAA GGATCTGATCATCAAACCTCCAAGTACTACTGTTTCAAGTGGAAAATGGTCCGAA	141

[0742]

	<p>GCGCATGCTGGCTTCGGCCGGAGAAGCTCCAAAAAGGAAATGAGCTGGCCTTGCCCTAG CAAGTACGTCAACTTCCTCTATCTTGCTTCGCACTACGAAAACTCAAAGGGTCACCG GAAGATAACGAACAGAAGCAGCTTTTCGTGGAGCAGCACAAGCATTATCTGGATGAA ATCATCGAACAAATCTCCGAGTTTCAAAGCGCGTGATCCTCGCCGACGCCAACCTCG ACAAAAGTCTGTCCGCCTACAATAAGCATAGAGATAAGCCGATCAGAGAACAGGCCG AGAACATTATCCACTTGTTCACCCTGACTAACCTGGGAGCCCCAGCCGCTTCAAGTA CTTCGATACTACTATCGATCGCAAAAGATACACGTCCACCAAGGAAGTTCTGGACGCG ACCCTGATCCACCAAGCATCACTGGACTCTACGAAACTAGGATCGATCTGTCGCAGC TGGGTGGCGAT</p>	
<p>使用表4的长 半衰期密码 子的 Cas9 ORF (无起始 或终止密码 子; 适于包括 在融合蛋白 质编码序列 中)</p>	<p>GACAAGAAGTACTCTATCGGTTTGGACATCGGTACCAACTCTGTCCGTTGGGCCGTCA TCACCGACGAATACAAGGTCCCATCTAAGAAGTTCAAGGTCTTGGGTAACACCGACA GACACTCTATCAAGAAGAAGTTGATCGGTGCCTTGTGTTGACTCTGGTGAACCCGC CGAAGCCACCAGATTGAAGAGAACCGCCAGAAGAAGATACACCAGAAGAAAGAACA GAATCTGCTACTTGAAGAAATCTTCTCTAACGAAATGGCCAAGGTGCAGACTCTTT CTTCCACAGATTGGAAGAATCTTTCTTGGTGAAGAAGACAAGAAGCAGCAAGAAC ACCAATCTTCGGTAACATCGTCGACGAAGTCGCCTACCACGAAAAGTACCCAACCAT CTACCCTTGAGAAAGAAGTTGGTGCAGCTTACCGACAAGGCCGACTTGAGATTGAT CTACTTGGCCTTGGCCACATGATCAAGTTCAGAGGTCACTTCTTGATCGAAGGTGAC TTGAACCCAGACAACCTCTGACGTGACAAGTTGTTTATCCAATTGGTCCAAACCTACA ACCAATTGTTGGAAGAAAACCCAATCAACGCCTCTGGTGTGACGCAAGGCCAATCT TGTCTGCCAGATTGTCTAAGAGCAGAAGATTGGAAAACCTTGATCGCCCAATTGCCAG GTGAAAAGAAGAACGGTTTGTTCGGTAACTTGATCGCCTGTCTTGGGTTTGACCC AACTTCAAGTCTAACTTCGACTTGGCCGAAGACGCCAAGTTGCAATTGTCTAAGGA ACCTACGACGACGACTTGGACAACCTGTTGGCCAAATCGGTGACCAATACGCCGA CTTGTCTTGGCCGCCAAGAAGTTGTCTGACGCCATCTTGTGTCTGATCTTGAGA GTCAACACCGAAATACCAAGGCCCCATTGTCTGCCTCTATGATCAAGAGATACGACG AACACCACCAAGACTTGACCTTGTGAAGGCCTTGGTCAGACAACAATTGCCAGAAA AGTACAAGGAAATCTTCTCGACCAATCTAAGAACGGTTACGCCGGTTACATCGACGG TGGTGCCTCTCAAGAAGAATTCTACAAGTTCATCAAGCCAATCTTGGAAAAGATGGA CGGTACCGAAGAATTGTTGGTCAAGTTGAACAGAGAAGACTTGTGAGAAAAGCAAA GAACCTTCGACAACGGTCTATCCCACACCAATCCACTTGGGTGAATTGCACGCCAT CTTGAGAAGACAAGAAGACTTCTACCCATTCTTGAAGGACAACAGAGAAAAAGATCG AAAAGATCTGACCTTCAAGATCCCATACTACGTCCGTTCCATTGGCCAGAGGTAACAG CAGATTCGCCTGGATGACCAGAAAAGTCTGAAGAAAACCATCACCCCATGGAATTCTGA AGAAGTCGTCGACAAGGGTGCCTCTGCCAATCTTTCATCGAAAAGAATGACCAACTT CGACAAGAAGCTTGCACAAACGAAAAGGTCTTGCACAAAGCACTCTTGTGTACGAATA CTTACCCTTCAACGAATTGACCAAGGTCAAGTACGTCACCGAAGGTTATGAGAAA GCCAGCCTTCTGTCTGGTGAACAAAAGAAGGCCATCGTCACTTGTGTTCAAGAC CAACAGAAAAGGTCAACGTCGAAGCAATTGAAGGAAGACTACTTCAAGAAGATCGAAT GCTTCGACTCTGTGAAATCTCTGGTGTGCAAGACAGATTCAACGCCTCTTGGGTAC CTACCAGACTTGTGAAGATCATCAAGGACAAGGACTTCTTGGACAACGAAGAAAA CGAAGACATCTTGAAGACATCGTCTTACCTTGACCTTGACCTTGTTCGAAGCAGAGAAAT GATCGAAGAAAAGATTGAAGACCTACGCCCACTTGTTCGACGACAAGGTCATGAAGCA ATTGAAGAGAAGAAGATACACCGGTTGGGGTAGATTGAGCAGAAAAGTTGATCAACGG TATCAGAGACAAGCAATCTGGTAAGACCATCTTGGACTTCTTGAAGTCTGACGGTTTC GCCAACAGAAAACCTCATGCAATTGATCCACGACGACTCTTGGACCTTCAAGGAAGAC ATCCAAAAGGCCAAGTCTCTGGTCAAGGTGACTCTTGGACGAAACCATCGCCAAAC TTGGCCGGTCTCCAGCCATCAAGAAGGTATCTTGCAAAACCGTCAAGGTCTGACG GAATTGGTCAAGGTCAAGGTAGACACAAGCCAGAAAACATCGTCATCGAAATGGCC AGAGAAAACCAACCACCAAAAAGGGTCAAAAAGAAGCAGAGAAAAGAAATGAAGA GATCAAGAAGGATCAAGGAATTGGGTTCTCAAATCTTGAAGGAACACCCAGTCTG AAAAACCCAATTGCAAAAACGAAAAGTTGACTTGTACTACTTGAAAAACGGTAGAG ACATGTACGTCGACCAAGAATTGGACATCAACAGATTGTCTGACTACGACGTCGACC ACATCGTCCACAATCTTCTTGAAGGACGACTCTATCGACAACAAGGTCTTGACCAG ATCTGACAAGAACAGAGGTAAGTCTGACAACGTCCATCTGAAGAAGTCGTCAAGAA GATGAAGAAGTACTGGAGACAATTGTTGAACGCCAAGTTGATCACCCAAAAGAAAGTT CGACAACCTTGAACAAGGCCGAAAAGAGGTGGTTTGTCTGAATTGGACAAGGCCGGTTT CATCAAGAGACAATTGGTTCGAAACCAGACAAATCACCAGACGTCGCCCAATCTT GGACAGCAGAATGAACACCAAGTACGACGAAAACGACAAGTTGATCAGAGAAGTCA AGGTCATCACCTTGAAGTCTAAGTTGGTCTCTGACTTCAGAAAAGGACTTCAACTCTA CAAGGTCAGAGAAATCAACAACCTACCACCACGCCACGACGCCTACTTGAACGCCGT CGTCCGGTACCGCCTTATCAAGAAGTACCCAAAGTTGGAATCTGAATTCGTCTACGGT GACTACAAGGTCTACGACGTCAGAAAAGATGATCGCCAAGTCTGAACAAGAAAACGGT AAGGCCACCGCCAAGTACTTCTTACTCTAACATCATGAACCTTCTTCAAGACCCGAAA TCACCTTGGCCAACGGTGAATCAGAAAAGAGACCAATTGATCGAAAACCAACGGTGAA ACCGGTGAAATCGTCTGGGACAAGGGTAGAGACTTCGCCACCGTCAGAAAAGGTCTTG TCTATGCCACAAGTCAACATCGTCAAGAAGACCCGAAGTCCAAACCGGTGGTTTCTCT</p>	<p>142</p>

[0743]

	<p>AAGGAATCTATCTTGCCAAAGAGAACTCTGACAAGTTGATCGCCAGAAAAGAAGGAC TGGGACCCAAAGAAAGTACGGTGGTTTTCGACTCTCCAACCGTCGCCTACTCTGTCTTG GTCGTCGCCAAGGTCGAAAAGGGTAAGTCTAAGAAGTTGAAGTCTGTCAAGGAATTG TTGGGTATCACCATCATGGAAAGATCTTCTTTGAAAAGAACCAATCGACTTCTTGG AAGCCAAGGGTTACAAGGAAGTCAAGAAGGACTTGATCATCAAGTTGCCAAAAGTACT CTTTGTTTCAATTGGAAAACGGTAGAAAAGAGAATGTTGGCCTCTGCCGGTGAATTGC AAAAGGGTAACGAATTGGCCTTGCCATCTAAGTACGTCAACTTCTGTACTTGGCCTC TCACTACGAAAAGTTGAAGGGTCTCCAGAAGACAACGAACAAAAGCAATGTTCGT CGAACAACACAAGCACTACTTGGACGAAATCATCGAACAAATCTCTGAATCTCTAA GAGAGTCATCTTGGCCGACGCCAACTTGGACAAGGCTTGTCTGCCTACAACAAGCA CAGAGACAAGCCAATCAGAGAACAAGCCGAAAACATCATCCACTTGTTCACCTTGAC CAACTTGGGTGCCCCAGCCGCTTCAAGTACTTCGACACCACCATCGACAGAAAAGAG ATACACCTTACCAAGGAAGTCTTGGACGCCACCTTGATCCACCAATCTATCACCGGT TTGTACGAAACCAGAATCGACTTGTCTCAATTGGGTGGTGACGGTGGTGGTTCTCAA AGAAGAAGAGAAAAGGTC</p>	
<p>使用表4的富含U的密码子的 Cas9 ORF (无起始或终止密码子; 适于包括在融合蛋白质编码序列中)</p>	<p>GATAAAAAATATTCTATTGGTTTATAGATATGGTACTAATTCTGTTGGTTGGGCTGTTATT ACTGATGAATATAAAGTTCCTTCTAAAAAATTTAAAGTTTTAGGTAATACTGATCGTCA TTCTATTAATAAAAAATTAATTGGTGCTTTATATTGATTCTGGTGAAACTGCTGAAG CTACTCGTTTAAAACGTAAGTCTGCTCGTCGTTATACTCGTCGTAATAAATCGTATTGTT ATTTACAAGAAATTTTTCTAATGAAATGGCTAAAGTTGATGATTCCTTTTTTTCATCGTT TAGAAGAATCTTTTTAGTTGAAGAAGATAAAAAACATGAACGTCATCCTATTTTTGGT AATATTGTTGATGAAGTTGCTTATCATGAAAAATATCCTACTATTTATCATTACGTAAA AAATTAGTTGATTCTACTGATAAAGCTGATTTACGTTTAAATTTATTTAGCTTTAGCTCATA TGATAAATTTTCGTGGTCATTTTTTAAATGAAGGTGATTTAAATCCTGATAATTCGATG TTGATAAATTTATTTATTCATAATAGTTCAAACTTATAATCAATTTTGAAGAAAATCTAT TAATGCTTCTGGTGTGATGCTAAAGCTATTTTATCTGCTCGTTTATCTAAATCTCGTCG TTTAGAAAATTTAATTGCTCAATTACCTGGTGAAAAAAAATGGTTTATTTGGTAATT TAATTGCTTTATCTTTAGGTTTAACTCCTAATTTTAAATCTAATTTTGAATTTAGCTGAAGA TGCTAAATTACAATTATCTAAAGATACTTATGATGATGATTTAGATAATTTATAGCTCAA ATTGGTGATCAATATGCTGATTTATTTTTAGCTGCTAAAAATTTATCTGATGCTATTTTTAT TATCTGATATTTACGTGTTAATACTGAAATTAAGTCTCTTTATCTGCTTCTATGAT TAAACGTTATGATGAACATCAAGATTTAACTTTATTTAAAGCTTTAGTTTCGTC AAC AATTACCTGAAAAATATAAGAAATTTTTTTGATCAATCAAAAATGGTTATGCTGGT TATATTGATGGTGGTCTCTCAAGAAAGAAATTTATAAAATTTATTAACCTATTTTAGAA AAAATGGATGGTACTGAAGAATTATTAGTTAAATTTAAATCGTGAAGATTTATTACGTAA ACAACGACTTTTGATAATGGTCTATTCCTCATCAAATTCATTTAGGTGAATTACATGC TATTTTACGTCGTC AAGAAATTTTATCCTTTTTTAAAAGATAATCGTGA AAAAATTTG AAAAAATTTTAACTTTTTCGTATTCCTTATTATGTTGGTCTTTAGCTCGTGGTAATCTC GTTTTGCTTGGATGACTCGTAAATCTGAAGAACTATTAATCTCCTTGGAAATTTTGAAGA AGTTGTTGATAAAGGTGCTTCTGCTCAATCTTTATTTGAACGATGACTAATTTTGATAA AAATTTACCTAATGAAAAAGTTTTACCTAAACATTTCTTTATTTATGATTAATTTTACTGTT TATAATGAATTAATAAGTTAAATATGTTACTGAAGGTATGCGTAAACCTGCTTTTTTTA TCTGGTGAACAAAAAAGCTATTTGTTGATTTATTTTAAAACTAATCGTAAAGTTTAC TGTTAAACAATTTAAAGAAGATTTTAAAAAATTTGAATGTTTTGATTCTGTTGAAA TTTCTGGTGTGGAAGATCGTTTTAATGCTTCTTTAGGTACTTATCATGATTTATTA AAAA TTATTAAGATAAAGATTTTTTAGATAATGAAGAAATGAAGATATTTTAGAAGATATT TTTTTAACTTTAACTTTATTTGAAGATCGTGAATGATTGAAGAACGTTTAAAAACTTA TGCTCATTATTTGATGATAAAGTTATGAAACAATTTAAACGTCGTCGTTATACTGGTT GGGGTCGTTTATCTCGTAAATTAATTAATGGTATTCGTGATAACAATCTGGTAAA ACTA TTTTAGATTTTTTAAATCTGATGGTTTTGCTAATCGTAAATTTTATGCAATTAATTCATGA TGATTTCTTAACTTTTAAAGAAGATTTCAAAAAGCTCAAGTTTCTGGTCAAGGTGATT CTTTACATGAACATATTGCTAATTTAGCTGGTCTCCTGCTATTA AAAAAGGTATTTTAC AACTGTTAAAGTTGTTGATGAATTAGTTAAAGTTATGGGTCGTCATAAACCTGAAAAT ATTGTTATTGAAATGGCTCGTGA AAATCAAACACTCAAAAAGGTCAAAAAAATTTCTC GTGAACGATGAAACGATTTGAAGAAGGTATTTAAAGAATTAGGTTCTCAAATTTTAAA AGAACATCCTGTTGAAAATACTCAATTACAAAATGAAAAATTATATTTATATTTTAC A AAATGGTCGTGATATGATGTTGATCAAGAATTAGATATTAATCGTTTATCTGATTATGAT GTTGATCATATTGTTCTCAATCTTTTTTAAAGATGATTTCTATTGATAATAAAGTTTFA ACTCGTTCGTGATAAAAATCGTGGTAAATCTGATAATGTTCTTCTGAAAGAAGTTGTTAA AAAAATGAAAAATTTTGGCGTCAATTTAAATGCTAAATTAATTACTCAACGTAAAT TTGATAATTTAACTAAAGCTGAACGTGGTGGTTTTATCTGAATTAGATAAAGCTGGTTTT ATTAACGTC AATTAGTTGAAACTCGTCAAATTAATAACATGTTGCTCAAATTTTAGA TTCTCGTATGAATACTAAATATGATGAAAATGATAAATTAATTCGTGAAGTTAAAGTTAT TACTTTAAATCTAAATTAGTTTCTGATTTTCGTAAGATTTTCAATTTTATAAAGTTTCG TGAAATTAATAATTATCATCATGCTCATGATGCTTATTAAATGCTGTTGTTGGTACTGC TTTAATTA AAAAATATCCTAAATTAAGAATCTGAATTTGTTTATGGTATTATAAAGTTTAT GATGTTCTGAAAATGATTGCTAAATCTGAACAAGAAATTTGGTAAAGCTACTGCTAAATA</p>	<p>143</p>

[0744]

	<p>TTTTTTTATTCTAATATTATGAATTTTTTTTAAAACGTAAATTACTTTAGCTAATGGTGAA ATTCGTAAACGTCTTTAATTGAAACTAATGGTGAAACTGGTGAAATTTGGGATA AAGGTCGTGATTTGCTACTGTTTCGTAAGTTTTATCTATGCCTCAAGTTAATATTGTTA AAAAAACTGAAGTTCAAACTGGTGGTTTTCTAAAGAATCTATTTTACCTAAACGTAA TTCTGATAAAATTAATTGCTCGTAAAAAAGATTGGGATCCTAAAAAATATGGTGGTTTTG ATTCCTACTGTTGCTTATTCTGTTTTAGTTGTTGCTAAAGTTGAAAAAGGTAATCT AAAAAATTAATCTGTAAAGAATTATTAGGTATTACTATTATGGAACGTTCTTCTTTT GAAAAAATCCTATTGATTTTTAGAAAGCTAAAGGTTATAAAGAAGTTAAAAAAGATT TAATTATTAATACCTAAATATTCTTATTGAAATGAAAAATGGTCGTAAACGTATGTT AGCTTCTGCTGGTGAATTACAAAAAGGTAATGAATTAGCTTTACCTTCTAAATATGTTA ATTTTTATATTAGCTTCTCATTATGAAAAATTAAGAAGTTCTCCTGAAGATAATGAAC AAAAACAATTATTTGTTGAACAACATAAACATTATTTAGATGAAATTATTGAACAAATT TCTGAATTTCTAAACGTGTTATTTAGCTGATGCTAATTAGATAAAGTTTTATCTGCT TATAATAAACATCGTGATAAACCTATTCTGTAACAAGCTGAAAAATATTATTCAATTATTT ACTTTAACTAATTTAGGTGCTCCTGCTTTTAAATATTTGATACTACTATTGATCGT AAACGTTATACTTCTACTAAAGAAGTTTTAGATGCTACTTTAATTCATCAATCTATTACT GGTTTATATGAAACTCGTATTGATTTATCTCAATTAGGTGGTGATGGTGGTGGTTCTCCT AAAAAAAACGTAAAGTT</p>	
<p>使用表4的低 G 密码子的 Cas9 ORF (无起始或终 止密码子; 适 于包括在融 合蛋白质编 码序列中)</p>	<p>GACAAAAAATACTCCATCGGCCTCGACATCGGCACCAACTCCGTCGGCTGGGCCGTC ATCACCGACGAATACAAAAGTCCCCTCCAAAAAATCAAAGTCCCTCGGCAACACCGAC AGACACTCCATCAAAAAAACCTCATCGGCGCCCTCCTCTCGACTCCGGCGAAACC GCCGAAGCCACCAGACTCAAAGAACCAGCCAGAAGAAGATACACCAGAAGAAAA ACAGAATCTGCTACCTCCAAGAAATCTTCTCCAACGAAATGGCCAAAGTCGACGACT CCTTCTCCACAGACTCGAAGAATCTTCTCCTCGTCAAGAAGACAAAAACAGAAA GACACCCATCTTCGGCAACATCGTTCGACGAAAGTCGCCTACCACGAAAAATCCCA CCATCTACCACCTCAGAAAAAACTCGTTCGACTCCACCGACAAAGCCGACCTCAGAC TCATCTACCTCGCCCTCGCCACATGATCAAATTCAGAGGCCACTTCCTCATCGAAGG CGACCTCAACCCGACAACCTCCGACGTCGACAAAACCTTTCATCCAACCTCGTCCAAAC CTACAACCAACTCTTCGAAGAAAACCCATCAACGCCTCCGGCTCGACGCCAAAGC CATCTCTCCGCCAGACTCTCAAATCCAGAAGACTCGAAAACTCATCGCCAAACTC CCCGGCGAAAAAAAACGGCTCTTCGGCAACCTCATCGCCCTCTCCCTCGGCCTC ACCCCAACTTCAAATCCAATTCGACCTCGCCGAAGACGCCAAACTCCAATCTCC AAAGACACTACGACGACGACCTCGACAACCTCCTCGCCAAATCGGCGACCAATAC GCCGACCTTCTCCTCGCCGCAAAAAACCTCTCCGACGCCATCCTCCTCCTCGACATCC TCAGAGTCAACACCGAAATCACCAAAGCCCCCTCTCCGCTCCATGATCAAAAGAT ACGACGAACACCACCAAGACCTCACCTCCTCAAAGCCCTCGTCAGACAACAACCTCC CCGAAAAATACAAAAGAAATCTTCTTCGACCAATCCAAAAACGGCTACGCCGGGTACA TCGACGGCGGGCCTCCCAAGAAGAAATCTACAAATTCATCAAACCTCATCTCGAAA AAATGGACGGCACCGAAGAACTCCTCGTCAAACCTCAACAGAGAAGACCTCCTCAGA AAACAAAAGAACCTTCGACAACGGCTCCATCCCCACCAATCCACCTCGGCGAACTC CACGCCATCTCAGAAGACAAGAAGACTTCTACCCCTTCTCAAAGACAACAGAGAA AAAATCGAAAAAATCCTCACCTCAGAATCCCCTACTACGTCGGCCCCCTCGCCAGAA GAACTCCAGATTCGCCTGGATGACCAAGAAATCCGAAGAAACCATCCCCCTGGAA ACTTCGAAGAAGTCGTGACAAAAGGGCCTCCGCCAATCCTTCATCGAAAGAATGA CCAACTTCGACAAAAACCTCCCCAACGAAAAGTCTCCCCAACACTCCCTCCTCT ACGAATACTTACCGTCTACAACGAACTCACCAAAGTCAAATACGTACCCGAAAGCA TGAGAAAACCCGCTTCTCTCCGGCGAACAAAAAAAAGCCATCGTCCGACTCCTCT TCAAAACCAACAGAAAAGTCAACGTAACAACCTCAAAGAAGACTACTTCAAAAA ATCGAATGCTTCGACTCCGTGAAATCTCCGGCGTCAAGACAGATTCAACGCCTCCC TCGGCACCTACCACGACCTCCTCAAATCATCAAAGACAAAGACTTCTCGACAACG AAGAAAACGAAGACATCTCGAAGACATCTCCTCACCTCACCTCCTCGAAGACA GAGAAATGATCGAAGAAAGACTCAAACCTACGCCACCTTTCGACGACAAAAGTCA TGAAACAACCTCAAAGAAGAAGATACACCGGCTGGGGCAGACTCTCCAGAAAATC ATCAACGGCATCAGAGACAAACAATCCGGCAAAACCATCTCGACTTCTCAAATCC GACGGCTTCGCCAACAGAAACTTATGCAACTCATCCACGACGACTCCCTCACCTTC AAAGAAGACATCCAAAAGCCCAAGTCTCCGGCCAAGGCGACTCCCTCCACGAACA CATCGCCAACTCGCCGGCTCCCCGCCATCAAAAAAGGCATCCTCAAACCGTCAA AGTCGTGACGAACTCGTCAAAGTCATGGGACAGACACAAACCCGAAAACATCGTCAT CGAAATGGCCAGAGAAAACCAAAACCCAAAAAGGCCAAAAAACTCCAGAGAA AGAATGAAAAGAATCGAAGAAGGCATCAAAGAAGTCCGCTCCAAATCCTCAAAGA ACACCCGTCGAAAACACCAACTCCAAAACGAAAAACTTACCTTACTACCTCCA AAACGGCAGAGACATGTACGTGACCAAGAAGTCAACAGACTCTCCGACTA CGACGTGACACATCGTCCCCAATCCTTCTCAAAGACGACTCCATCGACAACAA AGTCTCACAGATCCGACAAAACAGAGGCAATCCGACAACGTCCTCCCTCCGAAG AAGTCGTCAAAAAATGAAAAACTACTGGAGACAACCTCCTCAACGCCAAACTCATCA CCAAAAGAAAATTCGACAACCTACCAAAGCCGAAAAGAGGGCCTCTCCGAACTC GACAAAGCCGGCTCATCAAAGACAACCTCGTCAAAACAGACAATCACCAACA</p>	<p>144</p>

[0745]

[0746]

	<p>CGTCGCCAAATCCTCGACTCCAGAATGAACACCAAATACGACGAAAACGACAAACT CATCAGAGAAAGTCAAAGTCATCACCTCAAATCCAAACTCGTCTCCGACTTCAGAAA AGACTTCCAATTCTACAAAGTCAGAGAAATCAACAACCTACCACGCCCCACGACGC CTACCTCAACGCCGTCTCGTCCGCCACCGCCCTCATCAAAAAATACCCCAAACTCGAATCC GAATTCGTCTACGGCGACTACAAAGTCTACGACGTCAGAAAAATGATCGCCAAATCC GAAACAAGAAATCGGCAAAAGCCACCGCCAAATACTTCTTACTCCAACATCATGAAC TCTTCAAAACCGAAATCACCTCGCCAACGGCGAAATCAGAAAAAGACCCCTCATCG AAACCAACGGCGAAACCGGCCAAATCGTCTGGGACAAAGGCAGAGACTTCGCCACC GTCAGAAAAGTCTCTCCATGCCCAAGTCAACATCGTCAAAAAAACCGAAGTCCAA ACCGCGGGCTTCTCAAAGAATCCATCTCCCCAAAAGAACTCCGACAAAACATCATC GCCAGAAAAAAGACTGGGACCCCAAAAAATACGGCGGGCTTCGACTCCCCACCGT CGCCTACTCCGTCTCGTCTCGCCAAAGTCGAAAAAGGCAAATCAAAAAACTCAA ATCCGTCAAAGAACTCCTCGGCATCACCATCATGGAAAAGATCCTCCTTCGAAAAAAA CCCCATCGACTTCTCGAAGCCAAAGGCTACAAAGAAGTCAAAAAAGACCTCATCAT CAAACCTCCCCAAATACTCCCTCTTCGAACTCGAAAACGGCAGAAAAAGAATGCTCG CTCCGCCGGCGAACTCCAAAAAGGCAACGAACTCGCCCTCCCTCCAAATACGTCAA CTTCTCTACCTCGCTCCCACTACGAAAAACTCAAAGGCTCCCCGAAAGACAACGA ACAAAAACAACCTTTCGTGCAACAACACAAACACTACCTCGACGAAATCATCGAACA AATCTCCGAATCTCCAAAAGAGTCATCCTCGCCGACGCCAACCTCGACAAAAGTCT CTCCGCCACAAACAACACAGAGACAAACCCATCAGAGAACAAGCCGAAACATCA TCCACCTTTCACCCTCACCACCTCGGGCGCCCCGCGCCTTCAAATACTTCGACAC CACCATCGACAGAAAAAGATACACCTCCACCAAAAGAAGTCTCGACGCCACCCTCAT CCACCAATCCATCACCGGCCCTACGAAAACGAAATCGACCTTCCCAACTCGGGCG CGAGCGGGCGGGCTCCCCAAAAAAAAGAAAAGTCC</p>	
<p>使用表4的低 C 密码子的 Cas9 ORF (无起始或终 止密码子; 适 于包括在融 合蛋白质编 码序列中)</p>	<p>GATAAGAAGTATAGTATTGGATTGGATATTGGAACAAATAAGTGGGATGGGCTGTGAT TACAGATGAGTATAAGGTGCCTAGTAAGAAGTTAAAGGTGTTGGGAAATACAGATAGA CATAGTATTAAGAAGAATTTGATTGGAGCTTTGTTGTTTGATAGTGGAGAGACAGCTG AGGCTACAAGATTGAAGAGAACAGCTAGAAGAAGATATACAAGAAGAAAGAATAGA ATTTGTTATTTGCAGGAGATTTTTAGTAATGAGATGGCTAAGGTGGATGATAGTTTTTT CATAGATTGGAGGAGAGATTTTTGGTGGAGGAGGATAAGAAGCATGAGAGACATCCT ATTTTTGGAAATATTGTGGATGAGGTGGCTTATCATGAGAAGTATCCTACAATTTATCAT TTGAGAAAGAAGTTGGTGGATAGTACAGATAAGGCTGATTTGAGATTGATTTATTTGG CTTTGGCTCATATGATTAAGTTTAGAGGACATTTTTGATTGAGGGAGATTTGAATCCT GATAATAGTGATGTGGATAAGTTGTTTATTTCAGTTGGTGACAGACATATAATCAGTTGTT GAGGAGAATCCTATTAATGCTAGTGGAGTGGATGCTAAGGCTATTTTGGATGCTAGATT GAGTAAGAGTAGAAGATTGGAGAATTTGATTGCTCAGTTGCCTGGAGAGAAGAAGAA TGGATTGTTTGGAAATTTGATTGCTTTGAGTTTGGGATTGACACCTAATTTAAGAGTA ATTTTGGCTGAGGATGCTAAGTTGCAAGTTGAGTAAGGATACATATGATGATGAT TTGGATAATTTGTTGGCTCAGATTGGAGATCAGTATGCTGATTTGTTTTGGCTGCTAA GAATTTGAGTGATGCTATTTGTTGAGTGATATTTGAGAGTGAATACAGAGATTACAA AGGCTCCTTTGAGTGCTAGTATGATTAAGAGATATGATGAGCATCATCAGGATTTGACA TTGTTGAAGGCTTTGGTGAGACAGCAGTTGCCTGAGAAGTATAAGGAGATTTTTTTG ATCAGAGTAAGAATGGATATGCTGGATATATTGATGGAGGAGCTAGTCAGGAGGAGTT TTATAAGTTTATTAAGCCTATTTGGAGAAGATGGATGGAACAGAGGAGTTGTTGGTG AAGTTGAATAGAGAGGATTTGTTGAGAAAAGCAGAGAACATTTGATAATGGAAGTATTC CTCATCAGATTCATTTGGGAGAGTTGCATGCTATTTTGAAGAAGACAGGAGGATTTTTAT CCTTTTTGAAGGATAATAGAGAGAAGATTGAGAAGATTTTGCATTTAGAATTCCTTA TTATGTGGACCTTTGGCTAGAGGAAATAGTAGATTTGCTTGGATGACAAGAAAGAGT GAGGAGACAATTACACCTTGAATTTTGGAGGAGTGGTGGATAAGGGAGCTAGTGCT CAGAGTTTTATTGAGAGAATGACAAATTTGATAAGAATTTGCCTAATGAGAAGGTGT TGCTAAGCATAGTTTGTGTATGAGTATTTTACAGTGTATAATGAGTTGACAAAAGGTG AAGTATGTGACAGAGGGAATGAGAAAGCCTGCTTTTTTGGAGTGAGAGAGAGAGAAGAA GGCTATTGTGGATTGTTGTTAAGACAATAGAAAGGTGACAGTGAAGCAGTTGAA GGAGGATTATTTAAGAAGATTGAGTGTGTTGATAGTGTGGAGATTAGTGGAGTGGAG GATAGATTTAATGCTAGTTTGGGAACATATCATGATTTGTTGAAGATTATTAAGGATAAG GATTTTTGGATAATGAGGAGAATGAGGATATTTTGGAGGATATTGTGTTGACATTGAC ATTGTTTGGAGATAGAGAGATGATTGAGGAGAGATTGAAGACATATGCTCATTGTTT GATGATAAGGTGATGAAGCAGTTGAAGAGAAGAAGATATACAGGATGGGGAAGATTG AGTAGAAAAGTTGATTAATGGAATTAAGATAAGCAGAGTGGAAAAGACAATTTGGATT TTTTGAAGAGTGATGGATTGCTAATAGAAATTTATGCAAGTTGATTGATGATGATGAT TGACATTTAAGGAGGATATTCAGAAGGCTCAGGTGAGTGACAGGAGAGATGTTTGC ATGAGCATATTGCTAATTTGGCTGGAAGTCTGCTATTAAGAAGGGAATTTTGCAGAC AGTGAAGGTGGTGGATGAGTTGGTGAAGGTGATGGGAAGACATAAGCCTGAGAATAT TGTGATTGAGATGGCTAGAGAGAATCAGACAACACAGAAGGGACAGAAGAATAGTA GAGAGAAATGAAGAGAATTGAGGAGGGAATTAAGGAGTTGGGAAGTCAGATTG AAGGAGCATCCTGTGGAGAATACACAGTTGCAGAATGAGAAGTTGTATTGTATTATT TGCAGAATGGAAGAGATATGATGTGGATCAGGAGTTGGATATTAATAGATTGAGTGAT</p>	<p>145</p>

[0747]

	<p>TATGATGTGGATCATATTGTGCCTCAGAGTTTTTTGAAGGATGATAGTATTGATAATAAG GTGTTGACAAGAAGTGATAAGAATAGAGGAAAAGAGTGATAATGTGCCTAGTGAGGAG GTGGTGAAGAAGATGAAGAATTATTGGAGACAGTTGTTGAATGCTAAGTTGATTACAC AGAGAAAAGTTTTGATAATTTGACAAAAGGCTGAGAGAGGAGGATTGAGTGAGTTGGATA AGGCTGGATTTATTAAGAGACAGTTGGTGGAGACAAGACAGATTACAAAAGCATGTGG CTCAGATTTTGGATAGTGAATGAATACAAAAGTATGATGAGAATGATAAGTTGATTAGA GAGGTGAAGGTGATTACATTGAAGAGTAAGTTGGTGAAGTATTTAGAAAAGGATTTTC AGTTTTATAAGGTGAGAGAGATTAATAATTATCATCATGCTCATGATGCTTATTTGAATG CTGTGGTGGGAACAGCTTTGATTAAGAAGTATCCTAAGTTGGAGAGTGAGTTTGTGTA TGGAGATTATAAGGTGTATGATGTGAGAAAAGATGATTGCTAAGAGTGAGCAGGAGATT GGAAAAGGCTACAGCTAAGTATTTTTTTATAGTAATATTATGAATTTTTTAAGACAGAG ATTACATTGGCTAATGGAGAGATTAGAAAAGAGACCTTTGATTGAGACAAATGGAGAG ACAGGAGAGATTGTGTGGGATAAGGGAAGAGATTTTGCTACAGTGAGAAAAGGTGTTG AGTATGCCCTCAGGTGAATATTGTGAAGAAGACAGAGGTGCAGACAGGAGGATTAGT AAGGAGAGTATTTGCCTAAGAGAAAATAGTATAAGTTGATTGCTAGAAAAGAGGATT GGGATCCTAAGAAGTATGGAGGATTTGATAGTCTACAGTGGCTTATAGTGTGTTGGT GGTGGCTAAGGTGGAGAAGGGAAGAGTAAGAAGTTGAAGAGTGTGAAGGAGTTGT TGGGAATTACAATTATGGAGAGAAAGTAGTTTTGAGAAAAGTCTATTGATTTTTTGGGA GGTAAGGGATATAAGGAGGTGAAGAAGGATTGATTATTAAGTTGCCTAAGTATAGT TTGTTTGAGTTGGAGAATGGAAGAAAAGAGAATGTTGGCTAGTGCTGGAAGTTGCGAG AAGGGAATGAGTTGGCTTTGCCTAGTAAGTATGTGAATTTTTTGTATTTGGCTAGTCA TTATGAGAAGTTGAAGGGAAGTCCTGAGGATAATGAGCAGAAGCAGTTGTTTGTGGA GCAGCATAAGCATTATTTGGATGAGATTATTGAGCAGATTAGTGAAGTTAGTAAGAGA GTGATTTTGGCTGATGCTAATTTGGATAAGGTGTTGAGTGTATAATAAGCATTAGAGA TAAGCCTATTAGAGAGCAGGCTGAGAATATTATTCAATTTGTTTACATTGACAAATTTGG GAGCTCCTGCTGCTTTTAAAGTATTTTGATACAACAATTGATAGAAAAGAGATATACAAGT ACAAAAGGAGGTGTTGGATGCTACATTGATTATCAGAGTATTACAGGATTGTATGAGA CAAGAATTGATTGAGTCAGTTGGGAGGAGATGGAGGAGGAAGTCTAAGAAGAAG AGAAAAGGTG</p>	
<p>使用表4的低 A 密码子的 Cas9 ORF (无起始或终 止密码子; 适 于包括在融 合蛋白质编 码序列中)</p>	<p>GACAAGAAGTACTCCATCGGCCTGGACATCGGCACCAACTCCGTGGGCTGGGCCGTG ATCACCGACGAGTACAAGGTGCCCTCCAAGAAGTTCAAGGTGCTGGGCAACACCGA CCGGCACTCCATCAAGAAGAACCTGATCGGCGCCCTGCTGTTGACTCCGGCGAGAC CGCCGAGGCCACCCGGCTGAAGCGGACCCGCCGGCGGTACACCCGGGAAGA ACCGGATCTGCTACCTGCAGGAGATCTTCTCCAACGAGATGGCCAAGGTGGACGACT CCTTCTCCACCGGCTGGAGGAGTCTTCTGGTGGAGGAGACAAGAAGCAGGAG CGGCACCCATCTTCGGCAACATCGTGGACGAGGTGGCCTACCACGAGAAGTACCC ACCATCTACCACCTGCGGAAGAAGCTGGTGGACTCCACCGACAAGGCCGACCTGCGG CTGATCTACCTGGCCCTGGCCACATGATCAAGTTCCGGGGCCACTTCTGATCGAGG GCGACCTGAACCCCGACAACCTCCGACGTGGACAAGCTGTTTCATCCAGCTGGTGCAGA CCTACAACAGCTGTTTCGAGGAGAACCCATCAACGCCTCCGGCGTGGACGCCAAGG CCATCCTGTCCGCCCGGCTGTCCAAGTCCCGGCGGCTGGAGAACCTGATCGCCAGC TGCCCGCGAGAAGAAGAACCGCCTGTTCCGGCAACCTGATCGCCCTGTCCTGGCC TGACCCCAACTTCAAGTCCAACCTTCGACCTGGCCGAGGACGCCAAGCTGCAGCTGT CCAAGGACACCTACGACGACGACCTGGACAACCTGCTGGCCAGATCGGCGACCAAGT ACGCCGACCTGTTCTGGCCGCCAAGAACCTGTCCGACGCCATCCTGCTGTCCGACA TCTTCCGGGTGAACACCGAGATCACAAGGCCCCCTGTCCGCTCCATGATCAAGC GGTACGACGAGCACCACAGGACTGACCCTGCTGAAGGCCCTGGTGGCGCAGCAG CTGCCCGAGAAGTACAAGGAGATCTTCTTCGACAGTCCAAGAACGGCTACGCCGGC TACATCGACGGCGGCGCCTCCAGGAGGATTTCTACAAGTTCATCAAGCCATCCTG GAGAAGATGGACGGCACCGAGGAGCTGCTGGTGAAGCTGAACCGGGAGGACCTGCT GCGGAAGCAGCGGACCTTCGACAACCGCTCCCAACGAGAAGGTGCTGCCAAGCACTCC GCTGTACGAGTACTTACCCTGTACAACGAGCTGACCAAGGTGAAGTACGTGACCGA GGGCATGCGGAAGCCGCTTCTGTCGGCGGAGCAGAAGAAGGCCATCGTGGACCT GCTGTTCAAGACCAACCGGAAGGTGACCTGGAAGCAGCTGAAGGAGGACTACTTCA AGAAGATCGAGTGTTCGACTCCGTGGAGATCTCCGGCTGGAGGACCGGTTCAACG CCTCCCTGGGCACTACCACGACCTGCTGAAGATCATCAAGGACAAGGACTTCTGG ACAACGAGGAGAACGAGGACATCCTGGAGGACATCGTGTGACCCTGACCCTGTTCCG AGGACCGGGAGATGATCGAGGAGCGGCTGAAGACCTACGCCACCTGTTTCGACGAC AAGGTGATGAAGCAGCTGAAGCGGCGGCGGTACACCGGCTGGGGCCGGCTGTCCCG GAAGCTGATCAACGGCATCCGGGACAAGCAGTCCGGCAAGACCATCCTGGACTCCT GAAGTCCGACGGCTTCGCAACCGGAACCTCATGCAGCTGATCCACGACGACTCCCT GACCTTCAAGGAGGACATCCAGAAGGCCAGGTGTCGGCCAGGGCGACTCCCTGC</p>	<p>146</p>

[0748]

	<p>ACGAGCACATCGCCAACTGGCCGGCTCCCCGCCATCAAGAAGGGCATCCTGCAGACCGTGAAGGTGGTGGACGAGCTGGTGAAGGTGATGGGCCGGCACAAGCCCGAGAATCGTGATCGAGATGGCCCGGAGAACCAGACCACCCAGAAGGGCCAGAAGAACTCCGGGAGCGGATGAAGCGGATCGAGGAGGGCATCAAGGAGCTGGGCTCCCGATCCGAGGAGCAGCCCGTGGAGAACACCCAGCTGCAGAACGAGAAGCTGTACCTGTACTACCTGCAGAACCGCCGGACATGTACGTGGACCAGGAGCTGGACATCAACCCTGGTCCGACTACGACGTGGACCACATCGTGCCCCAGTCTTCTGAAGGACGACTCCATCGACAACAAGGTGCTGACCCGGTCCGACAAGAACCAGGGGCAAGTCCGACAACGTGCCCTCCGAGGAGGTGGTGAAGAAGATGAAGAATACTGGCGGCAGCTGCTGAACGCCAAGCTGATCACCCAGCGGAAGTTCGACAACCTGACCAAGGCCGAGCGGGGCGGCCTGTCCGAGCTGGACAAGGCCGGCTTCATCAAGCGGCAGCTGGTGGAGACCCGGCAGATCACCAAGCAGTGGCCAGATCCTGGACTCCCGGATGAACACCAAGTACGACGAGAACGACAAGCTGATCCGGGAGGTGAAGGTGATCACCTGAAGTCCAAGCTGGTGTCCGACTTCCGGAAGGACTTCCAGTTCTACAAGGTGCGGGAGATCAACAATACTACCACCAGCCCACGACCTACCTGAACGCCGTGGTGGGCACCGCCCTGATCAAGAAGTACCCCAAGCTGGAGTCCGAGTTCGTGTACGGCGACTACAAGGTGTACGACGTGCGGAAGATGATCGCAAGTCCGAGCAGGAGATCGGCAAGGCCACCGCAAGTACTTCTTACTCCAACATCATGAACCTTCTCAAGACCGAGATCACCTGGCCAACGGCGAGATCCGGAAGCGGCCCTGATCGAGACCAACGGCGAGACCGGCGAGATCGTGTGGGACAAGGGCCGGGACTTCGCCACCGTGGGAAGGTGCTGTCCATGCCCAAGGTGAACATCGTGAAGAAGACCGAGGTGCAGACCGGCGGCTTCTCCAAGGAGTCCATCCTGCCAAGCGGAACTCCGACAAGCTGATCGCCCGAAGAAGGACTGGGACCCCAAGAAGTACGGCGGCTTCGACTCCCCACCGTGGCCTACTCCGTGCTGGTGGTGGCCAAGGTGGAGAAGGGCAAGTCAAGAAGCTGAAGTCCGTGAAGGAGCTGCTGGGCATACCATCATGGAGCGGTCTCTTCGAGAAGAACCCATCGACTTCTGGAGGCCAAGGGCTACAAGGAGGTGAAGAAGGACCTGATCATCAAGCTGCCAAGTACTCCCTGTTTCGAGCTGGAGAACGGCCGGAAGCGGATGCTGGCCTCCGCCGGCGAGCTGCAGAAAGGGCAACGAGCTGGCCTGCCCTCCAAGTACGTGAACCTTCTGTACCTGGCCTCCACTACGAGAAGCTGAAGGGCTCCCGAGGACAACGAGCAGAAGCAGCTGTTCTGTGGAGCAGCACAAGCACTACCTGGACGAGATCATCGACAGATCTCCGAGTTCCTCAAGCGGGTATCCTGGCCGACGCCAACCTGGACAAGGTGCTGTCCGCTACAACAAGCACCGGGACAAGCCATCCGGGAGCAGGCCGAGAATCATCCACCTGTTACCCTGACCAACCTGGGCGCCCCCGCCGCTCAAGTACTTCGACACCACCTCGACCGGAAGCGGTACACCTCCACCAAGGAGGTGCTGGACGCCACCTGATCCACCAGTCCATACCGGCCTGTACGAGACCCGGATCGACTGTCCAGCTGGGCGGCGACGGCGGGCTCCCCAAGAAGAAGCGGAAGGTG</p>	
<p>使用表4的低A/U密码子的Cas9 ORF(无起始或终止密码子;适用于包括在融合蛋白质编码序列中)</p>	<p>GACAAGAAGTACAGCATCGGCCTGGACATCGGCACCAACAGCGTGGGCTGGGCCGTGATCACCGACGAGTACAAGGTGCCAGCAAGAAGTTCAGGTGCTGGCAACACCGACCCGGCACAGCATCAAGAAGAACCTGATCGGCGCCCTGCTGTTTCGACAGCGCGAGACCGCCGAGGCCACCCGGCTGAAGCGGACCGCCGGCGGCGGTACACCCGGCGGAA GAACCGGATCTGCTACCTGCAGGAGATCTTACGCAACGAGATGGCCAAGGTGGACGACAGCTTCTTCCACCGGCTGGAGGAGAGCTTCTGGTGGAGGAGGACAAGAAGCAGCAGCGGCACCCATCTTCGGCAACATCGTGGACGAGGTGGCCTACCACGAGAAGTACCACCATCTACCACCTGCCGAAGAAGCTGGTGGACAGCACCGACCAAGGCCACTGCGGCTGATCTACCTGGCCCTGGCCACATGATCAAGTTCGGGGGCCACTTCTGATCGAGGGCGACCTGAACCCGACAACAGCGACGTGGACAAGCTGTTTCATCCAGCTGGTG CAGACCTACAACAGCTGTTTCGAGGAGAACCCATCAACGCCAGCGGCGTGGACGCGCAAGGCCATCCTGAGCGCCCGGCTGAGCAAGAGCCGGCGGCTGGAGAACCTGATCGCCCTGAGCCTGGCCCTGACCCCAACTTCAAGAGCAACTTCGACCTGGCCGAGGACGCCAAGCTGCAGCTGAGCAAGGACACCTACGACGACGACCTGGACAACCTGCTGGCCAGATCGGCGACAGTACGCCGACCTGTTCTGGCCCAAGAACCTGAGCGACGCCATCTGCTGAGCGACATCCTGCGGGTGAACACCGAGATCACCAAGGCCCCCTGAGCGCCAGCATGATCAAGCGGTACGACGAGCACCACCAGGACCTGACCCTGCTGAAGGCCCTGGTGGCAGCAGCTGCCGAGAAGTACAAGGAGATCTTTCGACCAGAGCAAGAACGGCTACGCCGGCTACATCGACGGCGGCCAGCCAGGAGGAGTTCACAAGTTCATCAAGCCCATCTGGAGAAGATGGACGGCACCGAGGAGCTGCTGGTGAAGCTGAACCGGAGGACCTGCTGCGGAAGCAGCGGACCTTCGACAACGGCAGCATCCCCACCAGATCCACCTGGGCGAGCTGCACGCCATCCTGCGGCGGAGGAGGACTTCTACCCCTTCTGAA GGACAACCGGGAGAAGATCGAGAAGATCCTGACCTTCCGGATCCCTACTACGTGGGCCCCCTGGCCCGGGCAACAGCCGTTTCGCTGGATGACCCGGAAGAGCGAGGAGACCATCACCCCTGGAACCTTCGAGGAGGTGGTGGACAAGGGCGCCAGCGCCAGAGCTTCATCGAGCGGATGACCAACTTCGACAAGAACCTGCCCAACGAGAAGGTGCTGCCAAGCACAGCCTGCTGTACGAGTACTTACCCTGTACAACGAGCTGACCAAGGTGAAGTACGTGACCGAGGGCATGCGGAAGCCGCTTCTGAGCGGCGAGCAGAAGAAGGCATCGTGGACCTGTTCAAGACCAACCGGAAGGTGACCGTGAAGCAGCTGAAGGAGGACTACTTCAAGAAGATCGAGTGTTCGACAGCGTGGAGATCAGCGGCGTGGAGGACCGGTTCAACGCCAGCTGGGCACCTACCACGACCTGCTGAAGATCATCAAGGAC</p>	<p>147</p>

[0749]

	<p>AAGGACTTCCTGGACAACGAGGAGAACGAGGACATCCTGGAGGACATCGTGTGAC CCTGACCCTGTTTCGAGGACCGGGAGATGATCGAGGAGCGGCTGAAGACCTACGCCCA CCTGTTTCGACGACAAGGTGATGAAGCAGCTGAAGCGGGCGGGTACACCGGCTGGG GCCGGCTGAGCCGGAAGCTGATCAACGGCATCCGGGACAAGCAGAGCGGCAAGACC ATCCTGGACTTCCTGAAGAGCGACGGCTTCGCCAACCGGAACCTCATGCAGCTGATC CACGACGACAGCCTGACCTTCAAGGAGGACATCCAGAAGGCCAGGTGAGCGGCCA GGGCGACAGCCTGCACGAGCACATCGCCAACCTGGCCGGCAGCCCCGCCATCAAGA AGGGCATCCTGCAGACCGTGAAGGTGGTGGACGAGCTGGTGAAGGTGATGGCCGG CACAAGCCCCGAGAATCGTGTATCGAGATGGCCGGGAGAACCAGACCACCCAGAA GGGCCAGAAGAACAGCCGGGAGCGGATGAAGCGGATCGAGGAGGGCATCAAGGAG CTGGGCAGCCAGATCCTGAAGGAGCACCCCGTGGAGAACACCCAGTGCAGAACGA GAAGCTGTACCTGTACTACCTGCAGAACGGCCGGGACATGTACGTGGACCAGGAGCT GGACATCAACCGGCTGAGCGACTACGACGTGGACCACATCGTCCCCAGAGCTTCT GAAGGACGACAGCATCGACAACAAGGTGCTGACCCGGAGCGACAAGAACCAGGGGC AAGAGCGACAACGTGCCAGCGAGGAGGTGGTGAAGAAGATGAAGAACTACTGGCC GCAGCTGCTGAACGCCAAGCTGATCACCCAGCGGAAGTTCGACAACCTGACCAAGG CCGAGCGGGCGGCCCTGAGCGAGCTGGACAAGGCCGGCTTCATCAAGCGGCAGCTG GTGGAGACCCGGCAGATCACAAGCAGCTGGCCAGATCCTGGACAGCCGGATGAA CACCAAGTACGACGAGAACGACAAGCTGATCCGGGAGGTGAAGGTGATCACCTGA AGAGCAAGCTGGTGAAGGACTTCCGGAAGGACTTCCAGTTCTACAAGTGCAGGAG ATCAACAACCTACCACCGCCACGACGCCTACCTGAACGCCGTGGTGGGCACCGCC CTGATCAAGAAGTACCCCAAGCTGGAGAGCGAGTTCGTGTACGGCGACTACAAGGTG TACGACGTGCGGAAGATGATCGCCAAGAGCGAGCAGGAGATCGGCAAGGCCACCGC AAGTACTTCTTCTACAGCAACATCATGAACTTCTTCAAGACCGAGATCACCTGGCC AACGGCGAGATCCGGAAGCGGCCCTGATCGAGACCAACGGCGAGACCGGCAGAT CGTGTGGGACAAGGGCCGGACTTCGCCACCGTGGCGAAGGTGCTGAGCATGCCCC AGGTGAACATCGTGAAGAAGACCGAGGTGCAGACCGGGCGCTTCAGCAAGGAGAGC ATCTGCCAAGCGGAACAGCGACAAGCTGATCGCCCGAAGAAGGACTGGGACCC CAAGAAGTACGGCGGCTTCGACAGCCCCACCGTGGCCTACAGCGTGTGGTGGTGGC CAAGGTGGAGAAGGGCAAGAGCAAGAAGCTGAAGAGCGTGAAGGAGCTGCTGGGC ATCACCATCATGGAGCGGAGCAGCTTCGAGAAGAACCCATCGACTTCTGGAGGCC AAGGGCTACAAGGAGGTGAAGAAGGACCTGATCATCAAGCTGCCAAGTACAGCCT TTCGAGCTGGAGAACGGCCGGAAGCGGATGCTGGCCAGCGCCGGCGAGCTGCAGA AGGGCAACGAGCTGGCCCTGCCAGCAAGTACGTGAACTTCTGTACTTGGCCAGCC ACTACGAGAAGCTGAAGGGCAGCCCCGAGGACAACGAGCAGAAGCAGCTGTTCTGTG GAGCAGCACAAGCACTACCTGGACGAGATCATCGAGCAGATCAGCGAGTTCAGCAA GCCGGTGATCCTGGCCGACGCCAACCTGGACAAGGTGCTGAGCGCTACAACAAGC ACCGGGACAAGCCCATCCGGGAGCAGGCCGAGAACATCATCCACTGTTACCCTGA CCAACCTGGGCGCCCCCGCCCTTCAAGTACTTTCGACACCACCATCGACCCGGAAGC GGTACACCAGCACAAGGAGGTGCTGGACGCCACCTGATCCACCAGAGCATCACCG GCCTGTACGAGACCCGGATCGACCTGAGCCAGCTGGGCGGCGACGGCGGCGGACG CCCAAGAAGAAGCGGAAGGTG</p>	
<p>使用表4的低 A密码子, 具 有两个C端 NLS序列的 Cas9 ORF (无起始或终 止密码子; 适 于包括在融 合蛋白质编 码序列中)</p>	<p>GACAAGAAGTACTCCATCGGCCCTGGACATCGGCACCAACTCCGTGGGCTGGGCCGTG ATCACCGACGAGTACAAGGTGCCCTCCAAGAAGTTCAGGTGCTGGGCAACACCGA CCGGCACTCCATCAAGAAGAACCTGATCGGCGCCCTGCTGTTTCGACTCCGGCGAGAC CGCCGAGGCCACCCGGCTGAAGCGGACCGCCCGGGCGGGTACACCCGGCGGAAGA ACCGGATCTGCTACTTGCAGGAGATCTTCTCCAACGAGATGGCCAAGGTGGACGACT CCTTCTTCCACCGGCTGGAGGAGTCTTCTGGTGGAGGAGGACAAGAAGCACGAG CGGCACCCATCTTCGGCAACATCGTGGACGAGGTGGCCTACCACGAGAAGTACCC ACCATCTACCACCTGCGGAAGAAGCTGGTGGACTCCACCGACAAGGCCGACCTGCGG CTGATCTACCTGGCCCTGGCCACATGATCAAGTTCGGGGCCACTTCTGATCGAGG GCGACCTGAACCCCGACAACCTCGACGTGGACAAGCTGTTTCATCCAGCTGGTGCAGA CCTACAACAGCTGTTTCGAGGAGAACCCATCAACGCCTCCGGCGTGGACGCCAAGG CCATCCTGTCCGCCCGGCTGTCCAAGTCCCGCGGCTGGAGAACCTGATCGCCAGC TGCCCGGCGAGAAGAAGAACGGCCTGTTTCGGCAACCTGATCGCCCTGTCCCTGGGCC TGACCCCAACTTCAAGTCCAACCTTCGACCTGGCCGAGGACGCCAAGCTGCAGCTGT CCAAGGACACCTACGACGACGACCTGGACAACCTGCTGGCCAGATCGGGCAGCAGT ACGCCGACCTGTCTTGGCCGCCAAGAACCTGTCCGACGCCATCCTGCTGTCCGACA TCCTGCGGGTGAACACCGAGATCACAAGGCCCCCTGTCCGCCTCCATGATCAAGC GGTACGACGAGCACCACGAGCCTGACCCTGCTGAAGGCCCTGGTGGCGCAGCAG CTGCCCGAGAAGTACAAGGAGATCTTCTTCGACAGTCCAAGAACGGCTACGCGCCG TACATCGACGGCGGCGCCTCCAGGAGGAGTTCACAAGTTCATCAAGCCATCCTG GAGAAGATGGACGGCACCGAGGAGCTGCTGGTGAAGCTGAACCGGGAGGACCTGCT GCGGAAGCAGCGGACCTTCGACAACGGCTCCATCCCCACCAGATCCACCTGGGCGA GCTGCACGCCATCCTGCGGCGGAGGAGGACTTCTACCCCTTCTGAAGGACAACCG GGAGAAGATCGAGAAGATCCTGACCTTCCGGATCCCTACTACGTGGGCCCCCTGGC CCGGGCAACTCCCGTTCGCTGGATGACCCGGAAGTCCGAGGAGACCATCACCC</p>	<p>148</p>

[0750]

	<p>CTGGAAGTTCGAGGAGGTGGTGGACAAGGGCGCCTCCGCCAGTCCTTCATCGAGCG GATGACCAACTTCGACAAGAACCTGCCAACGAGAAGGTGCTGCCAAGCACTCCCT GCTGTACGAGTACTTCACCGTGTACAACGAGCTGACCAAGGTGAAGTACGTGACCGA GGGCATGCGGAAGCCCGCTTCTGTCCGGCGAGCAGAAGAAGGCCATCGTGGACCT GCTGTTCAAGACCAACCGGAAGGTGACCGTGAAGCAGCTGAAGGAGGACTACTTCA AGAAGATCGAGTGTCTCGACTCCGTGGAGATCTCCGGCGTGGAGGACTTCAACG CCTCCCTGGGCACCTACCACGACCTGCTGAAGATCATCAAGGACAAGGACTTCCTGG ACAACGAGGAGAACGAGGACATCCTGGAGGACATCGTGTGACCCTGACCCTGTTCG AGGACCGGGAGATGATCGAGGAGCGGCTGAAGACCTACGCCACCTGTTCCGACGAC AAGGTGATGAAGCAGCTGAAGCGGCGGCTACACCGGCTGGGGCCGGGTGTCCCG GAAGTGTATCAACGGCATCCGGGACAAGCAGTCCGGCAAGACCATCCTGGACTTCT GAAGTCCGACGGCTTCGCAACCGGAACCTCATGCAGCTGATCCACGACGACTCCCT GACCTTCAAGGAGGACATCCAGAAGGCCAGGTGTCCGGCCAGGGCGACTCCCTGC ACGAGCACATCGCAACCTGGCCGGCTCCCCGCCATCAAGAAGGGCATCCTGCAGA CCGTGAAGGTGGTGGACGAGCTGGTGAAGGTGATGGCCCGGCAACAAGCCCGAAGC ATCGTGTATCGAGATGGCCCGGAGAACCAGACCACCCAGAAGGGCCAGAAGAATC CCGGGAGCGGATGAAGCGGATCGAGGAGGGCATCAAGGAGCTGGGCTCCAGATCC TGAAGGAGCACCCCGTGGAGAACACCCAGCTGCAGAACGAGAAGCTGTACCTGTAC TACCTGCAGAACGGCCGGACATGTACGTGGACCAGGAGCTGGACATCAACCGGCTG TCCGACTACGACGTGGACACCATCGTGTCCCGAGTCCCTTCTGAAGGACCCGGCAGAT GACAACAAGGTGCTGACCCGGTCCGACAAGAACCAGGGGCAAGTCCGACAACGTGCC CTCCGAGGAGGTGGTGAAGAAGATGAAGAATACTGGCGGCAGCTGCTGAACGCCA AGTGTATCACCCAGCGGAAGTTCGACAACCTGACCAAGGCCGAGCGGGCCGGCCTG TCCGAGCTGGACAAGGCCGGTTCATCAAGCGGCAGCTGGTGGAGACCCGGCAGAT CACCAAGCAGTGGCCAGATCCTGGACTCCCGGATGAACACCAAGTACGACGAGA ACGACAAGCTGATCCGGGAGGTGAAGGTGATCACCTGAAGTCCAAGTGGTGTCCG ACTTCCGGAAGGACTTCCAGTTCATAAGGTGCGGGAGATCAACAATACTACCACCAG CCCACGACGCCTACTGAACGCCGTGGTGGGCACCGCCCTGATCAAGAAGTACCCCA AGCTGGAGTCCGAGTTCGTGTACGGCGACTACAAGGTGTACGACGTGCGGAAGATGA TCGCCAAGTCCGAGCAGGAGATCGGCAAGGCCACCGCCAAGTACTTCTTACTCCA ACATCATGAACTTCTTCAAGACCGAGATCACCTGGCCAACGGCGAGATCCGGAAGC GGCCCCTGATCGAGACCAACGGCGAGACCGGCGAGATCGTGTGGGACAAGGGCCGG GACTTCGCCACCGTGGGGAAGGTGCTGTCCATGCCCAAGGTGAACATCGTGAAGAAG ACCGAGGTGCAGACCGGCGGCTTCTCCAAGGAGTCCATCCTGCCAAGCGGAAGTCC GACAAGCTGATCGCCCGGAAGAAGGACTGGGACCCCAAGAAGTACGGCGGCTTCGA CTCCCCACCGTGGCCTACTCCGTGCTGGTGGTGGCCAAGGTGGAGAAGGGCAAGTC CAAGAAGCTGAAGTCCGTGAAGGAGCTGCTGGGCATCACCATCATGGAGCGGTCTC CTTCGAGAAGAACCCCATCGACTTCTGGAGGCCAAGGGCTACAAGGAGGATGAGA AGGACCTGATCATCAAGCTGCCAAGTACTCCCTGTTTCGAGCTGGAGAACGGCCGGA AGCGGATGCTGGCCTCCGCCGGCGAGCTGCAGAAGGGCAACGAGCTGGCCCTGCC TCCAAGTACGTGAACTTCTGTACTTGGCCTCCACTACGAGAAGCTGAAGGGCTCC CCCAGGACAACGAGCAGAAGCAGCTGTTCTGTGGAGCAGCACAAGACTACTTGGGA CGAGATCATCGAGCAGATCTCCGAGTTCCTCAAGCGGGTGTCTGGCCGACGCCAA CCTGGACAAGGTGCTGTCCGCTACAACAAGCACCGGGACAAGCCATCCGGGAGC AGGCCGAGAATCATCCACCTGTTACCCTGACCAACCTGGGCGCCCCCGCCGCT TCAAGTACTTCGACACCACCATCGACCGGAAGCGGTACACCTCCACCAAGGAGGTGC TGGACGCCACCCCTGATCCACAGTCCATCACCGCCCTGTACGAGACCCGGATCGACC TGTCCAGCTGGGCGGCGACGGCTCCGGCTCCCCCAAGAAGAAGCGGAAGGTGGAC GGTCCCCCAAGAAGAAGCGGAAGGTGGACTCCGGC</p>	
<p>使用表4的低 A 密码子的 Cas9 切口酶 ORF (无起始 或终止密码 子; 适于包括 在融合蛋白 质编码序列 中)</p>	<p>GACAAGAAGTACTCCATCGGCCTGGCCATCGGCACCAACTCCGTGGGCTGGGCCGTG ATCACCGACGAGTACAAGGTGCCCTCAAGAAGTTCAAGGTGCTGGGCAACACCGA CCGGCACTCCATCAAGAAGAACCTGATCGGCGCCCTGCTGTTGACTCCGGCGAGAC CGCCGAGGCCACCCGGCTGAAGCGGACCGCCCGGCGGCGGTACACCCGGCGGAAGA ACCGGATCTGCTACCTGCAGGAGATCTTCTCAACGAGATGGCCAAGGTGGACGACT CCTTCTTCCACCGGCTGGAGGAGTCTTCTGGTGGAGGAGGACAAGAAGCAGAG CGGCACCCATCTTCGGCAACATCGTGGACGAGGTGGCCTACCACGAGAAGTACCC ACCATCTACCACCTGCGGAAGAAGCTGGTGGACTCCACCGACAAGGCCGACCTGCGG CTGATCTACCTGGCCCTGGCCACATGATCAAGTTCGGGGCCACTTCTGATCGAGG GCGACCTGAACCCCGACAACCTCCGACGTGGACAAGCTGTTTATCCAGCTGGTGCAGA CCTACAACCAGCTGTTTCGAGGAGAACCCATCAACGCCTCCGGCGTGGACGCCAAGG CCATCCTGTCCGCCCGGTGTCCAAGTCCCGGCGGCTGGAGAACCTGATCGCCAGC TGCCCGGCGAGAAGAAGAAGCGCCTGTTCCGGCAACCTGATCGCCCTGTCCCTGGGCC TGACCCCAACTTCAAGTCCAATTCGACCTGGCCGAGGACGCCAAGCTGCAGCTGT CCAAGGACACCTACGACGACGACCTGGACAACCTGCTGGCCAGATCGGCGACCACT ACGCCAGCTGTTCTTCCGGCCCAAGAACCCTGTCCGACGCCATCCTGTCCGACA TCTTCCGGGTGAACACCGAGATACCAAGGCCCCCTGTCCGCTCCATGATCAAGC GGTACGACGAGCACCAAGGACCTGACCCTGCTGAAGGCCCTGGTGGCGACGAG</p>	<p>149</p>

[0751]

	<p>CTGCCCGAGAAGTACAAGGAGATCTTCTTCGACCAGTCCAAGAACGGCTACGCCGGC TACATCGACGGCGGCGCCTCCCAGGAGAGTTCTACAAGTTCATCAAGCCATCCTG GAGAAGATGGACGGCACCAGGAGCTGCTGGTGAAGCTGAACCGGGAGGACCTGCT GCGGAAGCAGCGGACCTTCGACAACGGCTCCATCCCCACCAGATCCACCTGGGCGA GCTGCACGCCATCTGCGGCGGCAGGAGGACTTCTACCCCTTCTGAAGGACAACCG GGGAAGATCGAGAAGATCCTGACCTTCCGGATCCCCACTACTACGTGGGCCCTTGG CCGGGGCAACTCCCGGTTTCGCTGGATGACCCGGAAGTCCGAGGAGACCATCACCCC CTGGAACCTCGAGGAGGTGGTGGACAAGGGCGCCTCCGCCAGTCTTCATCGAGCG GATGACCAACTTCGACAAGAACCTGCCAACGAGAAGGTGCTGCCAAGCACTCCCT GCTGTACGAGTACTTACCCTGTACAACGAGCTGACCAAGGTGAAGTACGTGACCGA GGGCATGCGGAAGCCCGCTTCTGTCCGGCAGCAGAAGAAGGCCATCGTGGACCT GCTGTTCAAGACCAACCGGAAGGTGACCGTGAAGCAGCTGAAGGAGGACTACTTCA AGAAGATCGAGTGTTCGACTCCGTGGAGATCTCCGGCGTGGAGGACCGGTTCAACG CCTCCCTGGGCACCTACCACGACCTGCTGAAGATCATCAAGGACAAGGACTTCTGG ACAACGAGGAGAACGAGGACATCCTGGAGGACATCGTGTGACCCTGACCCTGTTCG AGGACCGGGAGATGATCGAGGAGCGGCTGAAGACCTACGCCACCTGTTTCGACGAC AAGGTGATGAAGCAGCTGAAGCGGGCGGCTACACCGCTGGGGCCGGCTGTCCCG GAAGCTGATCAACGGCATCCGGGACAAGCAGTCCGGCAAGACCATCCTGGACTTCT GAAGTCCGACGGCTTCGCAACCGGAACCTCATGCAGTGTCCACGACGACTCCCT GACCTTCAAGGAGGACATCCAGAAGGCCAGGTGTCCGGCAGGGCAGCTCCCTGC ACGAGCACATCGCCAACCTGGCCGGCTCCCCGCCATCAAGAAGGGCATCCTGCAGA CCGTGAAGGTGGTGGACGAGCTGGTGAAGGTGATGGGCCGGCACAAGCCCGAGAAC ATCGTGATCGAGATGGCCCGGAGAACCAGACCACCCAGAAGGGCCAGAAGAAGTCC CCGGGAGCGGATGAAGCGGATCGAGGAGGGCATCAAGGAGCTGGGCTCCAGATCC TGAAGGAGCACCCCGTGGAGAACACCCAGCTGCAGAACGAGAAGCTGTACCTGTAC TACCTGCAGAACCGCCGGGACATGTACGTGGACCAGGAGCTGGACATCAACCGGCTG TCCGACTACGACGTGGACCACATCGTGCCCCAGTCTTCTGAAGGACGACTCCATC GACAACAAGGTGCTGACCCGGTCCGACAAGAACCAGGGGCAAGTCCGACAACGTGCC CTCCGAGGAGGTGGTGAAGAAGATGAAGAATACTGGCGGACAGCTGTGAACGCCA AGCTGATCACCCAGCGGAAGTTCGACAACCTGACCAAGGCCGAGCGGGCGGCTG TCCGAGCTGGACAAGGCCGGCTTCATCAAGCGGCAGCTGGTGGAGACCCGGCAGAT CACCAAGCAGTGGCCAGATCCTGGACTCCCGGATGAACACCAAGTACGAGTGAGA ACGACAAGCTGATCCGGGAGGTGAAGGTGATCACCTGAAGTCCAAGCTGGTGTCCG ACTTCCGGAAGGACTTCCAGTCTACAAGGTGCGGGAGATCAACAATACTACCACAG CCCACGACGCCTACCTGAACGCCGTGGTGGGCACCGCCCTGATCAAGAAGTACCCCA AGCTGGAGTCCGAGTTCGTGTACGGGACTACAAGGTGTACGACGTGCGGAAGATGA TCGCCAAGTCCGAGCAGGAGATCGGCAAGGCCACCGCCAAGTACTTCTTACTCCA ACATCATGAACTTCTTCAAGACCGAGATCACCTGGCCAACCGGCGAGATCCGGGAGC GGCCCTGATCGAGACCAACGGCGAGACCGGCGAGATCGTGTGGGACAAGGGCCGG GACTTCGCCACCGTGCAGGAAGGTGCTGTCCATGCCCCAGGTGAACATCGTGAAGAAG ACCGAGGTGCAGACCGGCGGCTTCTCCAAGGAGTCCATCTGCCAAGCGGAACTCC GACAAGCTGATCGCCCGGAAGAAGGACTGGGACCCCAAGAAGTACCGCGGCTTCA CTCCCCACCGTGGCCTACTCCGTGCTGGTGGTGGCCAAGGTGGAGAAGGGCAAGTC CAAGAAGCTGAAGTCCGTGAAGGAGCTGCTGGGCATCACCATATGGAGCGGTCCCT CTTCGAGAAGAACCCATCGACTTCTGGAGGCCAAGGGTACAAGGAGGTGAAGA AGGACCTGATCATCAAGCTGCCAAGTACTCCCTGTTTCGAGCTGGAGAACGGCCGGA AGCGGATGCTGGCTCCGCGGCGAGCTGCAGAAGGGCAACGAGCTGGCTGGTGCAG TCCAAGTACGTGAACCTTCTGTACTGGCCTCCACTACGAGAAGCTGAAGGGCTCC CCCAGGACAACGAGCAGAAGCAGCTGTTCGTGGAGCAGCACAAGCACTACCTGGA CGAGATCATCGAGCAGATCTCCGAGTCTCCAAGCGGGTATCCTGGCCGACGCCAA CCTGGACAAGGTGCTGTCCGCCTACAACAAGCACCGGGACAAGCCATCCGGGAGC AGGCCGAGAACATCATCACCTGTTACCCTGACCAACCTGGGCGCCCCCGCCGCT TCAAGTACTTCGACACCACATCGACCGGAAGCGGTACACCTCCACCAAGGAGGTGC TGGACGCCACCTGATCCACCAGTCCATCACCGGCTGTACGAGACCCGGATCGACC TGTCCAGCTGGGCGGCGACGGCGGCTCCCCAAGAAGAAGCGGAAGGTG</p>	
<p>使用表4的低 A 密码子的 Cas9 切口酶 ORF (无NLS 且无起始或 终止密码子; 适于包括在 融合蛋白质</p>	<p>GACAAGAAGTACTCCATCGGCCTGGCCATCGGCACCAACTCCGTGGGCTGGGCCGTG ATCACCGACGAGTACAAGGTGCCCTCCAAGAAGTTCAGGTGCTGGGCAACACCGA CCGGCACTCCATCAAGAAGAACCTGATCGGCGCCCTGCTGTTTCGACTCCGGCAGAC CGCCGAGGCCACCCGGCTGAAGCGGACCGCCCGGCGGCTACACCGGCGGAAGA ACCCGATCTGCTACTTGCAGGAGATCTTCTCCAACGAGATGGCCAAGGTGGACGACT CCTTCTCCACCGGCTGGAGGAGTCTTCTGGTGGAGGAGGACAAGAAGCACGAG CGGCACCCATCTTCGGCAACATCGTGGACGAGGTGGCCTACCACGAGAAGTACCC ACCATCTACCACCTGCGGAAGAAGCTGGTGGACTCCACGACAAGGCCGACCTGCGG CTGATCTACTGGCCCTGGCCACATGATCAAGTTCGGGGCCACTTCTGATCGAGG GCGACCTGAACCCGACAACCTCCGACGTGGACAAGCTGTTTCATCCAGCTGATCGAGA CCTACAACAGCTGTTTCGAGGAGAACCCATCAACGCCTCCGGCGTGGACGCCAAGG CCATCTGTCCGCCCGGCTGTCCAAGTCCCGGCGGCTGGAGAACCTGATCGCCAGC</p>	<p>150</p>

[0752]

<p>编码序列中)</p>	<p>TGCCCCGCGAGAAGAAGAACGGCCTGTTCCGGCAACCTGATCGCCCTGTCCCTGGGCC TGACCCCCAACTTCAAGTCCAACCTTCGACCTGGCCGAGGACGCCAAGCTGCAGCTGT CCAAGGACACCTACGACGACGACCTGGACAACCTGCTGGCCCAGATCGGGACCAGT ACGCCGACCTGTTCTGGCCGCCAAGAACCTGTCCGACGCCATCCTGCTGTCCGACA TCCTGCGGGTGAACACCGAGATCACCAAGGCCCCCTGTCCGCTCCATGATCAAGC GGTACGACGAGCACACCAGGACTGACCCTGCTGAAGGCCCTGGTGGCGCAGCAG CTGCCCGAGAAGTACAAGGAGATCTTCTTCGACCAGTCCAAGAACGGCTACGCCGGC TACATCGACGGCGGCGCCTCCAGGAGGAGTTCTACAAGTTCATCAAGCCATCCTG GAGAAGATGGACGGCACCCGAGGAGCTGCTGGTGAAGCTGAACCGGGAGGACCTGCT GCGGAAGCAGCGGACCTTCGACAACGGCTCCATCCCCACCAGATCCACTGGGCGA GCTGCACGCCATCCTGCGGGCGGAGGAGACTTCTACCCCTTCTGAAGGACAACCG GGAGAAGATCGAGAAGATCCTGACCTTCCGGATCCCCTACTACGTGGGCCCCCTGGC CCGGGGCAACTCCCGGTTCCGCTGGATGACCCGGAAGTCCGAGGAGACCATCACCC CTGGAACCTTCGAGGAGGTGGTGGACAAGGGCGCCTCCGCCAGTCTTTCATCGAGCG GATGACCAACTTCGACAAGAACCTGCCAACGAGAAGGTGCTGCCAAGCACTCCCT GCTGTACGAGTACTTACCCTGTACAACGAGCTGACCAAGGTGAAGTACGTGACCGA GGGCATGCGGAAGCCGCTTCTGTCCGGCGAGCAGAAGAAGGCCATCGTGGACCT GCTGTTCAAGACCAACCGGAAGGTGACCGTGAAGCAGCTGAAGGAGGACTACTTCA AGAAGATCGAGTGTTCGACTCCGTGGAGATCTCCGGCTGGAGGACCGGTTCAACG CCTCCCTGGGCACTACCACGACCTGCTGAAGATCATCAAGGACAAGGACTCCTGG ACAACGAGGAGAACGAGGACATCCTGGAGGACATCGTGTGACCCTGACCCTGTTCC AGGACCGGGAGATGATCGAGGAGCGGCTGAAGACCTACGCCACCTGTTCCGACGAC AAGGTGATGAAGCAGCTGAAGCGGGCGGCTACACCGGCTGGGGCCGGCTGTCCCG GAAGTGTATCAACGGCATCCGGGACAAGCAGTCCGGCAAGACCATCCTGGACTTCT GAAGTCCGACGGCTTCGCAACCGGAACCTCATGCAGCTGATCCACGACGACTCCCT GACCTTCAAGGAGGACATCCAGAAGGCCAGGTGTCCGGCCAGGGCGACTCCCTGC ACGAGCAGATCGCAACCTGGCCGGCTCCCCGCCATCAAGAAGGGCATCCTGCAGA CCGTGAAGGTGGTGGACGAGCTGGTGAAGGTGATGGGCGGCACAAGCCCGAGA ATCGTGATCGAGATGGCCCGGGAACCAAGACACCCAGACCCAGAAGGGCCAGAACTC CCGGGAGCGGATGAAGCGGATCGAGGAGGGCATCAAGGAGCTGGGCTCCAGATCC TGAAGGAGCACCCCGTGGAGAACACCCAGCTGCAGAACGAGAAGCTGTACCTGTAC TACCTGCAGAACCGCCGGGACATGTACGTGGACCAGGAGCTGGACATCAACCGGCTG TCCGACTACGACGTGGACCACATCGTGCCTCCAGTCTTCTGAAGGACGACTCCATC GACAACAAGGTGCTGACCCGGTCCGACAAGAACCAGGGGCAAGTCCGACAACGTGCC CTCCGAGGAGGTGGTGAAGAAGATGAAGAAGTACTGGCGGCAGCTGCTGAACGCCA AGCTGATCAACAGCGGAAGTTCGACAACCTGACCAAGGCCGAGCGGGGGCGGCTG TCCGAGCTGGACAAGGCCGGCTTTCATCAAGCGGCAGCTGGTGGAGACCCGGCAGAT CACCAAGCACGTGGCCAGATCCTGGACTCCCGGATGAACACCAAGTACGACGAGA ACGACAAGCTGATCCGGGAGGTGAAGGTGATCACCTGAAGTCCAAGCTGGTGTCCG ACTTCCGGAAGGACTTCCAGTTCATAAGGTGCGGGAGATCAACAACCTACCACACG CCCACGACGCCTACTGAACGCCGTGGTGGGCACCGCCCTGATCAAGAAGTACCCCA AGTGGAGTCCGAGTTCGTGTACGGCGACTACAAGGTGTACGACGTGCGGAAGATGA TCGCCAAGTCCGAGCAGGAGATCGGCAAGGCCACCGCCAAGTACTTCTTACTCCA ACATCATGAACCTTCTCAAGACCGAGATCACCTGGCCAACGGCGAGATCCGGAAGC GGCCCCTGATCGAGACCAACGGCGAGACCGGGAGATCGTGTGGGACAAGGGCCGG GACTTCGCCACCGTGGCGAAGGTGCTGTCCATGCCCCAGGTGAACATCGTGAAGAAG ACCGAGGTGCAGACCGCGGCTTCTCCAAGGAGTCCATCCTGCCCAAGCGGAACCTC GACAAGCTGATCGCCGGAAGAAGGACTGGGACCCCAAGAAGTACGGCGGCTTCGA CTCCCCACCGTGGCCTACTCCGTGCTGGTGGTGGCCAAGGTGGAGAAGGGCAAGTC CAAGAAGCTGAAGTCCGTGAAGGAGCTGCTGGGCATCACCATATGGAGCGGTCTCT CTTCGAGAAGAACCCCATCGACTTCTGGAGGCCAAGGGCTACAAGGAGGTGAAGA AGGACCTGATCATCAAGCTGCCAAGTACTCCCTGTTTCGAGCTGGAGAACGGCCGGA AGCGGATGCTGGCTCCGCCGGCGAGCTGCAAGAAGGGCAACGAGCTGGCCCTGCC TCCAAGTACGTGAACCTTCTGTACCTGGCTCCCACTACGAGAAGCTGAAGGGCTCC CCCAGGACAACGAGCAGAAGCAGCTGTTCTGTGGAGCAGCACAAGCACTACCTGGA CGAGATATCGAGCAGATCTCCGAGTTCCTCAAGCGGGTATCCTGGCCGACGCCAA CCTGGACAAGGTGCTGTCCGCTACAACAAGCACCGGGACAAGCCATCCGGGAGC AGGCCGAGAACATCATCCACCTGTTACCTGACCAACCTGGGCGCCCCCGCCGCT TCAAGTACTTCGACACCACATCGACCGGAAGCGGTACACCTCCACCAAGGAGGTGC TGGACGCCACCCTGATCCACCAGTCCATACCGGCCCTGTACGAGACCCGGATCGACC TGTCCAGCTGGGCGGCGAC</p>	
<p>使用表4的低 A密码子, 具 有两个C端 NLS序列的</p>	<p>GACAAGAAGTACTCCATCGGCCTGGCCATCGGCACCAACTCCGTGGGCTGGGCCGTG ATCACCGACGAGTACAAGGTGCCCTCCAAGAAGTTCAGGTGCTGGGCAACACCGA CCGGCACTCCATCAAGAAGAACCTGATCGGGCCCTGCTGTTTCGACTCCGGCGAGAC CGCCGAGGCCACCGGCTGAAGCGGACCGCCCGGGCGGATACACCCGGCGGAAGA ACCGGATCTGCTACCTGCAGGAGATCTTCTCCAACGAGATGGCCAAGGTGGACGACT CCTTCTCCACCGGCTGGAGGAGTCTTCTGGTGGAGGAGGACAAGAAGCACGAG</p>	<p>151</p>

<p>Cas9 切口酶 ORF (无起始或终止密码子; 适于包括在融合蛋白质编码序列中)</p>	<p>CGGCACCCCATCTTCGGCAACATCGTGACGAGGTGGCCTACCACGAGAAGTACCC ACCATCTACCACCTGCGGAAGAAGCTGGTGACTCCACCGACAAGGCCGACCTGCGG CTGATCTACCTGGCCCTGGCCACATGATCAAGTTCCGGGGCCACTTCTGATCGAGG GCGACCTGAACCCCGACAACCTCCGACGTGGACAAGCTGTTTCATCCAGCTGGTGCAGA CCTACAACCAGCTGTTTCGAGGAGAACCCCATCAACGCCTCCGGCGTGGACGCCAAGG CCATCCTGTCCCGCCGGCTGTCCAAGTCCCGCGCGCTGGAGAACCTGATCGCCACAGC TGCCCGGCGAGAAGAAGAACGGCCTGTTCCGGCAACCTGATCGCCCTGTCCCTGGGCC TGACCCCAACTTCAAGTCCAACCTCGACCTGGCCGAGGACGCCAAGCTGCAGCTGT CCAAGGACACCTACGACGACGACCTGGACAACCTGCTGGCCAGATCGGGCAGCAGT ACGGCAGCTGTTCTTGGCCGCAAGAACCTGTCCGACGCCATCTGCTGTCCGACA TCCTGCGGGTGAACACCGAGATCACCAAGGCCCCCTGTCCGCTCCATGATCAAGC GGTACGACGAGCACCACCAGGACCTGACCCTGCTGAAGGCCCTGGTGCAGCAGCAG CTGCCCGAGAAGTACAAGGAGATCTTCTTCGACCAGTCCAAGAACGGCTACGCCGGC TACATCGACGGCGCGCCTCCAGGAGGAGTTCTACAAGTTCATCAAGCCCATCTG GAGAAGATGGACGGCACCGAGGAGCTGCTGGTGAAGCTGAACCGGAGGACCTGCT GCGGAAGCAGCGGACCTTCGACAACGGCTCCATCCCCACCAGATCCACCTGGGCGA GCTGCACGCCATCTGCGGCGGACGAGGACTTCTACCCCTTCTGAAGGACAACCG GGAGAAGATCGAGAAGATCTGACCTTCCGGATCCCTACTACGTGGGCCCCCTGGC CCGGGCAACTCCCGGTTCCGCTGGATGACCCGGAAGTCCGAGGAGACCATCAGCC CTGGAACTTCGAGGAGGTGGTGGACAAGGGCGCCTCCGCCAGTCTCATCGAGCG GATGACCAACTTCGACAAGAACCTGCCAACGAGAAGGTGCTGCCAAGCACTCCCT GCTGTACGAGTACTTACCCTGTACAACGAGCTGACCAAGGTGAAGTACGTGACCGA GGCATGCGGAAGCCCGCCTTCTGTCCGGCAGCAGAAGAAGGCCATCGTGGACCT GCTGTTCAAGACCAACCGGAAGGTGACCGTGAAGCAGCTGAAGGAGGACTTCA AGAAGATCGAGTGCTTCGACTCCGTGGAGATCTCCGGCGTGGAGGACCGGTTCAACG CCTCCCTGGGCACCTACCAGACCTGCTGAAGATCATCAAGGACAAGGACTTCTGG ACAACGAGGAGAACGAGGACATCTGGAGGACATCGTGTGACCTGACCTGTTCC AGGACCGGAGATGATCGAGGAGCGGCTGAAGACCTACGCCACCTGTTTCGACGAC AAGGTGATGAAGCAGCTGAAGCGCGCGGTACACCGCTGGGGCCGGCTGTCCCG GAAGCTGATCAACGGCATCCGGGACAAGCAGTCCGGCAAGACCATCTGGACTTCT GAAGTCCGACGGCTTCGCCAACCGGAACCTCATGCAGCTGATCCACGACGACTCCCT GACCTTCAAGGAGGACATCCAGAAGGCCAGGTGTCCGGCCAGGGCGACTCCCTGC ACGACACATCGCAACCTGGCCGGCTCCCCGCCATCAAGAAGGCCATCTGCAGA CCGTGAAGGTGGTGGACGAGCTGGTGAAGGTGATGGGCCGACAAAGCCCGAGAAC ATCGTGATCGAGATGGCCCGGAGAACCAGACCACCCAGAAGGGCCAGAAGAACTC CCGGGAGCGGATGAAGCGGATCGAGGAGGGCATCAAGGAGCTGGGTCCTCCAGATCC TGAAGGAGCACCCCGTGGAGAACACCCAGCTGCAGAACGAGAAGCTGTACCTGTAC TACCTGCAGAACCGCCGGGACATGTACGTGGACAGGAGCTGGACATCAACCGGCTG TCCGACTACGACGTGGACCACATCGTGCCCCAGTCTTCTGAAGGACGACTCCATC GACAACAAGGTGCTGACCCGGTCCGACAAGAACCAGGGCAAGTCCGACAACGTGCC CTCCGAGGAGGTGGTGAAGAAGATGAAGAATACTGGCGGACGCTGCTGAACGCCA AGTGATACCCAGCGGAAGTTCGACAACCTGACCAAGGCCGAGCGGGCGGCTGTG TCCGAGCTGGACAAGGCCGGCTTCATCAAGCGGACGCTGGTGGAGACCCGGCAGAT CACCAAGCAGTGGCCAGATCCTGGACTCCCGGATGAACACCAAGTACGACGAGA ACGACAAGCTGATCCGGGAGGTGAAGGTGATCACCTGAAGTCCAAGCTGGTGTCCG ACTTCCGGAAGGACTTCCAGTTCTACAAGGTGCGGGAGATCAACAATAACACCACG CCACGACGCCACTTGAACGCCGTGGTGGGCACCGCCCTGATCAAGAAGCGGTCTCT AGCTGGAGTCCGAGTTCGTGTACGGCGACTACAAGGTGTACGACGTGCGGAAGATGA TCGCCAAGTCCGAGCAGGAGATCGGCAAGGCCACCGCCAAGTACTTCTTACTCCA ACATCATGAACTTCTTCAAGACCGAGATCACCTGGCCAACCGCGAGATCCGGAAGC GGCCCTGATCGAGACCAACGGCGAGACCGGCGAGATCGTGTGGGACAAGGGCCGG GACTTCGCCACCGTGGGAAGGTGCTGTCCATGCCCCAGGTGAACATCGTGAAGAAG ACCGAGGTGCAGACCGGCGGCTTCTCCAAGGAGTCCATCCTGCCAAGCGGAACCTC GACAAGCTGATCGCCCGGAAGAAGGACTGGGACCCCAAGAAGTACGGCGGCTTCGA CTCCCCACCGTGGCCTACTCCGTGCTGGTGGTGGCCAAGGTGGAGAAGGGCAAGTC CAAGAAGCTGAAGTCCGTGAAGGAGCTGCTGGGCATCACCATCATGGAGCGGTCTCT CTTCGAGAAGAACCCATCGACTTCTGGAGGCCAAGGGCTACAAGGAGGTGAAGA AGGACCTGATCATCAAGCTGCCAAGTACTCCCTGTTTCGAGCTGGAGAACGGCCGGA AGCGGATGCTGGCTCCGCGGCGAGCTGCAGAAGGGCAACGAGCTGGCCCTGCC TCCAAGTACGTGAACCTTCTGTACCTGGCCTCCACTACGAGAAGCTGAAGGGCTCC CCCAGGACAACGAGCAGAAGCAGCTGTTCTGTGGAGCAGCACAAAGCACTACCTGGA CGAGATCATCGAGCAGATCTCCGAGTTCTCCAAGCGGTGATCCTGGCCGACGCCAA CCTGGACAAGGTGCTGTCCGCCTACAACAAGCACCGGGACAAGCCATCCGGGAGC AGCCGAGAATCATCCACCTGTTACCTGACCAACCTGGGCGCCCCCGCCCT TCAAGTACTTCGACACCACATCGACCGGAAGCGGTACACCTCCAAGGAGGTGCT TGGACGCCACCTGATCCACAGTCCATACCGGCTGTACGAGACCCGGATCGACC TGTCCAGCTGGGCGGCGACGGCTCCGGCTCCCCAAGAAGAAGCGGAAGGTGGAC</p>
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[0753]

<p>使用表4的低A密码子的dCas9 ORF(无起始或终止密码子;适用于包括在融合蛋白质编码序列中)</p>	<p>GGCTCCCCAAGAAGAAGCGGAAGGTGGACTCCGGC GACAAGAAGTACTCCATCGGCCTGGCCATCGGCACCAACTCCGTGGGCTGGGCGGTG ATCACCGACGAGTACAAGGTGCCCTCCAAGAAGTTCAAGGTGCTGGGCAACACCGA CCGGCACTCCATCAAGAAGAACCTGATCGGGCCCTGCTGTTGACTCCGGCGAGAC CGCCGAGGCCACCCGGCTGAAGCGGACCCCGCGGCGGTACACCCGGCGGAAGA ACCGGATCTGCTACCTGCAGGAGATCTTCTCCAACGAGATGGCCAAGGTGGACGACT CCTTCTTCCACCGGCTGGAGGAGTCTTCTTCTGGTGGAGGAGGACAAGAAGCACGAG CGGCACCCCATCTTCGGCAACATCGTGGACGAGGTGGCCTACCACGAGAAGTACCCC ACCATCTACCACCTGCGGAAGAAGCTGGTGGACTCCACCGACAAGGCCGACTGCGG CTGATCTACCTGGCCCTGGCCACATGATCAAGTTCGGGGGCCACTTCTGATCGAGG GCGACCTGAACCCCGACAACCTCCGACGTGGACAAGCTGTTTCATCCAGCTGGTGCAGA CCTACAACCAAGCTGTTTCGAGGAGAACCCCATCAACGCCTCCGGCGTGGACGCCAAGG CCATCCTGTCGCCCGGCTGTCCAAGTCCCGCGGCTGGAGAACCTGATCGCCAGC TGCCCGGCGAGAAGAAGAAGCGCCTGTTCCGGCAACCTGATCGCCCTGTCCCTGGGCC TGACCCCAACTTCAAGTCCAACCTTCGACCTGGCCGAGGACGCCAAGCTGCAGTGT CCAAGGACACCTACGACGACGACCTGGACAACCTGCTGGCCAGATCGGCGACCAAGT ACGCCGACCTGTTCTGGCCGCCAAGAAGCTGTCGACGCCATCCTGCTGTCCGACA TCCTGCGGGTGAACACCGAGATCACCAGGCCCCCTGTCCGCTCCATGATCAAGC GGTACGACGAGCACCACCAGGACCTGACCCTGCTGAAGGCCCTGGTGCGGCAGCAG CTGACCGAGAAGTACAAGGAGATCTTCTTCGACCAAGTCCAAGAAGGACGACCGCGC TACATCGACGGCGCGCCTCCAGGAGGAGTTCTACAAGTTCATCAAGCCATCCTG GAGAAGATGGACGGCACCGAGGAGCTGCTGGTGAAGCTGAACCGGGAGGACCTGCT GCGGAAGCAGCGGACCTTCGACAACGGCTCCATCCCCACCAGATCCACCTGGGCGA GCTGCACGCCATCCTGCGGCGGCGAGGACTTCTACCCCTTCTGAAGGACAACCG GGAGAAGATCGAGAAGATCCTGACCTTCCGGATCCCTACTACGTGGGCCCTGGC CCGGGGCAACTCCCGGTTCCGCTGGATGACCCGGAAGTCCGAGGAGACCATCACCCC CTGGAACTTCGAGGAGGTGGTGGACAAGGGCGCTCCGCCAGTCTTCATCGAGCG GATGACCAACTTCGACAAGAACCTGCCAACGAGAAGGTGCTGCCAACGACTCCCT GCTGTACGAGTACTTACCCTGTACAACGAGCTGACCAAGGTGAAGTACGTGACCGA GGGCATGCGGAAGCCCGCTTCTGTCCGGCAGCAGAAGAAGGCCATCGTGGACCT GCTGTTCAAGACCAACCGGAAGGTGACCGTGAAGCAGCTGAAGGAGGACTACTTCA AGAAGATCGAGTGCTTCGACTCCGTGGAGATCTCCGGCGTGGAGGACCGGTTCAACG CCTCCCTGGCACCTACCACGACTGCTGAAGATCATCAAGGACAAGGACTTCTGTG ACAACGAGGAGAACGAGGACATCCTGGAGGACATCGTGTGACCTGACCTGACCTGTTCC AGGACCGGGAGATGATCGAGGAGCGGCTGAAGACCTACGCCACCTGTTTCGACGAC AAGGTGATGAAGCAGCTGAAGCGGCGGCGGTACACCGGCTGGGGCCGGCTGTCCCG GAAGCTGATCAACGGCATCCGGGACAAGCAGTCCGGCAAGACCATCCTGGACTTCT GAAGTCCGACGGCTTCGCCAACCGGAACCTTCATGACGCTGATCCACGACGACTCCCT GACCTTCAAGGAGGACATCCAGAAGGCCAGGTGTCCGGCCAGGGCGACTCCCTGC ACGAGCACATCGCAACCTGGCCGGCTCCCCGCCATCAAGAAGGGCATCCTGCAGA CCGTGAAGGTGGTGGACGAGCTGGTGAAGGTGATGGGCCGGCACAAGCCCGAGAAC ATCGTGATCGAGATGGCCGGGAGAACCAGACCACCAAGAAGGGCCAGAAGAACT CCGGGAGCGGATGAAGCGGATCGAGGAGGGCATCAAGGAGCTGGGCTCCAGATCC TGAAGGAGCACCCCGTGGAGAACACCCAGCTGCAGAACGAGAAGCTGTACCTGTAC TACCTGCAGAACGGCCGGGACATGTACGTGGACCAGGAGCTGGACATCAACCGGCTG TCCGACTACGACGTGGACGCCATCGTGCCCCAGTCTTCTGAAGGACGACTCCATC GACAACAAGGTGCTGACCCGGTCCGACAAGAACCAGGGGCAAGTCCGACAACCGTCC CTCCGAGGAGGTGGTGAAGAAGATGAAGAATACTGGCGGACGCTGCTGAACGCCA AGCTGATCACCCAGCGGAAGTTCGACAACCTGACCAAGGCCGAGCGGGCGGCTG TCCGAGCTGGACAAGGCCGGCTTCATCAAGCGGCAGCTGGTGGAGACCCGGCAGAT CACCAAGCACGTGGCCAGATCCTGGACTCCCGATGAACACCAAGTACGACGAGA ACGACAAGCTGATCCGGGAGGTGAAGGTGATCACCTGAAGTCCAAGCTGGTGTCCG ACTTCCGGAAGGACTTCCAGTTCTACAAGGTGCGGGAGATCAACAATACTACCACACG CCCACGACGCCTACCTGAACGCCGTGGTGGGCACCGCCCTGATCAAGAAGTACCCCA AGCTGGAGTCCGAGTTCGTGTACGGCGACTACAAGGTGTACGACGTGCGGAAGATGA TCGCCAAGTCCGAGCAGGAGATCGGCAAGGCCACCGCCAAGTACTTCTTACTTCCA ACATCATGAACCTTCAAGACCGAGATCACCTGGCCAACGGCGAGATCCGGAAGC GGCCCCTGATCGAGACCAACGGCGAGACCGGCGAGATCGTGTGGGACAAGGGCCGG GACTTCGCCACCGTGCAGGAAGGTGCTGTCCATGCCCAAGGTGAACATCGTGAAGAAG ACCGAGGTGCAGACCGGCGGCTTCTCCAAGGAGTCCATCTGCCAAGCGGAACCTCC GACAAGCTGATCGCCCGGAAGAAGGACTGGGACCCCAAGAAGTACGGCGGCTTCGA CTCCCCACCGTGGCCTACTCCGTGCTGGTGGTGGCCAAGGTGGAGAAGGGCAAGTC CAAGAAGCTGAAGTCCGTGAAGGAGCTGCTGGGCATCACCATCATGGAGCGGTCCCT CTTCGAGAAGAACCCATCGACTTCTGGAGGCCAAGGGCTACAAGGAGGTGAAGA AGGACTGATCATCAAGCTGCCAAGTACTCCCTGTTTCGAGCTGGAGAACGGCCGGA AGCGGATGCTGGCCTCCGCCGGCGAGCTGCAGAAGGGCAACGAGCTGGCCCTGCC TCCAAGTACGTGAACCTTCTGTACCTGGCCTCCACTACGAGAAGCTGAAGGGCTCC</p>	<p>152</p>
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[0754]

	<p>CCCAGGACAACGAGCAGAAGCAGCTGTTTCGTGGAGCAGCACAAAGCACTACCTGGA CGAGATCATCGAGCAGATCTCCGAGTTCTCCAAGCGGGTGATCCTGGCCGACGCCAA CCTGGACAAGGTGCTGTCCGCTACAACAAGCACCGGGACAAGCCCATCCGGGAGC AGGCCGAGAACATCATCCACCTGTTACCCCTGACCAACCTGGGCGCCCCGCCCT TCAAGTACTTCGACACCACCATCGACCGGAAGCGGTACACCTCCACCAAGGAGGTGC TGGACGCCACCCTGATCCACCAAGTCCATCACCGGCCCTGTACGAGACCCGGATCGACC TGTCCAGCTGGGCGGCGACGGCGGGCTCCCCAAGAAGAAGCGGAAGGTG</p>	
<p>使用表4的低 A 密码子的 dCas9 ORF (无NLS且无 起始或终止 密码子; 适于 包括在融合 蛋白质编码 序列中)</p>	<p>GACAAGAAGTACTCCATCGGCCCTGGCCATCGGCACCAACTCCGTGGGCTGGGCCGTG ATCACCGACGAGTACAAGGTGCCCTCCAAGAAGTTCAAGGTGCTGGGCAACACCGA CCGGCACTCCATCAAGAAGAACCTGATCGGCGCCCTGCTGTTGACTCCGGCGAGAC CGCCGAGGCCACCCGGCTGAAGCGGACCCGCCGGCGGTACACCCGGCGGAAGA ACCGGATCTGCTACCTGCAGGAGATCTTCTCCAACGAGATGGCCAAGGTGGACGACT CCTTCTCCACCGGCTGGAGGATCCTTCTGTTGGAGGAGGACAAGAAGCACGAG CGGCACCCATCTTCGGCAACATCGTGACGAGGTGGCCTACCACGAGAAGTACCCC ACCATCTACCACCTGCGGAAGAAGTGGTGGACTCCACCGACAAGGCCGACTGCGG TCGATCTACCTGGCCCTGGCCACATGATCAAGTTCCGGGGCCACTTCTGATCGAGG GCGACCTGAACCCGACAACCTCCGACGTGGACAAGCTGTTTCATCCAGCTGGTGCAGA CCTACAACAGCTGTTTCGAGGAGAACCCATCAACGCCTCCGGCGTGGACGCCAAGG CCATCTGTCCGCCCGGCTGTCCAAGTCCCGCGGCTGGAGAACCTGATCGCCCAGC TGCCCGGCGAGAAGAAGAACCGCCTGTTCCGGCAACCTGATCGCCCTGTCCCTGGCC TGACCCCAACTTCAAGTCCAACCTTCGACCTGGCCGAGGACGCCAAGCTGCAGCTGT CCAAGGACACCTACGACGACGACCTGGACAACCTGCTGGCCAGATCGGCGACCACT ACGCCGACCTGTTCTGGCCGCCAAGAACCTGTCCGACGCCATCCTGCTGTCCGACA TCCTGCGGGTGAACACCGAGATACCAAGGCCCTGTCCGCTCCATGATCAAGC GGTACGACGAGCACCACAGGACTGACCTGCTGAAGGCCCTGGTGGCGAGCAG CTGCCCGAGAAGTACAAGGAGATCTTCTTCGACCAGTCCAAGAACGGCTACGCCGGC TACATCGACGGCGGCGCCTCCAGGAGGAGTTTACAAGTTCATCAAGCCATCCTG GAGAAGATGGACGGCACCGAGGAGCTGCTGGTGAAGCTGAACCGGGAGGACCTGCT GCGGAAGCAGCGGACCTTCGACAACGGCTCCATCCCCACCAGATCCACCTGGGCGA GCTGCACGCCATCCTGCGGCGGCGAGGAGACTTCTACCCCTTCTGAAGGACAACCG GGAGAAGATCGAGAAGATCCTGACCTTCCGGATCCCCTACTACGTGGGCCCTGGC CCGGGGCAACTCCCGGTTGCGCTGGATGACCCGGAAGTCCGAGGAGACCATACCCC CTGGAACCTCGAGGAGTGGTGGACAAGGGCGCCTCCGCCAGTCCCTCATCGAGCG GTGACCAACTTCGACAAGAACCTGCCAACGAGAAGGTGCTGCCAACACTCCCT GCTGTACGAGTACTTACCCTGTACAACGAGCTGACCAAGGTGAAGTACGTGACCGA GGGCATCGGAAGCCCGCTTCTGTCGGCGAGCAGAAGAAGGCCATCGTGGACCT GCTGTTCAAGACCAACCGGAAGGTGACCGTGAAGCAGCTGAAGGAGGACTACTTCA AGAAGATCGAGTGTCTCGACTCCGTGGAGATCTCCGGCGTGGAGGACCGGTTCAACG CCTCCCTGGGCACCTACCACGACCTGCTGAAGATCATCAAGGACAAGGACTTCTGG ACAACGAGGAGAACGAGGACATCCTGGAGGACATCGTGTGACCTGACCTGTTCG AGGACCGGAGATGATCGAGGAGCGGCTGAAGACCTACGCCACCTGTTTCGACGAC AAGGTGATGAAGCAGCTGAAGCGGCGGCGGTACACCGGCTGGGGCCGGGTGTCCCG GAAGCTGATCAACGGCATCCGGGACAAGCAGTCCGGCAAGACCATCTGGACTTCT GAAGTCCGACGGCTTCGCAACCGGAACCTCATGCAGCTGATCCACGACGACTCCCT GACCTTCAAGGAGGACATCCAGAAGGCCAGGTGTCGGCCAGGGCGACTCCCTGC ACGAGCACATCGCAACCTGGCCGGCTCCCCGCCATCAAGAAGGGCATCCTGCAGA CCGTGAAGGTGGTGGACGAGCTGGTGAAGGTGATGGGCCGGCACAAGCCCGAGAT ATCGTGATCGAGATGGCCGGGAGAACCAGACCACCCAGAAGGGCCAGAAGAATC CCGGGAGCGGATGAAGCGGATCGAGGAGGGCATCAAGGAGCTGGGCTCCAGATCC TGAAGGAGCACCCCGTGGAGAACACCCAGCTGCAGAACGAGAAGCTGTACCTGTAC TACCTGCAGAACGGCCGGACATGTACGTGGACCAGGAGCTGGACATCAACCGGCTG TCCGACTACGACGTGGACGCCATCGTGCCCAAGTCTTCTGAAGGACGACTCCATC GACAACAAGGTGCTGACCCGGTCCGACAAGAACCAGGGCAAGTCCGACAACGTGCC CTCCGAGGAGGTGGTGAAGAAGATGAAGAATACTGGCGGCAGCTGCTGAACGCCA AGCTGATCACCCAGCGGAAGTTCGACAACCTGACCAAGGCCGAGCGGGCGGCGCTG TCCGAGCTGGACAAGGCCGGCTTCATCAAGCGGCGAGCTGGTGGAGACCCGGCAGAT CACCAAGCACGTGGCCAGATCCTGGACTCCCGGATGAACACCAAGTACGACGAGA ACGACAAGCTGATCCGGGAGGTGAAGGTGATCACCTGAAGTCCAAGTGGTGTCCG ACTTCCGGAAGGACTTCCAGTCTACAAGGTGCGGGAGATCAACAATACTACCACACG CCCACGACGCCTACCTGAACGCCGTGGTGGGCACCGCCCTGATCAAGAAGTACCCCA AGCTGGAGTCCGAGTTCGTGTACGGCGACTACAAGGTGTACGACGTGCGGAAGATGA TCGCCAAGTCCGAGCAGGAGATCGGCAAGGCCACCGCCAAGTACTTCTTACTCCA ACATCATGAACCTTCTCAAGACCGAGATCACCTGGCCAACGGCGAGATCCGGAAGC GGCCCCTGATCGAGACCAACGGCGAGACCGGCGAGATCGTGTGGGACAAGGGCCGG GACTCGCCACCGTGCAGGAAGGTGCTGTCATGCCCAAGGTGAACATCGTGAAGAAG ACCGAGGTGCAGACCGGCGGCTTCTCCAAGGAGTCCATCCTGCCAAGCGGAACCTC GACAAGCTGATCGCCCGGAAGAAGGACTGGGACCCCAAGAAGTACGGCGGCTTCGA</p>	<p>153</p>

[0755]

	<p>CTCCCCACCGTGGCCTACTCCGTGCTGGTGGTGGCCAAGGTGGAGAAGGGCAAGTC CAAGAAGCTGAAGTCCGTGAAGGAGCTGCTGGGCATCACCATCATGGAGCGGTCCTC CTTCGAGAAGAACCCCATCGACTTCTGGAGGCCAAGGGCTACAAGGAGGTGAAGA AGGACCTGATCATCAAGCTGCCAAGTACTCCCTGTTCGAGCTGGAGAACGGCCGGA AGCGGATGCTGGCCTCCGCCGGCGAGCTGCAGAAGGGCAACGAGCTGGCCCTGCC TCCAAGTACGTGAAGTCCGTGACTGGCCTCCCACTACGAGAAGTGAAGGCTCC CCCAGGACAACGAGCAGAAGCAGCTGTTCTGGAGCAGCACAAGCACTACCTGGA CGAGATCATCGAGCAGATCTCCGAGTTCCTCAAGCGGGTGATCCTGGCCGACGCCAA CCTGGACAAGGTGCTGTCCGCCTACAACAAGCACCAGGGACAAGCCATCCGGGAGC AGGCCGAGAATCATCCACCTGTTACCCCTGACCAACCTGGGCGCCCCGCCCT TCAAGTACTTCGACACCACCTCGACCCGGAAGCGGTACACCTCCACCAAGGAGGTGC TGGACGCCACCTGATCCACCAGTCCATCACCAGGCTGTACGAGACCCGGATCGACC TGTCCCAGCTGGGCGGCGAC</p>	
<p>使用表4的低 A密码子, 具 有两个C端 NLS序列的 dCas9 ORF (无起始或终 止密码子; 适 于包括在融 合蛋白质编 码序列中)</p>	<p>GACAAGAAGTACTCCATCGGCCTGGCCATCGGCACCAACTCCGTGGGCTGGGCCGTG ATCACCCGACGAGTACAAGGTGCCCTCCAAGAAGTTCAAGGTGCTGGGCAACACCGA CCGGCACTCCATCAAGAAGAACCTGATCGGCGCCTGCTGTTTCGACTCCGGCGAGAC CGCCGAGGCCACCCGGCTGAAGCGGACCCGCCGGCGGTTACACCCGGCGGAAGA ACCGGATCTGCTACCTGCAGGAGATCTTCTCAACGAGATGGCCAAGGTGGACGACT CCTTCTCCACCCGGCTGGAGGAGTCTTCTGGTGGAGGAGACAAGAAGCAGCAG CGGACCCCATCTTCGGCAACATCGTGGAGCAGGTTGGCCTACCACGAGAAGTACCC ACCATCTACCACCTGCGGAAGAAGCTGGTGGACTCCACCGACAAGGCCGACCTGCGG CTGATCTACCTGGCCCTGGCCACATGATCAAGTTCCGGGGCCACTTCTGATCGAGG GCGACCTGAACCCCGACAACCTCCGACGTGGACAAGCTGTTTATCCAGCTGGTGCAGA CCTACAACAGCTGTTTCGAGGAGAACCCCATCAACGCCTCCGGCGTGGACCCCAAG ACCTCCTGTCCGCCCGGCTGTCCAAGTCCCGCGGCTGGAGAACCTGATCGCCACG TGCCCGCGGAGAAGAAGAAGCAGGCTGTTTCGGCAACCTGATCGCCCTGTCCCTGGCC TGACCCCAACTTCAAGTCAACTTCGACCTGGCCGAGGACGCCAAGCTGCAGCTGT CCAAGGACACCTACGACGACGACCTGGACAACCTGCTGGCCAGATCGGCGACCACT ACGCCGACCTGTTCTTCGGCCCAAGAACCTGTCCGACGCCATCTGCTGTCCGACA TCTGCGGGTGAACACCGAGATCACCAGGCCCCCTGTCCGCCTCCATGATCAAGC GGTACGACGAGCACCACAGGACCTGACCCTGCTGAAGGCCCTGGTGCGGCAGCAG CTGCCGAGAAGTACAAGGAGATCTTCTTCGACCAGTCCAAGAACGGCTACGCCGGC TACATCGACGGCGCGCTCCAGGAGGAGTTCTACAAGTTCATCAAGCCATCCTG GAGAAGATGGACGGCACCGAGGAGCTGCTGGTGAAGCTGAACCGGGAGGACCTGCT GCGGAAGCAGCGGACCTTCGACAACGGCTCCATCCCCACCAGATCCACCTGGGCGA GCTGCACGCCATCTGCGGCGGCAGGAGGACTTCTACCCCTTCTGAAGGACAACCG GGAGAAGATCGAGAAGATCCTGACCTTCCGGATCCCCTACTACGTGGGCCCCCTGGC CCGGGCAACTCCGGTTCGCCTGGATGACCCGGAAGTCCGAGGAGACCATCACCC CTGGAACTTCGAGGAGGTGGTGGACAAGGGCGCCTCCGCCAGTCTTCATCGAGCG GATGACCAACTTCGACAAGAACCTGCCAACGAGAAGGTGCTGCCAAGCACTCCCT GCTGTACGAGTACTTACCCTGTACAACGAGCTGACCAAGGTGAAGTACGTGACCCGA GGCATGCGGAAGCCCGCTTCTGTCGGCGAGCAGAAGAAGGCCATCGTGGACCT GCTGTTCAAGACCAACCGAAGGTGACCGTGAAGCAGCTGAAGGAGGACTTCA AGAAGATCGAGTGTTCGACTCCGTGGAGATCTCCGGCGTGGAGGACCGGTTCAACG CCTCCCTGGGACCTACCACGACCTGCTGAAGATCATCAAGGACAAGGACTTCTGG ACAACGAGGAGAACGAGGACATCTGGAGGACATCGTGTGACCCTGACCCTGTTCCG AGGACCGGAGATGATCGAGGAGCGGCTGAAGACCTACGCCACCTGTTCCGACGAC AAGGTGATGAAGCAGCTGAAGCGGCGGCGGTACACCGGCTGGGGCCGGCTGTCCCG GAAGCTGATCAACGGCATCCGGGACAAGCAGTCCGGCAAGACCATCTGGACTTCT GAAGTCCGACGGCTTCGCCAACCAGCAACTTCATGCAGCTGATCCACGACGACTCCCT GACCTTCAAGGAGGACATCCAGAAGGCCAGGTGTCGGCCAGGGGACCTCCCTGC ACGACACATCGCCAACCTGGCCGGCTCCCCGCCATCAAGAAGGGACATCTGCAGA CCGTGAAGGTGGTGGACGAGCTGGTGAAGGTGATGGGCGGCACAAGCCCGAGAAC ATCGTGTGAGATGGCCCGGAGAACAGACCACCCAGAAGGGCCAGAAGAACTC CCGGGAGCGGATGAAGCGGATCGAGGAGGGCATCAAGGAGCTGGGCTCCCAGATCC TGAAGGAGCACCCCGTGGAGAACACCCAGCTGCAGAACGAGAAGCTGTACCTGTAC TACCTGCAGAACGGCCGGACATGTACGTGGACCAGGAGCTGGACATCAACCGGCTG TCCGACTACGACGTGGACGCCATCGTGCCCCAGTCTTCTGAAGGACGACTCCATC GACAACAAGGTGCTGACCCGGTCCGACAAGAACCAGGGGCAAGTCCGACAACGTGCC CTCCGAGGAGGTGGTGAAGAAGATGAAGAATACTGGCGGACGCTGCTGAACGCCA AGCTGATACCCAGCGGAAGTTCGACAACCTGACCAAGGCCGAGCGGGCGGCCTG TCCGAGCTGGACAAGGCCGGCTTCATCAAGCGGACGCTGGTGGAGACCCGGCAGAT CACCAAGCAGTGGCCAGATCCTGGACTCCCGGATGAACACCAAGTACGACGAGA ACGACAAGCTGATCCGGGAGGTGAAGGTGATCACCTGAAGTCAAGCTGGTGTCCG ACTCCGGAAGGACTTCCAGTTTACAAGGTGCGGGAGATCAACAATAACCCACG CCCACGACGCCTACCTGAACGCCGTGGTGGGACCGCCCTGATCAAGAAGTACCCCA AGCTGGAGTCCGAGTTCGTGTACGGCGACTACAAGGTGTACGACGTGCGGAAGATGA</p>	<p>154</p>

[0756]

	<p>TCGCCAAGTCCGAGCAGGAGATCGGCCAAGGCCACCGCCAAGTACTTCTTACTCCA ACATCATGAACCTTCTCAAGACCGAGATCACCCCTGGCCAACGGCGAGATCCGGAAAGC GGCCCCTGATCGAGACCAACGGCGAGACCGGCGAGATCGTGTGGGACAAGGGCCGG GACTTCGCCACCGTGCAGAAAGGTGCTGTCCATGCCCAAGTGAACATCGTGAAGAAG ACCGAGGTGCAGACCGGCGGCTTCTCCAAGGAGTCCATCTGCCCAAGCGGAACTCC GACAAGCTGATCGCCCGAAGAAGGACTGGGACCCCAAGAAGTACGGCCGGCTTCGA CTCCCCACCGTGGCCTACTCCGTGCTGGTGGTGGCCAAGGTGGAGAAGGGCAAGTC CAAGAAGCTGAAGTCCGTGAAGGAGCTGCTGGGCATCACCATATGGAGCGGTCTCT CTTCGAGAAGAACCCATCGACTTCTGGAGGCCAAGGGCTACAAGGAGGTGAAGA AGGACCTGATCATCAAGCTGCCAAGTACTCCCTGTTTCGAGCTGGAGAACGGCCGGA AGCGGATGCTGGCCTCCGCCGCGAGCTGCAGAAGGGCAACGAGCTGGCCCTGCC TCCAAGTACGTGAACCTTCTGTACTTGGCCTCCACTACGAGAAGCTGAAGGGCTCC CCCAGGACAACGAGCAGAAGCAGCTGTTCTGGAGCAGCACAAGCACTACCTGGA CGAGATCATCGAGCAGATCCGAGTTCTCCAAGCGGGTGTCTGGCCGACGCCAA CCTGGACAAGGTGCTGTCCGCTACAACAAGCACCGGGACAAGCCATCCGGGAGC AGGCCGAGAATCATCCACCTGTTACCCTGACCAACCTGGGCGCCCCGCCGCT TCAAGTACTTCGACACCACATCGACCGGAAGCGGTACACTCCACCAAGGAGGTGC TGGAGCCACCCGTATCCACCAGTCCATACCCGCCCTGTACGAGACCCGGATCGACC TGTCCAGCTGGGCGGCGACGGCTCCGGCTCCCCAAGAAGAAGCGGAAGGTGGAC GGTCCCCAAGAAGAAGCGGAAGGTGGACTCCGGC</p>	
<p>使用表4的低 A/U密码子, 具有两个C端 NLS序列的 Cas9 ORF (无起始或终 止密码子;适 于包括在融 合蛋白质编 码序列中)</p> <p>[0757]</p>	<p>GACAAGAAGTACAGCATCGGCCTGGACATCGGCACCAACAGCGTGGGCTGGCCGT GATCACCGACGAGTACAAGGTGCCAGCAAGAAGTTCAAGGTGCTGGCAACACCG ACCGGCACAGCATCAAGAAGAACCTGATCGGCGCCCTGCTGTTTCGACAGCGGCGAG ACCGCCGAGGCCACCGGCTGAAGCGGACCGCCGGCGGCGGTACACCGCCGGA GAACCGGATCTGCTACCTGCAGGAGATCTTCAGCAACGAGATGGCCAAGGTGGACGA CAGCTTCTTCCACCGGCTGGAGGAGAGCTTCTGGTGGAGGAGGACAAGAAGCAG AGCGGCACCCATCTTCGGCAACATCGTGGACGAGGTGGCCTACCACGAGAAGTACC CCACCATCTACCCTGCGGAAGAAGCTGGTGGACAGCACCGACAAGGCCGACCTG CGGTGATCTACCTGGCCCTGGCCACATGATCAAGTTCCGGGGCCACTTCTGATCG AGGGCGACCTGAACCCCGACAACAGCGACGTGGACAAGCTGTTTCATCCAGCTGGTG CAGACCTACAACAGCTGTTTCGAGGAGAACCCATCAACGCCAGCGCGGTGGACGC CAAGGCCATCTGAGCGCCCGGCTGAGCAAGAGCCGGCGGCTGGAGAACCTGATCG CCCAGCTGCCCGGAGAAGAAGACGGCCTGTTTCGCAACCTGATCGCCCTGAGC TGTGGCCTGACCCCAACTTCAAGAGCAACTTCGACCTGGCCGAGGACCGCAAGCT GCAGCTGAGCAAGGACACCTACGACGACGACCTGGACAACCTGCTGGCCAGATCG GCGACCAGTACGCCGACCTGTTCTTGGCCGCAAGAACCTGAGCGACGCCATCCTGC TGAGCGACATCTGCGGGTGAACACCGAGATCACCAAGGCCCCCTGAGCGCCAGCA TGATCAAGCGGTACGACGAGCACCAACAGGACCTGACCCTGTGAAGCCCTGGTGC GGCAGCAGCTGCCCGAGAAGTACAAGGAGATCTTCTTCGACCAGAGCAAGAACGGC TACGCCGGCTACATCGACGGCGGCCAGCCAGGAGGAGTTCTACAAGTTCATCAAG CCCATCTGGAGAAGATGGACGGCACCGAGGAGCTGCTGGTGAAGCTGAACCGGGA GGACCTGCTGCGGAAGCAGCGGACCTTCGACAACGGCAGCATCCCCACCAAGATCCA CCTGGCGAGCTGCACGCCATCTGCGCGCGCAGGAGGACTTCAACCTTCTGTAA GGACAACCGGGAGAAGATCGAGAAGATCCTGACCTTCGGATCCCTACTACGTGGG CCCCCTGGCCGGGGCAACAGCCGGTTCGCTGGATACCCGGAAGAGCGAGGAGA CCATACCCCTGGAACCTTCGAGGAGGTGGTGGACAAGGGCGCCAGCGCCAGAGC TTCATCGAGCGGATGACCAACTTCGACAAGAACCTGCCAACGAGAAGGTGCTGCC AAGCACAGCCTGCTGTACGAGTACTTACCCTGTACAACGAGCTGACCAAGGTGAAG TACGTGACCGAGGGCATGCGGAAGCCGCTTCTGAGCGGCGAGCAGAAGAAGGC CATCGTGGACCTGCTGTTCAAGACCAACCGGAAGGTGACCGTGAAGCAGCTGAAGG AGGACTACTTCAAGAAGATCGAGTGTCTTCGACAGCGTGGAGATCAGCGGCGTGGAG GACCGTTCAACGCCAGCTGGGCACCTACCACGACCTGCTGAAGATCATCAAGGAC AAGGACTTCTGGACAACGAGGAGAACGAGGACATCTGGAGGACATCGTGTGAC CCTGACCCTGTTTCGAGGACCGGGAGATGATCGAGGAGCGGCTGAAGACCTACGCCA CCTGTTTCGACGACAAGGTGATGAAGCAGCTGAAGCGGCGGCGGTACACCGGCTGGG GCCGGCTGAGCCGGAAGCTGATCAACGGCATCCGGGACAAGCAGAGCGGCAAGACC ATCCTGGACTTCTGAAGAGCGACGGCTTCGCCAACCAGCAACTTCATGCAGCTGATC CACGACGACAGCCTGACCTTCAAGGAGGACATCCAGAAGGCCAGGTGAGCGGCCA GGGCGACAGCCTGCACGACACATCGCCAACCTGGCCGGCAGCCCCGCCATCAAGA AGGGCATCTGCAGACCGTGAAGGTGGTGGACGAGCTGGTGAAGGTGATGGGCCGG CACAAGCCCAGAACATCGTGTATCGAGATGGCCCGGGAAGCAAGACCCACCAAGA GGGCCAGAAGAACAGCCGGGAGCGGATGAAGCGGATCGAGGAGGGCATCAAGGAG CTGGGCAGCCAGATCTGAAGGAGCACCCCTGGAGAACACCCAGCTGCAGAACGA GAAGCTGTACTGTACTACCTGCAGAACGGCCGGGACATGTACGTGGACCAGGAGCT GGACATCAACCGGCTGAGCGACTACGACGTGGACCACATCGTCCCCAGAGCTTCT GAAGGACGACAGCATCGACAACAAGGTGCTGACCCGAGCGACAAGAACCAGGGC AAGAGCGACAACGTGCCAGCGAGGAGGTGGTGAAGAAGATGAAGAACTACTGGCG</p>	<p>155</p>

[0758]

	<p>GCAGCTGCTGAACGCCAAGCTGATCACCCAGCGGAAGTTCGACAACCTGACCAAGG CCGAGCGGGCGGCCTGAGCGAGCTGGACAAGGCCGGCTTCATCAAGCGGCAGCTG GTGGAGACCCGGCAGATACCAAGCACGTGGCCAGATCCTGGACAGCCGGATGAA CACCAAGTACGACGAGAACGACAAGCTGATCCGGGAGGTGAAGGTGATCACCTGA AGAGCAAGCTGGTGAAGGACTTCCGGGAAGGACTTCCAGTTCTACAAGGTGCGGGAG ATCAACAACCTACCACCACGCCACGACGCTACCTGAACGCCGTGGTGGCCACCGCC CTGATCAAGAAGTACCCCAAGCTGGAGAGCGAGTTCGTGTACGGCGACTACAAGGTG TACGACGTGCGGAAGATGATCGCCAAGAGCGAGCAGGAGATCGGCAAGGCCACCGC CAAGTACTTCTTCTACAGCAACATCATGAACCTTCTCAAGACCGAGATCACCTGGCC AACGGCGAGATCCGGAAGCGGCCCTGATCGAGACCAACGGCGAGACCCGGCGAGAT CGTGTGGGACAAGGGCCGGGACTTCGCCACCGTGCAGGAAGGTGCTGAGCATGCCCC AGGTGAACATCGTGAAGAAGACCGAGGTGCAGACCCGGCGGCTTCAGCAAGGAGAGC ATCCTGCCAAGCGGAACAGCGACAAGCTGATCGCCCGGAAGAAGGACTGGGACCC CAAGAAGTACGGCGGCTTCGACAGCCCCACCGTGGCCTACAGCGTGCTGGTGGTGGC CAAGGTGGAGAAGGGCAAGAGCAAGAAGCTGAAGAGCGTGAAGGAGCTGCTGGGC ATCACCATCATGGAGCGGAGCAGCTTCGAGAAGAACCCCATCGACTTCCTGGAGGCC AAGGGCTACAAGGAGGTGAAGAAGGACCTGATCATCAAGCTGCCAAGTACAGCCT GTTCGAGCTGGAGAACGGCCGGAAGCGGATGCTGGCCAGCGCCGGCGAGCTGCAGA AGGGCAACGAGCTGGCCCTGCCAGCAAGTACGTGAACCTTCTGTACTGCTGGCCAGC CTAACGAGAAGCTGAAGGGCAGCCCCGAGGACAACGAGCAGAGAAGCAGCTGTTCTGT GAGCAGCACAAGCACTACCTGGACGAGATCATCGAGCAGATCAGCGAGTTCAGCAA GCGGGTGATCCTGGCCGACGCCAACCTGGACAAGGTGCTGAGCGCTACAACAAGC ACCGGGACAAGCCATCCGGGAGCAGGCCGAGAACATCATCCACCTGTTACCCCTGA CCAAGCTGGGCGCCCCCGCCCTTCAAGTACTTCGACACCACCATCGACCCGGAAGC GGTACACCAGCACCAAGGAGGTGCTGGACGCCACCCTGATCCACCAGAGCATCACCG GCCTGTACGAGACCCGGATCGACCTGAGCCAGCTGGGCGGCGACGGCAGCGGCAGC CCCAAGAAGAAGCGGAAGGTGGACGGCAGCCCCAAGAAGAAGCGGAAGGTGGACA GCGGC</p>	
<p>使用表4的低 A/U 密码子 的Cas9 ORF (无NLS且无 起始或终止 密码子; 适于 包括在融合 蛋白质编码 序列中)</p>	<p>GACAAGAAGTACAGCATCGGCCTGGACATCGGCACCAACAGCGTGGGCTGGGCCGT GATCACCCGACGAGTACAAGGTGCCAGCAAGAAGTTCAAGGTGCTGGGCAACACCG ACCGGCACAGCATCAAGAAGAACCTGATCGCGCCCTGCTGTTCGACAGCGGCGAG ACCGCCGAGGCCACCCGGCTGAAGCGGACCCGCCGGCGGTTACACCCGGCGGAA GAACCGGATCTGCTACCTGCAGGAGATTTTCAGCAACGAGATGGCCAAGGTGGACGA CAGCTTCTTCCACCGGCTGGAGGAGAGCTTCTGGTGGAGGAGGACAAGGACACG AGCGGCACCCCATCTTCGGCAACATCGTGGACGAGGTGGCCTACCACGAGAAGTACC CCACCATCTACCACCTGCGGAAGAAGCTGGTGGACAGCACCGACAAGGCCGACCTG CGGCTGATCTACCTGGCCCTGGCCACATGATCAAGTTCGGGGCCACTTCTGTATCG AGGGCGACTGAACCCCGACAACAGCGACGTGGACAAGCTGTTTCATCCAGCTGGTG CAGACCTACAACCAGCTGTTTCGAGGAGAACCCCATCAACGCCAGCGCGTGGACGC CAAGGCCATCTGAGCGCCCGGCTGAGCAAGAGCCGGCGGCTGGAGAACCTGATCG CCCAGCTGCCCGGCGAGAAGAAGAAGCGCCTGTTTCGGCAACCTGATCGCCCTGAGC CTGGCCCTGACCCCAACTTCAAGAGCAACTTCGACCTGGCCGAGGACGCCAAGCT GCAGCTGAGCAAGGACACCTACGACGACGACCTGGACAACCTGCTGGCCACTACGTCG GCGACCAGTACGCCGACCTGTTCTGGCCGCAAGAACCTGAGCGACGCCATCCTGC TGAGCGACATCTGCGGGTGAACACCGAGATACCAAGGCCCCCTGAGCGCCAGCA TGATCAAGCGGTACGACGAGCACCACCAGGACCTGACCCTGTGAAGGCCCTGGTGC GGCAGCAGCTGCCGAGAAGTACAAGGAGATCTTCTTCGACCAGAGCAAGAACGGC TACGCCGGCTACATCGACGGCGGCCAGCCAGGAGGAGTTCTACAAGTTCATCAAG CCCATCTGGAGAAGATGGACGGCACCGAGGAGCTGCTGGTGAAGCTGAACCGGGA GGACCTGCTGCGGAAGCAGCGGACCTTCGACAACGGCAGCATCCCCACCAGATCCA CCTGGGCGAGCTGCACGCCATCTGCGGCGCAGGAGGACTTCTACCCCTTCTGAA GGACAACCGGGAGAAGATCGAGAAGATCTGACCTTCGGATCCCTACTACGTGGG CCCCCTGGCCCGGGCAACAGCCGGTTCGCTGGATGACCCGGAAGAGCGAGGAGA CCATACCCCTGGAACCTCGAGGAGGTGGTGGACAAGGGCGCCAGCGCCAGAGC TTCATCGAGCGGATGACCAACTTCGACAAGAACCTGCCAACGAGAAGGTGCTGCC AAGCACAGCTGCTGTACGAGTACTTACCCTGTACAACGAGCTGACCAAGGTGAAG TACGTGACCGAGGGCATGCGGAAGCCGCCTTCTGAGCGGCGAGCAGAAGAAGGC CATCGTGGACCTGCTGTTCAAGACCAACCGGAAGGTGACCGTGAAGCAGCTGAAGG AGGACTACTTCAAGAAGATCGAGTGTTCGACAGCGTGGAGATCAGCGGCGTGGAG GACCGTTCAACGCCAGCTGGGCACCTACCAGACCTGCTGAAGATCATCAAGGAC AAGGACTTCTGGACAACGAGGAGAACGAGGACATCTGGAGGACATCTGCTGAC CCTGACCTGTTTCGAGGACCGGGAGATGATCGAGGAGCGGCTGAAGACCTACGCCA CCTGTTTCGACGACAAGGTGATGAAGCAGCTGAAGCGGCGGCGGTACACCGCTGGG GCCGGCTGAGCCGGAAGCTGATCAACGGCATCCGGGACAAGCAGAGCGGCAAGACC ATCTGGACTTCTGAAGAGCGACGGCTTCGCCAACCAGGAACTTTCATGACGTGATC CACGACGACAGCCTGACCTTCAAGGAGGACATCCAGAAGGCCAGGTGAGCGGCCA GGGCGACAGCCTGCACGACATCGCCAACCTGGCCGGCAGCCCCGCATCAAGA</p>	<p>156</p>

[0759]

	<p>AGGGCATCCTGCAGACCGTGAAGGTGGTGGACGAGCTGGTGAAGGTGATGGGCCGG CACAAGCCCGAGAATCTGTGATCGAGATGGCCCGGAGAACCAGACCACCCAGAA GGGCCAGAAGAACAGCCGGGAGCGGATGAAGCGGATCGAGGAGGGCATCAAGGAG CTGGGCAGCCAGATCCTGAAGGAGCACCCCTGGGAGAACCAGCTGCAGAACGA GAAGCTGTACCTGTACTACCTGCAGAACGGCCGGGACATGTACGTGGACCAGGAGCT GGACATCAACCCGGCTGAGCGACTACGACGTGGACCACATCGTGCCCCAGAGCTTCT GAAGGACGACAGCATCGACAACAAGGTGCTGACCCGGAGCGACAAGAACCAGGGG AAGAGCGACAACGTGCCAGCGAGGAGGTGGTGAAGAAGATGAAGAACTACTGGCG GCAGCTGCTGAACGCCAAGCTGATCACCCAGCGGAAGTTCGACAACCTGACCAAGG CCGAGCGGGCGGCCTGAGCGAGCTGGACAAGGCCGGCTTCATCAAGCGGCAGCTG GTGGAGACCCGGCAGATCACCAAGCACGTGGCCAGATCCTGGACAGCCGGATGAA CACCAAGTACGACGAGAACGACAAGCTGATCCGGGAGGTGAAGGTGATCACCTGA AGAGCAAGCTGGTGAAGGACTTCCGGAAGGACTTCCAGTTCTACAAGGTGCGGGAG ATCAACAACCTACCACCACGCCACGACGCCTACCTGAACGCCGTGGTGGGACCCGC CTGATCAAGAAGTACCCCAAGCTGGAGAGCGAGTTCGTGTACGGCGACTACAAGGTG TACGACGTGCGGAAGATGATCGCCAAGAGCGAGCAGGAGATCGGCAAGGCCACCCG CAAGTACTTCTTACAGCAACATCATGAACCTTCTCAAGACCGAGATCACCTGGCC AACGGCGAGATCCGGAAGCGGCCCTGATCGAGACCAACGGCGAGACCCGGCGAGAT CGTGTGGGACAAGGGCCGGACTTCGCCACCGTGGGAAGGTGCTGAGCATGCCCC AGGTGAACATCGTGAAGAAGAGACCGAGGTGCAGACCCGGCGCTTACAGCAAGGAGC ATCCTGCCAAGCGGAACAGCGACAAGCTGATCGCCCGGAAGAAGGACTGGGACCC CAAGAAGTACGGCGGCTTCGACAGCCCCACCGTGGCTACAGCGTGTGGTGGTGGC CAAGGTGGAGAAGGGCAAGAGCAAGAAGCTGAAGAGCGTGAAGGAGCTGCTGGGC ATCACATCATGGAGCGGAGCAGCTTCGAGAAGAACCCTACGACTTCTGGAGGCC AAGGGCTACAAGGAGGTGAAGAAGGACCTGATCATCAAGCTGCCAAGTACAGCCT GTTGAGCTGGAGAACGGCCGGAAGCGGATGCTGGCCAGCGCCGGCGAGCTGCAGA AGGGCAACGAGCTGGCCCTGCCAGCAAGTACGTGAACCTTCTGTACTGGCCAGCC ACTACGAGAAGCTGAAGGGCAGCCCCGAGGACAACGAGCAGAAGCAGCTGTTCTGTG GAGCAGCACAAGCACTACCTGGACGAGATCATCGAGCAGATCAGCGAGTTCAGCAA GCGGGTATCCTGGCCGACGCCAACCTGGACAAGGTGCTGAGCGCCTACAACAAGC ACCGGGACAAGCCATCCGGGAGCAGGCCGAGAACATCATCCACCTGTTACCCCTGA CCAACCTGGGCGCCCCCGCCCTTCAAGTACTTCGACACCACCATCGACCCGGAAGC GATCACACGACCAAGGAGGTGCTGGACGCCACCTGATCCACCAGAGCATCACCG GCCTGTACGAGACCCGGATCGACCTGAGCCAGCTGGGCGGCGAC</p>	
<p>使用表4的低 A/U 密码子 的 Cas9 切口 酶ORF (无起 始或终止密 码子; 适于包 括在融合蛋 白质编码序 列中)</p>	<p>GACAAGAAGTACAGCATCGGCCTGGCCATCGGCACCAACAGCGTGGGCTGGGCCGT GATCACCGACGAGTACAAGGTGCCAGCAAGAAGTTCAAGGTGCTGGGCAACACCG ACCGGCACAGCATCAAGAAGAACCTGATCGGCGCCCTGCTGTTGACAGCGGGCGAG ACCGCCGAGGCCACCCGGCTGAAGCGGACCCGCCGGCGGCGGTACACCCGGCGGAA GAACCGGATCTGCTACCTGCAGGAGATCTTACGCAACGAGATGGCCAAGGTGGACGA CAGCTTCTCCACCGGCTGGAGGAGAGCTTCTGTTGGAGGAGGACAAGAAGCACG AGCGGCACCCATCTTCGGCAACATCGTGGACGAGGTGGCCCTACCACGAGAAGTACC CCACCATTACCACCTGCGGAAGAAGCTGGTGGACAGCACCAGACAAGGCCAGCTG CGGTGATCTACCTGGCCCTGGCCACATGATCAAGTTCCGGGGCCACTTCTGATCG AGGGCGACCTGAACCCCGACAACAGCGACGTGGACAAGCTGTTATCCAGCTGGTG CAGACCTACAACAGCTGTTGAGGAGAACCCATCAACGCCAGCGCGTGGACGC CAAGGCCATCCTGAGCGCCCGGCTGAGCAAGAGCCGGCGGCTGGAGAACCTGATCG CCCAGCTGCCCGGCGAGAAGAAGAAGCAAGCCGCTGTTCCGGCAACCTGATCGCCTGAGC CTGGGCTGACCCCAACTTCAAGAGCAACTTCGACCTGGCCGAGGACGCCAAGCT GCAGCTGAGCAAGGACACCTACGACGACGACCTGGACAACCTGCTGGCCAGATCG GCGACCAGTACGCCGACCTGTTCTGGCCGCAAGAACCTGAGCGACGCCATCCTGC TGAGCGACATCTGCGGGTGAACACCGAGATCACAAGGCCCCCTGAGCGCCAGCA TGATCAAGCGGTACGACGAGCACCACCGGACCTGACCTGCTGAAGGCCCTGGTGC GGCAGCAGCTGCCGAGAAGTACAAGGAGATCTTCTCGACCAGAGCAAGAACGGC TACGCCGGCTACATCGACGGCGGCCAGCCAGGAGGAGTTTACAAGTTTATCAAG CCCATCTGGAGAAGATGGACGGCACCGAGGAGCTGCTGGTGAAGCTGAACCGGGA GGACCTGCTGCGGAAGCAGCGGACCTTCGACAACGGCAGCATCCCCACAGATCCA CCTGGGCGAGCTGCACGCCATCTGCGGCGGAGGAGGACTTCTACCCCTTCTGAA GGACAACCGGGAGAAGATCGAGAAGATCCTGACCTTCCGGATCCCTACTACGTGGG CCCCCTGGCCCGGGGAACAGCCGGTTCGCTGGATGACCCGGAAGAGCGAGGAGA CCATACCCCTGGAACCTCGAGGAGGTGGTGGACAAGGGCGCCAGCGCCAGAGC TTCATCGAGCGGATGACCAACTTCGACAAGAACCTGCCAACGAGAAGGTGCTGCC AAGCACAGCCTGCTGTACGAGTACTTACCCTGTACAACGAGCTGACCAAGGTGAAG TACGTGACCGAGGGCATGCGGAAGCCCGCTTCTGAGCGGCGAGCAGAAGAAGGC CATCGTGGACCTGCTGTTCAAGACCAACCGGAAGGTGACCGTGAAGCAGCTGAAGG AGGACTTCAAGAAGATCGAGTGTCTGACAGCGTGGAGATCAGCGGCGTGGAG GACCGGTTCAACGCCAGCCTGGGCACCTACCACGACCTGCTGAAGATCATCAAGGAC AAGGACTTCTGGACAACGAGGAGAACGAGGACATCTGGAGGACATCGTGTGAC</p>	<p>157</p>

[0760]

	<p>CCTGACCCTGTTTCGAGGACCGGGAGATGATCGAGGAGCGGCTGAAGACCTACGCCCA CCTGTTGACGACAAAGGTGATGAAGCAGCTGAAGCGGCGGCTACACCGCTGGG GCCGGCTGAGCCGGAAGCTGATCAACGGCATCCGGGACAAGCAGAGCGGCAAGACC ATCCTGGACTTCTGAAGAGCGACGGCTTCGCCAACCGGAACTTCATGCAGCTGATC CACGACGACAGCCTGACCTTCAAGGAGGACATCCAGAAGGCCAGGTGAGCGGCCA GGGCGACAGCCTGCACGACACATCGCCAACTGGCCGGCAGCCCCATCAAGA AGGGCATCCTGCAGACCGTGAAGGTGGTGGACGAGCTGGTGAAGGTGATGGGCCG CACAAGCCCCGAGAATCTGTGATCGAGATGGCCCGGAGAACCAGACCACCCAGAA GGGCCAGAAGAACAGCCGGGAGCGGATGAAGCGGATCGAGGAGGGCATCAAGGAG CTGGGCAGCCAGATCCTGAAGGAGCACCCCGTGGAGAACACCCAGCTGCAGAACGA GAAGCTGTACTGTACTACCTGCAGAACCGGCCGGACATGTACGTGGTACCAGGACT GGACATCAACCGGCTGAGCGACTACGACGTGGACCACATCGTCCCCAGAGCTTCT GAAGGACGACAGCATCGACAACAAGGTGCTGACCCGGAGCGACAAGAACCAGGGG AAGAGCGACAACGTGCCAGCGAGGAGGTGGTGAAGAAGATGAAGAATACTGGCCG GCAGCTGTGAACGCCAAGCTGATCACCAGCGGAAGTTCGACAACCTGACCAAGG CCGAGCGGGGCGGCTGAGCGAGCTGGACAAGGCCGGCTTCATCAAGCGGCAGCTG GTGGAGACCCGGCAGATCACAAGCAGCTGGCCAGATCCTGGACAGCCGGATGAA CACCAAGTACGACGAGAACGACAAGCTGATCCGGGAGGTGAAGGTGATCACCTGA AGGCAAGCTGGTGAAGGACTTCCGGAAGGACTTCCAGTTCTACAAGGTGCGGGAG ATCAACAATAACACCACGCCACGACGCTACCTGAACGCCGTGGTACCAGCCAGG CTGATCAAGAAGTACCCCAAGCTGGAGAGCGAGTTCGTGTACGGCGACTACAAGGTG TACGACGTGCGGAAGATGATCGCCAAGAGCGAGCAGGAGATCGGCAAGGCCACCGC CAAGTACTTCTTCTACAGCAACATCATGAACTTCTTCAAGACCGAGATCACCCCTGGCC AACGGCGAGATCCGGAAGCGGCCCTGATCGAGACCAACGGCGAGACCCGGCAGAT CGTGTGGGACAAGGGCCGGGACTTCGCCACCCTGCGGAAGGTGCTGAGCATGCCCC AGGTGAACATCGTGAAGAAGACCGAGGTGCAGACCCGGCGGCTTCAGCAAGGAGAGC ATCCTGCCAAGCGGAACAGCGACAAGCTGATCGCCCGGAAGAAGGACTGGGACCC CAAGAAGTACGGCGGCTTCGACAGCCCCACCGTGGCCTACAGCGTGTGGTGGTGGC CAAGGTGGAGAAGGGCAAGAGCAAGAAGCTGAAGAGCGTGAAGGAGCTGCTGGGC ATCACCATCATGGAGCGGAGCAGCTTCGAGAAGAACCCCATCGACTTCTGGAGGCC AAGGGCTACAAGGAGGTGAAGAAGGACCTGATCATCAAGCTGCCAAGTACAGCCT GTTTCGAGCTGGAGAACGGCCGGAAGCGGATGCTGGCCAGCGCCGGCGAGCTGCAGA AGGGCAACGAGCTGGCCCTGCCAGCAAGTACGTGAACCTTCTGTACTTGGCCAGCC ACTACGAGAAGCTGAAGGGCAGCCCCGAGGACAACGAGCAGAAGCAGCTGTTCTGTG GAGCAGCACAAGCACTACCTGGACGAGATCATCGAGCAGATCAGCGAGTTCAGCAA GCGGGTATCCTGGCCGACGCCAACCTGGACAAGGTGCTGAGCGCTACAACAAGC ACCGGGACAAGCCATCCGGGAGCAGCCGAGAACATCATCCACCTGTTTACCCTGA CCAACCTGGGCGCCCCCGCCCTTCAAGTACTTCGACACCACCATCGACCCGGAAGC GGTACACCAGCACCAAGGAGGTGCTGGACGCCACCCTGATCCACCAGAGCATCACCG GCCTGTACGAGACCCGGATCGACCTGAGCCAGCTGGGCGGCGACGGCGGCGGACG CCCAAGAAGAAGCGGAAGGTG</p>	
<p>使用表4的低 A/U密码子, 具有两个C端 NLS 序列的 Cas9 切口酶 ORF (无起始 或终止密码 子; 适于包括 在融合蛋白 质编码序列 中)</p>	<p>GACAAGAAGTACAGCATCGGCTGGCCATCGGCACCAACAGCGTGGGCTGGGCCGT GATCACCGACGAGTACAAGGTGCCAGCAAGAAGTTCAAGGTGCTGGGCAACACCG ACCGGCACAGCATCAAGAAGAACCTGATCGGCGCCCTGCTGTTTCGACAGCGGCGAG ACCGCCGAGGCCACCCGGCTGAAGCGGACCCCGCGGCGGTTACACCCGGCGGAA GAACCCGATCTGCTACCTGCAGGAGATTTAGCAACGAGATGGCCAAGGTGGACGA CAGCTTCTCCACCGGTGGAGGAGCTTCTGGTGGAGGAGGACAAGAAGCAGC AGCGGCACCCCATCTTCGGCAACATCGTGGACGAGGTGGCCTACCACGAGAAGTACC CCACCATCTACCACCTGCGGAAGAAGCTGGTGGACAGCACCGACAAGGCCGACCTG CGGCTGATCTACCTGGCCCTGGCCACATGATCAAGTTCGGGGGCCACTTCTGATCG AGGGCGACCTGAACCCGACAACAGCGACGTGGACAAGCTGTTTATCCAGCTGGTG CAGACCTACAACCAGCTGTTTCGAGGAGAACCCCATCAACGCCAGCGGCGTGGACG CAAGGCCATCCTGAGCGCCCGGCTGAGCAAGAGCCGGCGGCTGGAGAACCCTGATCG CCCAGCTGCCGGCGGAGAAGAAGAAGCGCCTGTTTCGGCAACCTGATCGCCCTGAGC CTGGGCTGACCCCAACTTCAAGAGCAACTTCGACCTGGCCGAGGACGCCAAGCT GCAGCTGAGCAAGGACACCTACGACGACGACCTGGACAACCTGTTGGCCAGATCG GCGACCAGTACGCCGACCTGTTCTGGCCGCAAGAACCCTGAGCGACGCCATCCTGC TGAGCGACATCTGCGGGTGAACACCGAGATCACAAGGCCCCCTGAGCGCCAGCA TGATCAAGCGGTACGACGAGCACCACAGGACCTGACCCTGTGAAGGCCCTGGTGC GGCAGCAGCTGCCCAGAAAGTACAAGGAGATCTTCTTCGACCAGAGCAAGAACCGG TACGCCGGCTACATCGACGGCGGCGCCAGCCAGGAGGAGTTTACAAGTTTATCAAG CCCATCCTGGAGAAGATGGACGGCACCGAGGAGCTGCTGGTGAAGCTGAACCGGGA GGACCTGCTGCGGAAGCAGCGGACCTTCGACAACGGCAGCATCCCCACCAAGATCCA CCTGGGCGAGCTGCACGCCATCTGCGGCGGCGAGGAGGACTTCTACCCTTCTGTAA GGACAACCGGGAAGATCGAGAAGATCCTGACCTTCCGGATCCCTACTACCTGCGG CCCCCTGGCCCGGGCAACAGCCGTTTCGCTGGATGACCCGGAAGAGCGAGGAGA CCATACCCCTGGAACCTTCGAGGAGTGGTGGACAAGGGCGCCAGCGCCAGAGC</p>	<p>158</p>

[0761]

	<p>TTCATCGAGCGGATGACCAACTTCGACAAGAACCTGCCAACGAGAAGGTGCTGCC AAGCACAGCCTGCTGTACGAGTACTTACCGTGTACAACGAGCTGACCAAGGTGAAG TACGTGACCGAGGGCATGCGGAAGCCCGCTTCTGAGCGGCGAGCAGAAGAAGGC CATCGTGGACCTGCTGTTCAAGACCAACCGGAAGGTGACCGTGAAGCAGCTGAAGG AGGACTACTTCAAGAAGATCGAGTGCCTTCGACAGCGTGGAGATCAGCGGCGTGGAG GACCGGTTCAACGCCAGCTGGGCACCTACCACGACCTGCTGAAGATCATCAAGGAC AAGGACTTCTGGACAACGAGGAGAACGAGGACATCCTGGAGGACATCGTGTGAC CCTGACCCTGTTGAGGACCGGGAGATGATCGAGGAGCGGCTGAAGACCTACGCCCA CCTGTTGACGACAAGGTGATGAAGCAGCTGAAGCGGCGGCGGTACACCGGCTGGG GCGGCTGAGCCGGAAGCTGATCAACGGCATCCGGGACAAGCAGAGCGCAAGACC ATCCTGGACTTCTGAAGAGCGACGGCTTCGCCAACCGGAACTTCATGCAGCTGATC CACGACGACAGCCTGACCTTCAAGGAGGACATCCAGAAGGCCAGGTGAGCGGCCA GGGCGACAGCCTGCACGAGCACATCGCCAACCTGGCCGGCAGCCCCGCCATCAAGA AGGGCATCTGCAGACCGTGAAGGTGGTGGACGAGCTGGTGAAGGTGATGGGCCGG CACAAGCCCAGAAACATCGTATCGAGATGGCCCGGAGAACCAGACCACCCAGAA GGGCCAGAAGAACAGCCGGGAGCGGATGAAGCGGATCGAGGAGGGCATCAAGGAG CTGGGCAGCCAGATCCTGAAGGAGCACCCCTGGGAGAACACCCAGCTGCAGAACGA GAAGCTGTACCTGTACTACCTGCAGAACCGCCGGGACATGTACGTGGACCAGGAGCT GGACATCAACCGGCTGAGCGACTACGACGTGGACCACATCGTCCCCAGAGCTTCTCT GAAGGACGACAGCATCGACAACAAGGTGCTGACCCGGAGCGACAAGACCCGGGGC AAGAGCGACAACGTGCCAGCGAGGAGGTGGTGAAGAAGATGAAGAACTACTGGCC GCAGCTGCTGAACGCCAAGCTGATCACCCAGCGGAAGTTCGACAACCTGACCAAGG CCGAGCGGGGCGGCTGAGCGAGCTGGACAAGGCCGGCTTCATCAAGCGGACAGTGT CTGGAGACCCGGCAGATCACCAGCAGCTGGCCAGATCCTGGACAGCCGGATGAA CACCAAGTACGACGAGAACGACAAGCTGATCCGGGAGGTGAAGGTGATCACCTGA AGAGCAAGCTGGTGTGAGCGACTTCCGGAAGGACTTCCAGTTCTACAAGGTGCGGGAG ATCAACAACCTACCACCGCCACGACGCCTACCTGAACGCCGTGGTGGGCACCGCC CTGATCAAGAAGTACCCAAAGCTGGAGAGCGAGTTCGTGTACGGCGACTACAAGGTG TACGACGTGCGGAAGATGATCGCCAAGAGCGAGCAGGAGATCGGCAAGGCCACCGC CAAGTACTTCTTCTACAGCAACATCATGAACCTTCTTCAAGACCGAGATCACCTGGCC AACGGCGAGATCCGGAAGCGGCCCTGATCGAGACCAACGGCGAGACCGGCGAGAT CGTGTGGGACAAGGGCCGGGACTTCGCCACCGTGCAGGAGGTGCTGAGCATGCCCC AGGTGAACATCGTGAAGAAGACCAGGTGCAGACCGGCGGCTTCAGCAAGGAGAGC ATCCTGCCAAGCGGAACAGCGACAAGCTGATCGCCGGAAGAAGGACTGGGACCC CAAGAAGTACGGCGGCTTCGACAGCCCCACCGTGGCCTACAGCGTGTGGTGGTGGC CAAGGTGGAGAAGGGCAAGAGCAAGAAGCTGAAGAGCGTGAAGGAGCTGTGGGC ATCACCATCATGGAGCGGAGCAGCTTCGAGAAGAACCCATCGACTTCTTGGAGCC AAGGGCTACAAGGAGGTGAAGAAGGACCTGATCATCAAGCTGCCAAGCTGACGCT GTTGAGCTGGAGAACGGCCGGAAGCGGATGCTGGCCAGCGCCGGCGAGCTGCAGA AGGGCAACGAGCTGGCCCTGCCAGCAAGTACGTGAACCTTCTGTACCTGGCCAGCC ACTACGAGAAGCTGAAGGGCAGCCCCGAGGACAACGAGCAGAAGCAGCTGTTCTGTG GAGCAGCACAAGCACTACCTGGACGAGATCATCGAGCAGATCAGCGAGTTCAGCAAG GCGGGTATCCTGGCCGACGCCAACCTGGACAAGGTGCTGAGCGCTACAACAAGC ACCGGGACAAGCCATCCGGGAGCAGGCCGAGAACATCATCCACCTGTTACCCCTGA CCAACCTGGGCGCCCCCGCCGCTTCAAGTACTTCGACACCACCATCGACCGGAAGC GGTACACCAGCACAAGGAGGTGCTGGACGCCACCCTGATCCACCAGAGCATCACCG GCTGTACGAGACCCGGATCGACTGAGCCAGCTGGGCGGCGACGGCAGCGGACG CCCAAGAAGAAGCGGAAGGTGGACGGCAGCCCCAAGAAGAAGCGGAAGGTGGACA GCGGC</p>	
<p>使用表4的低 A/U 密码子 的 Cas9 切口 酶 ORF (无 NLS 且无起 始或终止密 码子; 适于包 括在融合蛋 白质编码序 列中)</p>	<p>GACAAGAAGTACAGCATCGGCTGGcCATCGGCACCAACAGCGTGGGCTGGGCCGTG ATCACCGACGAGTACAAGGTGCCAGCAAGAAGTTCAAGGTGCTGGGCAACCCGA CCGGCACAGCATCAAGAAGAACCTGATCGGCGCCCTGCTGTTGACAGCGGCGAGA CCGCCGAGGCCACCCGGCTGAAGCGGACCGCCCGGCGGCGGTACACCCGGCGGAAG AACCAGATGCTGCTACCTGCAGGAGATTTAGCAACGAGATGGCCAAGGTGGACGAC AGCTTCTTCCACCGGCTGGAGGAGAGCTTCTGGTGGAGGAGGACAAGAAGCACGA GCGGCACCCATCTTCGGCAACATCGTGGACGAGGTGGCCTACCACGAGAAGTACCC CACCATTACCACCTGCGGAAGAAGCTGGTGGACAGCACCGACAAGGCCGACCTGC GGTGATCTACCTGGCCCTGGCCACATGATCAAGTCCGGGGCCACTTCTGATCGA GGGCGACCTGAACCCGACAACAGCGACGTGGACAAGCTGTTTCATCCAGCTGGTGC AGACCTACAACAGCTGTTTCGAGGAGAACCCATCAACGCCAGCGGCGTGGACGCC AAGGCCATCCTGAGCGCCGGCTGAGCAAGAGCCGGCGGCTGGAGAACCTGATCGC CCAGCTGCCCGGCGAGAAGAAGAACGGCCTGTTCCGGCAACCTGATCGCCCTGAGCCT GGGCTGACCCCAACTTCAAGAGCAACTTCGACCTGGCCGAGGACGCCAAGCTGC AGCTGAGCAAGGACACCTACGACGACGACCTGGACAACCTGCTGGCCAGATCGGC GACCAAGTACGCGACCTGTTCTCGCCGCCAAGAACCTGAGCGACGCCATCCTGTG AGCGACATCTGCGGGTGAACACCGAGATCACAAGGCCCCCTGAGCGCCAGCATG ATCAAGCGGTACGACGAGCACCACCAGGACCTGACCTGCTGAAGGCCCTGGTGGC</p>	<p>159</p>

[0762]

	<p>GCAGCAGCTGCCCGAGAAGTACAAGGAGATCTTCTTCGACCAGAGCAAGAACGGCT ACGCCGGCTACATCGACGCGCGGCCAGCCAGGAGGAGTTCTACAAGTTCATCAAGC CCATCCTGGAGAAGATGGACGGCACCGAGGAGCTGCTGGTGAAGCTGAACCGGGAG GACCTGCTGCGGAAGCAGCGGACCTTCGACAACGGCAGCATCCCCACAGATCCAC CTGGGCGAGCTGCACGCCATCTGCGGCGGCAGGAGGACTTCTACCCCTTCTGAAG GACAACCGGGAGAAGATCGAGAAGATCCTGACCTTCCGGATCCCTACTACGTGGGC CCCCTGGCCCGGGCAACAGCCGGTTCGCCTGGATGACCCGGAAGAGCGAGGAGAC CATCACCCCTGGAACTTCGAGGAGGTGGTGGACAAGGGCGCCAGCGCCAGAGCT TCATCGAGCGGATGACCAACTTCGACAAGAACCTGCCAACGAGAAGGTGCTGCCCA AGCACAGCTGTGTACGAGTACTTCACCGTGTACAACGAGCTGACCAAGGTGAAGT ACGTGACCGAGGGCATGCGGAAGCCCGCTTCTGAGCGGGCAGCAGAAGAAGGCC ATCGTGGACCTGCTGTTCAAGACCAACCGGAAGGTGACCGTGAAGCAGCTGAAGGA GGACTACTCAAGAAGATCGAGTGTTCGACAGCGTGGAGATCAGCGGCGTGGAGG ACCGGTTCAACGCCAGCTGGGCACCTACCACGACCTGCTGAAGATCATCAAGGACA AGGACTTCTGGACAACGAGGAGAACGAGGACATCCTGGAGGACATCGTCTGAC CTGACCCTGTTTCGAGGACCGGGAGATGATCGAGGAGCGGCTGAAGACCTACGCCAC CTGTTTCGACGACAAGGTGATGAAGCAGCTGAAGCGGCGGCGGTACACCGGCTGGGG CCGGTGAGCCGGAAGCTGATCAACGGCATCCGGGACAAGCAGAGCGGCAAGACCA TCTGGACTTCTGAAGAGCGACGGCTTCGCCAACCGGAACCTCATGACGTGATCC ACGACGACGCCTGACCTTCAAGGAGGACATCCAGAAGGCCAGGTGACCGGCCAG GGCGACAGCCTGCACGAGCACATCGCCAACCTGGCCGGCAGCCCCGCCATCAAGAA GGGCATCCTCGAGACCGTGAAGGTGGTGGACGAGCTGGTGAAGGTGATGGGCCGGC ACAAGCCCGAGAACATCGTGATCGAGATGGCCCGGGAGAACCAGACCACCGAGAAG GGCCAGAAGAACAGCCGGGAGCGGATGAAGCGGATCGAGGAGGGCATCAAGGAGT GGGCGCCAGATCCTGAAGGAGCACCCCGTGGAGAACACCCAGCTGCAGAACGAGA AGCTGTACTGTACTACCTGCAGAACGGCCGGGACATGTACGTGGACCAGGAGCTGG ACATCAACCGGCTGAGCGACTACGACGTGGACCACATCGTCCCCAGAGCTTCTCTGA AGGACGACAGCATCGACAACAAGGTGCTGACCCGAGCGACAAGAACCAGGGGCAA GAGCGACAACGTGCCACGCGAGGAGGTGGTGAAGAAGATGAAGAAGTACTGGCGGC AGCTGCTGAACGCCAAGCTGATCACCCAGCGAAGTTCGACAACCTGACCAAGGCC GAGCGGGGCGGCTGAGCGAGCTGGACAAGGCCGGCTTCATCAAGCGGCAGCTGGT GGAGACCCGGCAGATCACCAAGCAGTGGCCAGATCCTGGACAGCCGGATGAACA CCAAGTACGACGAGAACAAGCTGATCCGGGAGGTGAAGGTGATCACCTGGAAG AGCAAGCTGGTGAACGACTTCCGGAAGGACTTCCAGTTCACAAGGTGCGGGAGATC AACAACTACCACCGCCACGACGCCTACCTGAACGCCGTGGTGGGCACCGCCCTG ATCAAGAAGTACCCCAAGCTGGAGAGCGAGTTCGTGTACGGCGACTACAAGGTGTAC GACGTGCGGAAGATGATCGCCAAGAGCGAGCAGGAGATCGGCAAGGCCACCGCCAA GTACTTCTTCTACAGCAACATCATGAACTTCTTCAAGACCGAGATCACCTGGCCAAC GGCGAGATCCGGAAGCGGCCCTGATCGAGACCAACGGCGAGACCGGCGAGATCGT GTGGGACAAGGGCCGGGACTTCGCCACCGTGCAGGAAAGGTGCTGAGCATGCCCCAGG TGAACATCGTGAAGAAGACCGAGGTGCAGACCGGCGGCTTCAGCAAGGAGAGCATC TGCCCAAGCGGAACAGCGACAAGCTGATCGCCCGGAAGAAGGACTGGGACCCCAA GAAGTACGGCGGCTTCGACAGCCCCACCGTGGCCTACAGCGTGTGGTGGTGGCCAA GGTGGAGAAGGGCAAGAGCAAGAAGCTGAAGAGCGTGAAGGAGCTGCTGGGCATC ACCATCATGGAGCGGAGCAGCTTCGAGAAGAACCCCATCGACTTCTGGAGGGCAAG GGTACAAGGAGGTGAAGAAGGACCTGATCATCAAGCTGCCAAGTACAGCCTGTTG GAGTGGAGAACCGCCGGAAGCGGATGCTGGCCAGCGCCGGCGAGATCGAGAAGG GCAACGAGCTGGCCCTGCCAGCAAGTACGTGAACTTCTGTACTTGGCCAGCCACT ACGAGAAGCTGAAGGGCAGCCCGAGGACAACGAGCAGAAGCAGCTGTTCTGTGGA GCAGCACAAGCACTACCTGGACGAGATCATCGAGCAGATCAGCGAGTTCAGCAAGCG GGTATCCTGGCCGACGCCAACCTGGACAAGGTGCTGAGCGCCTACAACAAGCACCC GGGACAAGCCCATCCGGGAGCAGGCCGAGAACATCATCCACCTGTTTACCCTGACCA ACCTGGGCGCCCCGCCCTTCAAGTACTTCGACACCACCATCGACCGGAAGCGGT ACACGACCAAGGAGGTGCTGGACGCCACCTGATCCACCAGAGCATCACCGGC CTGTACGAGACCCGGATCGACCTGAGCCAGCTGGGCGGCGAC</p>	
<p>使用表4的低 A/U 密码子 的 dCas9 ORF (无起始 或终止密码 子; 适于包括 在融合蛋白 质编码序列</p>	<p>GACAAGAAGTACAGCATCGCCTGGCCTCGGCACCAACAGCGTGGGCTGGGCCGTG ATCACCGACGAGTACAAGGTGCCAGCAAGAAGTTCAGGTGCTGGGCAACACCGA CCGGCACAGCATCAAGAAGAAGCTGATCGGCCTGCTGTTTCGACAGCGGCGAGA CCGCCGAGGGCACCCGGCTGAAGCGGACCGCCGGCGGCTACACCCGGCGGAAG AACCGGATCTGTACTGCAGGAGATTTAGCAACGAGATGGCCAAGGTGGACGAC AGCTTCTCCACCGCTGGAGGAGCTTCTGGTGGAGGAGGACAAGAAGCACGA GCGGCACCCATCTTCGGCAACATCGTGGACGAGGTGGCCTACCACGAGAAGTACCC CACCATCTACCACCTGCGGAAGAAGCTGGTGGACAGCACCGACAAGGCCGACCTGC GGTGTACTACTTGGCCCTGGCCACATGATCAAGTTCGGGGCCACTTCTGTATCGA GGCGACCTGAACCCGACAACAGCAGCGACGTGGACAAGTGTTCATCAAGCTGGTGC AGACCTACAACAGCTGTTTCAGGAGAACCCCATCAACGCCAGCGGCGTGGACGCC AAGCCATCTGAGCGCCCGCTGAGCAAGAGCCGGCGGCTGGAGAAGCTGATCGC</p>	<p>160</p>

[0763]

中)	<p>CCAGCTGCCCGGCGAGAAGAAGAACGGCCTGTTCGGCAACCTGATCGCCCTGAGCCT GGGCTGACCCCAACTTCAAGAGCAACTTCGACCTGGCCGAGGACGCCAAGCTGC AGCTGAGCAAGGACACCTACGACGACGACCTGGACAACCTGCTGGCCAGATCGGC GACCAGTACGCCGACCTGTTCTGGCCGCCAAGAACCTGAGCGACGCCATCCTGCTG ATCGACATCCTGCGGGTGAACACCGAGATACCAAGGCCCCCTGAGCGCCAGCATG ATCAAGCGGTACGACGAGCACCACAGGACCTGACCCTGCTGAAGGCCCTGGTGCG GCAGCAGCTGCCGAGAAGTACAAGGAGATCTTCTCGACCAGAGCAAGAACGGCT ACGCCGGCTACATCGACGGCGGCCAGCCAGGAGGATTCTACAAGTTTCATCAAGC CCATCCTGGAGAAGATGGACGGCACCGAGGAGCTGCTGGTGAAGCTGAACCGGGAG GACCTGCTGCGGAAGCAGCGGACCTTCGACAACGGCAGCATCCCCACCAAGGAC CTGGGCGAGCTGCACGCCATCTGCGGGCGCAGGAGGACTTCTACCCTTCTGAAAG GACAACCGGGAGAAGATCGAGAAGATCCTGACCTTCCGGATCCCCTACTACGTGGGC CCCCTGGCCCGGGCAACAGCCGGTTCGCTGGATGACCCGGAAGAGCGAGGAGAC CATCACCCCTGGAACCTCGAGGAGGTGGTGGACAAGGGCGCCAGCGCCAGAGCT TCATCGAGCGGATGACCAACTTCGACAAGAACCTGCCAACGAGAAGGTGCTGCCA AGCACAGCCTGCTGTACGAGTACTTACCCTGTACAACGAGCTGACCAAGGTGAAGT ACGTGACCGAGGGCATGCGGAAGCCCGCCTTCTGAGCGGCGAGCAGAAGAAGGCC ATCGTGGACCTGCTGTTCAAGACCAACCGGAAGGTGACCGTGAAGCAGCTGAAGGA GGACTACTCAAGAAGATCGAGTGTTCGACAGCGTGGAGATCAGCGCGCTGGAGG ACCGGTTCAACGCCAGCTGGCCACCTACCACGACCTGCTGAAGATCATCAAGGACA AGGACTTCTGGACAACGAGGAGAACGAGGACATCCTGGAGGACATCGTGTGACC CTGACCCTGTTTCGAGGACCGGGAGATGATCGAGGAGCGGCTGAAGACCTACGCCAC CTGTTTCGACGACAAGGTGATGAAGCAGCTGAAGCGGGCGGTACACCGGCTGGGG CCGGCTGAGCCGGAAGCTGATCAACGGCATCCGGGACAAGCAGAGCGCAAGACCA TCCTGGACTTCTGAAGAGCGACGGCTTCGCCAACCAGCAACTTCATGCAGCTGATCC ACGACGACAGCCTGACCTTCAAGGAGGACATCCAGAAGGCCAGGTGAGCGGCCAG GGCGACAGCCTGCACGAGCACATCGCCAACCTGGCCGGCAGCCCCGCCATCAAGAA GGGCATCTGCAGACCGTGAAGGTGGTGGACGAGCTGGTGAAGGTGATGGGCCGGC ACAAGCCCGAGAACATCGTGTGATCGAGATGGCCCGGGAAGCAGACCACCCAGAAG GGCCAGAAGAACAGCCGGGAGCGGATGAAGCGGATCGAGGAGGGCATCAAGGAGCT GGGCAGCCAGATCCTGAAGGAGCACCCCGTGGAGAACCCAGCTGCAGAACGAGA AGCTGTACCTGTACTACCTGCAGAACGGCCGGGACATGTACGTGGACCAGGAGCTGG ACATCAACCGGCTGAGCGACTACGACGTGGAC_{gc}CATCGTGCCCAAGAGCTTCTGAA GGACGACAGCATCGACAACAAGGTGCTGACCCGGAGCGACAAGAACCAGGGGCAAG AGCGACAACGTGCCAGCGAGGAGGTGGTGAAGAAGATGAAGAACTACTGGCGGCA GCTGCTGAACGCCAAGCTGATCACCCAGCGGAAGTTCGACAACCTGACCAAGGCCG AGCGGGCGGGCTGAGCGAGCTGGACAAGGCCGGCTTCATCAAGCGCGAGCTGGTG GAGACCCGGCAGATCACCAAGCACGTGGCCAGATCCTGGACAGCCGGATGAACAC CAAGTACGACGAGAACGACAAGCTGATCCGGGAGGTGAAGGTGATCACCTGAAGA GCAAGCTGGTGAAGCGACTTCCGGAAGGACTTCCAGTTCTACAAGGTGCGGGAGATCA ACAACCTACCACCGCCACGACGCCTACCTGAACGCCGTGGTGGGCAACCCGCCCTGA TCAAGAAGTACCCAAAGCTGGAGAGCGAGTTCGTGTACGGCGACTACAAGGTGTACG ACGTGCGGAAGATGATCGCCAAGAGCGAGCAGGAGATCGGCAAGGCCACCGCCAAG TACTTCTTCTACAGCAACATCATGAACCTTCTTCAAGACCGAGATCACCTGGCCAACG GCGAGATCCGGAAGCGGCCCTGATCGAGACCAACGGCGAGACCGGCGAGATCGTG TGGACAAGGGCCGGGACTTCGCCACCGTGCAGGAGGTGCTGAGCATGCCCAAGGT GAACATCGTGAAGAAGACCGAGGTGCAGACCGCGGGCTTCAGCAAGGAGAGCATCC TGCCCAAGCGGAACAGCGACAAGCTGATCGCCCGGAAGAAGGACTGGGACCCCAAG AAGTACGGCGGCTTCGACAGCCCCACCGTGGCTACAGCGTGTGGTGGTGGCCAAG GTGGAGAAGGGCAAGAGCAAGAAGCTGAAGAGCGTGAAGGAGCTGCTGGGCATCA CCATCATGGAGCGGAGCAGCTTCGAGAAGAACCCTACGACTTCTGGAGGCCAAGG GCTACAAGGAGGTGAAGAAGGACCTGATCATCAAGCTGCCAAGTACAGCCTGTTTCG AGCTGGAGAACGGCCGGAAGCGGATGCTGGCCAGCGCCGGCGAGCTGCAGAAGGGC AACGAGCTGGCCCTGCCAGCAAGTACGTGAACCTTCTGTACTTGGCCAGCCACTAC GAGAAGCTGAAGGGCAGCCCCGAGGACAACGAGCAGAAGCAGCTGTTCTGTGGAGC AGCACAAGCACTACCTGGACGAGATCATCGAGCAGATCAGCGAGTTCAGCAAGCGG GTGATCCTGGCCGACGCCAACCTGGACAAGGTGCTGAGCGCCTACAACAAGCACCG GGACAAGCCATCCGGGAGCAGGCCGAGAACATCATCCACCTGTTACCCCTGACCAA CCTGGGCGCCCCCGCCCTTCAAGTACTTCGACACCACATCGACCGGAAGCGGTA CACCAGCACAAGGAGGTGCTGGACGCCACCCTGATCCACCAGAGCATCACCCGGCT GTACGAGACCCGGATCGACCTGAGCCAGCTGGGCGGCGACGGCGGCGGCAGCCCA AGAAGAAGCGGAAGGTG</p>	
使用表4的低 A/U密码子, 具有两个C端	<p>GACAAGAAGTACAGCATCGGCCTGGCCATCGGCACCAACAGCGTGGGCTGGGCCGT GATCACCGACGAGTACAAGGTGCCAGCAAGAAGTTCAAGGTGCTGGGCAACACCG ACCGGCACAGCATCAAGAAGAACCTGATCGCGGCCCTGCTGTTTCGACAGCGCGAG ACCGCCGAGGCCACCCGGCTGAAGCGGACCGCCCGGCGGGTACACCCGGCGGAA GAACCGGATCTGCTACCTGCAGGAGATCTTACGCAACGAGATGGCCAAGGTGGACGA</p>	161

<p>NLS 序列的 dCas9 ORF (无起始或终止 密码子; 适于 包括在融合 蛋白质编 码序列中)</p>	<p>CAGCTTCTCCACCGGCTGGAGGAGAGCTTCTGGTGGAGGAGGACAAGAAGCACG AGCGGCACCCCATCTTCGCAACATCGTGGACGAGGTGGCCTACCACGAGAAGTACC CCACCATCTACCACCTGCGGAAGAAGCTGGTGGACAGCACCGACAAGGCCGACCTG CGGCTGATCTACCTGGCCCTGGCCACATGATCAAGTTCGGGGCCACTTCTGATCG AGGGCGACCTGAACCCCGACAACAGCGACGTGGACAAGCTGTTATCCAGCTGGTG CAGACCTACAACCAGCTGTTTCGAGGAGAACCCCATCAACGCCAGCGCGTGGACGC CAAGGCCATCCTGAGCGCCCGGCTGAGCAAGAGCCGGCGGCTGGAGAACCTGATCG CCCAGCTGCCGGCGGAGAAGAAGAACGGCCTGTTCCGCAACCTGATCGCCCTGAGC CTGGGCCTGACCCCAACTTCAAGAGCAACTTCGACCTGGCCGAGGACGCCAAGCT GCAGCTGAGCAAGGACACCTACGACGACGACCTGGACAACCTGCTGGCCAGATCG GCGACCAAGTACGCCGACCTGTTCTGGCCGCAAGAACCTGAGCGACGCCATCCTGC TGAGCGACATCCTGCGGGTGAACACCGAGATCACCAGGCCCCCTGAGCGCCAGCA TGATCAAGCGGTACGACGAGCACCACGACCTGACCTGCTGAAGGCCCTGGTGC GGCAGCAGCTGCCCGAGAAGTACAAGGAGATCTTTCGACCAGAGCAAGAACCGC TACGCCGGCTACATCGACGGCGGCCAGCCAGGAGGAGTTCTACAAGTTCATCAAG CCCATCCTGGAGAAGATGGACGGCACCGAGGAGCTGCTGGTGAAGCTGAACCGGA GGACCTGCTGCCGAAGCAGCGGACCTTCGACAACGGCAGCATCCCCACAGATCCA CCTGGGCGAGCTGCACGCCATCCTGCGGCGGCAGGAGGACTTCTACCCCTTCTGAA GGACAACCGGGAGAAGATCGAGAAGATCCTGACCTTCCGGATCCCCTACTACGTGGG CCCCCTGGCCCGGGCAACAGCCGGTTCGCTGGATGACCCGGAAGAGCGAGGAGA CCATCACCCCTGGAACCTCGAGGAGGTGGTGGACAAGGGCGCCAGCGCCAGAGC TTCATCGAGCGGATGACCAACTTCGACAAGAACCTGCCAACGAGAAGGTGCTGCC AAGCACAGCCTGCTGTACGAGTACTTACCCTGTACAACGAGCTGACCAAGGTGAAG TACGTGACCGAGGGCATCGGAAGCCCGCTTCTGAGCGGCAGCAAGAAGGAGG CATCGTGGACCTGCTGTTCAAGACCAACCGGAAGGTGACCGTGAAGCAGCTGAAG AGGACTACTCAAGAAGATCGAGTGTTCGACAGCGTGGAGATCAGCGGCGTGGAG GACCGGTTCAACGCCAGCCTGGGCACCTACCACGACCTGCTGAAGATCATCAAGGAC AAGGACTTCTGGACAACGAGGAGAACGAGGACATCCTGGAGGACATCGTGTGAC CCTGACCCTGTTTCGAGGACCGGGAGATGATCGAGGAGCGGCTGAAGACCTACGCCCA CCTGTTTCGACGACAAGGTGATGAAGCAGCTGAAGCGGCGGCGGTACACCGGCTGGG GCCGGCTGAGCCGGAAGCTGATCAACGGCATCCGGGACAAGCAGAGCGGCAAGACC ATCCTGGACTTCTGAAGAGCGACGGCTTCGCCAACCGGAACCTCATGCAGCTGATC CACGACGACAGCCTGACCTTCAAGGAGGACATCCAGAAGGCCAGGTGACCGGCCA GGGCGACAGCCTGCACGAGCACATCGCCAACCTGGCCGGCAGCCCCGCCATCAAGA AGGGCATCCTGCAGACCGTGAAGGTGGTGGACGAGCTGGTGAAGGTGATGGGCCGG CACAAGCCCAGAACATCGTGATCGAGATGGCCCGGGAACCAGACCACCCAGAA GGCCAGAAGAACAGCCGGGAGCGGATGAAGCGGATCGAGGAGGGCATCAAGGAG CTGGGCGAGCCAGATCCTGAAGGAGCACCCCGTGGAGAACCACCCAGCTGCAAGCA GAAGCTGTACCTGTACTACCTGCAGAACGGCCGGGACATGTACGTGGACCAGGAGCT GGACATCAACCGGCTGAGCGACTACGACGTGGACGCCATCGTCCCCAGAGCTTCT GAAGGACGACAGCATCGACAACAAGGTGCTGACCCGGAGCGACAAGAACCAGGGC AAGAGCGACAACCTGCCCAGCGAGGAGGTGGTGAAGAAGATGAAGAACTACTGGCC GCAGCTGCTGAACGCCAAGCTGATCACCCAGCGGAAGTTCGACAACCTGACCAAGG CCGAGCGGGCGGCCCTGAGCGAGCTGGACAAGGCCGGCTTCATCAAGCGGCAGCTG GTGGAGACCCGGCAGATCACCAGCACGTGGCCAGATCCTGGACAGCCGGATGAA CACCAAGTACGACGAGAACGACAAGCTGATCCGGGAGGTGAAGGTGATCACCTGA AGAGCAAGCTGGTGAAGGACTTCCGGAAGGACTTCCAGTTCTACAAGGTGCGGAG ATCAACAACCTACCACCGCCACGACGCCTACCTGAACGCCGTGGTGGGACCCGCC CTGATCAAGAAGTACCCCAAGCTGGAGAGCGAGTTCGTGTACGGCGACTACAAGGTG TACGACGTGCCGGAAGATGATCGCCAAGAGCGAGCAGGAGATCGGCAAGGCCACCGC CAAGTACTTCTTACAGCAACATCATGAACTTCTTCAAGACCGAGATCACCTGGCC AACGGCGAGATCCGGAAGCGGCCCTGATCGAGACCAACGGCGAGACCGGCAGAT CGTGTGGGACAAGGGCCGGACTTCGCCACCGTGCAGGAGGTGCTGAGCATGCCCC AGGTGAACATCGTGAAGAAGACCGAGGTGCAGACCGGCGGCTTCAGCAAGGAGAGC ATCTGCCAAGCGGAACAGCGACAAGCTGATCGCCCGGAAGAAGGACTGGGACCC CAAGAAGTACGGCGGCTTCGACAGCCCCACCGTGGCCTACAGCGTGTGGTGGTGGC CAAGGTGGAGAAGGGCAAGAGCAAGAAGCTGAAGAGCGTGAAGGAGCTGCTGGGC ATCACCATCATGGAGCGGAGCAGCTTCGAGAAGAACCCATCGACTTCTGGAGGCC AAGGGCTACAAGGAGGTGAAGAAGGACCTGATCATCAAGCTGCCAAGTACAGCCT GTTTCGAGCTGGAGAACCGCCGGAAGCGGATGCTGGCCAGCGCCGGCGAGCTGCAGA AGGGCAACGAGCTGGCCCTGCCAGCAAGTACGTGAACCTTCTGTACTTGGCCAGCC ACTACGAGAAGCTGAAGGCGAGCCCCGAGGACAACGAGCAGAAGCAGCTGTTCTGTG GAGCAGCACAAGCACTACCTGGACGAGATCATCGAGCAGATCAGCGAGTTCAGCAA CCGGGTGATCCTGGCCGACGCCAACCTGGACAAGGTGCTGAGCGCTTACAACAAGC ACCGGACAAGCCATCCGGGAGCAGCCGAGAACATCATCCACTGTACCTACCCTGA CCAACCTGGGCGCCCCCGCCCTTCAAGTACTTCGACACCACCATCGACCCGGAAGC GGTACACCAGCACCAAGGAGGTGCTGGACGCCACCTGATCCACCAGAGCATCACCG</p>
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[0764]

	GCCTGTACGAGACCCGGATCGACCTGAGCCAGCTGGGCGGCGACGGCAGCGGCAGC CCCAAGAAGAAGCGGAAGGTGGACGGCAGCCCAAGAAGAAGCGGAAGGTGGACA GCGGC	
使用表4的低 A/U 密码子 的 dCas9 ORF (无NLS 且无起始或 终止密码子; 适于包括在 融合蛋白质 编码序列中)	GACAAGAAGTACAGCATCGGCCTGGcCATCGGCACCAACAGCGTGGGCTGGGCCGTG ATCACCGACGAGTACAAGGTGCCAGCAAGAAGTTCAAGGTGCTGGGCAACACCGA CCGGCACAGCATCAAGAAGAACCTGATCGGCCTGCTGTTTCGACAGCGGCGAGA CCGCCGAGGCCACCCGGCTGAAGCGGACCGCCCGGCGGCGGTACACCCGGCGGAAG AACCGGATCTGCTACCTGCAGGAGATCTTCAGCAACGAGATGGCCAAGGTGGACGAC AGTTCTTCCACCGGCTGGAGGAGAGCTTCTGGTGGAGGAGGACAAGAACGACGGA GCGGCACCCATCTTCGGCAACATCGTGGACGAGGTGGCCTACCACGAGAAGTACCC CACCATCTACCACCTGCGGAAGAAGCTGGTGGACAGCACCGACAAGGCCGACCTGC GGTGATCTACCTGGCCCTGGCCACATGATCAAGTTCCGGGGCCACTTCTGATCGA GGGCGACCTGAACCCGACAACAGCGACGTGGACAAGCTGTTTCATCCAGCTGGTGC AGACCTACAACAGCTGTTTCGAGGAGAACCCCATCAACGCCAGCGGCGTGGACGCC AAGGCATCTGAGCGCCCGGTGAGCAAGAGCCGCGGCTGGAGAACCCTGATCGC CCAGCTGCCCGGCGAGAAGAAGAAGCGGCCTGTTTCGGCAACCTGATCCCGCTGAGCCT GGGCTGACCCCAACTTCAAGAGCAACTTCGACCTGGCCGAGGACGCCAAGCTGC AGCTGAGCAAGGACACCTACGACGACGACCTGGACAACCTGCTGGCCAGATCGGC GACCAGTACGCCGACCTGTTCTGGCCGCAAGAACCTGAGCGACGCCATCTGCTG AGCGACATCTGCGGGTGAACACCGAGATCACCAGGCCCCCTGAGCCGACGATG ATCAAGCGGTACGACGAGCACCACAGGACCTGACCCTGCTGAAGGCCCTGGTGC GCAGCAGCTGCCGAGAAGTACAAGGAGATCTTCTTCGACCAGAGCAAGAACGGCT ACGCCGGTACATCGACGCGCGGCCAGCCAGGAGGAGTTTACAAGTTTCATCAAGC CCATCTGGAGAAGATGGACGGCACCGAGGAGCTGCTGGTGAAGCTGAACCGGAG GACCTGCTGCGGAAGCAGCGGACCTTCGACAACGGCAGCATCCCCACAGATCCAC CTGGGCGAGCTGCACGCCATCTGCGGCGCAGGAGGACTTCTACCCCTTCTGAA GACAACCGGGAGAAGATCGAGAAGATCTGACCTTCCGGATCCCTACTACGTGGGC CCCCTGGCCCGGGCAACAGCCGGTTCGCTGGATGACCCGGAAGAGCGGAGGAGAC CATCACCCCTGGAACCTTCGAGGAGGTGGTGGACAAGGGCGCCAGCGCCAGAGCT TCATCGAGCGGATGACCAACTTCGACAAGAACCTGCCAACGAGAAGGTGCTGCCCA AGCACAGCCTGCTGTACGAGTACTTACCGTGTACACGAGCTGACCAAGGTGAAGT ACGTGACCGAGGGCATGCGGAAGCCCGCCTTCTGAGCGGCGAGCAGAAGAAGGCC ATCGTGGACCTGCTGTTCAAGCAACCGGAAGGTGACCGTGAAGCAGCTGAAGGA GGACTACTTCAAGAAGTACGAGTGTCTTCGACAGCGTGGAGATCAGCGGCTGGAGG ACCGGTTCAACGCCAGCCTGGGCACCTACCACGACCTGCTGAAGATCATCAAGGACA AGGACTTCTGGACAACGAGGAGAACGAGGACATCTGGAGGACATCGTCTGACC CTGACCCCTGTTTCGAGGACCGGGAGATGATCGAGGAGCGGCTGAAGACCTACGCCAC TGTTTCGACGACAAGGTGATGAAGCAGCTGAAGCGGCGGCGGTACACCGCTGGGG CCGGCTGAGCCGGAAGCTGATCAACGGCATCCGGGACAAGCAGAGCGGCAAGACCA TCCTGGACTTCTGAAGAGCGACGGCTTCGCCAACCAGCAACTTCATGCAGCTGATCC ACGACGACAGCCTGACCTTCAAGGAGGACATCCAGAAGGCCAGGTGAGCGGCCAG GGGACAGCCTGCACGAGCAGATCGCCAACCTGGCCGGCAGCCCGCCATCAAGAA GGGCATCCTGCAGACCGTGAAGGTGGTGGACGAGCTGGTGAAGGTGATGGCCGGC ACAAGCCCGAGAACATCGTATCGAGATGGCCCGGGAGAACCAGACCACCGAAG GGCCAGAAGAACAGCCGGGAGCGGATGAAGCGGATCGAGGAGGGCATCAAGGAGCT GGGACGCCAGATCTGAAGGAGCACCCCGTGGAGAACACCCAGCTGCAGAACGAGA AGCTGTACCTGTACTACCTGCAGAACGGCCGGACATGTACGTGGACCTGAGG ACATCAACCGGCTGAGCGACTACGACGTGGACgcCATCGTCCCCAGAGCTTCTGAA GGACGACAGCATCGACAACAAGGTGCTGACCCGGAGCGACAAGAACCAGGGGCAAG AGCGACAACGTGCCAGCGAGGAGGTGGTGAAGAAGATGAAGAATACTGGCGGCA GCTGCTGAACGCCAAGCTGATCACCCAGCGGAAGTTTCGACAACCTGACCAAGGCCG AGCGGGCGGCTGAGCGAGCTGGACAAGGCCGGCTTCATCAAGCGCGAGTGGTG GAGACCCGGCAGATCACAAGCACGTGGCCAGATCCTGGACAGCCGGATGAACAC CAAGTACGACGAGAACGACAAGCTGATCCGGGAGGTGAAGGTGATCACCTGAAGA GCAAGCTGGTGAAGGACTTCCGGAAGGACTTCCAGTTCTACAAGGTGCGGGAGATCA ACAATAACACACGCCACGACGCTTACCTGAACGCCGTGGTGGCACCCGCTGA TCAAGAAGTACCCCAAGCTGGAGAGCGAGTTCGTGTACGGCGACTACAAGGTGTACG ACGTGCGGAAGATGATCGCCAAGAGCGAGCAGGAGATCGGCAAGGCCACCGCCAAG TACTTCTTACAGCAACATCATGAACCTTCTTCAAGACCGAGATCACCTGGCCAACG GCGAGATCCGGAAGCGGCCCTGATCGAGACCAACGGCGAGACCGGCGAGATCGTG TGGACAAGGGCCGGGACTTCCACACCGTCCGGAAGGTGCTGAGCATGCCCAAGT GAACATCGTGAAGAAGACCGAGGTGCAGACCGGCGGCTTCAGCAAGGAGAGCATCC TGCCCAAGCGGAACAGCGACAAGCTGATCGCCCGGAAGAAGGACTGGGACCCCAAG AAGTACGGCGGCTTCGACAGCCCCACCGTGGCCTACAGCGTGTGGTGGTGGCCAAG GTGGAGAAGGGCAAGAGCAAGAAGCTGAAGAGCGTGAAGGAGCTGCTGGGCATCA CCATCATGGAGCGGAGCAGCTTCGAGAAGAACCCTCGACTTCTGGAGGCCAAGG GCTACAAGGAGGTGAAGAAGGACCTGATCATCAAGCTGCCCAAGTACAGCCTGTTTCG	162

[0765]

	<p>AGCTGGAGAACGGCCGGAAGCGGATGCTGGCCAGCGCCGGCGAGCTGCAGAAGGGC AACGAGCTGGCCCTGCCAGCAAGTACGTGAACCTTCTGTACCTGGCCAGCCACTAC GAGAAGCTGAAGGGCAGCCCGAGGACAACGAGCAGAAGCAGCTGTTCTGTGGAGC AGCACAAAGCACTACCTGGACGAGATCATCGAGCAGATCAGCGAGTTCAGCAAGCGG GTGATCTGGCCGACGCCAACCTGGACAAGGTGCTGAGCGCCTACAACAAGCACCG GGACAAGCCCATCCGGGAGCAGGCCGAGAACATCATCCACCTGTTCCACCTGACCAA CCTGGGCGCCCCGCCCTTCAAGTACTTTCGACACCACCATCGACCGGAAGCGGTA CACCAGACCAAGGAGGTGCTGGACGCCACCCTGATCCACCAGAGCATCACCGGCT GTACGAGACCCGGATCGACCTGAGCCAGCTGGGCGGGCAG</p>	
<p>使用表4的低 A 密码子的 Nme Cas9 ORF (无起始 或终止密码 子; 适于包括 在融合蛋白 质编码序列 中)</p>	<p>GCCGCCTCAAGCCAACTCCATCAACTACATCTGGGCCTGGACATCGGCATCGCCT CCGTGGGCTGGCCATGGTGGAGATCGACGAGGAGGAGAACCCATCCGGCTGATCG ACCTGGGCGTGCGGGTGTTTCGAGCGGGCCGAGGTGCCAAGACCGGCGACTCCCTG GCCATGGCCCGGCGGCTGGCCCGTCCGTGCGGGCGGCTGACCCGGCGGCGGGCCCA CCGGCTGCTGCGGACCCGGCGGCTGCTGAAGCGGGAGGGCGTGTGCAGGGCCCA ACTTCAGCAGAAACGGCTGATCAAGTCCCTGCCAACACCCCTGGCAGAGGACGGG CCGCGCCCTGGACCGAAGCTGACCCCTGGAGTGGTCCGCGTGTCTGCTGCACC TGATCAAGCACCGGGCTACCTGTCCAGCGGAAGAACGAGGGCGAGACCGCCGAC AAGGAGCTGGGCGCCCTGCTGAAGGGCGTGGCCGGCAACGCCACGCCCTGCAGAC CGGCGACTTCCGGACCCCGCGGAGCTGGCCCTGAACAAGTTCGAGAAGGAGTCCG GCCACATCCGGAACCAAGCGTCCGACTACTCCACACCTTCTCCCGGAAGGACCTGC AGGCCGAGCTGATCCTGCTGTTTCGAGAAGCAGAAGGAGTTCGGCAACCCACGCTGT CCGGCGGCTGAAGGAGGGCATCGAGACCCTGCTGATGACCCAGCGGCCCGCCCTGT CCGGCGACGCGGTGCAGAAGATGCTGGGCCACTGCACCTTCGAGCCCGGAGTCC AAGCCGCCAAGAACACCTACACCGCCGAGCGGTTTCATCTGGCTGACCAAGTGAAC AACCTGCGGATCCTGGAGCAGGGCTCCGAGCGGCCCTGACCGACACCGAGCGGGC CACCTGTGAGCAGGCCCTACCGAAGTCCAAGCTGACCTACGCCAGGCCCGGAA GCTGCTGGGCTGGAGGACACCGCCTTCTTCAAGGGCCTGCGGTACGGCAAGGACA ACGCCGAGGCCTCCACCCTGATGGAGATGAAGGCCTACCACGCCATCTCCCGGGCC TGGAGAAGGAGGGCCTGAAGGACAAGAAGTCCCCCTGAACCTGTCCCGGAGCTG CAGGACGAGATCGGCACCGCCTTCTCCCTGTTCAAGACCGACGAGGACATCACGGC CGGCTGAAGGACCGGATCCAGCCCGAGATCCTGGAGGCCCTGCTGAAGCACATCTCC TTCGACAAGTTCGTGCAGATCTCCCTGAAGGCCCTGCGGCGGATCGTCCCTGATG GAGCAGGGCAAGCGGTACGACGAGCCCTGCGCCGAGATCTACGGCGACCACGACCG CAAGAAGAACACCGAGGAGAAGATCTACCTGCCCCCATCCCGCCGACGAGTCCG GAACCCCGTGGTGTGCGGGCCCTGTCCAGGCCCGGAAGGTGATCAACGGCGTGGT GCGGCGGTACGGCTCCCGCGCCGATCCACATCGAGACCGCCCGGGAGGTGGGCAA GTCCTTCAAGGACCGGAAGGAGATCGAGAAGCGGCAGGAGGAGAACCGGAAGGAC CGGGAGAAGGCCCGCCCAAGTTCGCGGAGTACTTCCCAACTTCGTGGGCGAGCC AAGTCCAAGGACATCTGAAGCTGCGGCTGTACGAGCAGCAGCACGGCAAGTGCCT GTACTCCGGCAAGGAGATCAACCTGGGCGGCTGAACGAGAAGGGCTACGTGGAGA TCGACCACGCCCTGCCCTTCTCCCGGACCTGGGACGACTCCTTCAACAACAAGGTGC TGGTGTGGGCTCCGAGAACCAGAACAAGGGCAACCAGACCCCTACGAGTACTTC AACGGCAAGGACAACCTCCCGGAGTGGCAGGAGTTCAAGGCCCGGGTGGAGACCTC CCGTTCCCGGTCCAAGAAGCAGCGGATCCTGCTGCAGAAGTTCGACGAGGACG GCTTCAAGGAGCGGAACCTGAACGACACCCGGTACGTGAACCGGTTCTGTGCCAGT TCGTGGCCGACCGGATGCGGCTGACCGCAAGGGCAAGAAGCGGGTGTTCGCCTCC AACGCCAGATACCAACCTGCTGCGGGCTTCTGGGGCTGCGGAAGGTGCGGGC CGAGAACGACCGGCACCACGCCCTGGACGCCGTGGTGGTGGCCTGCTCCACCGTGG CCATGCAGCAGAAGATCACCCGGTTCGTGCGGTACAAGGAGATGAACGCCCTTCGACG GCAAGACCATCGACAAGGAGACCGGCGAGGTGCTGCACCAGAAGACCCACTTCCCC CAGCCCTGGGAGTTCCTTCGCCAGGAGGTGATGATCCGGGTGTTTCGGAAGCCCGAC GGCAAGCCCGAGTTCGAGGAGGCCGACACCCTGGAGAAGCTGCGGACCTGCTGGC CGAGAAGCTGTCTCCCGGCCGAGGCCGTGCACGAGTACGTGACCCCTGTTCTGT GTCCCGGGCCCAACCGGAAGATGTCCGGCCAGGGCCACATGGAGACCGTGAAGT CCGCCAAGCGGCTGGACGAGGGCGTGTCCGTGCTGCGGGTGCCTGACCCAGCTG AAGCTGAAGGACCTGGAGAAGATGGTGAACCGGGAGCGGGAGCCCAAGTGTACGA GGCCCTGAAGGCCCGGCTGGAGGCCACAAGGACGACCCCGCAAGGCCTTCGCCG AGCCCTTCTACAAGTACGACAAGGCCGGCAACCGGACCCAGCAGGTGAAGCCGTG CGGGTGGAGCAGGTGCAGAAGACCGGCGTGTGGGTGCGGAACCACAACGGCATCGC CGACAACGCCACCATGGTGCGGGTGGACGTGTTTCGAGAAGGGCGACAAGTACTACT GGTGCCATCTACTCTGGCAGGTGGCCAAGGGCATCCTGCCGACCGGGCCGTGGT GCAGGGCAAGGACGAGGAGGACTGGCAGCTGATCGACGACTCCTTCAACTTCAAGT TCTCCCTGCACCCCAACGACCTGGTGGAGGTGATACCAAGAAGGCCCGGATGTTTCG GTACTTTCGCTCCTGCCACCGGGGACCGGCAACATCAACATCCGGATCCACGACCT GGACCACAAGATCGGCAAGAACGGCATCCTGGAGGGCATCGGCGTGAAGACCGCC TGTCTTCCAGAAGTACCAGATCGACGAGCTGGGCAAGGAGATCCGGCCCTGCCGGC TGAAGAAGCGGCCCCCGTGCGGTCCGGCAAGCGGACCGCCGACGGCTCCGAGTTC</p>	<p>163</p>

[0766]

[0767]

	GAGTCCCCCAAGAAGAAGCGGAAGGTGGAG	
使用表4的低A/U密码子的Nme Cas9 ORF (无起始或终止密码子; 适于包括在融合蛋白质编码序列中)	GCCGCCTTCAAGCCCAACAGCATCAACTACATCCTGGGCTGGACATCGGCATCGCCA GCGTGGGCTGGGCCATGGTGGAGATCGACGAGGAGGAGAACCCATCCGGCTGATCG ACCTGGGCGTGCGGGTGTTTCGAGCGGGCCGAGGTGCCAAGACCGGCACAGCCTG GCCATGGCCCGCGGCTGGCCCGGAGCGTGCGGCGGCTGACCCGGCGGGGCCCA CCGGTGTGCGGACCCGGCGGCTGCTGAAGCGGAGGGCGTGTGACAGCCGCCA ACTTCGACGAGAACGGCTGATCAAGAGCCTGCCAACACCCCTGGCAGCTGCGG GCCCGCCCTGGACCGGAAGCTGACCCCTGGAGTGGAGCGCCGTGCTGCTGCA CCTGATCAAGCACCAGGGGCTACCTGAGCCAGCGGAAGAACGAGGGCGAGACCGCCG ACAAGGAGCTGGCGCCCTGCTGAAGGGCGTGGCCGCAACGCCACGCCCTGCAG ACCGGACACTTCGGACCCCGCCGAGCTGGCCCTGAACAAGTTCGAGAAGGAGAG CGGCCACATCCGGAACCAGCGGAGCGACTACAGCCACACCTTCAGCCGGAAGGACC TGCAGGCCGAGCTGATCCTGCTGTTTCGAGAAGCAGAAGGAGTTCGGCAACCCAC GTGAGCGGGCCCTGAAGGAGGGCATCGAGACCCTGCTGATGACCCAGCGGCCCGC CCTGAGCGGGACGCGCTGCAGAAGATGCTGGGCCACTGCACCTTCGAGCCCGCCG AGCCCAAGGCCGCAAGAACACCTACCCGCGGAGCGGTTTCATCTGGTACCAAGC TGAACAACCTGCGGATCCTGGAGCAGGGCAGCGAGCGGCCCTGACCGACACCGAG CGGGCCACCCTGATGGACGAGCCCTACCGGAAGAGCAAGCTGACCTACGCCAGGC CCGGAAGCTGCTGGGCTGGAGGACACCGCCTTCTTCAAGGGCTGCGGTACGGCAA GGACAACGCCGAGGCCAGCACCTGATGGAGATGAAGGCCTACCACGCATCAGCCG GGCCCTGGAGAAGGAGGGCCTGAAGGACAAGAAGAGCCCTGAACCTGAGCCCG AGCTGCAGGACGAGATCGGCACCGCCTTCAGCCTGTTCAAGACCGACGAGGACATCA CCGGCCGGCTGAAGGACCGGATCCAGCCGAGATCCTGGAGGCCCTGCTGAAGCACA TCAGCTTCGACAAGTTCGTGCAGATCAGCCTGAAGGCCCTGCGGCGGATGTGCCCC TGATGGAGCAGGGCAAGCGGTACGACGAGGCCTGCGCCGAGATCTAGCGCGCACT ACGGCAAGAAGAACACCGAGGAGAAGATCTACCTGCCCCCATCCCGCCGACGAG ATCCGGAACCCGTTGGTGTGCTGCGGGCCCTGAGCCAGGCCCGGAAGGTGATCAACGG CGTGGTGCGGCGGTACGGCAGCCCCGCCGATCCACATCGAGACCGCCCGGGAGGT GGGCAAGAGCTTCAAGGACCGGAAGGAGATCGAGAAGCGGCAGGAGGAGAACC AAGGACCGGGAGAAGGCCGCCCAAGTTCCGGGAGTACTTCCCAACTTCGTGGG CGAGCCCAAGAGCAAGGACATCCTGAAGCTGCGGTGTACGAGCAGCAGCAGCGCA AGTGCCTGTACAGCGGCAAGGAGATCAACCTGGGCCGGCTGAACGAGAAGGGCTAC GTGGAGATCGACCACGCCCTGCCCTTCAGCCGGACCTGGGACGACAGCTTCAACAAC AAGGTGCTGGTGTGGCCAGCGAGAACCAGAACAAGGGCAACCCAGACCTTACGGA GTACTTCAACGGCAAGGACAACAGCCGGGAGTGGCAGGAGTTCAAGGCCCGGGTGG AGACCAGCCGTTCCCGGAGCAAGAAGCAGCGGATCCTGCTGCAAGAAGTTCGAC GAGGACGGCTTCAAGGAGCGGAACCTGAACGACACCCGGTACGTGAACCGGTTCT GTGCCAGTTGCTGGCCGACCCGGATGCGGCTGACCGCAAGGGCAAGGAGCGGTTGT TCGCCAGCAACGGCCAGATCAACCAACCTGCTGCGGGGCTTCTGGGGCTGCGGAAG GTGCGGGCCGAGAACGACCGGCACCACGCCCTGGACGCCGTGGTGGTGGCCCTGCAG CACCGTGGCCATGCAGCAGAAGATCACCCGGTTCGTGCGGTACAAGGAGATGAACGC CTTCGACGGCAAGACCATGACAAGGAGACCGGCGAGGTGCTGCACGAGAAGACCA ACTTCCCGCAGCCCTGGGAGTTCTTCGCCAGGAGGTGATGATCCGGGTGTTCCGCA AGCCCGACGGCAAGCCGAGTTTCGAGGAGGCCGACACCCTGGAGAAGCTGCGGACC CTGCTGGCCGAGAAGCTGAGCAGCCGGCCGAGGCCGTGCACGAGTACGTGACCCC CCTGTTCTGTGAGCCGGGCCCCAACCGGAAGATGAGCGGCCAGGGCCACATGGAGA CCGTGAAGAGCGCCAAGCGGCTGGACGAGGGCGTGAGCGTGTGCGGTTGCCCTG ACCCAGCTGAAGCTGAAGGACCTGGAGAAGATGGTGAACCGGGAGCGGGAGCCCAA GCTGTACGAGGCCCTGAAGGCCCGGCTGGAGGCCACAAGGACGACCCCGCAAGG CCTTCGCCGAGCCCTTCTACAAGTACGACAAGGCCGGCAACCGGACCCAGCAGGTGA AGGCCGTGCGGGTGGAGCAGGTGCAGAAGACCGGCGTGTGGGTGCGGAAACACAAC GGCATCGCCGACAACGCCACCATGGTGCGGGTGACGTTTCGAGAAGGGCGACAA GTACTACCTGGTGCCATCTACAGCTGGCAGGTGGCCAAGGGCATCCTGCCGACCG GGCCGTGGTGCAGGGCAAGGACGAGGAGGACTGGCAGCTGATCGACGACAGCTTCA ACTTCAAGTTCAGCCTGCACCCCAACGACCTGGTGGAGGTGATCAACAAGAAGGCC GGATGTTCCGGTACTTCGCCAGCTGCCACCGGGGCACCGCAACATCAACATCCGGA TCCACGACCTGGACCACAAGATCGGCAAGAACGGCATCCTGGAGGGCATCGGCGTG AAGACCGCCCTGAGCTTCCAGAAGTACCAGATCGACGAGCTGGGCAGGAGATCCG GCCCTGCCGGCTGAAGAAGCGGCCCCCGTGCAGGAGCGGCAAGCGGACCGCCGACG GCAGCGATTCGAGAGCCCAAGAAGAAGCGGAAGGTGGAG	164
具有NLS1的Cas9的开放阅读框架(无起始或终止)	GACAAGAAGTACAGCATCGGACTGGACATCGGAACAAACAGCGTCGGATGGGCAGT CATCACAGACGAATAAAGGTCCCAGCAAGAAGTTCAAGGTCTGGGAAACACAG ACAGACACAGCATCAAGAAGAACCTGATCGGAGCACTGCTGTTCCAGACGGGAGAA ACAGCAGAAGCAACAAGACTGAAGAGAACGACGAAGAAGAAGATACACAAGAAGAA AGAACAAGATCTGTACTCTGCAGGAAATCTCAGCAACGAAATGGCAAAGGTTCGAG ACAGCTTCTCCACAGACTGGAAGAAAGTCTCTGGTCAAGAAGACAAAGGAC	165

密码子; 适于 包括在融合 蛋白质编码 序列中)	GAAAGACACCCGATCTTCGGAACATCGTCGACGAAGTCGCATACCACGAAAAGTAC CCGACAATCTACCACCTGAGAAAAGAAGCTGGTTCGACAGCACAGACAAGGCAGACCT GAGACTGATCTACCTGGCACTGGCACATGATCAAGTTCAGAGGACACTTCTGTATC GAAGGAGACCTGAACCCGGACAACAGCGACGTGACAAGCTGTTTCATCCAGCTGGT CCAGACATAACAACAGCTGTTTCGAAGAAAACCCGATCAACGCAAGCGGAGTGCAGC CAAAGGCAATCCTGAGCGCAAGACTGAGCAAGAGCAGAAGACTGGAAAACCTGATC GCACAGCTGCCGGGAGAAAAGAAGAACGGACTGTTTCGGAACCTGATCGCACTGAG CCTGGGACTGACACCGAACTTCAAGAGCAACTTCGACCTGGCAGAAGACGCAAAAGC TGCAGCTGAGCAAGGACACATACGACGACGACCTGGACAACCTGCTGGCACAGATC GGAGACCAGTACGCAGACCTGTTCTGGCAGCAAAGAACCTGAGCGACGCAATCTT GCTGAGCGACATCCTGAGAGTCAACACAGAAATCACAAAGGCACCGCTGAGCGCAA GCATGATCAAGAGATACGACGAACACCACCAGGACCTGACACTGCTGAAGGCACTGG TCAGACAGCAGCTGCCGGAAGTACAAGGAAATCTTCTTCGACCAGAGCAAGAAGC GGATACGCAGGATACATCGACGGAGGAGCAAGCCAGGAAGAATTCTACAAGTTCATC AAGCCGATCCTGGAAAAGATGGACGGAACAGAAGAACTGCTGGTCAAGTGAACAG AGAAGACCTGCTGAGAAAAGCAGAGAACATTCGACAACGGAAGCATCCCGCACCAGA TCCACCTGGGAGAACTGCACGCAATCCTGAGAAGACAGGAAGACTTCTACCCGTTCC TGAAGGACAACAGAGAAAAGATCGAAAAGATCCTGACATTCAGAATCCCGTACTACG TCGGACCGCTGGCAAGAGGAAACAGCAGATTCGCATGGATGACAAGAAAAGAGCGAA GAAACAATCACACCGTGGAACTTCGAAGAAGTCTGTCGACAAGGGAGCAAGCGACA GAGCTTCATCGAAAAGATGACAACTTCGACAAGAACCTGCCGAACGAAAAGGTCC TGCCGAAGCACAGCCTGCTGTACGAATACTTCACAGTCTACAACGAACTGACAAAAG TCAAGTACGTCACAGAAGGAATGAGAAAGCCGGCATTCTGAGCGGAGAACAGAAG AAGCAATCGTCGACCTGCTGTTCAAGACAAAACAGAAAAGTTCACAGTCAAGCAGT GAAGGAAGACTACTTCAAGAAAGATCGAATGCTTCGACAGCGTCGAAATCAGCGGAGT CGAAGACAGATTCAACGCAAGCCTGGGAACATACCACGACCTGCTGAAGATCATCAA GGACAAGGACTTCTGGACAACGAAGAAAACGAAGACATCCTGGAAGACATCGTCC TGACACTGACACTGTTTCGAAGACAGAGAAAATGATCGAAGAAAAGACTGAAGACATAC GCACACCTGTTTCGACGACAAGGTCATGAAGCAGCTGAAGAGAAGAAGATACACAGG ATGGGGAAGACTGAGCAGAAAAGCTGATCAACGGAATCAGAGACAAGCAGAGCGGAA AGACAATCCTGGACTTCTGAAGAGCGACGGATTTCGAAAACGAAAACCTTCATGCAGC TGATCCACGACGACAGCCTGACATTCAAGGAAGACATCCAGAAGGCACAGGTCAGC GGACAGGGAGACAGCCTGCACGAACACATCGCAAACCTGGCAGGAAGCCCGGCAAT CAAGAAGGGAATCTGCAGACAGTCAAGGTCGTCGACGAACTGGTCAAGGTCATGG GAAGACACAAGCCGAAAACATCGTCATCGAAATGGCAAGAGAAAACCAGACAACA CAGAAGGGACAGAAGAACAGCAGAGAAAAGAATGAAGAGAATCGAAGAAGGAATCA AGGAACTGGGAAGCCAGATCCTGAAGGAACACCCGGTCGAAAACACACAGCAGTGCAG AACGAAAAGCTGTACTTACTACTGTCAGAACCGGAAGAGACATGTACTGTCGACCCAG GAACTGGACATCAACAGACTGAGCGACTACGACGTCGACCACATCGTCCCGCAGAGC TTCCTGAAGGACGACAGCATCGACAACAAGGTCCTGACAAGAAGCGACAAGAACAG AGGAAAAGGCGACAACGTCCTCCGAGCGAAGAAAGTCTGTAAGAAGATGAAGAATCACT GGAGACAGTGTGAACGCAAAAGCTGATCACACAGAGAAAAGTTCGACAACCTGACA AAGGCAGAGAGAGGAGGACTGAGCGAACTGGACAAGGCAGGATTCATCAAGAGAC AGCTGGTCGAAAACAAGACAGATCACAAGACAGTTCGACAGATCCTGGACAGCAGA ATGAACACAAAGTACGACGAAAACGACAAGCTGATCAGAGAAAGTCAAGGTCATCAC ACTGAAGAGCAAGCTGGTCAGCGACTTCAGAAAAGGACTTCCAGTTCTACAAGGTC GAGAAAATCAACAACCTACCACCGCACACGACGACATACCTGAACGCAAGCTCGTGGAA CAGCACTGATCAAGAAGTACCCGAAGCTGGAAAAGCAATTCGTCACGGAGACTACA AGGTCTACGACGTACAGAAAAGATGATCGAAAAGAGCGAACAGGAAATCGGAAAAGCA ACAGCAAAGTACTTCTTCTACAGCAACATCATGAACTTCTTCAAGACAGAAATCACAC TGGCAAACGGAGAAAATCAGAAAAGAGACCGCTGATCGAAAACAAACGGAGAAAACAGG AGAAAATCGTCTGGGACAAGGGAAGAGACTTCGCAACAGTCAGAAAAGGTCCTGAGCA TGCCCGAGGTCACATCGTCAAGAAGACAGAAGTCCAGACAGGAGGATTCAGCAAG GAAAGCATCCTGCCGAAGAGAAAACAGCGACAAGCTGATCGCAAGAAAAGAAAGGACTG GGACCCGAAGAAGTACGGAGGATTCGACAGCCCGACAGTCGCATACAGCGTCTGGT CGTCGAAAAGGTCGAAAAGGGAAAAGAGCAAGAAGCTGAAGAGCGTCAAGGAACTG CTGGGAATCACAATCATGGAAAGAAGCAGCTTCGAAAAGAACCAGATCGACTTCTG GAAGCAAAGGGATACAAAGGAAGTCAAGAAGGACCTGATCATCAAGCTGCCGAAGTA CAGCCTGTTGAACTGGAAAACGGAAGAAAGAGAATGCTGGCAAGCGCAGGAGAAAC TGCAGAAGGGAACGAACTGGCACTGCCGAGCAAGTACGTCAACTTCTGTACTGCTGG CAAGCCACTACGAAAAGCTGAAGGGAAGCCCGGAAGACAACGAACAGAAGCAGCT GTTCTGTCGAACAGCACAAGCACTACCTGGACGAAATCATCGAACAGATCAGCGAAT CAGCAAGAGAGTATCCTGGCAGACGCAAACCTGGACAAGGTCCTGAGCGCATAACA ACAAGCACAGAGACAAGCCGATCAGAGAACAGGCAGAAAACATCATCCACCTGTTTC CACTGACAAAACCTGGGAGCACCGGACGATTCAAGTACTTCGACACAACAACCTGAC AGAAAAGATACACAAGCACAAGGAAGTCTGGACGCAACACTGATCCACCAGAG CATCACAGGACTGTACGAAAACAAGAATCGACCTGAGCCAGCTGGGAGGAGACGGAG
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[0768]

<p>具有NLS2的 Cas9的开放 阅读框架(无 起始或终止 密码子;适于 包括在融合 蛋白质编码 序列中)</p>	<p>GAGGAAGCCTGGCAGCAAAGAGAAGCAGAACAACA GACAAGAAGTACAGCATCGGACTGGACATCGGAACAAACAGCGTCGGATGGGCACT CATCACAGACGAATACAAGGTCCCAGCAAGAAGTTCAAGGTCTGGGAAACACAG ACAGACACAGCATCAAGAAGAACCTGATCGGAGCACTGCTGTTCCAGACGGAGAA ACAGCAGAAGCAACAAGACTGAAGAGAACAGCAAGAAGAAGATACACAAGAAGAA AGAACAAGTCTGCTACTCTGCAGGAAATCTTCAGCAACGAAATGGCAAAGGTTCGACG ACAGCTTCTTCCACAGACTGGAAGAAAAGCTTCTGGTCCGAAAGAAGACAAGAAGCAC GAAAGACACCCGATCTTCGGAACATCGTCGACGAAGTGCATACCACGAAAAGTAC CCGACAATCTACCACCTGAGAAAGAAGCTGGTCCGACAGCACAGACAAGGCAGACCT GAGACTGATCTACTGGCACTGGCACACATGATCAAGTTTCAGAGGACACTTCTGATC GAAGGAGACCTGAACCCGGACAACAGCGACGTCCGACAAGCTGTTTCATCCAGCTGGT CCAGACATAACAACAGCTGTTTCGAAGAAAACCCGATCAACGCAAGCGGAGTCCGACG CAAAGGCAATCCTGAGCGCAAGACTGAGCAAGAGCAGAAGACTGGAAAACCTGATC GCACAGCTGCCGGGAGAAAAGAAGAACGGACTGTTTCGAAAACCTGATCGCACTGAG CCTGGGACTGACACCGAATTCAAGAGCAACTTCGACCTGGCAGAAGACGCAAAAGC TGACGCTGAGCAAGGACACATACGACGACGACCTGGACAACCTGGTCCGACAGT GGAGACCAGTACGCAGACCTGTTCTGGCAGCAAAGAAGCTGAGCGACGCAATCCT GCTGAGCGACATCTGAGAGTCAACACAGAAATCACAAGGCACCCGCTGAGCGCAA GCATGATCAAGAGATACGACGAACACCACCAGGACCTGACACTGCTGAAGGCACTGG TCAGACAGCAGTCCCGGAAAAGTACAAGGAAATCTTCTTCGACCCAGCAAGAAGCA GGATACGCAGGATACATCGACGGAGGACAAAGCCAGGAAGAATTCTACAAGTTTCATC AAGCCGATCCTGGAAAAGATGGACGGAACAGAAGAAGCTGCTGGTCAAGCTGAACAG AGAAGACCTGCTGAGAAAAGCAGAGAACATTCGACAACGGAAAGCATCCCGCACAGGA TCCACCTGGGAGAACTGCACGCAATCCTGAGAAGACAGGAAGACTTCTACCCGTTCC TGAAGGACAACAGAGAAAAGATCGAAAAGATCCTGACATTCAGAATCCCGTACTACG TCGGACCCGCTGGCAAGAGGAAAACAGCAGATTTCGCATGGATGACAAGAAAAGAGCGAA GAAACAATCACACCGTGGAACTTCGAAGAAGTCTGTCGACAAGGGGAGCAAGCGCACA GAGCTTATCGAAAAGATGACAACTTCGACAAGAAGCTGCCGAACGAAAAGGTCC TGCCGAAGCACAGCCTGCTGTACGAATACTTCACAGTCTACAACGAAGTACAAAGG TCAAGTACGTCACAGAAGGAATGAGAAAAGCCGGCATTCTGAGCGGAGAACAGAAG AAGGCAATCGTCGACCTGCTGTTCAAGACAAACAGAAAAGGTCACAGTCAAGCAGCT GAAGGAAGACTACTTCAAGAAAGATCGAATGCTTCGACAGCGTCGAAATCAGCGGAGT CGAAGACAGATTCAACGCAAGCTGGGAACATACCACGACCTGCTGAAGATCATCAA GGACAAGGACTTCTGGACAACGAAGAAAACGAAGACATCCTGGAAAGACATCGCTCC TGACACTGACACTGTTTCGAAGACAGAGAAATGATCGAAGAAAAGACTGAAGACATAC GCACACCTGTTTCGACGACAAGGTCATGAAGCAGCTGAAGAGAAGAAGATACACAGG ATGGGGAAAGACTGAGCAGAAAAGCTGATCAACGGAATCAGAGACAAGCAGAGCGGAA ACAATCCTGGACTTCTGTAAGAGCGACGGATTTCGAAAACAGAAAAGTTCATGACG TGATCCACGACGACAGCCTGACATTCAAGGAAGACATCCAGAAGGCACAGGTCAGC GGACAGGGGAGACAGCCTGCACGAACACATCGCAAACCTGGCAGGAAGCCCGGCAAT CAAGAAGGGAATCCTGCAGACAGTCAAGGTCGTCGACGAACTGGTCAAGGTCATGG GAAGACACAAGCCGAAAACATCGTCATCGAAATGGCAAGAGAAAACAGACAACA CAGAAGGGACAGAAGAAGACAGCAGAGAAAAGAAATGAAGAGAATCGAAGAAAGGAATCA AGGAACTGGGAAGCCAGATCCTGAAGGAACACCCGGTCGAAAACACACAGCTGCAG AACGAAAAGCTGTACTCTGACTACTGTCGAGAAGGAAAGACATGTACGTCGACCAG GAACTGGACATCAACAGACTGAGCGACTACGACGTCGACCACATCGTCCCGCAGAGC TTCCTGAAGGACGACAGCATCGACAACAAAGGTCCTGACAAGAAGCGACAAAGACAG AGGAAAAGAGCGACAACGTCCTCCGAGCGAAGAAAGTCTGTAAGAAGATGAAGAAGTACT GGAGACAGCTGCTGAACGCAAGCTGATCACACAGAGAAAGTTCGACAACCTGACA AAGGCAGAGAGAGGAGGACTGAGCGAACTGGACAAGGCAGGATTCATCAAGAGAC AGCTGGTCCGAAACAAGACAGATCACAAGACAGTCCGACAGATCCTGGACAGCAGA ATGAACACAAGTACGACGAAAACGACAAGCTGATCAGAGAAGTCAAGGTCATCAC ACTGAAGAGCAAGCTGGTCAGCGACTTCAGAAAAGGACTTCCAGTTCTACAAGGTC GAGAAATCAACAATACCACCACGCACACGACGCATACCTGAACGCAAGTCTCGGAA CAGCACTGATCAAGAAGTACCCGAAGCTGGAAAAGCGAATTCGTTCTACGGAGACTACA AGGTCTACGACGTCAGAAAAGATGATCGAAAAGAGCGAACAGGAAATCGGAAAGGCA ACAGCAAAAGTACTTCTTCTACAGCAACATCATGAACTTCTTCAAGACAGAAATCACAC TGGCAAACCGGAGAAATCAGAAAAGAGACCCGCTGATCGAAAACAACCGGAGAAAACAGG AGAAAATCGTCTGGGACAAGGGAAGAGACTTCGCAACAGTCAAGAAAGGTCCTGAGCA TGCCGACAGTCAACATCGTCAAGAAGACAGAAGTCCAGACAGGAGGATTCAGCAAG GAAAAGCATCCTGCCGAAGAGAAAACAGCGACAAGCTGATCGCAAGAAGAAGGACTG GGACCCGAAGAAGTACGGAGGATTCGACAGCCCGACAGTCCGATACAGCGTCTCTGGT CGTCGCAAAAGGTCGAAAAGGGAAGAGCAAGAAGCTGAAGAGCGTCAAGGAACTG CTGGGAATACAATCATGGAAAAGAGCAGCTTCGAAAAGAACCCTGATCGACTTCTCTG GAAGCAAAAGGATACAAGGAAGTCAAGAAGGACCTGATCATCAAGCTGACCGGAAAGTA CAGCCTGTTTCGAACTGGAAAACGGAAGAAAAGAGAATGCTGGCAAGCGCAGGAGAAC TGCAGAAGGGAAACGAAGTGGCACTGCCGAGCAAGTACGTCAACTTCTGTACTCTGG</p>	<p>166</p>
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[0769]

	<p>CAAGCCACTACGAAAAGCTGAAGGGAAGCCCGGAAGACAACGAACAGAAGCAGCT GTTTCGTCGAACAGCACAAAGCACTACCTGGACGAAAATCATCGAACAGATCAGCGAATT CAGCAAGAGAGTTCATCTGGCAGACGCAAACCTGGACAAGGTCCTGAGCGCATAACA ACAAGCACAGAGACAAGCCGATCAGAGAACAGGCAGAAAACATCATCCACCTGTTTC ACACTGACAAACCTGGGAGCACCAGCAGCATTCAAGTACTTCGACACAACAATCGAC AGAAAAGAGATACACAAGCACAAAAGGAAGTCTGGACGC AACACTGATCCACAGAG CATCACAGGACTGTACGAAAACAAGAATCGACCTGAGCCAGCTGGGAGGAGACGGAG GAGGAAGCCAGGCAGCAAAGAGAAGCAGAAACAACA</p>	
<p>具有NLS3的 Cas9 的开放 阅读框架(无 起始或终止 密码子; 适于 包括在融合 蛋白质编码 序列中)</p>	<p>GACAAGAAGTACAGCATCGGACTGGACATCGGAACAAACAGCGTCGGATGGGCACT CATCACAGACGAATACAAGGTCCCAGCAAGAAGTTCAAGGTCTGGGAAAACACAG ACAGACACAGCATCAAGAAGAACCTGATCGGAGCACTGCTGTTTCGACAGCGGAGAA ACAGCAGAAGCAACAAGACTGAAGAGAACAGCAAGAAGAAGATACACAAGAAGAA AGAACAGAATCTGTACTCTGCAGGAAATCTTCAGCAACGAAATGGCAAAGGTCGACG ACAGCTTCTTCCACAGACTGGAAGAAAGCTTCTGGTCAAGAAGACAAGAAGCAC GAAAGACACCCGATCTTCGGAACATCGTCGACGAAGTCGCATACCACGAAAAGTAC CCGACAATCTACCACCTGAGAAAGAAGCTGGTTCGACAGCACAGACAAGGCAGCCT GAGACTGATCTACCTGGCACTGGCACACATGATCAAGTTCAGAGGACACTTCTGATC GAAGGAGACCTGAACCCGGACAACAGCGACGTCGACAAGCTGTTTCATCCAGCTGGT CCAGACATAACAACAGCTGTTTCGAAGAAAACCCGATCAACGCAAGCGGAGTTCGACG CAAAGGCAATCCTGAGCGCAAGACTGAGCAAGAGCAGAAGACTGGAAAACCTGATC GCACAGCTGCCGGGAGAAAAGAAGAACGGACTGTTTCGGAACCTGATCGCACTGAG CCTGGGACTGACACCGAATTCAGAGCAACTTCGACCTGGCAGAAGACGCAAAAGC TGCAGCTGAGCAAGGACATACGACGACGACCTGGACAACCTGCTGGCACAGATC GGAGACCAGTACGCAGACTGTTCTGGCAGCAAAGAACCTGAGCGACGCAATCCT GCTGAGCGACATCCTGAGAGTCAACACAGAAATCACAAGGCACCGCTGAGCGCAA GCATGATCAAGAGATACGACGAACACCACCAGGACCTGACACTGCTGAAGGCACTGG TCAGACAGCAGCTGCCGAAAAGTACAAGGAAATCTTCTTCGACCAGAGCAAGAAGC GGATACGCAGGATACATCGACGGAGGAGCAAGCCAGGAAGAATTCACAAGTTCATC AAGCCGATCCTGGAAAAGATGGACGGAAACAGAAGAACTGCTGGTCAAGCTGAACAG AGAAGACCTGCTGAGAAAAGCAGAGAACATTCGACAACGGAAGCATCCCGCACCAGA TCCACCTGGGAGAACTGCACGCAATCCTGAGAAGACAGGAAGACTTCTACCCGTTCC TGAAGGACAACAGAGAAAAGATCGAAAAGATCCTGACATTGAGAATCCCGTACTACG TCGGACCGCTGGCAAGAGAAAACAGCAGATTGCGATGGATGACAAGAAAAGAGCGAA GAAAACAATCACACCGTGGAACTTCGAAGAAGTCTGTCGACAAGGGAGAACGCGACA GAGCTTCATCGAAAAGATGACAAACTTCGACAAGAACCTGCCGAACGAAAAGGTCC TGCCGAAGCACAGCCTGCTGTACGAATACTTCACAGTCTACAACGAACTGACAAAAG TCAAGTACGTCACAGAAGGAATGAGAAAGCCGGCATTCTGAGCGGAGAACAGAAG AAGGCAATCGTCGACCTGCTGTTCAAGACAAAACAGAAAAGGTCACAGTCAAGCAGT GAAGGAAGACTACTTCAAGAAGATCGAATGCTTCGACAGCGTCGAAATCAGCGGAGT CGAAGACAGATTCAACGCAAGCCTGGGAACATACCACGACCTGCTGAAGATCATCAA GGACAAGGACTTCTGGACAACGAAGAAAACGAAGACATCCTGGAAGACATCGTCC TGCACTGACACTGTTTCGAAGACAGAGAAATGATCGAAGAAAAGACTGAAGACATAC GCACACCTGTTTCGACGACAAAGGTCATGAAGCAAGTGAAGAGAAGAAGATACAGG ATGGGGAAGACTGAGCAGAAAAGCTGATCAACGGAATCAGAGACAAGCAGAGCGGAA AGACAATCCTGGACTTCTGAAAGAGCGACGGATTTCGAAAACGAAAACCTCATGACG TGATCCACGACGACAGCCTGACATTCAAGGAAGACATCCAGAAGGCACAGGTCAGC GGACAGGGAGACAGCCTGCACGAACACATCGAAAACCTGGCAGGAACCCCGCAAT CAAGAAGGGAATCTGACAGAGTCAAGGTCGTCGACGAACTGGTCAAGGTCATGG GAAGACACAAGCCGAAAACATCGTCATCGAAATGGCAAGAGAAAACCAGACAACA CAGAAGGGACAGAAGAACAGCAGAGAAAAGAATGAAGAGAATCGAAGAAGGAATCA AGGAACTGGGAAGCCAGATCCTGAAGGAACACCCGGTCGAAAACACACAGCTGCAG AACGAAAAGCTGTACTTACTCCTGCAGAACGGAAGAGACATGATACGTCGACCAG GAACTGGACATCAACAGACTGAGCGACTACGACGTCGACCACATCGTCCCGCAGAGC TTCCTGAAGGACGACAGCATCGACAACAAGGTCCTGACAAGAAGCGACAAGAACAG AGGAAAAGAGCGACAACGTCGAGCGAAGAAAGTCTGTAAGAAGATGAAGAAGTACT GGAGACAGCTGCTGAACGCAAGCTGATCACACAGAGAAAAGTTCGACAACCTGACA AAGGCAGAGAGAGGAGGACTGAGCGAACTGGACAAGGCAGGATTCATCAAGAGAC AGCTGGTCGAAAACAAGACAGATCACAAGACAGTGCACAGATCCTGGACAGCAGA ATGAACACAAAGTACGACGAAAACGACAAGCTGATCAGAGAAAGTCAAGGTCATCAC ACTGAAGAGCAAGCTGGTCAGCGACTTCAGAAAAGGACTTCCAGTTTACAAGGTC GAGAAATCAACAACCTACCACCGCACACGACGCATACCTGAACGCAAGTCTGTCGGAA CAGCACTGATCAAGAAGTACCCGAAGCTGGAAAAGCAATTCGTCATCGGAGACTACA AGGTCTACGACGTCAGAAAAGATGATCGAAAAGAGCGAACAGGAAATCGGAAAAGGCA ACAGCAAAGTACTTCTTACAGCAACATCATGAACTTCTTCAAGACAGAAAATCACAC TGGCAAACGGAGAAATCAGAAAAGAGACCGCTGATCGAAAACAACGGAGAAAACAGG AGAAATCGTCTGGGACAAGGGAAGAGACTTCGCAACAGTCAGAAAAGGTCCTGAGCA TGCCCGAGGTCAACATCGTCAAGAAGACAGAAGTCCAGACAGGAGGATTCAGCAAG</p>	<p>167</p>

[0770]

	<p>GAAAGCATCCTGCCGAAGAGAAAACAGCGACAAGCTGATCGCAAGAAAAGAAGGACTG GGACCCGAAGAAGTACGGAGGATTTCAGACAGCCGACAGTTCGCATACAGCGTCTGGT CGTCGCAAAGGTCGAAAAGGGAAAAGCAAGAAGCTGAAGAGCGTCAAGGAACTG CTGGGAATCACAATCATGGAAAAGCAGCTTCGAAAAGAACCCTGATCGACTTCCTG GAAGCAAAGGGATACAAGGAAGTCAAGAAGGACCTGATCATCAAGCTGCCGAAGTA CAGCCTGTTTCTGAACTGGAAAACGGAAAAGAAAAGAGAATGCTGGCAAGCGCAGGAGAAC TGCAGAAGGGAAACGAACTGGCACTGCCGAGCAAGTACGTCAACTTCTGTACTCTGG CAAGCCACTACGAAAAGCTGAAGGGAAAGCCCGGAAGACAACGAACAGAAGCAGCT GTTTCGTGAAACAGCACAAGCACTACCTGGACGAAATCATCGAACAGATCAGCGAATT CAGCAAGAGAGTTCCTGGCAGACGCAAACTGGACAAGGTCTGAGCGCATACA ACAAGCACAGAGACAAGCCGATCAGAGAACAGGCAGAAAACATCATCCACCTGTTT ACACTGACAAACCTGGGAGCACCGGCAGCATTCAAGTACTTCGACACAACAATCGAC AGAAAAGATACACAAGCACAAAAGGAAGTCTGGACGCAACTGATCCACCAGAG CATCACAGGACTGTACGAAAACAAGAATCGACCTGAGCCAGCTGGGAGGAGACGGAG GAGGAAGCCCGGCACCGGCAAGAGAGAGAAAAGAACAACA</p>	
<p>具有NLS4的 Cas9 的开放 阅读框架(无 起始或终止 密码子; 适于 包括在融合 蛋白质编码 序列中)</p>	<p>GACAAGAAGTACAGCATCGGACTGGACATCGGAACAAAACAGCTCGGATGGGCACT CATCACAGACGAATACAAGGTCCCGAGCAAGAAGTTCAAGGTCTGGGAAAACACAG ACAGACACAGCATCAAGAAGAACCTGATCGGAGCACTGCTGTTTCGACAGCGGAGAA ACAGCAGAAGCAACAAGACTGAAGAGAACAGCAAGAAGAAGATACACAAGAAGAA AGAACAGAATCTGCTACTGCAGGAAATCTTCAGCAACGAAATGGCAAAGGTCGACG ACAGCTTCTTCCACAGACTGGAAGAAAGCTTCTGGTCAAGAAGACAAGAAGCAC GAAAGACACCCGATCTTCGGAACATCGTCGACGAAGTTCGATACCACGAAAAGTAC CCGACAATCTACCACCTGAGAAAAGAAGCTGGTTCGACAGCACAGACAAGGCAGACCT GAGACTGATCTACCTGGCACTGGCACACATGATCAAGTTCAGAGGACATCTCTCTG GAAGGAGACCTGAACCCGGACAACAGCGACGTCGACAAGCTGTTTCATCCAGCTGGT CCAGACATACAACCAGCTGTTTCGAAGAAAACCCGATCAACGCAAGCGGAGTTCGACG CAAAGGCAATCTGAGCGCAAGACTGAGCAAGAGCAGAAGACTGGAAAACCTGATC GCACAGCTGCCGGGAGAAAAGAAGAACGGACTGTTTCGAAAACCTGATCGCACTGAG CCTGGGACTGACACCGAATTCAGAGCAACTTCGACCTGGCAGAAGACGCAAAAGC TGCAGCTGAGCAAGGACACATACGACGACGACCTGGACAACCTGCTGGCACAGATC GGAGACCAGTACGCAGACCTGTTCTGGCAGCAAAGAAGCTGAGCGACGCAATCCT GCTGAGCGACATCCTGAGAGTCAACACAGAAATCACAAGGCACCCGCTGAGCGCAA GCTGATCAAGAGATACAGCAACACCACCAGGACCTGACACTGCTGAAGGCACTGG TCAGACAGCAGCTGCCGGAAAAGTACAAGGAAATCTTCTTCGACCAGCAAGAAGC GGATACGCAGGATACATCGACGGAGGACAAGCCAGGAAGAATTCTACAAGTTCATC AAGCCGATCTGGAAAAGATGGACGGAACAGAAGAAGTCTGCTGGTCAAGCTGAACAG AGAAGACCTGCTGAGAAAAGCAGAGAATTCGACAACGGAAAGCATCCCGCACAGGA TCCACCTGGGAGAACTGCACGCAATCCTGAGAAGACAGGAAGACTTCTACCCGTTCC TGAAGGACAACAGAGAAAAGATCGAAAAGATCCTGACATTCAGAATCCCGTACTACG TCGGACCCGCTGGCAAGAGGAAAACAGCAGATTTCGATGGATGACAAGAAAAGAGCGAA GAAACAATCACACCGTGGAACTTCGAAGAAGTCTGTCGACAAGGGAGCAAGCGCACAA GAGCTTTCATCGAAAAGATGACAACTTCGACAAGAAGCTGCCGAACGAAAAGGTCC TGCCGAAAGCACAGCCTGCTGTACGAATACTTCACAGTCTACAACGAAGTACAAAAG TCAAGTACGTCACAGAAGGAATGAGAAAGCCGGCATTCTGAGCGGAGAACAGAAG AAGGCAATCGTGCAGCTGCTGTTCAAGACAACAGAAAAGGTCACAGTCAAGCAGCT GAAGGAAGACTACTTCAAGAAGATCGAATGCTTCGACAGCGTCAAGTCAAGCGGAGT CGAAGACAGATTCAACGCAAGCCTGGGAACATACCAGACCTGCTGAAAGATCATCAA GGACAAGGACTTCTGGACAACGAAGAAAACGAAGACATCCTGGAAGACATCGTCC TGACACTGACTGTTTCGAAGACAGAGAAATGATCGAAGAAAAGACTGAAGACATAC GCACACCTGTTTCGACGACAAGGTCATGAAGCAGCTGAAGAGAAGAAGATACACAGG ATGGGGAAGACTGAGCAGAAAAGCTGATCAACGGAATCAGAGACAAGCAGAGCGGAA AGACAATCTGGACTTCTGAAAGAGCGACGGATTTCGCAAACAGAACTTCATGCAGC TGATCCACGACGACAGCCTGACATTCAAGGAAGACATCCAGAAGGCACAGGTCAGC GGACAGGGAGACAGCCTGCACGAACACATCGCAAACCTGGCAGGAAGCCCGGCAAT CAAGAAGGGAACTCTGCAGACAGTCAAGGTCTGTCGACGAACTGGTCAAGGTCATGG GAAGACACAAGCCGAAAACATCGTTCATCGAAATGGCAAAGAGAAAACAGACAACA CAGAAGGGACAGAAGAACAGCAGAGAAAAGAATGAAGAGAATCGAAGAAGGAATCA AGGAACTGGGAAGCCAGATCCTGAAGGAACACCCGGTTCGAAAACACACAGCTGCAG AACGAAAAGCTGTACTCTGACTACTGACAGAACGGAAGAGACATGTACGTCGACCAG GAACTGGACATCAACAGACTGAGCGACTACGACGTCGACCACATCGTCCCGCAGAGC TTCCTGAAGGACGACAGCATCGACAACAAGGTCTGACAAGAAGCGACAAGAACAG AGGAAAAGAGCGACAACGTCCCGAGCGAAGAAGTCTGTAAGAAGATGAAGAAGTACT GGAGACAGCTGCTGAACGAAAAGCTGATCACACAGAGAAAAGTTCGACAACCTGACA AAGGCAGAGAGAGGAGGACTGAGCGAACTGGACAAGGCAGGATTCATCAAGAGAC AGCTGGTCAAACAAGACAGATCACAAGCACAGTTCGACAGATCCTGGACAGCAGA ATGAACACAAAGTACGACGAAAACGACAAGCTGATCAGAGAAGTCAAGGTCATCAC ACTGAAGAGCAAGCTGGTACGCGACTTCAGAAAAGGACTTCCAGTTCACAAGGTC</p>	<p>168</p>

[0771]

[0772]

	<p>GAGAAATCAACAACACTACCACCACGCACACGACGCATACCTGAACGCAGTCGTCGGAA CAGCACTGATCAAGAAGTACCCGAAGCTGGAAAAGCGAATTTCGTCTACGGAGACTACA AGGTCTACGACGTCAGAAAAGATGATCGCAAAGAGCGAACAGGAAATCGGAAAAGCA ACAGCAAAGTACTTCTTCTACAGCAACATCATGAACTTCTTCAAGACAGAAAATCACAC TGGCAAACGGAGAAATCAGAAAAGAGACCGCTGATCGAAAACAAACGGAGAAAACAGG AGAAATCGTCTGGGACAAGGGAAGAGACTTCGCAACAGTCAGAAAAGGTCCTGAGCA TGCCCGAGGTCAACATCGTCAAGAAGACAGAAGTCCAGACAGGAGGATTTCAGCAAG GAAAGCATCTGCCGAAGAGAAAACAGCGACAAGCTGATCGCAAGAAAAGAAGGACTG GGACCCGAAGAAGTACGGAGGATTTCGACAGCCCGACAGTCGCATACAGCGTCTGGT CGTCGCAAAGGTCGAAAAGGGAAAAGCAAGAAGCTGAAGAGCGTCAAGGAACTG CAAGCCACTACGAAAAGCTGAAGGGAAGCCCGAAGACAACGAACAGAAAGCAGCT CTGGGAATCACAAATCATGGAAAAGCAGCTTCGAAAAGAACCCTGATCGACTTCTG GAAGCAAAGGGATACAAGGAAGTCAAGAAGGACCTGATCATCAAGCTGCCGAAGTA CAGCCTGTTGAACTGGAAAACGGAAGAAAAGAGAATGCTGGCAAGCGCAGGAGAAC TGCAGAAGGGAAACGAACTGGCACTGCCGAGCAAGTACGTCAACTTCTGTACCTGG CAAGCACTACGAAAAGCTGAAGGGAAGCCCGAAGACAACGAACAGAAAGCAGCT GTTCTGTCGAACAGCACAAGCACTACCTGGACGAAATCATCGAACAGATCAGCGAATT CAGCAAGAGAGTCACTCTGGCAGACGCAAACCTGGACAAGGTCCTGAGCGCATACA ACAAGCACAGAGACAAGCCGATCAGAGAACAGGCAGAAAACATCATCCACCTGTTT ACACTGACAAACCTGGGAGCACCGGACGATTCAAGTACTTCGACACAACAATCGAC AGAAAAGAGATACACAAGCAAAAAGGAAGTCTGGACGCAACACTGATCCACCAAGAG CATCACAGGACTGTACGAAACAAGAATCGACCTGAGCCAGCTGGGAGGAGACGGAG GAGGAAGCCAGGCAGCAAAGAGACCGAGAACAACA</p>	
<p>具有NLS5的 Cas9的开放 阅读框架(无 起始或终止 密码子;适于 包括在融合 蛋白质编码 序列中)</p>	<p>GACAAGAAGTACAGCATCGGACTGGACATCGGAACAAAACAGCGTCGGATGGGCAGT CATCACAGCAGCAATACAAGTCCCGAGCAAGAAGTTCAAGGTCCTGGGAAAACACAG ACAGACACAGCATCAAGAAGAACTGATCGGAGCACTGCTGTTTCGACAGCGGAGAA ACAGCAGAAGCAACAAGACTGAAGAGAACAGCAAGAAGAAGATACACAAGAAGAA AGAACAGAATCTGCTACCTGCAGGAAATCTTCAGCAACGAAATGGCAAAGGTCGACG ACAGCTTCTTCCACAGACTGGAAGAAAGCTTCTGGTTCGAAGAAGACAAGAAGCAC GAAAGACACCCGATCTTCGAAAACATCGTCGACGAAGTCGCATACCACGAAAAGTAC CCGACAATCTACCACCTGAGAAAAGAAGCTGGTTCGACAGCACAGACAAGGCAGACCT GAGACTGATCTACCTGGCACTGGCACACATGATCAAGTTCAGAGGACACTTCTGATC GAAGGAGACCTGAACCCGGACAACAGCGACGTCGACAAGCTGTTTCATCCAGCTGGT CCAGACATACAACAGCTGTTTCGAAGAAAACCCGATCAACGCAAGCCGAGTCGACG CAAAGGCAATCCTGGAAAAGCTGAGCAAGAGCAGAAAGACTGGAAAACCTGATC GCACAGCTGCCGGGAGAAAAGAAGAACGGACTGTTTCGAAAACCTGATCGCACTGAG CCTGGGACTGACACCGAATTCAAGAGCAACTTCGACCTGGCAGAAGACGCAAAAGC TGCAGCTGAGCAAGGACACATACGACGACGACCTGGACAACCTGCTGGCAGATC GGAGACCAGTACGCGACCTGTTCTGGCAGCAAAGAACTGAGCGACGCAATCCT GCTGAGCGACATCTGAGAGTCAACACAGAAATCACAAGGCACCGCTGAGCGCAA GCATGATCAAGAGATACGACGAACACCACAGGACCTGACACTGCTGAAGGCACTGG TCAGACAGCAGCTGCCGAAAAGTACAAGGAAATCTTCTTCGACCAGAGCAAGAAGC GGATACGCAGGATACATCGACGGAGGAGCAAGCCAGGAAGAATTCACAAGTTCATC AAGCCGATCCTGGAAAAGATGGACGGAACAGAAGAAGTCTGTTGATGACAAGAAGCGAA AGAAGACCTGCTGAGAAAGCAGAGAACATTCGACAACGGAAAGCATCCCGCACCAGA TCCACCTGGGAGAACTGCACGCAATCCTGAGAAGACAGGAAGACTTCTACCCGTTCC TGAAGGACAACAGAGAAAAGATCGAAAAGATCTGACATTCAGAATCCCGTACTACG TCGGACCGCTGGCAAAGAGGAAAACAGCAGATTTCGATGGATGACAAGAAGAGCGAA GAAACAATCACACCGTGGAACTTCGAAGAAGTCGTCGACAAGGGAGCAAGCGCACA GAGCTTTCATCGAAAAGATGACAACTTCGACAAGAACCTGCCGAACGAAAAGGTCC TGCCGAAGCACAGCCTGCTGTACGAATACTTCACAGTCTACAACGAACTGACAAAAG TCAAGTACGTCACAGAAGGAATGAGAAAGCCGGCATTCTGAGCGGAGAACAGAAAG AAGGCAATCGTCGACCTGCTGTTCAAGACAAAACAGAAAAGGTCACAGTCAAGCAGCT GAAGGAAGACTACTTCAAGAAGATCGAATGCTTCGACAGCGTCGAAATCAGCGGAGT CGAAGACAGATTCAACGCAAGCCTGGGAACATACCACGACCTGCTGAAGATCATCAA GGACAAGGACTTCTGGACAACGAAGAAAACGAAGACATCTGGAAGACATCGTCC TGACACTGACACTGTTTCGAAGACAGAGAAATGATCGAAGAAAAGACTGAAGACATAC GCACACCTGTTTCGACGACAAGGTCATGAAGCAGCTGAAGAGAAGAAGATACACAGG ATGGGGAAGACTGAGCAGAAAGCTGATCAACGGAATCAGAGACAAGCAGAGCGGAA AGACAATCCTGGACTTCTGAAGAGCGACGGATTTCGAAAACAGAAAACCTCATGCAGC TGATCCACGACGACAGCCTGACATTCAAGGAAGACATCCAGAAGGCACAGGTCAGC GGACAGGGAGACAGCCTGCACGAACACATCGAAAACCTGGCAGGAAGCCGGCAAT CAAGAAGGGAATCCTGCAGACAGTCAAGGTCGTCGACGAACTGGTCAAGGTCATGG GAAGACACAAGCCGAAAACATCGTCATCGAAATGGCAAAGAGAAAACAGACAACA CAGAAGGGACAGAAGAACAGCAGAGAAAAGAATGAAGAGAATCGAAGAAGGAATCA AGAACTGGGAAGCCAGATCCTGAAGGAACACCCGGTTCGAAAACACACAGACTGCAG AACGAAAAGCTGTACTCTGACTACCTGCAGAACGGAAGAGACATGTACGTCGACCAG GAACTGGACATCAACAGACTGAGCGACTACGACGTCGACCACATCGTCCCGCAGAGC</p>	<p>169</p>

[0773]

	<p>TTCCTGAAGGACGACAGCATCGACAACAAGTCTGACAAGAAGCGACAAGAACAG AGGAAAAGAGCGACAACGTCCTCGAGCGAAGAAGTCGTCAAGAAGATGAAGAATACT GGAGACAGCTGCTGAACGCAAAAGCTGATCACACAGAGAAAGTTCGACAACCTGACA AAGGCAGAGAGAGGAGGACTGAGCGAACTGGACAAGGCAGGATTCATCAAGAGAC AGCTGGTTCGAAAACAAGACAGATCACAAGCAGTTCGCACAGATCCTGGACAGCAGA ATGAACACAAAAGTACGACGAAAACGACAAGCTGATCAGAGAAGTCAAGGTCATCAC ACTGAAGAGCAAGCTGGTCAGCGACTTCAGAAAGGACTTCCAGTTCATAAGGTCA GAGAAATCAACAATACTACCACCACGCACACGACGCATACCTGAACGCAGTCGTCGGAA CAGCACTGATCAAGAAGTACCCGAAGCTGGAAAAGCGAATTCGTCTACGGAGACTACA AGGTCTACGACGTCAGAAAAGATGATCGCAAAGAGCGAAGCAAGGAAATCGAAAAGGCA ACAGCAAAGTACTTCTTACAGCAACATCATGAACCTTCTCAAGACAGAAAATCACAC TGGCAAACGGAGAAATCAGAAAAGAGACCGCTGATCGAAAACAACGGAGAAAACAGG AGAAATCGTCTGGGACAAGGGAAGAGACTTCGCAACAGTCAGAAAAGGTCCTGAGCA TGCCCGAGGTCAACATCGTCAAGAAGACAGAAGTCCAGACAGGAGGATTCAGCAAG GAAAGCATCCTGCCGAAGAGAAAACAGCGACAAGCTGATCGCAAGAAAAGAGGACTG GGACCCGAAGAAGTACGGAGGATTCGACAGCCCGACAGTCGCATACAGCGTCTGGT CGTCGCAAAGGTGCAAAAAGGAAAGAGCAAGAAGCTGAAGAGCGTCAAGGAACTG CTGGGAATCACAATCATGGAAAGAACGAGCTTCGAAAAGAACCCGATCGACTTCCTG GAAGCAAAGGGATACAAGGAAGTCAAGAAGGACCTGATCATCAAGTCGCCGAAGTA CAGCCTGTTCGAACTGGAAAACGGAAAGAAAAGAGAATGCTGGCAAGCGCAGGAGAAC TGCAGAAGGGAAACGAACTGGCACTGCCGAGCAAGTACGTCAACTTCTGTACTCTGG CAAGCCACTACGAAAAGCTGAAGGGAAAGCCCGAAGACAACGAACAGAAAGCAGCT GTTCTGTCGAACAGCACAAGCACTACCTGGACGAAATCATCGAACAGATCAGCGAATT CAGCAAGAGAGTTCCTGGCAGCAGCAAACTGGACAAGGTCCTGAGCGATACACA ACAAGCACAGAGACAAGCCGATCAGAGAACAGGCAGAAAACATCATCCACCTGTTC ACACTGACAAACCTGGGAGCACCAGCAGCATTCAAGTACTTCGACACAACAATCGAC AGAAAAGAGATACACAAGCACAAGGAAGTCTGGACGCAACACTGATCCACCAGAG CATCACAGGACTGTACGAAAACAAGAATCGACTGAGCCAGCTGGGAGGAGACGGAG GAGGAAGCAGAGCAGCAAAGAGACCCGAGAACAACA</p>	
<p>具有NLS6的 Cas9的开放 阅读框架(无 起始或终止 密码子;适于 包括在融合 蛋白质编码 序列中)</p>	<p>GACAAGAAGTACAGCATCGGACTGGACATCGGAACAAAACAGCGTCGGATGGGCAGT CATCACAGACGAATACAAGGTCCCAGCAAGAAGTTCAAGGTCTGGGAAACACAG ACAGACACAGCATCAAGAAGAACTGATCGGAGCACTGCTGTTCCGACAGCGGAGAA ACAGCAGAAGCAACAAGACTGAAGAGAACAGCAAGAAGAAGATACACAAGAAGAA AGAAACAGAATCTGCTACTCTGCAGGAAATCTTCAGCAACGAAATGGCAAAGGTCAGC ACAGCTTCTTCCACAGACTGGAAGAAAGCTTCTGGTTCGAAGAAGACAAGAAGCAC GAAAGACACCCGATCTTCGGAACATCGTTCGACGAAGTCGCATACCACGAAAAGTAC CCGACAATCTACCACCTGAGAAAGAAGCTGGTTCGACAGCACAGACAAGGCAGACT GAGACTGATCTACTGGCACTGGCACACATGATCAAGTTTCAGAGGACACTTCTGATC GAAGGAGACCTGAACCCGGACAACAGCGACGTCGACAAGCTGTTTCATCCAGCTGGT CCAGACATACAACCAGCTGTTTCGAAGAAAACCCGATCAACGCAAGCGGAGTCGACG CAAAGGCAATCTGAGCGCAAGACTGAGCAAGAGCAGAAGACTGGAAAACCTGATC GCACAGCTGCCGGGAGAAAAGAAGACCGACTGTTTCGAAAACCTGATCGCACTGAG CCTGGGACTGACACCGAACTTCAAGAGCAACTTCGACCTGGCAGAAAGCAGCAAAAGC TGCAGCTGAGCAAGGACACATACGACGACGACCTGGACAACCTGCTGGCACAGATC GGAGACCAGTACGCAGACCTGTTCTGGCAGCAAAGAAGCTGAGCGACGCAATCCT GCTGAGCGACATCTGAGAGTCAACACAGAAATCACAAGGCACCCGCTGAGCGCAA GCATGATCAAGAGATACGCAACACCACAGGACCTGACACTGCTGAAGGCACTGG TCAGACAGCAGCTGCCGAAAAGTACAAGGAAATCTTCTTCGACCAGAGCAAGAAGC GGATACGCAGGATACATCGACGGAGGACAAGCCAGGAAGAATTCTACAAGTTCATC AAGCCGATCTGGAAAAGATGGACGGAACAGAAGAAGTCTGGTCAAGCTGAACAG AGAAGACCTGCTGAGAAAGCAGAGAACATTCGACAACGGAAGCATCCCAGCAGCA TCCACCTGGGAGAACTGCACGCAATCCTGAGAAGACAGGAAGACTTCTACCCGTTCC TGAAGGACAACAGAGAAAAGATCGAAAAGATCCTGACATTGAGAATCCCGTACTACG TCGGACCCGCTGGCAAGAGGAAAACAGCAGATTTCGCATGGATGACAAGAAAAGAGCGAA GAAACAATCACACCGTGGAACTTCGAAGAAGTCGTCGACAAGGGAGCAAGCGCACA GAGCTTCATCGAAAAGAAATGACAAAATTCGACAAGAAGCTGCCGAACGAAAAGGTCC TGCCGAAGCACAGCCTGCTGTACGAATACTTCACAGTCTACAACGAACTGACAAAAG TCAAGTACGTACAGAAGGAATGAGAAAGCCGGCATTCTGAGCGGAGAACAGAAG AAGGCAATCGTCGACCTGCTGTTCAAGACAAAACAGAAAAGGTCACAGTCAAGCAGCT GAAGGAAGACTACTTCAAGAAGATCGAATGCTTCGACAGCGTCGAAATCAGCGGAGT CGAAGACAGATTCAACGCAAGCCTGGGAACATACCACGACCTGCTGAAGATCATCAA GGACAAGGACTTCTGGACAACGAAGAAAACGAAGACATCCTGGAAGACATCGTCC TGACACTGACACTGTTTCGAAGACAGAGAAAATGATCGAAGAAAAGACTGAAGACATC GCACACCTGTTTCGACGACAAGGTTCATGAAGCAGCTGAAGAGAAGAAGATACACAGG ATGGGGAAGACTGAGCAGAAAAGCTGATCAACGGAATCAGAGACAAGCAGAGCGGAA AGACAATCCTGGACTTCTGAAGAGCGACGGATTTCGAAAACAGAAAACCTTCATGCAGC TGATCCACGACGACAGCCTGACATTCAAGGAAGACATCCAGAAGGCACAGGTCAGC</p>	<p>170</p>

[0774]

	<p>GGACAGGGAGACAGCCTGCACGAACACATCGCAAACCTGGCAGGAAGCCCGGCAAT CAAGAAGGGAATCCTGCAGACAGTCAAGGTCGTGACGAACTGGTCAAGGTCATGG GAAGACACAAGCCGAAAACATCGTCATCGAAATGGCAAGAGAAAACCAGACAACA CAGAAGGGACAGAAGAACAGCAGAGAAAAGAAATGAAGAGAATCGAAGAAGGAATCA AGGAACTGGGAAGCCAGATCCTGAAGGAACACCCGGTCGAAAAACACACAGCTGCAG AGAAAAGCTGTACCTGTACTACCTGCAGAACGGAAGAGACATGTACGTGACCAG GAACTGGACATCAACAGACTGAGCGACTACGACGTGACCACATCGTCCCAGAGAGC TTCCTGAAGGACGACAGCATCGACAACAAGGTCCTGACAAGAAGCGACAAGAACAG AGGAAAAGAGCGACAACGTCCCGAGCGAAGAAAGTCGTCAAGAAGATGAAGAAGTACT GGAGACAGCTGTGAACGCAAAGCTGATCACACAGAGAAAAGTTTCGACAACCTGACA AAGGCAGAGAGAGGAGGACTGAGCGAACTGGACAAGGCAGGATTCATCAAGAGAC AGCTGGTCGAAACAAGACAGATCACAAGCACGTGCGACAGATCCTGGACAGCAGA ATGAACACAAAAGTACGACGAAAACGACAAGCTGATCAGAGAAGTCAAGGTCATCAC ACTGAAGAGCAAGCTGGTCAGCGACTTCAGAAAAGGACTTCCAGTTCTACAAGGTCA GAGAAATCAACAACACTACCACCAGCACACGACGCATACCTGAAACGAGTCCGGA CAGCACTGATCAAGAAGTACCCGAAGCTGGAAAAGCAATTTCGTCTACGGAGACTACA AGGTCTACGACGTGAGAAAGATGATCGAAAAGAGCGAACAGGAAATCGGAAAAGGCA ACAGCAAAAGTACTTCTTCTACAGCAACATCATGAACTTCTTCAAGACAGAAAATCACAC TGGCAAAACGGAGAAATCAGAAAAGAGACCGCTGATCGAAAACAAACGGGAAAACAGG AGAAAATCGTCTGGGACAAGGGAAGAGACTTCGCAACAGTCAGAAAAGGTCCTGAGCA TGCCCGAGGTCAACATCGTCAAGAAGACAGAAGTCCAGACAGGAGGATTCAGCAAG GAAAGCATCCTGCCGAAGAGAAAACAGCGACAAGCTGATCGCAAGAAAAGAAAGGACTG GGACCCGAAGAAGTACGGAGGATTCGACAGCCCGACAGTCCGATACAGCGTCTTGGT CGTCGAAAAGGTCGAAAAGGGAAGAGCAAGAAGTGAAGAGCGTCAAGGAATTCG CTGGGAATACAATCATGGAAAGAAGCAGCTTCGAAAAGAACCAGATCGACTTCTG GAAGCAAAGGGATACAAGGAAGTCAAGAAGGACCTGATCATCAAGCTGCCGAAGTA CAGCCTGTTGAACTGGAAAACGGAAAGAGAAATGCTGGCAAGCGCAGGAGAAAC TGCAGAAGGGAAACGAACTGGCCTGCGGAGCAAGTACGTCAACTTCTGTACTCTGG CAAGCCACTACGAAAAGCTGAAGGGAAGCCCGGAAGACAACGAACAGAAAGCAAGCT GTTCTGTCGAACAGCACAAAGCACTACCTGGACGAAATCATCGAACAGATCAGCGAATT CAGCAAGAGAGTACCTGGCAGACGCAAACCTGGACAAGGTCCTGAGCGCATACA ACAAGCACAGAGACAAGCCGATCAGAGAACAGGCAGAAAACATCATCCACCTGTTT CAAGTACAAAACCTGGGAGCACCCGAGCATTCAAGTACTTCGACACAACAGAAAGTGC AGAAAAGATACACAAGCACAAAAGGAAGTCTGGACGCAACACTGATCCACCAGAG CATCACAGGACTGTACGAAAACAAGAATCGACCTGAGCCAGCTGGGAGGAGACGGAG GAGGAAGCGCAGCAGCAAAGAGAAGCTGGAGCATGGCAGCA</p>	
<p>具有NLS7的 Cas9 的开放 阅读框架(无 起始或终止 密码子; 适于 包括在融合 蛋白质编码 序列中)</p>	<p>GACAAGAAGTACAGCATCGGACTGGACATCGGAACAAACAGCGTCGGATGGGCAGT CATCACAGACGAAATACAAGTCCCGAGCAAGAAGTTCAAGGTCCTGGGAAAACACAG ACAGACACAGCATCAAGAAGAACCTGATCGGAGCACTGCTGTTTCGACAGCGGAGAA ACAGCAGAAGCAACAAGACTGAAGAGAACAGCAAGAAGAAGATACACAAGAAGAA AGAACAGAATCTGCTACCTGCAGGAAATCTTCAGCAACGAAATGGCAAAGGTCGACG ACAGCTTCTTCCACAGACTGGAAGAAAGTCTTCTGGTCGAAGAAGACAAGAAGCAC GAAAGACACCCGATCTTCGGAACATCGTTCGACGAAAGTCCGATACACAGAAAGTAC CCGACAATCTACCACCTGAGAAAGAAGCTGGTCGACAGCACAGACAAGGCAGACCT GAGACTGATCTACCTGGCACTGGCACACATGATCAAGTTCAGAGGACACTTCTGATC GAAGGAGACCTGAACCCGGACAACAGCGACGTGACAAGCTGTTTATCCAGCTGGT CCAGACATAACAACAGCTGTTTCGAAGAAAACCCGATCAACGCAAGCGGAGTCCGACG CAAAGGCAATCTGAGCGCAAGACTGAGCAAGAGCAGAAGACTGGAAAACCTGATC GCACAGCTGCCGGGAGAAAAGAAGAACGGACTGTTTCGAAAACCTGATCGCACTGAG CCTGGGACTGACACCGAACTTCAAGAGCAACTTCGACCTGGCAGAAGACGCAAAAGC TGCAGCTGAGCAAGGACACATACGACGACGACCTGGACAACCTGCTGGCAGACAGATC GGAGACCAAGTACGACGACCTGTTCTGGCAGCAAGAAGAACTGAGCGACGCAATCCT GCTGAGCGACATCTGAGAGTCAACACAGAAATCACAAGGCACCGCTGAGCGCAA GCATGATCAAGAGATACGACGAACACCACAGGACCTGACACTGCTGAAGGCAGTGG TCAGACAGCAGCTGCCGAAAAGTACAAGGAAATCTTCTTCGACCAGAGCAAGAAGC GGATACGCAAGGATACATCGACGGAGGAGCAAGCCAGGAAGAATTCACAAGTTTATC AAGCCGATCTGGAAAAGATGGACGGAACAGAAGAAGTCTGGTCAAGCTGAACAG AGAAGACCTGCTGAGAAAGCAGAGAACATTCGACAACGGAAGCATCCCGCACCAGA TCCACCTGGGAGAACTGCACGCAATCTGAGAAGACAGGAAGACTTCTACCCGTTCC TGAAGGACAACAGAGAAAAGATCGAAAAGATCTGACATTCAGAATCCCGTACTACG TCGGACCGCTGGCAAGAGGAAAACAGCAGATTTCGATGGATGACAAGAAAAGAGCGAA GAAACAATCACACCGTGGAACTTCGAAGAAGTCGTGACAAGGGAGCAAGCGCACA GAGCTTATCGAAAAGAAATGACAACTTCGACAAGAACCTGCCGAACGAAAAGGTCC TGCCGAAGCACAGCCTGCTGTACGAATACTTCACAGTCTACAACGAACTGACAAAAG TCAAGTACGTACAGAAGGAATGAGAAAAGCCGGCATTCCTGAGCGGAGAACAGAAAG AAGGCAATCGTCGACCTGCTGTTCAAGACAAAACAGAAAAGGTCACAGTCAAGCAGCT GAAGGAAGACTACTCAAGAAGATCGAATGCTTCGACAGCGTCGAAATCAGCGGAGT</p>	<p>171</p>

[0775]

	<p>CGAAGACAGATTCAACGCAAGCCTGGGAACATACCACGACCTGCTGAAGATCATCAA GGACAAGGACTTCTGGACAACGAAGAAAACGAAGACATCCTGGAAGACATCGTCC TGACACTGACACTGTTTGAAGACAGAGAAATGATCGAAGAAAGACTGAAGACATAC GCACACCTGTTTCGACGACAAGGTCATGAAGCAGCTGAAGAGAAAGATACACAGG ATGGGGAAAGACTGAGCAGAAAAGCTGATCAACGGAATCAGAGACAAGCAGAGCGGAA AGACAATCTGGACTTCTGAAAGAGCGACGGATTTCGCAAACAGAAAATTCATGCAGC TGATCCACGACGACAGCCTGACATTCAAGGAAGACATCCAGAAGGCACAGGTCAGC GGACAGGGGAGACAGCCTGCACGAACACATCGCAAACCTGGCAGGAAGCCCGGCAAT CAAGAAGGGAATCCTGCAGACAGTCAAGGTCGTCGACGAACTGGTCAAGGTCATGG GAAGACACAAGCCGAAAACATCGTCATCGAAATGGCAAGAGAAAACAGACAACA CAGAAGGGACAGAAGAACAGCAGAGAAAAGAAATGAAGAGAATCGAAGGAATCA AGGAACTGGGAAGCCAGATCCTGAAGGAACACCCGGTCGAAAACACACAGCTGCAG AACGAAAAGCTGTACTCTGACTACCTGCAGAACGGAAGAGACATGTACGTCGACCAG GAACTGGACATCAACAGACTGAGCGACTACGACGTCGACCACATCGTCCCAGAGAGC TTCTGAAAGGACGACAGCATCGACAACAAGGTCCTGACAAGAAGCGACAAGAAGAG AGGAAAAGAGCGACAACGTCCCGAGCGAAGAAGTCGTCAAGAAGATGAAGAAGTACT GGAGACAGCTGCTGAACGCAAAGCTGATCACACAGAGAAAGTTCGACAACCTGACA AAGGCAGAGAGAGGAGGACTGAGCGAACTGGACAAGGCAGGATTCATCAAGAGAC AGCTGGTCGAAAACAAGACAGATCACAAAGCAGTCGCACAGATCCTGGACAGCAGA ATGAACACAAGTACGACGAAAACGACAAGCTGATCAGAGAAGTCAAGGTCATCAC ACTGAAGAGCAAGCTGGTCAGCGACTTCAGAAAAGGACTTCCAGTTCTACAAGGTCA GAGAAATCAACAATACCACCACGCACACGACGCATACCTGAACGCAGTCGTCCGAA CAGCACTGATCAAGAAGTACCCGAAGCTGGAAAAGCGAATTCGTCTACGGAGACTACA AGGTCACGACGTACGAAAGATGATCGAAAAGAGCGAACAGGAAATCGGAAAGAG ACAGCAAAGTACTTCTTCTACAGCAACATCATGAACTTCTTCAAGACAGAAATCACAC TGGCAAACCGGAGAAATCAGAAAAGAGACCGCTGATCGAAAACAACCGGAGAAACAGG AGAAATCGTCTGGGACAAGGGAAGAGACTTCGCAACAGTCAGAAAAGGTCCTGAGCA TGCCGCAGGTCAACATCGTCAAGAAGACAGAAGTCCAGACAGGAGGATTCAGCAAG GAAAGCATCCTGCCGAAAGAGAAAACAGCGACAAGCTGATCGCAAGAAGAAGGACTG GGACCCGAAGAAGTACGGAGGATTCGACAGCCCGACAGTCGCATACAGCGTCTGGT CGTCGCAAAGGTCGAAAAGGGAAGAGCAAGAAGCTGAAGAGCGTCAAGGAACTG CTGGGAATCACAATCATGGAAAGAAGCAGCTTCGAAAAGAACCCTGATCGACTTCTG GAAGCAAAGGGATACAAGGAAGTCAAGAAGGACCTGATCATCAAGTCCCGCAAGTA CAGCCTGTTGAACTGGAAAACGGAAGAAAGAGAATGCTGGCAAGCGCAGGAGAAC TGCAGAAGGGAAACGAACTGGCACTGCCGAGCAAGTACGTCAACTTCTGTACCTGG CAAGCCACTACGAAAAGCTGAAGGGAAGCCCGGAAGACAACGAAACAGAAGCAGCT GTTCCGTCGAACAGCACAAGCACTACCTGGACGAAATCATCGAACAGATCAGCGAAT CAGCAAGAGAGTCTCCTGGCAGACGCAAACTGGACAAGGTCCTGAGCCATACA ACAAGCACAGAGACAAGCCGATCAGAGAACAGGCAGAAAACATCATCCACCTGTTC ACACTGACAAACCTGGGAGCACCAGCAGCATTCAAGTACTTCGACACAACAATCGAC AGAAAAGATACACAAGCACAAGGAAGTCTGGACGCAACACTGATCCACCAGAG CATCACAGGACTGTACGAAAACAAGAATCGACCTGAGCCAGCTGGGAGGAGACGGAG GAGGAAGCGCAGCAGCAAAGAGAGTCTGGAGCATGGCATT</p>
<p>具有NLS8的 Cas9的开放 阅读框架(无 起始或终止 密码子;适于 包括在融合 蛋白质编码 序列中)</p>	<p>GACAAGAAGTACAGCATCGGACTGGACATCGGAACAAACAGCGTCGGATGGGCAGT CATCACAGACGAATACAAGGTCCTGGAGCAAGAAGTTCAAGGTCCTGGGAAAACACAG ACAGACACAGCATCAAGAAGAACCTGATCGGAGCACTGCTGTTTCGACAGCGGAGAA ACAGCAGAAGCAACAAGACTGAAGAGAACAGCAAGAAGAAGATACACAAGAAGAA AGAACAGAATCTGCTACCTGCAGGAAATCTTCAGCAACGAAATGGCAAAGGTCGACG ACAGCTTCTCCACAGACTGGAAGAAAGTCTCTGGTCAAGAAGACAAGAAGCAC GAAAGACACCCGATCTTCGAAAACATCGTCGACGAAAGTCGCATACCACGAAAAGTAC CCGACAATCTACCACCTGAGAAAAGAAGCTGGTCGACAGCACAGACAAGGCAGACCT GAGACTGATCTACTGGCACTGGCACACATGATCAAGTTTACAGAGGACACTTCTGATC GAAGGAGACCTGAACCCGGACAACAGCGACGTCGACAAGCTGTTTATCCAGCTGGT CCAGACATACAACCAGCTGTTTCGAAGAAAACCCGATCAACGCAAGCGGAGTCGACG CAAAGGCAATCTGAGCGAAGACTGAGCAAGAGCAGAAGACTGGAAAACCTGATC GCACAGCTGCCGGGAGAAAAGAAGACCGGACTGTTTCGAAAACCTGATCGCACTGAG CCTGGGACTGACACCGAACTTCAAGAGCAACTTCGACCTGGCAGAAGACGCAAAAGC TGCAGCTGAGCAAGGACACATACGACGACGACCTGGACAACCTGCTGGCACAGATC GGAGACCAAGTACGCAGACCTGTTCTGGCAGCAAAAGAAGCTGAGCGACGCAATCCT GCTGAGCGACATCCTGAGAGTCAACACAGAAATCACAAGGCACCGCTGAGCGCAA GCATGATCAAGAGATACGACGAACACCACAGGACCTGACACTGCTGAAGGCACTGG TCAGACAGCAGCTGCCGAAAAGTACAAGGAAATCTTCTTCGACCAGAGCAAGAAGC GGATACGCAGGATACATCGACGGAGGAGCAAGCCAGGAAGAATTCTACAAGTTTATC AAGCCGATCTGGAAAAGATGGACGGAACAGAAGAAGTCTGGTCAAGCTGAACAG AGAAGACCTGTGAGAAAGCAGAGAACATTTCGACAACGGAAGCATCCCGACCAGA TCCACCTGGGAGAACTGCACGCAATCCTGAGAAGACAGGAAGACTTCTACCCGTTCC TGAAGGACAACAGAGAAAAGATCGAAAAGATCCTGACATTCAGAATCCCGTACTACG</p>

[0776]

	<p>TCGGACCGCTGGCAAGAGGAAACAGCAGATTTCGCATGGATGACAAGAAAGAGCGAA GAAACAATCACACCGTGGAACTTTCGAAGAAGTCGTCGACAAGGGAGCAAGCGCAC GAGCTTCATCGAAAGAATGACAACTTCGACAAGAACCTGCCGAACGAAAAGGTCC TGCCGAAGCACAGCCTGCTGTACGAATACTTCACAGTCTACAACGAAGTACAAAAG TCAAGTACGTCACAGAAGGAATGAGAAAGCCGGCATTCTGAGCGGAGAACAGAAG AAGGCAATCGTCGACCTGCTGTTCAAGACAAACAGAAAAGGTCACAGTCAAGCAGCT GAAGGAAGACTACTTCAAGAAAGATCGAATGCTTCGACAGCGTCGAAATCAGCGGAGT CGAAGACAGATTCAACGCAAGCCTGGGAACATACCACGACCTGTGAAGATCATCAA GGACAAGGACTTCTGGACAACGAAGAAAACGAAGACATCTGGAAAGACATCGTCC TGACACTGACACTGTTTCAAGACAGAGAAAATGATCGAAGAAAAGACTGAAGACATAC GCACACCTGTTTCGACGACAAAGTTCATGAAGCAGCTGAAGAGAAGAAGATACACAGG ATGGGGAAGACTGAGCAGAAAAGCTGATCAACGGAATCAGAGACAAGCAGAGCGGAA AGACAATCCTGGACTTCTGAAGAGCGACGGATTTCGAAAACGAAAACCTTCATGCAGC TGATCCACGACGACAGCCTGACATTCAAGGAAGACATCCAGAAGGCACAGGTTCAGC GGACAGGGAGACAGCCTGCACGAACACATCGCAAACCTGGCAGGAAGCCCGGCAAT CAAGAAGGGAATCCTGCAGACAGTCAAGGTCGTCGACGAACTGGTCAAGGTCATGG GAAGACACAAGCCGAAAACATCGTCATCGAAATGGCAAGAGAAAACAGACAACA CAGAAGGGACAGAGAACAGCAGAGAAAAGAAATGAAGAGAATCGAAGAAGGAATCA AGGAAGTGGGAAGCCAGATCCTGAAGGAACACCCGGTCGAAAACACACAGCTGCAG AACGAAAAGCTGTACTTACTCCTGCAGAACGGAAGAGACATGTCAGTCTGCGACCAG GAACTGGACATCAACAGACTGAGCGACTACGACGTCGACCACATCGTCCCAGAGC TTCCTGAAGGACGACAGCATCGACAACAAGGTCCTGACAAGAAGCGACAAGAACAG AGGAAAAGAGCGACAACGTCCTGAGCGAAGAAGTTCGTAAGAAGATGAAGAAGTACT GGACAGCTGCTGAACGCAAGCTGATCACACAGAGAAAAGTTCGACAACAGCAATCA AAGGCAGAGAGAGGAGGACTGAGCGAACTGGACAAGGCAGGATTCATCAAGAGAC AGCTGGTCGAAACAAGACAGATCACAAGCACGTCGCACAGATCCTGGACAGCAGA ATGAACACAAAGTACGACGAAAACGCAAGCTGATCAGAGAAAGTCAAGGTCATCAC ACTGAAGAGCAAGCTGGTCAGCGACTTCAGAAAAGGACTTCCAGTTTACAAGGTCAG GAGAAATCAACAACCTACCACCGCACACGACGCATACCTGAACGAGCTCAGGAA CAGCACTGATCAAGAAGTACCCGAAGCTGGAAAAGCAATTCGTCACGGAGACTACA AGGTCTACGACGTCAGAAAAGATGATCGAAAAGAGCGAACAGGAAATCGGAAAAGGCA ACAGCAAAGTACTTCTTACAGCAACATCATGAACTTCTTCAAGACAGAAAATCACAC TGGCAAACGGAGAAAATCAGAAAAGAGACCGCTGATCGAAAACAAACGGAGAAAACAG AGAAATCGTCTGGGACAAGGGAAGAGACTTCGCAACAGTCAGAAAAGGTCCTGAGCA TGCCCGAGGTCAACATCGTCAAGAAGACAGAAGTCCAGACAGGAGGATTACGAAG GAAAGCATCCTGCCGAAGAGAAAACAGCGACAAGCTGATCGCAAGAAAAGAAAGGACTG GGACCCGAAGAAGTACGGAGGATTTCGACAGCCGACAGTTCGCATACAGCGTCTGGT CGTCGCAAAGGTCGAAAAGGGGAAAAGAGCAAGAAGCTGAAGAGCGTCAAGGAACTG CTGGGAATCACAATCATGGAAAGAAGCAGCTTCGAAAAGAACCCGATCGACTTCTG GAAGCAAAGGGATACAAAGGAAGTCAAGAAGGACCTGATCATCAAGCTGCCGAAGTA CAGCCTGTTTCAAGTGGAAAACGGAAGAAAGAGAATGCTGGCAAGCGCAGGAGAAC TGCAGAAGGGAACGAACCTGGCACTGCCGAGCAAGTACGTCAACTTCTGTACTTGG CAAGCCACTACGAAAAGCTGAAGGGAAAGCCCGAAGACAACGAACAGAAGCAGCT GTTTCGTCGAACAGCACAAGCACTACCTGGACGAAATCATCGAACAGATCAGCGAATT CAGCAAGAGAGTATCCTGGCAGACGCAAACCTGGACAAGGTCCTGAGCGCATAACA ACAAGCAGAGACAAGCCGATCAGAGAACAGGCAGAAAACATCATCCACCTGTTT CACTGACAAAACCTGGGAGCACCGGACGATTCGAAGTACTTCGACACAACAATCGAC AGAAAAGATACACAAGCACAAGGAAGTCTGGACGCAACACTGATCCACCAGAG CATCACAGGACTGTACGAAAACAAGAATCGACCTGAGCCAGCTGGGAGGAGACGGAG GAGGAAGCGCAGCAGCAAAGAGAAGCTGGAGCATGGCATT</p>	
<p>具有NLS9的 Cas9的开放 阅读框架(无 起始或终止 密码子;适于 包括在融合 蛋白质编码 序列中)</p>	<p>GACAAGAAGTACAGCATCGGACTGGACATCGAAACAAACAGCGTCGGATGGGCAGT CATCACAGACGAATACAAGTCCCAGCAAGAAGTTCAAGGTCCTGGGAAAACACAG ACAGACACAGCATCAAGAAGAACCTGATCGGAGCACTGCTGTTTCGACAGCGGAGAA ACAGCAGAAGCAACAAGACTGAAGAGAACAGCAAGAAGAAGATACACAAGAAGAA AGAACAGAATCTGCTACTTGCAGGAAATCTTTCAGCAACGAAATGGCAAAGGTCGACG ACAGCTTCTCCACAGACTGGAAGAAAGCTTCTGGTTCGAAGAAGACAAGAAGCAC GAAAGACACCCGATCTTCGGAACATCGTCGACGAAAGTTCGCATACCACGAAAAGTAC CCGACAATCTACCACCTGAGAAAAGAAGCTGGTCGACAGCACAGACAAGGCAGACCT GAGACTGATCTACTTGGCACTGGCACACATGATCAAGTTTCAGAGGACACTTCTGATC GAAGGAGACCTGAACCCGGACAACAGCGACGTCGACAAGCTGTTTCATCCAGCTGGT CCAGACATAACCAAGCTGTTTCGAAGAAAACCCGATCAACGCAAGCGGAGTCGACG CAAAGGCAATCCTGAGCGCAAGACTGAGCAAGAGCAGAAGACTGGAAAACCTGATC GCACAGCTGCCGGGAGAAAAGAAGACGGACTGTTTCGAAAACCTGATCGCACTGAG CCTGGGACTGACACCGAATTCGAAGCAACTTCGACCTGGCAGAAGACGCAAAAGC TGCAGCTGAGCAAGGACACATACGACGACGACCTGGACAACCTGTCGACACAGATC GGAGACCAAGTACGACAGCTGTTTCTGGCAGCAAAGAAGCTGAGCGACGCAATCCT GCTGAGCGACATCCTGAGAGTCAACACAGAAATCACAAGGCACCGCTGAGCGCAA</p>	<p>173</p>

[0777]

	<p>GCATGATCAAGAGATACGACGAACACCACCAGGACCTGACACTGCTGAAGGCACTGG TCAGACAGCAGCTGCCGAAAAAGTACAAGGAAATCTTCTCGACCAGAGCAAGAAC GGATACGCAGGATACATCGACGGAGGAGCAAGCCAGGAAGAATTCTACAAGTTCATC AAGCCGATCCTGGAAAAAGATGGACGGAACAGAAGAACTGCTGGTCAAGCTGAACAG AGAAGACCTGCTGAGAAAAGCAGAGAACATTCGACAACGGAAGCATCCCCGACCAGA TCCACCTGGGAGAACTGCACGCAATCCTGAGAAGACAGGAAGACTTACCCTGTTCC TGAAGGACAACAGAGAAAAGATCGAAAAAGATCCTGACATTCAGAATCCCGTACTACG TCGGACCCGCTGGCAAGAGGAAAACAGCAGATTTCGCATGGATGACAAGAAAAGAGCGAA GAAACAATCACACCGTGGAACTTCGAAGAAGTCGTCGACAAGGGGAGCAAGCGCAC GAGCTTCATCGAAAAGAAATGACAAACTTCGACAAGAACCTGCCGAACGAAAAGGTCC TGCCGAAGCACAGCCTGTGTACGAATACTTCACAGTCTACAACGAACTGACAAAAGG TCAAGTACGTCACAGAAGGAATGAGAAAGCCGGCATTCTGAGCGGAGAACAGAAG AAGGCAATCGTCGACCTGCTGTTCAAGACAAACAGAAAAGGTCACAGTCAAGCAGCT GAAGGAAGACTACTTCAAGAAAGATCGAATGCTTCGACAGCGTCGAAATCAGCGGAGT CGAAGACAGATTCAACGCAAGCTGGGAACATACCACGACCTGCTGAAGATCATCAA GGACAAGGACTTCTGGACAACGAAGAAAACGAAGACATCCTGGAAGACATCGTCC TGACACTGACTGTTTGAAGACAGAGAAATGATCGAAGAAAAGACTGAAGACATAC GCACACCTGTTGACGACAAGGTCATGAAGCAGCTGAAGAGAAAAGATACACAGG ATGGGGAAAGACTGAGCAGAAAAGCTGATCAACGGAATCAGAGACAAGCAGACGCGAA AGACAATCCTGGACTTCTGAAGAGCGGACGGATTTCGAAAACAGAAAACCTCATGCAGC TGATCCACGACGACAGCCTGACATTCAAGGAAGACATCCAGAAGGCACAGGTCAGC GGACAGGGAGACAGCCTGCACGAACACATCGCAAACCTGGCAGGAAGCCCGGCAAT CAAGAAGGGAATCCTGCAGACAGTCAAGGTCGTCGACGAACTGGTCAAGGTCATGG GAAGACACAAGCCGAAAACATCGTTCATCGAAATGGCAAGAGAAAACCCAGACAACA CAGAAGGGACAGAAGAACAGCAGAGAAAAGAAATGAAGAGAATCGAAGAAGGAATCA AGGAACTGGGAAGCCAGATCCTGAAGGAACACCCGGTCGAAAACACACAGCTGCAG AACGAAAAGCTGTACTTGTACTCTGACGAAACGGAAGAGACATGTACGTCGACCAG GAACTGGACATCAACAGACTGAGCGACTACGACGTCGACCACATCGTCCCAGAGAGC TTCCTGAAGGACGACAGCATCGACAACAAAGGTCCTGACAAGAAGCGACAAGAACAG AGGAAAAGAGCGACAACGTCGAGCGAAGAAAGTCTGCAAGAAGATGAAGAAGTACT GGAGACAGCTGCTGAACGCAAGGTCATCACACAGAGAAAAGTTCGACAACCTGACA AAGGCAGAGAGAGGGAGGACTGAGCGAACTGGACAAGGCAGGATTCATCAAGAGAC AGTGGTCGAAAACAAGACAGATCACAAGCAGCTCGCACAGATCCTGGACAGCAGAGA ATGAACACAAAGTACGACGAAAACGACAAGCTGATCAGAGAAAGTCAAGGTCATCAC ACTGAAGAGCAAGCTGGTACGCGACTTCAGAAAAGGACTTCCAGTTCACAAGGTC GAGAAATCAACAATACCACCACGCACACGACGCATACCTGAACGCAGTCGTCGGAA CAGACTGATCAAGAAGTACCCGAAGCTGGAAAAGCGAATTCGTCACGGAGACTACA AGGTCTACGACGTACAGAAAAGATGATCGAAAAGAGCGAACAGGAAATCGGAAAGGA ACAGCAAAGTACTTCTTCTACAGCAACATCATGAACTTCTTCAAGACAGAAATCACAC TGGCAAACCGGAGAAATCAGAAAAGAGACCGCTGATCGAAAACAAACGGAGAAAACAGG AGAAATCGTCTGGGACAAGGGAAGAGACTTCGCAACAGTCAGAAAAGGTCCTGAGCA TGCCGACGGTCAACATCGTCAAGAAGACAGAAAGTCCAGACAGGAGGATTCAGAAAG GAAAGCATCTGCCGAAGAGAAAACAGCGACAAGCTGATCGAAGAAAAGAAAGGACTG GGACCCGAAGAAGTACGGAGGATTCGACAGCCCGACAGTCGCATACAGCGTCTGGT CGTCGCAAAGGTCGAAAAGGGAAAAGAGCAAGAAAGTGAAGAGCGTCAAGGAACTG CTGGGAATCACAATCATGGAAAGAAGCAGCTTCGAAAAGAACCCTGATCGACTTCTG GAAGCAAAGGGATACAAAGGAAAGTCAAGAAGGACCTGATCATCAAGCTGCCGAAAGTA CAGCCTGTTGAACTGGAAAACGGAAGAAAGAGAATGCTGGCAAGCGCAGGAGAAC TGCAGAAGGGAAACGAACTGGCACTGCCGAGCAAGTACGTCAACTTCTGTACCTGG CAAGCCACTACGAAAAGCTGAAGGGAAAGCCCGAAGACAACGAACAGAAGCAGCT GTTCTGTCGAACAGCACAAAGCACTACCTGGACGAAATCATCGAACAGATCAGCGAAT CAGCAAGAGAGTATCCTGGCAGACGCAAACTGGACAAGGTCCTGAGCGCATAACA ACAAGCACAGAGACAAGCCGATCAGAGAACAGGCAGAAAACATCATCCACCTGTTT ACACTGACAAACCTGGGAGCACCAGGACATCAAGTACTTCGACACAACAATCGAC AGAAAAGAGATACACAAGCACAAAGGAAGTCTGGACGCAACACTGATCCACCAGAG CATCACAGGACTGTACGAAAACAAGAATCGACCTGAGCCAGCTGGGAGGAGACGGAG GAGGAAGCGCAGCAGCAAAGAGAAAGTACTTCGCAGCA</p>	
<p>具有 NLS10 的 Cas9 的 开放阅读框 (无起始或终 止密码子; 适 于包括在融</p>	<p>GACAAGAAGTACAGCATCGGACTGGACATCGGAACAAACAGCGTCGGATGGGCACT CATCACAGACGAATACAAGGTCCCGAGCAAGAAGTTCAAGGTCCTGGGAAAACACAG ACAGACACAGCATCAAGAAGAACCTGATCGGAGCACTGCTGTTTCGACAGCGGAGAA ACAGCAGAAGCAACAAGACTGAAGAGAACAGCAAGAAGAAGATACACAAGAAGAA AGAACAGAATCTGCTACTCTGCAGGAAATCTTCAGCAACGAAATGGCAAAGGTCGACG ACAGCTTCTCCACAGACTGGAAGAAAAGTCTCTGGTCAAGAAAGACAAGAAGCAC GAAAGACACCCGATCTTCGGAACATCGTCGACGAAAGTTCGATACACCAGAAAAGTAC CCGACAATACCACCTGAGAAAGAAGTGGTTCGACAGCACAGACAAGGAGACCT GAGACTGATCTACTGGCACTGGCACACATGATCAAGTTTCAGAGGACACTTCTGATC GAAGGAGACCTGAACCCGACAACAGCGACGTCGACAAGCTGTTTCATCCAGCTGGT</p>	<p>174</p>

[0778]

合蛋白质编 码序列中)	<p>CCAGACATACAACCAGCTGTTTCGAAGAAAACCCGATCAACGCAAGCGGAGTCGACG CAAAGGCAATCCTGAGCGCAAGACTGAGCAAGAGCAGAAGACTGGAAAACCTGATC GCACAGCTGCCGGGAGAAAAGAAGACGGACTGTTCCGAAACCTGATCGCACTGAG CCTGGGACTGACACCGAACTTCAAGAGCAACTTCGACCTGGCAGAAGACGCAAAAGC TGCAGCTGAGCAAGGACACATACGACGACGACCTGGACAACCTGCTGGCACAGATC GGAGACCAGTACGCAGACCTGTTCTTGGCAGCAAAGAACCTGAGCGACGCAATCCT GCTGAGCGACATCCTGAGAGTCAACACAGAAATCACAAAGGCACCGCTGAGCGCAA GCATGATCAAGATACGACGAACACCACAGGACCTGACACTGCTGAAGGCACTGG TCAGACAGCAGCTGCCGGAAGTACAAGGAAATCTTCTCGACCAGAGCAAGAAGC GGATACGCAGGATACATCGACGGAGGAGCAAGCCAGGAAGAATTCTACAAGTTCATC AAGCCGATCCTGGAAAAGATGGACGGAACAGAAGAAGTCTGGTCAAGTGAACAG AGAAGACCTGCTGAGAAAGCAGAGAACATTCGACAACGGAAGCATCCCGCACCAGA TCCACCTGGGAGAACTGCACGCAATCCTGAGAAGACAGGAAGACTTCTACCCGTTCC TGAAGGACAACAGAGAAAAGATCGAAAAGATCCTGACATTGAGAATCCCGTACTACG TCGGACCGTGGCAAGAGGAAACAGCAGATTTCGATGGATGACAAGAAAAGCGCAA GAAACAATCACACCGTGGAACTTCGAAGAAGTCGTCGACAAGGGAGCAAGCGCACA GAGCTTCATCGAAAAGATGACAACTTCGACAAGAAGCTGCCGAACGAAAAGGTCC TGCCGAAGCACAGCCTGCTGTACGAATACTTCACAGTCTACAACGAACTGACAAAAG TCAAGTACGTCACAGAAGGAATGAGAAAAGCCGGCATTCTGAGCGGAGAACAGAAG AAGGCAATCGTCGACCTGCTGTTCAAGACAAAACAGAAAAGGTACAGTCAAGCAGCT GAAGGAAGACTACTTCAAGAAGATCGAATGCTTCGACAGCGTCGAAATCAGCGGAGT CGAAGACAGATTCAACGCAAGCCTGGGAACATACCACGACCTGCTGAAGATCATCAA GGACAAGGACTTCTGGACAACGAAGAAAACGAAGACATCCTGGAAGACATCGTCC TGCACTGACACTGTTTCGAAGACAGAGAAATGATCGAAGAAAAGACTGAAGACATAC GCACACCTGTTTCGACGACAAGGTCATGAAGCAGCTGAAGAGAAGAAGATACACAGG ATGGGGAAGACTGAGCAGAAAGCTGATCAACGGAATCAGAGACAAGCAGAGCGGAA AGACAATCCTGGACTTCTGAAGAGCGACGGATTTCGAAAACAGAAAACCTCATGACG TGATCCACGACGACAGCCTGACATTCAAGGAAGACATCCAGAAGGCACAGGTGACG GGACAGGGAGACAGCCTGCACGAACACATCGAAAACCTGGCAGGAAGCCCGCAAT CAAGAAGGGAATCCTGCAGACAGTCAAGGTCGTCGACGAACTGGTCAAGGTCATGG GAAGACACAAGCCGAAAACATCGTCATCGAAATGGCAAGAGAAAACCAGACAACA CAGAAGGGACAGAAGAACAGCAGAGAAAAGAATGAAGAGAATCGAAGAAGGAATCA AGGAAGTGGGAAGCCAGATCCTGAAGGAACACCCGGTTCGAAAACACACAGCTGCAG AACGAAAAGCTGTACTCTGACTACTGACAGAACGGAAGAGACATGTACGTCGACCAG GAACTGGACATCAACAGACTGAGCGACTACGACGTCGACCACATCGTCCCGCAGAGC TTCCTGAAGGACGACAGCATCGACAACAGGTCCTGACAAGAAGCGACAAGAACAG AGGAAAAGAGCGACAACGTCCTGAGCGAAGAAAGTGTCAAGAAGATGAAGAAGTCACT GGACAGCTGCTGAACGCAAAAGCTGATCACACAGAGAAAAGTTCGACAACCTGACA AAGGCAGAGAGAGGAGGACTGAGCGAACTGGACAAGGCAGGATTCATCAAGAGAC AGCTGGTCGAAAACAAGACAGATCACAAGACAGTTCGACACAGATCCTGGACAGCAGA ATGAACACAAAGTACGACGAAAACGACAAGCTGATCAGAGAAGTCAAGGTCATCAC ACTGAAGAGCAAGCTGGTTCAGCGACTTCAGAAAAGGACTTCCAGTTTACAAGGTC GAGAAATCAACAATACTACCACACGCACACGACGCATACCTGAACGCAGTCTCGGAA CAGCACTGATCAAGAAGTACCCGAAGCTGGAAAAGCGAATTCGTCTACGGAGACTACA AGGTCTACGACGTACAGAAAAGATGATCGAAAAGAGCGAACAGGAAATCGGAAAAGCA ACAGCAAAGTACTTCTTCTACAGCAACATCATGAACTTCTTCAAGACAGAAATCACAC TGGCAAACGGAGAAAATCAGAAAAGAGACCGCTGATCGAAAACAAAACGGAGAAAACAGG AGAAATCGTCTGGGACAAGGGAAGAGACTTCGCAACAGTCAGAAAAGGTCCTGAGCA TGCCCGAGGTCAACATCGTCAAGAAGACAGAAGTCCAGACAGGAGGATTCAGCAAG GAAAGCATCTGCCGAAGAGAAAACAGCGACAAGCTGATCGCAAGAAAAGAAAGGACTG GGACCCGAAGAAGTACGGAGGATTCGACAGCCGACAGTTCGATACAGCGTCTGGT CGTCGCAAAGGTCGAAAAGGGAAGAGCAAGAAGCTGAAGAGCGTCAAGGAACTG CTGGGAATCACAATCATGGAAAGAAGCAGCTTCGAAAAGAACCCTGACTTCTG GAAGCAAAGGGATACAAGGAAGTCAAGAAGGACCTGATCATCAAGCTGCCGAAGTA CAGCCTGTTGAACTGGAAAACGGAAGAAGAGAATGCTGGCAAGCGCAGGAGAAAC TGCAGAAGGGAACGAACTGGCACTGCCGAGCAAGTACGTCAACTTCTGTACTGGT CAAGCCACTACGAAAAGCTGAAGGGAAGCCCGGAAGACAACGAACAGAAGCAGCT GTTCTGTCGAACAGCACAAGCACTACCTGGACGAAATCATCGAACAGATCAGCGAAT CAGCAAGAGAGTATCCTGGCAGACGCAACCTGGACAAGGTCCTGAGCGCATAACA ACAAGCACAGAGACAAGCCGATCAGAGAACAGGAGGAGAAAACATCACCACCTGTT ACACTGACAAAACCTGGGAGCACCAGCAGTTCAGTACTTCGACACAACAATCGAC AGAAAAGAGATACACAAGCACAAGGAAGTCTGGACGCAACACTGATCCACCAGAG CATCACAGGACTGTACGAAAACAAGAATCGACCTGAGCCAGCTGGGAGGAGACGGAG GAGGAAGCAGAGCAGCAAAGAGAAAAGGCATTTCGACGA</p>	
具有 NLS11 的 Cas9 的开	<p>GACAAGAAGTACAGCATCGGACTGGACATCGGAACAAAACAGCGTCGGATGGGCACT CATCACAGACGAATACAAGGTCCCGAGCAAGAAGTTCAAGGTCCTGGGAAAACACAG ACAGACACAGCATCAAGAAGAACCTGATCGGAGCACTGCTGTTTCGACAGCGGAGAA</p>	175

<p>放阅读框架 (无起始或终 止密码子; 适 于包括在融 合蛋白质编 码序列中)</p>	<p>ACAGCAGAAGCAACAAGACTGAAGAGAACAGCAAGAAGAAGATACACAAGAAGAA AGAACAGAAATCTGCTACCTGCAGGAAATCTTCAGCAACGAAATGGCAAAGGTCGACG ACAGCTTCTTCCACAGACTGGAAGAAAGCTTCTGGTCTGAAGAAGACAAGAAGCAC GAAAGACACCCGATCTTCGGAACATCGTCGACGAAGTCGCATACCACGAAAAGTAC CCGACAATCTACCACCTGAGAAAGAAGCTGGTGCACAGCACAGACAAGGCAGACCT GAGACTGATCTACCTGGCACTGGCACACATGATCAAGTTCAGAGGACACTTCTGATC GAAGGAGACCTGAACCCGGACAACAGCGACGTCGACAAGCTGTTTCATCCAGCTGGT CCAGACATAACAACAGCTGTTTCAAGAAAACCCGATCAACGCAAGCGGAGTCGACG CAAAGGCAATCTGAGCGCAAGACTGAGCAAGAGCAGAAGACTGGAAAACCTGATC GCACAGCTGCCGGGAGAAAAGAAGACGACTGTTTCGAAAACCTGATCGCACTGAG CCTGGGACTGACACCGAACTTCAAGAGCAACTTCGACCTGGCAGAAAGCAAAGC TGCAGCTGAGCAAGGACACATACGACGACGACCTGGACAACCTGCTGGCACAGATC GGAGACCAGTACGCAGACCTGTTTCTGGCAGCAAAGAACCTGAGCGACGCAATCCT GCTGAGCGACATCTGAGAGTCAACACAGAAATCACAAGGCACCCGCTGAGCGCAA GCATGATCAAGAGATACGACGAACACCACCAGGACCTGACACTGCTGAAGGCATG TCAGACAGCAGCTGCCGAAAAGTACAAGGAAATCTTCTTCGACCAGAGCAAGAAC GGATACGCAGGATACATCGACGGAGGAGCAAGCCAGGAAGAATTCTACAAGTTCATC AAGCCGATCTGGAAAAGATGGACGGAACAGAAGAACTGCTGGTCAAGCTGAACAG AGAAGACCTGCTGAGAAAGCAGAGAACATTCGACAACGGAAGCATCCCGCACAGCA TCCACCTGGGAGAACTGCACGCAATCCTGAGAAGACAGGAAGACTTCTACCCGTTCC TGAAGGACAACAGAGAAAAGATCGAAAAGATCCTGACATTGAGAATCCCGTACTACG TCGGACCCGCTGGCAAGAGGAAAACAGCAGATTTCGCATGGATGACAAGAAAAGAGCGAA GAAACAATCACACCGTGGAACTTCAAGAAGTCTGTCGACAAGGGAGCAAGCGCAC GAGCTTTCGAAAAGAAATGACAAAATTCGACAAGAACCTGCCGAAACGAAAAGTCC TGCCGAAGCACAGCCTGCTGTACGAATACTTACAGTCTACAACGAACTGACAAAAG TCAAGTACGTACAGAAAGGAATGAGAAAGCCGGCATTCTGAGCGGAGAACAGAAAG AAGGCAATCGTCGACCTGCTGTTCAAGACAAAACAGAAAAGGTCACAGTCAAGCAGCT GAAGGAAGACTACTTCAAGAAGATCGAATGCTTTCGACAGCGTCGAAATCAGCGAGT CGAAGACAGATTCAACGCAAGCTGGGAACATACCACGACCTGCTGAAAGATCATCAA GGACAAGGACTTCTGGACAACGAAGAAAACGAAGACATCCTGGAAGACATCGTCC TGACACTGACACTGTTTCAAGACAGAGAAAATGATCGAAGAAAAGACTGAAGACATAC GCACACCTGTTTCGACGACAAGGTTCATGAAGCAGCTGAAGAGAAGAAGATACACAGG ATGGGGAAGACTGAGCAGAAAAGCTGATCAACGGAATCAGAGACAAGCAGAGCGGAA AGACAATCCTGGACTTCTGAAGAGCGACGGATTTCGAAAACAGAAAATTCATGCAGC TGATCCACGACGACAGCCTGACATTCAAGGAAGACATCCAGAAGGCACAGGTCAGC GGACAGGGGAGACAGCCTGCACGAACACATCGCAAACCTGGCAGGAAAGCCCGGCAAT CAAGAAGGGAATCCTGCAGACAGTCAAGGTCTGTCGACGAACTGGTCAAGGTCATGG GAAGACACAAGCCGAAAACATCGTCATCGAAATGGCAAGAGAAAACGAGACAACA CAGAAGGGACAGAAGAACAGCAGAGAAAAGAAATGAAGAGAATCGAAGAAGGAATCA AGGAACTGGGAAGCCAGATCCTGAAGGAACACCCGGTTCGAAAACACACAGCTGCAG AACGAAAAGCTGTACTTACTACTGCAGAACGGAAGAGACATGTACGTCGACCAG GAACTGGACATCAACAGACTGAGCGACTACGACGTCGACCACATCGTCCCGCAGAGC TTCCTGAAGGACGACAGCATCGACAACAAGGTCCTGACAAGAAGCGACAAGAACAG AGGAAAGAGCGACAACGTCCTCGAGCGAAGAAGTCGTCAGAAGATGAAGAAGTACT GGAGACAGCTGCTGAACGCAAAAGCTGATCACACAGAGAAAAGTTCGACAACCTGACA AAGGCAGAGAGAGGAGGACTGAGCGAACTGGACAAGGCAGGATTCATCAAGAGAC AGTGGTTCGAAAACAAGACAGATCACAAAAGCACGTCGCACAGATCTGGACAGAGA ATGAACACAAAGTACGACGAAAACGACAAGCTGATCAGAGAAGTCAAGGTCATCAC ACTGAAGAGCAAGCTGGTACGCGACTTCAGAAAAGGACTTCCAGTTCACAAGGTCA GAGAAATCAACAATACCACCACGACACGACGCATACCTGAACGCAGTCTGTCGGAA CAGCACTGATCAAGAAGTACCCGAAGCTGGAAAAGCGAATTCGTCTACGGAGACTACA AGGTCTACGACGTCAGAAAAGATGATCGAAAAGAGCGAACAGGAAATCGGAAAAGGCA ACAGCAAAGTACTTCTTCTACAGCAACATCATGAACTTCTTCAAGACAGAAATCACAC TGGCAAACCGGAGAAATCAGAAAAGAGACCCGCTGATCGAAAACAAAACGGAGAAAACAGG AGAAATCGTCTGGGACAAGGGAAGAGACTTCGCAACAGTCAGAAAAGGTCCTGAGCA TGCCGCAGGTCAACATCGTCAAGAAGACAGAAGTCCAGACAGGAGGATTCAGCAAAG GAAAGCATCCTGCCAAGAGAAAACAGCGACAAGCTGATCGCAAGAAAAGAAAGGACTG GGACCCGAAGAAGTACGGAGGATTCGACAGCCGACAGTCGCATACAGCGTCTGCTGGT CGTCGCAAAGGTCGAAAAGGAAAAGAGCAAGAAGCTGAAGAGCGTCAAGGAACTG CTGGGAATCACAATCATGGAAAAGAGCAGCTTCGAAAAGAACCAGTCTGACTTCTG GAAGCAAAGGGATACAAGGAAGTCAAGAAGGACCTGATCATCAAGCTGCCGAAGTA CAGCCTGTTGAACTGGAAAACGGAAGAAAAGAGAATGCTGGCAAGCGCAGGAGAAC TGCAAGGGGAAACGAACTGGCACTGCCGAGCAAGTACGTCAACTTCTGTACTCTGG CAAGCCACTACGAAAAGCTGAAGGGAAGCCCGAAGACAACGAACAGAAAGCAGCT GTTCTCGAACAGCACAAAGCACTACCTGGACGAAATCATCGAACAGATCAGCGAATT CAGCAAGAGAGTATCCTGGCAGACGCAACCTGGACAAGGTCCTGAGCGCATAACA ACAAGCACAGAGACAAGCCGATCAGAGAACAGGCAGAAAACATCATCCACCTGTTT</p>
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[0779]

	<p>ACACTGACAAACCTGGGAGCACCGGCAGCATTCAAGTACTTCGACACAACAATCGAC AGAAAAGAGATACACAAGCACAAAAGGAAGTCCTGGACGCAACACTGATCCACCAGAG CATCACAGGACTGTACGAAACAAGAATCGACCTGAGCCAGCTGGGAGGAGACGGAG GAGGAAGCAGAGCAGCAAAGAGAAAGTACTTTCGCAGTC</p>	
<p>具有 XBG UTR 及含有 表4的低U 1 密码子的 Cas9 ORF的 mRNA 转录 物</p>	<p>GGGAAGCUCAGAAUAAACGCUCAACUUGGCCGGAUCUGCCACCAUGGACAAGAA GUACAGCAUCGGCCUGGACAUCCGACCAACAGCGUGGGCUGGGCCUGAUCACC GACGAGUACAAGGUGCCAGCAAGAAAGUUAAGGUGCUGGGCAACACCCGACAGAC ACAGCAUCAAGAAGAACCUGAUCGGCGCCUGCUGUUCGACAGCGGCGAGACCGC CGAGGCCACCAGACUGAAGAGAACCGCCAGAAGAAGAUACACCAGAAGAAAGAAC AGAAUCUGCUACCUGCAGGAGAUUCAGCAACGAGAUGGCCAAGGUGGACGACA GCUUCUCCACAGACUGGAGGAGAGCUUCUUGGUGGAGGAGGACAAGAAGCACGA GAGACACCCCAUCUUCGGCAACAUCGUGGACGAGGUGGCCUACCACGAGAAGUAC CCCACCAUCUACCACUGAGAAAGAAGCUGGUGGACAGCACCCGACAAGGCCGACC UGAGACUGAUCUACCUGGCCUGGCCACAUGAUCAGUUCAGAGGCCACUUCU GAUCGAGGGCGACCUGAACCCCGACAACAGCGACGUGGACAAGCUUUCACCCAG CUGGUGCAGACCUACAACCAGCUGUUCGAGGAGAACCCTCAUCAAGGUGGCGG UGGACGCCAAGGCCAUCCUGAGCGCCAGACUGAGCAAGAGCAGAAGACUGGAGAA CCUGAUCGCCAGCUGCCGGCGAGAAGAAGAACGGCCUGUUCGGCAACCUGAUC GCCUGAGCCUGGGCCUGACCCCAACUUAAGAGCAACUUCGACCUGGCCGAGG ACGCCAAGCUGCAGCUGAGCAAGGACACCUACGACGACGACCCUGGACUUCGCU GGCCAGAUCCGGCGACCAGUACGCCGACCUGUUCUUGGCCGCAAGAACCUGAGC GACGCCAUCCUGCUGAGCGACAUCUUGAGAGUGAACACCCGAGAUCACCAAGGCC CCUGAGCGCCAGCAUGAUAAGAGAUACGACGAGCACCACCAGGACCUAGCCU GCUGAAGGCCUGGUGAGACAGCAGCUGCCCGAGAAGUACAAGGAGAUUCUUC GACCAGACAAGAACGGCUACGCCGGCUACAUCGACGGCGGCGCCAGCAGGAGG AGUUCUACAAGUUCAUCAAGCCCAUCUUGGAGAAGAUGGACGGCACCCGAGGAGCU GCUUGGUGAAGCUGAACAGAGAGGACCUGCUGAGAAAAGCAGAGAACCUUCGACAAC GGCAGCAUCCCCACCAGAUCCACCUGGGCGAGCUGCACGCCAUCCUGAGAAGAC AGGAGGACUUCUACCCUUCUGAAGGACAACAGAGAGAAGAUCCGAGAAGAUCCU GACCUUCAGAAUCCCCUACUACGUGGGCCCCUGGCCAGAGGCAACAGCAGAUUC GCCUGGAUGACCAGAAAGAGCGAGGAGACCAUACCCCCUGGAACUUCGAGGAGG UGGUGGACAAGGGCGCCAGCGCCAGAGCUUCAUCGAGAGAAUGACCAACUUCGA CAAGAACCUGCCCAACGAGAAGGUGCUGCCCAAGCAGCCUGCUGUACGAGUAC UUCACCGUGUACAACGAGCUGACCAAGGUGAAGUACGUGACCGAGGGCAUGAGAA AGCCCCCUUCCUGAGCGCGAGCAGAAGAAGGCCAUCGUGGACCUGCUGUUCAA GACCAACAGAAAGGUGACCGUGAAGCAGCUGAAGGAGGACUACUUAAGAAGAU CGAGUGCUUCGACAGCGUGGAGAUACGCGGCGUGGAGGACAGAUUCAACGCCAGC CUGGGCACCUACCACGACCUGCUGAAGAUCAUCAAGGACAAGGACUUCUGGACA ACGAGGAGAACGAGGACAUCUUGGAGGACAUCGUGCUGACCCUGACCCUGUUCGA GGACAGAGAGAUUGAUCGAGGAGAGACUGAAGACCUACGCCACCUGUUCGACGAC AAGGUGAUGAAGCAGCUGAAGAGAAGAAGAUACACCGCCUGGGGCGAGCUGAGC AGAAAGCUGAUAACGGCAUCAGAGACAAGCAGAGCGGCAAGACCAUCUGGACU UCCUGAAGAGCGACGGCUUCGCCAACAGAAAACUUAUGCAGCUGAUCACGACGGA CAGCCUGACCUUCAAGGAGGACAUCCAGAAGGCCAGGUGAGCGGCCAGGGCGAC AGCCUGCACGAGCACAUCCGCAACCUUGCCGGCAGCCCCGCCAUCAAGAAGGGCA UCCUGCAGACCGUGAAGGUGGUGGACGAGCUGGUGAAGGUGAUGGGCAGACACA AGCCCCGAGAACAUCGUGAUCGAGAUGGCCAGAGAGAACCAGACCCAGUCCUGGAGG CCAGAAGAACAGCAGAGAGAGAAUGAAGAGAAUCGAGGAGGGCAUCAAGGAGCU GGGAGCCAGAUCCUGAAGGAGCACCCCGUGGAGAACACCCAGCUGCAGAACGAG AAGCUGUACCUGUACUACCUGCAGAACGGCAGAGACAUGUACGUGGACCAGGAGC UGGACAUCAACAGACUGAGCGACUACGACGUGGACCACAUCGUGCCCCAGAGCUU CCUGAAGGACGACAGCAUCGACAACAAGGUGCUGACCAAGAAGCGACAAGAACAGA GGCAAGAGCGACAACGUGCCCAGCGAGGAGGUGGUGAAGAAGAUGAAGAACUAC UGGAGACAGCUGCUGAACGCCAAGCUGAUCACCCAGAGAAAGUUCGACAACCUGA CCAAGGCCGAGAGAGGCGGCCUGAGCGAGCUGGACAAGGCCGGCUUCAUCAAGAG ACAGCUGGUGGAGACCAGACAGAUACCAAGCAGCUGGCCAGAUCCUGGACAGC AGAAUGAACACCAAGUACGACGAGAACGACAAGCUGAUCAGAGAGGUGAAGGUG AUCACCCUGAAGAGCAAGCUGGUGAGCGACUUCAGAAAGGACUUCAGUUCUACA AGGUGAGAGAGAUCAACAACUACCACCACGCCACGACGCCUACCUGAACGCCGU GGUGGGCACCCGCCUGAUCAGAAGUACCCCAAGCUGGAGAGCGAGUUCGUGUAC GGCGACUACAAGGUGUACGACGUGAGAAAGAUUGAUCGCCAAGAGCGAGCAGGAG AUCGGCAAGGCCACCCCAAGUACUUCUUCUACAGCAACAUCAUGAACUUCUUC AGACCGAGAUACCCUGGCCAACGGCGAGAUCAAGAAAGAGACCCUGAUCGAGAC CAACGGCGAGACCGGCGAGAUCCUGUGGGACAAGGGCAGAGACUUCGCCACCCGUG AGAAAGGUGCUGAGCAUGCCCAAGGUGAACUUCGUGAAGAAGACCCGAGGUGCAG ACCGGGCGCUUCAGCAAGGAGAGCAUCCUGCCCAAGAGAAACAGCGACAAGCUGA UCGCCAGAAAGAAGGACUGGGACCCCAAGAAGUACGGCGGCUUCGACAGCCCCAC</p>	<p>176</p>

[0780]

[0782]

	<p>AGCUGCUGAACGCCAAGCUGAUCACCCAGCGGAAGUUCGACAACCCUGACCAAGGC CGAGCGGGGCGGCCUGUCCGAGCUGGACAAGGCCGGCUUCAAGCGGCAGCUG GUGGAGACCCGGCAGAUACCAAGCAGUGGCCAGAUCCUGGACUCCCGGAUGA ACACCAAGUACGACGAGAACGACAAGCUGAUCGGGAGGUGAAGGUGAUCACCCU GAGUCCAAGCUGGUUCCGACUUCGGGAAGGACUUCAGUUCUACAAGGUGCGG GAGAUACAACAACUACCACCGCCACGACGCCUACCUGAACGCCGUGGUGGGCA CCGCCUGAUCAGAAGUACCCCAAGCUGGAGUCCGAGUUCGUGUACGGCGACUA CAAGGUGUACGACGUGCGGAAGAUAGUCCGAAGUCCGAGCAGGAGAUCCGGAAG GCCACCGCCAAGUACUUCUUCUACUCCAACAUCUAGAACUUCUUAAGACCGGAGA UCACCCUGGCCAACGGCGAGAUCCGGAAGCGGCCCCUGAUCGACCAACCGGCGA GACCGGCGAGAUCCGUGGGACAAGGGCCGGGACUUCGCCACCGUGCGGAAGGUG CUGUCCAUGCCCCAGGUGAACAUCCGUAAGAAGACCGAGGUGCAGACCGGCGGCU UCUCCAAGGAGUCCAUCUGCCCAAGCGGAACUCCGACAAGCUGAUCGCCCGGAA GAAGGACUGGGACCCCAAGAAGUACGGCGGCUUCGACUCCCCACCGUGGCCUAC UCCGUGCUGGUGGGCCAAGGUGGAGAAGGGCAAGUCCAAGAAGCUGAAGUCC GUGAAGGAGCUGCUGGGCAUCACCAUCAUGGAGCGGUCCUCCUUCGAGAAGAACC CCAUCGACUCCUGGAGGCCAAGGGCUACAAGGAGGUGAAGAAGGACCUGAUCAU CAAGCUGCCCAAGUACUCCUGUUCGAGCUGGAGAACGGCCGGAAGCGGAUGCUG GCCUCCGCCGGCGAGCUGCAGAAGGGCAACGAGCUGGCCUCCUCCAAGUACG UGAACUCCUGUACCUCCUGGCCUCCACUACGAGAAGCUGAAGGGCCUCCCGGGA CAACGAGCAGAAGCAGCUGUUCGUGGAGCAGCACAAGCACUACCUGGACGAGAU AUCGAGCAGAUCCGAGUUCUCCAAGCGGGUGAUCUCCGCGACGCCAACCUUG ACAAGGUGCUGUCCGCCUACAACAAGCACCGGGACAAGCCAUCCGGGAGCAGGC CGAGAACAUAUCCACCGUUCACCCUGACCAACCUCCGCGCCUCCCGGCGUUA AGUACUUCGACACCACCAUCGACCGGAAGCGGUACACCUCCACCAAGGAGGUGCU GGACGCCACCCUGAUCCACAGUCCAUCACCGGCCUGUACGAGACCCGGAUCGAC CUGUCCAGCUGGGCGGCGACGGCGGCGGCUCCCAAGAAGAAGCGGAAGGUGU GACUAGCACAGCCUCAAGAACACCCGAAUGGAGUCUCAAGCUACAUAUACCA ACUUAACAUUUACAAAUGUUGUCCCAAAAUGUAGCCAUUCGUAUCUGCUCU AAUAAAAAGAAAGUUCUUCACAUUCUCUCGAGAAAAAAAAAAAAAAAAAAAAAA AA AAAAAAAAAAAAAAAAAAAAAAAAAUCUAG</p>	
<p>具有 XBG UTR 及含有 表4的低U/A 密码子的 Cas9 ORF的 mRNA 转录 物</p>	<p>GGGAAGCUCAGAAUAAACGCUCAACUUGGCCGGAUCUGCCACCAUGGACAAGAA GUACAGAUCCGGCCUGGACAUCCGGCACCAACAGCGUGGGGCGGUGAUCACC GACGAGUACAAGGUGCCAGCAAGAAGUUCAGGUGCUGGGCAACACCGACCGGC ACAGCAUCAAGAAGAACCUGAUCGGCGCCUUCGUGUUCGACAGCGGCGAGACCGC CGAGGCCACCCGGCUGAAGCGGACCGCCGGCGGCGGUACACCCGGCGGAAGAAC CGGAUCUGCUACCUCCGAGGAGAUUCUACGCAACGAGAUUGGCCAAGGUGGACACA GCUUCUCCACCGGCUUGGAGGAGCUCUCCUGGUGGAGGAGGACAAGAAGCACGA GCGGCACCCCAUCUUCGGCAACAUCGUGGACGAGGUGGCCUACACGAGAAGUAC CCCACCAUCUACCAUCUGCGGAAGAAGCUGGUGGACAGCACCGACAAGGCCGACC UGCGGCUGAUCUACCUGCCUUGGCCACAUGAUAAGUUCGGGGCCACUUCU GAUCGAGGGCGACCUGAACCCCGACAACAGCGACGUGGACAAGCUGUUCUACUCCAG CUGGUGCAGACCUACAACCAGCUGUUCGAGGAGAACCCCAUCAACGCCAGCGGCG UGGACGCCAAGGCCAUCCUGAGCGCCGGCUGAGCAAGAGCCGGCGGCUUGGAGAA CCUGAUCGCCAGCUGCCGGCGAGAAGAAGAAGCGGCUUUCGGCAACCUGAUC CCCCUGAGCCUGGGCCUGACCCCAACUUCAGAGCAACUUCGACUCCGCGGAGG ACGCCAAGCUGCAGCUGAGCAAGGACACCUACGACGACGACCUGGACAACCUUCU GGCCCAGAUCCGGCGACAGUACGCCGACCUUUCUGGCCGCAAGAACCUGAGC GACGCCAUCCUGCUGAGCGACAUCUUCGCGGUGAACACCGAGAUACCAAGGCC CCCUGAGCGCCAGCAUGAUAAGCGGUACGACGAGCACACCAGGACCUGACCCU GCUGAAGGCCUUGGUGCGGCAGCAGCUGCCCGAGAAGUACAAGGAGAUUCUUCU GACCAGAGCAAGAACGGCUACGCCGGCUACAUCGACGGCGGCCAGCCAGGAGG AGUUCUACAAGUUCUACAAGCCAUCCUGGAGAAGAUUGGACGGCACCGAGGAGCU GCUGGUGAAGCUGAACCGGGAGGACCUGCUGCGGAAGCAGCGGACCUUCGACAAC GGCAGAUCCCCACCAGAUCCACCUCCGAGCUGCAGCAGCAUCCUGCGGCGGC AGGAGGACUUCUACCCUUCUUGAAGGACAACCGGGAGAAGAUUCGAGAAGAUCCU GACCUUCGGAUCCCUACUACGUGGGCCCCUGGCCCGGGGAACAGCCGGUUC GCCUGGAUGACCCGGAAGAGCGAGGAGACCAUCACCCUUGGAACUUCGAGGAGG UGGUGGACAAGGGCGCCAGCGCCAGAGCUUCAUCGAGCGGAUGACCAACUUCGA CAAGAACCUGCCCAACGAGAAGGUGCUGCCCAAGCACAGCCUGCUGUACGAGUAC UUCACCGUGUACAACGAGCUGACCAAGGUGAAGUACGUGACCGAGGGCAUCGCGA AGCCCGCCUUCUGAGCGGCGAGCAGAAGAAGGCCAUCGUGGACCUGCUGUUCAA GACCAACCGGAAGGUGACCGUGAAGCAGCUGAAGGAGGACUACUUAAGAAGAU GAGUUCUUCGACAGCUGGAGAUACGCGGCGUGGAGGACCGGUUCAACGCCAGCC UGGGCACCUACCAGCACCUGCUGAAGAUCAUCAAGGACAAGGACUUCUUGGACAA CGAGGAGAACGAGGACAUCUGGAGGACUUCGUGCUGACCCUGACCCUGUUCGAG</p>	<p>178</p>

[0783]

	<p>GACCGGGAGAUGAUCGAGGAGCGGCUGAAGACCUACGCCACCUGUUCGACGACA AGGUGAUGAAGCAGCUGAAGCGGCGGCGGUACACCGGCUGGGGCCGGCUGAGCCG GAAGCUGAUGAAGCAGCUGAAGCGGCGGCGGUACACCGGCUGGGGCCGGCUGAGCCG CUGAAGAGCGACGGCUUCGCCAACCGGAACUUAUGCAGCUGAUCCACGACGACA GCCUGACCUUCAAGGAGGACAUCAGAAAGGCCAGGUGAGCGGGCAGGGCGACAG CCUGCAGCAGCACAUCGCCAACCUUGGCCGGCAGCCCGCCAUAAGAAGGGCAUC CUGCAGACCGUGAAGGUGGUGGACGAGCUGGUGAAGGUGAUGGGCCGGCACAAG CCCAGAACAUUCGUGAUCGAGAUUGGCCCGGGAGAACCAGACCACCCAGAAGGGCC AGAAGAACAGCCGGGAGCGGAUGAAGCGGAUCGAGGAGGGCAUCAAGGAGCUGG GCAGCCAGAUCCUGAAGGAGCACCCCGUGGAGAACACCCAGCUGCAGAACGAGAA GCUGUACCUGUACUACCGGCAAGCAGAACCGCCGGGACAUGUACGUGACCAGGAGCUG GACAUCAACCGGCUGAGCGACUACGACGUGGACCACAUCGUGCCCCAGAGCUUCC UGAAGGACGACAGCAUCGACAACAAGGUGCUGACCCGGAGCGACAAGAACCAGGGG CAAGAGCGACAACGUGCCCAGCGAGGAGGUGGUGAAGAAGAUGAAGAACUACUG CGGCGAGCUGCUGAACGCCAAGCUGAUCACCCAGCGGAAGUUCGACAGGAGACC AAGGCCGAGCGGGCGGCCUGAGCGAGCUGGACAAGGCCGGCUUCAUAAGCGGC AGCUGGUGGAGACCCGGCAGAUACCAAGCACGUGGCCAGAUCCUGGACAGCCG GAUGAACACCAAGUACGACGAGAACGACAAGCUGAUCGGGAGGUGAAGGUGAU CACCCUGAAGAGCAAGCUGGUGAGCGACUUCGGAAAGGACUUCAGUUCUACAAG GUCGCGGGAUCAACAACUACCCACGCCCACGACGCCUACCCUGAACCCGAGGUGG UGGGCACCCGCCUGAUCAGAAGUACCCCAAGCUGGAGAGCGAGUUCGUGUACGG CGACUACAAGGUGUACGACGUGCGGAAGAUCAUCGCAAGAGCGAGCAGGAGAUC GGCAAGGCCACCCCAAGUACUUCUUCUACAGCAACAUCAUAGAACUUCUUAAGA CCGAGAUACCCUGGCCAACGGCGAGAUCCGGAAGCGGCCCCUGAUCGAGGACAA CGGCGAGACCGGCGAGAUUCGUGGGACAAGGGCCGGGACUUCGCCACCCGUGCGG AAGGUGCUGAGCAUGCCCCAGGUGAACAUUCGUGAAGAAGACCCGAGGUGCAGACCG GCGGCUUCAGCAAGGAGAGCAUCCUGCCCAAGCGGAACAGCGACAAGCUGAUCGC CCGGAAGAAGGACUGGGACCCCAAGAAGUACGGCGGCUUCGACAGCCCCACCGUG GCCUACAGCGUGCUGGUGGUGGCCAAGGUGGAGAAAGGGCAAGAGCAAGAAGCUG AAGAGCGUGAAGGAGCUGCUGGGCAUCACCAUCAUGGAGCGGAGCAGCUUCGAGA AGAACCCCAUCGACUUCUGGAGGCCAAGGGCUACAAGGAGGUGAAGAAGGACCU GAUCAUCAAGCUGCCCAAGUACAGCCUGUUCGAGCUGGAGAACGGCCGGAAGCGG AGUACGUGAACUUCUGUACCCUGGCCAGCCACUACGAGAAGCUGAAGGGCAGCCC CGAGGACAACGAGCAGAAGCAGCUGUUCGUGGAGCAGCACAAGCACUACCCUGGAC GAGAUCAUCGAGCAGAUACGCGAGUUCAGCAAGCGGGUGAUCCUGGCCGACGCCA ACCCUGGACAAGGUGCUGAGCGCCUACAACAAGCACCCGGGACAAGCCCAUCCCGGA GCAGGCCGAGAACAUCUACCCUUGUACCCUGACCAACCCUGGGCGCCUCCCGCCG CCUUAAGUACUUCGACACCACCAUCGACCCGGAAGCGGUACACCAGCACCAAGGA GGUGCUGGACGCCACCCUGAUCCACCAGAGCAUACCCGGCCUGUACGAGACCCGG AUCGACCUAGCCAGCUGGGCGGCGACGGCGGCGGACGCCCAAGAAGAAGCGGA AGGUGAGACUAGCACCCAGCCUCAAGAACACCCGAAUGGAGUCUCUAAGCUACAUA AUACCAACUACACUUUACAAAUGUUGUCCCCCAAAAUGUAGCCAUUCGUUAUCU GCUCCUAAUAAAAAGAAAGUUUCUUCACAUUCUCUCGAGAAAAAAAAAAAAAAAAAA AA AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAUCUAG</p>	
<p>具有编码带 有HiBiT标记 标签的 Cas9 的 ORF、HSD 5' UTR 及 人类 ALB 3' UTR 的 mRNA 转录 物</p>	<p>GGGTCCCAGTCGGCGTCCAGCGGCTTGCTTGTTCTGTGTGTGTCTGTCAGGC CTTATTCGGATCCGCCACCATGGACAAGAAGTACAGCATCGGACTGGACATCGGAAC AAACAGCGTCGGATGGGCAGTCATCACAGACGAATACAAGGTCCCGAGCAAGAAGT TCAAGGTCCTGGGAAAACAGACAGACACAGCATCAAGAAGAACCTGATCGGAGCA CTGCTGTTGACAGCGGAGAAAACAGCAGAAGCAACAAGACTGAAGAGAACAGCAA GAAGAAGATACACAAGAAGAAAGAACAAGAATCTGCTACTGCAAGGAAATCTTCAGC AACGAAATGGCAAAGGTCGACGACAGCTTCTTCCACAGACTGGAAGAAAGCTTCT GGTCAAGAAGACAAGAAGCACGAAAGACACCCGATCTTCGGAACATCGTCGACG AAGTTCGCATACCACGAAAAGTACCCGACAATCTACCACCTGAGAAAAGAAGCTGGTCG ACAGCACAGACAAGGCAGACTGAGACTGATCTACTGGCACTGGCACACATGATCA AGTTTCAGAGGACACTTCTGATCGAAGGAGACTGAACCCGGACAACAGCGACGTC GACAAGCTGTTATCCAGCTGGTCCAGACATACAACCAGCTGTTCAAGAAAACCCG ATCAACGCAAGCGGAGTCGACGCAAAAGGCAATCCTGAGCGCAAGACTGAGCAAGAG CAGAAGACTGGAAAACCTGATCGCACAGCTGCCGGGAGAAAAGAAGAACGGACTGT TCGAAAACCTGATCGCACTGAGCCTGGGACTGACACCCAACTTCAAGAGCAACTTCG ACCTGGCAGAAGACGCAAAGCTGACGCTGAGCAAGGACACATACGACGACGACCTG GACAACCTGCTGGCACAGATCGGAGACCACTACGACAGCCTGTTCTGGCAGCAAAA GAACCTGAGCGACGCAATCTGCTGAGCGACATCTGAGAGTCAACACAGAAATCAC AAAGGCACCGCTGAGCGCAAGCATGATCAAGAGATACGACGAACACCACAGGACC TGACACTGCTGAAGGCACTGGTCAGACAGCAGCTGCCGAAAAGTACAAGGAAATC TTCTTCGACCAGAGCAAGAACGGATACGACGATACATCGACGGAGGAGCAAGCCA</p>	<p>179</p>

[0784]

	<p>GGAAGAATTCTACAAGTTCATCAAGCCGATCCTGGAAAAGATGGACGGAACAGAAGA ACTGCTGGTCAAGCTGAACAGAGAAAGACCTGCTGAGAAAAGCAGAGAACATTCGACA ACGGAAGCATCCCACCAGATCCACCTGGGAGAAGTGCACGCAATCCTGAGAAGA CAGGAAGACTTCTACCCGTTCTGAAGGACAACAGAGAAAAGATCGAAAAGATCCT GACATTCAGAATCCCGTACTACGTCGGACCGCTGGCAAGAGGAAAACGACGATTCGC ATGGATGACAAGAAAAGAGCGAAGAAAACAATCACACCGTGGAACTTCGAAGAAAGTCG TCGACAAGGGAGCAAGCGCACAGAGCTTCATCGAAAAGAAATGACAAACTTCGACAAG AACCTGCCGAACGAAAAGGTCTGCCGAAGCACAGCTGCTGTACGAATACTTCACA GTCTACAACGAACTGACAAAAGGTCAAGTACGTCACAGAAGGAATGAGAAAAGCCGGC ATTCTGAGCGGAGAACAGAAGAAGGCAATCGTCGACCTGCTGTTCAAGACAAAACA GAAAAGTTCACAGTCAAGCAGCTGAAGGAAGACTACTTCAAGAAGATCGAATGCTTC GACAGCGTCGAAATCAGCGGAGTCGAAGACAGATTCAACGCAAGCCTGGGAACATA CCACGACCTGCTGAAGATCATCAAGGACAAGGACTTCCTGGACAACGAAGAAAACG AAGACATCCTGGAAGACATCGTCTGACACTGACACTGTTGGAAGACAGAGAAATGA TCGAAGAAAAGACTGAAGACATACGCACACCTGTTTCGACGACAAGGTATGAAGCAG CTGAAGAGAAGAAGATACACAGGATGGGGAAGACTGAGCAGAAAAGCTGATCAACGG AATCAGAGACAAGCAGAGCGGAAAAGACAATCCTGGACTTCTGAAGAGCGACGGAT TCGCAAAACAGAACTTCATGCAGCTGATCCACGACGACAGCCTGACATTCAAGGAAG ACATCCAGAAGGCACAGGTCAGCGGACAGGGAGACAGCCTGCACGAACACATCGCA AACCTGGCAGGAAGCCCGGCAATCAAGAAGGGAATCCTGCAGACAGTCAAGTCTGT CGACGAACTGGTCAAGGTTCATGGGAAGACACAAGCCGAAAAACATCGTATCGAAA TGGCAAGAGAAAACCAGACAACACAGAAGGGACAGAAGAACAGCAGAGAAAAGAAT GAAGAGAATCGAAGAAGGAATCAAGGAAGTGGGAAGCCAGATCCTGAAGGAACACC CGGTCGAAAACACACAGCTGCAGAACGAAAAGTGTACTGTACTGACGACAC GGAAGAGACATGTACGTCGACCAGGAACTGGACATCAACAGACTGAGCGACTACGA CGTCGACCACATCGTCCCGCAGAGCTTCTGAAGGACGACAGCATCGACAACAAGGT CCTGACAAGAAGCGACAAGAACAGAGGAAAAGAGCGACAACGTCCCGAGCGAAGAA GTGCTCAAGAAGATGAAGAAGTACTGGAGACAGCTGCTGAACGCAAAGCTGATCAC ACAGAGAAAAGTTCGACAACCTGACAAAAGGCAGAGAGAGGAGGACTGAGCGAACTG GACAAGGCAGGATTCATCAAGAGACAGCTGGTCGAAAACAAGACAGATCACAAAAGCA CGTCGCACAGATCCTGGACAGCAGAATGAACACAAGTACGACGAAAACGACAAGC TGATCAGAGAAGTCAAGGTTCATCAGTGAAGAGCAAGCTGGTCAGCGACTTCAGA AAGGACTTCCAGTTCATCAAGGTTCAGAGAAATCAACAAGTACCACACGACACGAC GCATACCTGAACGCAGTTCGGAACAGCACTGATCAAGAAGTACCCGAAGCTGGAA AGCGAATTCGTCTACGGAGACTACAAGGTCTACGACGTGAGAAAAGATGATCGCAAAG AGCGAACAGGAAATCGGAAAAGGCAACAGCAAAGTACTTCTTCTACAGCAACATCATG AACTTCTCAAGACAGAAATCACACTGGCAAACGGAGAAATCAGAAAAGAGACCGCT GATCGAAAACAAACGGAGAAAACAGGAGAAAATCGTCTGGGACAAGGGAAAGAGACTTCG CAACAGTCAGAAAGGTCTGAGCATGCCGACGGTCAACATCGTCAAGAAGACAGAA GTCCAGACAGGAGGATTCAGCAAGGAAAGCATCCTGCCGAAGAGAAAACAGCGACAA GCTGATCGCAAGAAAAGAGGACTGGGACCCGAAGAAGTACGGAGGATTCGACAGCC CGTAGTCGCATACAGGTCCTGGTCTGCAAAAGGTGCAAAAAGGGAAGGAAAGCAAG AAGCTGAAGAGCGTCAAGGAACTGCTGGGAATCACAATCATGGAAAAGAGCAGCTT CGAAAAGAACCCTGATCGACTTCTGGAAGCAAAGGATACAAGGAAGTCAAGAAGG ACCTGATCATCAAGTCCGAAAGTACAGCCTGTTGCAACTGGAAAACGGAAAGAAAG AGAATGCTGGCAAGCGCAGGAGAACTGCAGAAGGGAAACGAACTGGCACTGCCGA GCAAGTACGTCAACTTCTGTACTGCAAGCCACTACGAAAAGTGAAGGGAAGCC CGGAAGACAACGAACAGAAGCAGCTGTTGTCGAACAGCACAAGCACTACCTGGAC GAAATCATCGAACAGATCAGCGAATTCAGCAAGAGAGTATCCTGGCAGACGCAAAC CTGGACAAGGTCTGAGCGCATAACAAGCACAGAGACAAGCCGATCAGAGAACA GGCAGAAAACATCATCCACCTGTTCAACTGACAAAACCTGGGAGCACCCGGCAGCATT CAAGTACTTCGACACAACAATCGACAGAAAAGAGATACACAAGCACAAAAGGAAGTCC TGGACGCAACTGATCCACCAGAGCATCACAGGACTGTACGAAAACAAGAATCGACC TGAGCCAGCTGGGAGGAGACGGAGGAGGAAGCCCGAAGAAGAAGAGAAAAGGTCAG CGAAAAGCGCAACACCGGAAAGCGTCAGCGGATGGAGACTGTTCAAGAAGATCAGCT AGCTAGCCATCACATTTAAAAGCATCTCAGCCTACCATGAGAATAAGAGAAAAGAAAT GAAGATCAATAGCTTATTCATCTCTTTTCTTTTCTGTTGGTGTAAGCCAACACCCTG TCTAAAAAACATAAATTTCTTTAATCATTTTGCCTCTTTTCTCTGTGCTTCAATTAATAA AAAATGGAAGAAGCTCGAGAAA AA AAATCTAG</p>	
<p>具有编码带 有HiBiT标记 标签的 Cas9 的 ORF、</p>	<p>GGGAGATCGCCTGGAGACGCCATCCACGCTGTTTTGACCTCCATCGCCACCATGGAC AAGAAGTACAGCATCGGACTGGACATCGGAACAAAACAGCGTCCGGATGGGCAGTCATC ACAGACGAATACAAGGTCCCAGCAAGAAGTTCAAGGTCCTGGGAAACACAGACAG ACACAGCATCAAGAAGAACCTGATCGGAGCACTGCTGTTTCGACAGCGGAGAAAACAG CAGAAGCAACAAGACTGAAGAGAACAGCAAGAAGAAGATACACAAGAAGAAAAGAA CAGAATCTGCTACTGTCAGGAAATCTTCAGCAACGAAATGGCAAAGGTTCGACGACAG</p>	<p>180</p>

<p>CMV-1 5' UTR 及人类 ALB 3' UTR 的 mRNA 转录 物</p>	<p>CTTCTTCCACAGACTGGAAGAAAGCTTCTTGGTCTGGAAGAAGACAAGAAGCACGAAA GACACCCGATCTTCGGAAACATCGTCGACGAAAGTCGCATACCACGAAAAGTACCCGA CAATCTACCACCTGAGAAAAGAAGCTGGTCGACAGCACAGACAAGGCAGACCTGAGA CTGATCTACCTGGCACTGGCACACATGATCAAGTTTACAGAGGACACTTCTGATCGAAG GAGACCTGAACCCGGACAACAGCGACGTCGACAAGCTGTTTATCCAGCTGGTCCAG ACATACAACCAGCTGTTCTGAAGAAAACCCGATCAACGCAAGCGGAGTGCAGCAGAAA GGCAATCCTGAGCGCAAGACTGAGCAAGAGCAGAAGACTGGAAAACCTGATCGCAC AGCTGCCGGGAGAAAAGAAGAACGGACTGTTCCGGAAACCTGATCGCACTGAGCCTG GGACTGACACCGAACTTCAAGAGCAACTTCGACCTGGCAGAAGACGCAAAAGCTGCA GCTGAGCAAGGACACATACGACGACGACCTGGACAACCTGCTGGCAGATCGGAG ACCAGTACGCAGACCTGTTCTGGCAGCAAAAGAACCTGAGCGACGCAATCCTGTGA GCGACATCCTGAGAGTCAACACAGAAATCACAAAGGCACCGCTGAGCGCAAGCATG ATCAAGAGATACGACGAACACCACCAGGACCTGACACTGCTGAAGGCACTGGTCAG ACAGCAGCTGCCGAAAAGTACAAGGAAATCTTCTTCGACCAGAGCAAGAAGCGGAT ACGAGATAATCGACGGAGGAGCAAGCCAGGAAGAAATTCTACAAGTTTCAATCAAGC CGATCCTGAAAAAGATGGACGGAACAGAAGAAGTCTGGTCAAGCTGAACAGAGAA GACCTGCTGAGAAAAGCAGAGAACATTCGACAACGGAAAGCATCCCGCACCAGATCCA CCTGGGAGAACTGCACGCAATCCTGAGAAGACAGGAAGACTTCTACCCGTTTCTGAA GGACAACAGAGAAAAGATCGAAAAGATCCTGACATTCAGAATCCCGTACTACGTCGG ACCGTGGCAAGAGGAAACAGCAGATTTCGATGGATGACAAGAAAAGCGAAGAAA CAATCACACCGTGGAACTTTCGAAGAAGTCGTCGACAAGGGAGCAAGCGCACAGAGC TTCATCGAAAAGATGACAAACTTCGACAAGAACCTGCCGAACGAAAAGGTCTGCC GAAGCACAGCCTGCTGTACGAATACTTACAGTCTACAACGAACTGACAAAAGGTCAA GTACGTCACAGAAGGAATGAGAAAAGCCGGCATTCTGAGCGGAGAAAGCAAGAAAGG CAATCGTCGACCTGCTGTTCAAGACAAAACAGAAAAGGTACAGTCAAGCAGCTGAAG GAAGACTACTTCAAGAAGATCGAATGCTTCGACAGCGTCAAATCAGCGGAGTCAA GACAGATTCAACGCAAGCCTGGGAACATACCACGACCTGCTGAAGATCATCAAGGAC AAGGACTTCTGGACAACGAAGAAAACGAAGACATCCTGGAAGACATCGTCTGAC ACTGACACTGTTGGAAGACAGAGAAAATGATCGAAGAAAAGACTGAAGACATACGCAC ACCTGTTGACGACAAGGTGATGAAGCAGCTGAAGAGAAGAAGATACACAGGATGG GGAAGACTGAGCAGAAAAGCTGATCAACGGAATCAGAGACAAGCAGAGCGGAAAAGA CAATCCTGGACTTCTGAAAGAGCGACGGATTTCGAAAACAGAAAATTCATGCAGCTGA TCCACGACGACAGCCTGACATTCAGGAAGACATCCAGAAGGCACAGGTCAGCGGA CAGGGAGACAGCCTGCACGAACACATCGCAAACCTGGCAGGAAGCCCGGCAATCAA GAAGGGAATCCTGCAGACAGTCAAGGTGCTGACGAACTGGTCAAGGTATGGGAA GACACAAGCCGAAAACATCGTCATCGAAATGGCAAGAGAAAACAGACAACACAG AAGGGACAGAAGAACAGCAGAGAAAAGAATGAAGAGAATCGAAGAAGGAATCAAGG AACTGGGAAGCCAGATCTGAAAGGAACACCCCGTTCGAAAACACACAGCTGCAAGC GAAAAGCTGTACTGTACTACCTGCAGAACGGAAGAGACATGTACGTCGACCAGGAA CTGGACATCAACAGACTGAGCGACTACGACGTCGACCACATCGTCCCGCAGAGCTTC TGAAGGACGACAGCATCGACAACAAGGTCTGACAAGAAGCGCAAGAAGAACAGAG GAAAGAGCGACAACGTCCGAGCGAAGAAGTCTGTCGAAGAAGATGAAGAAGTCACTGG AGACAGCTGCTGAACGCAAAAGCTGATCACACAGAGAAAAGTTCGACAACCTGACAAA GGCAGAGAGAGGAGGACTGAGCGAACTGGACAAGGCAGGATTCATCAAGAGACAG CTGGTTCGAAAACAAGACAGATCACAAGCAGTTCGACAGATCCTGGACAGCAGAAT GAACACAAAAGTACGACGAAAACGACAAGCTGATCAGAGAAGTCAAGGTATCACAC TGAAGAGCAAGCTGGTCAAGCACTTCAGAAAGGACTTCCAGTTTACAAGGTCAAG GAAATCAACAACCTACCACCACGCACACGACGCATACCTGAACGCAGTCTGTCGGAACA GCACTGATCAAGAAGTACCCGAAGCTGGAAAAGCGAATTTCGTCTACGGAGACTACAAG GTCTACGACGTCAGAAAAGATGATCGAAAAGAGCGAACAGGAAATCGGAAAAGGCAAC AGCAAAAGTACTTCTTACAGCAACATCATGAACTTCTTCAAGACAGAAAATCACACTG GCAAAACGGAGAAATCAGAAAAGAGACCCTGATCGAAAACAAACGGAGAAAACAGGAG AAATCGTCTGGGACAAGGGAAAGAGACTTCGCAACAGTCAAGAAAGGTCTGAGCATG CCGAGGTCAACATCGTCAAGAAGACAGAAGTCCAGACAGGAGGATTCAGCAAGGA AAGCATCTGCCGAAGAGAAAACAGCGACAAGCTGATCGCAAGAAAAGAAGGACTGGG ACCCGAAGAAGTACGGAGGATTCGACAGCCCGACAGTTCGCATACAGCGTCTGGTCCG TCGCAAAAGGTTCGAAAAGGGAAAAGAGCAAGAAGCTGAAGAGCGTCAAGGAACTGCT GGGAATCACAATCATGAAAAGAAGCAGCTTCGAAAAGAACCAGATCGACTTCTGGAA AGCAAAAGGGATACAAGGAAGTCAAGAAAGGACCTGATCATCAAGTCCGCAAGTACA GCCTGTTTCAACTGGAAAACGGAAGAAAAGAGAATGCTGGCAAGCGCAGGAGAAGT CAGAAGGGAAAACGAACTGGCACTGCCGAGCAAGTACGTCAACTTCTGTACTCTGGC AAGCCACTACGAAAAGCTGAAGGGAAAGCCCGAAGACAACGAACAGAAGCAGCTG TTCGTGCAACAGCACAAGCACTACCTGGACGAAATCATCGAACAGATCAGCGAATTC AGCAAGAGAGTATCCTGGCAGACGCAAACTGGACAAGGTCTGAGCGCATAACA CAAGCACAGAGACAAGCCGATCAGAGAACAGGCAGAAAACATCATCCACCTGTTCA CACTGACAAAACCTGGGAGCACCGGCAGCATTCAAGTACTTCGACACAACAATCGACA GAAAGAGATACACAAGCACAAGGAAGTCTGGACGCAACTGATCCACCAGAGC</p>
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[0786]

	<p>ATCACAGGACTGTACGAAACAAGAATCGACCTGAGCCAGCTGGGAGGAGACGGAGG AGGAAGCCCGAAGAAGAAGAGAAAAGGTCAGCGAAAAGCGCAACACCCGAAAAGCGTC AGCGGATGGAGACTGTTCAAGAAGATCAGCTAGCTAGCCATCACATTTAAAAGCATCT CAGCCTACCATGAGAATAAGAGAAAAGAAAATGAAGATCAATAGCTTATTCATCTCTTT TTCTTTTTCGTTGGTGTAAAGCCAACACCCCTGTCTAAAAAACATAATTTCTTTAATCA TTTTGCCCTTTTTCTGTGCTTCAATTAATAAAAAATGGAAAGAACCCTCGAGAAAAA AAA AAA</p>	
<p>具有编码带 有HiBiT标记 标签的 Cas9 的 ORF、 CMV-2 5' UTR 及人类 ALB 3' UTR 的 mRNA 转录 物</p>	<p>GGGAGAAGACACCGGGACCGATCCAGCCTCCGCGGCCGGGAACGGCGCCACCATGG ACAAGAAGTACAGCATCGGACTGGACATCGGAACAAAACAGCGTCGGATGGGCAGTC ATCACAGACGAATACAAGGTCCCGAGCAAGAAGTTCAAGGTCCTGGGAAACACAGA CAGACACAGCATCAAGAAGAACCCTGATCGGAGCACTGCTGTTTCGACAGCGGAGAAA CAGCAGAAGCAACAAGACTGAAGAGAACAGCAAGAAGAAGATACACAAGAAGAAA GAACAGAATCTGCTACCTGCAGGAAATCTTCAGCAACGAAATGGCAAAGGTCGACGA CAGCTTCTCCACAGACTGGAAGAAAGCTTCTGGTCGAAGAAGACAAGAAGCAGC AAAAGACACCCGATCTTCGAAACATCGTCGACGAAGTCGCATACCACGAAAAGTACC CGACAATCTACCACCTGAGAAAGAAGCTGGTCGACAGCACAGACAAGGCAGACCTG AGACTGATCTACCTGGCACTGGCACACATGATCAAGTTTCAGAGGACACTTCTGATCG AAGGAGACCTGAACCCGGACAACAGCGACGTCGACAAGCTGTTTCATCCAGCTGGTC CAGACATACACCAGCTGTTTCGAAGAAAACCCGATCAACGCAAGCGGAGTCGACGC AAAGGCAATCCTGAGCGCAAGACTGAGCAAGAGCAGAAGACTGGAAAACCTGATCG CACAGCTGCCGGGAGAAAAGAAGAACGGACTGTTTCGAAACCTGATCGCACTGAGC CTGGGACTGACACCGAACTTCAAGAGCAACTTCGACCTGGCAGAAGACGCAAAAGT GCAGCTGAGCAAGGACACATACGACGACGACCTGGACAACCTGCTGGCAGATCGT GAGACCAAGTACGCAGACCTGTTCTGGCAGCAAAAGAACCCTGAGCGCAGCAATCCTGC TGAGCGACATCTGAGAGTCAACACAGAAATCAAAAGGCACCCGCTGAGCGCAAGC ATGATCAAGAGATACGACGAACACCACAGGACCTGACACTGCTGAAGGCAGTGGTC AGACAGCAGCTGCCGAAAAGTACAAGGAAATCTTTCGACCAGAGCAAGAACCGG ATACGCAGGATACATCGACGGAGGAGCAAGCCAGGAAGAATTCTACAAGTTCATCAA GCCGATCTGAAAAGATGGACGGAACAGAAGAAGTCTGGTCAAGCTGAACAGAG AAGACCTGCTGAGAAAAGCAGAGAACATTCGACAACGGAAGCATCCCGCACCAGATC CACCTGGGAGAACTGCACGCAATCCTGAGAAGACAGGAAGACTTCTACCCGTTTCTG AAGGACAACAGAGAAAAGATCGAAAAGATCTGACATTCAGAATCCCGTACTACGTC GGACCGCTGGCAAGAGGAAACAGCAGATTTCGCATGGATGACAAGAAGAGCGAAGA ACAATCACACCGTGAACCTTCAAGAAGTCTGTCGACAAGGGAGCAAGCGCACAGA GCTTCATCGAAAAGAAATGACAACTTCGACAAGAACCCTGCCGAACGAAAAGGTCCTG CCGAAGCACAGCCTGCTGTACGAATACTTCACAGTCTACAACGAACTGACAAAAGGTC AAGTACGTCACAGAAGGAATGAGAAAAGCCGGCATTCTGAGCGGAGAACAGAAGAA GGCAATCGTCGACCTGCTGTTCAAGACAAAACAGAAAAGGTCACAGTCAAGCAGCTGA AGGAAGACTACTTCAAGAAGATCGAATGCTTCGACAGCGTCAAATCAGCGGAGTGC AAGACAGATTCAACGCAAGCCTGGGAACATACCACGACCTGCTGAAGATCATCAAGG ACAAGGACTTCTGGACAACGAAGAAAACGAAGACATCTGGAAGACATCGTCTCTG ACACTGACACTGTTTCGAAGACAGAGAAATGATCGAAGAAAAGACTGAAGACATACG ACACCTGTTTCGACGACAAGGTCATGAAGCAGCTGAAGAGAAGAAGATACACAGGAT GGGGAAGACTGAGCAGAAAAGCTGATCAACGGAATCAGAGACAAGCAGAGCGGAAA GACAATCTGGACTTCTGAAGAGCGACGGATTTCGAAAACAGAACTTCATGCAGCT GATCCACGACGACAGCTGACATTCAGGAAGACATCCAGAAGGCACAGGTCAGCG GACAGGGAGACAGCCTGCACGAACACATCGCAAACCTGGCAGGAAGCCCGGCAATC AAGAAGGGAATCCTGCAGACAGTCAAGGTCGTCGACGAACTGGTCAAGGTCATGGG AAGACACAAGCCGAAAACATCGTCATCGAAATGGCAAGAGAAAACAGACAACAC AGAAGGGACAGAAGAACAGCAGAGAAAAGAATGAAGAGAATCGAAGAAGGAATCAA GGAACTGGGAAGCCAGATCTGAAGGAACACCCGGTTCGAAAACACACAGACTGCAGA ACGAAAAGCTGTACCTGTACTACCTGCAGAACGGAAGAGACATGTACGTCGACCAGG AACTGGACATCAACAGACTGAGCGACTACGACGTCGACCACATCGTCCCGCAGAGCT TCCTGAAGGACGACAGCATCGACAACAAGGTCCTGACAAGAAGCGACAAGAACAGA GGAAAAGAGCGACAACGTCCTCCGAGCGAAGAAGTCTGTCGAAGAAGATGAAGAACTACTG GAGACAGCTGCTGAACGCAAAGCTGATCACACAGAGAAAAGTTTCGACAACCTGACAA AGGCAGAGAGAGGAGGACTGAGCGAACTGGACAAGGCAGGATTATCAAGAGACA GCTGGTCAAAACAAGACAGATCACAAGCAGCTCGCACAGATCCTGGACAGCAGAA TGAACACAAGTACGACGAAAACGACAAGCTGATCAGAGAAGTCAAGGTCATCACA CTGAAGAGCAAGCTGGTCAAGCAGCTTCAGAAAAGGACTTCAGTTCTACAAGGTCAG AGAAATCAACAACCTACCACCGCACACGACGCATACCTGAACGCAGTCGTCGGAAC AGCATGATCAAGAAGTACCCGAAGCTGGAAAGCGAATTCGTCACGGAGACTACAA GGTCTACGACGTCAGAAAAGATGATCGAAAAGAGCGAACAGGAAATCGGAAAAGGCAA CAGCAAAGTACTTCTTCTACAGCAACATCATGAACCTTCTCAAGACAGAAATCACACT GGCAAACGGAGAAATCAGAAAAGAGACCGCTGATCGAAAACAAACGGAGAAAACAGGA GAAATCGTCTGGGACAAGGGAAGAGACTTCGCAACAGTCAGAAAAGGTCCTGAGCAT</p>	<p>181</p>

[0787]

	<p>GCCGCAGGTCAACATCGTCAAGAAGACAGAAGTCCAGACAGGAGGATTGAGCAAGG AAAAGCATCCTGCCGAAGAGAAAACAGCGACAAGCTGATCGCAAGAAAAGAAGGACTGG GACCCGAAGAAGTACGGAGGATTTCGACAGCCCAGAGTTCGCATACAGCGTCTCTGGTC GTTCGCAAAGGTCGAAAAGGGAAAGAGCAAGAAGCTGAAGAGCGTCAAGGAACTGC TGGGAATCACAATCATGGAAGAAGAGCAGCTTCGAAAAGAACCCGATCGACTTCTCTGG AAGCAAAGGGATACAAGGAAGTCAAGAAGGACCTGATCATCAAGCTGCCGAAGTAC AGCCTGTTTGAAGTGGAAAACGGAAGAAGAGAATGCTGGCAAGCGCAGGAGAAGT GCAGAAGGGAAACGAAGTGGCACTGCCGAGCAAGTACGTAACCTTCTGTACCTGG CAAGCCACTACGAAAAGCTGAAGGGAAAGCCGGAAGACAACGAACAGAAGCAGT GTTTCGTCGAACAGCACAAGCACTACCTGGACGAAATCATCGAACAGATCAGCGAAT CAGCAAGAGAGTATCCTGGCAGACGCAAAACCTGGACAAGGTCCTGATCGCATAACA ACAAGCACAGAGACAAGCCGATCAGAGAACAGGCAGAAAACATCATCCACCTGTTC ACACTGACAAACCTGGGAGCACCAGCAGCATTCAAGTACTTCGACACAACAATCGAC AGAAAAGAGATACACAAGCACAAGGAAGTCTGGACGCAACACTGATCCACCAGAG CATCAAGGACTGTACGAAAACAAGAAATCGACCTGAGCCAGCTGGGAGGAGACGGAG GAGGAAGCCGAAGAAGAAGAGAAAGGTCAGCGAAAAGCGCAACACCCGAAAGCGT CAGCGGATGGAGACTGTTCAAGAAGATCAGCTAGCTAGCCATCACATTTAAAAGCATC TCAGCCTACCATGAGAATAAGAGAAAAGAAAATGAAGATCAATAGCTTATTCATCTCTT TTTTTTTTCGTTGGTGTAAGGCCAACCCCTGTCTAAAAAACATAAATTTCTTTAATC ATTTTGCCTTTTTCTGTGCTTCAATTAATAAAAAAATGGAAAAGAACCTCGAGAAAA AA AA</p>	
<p>具有编码带 有HiBiT标记 标签的 Cas9 的 ORF、 CMV-3' 5' UTR 及人类 ALB 3' UTR 的 mRNA 转录 物</p>	<p>GGGTGCATTGGAACCGCGGATTCCCGTGC AAGAGTGACTCACCGCGCCACCATGGA CAAGAAGTACAGCATCGGACTGGACATCGGAACAACAGCGTCGGATGGGCGATCAT CACAGACGAATACAAGTCCCGAGCAAGAAGTTCAAGGTCCTGGGAAAACAGACA GACACAGCATCAAGAAGAACCTGATCGGAGCACTGCTGTTTCGACAGCGGAGAAAACA GCAGAAGCAACAAGACTGAAGAGAACAGCAAGAAGAAGATACACAAGAAGAAAAGA ACAGAATCTGCTACCTGCAGGAAATCTTCAGCAACGAAATGGCAAAGGTCGACGACA 5' AGACACCCGATCTTCGAAAACATCGTCGACGAAGTTCGCATACCACGAAAAGTACCCG ACAATCTACCACCTGAGAAAAGAGCTGGTCGACAGCACAGACAAGGCAGACCTGAG 3' ACTGATCTACCTGGCACTGGCACACATGATCAAGTTTCAGAGGACACTTCTGATCGAA GACGACCTGAACCCGGCAACAACAGCGACGTCGACAAGCTGTTTCATCCAGTGGTCCA GACATACAACCAGCTGTTTCGAAAAGAAAACCCGATCAACGCAAGCGGAGTTCGACAA AGGCAATCCTGAGCGCAAGACTGAGCAAGAGCAGAAGACTGGAAAACCTGATCGCA CAGCTGCCGGGAGAAAAGAAAGAACGGACTGTTTCGAAAACCTGATCGCACTGAGCCT GGGACTGACACCGAACTTCAAGAGCAACTTCGACCTGGCAGAAGACGCAAGCTGC AGCTGAGCAAGGACACATACGACGACGACCTGGACAACCTGCTGGCACAGATCGGA GACCAGTACGCAGACCTGTTCTGGCAGCAAAAGAACCTGAGCGACGCAATCCTGCTG AGCGACATCCTGAGAGTCAACACAGAAATCAAAAAGGCACCGCTGAGCGCAAGCAT GATCAAGAGATACGACGAACACCACAGGACCTGACACTGCTGAAGGCACTGGTCA GACAGCAGCTGCCGAAAAGTCAAGGAAATCTTTCGACCAGAGCAAGAACCGGA TACGCAGGATACATCGAGGAGCAAGCCAGGAAGAATTCTACAAGTTCATCAAG CCGATCCTGAAAAGATGGACGGAAACAGAAGAACTGCTGGTCAAGCTGAACAGAGA AGACCTGCTGAGAAAAGCAGAGAACATTTCGACAACGGAAGCATCCCGCACAGATCC ACCTGGGAGAAGTGCACGCAATCCTGAGAAGACAGGAAGACTTCTACCCGTTCTGGA AGGACAACAGAGAAAAGATCGAAAAGATCCTGACATTCAGAATCCCGTACTACGTCG GACCGCTGGCAAGAGGAAACAGCAGATTTCGATGGATGACAAGAAAGAGCGAAGAA ACAATCACACCGTGGAACTTCAAGAAGTCTGTCGACAAGGGAGCAAGCGCACAGAG CTTCATCGAAAAGAAATGACAACTTCGACAAGAACCTGCCGAACGAAAAGGTCCTGCC GAAGCACAGCCTGCTGTACGAATACTTCACAGTCTACAACGAAGTACAAAAGGTCAA GTACGTCACAGAAGGAATGAGAAAAGCCGGCATTCTGAGCGGAGAACAGAAGAAAG CAATCGTCGACCTGCTGTTCAAGACAAAACAGAAAAGGTCACAGTCAAGCAGCTGAAG GAAGACTACTTCAAGAAGATCGAATGCTTCGACAGCGTCGAAATCAGCGGAGTTCGAA GACAGATTCAACGCAAGCCTGGGAACATACCACGACCTGCTGAAGATCATCAAGGAC AAGGACTTCTGGACAACGAAGAAAACGAAGACATCCTGGAAAGACATCGTCTGAC ACTGACACTGTTTCGAAAGACAGAGAAATGATCGAAGAAAAGACTGAAGACATACGCAC ACCTGTTTCGACGACAAGGTCATGAAGCAGCTGAAGAGAAGAAGATACACAGGATGG GGAAGACTGAGCAGAAAAGCTGATCAACGGAATCAGAGACAAGCAGAGCGGAAAAGA CAATCCTGGACTTCTGAAGAGCGACGGATTTCGAAAACAGAAAACCTCATGCAGCTGA TCCACGACGACAGCTGACATTCAGAAGGACATCCAGAAGGCACAGGTCAGCGGA CAGGGAGACAGCCTGCACGAACACATCGCAAACCTGGCAGGAAGCCCGGCAATCAA GAAGGGAATCCTGCAGACAGTCAAGGTCGTCGACGAACTGGTCAAGGTCATGGGAA GACACAAGCCGAAAACATCGTCATCGAAATGGCAAGAGAAAACAGACAACACAG AAGGGACAGAAAGAACAGCAGAGAAAAGAAATGAAGAGAATCGAAGAAGGAATCAAG AACTGGGAAGCCAGATCCTGAAGGAACACCCGGTCGAAAACACACAGCTGCAGAAC GAAAAGCTGTACTACTGACGAGAACCGGAAGAGACATGTACGTCGACCAGGAA</p>	<p>182</p>

[0788]

	<p>CTGGACATCAACAGACTGAGCGACTACGACGTCGACCACATCGTCCCAGAGCTTC CTGAAGGACGACAGCATCGACAACAAGGTCCTGACAAGAAAGCGACAAGAACAGAG GAAAGAGCGACAACGTCCCAGCGAAGAAGTCGTCAAGAAGATGAAGAACTACTGG AGACAGCTGCTGAACGCAAAAGCTGATCACACAGAGAAAAGTTCGACAACCTGACAAA GGCAGAGAGAGGAGGACTGAGCGAACTGGACAAGGCAGGATTCATCAAGAGACAG CTGGTCGAAAACAAGACAGATCACAAAAGCACGTCGCACAGATCCTGGACAGCAAGAT GAACACAAAAGTACGACGAAAACGACAAGCTGATCAGAGAAGTCAAGGTCATCACAC TGAAGAGCAAGCTGGTCAGCGACTTCAGAAAAGGACTTCCAGTTCACAAGGTCAGA GAAATCAACAACCTACCACCACGCACACGACGCATACCTGAACGCAGTCGTCCGAAACA GCACTGATCAAGAAGTACCCGAAGCTGGAAAAGCGAATTCGTCTACGGAGACTACAAG GTCTACGACGTCAGAAAAGATGATCGCAAAGAGCGAACAGGAAATCGCAAAGCAAC AGCAAAGTACTTCTTCTACAGCAACATCATGAACTTCTTCAAGACAGAAATCACACTG GCAAACGGAGAAATCAGAAAAGAGACCGCTGATCGAAAACAAACGGAGAAAACAGGAG AAATCGTCTGGGACAAGGGAAGAGACTTCGCAACAGTCAGAAAAGGTCCTGAGCATG CCGACGGTCAACATCGTCAAGAAGACAGAAGTCCAGACAGGAGGATTCAGCAAGGA AAGCATCCTGCCGAAGAGAAAACAGCGACAAGCTGATCGCAAGAAAAGGACTGGG ACCCGAAGAAGTACGGAGGATTCGACAGCCGACAGTCGCATACAGCGTCTGGTTCG TCGCAAAGGTCGAAAAGGGAAGAGACAAGAAAGCTGAAGAGCGTCAAGGAACTGCT GGGAATACAATCATGGAAGAAGCAGCTTCGAAAAGAACCCTGATCGACTTCTCTGGA AGCAAAGGGATACAAGGAAGTCAAGAAGGACCTGATCATCAAGCTGCCAAAGTACA GCCTGTTGAACTGGAAAACGGAAGAAAAGAGAATGCTGGCAAGCGCAGGAGAAGTGC CAGAAGGGAAACGAACTGGCACTGCCGAGCAAGTACGTCAAACTTCTGTACCTGGC AAGCCACTACGAAAAGCTGAAGGGAAGCCCGGAAGACAACGAACAGAAGCAGCTG TTCGTGAAACAGCACAAAGCACTACCTGGACGAAATCATCGAACAGATCAGCGAATTC AGCAAAGAGAGTCATCCTGGCAGACGCAAACTGGACAAGGTCCTGAGCGCATACAA CAAGCACAGAGACAAGCCGATCAGAGAACAGGCAGAAAACATCATCCACCTGTTCA CACTGACAAAACCTGGGAGCACCCGGCAGCATTCAAGTACTTCGACACAACAATCGACA GAAAGAGATACACAAGCACAAGGAAGTCTGGACGCAACACTGATCCACCAGAGC ATCACAGGACTGTACGAAAACAAGAATCGACCTGAGCCAGCTGGGAGGAGACGGAGG AGGAAGCCCGAAGAAGAAGAGAAAAGGTCAGCGAAAAGCGCAACACCCGAAAGCGTC AGCGGATGGAGACTGTTCAAGAAGATCAGCTAGCTAGCCATCACATTTAAAAGCATCT CAGCCTACCATGAGAATAAGAGAAAAGAAAATGAAGATCAATAGCTTATTTCATCTTTT TTTTTTTTCGTTGGTGTAAAAGCCAACCCCTGTCTAAAAAACATAAAATTTTAAATCA TTTTGCCTCTTTTCTCTGTGCTCAATTAATAAAAAATGGAAGAACCCTCGAGAAAAA AAA AAA</p>	
<p>具有编码带 有HiBiT标记 标签的 Cas9 的 ORF、HBA 5' UTR 及 人类 ALB 3' UTR 的 mRNA 转录 物</p>	<p>GGGCATAAACCCCTGGCGCGCTCGCGGCCCGGCACTTCTGGTCCCCACAGACTCAG AGAGAACCACCCGCCACCATGGACAAGAAGTACAGCATCGGACTGGACATCGGAA CAAAACAGCGTCGGATGGGCAGTCATCACAGACGAATACAAGGTCCTGAGCAAGAAG TTCAAGGTCCTGGGAAACACAGACAGACACAGCATCAAGAAGAACCCTGATCGGAGC ACTGCTGTTGACAGCGGAGAAAACAGCAGAAGCAACAAAGACTGAAGAGAAACAGCA AGAAGAAGATACACAAGAAGAAGAAAGACAAGAAATCTGCTACCTGCAGGAAATCTTTCAG CAACGAAATGGCAAAGGTCGACAGACGCTTCTTCCACAGACTGGAAGAAGAAAGTTC TGGTTCGAAGAAGACAAGAAGCAGAAAAGACACCCGATCTTCGGAACATCGTTCGAC GAAGTCGCATACCACGAAAAGTACCCGACAATCTACCCTGAGAAAAGAAGCTGGTTC GACAGCACAGACAAGGCAGACTGAGACTGATCTACCTGGCACTGGCACACATGATC AAGTTTCAGAGGACTTCTGATCGAAGGAGACCTGAACCCGGACAACAGCGACGT CGACAAGCTGTTTCATCCAGCTGGTCCAGACATACAACCAGCTGTTTCGAAGAAAACCC GATCAACGCAAGCGGAGTCGACGCAAAAGGCAATCTGAGCGCAAGACTGAGCAAGA GCAGAAAGACTGGAACCTGATCGCACAGCTGCCGGGAGAAAAGAAAGACGGACT GTTCCGAAACCTGATCGCACTGAGCCTGGGACTGACACCGAACTTCAAGAGCAACTT GTACCTGGCAGAAGACGCAAAAGCTGCAGCTGAGCAAGGACACATACAGCAGCAGC TGGACAACCTGCTGGCACAGATCGGAGACCAGTACGCAGACCTGTTCTGGCAGCAA AGAACCTGAGCGACGCAATCCTGCTGAGCGACATCCTGAGAGTCAACACAGAAATCA CAAAGGCACCGCTGAGCGCAAGCATGATCAAGAGATACGACGAACACCACCAGGAC CTGACACTGCTGAAGGCACTGGTTCAGACAGCAGCTGCCGAAAAGTCAAGGAAAT CTTCTTCGACCAGAGCAAGAACGGATACGCAGGATACATCGACGGAGGAGCAAGCCA GGAAGAATTCTACAAGTTCATCAAGCCGATCCTGGAAGAAGATGGACGGAACAGAAGA ACTGCTGGTCAAGCTGAACAGAGAAGACCTGCTGAGAAAAGCAGAGAACATTCGACA ACGGAAGCATCCCGACCAAGATCCACTGGGAGAAGTGCACGCAATCCTGAGAAGA CAGGAAGACTTCTACCCGTTCTGAAAGGACAACAGAGAAAAGATCGAAAAGATCCT GACATTCAGAATCCCGTACTACGTCGGACCGCTGGCAAGAGGAAAACAGCAGATTCGC ATGGATGACAAGAAAAGAGCGAAGAAAACAATCACACCGTGGAACTTCGAAGAAGTTCG TCGACAAGGGAGCAAGCGCACAGAGCTTCATCGAAAAGATGACAAACTTCGACAAG AACTGCCGAACGAAAAGGTCCTGCCGAAGCACAGCCTGCTGTACGAATACTCACAC GTCTACAACGAACTGACAAAAGGTCAGTACGTCACAGAAGGAATGAGAAAAGCCGGC ATTCCTGAGCGGAGAACAGAAGAAGGCAATCGTCGACCTGCTGTTCAAGACAAAACA</p>	<p>183</p>

[0789]

	<p>GAAAGGTCACAGTCAAGCAGCTGAAGGAAGACTACTTCAAGAAGATCGAATGCTTC GACAGCGTCGAAATCAGCGGAGTCAAGACAGATTCAACGCAAGCCTGGGAACATA CCACGACCTGCTGAAGATCATCAAGGACAAGGACTTCTGGACAACGAAGAAAACG AAGACATCCTGGAAGACATCGTCTGACACTGACACTGTTGGAAGACAGAGAAATGA TCGAAGAAAAGACTGAAGACATACGCACACCTGTTTCGACGACAAGGTCATGAAGCAG CTGAAGAGAAGAAGATACACAGGATGGGAAGACTGAGCAGAAAAGCTGATCAACGG AATCAGAGACAAGCAGAGCGGAAAAGACAATCCTGGACTTCTGAAGAGCGACGGAT TCGCAAACAGAAAATTCATGCAGCTGATCCACGACGACAGCCTGACATTCAAGGAAG ACATCCAGAAGGCACAGGTCAGCGGACAGGGAGACAGCCTGCACGAACACATCGCA AACCTGGCAGGAAGCCCGCAATCAAGAAGGGAATCCTGCAGACAGTCAAGGTCGT CGACGAACTGGTCAAGGTCATGGGAAGACACAAGCCGGAACATCGTCAATCGAAA TGGCAAGAGAAAACCAGACAACACAGAAGGGACAGAAGAACAGCAGAGAAAAGAA GAAGAGAATCGAAGAAGGAATCAAGGAACTGGGAAGCCAGATCCTGAAGGAACACC CGGTGCAAAAACACACAGCTGCAGAACGAAAAGCTGTACTGTACTACTGCAGAAC GGAAGAGACATGTACGTCGACCAGGAAGTGGACATCAACAGACTGAGCGACTACGA CGTCGACCACATCGTCCCGCAGAGCTTCTGAAGGACGACAGCATCGACAACAAGGT CCTGACAAGAAGCGACAAGAACAGAGGAAAGAGCGACAACGTCCCGAGCGAAGAA GTGCTCAAGAAGATGAAGAATACTGGAGACAGCTGCTGAACGCAAAGCTGATCAC ACAGAGAAAAGTTCGACAACCTGACAAAAGGCAGAGAGAGGAGGACTGAGCGAACTG GACAAGGCAGGATTCATCAAGAGACAGCTGGTTCGAAAACAAGACAGATCACAAAAGCA CGTCGCACAGATCCTGGACAGCAGAATGAACACAAAAGTACGACGAAAACGACAAGC TGATCAGAGAAGTCAAGGTCATCACACTGAAGAGCAAGCTGGTCAGCGACTTCAGA AAGGACTTCCAGTTCTACAAGGTCAGAGAAAATCAACAACACTACCACCACGCACACGAC GCATACCTGAACGCAGTCGTGGAAACAGCACTGATCAAGAAGTACCCGAGCGGAA AGCGAATTCGTCTACGGAGACTACAAGGTCACGACGTCAGAAAAGATGATCGCAAAG AGCGAACAGGAAATCGGAAAGGCAACAGCAAAGTACTTCTTACAGCAACATCATG AACTTCTCAAGACAGAAATCACACTGGCAAACGGAGAAATCAGAAAAGAGACCGCT GATCGAAAACAAACGGAGAAACAGGAGAAATCGTCTGGGACAAGGGAAGAGACTTCG CAACAGTCAGAAAAGGTCCTGAGCATGCCGCAAGTCAACATCGTCAAGAAGACAGAA GTCCAGACAGGAGGATTCAGCAAGGAAAGCATCCTGCCGAAGAGAAAACAGCGACAA GCTGATCGCAAGAAAGAAAGGACTGGGACCCGAAGAAGTACGGAGGATTCGACAGCC CGACAGTCGCATACAGCGTCTGGTCTGCGCAAAGGTCGAAAAGGGAAAAGAGCAAG AAGCTGAAGAGCGTCAAGGAACTGCTGGGAATCAACAATCATGGAAGAAGCAAGCTT CGAAAAGAACCCTGATCGACTTCTGGAAAGCAAAGGATACAAGGAAGTCAAGAAGG ACCTGATCATCAAGCTGCCGAAGTACAGCCTGTTGCAACTGGAAAACCGAAGAAAG AGAATGCTGGCAAGCGCAGGAGAACTGCAGAAGGGAAACGAACTGGCACTGCCGA GCAAGTACGTCAACTTCTGTACTTGGCAAGCCACTACGAAAAGCTGAAGGGGAAGCC CGGAAGACAACGAACAGAAGCAGCTGTTTCGTCAACAGCACAAGCAACACTACCTGGAC GAAATCATCGAACAGATCAGCGAATTCAGCAAGAGAGTCACTTGGCAGACGCAAAC CTGGACAAGGTCCTGAGCGCATACAACAAGCACAGAGACAAGCCGATCAGAGAACA GGCAGAAAACATCATCCACTGTTCACTGACAAAACCTGGGAGCACCCGGCAGCATT CAAGTACTTCGACACAACAATCGACAGAAAGAGATACACAAGCACAAGGAAAGTCC TGGACGCAACACTGATCCACCAGAGCATCACAGGACTGTACGAAAACAAGAATCGACC TGAGCCAGCTGGGAGGAGACGGAGGAGGAAGCCC GAAGAAGAAGAGAAAGGTCAG CGAAAAGCGCAACACCCGAAAGCGTCAAGCGGATGGAGACTGTTCAAGAAGATCAGCT AGTAGCCATCACATTTAAAAGCATCTCAGCCTACCATGAGAATAAGAGAAAAGAAAAT GAAGATCAATAGCTTATTCATCTTTTTCTTTTTCTTTTCTGTTGGTGTAAGCAACACCTG TCTAAAAACATAAATTTCTTAAATCATTTCCTTTTTCTCTGTGCTTCAATTAATAA AAAATGGAAAAGAACCTCGAGAAA AA AAAAAAAAAAAAAAAA</p>
<p>具有编码带 有HiBiT标记 标签的 Cas9 的 ORF、HBB 5' UTR 及 人类 ALB 3' UTR 的 mRNA 转录 物</p>	<p>GGGACATTTGCTTCTGACACAACCTGTGTTCACTAGCAACCTCAAACAGACACCGGAT CTCGCCACCATGGACAAGAAGTACAGCATCGGACTGGACATCGGAACAAAACAGCGTC GGATGGGCAGTCAACAGACGAATACAAGGTCCCAGCAAGAAGTCAAGGTCCTG GGAAAACACAGACAGACACAGCATCAAGAAGAACCTGATCGGAGCACTGCTGTTTCA CAGCGGAGAAAACAGCAGAAGCAACAGACTGAAGAGAACAGCAAGAAGAAGATAC ACAAGAAGAAAAGAACAGAATCTGCTACCTGCAGGAAATCTTACGCAACGAAATGGC AAAGGTCGACGACAGCTTCTTCCACAGACTGGAAGAAAGCTTCTGGTTCGAAGAAG ACAAGAAGCACGAAAGACACCCGATCTTCGAAAACATCGTCGACGAAAGTCCGATACC ACGAAAAGTACCCGACAATCTACCCTGAGAAAAGAAGCTGGTCGACAGCACAGAC AAGGCAGACCTGAGACTGATCTACCTGGCACTGGCACACATGATCAAGTTCAGAGGA CACTTCTGATCGAAGGAGACCTGAACCCGACAACAGCGACGTCGACAAGCTGTTT ATCCAGCTGGTCCAGACATAAACCAGCTGTTTCAAGAAAACCCGATCAACGCAAGC GGAGTCGACGCAAAGGCAATCCTGAGCGCAAGACTGAGCAAGAGCAGAAAGACTGG AAAACCTGATCGCACAGCTGCCGGGAGAAAAGAAGAAGCAAGGACTGTTTCGAAAACCTG ATCGCACTGAGCCTGGGACTGACACCGAACTTCAAGAGCAACTTCGACCTGGCAGA AGACGCAAAGCTGCAGCTGAGCAAGGACACATACGACGACGACCTGGACAACCTGC</p>

[0790]

	<p>TGGCACAGATCGGAGACCAGTACGCAGACCTGTTCTGCGCAGCAAAGAACCTGAGC GACGCAATCCTGCTGAGCGACATCCTGAGAGTCAACACAGAAATCACAAAAGGCACC GCTGAGCGCAAGCATGATCAAGAGATACGACGAACACCACCAGGACCTGACACTGCT GAAGGCACTGGTCAGACAGCAGCTGCCGGAAGTACAAGGAAATCTTCTTCGACC AGAGCAAGAACGGATACGCAGGATACATCGACGGAGGAGCAAGCCAGGAAGAATTC TACAAGTTCATCAAGCCGATCCTGGAAAAAGATGGACGGAAACAGAAGAATCTGGTC AAGCTGAACAGAGAAGACCTGCTGAGAAAAGCAGAGAACATTCGACAACCGAAGCAT CCCGCACCAGATCCACCTGGGAGAACTGCACGCAATCCTGAGAAAGACAGGAAGACT TCTACCCGTTCTGAAGGACAACAGAGAAAAGATCGAAAAGATCCTGACATTCAGAA TCCCCTACTACGTCGGACCGCTGGCAAGAGGAAAACAGCAGATTTCGATGGATGACAA GAAAGAGCGAAGAAACAATCACACCGTGGAACTTCGAAGAAGTCGTCGACAAGGGA GCAAGCGCACAGAGCTTCATCGAAAGAATGACAAACTTCGACAAGAACCTGCCGAA CGAAAAGGTCTGCCGAAAGCACAGCCTGCTGTACGAATACTTCACAGTCTACAACGA ACTGACAAAAGGTCAAGTACGTCACAGAAGGAATGAGAAAAGCCGGCATTCTGAGCG GAGAACAGAAAGGAATCGTCGACCTGCTGTTCAAGACAAAACAGAAAAGGTCACA GTCAAGCAGCTGAAGGAAGACTACTTCAAGAAGATCGAATGCTTCGACAGCGTCGAA ATCAGCGGAGTCGAAGACAGATTCAACGCAAGCCTGGGAACATACCACGACCTGCTG AAGATCATCAAGGACAAGGACTTCTGGAACAACGAAGAAAACGAAGACATCCTGGA AGACATCGTCTGACACTGACACTGTTTCAAGACAGAGAAAATGATCGAAGAAAAGACT GAAGACATACGCACACCTGTTTCGACGACAAGGTCATGAAGCAGCTGAGGAAAGAA GATACACAGGATGGGGAAGACTGAGCAGAAAAGCTGATCAACGGAATCAGAGACAAG CAGAGCGGAAAAGACAATCCTGGACTTCTGAAGAGCGACGGATTCCGAAAACAGAAA CTTCATGCAGCTGATCCACGACGACAGCCTGACATTCAAGGAAGACATCCAGAAGGC ACAGGTCAGCGGACAGGGAGACGCCTGCACGAACACATCGCAAACCTGGCAGGAA GCCCGGAATCAAGAAGGGAATCCTGCAGACAGTCAAGGTCTGTCGACGAACTGGTC AAGGTCATGGGAAGACACAAGCCGGAACATCGTCATCGAAATGGCAAGAGAAA CCAGACAACACAGAAGGGACAGAAGAACAGCAGAGAAAAGAAATGAAGAGAATCGAA GAAGGAATCAAGGAAGTGGGAAGCCAGATCCTGAAGGAACACCCGGTCGAAAACAC ACAGCTGCAGAACGAAAAGCTGTACTTACCTGCAGAACGGAAGAGACATGTA CGTCGACCAGGAAGTGGACATCAACAGACTGAGCGACTACGACGTCGACCACATCGT CCCGCAGAGCTTCTGAAGGACGACAGCATCGACAACAAGGTCCTGACAAGAAAGCG ACAAGAACAGAGGAAAGAGCGACAACGTCCCGAGCGAAGAAAGTCTGTAAGAAGAT GAAGAATACTGGAGACAGCTGTGAACGCAAAAGCTGATCACACAGAGAAAAGTTCG ACAACCTGACAAAGGCAGAGAGAGGAGGACTGAGCGAACTGGACAAGGCAGGATT CATCAAGAGACAGTGGTCGAAAACAAGACAGATCACAAGACAGTCCGACAGATCC TGGACAGCAGAAATGAACACAAGGTACGACGAAAACGACAAGCTGATCAGAGAAGTC AAGGTCATCACACTGAAGAGCAAGCTGGTCAGCGACTTCAGAAAAGGACTTCCAGTTC TACAAGGTCAGAGAAATCAACAATACTACCACACGACACGACGATACCTGAACGCA GTGTCGGAACAGCACTGATCAAGAAGTACCCGAAGCTGGAAAGCGAATTCGTCTAC GGAGACTACAAGGTCTACGACGTCAGAAAAGATGATCGCAAAGAGCGAACAGGAAAT CGGAAAAGGCAACAGCAAAGTACTTCTTACAGCAACATCATGAACTTCTTCAAGAC AGAAATCACACTGGCAAAACGGAGAAAATCAGAAAAGAGACCCTGATCGAAAACAAACG GAGAAAACAGGAGAAAATCGTCTGGGACAAGGGAAAGAGACTTCGCAACAGTCAGAAA GGTCTGAGCATGCCGAGGTCAACATCGTCAAGAAGACAGAAGTCCAGACAGGAG GATTCAGCAAGGAAAGCATCCTGCCGAAGAGAAAACAGCGACAAGCTGATCGCAAGA AAGAAGGACTGGGACCCGAAGAAGTACGGAGGATTCGACAGCCGACAGTCCGATA CAGCTCCTGGTCTGTCGAAAAGGTCGAAAAGGGAAAGAGCAAGAAGAAAGTGAAGC GTCAAGGAAGTCTGGGAATCAACAATCATGGAAAAGAGCAGCTTCGAAAAGAACCC GATCGACTTCTGGAAGCAAAGGGATACAAGGAAGTCAAGAAGGACCTGATCATCAA GCTGCCGAAGTACAGCCTGTTTCAACTGGAAAACGGAAGAAAAGAGAATGCTGGCAA GCGCAGGAGAACTGCAGAAGGGAAACGAACTGGCAGTCCGAGCAAGTACGTCAAC TTCCTGTACTGGCAAGCCACTACGAAAAGCTGAAGGGAAAGCCCGGAAGACAACGA ACAGAAGCAGCTGTTCTGTCGAACAGCACAAGCACTACCTGGACGAAATCATCGAACA GATCAGCGAATTCAGCAAGAGAGTCACTTGGCAGACGCAAACTGGACAAGGTCTCT GAGCGCATAACAAGCACAGAGACAAGCCGATCAGAGAACAGGCAGAAAACATCA TCCACCTGTTACACTGACAAACCTGGGAGCACCAGCAGCATTCAAGTACTTCGACA CAACAATCGACAGAAAAGAGATACACAAGCACAAAGGAAGTCTGGACGCAACACTG ATCCACCAGAGCATCACAGGACTGTACGAAAACAAGAATCGACCTGAGCCAGCTGGGA GGAGACGGAGGAGGAAGCCGAAGAAGAAGAGAAAAGGTCAGCGAAAAGCGCAACAC CGGAAAAGCAGTCCAGCGGATGGAGACTGTTCAAGAAGATCAGCTAGTACGATCAGT TTAAAAGCATCTCAGCCTACCATGAGAATAAGAGAAAAGAAAATGAAGATCAATAGCTT ATTCATCTTTTTCTTTTTCTGTTGGTGTAAAGCCAACACCCTGTCTAAAAAACATAAA TTTTTTAATCATTTTGCCTTTTTCTGTGTCTCAATTAATAAAAAATGGAAAAGAAC CTCGAGAAAAA AA AA</p>	
具有编码带	GGGAAGCTCAGAATAAACGCTCAACTTTGGCCGGATCTCGCCACCATGGACAAGAAG TACAGCATCGGACTGGACATCGGAACAAACAGCGTCCGATGGGCAGTCATCACAGAC	185

<p>有HiBiT标记 标签的 Cas9 的ORF、XBG 5' UTR 及 人类ALB 3' UTR 的 mRNA 转录 物</p>	<p>GAATACAAGGTCCCAGCAAGAAGTTCAAGGTCTGGGAAACACAGACAGACACAG CATCAAGAAGAACCCTGATCGGAGCACTGCTGTTTCGACAGCGGAGAAACAGCAGAAG CAACAAGACTGAAGAGAACAGCAAGAAGATACACAAGAAGAAAGAACAGAAT CTGCTACCTGCAGGAAATCTTCAGCAACGAAATGGCAAAGGTGACGACAGCTTCTT CCACAGACTGGAAGAAAGCTTCTGGTGAAGAAGACAAGAAGCACGAAAGACAC CCGATCTTCGGAACATCGTCGACGAAGTCGCATACCACGAAAAGTACCCGCAATCT ACCACCTGAGAAAGAAGCTGGTTCGACAGCAGACAAAGGCAGACCTGAGACTGATC TACCTGGCACTGGCACACATGATCAAGTTCAGAGGACACTTCCTGATCGAAGGAGAC CTGAACCCGGACAACAGCGACGTCGACAAGCTGTTTCATCCAGCTGGTCCAGACATAC AACCAGCTGTTCAAGAAAACCCGATCAACGCAAGCGGAGTCGACGCAAAGGCAAT CCTGAGCGCAAGACTGAGCAAGAGCAGAAGACTGGAAAACCTGATCGACAGCTGC CGGGAGAAAAGAAGAACGGACTGTTTCGAAAACCTGATCGCACTGAGCCTGGGACTG ACACCGAACTTCAAGAGCAACTTCGACCTGGCAGAAGACGCAAAGCTGCAGCTGAG CAAGGACACATACGACGACGACCTGGACAACCTGCTGGCACAGATCGGAGACCAGT ACGCAGACCTGTTCTGGCAGCAAAGAACCCTGAGCGACGCAATCTGCTGAGCGACA TCCTGAGAGTCAACACAGAAATCACAAGGCACCGCTGAGCGCAAGCATGATCAAG AGATACGACGAACACCACAGGACCTGACTGCTGAAGGCACTGGTTCAGACAGCA GCTGCCGAAAAGTACAAGGAAATCTTCTTCGACCAGAGCAAGAACGGATACGCAG GATACATCGACGGAGGAGCAAGCCAGGAAGAATTCTACAAGTTCATCAAGCCGATCC TGGAAAAGATGGACGGAAACAGAAGAACTGCTGGTCAAGCTGAACAGATACGCAACCTG CTGAGAAAAGCAGAGAACATTCGACAACGGAAAGCATCCCGCACCAGATCCACCTGGG AGAACTGCACGCAATCCTGAGAAGACAGGAAGACTTCTACCCGTTCTGAAGGACA ACAGAGAAAAGATCGAAAAGATCCTGACATTCAGAATCCCGTACTACGTCGGACCCG TGGCAAGAGGAAACAGCAGATTCGCATGGATGACAAGAAAAGAGCAGAAAGCAATC ACACCGTGGAACTTCGAAGAAGTCGTCGACAAGGGAGCAAGCGCACAGAGCTTCAT CGAAAAGATGACAACTTCGACAAGAACCCTGCCGAACGAAAAGGTCTGCCGAAGC ACAGCCTGCTGTACGAATACTTCACAGTCTACAACGAACTGACAAAAGGTCAAGTACG TCACAGAAGGAATGAGAAAGCCGGCATTCTGAGCGGAGAACAGAAGAAGGCAATC GTCGACCTGCTGTTCAAGCAAACAGAAAAGGTACACAGTCAAGCAGCTGAAGGAAAG CTACTTCAAGAAGATCGAATGCTTCGACAGCGTCGAAAATCAGCGGAGTCAAGACAG ATTCACGCAAGCCTGGGAACATACCACGACCTGCTGAAGATCATCAAGGACAAGGA CTTCTGGACAACGAAGAAAACGAAGACATCCTGGAAGACATCGTCTGACACTGAC ACTGTTTCGAAGACAGAGAAATGATCGAAGAAAGACTGAAGACATACGCAACCTGTT CGACGACAAGGTTCATGAAGCAGCTGAAGAGAAGAAGATACACAGGATGGGGAAGAC TGAGCAGAAAAGCTGATCAACGGAATCAGAGACAAGCAGAGCGGAAAAGACAATCCTG GACTTCTGAAGAGCGACGGATTTCGAAAACAGAAAATTCATGCAGCTGATCCACGAC GACAGCCTGACATTCAGGAAGACATCCAGAAGGCACAGGTCAGCGCACAGGAGGAGA CAGCCTGCACGAACACATCGAAAACCTGGCAGGAAGCCCGCAATCAAGAAGGAA TCCTGCAGACAGTCAAGGTTCGTCGACGAACTGGTCAAGGTTCATGGGAAGACACAAG CCGAAAACATCGTCATCGAAATGGCAAGAGAAAACAGACAACACAGAAGGGACA GAAGAACAGCAGAGAAAGAATGAAGAGAATCGAAGAAGGAATCAAGGAACTGGGA AGCAGATCCTGAAGGAACACCCTGGTTCGAAAACACACAGCTGCAGAGAAGAAAGT GTACCTGTACTACCTGCAGAACGGAAGAGACATGTACGTCGACCAGGAACTGGACAT CAACAGACTGAGCGACTACGACGTCGACCACATCGTCCCGCAGAGCTTCTGAAGGA CGACAGCATCGACAACAAGGTCTGACAAGAAGCGACAAGAACAGAGGAAAAGAGC GACAACGTCCCAGCGAAGAAGTCGTCAAGAAGATGAAGAATACTGGAGACAGCT GCTGAACGCAAAGCTGATCACACAGAGAAAAGTTCGACAACCTGACAAAAGCAGAGA GAGGAGGACTGAGCGAACTGGACAAGGCAGGATTCATCAAGAGACAGCTGGTTCGAA ACAAGACAGATCACAAAGCAGTTCGACAGATCCTGGACAGCAGAATGAACACAAA GTACGACGAAAACGACAAGCTGATCAGAGAAGTCAAGGTTCATCAACTGAAGAGCA AGCTGGTTCAGCGACTTCAGAAAAGGACTTCCAGTTCTACAAGGTTCAGAGAAGAA ACTACCACCACGACACGACGCATACCTGAACGCAATCGTTCGGAACAGCACTGATCA AGAAGTACCCGAAGCTGGAAAGCGAATTCGTCTACGGAGACTACAAGGTCTACGACG TCAGAAAAGATGATCGAAAAGAGCGAACAGGAAATCGGAAAAGGCAACAGCAAAGTAC TTCTTACAGCAACATCATGAATCTTCAAGACAGAAATCACACTGGCAAACCGGA GAAATCAGAAAAGAGACCGCTGATCGAAAACAAACGGAGAAACAGGAGAAAATCGTCTG GGACAAGGGAAGAGACTTCGCAACAGTCAGAAAAGGTCTGAGCATGCCCGAGGTCA ACATCGTCAAGAAGACAGAAAGTCCAGACAGGAGGATTCAGCAAGGAAAGCATCCTG CCGAAGAGAAAACAGCGACAAGCTGATCGCAAGAAGAAGGACTGGGACCCGAAAGA AGTACGGAGGATTCGACAGCCCGACAGTTCGCATACAGCGTCTGGTTCGTCGCAAGG TCGAAAAGGGAAGAGCAAGAAGCTGAAGAGCGTCAAGGAACTGCTGGGAATCAC AATCATGGAAGAAGCAGCTTCGAAAAGAACCCTGATCGACTTCTGGAAGCAAAGG GATACAAGGAAGTCAAGAAGGACCTGATCATCAAGCTGCCGAAGTACAGCCTGTTTCG AACTGGAAAACGGAAGAAGAGAATGCTGGCAAGCGCAGGAGAAGTTCAGAAAGG AAAAGAACTGGCACTGCCGAGCAAGTACGTCAACTTCTGATCCTGGCAAGCCACTA CGAAAAGCTGAAGGGAAGCCCGAAAGACAACGAACAGAAGCAGCTGTTCTGTCGAA CAGACAAGCACTACCTGGACGAAATCATCGAACAGATCAGCGAATTCAGCAAGAGA</p>
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[0791]

[0792]

	GTCATCCTGGCAGACGCAAACCTGGACAAGTCTGAGCGCATACAACAAGCACAG AGACAAGCCGATCAGAGAACAGGCAGAAAAACATCACCCTGTTCACACTGACAA ACCTGGGAGCACCAGCAGCATTCAAGTACTTCGACACAACAATCGACAGAAAGAGAT ACACAAGCACAAAGGAAGTCTGGACGCAACACTGATCCACCAGAGCATCACAGGA CTGTACGAAACAAGAATCGACCTGAGCCAGCTGGGAGGAGACGGAGGAGGAAGCCC GAAGAAGAAGAGAAAGGTGAGCGAAAGCGCAACACCGGAAAGCGTCAGCGGATGG AGACTGTTCAAGAAAGATCAGCTAGCTAGCCATCACATTTAAAAGCATCTCAGCCTACC ATGAGAATAAGAGAAAGAAAATGAAGATCAATAGCTTATTCATCTCTTTTCTTTTTCG TTGGTGTAAGCCAAACACCCTGTCTAAAAAACATAAATTTCTTAAATCATTTCGCTCT TTTTCTGTGCTTCAATTAATAAAAAATGAAAAGAACCCTCGAGAAAAAAAAAAAAAA AA AA	
具有NLS1的 Cas9的氨基 酸序列	MDKKYSIGLDIGTNSVGVAVITDEYKVPSSKFKVLGNTRHSIKKNLIGALLFDSGETAE ATRLKRTARRRYTRRNKRYLQEIFSNEMAKVDDSFHRLSEESFLVEEDKKHERHPFIGN IVDEVAYHEKYPTIYHLRKKLVDSTDKADLRILIYLAHMIKFRGHFLIEGDLNPDNSDV DKLFIQLVQTYNQLFEENPINASGVDAKAILSARLSKSRRLLENLIALPGEKKNLGFNLI ALSLGLTPNFKSNFDLAEDAKLQLSKDTYDDDLNLLAQIGDQYADLFLAAKNLSDAIL LSDILRVNTEITKAPLSASMIKRYDEHHQDLTLLKALVRQQLPEKYKEIFFDQSKNGYAGY IDGGASQEEFYKFIKPILEKMDGTEELLVKNLREDLLRKQRTFDNGSIPHQIHLGELHAILR IQEDFYFLKDNREKIEKILTRIPYYVGPLARGNSRFAMWTRKSEETITPWNFEVVDK GASAQSFIERMTNFDKNLPNEKVLPHKSLLYEYFTVYNELTKVKYVTEGMRKPAFLSGE QKKAIVDLLFKTNRKVTVKQLKEDYFKKIECFDSVEISGVEDRFNASLGTYHDLKIKD KDFLDNEENEDILEDIVLTLTFEDREMIEERLKYAHLFDDKVMKQLKRRRYTGWRSL RKLINGIRDKQSGKTILDFLKSDFANRNFMLIHDDSLTFKEDIQKAQVSGQGDSLHEHI ANLAGSPAIKKILQTVKVVDELKVMGRHKPENIVIEMARENQTTQKGGQNSRERMK RIEFIGELGSQLKEHPVENTQLQNEKLYLYLQNGRDMYVDQELDINRLSDYDVDHIV PQSFLKDDSIDNKVLTRSDKNRGSNDVPSEEVVKMKMKNYWRQLLNAKLITQRKFDNLT KAERGGSELSEDKAGFIKRLVETRQITKHVAQILDSRMNTKYDENDKLIREVKVITLKS LVSDFRKDFQFYKVRINNYHHAHDAYLNAVVGTAALIKKYPKLESEFVYGDYKVVYDVR KMIKSEQEIQKATAKYFFYSNIMNFFKTEITLANGEIRKRPLIETNGETGEIVWDKGRDF ATVRKVLSPQVNVKKTVEVQTGGFSKESILPKRNSDKLIARCKDWDPKKYGGFDSPTV AYSVLVVAKEVGKSKKLLSVKELLGITIMERSSEFKNPIDFLEAKGYKEVKKDLIHLKPK YSLFELENGRKRMLASAGELQKGNELALPSKYVNFYLYLASHYEKLGSPEDNEQKQLFV EQHKHYLDEIIEQISEFSKRVLADANLKVLSAYNKHRRDKPIREQAENIHLFTLNLGAP AAFKYFDTTIDRKRYTSTKEVLDATLIHQISITGLYETRIDLSQLGGDGGGSLAAKRSRTT	186
具有NLS2的 Cas9的氨基 酸序列	MDKKYSIGLDIGTNSVGVAVITDEYKVPSSKFKVLGNTRHSIKKNLIGALLFDSGETAE ATRLKRTARRRYTRRNKRYLQEIFSNEMAKVDDSFHRLSEESFLVEEDKKHERHPFIGN IVDEVAYHEKYPTIYHLRKKLVDSTDKADLRILIYLAHMIKFRGHFLIEGDLNPDNSDV DKLFIQLVQTYNQLFEENPINASGVDAKAILSARLSKSRRLLENLIALPGEKKNLGFNLI ALSLGLTPNFKSNFDLAEDAKLQLSKDTYDDDLNLLAQIGDQYADLFLAAKNLSDAIL LSDILRVNTEITKAPLSASMIKRYDEHHQDLTLLKALVRQQLPEKYKEIFFDQSKNGYAGY IDGGASQEEFYKFIKPILEKMDGTEELLVKNLREDLLRKQRTFDNGSIPHQIHLGELHAILR IQEDFYFLKDNREKIEKILTRIPYYVGPLARGNSRFAMWTRKSEETITPWNFEVVDK GASAQSFIERMTNFDKNLPNEKVLPHKSLLYEYFTVYNELTKVKYVTEGMRKPAFLSGE QKKAIVDLLFKTNRKVTVKQLKEDYFKKIECFDSVEISGVEDRFNASLGTYHDLKIKD KDFLDNEENEDILEDIVLTLTFEDREMIEERLKYAHLFDDKVMKQLKRRRYTGWRSL RKLINGIRDKQSGKTILDFLKSDFANRNFMLIHDDSLTFKEDIQKAQVSGQGDSLHEHI ANLAGSPAIKKILQTVKVVDELKVMGRHKPENIVIEMARENQTTQKGGQNSRERMK RIEFIGELGSQLKEHPVENTQLQNEKLYLYLQNGRDMYVDQELDINRLSDYDVDHIV PQSFLKDDSIDNKVLTRSDKNRGSNDVPSEEVVKMKMKNYWRQLLNAKLITQRKFDNLT KAERGGSELSEDKAGFIKRLVETRQITKHVAQILDSRMNTKYDENDKLIREVKVITLKS LVSDFRKDFQFYKVRINNYHHAHDAYLNAVVGTAALIKKYPKLESEFVYGDYKVVYDVR KMIKSEQEIQKATAKYFFYSNIMNFFKTEITLANGEIRKRPLIETNGETGEIVWDKGRDF ATVRKVLSPQVNVKKTVEVQTGGFSKESILPKRNSDKLIARCKDWDPKKYGGFDSPTV AYSVLVVAKEVGKSKKLLSVKELLGITIMERSSEFKNPIDFLEAKGYKEVKKDLIHLKPK YSLFELENGRKRMLASAGELQKGNELALPSKYVNFYLYLASHYEKLGSPEDNEQKQLFV EQHKHYLDEIIEQISEFSKRVLADANLKVLSAYNKHRRDKPIREQAENIHLFTLNLGAP AAFKYFDTTIDRKRYTSTKEVLDATLIHQISITGLYETRIDLSQLGGDGGGSLAAKRSRTT	187
具有NLS3的 Cas9的氨基 酸序列	MDKKYSIGLDIGTNSVGVAVITDEYKVPSSKFKVLGNTRHSIKKNLIGALLFDSGETAE ATRLKRTARRRYTRRNKRYLQEIFSNEMAKVDDSFHRLSEESFLVEEDKKHERHPFIGN IVDEVAYHEKYPTIYHLRKKLVDSTDKADLRILIYLAHMIKFRGHFLIEGDLNPDNSDV DKLFIQLVQTYNQLFEENPINASGVDAKAILSARLSKSRRLLENLIALPGEKKNLGFNLI ALSLGLTPNFKSNFDLAEDAKLQLSKDTYDDDLNLLAQIGDQYADLFLAAKNLSDAIL LSDILRVNTEITKAPLSASMIKRYDEHHQDLTLLKALVRQQLPEKYKEIFFDQSKNGYAGY IDGGASQEEFYKFIKPILEKMDGTEELLVKNLREDLLRKQRTFDNGSIPHQIHLGELHAILR IQEDFYFLKDNREKIEKILTRIPYYVGPLARGNSRFAMWTRKSEETITPWNFEVVDK	188

[0793]

	GASAQSFIERMTNFDKNLPNEKVLPHKSHLLYEYFTVYNELTKVKYVTEGMRKPAFLSGE QKKAIVDLLFKTNRKVTYKQLKEDYFKKIECFDSVEISGVEDRFNASLGTYHDLKLIKD KDFLDNEENEDILEDIVLTLTLFEDREMIEERLKYAHLFDDKVMKQLKRRRYTGWGRSL RKLINGIRDKQSGKTILDFLKSDFANRNFMLIHDDSLTFKEDIQKAQVSGQGDSLHEHI ANLAGSPAIKKGILQTVKVVDELVKVMGRHKPENVIEMARENQTTQKGQKNSRERMK RIEEGIKELGSQLKEHPVENTQLQNEKLYLYLQNGRDMYVDQELDINRSLSDYDVDHIV PQSFLKDDSIDNKVLTRSDKNRKGSDNVPSEEVVKMKMKNYWRQLLNAKLITQRKFDNLT KAERGGSELDDKAGFIKRVLQVETQITKHVAQILDSRMNTKYDENDKLIREVKVITLKS LVSDFRKDFQFYKVRINNYHHAHDAYLNAVGTALIKKYPKLESEFVYGDYKVVYDVR KMAKSEQEIGKATAKYFFYSNIMNFFKTEITLANGEIRKPLIETNGETGEIVWDKGRDF ATVRKVLSPQVNIKKTEVQTGGFSKESILPKRNSDKLIARKKDWDPKKYGGFDSPTV AYSVLVAVKVEKGKSKKLSVKELLGITIMERSSEFKNPIDFLEAKGYKEVKKDLIILPK YSLFEENGRKRLASAGELQKGNELALPSKYVNFLYLASHYEKLGKSPEDNEQKQLFV EQHKHYLDEIIEQISEFSKRVILADANLDKVL SAYNKHRDKPIREQAENIIHFLTTLNLGAP AAFKYFDTTIDRKRYTSTKEVLDATLIHQSIITGLYETRIDLSQLGGDGGSPAPAKRERTT	
具有NLS4的 Cas9的氨基 酸序列	MDKKYSIGLDIGTNSVGVAVITDEYK VPSKKFKVLGNTDRHSIKKNLIGALLFDSGETAE ATRLKRTARRRYTRRKNRICYLQEIFSNEMAKVDDSFHRLSEESFLVEEDKKHERHPFGN IVDEVAYHEKYPTIYHLRKKLVDSTDKADLRLIYLALAHMIKFRGHFLIEGDLNPDNSDV DKLFIQLVQTYNQLFEENPINASGVDAKAILSARLSKSRRLLENLIAQLPGEKKNLFGNLI ALSLGLTPNFKSNFDLAEDAQLQSKDQYDQDLDNLLAQIGDQYADLFLAAKNLSDAIL LSDILRVNTEITKAPLSASMIKRYDEHHQDLTLLKALVRQQLPEKYKEIFFDQSKNGYAGY IDGGASQEEFYKFIKPILEKMDGTEELLVKNLREDLLRKQRTFDNGSIPHQIHLGELHAILR RQEDFYFLKDNREKIEKILTRIPYYVGPLARGNSRFAMTRKSEETITPWNFEFVVDK GASAQSFIERMTNFDKNLPNEKVLPHKSHLLYEYFTVYNELTKVKYVTEGMRKPAFLSGE QKKAIVDLLFKTNRKVTYKQLKEDYFKKIECFDSVEISGVEDRFNASLGTYHDLKLIKD KDFLDNEENEDILEDIVLTLTLFEDREMIEERLKYAHLFDDKVMKQLKRRRYTGWGRSL RKLINGIRDKQSGKTILDFLKSDFANRNFMLIHDDSLTFKEDIQKAQVSGQGDSLHEHI ANLAGSPAIKKGILQTVKVVDELVKVMGRHKPENVIEMARENQTTQKGQKNSRERMK RIEEGIKELGSQLKEHPVENTQLQNEKLYLYLQNGRDMYVDQELDINRSLSDYDVDHIV PQSFLKDDSIDNKVLTRSDKNRKGSDNVPSEEVVKMKMKNYWRQLLNAKLITQRKFDNLT KAERGGSELDDKAGFIKRVLQVETQITKHVAQILDSRMNTKYDENDKLIREVKVITLKS LVSDFRKDFQFYKVRINNYHHAHDAYLNAVGTALIKKYPKLESEFVYGDYKVVYDVR KMAKSEQEIGKATAKYFFYSNIMNFFKTEITLANGEIRKPLIETNGETGEIVWDKGRDF ATVRKVLSPQVNIKKTEVQTGGFSKESILPKRNSDKLIARKKDWDPKKYGGFDSPTV AYSVLVAVKVEKGKSKKLSVKELLGITIMERSSEFKNPIDFLEAKGYKEVKKDLIILPK YSLFEENGRKRLASAGELQKGNELALPSKYVNFLYLASHYEKLGKSPEDNEQKQLFV EQHKHYLDEIIEQISEFSKRVILADANLDKVL SAYNKHRDKPIREQAENIIHFLTTLNLGAP AAFKYFDTTIDRKRYTSTKEVLDATLIHQSIITGLYETRIDLSQLGGDGGSPAPAKRERTT	189
具有NLS5的 Cas9的氨基 酸序列	MDKKYSIGLDIGTNSVGVAVITDEYK VPSKKFKVLGNTDRHSIKKNLIGALLFDSGETAE ATRLKRTARRRYTRRKNRICYLQEIFSNEMAKVDDSFHRLSEESFLVEEDKKHERHPFGN IVDEVAYHEKYPTIYHLRKKLVDSTDKADLRLIYLALAHMIKFRGHFLIEGDLNPDNSDV DKLFIQLVQTYNQLFEENPINASGVDAKAILSARLSKSRRLLENLIAQLPGEKKNLFGNLI ALSLGLTPNFKSNFDLAEDAQLQSKDQYDQDLDNLLAQIGDQYADLFLAAKNLSDAIL LSDILRVNTEITKAPLSASMIKRYDEHHQDLTLLKALVRQQLPEKYKEIFFDQSKNGYAGY IDGGASQEEFYKFIKPILEKMDGTEELLVKNLREDLLRKQRTFDNGSIPHQIHLGELHAILR RQEDFYFLKDNREKIEKILTRIPYYVGPLARGNSRFAMTRKSEETITPWNFEFVVDK GASAQSFIERMTNFDKNLPNEKVLPHKSHLLYEYFTVYNELTKVKYVTEGMRKPAFLSGE QKKAIVDLLFKTNRKVTYKQLKEDYFKKIECFDSVEISGVEDRFNASLGTYHDLKLIKD KDFLDNEENEDILEDIVLTLTLFEDREMIEERLKYAHLFDDKVMKQLKRRRYTGWGRSL RKLINGIRDKQSGKTILDFLKSDFANRNFMLIHDDSLTFKEDIQKAQVSGQGDSLHEHI ANLAGSPAIKKGILQTVKVVDELVKVMGRHKPENVIEMARENQTTQKGQKNSRERMK RIEEGIKELGSQLKEHPVENTQLQNEKLYLYLQNGRDMYVDQELDINRSLSDYDVDHIV PQSFLKDDSIDNKVLTRSDKNRKGSDNVPSEEVVKMKMKNYWRQLLNAKLITQRKFDNLT KAERGGSELDDKAGFIKRVLQVETQITKHVAQILDSRMNTKYDENDKLIREVKVITLKS LVSDFRKDFQFYKVRINNYHHAHDAYLNAVGTALIKKYPKLESEFVYGDYKVVYDVR KMAKSEQEIGKATAKYFFYSNIMNFFKTEITLANGEIRKPLIETNGETGEIVWDKGRDF ATVRKVLSPQVNIKKTEVQTGGFSKESILPKRNSDKLIARKKDWDPKKYGGFDSPTV AYSVLVAVKVEKGKSKKLSVKELLGITIMERSSEFKNPIDFLEAKGYKEVKKDLIILPK YSLFEENGRKRLASAGELQKGNELALPSKYVNFLYLASHYEKLGKSPEDNEQKQLFV EQHKHYLDEIIEQISEFSKRVILADANLDKVL SAYNKHRDKPIREQAENIIHFLTTLNLGAP AAFKYFDTTIDRKRYTSTKEVLDATLIHQSIITGLYETRIDLSQLGGDGGSPAPAKRERTT	190
具有NLS6的 Cas9的氨基 酸序列	MDKKYSIGLDIGTNSVGVAVITDEYK VPSKKFKVLGNTDRHSIKKNLIGALLFDSGETAE ATRLKRTARRRYTRRKNRICYLQEIFSNEMAKVDDSFHRLSEESFLVEEDKKHERHPFGN IVDEVAYHEKYPTIYHLRKKLVDSTDKADLRLIYLALAHMIKFRGHFLIEGDLNPDNSDV DKLFIQLVQTYNQLFEENPINASGVDAKAILSARLSKSRRLLENLIAQLPGEKKNLFGNLI ALSLGLTPNFKSNFDLAEDAQLQSKDQYDQDLDNLLAQIGDQYADLFLAAKNLSDAIL ALSGLTPNFKSNFDLAEDAQLQSKDQYDQDLDNLLAQIGDQYADLFLAAKNLSDAIL	191

[0794]

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<p>具有NLS7的 Cas9的氨基 酸序列</p>	<p>MDKKYSIGLDIGTNSVGWAVITDEYKVPSSKFKVLGNTDRHSIKKNLIGALLFDSGETAE ATRLKRTARRRYTRRKNRICYLQEIFSNEMAKVDDSFHRL EESFLVEEDKKHERHPFIGN IVDEVAYHEKYPTIYHLRKLVDSTDKADLRLIYLA LAHMIKFRGHFLIEGDLNPDNSDV DKLFIQLVQTYNQLFEENPINASGVDAKAILSARLSKSRRLLENLIAQLPGEKKNGLFGNLI ALSLGLTPNFKSNFDLAEDAQLSKDQYDQYADLFLAAKNLSDAIL LSDILRVNTEITKAPLSASMIKRYDEHHQDLTLLKALVRQQLPEKYKEIFFDQSKNGYAGY IDGGASQEEFYKFIKPILEKMDGTEELLVKNREDLLRKQRTFDNGSIPHQIHLGELHAILR RQEDFYFPLKDNREKIEKILTRIPYYVGPLARGNSRFAMTRKSEETITPWNFEVVVK GASAQSFIERMTNFDKNLPNEKVLPHSLLYEYFTVYNELTKVKYVTEGMRKPAFLSGE QKKAIVDLLFKTNRKVTVKQLKEDYFKKIECFDSVEISGVEDRFNASLGTYHDLKIIKD KDFLDNEENEDILEDIVLTLTLFEDREMIEERLKYAHLFDDKVMKQLKRRRYTGWRLS RKLINGIRDKQSGKTILDFLKSDFANRNFQMLIHDDSLTFKEDIQKAQVSGQGDSLHEHI ANLAGSPAIKKGILQTVKVVDELVKVMGRHKPENIVIAMARENQTTQKGQKNSRERMK RIEIEGKELGSQILKEHPVENTQLQNEKLYLYLQNGRDMYVDQELDINRLSDYDVDHIV PQSFLKDDSIDNKVLTRSDKNRGSNDVPSEEVVKMKMKNYWRQLNAKLITQRKFDNLT KAERGGSELKAGFIKQRLVETROITKHVAQILDSRMNTKYDENDKLIREVKVITLKS LVSDFRKDFQFYKVRINNYHHAHDAYLNAVGTALIKKYPKLESEFVYGDYKVVYDVR KMIKSEQEI GKATAKYFFYSNIMNFFKTEITLANGEIRKRPLIETNGETGEIVWDKGRDF ATVRKVL SMPQVNIKKTEVQTGGFSKESILPKRNSDKLIARKKDWDPKKGFFDSPTV AYSVLVAKVEKGKSKKLSVKELLGITIMERSSEKPNIDFLEAKGYKEVKKDLIILPK YSLFELENGRKRMLASAGELQKGNELALPSKYVNFLYLASHYEKLGSPEDNEQKQLFV EQHKHYLDEIIEQISEFSKRVLADANLDKVL SAYNKHDKPIREQAENIHLFTLNLGAP AAFKYFDTTIDRKRYTSTKEVL DATLIHQSI TGLYETRIDLSQLGGGGGSAAKRVWSM AF</p>	<p>192</p>
<p>具有NLS8的 Cas9的氨基 酸序列</p>	<p>MDKKYSIGLDIGTNSVGWAVITDEYKVPSSKFKVLGNTDRHSIKKNLIGALLFDSGETAE ATRLKRTARRRYTRRKNRICYLQEIFSNEMAKVDDSFHRL EESFLVEEDKKHERHPFIGN IVDEVAYHEKYPTIYHLRKLVDSTDKADLRLIYLA LAHMIKFRGHFLIEGDLNPDNSDV DKLFIQLVQTYNQLFEENPINASGVDAKAILSARLSKSRRLLENLIAQLPGEKKNGLFGNLI ALSLGLTPNFKSNFDLAEDAQLSKDQYDQYADLFLAAKNLSDAIL LSDILRVNTEITKAPLSASMIKRYDEHHQDLTLLKALVRQQLPEKYKEIFFDQSKNGYAGY IDGGASQEEFYKFIKPILEKMDGTEELLVKNREDLLRKQRTFDNGSIPHQIHLGELHAILR RQEDFYFPLKDNREKIEKILTRIPYYVGPLARGNSRFAMTRKSEETITPWNFEVVVK GASAQSFIERMTNFDKNLPNEKVLPHSLLYEYFTVYNELTKVKYVTEGMRKPAFLSGE QKKAIVDLLFKTNRKVTVKQLKEDYFKKIECFDSVEISGVEDRFNASLGTYHDLKIIKD KDFLDNEENEDILEDIVLTLTLFEDREMIEERLKYAHLFDDKVMKQLKRRRYTGWRLS RKLINGIRDKQSGKTILDFLKSDFANRNFQMLIHDDSLTFKEDIQKAQVSGQGDSLHEHI ANLAGSPAIKKGILQTVKVVDELVKVMGRHKPENIVIAMARENQTTQKGQKNSRERMK RIEIEGKELGSQILKEHPVENTQLQNEKLYLYLQNGRDMYVDQELDINRLSDYDVDHIV PQSFLKDDSIDNKVLTRSDKNRGSNDVPSEEVVKMKMKNYWRQLNAKLITQRKFDNLT KAERGGSELKAGFIKQRLVETROITKHVAQILDSRMNTKYDENDKLIREVKVITLKS LVSDFRKDFQFYKVRINNYHHAHDAYLNAVGTALIKKYPKLESEFVYGDYKVVYDVR KMIKSEQEI GKATAKYFFYSNIMNFFKTEITLANGEIRKRPLIETNGETGEIVWDKGRDF ATVRKVL SMPQVNIKKTEVQTGGFSKESILPKRNSDKLIARKKDWDPKKGFFDSPTV AYSVLVAKVEKGKSKKLSVKELLGITIMERSSEKPNIDFLEAKGYKEVKKDLIILPK YSLFELENGRKRMLASAGELQKGNELALPSKYVNFLYLASHYEKLGSPEDNEQKQLFV EQHKHYLDEIIEQISEFSKRVLADANLDKVL SAYNKHDKPIREQAENIHLFTLNLGAP AAFKYFDTTIDRKRYTSTKEVL DATLIHQSI TGLYETRIDLSQLGGGGGSAAKRSWSM AA</p>	<p>193</p>

具有 NLS9 的 Cas9 的氨基酸序列	<p>AF</p> <p>MDKKYSIGLDIGTNSVGVAVITDEYKVPSSKFKVLGNTDRHSIKKNLIGALLFDSGETAE ATRLKRTARRRYTRRKNRICYLQEIFSNEMAKVDDSFHRLVESFLVEEDKKHERHPFIGN IVDEVAYHEKYPTIYHLRKLVDSTDKADRLRIYLALAHMIKFRGHFLIEGDLNPDNSDV DKLFIQLVQTYNQLFEEENPINASGVDAKAILSARLSKSRRLLENLIAQLPGEKKNLFGNLI ALSLGLTPNFKSNFDLAEDAKLQLSKDYDDDLNLLAQIGDQYADLFLAAKNLSDAIL LSDILRVNTEITKAPLSASMIKRYDEHHQDLTLLKALVRQQLPEKYKEIFFDQSKNGYAGY IDGGASQEEFYKFIKPILEKMDGTEELLVKNLREDLLRKQRTFDNGSIPHQIHLGELHAILR RQEDFYPFKLDNREKIEKILTRIPYYVGPLARGNSRFAMWTRKSEETITPWNFEVVDK GASAQSFIERMTNFDKNLPNEKVLPHSLLYEYFTVYNELTKVKYVTEGMRKPAFLSGE QKKAIVDLLFKTNRKVTVKQLKEDYFKKIECFDSVEISGVEDRFNASLGTIYHDLKIIKD KDFLDNEENEDILEDIVLTLTLFEDREMIEERLKYAHLFDDKVMKQLKRRRYTGWRLS RKLINGIRDKQSGKTILDFLKSDFANRNFMLIHDDSLTFKEDIQKAQVSGQGDSLHEHI ANLAGSPAIKKGILQTVKVVDELVKVMGRHKPENIVIAMARENQTTQKGQKNSRERMK RIEEGIKELGSQILKEHPVENTQLQNEKLYLYLQNGRDMYVDQELDINRLSDYDVDHIV PQSFLKDDSIDNKVLTRSDKNRGSNDVPSEEVVKMKMKNYWRQLLNAKLITQRKFDNLT KAERGGSELKAGFIKRLVETROITKHVAQILDSRMNTKYDENDKLIREVKVITLKS LVSDFRKDFQFYKVRINNYHHAHDAYLNAVGTALIKKYPKLESEFVYGDYKVDVDR KMIAKSEQEIGKATAKYFFYSNIMNFFKTEITLANGEIRKRPLIETNGETGEIVWDKGRDF ATVRKVL SMPQVNVKKTVEVQTGGFSKESILPKRNSDKLIARKKDWDPKYYGGFDSPTV AYSVLVVAKEVGKSKKLSVKELGITIMERSSEFKNPIDFLEAKGYKEVKKDLIILPK YSLFELENGRKRMLASAGELQKGNELALPSKYVNFLYLASHYEKLGKSPEDNEQKQLFV EQHKHYLDEIIEQISEFSKRVLADANLDKVL SAYNKHRDKPIREQAENIIHFLTTLNLGAP AAFKYFDTTIDRKRYTSTKEVLDATLIHQISITGLYETRIDLSQLGGGGGSAAKRKYFA A</p>	194
具有 NLS10 的 Cas9 的氨基酸序列	<p>MDKKYSIGLDIGTNSVGVAVITDEYKVPSSKFKVLGNTDRHSIKKNLIGALLFDSGETAE ATRLKRTARRRYTRRKNRICYLQEIFSNEMAKVDDSFHRLVESFLVEEDKKHERHPFIGN IVDEVAYHEKYPTIYHLRKLVDSTDKADRLRIYLALAHMIKFRGHFLIEGDLNPDNSDV DKLFIQLVQTYNQLFEEENPINASGVDAKAILSARLSKSRRLLENLIAQLPGEKKNLFGNLI ALSLGLTPNFKSNFDLAEDAKLQLSKDYDDDLNLLAQIGDQYADLFLAAKNLSDAIL LSDILRVNTEITKAPLSASMIKRYDEHHQDLTLLKALVRQQLPEKYKEIFFDQSKNGYAGY IDGGASQEEFYKFIKPILEKMDGTEELLVKNLREDLLRKQRTFDNGSIPHQIHLGELHAILR RQEDFYPFKLDNREKIEKILTRIPYYVGPLARGNSRFAMWTRKSEETITPWNFEVVDK GASAQSFIERMTNFDKNLPNEKVLPHSLLYEYFTVYNELTKVKYVTEGMRKPAFLSGE QKKAIVDLLFKTNRKVTVKQLKEDYFKKIECFDSVEISGVEDRFNASLGTIYHDLKIIKD KDFLDNEENEDILEDIVLTLTLFEDREMIEERLKYAHLFDDKVMKQLKRRRYTGWRLS RKLINGIRDKQSGKTILDFLKSDFANRNFMLIHDDSLTFKEDIQKAQVSGQGDSLHEHI ANLAGSPAIKKGILQTVKVVDELVKVMGRHKPENIVIAMARENQTTQKGQKNSRERMK RIEEGIKELGSQILKEHPVENTQLQNEKLYLYLQNGRDMYVDQELDINRLSDYDVDHIV PQSFLKDDSIDNKVLTRSDKNRGSNDVPSEEVVKMKMKNYWRQLLNAKLITQRKFDNLT KAERGGSELKAGFIKRLVETROITKHVAQILDSRMNTKYDENDKLIREVKVITLKS LVSDFRKDFQFYKVRINNYHHAHDAYLNAVGTALIKKYPKLESEFVYGDYKVDVDR KMIAKSEQEIGKATAKYFFYSNIMNFFKTEITLANGEIRKRPLIETNGETGEIVWDKGRDF ATVRKVL SMPQVNVKKTVEVQTGGFSKESILPKRNSDKLIARKKDWDPKYYGGFDSPTV AYSVLVVAKEVGKSKKLSVKELGITIMERSSEFKNPIDFLEAKGYKEVKKDLIILPK YSLFELENGRKRMLASAGELQKGNELALPSKYVNFLYLASHYEKLGKSPEDNEQKQLFV EQHKHYLDEIIEQISEFSKRVLADANLDKVL SAYNKHRDKPIREQAENIIHFLTTLNLGAP AAFKYFDTTIDRKRYTSTKEVLDATLIHQISITGLYETRIDLSQLGGGGGSAAKRKAFA A</p>	195
具有 NLS11 的 Cas9 的氨基酸序列	<p>MDKKYSIGLDIGTNSVGVAVITDEYKVPSSKFKVLGNTDRHSIKKNLIGALLFDSGETAE ATRLKRTARRRYTRRKNRICYLQEIFSNEMAKVDDSFHRLVESFLVEEDKKHERHPFIGN IVDEVAYHEKYPTIYHLRKLVDSTDKADRLRIYLALAHMIKFRGHFLIEGDLNPDNSDV DKLFIQLVQTYNQLFEEENPINASGVDAKAILSARLSKSRRLLENLIAQLPGEKKNLFGNLI ALSLGLTPNFKSNFDLAEDAKLQLSKDYDDDLNLLAQIGDQYADLFLAAKNLSDAIL LSDILRVNTEITKAPLSASMIKRYDEHHQDLTLLKALVRQQLPEKYKEIFFDQSKNGYAGY IDGGASQEEFYKFIKPILEKMDGTEELLVKNLREDLLRKQRTFDNGSIPHQIHLGELHAILR RQEDFYPFKLDNREKIEKILTRIPYYVGPLARGNSRFAMWTRKSEETITPWNFEVVDK GASAQSFIERMTNFDKNLPNEKVLPHSLLYEYFTVYNELTKVKYVTEGMRKPAFLSGE QKKAIVDLLFKTNRKVTVKQLKEDYFKKIECFDSVEISGVEDRFNASLGTIYHDLKIIKD KDFLDNEENEDILEDIVLTLTLFEDREMIEERLKYAHLFDDKVMKQLKRRRYTGWRLS RKLINGIRDKQSGKTILDFLKSDFANRNFMLIHDDSLTFKEDIQKAQVSGQGDSLHEHI ANLAGSPAIKKGILQTVKVVDELVKVMGRHKPENIVIAMARENQTTQKGQKNSRERMK RIEEGIKELGSQILKEHPVENTQLQNEKLYLYLQNGRDMYVDQELDINRLSDYDVDHIV PQSFLKDDSIDNKVLTRSDKNRGSNDVPSEEVVKMKMKNYWRQLLNAKLITQRKFDNLT KAERGGSELKAGFIKRLVETROITKHVAQILDSRMNTKYDENDKLIREVKVITLKS LVSDFRKDFQFYKVRINNYHHAHDAYLNAVGTALIKKYPKLESEFVYGDYKVDVDR</p>	196
[0796]	<p>KMIAKSEQEIGKATAKYFFYSNIMNFFKTEITLANGEIRKRPLIETNGETGEIVWDKGRDF ATVRKVL SMPQVNVKKTVEVQTGGFSKESILPKRNSDKLIARKKDWDPKYYGGFDSPTV AYSVLVVAKEVGKSKKLSVKELGITIMERSSEFKNPIDFLEAKGYKEVKKDLIILPK YSLFELENGRKRMLASAGELQKGNELALPSKYVNFLYLASHYEKLGKSPEDNEQKQLFV EQHKHYLDEIIEQISEFSKRVLADANLDKVL SAYNKHRDKPIREQAENIIHFLTTLNLGAP AAFKYFDTTIDRKRYTSTKEVLDATLIHQISITGLYETRIDLSQLGGGGGSAAKRKYFAV</p>	

[0797] * = PS键; 'm' = 2'-O-Me核苷酸。

序列表

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Ile Leu Gln Thr Val Lys Val Val Asp Glu Leu Val Lys Val Met Gly
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Leu Ser Asp Tyr Asp Val Asp His Ile Val Pro Gln Ser Phe Leu Lys
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 35 40 45
 Gly Ala Leu Leu Phe Asp Ser Gly Glu Thr Ala Glu Ala Thr Arg Leu
 50 55 60
 Lys Arg Thr Ala Arg Arg Arg Tyr Thr Arg Arg Lys Asn Arg Ile Cys
 65 70 75 80
 Tyr Leu Gln Glu Ile Phe Ser Asn Glu Met Ala Lys Val Asp Asp Ser
 85 90 95
 Phe Phe His Arg Leu Glu Glu Ser Phe Leu Val Glu Glu Asp Lys Lys
 100 105 110
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 115 120 125
 His Glu Lys Tyr Pro Thr Ile Tyr His Leu Arg Lys Lys Leu Val Asp
 130 135 140
 Ser Thr Asp Lys Ala Asp Leu Arg Leu Ile Tyr Leu Ala Leu Ala His
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 165 170 175
 Asp Asn Ser Asp Val Asp Lys Leu Phe Ile Gln Leu Val Gln Thr Tyr
 180 185 190
 Asn Gln Leu Phe Glu Glu Asn Pro Ile Asn Ala Ser Gly Val Asp Ala
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 Lys Ala Ile Leu Ser Ala Arg Leu Ser Lys Ser Arg Arg Leu Glu Asn
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 225 230 235 240
 Leu Ile Ala Leu Ser Leu Gly Leu Thr Pro Asn Phe Lys Ser Asn Phe
 245 250 255
 Asp Leu Ala Glu Asp Ala Lys Leu Gln Leu Ser Lys Asp Thr Tyr Asp
 260 265 270

Asp Asp Leu Asp Asn Leu Leu Ala Gln Ile Gly Asp Gln Tyr Ala Asp
 275 280 285
 Leu Phe Leu Ala Ala Lys Asn Leu Ser Asp Ala Ile Leu Leu Ser Asp
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 Ile Leu Arg Val Asn Thr Glu Ile Thr Lys Ala Pro Leu Ser Ala Ser
 305 310 315 320
 Met Ile Lys Arg Tyr Asp Glu His His Gln Asp Leu Thr Leu Leu Lys
 325 330 335
 Ala Leu Val Arg Gln Gln Leu Pro Glu Lys Tyr Lys Glu Ile Phe Phe
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 Asp Gln Ser Lys Asn Gly Tyr Ala Gly Tyr Ile Asp Gly Gly Ala Ser
 355 360 365
 Gln Glu Glu Phe Tyr Lys Phe Ile Lys Pro Ile Leu Glu Lys Met Asp
 370 375 380
 Gly Thr Glu Glu Leu Leu Val Lys Leu Asn Arg Glu Asp Leu Leu Arg
 385 390 395 400
 Lys Gln Arg Thr Phe Asp Asn Gly Ser Ile Pro His Gln Ile His Leu
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 Val Val Asp Lys Gly Ala Ser Ala Gln Ser Phe Ile Glu Arg Met Thr
 485 490 495
 Asn Phe Asp Lys Asn Leu Pro Asn Glu Lys Val Leu Pro Lys His Ser
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 Tyr Val Thr Glu Gly Met Arg Lys Pro Ala Phe Leu Ser Gly Glu Gln
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 Val Lys Gln Leu Lys Glu Asp Tyr Phe Lys Lys Ile Glu Cys Phe Asp
 565 570 575

Ser Val Glu Ile Ser Gly Val Glu Asp Arg Phe Asn Ala Ser Leu Gly
 580 585 590

Thr Tyr His Asp Leu Leu Lys Ile Ile Lys Asp Lys Asp Phe Leu Asp
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Asn Glu Glu Asn Glu Asp Ile Leu Glu Asp Ile Val Leu Thr Leu Thr
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Leu Phe Glu Asp Arg Glu Met Ile Glu Glu Arg Leu Lys Thr Tyr Ala
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His Leu Phe Asp Asp Lys Val Met Lys Gln Leu Lys Arg Arg Arg Tyr
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Thr Gly Trp Gly Arg Leu Ser Arg Lys Leu Ile Asn Gly Ile Arg Asp
 660 665 670

Lys Gln Ser Gly Lys Thr Ile Leu Asp Phe Leu Lys Ser Asp Gly Phe
 675 680 685

Ala Asn Arg Asn Phe Met Gln Leu Ile His Asp Asp Ser Leu Thr Phe
 690 695 700

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Arg His Lys Pro Glu Asn Ile Val Ile Glu Met Ala Arg Glu Asn Gln
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Thr Thr Gln Lys Gly Gln Lys Asn Ser Arg Glu Arg Met Lys Arg Ile
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Glu Glu Gly Ile Lys Glu Leu Gly Ser Gln Ile Leu Lys Glu His Pro
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Lys Ala Gly Phe Ile Lys Arg Gln Leu Val Glu Thr Arg Gln Ile Thr	915	920	925
Lys His Val Ala Gln Ile Leu Asp Ser Arg Met Asn Thr Lys Tyr Asp	930	935	940
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Lys Leu Val Ser Asp Phe Arg Lys Asp Phe Gln Phe Tyr Lys Val Arg	965	970	975
Glu Ile Asn Asn Tyr His His Ala His Asp Ala Tyr Leu Asn Ala Val	980	985	990
Val Gly Thr Ala Leu Ile Lys Lys Tyr Pro Lys Leu Glu Ser Glu Phe	995	1000	1005
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Arg Lys Val Leu Ser Met Pro Gln Val Asn Ile Val Lys Lys Thr	1085	1090	1095
Glu Val Gln Thr Gly Gly Phe Ser Lys Glu Ser Ile Leu Pro Lys	1100	1105	1110
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Lys Lys Tyr Gly Gly Phe Asp Ser Pro Thr Val Ala Tyr Ser Val	1130	1135	1140
Leu Val Val Ala Lys Val Glu Lys Gly Lys Ser Lys Lys Leu Lys	1145	1150	1155

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	Phe Glu	Lys Asn Pro Ile Asp	Phe Leu Glu Ala Lys Gly Tyr Lys
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	Glu Val	Lys Lys Asp Leu Ile	Ile Lys Leu Pro Lys Tyr Ser Leu
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	Phe Glu	Leu Glu Asn Gly Arg	Lys Arg Met Leu Ala Ser Ala Gly
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	Glu Leu	Gln Lys Gly Asn Glu	Leu Ala Leu Pro Ser Lys Tyr Val
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	Pro Glu	Asp Asn Glu Gln Lys	Gln Leu Phe Val Glu Gln His Lys
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	His Tyr	Leu Asp Glu Ile Ile	Glu Gln Ile Ser Glu Phe Ser Lys
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	Arg Val	Ile Leu Ala Asp Ala	Asn Leu Asp Lys Val Leu Ser Ala
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	Ile Ile	His Leu Phe Thr Leu	Thr Asn Leu Gly Ala Pro Ala Ala
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	Phe Lys	Tyr Phe Asp Thr Thr	Ile Asp Arg Lys Arg Tyr Thr Ser
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<213> 人工序列

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<223> 合成的: dCas9 (D10A H840A) 氨基酸序列

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 35 40 45
 Gly Ala Leu Leu Phe Asp Ser Gly Glu Thr Ala Glu Ala Thr Arg Leu
 50 55 60
 Lys Arg Thr Ala Arg Arg Arg Tyr Thr Arg Arg Lys Asn Arg Ile Cys
 65 70 75 80
 Tyr Leu Gln Glu Ile Phe Ser Asn Glu Met Ala Lys Val Asp Asp Ser
 85 90 95
 Phe Phe His Arg Leu Glu Glu Ser Phe Leu Val Glu Glu Asp Lys Lys
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 His Glu Arg His Pro Ile Phe Gly Asn Ile Val Asp Glu Val Ala Tyr
 115 120 125
 His Glu Lys Tyr Pro Thr Ile Tyr His Leu Arg Lys Lys Leu Val Asp
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 Ser Thr Asp Lys Ala Asp Leu Arg Leu Ile Tyr Leu Ala Leu Ala His
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 245 250 255
 Asp Leu Ala Glu Asp Ala Lys Leu Gln Leu Ser Lys Asp Thr Tyr Asp
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 275 280 285
 Leu Phe Leu Ala Ala Lys Asn Leu Ser Asp Ala Ile Leu Leu Ser Asp
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 Ile Leu Arg Val Asn Thr Glu Ile Thr Lys Ala Pro Leu Ser Ala Ser
 305 310 315 320
 Met Ile Lys Arg Tyr Asp Glu His His Gln Asp Leu Thr Leu Leu Lys
 325 330 335

Ala Leu Val Arg Gln Gln Leu Pro Glu Lys Tyr Lys Glu Ile Phe Phe
340 345 350

Asp Gln Ser Lys Asn Gly Tyr Ala Gly Tyr Ile Asp Gly Gly Ala Ser
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Gln Glu Glu Phe Tyr Lys Phe Ile Lys Pro Ile Leu Glu Lys Met Asp
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Gly Thr Glu Glu Leu Leu Val Lys Leu Asn Arg Glu Asp Leu Leu Arg
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Lys Gln Arg Thr Phe Asp Asn Gly Ser Ile Pro His Gln Ile His Leu
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Gly Glu Leu His Ala Ile Leu Arg Arg Gln Glu Asp Phe Tyr Pro Phe
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Leu Lys Asp Asn Arg Glu Lys Ile Glu Lys Ile Leu Thr Phe Arg Ile
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Pro Tyr Tyr Val Gly Pro Leu Ala Arg Gly Asn Ser Arg Phe Ala Trp
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465 470 475 480

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Tyr Val Thr Glu Gly Met Arg Lys Pro Ala Phe Leu Ser Gly Glu Gln
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Lys Lys Ala Ile Val Asp Leu Leu Phe Lys Thr Asn Arg Lys Val Thr
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Val Lys Gln Leu Lys Glu Asp Tyr Phe Lys Lys Ile Glu Cys Phe Asp
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Ser Val Glu Ile Ser Gly Val Glu Asp Arg Phe Asn Ala Ser Leu Gly
580 585 590

Thr Tyr His Asp Leu Leu Lys Ile Ile Lys Asp Lys Asp Phe Leu Asp
595 600 605

Asn Glu Glu Asn Glu Asp Ile Leu Glu Asp Ile Val Leu Thr Leu Thr
610 615 620

Leu Phe Glu Asp Arg Glu Met Ile Glu Glu Arg Leu Lys Thr Tyr Ala

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His Leu Phe Asp	Asp Lys Val Met Lys	Gln Leu Lys Arg Arg	Arg Tyr
	645	650	655
Thr Gly Trp Gly	Arg Leu Ser Arg Lys	Leu Ile Asn Gly	Ile Arg Asp
	660	665	670
Lys Gln Ser Gly	Lys Thr Ile Leu Asp Phe	Leu Lys Ser Asp	Gly Phe
	675	680	685
Ala Asn Arg Asn	Phe Met Gln Leu Ile His	Asp Asp Ser	Leu Thr Phe
	690	695	700
Lys Glu Asp Ile	Gln Lys Ala Gln Val Ser	Gly Gln Gly Asp	Ser Leu
705	710	715	720
His Glu His Ile	Ala Asn Leu Ala Gly	Ser Pro Ala Ile	Lys Lys Gly
	725	730	735
Ile Leu Gln Thr	Val Lys Val Val Asp	Glu Leu Val Lys	Val Met Gly
	740	745	750
Arg His Lys Pro	Glu Asn Ile Val Ile	Glu Met Ala Arg	Glu Asn Gln
	755	760	765
[0023] Thr Thr Gln Lys	Gly Gln Lys Asn Ser Arg	Glu Arg Met	Lys Arg Ile
	770	775	780
Glu Glu Gly Ile	Lys Glu Leu Gly Ser	Gln Ile Leu Lys	Glu His Pro
785	790	795	800
Val Glu Asn Thr	Gln Leu Gln Asn Glu	Lys Leu Tyr Leu	Tyr Tyr Leu
	805	810	815
Gln Asn Gly Arg	Asp Met Tyr Val Asp	Gln Glu Leu Asp	Ile Asn Arg
	820	825	830
Leu Ser Asp Tyr	Asp Val Asp Ala Ile	Val Pro Gln Ser	Phe Leu Lys
	835	840	845
Asp Asp Ser Ile	Asp Asn Lys Val Leu Thr	Arg Ser Asp	Lys Asn Arg
	850	855	860
Gly Lys Ser Asp	Asn Val Pro Ser Glu	Glu Val Val Lys	Lys Met Lys
865	870	875	880
Asn Tyr Trp Arg	Gln Leu Leu Asn Ala	Lys Leu Ile Thr	Gln Arg Lys
	885	890	895
Phe Asp Asn Leu	Thr Lys Ala Glu Arg	Gly Gly Leu Ser	Glu Leu Asp
	900	905	910
Lys Ala Gly Phe	Ile Lys Arg Gln Leu	Val Glu Thr Arg	Gln Ile Thr
	915	920	925

Lys His Val Ala Gln Ile Leu Asp Ser Arg Met Asn Thr Lys Tyr Asp
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 Glu Asn Asp Lys Leu Ile Arg Glu Val Lys Val Ile Thr Leu Lys Ser
 945 950 955 960
 Lys Leu Val Ser Asp Phe Arg Lys Asp Phe Gln Phe Tyr Lys Val Arg
 965 970 975
 Glu Ile Asn Asn Tyr His His Ala His Asp Ala Tyr Leu Asn Ala Val
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 Val Gly Thr Ala Leu Ile Lys Lys Tyr Pro Lys Leu Glu Ser Glu Phe
 995 1000 1005
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 Tyr Ser Asn Ile Met Asn Phe Phe Lys Thr Glu Ile Thr Leu Ala
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 1055 1060 1065
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 1115 1120 1125
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 1130 1135 1140
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 1145 1150 1155
 Ser Val Lys Glu Leu Leu Gly Ile Thr Ile Met Glu Arg Ser Ser
 1160 1165 1170
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 1175 1180 1185
 Glu Val Lys Lys Asp Leu Ile Ile Lys Leu Pro Lys Tyr Ser Leu
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Glu Leu Gln Lys Gly Asn Glu Leu Ala Leu Pro Ser Lys Tyr Val
1220 1225 1230

Asn Phe Leu Tyr Leu Ala Ser His Tyr Glu Lys Leu Lys Gly Ser
1235 1240 1245

Pro Glu Asp Asn Glu Gln Lys Gln Leu Phe Val Glu Gln His Lys
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His Tyr Leu Asp Glu Ile Ile Glu Gln Ile Ser Glu Phe Ser Lys
1265 1270 1275

Arg Val Ile Leu Ala Asp Ala Asn Leu Asp Lys Val Leu Ser Ala
1280 1285 1290

Tyr Asn Lys His Arg Asp Lys Pro Ile Arg Glu Gln Ala Glu Asn
1295 1300 1305

Ile Ile His Leu Phe Thr Leu Thr Asn Leu Gly Ala Pro Ala Ala
1310 1315 1320

Phe Lys Tyr Phe Asp Thr Thr Ile Asp Arg Lys Arg Tyr Thr Ser
1325 1330 1335

Thr Lys Glu Val Leu Asp Ala Thr Leu Ile His Gln Ser Ile Thr
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 35 40 45

Gly Ala Leu Leu Phe Asp Ser Gly Glu Thr Ala Glu Ala Thr Arg Leu
 50 55 60

Lys Arg Thr Ala Arg Arg Arg Tyr Thr Arg Arg Lys Asn Arg Ile Cys
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Tyr Leu Gln Glu Ile Phe Ser Asn Glu Met Ala Lys Val Asp Asp Ser
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Phe Phe His Arg Leu Glu Glu Ser Phe Leu Val Glu Glu Asp Lys Lys
 100 105 110

His Glu Arg His Pro Ile Phe Gly Asn Ile Val Asp Glu Val Ala Tyr
 115 120 125
 His Glu Lys Tyr Pro Thr Ile Tyr His Leu Arg Lys Lys Leu Val Asp
 130 135 140
 Ser Thr Asp Lys Ala Asp Leu Arg Leu Ile Tyr Leu Ala Leu Ala His
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Thr Gly Trp Gly Arg Leu Ser Arg Lys Leu Ile Asn Gly Ile Arg Asp
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Ala Asn Arg Asn Phe Met Gln Leu Ile His Asp Asp Ser Leu Thr Phe
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 Val Gly Thr Ala Leu Ile Lys Lys Tyr Pro Lys Leu Glu Ser Glu Phe
 995 1000 1005
 Val Tyr Gly Asp Tyr Lys Val Tyr Asp Val Arg Lys Met Ile Ala

1010	1015	1020
Lys Ser Glu Gln Glu Ile Gly 1025	Lys Ala Thr Ala 1030	Lys Tyr Phe Phe 1035
Tyr Ser Asn Ile Met Asn Phe 1040	Phe Lys Thr Glu 1045	Ile Thr Leu Ala 1050
Asn Gly Glu Ile Arg Lys Arg 1055	Pro Leu Ile Glu 1060	Thr Asn Gly Glu 1065
Thr Gly Glu Ile Val Trp 1070	Asp Lys Gly Arg Asp 1075	Phe Ala Thr Val 1080
Arg Lys Val Leu Ser Met Pro 1085	Gln Val Asn Ile 1090	Val Lys Lys Thr 1095
Glu Val Gln Thr Gly Gly Phe 1100	Ser Lys Glu Ser 1105	Ile Leu Pro Lys 1110
Arg Asn Ser Asp Lys Leu Ile 1115	Ala Arg Lys Lys 1120	Asp Trp Asp Pro 1125
Lys Lys Tyr Gly Gly Phe Asp 1130	Ser Pro Thr Val 1135	Ala Tyr Ser Val 1140
[0037] Leu Val Val Ala Lys Val Glu 1145	Lys Gly Lys Ser 1150	Lys Lys Leu Lys 1155
Ser Val Lys Glu Leu Leu Gly 1160	Ile Thr Ile Met 1165	Glu Arg Ser Ser 1170
Phe Glu Lys Asn Pro Ile Asp 1175	Phe Leu Glu Ala 1180	Lys Gly Tyr Lys 1185
Glu Val Lys Lys Asp Leu Ile 1190	Ile Lys Leu Pro 1195	Lys Tyr Ser Leu 1200
Phe Glu Leu Glu Asn Gly Arg 1205	Lys Arg Met Leu 1210	Ala Ser Ala Gly 1215
Glu Leu Gln Lys Gly Asn Glu 1220	Leu Ala Leu Pro 1225	Ser Lys Tyr Val 1230
Asn Phe Leu Tyr Leu Ala Ser 1235	His Tyr Glu Lys 1240	Leu Lys Gly Ser 1245
Pro Glu Asp Asn Glu Gln Lys 1250	Gln Leu Phe Val 1255	Glu Gln His Lys 1260
His Tyr Leu Asp Glu Ile Ile 1265	Glu Gln Ile Ser 1270	Glu Phe Ser Lys 1275
Arg Val Ile Leu Ala Asp Ala 1280	Asn Leu Asp Lys 1285	Val Leu Ser Ala 1290

Tyr Asn Lys His Arg Asp Lys Pro Ile Arg Glu Gln Ala Glu Asn
 1295 1300 1305
 Ile Ile His Leu Phe Thr Leu Thr Asn Leu Gly Ala Pro Ala Ala
 1310 1315 1320
 Phe Lys Tyr Phe Asp Thr Thr Ile Asp Arg Lys Arg Tyr Thr Ser
 1325 1330 1335
 Thr Lys Glu Val Leu Asp Ala Thr Leu Ile His Gln Ser Ile Thr
 1340 1345 1350
 Gly Leu Tyr Glu Thr Arg Ile Asp Leu Ser Gln Leu Gly Gly Asp
 1355 1360 1365

<210> 14
 <211> 4107
 <212> RNA
 <213> 人工序列

<220>
 <223> 合成的:使用如表3中所列的最小尿苷密码子编码SEQ ID NO: 13的, 具有起始和终止密码子的Cas9 mRNA ORF

[0038]

<400> 14
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 aucacagacg aauacaaggu cccgagcaag aaguucaagg uccugggaaa cacagacaga 120
 cacagcauca agaagaaccu gaucggagca cugcuguucg acagcggaga aacagcagaa 180
 gcaacaagac ugaagagaac agcaagaaga agauacacaa gaagaaagaa cagaaucugc 240
 uaccugcagg aauucucag caacgaaaug gcaaaggucg acgacagcuu cuuccacaga 300
 cuggaagaaa gcuuccuggu cgaagaagac aagaagcagc aaagacacc gaucucggga 360
 aaucugucg acgaagucg auaccacgaa aaguaccgca caaucuacca ccugagaaag 420
 aagcuggucg acagcacaga caaggcagac cugagacuga ucuaccuggc acuggcacac 480
 augaucaagu ucagaggaca cuuccugauc gaaggagacc ugaaccggga caacagcgac 540
 gucgacaagc uguucaucca gcugguccag acauacaacc agcuguucga agaaaaccg 600
 aucaacgcaa gcggagucga cgcaaaggca auccugagcg caagacugag caagagcaga 660
 agacuggaaa accugaucg acagcugccg ggagaaaaga agaaccggcu guucggaaac 720
 cugaucgac ugagccuggg acugacaccg aacuucaaga gcaacuucga ccuggcagaa 780
 gacgcaaagc ugcagcugag caaggacaca uacgacgacg accuggacaa ccugcuggca 840
 cagaucggag accaguacgc agaccuguuc cuggcagcaa agaaccugag cgacgcaauc 900
 cugcugagcg acauccugag agucaacaca gaaaucaaaa aggcaccgcu gacgcaagc 960
 augaucaaga gauacgacga acaccaccag gaccugacac ugcugaaggc acugucaga 1020
 cagcagcugc cggaaaagua caaggaaauc uucucgacc agagcaagaa cggauacgca 1080
 ggauacaucg acggaggagc aagccaggaa gaaucuaca aguucauca gccgauccug 1140
 gaaaagauag acggaacaga agaacugcug gucaagcuga acagagaaga ccugcugaga 1200
 aagcagagaa cauucgacaa cggaagcauc ccgaccaga uccaccuggg agaacugcac 1260
 gcaauccuga gaagacagga agacuucua cccguuccuga aggacaacag agaaaagauc 1320
 gaaaagaucg ugacaucag aauccgucac uacgucggac cgcuggcaag aggaaacagc 1380

agauucgcau ggaugacaag aaagagcgaa gaaacaauca caccguggaa cuucgaagaa	1440
gucgucgaca agggagcaag cgcacagagc uucaucgaaa gaaugacaaa cuucgacaag	1500
aaccugccga acgaaaaggu ccugccgaag cacagccugc uguacgaaua cuucacaguc	1560
uacaacgaac ugacaaaaggu caaguacguc acagaaggaa ugagaaagcc ggcauuccug	1620
agcggagaac agaagaagc aaucgucgac cugcuguuca agacaaacag aaaggucaca	1680
gucaagcagc ugaaggaaga cuacuucaag aagaucgaau gcuucgacag cgucgaaauc	1740
agcggagucg aagacagauu caacgcaagc cugggaacau accacgaccu gcugaagauc	1800
aucaaggaca aggacuuccu ggacaacgaa gaaaacgaag acauccugga agacaucguc	1860
cugacacuga cacuguuca agacagagaa augaucgaag aaagacugaa gacauacgca	1920
caccuguucg acgacaaggu caugaagcag cugaagagaa gaagauacac aggaugggga	1980
agacugagca gaaagcugau caacggaauc agagacaagc agagcggaaa gacaauccug	2040
gacuuccuga agagcgacgg auucgcaaac agaaacuua ugcagcugau ccacgacgac	2100
agccugacau ucaaggaaga cauccagaag gcacagguca gggacaggg agacagccug	2160
cacgaacaca ucgcaaaccu ggcaggaagc ccggcaauca agaagggaau ccugcagaca	2220
gucaaggucg ucgacgaacu ggucaggguc augggaagac acaagccgga aaacaucguc	2280
aucgaaaug caagagaaaa ccagacaaca cagaaggac agaagaacag cagagaaaga	2340
augaagagaa ucgaagaagg aaucaggaag cugggaagcc agauccugaa ggaacaccg	2400
gucgaaaaca cacagcuga gaacgaaaag cuguaccugu acuaccugca gaacggaaga	2460
gacauguacg ucgaccagga acuggacauc aacagacuga gcgacuacga cgucgaccac	2520
[0039] aucgucccg agagcuuccu gaagcagcag agcaucgaca acaagguccu gacaagaagc	2580
gacaagaaca gaggaaagag cgacaacguc ccgagcgaag aagucgucaa gaagaugaag	2640
aacuacugga gacagcugcu gaacgcaaag cugaucacac agagaaaguu cgacaaccug	2700
acaaaggcag agagaggagg acugagcga cuggacaagg caggauucau caagagacag	2760
cuggucgaaa caagacagau cacaagcagc gucgcacaga uccuggacag cagaaugaac	2820
acaaaguacg acgaaaacga caagcugauc agagaaguca aggucaucac acugaagagc	2880
aagcugguca gcgacuucag aaaggacuuc caguucuaca aggucaagaa aaucacaac	2940
uaccaccagc cacacgagc auaccugaac gcagucgucg gaacagcacu gaucaagaag	3000
uaccgaagc uggaagcga auucgucuc ggagacuaca agguacuacga cgucagaaag	3060
augaucgcaa agagcgaaca ggaaucgga aaggcaacag caaaguacuu cuucuacagc	3120
aacaucauga acuucuuaa gacagaaauc acacuggcaa acggagaaau cagaaaagaa	3180
ccgucgaucg aaacaaacgg agaaacagga gaaucgucu gggacaaggg aagagacuuc	3240
gcaacaguca gaaagguccu gagcaugccg cagguaaca ucgucaagaa gacagaaguc	3300
cagacaggag gauucagcaa ggaagcauc cugccgaaga gaaacagcga caagcugauc	3360
gcaagaaaga aggacuggga cccgaagaag uacggaggau ucgacagccc gacagucgca	3420
uacagcucc ugguucguc aaaggucgaa aagggaaga gcaagaagcu gaagagcuc	3480
aaggaaucgc uggaauac aaucaugga agaagcagcu ucgaaaagaa ccgaucgac	3540
uuccuggaag caaagggaau caaggaaguc aagaaggacc ugaucaucaa gcugccgaag	3600
uacagccugu ucgaucgga aaacggaaga aagagaaucgc uggcaagcgc aggagaacug	3660

cagaaggaa acgaacuggc acugccgagc aaguacguca acuuccugua ccuggcaagc	3720
cacuacgaaa agcugaaggg aagcccggaa gacaacgaac agaagcagcu guucgucgaa	3780
cagcacaagc acuaccugga cgaaaucauc gaacagauca gcgaaauucag caagagaguc	3840
auccugcgag acgcaaacu ggacaagguc cugagcgcau acaacaagca cagagacaag	3900
ccgaucagag aacaggcaga aaacaucauc caccuguuca cacugacaaa ccugggagca	3960
ccggcagcau ucaaguacuu cgacacaaca aucgacagaa agagauacac aagcacaag	4020
gaaguccug acgcaacacu gaucaccag agcaucacag gacuguacga aacaagaauc	4080
gaccugagcc agcugggagg agacuag	4107

<210> 15
 <211> 4101
 <212> RNA
 <213> 人工序列

<220>
 <223> 合成的：使用如表3中所列的最小尿苷密码子编码SEQ ID NO: 13的Cas9编码序列(无起始或终止密码子；适于包括在融合蛋白质编码序列中)

[0040]

<400> 15	
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acagacgaau acaagguccc gagcaagaag uucaaggucc ugggaaacac agacagacac	120
agcaucaaga agaaccugau cggagcacug cuguucgaca gcggagaaac agcagaagca	180
acaagacuga agagaacagc aagaagaaga uacacaagaa gaaagaacag aaucugcuac	240
cugcaggaaa ucuucagcaa cgaaauugca aaggucgacg acagcuucuu ccacagacug	300
gaagaaagcu uccuggucga agaagacaag aagcacgaaa gacaccgcau cuucggaac	360
aucgucgacg aagucgcaua ccacgaaaag uaccgacaa ucuaccaccu gagaaaagag	420
cuggucgaca gcacagacaa ggcagaccug agacugaucu accuggcacu ggcacacaug	480
aucaaguuca gaggacacuu ccugaucgaa ggagaccuga acccggacaa cagcagacguc	540
gacaagcugu ucauccagcu gguccagaca uacaaccagc uguucgaaga aaaccgcauc	600
aacgcaagcg gagucgacgc aaaggcaauc cugagcgcaa gacugagcaa gagcagaaga	660
cuggaaaacc ugaucgcaca gcugccggga gaaaagaaga acggacuguu cggaaaccug	720
aucgcacuga gccugggacu gacaccgaac uucaagagca acuucgaccu ggcagaagac	780
gcaaaugcgc agcugagcaa ggacacauac gacgacgacc uggacaaccu gcuggcacag	840
aucggagacc aguacgcaga ccuguuccug gcagcaaaga accugagcga cgcaauccug	900
cugagcgaca uccugagagu caacacagaa aucacaaagg caccgcugag cgcaagcaug	960
aucaagagau acgacgaaca ccaccaggac cugacacugc ugaaggcacu ggucagacag	1020
cagcugccgg aaaaguacaa ggaaauucuu uucgaccaga gcaagaacgg auacgcagga	1080
uacaucgacg gaggagcaag ccaggaagaa uucaacaagu ucaucaagcc gaucugggaa	1140
aagauggacg gaacagaaga acugcugguc aagcugaaca gagaagaccu gcugagaaag	1200
cagagaacau ucgacaacgg aagcauuccg caccagauc accugggaga acugcacgca	1260
auccugagaa gacaggaaga cuucuaaccg uuccugaagg acaacagaga aaagaucgaa	1320
aagaucgcau caucagaau cccguacuac gucggaccgc uggcaagagg aaacagcaga	1380
uucgcaugga ugacaagaaa gagcgaagaa acaaucacac cguggaacuu cgaagaaguc	1440

	gucgacaagg gagcaagcgc acagagcuuc aucgaaagaa ugacaaacuu cgacaagaac	1500
	cugccgaacg aaaagguccu gccgaagcac agccugcugu acgaauacuu cacagucuac	1560
	aacgaacuga caaaggucua guacgucaca gaaggaauga gaaagccggc auuccugagc	1620
	ggagaacaga agaaggcaau cgucgaccug cuguucaaga caaacagaaa ggucacaguc	1680
	aagcagcuga aggaagacua cuucaagaag aucgaaugcu ucgacagcgu cgaaaucagc	1740
	ggagucgaag acagauucaa cgcaagccug ggaacauacc acgaccugcu gaagaucauc	1800
	aaggacaagg acuuccugga caacgaagaa aacgaagaca uccuggaaga caucguccug	1860
	acacugacac uguucgaaga cagagaaaug aucgaagaaa gacugaagac auacgcacac	1920
	cuguucgacg acaaggucua gaagcagcug aagagaagaa gauacacagg auggggaaga	1980
	cugagcagaa agcugaucaa cggaucaga gacaagcaga gcggaagac aaucuggac	2040
	uuccugaaga gcgacggauu cgcaaacaga aacuucaugc agcugaucca cgacgacagc	2100
	cugacauuca aggaagacau ccagaaggca caggucagcg gacagggaga cagccugcac	2160
	gaacacaucg caaacccggc aggaagcccg gcaaucaaga agggaaucuu gcagacaguc	2220
	aaggucgucg acgaacuggu caaggucaug ggaagacaca agccggaaaa caucgucauc	2280
	gaaauggcaa gaaaaacca gacaacacag aaggacaga agaacagcag agaaagaaug	2340
	aagagaaucg aagaaggaau caaggaacug ggaagccaga uccugaagga acaccgguc	2400
	gaaaacacac agcugcagaa cgaaaagcug uaccuguacu accugcagaa cggaagagac	2460
	auguacgucg accaggaacu ggacaucaac agacugagcg acuacgacgu cgaccacauc	2520
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	aagaacagag gaaagagcga caacgucgag agcgaagaag ucgucaagaa gaugaagaac	2640
	uacuggagac agcugcugaa cgcaaagcug aucacacaga gaaaguucga caaccugaca	2700
	aaggcagaga gaggaggacu gagcgaacug gacaagcag gauucaucaa gagacagcug	2760
	gucgaaacaa gacagaucaac aaagcacguc gcacagauc uggacagcag aaugaacaca	2820
	aaguacgacg aaaacgacaa gcugaucaga gaagucaagg ucaucacacu gaagagcaag	2880
	cuggucagcg acuuacagaaa ggacuuccag uucuacaagg ucagagaaa caacaacuac	2940
	caccacgcac acgacgcaua ccugaacgca gucgucggaa cagcacugau caagaaguac	3000
	ccgaagcugg aaagcgaauu cgucucgga gacuacaagg ucucagcgu cagaaagaug	3060
	aucgcaaaga gcgaacagga aaucggaaag gcaacagcaa aguacuucu cuacagcaac	3120
	aucaugaacu ucuucaagac agaaaucaca cuggcaaagc gagaaaucag aaagagaccg	3180
	cugaucgaaa caaacggaga aacaggagaa aucgucuggg acaaggaag agacuucgca	3240
	acagucagaa agguccugag caugccgag gucaacaucg ucaagaagac agaaguccag	3300
	acaggaggau ucagcaagga aagcauccug ccgaagagaa acagcgacaa gcugaucgca	3360
	agaaagaagg acugggaccg gaagaaguac ggaggauucg acagcccagc agucgcauc	3420
	agcguccugg ucgucgcaaa ggucgaaaag ggaagagca agaagcugaa gagcgucaag	3480
	gaucgucgag gaauacacau cauggaaaga agcagcuucg aaaagaacc gaucgacuuc	3540
	cuggaagcaa agggauacaa ggaagucaag aaggaccuga ucaucaagcu gccgaaguac	3600
	agccuguucg aaucggaaaa cggaagaaag agaauagcug caagcgcagg agaacugcag	3660

aagggaaaacg aacuggcacu gccgagcaag uacgucaacu uccuguaccu ggcaagccac 3720
 uacgaaaagc ugaagggaag cccggaagac aacgaacaga agcagcuguu cgucgaacag 3780
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 aucagagaac aggcagaaaa caucauccac cuguucacac ugacaaaccu gggagaccg 3960
 gcagcauua aguacuucga cacaacauc gacagaaaga gauacacaag cacaaggaa 4020
 guccuggacg caacacugau ccaccagagc aucacaggac uguacgaaac aagaaucgac 4080
 cugagccagc ugggaggaga c 4101

<210> 16
 <211> 1368
 <212> PRT
 <213> 人工序列

<220>
 <223> 合成的: Cas9切口酶(无NLS)的氨基酸序列

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

[0042]

Lys Val Leu Gly Asn Thr Asp Arg His Ser Ile Lys Lys Asn Leu Ile
 35 40 45

Gly Ala Leu Leu Phe Asp Ser Gly Glu Thr Ala Glu Ala Thr Arg Leu
 50 55 60

Lys Arg Thr Ala Arg Arg Arg Tyr Thr Arg Arg Lys Asn Arg Ile Cys
 65 70 75 80

Tyr Leu Gln Glu Ile Phe Ser Asn Glu Met Ala Lys Val Asp Asp Ser
 85 90 95

Phe Phe His Arg Leu Glu Glu Ser Phe Leu Val Glu Glu Asp Lys Lys
 100 105 110

His Glu Arg His Pro Ile Phe Gly Asn Ile Val Asp Glu Val Ala Tyr
 115 120 125

His Glu Lys Tyr Pro Thr Ile Tyr His Leu Arg Lys Lys Leu Val Asp
 130 135 140

Ser Thr Asp Lys Ala Asp Leu Arg Leu Ile Tyr Leu Ala Leu Ala His
 145 150 155 160

Met Ile Lys Phe Arg Gly His Phe Leu Ile Glu Gly Asp Leu Asn Pro
 165 170 175

Asp Asn Ser Asp Val Asp Lys Leu Phe Ile Gln Leu Val Gln Thr Tyr
 180 185 190

Asn Gln Leu Phe Glu Glu Asn Pro Ile Asn Ala Ser Gly Val Asp Ala
 195 200 205

Lys Ala Ile Leu Ser Ala Arg Leu Ser Lys Ser Arg Arg Leu Glu Asn
 210 215 220

Leu Ile Ala Gln Leu Pro Gly Glu Lys Lys Asn Gly Leu Phe Gly Asn
 225 230 235 240

Leu Ile Ala Leu Ser Leu Gly Leu Thr Pro Asn Phe Lys Ser Asn Phe
 245 250 255

Asp Leu Ala Glu Asp Ala Lys Leu Gln Leu Ser Lys Asp Thr Tyr Asp
 260 265 270

Asp Asp Leu Asp Asn Leu Leu Ala Gln Ile Gly Asp Gln Tyr Ala Asp
 275 280 285

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

Ile Leu Arg Val Asn Thr Glu Ile Thr Lys Ala Pro Leu Ser Ala Ser
 305 310 315 320

Met Ile Lys Arg Tyr Asp Glu His His Gln Asp Leu Thr Leu Leu Lys
 325 330 335

[0043] Ala Leu Val Arg Gln Gln Leu Pro Glu Lys Tyr Lys Glu Ile Phe Phe
 340 345 350

Asp Gln Ser Lys Asn Gly Tyr Ala Gly Tyr Ile Asp Gly Gly Ala Ser
 355 360 365

Gln Glu Glu Phe Tyr Lys Phe Ile Lys Pro Ile Leu Glu Lys Met Asp
 370 375 380

Gly Thr Glu Glu Leu Leu Val Lys Leu Asn Arg Glu Asp Leu Leu Arg
 385 390 395 400

Lys Gln Arg Thr Phe Asp Asn Gly Ser Ile Pro His Gln Ile His Leu
 405 410 415

Gly Glu Leu His Ala Ile Leu Arg Arg Gln Glu Asp Phe Tyr Pro Phe
 420 425 430

Leu Lys Asp Asn Arg Glu Lys Ile Glu Lys Ile Leu Thr Phe Arg Ile
 435 440 445

Pro Tyr Tyr Val Gly Pro Leu Ala Arg Gly Asn Ser Arg Phe Ala Trp
 450 455 460

Met Thr Arg Lys Ser Glu Glu Thr Ile Thr Pro Trp Asn Phe Glu Glu
 465 470 475 480

Val Val Asp Lys Gly Ala Ser Ala Gln Ser Phe Ile Glu Arg Met Thr
 485 490 495

Asn Phe Asp Lys Asn Leu Pro Asn Glu Lys Val Leu Pro Lys His Ser
 500 505 510

Leu Leu Tyr Glu Tyr Phe Thr Val Tyr Asn Glu Leu Thr Lys Val Lys
 515 520 525

Tyr Val Thr Glu Gly Met Arg Lys Pro Ala Phe Leu Ser Gly Glu Gln
 530 535 540

Lys Lys Ala Ile Val Asp Leu Leu Phe Lys Thr Asn Arg Lys Val Thr
 545 550 555 560

Val Lys Gln Leu Lys Glu Asp Tyr Phe Lys Lys Ile Glu Cys Phe Asp
 565 570 575

Ser Val Glu Ile Ser Gly Val Glu Asp Arg Phe Asn Ala Ser Leu Gly
 580 585 590

Thr Tyr His Asp Leu Leu Lys Ile Ile Lys Asp Lys Asp Phe Leu Asp
 595 600 605

Asn Glu Glu Asn Glu Asp Ile Leu Glu Asp Ile Val Leu Thr Leu Thr
 610 615 620

Leu Phe Glu Asp Arg Glu Met Ile Glu Glu Arg Leu Lys Thr Tyr Ala
 625 630 635 640

[0044] His Leu Phe Asp Asp Lys Val Met Lys Gln Leu Lys Arg Arg Arg Tyr
 645 650 655

Thr Gly Trp Gly Arg Leu Ser Arg Lys Leu Ile Asn Gly Ile Arg Asp
 660 665 670

Lys Gln Ser Gly Lys Thr Ile Leu Asp Phe Leu Lys Ser Asp Gly Phe
 675 680 685

Ala Asn Arg Asn Phe Met Gln Leu Ile His Asp Asp Ser Leu Thr Phe
 690 695 700

Lys Glu Asp Ile Gln Lys Ala Gln Val Ser Gly Gln Gly Asp Ser Leu
 705 710 715 720

His Glu His Ile Ala Asn Leu Ala Gly Ser Pro Ala Ile Lys Lys Gly
 725 730 735

Ile Leu Gln Thr Val Lys Val Val Asp Glu Leu Val Lys Val Met Gly
 740 745 750

Arg His Lys Pro Glu Asn Ile Val Ile Glu Met Ala Arg Glu Asn Gln
 755 760 765

Thr Thr Gln Lys Gly Gln Lys Asn Ser Arg Glu Arg Met Lys Arg Ile
 770 775 780

Glu Glu Gly Ile Lys Glu Leu Gly Ser Gln Ile Leu Lys Glu His Pro
 785 790 795 800

Val Glu Asn Thr Gln Leu Gln Asn Glu Lys Leu Tyr Leu Tyr Tyr Leu
 805 810 815
 Gln Asn Gly Arg Asp Met Tyr Val Asp Gln Glu Leu Asp Ile Asn Arg
 820 825 830
 Leu Ser Asp Tyr Asp Val Asp His Ile Val Pro Gln Ser Phe Leu Lys
 835 840 845
 Asp Asp Ser Ile Asp Asn Lys Val Leu Thr Arg Ser Asp Lys Asn Arg
 850 855 860
 Gly Lys Ser Asp Asn Val Pro Ser Glu Glu Val Val Lys Lys Met Lys
 865 870 875 880
 Asn Tyr Trp Arg Gln Leu Leu Asn Ala Lys Leu Ile Thr Gln Arg Lys
 885 890 895
 Phe Asp Asn Leu Thr Lys Ala Glu Arg Gly Gly Leu Ser Glu Leu Asp
 900 905 910
 Lys Ala Gly Phe Ile Lys Arg Gln Leu Val Glu Thr Arg Gln Ile Thr
 915 920 925
 Lys His Val Ala Gln Ile Leu Asp Ser Arg Met Asn Thr Lys Tyr Asp
 930 935 940
 [0045] Glu Asn Asp Lys Leu Ile Arg Glu Val Lys Val Ile Thr Leu Lys Ser
 945 950 955 960
 Lys Leu Val Ser Asp Phe Arg Lys Asp Phe Gln Phe Tyr Lys Val Arg
 965 970 975
 Glu Ile Asn Asn Tyr His His Ala His Asp Ala Tyr Leu Asn Ala Val
 980 985 990
 Val Gly Thr Ala Leu Ile Lys Lys Tyr Pro Lys Leu Glu Ser Glu Phe
 995 1000 1005
 Val Tyr Gly Asp Tyr Lys Val Tyr Asp Val Arg Lys Met Ile Ala
 1010 1015 1020
 Lys Ser Glu Gln Glu Ile Gly Lys Ala Thr Ala Lys Tyr Phe Phe
 1025 1030 1035
 Tyr Ser Asn Ile Met Asn Phe Phe Lys Thr Glu Ile Thr Leu Ala
 1040 1045 1050
 Asn Gly Glu Ile Arg Lys Arg Pro Leu Ile Glu Thr Asn Gly Glu
 1055 1060 1065
 Thr Gly Glu Ile Val Trp Asp Lys Gly Arg Asp Phe Ala Thr Val
 1070 1075 1080
 Arg Lys Val Leu Ser Met Pro Gln Val Asn Ile Val Lys Lys Thr

	1085		1090		1095
	Glu Val 1100	Gln Thr Gly Gly	Phe 1105	Ser Lys Glu Ser	Ile Leu Pro Lys 1110
	Arg Asn 1115	Ser Asp Lys Leu	Ile 1120	Ala Arg Lys Lys	Asp Trp Asp Pro 1125
	Lys Lys 1130	Tyr Gly Gly Phe	Asp 1135	Ser Pro Thr Val	Ala Tyr Ser Val 1140
	Leu Val 1145	Val Ala Lys Val	Glu 1150	Lys Gly Lys Ser	Lys Lys Leu Lys 1155
	Ser Val 1160	Lys Glu Leu Leu	Gly 1165	Ile Thr Ile Met	Glu Arg Ser Ser 1170
	Phe Glu 1175	Lys Asn Pro Ile	Asp 1180	Phe Leu Glu Ala	Lys Gly Tyr Lys 1185
	Glu Val 1190	Lys Lys Asp Leu	Ile 1195	Ile Lys Leu Pro	Lys Tyr Ser Leu 1200
	Phe Glu 1205	Leu Glu Asn Gly	Arg 1210	Lys Arg Met Leu	Ala Ser Ala Gly 1215
[0046]	Glu Leu 1220	Gln Lys Gly Asn	Glu 1225	Leu Ala Leu Pro	Ser Lys Tyr Val 1230
	Asn Phe 1235	Leu Tyr Leu Ala	Ser 1240	His Tyr Glu Lys	Leu Lys Gly Ser 1245
	Pro Glu 1250	Asp Asn Glu Gln	Lys 1255	Gln Leu Phe Val	Glu Gln His Lys 1260
	His Tyr 1265	Leu Asp Glu Ile	Ile 1270	Glu Gln Ile Ser	Glu Phe Ser Lys 1275
	Arg Val 1280	Ile Leu Ala Asp	Ala 1285	Asn Leu Asp Lys	Val Leu Ser Ala 1290
	Tyr Asn 1295	Lys His Arg Asp	Lys 1300	Pro Ile Arg Glu	Gln Ala Glu Asn 1305
	Ile Ile 1310	His Leu Phe Thr	Leu 1315	Thr Asn Leu Gly	Ala Pro Ala Ala 1320
	Phe Lys 1325	Tyr Phe Asp Thr	Thr 1330	Ile Asp Arg Lys	Arg Tyr Thr Ser 1335
	Thr Lys 1340	Glu Val Leu Asp	Ala 1345	Thr Leu Ile His	Gln Ser Ile Thr 1350
	Gly Leu 1355	Tyr Glu Thr Arg	Ile 1360	Asp Leu Ser Gln	Leu Gly Gly Asp 1365

<210> 17
 <211> 4107
 <212> RNA
 <213> 人工序列

<220>

<223> 合成的:使用如表3中所列的最小尿苷密码子编码SEQ ID NO: 16的, 具有起始和终止密码子的Cas9切口酶mRNA ORF

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cacagcauca	agaagaaccu	gaucggagca	cugcuguucg	acagcggaga	aacagcagaa	180
gcaacaagac	ugaagagAAC	agcaagaaga	agauacaca	gaagaagaa	cagaaucugc	240
uaccugcagg	aaauucucag	caacgaaug	gcaaaggucg	acgacagcuu	cuuccacaga	300
cuggaagaaa	gcuuccuggu	cgaagaagac	aagaagcagc	aaagacacc	gaucuucgga	360
aacaucuguc	acgaagucgc	auaccacgaa	aaguaccgca	caaucuacca	ccugagaaag	420
aagcuguguc	acagcacaga	caaggcagac	cugagacuga	ucuaccuggc	acuggcacac	480
augaucaagu	ucagaggaca	cuuccugauc	gaaggagacc	ugaaccggga	caacagcgac	540
gucgacaagc	uguucaucca	gcugguccag	acauacaacc	agcuguucga	agaaaaccg	600
aucaacgcaa	gcggagucga	cgcaaggca	auccugagcg	caagacugag	caagagcaga	660
agacuggaaa	accugaucgc	acagcugccg	ggagaaaaga	agaacggacu	guucggaaac	720
cugaucgcac	ugagccuggg	acugacaccg	aacuucaga	gcaacuucga	ccuggcagaa	780
gacgcaaagc	ugcagcugag	caaggacaca	uacgacgacg	accuggacaa	ccugcuggca	840
cagaucggag	accaguacgc	agaccuguuc	cuggcagcaa	agaaccugag	cgacgcaauc	900
cugcugagcg	acauccugag	agucaacaca	gaaucacaa	aggcaccgcu	gagcgaagc	960
augaucaaga	gauacgacga	acaccaccag	gaccugacac	ugcugaagcg	acuggucaga	1020
cagcagcugc	cggaaaagua	caaggaauc	uucucgacc	agagcaagaa	cggauacgca	1080
ggaucaaucg	acggaggagc	aagccaggaa	gaaucuaca	aguucaucaa	gccgauccug	1140
gaaaagauug	acggaacaga	agaacugcug	gucaagcuga	acagagaaga	ccugcugaga	1200
aagcagagaa	cauucgacaa	cggaagcauc	ccgcaccaga	uccaccuggg	agaacugcac	1260
gcaauccuga	gaagacagga	agacuucuc	ccguuccuga	aggacaacag	agaaaagauc	1320
gaaaagaucc	ugacauucag	aaucuccguac	uacgucggac	cgucggcaag	aggaaacagc	1380
agauucgcau	ggaugacaag	aaagagcgaa	gaaacaauca	caccguggaa	cuucgaagaa	1440
gucgucgaca	aggagcaag	cgcacagagc	uucaucgaaa	gaaugacaaa	cuucgacaag	1500
aaccugccga	acgaaaaggu	ccugccgaag	cacagccugc	uguacgaaua	cuucacaguc	1560
uacaacgaac	ugacaaaggu	caaguacguc	acagaaggaa	ugagaaagcc	ggcauuccug	1620
agcggagaac	agaagaaggc	aaucgucgac	cugcuguuca	agacaacag	aaaggucaca	1680
gucaagcagc	ugaaggaaga	cuacuucag	aagaucgaau	gcuucgacag	cgucgaaauc	1740
agcggagucg	aagacagauu	caacgcaagc	cugggaacau	accacgaccu	gcugaagauc	1800
aucaaggaca	aggacuuccu	ggacaacgaa	gaaaacgaag	acauccugga	agacaucguc	1860
cugacacuga	cacuguucga	agacagagaa	augaucgaag	aaagacugaa	gacauacgca	1920
caccuguucg	acgacaaggu	caugaagcag	cugaagagaa	gaagauacac	aggauuggga	1980

[0047]

	agacugagca gaaagcugau caacggauc agagacaagc agagcggaaa gacaauccug	2040
	gacuuccuga agagcgcgag auucgcaaac agaaacuua ugcagcugau ccacgacgac	2100
	agccugacau ucaaggaaga cauccagaag gcacagguca gcggacaggg agacagccug	2160
	cacgaacaca ucgcaaaccu ggacggaagc ccggcaauca agaagggaau ccugcagaca	2220
	gucaaggucg ucgacgaacu ggucagguc augggaagac acaagccgga aaacaucguc	2280
	aucgaaaugg caagagaaaa ccagacaaca cagaaggac agaagaacag cagagaaaga	2340
	augagagaa ucgaagaagg aaucaggaa cugggaagcc agauccugaa ggaacaccg	2400
	gucgaaaaca cacagcugca gaacgaaaag cuguaccugu acuaccugca gaacggaaga	2460
	gacauguacg ucgaccagga acuggacauc aacagacuga gcgacuacga cgucgaccac	2520
	aucgucccg agagcuuccu gaaggacgac agcaucgaca acaagguccu gacaagaagc	2580
	gacaagaaca gaggaaagag cgacaacguc ccgagcgaag aagucgucaa gaagaugaag	2640
	aaucacugga gacagcugcu gaacgcaaag cugaucacac agagaaaguu cgacaaccug	2700
	acaaaggcag agagaggagg acugagcga cuggacaagg caggauucau caagagacag	2760
	cuggucgaaa caagacagau cacaaagcac gucgcacaga uccuggacag cagaaugaac	2820
	acaaaguacg acgaaaacga caagcugauc agagaaguca aggucaucac acugaagagc	2880
	aagcugguca gcgacuucag aaaggacuuc caguucuaca aggucaagaga aaucacaac	2940
	uaccaccag cacacgacgc auaccugaac gcagucgucg gaacagcacu gaucaagaag	3000
	uaccggaagc uggaaagcga auucgucuc ggagacuaca agguacuacga cgucagaaag	3060
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	ccgucgucg aaacaaaccg agaaacagga gaaaucgucu gggacaaggg aagagacuuc	3240
	gcaacaguca gaaagguccu gagcaugccg caggucaaca ucgucaagaa gacagaaguc	3300
	cagacaggag gauucagcaa ggaaagcauc cugccgaaga gaaacagcga caagcugauc	3360
	gcaagaaaga aggacuggga cccgaagaag uacggaggau ucgacagccc gacagucgca	3420
	uacagcgucc uggucgucgc aaaggucgaa aagggaaaga gcaagaagcu gaagagcuc	3480
	aaggaacugc ugggaaucac aaucauggaa agaagcagcu ucgaaaagaa cccgaucgac	3540
	uuccuggaag caaagggaau caaggaaguc aagaaggacc ugaucaucau gcugccgaag	3600
	uacagccugu ucgaacugga aaacggaaga aagagaauuc uggcaagcgc aggagaacug	3660
	cagaagggaa acgaacuggc acugccgagc aaguacguca acuuuccugua ccuggcaagc	3720
	cacuacgaaa agcugaaggg aagcccggaa gacaacgaac agaagcagcu guucgucgaa	3780
	cagcacaagc acuaccugga cgaaaaucau gaacagauca gcgaaauucag caagagaguc	3840
	auccuggcag acgcaaaccu ggacaagguc cugagcgcau acaacaagca cagagacaag	3900
	ccgaucagag aacaggcaga aaacaucac caccuguuca cacugacaaa ccugggagca	3960
	ccggcagcau ucaaguacuu cgacacaaca aucgacagaa agagauacac aagcacaag	4020
	gaaguccugg acgcaacacu gauccaccag agcaucacag gacugucgca aacaagauc	4080
	gaccugagcc agcugggagg agacuag	4107

<210> 18
<211> 4101

<212> RNA
<213> 人工序列

<220>

<223> 合成的：使用如表3中所列的最小尿苷密码子编码SEQ ID NO: 16的Cas9切口酶编码序列(无起始或终止密码子；适于包括在融合蛋白质编码序列中)

<400> 18

[0049]

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acagacgaau acaaggucc gagcaagaag uucaaggucc uggaaacac agacagacac      120
agcaucaaga agaaccugau cggagcacug cuguucgaca gcggagaaac agcagaagca      180
acaagacuga agagaacagc aagaagaaga uacacaagaa gaaagaacag aaucugcuac      240
cugcagaaaa ucuucagcaa cgaaauggca aaggucgacg acagcuucuu ccacagacug      300
gaagaagcu uccuggucga agaagacaag aagcacgaaa gacacccgau cuucgaaac      360
aucgucgacg aagucgcaua ccacgaaaag uacccgacaa ucuaccaccu gagaaagaag      420
cuggucgaca gcacagacaa ggacagaccug agacugaucu accuggcacu ggcacacaug      480
aucaaguuca gaggacacuu ccugaucgaa ggagaccuga acccgacaa cagcagcugc      540
gacaagcugu ucauccagcu ggucagaca uacaaccagc uguucgaaga aaacccgauc      600
aacgcaagcg gagucgacgc aaaggcaauc cugagcgcaa gacugagcaa gacgagaaga      660
cuggaaaacc ugaucgcaca gcugccggga gaaaagaaga acggacuguu cggaaaccug      720
aucgcacuga gccugggacu gacaccgaac uucaagagca acuucgaccu ggcagaagac      780
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aucggagacc aguacgcaga ccuguuccug gcagcaaaga accugagcga cgcaauccug      900
cugagcgaca uccugagagu caacacagaa aucacaaagg caccgcugag cgcaagcaug      960
aucaagagau acgacgaaca ccaccaggac cugacacugc ugaaggcacu ggucagacag     1020
cagcugccgg aaaaguacaa ggaaauuc uucgaccaga gcaagaacgg auacgcagga     1080
uacaucgacg gaggagcaag ccaggaaaga uucuacaagu ucaucaagcc gauccuggaa     1140
aagauggacg gaacagaaga acugcugguc aagcugaaca gagaagaccu gcugagaaaag     1200
cagagaacau ucgacaacgg aagcaucccg caccagauc accugggaga acugcacgca     1260
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uucgcaugga ugacaagaaa gagcgaagaa acaaucacac cguggaacuu cgaagaaguc     1440
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ggagaacaga agaaggcaau cgucgaccug cuguucaaga caaacagaaa ggucacaguc     1680
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ggagucgaag acagauucua cgaaagccug ggaacauacc acgaccugcu gaagaucauc     1800
aaggacaagg acuuccugga caacgaagaa aacgaagaca uccuggaaga caucguccug     1860
acacugacac uguucgaaga cagagaaaug aucgaagaaa gacugaagac auacgcacac     1920
cuguucgacg acaaggucua gaagcagcug aagagaagaa gauacacagg auggggaaga     1980
cugagcagaa agcugaucaa cggaaucaga gacaagcaga gcggaaagac aauccuggac     2040

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uuccugaaga gcgacggauu cgcaaacaga aacuucaugc agcugaucca cgacgacagc	2100
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gaaauggcaa gagaaaacca gacaacacag aaggacaga agaacagcag agaaagaug	2340
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gaacugcugg gaaucaacu cauggaaaga agcagcuucg aaaagaacc gaucgacuuc	3540
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gcagcauua aguacuucg cacaacaauc gacagaaaga gauacacaag cacaagga	4020
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cugagccagc ugggaggaga c	4101
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<211> 1368	
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<213> 人工序列

<220>

<223> 合成的: dCas9 (无NLS)的氨基酸序列

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Gly Trp Ala Val Ile Thr Asp Glu Tyr Lys Val Pro Ser Lys Lys Phe
20 25 30

Lys Val Leu Gly Asn Thr Asp Arg His Ser Ile Lys Lys Asn Leu Ile
35 40 45

Gly Ala Leu Leu Phe Asp Ser Gly Glu Thr Ala Glu Ala Thr Arg Leu
50 55 60

Lys Arg Thr Ala Arg Arg Arg Tyr Thr Arg Arg Lys Asn Arg Ile Cys
65 70 75 80

Tyr Leu Gln Glu Ile Phe Ser Asn Glu Met Ala Lys Val Asp Asp Ser
85 90 95

Phe Phe His Arg Leu Glu Glu Ser Phe Leu Val Glu Glu Asp Lys Lys
100 105 110

[0051]

His Glu Arg His Pro Ile Phe Gly Asn Ile Val Asp Glu Val Ala Tyr
115 120 125

His Glu Lys Tyr Pro Thr Ile Tyr His Leu Arg Lys Lys Leu Val Asp
130 135 140

Ser Thr Asp Lys Ala Asp Leu Arg Leu Ile Tyr Leu Ala Leu Ala His
145 150 155 160

Met Ile Lys Phe Arg Gly His Phe Leu Ile Glu Gly Asp Leu Asn Pro
165 170 175

Asp Asn Ser Asp Val Asp Lys Leu Phe Ile Gln Leu Val Gln Thr Tyr
180 185 190

Asn Gln Leu Phe Glu Glu Asn Pro Ile Asn Ala Ser Gly Val Asp Ala
195 200 205

Lys Ala Ile Leu Ser Ala Arg Leu Ser Lys Ser Arg Arg Leu Glu Asn
210 215 220

Leu Ile Ala Gln Leu Pro Gly Glu Lys Lys Asn Gly Leu Phe Gly Asn
225 230 235 240

Leu Ile Ala Leu Ser Leu Gly Leu Thr Pro Asn Phe Lys Ser Asn Phe
245 250 255

Asp Leu Ala Glu Asp Ala Lys Leu Gln Leu Ser Lys Asp Thr Tyr Asp
260 265 270

Asp Asp Leu Asp Asn Leu Leu Ala Gln Ile Gly Asp Gln Tyr Ala Asp
 275 280 285

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

Ile Leu Arg Val Asn Thr Glu Ile Thr Lys Ala Pro Leu Ser Ala Ser
 305 310 315 320

Met Ile Lys Arg Tyr Asp Glu His His Gln Asp Leu Thr Leu Leu Lys
 325 330 335

Ala Leu Val Arg Gln Gln Leu Pro Glu Lys Tyr Lys Glu Ile Phe Phe
 340 345 350

Asp Gln Ser Lys Asn Gly Tyr Ala Gly Tyr Ile Asp Gly Gly Ala Ser
 355 360 365

Gln Glu Glu Phe Tyr Lys Phe Ile Lys Pro Ile Leu Glu Lys Met Asp
 370 375 380

Gly Thr Glu Glu Leu Leu Val Lys Leu Asn Arg Glu Asp Leu Leu Arg
 385 390 395 400

Lys Gln Arg Thr Phe Asp Asn Gly Ser Ile Pro His Gln Ile His Leu
 405 410 415

[0052] Gly Glu Leu His Ala Ile Leu Arg Arg Gln Glu Asp Phe Tyr Pro Phe
 420 425 430

Leu Lys Asp Asn Arg Glu Lys Ile Glu Lys Ile Leu Thr Phe Arg Ile
 435 440 445

Pro Tyr Tyr Val Gly Pro Leu Ala Arg Gly Asn Ser Arg Phe Ala Trp
 450 455 460

Met Thr Arg Lys Ser Glu Glu Thr Ile Thr Pro Trp Asn Phe Glu Glu
 465 470 475 480

Val Val Asp Lys Gly Ala Ser Ala Gln Ser Phe Ile Glu Arg Met Thr
 485 490 495

Asn Phe Asp Lys Asn Leu Pro Asn Glu Lys Val Leu Pro Lys His Ser
 500 505 510

Leu Leu Tyr Glu Tyr Phe Thr Val Tyr Asn Glu Leu Thr Lys Val Lys
 515 520 525

Tyr Val Thr Glu Gly Met Arg Lys Pro Ala Phe Leu Ser Gly Glu Gln
 530 535 540

Lys Lys Ala Ile Val Asp Leu Leu Phe Lys Thr Asn Arg Lys Val Thr
 545 550 555 560

Val Lys Gln Leu Lys Glu Asp Tyr Phe Lys Lys Ile Glu Cys Phe Asp
 565 570 575

Ser Val Glu Ile Ser Gly Val Glu Asp Arg Phe Asn Ala Ser Leu Gly
 580 585 590

Thr Tyr His Asp Leu Leu Lys Ile Ile Lys Asp Lys Asp Phe Leu Asp
 595 600 605

Asn Glu Glu Asn Glu Asp Ile Leu Glu Asp Ile Val Leu Thr Leu Thr
 610 615 620

Leu Phe Glu Asp Arg Glu Met Ile Glu Glu Arg Leu Lys Thr Tyr Ala
 625 630 635 640

His Leu Phe Asp Asp Lys Val Met Lys Gln Leu Lys Arg Arg Arg Tyr
 645 650 655

Thr Gly Trp Gly Arg Leu Ser Arg Lys Leu Ile Asn Gly Ile Arg Asp
 660 665 670

Lys Gln Ser Gly Lys Thr Ile Leu Asp Phe Leu Lys Ser Asp Gly Phe
 675 680 685

Ala Asn Arg Asn Phe Met Gln Leu Ile His Asp Asp Ser Leu Thr Phe
 690 695 700

Lys Glu Asp Ile Gln Lys Ala Gln Val Ser Gly Gln Gly Asp Ser Leu
 705 710 715 720

[0053] His Glu His Ile Ala Asn Leu Ala Gly Ser Pro Ala Ile Lys Lys Gly
 725 730 735

Ile Leu Gln Thr Val Lys Val Val Asp Glu Leu Val Lys Val Met Gly
 740 745 750

Arg His Lys Pro Glu Asn Ile Val Ile Glu Met Ala Arg Glu Asn Gln
 755 760 765

Thr Thr Gln Lys Gly Gln Lys Asn Ser Arg Glu Arg Met Lys Arg Ile
 770 775 780

Glu Glu Gly Ile Lys Glu Leu Gly Ser Gln Ile Leu Lys Glu His Pro
 785 790 795 800

Val Glu Asn Thr Gln Leu Gln Asn Glu Lys Leu Tyr Leu Tyr Tyr Leu
 805 810 815

Gln Asn Gly Arg Asp Met Tyr Val Asp Gln Glu Leu Asp Ile Asn Arg
 820 825 830

Leu Ser Asp Tyr Asp Val Asp Ala Ile Val Pro Gln Ser Phe Leu Lys
 835 840 845

Asp Asp Ser Ile Asp Asn Lys Val Leu Thr Arg Ser Asp Lys Asn Arg
 850 855 860

Gly Lys Ser Asp Asn Val Pro Ser Glu Glu Val Val Lys Lys Met Lys
 865 870 875 880

Asn Tyr Trp Arg Gln Leu Leu Asn Ala Lys Leu Ile Thr Gln Arg Lys
 885 890 895

Phe Asp Asn Leu Thr Lys Ala Glu Arg Gly Gly Leu Ser Glu Leu Asp
 900 905 910

Lys Ala Gly Phe Ile Lys Arg Gln Leu Val Glu Thr Arg Gln Ile Thr
 915 920 925

Lys His Val Ala Gln Ile Leu Asp Ser Arg Met Asn Thr Lys Tyr Asp
 930 935 940

Glu Asn Asp Lys Leu Ile Arg Glu Val Lys Val Ile Thr Leu Lys Ser
 945 950 955 960

Lys Leu Val Ser Asp Phe Arg Lys Asp Phe Gln Phe Tyr Lys Val Arg
 965 970 975

Glu Ile Asn Asn Tyr His His Ala His Asp Ala Tyr Leu Asn Ala Val
 980 985 990

Val Gly Thr Ala Leu Ile Lys Lys Tyr Pro Lys Leu Glu Ser Glu Phe
 995 1000 1005

Val Tyr Gly Asp Tyr Lys Val Tyr Asp Val Arg Lys Met Ile Ala
 1010 1015 1020

[0054] Lys Ser Glu Gln Glu Ile Gly Lys Ala Thr Ala Lys Tyr Phe Phe
 1025 1030 1035

Tyr Ser Asn Ile Met Asn Phe Phe Lys Thr Glu Ile Thr Leu Ala
 1040 1045 1050

Asn Gly Glu Ile Arg Lys Arg Pro Leu Ile Glu Thr Asn Gly Glu
 1055 1060 1065

Thr Gly Glu Ile Val Trp Asp Lys Gly Arg Asp Phe Ala Thr Val
 1070 1075 1080

Arg Lys Val Leu Ser Met Pro Gln Val Asn Ile Val Lys Lys Thr
 1085 1090 1095

Glu Val Gln Thr Gly Gly Phe Ser Lys Glu Ser Ile Leu Pro Lys
 1100 1105 1110

Arg Asn Ser Asp Lys Leu Ile Ala Arg Lys Lys Asp Trp Asp Pro
 1115 1120 1125

Lys Lys Tyr Gly Gly Phe Asp Ser Pro Thr Val Ala Tyr Ser Val
 1130 1135 1140

Leu Val Val Ala Lys Val Glu Lys Gly Lys Ser Lys Lys Leu Lys
 1145 1150 1155

Ser Val Lys Glu Leu Leu Gly Ile Thr Ile Met Glu Arg Ser Ser

1160 1165 1170
 Phe Glu Lys Asn Pro Ile Asp Phe Leu Glu Ala Lys Gly Tyr Lys
 1175 1180 1185
 Glu Val Lys Lys Asp Leu Ile Ile Lys Leu Pro Lys Tyr Ser Leu
 1190 1195 1200
 Phe Glu Leu Glu Asn Gly Arg Lys Arg Met Leu Ala Ser Ala Gly
 1205 1210 1215
 Glu Leu Gln Lys Gly Asn Glu Leu Ala Leu Pro Ser Lys Tyr Val
 1220 1225 1230
 Asn Phe Leu Tyr Leu Ala Ser His Tyr Glu Lys Leu Lys Gly Ser
 1235 1240 1245
 Pro Glu Asp Asn Glu Gln Lys Gln Leu Phe Val Glu Gln His Lys
 1250 1255 1260
 His Tyr Leu Asp Glu Ile Ile Glu Gln Ile Ser Glu Phe Ser Lys
 1265 1270 1275
 Arg Val Ile Leu Ala Asp Ala Asn Leu Asp Lys Val Leu Ser Ala
 1280 1285 1290
 Tyr Asn Lys His Arg Asp Lys Pro Ile Arg Glu Gln Ala Glu Asn
 1295 1300 1305
 Ile Ile His Leu Phe Thr Leu Thr Asn Leu Gly Ala Pro Ala Ala
 1310 1315 1320
 Phe Lys Tyr Phe Asp Thr Thr Ile Asp Arg Lys Arg Tyr Thr Ser
 1325 1330 1335
 Thr Lys Glu Val Leu Asp Ala Thr Leu Ile His Gln Ser Ile Thr
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[0055]

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<223> 合成的:使用如表3中所列的最小尿苷密码子编码SEQ ID NO: 19的, 具有起始和终止密码子的dCas9 mRNA ORF

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 gcaacaagac ugaagagaac agcaagaaga agauacacaa gaagaaagaa cagaaucugc 240
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gucgacaagc uguucaucca gcugguccag acauacaacc agcuguucga agaaaaccg	600
aucaacgcaa gcggagucga cgcaaaggca auccugagcg caagacugag caagagcaga	660
agacuggaaa accugaucgc acagcugccg ggagaaaaga agaaccgacu guucggaaac	720
cugaucgcac ugagccuggg acugacaccg aacuucaaga gcaacuucga ccuggcagaa	780
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gacuuccuga agagcagcgg auucgcaaac agaacuucg ugcagcugau ccacgacgac	2100
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	acaaaguacg acgaaaacga caagcugauc agagaaguca aggucaucac acugaagagc	2880
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	aaggaaucg uggaaucac auucaugaa agaagcagcu ucgaaaagaa cccgaucgac	3540
	uuccuggaag caaagggau caaggaaguc aagaaggacc ugaucaucau gcugccgaag	3600
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	cagcacaagc acuaaccuga cgaaucauc gaacagauca gcgaaucag caagagaguc	3840
	auccuggcag acgcaaaccu ggacaagguc cugagcgcau acaacaagca cagagacaag	3900
	ccgaucagag aacaggcaga aaacaucauc caccuguuca cacugacaaa ccugggagca	3960
	ccggcagcau ucaaguacuu cgacacaaca aucgacagaa agagauacac aagcacaag	4020
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	括在融合蛋白质编码序列中)	
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	agcaucaaga agaaccugau cggagcacug cuguucgaca gcggagaaac agcagaagca	180
	acaagacuga agagaacagc aagaagaaga uacacaagaa gaaagaacag aaucugcuac	240
	cugcagggaaa ucuucagcaa cgaauugcga aaggucgacg acagcuucuu ccacagacug	300
	gaagaagcu uccugucgca agaagacaag aagcacgaaa gacaccgcau cuucggaac	360

aucgucgacg aagucgcaua ccacgaaaag uacccgacaa ucuaccaccu gagaaaagaag	420
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aucaaguuca gaggacacuu ccugaucgaa ggagaccuga acccggacaa cagcgacguc	540
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cugagcgaca uccugagagu caacacagaa aucacaaagg caccgcugag cgcaagcaug	960
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<223> 合成的：具有两个核定位信号作为C端氨基酸的Cas9的氨基酸序列

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Gly Trp Ala Val Ile Thr Asp Glu Tyr Lys Val Pro Ser Lys Lys Phe
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Lys Val Leu Gly Asn Thr Asp Arg His Ser Ile Lys Lys Asn Leu Ile
 35 40 45

Gly Ala Leu Leu Phe Asp Ser Gly Glu Thr Ala Glu Ala Thr Arg Leu

50	55	60
Lys Arg Thr Ala Arg Arg Arg Tyr Thr Arg Arg Lys Asn Arg Ile Cys 65 70 75 80		
Tyr Leu Gln Glu Ile Phe Ser Asn Glu Met Ala Lys Val Asp Asp Ser 85 90 95		
Phe Phe His Arg Leu Glu Glu Ser Phe Leu Val Glu Glu Asp Lys Lys 100 105 110		
His Glu Arg His Pro Ile Phe Gly Asn Ile Val Asp Glu Val Ala Tyr 115 120 125		
His Glu Lys Tyr Pro Thr Ile Tyr His Leu Arg Lys Lys Leu Val Asp 130 135 140		
Ser Thr Asp Lys Ala Asp Leu Arg Leu Ile Tyr Leu Ala Leu Ala His 145 150 155 160		
Met Ile Lys Phe Arg Gly His Phe Leu Ile Glu Gly Asp Leu Asn Pro 165 170 175		
Asp Asn Ser Asp Val Asp Lys Leu Phe Ile Gln Leu Val Gln Thr Tyr 180 185 190		
[0060] Asn Gln Leu Phe Glu Glu Asn Pro Ile Asn Ala Ser Gly Val Asp Ala 195 200 205		
Lys Ala Ile Leu Ser Ala Arg Leu Ser Lys Ser Arg Arg Leu Glu Asn 210 215 220		
Leu Ile Ala Gln Leu Pro Gly Glu Lys Lys Asn Gly Leu Phe Gly Asn 225 230 235 240		
Leu Ile Ala Leu Ser Leu Gly Leu Thr Pro Asn Phe Lys Ser Asn Phe 245 250 255		
Asp Leu Ala Glu Asp Ala Lys Leu Gln Leu Ser Lys Asp Thr Tyr Asp 260 265 270		
Asp Asp Leu Asp Asn Leu Leu Ala Gln Ile Gly Asp Gln Tyr Ala Asp 275 280 285		
Leu Phe Leu Ala Ala Lys Asn Leu Ser Asp Ala Ile Leu Leu Ser Asp 290 295 300		
Ile Leu Arg Val Asn Thr Glu Ile Thr Lys Ala Pro Leu Ser Ala Ser 305 310 315 320		
Met Ile Lys Arg Tyr Asp Glu His His Gln Asp Leu Thr Leu Leu Lys 325 330 335		
Ala Leu Val Arg Gln Gln Leu Pro Glu Lys Tyr Lys Glu Ile Phe Phe 340 345 350		

Asp Gln Ser Lys Asn Gly Tyr Ala Gly Tyr Ile Asp Gly Gly Ala Ser
 355 360 365

Gln Glu Glu Phe Tyr Lys Phe Ile Lys Pro Ile Leu Glu Lys Met Asp
 370 375 380

Gly Thr Glu Glu Leu Leu Val Lys Leu Asn Arg Glu Asp Leu Leu Arg
 385 390 395 400

Lys Gln Arg Thr Phe Asp Asn Gly Ser Ile Pro His Gln Ile His Leu
 405 410 415

Gly Glu Leu His Ala Ile Leu Arg Arg Gln Glu Asp Phe Tyr Pro Phe
 420 425 430

Leu Lys Asp Asn Arg Glu Lys Ile Glu Lys Ile Leu Thr Phe Arg Ile
 435 440 445

Pro Tyr Tyr Val Gly Pro Leu Ala Arg Gly Asn Ser Arg Phe Ala Trp
 450 455 460

Met Thr Arg Lys Ser Glu Glu Thr Ile Thr Pro Trp Asn Phe Glu Glu
 465 470 475 480

Val Val Asp Lys Gly Ala Ser Ala Gln Ser Phe Ile Glu Arg Met Thr
 485 490 495

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Leu Leu Tyr Glu Tyr Phe Thr Val Tyr Asn Glu Leu Thr Lys Val Lys
 515 520 525

Tyr Val Thr Glu Gly Met Arg Lys Pro Ala Phe Leu Ser Gly Glu Gln
 530 535 540

Lys Lys Ala Ile Val Asp Leu Leu Phe Lys Thr Asn Arg Lys Val Thr
 545 550 555 560

Val Lys Gln Leu Lys Glu Asp Tyr Phe Lys Lys Ile Glu Cys Phe Asp
 565 570 575

Ser Val Glu Ile Ser Gly Val Glu Asp Arg Phe Asn Ala Ser Leu Gly
 580 585 590

Thr Tyr His Asp Leu Leu Lys Ile Ile Lys Asp Lys Asp Phe Leu Asp
 595 600 605

Asn Glu Glu Asn Glu Asp Ile Leu Glu Asp Ile Val Leu Thr Leu Thr
 610 615 620

Leu Phe Glu Asp Arg Glu Met Ile Glu Glu Arg Leu Lys Thr Tyr Ala
 625 630 635 640

His Leu Phe Asp Asp Lys Val Met Lys Gln Leu Lys Arg Arg Arg Tyr
 645 650 655

Thr Gly Trp Gly Arg Leu Ser Arg Lys Leu Ile Asn Gly Ile Arg Asp
 660 665 670
 Lys Gln Ser Gly Lys Thr Ile Leu Asp Phe Leu Lys Ser Asp Gly Phe
 675 680 685
 Ala Asn Arg Asn Phe Met Gln Leu Ile His Asp Asp Ser Leu Thr Phe
 690 695 700
 Lys Glu Asp Ile Gln Lys Ala Gln Val Ser Gly Gln Gly Asp Ser Leu
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 His Glu His Ile Ala Asn Leu Ala Gly Ser Pro Ala Ile Lys Lys Gly
 725 730 735
 Ile Leu Gln Thr Val Lys Val Val Asp Glu Leu Val Lys Val Met Gly
 740 745 750
 Arg His Lys Pro Glu Asn Ile Val Ile Glu Met Ala Arg Glu Asn Gln
 755 760 765
 Thr Thr Gln Lys Gly Gln Lys Asn Ser Arg Glu Arg Met Lys Arg Ile
 770 775 780
 Glu Glu Gly Ile Lys Glu Leu Gly Ser Gln Ile Leu Lys Glu His Pro
 785 790 800
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 820 825 830
 Leu Ser Asp Tyr Asp Val Asp His Ile Val Pro Gln Ser Phe Leu Lys
 835 840 845
 Asp Asp Ser Ile Asp Asn Lys Val Leu Thr Arg Ser Asp Lys Asn Arg
 850 855 860
 Gly Lys Ser Asp Asn Val Pro Ser Glu Glu Val Val Lys Lys Met Lys
 865 870 875 880
 Asn Tyr Trp Arg Gln Leu Leu Asn Ala Lys Leu Ile Thr Gln Arg Lys
 885 890 895
 Phe Asp Asn Leu Thr Lys Ala Glu Arg Gly Gly Leu Ser Glu Leu Asp
 900 905 910
 Lys Ala Gly Phe Ile Lys Arg Gln Leu Val Glu Thr Arg Gln Ile Thr
 915 920 925
 Lys His Val Ala Gln Ile Leu Asp Ser Arg Met Asn Thr Lys Tyr Asp
 930 935 940
 Glu Asn Asp Lys Leu Ile Arg Glu Val Lys Val Ile Thr Leu Lys Ser
 945 950 955 960

Lys Leu Val Ser Asp Phe Arg Lys Asp Phe Gln Phe Tyr Lys Val Arg
 965 970 975
 Glu Ile Asn Asn Tyr His His Ala His Asp Ala Tyr Leu Asn Ala Val
 980 985 990
 Val Gly Thr Ala Leu Ile Lys Lys Tyr Pro Lys Leu Glu Ser Glu Phe
 995 1000 1005
 Val Tyr Gly Asp Tyr Lys Val Tyr Asp Val Arg Lys Met Ile Ala
 1010 1015 1020
 Lys Ser Glu Gln Glu Ile Gly Lys Ala Thr Ala Lys Tyr Phe Phe
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 1070 1075 1080
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 1115 1120 1125
 Lys Lys Tyr Gly Gly Phe Asp Ser Pro Thr Val Ala Tyr Ser Val
 1130 1135 1140
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 Ser Val Lys Glu Leu Leu Gly Ile Thr Ile Met Glu Arg Ser Ser
 1160 1165 1170
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 1175 1180 1185
 Glu Val Lys Lys Asp Leu Ile Ile Lys Leu Pro Lys Tyr Ser Leu
 1190 1195 1200
 Phe Glu Leu Glu Asn Gly Arg Lys Arg Met Leu Ala Ser Ala Gly
 1205 1210 1215
 Glu Leu Gln Lys Gly Asn Glu Leu Ala Leu Pro Ser Lys Tyr Val
 1220 1225 1230
 Asn Phe Leu Tyr Leu Ala Ser His Tyr Glu Lys Leu Lys Gly Ser

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His Tyr Leu Asp Glu Ile Ile	Glu Gln Ile Ser	Glu Phe Ser Lys
1265	1270	1275
Arg Val Ile Leu Ala Asp Ala	Asn Leu Asp Lys	Val Leu Ser Ala
1280	1285	1290
Tyr Asn Lys His Arg Asp Lys	Pro Ile Arg Glu	Gln Ala Glu Asn
1295	1300	1305
Ile Ile His Leu Phe Thr Leu	Thr Asn Leu Gly	Ala Pro Ala Ala
1310	1315	1320
Phe Lys Tyr Phe Asp Thr Thr	Ile Asp Arg Lys	Arg Tyr Thr Ser
1325	1330	1335
Thr Lys Glu Val Leu Asp Ala	Thr Leu Ile His	Gln Ser Ile Thr
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Gly Leu Tyr Glu Thr Arg Ile	Asp Leu Ser Gln	Leu Gly Gly Asp
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[0064]

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 <212> RNA
 <213> 人工序列

<220>
 <223> 合成的：使用如表3中所列的最小尿苷密码子编码SEQ ID NO: 22的，具有起始和终止密码子的Cas9 mRNA ORF

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cacagcauca agaagaaccu gaucggagca cugcuguucg acagcggaga aacagcagaa	180
gcaacaagac ugaagagaac agcaagaaga agauacacaa gaagaaagaa cagaaucugc	240
uaccugcagg aaauucucag caacgaaaug gcaaaggucg acgacagcuu cuuccacaga	300
cuggaagaaa gcuuccuggu cgaagaagac aagaagcacg aaagacaccc gaucuucgga	360
aacaucgucg acgaagucgc auaccacgaa aaguaccgca caaucuacca ccugagaaag	420
aagcuggucg acagcacaga caaggcagac cugagacuga ucuaccuggc acuggcacac	480
augaucaagu ucagaggaca cuuccugauc gaaggagacc ugaaccggga caacagcgac	540
gucgacaagc uguucaucca gcugguccag acauacaacc agcuguucga agaaaaccg	600
aucaacgcaa gcgagucga cgcaaaggca auccugagcg caagacugag caagagcaga	660
agacuggaaa accugaucgc acagcugccg ggagaaaaga agaacggacu guucggaaac	720

cugaucgcac	ugagccuggg	acugacaccg	aacuucaaga	gcaacuucga	ccuggcagaa	780	
gacgcaaagc	ugcagcugag	caaggacaca	uacgacgacg	accuggacaa	ccugcuggca	840	
cagaucggag	accaguacgc	agaccuguuc	cuggcagcaa	agaaccugag	cgacgcaauc	900	
cugcugagcg	acauccugag	agucaacaca	gaaaucacaa	aggcaccgcu	gagcgcaagc	960	
augaucaaga	gauacgacga	acaccaccag	gaccugacac	ugcugaaggc	acuggucaga	1020	
cagcagcugc	cgghaaagua	caaggaaauc	uucuuugacc	agagcaagaa	cggaauacga	1080	
ggauacaucg	acggaggagc	aagccaggaa	gaauucuaca	aguucaucaa	gccgaucug	1140	
gaaaagaugg	acggaacaga	agaacugcug	gucaagcuga	acagagaaga	ccugcugaga	1200	
aagcagagaa	cauucgacaa	cggaagcauc	ccgcaccaga	uccaccuggg	agaacugcac	1260	
gcaauccuga	gaagacagga	agacuucac	ccguuccuga	aggacaacag	agaaaagauc	1320	
gaaaagauc	ugacauucag	aaucgccuac	uacgucggac	cgucggcaag	aggaaacagc	1380	
agauucgcau	ggauagacaag	aaagagcgaa	gaaacaauca	caccguggaa	cuucgaagaa	1440	
gucgucgaca	agggagcaag	cgcacagagc	uucaucgaaa	gaaugacaaa	cuucgacaag	1500	
aaccugcccga	acghaaaggu	ccugccgaag	cacagccugc	uguacgaaua	cuucacaguc	1560	
uacaacgaac	ugacaaaggu	caaguacguc	acagaaggaa	ugagaaagcc	ggcauuccug	1620	
agcggagaac	agaagaaggc	aaucgucgac	cugcuguuca	agacaaacag	aaaggucaca	1680	
gucaagcagc	ugaaggaaga	cuacuuaag	aagaucgaau	gcuucgacag	cgucgaaauc	1740	
agcggagucg	aagacagauu	caacgcaagc	cugggaacau	accacgaccu	gcugaagauc	1800	
[0065]	aucaaggaca	aggacuuccu	ggacaacgaa	gaaaacgaag	acaucuggga	agacaucguc	1860
cugacacuga	cacuguucga	agacagagaa	augaucgaag	aaagacugaa	gacauacgca	1920	
caccuguucg	acgacaaggu	caugaagcag	cugaagagaa	gaagauacac	aggaugggga	1980	
agacugagca	gaaagcugau	caacggauc	agagacaagc	agagcggaaa	gacaaucug	2040	
gacuuccuga	agagcgacgg	auucgcaaac	agaaacuua	ugcagcugau	ccacgacgac	2100	
agccugacau	ucaaggaaga	cauccagaag	gcacagguca	gcggacaggg	agacagccug	2160	
cacgaacaca	ucgcaaaccu	ggcaggaagc	ccgcaauca	agaagggaa	ccugcagaca	2220	
gucaaggucg	ucgacgaacu	ggucaagguc	augggaagac	acaagccgga	aaacaucguc	2280	
aucgaaaugg	caagagaaaa	ccagacaaca	cagaaggac	agaagaacag	cagagaaaga	2340	
augaagagaa	ucgaagaagg	aaucaaggaa	cugggaagcc	agaucugaa	ggaacacccg	2400	
gucgaaaaca	cacagcugca	gaacgaaaag	cuguaccugu	acuaccugca	gaacggaaga	2460	
gacauguacg	ucgaccagga	acuggacauc	aacagacuga	gcgacuacga	cgucgaccac	2520	
aucgucccgc	agagcuuccu	gaaggacgac	agcaucgaca	acaagguccu	gacaagaagc	2580	
gacaagaaca	gaggaaagag	cgacaacguc	ccgagcgaag	aagucgucaa	gaagaugaag	2640	
aacuacugga	gacagcugcu	gaacgcaaag	cugaucacac	agagaaaguu	cgacaaccug	2700	
acaaaggcag	agagaggagg	acugagcgaa	cuggacaagg	caggauucau	caagagacag	2760	
cuggucgaaa	caagacagau	cacaaagcac	gucgcacaga	uccuggacag	cagaaugaac	2820	
acaaaguacg	acghaaacga	caagcugauc	agagaaguca	aggucaucac	acugaagagc	2880	
aagcugguca	gcgacuucag	aaaggacuuc	caguucuaca	aggucagaga	aaucaacaac	2940	

uaccaccacg cacacgacgc auaccugaac gcagucgucg gaacagcacu gaucaagaag	3000
uacccgaagc uggaaagcga auucgucuaac ggagacuaca aggucuaacga cgucagaaaag	3060
augaucgcaa agagcgaaca ggaaaucgga aaggcaacag caaaguacuu cuucuacagc	3120
aacaucauga acuucuuaa gacagaaauc acacuggcaa acggagaaaau cagaaaagaga	3180
ccgucgaucg aaacaaacgg agaaacagga gaaaucgucu gggacaaggg aagagacuuc	3240
gcaacaguca gaaagguccu gagcaugccg caggucaaca ucgucaagaa gacagaaguc	3300
cagacaggag gauucagcaa gaaagcauc cugccgaaga gaaacagcga caagcugauc	3360
gcaagaaaaga aggacuggga cccgaagaag uacggaggau ucgacagccc gacagucgca	3420
uacagcgucc uggucgucg aaaggucgaa aagggaaga gcaagaagcu gaagagcguc	3480
aaggaacugc ugggaauac aucaugaa agaagcagcu ucgaaaagaa cccgaucgac	3540
uuccuggaag caaagggua caaggaaguc aagaaggacc ugaucauaa gcugccgaag	3600
uacagccugu ucgaacugga aaacggaaga aagagaaugc uggcaagcg aggagaacug	3660
cagaaggaa acgaacuggc acugccgagc aaguacguca acuuccugua ccuggcaagc	3720
cacuacgaaa agcugaaggg aagccggaa gacaacgaac agaagcagcu guucgucgaa	3780
cagcacaagc acuaccugga gaaaaucauc gaacagauca gcgaaauacg caagagaguc	3840
auccuggcag acgcaaacu ggacaagguc cugagcgcau acaacaagca cagagacaag	3900
ccgaucagag aacagcgaga aaacaucauc caccuguuca cacugacaaa ccugggagca	3960
ccggcagcau ucaaguacuu cgacacaaca aucgacagaa agagauacac aagcacaag	4020
gaaguccug acgcaacacu gauccaccag agcaucacag gacuguacga aacaagaauc	4080
gaccugagcc agcugggag agacggaagc ggaagcccga agaagaagag aaaggucgac	4140
ggaagcccga agaagaagag aaaggucgac agcggauag	4179
<210> 24	
<211> 4173	
<212> RNA	
<213> 人工序列	
<220>	
<223> 合成的：使用如表3中所列的最小尿苷密码子编码SEQ ID NO：23的Cas9编码序列(无起始或终止密码子；适于包括在融合蛋白质编码序列中)	
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agcaucaaga agaaccugau cggagcacug cuguucgaca gcggagaaac agcagaagca	180
acaagacuga agagaacagc aagaagaaga uacacaagaa gaaagaacag aaucugcuac	240
cugcagaaaa ucuucagcaa cgaaauggca aaggucgacg acagcuucuu ccacagacug	300
gaagaaagcu uccuggucg agaagacaag aagcacgaaa gacacccgau cuucggaac	360
aucgucgacg aagucgcaua ccacgaaaag uaccgacaa ucuaccaccu gagaaagaag	420
cuggucgaca gcacagacaa ggcagaccug agacugaucu accuggcacu ggcacacaug	480
aucaaguuca gaggacacuu ccugaucgaa ggagaccuga acccgacaa cagcagcugc	540
gacaagcugu ucauccagcu gguccagaca uacaaccagc uguucgaaga aaaccgauc	600
aacgcaagcg gagucgacgc aaaggcauc cugagcgcaa gacugagcaa gacagaaga	660

cuggaaaacc	ugaucgcaca	gcugccggga	gaaaagaaga	acggacuguu	cggaaccug	720
aucgcacuga	gccugggacu	gacaccgaac	uucaagagca	acuucgaccu	ggcagaagac	780
gcaaagcugc	agcugagcaa	ggacacauac	gacgacgacc	uggacaaccu	gcuggcacag	840
aucggagacc	aguacgcaga	ccuguuccug	gcagcaaaga	accugagcga	cgcaauccug	900
cugagcgaca	uccugagagu	caacacagaa	aucacaaagg	caccgcugag	cgcaagcaug	960
aucaagagau	acgacgaaca	ccaccaggac	cugacacugc	ugaaggcacu	ggucagacag	1020
cagcugccgg	aaaaguacaa	ggaaaucuuc	uucgaccaga	gcaagaacgg	auacgcagga	1080
uacaucgacg	gaggagcaag	ccaggaagaa	uucuacaagu	ucaucaagcc	gauccuggaa	1140
aagauggacg	gaacagaaga	acugcugguc	aagcugaaca	gagaagaccu	gcugagaaag	1200
cagagaacau	ucgacaacgg	aagcaucccg	caccagauc	accugggaga	acugcacgca	1260
auccugagaa	gacaggaaga	cuucuacccg	uuccugaagg	acaacagaga	aaagaucgaa	1320
aagauccuga	cauucagaau	cccguacuac	gucggaccgc	uggcaagagg	aaacagcaga	1380
uucgcaugga	ugacaagaaa	gagcgaagaa	acaaucacac	cguggaacuu	cgaagaaguc	1440
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cuguucgacg	acaaggucua	gaagcagcug	aagagaagaa	gauacacagg	auggggaaga	1980
cugagcagaa	agcugaucaa	cggaaucaga	gacaagcaga	gcggaagac	aauccuggac	2040
uuccugaaga	gcgacggauu	cgcaaacaga	aacuucaugc	agcugaacca	cgacgacagc	2100
cugacauuca	aggaagacau	ccagaaggca	caggucagc	gacagggaga	cagccugcac	2160
gaacacaucg	caaaccuggc	aggaagccc	gcaaucaaga	agggaauccu	gcagacaguc	2220
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gaaaacacac	agcugcagaa	cgaaaagcug	uaccuguacu	accugcagaa	cggaagagac	2460
auguacgucg	accaggaacu	ggacauaac	agacugagcg	acuacgacgu	cgaccacauc	2520
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aagaacagag	gaaagagcga	caacguccc	agcgaagaag	ucgucaagaa	gaugaagaac	2640
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aaguacgacg	aaaacgacaa	gcugaucaga	gaagucaagg	ucaucacacu	gaagagcaag	2880
cuggucagcg	acuucagaaa	ggacuuccag	uucuacaagg	ucagagaaau	caacaacuac	2940

[0067]

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aucgcaaaga gcgaacagga aaucggaaag gcaacagcaa aguacuucuu cuacagcaac	3120
aucaugaacu ucuucaagac agaaaucaca cuggcaaacg gagaaaucag aaagagaccg	3180
cugaucgaaa caaacggaga aacaggagaa aucgucuggg acaagggag agacuucgca	3240
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gaacugcugg gaucacaa cauggaaaga agcagcuucg aaaagaacc gaucgacuuc	3540
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aucagagaac aggcagaaaa caucauccac cuguucacac ugacaaaccu gggagcaccg	3960
gcagcauua aguacuucg cacaacauc gacagaaaga gauacacaag cacaaggaa	4020
[0068] guccuggacg caacacugau ccaccagac aucacaggac uguacgaaac aagaaucgac	4080
cugagccagc ugggaggaga cggaagcgga agcccgaaga agaagagaaa ggucgacgga	4140
agcccgaaga agaagagaaa ggucgacagc gga	4173

<210> 25

<211> 1392

<212> PRT

<213> 人工序列

<220>

<223> 合成的：具有两个核定位信号作为C端氨基酸的Cas9切口酶的氨基酸序列

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Met Asp Lys Lys Tyr Ser Ile Gly Leu Ala Ile Gly Thr Asn Ser Val
1 5 10 15

Gly Trp Ala Val Ile Thr Asp Glu Tyr Lys Val Pro Ser Lys Lys Phe
20 25 30

Lys Val Leu Gly Asn Thr Asp Arg His Ser Ile Lys Lys Asn Leu Ile
35 40 45

Gly Ala Leu Leu Phe Asp Ser Gly Glu Thr Ala Glu Ala Thr Arg Leu
50 55 60

Lys Arg Thr Ala Arg Arg Arg Tyr Thr Arg Arg Lys Asn Arg Ile Cys
65 70 75 80

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

	85	90	95	
	Phe Phe His Arg Leu Glu Glu Ser Phe Leu Val Glu Glu Asp Lys Lys 100 105 110			
	His Glu Arg His Pro Ile Phe Gly Asn Ile Val Asp Glu Val Ala Tyr 115 120 125			
	His Glu Lys Tyr Pro Thr Ile Tyr His Leu Arg Lys Lys Leu Val Asp 130 135 140			
	Ser Thr Asp Lys Ala Asp Leu Arg Leu Ile Tyr Leu Ala Leu Ala His 145 150 155 160			
	Met Ile Lys Phe Arg Gly His Phe Leu Ile Glu Gly Asp Leu Asn Pro 165 170 175			
	Asp Asn Ser Asp Val Asp Lys Leu Phe Ile Gln Leu Val Gln Thr Tyr 180 185 190			
	Asn Gln Leu Phe Glu Glu Asn Pro Ile Asn Ala Ser Gly Val Asp Ala 195 200 205			
	Lys Ala Ile Leu Ser Ala Arg Leu Ser Lys Ser Arg Arg Leu Glu Asn 210 215 220			
[0069]	Leu Ile Ala Gln Leu Pro Gly Glu Lys Lys Asn Gly Leu Phe Gly Asn 225 230 235 240			
	Leu Ile Ala Leu Ser Leu Gly Leu Thr Pro Asn Phe Lys Ser Asn Phe 245 250 255			
	Asp Leu Ala Glu Asp Ala Lys Leu Gln Leu Ser Lys Asp Thr Tyr Asp 260 265 270			
	Asp Asp Leu Asp Asn Leu Leu Ala Gln Ile Gly Asp Gln Tyr Ala Asp 275 280 285			
	Leu Phe Leu Ala Ala Lys Asn Leu Ser Asp Ala Ile Leu Leu Ser Asp 290 295 300			
	Ile Leu Arg Val Asn Thr Glu Ile Thr Lys Ala Pro Leu Ser Ala Ser 305 310 315 320			
	Met Ile Lys Arg Tyr Asp Glu His His Gln Asp Leu Thr Leu Leu Lys 325 330 335			
	Ala Leu Val Arg Gln Gln Leu Pro Glu Lys Tyr Lys Glu Ile Phe Phe 340 345 350			
	Asp Gln Ser Lys Asn Gly Tyr Ala Gly Tyr Ile Asp Gly Gly Ala Ser 355 360 365			
	Gln Glu Glu Phe Tyr Lys Phe Ile Lys Pro Ile Leu Glu Lys Met Asp 370 375 380			

Gly Thr Glu Glu Leu Leu Val Lys Leu Asn Arg Glu Asp Leu Leu Arg
 385 390 395 400
 Lys Gln Arg Thr Phe Asp Asn Gly Ser Ile Pro His Gln Ile His Leu
 405 410 415
 Gly Glu Leu His Ala Ile Leu Arg Arg Gln Glu Asp Phe Tyr Pro Phe
 420 425 430
 Leu Lys Asp Asn Arg Glu Lys Ile Glu Lys Ile Leu Thr Phe Arg Ile
 435 440 445
 Pro Tyr Tyr Val Gly Pro Leu Ala Arg Gly Asn Ser Arg Phe Ala Trp
 450 455 460
 Met Thr Arg Lys Ser Glu Glu Thr Ile Thr Pro Trp Asn Phe Glu Glu
 465 470 475 480
 Val Val Asp Lys Gly Ala Ser Ala Gln Ser Phe Ile Glu Arg Met Thr
 485 490 495
 Asn Phe Asp Lys Asn Leu Pro Asn Glu Lys Val Leu Pro Lys His Ser
 500 505 510
 Leu Leu Tyr Glu Tyr Phe Thr Val Tyr Asn Glu Leu Thr Lys Val Lys
 515 520 525
 [0070] Tyr Val Thr Glu Gly Met Arg Lys Pro Ala Phe Leu Ser Gly Glu Gln
 530 535 540
 Lys Lys Ala Ile Val Asp Leu Leu Phe Lys Thr Asn Arg Lys Val Thr
 545 550 555 560
 Val Lys Gln Leu Lys Glu Asp Tyr Phe Lys Lys Ile Glu Cys Phe Asp
 565 570 575
 Ser Val Glu Ile Ser Gly Val Glu Asp Arg Phe Asn Ala Ser Leu Gly
 580 585 590
 Thr Tyr His Asp Leu Leu Lys Ile Ile Lys Asp Lys Asp Phe Leu Asp
 595 600 605
 Asn Glu Glu Asn Glu Asp Ile Leu Glu Asp Ile Val Leu Thr Leu Thr
 610 615 620
 Leu Phe Glu Asp Arg Glu Met Ile Glu Glu Arg Leu Lys Thr Tyr Ala
 625 630 635 640
 His Leu Phe Asp Asp Lys Val Met Lys Gln Leu Lys Arg Arg Arg Tyr
 645 650 655
 Thr Gly Trp Gly Arg Leu Ser Arg Lys Leu Ile Asn Gly Ile Arg Asp
 660 665 670
 Lys Gln Ser Gly Lys Thr Ile Leu Asp Phe Leu Lys Ser Asp Gly Phe
 675 680 685

Ala Asn Arg Asn Phe Met Gln Leu Ile His Asp Asp Ser Leu Thr Phe
690 695 700

Lys Glu Asp Ile Gln Lys Ala Gln Val Ser Gly Gln Gly Asp Ser Leu
705 710 715 720

His Glu His Ile Ala Asn Leu Ala Gly Ser Pro Ala Ile Lys Lys Gly
725 730 735

Ile Leu Gln Thr Val Lys Val Val Asp Glu Leu Val Lys Val Met Gly
740 745 750

Arg His Lys Pro Glu Asn Ile Val Ile Glu Met Ala Arg Glu Asn Gln
755 760 765

Thr Thr Gln Lys Gly Gln Lys Asn Ser Arg Glu Arg Met Lys Arg Ile
770 775 780

Glu Glu Gly Ile Lys Glu Leu Gly Ser Gln Ile Leu Lys Glu His Pro
785 790 795 800

Val Glu Asn Thr Gln Leu Gln Asn Glu Lys Leu Tyr Leu Tyr Tyr Leu
805 810 815

Gln Asn Gly Arg Asp Met Tyr Val Asp Gln Glu Leu Asp Ile Asn Arg
820 825 830

[0071] Leu Ser Asp Tyr Asp Val Asp His Ile Val Pro Gln Ser Phe Leu Lys
835 840 845

Asp Asp Ser Ile Asp Asn Lys Val Leu Thr Arg Ser Asp Lys Asn Arg
850 855 860

Gly Lys Ser Asp Asn Val Pro Ser Glu Glu Val Val Lys Lys Met Lys
865 870 875 880

Asn Tyr Trp Arg Gln Leu Leu Asn Ala Lys Leu Ile Thr Gln Arg Lys
885 890 895

Phe Asp Asn Leu Thr Lys Ala Glu Arg Gly Gly Leu Ser Glu Leu Asp
900 905 910

Lys Ala Gly Phe Ile Lys Arg Gln Leu Val Glu Thr Arg Gln Ile Thr
915 920 925

Lys His Val Ala Gln Ile Leu Asp Ser Arg Met Asn Thr Lys Tyr Asp
930 935 940

Glu Asn Asp Lys Leu Ile Arg Glu Val Lys Val Ile Thr Leu Lys Ser
945 950 955 960

Lys Leu Val Ser Asp Phe Arg Lys Asp Phe Gln Phe Tyr Lys Val Arg
965 970 975

Glu Ile Asn Asn Tyr His His Ala His Asp Ala Tyr Leu Asn Ala Val
980 985 990

Val Gly Thr Ala Leu Ile Lys Lys Tyr Pro Lys Leu Glu Ser Glu Phe
 995 1000 1005

Val Tyr Gly Asp Tyr Lys Val Tyr Asp Val Arg Lys Met Ile Ala
 1010 1015 1020

Lys Ser Glu Gln Glu Ile Gly Lys Ala Thr Ala Lys Tyr Phe Phe
 1025 1030 1035

Tyr Ser Asn Ile Met Asn Phe Phe Lys Thr Glu Ile Thr Leu Ala
 1040 1045 1050

Asn Gly Glu Ile Arg Lys Arg Pro Leu Ile Glu Thr Asn Gly Glu
 1055 1060 1065

Thr Gly Glu Ile Val Trp Asp Lys Gly Arg Asp Phe Ala Thr Val
 1070 1075 1080

Arg Lys Val Leu Ser Met Pro Gln Val Asn Ile Val Lys Lys Thr
 1085 1090 1095

Glu Val Gln Thr Gly Gly Phe Ser Lys Glu Ser Ile Leu Pro Lys
 1100 1105 1110

Arg Asn Ser Asp Lys Leu Ile Ala Arg Lys Lys Asp Trp Asp Pro
 1115 1120 1125

[0072] Lys Lys Tyr Gly Gly Phe Asp Ser Pro Thr Val Ala Tyr Ser Val
 1130 1135 1140

Leu Val Val Ala Lys Val Glu Lys Gly Lys Ser Lys Lys Leu Lys
 1145 1150 1155

Ser Val Lys Glu Leu Leu Gly Ile Thr Ile Met Glu Arg Ser Ser
 1160 1165 1170

Phe Glu Lys Asn Pro Ile Asp Phe Leu Glu Ala Lys Gly Tyr Lys
 1175 1180 1185

Glu Val Lys Lys Asp Leu Ile Ile Lys Leu Pro Lys Tyr Ser Leu
 1190 1195 1200

Phe Glu Leu Glu Asn Gly Arg Lys Arg Met Leu Ala Ser Ala Gly
 1205 1210 1215

Glu Leu Gln Lys Gly Asn Glu Leu Ala Leu Pro Ser Lys Tyr Val
 1220 1225 1230

Asn Phe Leu Tyr Leu Ala Ser His Tyr Glu Lys Leu Lys Gly Ser
 1235 1240 1245

Pro Glu Asp Asn Glu Gln Lys Gln Leu Phe Val Glu Gln His Lys
 1250 1255 1260

His Tyr Leu Asp Glu Ile Ile Glu Gln Ile Ser Glu Phe Ser Lys

1265 1270 1275

Arg Val Ile Leu Ala Asp Ala Asn Leu Asp Lys Val Leu Ser Ala
1280 1285 1290

Tyr Asn Lys His Arg Asp Lys Pro Ile Arg Glu Gln Ala Glu Asn
1295 1300 1305

Ile Ile His Leu Phe Thr Leu Thr Asn Leu Gly Ala Pro Ala Ala
1310 1315 1320

Phe Lys Tyr Phe Asp Thr Thr Ile Asp Arg Lys Arg Tyr Thr Ser
1325 1330 1335

Thr Lys Glu Val Leu Asp Ala Thr Leu Ile His Gln Ser Ile Thr
1340 1345 1350

Gly Leu Tyr Glu Thr Arg Ile Asp Leu Ser Gln Leu Gly Gly Asp
1355 1360 1365

Gly Ser Gly Ser Pro Lys Lys Lys Arg Lys Val Asp Gly Ser Pro
1370 1375 1380

Lys Lys Lys Arg Lys Val Asp Ser Gly
1385 1390

[0073]

<210> 26
<211> 4179
<212> RNA
<213> 人工序列

<220>
<223> 合成的：使用如表3中所列的最小尿苷密码子编码SEQ ID NO: 25的，具有起始和终止密码子的Cas9切口酶mRNA ORF

<400> 26
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 aucacagacg aaaucaaggu cccgagcaag aaguucaagg uccugggaaa cacagacaga 120
 cacagcauca agaagaaccu gaucggagca cugcuguucg acagcggaga aacagcagaa 180
 gcaacaagac ugaagagaac agcaagaaga agauacacaa gaagaaagaa cagaaucugc 240
 uaccugcagg aaauucucag caacgaaaug gcaaaggucg acgacagcuu cuuccacaga 300
 cuggaagaaa gcuuccuggu cgaagaagac aagaagcacg aaagacacc gaucucgga 360
 acaucugucg acgaagucg auaccacgaa aaguaccga caaucuacca ccugagaaag 420
 aagcuggucg acagcacaga caaggcagac cugagacuga ucuaccuggc acuggcacac 480
 augaucaagu ucagaggaca cuuccugauc gaaggagacc ugaaccggga caacagcgac 540
 gucgacaagc uguucaucaa gcugguccag acauacaacc agcuguucga agaaaaccg 600
 aucaacgcaa gcggagucga cgcaaagca auccugagcg caagacugag caagagcaga 660
 agacuggaaa accugaucg acagcugccg ggagaaaaga agaaccgacu guucggaaac 720
 cugaucgcac ugagccuggg acugacaccg aacuucaaga gcaacuucga ccuggcagaa 780
 gacgcaaagc ugcagcugag caaggacaca uacgacgacg accuggacaa ccugcuggca 840
 cagaucggag accaguacgc agaccuguuc cuggcagcaa agaaccugag cgacgcaauc 900

cugcugagcg	acauccugag	agucaacaca	gaaaucacaa	aggcaccgcu	gagcgcgaagc	960
augaucaaga	gauacgacga	acaccaccag	gaccugacac	ugcugaaggc	acuggucaga	1020
cagcagcugc	cggaaaagua	caaggaaauc	uucuucgacc	agagcaagaa	cggauacgca	1080
ggauacaucg	acggaggagc	aagccaggaa	gaauuuaca	aguucaucaa	gccgauccug	1140
gaaaagaugg	acggaacaga	agaacugcug	gucaagcuga	acagagaaga	ccugcugaga	1200
aagcagagaa	cauucgacaa	cggaagcauc	ccgcaccaga	uccaccuggg	agaacugcac	1260
gcaauccuga	gaagacagga	agacuucuc	ccguuccuga	aggacaacag	agaaaagauc	1320
gaaaagaucc	ugacauucag	aaucccguc	uacgucggac	cgcuggcaag	aggaaacagc	1380
agauucgcau	ggauacaaag	aaagagcga	gaaacaauc	caccguggaa	cuucgaagaa	1440
gucgucgaca	aggagcgaag	cgcacagagc	uucaucgaaa	gaaugacaaa	cuucgacaag	1500
aaccugccga	acgaaaaggu	ccugccgaag	cacagccugc	uguacgaaua	cuucacaguc	1560
uacaacgaac	ugacaaaaggu	caaguacguc	acagaaggaa	ugagaagcc	ggcauuccug	1620
agcggagaac	agaagaaggc	aaucgucgac	cugcuguuca	agacaaacag	aaaggucaca	1680
gucaagcagc	ugaaggaaga	cuacuucag	aagaucgaau	gcuucgacag	cgucgaaauc	1740
agcggagucg	aagacagauu	caacgcaagc	cugggaacau	accacgaccu	gcugaagauc	1800
aucaaggaca	aggacuuccu	ggacaacgaa	gaaaacgaag	acauccugga	agacaucguc	1860
cugacacuga	cacuguucga	agacagagaa	augaucgaag	aaagacugaa	gacauacgca	1920
caccuguucg	acgacaaggu	caugaagcag	cugaagagaa	gaagauacac	aggauaggga	1980
agacugagca	gaaagcugau	caacggauc	agagacaagc	agagcggaaa	gacaauccug	2040
gacuuccuga	agagcgcagc	auucgcaaac	agaaacuuc	ugcagcugau	ccacgacgac	2100
agccugacau	ucaaggaaga	cauccagaag	gcacagguca	gcggacaggg	agacagccug	2160
cacgaacaca	ucgcaaaccu	ggcagggaagc	ccggcaauca	agaagggaau	ccugcagaca	2220
gucaaggucg	ucgacgaacu	ggucaagguc	augggaagac	acaagccgga	aaacaucguc	2280
aucgaaaugg	caagagaaaa	ccagacaaca	cagaagggac	agaagaacag	cagagaaaga	2340
augaagagaa	ucgaagaagg	aaucgaagg	cugggaagcc	agauccugaa	ggaacaccgc	2400
gucgaaaaca	cacagcugca	gaacgaaaag	cuguaccugu	acuaccugca	gaacggaaga	2460
gacauguacg	ucgaccagga	acuggacauc	aacagacuga	gcgacuacga	cugcagaccac	2520
aucguccgc	agagcuuccu	gaaggacgac	agcaucgaca	acaagguccu	gacaagaagc	2580
gacaagaaca	gaggaaagag	cgacaacguc	ccgagcgaag	aagucgucaa	gaagaugaag	2640
aacuacugga	gacagcugcu	gaacgcaaag	cugaucacac	agagaaguu	cgacaaccug	2700
acaaaggcag	agagaggagg	acugagcga	cuggacaagg	caggauucau	caagagacag	2760
cuggucgaaa	caagacagau	cacaaagcac	gucgcacaga	uccuggacag	cagaaugaac	2820
acaaaguacg	acgaaaacga	caagcugauc	agagaaguca	aggucaucac	acugaagagc	2880
aagcugguca	gcgacuucag	aaaggacuuc	caguucuaa	aggucagaga	aaucacaac	2940
uaccaccacg	cacacgacgc	auaccugaac	gcagucgucg	gaacagcacu	gaucaagaag	3000
uaccggaagc	uggaaagcga	auucgucuc	ggagacuaca	aggucucgca	cugcagaaaag	3060
augaucgcaa	agagcgaaca	ggaaucgga	aaggcaacag	caaaguacuu	cuucucagc	3120
aaaucauga	acuucuucaa	gacagaaauc	acacuggcaa	acggagaaau	cagaaaagaa	3180

[0074]

ccgcugaucg	aaacaaacgg	agaacacagga	gaaaucgucu	gggacaaggg	aagagacuuc	3240
gcaacaguca	gaaagguccu	gagcaugccg	caggucaaca	ucgucaagaa	gacagaaguc	3300
cagacaggag	gauucagcaa	ggaaagcauc	cugccgaaga	gaaacagcga	caagcugauc	3360
gcaagaaaaga	aggacuggga	cccgaagaag	uacggaggau	ucgacagecc	gacagucgca	3420
uacagcgucc	uggucgucg	aaaggucgaa	aagggaaga	gcaagaagcu	gaagagcguc	3480
aaggaacugc	ugggaauac	aaucauggaa	agaagcagcu	ucgaaaagaa	cccgaucgac	3540
uuccuggaag	caaagggua	caaggaaguc	aagaaggacc	ugaucaucua	gcugccgaag	3600
uacagccugu	ucgaacugga	aaacggaaga	aagagaauuc	uggcaagcgc	aggagaacug	3660
cagaaggga	acgaacuggc	acugccgagc	aaguacguca	acuuccugua	ccuggcaage	3720
cacuacgaaa	agcugaaggg	aagcccggaa	gacaacgaac	agaagcagcu	guucgucgaa	3780
cagcacaagc	acuaccugga	cgaaaucauc	gaacagauca	gcgaaauucag	caagagaguc	3840
auccuggcag	acgcaaaccu	ggacaagguc	cugagcgcau	acaacaagca	cagagacaag	3900
ccgauccagag	aacaggcaga	aaacaucauc	caccuguuca	cacugacaaa	ccugggagca	3960
ccggcagcau	ucaaguacuu	cgacacaaca	aucgacagaa	agagauacac	aagcacaag	4020
gaaguccugg	acgcaacacu	gauccaccag	agcaucacag	gacuguacga	aacaagaauc	4080
gaccugagcc	agcuggggag	agacggaagc	ggaagcccga	agaagaagag	aaaggucgac	4140
ggaagcccga	agaagaagag	aaaggucgac	agcggauag			4179

[0075]

<210> 27
 <211> 4173
 <212> RNA
 <213> 人工序列

<220>
 <223> 合成的：使用如表3中所列的最小尿苷密码子编码SEQ ID NO: 25的Cas9切口酶编码序列(无起始或终止密码子；适于包括在融合蛋白质编码序列中)

<400> 27						
gacaagaagu	acagcaucgg	acuggcaauc	ggaacaaaca	gcgucggaug	ggcagucauc	60
acagacgaau	acaaggucc	gagcaagaag	uucaaggucc	ugggaaacac	agacagacac	120
agcaucaaga	agaaccugau	cggagcacug	cuguucgaca	gcggagaaac	agcagaagca	180
acaagacuga	agagaacagc	aagaagaaga	uacacaagaa	gaaagaacag	aaucugcuac	240
cugcaggaaa	ucuucagcaa	cgaaauggca	aaggucgacg	acagcuucuu	ccacagacug	300
gaagaaagcu	uccugucga	agaagacaag	aagcacgaaa	gacaccgcau	cuucggaaac	360
aucgucgacg	aagucgcaua	ccacgaaaag	uacccgacaa	ucuaccaacu	gagaaagaag	420
cuggucgaca	gcacagacaa	ggcagaccug	agacugaucu	accuggcacu	ggcacacaug	480
aucaaguuca	gaggacacuu	ccugaucgaa	ggagaccuga	acccggacaa	cagcagcugc	540
gacaagcugu	ucauccagcu	gguccagaca	uacaaccagc	uguucgaaga	aaaccgcauc	600
aacgcaagcg	gagucgacgc	aaaggcaauc	cugagcgcaa	gacugagcaa	gagcagaaga	660
cuggaaaacc	ugaucgcaca	gcugccggga	gaaaagaaga	acggacuguu	cggaaaccug	720
aucgcacuga	gccugggacu	gacaccgaac	uucaagagca	acuucgaccu	ggcagaagac	780
gcaaagcugc	agcugagcaa	ggacacauc	gacgacgacc	uggacaaccu	gcuggcagac	840
aucggagacc	aguacgcaga	ccuguuccug	gcagcaaga	accugagcga	cgaaucug	900

	cugagcgaca uccugagagu caacacagaa aucacaaagg caccgcugag cgcaagcaug	960
	aucaagagau acgacgaaca ccaccaggac cugacacugc ugaaggcacu ggucagacag	1020
	cagcugccgg aaaaguacaa ggaaaucuuc uucgaccaga gcaagaacgg auacgcagga	1080
	uacaucgacg gaggagcaag ccaggaagaa uucuacaagu ucaucaagcc gaucuggaa	1140
	aagauggacg gaacagaaga acugcugguc aagcugaaca gagaagaccu gcugagaaag	1200
	cagagaacau ucgacaacgg aagcaucccg caccagaucc accugggaga acugcacgca	1260
	auccugagaa gacaggaaga cuucuaccg uuccugaagg acaacagaga aaagaucgaa	1320
	aagauccuga cauucagaau cccguacuac gucggaccgc uggcaagagg aaacagcaga	1380
	uucgcaugga ugacaagaaa gagcgaagaa acaaucacac cguggaacuu cgaagaaguc	1440
	gucgacaagg gagcaagcgc acagagcuuc aucgaaagaa ugacaacuu cgacaagaac	1500
	cugccgaacg aaaagguccu gccgaagcac agccugcugu acgaaucuu cacagucuauc	1560
	aacgaacuga caaaggucaa guacgucaca gaaggaauga gaaagccggc auuccugagc	1620
	ggagaacaga agaaggcaau cgucgaccug cuguucaaga caaacagaaa ggucacaguc	1680
	aagcagcuga aggaagacua cuucaagaag aucgaaugcu ucgacagcgu cgaaaucagc	1740
	ggagucgaag acagauucua cgcaagccug ggaacauacc acgaccugcu gaagaucauc	1800
	aaggaacagg acuuccugga caacgaagaa aacgaagaca uccuggaaga caucguccug	1860
	acacugacac uguucgaaga cagagaaaug aucgaagaaa gacugaagac auacgcacac	1920
	cuguucgacg acaaggucau gaagcagcug aagagaagaa gauacacagg auggggaaga	1980
[0076]	cugagcagaa agcugaucaa cggaaucaga gacaagcaga gccgaaagac aauccuggac	2040
	uuccugaaga gcgacggauu cgcaaacaga aacuucagc agcugaucca cgacgacagc	2100
	cugacauuca aggaagacau ccagaaggca caggucagcg gacagggaga cagccugcac	2160
	gaacacaucg caaacuggc aggaagccc gcaaucaaga agggaauccu gcagacaguc	2220
	aaggucgucg acgaacuggu caaggucaug ggaagacaca agccggaaaa caucgucauc	2280
	gaaauggcaa gagaaaacca gacaacacag aaggacaga agaacagcag agaaagaau	2340
	aagagaaucg aagaaggaau caaggaacug ggaagccaga uccugaagga acaccgguc	2400
	gaaaacacac agcugcagaa cgaaaagcug uaccuguacu accugcagaa cggaagagac	2460
	auguacgucg accaggaacu ggacaucaac agacugagcg acuacgacgu cgaccacauc	2520
	gucccgcaga gcuuccugaa ggacgacagc aucgacaaca agguccugac aagaagcagc	2580
	aagaacagag gaaagagcga caacguccc agcgaagaag ucgucaagaa gaugaagaac	2640
	uacuggagac agcugcugaa cgcaaagcug aucacacaga gaaaguucga caaccugaca	2700
	aaggcagaga gaggaggacu gagcgaacug gacaagcgag gauucaucaa gagacagcug	2760
	gucgaaacaa gacagaucaac aaagcagcuc gcacagaucc uggacagcag aaugaacaca	2820
	aaguacgacg aaaacgacaa gcugaucaga gaagucaagg ucaucacacu gaagagcaag	2880
	cuggucagcg acuucagaaa ggacuuccag uucuacaagg ucagagaaa caacaacuac	2940
	caccacgac acgacgcaua ccugaacgca gucgucggaa cagcagcugau caagaaguac	3000
	ccgaagcugg aaagcgaauu cgucucgga gacuacaagg ucuacgacgu cagaaagaug	3060
	aucgcaaaaga gcgaacagga aaucggaag gcaacagcaa aguacuucuu cuacagcaac	3120

aucaugaacu ucuucaagac agaaaucaca cuggcaaacg gagaaaucag aaagagaccg	3180
cugaucgaaa caaacggaga aacaggagaa aucgucuggg acaagggaag agacuucgca	3240
acagucagaa agguccugag caugcccgag gucaacaucg ucaagaagac agaaguccag	3300
acaggaggau ucagcaagga aagcauccug ccgaagagaa acagcgacaa gcugaucgca	3360
agaaagaagg acugggaccc gaagaaguac ggaggauucg acagcccgcac agucgcauac	3420
agcguccugg ucgucgcaaa ggucgaaaag ggaaagagca agaagcugaa gacgcucaag	3480
gaucgucugg gaaucacaau cauggaaaga agcagcuucg aaaagaaccc gaucgacuuc	3540
cuggaagcaa agggauacaa ggaagucaag aaggaccuga ucaucaageu gccgaaguac	3600
agccuguucg aacuggaaaa cggaagaaag agaaucugg caagcgagg agaacugcag	3660
aagggaaacg aacuggcacu gccgagcaag uacgucaacu uccuguaccu ggcaagccac	3720
uacgaaaagc ugaagggaag cccggaagac aacgaacaga agcagcuguu cgucgaacag	3780
cacaagcacu accuggacga aaucaucgaa cagaucagcg aaucagcaa gagagucauc	3840
cuggcagacg caaacugga caagguccug agcgcauaca acaagcacag agacaagccg	3900
aucagagaac aggcagaaaa caucauccac cuguucacac ugacaaaccu gggagcaccg	3960
gcagcauua aguacuucg cacaacauc gacagaaaaga gauacacaag cacaagggaa	4020
guccuggacg caacacugau ccaccagagc aucacaggac uguacgaaac aagaaucgac	4080
cugagccagc ugggaggaga cggaagcgga agcccgaaga agaagagaaa ggucgacgga	4140
agcccgaaga agaagagaaa ggucgacagc gga	4173

[0077]

<210> 28
 <211> 1392
 <212> PRT
 <213> 人工序列

<220>
 <223> 合成的：具有两个核定位信号作为C端氨基酸的dCas9的氨基酸序列

<400> 28

Met Asp Lys Lys Tyr Ser Ile Gly Leu Ala Ile Gly Thr Asn Ser Val
 1 5 10 15

Gly Trp Ala Val Ile Thr Asp Glu Tyr Lys Val Pro Ser Lys Lys Phe
 20 25 30

Lys Val Leu Gly Asn Thr Asp Arg His Ser Ile Lys Lys Asn Leu Ile
 35 40 45

Gly Ala Leu Leu Phe Asp Ser Gly Glu Thr Ala Glu Ala Thr Arg Leu
 50 55 60

Lys Arg Thr Ala Arg Arg Arg Tyr Thr Arg Arg Lys Asn Arg Ile Cys
 65 70 75 80

Tyr Leu Gln Glu Ile Phe Ser Asn Glu Met Ala Lys Val Asp Asp Ser
 85 90 95

Phe Phe His Arg Leu Glu Glu Ser Phe Leu Val Glu Glu Asp Lys Lys
 100 105 110

His Glu Arg His Pro Ile Phe Gly Asn Ile Val Asp Glu Val Ala Tyr
 115 120 125
 His Glu Lys Tyr Pro Thr Ile Tyr His Leu Arg Lys Lys Leu Val Asp
 130 135 140
 Ser Thr Asp Lys Ala Asp Leu Arg Leu Ile Tyr Leu Ala Leu Ala His
 145 150 155 160
 Met Ile Lys Phe Arg Gly His Phe Leu Ile Glu Gly Asp Leu Asn Pro
 165 170 175
 Asp Asn Ser Asp Val Asp Lys Leu Phe Ile Gln Leu Val Gln Thr Tyr
 180 185 190
 Asn Gln Leu Phe Glu Glu Asn Pro Ile Asn Ala Ser Gly Val Asp Ala
 195 200 205
 Lys Ala Ile Leu Ser Ala Arg Leu Ser Lys Ser Arg Arg Leu Glu Asn
 210 215 220
 Leu Ile Ala Gln Leu Pro Gly Glu Lys Lys Asn Gly Leu Phe Gly Asn
 225 230 235 240
 Leu Ile Ala Leu Ser Leu Gly Leu Thr Pro Asn Phe Lys Ser Asn Phe
 245 250 255
 [0078] Asp Leu Ala Glu Asp Ala Lys Leu Gln Leu Ser Lys Asp Thr Tyr Asp
 260 265 270
 Asp Asp Leu Asp Asn Leu Leu Ala Gln Ile Gly Asp Gln Tyr Ala Asp
 275 280 285
 Leu Phe Leu Ala Ala Lys Asn Leu Ser Asp Ala Ile Leu Leu Ser Asp
 290 295 300
 Ile Leu Arg Val Asn Thr Glu Ile Thr Lys Ala Pro Leu Ser Ala Ser
 305 310 315 320
 Met Ile Lys Arg Tyr Asp Glu His His Gln Asp Leu Thr Leu Leu Lys
 325 330 335
 Ala Leu Val Arg Gln Gln Leu Pro Glu Lys Tyr Lys Glu Ile Phe Phe
 340 345 350
 Asp Gln Ser Lys Asn Gly Tyr Ala Gly Tyr Ile Asp Gly Gly Ala Ser
 355 360 365
 Gln Glu Glu Phe Tyr Lys Phe Ile Lys Pro Ile Leu Glu Lys Met Asp
 370 375 380
 Gly Thr Glu Glu Leu Leu Val Lys Leu Asn Arg Glu Asp Leu Leu Arg
 385 390 395 400
 Lys Gln Arg Thr Phe Asp Asn Gly Ser Ile Pro His Gln Ile His Leu
 405 410 415

Gly Glu Leu His Ala Ile Leu Arg Arg Gln Glu Asp Phe Tyr Pro Phe
 420 425 430

Leu Lys Asp Asn Arg Glu Lys Ile Glu Lys Ile Leu Thr Phe Arg Ile
 435 440 445

Pro Tyr Tyr Val Gly Pro Leu Ala Arg Gly Asn Ser Arg Phe Ala Trp
 450 455 460

Met Thr Arg Lys Ser Glu Glu Thr Ile Thr Pro Trp Asn Phe Glu Glu
 465 470 475 480

Val Val Asp Lys Gly Ala Ser Ala Gln Ser Phe Ile Glu Arg Met Thr
 485 490 495

Asn Phe Asp Lys Asn Leu Pro Asn Glu Lys Val Leu Pro Lys His Ser
 500 505 510

Leu Leu Tyr Glu Tyr Phe Thr Val Tyr Asn Glu Leu Thr Lys Val Lys
 515 520 525

Tyr Val Thr Glu Gly Met Arg Lys Pro Ala Phe Leu Ser Gly Glu Gln
 530 535 540

Lys Lys Ala Ile Val Asp Leu Leu Phe Lys Thr Asn Arg Lys Val Thr
 545 550 555 560

[0079] Val Lys Gln Leu Lys Glu Asp Tyr Phe Lys Lys Ile Glu Cys Phe Asp
 565 570 575

Ser Val Glu Ile Ser Gly Val Glu Asp Arg Phe Asn Ala Ser Leu Gly
 580 585 590

Thr Tyr His Asp Leu Leu Lys Ile Ile Lys Asp Lys Asp Phe Leu Asp
 595 600 605

Asn Glu Glu Asn Glu Asp Ile Leu Glu Asp Ile Val Leu Thr Leu Thr
 610 615 620

Leu Phe Glu Asp Arg Glu Met Ile Glu Glu Arg Leu Lys Thr Tyr Ala
 625 630 635 640

His Leu Phe Asp Asp Lys Val Met Lys Gln Leu Lys Arg Arg Arg Tyr
 645 650 655

Thr Gly Trp Gly Arg Leu Ser Arg Lys Leu Ile Asn Gly Ile Arg Asp
 660 665 670

Lys Gln Ser Gly Lys Thr Ile Leu Asp Phe Leu Lys Ser Asp Gly Phe
 675 680 685

Ala Asn Arg Asn Phe Met Gln Leu Ile His Asp Asp Ser Leu Thr Phe
 690 695 700

Lys Glu Asp Ile Gln Lys Ala Gln Val Ser Gly Gln Gly Asp Ser Leu
 705 710 715 720

His Glu His Ile Ala Asn Leu Ala Gly Ser Pro Ala Ile Lys Lys Gly
 725 730 735
 Ile Leu Gln Thr Val Lys Val Val Asp Glu Leu Val Lys Val Met Gly
 740 745 750
 Arg His Lys Pro Glu Asn Ile Val Ile Glu Met Ala Arg Glu Asn Gln
 755 760 765
 Thr Thr Gln Lys Gly Gln Lys Asn Ser Arg Glu Arg Met Lys Arg Ile
 770 775 780
 Glu Glu Gly Ile Lys Glu Leu Gly Ser Gln Ile Leu Lys Glu His Pro
 785 790 795 800
 Val Glu Asn Thr Gln Leu Gln Asn Glu Lys Leu Tyr Leu Tyr Tyr Leu
 805 810 815
 Gln Asn Gly Arg Asp Met Tyr Val Asp Gln Glu Leu Asp Ile Asn Arg
 820 825 830
 Leu Ser Asp Tyr Asp Val Asp Ala Ile Val Pro Gln Ser Phe Leu Lys
 835 840 845
 Asp Asp Ser Ile Asp Asn Lys Val Leu Thr Arg Ser Asp Lys Asn Arg
 850 855 860
 [0080] Gly Lys Ser Asp Asn Val Pro Ser Glu Glu Val Val Lys Lys Met Lys
 865 870 875 880
 Asn Tyr Trp Arg Gln Leu Leu Asn Ala Lys Leu Ile Thr Gln Arg Lys
 885 890 895
 Phe Asp Asn Leu Thr Lys Ala Glu Arg Gly Gly Leu Ser Glu Leu Asp
 900 905 910
 Lys Ala Gly Phe Ile Lys Arg Gln Leu Val Glu Thr Arg Gln Ile Thr
 915 920 925
 Lys His Val Ala Gln Ile Leu Asp Ser Arg Met Asn Thr Lys Tyr Asp
 930 935 940
 Glu Asn Asp Lys Leu Ile Arg Glu Val Lys Val Ile Thr Leu Lys Ser
 945 950 955 960
 Lys Leu Val Ser Asp Phe Arg Lys Asp Phe Gln Phe Tyr Lys Val Arg
 965 970 975
 Glu Ile Asn Asn Tyr His His Ala His Asp Ala Tyr Leu Asn Ala Val
 980 985 990
 Val Gly Thr Ala Leu Ile Lys Lys Tyr Pro Lys Leu Glu Ser Glu Phe
 995 1000 1005
 Val Tyr Gly Asp Tyr Lys Val Tyr Asp Val Arg Lys Met Ile Ala

1010	1015	1020
Lys Ser Glu Gln Glu Ile Gly 1025	Lys Ala Thr Ala 1030	Lys Tyr Phe Phe 1035
Tyr Ser Asn Ile Met Asn Phe 1040	Phe Lys Thr Glu 1045	Ile Thr Leu Ala 1050
Asn Gly Glu Ile Arg Lys Arg 1055	Pro Leu Ile Glu 1060	Thr Asn Gly Glu 1065
Thr Gly Glu Ile Val Trp Asp 1070	Lys Gly Arg Asp 1075	Phe Ala Thr Val 1080
Arg Lys Val Leu Ser Met Pro 1085	Gln Val Asn Ile 1090	Val Lys Lys Thr 1095
Glu Val Gln Thr Gly Gly Phe 1100	Ser Lys Glu Ser 1105	Ile Leu Pro Lys 1110
Arg Asn Ser Asp Lys Leu Ile 1115	Ala Arg Lys Lys 1120	Asp Trp Asp Pro 1125
Lys Lys Tyr Gly Gly Phe Asp 1130	Ser Pro Thr Val 1135	Ala Tyr Ser Val 1140
[0081] Leu Val Val Ala Lys Val Glu 1145	Lys Gly Lys Ser 1150	Lys Lys Leu Lys 1155
Ser Val Lys Glu Leu Leu Gly 1160	Ile Thr Ile Met 1165	Glu Arg Ser Ser 1170
Phe Glu Lys Asn Pro Ile Asp 1175	Phe Leu Glu Ala 1180	Lys Gly Tyr Lys 1185
Glu Val Lys Lys Asp Leu Ile 1190	Ile Lys Leu Pro 1195	Lys Tyr Ser Leu 1200
Phe Glu Leu Glu Asn Gly Arg 1205	Lys Arg Met Leu 1210	Ala Ser Ala Gly 1215
Glu Leu Gln Lys Gly Asn Glu 1220	Leu Ala Leu Pro 1225	Ser Lys Tyr Val 1230
Asn Phe Leu Tyr Leu Ala Ser 1235	His Tyr Glu Lys 1240	Leu Lys Gly Ser 1245
Pro Glu Asp Asn Glu Gln Lys 1250	Gln Leu Phe Val 1255	Glu Gln His Lys 1260
His Tyr Leu Asp Glu Ile Ile 1265	Glu Gln Ile Ser 1270	Glu Phe Ser Lys 1275
Arg Val Ile Leu Ala Asp Ala 1280	Asn Leu Asp Lys 1285	Val Leu Ser Ala 1290

Tyr Asn Lys His Arg Asp Lys Pro Ile Arg Glu Gln Ala Glu Asn
 1295 1300 1305

Ile Ile His Leu Phe Thr Leu Thr Asn Leu Gly Ala Pro Ala Ala
 1310 1315 1320

Phe Lys Tyr Phe Asp Thr Thr Ile Asp Arg Lys Arg Tyr Thr Ser
 1325 1330 1335

Thr Lys Glu Val Leu Asp Ala Thr Leu Ile His Gln Ser Ile Thr
 1340 1345 1350

Gly Leu Tyr Glu Thr Arg Ile Asp Leu Ser Gln Leu Gly Gly Asp
 1355 1360 1365

Gly Ser Gly Ser Pro Lys Lys Lys Arg Lys Val Asp Gly Ser Pro
 1370 1375 1380

Lys Lys Lys Arg Lys Val Asp Ser Gly
 1385 1390

<210> 29
 <211> 4179
 <212> RNA
 <213> 人工序列

<220>
 <223> 合成的：使用如表3中所列的最小尿苷密码子编码SEQ ID NO: 28的，具有起始和终止密码子的dCas9 mRNA ORF

[0082]

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 cacagcauca agaagaaccu gaucggagca cugcuguuug acagcggaga aacagcagaa 180
 gcaacaagac ugaagagaac agcaagaaga agauacacaa gaagaagaa cagaaucugc 240
 uaccugcagg aaaucucag caacgaaaug gcaaaggucg acgacagcuu cuuccacaga 300
 cuggaagaaa gcuuccuggu cgaagaagac aagaagcacg aaagacaccc gaucucgga 360
 aacaucgucg acgaagucgc auaccacgaa aaguaccga caaucuacca ccugagaaag 420
 aagcuggucg acagcacaga caaggcagac cugagacuga ucuaccuggc acuggcacac 480
 augaucaagu ucagaggaca cuuccugauc gaaggagacc ugaaccgga caacagcgac 540
 gucgacaagc uguucaucca gcugguccag acauacaacc agcuguucga agaaaaccg 600
 aucaacgcaa gcggagucga cgcaaaggca auccugagcg caagacugag caagagcaga 660
 agacuggaaa accugaucgc acagcugccg ggagaaaaga agaacggacu guucggaac 720
 cugaucgcac ugagccuggg acugacaccg aacuucaaga gcaacuucga ccuggcagaa 780
 gagcgaagc ugcagcugag caaggacaca uacgacgacg accuggacaa ccugcuggca 840
 cagaucggag accaguacgc agaccuguuc cuggcagcaa agaaccugag cgacgcaauc 900
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 cagcagcugc cggaaaagua caaggaauc uucucgacc agagcaagaa cggauacgca 1080
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	gcaauccuga	gaagacagga	agacuucua	ccguuccuga	aggacaacag	agaaaagauc	1320
	gaaaagaucc	ugacauucag	aaucccgua	uacgucggac	cgucggcaag	aggaaacagc	1380
	agauucgcau	ggaugacaag	aaagagcgaa	gaaacaauca	caccguggaa	cuucgaagaa	1440
	gucgucgaca	aggagcaag	cgcacagagc	uucaucgaaa	gaaugacaaa	cuucgacaag	1500
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	uacaacgaac	ugacaaaggu	caaguacguc	acagaaggaa	ugagaaagcc	ggcauuccug	1620
	agcggagaac	agaagaagc	aaucgucgac	cugcuguuca	agacaaacag	aaaggucaca	1680
	gucaagcagc	ugaaggaaga	cuacuucua	aagaucgaau	gcuucgacag	cgucgaaauc	1740
	agcggagucg	aagacagauu	caacgcaagc	cugggaacau	accacgaccu	gcugaagauc	1800
	aucaaggaca	aggacuuccu	ggacaacgaa	gaaaacgaag	acauccugga	agacaucguc	1860
	cugacacuga	cacuguucga	agacagagaa	augaucgaag	aaagacugaa	gacauacgca	1920
	caccuguucg	acgacaaggu	caugaagcag	cugaagagaa	gaagauacac	aggaugggga	1980
	agacugagca	gaaagcugau	caacggaau	agagacaagc	agagcggaaa	gacaauccug	2040
	gacuuccuga	agagcgacgg	auucgcaaac	agaaacuuca	ugcagcugau	ccacgacgac	2100
	agccugacau	ucaaggaaga	cauccagaag	gcacaggua	gaggacaggg	agacagccug	2160
	cacgaacaca	ucgcaaaccu	ggcaggaagc	ccggcaauca	agaagggaau	ccugcagaca	2220
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	gucgaaaaca	cacagcugca	gaacgaaaa	cuguaccugu	acuaccugca	gaacggaaga	2460
	gacauguacg	ucgaccagga	acuggacauc	aacagacuga	gagacuacga	cgucgacgca	2520
	aucgucccgc	agagcuuccu	gaaggacgac	agcaucgaca	acaagguccu	gacaagaagc	2580
	gacaagaaca	gaggaaagag	cgacaacguc	ccgagcgaag	aagucgucaa	gaagaugaag	2640
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	acaaaggcag	agagaggagg	acugagcgaa	cuggacaagg	caggauucau	caagagacag	2760
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	aagcugguca	gagacuucag	aaaggacuuc	caguucuaca	aggucagaga	aaucaacaac	2940
	uaccaccacg	cacacgacgc	auaccugaac	gcagucgucg	gaacagcacu	gaucaagaag	3000
	uaccggaagc	uggaaagcga	auucgucua	ggagacuaca	aggucuaacga	cgucagaaag	3060
	augaucgcaa	agagcgaaca	ggaaaucgga	aaggcaacag	caaaguacuu	cuucacagc	3120
	aacaucauga	acuucuucaa	gacagaaauc	acacuggcaa	acggagaaau	cagaaagaga	3180
	ccgcugaucg	aaacaaacgg	agaaacagga	gaaaucgucu	gggacaaggg	aagagacuuc	3240
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	cagacagggg	gauucagcaa	ggaaagcauc	cugccgaaga	gaaacagcga	caagcugauc	3360
	gcaagaaaga	aggacuggga	cccgaagaag	uacggaggau	ucgacagccc	gacagucgca	3420

uacagcgucc	uggucgucgc	aaaggucgaa	aagggaaaga	gcaagaagcu	gaagagcguc	3480
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cagaagggaa	acgaacuggc	acugccgagc	aaguacguca	acuuccugua	ccuggcaagc	3720
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cagcacaagc	acuaccugga	cgaaucauc	gaacagauca	gcgaaucag	caagagaguc	3840
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ccgaucagag	aacaggcaga	aaacaucauc	caccuguuca	cacugacaaa	ccugggagca	3960
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gaaguccugg	acgcaacacu	gauccaccag	agcaucacag	gacugucga	aacaagauc	4080
gaccugagcc	agcugggagg	agacggaagc	ggaagcccga	agaagaagag	aaaggucgac	4140
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<210> 30
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 <223> 合成的：使用如表3中所列的最小尿苷密码子编码SEQ ID NO: 28的dCas9编码序列(无起始或终止密码子；适于包括在融合蛋白质编码序列中)

[0084]

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	agcaucaaga	agaaccugau	cggagcacug	cuguucgaca	gcggagaaac	agcagaagca	180
	acaagacuga	agagaacagc	aagaagaaga	uacacaagaa	gaaagaacag	aaucugcuac	240
	cugcaggaaa	ucuucagcaa	gaaauggca	aaggucgacg	acagcuucuu	ccacagacug	300
	gaagaaagcu	uccuggucca	agaagacaag	aagcacgaaa	gacaccgcau	cuucggaaac	360
	aucgucgacg	aagucgcaua	ccacgaaaag	uaccgacaaa	ucuaccaccu	gagaaagaag	420
	cuggucgaca	gcacagacaa	ggcagaccug	agacugaucu	accuggcacu	ggcacacaug	480
	aucaaguuca	gaggacacuu	ccugaucgaa	ggagaccuga	acccggacaa	cagcagcugc	540
	gacaagcugu	ucauccagcu	gguccagaca	uacaaccagc	uguucgaaaga	aaaccgcauc	600
	aacgcaagcg	gagucgacgc	aaaggcaauc	cugagcgcaa	gacugagcaa	gagcagaaga	660
	cuggaaaacc	ugaucgcaca	gcugccggga	gaaaagaaga	acggacuguu	cggaaaccug	720
	aucgcacuga	gccugggacu	gacaccgaac	uucaagagca	acuucgaccu	ggcagaagac	780
	gcaaagcugc	agcugagcaa	ggacacauac	gacgacgacc	uggacaaccu	gcuggcacag	840
	aucggagacc	aguacgcaga	ccuguuccug	gcagcaaaga	accugagcga	cgcaauccug	900
	cugagcgaca	uccugagagu	caacacagaa	aucacaaagg	caccgcugag	cgcaagcaug	960
	aucaagagau	acgacgaaca	ccaccaggac	cugacacugc	ugaaggcacu	ggucagacag	1020
	cagcugccgg	aaaaguacaa	gaaaauuc	uucgaccaga	gcaagaacgg	auacgcagga	1080
	uacaucgacg	gaggagcaag	ccaggaagaa	uucuacaagu	ucaucaagcc	gaucuggaa	1140

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cugagcagaa agcugaucaa cggaaucaga gacaagcaga gcggaaagac aauccuggac	2040
uuccugaaga gcgacggauu cgcaaacaga aacuucagc agcugaucca cgacgacagc	2100
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acaggaggau ucagcaagga aagcauccug ccgaagagaa acagcgacaa gcugaucgca	3360

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	cuggaagcaa agggauacaa ggaagucaag aaggaccuga ucaucaagcu gccgaaguac	3600
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	aucagagaac aggcagaaaa caucauccac cuguucacac ugacaaaccu gggagcaccg	3960
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	cugagccagc ugggaggaga cggaagcggga agcccgaaga agaagagaaa ggucgacgga	4140
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	tattttcatt gc	132

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	cccacc	66
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	ttcacattct	130
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<222>	(97)..(100)		
<223>	PS键, 2'-O-Me 核苷酸		
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	cguuaucaac uugaaaaagu ggcaccgagu cggugcuuuu	100	
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<223>	合成的: 具有HSD的5' UTR、对应于SEQ ID NO: 4的ORF、Kozak序列及ALB的3' UTR的Cas9转录物		
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	cgtcggatgg gcagtcatca cagacgaata caaggtccc agcaagaagt tcaagtcct	180	
	gggaaacaca gacagacaca gcatcaagaa gaacctgac ggagcactgc tgttcgacag	240	
	cggagaaaca gcagaagcaa caagactgaa gagaacagca agaagaagat acacaagaag	300	
	aaagaacaga atctgtacc tgcaggaaat cttcagcaac gaaatggcaa aggtcgacga	360	
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<213> 人工序列	
<220>	
<223> 合成的: 具有HSD的5' UTR、对应于SEQ ID NO: 4的ORF及ALB的3' UTR的Cas9转录物	
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 <212> DNA
 <213> 人工序列

[0093]

<220>
 <223> 合成的: 具有19.36% U含量的替代Cas9 ORF

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[0094]

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 <212> DNA
 <213> 人工序列

[0095]

<220>
 <223> 合成的：具有HSD的5' UTR、对应于SEQ ID NO: 45的ORF、Kozak序列及ALB的3' UTR的Cas9转录物

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	ttcctagaag cgaaagggt	3600
	caaagaagta aaaaagacc taataataaa actaccgaaa	3660
	tacagcctat tcgaactaga aaacggcgca aaacgaatgc tagcgagcgc gggggaacta	3720
	caaaaaggga acgaactagc gctaccgagc aaatagcgtaa acttctata cctagcgagc	3780
	cactacgaaa aactaaaagg gagcccgaa gacaacgaac aaaaacaact attcgtagaa	3840
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	ccggcggcgt tcaaaactt cgacacgacg atagaccgaa aacgatacac gagcacgaaa	4080
	gaagtactag acgcgacgct aatacaccaa agcataacgg ggctatacga aacgcgaata	4080

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	<211> 4411	
	<212> DNA	
	<213> 人工序列	
	<220>	
	<223> 合成的: 具有HSD的5' UTR、对应于SEQ ID NO: 54的ORF、Kozak序列及ALB的3' UTR的Cas9转录物	
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	cgtaggggtgg gcgtaataa cggacgaata caaagtaccg agcaaaaaat tcaaagtact	180
	agggaacacg gaccgacaca gcataaaaaa aaacctaata gggcgctac tattegacag	240
	cggggaaacg gcggaagcga cgcgactaaa acgaacggcg cgacgacgat acacgcgacg	300
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	ataccaccta cgaaaaaac tagtagacag cacggacaaa gcggacctac gactaatata	540
	cctagcgeta gcgcacatga taaaattccg agggcacttc ctaatagaag gggacctaaa	600
	cccggacaac agcgacgtag acaactatt catacaacta gtacaaacgt acaaccaact	660
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<210> 56
 <211> 4411
 <212> DNA
 <213> 人工序列

<220>
 <223> 合成的：具有AGG作为供与CleanCap™一起使用之前三个核苷酸、HSD的5' UTR、对应于SEQ ID NO: 4的ORF、Kozak序列及ALB的3' UTR的Cas9转录物

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<210> 57

<211> 4481

<212> DNA

<213> 人工序列

<220>

<223> 合成的：具有来自CMV的5' UTR、对应于SEQ ID NO: 4的ORF、Kozak序列及ALB的3' UTR的Cas9转录物

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<211> 4325

<212> DNA

<213> 人工序列

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<223> 合成的: 具有AGG作为供与CleanCap™一起使用之前三个核苷酸、来自XBG的5' UTR、对应于SEQ ID NO: 4的ORF、Kozak序列及XBG的3' UTR的Cas9转录物	
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<212> DNA	

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<213> 人工序列

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[0134]

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Leu Arg Ala Ala Ala Leu Asp Arg Lys Leu Thr Pro Leu Glu Trp Ser
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Lys Asn Glu Gly Glu Thr Ala Asp Lys Glu Leu Gly Ala Leu Leu Lys
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Gly Val Ala Gly Asn Ala His Ala Leu Gln Thr Gly Asp Phe Arg Thr
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Pro Ala Glu Leu Ala Leu Asn Lys Phe Glu Lys Glu Ser Gly His Ile
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Arg Ala Val Val Gln Gly Lys Asp Glu Glu Asp Trp Gln Leu Ile Asp
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[0138]

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	<212> DNA	
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	<220>	
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<210> 113
 <211> 4179
 <212> DNA
 <213> 人工序列

<220>

<223> 合成的：使用表4的低A密码子，具有两个C端NLS序列及起始及终止密码子的Cas9 ORF

<400> 113

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[0160]

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<210> 114
 <211> 4140
 <212> DNA
 <213> 人工序列

<220>

<223> 合成的：使用表4的低A密码子，具有起始及终止密码子的Cas9切口酶ORF

<400> 114

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[0162]

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<213> 人工序列

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<223> 合成的：使用表4的低A密码子，具有两个C端NLS序列及起始及终止密码子的Cas9切口酶ORF

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<210> 118	
<211> 4107	
<212> DNA	
<213> 人工序列	

	<220>		
	<223>	合成的：使用表4的低A密码子，具有起始及终止密码子且无NLS的dCas9 ORF	
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		cactccatca agaagaacct gatcggcgcc ctgctgttcc actccggcga gaccgccgag	180
		gccaccggcg tgaagcggac cgcccggcgg cggtagaccc ggcggaagaa cgggatctgc	240
		tacctgcagg agatcttctc caacgagatg gccaaaggtg acgactcctt ctccaccgg	300
		ctggaggagt cttcctcgtt ggaggaggac aagaagcacg agcggcaccc catcttcggc	360
		aacatcgtgg acgaggtggc ctaccacgag aagtaccca ccatctacca cctgcggaag	420
		aagctggtgg actccaccga caaggccgac ctgcggctga tctacctggc cctggcccac	480
		atgatcaagt tccggggcca cttcctgatc gagggcgacc tgaaccccca caactccgac	540
		gtggacaagc tgttcatcca gctggtgcag acctacaacc agctgttcga ggagaacccc	600
		atcaacgcct ccggcgtgga cgccaaggcc atcctgtccg cccggtgtc caagtcccgg	660
		cggctggaga acctgatcgc ccagctgccc ggcgagaaga agaacggcct gttcggcaac	720
		ctgatcggcc tgtccctggg cctgaccccc aacttcaagt ccaacttga cctggcccag	780
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		ggctacatcg acggcggcgc ctcccaggag gagttctaca agttcatcaa gcccatcctg	1140
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		aagcagcggc ccttcgacaa cggtccatc ccccaccaga tccacctggg cgagctgcac	1260
		gccatcctgc ggcggcagga ggacttttac ccttctctga aggacaaccg ggagaagate	1320
		gagaagatec tgaccttccg gatccctac tacgtgggcc cctggcccc gggaactcc	1380
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<210> 119

<211> 4179

<212> DNA

<213> 人工序列

<220>

<223> 合成的：使用表4的低A密码子，具有两个C端NLS序列及起始及终止密码子的dCas9 ORF

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	gaggtgctgg acgccacct gateccaccg tccatcaccg gcctgtacga gaccggatc	4080
	gacctgtccc agctgggcgg cgacggctcc gctccccca agaagaagcg gaaggtggac	4140
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<210> 120

<211> 4179

<212> DNA

<213> 人工序列

<220>

<223> 合成的：使用表4的低A/U密码子，具有两个C端NLS序列及起始及终止密码子的Cas9 ORF

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<213> 人工序列

<220>

<223> 合成的：使用表4的低A/U密码子，具有起始及终止密码子且无NLS的Cas9 ORF

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 tacctgcagg aaatcttcag caacgaaatg gcaaaggctc acgacagctt cttccacaga 300
 ctggaagaaa gcttctcgtt cgaagaagac aagaagcac aaagacaccc gatcttcgga 360
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 aagctggtcg acagcacaga caaggcagac ctgagactga tctacctggc actggcacac 480
 atgatcaagt tcagaggaca ctctctgac gaaggagacc tgaaccggga caacagcgcac 540
 gtcgacaagc tgttcatcca gctggtccag acatacaacc agctgttcga agaaaacccg 600
 atcaacgcaa cgggagtcga cggaaaggca atcctgagcg caagactgag caagagcaga 660
 agactggaaa acctgatcgc acagctgccg ggagaaaaga agaacggact gttcggaaac 720
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 ctgctgagcg acatcctgag agtcaacaca gaaatcaca aggcaccgct gagcgaagc 960
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 aacctgccga acgaaaaggt cctgccgaag cacagcctgc tgtacgaata cttcacagtc 1560
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cacctgttcg acgacaaggt catgaagcag ctgaagagaa gaagatacac aggatgggga	1980
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tacagcctgt tcgaactgga aaacggaaga aagagaatgc tggcaagcgc aggagaactg	3660
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cagcacaage actacctgga cgaaatcadc gaacagatca gcgaattcag caagagagtc	3840
atcctggcag acgcaaacct ggacaaggtc ctgagcgcac acaacaagca cagagacaag	3900
ccgatcagag aacagcgaga aaacatcadc cacctgttca cactgacaaa cctgggagca	3960
ccggcagcat tcaagtactt cgacacaaca atcgacagaa agagatacac aagcacaag	4020
gaagtcctgg acgcaaacct gatccaccag agcatcacag gactgtacga aacaagaatc	4080
gacctgagcc agctgggagg agacggagga ggaagcctgg cagcaagag aagcagaaca	4140
acatag	4146

[0194]

<210> 131
 <211> 4146
 <212> DNA
 <213> 人工序列

<220>
 <223> 合成的: 具有NLS2的Cas9的开放阅读框架, 其具有起始及终止密码子

<400> 131
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 cacagcatca agaagaacct gatcggagca ctgctgttcg acagcggaga aacagcagaa 180
 gcaacaagac tgaagagaac agcaagaaga agatacaca gaagaaagaa cagaatctgc 240
 tacctgcagg aaatcttcag caacgaaatg gcaaaggctc acgacagctt cttccacaga 300
 ctggaagaaa gcttctcgtt cgaagaagac aagaagcac aaagacaccc gatcttcgga 360
 aacatcgtcg acgaagtcgc ataccacgaa aagtaccgca caatctacca cctgagaaaag 420
 aagctggtcg acagcacaga caaggcagac ctgagactga tctacctggc actggcacac 480
 atgatcaagt tcagaggaca ctctctgac gaaggagacc tgaaccggga caacagcagc 540
 gtcgacaagc tgttcatcca gctggtccag acatacaacc agctgttcga agaaaacccg 600
 atcaacgcaa cgggagtcga cggaaaggca atcctgagcg caagactgag caagagcaga 660
 agactggaaa acctgatcgc acagctgccg ggagaaaaga agaacggact gttcggaaac 720
 ctgatcgcac tgagctggg actgacaccg aacttcaaga gcaacttcga cctggcagaa 780
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 cagcagctgc cggaaaagta caaggaaatc ttcttcgacc agagcaagaa cggatacga 1080
 ggatacatcg acggaggagc aagccaggaa gaattctaca agttcatcaa gccgatcctg 1140
 gaaaagatgg acggaacaga agaactgctg gtcaagctga acagagaaga cctgctgaga 1200
 aagcagagaa cattcgacaa cggaaagcgc ccgaccaga tccacctggg agaactgcac 1260
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 gaaaagatcc tgacattcag aatcccgtac tacgtcggac cgctggcaag aggaacagc 1380
 agattcgcac ggatgacaag aaagagcga gaaacaatca caccgtggaa cttcgaagaa 1440
 gtcgtcgaca agggagcaag cgcacagagc ttcatgaaa gaatgacaaa cttcgacaag 1500
 aacctgccga acgaaaaggt cctgccgaag cacagcctgc tgtacgaata cttcacagtc 1560
 tacaacgaac tgacaaaggt caagtacgtc acagaaggaa tgagaaagcc ggcattcctg 1620
 agcggagaac agaagaagc aatcgtcgac ctgctgttca agacaaacag aaagtcaca 1680
 gtcaagcagc tgaaggaaga ctacttcaag aagatcgaat gcttcgacag cgtcgaaatc 1740
 agcggagtcg aagacagatt caacgcaagc ctgggaacat accacgacct gctgaagatc 1800
 atcaaggaca aggacttctt ggacaacgaa gaaaacgaag acatcctgga agacatcgtc 1860
 ctgacactga cactgttcga agacagagaa atgatcgaag aaagactgaa gacatacga 1920

cacctgttcg acgacaaggt catgaagcag ctgaagagaa gaagatacac aggatgggga	1980
agactgagca gaaagctgat caacggaatc agagacaagc agagcggaaa gacaatcctg	2040
gacttctctga agagcgacgg attcgcaaac agaaacttca tgcagctgat ccacgacgac	2100
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acaaagtacg acgaaaacga caagctgatc agagaagtca aggtcatcac actgaagagc	2880
aagctggtca gcgacttcag aaaggacttc cagttctaca aggtcagaga aatcaacaac	2940
taccaccacg cacacgacgc atacctgaac gcagtcgtcg gaacagcact gatcaagaag	3000
taccgaagc tggaagcga attcgtctac ggagactaca aggtctacga cgtcagaaaag	3060
atgatgcaa agagcgaaca ggaaatcgga aaggcaacag caaagtactt ctctacagc	3120
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ccgctgatcg aaacaaacgg agaacagga gaaatcgtct gggacaaggg aagagacttc	3240
gcaacagtca gaaaggtcct gagcatgccg caggtcaaca tcgtcaagaa gacagaagtc	3300
cagacaggag gattcagcaa ggaaagcadc ctgccgaaga gaaacagcga caagctgatc	3360
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ttcttgaag caaagggata caaggaagtc aagaaggacc tgatcatcaa gctgccgaag	3600
tacagcctgt tcgaactgga aaacggaaga aagagaatgc tggcaagcgc aggagaactg	3660
cagaagggaa acgaactggc actgccgagc aagtacgtca acttctgta cctggcaagc	3720
cactacgaaa agctgaaggg aagcccggaa gacaacgaac agaagcagct gttcgtcgaa	3780
cagcacaagc actacctgga cgaaatcadc gaacagatca gcgaattcag caagagagtc	3840
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gaagtcctgg acgcaaacct gatccaccag agcatcacag gactgtacga aacaagaatc	4080
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acatag	4146

[0196]

<210> 132
 <211> 4149
 <212> DNA
 <213> 人工序列

<220>
 <223> 合成的: 具有NLS3的Cas9的开放阅读框架, 其具有起始及终止密码子

<400> 132
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 cacagcatca agaagaacct gatcggagca ctgctgttcg acagcggaga aacagcagaa 180
 gcaacaagac tgaagagaac agcaagaaga agatacaca gaagaaagaa cagaatctgc 240
 tacctgcagg aaatcttcag caacgaaatg gcaaaggctc acgacagctt cttccacaga 300
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 aacatcgtcg acgaagtcgc ataccacgaa aagtaccgca caatctacca cctgagaaaag 420
 aagctggtcg acagcacaga caaggcagac ctgagactga tctacctggc actggcacac 480
 atgatcaagt tcagaggaca ctctctgac gaaggagacc tgaaccggga caacagcagc 540
 gtcgacaagc tgttcatcca gctggtccag acatacaacc agctgttcga agaaaaccg 600
 atcaacgcaa cgggagtcga cggaaaggca atcctgagcg caagactgag caagagcaga 660
 agactggaaa acctgatcgc acagctgccg ggagaaaaga agaaccgact gttcggaaac 720
 ctgatcgcac tgagcctggg actgacaccg aacttcaaga gcaacttcga cctggcagaa 780
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 ctgctgagcg acatcctgag agtcaacaca gaaatcaca aggcaccgct gagcgaagc 960
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 cagcagctgc cggaaaagta caaggaaatc ttcttcgacc agagcaagaa cggatacga 1080
 ggatacatcg acggaggagc aagccaggaa gaattctaca agttcatcaa gccgatcctg 1140
 gaaaagatgg acggaacaga agaactgctg gtcaagctga acagagaaga cctgctgaga 1200
 aagcagagaa cattcgacaa cggaaagcgc ccgaccaga tccacctggg agaactgcac 1260
 gcaatcctga gaagacagga agacttctac ccgttctga aggacaacag agaaaagatc 1320
 gaaaagatcc tgacattcag aatcccgtac tacgtcggac cgctggcaag aggaacagc 1380
 agattcgcac ggatgacaag aaagagcga gaaacaatca caccgtggaa cttcgaagaa 1440
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 aacctgccga acgaaaaggt cctgccgaag cacagcctgc tgtacgaata cttcacagtc 1560
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 agcggagaac agaagaagc aatcgtcgac ctgctgttca agacaaacag aaagtcaca 1680
 gtcaagcagc tgaaggaaga ctacttcaag aagatcgaat gcttcgacag cgtcgaaatc 1740
 agcggagtcg aagacagatt caacgcaagc ctgggaacat accacgacct gctgaagatc 1800
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cacctgttcg acgacaaggt catgaagcag ctgaagagaa gaagatacac aggatgggga	1980
agactgagca gaaagctgat caacggaatc agagacaagc agagcggaaa gacaatcctg	2040
gacttctctga agagcgacgg attcgcaaac agaaacttca tgcagctgat ccacgacgac	2100
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gacaagaaca gaggaaagag cgacaacgtc ccgagcgaag aagtcgtcaa gaagatgaag	2640
aaactactgga gacagctgct gaacgcaaaag ctgatcacac agagaaagt cgacaacctg	2700
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gcaagaaaga aggactggga cccgaagaag tacggaggat tcgacagccc gacagtcgca	3420
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gacctgagcc agctgggagg agacggagga ggaagcccgg caccggcaaa gagagaaaga	4140
acaacatag	4149

<210>	133	
<211>	4146	
<212>	DNA	
<213>	人工序列	
<220>		
<223>	合成的: 具有NLS4的Cas9的开放阅读框架, 其具有起始及终止密码子	
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	atcacagacg aatacaaggt cccgagcaag aagttcaagg tcttgggaaa cacagacaga	120
	cacagcatca agaagaacct gatcggagca ctgctgttcg acagcggaga aacagcagaa	180
	gcaacaagac tgaagagaac agcaagaaga agatacaca gaagaaagaa cagaatctgc	240
	tacctgcagg aaatcttcag caacgaaatg gcaaaggctc acgacagctt cttccacaga	300
	ctggaagaaa gcttcttggc cgaagaagac aagaagcac aaagacaccc gatcttcgga	360
	aacatcgtcg acgaagtcgc ataccacgaa aagtaccgca caatctacca cctgagaaaag	420
	aagctggtcg acagcacaga caaggcagac ctgagactga tctacctggc actggcacac	480
	atgatcaagt tcagaggaca ctctctgac gaaggagacc tgaaccggga caacagcagc	540
	gtcgacaagc tgttcatcca gctggtccag acatacaacc agctgttcga agaaaacccg	600
	atcaacgcaa cgggagtcga cggaaaggca atcctgagcg caagactgag caagagcaga	660
	agactggaaa acctgatcgc acagctgccg ggagaaaaga agaaccggact gttcggaaac	720
	ctgatcgcac tgagctggg actgacaccg aacttcaaga gcaacttcga cctggcagaa	780
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	ctgctgagcg acatcctgag agtcaacaca gaaatcaca aggcaccgct gagcgaagc	960
	atgatcaaga gatacagca acaccaccag gacctgacac tgctgaaggc actggtcaga	1020
	cagcagctgc cggaaaagta caaggaaatc ttcttcgacc agagcaagaa cggatacga	1080
	ggatacatcg acggaggagc aagccaggaa gaattctaca agttcatcaa gccgatcctg	1140
	gaaaagatgg acggaacaga agaactgctg gtcaagctga acagagaaga cctgctgaga	1200
	aagcagagaa cattcgacaa cggaaagcgc ccgcaccaga tccacctggg agaactgcac	1260
	gcaatcctga gaagacagga agacttctac ccgttctga aggacaacag agaaaagatc	1320
	gaaaagatcc tgacattcag aatcccgtac tacgtcggac cgctggcaag aggaacacgc	1380
	agattcgcac ggatgacaag aaagagcga gaaacaatca caccgtggaa cttcgaagaa	1440
	gtcgtcgaca agggagcaag cgcacagagc ttcatgaaa gaatgacaaa cttcgacaag	1500
	aacctgccga acgaaaaggt cctgccgaag cacagcctgc tgtacgaata cttcacagtc	1560
	tacaacgaac tgacaaaggt caagtacgtc acagaaggaa tgagaaagcc ggcattcctg	1620
	agcggagaac agaagaagc aatcgtcgac ctgctgttca agacaaacag aaagtcaca	1680
	gtcaagcagc tgaaggaaga ctacttcaag aagatcgaat gcttcgacag cgtcgaaatc	1740
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	atcaaggaca aggacttctt ggacaacgaa gaaaacgaag acatcctgga agacatcgtc	1860
	ctgacactga cactgttcga agacagagaa atgatcgaag aaagactgaa gacatacga	1920

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ccggcagcat tcaagtactt cgacacaaca atcgacagaa agagatacac aagcacaag	4020
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acatag	4146

[0200]

<210>	134	
<211>	4146	
<212>	DNA	
<213>	人工序列	
<220>		
<223>	合成的：具有NLS5的Cas9的开放阅读框架，其具有起始及终止密码子	
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	cacagcatca agaagaacct gatcggagca ctgctgttcg acagcggaga aacagcagaa	180
	gcaacaagac tgaagagaac agcaagaaga agatacaca gaagaaagaa cagaatctgc	240
	tacctgcagg aaatcttcag caacgaaatg gcaaaggctc acgacagctt cttccacaga	300
	ctggaagaaa gcttcttggc cgaagaagac aagaagcac aaagacaccc gatcttcgga	360
	aacatcgtcg acgaagtcgc ataccacgaa aagtaccgca caatctacca cctgagaaaag	420
	aagctggtcg acagcacaga caaggcagac ctgagactga tctacctggc actggcacac	480
	atgatcaagt tcagaggaca ctctctgac gaaggagacc tgaaccggga caacagcagc	540
	gtcgacaagc tgttcatcca gctggtccag acatacaacc agctgttcga agaaaacccg	600
	atcaacgcaa cgggagtcga cggaaaggca atcctgagcg caagactgag caagagcaga	660
	agactggaaa acctgatcgc acagctgccc ggagaaaaga agaaccgact gttcggaaac	720
	ctgatcgcac tgagctggg actgacaccg aacttcaaga gcaacttcga cctggcagaa	780
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	ctgctgagcg acatcctgag agtcaacaca gaaatcaca aggcaccgct gagcgaagc	960
	atgatcaaga gatacagca acaccaccag gacctgacac tgctgaaggc actggtcaga	1020
	cagcagctgc cggaaaagta caaggaaatc ttcttcgacc agagcaagaa cggatacga	1080
	ggatacatcg acggaggagc aagccaggaa gaattctaca agttcatcaa gccgatcctg	1140
	gaaaagatgg acggaacaga agaactgctg gtcaagctga acagagaaga cctgctgaga	1200
	aagcagagaa cattcgacaa cggaaagcgc ccgcaccaga tccacctggg agaactgcac	1260
	gcaatcctga gaagacagga agacttctac ccgttctga aggacaacag agaaaagatc	1320
	gaaaagatcc tgacattcag aatcccgtac tacgtcggac cgctggcaag aggaacagc	1380
	agattcgcac ggatgacaag aaagagcga gaaacaatca caccgtggaa cttcgaagaa	1440
	gtcgtcgaca agggagcaag cgcacagagc ttcatgaaa gaatgacaaa cttcgacaag	1500
	aacctgccga acgaaaaggt cctgccgaag cacagcctgc tgtacgaata cttcacagtc	1560
	tacaacgaac tgacaaaggt caagtacgtc acagaaggaa tgagaaagcc ggcattcctg	1620
	agcggagaac agaagaagc aatcgtcgac ctgctgttca agacaaacag aaagtcaca	1680
	gtcaagcagc tgaaggaaga ctacttcaag aagatcgaat gcttcgacag cgtcgaaatc	1740
	agcggagtcg aagacagatt caacgcaagc ctgggaacat accacgacct gctgaagatc	1800
	atcaaggaca aggacttctt ggacaacgaa gaaaacgaag acatcctgga agacatcgtc	1860
	ctgacactga cactgttcga agacagagaa atgatcgaag aaagactgaa gacatacga	1920

cacctgttcg acgacaaggt catgaagcag ctgaagagaa gaagatacac aggatgggga	1980
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gaagtcctgg acgcaaacct gatccaccag agcatcacag gactgtacga aacaagaatc	4080
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acatag	4146

[0202]

<210> 135
 <211> 4152
 <212> DNA
 <213> 人工序列

<220>
 <223> 合成的: 具有NLS6的Cas9的开放阅读框架, 其具有起始及终止密码子

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 cacagcatca agaagaacct gatcggagca ctgctgttcg acagcggaga aacagcagaa 180
 gcaacaagac tgaagagaac agcaagaaga agatacaca gaagaaagaa cagaatctgc 240
 tacctgcagg aaatcttcag caacgaaatg gcaaaggctc acgacagctt cttccacaga 300
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 aacatcgtcg acgaagtcgc ataccacgaa aagtaccgca caatctacca cctgagaaaag 420
 aagctggctg acagcacaga caaggcagac ctgagactga tctacctggc actggcacac 480
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 agactggaaa acctgatcgc acagctgccg ggagaaaaga agaacggact gttcggaaac 720
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 aacctgccga acgaaaaggt cctgccgaag cacagcctgc tgtacgaata cttcacagtc 1560
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[0204]

<210>	136	
<211>	4152	
<212>	DNA	
<213>	人工序列	
<220>		
<223>	合成的：具有NLS7的Cas9的开放阅读框架，其具有起始及终止密码子	
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	gcaacaagac tgaagagaac agcaagaaga agatacaca gaagaaagaa cagaatctgc	240
	tacctgcagg aaatcttcag caacgaaatg gcaaaggctc acgacagctt cttccacaga	300
	ctggaagaaa gcttcctggt cgaagaagac aagaagcac aaagacacc gatcttcgga	360
	aacatcgtcg acgaagtcgc ataccacgaa aagtaccgca caatctacca cctgagaaaag	420
	aagctggtcg acagcacaga caaggcagac ctgagactga tctacctggc actggcacac	480
	atgatcaagt tcagaggaca cttcctgate gaaggagacc tgaaccggga caacagcagc	540
	gtcgacaagc tgttcatcca gctggtccag acatacaacc agctgttcga agaaaaccg	600
	atcaacgcaa cgggagtcga cggaaaggca atcctgagcg caagactgag caagagcaga	660
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	ctgatcgcac tgagcctggg actgacaccg aacttcaaga gcaacttca cctggcagaa	780
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	ctgctgagcg acatcctgag agtcaacaca gaaatcaca aggcaccgct gagcgaagc	960
	atgatcaaga gatacagca acaccaccag gacctgacac tgctgaaggc actggtcaga	1020
	cagcagctgc cggaaaagta caaggaaatc ttcttcgacc agagcaagaa cggatagca	1080
	ggatacatcg acggaggagc aagccaggaa gaattctaca agttcatcaa gccgatcctg	1140
	gaaaagatgg acggaacaga agaactgctg gtcaagctga acagagaaga cctgctgaga	1200
	aagcagagaa cattcgacaa cggaaagcgc ccgaccaga tccacctggg agaactgcac	1260
	gcaatcctga gaagacagga agacttctac ccgttctga aggacaacag agaaaagatc	1320
	gaaaagatcc tgacattcag aatcccgtac tacgtcggac cgctggcaag aggaacagc	1380
	agattcgcac ggatgacaag aaagagcga gaaacaatca caccgtggaa cttcgaagaa	1440
	gtcgtcgaca agggagcaag cgcacagagc ttcatgaaa gaatgacaaa cttcgacaag	1500
	aacctgccga acgaaaaggt cctgccgaag cacagcctgc tgtacgaata cttcacagtc	1560
	tacaacgaac tgacaaaggt caagtacgtc acagaaggaa tgagaaagcc ggcattcctg	1620
	agcggagaac agaagaagc aatcgtcgac ctgctgttca agacaaacag aaagtcaca	1680
	gtcaagcagc tgaaggaaga ctacttcaag aagatcgaat gcttcgacag cgtcgaaatc	1740
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	atcaaggaca aggacttctt ggacaacgaa gaaaacgaag acatcctgga agacatcgtc	1860
	ctgacactga cactgttcga agacagagaa atgatcgaag aaagactgaa gacatagca	1920

cacctgttcg acgacaaggt catgaagcag ctgaagagaa gaagatacac aggatgggga	1980
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gacttctctga agagcgacgg attcgcaaac agaaacttca tgcagctgat ccacgacgac	2100
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atggcattct ag	4152

[0206]

<210>	137	
<211>	4152	
<212>	DNA	
<213>	人工序列	
<220>		
<223>	合成的: 具有NLS8的Cas9的开放阅读框架, 其具有起始及终止密码子	
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	cacagcatca agaagaacct gatcggagca ctgctgttcg acagcggaga aacagcagaa	180
	gcaacaagac tgaagagaac agcaagaaga agatacaca gaagaaagaa cagaatctgc	240
	tacctgcagg aaatcttcag caacgaaatg gcaaaggctc acgacagctt cttccacaga	300
	ctggaagaaa gcttcttggc cgaagaagac aagaagcac aaagacaccc gatcttcgga	360
	aacatcgtcg acgaagtcgc ataccacgaa aagtaccgca caatctacca cctgagaaaag	420
	aagctggtcg acagcacaga caaggcagac ctgagactga tctacctggc actggcacac	480
	atgatcaagt tcagaggaca cttctgatc gaaggagacc tgaaccggga caacagcagc	540
	gtcgacaagc tgttcatcca gctggtccag acatacaacc agctgttcga agaaaaccg	600
	atcaacgcaa cgggagtcga cggaaaggca atcctgagcg caagactgag caagagcaga	660
	agactggaaa acctgatcgc acagctgccg ggagaaaaga agaaccgact gttcggaaac	720
	ctgatcgcac tgagcctggg actgacaccg aacttcaaga gcaacttcga cctggcagaa	780
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	cagatcggag accagtacgc agacctgttc ctggcagcaa agaacctgag cgacgcaatc	900
	ctgctgagcg acatcctgag agtcaacaca gaaatcaca aggcaccgct gacgcaagc	960
	atgatcaaga gatacagca acaccaccag gacctgacac tgctgaaggc actggtcaga	1020
	cagcagctgc cggaaaagta caaggaaatc ttcttcgacc agagcaagaa cggatacga	1080
	ggatacatcg acggaggagc aagccaggaa gaattctaca agttcatcaa gccgatcctg	1140
	gaaaagatgg acggaacaga agaactgctg gtcaagctga acagagaaga cctgctgaga	1200
	aagcagagaa cattcgacaa cggaaagcgc ccgcaccaga tccacctggg agaactgcac	1260
	gcaatcctga gaagacagga agacttctac ccgttctga aggacaacag agaaaagatc	1320
	gaaaagatcc tgacattcag aatcccgtac tacgtcggac cgctggcaag aggaacacgc	1380
	agattcgcac ggatgacaag aaagagcga gaaacaatca caccgtggaa cttcgaagaa	1440
	gtcgtcgaca agggagcaag cgcacagagc ttcacgaaa gaatgacaaa cttcgacaag	1500
	aacctgccga acgaaaaggt cctgccgaag cacagcctgc tgtacgaata cttcacagtc	1560
	tacaacgaac tgacaaaggt caagtacgtc acagaaggaa tgagaaagcc ggcattcctg	1620
	agcggagaac agaagaaggc aatcgtcgac ctgctgttca agacaaacag aaagtcaca	1680
	gtcaagcagc tgaaggaaga ctacttcaag aagatcgaat gcttcgacag cgtcgaaatc	1740
	agcggagtcg aagacagatt caacgcaagc ctgggaacat accacgacct gctgaagatc	1800
	atcaaggaca aggacttctt ggacaacgaa gaaaacgaag acatcctgga agacatcgtc	1860
	ctgacactga cactgttcga agacagagaa atgatcgaag aaagactgaa gacatacga	1920

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atggcattct ag	4152

[0208]

<210> 138
 <211> 4149
 <212> DNA
 <213> 人工序列

<220>
 <223> 合成的: 具有NLS9的Cas9的开放阅读框架, 其具有起始及终止密码子

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 cacagcatca agaagaacct gatcggagca ctgctgttcg acagcggaga aacagcagaa 180
 gcaacaagac tgaagagaac agcaagaaga agatacaca gaagaaagaa cagaatctgc 240
 tacctgcagg aaatcttcag caacgaaatg gcaaaggctc acgacagctt cttccacaga 300
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 aagctggtcg acagcacaga caaggcagac ctgagactga tctacctggc actggcacac 480
 atgatcaagt tcagaggaca ctctctgatc gaaggagacc tgaaccggga caacagcagc 540
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 aacctgccga acgaaaaggt cctgccgaag cacagcctgc tgtacgaata cttcacagtc 1560
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[0210]

<210>	139	
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<212>	DNA	
<213>	人工序列	
<220>		
<223>	合成的：具有NLS10的Cas9的开放阅读框架，其具有起始及终止密码子	
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	gaaaagatcc tgacattcag aatcccgtac tacgtcggac cgctggcaag aggaacagc	1380
	agattcgcac ggatgacaag aaagagcga gaaacaatca caccgtggaa cttcgaagaa	1440
	gtcgtcgaca agggagcaag cgcacagagc ttcacgaaa gaatgacaaa cttcgacaag	1500
	aacctgccga acgaaaaggt cctgccgaag cacagcctgc tgtacgaata cttcacagtc	1560
	tacaacgaac tgacaaaggt caagtacgtc acagaaggaa tgagaaagcc ggcattcctg	1620
	agcggagaac agaagaagc aatcgtcgc ctgctgttca agacaaacag aaagtcaca	1680
	gtcaagcagc tgaaggaaga ctacttcaag aagatcgaat gcttcgacag cgtcgaaatc	1740
	agcggagtcg aagacagatt caacgcaagc ctgggaacat accacgacct gctgaagatc	1800
	atcaaggaca aggacttctt ggacaacgaa gaaaacgaag acatcctgga agacatcgtc	1860
	ctgacactga cactgttcga agacagagaa atgatcgaag aaagactgaa gacatacga	1920

cacctgttcg acgacaaggt catgaagcag ctgaagagaa gaagatacac aggatgggga	1980
agactgagca gaaagctgat caacggaatc agagacaagc agagcggaaa gacaatcctg	2040
gacttctctga agagcgacgg attcgcaaac agaaacttca tgcagctgat ccacgacgac	2100
agcctgacat tcaaggaaga catccagaag gcacaggtca gcggacaggg agacagcctg	2160
cacgaacaca tcgcaaacct ggcaggaagc ccggcaatca agaaggggat cctgcagaca	2220
gtcaaggtcg tcgacgaact ggtcaaggtc atgggaagac acaagccgga aaacatcgtc	2280
atcgaatgga caagagaaaa ccagacaaca cagaaggac agaagaacag cagagaaaa	2340
atgaagagaa tcgaagaagg aatcaaggaa ctgggaagcc agatcctgaa ggaacaccg	2400
gtcgaataca cacagctgca gaacgaaaag ctgtacctgt actacctgca gaacggaaga	2460
gacatgtiac tcgaccagga actggacatc aacagactga gcgactacga cgtcgaccac	2520
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gacaagaaca gaggaaagag cgacaacgtc ccgagcgaag aagtcgtcaa gaagatgaag	2640
aaactactgga gacagctgct gaacgcaaaag ctgatcacac agagaaagt cacaacctg	2700
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aagctggtca gcgacttcag aaaggactc cagttctaca aggtcagaga aatcaacaac	2940
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taccgaagc tggaagcga attcgtctac ggagactaca aggtctacga cgtcagaaaag	3060
atgatgcaa agagcgaaca ggaaatcgga aaggcaacag caaagtactt ctctacagc	3120
aacatcatga acttcttcaa gacagaaatc acactggcaa acggagaaat cagaaaagaga	3180
ccgctgatcg aaacaaacgg agaaacagga gaaatcgtc gggacaaggg aagagacttc	3240
gcaacagtca gaaaggtcct gagcatgccg caggtcaaca tcgtcaagaa gacagaagtc	3300
cagacaggag gattcagcaa ggaaagcacc ctgccgaaga gaaacagcga caagctgatc	3360
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tacagcctgt tcgaactgga aaacggaaga aagagaatgc tggcaagcgc aggagaactg	3660
cagaagggaa acgaactggc actgccgagc aagtacgtca acttctgta cctggcaagc	3720
cactacgaaa agctgaaggg aagcccggaa gacaacgaac agaagcagct gttcgtcgaa	3780
cagcacaagc actacctgga cgaaatcacc gaacagatca gcgaattcag caagagagtc	3840
atcctggcag acgcaaacct ggacaaggtc ctgagcgcac acaacaagca cagagacaag	3900
ccgatcagag aacagcgaga aaacatcacc cacctgttca cactgacaaa cctgggagca	3960
ccggcagcat tcaagtactt cgacacaaca atcgacagaa agagatacac aagcacaag	4020
gaagtcctgg acgcaaacct gatccaccag agcatcacag gactgtacga aacaagaatc	4080
gacctgagcc agctgggagg agacggagga ggaagcagag cagcaagag aaaggcattc	4140
gcagcatag	4149

[0212]

<210>	140	
<211>	4149	
<212>	DNA	
<213>	人工序列	
<220>		
<223>	合成的: 具有NLS11的Cas9的开放阅读框架, 其具有起始及终止密码子	
<400>	140	
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	atcacagacg aatacaaggt cccgagcaag aagttcaagg tcttgggaaa cacagacaga	120
	cacagcatca agaagaacct gatcggagca ctgctgttcg acagcggaga aacagcagaa	180
	gcaacaagac tgaagagaac agcaagaaga agatacaca gaagaaagaa cagaatctgc	240
	tacctgcagg aaatcttcag caacgaaatg gcaaaggctc acgacagctt cttccacaga	300
	ctggaagaaa gcttcttggc cgaagaagac aagaagcac aaagacaccc gatcttcgga	360
	aacatcgtcg acgaagtcgc ataccacgaa aagtaccgca caatctacca cctgagaaaag	420
	aagctggtcg acagcacaga caaggcagac ctgagactga tctacctggc actggcacac	480
	atgatcaagt tcagaggaca ctctctgac gaaggagacc tgaaccggga caacagcgc	540
	gtcgacaagc tgttcatcca gctgttcag acatacaacc agctgttcga agaaaaccg	600
	atcaacgcaa cgggagtcga cggaaaggca atcctgagcg caagactgag caagagcaga	660
	agactggaaa acctgatcgc acagctgccg ggagaaaaga agaaccgact gttcggaaac	720
	ctgatcgcac tgagctggg actgacaccg aacttcaaga gcaacttca cctggcagaa	780
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	ctgctgagcg acatcctgag agtcaacaca gaaatcaca aggcaccgct gagcgaagc	960
	atgatcaaga gatacagca acaccaccag gacctgacac tgctgaaggc actggtcaga	1020
	cagcagctgc cggaaaagta caaggaaatc ttcttcgacc agagcaagaa cggatacga	1080
	ggatacatcg acggaggagc aagccaggaa gaattctaca agttcatcaa gccgatcctg	1140
	gaaaagatgg acggaacaga agaactgctg gtcaagctga acagagaaga cctgctgaga	1200
	aagcagagaa cattcgacaa cggaaagcgc ccgaccaga tccacctggg agaactgcac	1260
	gcaatcctga gaagacagga agacttctac ccgttctga aggacaacag agaaaagatc	1320
	gaaaagatcc tgacattcag aatcccgtac tacgtcggac cgctggcaag aggaacagc	1380
	agattcgcac ggatgacaag aaagagcga gaaacaatca caccgtggaa cttcgaagaa	1440
	gtcgtcgaca agggagcaag cgcacagagc ttcacgaaa gaatgacaaa cttcgacaag	1500
	aacctgccga acgaaaaggt cctgccgaag cacagcctgc tgtacgaata cttcacagtc	1560
	tacaacgaac tgacaaaggt caagtacgtc acagaaggaa tgagaaagcc ggcattcctg	1620
	agcggagaac agaagaagc aatcgtcgac ctgctgttca agacaaacag aaagtcaca	1680
	gtcaagcagc tgaaggaaga ctacttcaag aagatcgaat gcttcgacag cgtcgaaatc	1740
	agcggagtcg aagacagatt caacgcaagc ctgggaacat accacgacct gctgaagatc	1800
	atcaaggaca aggacttctt ggacaacgaa gaaaacgaag acatcctgga agacatcgtc	1860
	ctgacactga cactgttcga agacagagaa atgatcgaag aaagactgaa gacatacga	1920

cacctgttcg acgacaaggt catgaagcag ctgaagagaa gaagatacac aggatgggga	1980
agactgagca gaaagctgat caacggaatc agagacaagc agagcggaaa gacaatcctg	2040
gacttctctga agagcgacgg attcgcaaac agaaacttca tgcagctgat ccacgacgac	2100
agcctgacat tcaaggaaga catccagaag gcacaggtca gcggacaggg agacagcctg	2160
cacgaacaca tcgcaaacct ggcaggaagc cggcaatca agaagggaat cctgcagaca	2220
gtcaaggtcg tcgacgaact ggtcaaggtc atgggaagac acaagccgga aaacatcgtc	2280
atcgaatgga caagagaaaa ccagacaaca cagaaggac agaagaacag cagagaaaa	2340
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gtcgaataca cacagctgca gaacgaaaag ctgtacctgt actacctgca gaacggaaga	2460
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gacaagaaca gaggaaagag cgacaacgtc ccgagcgaag aagtcgtcaa gaagatgaag	2640
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acaaagtacg acgaaaacga caagctgatc agagaagtca aggtcatcac actgaagagc	2880
aagctggtca gcgacttcag aaaggacttc cagttctaca aggtcagaga aatcaacaac	2940
taccaccacg cacacgacgc atacctgaac gcagtcgtcg gaacagcact gatcaagaag	3000
taccgaagc tggaagcga attcgtctac ggagactaca aggtctacga cgtcagaaaag	3060
atgatgcaa agagcgaaca ggaaatcgga aaggcaacag caaagtactt ctctacagc	3120
aacatcatga acttcttcaa gacagaaatc acactggcaa acggagaaat cagaaaagaga	3180
ccgctgatcg aaacaaacgg agaacagga gaaatcgtct gggacaaggg aagagacttc	3240
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cagacaggag gattcagcaa ggaaagcctc ctgccgaaga gaaacagcga caagctgatc	3360
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tacagctcc tggtcgtcgc aaaggctgaa aagggaaga gcaagaagct gaagagcgtc	3480
aaggaaactc tgggaatcac aatcatggaa agaagcagct tcgaaaagaa cccgatcgac	3540
ttcttgaag caaagggata caaggaagtc aagaaggacc tgatcatcaa gctgccgaag	3600
tacagcctgt tcgaactgga aaacggaaga aagagaatgc tggcaagcgc aggagaactg	3660
cagaagggaa acgaactggc actgccgagc aagtacgtca acttctgta cctggcaagc	3720
cactacgaaa agctgaaggg aagcccggaa gacaacgaac agaagcagct gttcgtcgaa	3780
cagcacaage actacctgga cgaaatcctc gaacagatca gcgaattcag caagagagtc	3840
atcctggcag acgcaaacct ggacaaggtc ctgagcgcac acaacaagca cagagacaag	3900
ccgatcagag aacagcgaga aaacatcctc cacctgttca cactgacaaa cctgggagca	3960
ccggcagcat tcaagtactt cgacacaaca atcgacagaa agagatacac aagcacaag	4020
gaagtcctgg acgcaacact gatccaccag agcatcacag gactgtacga aacaagaatc	4080
gacctgagcc agctgggagg agacggagga ggaagcagag cagcaaagag aaagtacttc	4140
gcagtctag	4149

[0214]

<210> 141
 <211> 4128
 <212> DNA
 <213> 人工序列

<220>
 <223> 合成的：使用通常在人类中高度表达的密码子的Cas9 ORF（无起始或终止密码子；适于包括在融合蛋白质编码序列中）

<400> 141
 cctaagaaaa agcggaaagt cgacgggat aagaagtact caatcgggct ggatatcgga 60
 actaatccg tgggttggge agtgatecag gatgaataca aagtgcgctc caagaagttc 120
 aaggctctgg ggaacaccga tagacacagc atcaagaaaa atctcatcgg agccctgctg 180
 ttgactcgc gcaaacccgc agaagcgacc cggtcaaac gtaccgcgag gcgacgctac 240
 acccgcgga agaategcat ctgctatctc caagagatct tttcgaacga aatggcaaag 300
 gtcgacgaca gcttcttcca ccgectggaa gaatctttcc tgggtggagg gacaagaag 360
 catgaacggc atcctatctt tggaaacatc gtcgacgaag tggegtacca cgaagaagtac 420
 ccgacctct accatctgcg gaagaagtgt gttgactcaa ctgacaagge cgacctcaga 480
 ttgatctact tggcctcgc ccatatgac aaattccgcg gacacttctt gatcgaagge 540
 gatctgaacc ctgataacte cgactgggat aagcttttca ttcaactggt gcagacctac 600
 aaccaactgt tcgaagaaaa cccaatcaat gctagcggcg tcgatccaa gccatcctg 660
 tcgccccgc tgtcgaagtc gcggcgctc gaaaacctga tcgcacagct gccgggagag 720
 aaaaagaacg gacttttcgg caactgacg gctctctcac tgggactcac tccaatttc 780
 aagtccaatt ttgacctggc cgaggacgcg aagctgcaac tctcaaagga cacctacgac 840
 gacgacttgg acaatttget ggcacaaatt ggcgatcagt acgcgatctt gtctcttgcc 900
 gctaagaacc tttcggacgc aatcttctgt tccgatatcc tgcgcgtgaa caccgaaata 960
 accaaagcgc cgettagcgc ctgatgatt aagcggtacg acgagatca ccaggatctc 1020
 acgtctctca aagcgtctgt gagacagcaa ctgcctgaaa agtacaagga gatctctctc 1080
 gaccagtcca agaattggta cgcagggtac atcgatggag gcgctagcca ggaagagttc 1140
 tataagtcca tcaagccaat cctgaaaaag atggacggaa ccgaagaact gctggtcaag 1200
 ctgaacaggg aggatctget ccgaaaacag agaacctttg acaacggate cattccccac 1260
 cagatccatc tgggtgagct gcacccatc ttgcggcgc aggaggactt ttaccattc 1320
 ctcaagaca accgggaaaa gatcagaaaa attctgacgt tccgatccc gtattacgtg 1380
 ggcccactgg cgcgcggcaa ttcgcgttc gcgtggatga ctagaaaate agaggaaacc 1440
 atcactcctt ggaatttcga ggaagtgtg gataaggag ettcggcaca aagcttctc 1500
 gaacgaatga ccaacttga caagaatctc caaaacgaga aggtgtctcc taagcacagc 1560
 ctcttttac aatacttcc tgtctaac gaactgacta aagtgaata cgttactgaa 1620
 ggaatgagga agccggcctt tctgtccgga gaacagaaga aagcaattgt cgatctgctg 1680
 ttcaagacca accgcaaggt gaccgtcaag cagcttaaag aggactactt caagaagatc 1740
 gagtgtttc actcagtga aatcagcggg gtggaggaca gattcaacgc ttcgctggga 1800
 acctatcatg atctctgaa gatcatcaag gacaaggact tcttgacaa cgaggagaac 1860
 gaggacatcc tggaagatat cgtctgacc ttgaccttt tcgaggatcg cgagatgatc 1920

[0215]

gaggagaggc ttaagaccta cgctcatctc ttcgacgata aggtcatgaa acaactcaag	1980
cgccgccggt acactgggtt gggccgcctc tcccgaagc tgatcaacgg tattcggat	2040
aaacagagcg gtaaaactat cctggatttc ctcaaactcg atggcttcgc taatcgtaac	2100
ttcatgcaat tgatccacga cgacagcctg acctttaagg aggacatcca aaaagcacia	2160
gtgtccggac agggagactc actccatgaa cacatcgcga atctggccgg ttcgccggcg	2220
attaagaagg gaattctgca aactgtgaag gtggtcgcag agctgggtgaa ggtcatggga	2280
cggcacaaa cggagaatat cgtgattgaa atggcccag aaaaccagac taccagaag	2340
ggccagaaaa actcccgcga aaggatgaag cggatcgaag aaggaatcaa ggagctgggc	2400
agccagatcc tgaagagca cccggtggaa aacacgcagc tgcagaacga gaagctctac	2460
ctgtactatt tgcaaatgg acgggacatg tacgtggacc aagagctgga catcaatcgg	2520
ttgtctgatt acgacgtgga ccacatcgtt ccacagtctt ttctgaagga tgactcgate	2580
gataacaagg tgttgactcg cagcgacaag aacagaggga agtcagataa tgtgccatcg	2640
gaggaggtcg tgaagaagat gaagaattac tggcgcgcag tcctgaatgc gaagctgatt	2700
accagagaa agtttgacaa tctcactaaa gccgagcgcg gcggactctc agagctggat	2760
aaggctggat tcatcaaacg gcagctggtc gagactcggc agattaccaa gcacgtggcg	2820
cagatcttgg actcccgcac gaacactaaa tacgacgaga acgataagct catccgggaa	2880
gtgaaggtga ttaccctgaa aagcaactt gtgtcggact ttcggaagga ctttcagttt	2940
tacaaagtga gagaaatcaa caactacat cacgcgatg acgcatacct caacgtgtg	3000
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tacaaggtct acgacgtgag gaagatgata gccaaagtcg aacaggaaat cgggaaagca	3120
actgcgaaat acttctttta ctcaaactc atgaactttt tcaagactga aattacgctg	3180
gccaatggag aaatcaggaa gaggccactg atcgaaacta acggagaaac gggcgaaatc	3240
gtgtgggaca agggcaggga cttcgcaact gttcgcaaag tgctctctat gccgcaagtc	3300
aatattgtga agaaaaccga agtgcaaacc ggcggatttt caaaggaatc gatcctccca	3360
aagagaaata gcgacaagct cattgcagc aagaaagact gggaccgaa gaagtacgga	3420
ggattcgatt cgccgactgt cgcatactcc gtctctgtg tggccaaggt ggagaaggga	3480
aagagcaaaa agctcaaatc cgtcaagag ctgctgggga ttaccatcat ggaacgatcc	3540
tcgttcgaga agaaccgat tgatttctc gagcgaagg gttacaagga ggtgaagaag	3600
gatctgatca tcaaaactcc caagtactca ctgttcgaac tggaaaatgg tcggaagcgc	3660
atgctggctt cggccggaga actccaaaaa ggaatgagc tggccttgcc tagcaagtac	3720
gtcaacttcc tctatcttgc ttcgactac gaaaaactca aagggtcacc ggaagataac	3780
gaacagaagc agcttttctg ggagcagcac aagcattatc tggatgaaat catcgaacaa	3840
atctccgagt tttcaaagcg cgtgatctc gccgacgcca acctcgacaa agtctgtcg	3900
gcctacaata agcatagaga taagccgatc agagaacagg ccgagaacat tatccacttg	3960
ttaccctga ctaactggg agccccagcc gccttcaagt acttcgatac tactatcgat	4020
cgcaaaagat acacgtccac caaggaagtt ctggacgcga ccctgateca ccaaagcatc	4080
actggactct acgaaactag gatcgatctg tcgcagctgg gtggcgat	4128

<210> 142
 <211> 4134
 <212> DNA
 <213> 人工序列

<220>

<223> 合成的：使用表4的长半衰期密码子的Cas9 ORF（无起始或终止密码子；适于包括在融合蛋白质编码序列中）

<400> 142

gacaagaagt actctatcgg ttggacatc ggtaccaact ctgtcggttg ggccgtcacc 60
 accgacgaat acaaggtccc atctaagaag ttcaaggtct tgggtaacac cgacagacac 120
 tetatcaaga agaacttgat cgggtccctg ttgttcgact ctggtgaaac cgccgaagcc 180
 accagattga agagaaccgc cagaagaaga tacaccagaa gaaagaacag aatctgctac 240
 ttgcaagaaa tcttctctaa cgaatggcc aaggtcgacg actctttctt ccacagattg 300
 gaagaatctt tcttggtcga agaagacaag aagcacgaaa gacaccaat ctctcgtaac 360
 atcgtcgacg aagtcgceta ccacgaaaag taccacaacca tetaccactt gagaagaag 420
 ttggtcgact ctaccgacaa ggccgacttg agattgatct acttgccctt ggcccacatg 480
 atcaagttca gaggtcactt cttgatcgaa ggtgacttga acccagacaa ctctgacgtc 540
 gacaagttgt tcatccaatt ggtccaaacc tacaaccaat tgttcgaaga aaaccaatc 600
 aacgcctctg gtgtcgacgc caaggccate ttgtctgcca gattgtctaa gacgagaaga 660
 ttgaaaaact tgatcgccca attgccaggt gaaaagaaga acggtttgtt cggttaactg 720
 atcgccttgt ctttgggttt gaccccaaac ttcaagtcta acttcgactt ggccgaagac 780
 gccaaagttg aattgtctaa ggacacctac gacgacgact tggacaactt gttggcccaa 840
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 atcaagagat acgacgaaca ccaccaagac ttgacctgt tgaaggcctt ggteagacaa 1020
 caattgccag aaaagtacaa ggaatcttc ttcgaccaat ctaagaacgg ttacgccggt 1080
 tacatcgacg gtggtgcctc tcaagaagaa ttctacaagt tcatcaagcc aatcttggaa 1140
 aagatggacg gtaccgaaga attgttggtc aagttgaaca gagaagactt gttgagaag 1200
 caaagaacct tgcacaacgg ttctatccca caccaaatcc acttgggtga attgcacgcc 1260
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 ttccaaaacg aaaaggtctt gccaaagcac tcttgttgt acgaatactt caccgtctac 1560
 aacgaattga ccaaggtcaa gtactgcacc gaaggtatga gaaagccagc cttcttgtct 1620
 ggtgaacaaa agaaggecat cgtcgacttg ttgttcaaga ccaacagaaa ggtcaccgtc 1680
 aagcaattga aggaagacta cttcaagaag atcgaatget tgcactctgt cgaaatctct 1740
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 aaggacaagg acttcttggc caacgaagaa aacgaagaca tcttgaaga catcgtcttg 1860
 accttgacct tgttcgaaga cagagaaatg atcgaagaaa gattgaagac ctacgccacc 1920
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<211> 4134
 <212> DNA
 <213> 人工序列
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 <223> 合成的：使用表4的富含U的密码子的Cas9 ORF（无起始或终止密码子；适于包括在融合蛋白质编码序列中）
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 tctattaaaa aaaatttaat tgggtcttta ttatttgatt ctggtgaaac tgctgaagct 180
 actcgtttaa aacgtactgc tcgtcgtcgt tatactcgtc gtaaaaatcg tatttgttat 240
 ttacaagaaa ttttttctaa tgaatggct aaagttagatg attctttttt tcatcgttta 300
 gaagaatcct ttttagttga agaagataaa aaacatgaac gtcacccat ttttgtaat 360
 attgttagatg aagttgctta tcatgaaaa taccctacta tttatcattt acgtaaaaaa 420
 ttagttgatt ctactgataa agctgattta cgtttaattt atttagcttt agctcatatg 480
 attaaatttc gtggtcattt ttaattgaa ggtgatttaa atcctgataa ttctgatggt 540
 gataaattat ttattcaatt agttcaaact tataatcaat ttttgaaga aaatccattt 600
 aatgcttctg gtgttagatc taaagctatt ttatctgctc gtttatctaa atctcgtcgt 660
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 tatattgatg gtggtgcttc tcaagaagaa ttttataaat ttattaaacc tattttagaa 1140
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 caacgtactt ttgataatgg ttctattcct catcaaattc atttaggtga attacatgct 1260
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<212> DNA	

<213> 人工序列

<220>

<223> 合成的：使用表4的低G密码子的Cas9 ORF（无起始或终止密码子；适于包括在融合蛋白质编码序列中）

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tccatcaaaa aaaacctcat eggcgcctc ctcttcgact cggcgaaac cgccgaagcc	180
accgactca aaagaaccgc cagaagaaga tacaccagaa gaaaaaacag aatctgtctac	240
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<220>		
<223>	合成的：使用表4的低C密码子的Cas9 ORF (无起始或终止密码子；适于包括在融合蛋白质编码序列中)	
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	agtattaaga agaatttggat tggagctttg ttgtttgata gtggagagac agctgaggct	180
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	agccagcga agaacaggg cgagaccgca gacaaggagc tggcgccct getgaagggc	480
	gtggccgca acgcccacgc cctgcagacc ggcgacttcc ggacccccgc cgagctggcc	540
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	accttcagcc ggaaggacct gcagcccgag ctgacatcctg ttttcgagaa gcagaaggag	660
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	aagctgaaca acctgcggat cctggagcag ggcagcagc ggccccctgac cgacaccgag	900
	cgggccacc tgatggacga gccctaccgg aagagcaagc tgacctacgc ccaggcccgg	960
	aagctgctgg gcctggagga caccgccttc ttcaagggcc tgcggtacgg caagacaac	1020
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cagatcgacg	agetgggcaa	ggagatccgg	ccctgccggc	tgaagaagcg	gcccccggtg	3240
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<211> 4140

<212> DNA

<213> 人工序列

<220>

<223> 合成的：具有NLS1的Cas9的开放阅读框架(无起始或终止密码子；适于包括在融合蛋白质编码序列中)

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agcatcaaga agaacctgat cggagcactg ctgttcgaca gcggagaaac agcagaagca	180
acaagactga agagaacagc aagaagaaga tacacaagaa gaaagaacag aatctgctac	240
ctgcaggaaa tcttcagcaa cgaaatggca aaggtcgacg acagcttctt ccacagactg	300
gaagaaaagt tcttggtcga agaagacaag aagcacgaaa gacaccgat cttcggaaac	360
atcgtcgacg aagtcgata ccacgaaaag taccgacaa tctaccacct gagaaaagag	420
ctggtcgaca gcacagacaa ggcagacctg agactgatct acctggcact ggcacacatg	480
atcaagtcca gaggacactt cctgatcgaa ggagacctga acccgacaa cagcgcgctc	540
gacaagctgt tcatccagct ggtccagaca tacaaccagc tgttcgaaga aaaccgatc	600
aacgcaagcg ggtcgcagc aaaggcaatc ctgagcgcga gactgagcaa gacgagaaga	660
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cagctgccgg aaaagtacaa gaaatcttc ttcgaccaga gcaagaacgg atacgcagga	1080
tacatcgacg gaggagcaag ccaggaagaa ttctacaagt tcatcaagcc gatcctggaa	1140
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aagcagctga aggaagacta cttcaagaag atcgaatgct tcgacagcgt cgaatcagc	1740
ggagtccaag acagattcaa cgcaagcctg ggaacatacc acgacctgct gaagatcacc	1800
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ctgagcagaa agctgatcaa cggaatcaga gacaagcaga gcggaagac aatcctggac	2040

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gaacacatcg caaacctggc aggaagcccg gcaatcaaga agggaatcct gcagacagtc	2220
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gaaatggcaa gagaaaacca gacaacacag aaggacaga agaacagcag agaaagaatg	2340
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gaaaacacac agctgcagaa cgaaaagctg tacctgtact acctgcagaa cggaagagac	2460
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<211> 4140	
<212> DNA	
<213> 人工序列	

<220>					
<223>	合成的：具有NLS2的Cas9的开放阅读框架(无起始或终止密码子；适于包括在融合蛋白质编码序列中)				
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	agcatcaaga	agaacctgat	cggagcactg	ctgttcgaca	gcggagaaac agcagaagca 180
	acaagactga	agagaacagc	aagaagaaga	tacacaagaa	gaaagaacag aatctgctac 240
	ctgcaggaaa	tcttcagcaa	cgaaatggca	aaggtcgacg	acagcttctt ccacagactg 300
	gaagaaagct	tcctggtcga	agaagacaag	aagcacgaaa	gacacccgat cttcgaaac 360
	atcgtcgacg	aagtcgata	ccacgaaaag	taccgacaa	tctaccacct gagaaagaag 420
	ctggtcgaca	gcacagacaa	ggcagacctg	agactgatct	acctggcact ggcacacatg 480
	atcaagtcca	gaggacactt	cctgatcgaa	ggagacctga	accggacaa cagcgcgctc 540
	gacaagctgt	tcatccagct	ggtccagaca	tacaaccagc	tgttcgaaga aaacccgatc 600
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	ctggaaaacc	tgatcgacaa	gctgccggga	gaaaagaaga	acggactggt cggaaaacctg 720
	atcgactga	gcctgggact	gacaccgaac	ttcaagagca	acttcgacct ggcagaagac 780
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	ctgccgaacg	aaaaggtcct	gccgaagcac	agcctgctgt	acgaatactt cacagtctac 1560
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	ttcctgaaga	gcgacggatt	cgcaaacaga	aacttcatgc	agctgatcca cgacgacagc 2100

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<210> 167	
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<223> 合成的：具有NLS3的Cas9的开放阅读框架(无起始或终止密码子；适于包括在融合蛋白质编码序列中)

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aca	4143
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<211> 4140	
<212> DNA	
<213> 人工序列	
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<223> 合成的：具有NLS4的Cas9的开放阅读框架(无起始或终止密码子；适于包括在融合蛋白质编码序列中)

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<223> 合成的：具有NLS5的Cas9的开放阅读框架(无起始或终止密码子；适于包括在融合蛋白质编码序列中)5	

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agcatcaaga agaacctgat cggagcactg ctgttcgaca gcggagaaac agcagaagca	180
acaagactga agagaacagc aagaagaaga tacacaagaa gaaagaacag aatctgctac	240
ctgcaggaaa tcttcagcaa cgaaatggca aaggctgacg acagcttctt ccacagactg	300
gaagaaagct tcctggtcga agaagacaag aagcacgaaa gacacccgat ctteggaaac	360
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<223> 合成的：具有NLS6的Cas9的开放阅读框架(无起始或终止密码子；适于包括在融合蛋白质编码序列中)	
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gcattc	4146
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ttctgaaga gcgacggatt cgcaaacaga aacttcatgc agctgatcca cgacgacagc	2100
ctgacattca aggaagacat ccagaaggca caggtcagcg gacagggaga cagcctgcac	2160
gaacacatcg caaacctggc aggaagcccg gcaatcaaga agggaatect gcagacagtc	2220
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ccgaagctgg aaagcgaatt cgtctacgga gactacaagg tctacgacgt cagaagatg	3060
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atcagagaac aggcagaaaa catcatccac ctgttcacac tgacaaacct gggagcaccg	3960
gcagcattca agtacttcga cacaacaatc gacagaaaga gatacacaag cacaagga	4020
gtcctggacg caacactgat ccaccagagc atcacaggac tgtacgaaac aagaatcgac	4080
ctgagccagc tgggaggaga cggaggagga agcgcagcag caaagagaaa gtacttcgca	4140
gca	4143
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<213> 人工序列	
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agcatcaaga agaacctgat cggagcactg ctgttcgaca gcggagaaac agcagaagca	180
acaagactga agagaacagc aagaagaaga tacacaagaa gaaagaacag aatctgtctac	240
ctgcaggaaa tcttcagcaa cgaaatggca aaggtcgacg acagettctt ccacagactg	300
gaagaaagct tcttggtcga agaagacaag aagcacgaaa gacacccgat cttcggaaac	360
atctgcgacg aagtcgcata ccacgaaaag tacccgacaa tctaccacct gagaaagaag	420
ctggtcgaca gcacagacaa ggacagactg agactgatct acctggcact ggcacacatg	480
atcaagtcca gaggacactt cctgatcgaa ggagacctga acccggacaa cagcgcagtc	540
gacaagctgt tcatccagct ggtccagaca tacaaccagc tgttcgaaga aaacccgatc	600
aacgaagcg gagtcgacgc aaaggcaatc ctgagcgcga gactgagcaa ggcagaaga	660
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ctgagcgaca tcttgagagt caacacagaa atcacaaagg caccgctgag cgcaagcatg	960
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cagctgccgg aaaagtacaa ggaatcttc ttcgaccaga gcaagaacgg atacgcagga	1080
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caccacgca cgcagcagata cctgaacgca gtcgtcggaa cagcactgat caagaagtac	3000
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gca	4143
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acagacgaat acaaggtccc gagcaagaag ttcaaggtcc tgggaaacac agacagacac	120
agcatcaaga agaacctgat cggagcactg ctgttcgaca gcggagaaac agcagaagca	180
acaagactga agagaacagc aagaagaaga tacacaagaa gaaagaacag aatctgtctac	240
ctgcaggaaa tcttcagcaa cgaaatggca aaggtcgacg acagettctt ccacagactg	300
gaagaaagct tcttggtcga agaagacaag aagcacgaaa gacacccgat cttcggaaac	360
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ctggtcgaca gcacagacaa ggacagctg agactgatct acctggcact ggcacacatg	480
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ctggaaaacc tgatcgaca gctgccggga gaaaagaaga acggactgtt cggaaacctg	720
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cagctgccgg aaaagtacaa ggaatcttc ttcgaccaga gcaagaacgg atacgcagga	1080
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gtc	4143
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	ctgggactga caccgaactt caagagcaac ttcgacctgg cagaagacgc aaagctgcag	840
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	ctgagagtca acacagaaat cacaaggca ccgctgagcg caagcatgat caagagatac	1020
	gacgaacacc accaggacct gacctgctg aaggcactgg tcagacagca gctgccggaa	1080
	aagtacaagg aaatcttctt cgaccagagc aagaacggat acgcaggata catcgcagga	1140
	ggagcaagcc aggaagaatt ctacaagttc atcaagccga tcctggaaaa gatggacgga	1200
	acagaagaac tgctggtcaa gctgaacaga gaagacctgc tgagaaagca gagaacattc	1260
	gacaacggaa gcatcccga ccagatccac ctgggagaac tgcacgcaat cctgagaaga	1320
	caggaagact tctaccggtt cctgaaggac aacagagaaa agatcgaaaa gatcctgaca	1380
	ttcagaatcc cgtactacgt cggaccgctg gcaagaggaa acagcagatt cgcattgatg	1440
	acaagaaaga gcgaagaaac aatcacaccg tggaaacttc aagaagtcgt cgacaaggga	1500
	gcaagcgcac agagcttcat cgaaagaatg acaaaacttc acaagaacct gccgaacgaa	1560

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aaggtcaagt acgtcacaga aggaatgaga aagccggcat tcctgagcgg agaacagaag	1680
aaggcaatcg tcgacctgct gttcaagaca aacagaaaagg tcacagtcaa gcagctgaag	1740
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ttcctggaca acgaagaaaa cgaagacatc ctggaagaca tcgtcctgac actgacactg	1920
ttcgaagaca gagaatgat cgaagaaaga ctgaagacat acgcacacct gttcgacgac	1980
aaggtcatga agcagctgaa gagaagaaga tacacaggat ggggaagact gacgagaaag	2040
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gacgcatacc tgaacgcagt cgtcggaaaca gcaactgatca agaagtacce gaagctggaa	3060
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agcaaggaaa gcatcctgcc gaagagaaac agcgacaagc tgatcgaag aaagaaggac	3420
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ctggcactgc cgagcaagta cgtcaacttc ctgtacctgg caagccacta cgaagactgc	3780

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 aacctggaca aggtcctgag cgcatacaac aagcacagag acaagccgat cagagaacag 3960
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 tctttttctt tttcgttggg gtaaagecaa caccctgtct aaaaaacata aattttctta 4380
 atcattttgc ctctttttct tgtgtctcaa ttaataaaaa atggaagaa cctcgagaaa 4440
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- <211> 1381
- <212> PRT
- <213> 人工序列
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- <223> 合成的：具有NLS1的Cas9的氨基酸序列
- <400> 186

[0305]

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

Met Ile Lys Phe Arg Gly His Phe Leu Ile Glu Gly Asp Leu Asn Pro
 165 170 175

Asp Asn Ser Asp Val Asp Lys Leu Phe Ile Gln Leu Val Gln Thr Tyr
 180 185 190

Asn Gln Leu Phe Glu Glu Asn Pro Ile Asn Ala Ser Gly Val Asp Ala
 195 200 205

Lys Ala Ile Leu Ser Ala Arg Leu Ser Lys Ser Arg Arg Leu Glu Asn
 210 215 220

Leu Ile Ala Gln Leu Pro Gly Glu Lys Lys Asn Gly Leu Phe Gly Asn
 225 230 235 240

Leu Ile Ala Leu Ser Leu Gly Leu Thr Pro Asn Phe Lys Ser Asn Phe
 245 250 255

Asp Leu Ala Glu Asp Ala Lys Leu Gln Leu Ser Lys Asp Thr Tyr Asp
 260 265 270

Asp Asp Leu Asp Asn Leu Leu Ala Gln Ile Gly Asp Gln Tyr Ala Asp
 275 280 285

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

[0306] Ile Leu Arg Val Asn Thr Glu Ile Thr Lys Ala Pro Leu Ser Ala Ser
 305 310 315 320

Met Ile Lys Arg Tyr Asp Glu His His Gln Asp Leu Thr Leu Leu Lys
 325 330 335

Ala Leu Val Arg Gln Gln Leu Pro Glu Lys Tyr Lys Glu Ile Phe Phe
 340 345 350

Asp Gln Ser Lys Asn Gly Tyr Ala Gly Tyr Ile Asp Gly Gly Ala Ser
 355 360 365

Gln Glu Glu Phe Tyr Lys Phe Ile Lys Pro Ile Leu Glu Lys Met Asp
 370 375 380

Gly Thr Glu Glu Leu Leu Val Lys Leu Asn Arg Glu Asp Leu Leu Arg
 385 390 395 400

Lys Gln Arg Thr Phe Asp Asn Gly Ser Ile Pro His Gln Ile His Leu
 405 410 415

Gly Glu Leu His Ala Ile Leu Arg Arg Gln Glu Asp Phe Tyr Pro Phe
 420 425 430

Leu Lys Asp Asn Arg Glu Lys Ile Glu Lys Ile Leu Thr Phe Arg Ile
 435 440 445

Pro Tyr Tyr Val Gly Pro Leu Ala Arg Gly Asn Ser Arg Phe Ala Trp

Arg His Lys Pro Glu Asn Ile Val Ile Glu Met Ala Arg Glu Asn Gln
 755 760 765
 Thr Thr Gln Lys Gly Gln Lys Asn Ser Arg Glu Arg Met Lys Arg Ile
 770 775 780
 Glu Glu Gly Ile Lys Glu Leu Gly Ser Gln Ile Leu Lys Glu His Pro
 785 790 795 800
 Val Glu Asn Thr Gln Leu Gln Asn Glu Lys Leu Tyr Leu Tyr Tyr Leu
 805 810 815
 Gln Asn Gly Arg Asp Met Tyr Val Asp Gln Glu Leu Asp Ile Asn Arg
 820 825 830
 Leu Ser Asp Tyr Asp Val Asp His Ile Val Pro Gln Ser Phe Leu Lys
 835 840 845
 Asp Asp Ser Ile Asp Asn Lys Val Leu Thr Arg Ser Asp Lys Asn Arg
 850 855 860
 Gly Lys Ser Asp Asn Val Pro Ser Glu Glu Val Val Lys Lys Met Lys
 865 870 875 880
 Asn Tyr Trp Arg Gln Leu Leu Asn Ala Lys Leu Ile Thr Gln Arg Lys
 885 890 895
 [0308] Phe Asp Asn Leu Thr Lys Ala Glu Arg Gly Gly Leu Ser Glu Leu Asp
 900 905 910
 Lys Ala Gly Phe Ile Lys Arg Gln Leu Val Glu Thr Arg Gln Ile Thr
 915 920 925
 Lys His Val Ala Gln Ile Leu Asp Ser Arg Met Asn Thr Lys Tyr Asp
 930 935 940
 Glu Asn Asp Lys Leu Ile Arg Glu Val Lys Val Ile Thr Leu Lys Ser
 945 950 955 960
 Lys Leu Val Ser Asp Phe Arg Lys Asp Phe Gln Phe Tyr Lys Val Arg
 965 970 975
 Glu Ile Asn Asn Tyr His His Ala His Asp Ala Tyr Leu Asn Ala Val
 980 985 990
 Val Gly Thr Ala Leu Ile Lys Lys Tyr Pro Lys Leu Glu Ser Glu Phe
 995 1000 1005
 Val Tyr Gly Asp Tyr Lys Val Tyr Asp Val Arg Lys Met Ile Ala
 1010 1015 1020
 Lys Ser Glu Gln Glu Ile Gly Lys Ala Thr Ala Lys Tyr Phe Phe
 1025 1030 1035
 Tyr Ser Asn Ile Met Asn Phe Phe Lys Thr Glu Ile Thr Leu Ala
 1040 1045 1050

	Asn Gly 1055	Glu Ile Arg Lys Arg 1060	Pro Leu Ile Glu Thr 1065	Asn Gly Glu
	Thr Gly 1070	Glu Ile Val Trp Asp 1075	Lys Gly Arg Asp Phe 1080	Ala Thr Val
	Arg Lys 1085	Val Leu Ser Met Pro 1090	Gln Val Asn Ile Val 1095	Lys Lys Thr
	Glu Val 1100	Gln Thr Gly Gly Phe 1105	Ser Lys Glu Ser Ile 1110	Leu Pro Lys
	Arg Asn 1115	Ser Asp Lys Leu Ile 1120	Ala Arg Lys Lys Asp 1125	Trp Asp Pro
	Lys Lys 1130	Tyr Gly Gly Phe Asp 1135	Ser Pro Thr Val Ala 1140	Tyr Ser Val
	Leu Val 1145	Val Ala Lys Val Glu 1150	Lys Gly Lys Ser Lys 1155	Lys Leu Lys
	Ser Val 1160	Lys Glu Leu Leu Gly 1165	Ile Thr Ile Met Glu 1170	Arg Ser Ser
	Phe Glu 1175	Lys Asn Pro Ile Asp 1180	Phe Leu Glu Ala Lys 1185	Gly Tyr Lys
[0309]	Glu Val 1190	Lys Lys Asp Leu Ile 1195	Ile Lys Leu Pro Lys 1200	Tyr Ser Leu
	Phe Glu 1205	Leu Glu Asn Gly Arg 1210	Lys Arg Met Leu Ala 1215	Ser Ala Gly
	Glu Leu 1220	Gln Lys Gly Asn Glu 1225	Leu Ala Leu Pro Ser 1230	Lys Tyr Val
	Asn Phe 1235	Leu Tyr Leu Ala Ser 1240	His Tyr Glu Lys Leu 1245	Lys Gly Ser
	Pro Glu 1250	Asp Asn Glu Gln Lys 1255	Gln Leu Phe Val Glu 1260	Gln His Lys
	His Tyr 1265	Leu Asp Glu Ile Ile 1270	Glu Gln Ile Ser Glu 1275	Phe Ser Lys
	Arg Val 1280	Ile Leu Ala Asp Ala 1285	Asn Leu Asp Lys Val 1290	Leu Ser Ala
	Tyr Asn 1295	Lys His Arg Asp Lys 1300	Pro Ile Arg Glu Gln 1305	Ala Glu Asn
	Ile Ile 1310	His Leu Phe Thr Leu 1315	Thr Asn Leu Gly Ala 1320	Pro Ala Ala
	Phe Lys 1325	Tyr Phe Asp Thr Thr 1330	Ile Asp Arg Lys Arg 1335	Tyr Thr Ser

Thr Lys Glu Val Leu Asp Ala Thr Leu Ile His Gln Ser Ile Thr
 1340 1345 1350
 Gly Leu Tyr Glu Thr Arg Ile Asp Leu Ser Gln Leu Gly Gly Asp
 1355 1360 1365
 Gly Gly Gly Ser Leu Ala Ala Lys Arg Ser Arg Thr Thr
 1370 1375 1380
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 20 25 30
 Lys Val Leu Gly Asn Thr Asp Arg His Ser Ile Lys Lys Asn Leu Ile
 35 40 45
 Gly Ala Leu Leu Phe Asp Ser Gly Glu Thr Ala Glu Ala Thr Arg Leu
 50 55 60
 Lys Arg Thr Ala Arg Arg Arg Tyr Thr Arg Arg Lys Asn Arg Ile Cys
 65 70 75 80
 Tyr Leu Gln Glu Ile Phe Ser Asn Glu Met Ala Lys Val Asp Asp Ser
 85 90 95
 Phe Phe His Arg Leu Glu Glu Ser Phe Leu Val Glu Glu Asp Lys Lys
 100 105 110
 His Glu Arg His Pro Ile Phe Gly Asn Ile Val Asp Glu Val Ala Tyr
 115 120 125
 His Glu Lys Tyr Pro Thr Ile Tyr His Leu Arg Lys Lys Leu Val Asp
 130 135 140
 Ser Thr Asp Lys Ala Asp Leu Arg Leu Ile Tyr Leu Ala Leu Ala His
 145 150 155 160
 Met Ile Lys Phe Arg Gly His Phe Leu Ile Glu Gly Asp Leu Asn Pro
 165 170 175
 Asp Asn Ser Asp Val Asp Lys Leu Phe Ile Gln Leu Val Gln Thr Tyr
 180 185 190
 Asn Gln Leu Phe Glu Glu Asn Pro Ile Asn Ala Ser Gly Val Asp Ala
 195 200 205

[0310]

Lys Ala Ile Leu Ser Ala Arg Leu Ser Lys Ser Arg Arg Leu Glu Asn
 210 215 220
 Leu Ile Ala Gln Leu Pro Gly Glu Lys Lys Asn Gly Leu Phe Gly Asn
 225 230 235 240
 Leu Ile Ala Leu Ser Leu Gly Leu Thr Pro Asn Phe Lys Ser Asn Phe
 245 250 255
 Asp Leu Ala Glu Asp Ala Lys Leu Gln Leu Ser Lys Asp Thr Tyr Asp
 260 265 270
 Asp Asp Leu Asp Asn Leu Leu Ala Gln Ile Gly Asp Gln Tyr Ala Asp
 275 280 285
 Leu Phe Leu Ala Ala Lys Asn Leu Ser Asp Ala Ile Leu Leu Ser Asp
 290 295 300
 Ile Leu Arg Val Asn Thr Glu Ile Thr Lys Ala Pro Leu Ser Ala Ser
 305 310 315 320
 Met Ile Lys Arg Tyr Asp Glu His His Gln Asp Leu Thr Leu Leu Lys
 325 330 335
 Ala Leu Val Arg Gln Gln Leu Pro Glu Lys Tyr Lys Glu Ile Phe Phe
 340 345 350
 [0311] Asp Gln Ser Lys Asn Gly Tyr Ala Gly Tyr Ile Asp Gly Gly Ala Ser
 355 360 365
 Gln Glu Glu Phe Tyr Lys Phe Ile Lys Pro Ile Leu Glu Lys Met Asp
 370 375 380
 Gly Thr Glu Glu Leu Leu Val Lys Leu Asn Arg Glu Asp Leu Leu Arg
 385 390 395 400
 Lys Gln Arg Thr Phe Asp Asn Gly Ser Ile Pro His Gln Ile His Leu
 405 410 415
 Gly Glu Leu His Ala Ile Leu Arg Arg Gln Glu Asp Phe Tyr Pro Phe
 420 425 430
 Leu Lys Asp Asn Arg Glu Lys Ile Glu Lys Ile Leu Thr Phe Arg Ile
 435 440 445
 Pro Tyr Tyr Val Gly Pro Leu Ala Arg Gly Asn Ser Arg Phe Ala Trp
 450 455 460
 Met Thr Arg Lys Ser Glu Glu Thr Ile Thr Pro Trp Asn Phe Glu Glu
 465 470 475 480
 Val Val Asp Lys Gly Ala Ser Ala Gln Ser Phe Ile Glu Arg Met Thr
 485 490 495
 Asn Phe Asp Lys Asn Leu Pro Asn Glu Lys Val Leu Pro Lys His Ser
 500 505 510

Leu Leu Tyr Glu Tyr Phe Thr Val Tyr Asn Glu Leu Thr Lys Val Lys
 515 520 525

Tyr Val Thr Glu Gly Met Arg Lys Pro Ala Phe Leu Ser Gly Glu Gln
 530 535 540

Lys Lys Ala Ile Val Asp Leu Leu Phe Lys Thr Asn Arg Lys Val Thr
 545 550 555 560

Val Lys Gln Leu Lys Glu Asp Tyr Phe Lys Lys Ile Glu Cys Phe Asp
 565 570 575

Ser Val Glu Ile Ser Gly Val Glu Asp Arg Phe Asn Ala Ser Leu Gly
 580 585 590

Thr Tyr His Asp Leu Leu Lys Ile Ile Lys Asp Lys Asp Phe Leu Asp
 595 600 605

Asn Glu Glu Asn Glu Asp Ile Leu Glu Asp Ile Val Leu Thr Leu Thr
 610 615 620

Leu Phe Glu Asp Arg Glu Met Ile Glu Glu Arg Leu Lys Thr Tyr Ala
 625 630 635 640

His Leu Phe Asp Asp Lys Val Met Lys Gln Leu Lys Arg Arg Arg Tyr
 645 650 655

[0312] Thr Gly Trp Gly Arg Leu Ser Arg Lys Leu Ile Asn Gly Ile Arg Asp
 660 665 670

Lys Gln Ser Gly Lys Thr Ile Leu Asp Phe Leu Lys Ser Asp Gly Phe
 675 680 685

Ala Asn Arg Asn Phe Met Gln Leu Ile His Asp Asp Ser Leu Thr Phe
 690 695 700

Lys Glu Asp Ile Gln Lys Ala Gln Val Ser Gly Gln Gly Asp Ser Leu
 705 710 715 720

His Glu His Ile Ala Asn Leu Ala Gly Ser Pro Ala Ile Lys Lys Gly
 725 730 735

Ile Leu Gln Thr Val Lys Val Val Asp Glu Leu Val Lys Val Met Gly
 740 745 750

Arg His Lys Pro Glu Asn Ile Val Ile Glu Met Ala Arg Glu Asn Gln
 755 760 765

Thr Thr Gln Lys Gly Gln Lys Asn Ser Arg Glu Arg Met Lys Arg Ile
 770 775 780

Glu Glu Gly Ile Lys Glu Leu Gly Ser Gln Ile Leu Lys Glu His Pro
 785 790 795 800

Val Glu Asn Thr Gln Leu Gln Asn Glu Lys Leu Tyr Leu Tyr Tyr Leu

	805	810	815
	Gln Asn Gly Arg Asp Met Tyr Val Asp Gln Glu Leu Asp Ile Asn Arg 820	825	830
	Leu Ser Asp Tyr Asp Val Asp His Ile Val Pro Gln Ser Phe Leu Lys 835	840	845
	Asp Asp Ser Ile Asp Asn Lys Val Leu Thr Arg Ser Asp Lys Asn Arg 850	855	860
	Gly Lys Ser Asp Asn Val Pro Ser Glu Glu Val Val Lys Lys Met Lys 865	870	875
	Asn Tyr Trp Arg Gln Leu Leu Asn Ala Lys Leu Ile Thr Gln Arg Lys 885	890	895
	Phe Asp Asn Leu Thr Lys Ala Glu Arg Gly Gly Leu Ser Glu Leu Asp 900	905	910
	Lys Ala Gly Phe Ile Lys Arg Gln Leu Val Glu Thr Arg Gln Ile Thr 915	920	925
	Lys His Val Ala Gln Ile Leu Asp Ser Arg Met Asn Thr Lys Tyr Asp 930	935	940
[0313]	Glu Asn Asp Lys Leu Ile Arg Glu Val Lys Val Ile Thr Leu Lys Ser 945	950	955
	Lys Leu Val Ser Asp Phe Arg Lys Asp Phe Gln Phe Tyr Lys Val Arg 965	970	975
	Glu Ile Asn Asn Tyr His His Ala His Asp Ala Tyr Leu Asn Ala Val 980	985	990
	Val Gly Thr Ala Leu Ile Lys Lys Tyr Pro Lys Leu Glu Ser Glu Phe 995	1000	1005
	Val Tyr Gly Asp Tyr Lys Val Tyr Asp Val Arg Lys Met Ile Ala 1010	1015	1020
	Lys Ser Glu Gln Glu Ile Gly Lys Ala Thr Ala Lys Tyr Phe Phe 1025	1030	1035
	Tyr Ser Asn Ile Met Asn Phe Phe Lys Thr Glu Ile Thr Leu Ala 1040	1045	1050
	Asn Gly Glu Ile Arg Lys Arg Pro Leu Ile Glu Thr Asn Gly Glu 1055	1060	1065
	Thr Gly Glu Ile Val Trp Asp Lys Gly Arg Asp Phe Ala Thr Val 1070	1075	1080
	Arg Lys Val Leu Ser Met Pro Gln Val Asn Ile Val Lys Lys Thr 1085	1090	1095

	Glu Val 1100	Gln Thr Gly Gly	Phe 1105	Ser Lys Glu Ser	Ile 1110	Leu Pro Lys
	Arg Asn 1115	Ser Asp Lys Leu	Ile 1120	Ala Arg Lys Lys	Asp 1125	Trp Asp Pro
	Lys Lys 1130	Tyr Gly Gly Phe	Asp 1135	Ser Pro Thr Val	Ala 1140	Tyr Ser Val
	Leu Val 1145	Val Ala Lys Val	Glu 1150	Lys Gly Lys Ser	Lys 1155	Lys Leu Lys
	Ser Val 1160	Lys Glu Leu Leu	Gly 1165	Ile Thr Ile Met	Glu 1170	Arg Ser Ser
	Phe Glu 1175	Lys Asn Pro Ile	Asp 1180	Phe Leu Glu Ala	Lys 1185	Gly Tyr Lys
	Glu Val 1190	Lys Lys Asp Leu	Ile 1195	Ile Lys Leu Pro	Lys 1200	Tyr Ser Leu
	Phe Glu 1205	Leu Glu Asn Gly	Arg 1210	Lys Arg Met Leu	Ala 1215	Ser Ala Gly
	Glu Leu 1220	Gln Lys Gly Asn	Glu 1225	Leu Ala Leu Pro	Ser 1230	Lys Tyr Val
[0314]	Asn Phe 1235	Leu Tyr Leu Ala	Ser 1240	His Tyr Glu Lys	Leu 1245	Lys Gly Ser
	Pro Glu 1250	Asp Asn Glu Gln	Lys 1255	Gln Leu Phe Val	Glu 1260	Gln His Lys
	His Tyr 1265	Leu Asp Glu Ile	Ile 1270	Glu Gln Ile Ser	Glu 1275	Phe Ser Lys
	Arg Val 1280	Ile Leu Ala Asp	Ala 1285	Asn Leu Asp Lys	Val 1290	Leu Ser Ala
	Tyr Asn 1295	Lys His Arg Asp	Lys 1300	Pro Ile Arg Glu	Gln 1305	Ala Glu Asn
	Ile Ile 1310	His Leu Phe Thr	Leu 1315	Thr Asn Leu Gly	Ala 1320	Pro Ala Ala
	Phe Lys 1325	Tyr Phe Asp Thr	Thr 1330	Ile Asp Arg Lys	Arg 1335	Tyr Thr Ser
	Thr Lys 1340	Glu Val Leu Asp	Ala 1345	Thr Leu Ile His	Gln 1350	Ser Ile Thr
	Gly Leu 1355	Tyr Glu Thr Arg	Ile 1360	Asp Leu Ser Gln	Leu 1365	Gly Gly Asp
	Gly Gly 1370	Gly Ser Gln Ala	Ala 1375	Lys Arg Ser Arg	Thr 1380	Thr

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 20 25 30

 Lys Val Leu Gly Asn Thr Asp Arg His Ser Ile Lys Lys Asn Leu Ile
 35 40 45

 Gly Ala Leu Leu Phe Asp Ser Gly Glu Thr Ala Glu Ala Thr Arg Leu
 50 55 60

 Lys Arg Thr Ala Arg Arg Arg Tyr Thr Arg Arg Lys Asn Arg Ile Cys
 65 70 75 80

 Tyr Leu Gln Glu Ile Phe Ser Asn Glu Met Ala Lys Val Asp Asp Ser
 85 90 95

 Phe Phe His Arg Leu Glu Glu Ser Phe Leu Val Glu Glu Asp Lys Lys
 100 105 110

 His Glu Arg His Pro Ile Phe Gly Asn Ile Val Asp Glu Val Ala Tyr
 115 120 125

 His Glu Lys Tyr Pro Thr Ile Tyr His Leu Arg Lys Lys Leu Val Asp
 130 135 140

 Ser Thr Asp Lys Ala Asp Leu Arg Leu Ile Tyr Leu Ala Leu Ala His
 145 150 155 160

 Met Ile Lys Phe Arg Gly His Phe Leu Ile Glu Gly Asp Leu Asn Pro
 165 170 175

 Asp Asn Ser Asp Val Asp Lys Leu Phe Ile Gln Leu Val Gln Thr Tyr
 180 185 190

 Asn Gln Leu Phe Glu Glu Asn Pro Ile Asn Ala Ser Gly Val Asp Ala
 195 200 205

 Lys Ala Ile Leu Ser Ala Arg Leu Ser Lys Ser Arg Arg Leu Glu Asn
 210 215 220

 Leu Ile Ala Gln Leu Pro Gly Glu Lys Lys Asn Gly Leu Phe Gly Asn
 225 230 235 240

 Leu Ile Ala Leu Ser Leu Gly Leu Thr Pro Asn Phe Lys Ser Asn Phe
 245 250 255

[0315]

Asp Leu Ala Glu Asp Ala Lys Leu Gln Leu Ser Lys Asp Thr Tyr Asp
 260 265 270

Asp Asp Leu Asp Asn Leu Leu Ala Gln Ile Gly Asp Gln Tyr Ala Asp
 275 280 285

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

Ile Leu Arg Val Asn Thr Glu Ile Thr Lys Ala Pro Leu Ser Ala Ser
 305 310 315 320

Met Ile Lys Arg Tyr Asp Glu His His Gln Asp Leu Thr Leu Leu Lys
 325 330 335

Ala Leu Val Arg Gln Gln Leu Pro Glu Lys Tyr Lys Glu Ile Phe Phe
 340 345 350

Asp Gln Ser Lys Asn Gly Tyr Ala Gly Tyr Ile Asp Gly Gly Ala Ser
 355 360 365

Gln Glu Glu Phe Tyr Lys Phe Ile Lys Pro Ile Leu Glu Lys Met Asp
 370 375 380

Gly Thr Glu Glu Leu Leu Val Lys Leu Asn Arg Glu Asp Leu Leu Arg
 385 390 395 400

[0316] Lys Gln Arg Thr Phe Asp Asn Gly Ser Ile Pro His Gln Ile His Leu
 405 410 415

Gly Glu Leu His Ala Ile Leu Arg Arg Gln Glu Asp Phe Tyr Pro Phe
 420 425 430

Leu Lys Asp Asn Arg Glu Lys Ile Glu Lys Ile Leu Thr Phe Arg Ile
 435 440 445

Pro Tyr Tyr Val Gly Pro Leu Ala Arg Gly Asn Ser Arg Phe Ala Trp
 450 455 460

Met Thr Arg Lys Ser Glu Glu Thr Ile Thr Pro Trp Asn Phe Glu Glu
 465 470 475 480

Val Val Asp Lys Gly Ala Ser Ala Gln Ser Phe Ile Glu Arg Met Thr
 485 490 495

Asn Phe Asp Lys Asn Leu Pro Asn Glu Lys Val Leu Pro Lys His Ser
 500 505 510

Leu Leu Tyr Glu Tyr Phe Thr Val Tyr Asn Glu Leu Thr Lys Val Lys
 515 520 525

Tyr Val Thr Glu Gly Met Arg Lys Pro Ala Phe Leu Ser Gly Glu Gln
 530 535 540

Lys Lys Ala Ile Val Asp Leu Leu Phe Lys Thr Asn Arg Lys Val Thr
 545 550 555 560

Val Lys Gln Leu Lys Glu Asp Tyr Phe Lys Lys Ile Glu Cys Phe Asp
 565 570 575

Ser Val Glu Ile Ser Gly Val Glu Asp Arg Phe Asn Ala Ser Leu Gly
 580 585 590

Thr Tyr His Asp Leu Leu Lys Ile Ile Lys Asp Lys Asp Phe Leu Asp
 595 600 605

Asn Glu Glu Asn Glu Asp Ile Leu Glu Asp Ile Val Leu Thr Leu Thr
 610 615 620

Leu Phe Glu Asp Arg Glu Met Ile Glu Glu Arg Leu Lys Thr Tyr Ala
 625 630 635 640

His Leu Phe Asp Asp Lys Val Met Lys Gln Leu Lys Arg Arg Arg Tyr
 645 650 655

Thr Gly Trp Gly Arg Leu Ser Arg Lys Leu Ile Asn Gly Ile Arg Asp
 660 665 670

Lys Gln Ser Gly Lys Thr Ile Leu Asp Phe Leu Lys Ser Asp Gly Phe
 675 680 685

Ala Asn Arg Asn Phe Met Gln Leu Ile His Asp Asp Ser Leu Thr Phe
 690 695 700

[0317] Lys Glu Asp Ile Gln Lys Ala Gln Val Ser Gly Gln Gly Asp Ser Leu
 705 710 715 720

His Glu His Ile Ala Asn Leu Ala Gly Ser Pro Ala Ile Lys Lys Gly
 725 730 735

Ile Leu Gln Thr Val Lys Val Val Asp Glu Leu Val Lys Val Met Gly
 740 745 750

Arg His Lys Pro Glu Asn Ile Val Ile Glu Met Ala Arg Glu Asn Gln
 755 760 765

Thr Thr Gln Lys Gly Gln Lys Asn Ser Arg Glu Arg Met Lys Arg Ile
 770 775 780

Glu Glu Gly Ile Lys Glu Leu Gly Ser Gln Ile Leu Lys Glu His Pro
 785 790 795 800

Val Glu Asn Thr Gln Leu Gln Asn Glu Lys Leu Tyr Leu Tyr Tyr Leu
 805 810 815

Gln Asn Gly Arg Asp Met Tyr Val Asp Gln Glu Leu Asp Ile Asn Arg
 820 825 830

Leu Ser Asp Tyr Asp Val Asp His Ile Val Pro Gln Ser Phe Leu Lys
 835 840 845

Asp Asp Ser Ile Asp Asn Lys Val Leu Thr Arg Ser Asp Lys Asn Arg
 850 855 860

Gly Lys Ser Asp Asn Val Pro Ser Glu Glu Val Val Lys Lys Met Lys
 865 870 875 880
 Asn Tyr Trp Arg Gln Leu Leu Asn Ala Lys Leu Ile Thr Gln Arg Lys
 885 890 895
 Phe Asp Asn Leu Thr Lys Ala Glu Arg Gly Gly Leu Ser Glu Leu Asp
 900 905 910
 Lys Ala Gly Phe Ile Lys Arg Gln Leu Val Glu Thr Arg Gln Ile Thr
 915 920 925
 Lys His Val Ala Gln Ile Leu Asp Ser Arg Met Asn Thr Lys Tyr Asp
 930 935 940
 Glu Asn Asp Lys Leu Ile Arg Glu Val Lys Val Ile Thr Leu Lys Ser
 945 950 955 960
 Lys Leu Val Ser Asp Phe Arg Lys Asp Phe Gln Phe Tyr Lys Val Arg
 965 970 975
 Glu Ile Asn Asn Tyr His His Ala His Asp Ala Tyr Leu Asn Ala Val
 980 985 990
 Val Gly Thr Ala Leu Ile Lys Lys Tyr Pro Lys Leu Glu Ser Glu Phe
 995 1000 1005
 [0318] Val Tyr Gly Asp Tyr Lys Val Tyr Asp Val Arg Lys Met Ile Ala
 1010 1015 1020
 Lys Ser Glu Gln Glu Ile Gly Lys Ala Thr Ala Lys Tyr Phe Phe
 1025 1030 1035
 Tyr Ser Asn Ile Met Asn Phe Phe Lys Thr Glu Ile Thr Leu Ala
 1040 1045 1050
 Asn Gly Glu Ile Arg Lys Arg Pro Leu Ile Glu Thr Asn Gly Glu
 1055 1060 1065
 Thr Gly Glu Ile Val Trp Asp Lys Gly Arg Asp Phe Ala Thr Val
 1070 1075 1080
 Arg Lys Val Leu Ser Met Pro Gln Val Asn Ile Val Lys Lys Thr
 1085 1090 1095
 Glu Val Gln Thr Gly Gly Phe Ser Lys Glu Ser Ile Leu Pro Lys
 1100 1105 1110
 Arg Asn Ser Asp Lys Leu Ile Ala Arg Lys Lys Asp Trp Asp Pro
 1115 1120 1125
 Lys Lys Tyr Gly Gly Phe Asp Ser Pro Thr Val Ala Tyr Ser Val
 1130 1135 1140
 Leu Val Val Ala Lys Val Glu Lys Gly Lys Ser Lys Lys Leu Lys

	1145		1150		1155
	Ser Val 1160	Lys Glu Leu Leu	Gly Ile Thr Ile Met 1165	Glu Arg Ser Ser 1170	
	Phe Glu 1175	Lys Asn Pro Ile	Asp Phe Leu Glu Ala 1180	Lys Gly Tyr Lys 1185	
	Glu Val 1190	Lys Lys Asp Leu	Ile Ile Lys Leu Pro 1195	Lys Tyr Ser Leu 1200	
	Phe Glu 1205	Leu Glu Asn Gly	Arg Lys Arg Met Leu 1210	Ala Ser Ala Gly 1215	
	Glu Leu 1220	Gln Lys Gly Asn	Glu Leu Ala Leu Pro 1225	Ser Lys Tyr Val 1230	
	Asn Phe 1235	Leu Tyr Leu Ala	Ser His Tyr Glu Lys 1240	Leu Lys Gly Ser 1245	
	Pro Glu 1250	Asp Asn Glu Gln	Lys Gln Leu Phe Val 1255	Glu Gln His Lys 1260	
	His Tyr 1265	Leu Asp Glu Ile	Ile Glu Gln Ile Ser 1270	Glu Phe Ser Lys 1275	
[0319]	Arg Val 1280	Ile Leu Ala Asp	Ala Asn Leu Asp Lys 1285	Val Leu Ser Ala 1290	
	Tyr Asn 1295	Lys His Arg Asp	Lys Pro Ile Arg Glu 1300	Gln Ala Glu Asn 1305	
	Ile Ile 1310	His Leu Phe Thr	Leu Thr Asn Leu Gly 1315	Ala Pro Ala Ala 1320	
	Phe Lys 1325	Tyr Phe Asp Thr	Thr Ile Asp Arg Lys 1330	Arg Tyr Thr Ser 1335	
	Thr Lys 1340	Glu Val Leu Asp	Ala Thr Leu Ile His 1345	Gln Ser Ile Thr 1350	
	Gly Leu 1355	Tyr Glu Thr Arg	Ile Asp Leu Ser Gln 1360	Leu Gly Gly Asp 1365	
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Gly Trp Ala Val Ile Thr Asp Glu Tyr Lys Val Pro Ser Lys Lys Phe
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Lys Val Leu Gly Asn Thr Asp Arg His Ser Ile Lys Lys Asn Leu Ile
 35 40 45

Gly Ala Leu Leu Phe Asp Ser Gly Glu Thr Ala Glu Ala Thr Arg Leu
 50 55 60

Lys Arg Thr Ala Arg Arg Arg Tyr Thr Arg Arg Lys Asn Arg Ile Cys
 65 70 75 80

Tyr Leu Gln Glu Ile Phe Ser Asn Glu Met Ala Lys Val Asp Asp Ser
 85 90 95

Phe Phe His Arg Leu Glu Glu Ser Phe Leu Val Glu Glu Asp Lys Lys
 100 105 110

His Glu Arg His Pro Ile Phe Gly Asn Ile Val Asp Glu Val Ala Tyr
 115 120 125

His Glu Lys Tyr Pro Thr Ile Tyr His Leu Arg Lys Lys Leu Val Asp
 130 135 140

Ser Thr Asp Lys Ala Asp Leu Arg Leu Ile Tyr Leu Ala Leu Ala His
 145 150 155 160

[0320] Met Ile Lys Phe Arg Gly His Phe Leu Ile Glu Gly Asp Leu Asn Pro
 165 170 175

Asp Asn Ser Asp Val Asp Lys Leu Phe Ile Gln Leu Val Gln Thr Tyr
 180 185 190

Asn Gln Leu Phe Glu Glu Asn Pro Ile Asn Ala Ser Gly Val Asp Ala
 195 200 205

Lys Ala Ile Leu Ser Ala Arg Leu Ser Lys Ser Arg Arg Leu Glu Asn
 210 215 220

Leu Ile Ala Gln Leu Pro Gly Glu Lys Lys Asn Gly Leu Phe Gly Asn
 225 230 235 240

Leu Ile Ala Leu Ser Leu Gly Leu Thr Pro Asn Phe Lys Ser Asn Phe
 245 250 255

Asp Leu Ala Glu Asp Ala Lys Leu Gln Leu Ser Lys Asp Thr Tyr Asp
 260 265 270

Asp Asp Leu Asp Asn Leu Leu Ala Gln Ile Gly Asp Gln Tyr Ala Asp
 275 280 285

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

Ile Leu Arg Val Asn Thr Glu Ile Thr Lys Ala Pro Leu Ser Ala Ser

	305		310		315		320									
	Met	Ile	Lys	Arg	Tyr	Asp	Glu	His	His	Gln	Asp	Leu	Thr	Leu	Leu	Lys
					325					330					335	
	Ala	Leu	Val	Arg	Gln	Gln	Leu	Pro	Glu	Lys	Tyr	Lys	Glu	Ile	Phe	Phe
				340					345					350		
	Asp	Gln	Ser	Lys	Asn	Gly	Tyr	Ala	Gly	Tyr	Ile	Asp	Gly	Gly	Ala	Ser
			355					360					365			
	Gln	Glu	Glu	Phe	Tyr	Lys	Phe	Ile	Lys	Pro	Ile	Leu	Glu	Lys	Met	Asp
		370					375						380			
	Gly	Thr	Glu	Glu	Leu	Leu	Val	Lys	Leu	Asn	Arg	Glu	Asp	Leu	Leu	Arg
	385					390					395					400
	Lys	Gln	Arg	Thr	Phe	Asp	Asn	Gly	Ser	Ile	Pro	His	Gln	Ile	His	Leu
					405					410					415	
	Gly	Glu	Leu	His	Ala	Ile	Leu	Arg	Arg	Gln	Glu	Asp	Phe	Tyr	Pro	Phe
				420					425					430		
	Leu	Lys	Asp	Asn	Arg	Glu	Lys	Ile	Glu	Lys	Ile	Leu	Thr	Phe	Arg	Ile
			435					440					445			
[0321]	Pro	Tyr	Tyr	Val	Gly	Pro	Leu	Ala	Arg	Gly	Asn	Ser	Arg	Phe	Ala	Trp
		450					455					460				
	Met	Thr	Arg	Lys	Ser	Glu	Glu	Thr	Ile	Thr	Pro	Trp	Asn	Phe	Glu	Glu
	465					470					475					480
	Val	Val	Asp	Lys	Gly	Ala	Ser	Ala	Gln	Ser	Phe	Ile	Glu	Arg	Met	Thr
					485					490					495	
	Asn	Phe	Asp	Lys	Asn	Leu	Pro	Asn	Glu	Lys	Val	Leu	Pro	Lys	His	Ser
				500					505					510		
	Leu	Leu	Tyr	Glu	Tyr	Phe	Thr	Val	Tyr	Asn	Glu	Leu	Thr	Lys	Val	Lys
			515					520					525			
	Tyr	Val	Thr	Glu	Gly	Met	Arg	Lys	Pro	Ala	Phe	Leu	Ser	Gly	Glu	Gln
		530					535					540				
	Lys	Lys	Ala	Ile	Val	Asp	Leu	Leu	Phe	Lys	Thr	Asn	Arg	Lys	Val	Thr
	545					550					555					560
	Val	Lys	Gln	Leu	Lys	Glu	Asp	Tyr	Phe	Lys	Lys	Ile	Glu	Cys	Phe	Asp
					565					570					575	
	Ser	Val	Glu	Ile	Ser	Gly	Val	Glu	Asp	Arg	Phe	Asn	Ala	Ser	Leu	Gly
				580					585					590		
	Thr	Tyr	His	Asp	Leu	Leu	Lys	Ile	Ile	Lys	Asp	Lys	Asp	Phe	Leu	Asp
			595					600					605			

Asn Glu Glu Asn Glu Asp Ile Leu Glu Asp Ile Val Leu Thr Leu Thr
 610 615 620
 Leu Phe Glu Asp Arg Glu Met Ile Glu Glu Arg Leu Lys Thr Tyr Ala
 625 630 635 640
 His Leu Phe Asp Asp Lys Val Met Lys Gln Leu Lys Arg Arg Arg Tyr
 645 650 655
 Thr Gly Trp Gly Arg Leu Ser Arg Lys Leu Ile Asn Gly Ile Arg Asp
 660 665 670
 Lys Gln Ser Gly Lys Thr Ile Leu Asp Phe Leu Lys Ser Asp Gly Phe
 675 680 685
 Ala Asn Arg Asn Phe Met Gln Leu Ile His Asp Asp Ser Leu Thr Phe
 690 695 700
 Lys Glu Asp Ile Gln Lys Ala Gln Val Ser Gly Gln Gly Asp Ser Leu
 705 710 715 720
 His Glu His Ile Ala Asn Leu Ala Gly Ser Pro Ala Ile Lys Lys Gly
 725 730 735
 Ile Leu Gln Thr Val Lys Val Val Asp Glu Leu Val Lys Val Met Gly
 740 745 750
 [0322] Arg His Lys Pro Glu Asn Ile Val Ile Glu Met Ala Arg Glu Asn Gln
 755 760 765
 Thr Thr Gln Lys Gly Gln Lys Asn Ser Arg Glu Arg Met Lys Arg Ile
 770 775 780
 Glu Glu Gly Ile Lys Glu Leu Gly Ser Gln Ile Leu Lys Glu His Pro
 785 790 795 800
 Val Glu Asn Thr Gln Leu Gln Asn Glu Lys Leu Tyr Leu Tyr Tyr Leu
 805 810 815
 Gln Asn Gly Arg Asp Met Tyr Val Asp Gln Glu Leu Asp Ile Asn Arg
 820 825 830
 Leu Ser Asp Tyr Asp Val Asp His Ile Val Pro Gln Ser Phe Leu Lys
 835 840 845
 Asp Asp Ser Ile Asp Asn Lys Val Leu Thr Arg Ser Asp Lys Asn Arg
 850 855 860
 Gly Lys Ser Asp Asn Val Pro Ser Glu Glu Val Val Lys Lys Met Lys
 865 870 875 880
 Asn Tyr Trp Arg Gln Leu Leu Asn Ala Lys Leu Ile Thr Gln Arg Lys
 885 890 895
 Phe Asp Asn Leu Thr Lys Ala Glu Arg Gly Gly Leu Ser Glu Leu Asp
 900 905 910

Lys Ala Gly Phe Ile Lys Arg Gln Leu Val Glu Thr Arg Gln Ile Thr
 915 920 925

Lys His Val Ala Gln Ile Leu Asp Ser Arg Met Asn Thr Lys Tyr Asp
 930 935 940

Glu Asn Asp Lys Leu Ile Arg Glu Val Lys Val Ile Thr Leu Lys Ser
 945 950 955 960

Lys Leu Val Ser Asp Phe Arg Lys Asp Phe Gln Phe Tyr Lys Val Arg
 965 970 975

Glu Ile Asn Asn Tyr His His Ala His Asp Ala Tyr Leu Asn Ala Val
 980 985 990

Val Gly Thr Ala Leu Ile Lys Lys Tyr Pro Lys Leu Glu Ser Glu Phe
 995 1000 1005

Val Tyr Gly Asp Tyr Lys Val Tyr Asp Val Arg Lys Met Ile Ala
 1010 1015 1020

Lys Ser Glu Gln Glu Ile Gly Lys Ala Thr Ala Lys Tyr Phe Phe
 1025 1030 1035

Tyr Ser Asn Ile Met Asn Phe Phe Lys Thr Glu Ile Thr Leu Ala
 1040 1045 1050

[0323] Asn Gly Glu Ile Arg Lys Arg Pro Leu Ile Glu Thr Asn Gly Glu
 1055 1060 1065

Thr Gly Glu Ile Val Trp Asp Lys Gly Arg Asp Phe Ala Thr Val
 1070 1075 1080

Arg Lys Val Leu Ser Met Pro Gln Val Asn Ile Val Lys Lys Thr
 1085 1090 1095

Glu Val Gln Thr Gly Gly Phe Ser Lys Glu Ser Ile Leu Pro Lys
 1100 1105 1110

Arg Asn Ser Asp Lys Leu Ile Ala Arg Lys Lys Asp Trp Asp Pro
 1115 1120 1125

Lys Lys Tyr Gly Gly Phe Asp Ser Pro Thr Val Ala Tyr Ser Val
 1130 1135 1140

Leu Val Val Ala Lys Val Glu Lys Gly Lys Ser Lys Lys Leu Lys
 1145 1150 1155

Ser Val Lys Glu Leu Leu Gly Ile Thr Ile Met Glu Arg Ser Ser
 1160 1165 1170

Phe Glu Lys Asn Pro Ile Asp Phe Leu Glu Ala Lys Gly Tyr Lys
 1175 1180 1185

Glu Val Lys Lys Asp Leu Ile Ile Lys Leu Pro Lys Tyr Ser Leu
 1190 1195 1200

Phe Glu Leu Glu Asn Gly Arg Lys Arg Met Leu Ala Ser Ala Gly
 1205 1210 1215
 Glu Leu Gln Lys Gly Asn Glu Leu Ala Leu Pro Ser Lys Tyr Val
 1220 1225 1230
 Asn Phe Leu Tyr Leu Ala Ser His Tyr Glu Lys Leu Lys Gly Ser
 1235 1240 1245
 Pro Glu Asp Asn Glu Gln Lys Gln Leu Phe Val Glu Gln His Lys
 1250 1255 1260
 His Tyr Leu Asp Glu Ile Ile Glu Gln Ile Ser Glu Phe Ser Lys
 1265 1270 1275
 Arg Val Ile Leu Ala Asp Ala Asn Leu Asp Lys Val Leu Ser Ala
 1280 1285 1290
 Tyr Asn Lys His Arg Asp Lys Pro Ile Arg Glu Gln Ala Glu Asn
 1295 1300 1305
 Ile Ile His Leu Phe Thr Leu Thr Asn Leu Gly Ala Pro Ala Ala
 1310 1315 1320
 Phe Lys Tyr Phe Asp Thr Thr Ile Asp Arg Lys Arg Tyr Thr Ser
 1325 1330 1335
 [0324] Thr Lys Glu Val Leu Asp Ala Thr Leu Ile His Gln Ser Ile Thr
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 Gly Leu Tyr Glu Thr Arg Ile Asp Leu Ser Gln Leu Gly Gly Asp
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 Gly Gly Gly Ser Gln Ala Ala Lys Arg Pro Arg Thr Thr
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 Lys Val Leu Gly Asn Thr Asp Arg His Ser Ile Lys Lys Asn Leu Ile
 35 40 45
 Gly Ala Leu Leu Phe Asp Ser Gly Glu Thr Ala Glu Ala Thr Arg Leu
 50 55 60

Lys Arg Thr Ala Arg Arg Arg Tyr Thr Arg Arg Lys Asn Arg Ile Cys
 65 70 75 80
 Tyr Leu Gln Glu Ile Phe Ser Asn Glu Met Ala Lys Val Asp Asp Ser
 85 90 95
 Phe Phe His Arg Leu Glu Glu Ser Phe Leu Val Glu Glu Asp Lys Lys
 100 105 110
 His Glu Arg His Pro Ile Phe Gly Asn Ile Val Asp Glu Val Ala Tyr
 115 120 125
 His Glu Lys Tyr Pro Thr Ile Tyr His Leu Arg Lys Lys Leu Val Asp
 130 135 140
 Ser Thr Asp Lys Ala Asp Leu Arg Leu Ile Tyr Leu Ala Leu Ala His
 145 150 155 160
 Met Ile Lys Phe Arg Gly His Phe Leu Ile Glu Gly Asp Leu Asn Pro
 165 170 175
 Asp Asn Ser Asp Val Asp Lys Leu Phe Ile Gln Leu Val Gln Thr Tyr
 180 185 190
 Asn Gln Leu Phe Glu Glu Asn Pro Ile Asn Ala Ser Gly Val Asp Ala
 195 200 205
 [0325] Lys Ala Ile Leu Ser Ala Arg Leu Ser Lys Ser Arg Arg Leu Glu Asn
 210 215 220
 Leu Ile Ala Gln Leu Pro Gly Glu Lys Lys Asn Gly Leu Phe Gly Asn
 225 230 235 240
 Leu Ile Ala Leu Ser Leu Gly Leu Thr Pro Asn Phe Lys Ser Asn Phe
 245 250 255
 Asp Leu Ala Glu Asp Ala Lys Leu Gln Leu Ser Lys Asp Thr Tyr Asp
 260 265 270
 Asp Asp Leu Asp Asn Leu Leu Ala Gln Ile Gly Asp Gln Tyr Ala Asp
 275 280 285
 Leu Phe Leu Ala Ala Lys Asn Leu Ser Asp Ala Ile Leu Leu Ser Asp
 290 295 300
 Ile Leu Arg Val Asn Thr Glu Ile Thr Lys Ala Pro Leu Ser Ala Ser
 305 310 315 320
 Met Ile Lys Arg Tyr Asp Glu His His Gln Asp Leu Thr Leu Leu Lys
 325 330 335
 Ala Leu Val Arg Gln Gln Leu Pro Glu Lys Tyr Lys Glu Ile Phe Phe
 340 345 350
 Asp Gln Ser Lys Asn Gly Tyr Ala Gly Tyr Ile Asp Gly Gly Ala Ser
 355 360 365

Gln Glu Glu Phe Tyr Lys Phe Ile Lys Pro Ile Leu Glu Lys Met Asp
 370 375 380

Gly Thr Glu Glu Leu Leu Val Lys Leu Asn Arg Glu Asp Leu Leu Arg
 385 390 395 400

Lys Gln Arg Thr Phe Asp Asn Gly Ser Ile Pro His Gln Ile His Leu
 405 410 415

Gly Glu Leu His Ala Ile Leu Arg Arg Gln Glu Asp Phe Tyr Pro Phe
 420 425 430

Leu Lys Asp Asn Arg Glu Lys Ile Glu Lys Ile Leu Thr Phe Arg Ile
 435 440 445

Pro Tyr Tyr Val Gly Pro Leu Ala Arg Gly Asn Ser Arg Phe Ala Trp
 450 455 460

Met Thr Arg Lys Ser Glu Glu Thr Ile Thr Pro Trp Asn Phe Glu Glu
 465 470 475 480

Val Val Asp Lys Gly Ala Ser Ala Gln Ser Phe Ile Glu Arg Met Thr
 485 490 495

Asn Phe Asp Lys Asn Leu Pro Asn Glu Lys Val Leu Pro Lys His Ser
 500 505 510

[0326] Leu Leu Tyr Glu Tyr Phe Thr Val Tyr Asn Glu Leu Thr Lys Val Lys
 515 520 525

Tyr Val Thr Glu Gly Met Arg Lys Pro Ala Phe Leu Ser Gly Glu Gln
 530 535 540

Lys Lys Ala Ile Val Asp Leu Leu Phe Lys Thr Asn Arg Lys Val Thr
 545 550 555 560

Val Lys Gln Leu Lys Glu Asp Tyr Phe Lys Lys Ile Glu Cys Phe Asp
 565 570 575

Ser Val Glu Ile Ser Gly Val Glu Asp Arg Phe Asn Ala Ser Leu Gly
 580 585 590

Thr Tyr His Asp Leu Leu Lys Ile Ile Lys Asp Lys Asp Phe Leu Asp
 595 600 605

Asn Glu Glu Asn Glu Asp Ile Leu Glu Asp Ile Val Leu Thr Leu Thr
 610 615 620

Leu Phe Glu Asp Arg Glu Met Ile Glu Glu Arg Leu Lys Thr Tyr Ala
 625 630 635 640

His Leu Phe Asp Asp Lys Val Met Lys Gln Leu Lys Arg Arg Arg Tyr
 645 650 655

Thr Gly Trp Gly Arg Leu Ser Arg Lys Leu Ile Asn Gly Ile Arg Asp

	660		665		670
	Lys Gln Ser Gly Lys Thr Ile Leu Asp Phe Leu Lys Ser Asp Gly Phe		680		685
	675				
	Ala Asn Arg Asn Phe Met Gln Leu Ile His Asp Asp Ser Leu Thr Phe		695		700
	690				
	Lys Glu Asp Ile Gln Lys Ala Gln Val Ser Gly Gln Gly Asp Ser Leu		710		720
	705				
	His Glu His Ile Ala Asn Leu Ala Gly Ser Pro Ala Ile Lys Lys Gly		725		735
	Ile Leu Gln Thr Val Lys Val Val Asp Glu Leu Val Lys Val Met Gly		745		750
	Arg His Lys Pro Glu Asn Ile Val Ile Glu Met Ala Arg Glu Asn Gln		760		765
	Thr Thr Gln Lys Gly Gln Lys Asn Ser Arg Glu Arg Met Lys Arg Ile		775		780
	Glu Glu Gly Ile Lys Glu Leu Gly Ser Gln Ile Leu Lys Glu His Pro		790		800
	785				
[0327]	Val Glu Asn Thr Gln Leu Gln Asn Glu Lys Leu Tyr Leu Tyr Tyr Leu		805		815
	Gln Asn Gly Arg Asp Met Tyr Val Asp Gln Glu Leu Asp Ile Asn Arg		820		830
	Leu Ser Asp Tyr Asp Val Asp His Ile Val Pro Gln Ser Phe Leu Lys		840		845
	Asp Asp Ser Ile Asp Asn Lys Val Leu Thr Arg Ser Asp Lys Asn Arg		855		860
	Gly Lys Ser Asp Asn Val Pro Ser Glu Glu Val Val Lys Lys Met Lys		870		880
	865				
	Asn Tyr Trp Arg Gln Leu Leu Asn Ala Lys Leu Ile Thr Gln Arg Lys		885		895
	Phe Asp Asn Leu Thr Lys Ala Glu Arg Gly Gly Leu Ser Glu Leu Asp		900		910
	Lys Ala Gly Phe Ile Lys Arg Gln Leu Val Glu Thr Arg Gln Ile Thr		915		925
	Lys His Val Ala Gln Ile Leu Asp Ser Arg Met Asn Thr Lys Tyr Asp		930		940
	Glu Asn Asp Lys Leu Ile Arg Glu Val Lys Val Ile Thr Leu Lys Ser		950		960
	945				

Lys Leu Val Ser Asp Phe Arg Lys Asp Phe Gln Phe Tyr Lys Val Arg
 965 970 975
 Glu Ile Asn Asn Tyr His His Ala His Asp Ala Tyr Leu Asn Ala Val
 980 985 990
 Val Gly Thr Ala Leu Ile Lys Lys Tyr Pro Lys Leu Glu Ser Glu Phe
 995 1000 1005
 Val Tyr Gly Asp Tyr Lys Val Tyr Asp Val Arg Lys Met Ile Ala
 1010 1015 1020
 Lys Ser Glu Gln Glu Ile Gly Lys Ala Thr Ala Lys Tyr Phe Phe
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 Tyr Ser Asn Ile Met Asn Phe Phe Lys Thr Glu Ile Thr Leu Ala
 1040 1045 1050
 Asn Gly Glu Ile Arg Lys Arg Pro Leu Ile Glu Thr Asn Gly Glu
 1055 1060 1065
 Thr Gly Glu Ile Val Trp Asp Lys Gly Arg Asp Phe Ala Thr Val
 1070 1075 1080
 Arg Lys Val Leu Ser Met Pro Gln Val Asn Ile Val Lys Lys Thr
 1085 1090 1095
 [0328] Glu Val Gln Thr Gly Gly Phe Ser Lys Glu Ser Ile Leu Pro Lys
 1100 1105 1110
 Arg Asn Ser Asp Lys Leu Ile Ala Arg Lys Lys Asp Trp Asp Pro
 1115 1120 1125
 Lys Lys Tyr Gly Gly Phe Asp Ser Pro Thr Val Ala Tyr Ser Val
 1130 1135 1140
 Leu Val Val Ala Lys Val Glu Lys Gly Lys Ser Lys Lys Leu Lys
 1145 1150 1155
 Ser Val Lys Glu Leu Leu Gly Ile Thr Ile Met Glu Arg Ser Ser
 1160 1165 1170
 Phe Glu Lys Asn Pro Ile Asp Phe Leu Glu Ala Lys Gly Tyr Lys
 1175 1180 1185
 Glu Val Lys Lys Asp Leu Ile Ile Lys Leu Pro Lys Tyr Ser Leu
 1190 1195 1200
 Phe Glu Leu Glu Asn Gly Arg Lys Arg Met Leu Ala Ser Ala Gly
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 Glu Leu Gln Lys Gly Asn Glu Leu Ala Leu Pro Ser Lys Tyr Val
 1220 1225 1230
 Asn Phe Leu Tyr Leu Ala Ser His Tyr Glu Lys Leu Lys Gly Ser
 1235 1240 1245

Pro Glu Asp Asn Glu Gln Lys Gln Leu Phe Val Glu Gln His Lys
1250 1255 1260

His Tyr Leu Asp Glu Ile Ile Glu Gln Ile Ser Glu Phe Ser Lys
1265 1270 1275

Arg Val Ile Leu Ala Asp Ala Asn Leu Asp Lys Val Leu Ser Ala
1280 1285 1290

Tyr Asn Lys His Arg Asp Lys Pro Ile Arg Glu Gln Ala Glu Asn
1295 1300 1305

Ile Ile His Leu Phe Thr Leu Thr Asn Leu Gly Ala Pro Ala Ala
1310 1315 1320

Phe Lys Tyr Phe Asp Thr Thr Ile Asp Arg Lys Arg Tyr Thr Ser
1325 1330 1335

Thr Lys Glu Val Leu Asp Ala Thr Leu Ile His Gln Ser Ile Thr
1340 1345 1350

Gly Leu Tyr Glu Thr Arg Ile Asp Leu Ser Gln Leu Gly Gly Asp
1355 1360 1365

Gly Gly Gly Ser Arg Ala Ala Lys Arg Pro Arg Thr Thr
1370 1375 1380

[0329]

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Gly Trp Ala Val Ile Thr Asp Glu Tyr Lys Val Pro Ser Lys Lys Phe
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Lys Val Leu Gly Asn Thr Asp Arg His Ser Ile Lys Lys Asn Leu Ile
35 40 45

Gly Ala Leu Leu Phe Asp Ser Gly Glu Thr Ala Glu Ala Thr Arg Leu
50 55 60

Lys Arg Thr Ala Arg Arg Arg Tyr Thr Arg Arg Lys Asn Arg Ile Cys
65 70 75 80

Tyr Leu Gln Glu Ile Phe Ser Asn Glu Met Ala Lys Val Asp Asp Ser
85 90 95

Phe Phe His Arg Leu Glu Glu Ser Phe Leu Val Glu Glu Asp Lys Lys
100 105 110

His Glu Arg His Pro Ile Phe Gly Asn Ile Val Asp Glu Val Ala Tyr
 115 120 125

His Glu Lys Tyr Pro Thr Ile Tyr His Leu Arg Lys Lys Leu Val Asp
 130 135 140

Ser Thr Asp Lys Ala Asp Leu Arg Leu Ile Tyr Leu Ala Leu Ala His
 145 150 155 160

Met Ile Lys Phe Arg Gly His Phe Leu Ile Glu Gly Asp Leu Asn Pro
 165 170 175

Asp Asn Ser Asp Val Asp Lys Leu Phe Ile Gln Leu Val Gln Thr Tyr
 180 185 190

Asn Gln Leu Phe Glu Glu Asn Pro Ile Asn Ala Ser Gly Val Asp Ala
 195 200 205

Lys Ala Ile Leu Ser Ala Arg Leu Ser Lys Ser Arg Arg Leu Glu Asn
 210 215 220

Leu Ile Ala Gln Leu Pro Gly Glu Lys Lys Asn Gly Leu Phe Gly Asn
 225 230 235 240

Leu Ile Ala Leu Ser Leu Gly Leu Thr Pro Asn Phe Lys Ser Asn Phe
 245 250 255

[0330] Asp Leu Ala Glu Asp Ala Lys Leu Gln Leu Ser Lys Asp Thr Tyr Asp
 260 265 270

Asp Asp Leu Asp Asn Leu Leu Ala Gln Ile Gly Asp Gln Tyr Ala Asp
 275 280 285

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

Ile Leu Arg Val Asn Thr Glu Ile Thr Lys Ala Pro Leu Ser Ala Ser
 305 310 315 320

Met Ile Lys Arg Tyr Asp Glu His His Gln Asp Leu Thr Leu Leu Lys
 325 330 335

Ala Leu Val Arg Gln Gln Leu Pro Glu Lys Tyr Lys Glu Ile Phe Phe
 340 345 350

Asp Gln Ser Lys Asn Gly Tyr Ala Gly Tyr Ile Asp Gly Gly Ala Ser
 355 360 365

Gln Glu Glu Phe Tyr Lys Phe Ile Lys Pro Ile Leu Glu Lys Met Asp
 370 375 380

Gly Thr Glu Glu Leu Leu Val Lys Leu Asn Arg Glu Asp Leu Leu Arg
 385 390 395 400

Lys Gln Arg Thr Phe Asp Asn Gly Ser Ile Pro His Gln Ile His Leu
 405 410 415

Gly Glu Leu His Ala Ile Leu Arg Arg Gln Glu Asp Phe Tyr Pro Phe
 420 425 430

Leu Lys Asp Asn Arg Glu Lys Ile Glu Lys Ile Leu Thr Phe Arg Ile
 435 440 445

Pro Tyr Tyr Val Gly Pro Leu Ala Arg Gly Asn Ser Arg Phe Ala Trp
 450 455 460

Met Thr Arg Lys Ser Glu Glu Thr Ile Thr Pro Trp Asn Phe Glu Glu
 465 470 475 480

Val Val Asp Lys Gly Ala Ser Ala Gln Ser Phe Ile Glu Arg Met Thr
 485 490 495

Asn Phe Asp Lys Asn Leu Pro Asn Glu Lys Val Leu Pro Lys His Ser
 500 505 510

Leu Leu Tyr Glu Tyr Phe Thr Val Tyr Asn Glu Leu Thr Lys Val Lys
 515 520 525

Tyr Val Thr Glu Gly Met Arg Lys Pro Ala Phe Leu Ser Gly Glu Gln
 530 535 540

Lys Lys Ala Ile Val Asp Leu Leu Phe Lys Thr Asn Arg Lys Val Thr
 545 550 555 560

[0331] Val Lys Gln Leu Lys Glu Asp Tyr Phe Lys Lys Ile Glu Cys Phe Asp
 565 570 575

Ser Val Glu Ile Ser Gly Val Glu Asp Arg Phe Asn Ala Ser Leu Gly
 580 585 590

Thr Tyr His Asp Leu Leu Lys Ile Ile Lys Asp Lys Asp Phe Leu Asp
 595 600 605

Asn Glu Glu Asn Glu Asp Ile Leu Glu Asp Ile Val Leu Thr Leu Thr
 610 615 620

Leu Phe Glu Asp Arg Glu Met Ile Glu Glu Arg Leu Lys Thr Tyr Ala
 625 630 635 640

His Leu Phe Asp Asp Lys Val Met Lys Gln Leu Lys Arg Arg Arg Tyr
 645 650 655

Thr Gly Trp Gly Arg Leu Ser Arg Lys Leu Ile Asn Gly Ile Arg Asp
 660 665 670

Lys Gln Ser Gly Lys Thr Ile Leu Asp Phe Leu Lys Ser Asp Gly Phe
 675 680 685

Ala Asn Arg Asn Phe Met Gln Leu Ile His Asp Asp Ser Leu Thr Phe
 690 695 700

Lys Glu Asp Ile Gln Lys Ala Gln Val Ser Gly Gln Gly Asp Ser Leu
 705 710 715 720

His Glu His Ile Ala Asn Leu Ala Gly Ser Pro Ala Ile Lys Lys Gly
 725 730 735
 Ile Leu Gln Thr Val Lys Val Val Asp Glu Leu Val Lys Val Met Gly
 740 745 750
 Arg His Lys Pro Glu Asn Ile Val Ile Glu Met Ala Arg Glu Asn Gln
 755 760 765
 Thr Thr Gln Lys Gly Gln Lys Asn Ser Arg Glu Arg Met Lys Arg Ile
 770 775 780
 Glu Glu Gly Ile Lys Glu Leu Gly Ser Gln Ile Leu Lys Glu His Pro
 785 790 795 800
 Val Glu Asn Thr Gln Leu Gln Asn Glu Lys Leu Tyr Leu Tyr Tyr Leu
 805 810 815
 Gln Asn Gly Arg Asp Met Tyr Val Asp Gln Glu Leu Asp Ile Asn Arg
 820 825 830
 Leu Ser Asp Tyr Asp Val Asp His Ile Val Pro Gln Ser Phe Leu Lys
 835 840 845
 Asp Asp Ser Ile Asp Asn Lys Val Leu Thr Arg Ser Asp Lys Asn Arg
 850 855 860
 [0332] Gly Lys Ser Asp Asn Val Pro Ser Glu Glu Val Val Lys Lys Met Lys
 865 870 875 880
 Asn Tyr Trp Arg Gln Leu Leu Asn Ala Lys Leu Ile Thr Gln Arg Lys
 885 890 895
 Phe Asp Asn Leu Thr Lys Ala Glu Arg Gly Gly Leu Ser Glu Leu Asp
 900 905 910
 Lys Ala Gly Phe Ile Lys Arg Gln Leu Val Glu Thr Arg Gln Ile Thr
 915 920 925
 Lys His Val Ala Gln Ile Leu Asp Ser Arg Met Asn Thr Lys Tyr Asp
 930 935 940
 Glu Asn Asp Lys Leu Ile Arg Glu Val Lys Val Ile Thr Leu Lys Ser
 945 950 955 960
 Lys Leu Val Ser Asp Phe Arg Lys Asp Phe Gln Phe Tyr Lys Val Arg
 965 970 975
 Glu Ile Asn Asn Tyr His His Ala His Asp Ala Tyr Leu Asn Ala Val
 980 985 990
 Val Gly Thr Ala Leu Ile Lys Lys Tyr Pro Lys Leu Glu Ser Glu Phe
 995 1000 1005
 Val Tyr Gly Asp Tyr Lys Val Tyr Asp Val Arg Lys Met Ile Ala

Tyr Asn Lys His Arg Asp Lys Pro Ile Arg Glu Gln Ala Glu Asn
1295 1300 1305

Ile Ile His Leu Phe Thr Leu Thr Asn Leu Gly Ala Pro Ala Ala
1310 1315 1320

Phe Lys Tyr Phe Asp Thr Thr Ile Asp Arg Lys Arg Tyr Thr Ser
1325 1330 1335

Thr Lys Glu Val Leu Asp Ala Thr Leu Ile His Gln Ser Ile Thr
1340 1345 1350

Gly Leu Tyr Glu Thr Arg Ile Asp Leu Ser Gln Leu Gly Gly Asp
1355 1360 1365

Gly Gly Gly Ser Ala Ala Ala Lys Arg Ser Trp Ser Met Ala Ala
1370 1375 1380

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<211> 1383

<212> PRT

<213> 人工序列

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<223> 合成的: 具有NLS7的Cas9的氨基酸序列

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1 5 10 15

[0334]

Gly Trp Ala Val Ile Thr Asp Glu Tyr Lys Val Pro Ser Lys Lys Phe
20 25 30

Lys Val Leu Gly Asn Thr Asp Arg His Ser Ile Lys Lys Asn Leu Ile
35 40 45

Gly Ala Leu Leu Phe Asp Ser Gly Glu Thr Ala Glu Ala Thr Arg Leu
50 55 60

Lys Arg Thr Ala Arg Arg Arg Tyr Thr Arg Arg Lys Asn Arg Ile Cys
65 70 75 80

Tyr Leu Gln Glu Ile Phe Ser Asn Glu Met Ala Lys Val Asp Asp Ser
85 90 95

Phe Phe His Arg Leu Glu Glu Ser Phe Leu Val Glu Glu Asp Lys Lys
100 105 110

His Glu Arg His Pro Ile Phe Gly Asn Ile Val Asp Glu Val Ala Tyr
115 120 125

His Glu Lys Tyr Pro Thr Ile Tyr His Leu Arg Lys Lys Leu Val Asp
130 135 140

Ser Thr Asp Lys Ala Asp Leu Arg Leu Ile Tyr Leu Ala Leu Ala His
145 150 155 160

Met Ile Lys Phe Arg Gly His Phe Leu Ile Glu Gly Asp Leu Asn Pro

	165	170	175
	Asp Asn Ser Asp Val Asp Lys Leu Phe Ile Gln Leu Val Gln Thr Tyr 180	185	190
	Asn Gln Leu Phe Glu Glu Asn Pro Ile Asn Ala Ser Gly Val Asp Ala 195	200	205
	Lys Ala Ile Leu Ser Ala Arg Leu Ser Lys Ser Arg Arg Leu Glu Asn 210	215	220
	Leu Ile Ala Gln Leu Pro Gly Glu Lys Lys Asn Gly Leu Phe Gly Asn 225	230	235
	Leu Ile Ala Leu Ser Leu Gly Leu Thr Pro Asn Phe Lys Ser Asn Phe 245	250	255
	Asp Leu Ala Glu Asp Ala Lys Leu Gln Leu Ser Lys Asp Thr Tyr Asp 260	265	270
	Asp Asp Leu Asp Asn Leu Leu Ala Gln Ile Gly Asp Gln Tyr Ala Asp 275	280	285
	Leu Phe Leu Ala Ala Lys Asn Leu Ser Asp Ala Ile Leu Leu Ser Asp 290	295	300
[0335]	Ile Leu Arg Val Asn Thr Glu Ile Thr Lys Ala Pro Leu Ser Ala Ser 305	310	315
	Met Ile Lys Arg Tyr Asp Glu His His Gln Asp Leu Thr Leu Leu Lys 325	330	335
	Ala Leu Val Arg Gln Gln Leu Pro Glu Lys Tyr Lys Glu Ile Phe Phe 340	345	350
	Asp Gln Ser Lys Asn Gly Tyr Ala Gly Tyr Ile Asp Gly Gly Ala Ser 355	360	365
	Gln Glu Glu Phe Tyr Lys Phe Ile Lys Pro Ile Leu Glu Lys Met Asp 370	375	380
	Gly Thr Glu Glu Leu Leu Val Lys Leu Asn Arg Glu Asp Leu Leu Arg 385	390	395
	Lys Gln Arg Thr Phe Asp Asn Gly Ser Ile Pro His Gln Ile His Leu 405	410	415
	Gly Glu Leu His Ala Ile Leu Arg Arg Gln Glu Asp Phe Tyr Pro Phe 420	425	430
	Leu Lys Asp Asn Arg Glu Lys Ile Glu Lys Ile Leu Thr Phe Arg Ile 435	440	445
	Pro Tyr Tyr Val Gly Pro Leu Ala Arg Gly Asn Ser Arg Phe Ala Trp 450	455	460

Met Thr Arg Lys Ser Glu Glu Thr Ile Thr Pro Trp Asn Phe Glu Glu
465 470 475 480

Val Val Asp Lys Gly Ala Ser Ala Gln Ser Phe Ile Glu Arg Met Thr
485 490 495

Asn Phe Asp Lys Asn Leu Pro Asn Glu Lys Val Leu Pro Lys His Ser
500 505 510

Leu Leu Tyr Glu Tyr Phe Thr Val Tyr Asn Glu Leu Thr Lys Val Lys
515 520 525

Tyr Val Thr Glu Gly Met Arg Lys Pro Ala Phe Leu Ser Gly Glu Gln
530 535 540

Lys Lys Ala Ile Val Asp Leu Leu Phe Lys Thr Asn Arg Lys Val Thr
545 550 555 560

Val Lys Gln Leu Lys Glu Asp Tyr Phe Lys Lys Ile Glu Cys Phe Asp
565 570 575

Ser Val Glu Ile Ser Gly Val Glu Asp Arg Phe Asn Ala Ser Leu Gly
580 585 590

Thr Tyr His Asp Leu Leu Lys Ile Ile Lys Asp Lys Asp Phe Leu Asp
595 600 605

[0336] Asn Glu Glu Asn Glu Asp Ile Leu Glu Asp Ile Val Leu Thr Leu Thr
610 615 620

Leu Phe Glu Asp Arg Glu Met Ile Glu Glu Arg Leu Lys Thr Tyr Ala
625 630 635 640

His Leu Phe Asp Asp Lys Val Met Lys Gln Leu Lys Arg Arg Arg Tyr
645 650 655

Thr Gly Trp Gly Arg Leu Ser Arg Lys Leu Ile Asn Gly Ile Arg Asp
660 665 670

Lys Gln Ser Gly Lys Thr Ile Leu Asp Phe Leu Lys Ser Asp Gly Phe
675 680 685

Ala Asn Arg Asn Phe Met Gln Leu Ile His Asp Asp Ser Leu Thr Phe
690 695 700

Lys Glu Asp Ile Gln Lys Ala Gln Val Ser Gly Gln Gly Asp Ser Leu
705 710 715 720

His Glu His Ile Ala Asn Leu Ala Gly Ser Pro Ala Ile Lys Lys Gly
725 730 735

Ile Leu Gln Thr Val Lys Val Val Asp Glu Leu Val Lys Val Met Gly
740 745 750

Arg His Lys Pro Glu Asn Ile Val Ile Glu Met Ala Arg Glu Asn Gln
755 760 765

Thr Thr Gln Lys Gly Gln Lys Asn Ser Arg Glu Arg Met Lys Arg Ile
 770 775 780
 Glu Glu Gly Ile Lys Glu Leu Gly Ser Gln Ile Leu Lys Glu His Pro
 785 790 795 800
 Val Glu Asn Thr Gln Leu Gln Asn Glu Lys Leu Tyr Leu Tyr Tyr Leu
 805 810 815
 Gln Asn Gly Arg Asp Met Tyr Val Asp Gln Glu Leu Asp Ile Asn Arg
 820 825 830
 Leu Ser Asp Tyr Asp Val Asp His Ile Val Pro Gln Ser Phe Leu Lys
 835 840 845
 Asp Asp Ser Ile Asp Asn Lys Val Leu Thr Arg Ser Asp Lys Asn Arg
 850 855 860
 Gly Lys Ser Asp Asn Val Pro Ser Glu Glu Val Val Lys Lys Met Lys
 865 870 875 880
 Asn Tyr Trp Arg Gln Leu Leu Asn Ala Lys Leu Ile Thr Gln Arg Lys
 885 890 895
 Phe Asp Asn Leu Thr Lys Ala Glu Arg Gly Gly Leu Ser Glu Leu Asp
 900 905 910
 [0337] Lys Ala Gly Phe Ile Lys Arg Gln Leu Val Glu Thr Arg Gln Ile Thr
 915 920 925
 Lys His Val Ala Gln Ile Leu Asp Ser Arg Met Asn Thr Lys Tyr Asp
 930 935 940
 Glu Asn Asp Lys Leu Ile Arg Glu Val Lys Val Ile Thr Leu Lys Ser
 945 950 955 960
 Lys Leu Val Ser Asp Phe Arg Lys Asp Phe Gln Phe Tyr Lys Val Arg
 965 970 975
 Glu Ile Asn Asn Tyr His His Ala His Asp Ala Tyr Leu Asn Ala Val
 980 985 990
 Val Gly Thr Ala Leu Ile Lys Lys Tyr Pro Lys Leu Glu Ser Glu Phe
 995 1000 1005
 Val Tyr Gly Asp Tyr Lys Val Tyr Asp Val Arg Lys Met Ile Ala
 1010 1015 1020
 Lys Ser Glu Gln Glu Ile Gly Lys Ala Thr Ala Lys Tyr Phe Phe
 1025 1030 1035
 Tyr Ser Asn Ile Met Asn Phe Phe Lys Thr Glu Ile Thr Leu Ala
 1040 1045 1050
 Asn Gly Glu Ile Arg Lys Arg Pro Leu Ile Glu Thr Asn Gly Glu
 1055 1060 1065

	Thr Gly 1070	Glu Ile Val Trp	Asp 1075	Lys Gly Arg Asp	Phe 1080	Ala Thr Val
	Arg Lys 1085	Val Leu Ser Met	Pro 1090	Gln Val Asn Ile	Val 1095	Lys Lys Thr
	Glu Val 1100	Gln Thr Gly Gly	Phe 1105	Ser Lys Glu Ser	Ile 1110	Leu Pro Lys
	Arg Asn 1115	Ser Asp Lys Leu	Ile 1120	Ala Arg Lys Lys	Asp 1125	Trp Asp Pro
	Lys Lys 1130	Tyr Gly Gly Phe	Asp 1135	Ser Pro Thr Val	Ala 1140	Tyr Ser Val
	Leu Val 1145	Val Ala Lys Val	Glu 1150	Lys Gly Lys Ser	Lys 1155	Lys Leu Lys
	Ser Val 1160	Lys Glu Leu Leu	Gly 1165	Ile Thr Ile Met	Glu 1170	Arg Ser Ser
	Phe Glu 1175	Lys Asn Pro Ile	Asp 1180	Phe Leu Glu Ala	Lys 1185	Gly Tyr Lys
	Glu Val 1190	Lys Lys Asp Leu	Ile 1195	Ile Lys Leu Pro	Lys 1200	Tyr Ser Leu
[0338]	Phe Glu 1205	Leu Glu Asn Gly	Arg 1210	Lys Arg Met Leu	Ala 1215	Ser Ala Gly
	Glu Leu 1220	Gln Lys Gly Asn	Glu 1225	Leu Ala Leu Pro	Ser 1230	Lys Tyr Val
	Asn Phe 1235	Leu Tyr Leu Ala	Ser 1240	His Tyr Glu Lys	Leu 1245	Lys Gly Ser
	Pro Glu 1250	Asp Asn Glu Gln	Lys 1255	Gln Leu Phe Val	Glu 1260	Gln His Lys
	His Tyr 1265	Leu Asp Glu Ile	Ile 1270	Glu Gln Ile Ser	Glu 1275	Phe Ser Lys
	Arg Val 1280	Ile Leu Ala Asp	Ala 1285	Asn Leu Asp Lys	Val 1290	Leu Ser Ala
	Tyr Asn 1295	Lys His Arg Asp	Lys 1300	Pro Ile Arg Glu	Gln 1305	Ala Glu Asn
	Ile Ile 1310	His Leu Phe Thr	Leu 1315	Thr Asn Leu Gly	Ala 1320	Pro Ala Ala
	Phe Lys 1325	Tyr Phe Asp Thr	Thr 1330	Ile Asp Arg Lys	Arg 1335	Tyr Thr Ser
	Thr Lys	Glu Val Leu Asp	Ala	Thr Leu Ile His	Gln	Ser Ile Thr

Leu Ile Ala Gln Leu Pro Gly Glu Lys Lys Asn Gly Leu Phe Gly Asn
 225 230 235 240

Leu Ile Ala Leu Ser Leu Gly Leu Thr Pro Asn Phe Lys Ser Asn Phe
 245 250 255

Asp Leu Ala Glu Asp Ala Lys Leu Gln Leu Ser Lys Asp Thr Tyr Asp
 260 265 270

Asp Asp Leu Asp Asn Leu Leu Ala Gln Ile Gly Asp Gln Tyr Ala Asp
 275 280 285

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

Ile Leu Arg Val Asn Thr Glu Ile Thr Lys Ala Pro Leu Ser Ala Ser
 305 310 315 320

Met Ile Lys Arg Tyr Asp Glu His His Gln Asp Leu Thr Leu Leu Lys
 325 330 335

Ala Leu Val Arg Gln Gln Leu Pro Glu Lys Tyr Lys Glu Ile Phe Phe
 340 345 350

Asp Gln Ser Lys Asn Gly Tyr Ala Gly Tyr Ile Asp Gly Gly Ala Ser
 355 360 365

[0340] Gln Glu Glu Phe Tyr Lys Phe Ile Lys Pro Ile Leu Glu Lys Met Asp
 370 375 380

Gly Thr Glu Glu Leu Leu Val Lys Leu Asn Arg Glu Asp Leu Leu Arg
 385 390 395 400

Lys Gln Arg Thr Phe Asp Asn Gly Ser Ile Pro His Gln Ile His Leu
 405 410 415

Gly Glu Leu His Ala Ile Leu Arg Arg Gln Glu Asp Phe Tyr Pro Phe
 420 425 430

Leu Lys Asp Asn Arg Glu Lys Ile Glu Lys Ile Leu Thr Phe Arg Ile
 435 440 445

Pro Tyr Tyr Val Gly Pro Leu Ala Arg Gly Asn Ser Arg Phe Ala Trp
 450 455 460

Met Thr Arg Lys Ser Glu Glu Thr Ile Thr Pro Trp Asn Phe Glu Glu
 465 470 475 480

Val Val Asp Lys Gly Ala Ser Ala Gln Ser Phe Ile Glu Arg Met Thr
 485 490 495

Asn Phe Asp Lys Asn Leu Pro Asn Glu Lys Val Leu Pro Lys His Ser
 500 505 510

Leu Leu Tyr Glu Tyr Phe Thr Val Tyr Asn Glu Leu Thr Lys Val Lys

Gln Asn Gly Arg Asp Met Tyr Val Asp Gln Glu Leu Asp Ile Asn Arg
 820 825 830

Leu Ser Asp Tyr Asp Val Asp His Ile Val Pro Gln Ser Phe Leu Lys
 835 840 845

Asp Asp Ser Ile Asp Asn Lys Val Leu Thr Arg Ser Asp Lys Asn Arg
 850 855 860

Gly Lys Ser Asp Asn Val Pro Ser Glu Glu Val Val Lys Lys Met Lys
 865 870 875 880

Asn Tyr Trp Arg Gln Leu Leu Asn Ala Lys Leu Ile Thr Gln Arg Lys
 885 890 895

Phe Asp Asn Leu Thr Lys Ala Glu Arg Gly Gly Leu Ser Glu Leu Asp
 900 905 910

Lys Ala Gly Phe Ile Lys Arg Gln Leu Val Glu Thr Arg Gln Ile Thr
 915 920 925

Lys His Val Ala Gln Ile Leu Asp Ser Arg Met Asn Thr Lys Tyr Asp
 930 935 940

Glu Asn Asp Lys Leu Ile Arg Glu Val Lys Val Ile Thr Leu Lys Ser
 945 950 955 960

[0342] Lys Leu Val Ser Asp Phe Arg Lys Asp Phe Gln Phe Tyr Lys Val Arg
 965 970 975

Glu Ile Asn Asn Tyr His His Ala His Asp Ala Tyr Leu Asn Ala Val
 980 985 990

Val Gly Thr Ala Leu Ile Lys Lys Tyr Pro Lys Leu Glu Ser Glu Phe
 995 1000 1005

Val Tyr Gly Asp Tyr Lys Val Tyr Asp Val Arg Lys Met Ile Ala
 1010 1015 1020

Lys Ser Glu Gln Glu Ile Gly Lys Ala Thr Ala Lys Tyr Phe Phe
 1025 1030 1035

Tyr Ser Asn Ile Met Asn Phe Phe Lys Thr Glu Ile Thr Leu Ala
 1040 1045 1050

Asn Gly Glu Ile Arg Lys Arg Pro Leu Ile Glu Thr Asn Gly Glu
 1055 1060 1065

Thr Gly Glu Ile Val Trp Asp Lys Gly Arg Asp Phe Ala Thr Val
 1070 1075 1080

Arg Lys Val Leu Ser Met Pro Gln Val Asn Ile Val Lys Lys Thr
 1085 1090 1095

Glu Val Gln Thr Gly Gly Phe Ser Lys Glu Ser Ile Leu Pro Lys
 1100 1105 1110

	Arg Asn Ser Asp Lys Leu Ile Ala Arg Lys Lys Asp Trp Asp Pro 1115 1120 1125
	Lys Lys Tyr Gly Gly Phe Asp Ser Pro Thr Val Ala Tyr Ser Val 1130 1135 1140
	Leu Val Val Ala Lys Val Glu Lys Gly Lys Ser Lys Lys Leu Lys 1145 1150 1155
	Ser Val Lys Glu Leu Leu Gly Ile Thr Ile Met Glu Arg Ser Ser 1160 1165 1170
	Phe Glu Lys Asn Pro Ile Asp Phe Leu Glu Ala Lys Gly Tyr Lys 1175 1180 1185
	Glu Val Lys Lys Asp Leu Ile Ile Lys Leu Pro Lys Tyr Ser Leu 1190 1195 1200
	Phe Glu Leu Glu Asn Gly Arg Lys Arg Met Leu Ala Ser Ala Gly 1205 1210 1215
	Glu Leu Gln Lys Gly Asn Glu Leu Ala Leu Pro Ser Lys Tyr Val 1220 1225 1230
	Asn Phe Leu Tyr Leu Ala Ser His Tyr Glu Lys Leu Lys Gly Ser 1235 1240 1245
[0343]	Pro Glu Asp Asn Glu Gln Lys Gln Leu Phe Val Glu Gln His Lys 1250 1255 1260
	His Tyr Leu Asp Glu Ile Ile Glu Gln Ile Ser Glu Phe Ser Lys 1265 1270 1275
	Arg Val Ile Leu Ala Asp Ala Asn Leu Asp Lys Val Leu Ser Ala 1280 1285 1290
	Tyr Asn Lys His Arg Asp Lys Pro Ile Arg Glu Gln Ala Glu Asn 1295 1300 1305
	Ile Ile His Leu Phe Thr Leu Thr Asn Leu Gly Ala Pro Ala Ala 1310 1315 1320
	Phe Lys Tyr Phe Asp Thr Thr Ile Asp Arg Lys Arg Tyr Thr Ser 1325 1330 1335
	Thr Lys Glu Val Leu Asp Ala Thr Leu Ile His Gln Ser Ile Thr 1340 1345 1350
	Gly Leu Tyr Glu Thr Arg Ile Asp Leu Ser Gln Leu Gly Gly Asp 1355 1360 1365
	Gly Gly Gly Ser Ala Ala Ala Lys Arg Ser Trp Ser Met Ala Phe 1370 1375 1380
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 35 40 45
 Gly Ala Leu Leu Phe Asp Ser Gly Glu Thr Ala Glu Ala Thr Arg Leu
 50 55 60
 Lys Arg Thr Ala Arg Arg Arg Tyr Thr Arg Arg Lys Asn Arg Ile Cys
 65 70 75 80
 Tyr Leu Gln Glu Ile Phe Ser Asn Glu Met Ala Lys Val Asp Asp Ser
 85 90 95
 Phe Phe His Arg Leu Glu Glu Ser Phe Leu Val Glu Glu Asp Lys Lys
 100 105 110
 [0344] His Glu Arg His Pro Ile Phe Gly Asn Ile Val Asp Glu Val Ala Tyr
 115 120 125
 His Glu Lys Tyr Pro Thr Ile Tyr His Leu Arg Lys Lys Leu Val Asp
 130 135 140
 Ser Thr Asp Lys Ala Asp Leu Arg Leu Ile Tyr Leu Ala Leu Ala His
 145 150 155 160
 Met Ile Lys Phe Arg Gly His Phe Leu Ile Glu Gly Asp Leu Asn Pro
 165 170 175
 Asp Asn Ser Asp Val Asp Lys Leu Phe Ile Gln Leu Val Gln Thr Tyr
 180 185 190
 Asn Gln Leu Phe Glu Glu Asn Pro Ile Asn Ala Ser Gly Val Asp Ala
 195 200 205
 Lys Ala Ile Leu Ser Ala Arg Leu Ser Lys Ser Arg Arg Leu Glu Asn
 210 215 220
 Leu Ile Ala Gln Leu Pro Gly Glu Lys Lys Asn Gly Leu Phe Gly Asn
 225 230 235 240
 Leu Ile Ala Leu Ser Leu Gly Leu Thr Pro Asn Phe Lys Ser Asn Phe
 245 250 255
 Asp Leu Ala Glu Asp Ala Lys Leu Gln Leu Ser Lys Asp Thr Tyr Asp
 260 265 270

Asp Asp Leu Asp Asn Leu Leu Ala Gln Ile Gly Asp Gln Tyr Ala Asp
 275 280 285

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

Ile Leu Arg Val Asn Thr Glu Ile Thr Lys Ala Pro Leu Ser Ala Ser
 305 310 315 320

Met Ile Lys Arg Tyr Asp Glu His His Gln Asp Leu Thr Leu Leu Lys
 325 330 335

Ala Leu Val Arg Gln Gln Leu Pro Glu Lys Tyr Lys Glu Ile Phe Phe
 340 345 350

Asp Gln Ser Lys Asn Gly Tyr Ala Gly Tyr Ile Asp Gly Gly Ala Ser
 355 360 365

Gln Glu Glu Phe Tyr Lys Phe Ile Lys Pro Ile Leu Glu Lys Met Asp
 370 375 380

Gly Thr Glu Glu Leu Leu Val Lys Leu Asn Arg Glu Asp Leu Leu Arg
 385 390 395 400

Lys Gln Arg Thr Phe Asp Asn Gly Ser Ile Pro His Gln Ile His Leu
 405 410 415

[0345] Gly Glu Leu His Ala Ile Leu Arg Arg Gln Glu Asp Phe Tyr Pro Phe
 420 425 430

Leu Lys Asp Asn Arg Glu Lys Ile Glu Lys Ile Leu Thr Phe Arg Ile
 435 440 445

Pro Tyr Tyr Val Gly Pro Leu Ala Arg Gly Asn Ser Arg Phe Ala Trp
 450 455 460

Met Thr Arg Lys Ser Glu Glu Thr Ile Thr Pro Trp Asn Phe Glu Glu
 465 470 475 480

Val Val Asp Lys Gly Ala Ser Ala Gln Ser Phe Ile Glu Arg Met Thr
 485 490 495

Asn Phe Asp Lys Asn Leu Pro Asn Glu Lys Val Leu Pro Lys His Ser
 500 505 510

Leu Leu Tyr Glu Tyr Phe Thr Val Tyr Asn Glu Leu Thr Lys Val Lys
 515 520 525

Tyr Val Thr Glu Gly Met Arg Lys Pro Ala Phe Leu Ser Gly Glu Gln
 530 535 540

Lys Lys Ala Ile Val Asp Leu Leu Phe Lys Thr Asn Arg Lys Val Thr
 545 550 555 560

Val Lys Gln Leu Lys Glu Asp Tyr Phe Lys Lys Ile Glu Cys Phe Asp
 565 570 575

Ser Val Glu Ile Ser Gly Val Glu Asp Arg Phe Asn Ala Ser Leu Gly
 580 585 590

Thr Tyr His Asp Leu Leu Lys Ile Ile Lys Asp Lys Asp Phe Leu Asp
 595 600 605

Asn Glu Glu Asn Glu Asp Ile Leu Glu Asp Ile Val Leu Thr Leu Thr
 610 615 620

Leu Phe Glu Asp Arg Glu Met Ile Glu Glu Arg Leu Lys Thr Tyr Ala
 625 630 635 640

His Leu Phe Asp Asp Lys Val Met Lys Gln Leu Lys Arg Arg Arg Tyr
 645 650 655

Thr Gly Trp Gly Arg Leu Ser Arg Lys Leu Ile Asn Gly Ile Arg Asp
 660 665 670

Lys Gln Ser Gly Lys Thr Ile Leu Asp Phe Leu Lys Ser Asp Gly Phe
 675 680 685

Ala Asn Arg Asn Phe Met Gln Leu Ile His Asp Asp Ser Leu Thr Phe
 690 695 700

Lys Glu Asp Ile Gln Lys Ala Gln Val Ser Gly Gln Gly Asp Ser Leu
 705 710 715 720

[0346] His Glu His Ile Ala Asn Leu Ala Gly Ser Pro Ala Ile Lys Lys Gly
 725 730 735

Ile Leu Gln Thr Val Lys Val Val Asp Glu Leu Val Lys Val Met Gly
 740 745 750

Arg His Lys Pro Glu Asn Ile Val Ile Glu Met Ala Arg Glu Asn Gln
 755 760 765

Thr Thr Gln Lys Gly Gln Lys Asn Ser Arg Glu Arg Met Lys Arg Ile
 770 775 780

Glu Glu Gly Ile Lys Glu Leu Gly Ser Gln Ile Leu Lys Glu His Pro
 785 790 795 800

Val Glu Asn Thr Gln Leu Gln Asn Glu Lys Leu Tyr Leu Tyr Tyr Leu
 805 810 815

Gln Asn Gly Arg Asp Met Tyr Val Asp Gln Glu Leu Asp Ile Asn Arg
 820 825 830

Leu Ser Asp Tyr Asp Val Asp His Ile Val Pro Gln Ser Phe Leu Lys
 835 840 845

Asp Asp Ser Ile Asp Asn Lys Val Leu Thr Arg Ser Asp Lys Asn Arg
 850 855 860

Gly Lys Ser Asp Asn Val Pro Ser Glu Glu Val Val Lys Lys Met Lys

865	870	875	880
Asn Tyr Trp Arg Gln Leu Leu Asn Ala Lys Leu Ile Thr Gln Arg Lys 885 890 895			
Phe Asp Asn Leu Thr Lys Ala Glu Arg Gly Gly Leu Ser Glu Leu Asp 900 905 910			
Lys Ala Gly Phe Ile Lys Arg Gln Leu Val Glu Thr Arg Gln Ile Thr 915 920 925			
Lys His Val Ala Gln Ile Leu Asp Ser Arg Met Asn Thr Lys Tyr Asp 930 935 940			
Glu Asn Asp Lys Leu Ile Arg Glu Val Lys Val Ile Thr Leu Lys Ser 945 950 955 960			
Lys Leu Val Ser Asp Phe Arg Lys Asp Phe Gln Phe Tyr Lys Val Arg 965 970 975			
Glu Ile Asn Asn Tyr His His Ala His Asp Ala Tyr Leu Asn Ala Val 980 985 990			
Val Gly Thr Ala Leu Ile Lys Lys Tyr Pro Lys Leu Glu Ser Glu Phe 995 1000 1005			
[0347] Val Tyr Gly Asp Tyr Lys Val Tyr Asp Val Arg Lys Met Ile Ala 1010 1015 1020			
Lys Ser Glu Gln Glu Ile Gly Lys Ala Thr Ala Lys Tyr Phe Phe 1025 1030 1035			
Tyr Ser Asn Ile Met Asn Phe Phe Lys Thr Glu Ile Thr Leu Ala 1040 1045 1050			
Asn Gly Glu Ile Arg Lys Arg Pro Leu Ile Glu Thr Asn Gly Glu 1055 1060 1065			
Thr Gly Glu Ile Val Trp Asp Lys Gly Arg Asp Phe Ala Thr Val 1070 1075 1080			
Arg Lys Val Leu Ser Met Pro Gln Val Asn Ile Val Lys Lys Thr 1085 1090 1095			
Glu Val Gln Thr Gly Gly Phe Ser Lys Glu Ser Ile Leu Pro Lys 1100 1105 1110			
Arg Asn Ser Asp Lys Leu Ile Ala Arg Lys Lys Asp Trp Asp Pro 1115 1120 1125			
Lys Lys Tyr Gly Gly Phe Asp Ser Pro Thr Val Ala Tyr Ser Val 1130 1135 1140			
Leu Val Val Ala Lys Val Glu Lys Gly Lys Ser Lys Lys Leu Lys 1145 1150 1155			

Ser Val Lys Glu Leu Leu Gly Ile Thr Ile Met Glu Arg Ser Ser
 1160 1165 1170
 Phe Glu Lys Asn Pro Ile Asp Phe Leu Glu Ala Lys Gly Tyr Lys
 1175 1180 1185
 Glu Val Lys Lys Asp Leu Ile Ile Lys Leu Pro Lys Tyr Ser Leu
 1190 1195 1200
 Phe Glu Leu Glu Asn Gly Arg Lys Arg Met Leu Ala Ser Ala Gly
 1205 1210 1215
 Glu Leu Gln Lys Gly Asn Glu Leu Ala Leu Pro Ser Lys Tyr Val
 1220 1225 1230
 Asn Phe Leu Tyr Leu Ala Ser His Tyr Glu Lys Leu Lys Gly Ser
 1235 1240 1245
 Pro Glu Asp Asn Glu Gln Lys Gln Leu Phe Val Glu Gln His Lys
 1250 1255 1260
 His Tyr Leu Asp Glu Ile Ile Glu Gln Ile Ser Glu Phe Ser Lys
 1265 1270 1275
 Arg Val Ile Leu Ala Asp Ala Asn Leu Asp Lys Val Leu Ser Ala
 1280 1285 1290
 Tyr Asn Lys His Arg Asp Lys Pro Ile Arg Glu Gln Ala Glu Asn
 [0348] 1295 1300 1305
 Ile Ile His Leu Phe Thr Leu Thr Asn Leu Gly Ala Pro Ala Ala
 1310 1315 1320
 Phe Lys Tyr Phe Asp Thr Thr Ile Asp Arg Lys Arg Tyr Thr Ser
 1325 1330 1335
 Thr Lys Glu Val Leu Asp Ala Thr Leu Ile His Gln Ser Ile Thr
 1340 1345 1350
 Gly Leu Tyr Glu Thr Arg Ile Asp Leu Ser Gln Leu Gly Gly Asp
 1355 1360 1365
 Gly Gly Gly Ser Ala Ala Ala Lys Arg Lys Tyr Phe Ala Ala
 1370 1375 1380
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 <211> 1382
 <212> PRT
 <213> 人工序列
 <220>
 <223> 合成的: 具有NLS10的Cas9的氨基酸序列
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 1 5 10 15
 Gly Trp Ala Val Ile Thr Asp Glu Tyr Lys Val Pro Ser Lys Lys Phe

	20	25	30
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	Gly Ala Leu Leu Phe Asp Ser Gly Glu Thr Ala Glu Ala Thr Arg Leu 50 55 60		
	Lys Arg Thr Ala Arg Arg Arg Tyr Thr Arg Arg Lys Asn Arg Ile Cys 65 70 75 80		
	Tyr Leu Gln Glu Ile Phe Ser Asn Glu Met Ala Lys Val Asp Asp Ser 85 90 95		
	Phe Phe His Arg Leu Glu Glu Ser Phe Leu Val Glu Glu Asp Lys Lys 100 105 110		
	His Glu Arg His Pro Ile Phe Gly Asn Ile Val Asp Glu Val Ala Tyr 115 120 125		
	His Glu Lys Tyr Pro Thr Ile Tyr His Leu Arg Lys Lys Leu Val Asp 130 135 140		
	Ser Thr Asp Lys Ala Asp Leu Arg Leu Ile Tyr Leu Ala Leu Ala His 145 150 155 160		
[0349]	Met Ile Lys Phe Arg Gly His Phe Leu Ile Glu Gly Asp Leu Asn Pro 165 170 175		
	Asp Asn Ser Asp Val Asp Lys Leu Phe Ile Gln Leu Val Gln Thr Tyr 180 185 190		
	Asn Gln Leu Phe Glu Glu Asn Pro Ile Asn Ala Ser Gly Val Asp Ala 195 200 205		
	Lys Ala Ile Leu Ser Ala Arg Leu Ser Lys Ser Arg Arg Leu Glu Asn 210 215 220		
	Leu Ile Ala Gln Leu Pro Gly Glu Lys Lys Asn Gly Leu Phe Gly Asn 225 230 235 240		
	Leu Ile Ala Leu Ser Leu Gly Leu Thr Pro Asn Phe Lys Ser Asn Phe 245 250 255		
	Asp Leu Ala Glu Asp Ala Lys Leu Gln Leu Ser Lys Asp Thr Tyr Asp 260 265 270		
	Asp Asp Leu Asp Asn Leu Leu Ala Gln Ile Gly Asp Gln Tyr Ala Asp 275 280 285		
	Leu Phe Leu Ala Ala Lys Asn Leu Ser Asp Ala Ile Leu Leu Ser Asp 290 295 300		
	Ile Leu Arg Val Asn Thr Glu Ile Thr Lys Ala Pro Leu Ser Ala Ser 305 310 315 320		

Met Ile Lys Arg Tyr Asp Glu His His Gln Asp Leu Thr Leu Leu Lys
325 330 335

Ala Leu Val Arg Gln Gln Leu Pro Glu Lys Tyr Lys Glu Ile Phe Phe
340 345 350

Asp Gln Ser Lys Asn Gly Tyr Ala Gly Tyr Ile Asp Gly Gly Ala Ser
355 360 365

Gln Glu Glu Phe Tyr Lys Phe Ile Lys Pro Ile Leu Glu Lys Met Asp
370 375 380

Gly Thr Glu Glu Leu Leu Val Lys Leu Asn Arg Glu Asp Leu Leu Arg
385 390 395 400

Lys Gln Arg Thr Phe Asp Asn Gly Ser Ile Pro His Gln Ile His Leu
405 410 415

Gly Glu Leu His Ala Ile Leu Arg Arg Gln Glu Asp Phe Tyr Pro Phe
420 425 430

Leu Lys Asp Asn Arg Glu Lys Ile Glu Lys Ile Leu Thr Phe Arg Ile
435 440 445

Pro Tyr Tyr Val Gly Pro Leu Ala Arg Gly Asn Ser Arg Phe Ala Trp
450 455 460

[0350] Met Thr Arg Lys Ser Glu Glu Thr Ile Thr Pro Trp Asn Phe Glu Glu
465 470 475 480

Val Val Asp Lys Gly Ala Ser Ala Gln Ser Phe Ile Glu Arg Met Thr
485 490 495

Asn Phe Asp Lys Asn Leu Pro Asn Glu Lys Val Leu Pro Lys His Ser
500 505 510

Leu Leu Tyr Glu Tyr Phe Thr Val Tyr Asn Glu Leu Thr Lys Val Lys
515 520 525

Tyr Val Thr Glu Gly Met Arg Lys Pro Ala Phe Leu Ser Gly Glu Gln
530 535 540

Lys Lys Ala Ile Val Asp Leu Leu Phe Lys Thr Asn Arg Lys Val Thr
545 550 555 560

Val Lys Gln Leu Lys Glu Asp Tyr Phe Lys Lys Ile Glu Cys Phe Asp
565 570 575

Ser Val Glu Ile Ser Gly Val Glu Asp Arg Phe Asn Ala Ser Leu Gly
580 585 590

Thr Tyr His Asp Leu Leu Lys Ile Ile Lys Asp Lys Asp Phe Leu Asp
595 600 605

Asn Glu Glu Asn Glu Asp Ile Leu Glu Asp Ile Val Leu Thr Leu Thr
610 615 620

Leu Phe Glu Asp Arg Glu Met Ile Glu Glu Arg Leu Lys Thr Tyr Ala
 625 630 635 640
 His Leu Phe Asp Asp Lys Val Met Lys Gln Leu Lys Arg Arg Arg Tyr
 645 650 655
 Thr Gly Trp Gly Arg Leu Ser Arg Lys Leu Ile Asn Gly Ile Arg Asp
 660 665 670
 Lys Gln Ser Gly Lys Thr Ile Leu Asp Phe Leu Lys Ser Asp Gly Phe
 675 680 685
 Ala Asn Arg Asn Phe Met Gln Leu Ile His Asp Asp Ser Leu Thr Phe
 690 695 700
 Lys Glu Asp Ile Gln Lys Ala Gln Val Ser Gly Gln Gly Asp Ser Leu
 705 710 715 720
 His Glu His Ile Ala Asn Leu Ala Gly Ser Pro Ala Ile Lys Lys Gly
 725 730 735
 Ile Leu Gln Thr Val Lys Val Val Asp Glu Leu Val Lys Val Met Gly
 740 745 750
 Arg His Lys Pro Glu Asn Ile Val Ile Glu Met Ala Arg Glu Asn Gln
 755 760 765
 [0351] Thr Thr Gln Lys Gly Gln Lys Asn Ser Arg Glu Arg Met Lys Arg Ile
 770 775 780
 Glu Glu Gly Ile Lys Glu Leu Gly Ser Gln Ile Leu Lys Glu His Pro
 785 790 795 800
 Val Glu Asn Thr Gln Leu Gln Asn Glu Lys Leu Tyr Leu Tyr Tyr Leu
 805 810 815
 Gln Asn Gly Arg Asp Met Tyr Val Asp Gln Glu Leu Asp Ile Asn Arg
 820 825 830
 Leu Ser Asp Tyr Asp Val Asp His Ile Val Pro Gln Ser Phe Leu Lys
 835 840 845
 Asp Asp Ser Ile Asp Asn Lys Val Leu Thr Arg Ser Asp Lys Asn Arg
 850 855 860
 Gly Lys Ser Asp Asn Val Pro Ser Glu Glu Val Val Lys Lys Met Lys
 865 870 875 880
 Asn Tyr Trp Arg Gln Leu Leu Asn Ala Lys Leu Ile Thr Gln Arg Lys
 885 890 895
 Phe Asp Asn Leu Thr Lys Ala Glu Arg Gly Gly Leu Ser Glu Leu Asp
 900 905 910
 Lys Ala Gly Phe Ile Lys Arg Gln Leu Val Glu Thr Arg Gln Ile Thr
 915 920 925

Lys His Val Ala Gln Ile Leu Asp Ser Arg Met Asn Thr Lys Tyr Asp
 930 935 940

Glu Asn Asp Lys Leu Ile Arg Glu Val Lys Val Ile Thr Leu Lys Ser
 945 950 955 960

Lys Leu Val Ser Asp Phe Arg Lys Asp Phe Gln Phe Tyr Lys Val Arg
 965 970 975

Glu Ile Asn Asn Tyr His His Ala His Asp Ala Tyr Leu Asn Ala Val
 980 985 990

Val Gly Thr Ala Leu Ile Lys Lys Tyr Pro Lys Leu Glu Ser Glu Phe
 995 1000 1005

Val Tyr Gly Asp Tyr Lys Val Tyr Asp Val Arg Lys Met Ile Ala
 1010 1015 1020

Lys Ser Glu Gln Glu Ile Gly Lys Ala Thr Ala Lys Tyr Phe Phe
 1025 1030 1035

Tyr Ser Asn Ile Met Asn Phe Phe Lys Thr Glu Ile Thr Leu Ala
 1040 1045 1050

Asn Gly Glu Ile Arg Lys Arg Pro Leu Ile Glu Thr Asn Gly Glu
 1055 1060 1065

[0352] Thr Gly Glu Ile Val Trp Asp Lys Gly Arg Asp Phe Ala Thr Val
 1070 1075 1080

Arg Lys Val Leu Ser Met Pro Gln Val Asn Ile Val Lys Lys Thr
 1085 1090 1095

Glu Val Gln Thr Gly Gly Phe Ser Lys Glu Ser Ile Leu Pro Lys
 1100 1105 1110

Arg Asn Ser Asp Lys Leu Ile Ala Arg Lys Lys Asp Trp Asp Pro
 1115 1120 1125

Lys Lys Tyr Gly Gly Phe Asp Ser Pro Thr Val Ala Tyr Ser Val
 1130 1135 1140

Leu Val Val Ala Lys Val Glu Lys Gly Lys Ser Lys Lys Leu Lys
 1145 1150 1155

Ser Val Lys Glu Leu Leu Gly Ile Thr Ile Met Glu Arg Ser Ser
 1160 1165 1170

Phe Glu Lys Asn Pro Ile Asp Phe Leu Glu Ala Lys Gly Tyr Lys
 1175 1180 1185

Glu Val Lys Lys Asp Leu Ile Ile Lys Leu Pro Lys Tyr Ser Leu
 1190 1195 1200

Phe Glu Leu Glu Asn Gly Arg Lys Arg Met Leu Ala Ser Ala Gly

Tyr Leu Gln Glu Ile Phe Ser Asn Glu Met Ala Lys Val Asp Asp Ser
 85 90 95

Phe Phe His Arg Leu Glu Glu Ser Phe Leu Val Glu Glu Asp Lys Lys
 100 105 110

His Glu Arg His Pro Ile Phe Gly Asn Ile Val Asp Glu Val Ala Tyr
 115 120 125

His Glu Lys Tyr Pro Thr Ile Tyr His Leu Arg Lys Lys Leu Val Asp
 130 135 140

Ser Thr Asp Lys Ala Asp Leu Arg Leu Ile Tyr Leu Ala Leu Ala His
 145 150 155 160

Met Ile Lys Phe Arg Gly His Phe Leu Ile Glu Gly Asp Leu Asn Pro
 165 170 175

Asp Asn Ser Asp Val Asp Lys Leu Phe Ile Gln Leu Val Gln Thr Tyr
 180 185 190

Asn Gln Leu Phe Glu Glu Asn Pro Ile Asn Ala Ser Gly Val Asp Ala
 195 200 205

Lys Ala Ile Leu Ser Ala Arg Leu Ser Lys Ser Arg Arg Leu Glu Asn
 210 215 220

[0354] Leu Ile Ala Gln Leu Pro Gly Glu Lys Lys Asn Gly Leu Phe Gly Asn
 225 230 235 240

Leu Ile Ala Leu Ser Leu Gly Leu Thr Pro Asn Phe Lys Ser Asn Phe
 245 250 255

Asp Leu Ala Glu Asp Ala Lys Leu Gln Leu Ser Lys Asp Thr Tyr Asp
 260 265 270

Asp Asp Leu Asp Asn Leu Leu Ala Gln Ile Gly Asp Gln Tyr Ala Asp
 275 280 285

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

Ile Leu Arg Val Asn Thr Glu Ile Thr Lys Ala Pro Leu Ser Ala Ser
 305 310 315 320

Met Ile Lys Arg Tyr Asp Glu His His Gln Asp Leu Thr Leu Leu Lys
 325 330 335

Ala Leu Val Arg Gln Gln Leu Pro Glu Lys Tyr Lys Glu Ile Phe Phe
 340 345 350

Asp Gln Ser Lys Asn Gly Tyr Ala Gly Tyr Ile Asp Gly Gly Ala Ser
 355 360 365

Gln Glu Glu Phe Tyr Lys Phe Ile Lys Pro Ile Leu Glu Lys Met Asp

370	375	380
Gly Thr Glu Glu Leu Leu Val Lys Leu Asn Arg Glu Asp Leu Leu Arg 385 390 395 400		
Lys Gln Arg Thr Phe Asp Asn Gly Ser Ile Pro His Gln Ile His Leu 405 410 415		
Gly Glu Leu His Ala Ile Leu Arg Arg Gln Glu Asp Phe Tyr Pro Phe 420 425 430		
Leu Lys Asp Asn Arg Glu Lys Ile Glu Lys Ile Leu Thr Phe Arg Ile 435 440 445		
Pro Tyr Tyr Val Gly Pro Leu Ala Arg Gly Asn Ser Arg Phe Ala Trp 450 455 460		
Met Thr Arg Lys Ser Glu Glu Thr Ile Thr Pro Trp Asn Phe Glu Glu 465 470 475 480		
Val Val Asp Lys Gly Ala Ser Ala Gln Ser Phe Ile Glu Arg Met Thr 485 490 495		
Asn Phe Asp Lys Asn Leu Pro Asn Glu Lys Val Leu Pro Lys His Ser 500 505 510		
[0355] Leu Leu Tyr Glu Tyr Phe Thr Val Tyr Asn Glu Leu Thr Lys Val Lys 515 520 525		
Tyr Val Thr Glu Gly Met Arg Lys Pro Ala Phe Leu Ser Gly Glu Gln 530 535 540		
Lys Lys Ala Ile Val Asp Leu Leu Phe Lys Thr Asn Arg Lys Val Thr 545 550 555 560		
Val Lys Gln Leu Lys Glu Asp Tyr Phe Lys Lys Ile Glu Cys Phe Asp 565 570 575		
Ser Val Glu Ile Ser Gly Val Glu Asp Arg Phe Asn Ala Ser Leu Gly 580 585 590		
Thr Tyr His Asp Leu Leu Lys Ile Ile Lys Asp Lys Asp Phe Leu Asp 595 600 605		
Asn Glu Glu Asn Glu Asp Ile Leu Glu Asp Ile Val Leu Thr Leu Thr 610 615 620		
Leu Phe Glu Asp Arg Glu Met Ile Glu Glu Arg Leu Lys Thr Tyr Ala 625 630 635 640		
His Leu Phe Asp Asp Lys Val Met Lys Gln Leu Lys Arg Arg Arg Tyr 645 650 655		
Thr Gly Trp Gly Arg Leu Ser Arg Lys Leu Ile Asn Gly Ile Arg Asp 660 665 670		

Lys Gln Ser Gly Lys Thr Ile Leu Asp Phe Leu Lys Ser Asp Gly Phe
 675 680 685

Ala Asn Arg Asn Phe Met Gln Leu Ile His Asp Asp Ser Leu Thr Phe
 690 695 700

Lys Glu Asp Ile Gln Lys Ala Gln Val Ser Gly Gln Gly Asp Ser Leu
 705 710 715 720

His Glu His Ile Ala Asn Leu Ala Gly Ser Pro Ala Ile Lys Lys Gly
 725 730 735

Ile Leu Gln Thr Val Lys Val Val Asp Glu Leu Val Lys Val Met Gly
 740 745 750

Arg His Lys Pro Glu Asn Ile Val Ile Glu Met Ala Arg Glu Asn Gln
 755 760 765

Thr Thr Gln Lys Gly Gln Lys Asn Ser Arg Glu Arg Met Lys Arg Ile
 770 775 780

Glu Glu Gly Ile Lys Glu Leu Gly Ser Gln Ile Leu Lys Glu His Pro
 785 790 795 800

Val Glu Asn Thr Gln Leu Gln Asn Glu Lys Leu Tyr Leu Tyr Tyr Leu
 805 810 815

[0356] Gln Asn Gly Arg Asp Met Tyr Val Asp Gln Glu Leu Asp Ile Asn Arg
 820 825 830

Leu Ser Asp Tyr Asp Val Asp His Ile Val Pro Gln Ser Phe Leu Lys
 835 840 845

Asp Asp Ser Ile Asp Asn Lys Val Leu Thr Arg Ser Asp Lys Asn Arg
 850 855 860

Gly Lys Ser Asp Asn Val Pro Ser Glu Glu Val Val Lys Lys Met Lys
 865 870 875 880

Asn Tyr Trp Arg Gln Leu Leu Asn Ala Lys Leu Ile Thr Gln Arg Lys
 885 890 895

Phe Asp Asn Leu Thr Lys Ala Glu Arg Gly Gly Leu Ser Glu Leu Asp
 900 905 910

Lys Ala Gly Phe Ile Lys Arg Gln Leu Val Glu Thr Arg Gln Ile Thr
 915 920 925

Lys His Val Ala Gln Ile Leu Asp Ser Arg Met Asn Thr Lys Tyr Asp
 930 935 940

Glu Asn Asp Lys Leu Ile Arg Glu Val Lys Val Ile Thr Leu Lys Ser
 945 950 955 960

Lys Leu Val Ser Asp Phe Arg Lys Asp Phe Gln Phe Tyr Lys Val Arg
 965 970 975

Glu Ile Asn Asn Tyr His His Ala His Asp Ala Tyr Leu Asn Ala Val
 980 985 990

Val Gly Thr Ala Leu Ile Lys Lys Tyr Pro Lys Leu Glu Ser Glu Phe
 995 1000 1005

Val Tyr Gly Asp Tyr Lys Val Tyr Asp Val Arg Lys Met Ile Ala
 1010 1015 1020

Lys Ser Glu Gln Glu Ile Gly Lys Ala Thr Ala Lys Tyr Phe Phe
 1025 1030 1035

Tyr Ser Asn Ile Met Asn Phe Phe Lys Thr Glu Ile Thr Leu Ala
 1040 1045 1050

Asn Gly Glu Ile Arg Lys Arg Pro Leu Ile Glu Thr Asn Gly Glu
 1055 1060 1065

Thr Gly Glu Ile Val Trp Asp Lys Gly Arg Asp Phe Ala Thr Val
 1070 1075 1080

Arg Lys Val Leu Ser Met Pro Gln Val Asn Ile Val Lys Lys Thr
 1085 1090 1095

Glu Val Gln Thr Gly Gly Phe Ser Lys Glu Ser Ile Leu Pro Lys
 1100 1105 1110

[0357] Arg Asn Ser Asp Lys Leu Ile Ala Arg Lys Lys Asp Trp Asp Pro
 1115 1120 1125

Lys Lys Tyr Gly Gly Phe Asp Ser Pro Thr Val Ala Tyr Ser Val
 1130 1135 1140

Leu Val Val Ala Lys Val Glu Lys Gly Lys Ser Lys Lys Leu Lys
 1145 1150 1155

Ser Val Lys Glu Leu Leu Gly Ile Thr Ile Met Glu Arg Ser Ser
 1160 1165 1170

Phe Glu Lys Asn Pro Ile Asp Phe Leu Glu Ala Lys Gly Tyr Lys
 1175 1180 1185

Glu Val Lys Lys Asp Leu Ile Ile Lys Leu Pro Lys Tyr Ser Leu
 1190 1195 1200

Phe Glu Leu Glu Asn Gly Arg Lys Arg Met Leu Ala Ser Ala Gly
 1205 1210 1215

Glu Leu Gln Lys Gly Asn Glu Leu Ala Leu Pro Ser Lys Tyr Val
 1220 1225 1230

Asn Phe Leu Tyr Leu Ala Ser His Tyr Glu Lys Leu Lys Gly Ser
 1235 1240 1245

Pro Glu Asp Asn Glu Gln Lys Gln Leu Phe Val Glu Gln His Lys
 1250 1255 1260

His Tyr Leu Asp Glu Ile Ile Glu Gln Ile Ser Glu Phe Ser Lys
 1265 1270 1275

Arg Val Ile Leu Ala Asp Ala Asn Leu Asp Lys Val Leu Ser Ala
 1280 1285 1290

Tyr Asn Lys His Arg Asp Lys Pro Ile Arg Glu Gln Ala Glu Asn
 1295 1300 1305

Ile Ile His Leu Phe Thr Leu Thr Asn Leu Gly Ala Pro Ala Ala
 1310 1315 1320

Phe Lys Tyr Phe Asp Thr Thr Ile Asp Arg Lys Arg Tyr Thr Ser
 1325 1330 1335

Thr Lys Glu Val Leu Asp Ala Thr Leu Ile His Gln Ser Ile Thr
 1340 1345 1350

Gly Leu Tyr Glu Thr Arg Ile Asp Leu Ser Gln Leu Gly Gly Asp
 1355 1360 1365

Gly Gly Gly Ser Arg Ala Ala Lys Arg Lys Tyr Phe Ala Val
 1370 1375 1380

[0358]

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 <213> 人工序列

<220>
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<220>
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 <222> (1)..(3)
 <223> PS键, 2'-O-Me 核苷酸

<220>
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<220>
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 <223> 2'-O-Me 核苷酸

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 <222> (97)..(100)
 <223> PS键, 2'-O-Me 核苷酸

<400> 197
 auaccagucc agcgaggcag guuuuagagc uagaaauagc aaguuaaaau aaggcuaguc 60
 cguuaucaac uugaaaaagu ggcaccgagu cggugcuuuu 100

<210> 198
 <211> 100
 <212> RNA
 <213> 人工序列

<220>

	<223> 合成的: G510 引导 RNA	
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	<222> (1)..(3)	
	<223> PS键, 2'-O-Me 核苷酸	
	<220>	
	<221> 修饰的_碱基	
	<222> (29)..(40)	
	<223> 2'-O-Me 核苷酸	
[0359]	<220>	
	<221> 修饰的_碱基	
	<222> (69)..(96)	
	<223> 2'-O-Me 核苷酸	
	<220>	
	<221> 修饰的_碱基	
	<222> (97)..(100)	
	<223> PS键, 2'-O-Me 核苷酸	
	<400> 198	
	acuugucuuc ucuauacca guuuuagagc uagaaauagc aaguuaaaau aaggcuaguc	60
	cguaaucaac uugaaaaagu ggcaccgagu cggugcuuuu	100

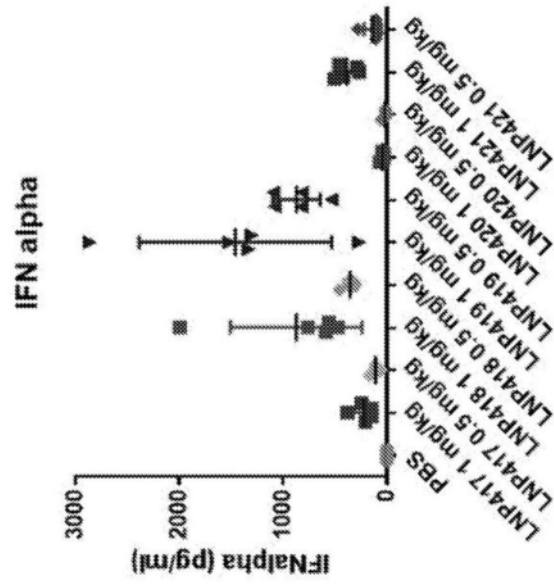


图1A

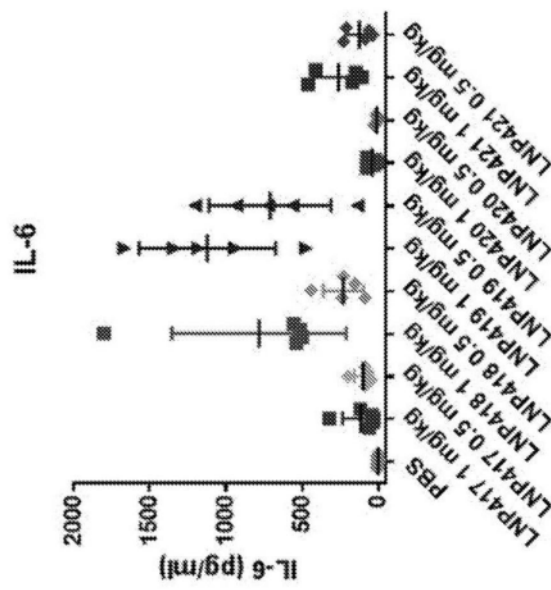


图1B

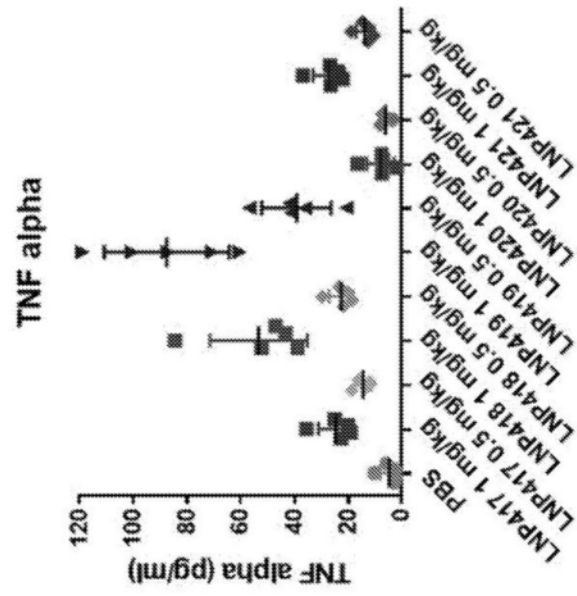


图1C

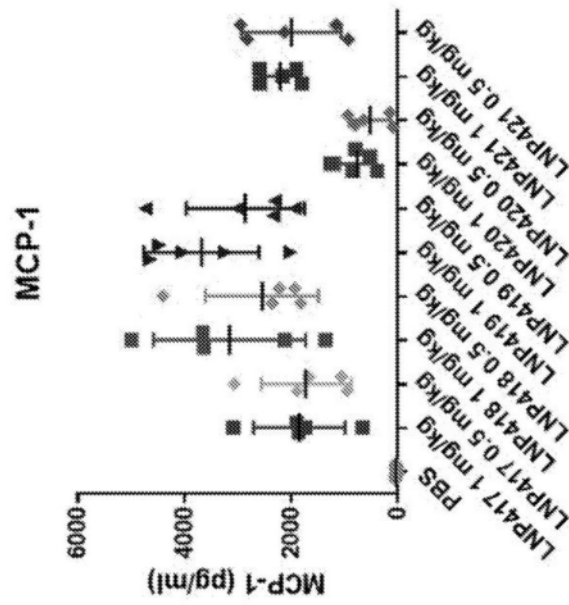


图1D

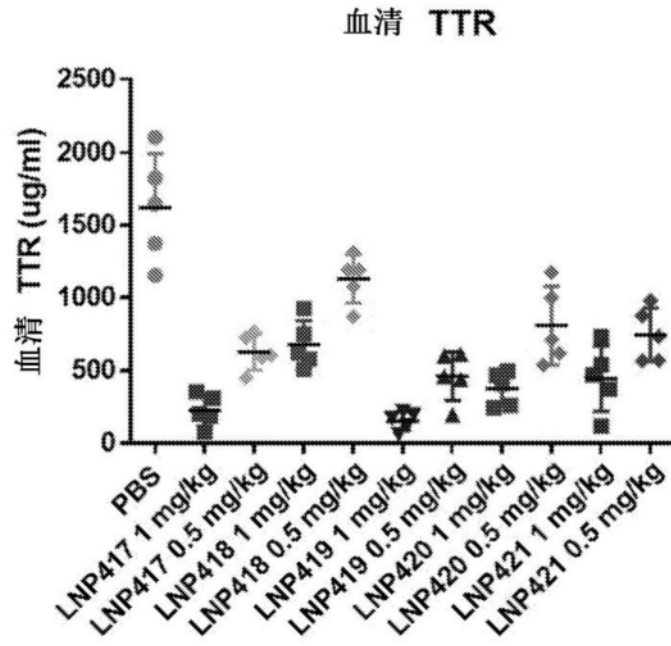


图2A

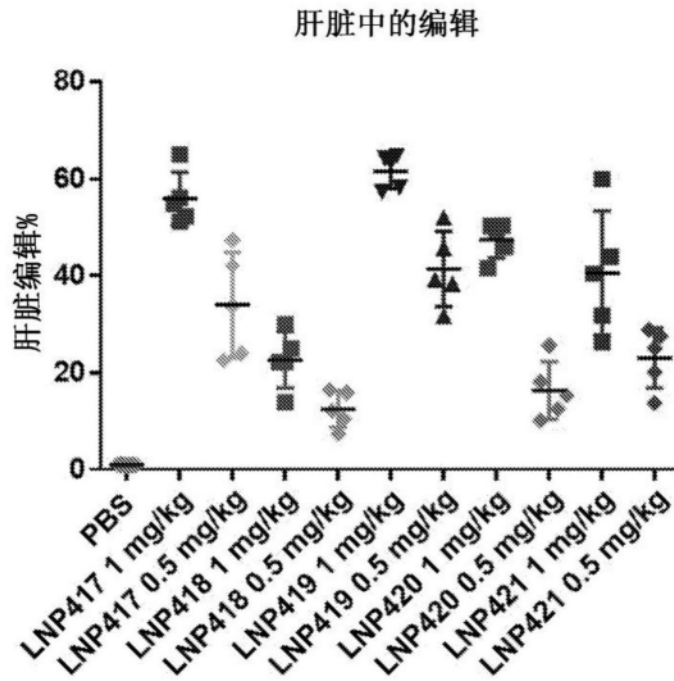


图2B

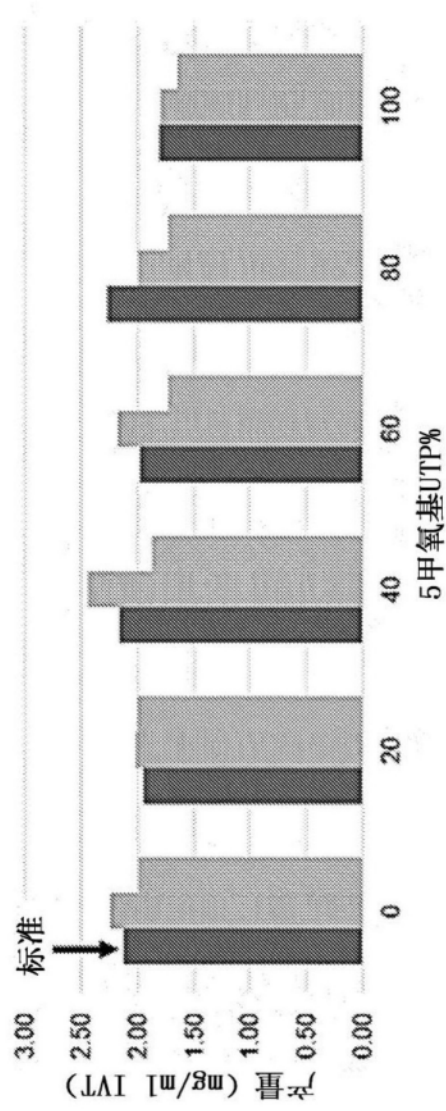


图3

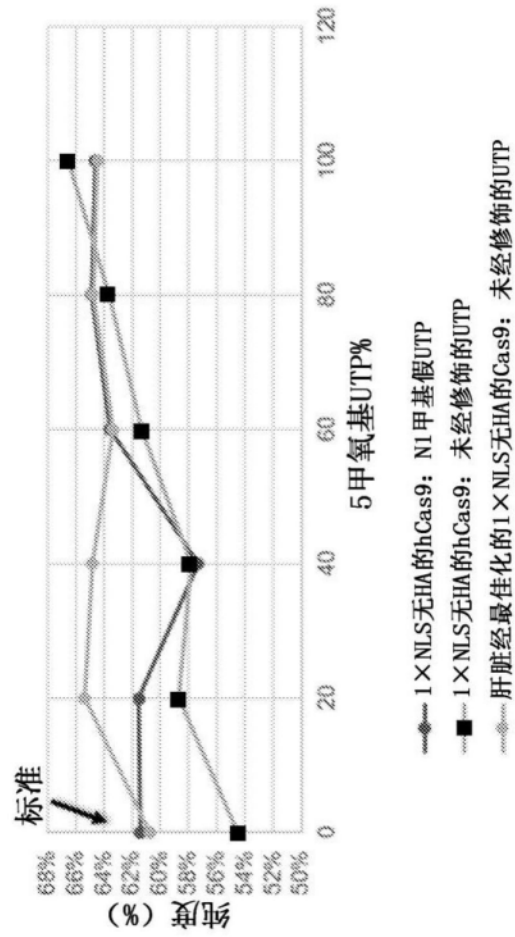


图4

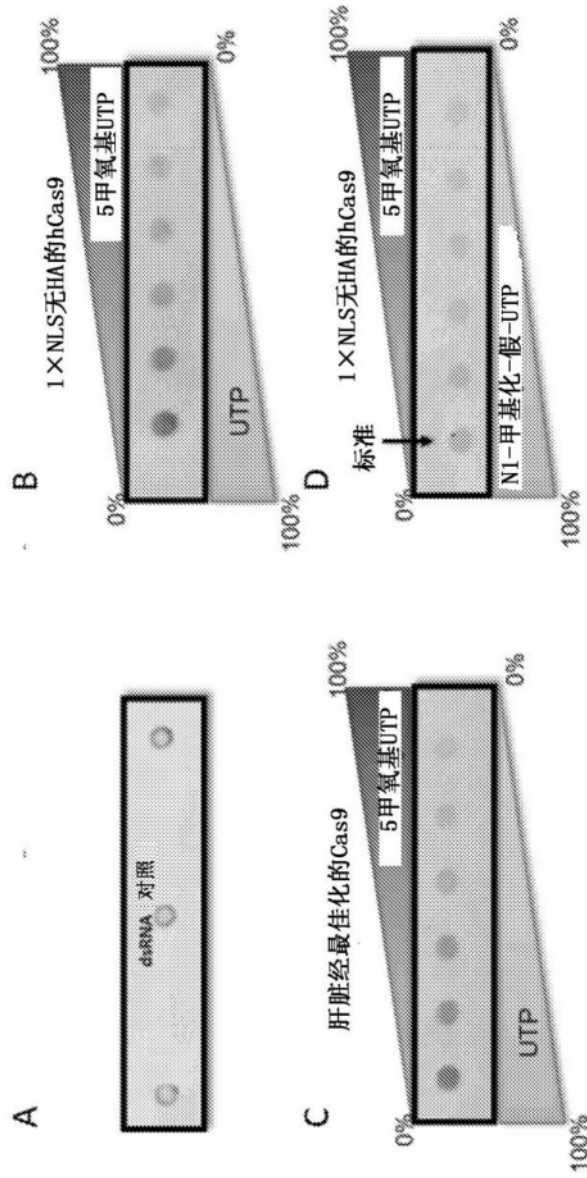


图5

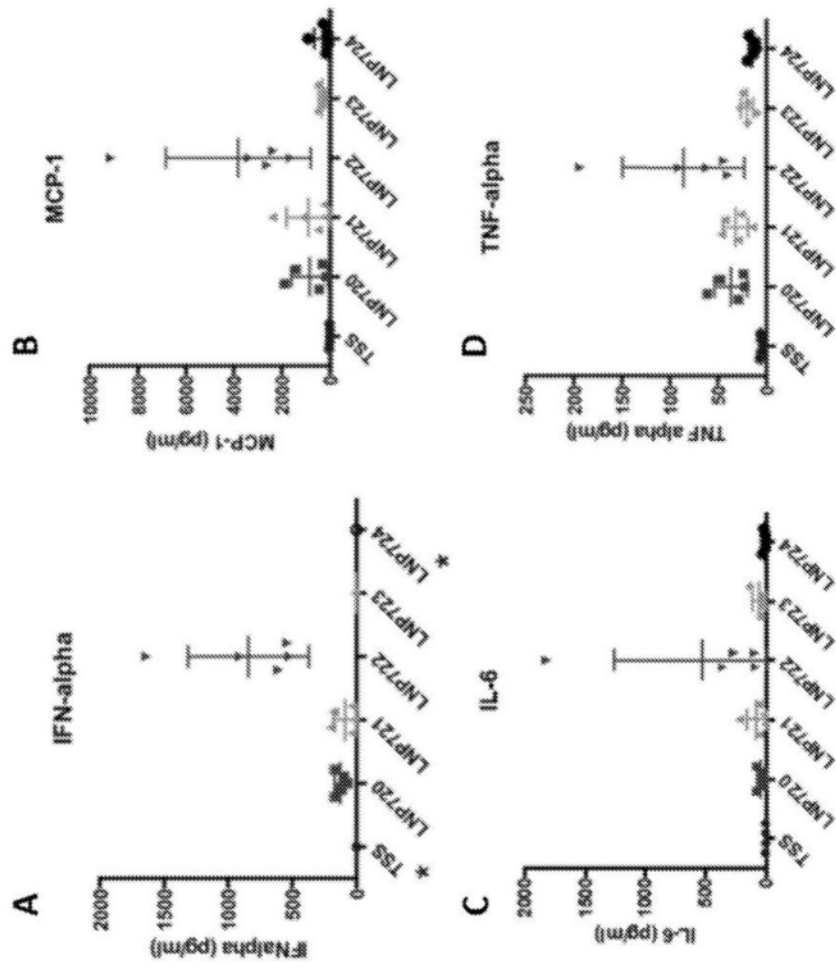


图7

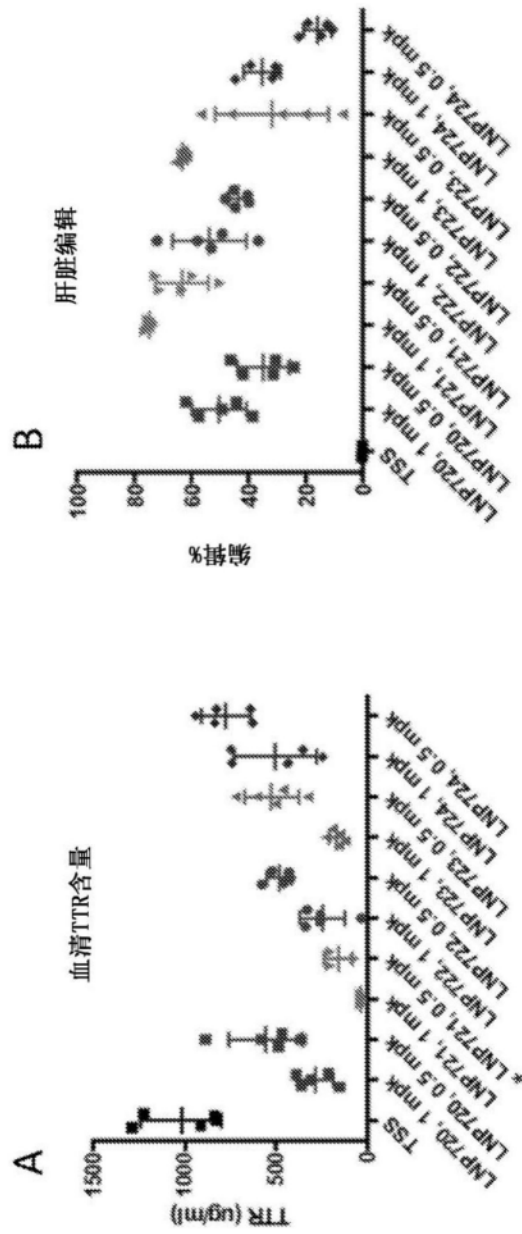


图8

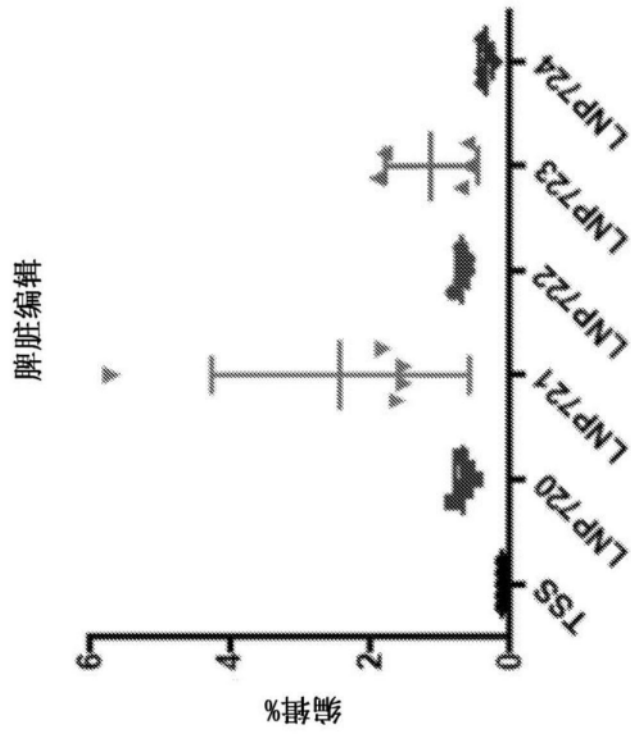


图9

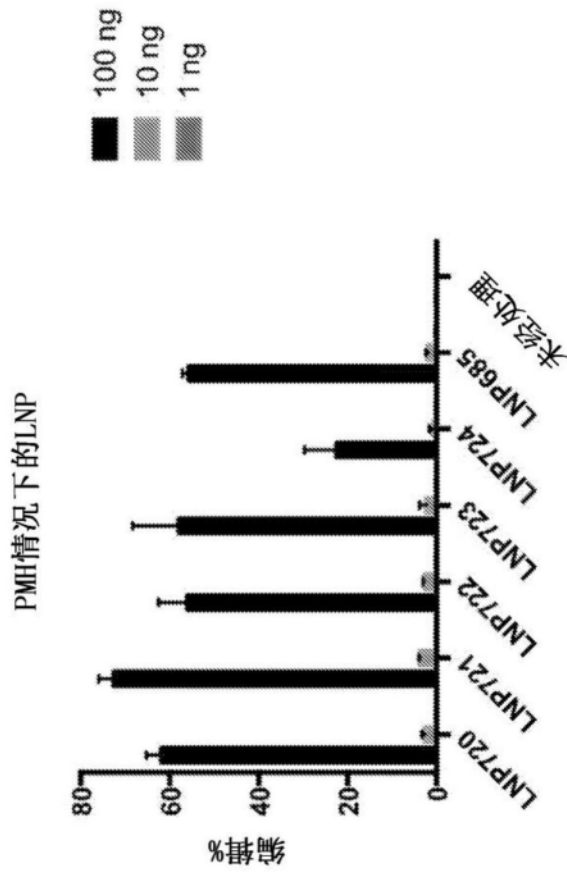


图10

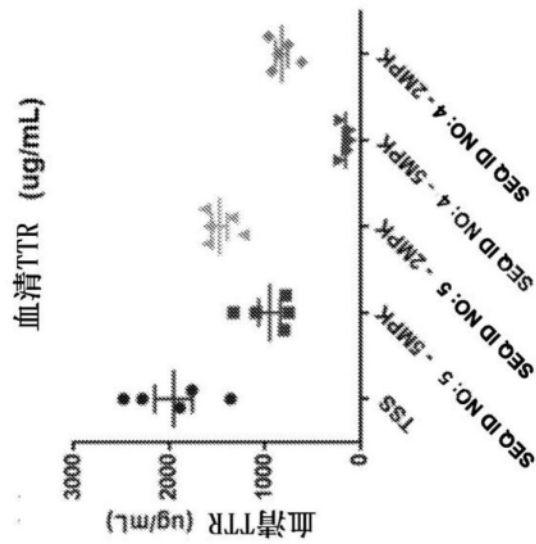


图11A

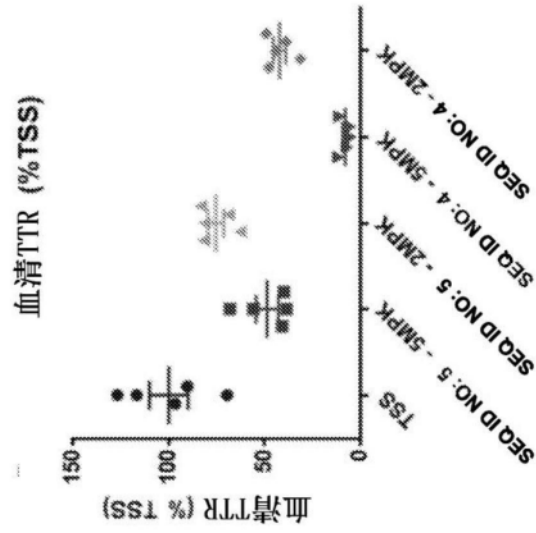


图11B

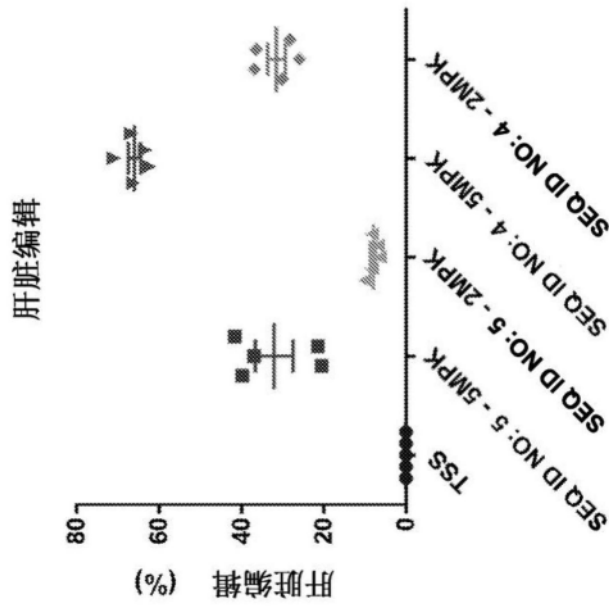


图12

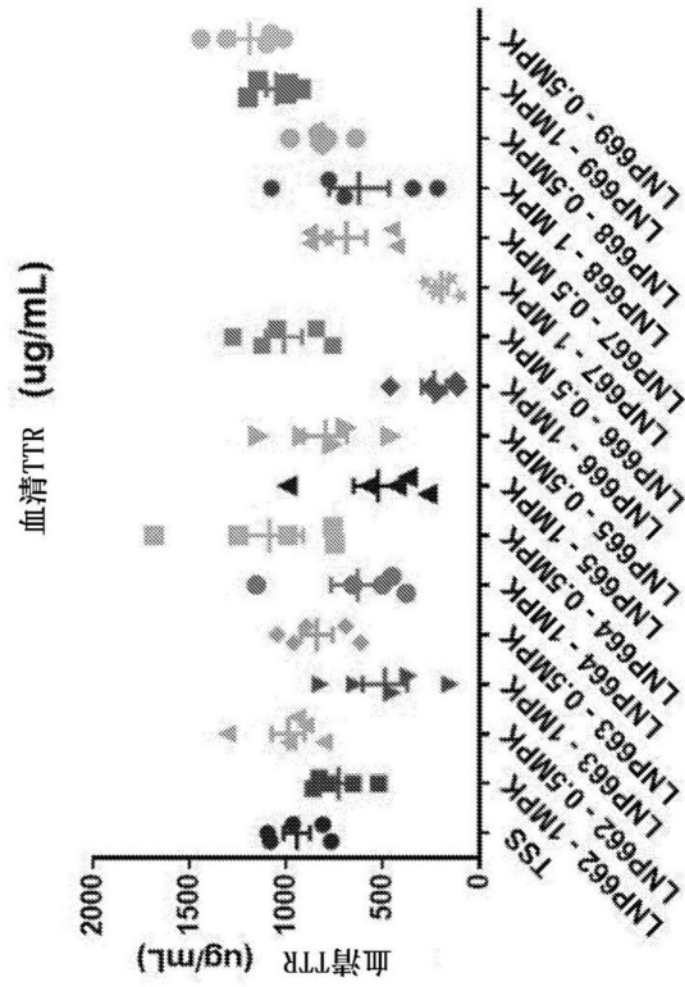


图13A

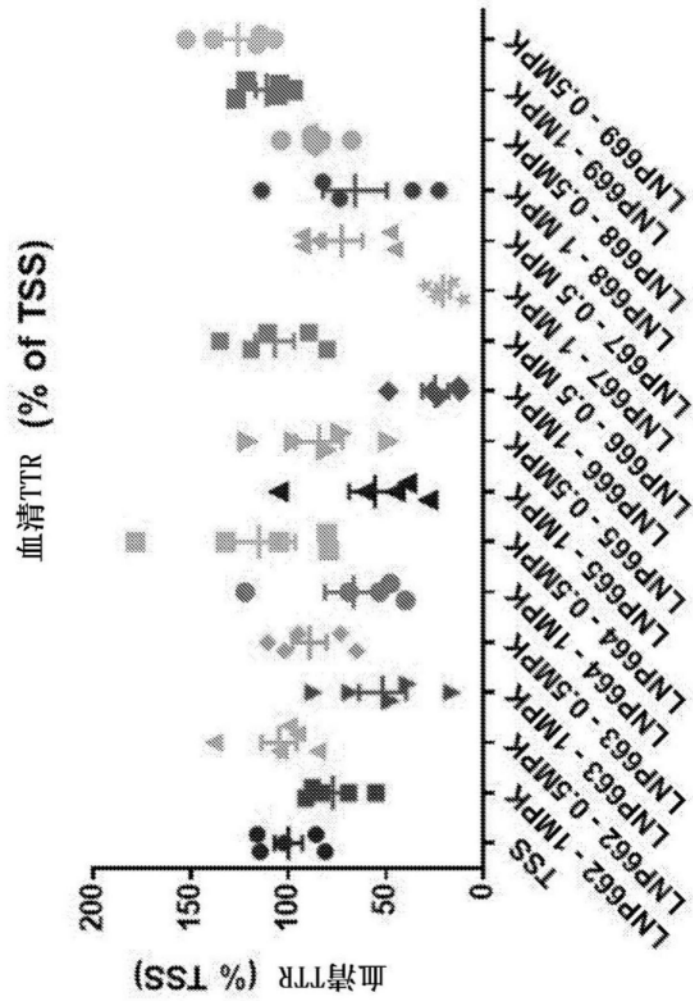


图13B

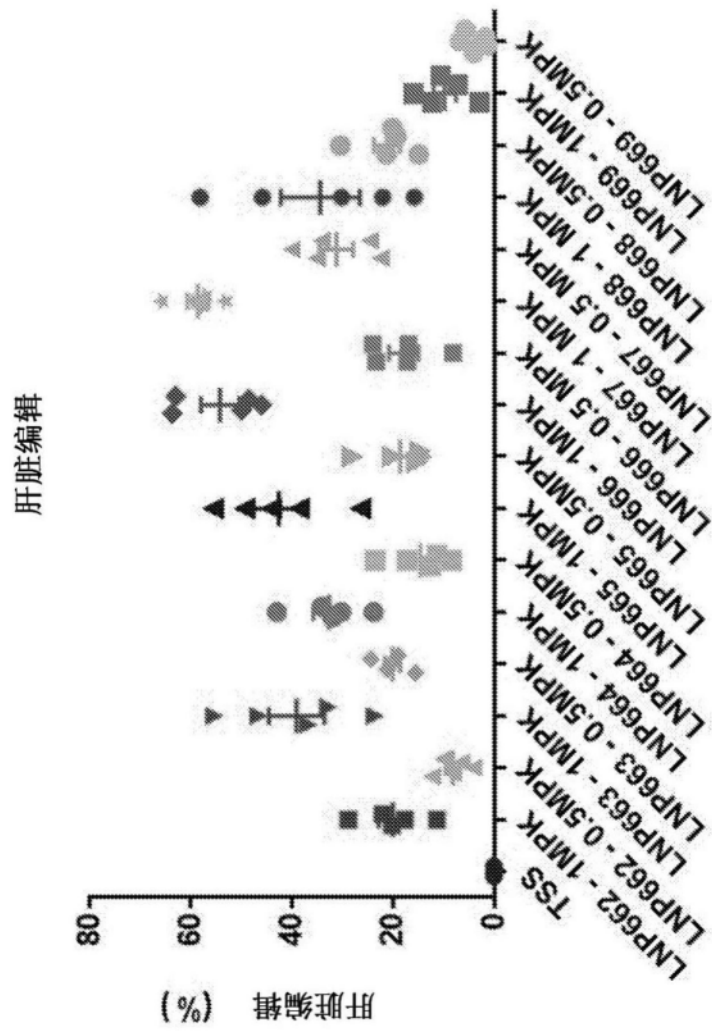


图13C

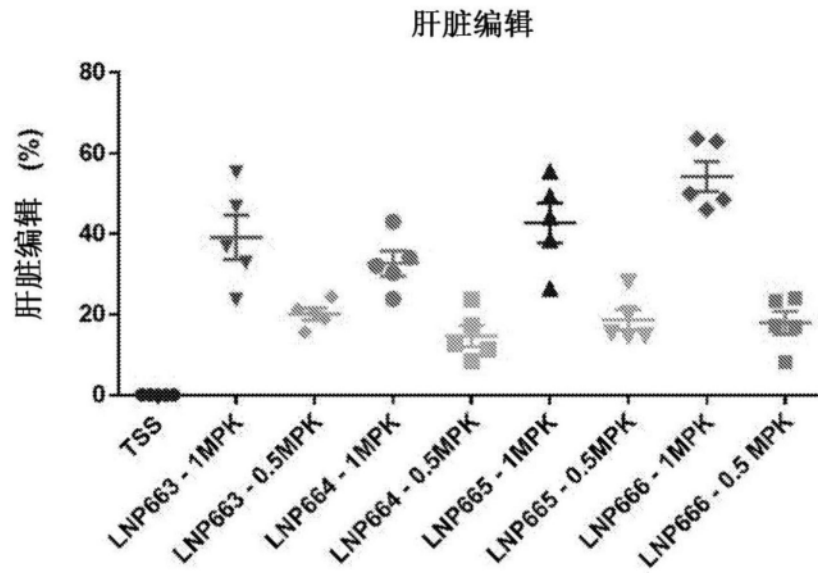


图13D

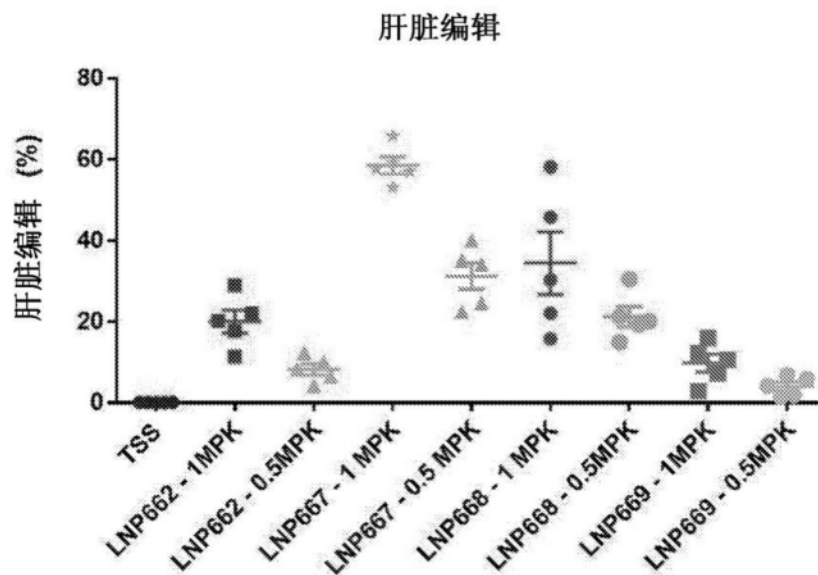


图13E

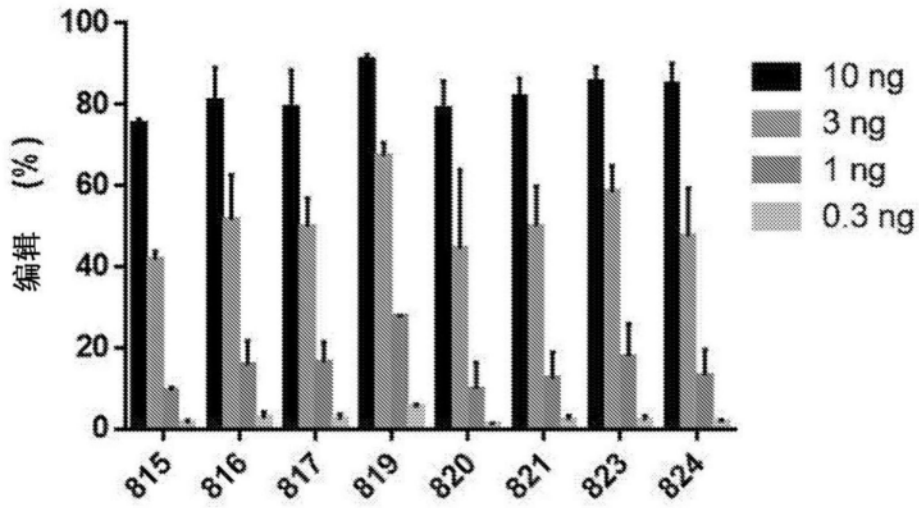


图14

血清TTR含量- SEQ ID NO:5

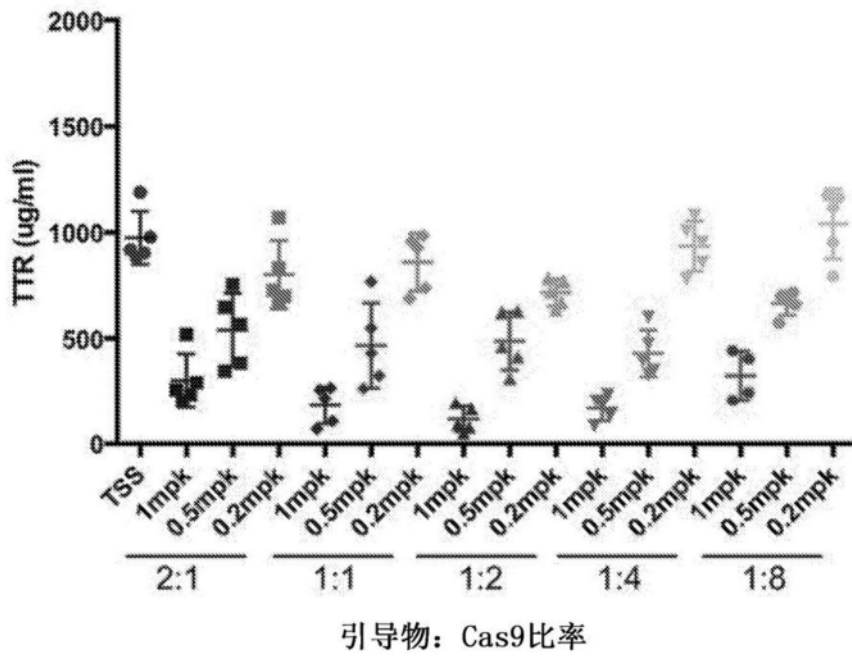


图15A

血清TTR含量- SEQ ID NO:4

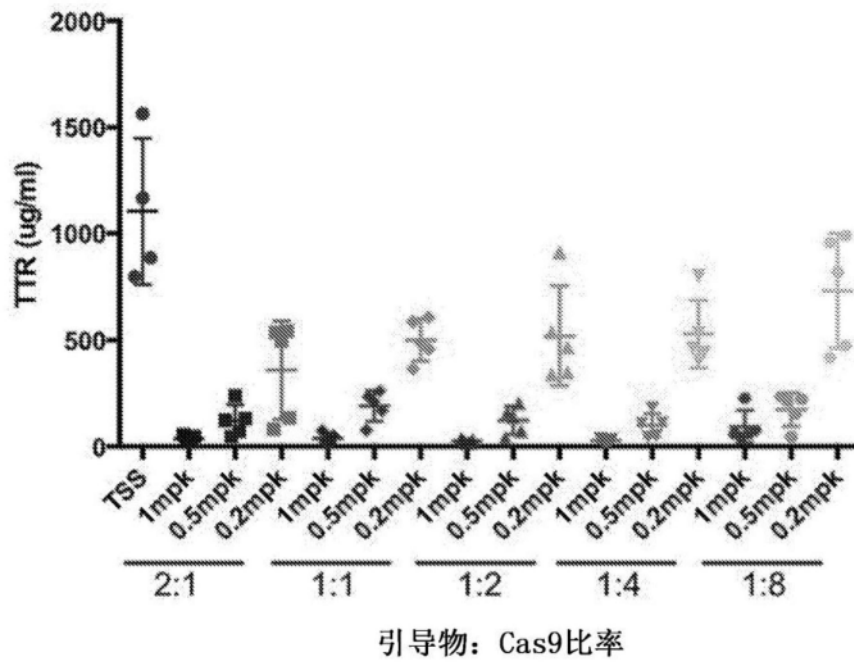


图15B

肝脏编辑- SEQ ID NO:5

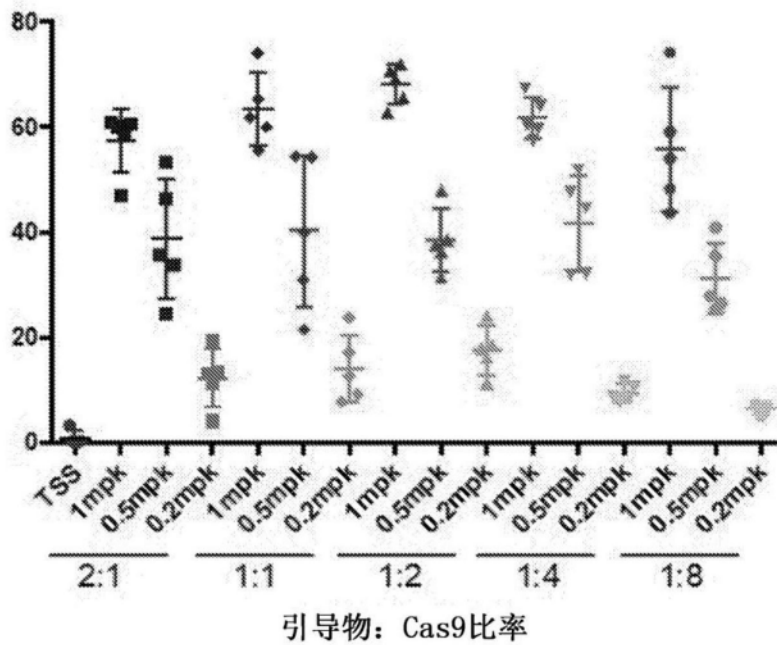


图16A

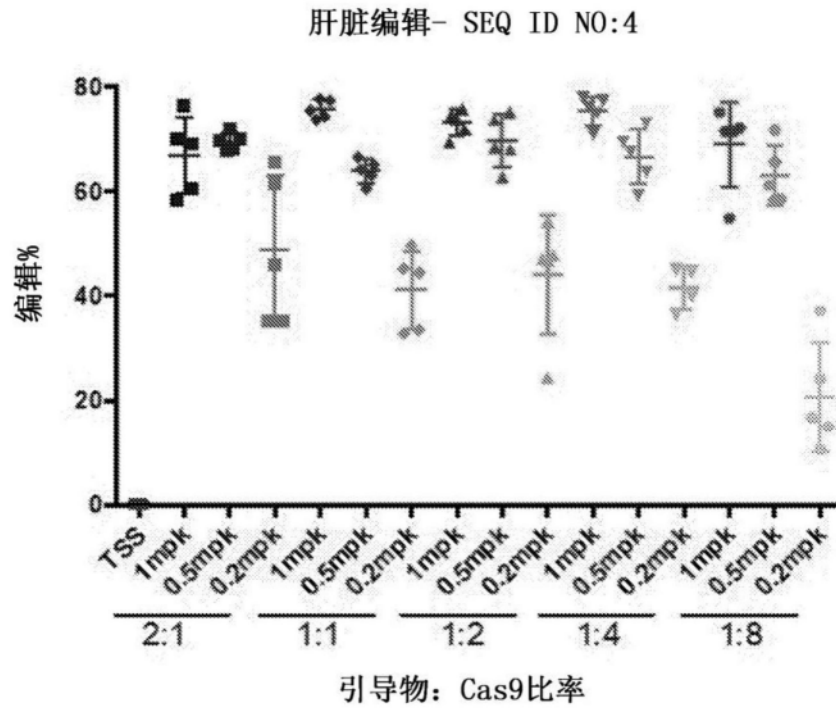


图16B

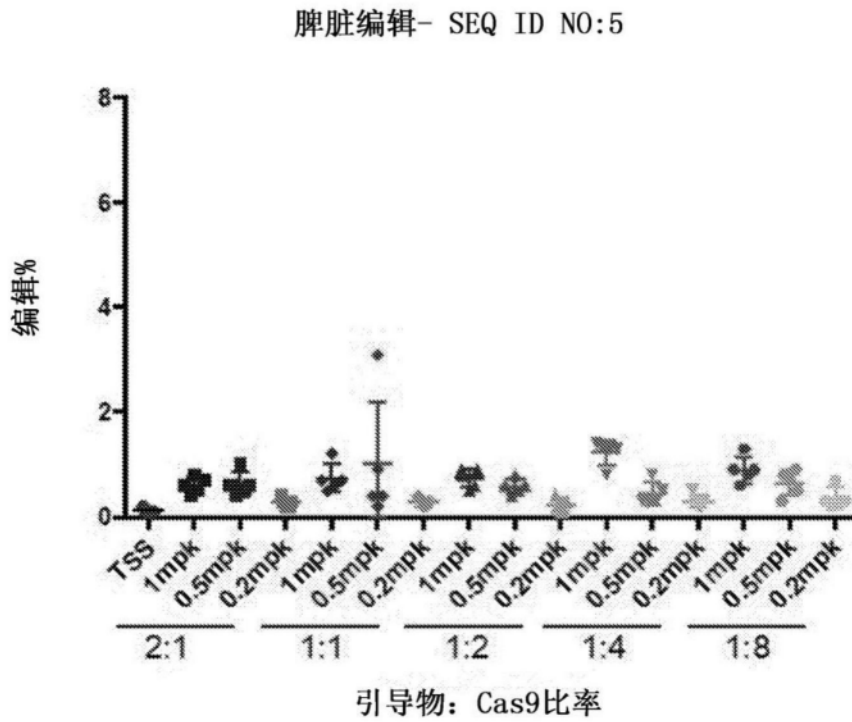


图17A

脾脏编辑- SEQ ID NO:4

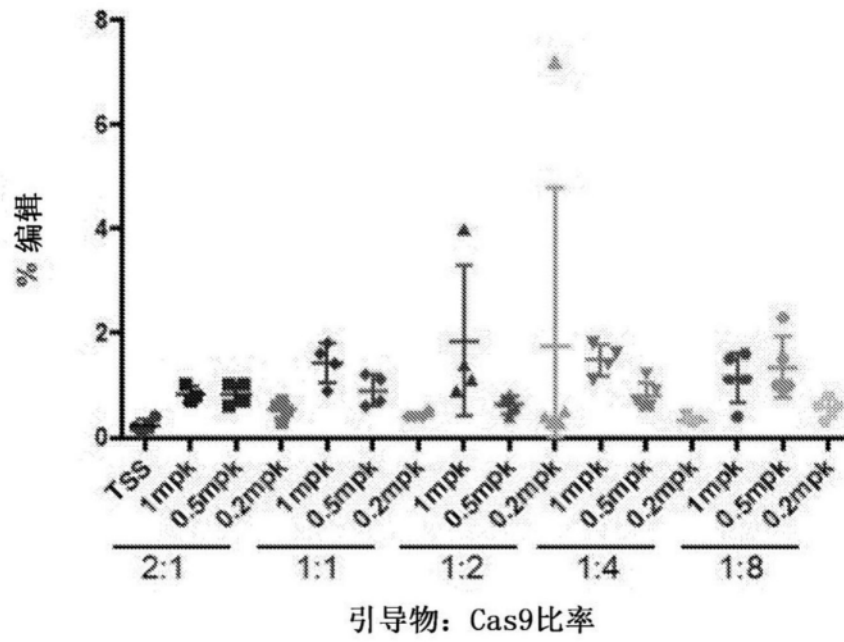


图17B

SEQ ID NO: 5 | SEQ ID NO: 4 | WT
1:1 | 4:1 | 1:1 | 4:1

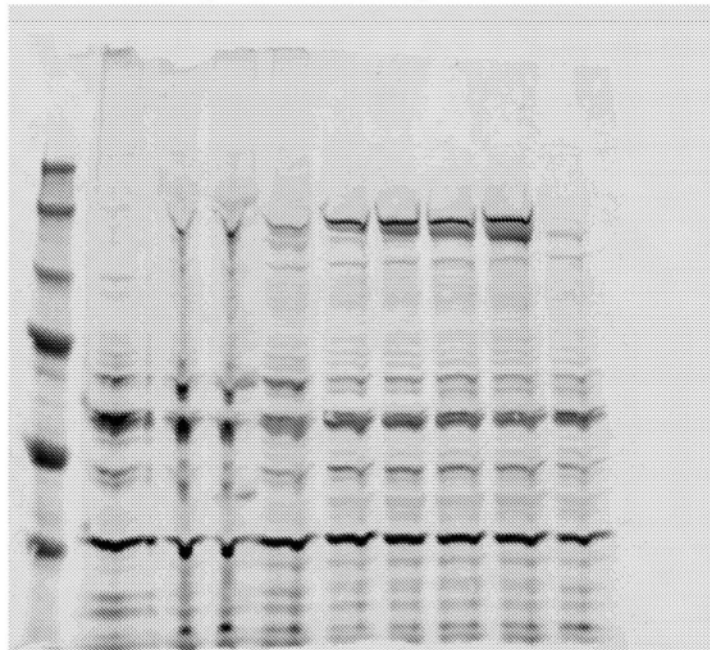


图18

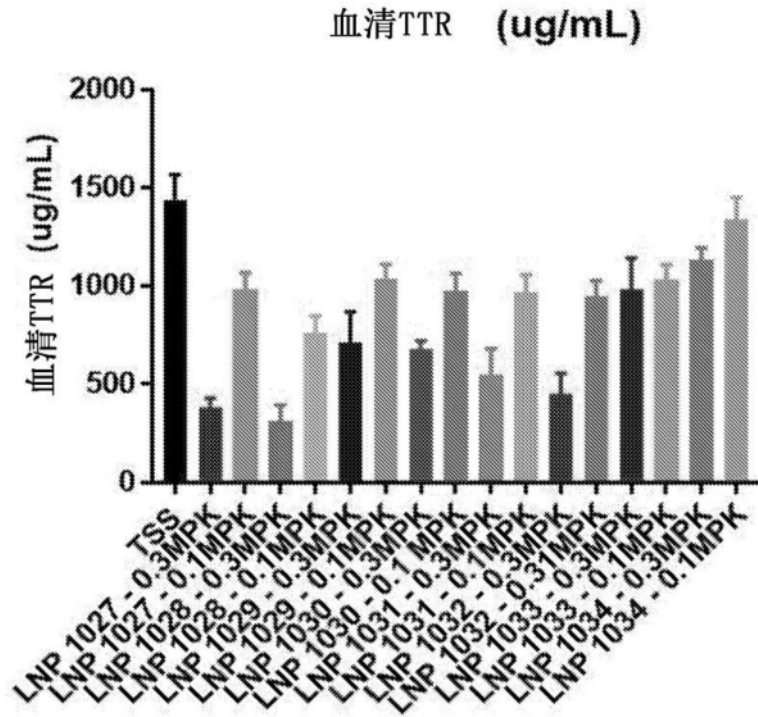


图19A

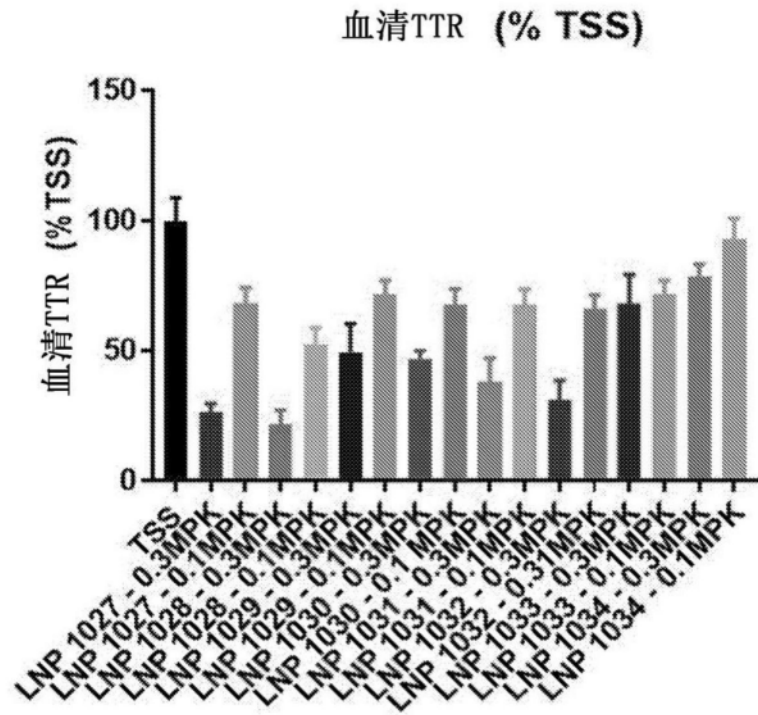


图19B

肝脏编辑

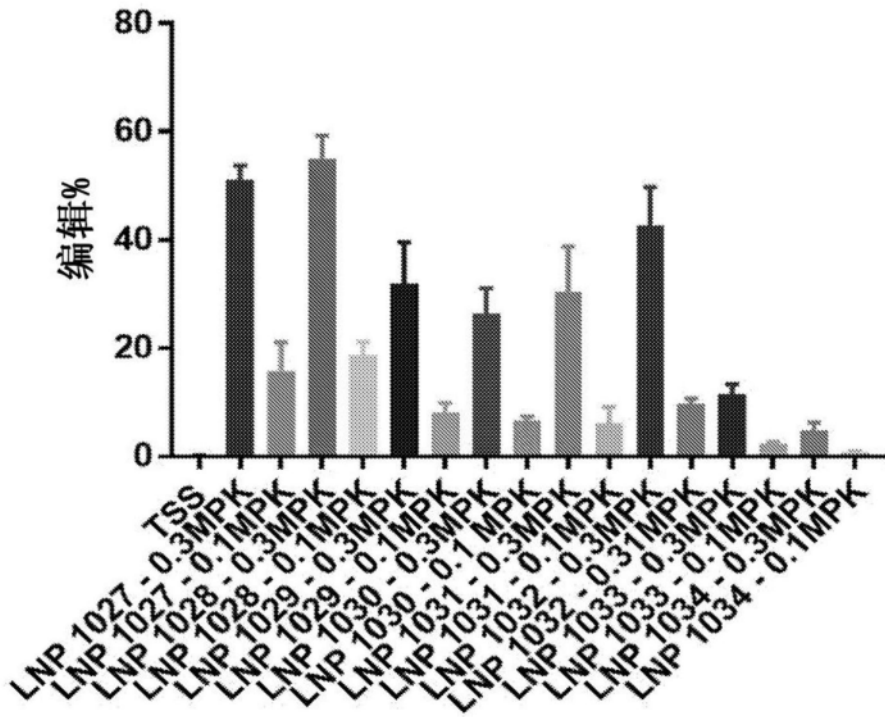


图20

肝脏编辑

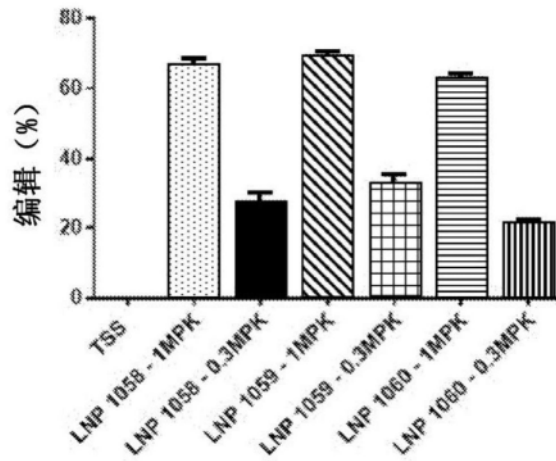


图21A

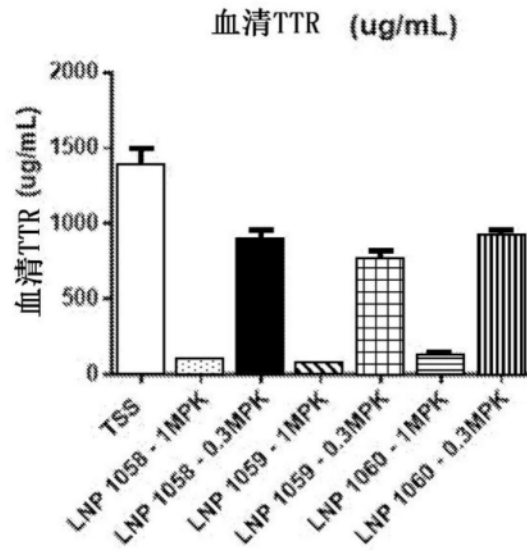


图21B

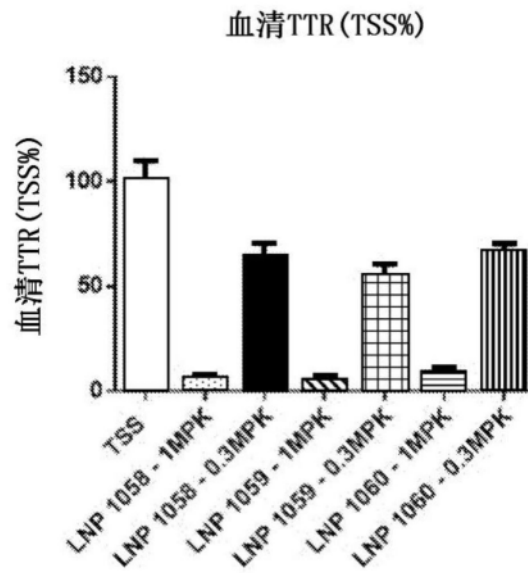


图21C

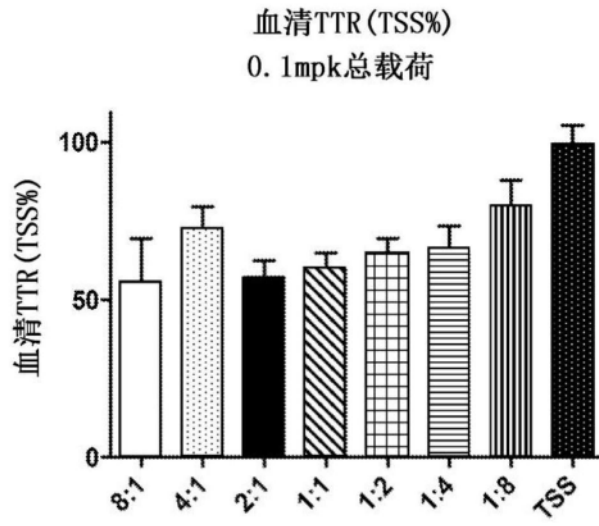


图22A

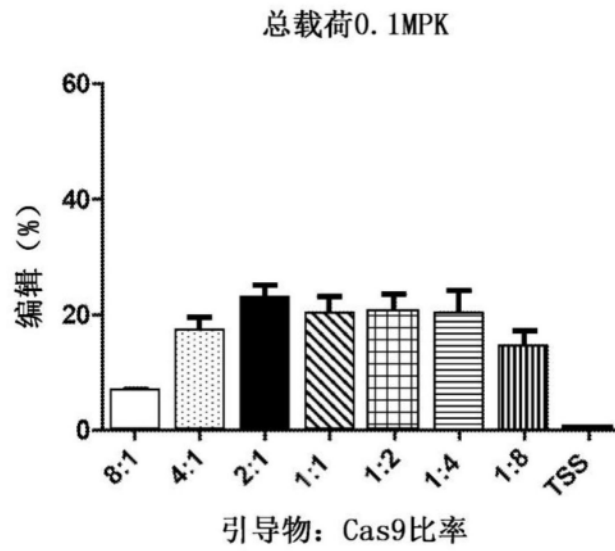


图22B

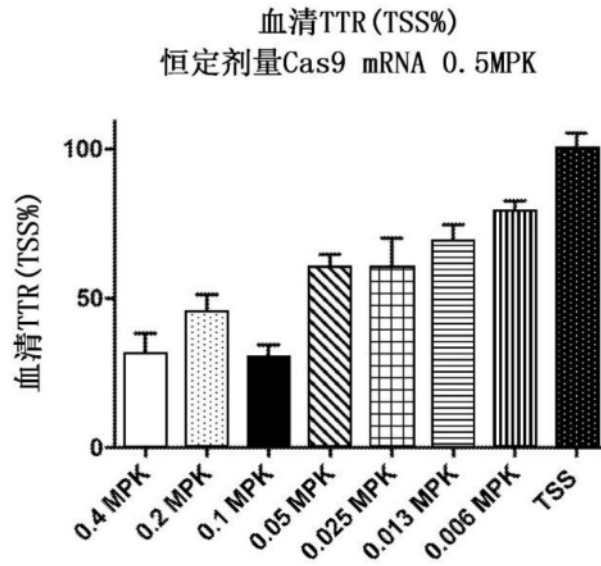


图22C

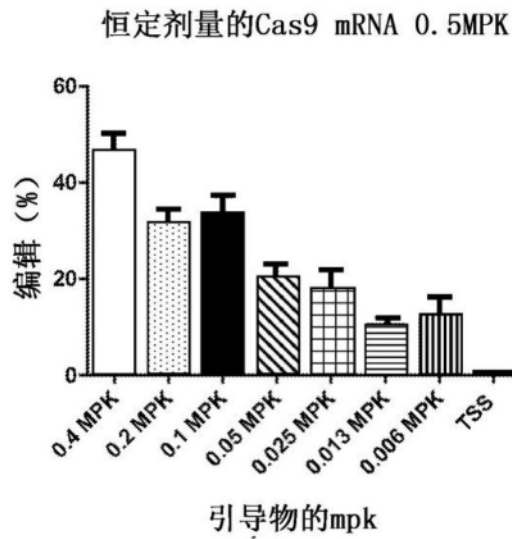


图22D

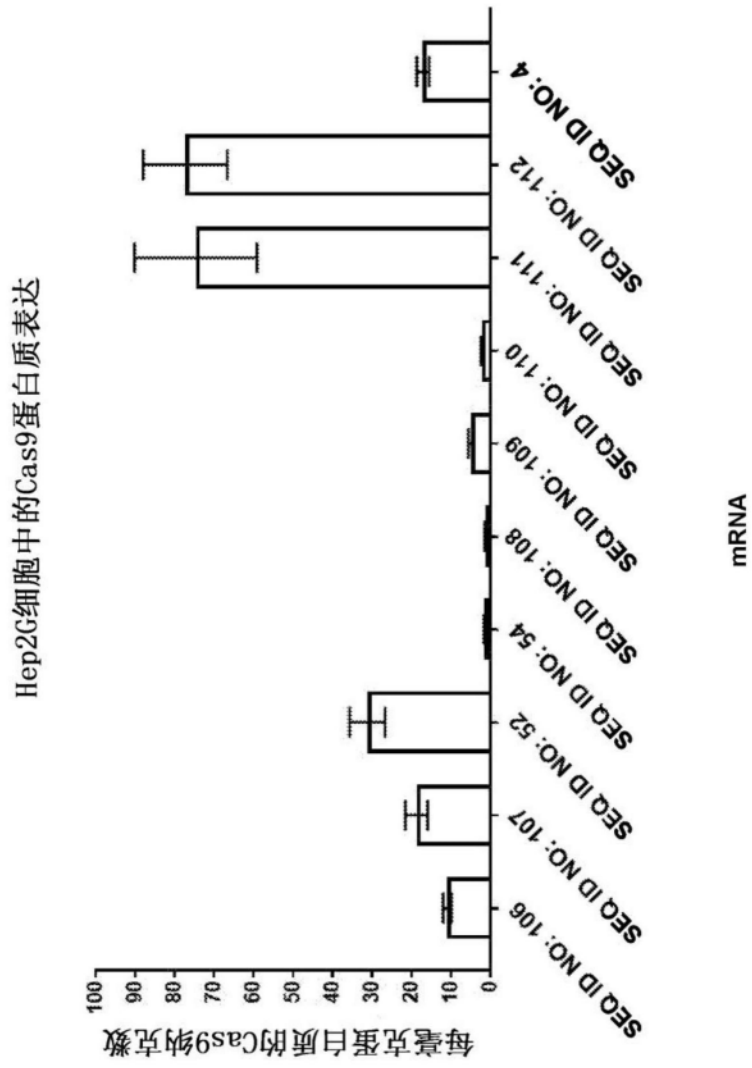


图23

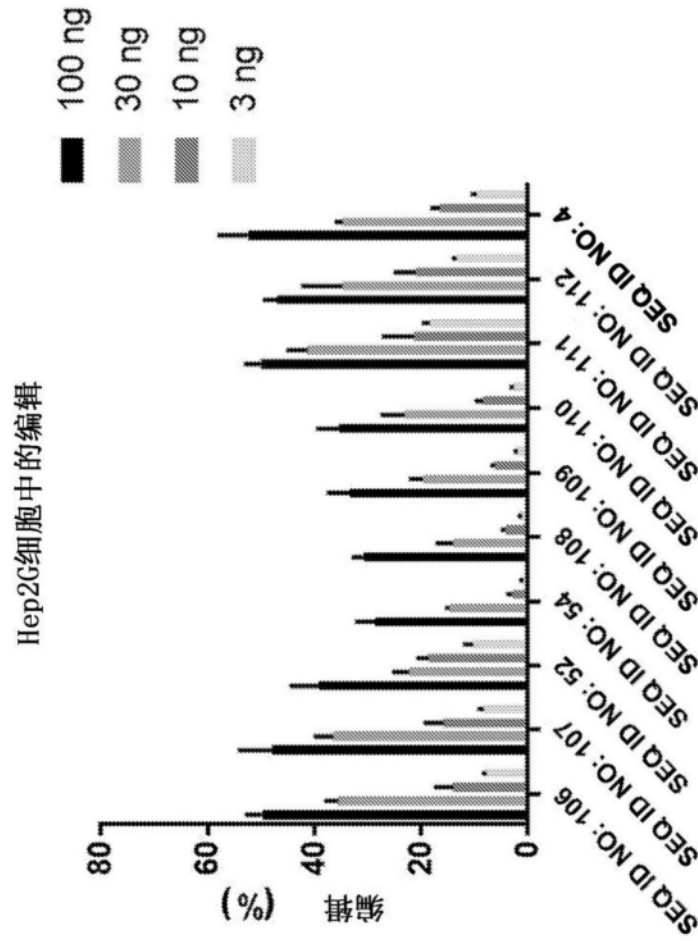


图24

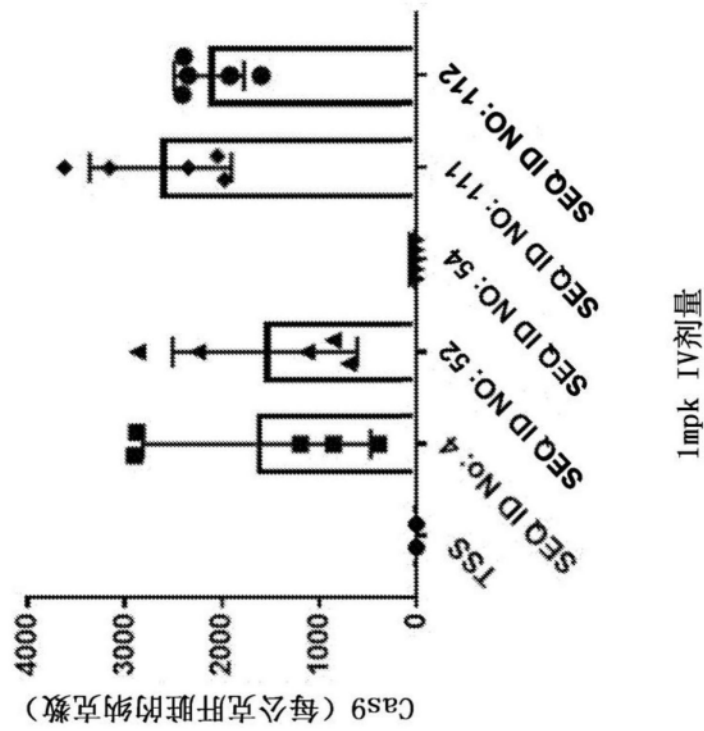


图25

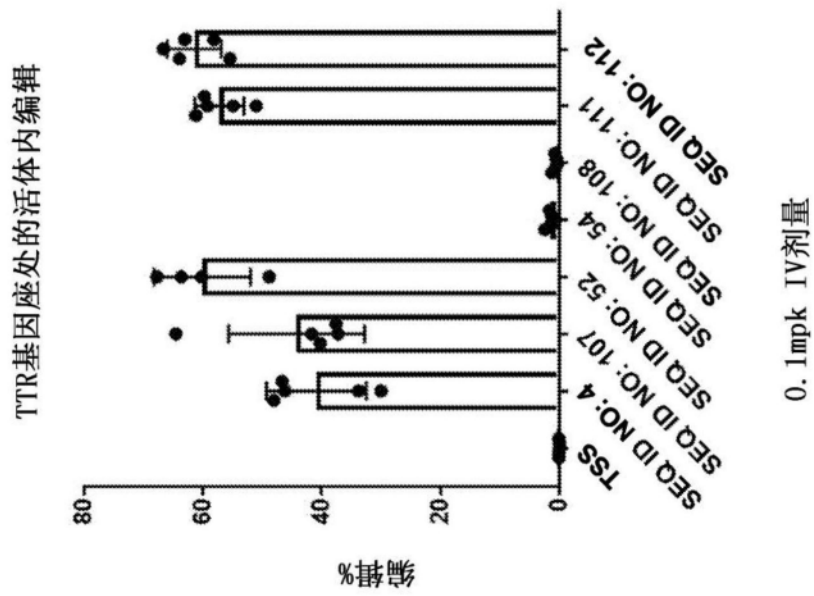


图26

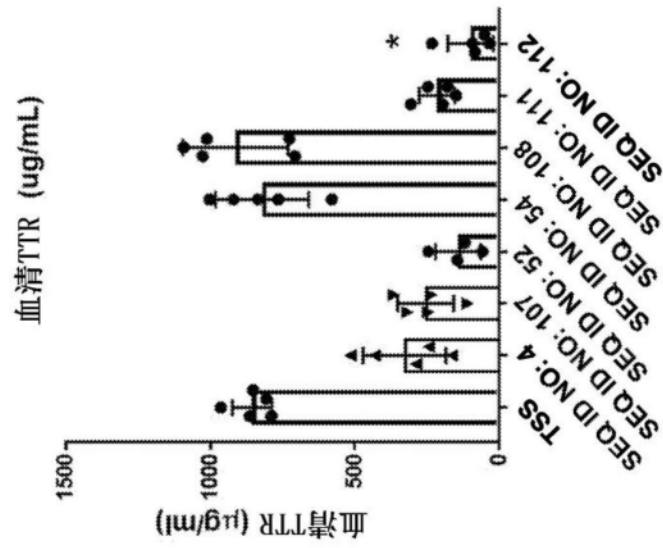


图27A

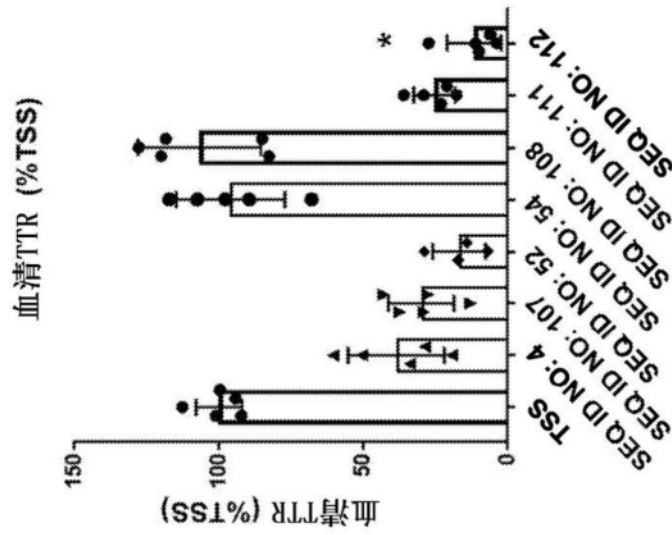


图27B

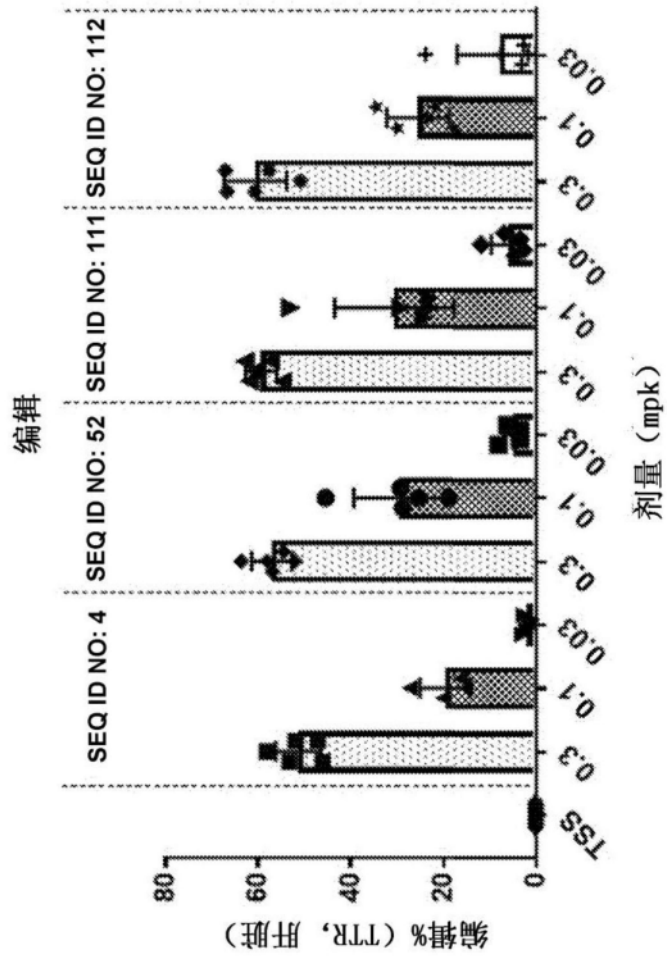


图28

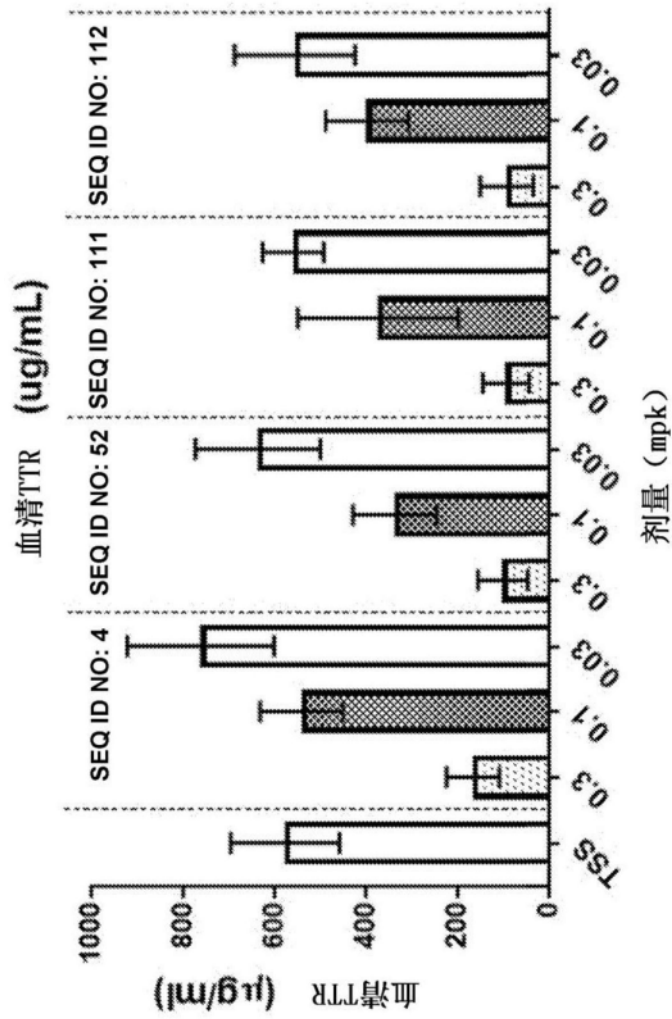


图29A

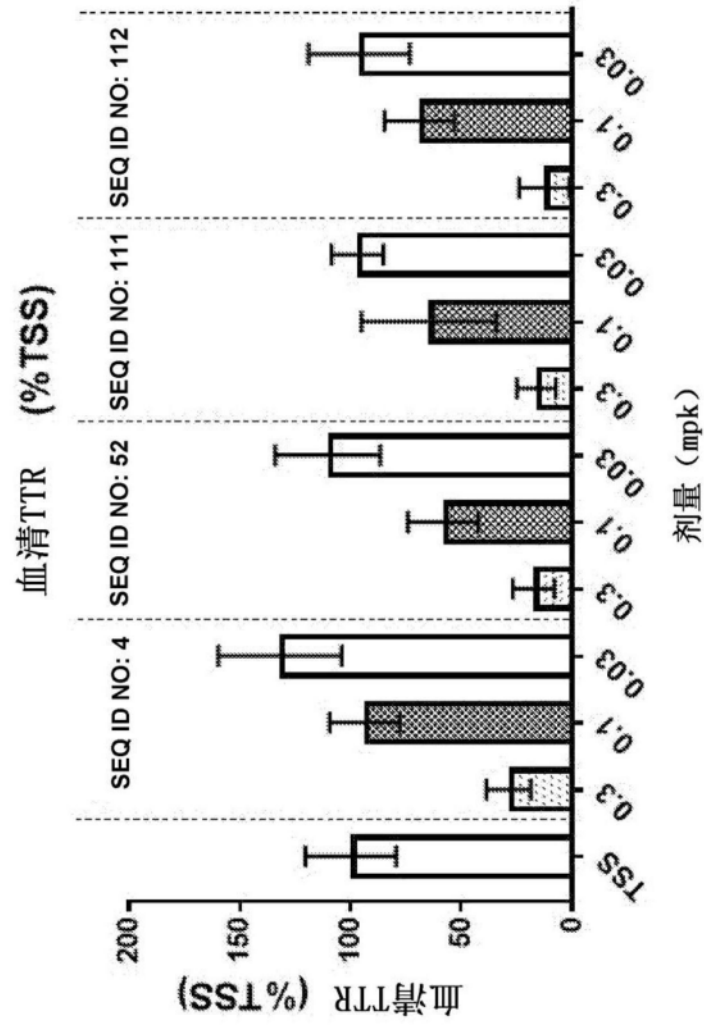


图29B

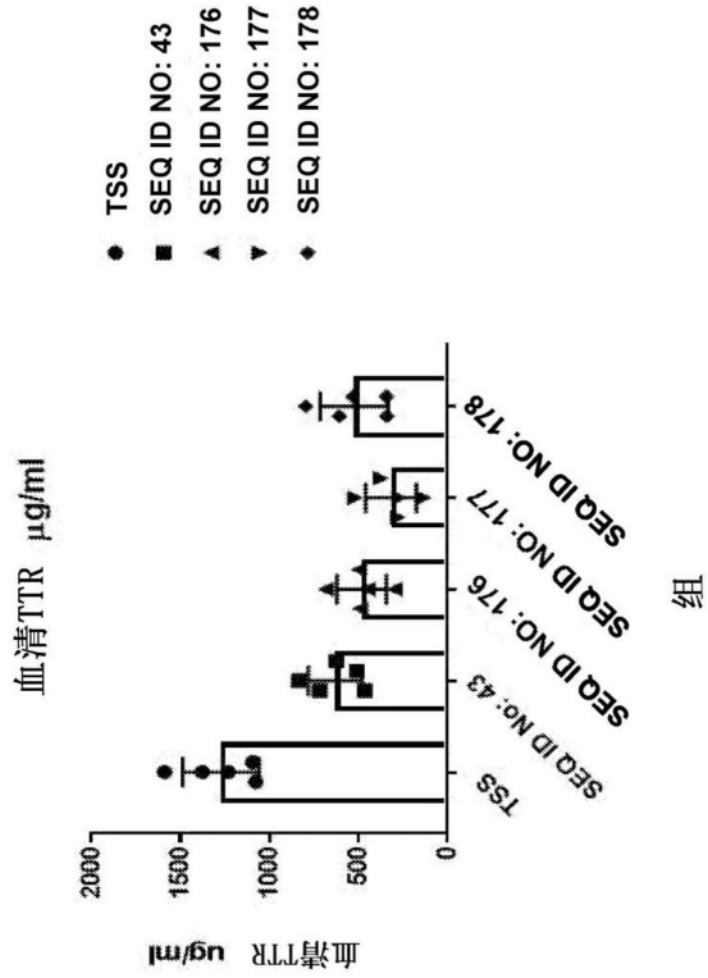


图30A

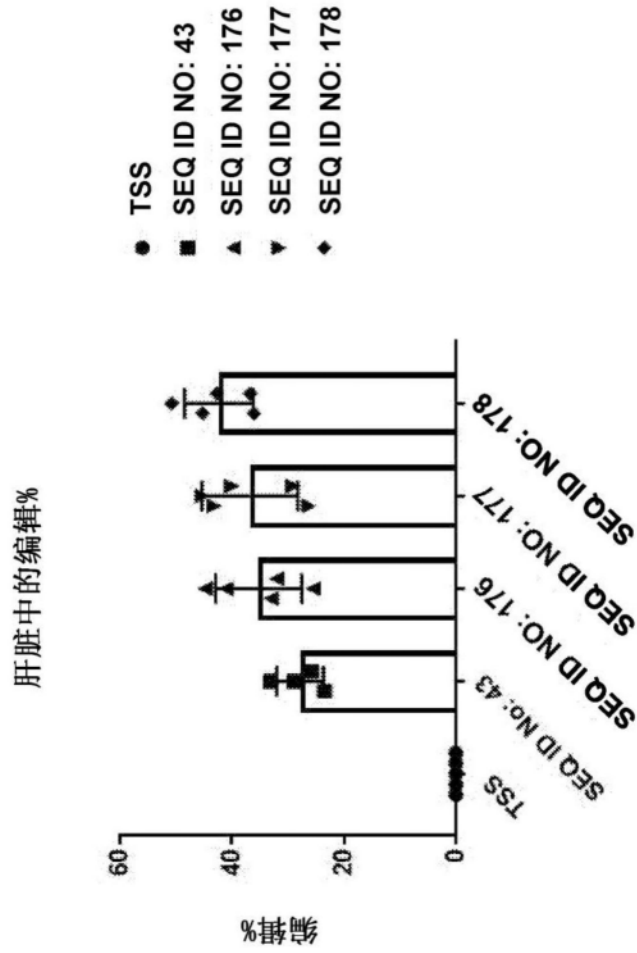


图30B

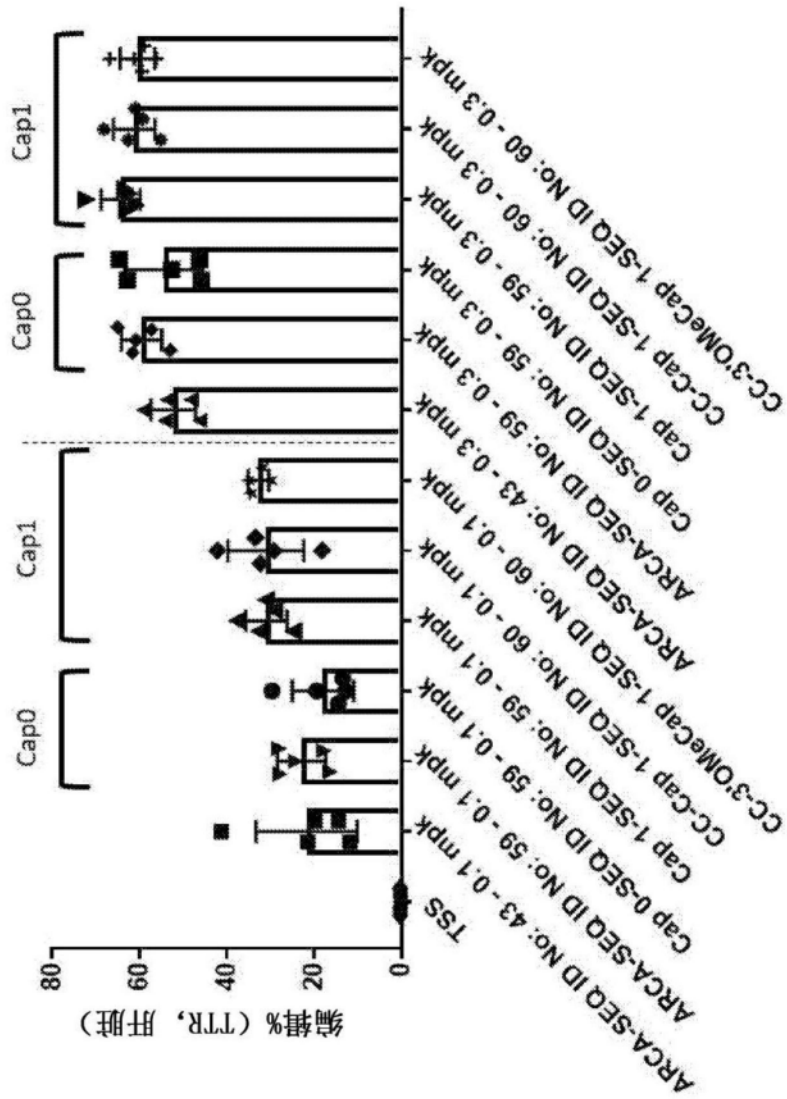


图31

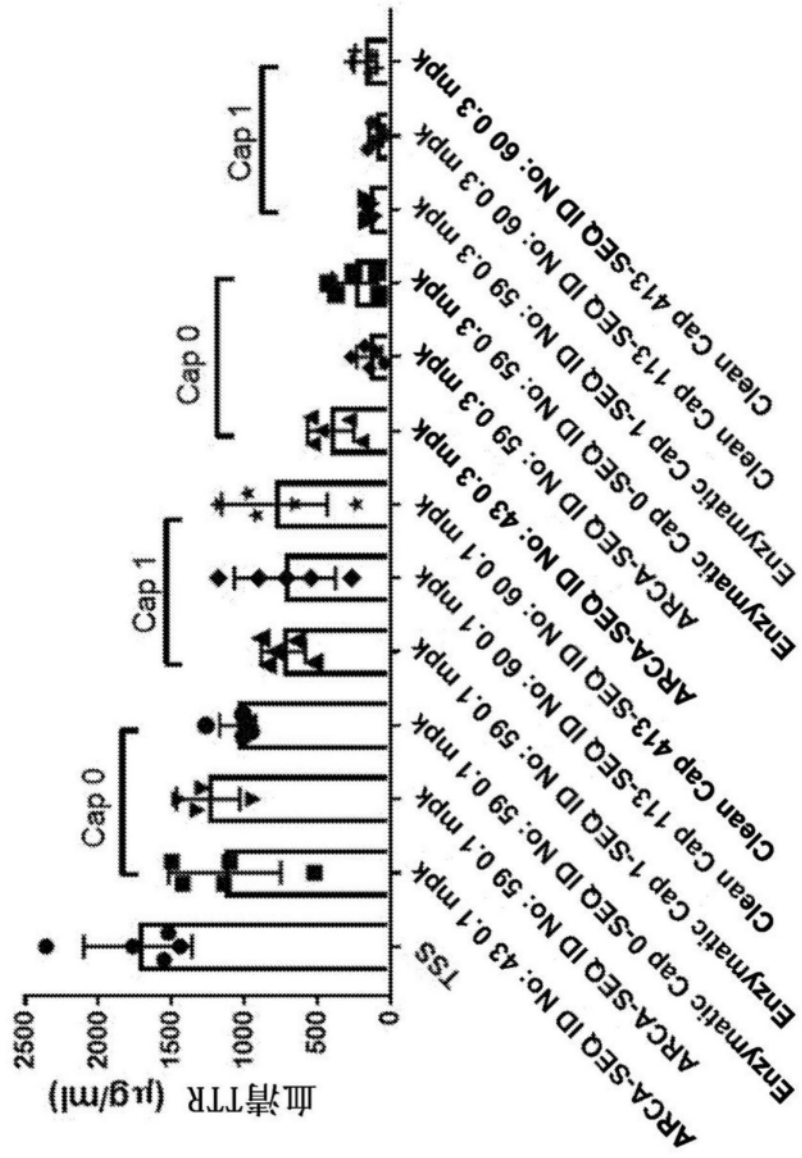


图32

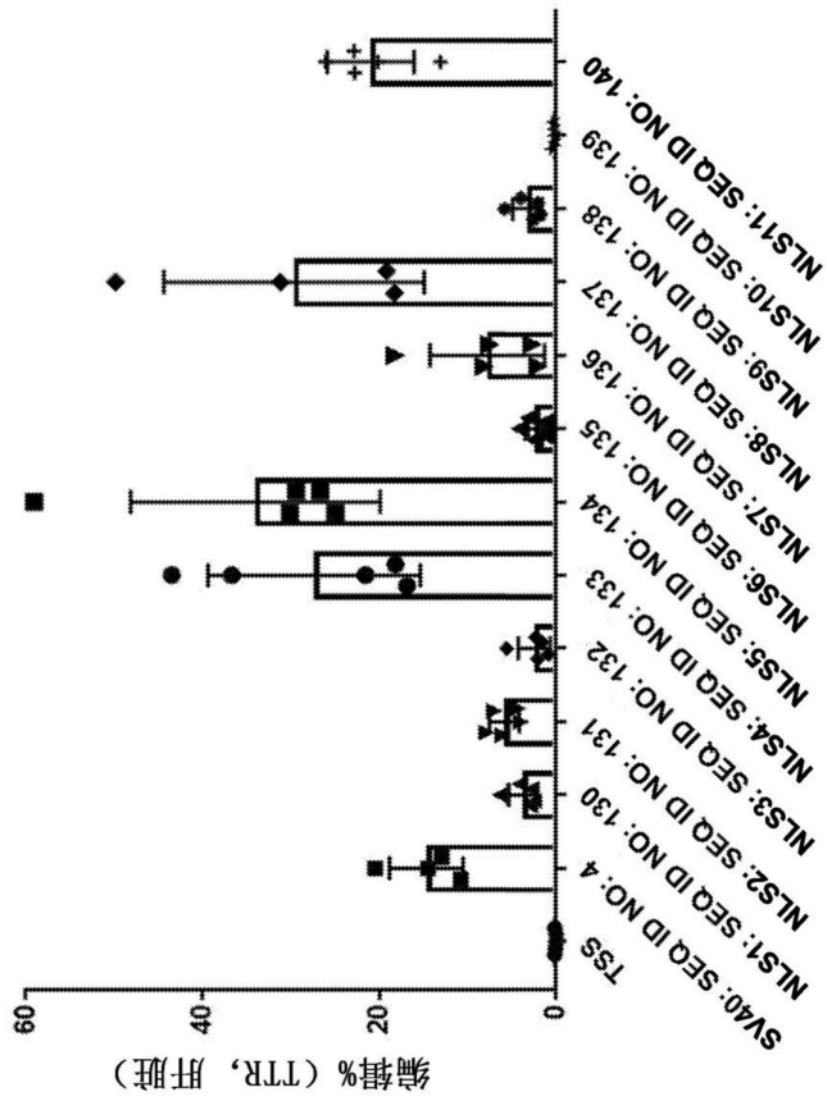


图33

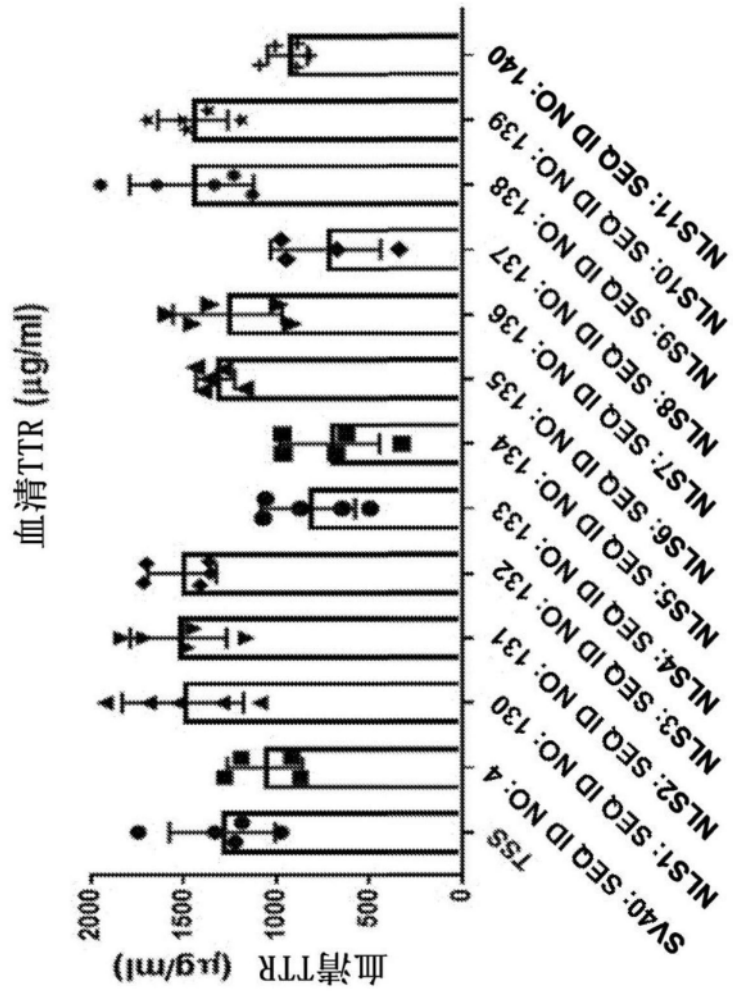


图34A

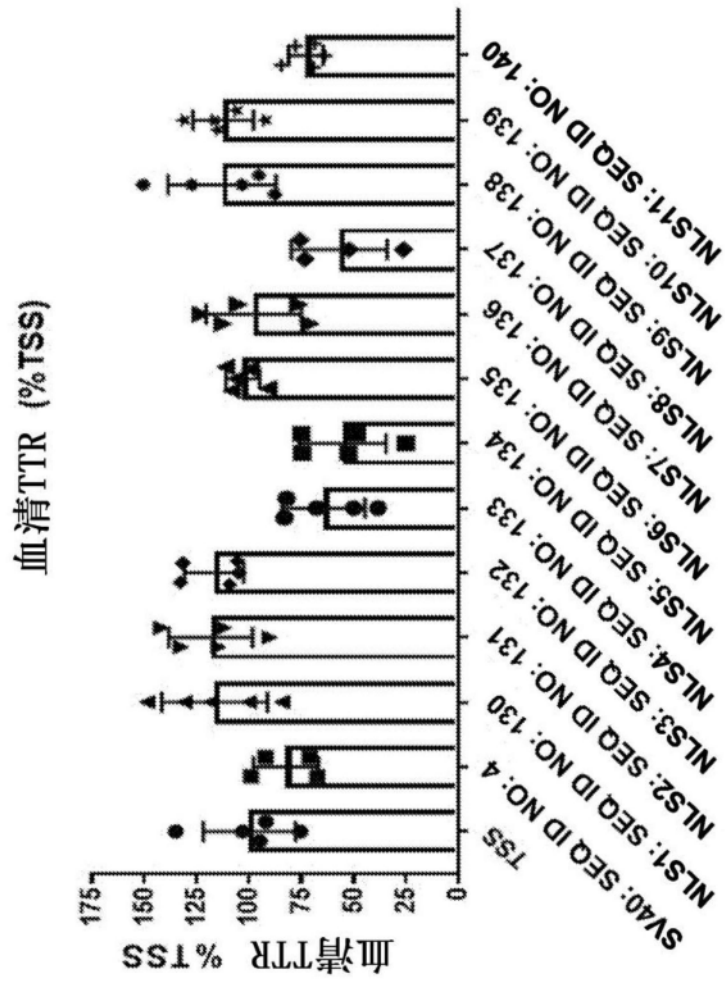


图34B

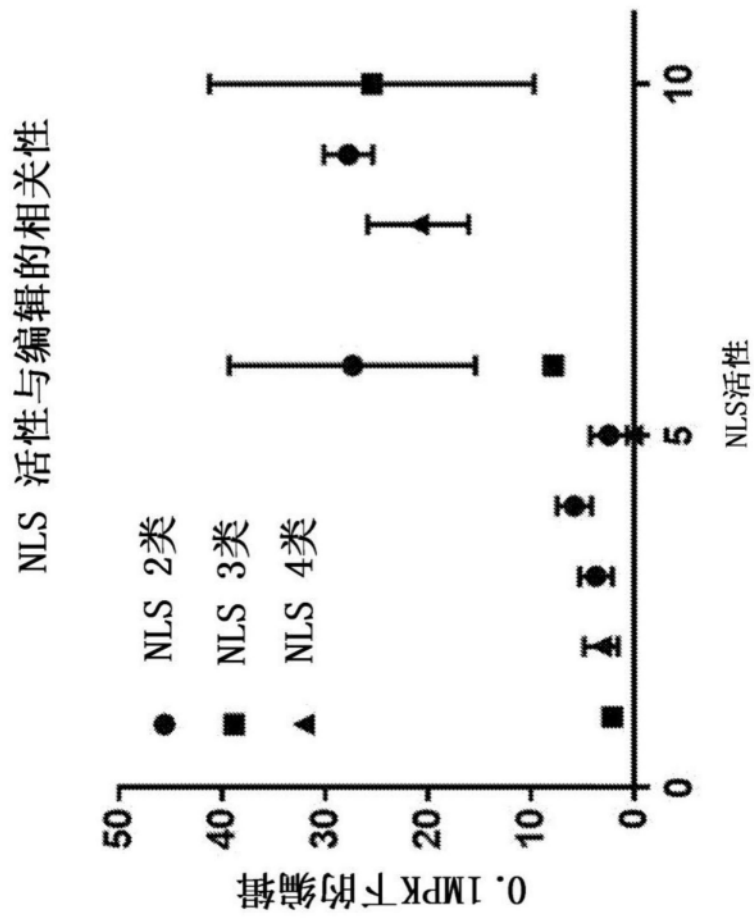


图35

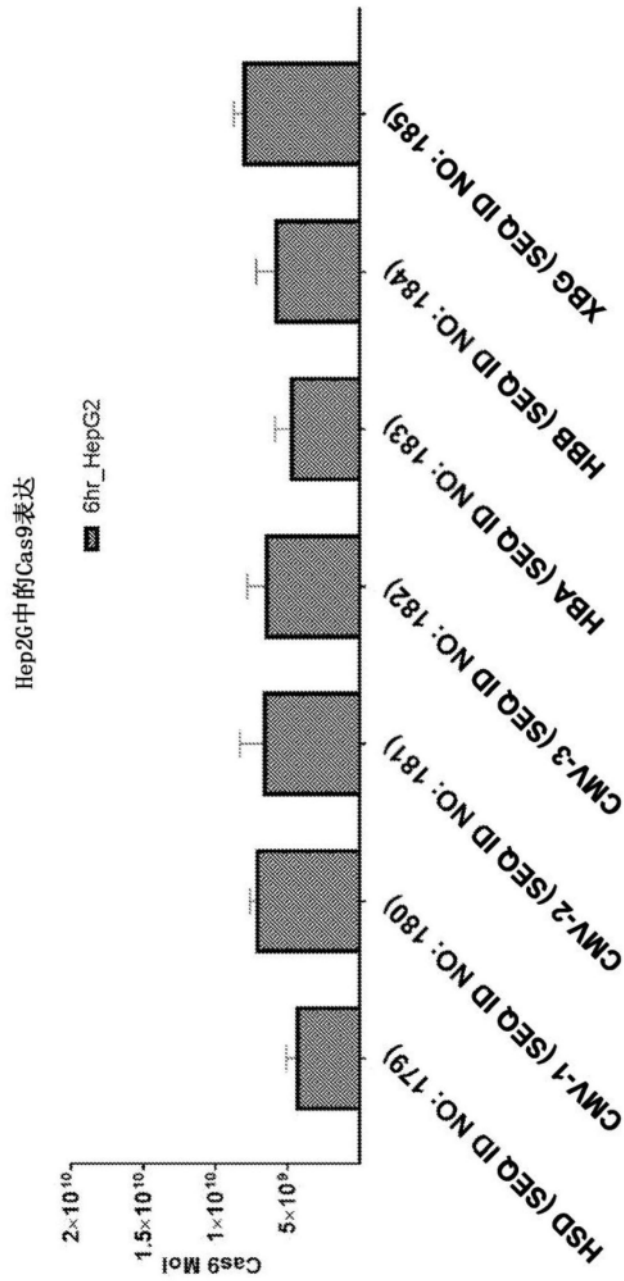


图36