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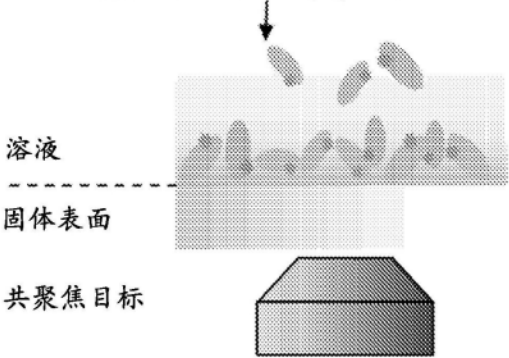
(54) 发明名称

用于在低蛋白浓度下使蛋白损失最小化的组合物和方法

(57) 摘要

本发明涉及用于在低蛋白浓度下使蛋白损失(例如,由于吸附到固体表面)最小化的组合物和方法。本文披露的发明总体上涉及包含蛋白的组合物、特别是包含低蛋白浓度的治疗性蛋白的药物组合物的领域。本文披露的发明还涉及向有需要的受试者施用该组合物的方法。

用于测量蛋白与固体表面结合的测定的示意图
荧光团标记的双特异性抗体



1. 一种水性组合物, 该水性组合物包含浓度介于约0.001 μ g/ml与约100 μ g/ml之间的双特异性抗体构建体以及浓度为表面活性剂的临界胶束浓度(CMC)的至少约0.25倍的该表面活性剂, 其中该双特异性抗体构建体包含与靶细胞表面抗原结合的第一结合结构域、与T细胞表面上的人CD3结合的第二结合结构域, 以及任选地按氨基到羧基的顺序包含铰链-CH2结构域-CH3结构域-接头-铰链-CH2结构域-CH3结构域的第三结构域, 其中该第二结合结构域包含具有SEQ ID NO:201的序列的多肽。

2. 如权利要求1所述的组合物, 其中该双特异性抗体构建体以介于约0.001 μ g/ml与约50 μ g/ml之间的浓度存在。

3. 如权利要求1或2所述的组合物, 其中该双特异性抗体构建体以介于约0.01 μ g/ml至约50 μ g/ml之间、或介于0.1 μ g/ml至约50 μ g/ml、或0.1 μ g/ml至约10 μ g/ml、或1 μ g/ml至约10 μ g/ml之间的浓度存在。

4. 如权利要求1-3中任一项所述的组合物, 其中该表面活性剂是聚山梨醇酯、泊洛沙姆或曲拉通x-100。

5. 如权利要求1-4中任一项所述的组合物, 其中该表面活性剂是聚山梨醇酯80、聚山梨醇酯60、聚山梨醇酯40、聚山梨醇酯20或曲拉通X-100。

6. 如权利要求1-4中任一项所述的组合物, 其中该表面活性剂是泊洛沙姆188或泊洛沙姆407。

7. 如权利要求1-6中任一项所述的组合物, 其中该表面活性剂以介于该表面活性剂的该CMC的约0.25倍与约20倍之间、或介于该CMC的约0.25倍与约10倍之间的浓度存在。

8. 如权利要求1-7中任一项所述的组合物, 其中该组合物进一步包含盐、氨基酸、糖类或糖类衍生物或它们的组合。

9. 如权利要求8所述的组合物, 其中该组合物进一步包含缓冲剂或防腐剂。

10. 如权利要求8或9所述的组合物, 其中该组合物的pH介于约3.5与约7.5之间。

11. 如权利要求10所述的组合物, 其中该组合物的pH介于约4.2与约7.0之间。

12. 如权利要求8-11中任一项所述的组合物, 其中该盐是NaCl。

13. 如权利要求8-12中任一项所述的组合物, 其中该糖类或糖类衍生物是单糖、二糖、环状多糖或糖醇。

14. 如权利要求8-13所述的组合物, 其中该糖类是蔗糖、海藻糖、甘露糖醇或山梨糖醇。

15. 如权利要求8-14中任一项所述的组合物, 其中该氨基酸是赖氨酸。

16. 如权利要求9-15中任一项所述的组合物, 其中该缓冲剂是乙酸盐缓冲剂、谷氨酸盐缓冲剂、柠檬酸盐缓冲剂、琥珀酸盐缓冲剂、酒石酸盐缓冲剂、富马酸盐缓冲剂、马来酸盐缓冲剂、组氨酸缓冲剂或磷酸盐缓冲剂。

17. 如权利要求1-16中任一项所述的组合物, 其中该双特异性抗体构建体的该第一结合结构域和该第二结合结构域中的每一者包含VH区和VL区。

18. 如权利要求1-17中任一项所述的组合物, 其中该双特异性抗体构建体是单链抗体构建体。

19. 如权利要求1-18中任一项所述的组合物, 其中该双特异性抗体构建体包含具有选自SEQ ID NO:11、SEQ ID NO:13、SEQ ID NO:15、SEQ ID NO:24、SEQ ID NO:25、SEQ ID NO:47、SEQ ID NO:48、SEQ ID NO:66、SEQ ID NO:67、SEQ ID NO:76、SEQ ID NO:78、SEQ ID

NO:87、SEQ ID NO:88、SEQ ID NO:108、SEQ ID NO:109、SEQ ID NO:110、SEQ ID NO:165、SEQ ID NO:166、SEQ ID NO:167、SEQ ID NO:176、SEQ ID NO:178和SEQ ID NO:192的氨基酸序列的多肽。

20. 如权利要求1-19中任一项所述的组合物,其中该组合物是药物组合物。

21. 如权利要求1-20中任一项所述的组合物,其中该组合物容纳在塑料容器中。

22. 如权利要求21所述的组合物,其中该容器由包含聚烯烃、PVC、EVA或聚氨酯的材料制成。

23. 如权利要求22所述的组合物,其中该容器由包含PVC的材料制成,并且其中该PVC基本上不含DEHP或TOTM。

24. 如权利要求21-23中任一项所述的组合物,其中该容器是IV袋或IV管。

25. 一种包含容纳在容器内的水性药物组合物的药物制剂,其中该水性药物组合物包含:

a) 浓度介于约0.001 μ g/ml与约100 μ g/ml之间的双特异性抗体构建体,以及

b) 浓度为表面活性剂的CMC的至少约0.25倍的该表面活性剂,其中该表面活性剂具有至少20的HLB值。

26. 如权利要求25所述的药物制剂,其中该水性药物组合物包含浓度介于约0.001 μ g/ml与约50 μ g/ml之间的该双特异性抗体构建体。

27. 如权利要求25或26所述的药物制剂,其中该水性药物组合物包含浓度介于该表面活性剂的该CMC的约0.25倍与约20倍之间、或介于该CMC的约0.25倍与约10倍之间的该表面活性剂。

28. 如权利要求25-27中任一项所述的药物制剂,其中该水性药物组合物进一步包含盐、缓冲剂、氨基酸、糖类或糖类衍生物或它们的组合。

29. 如权利要求25-28中任一项所述的药物制剂,其中该水性药物组合物具有介于约4.2与约7.0之间的pH。

30. 如权利要求25-29中任一项所述的药物制剂,其中该容器由包含聚烯烃、PVC、EVA或聚氨酯的材料制成。

31. 如权利要求25-30中任一项所述的药物制剂,其中该双特异性抗体构建体包含具有选自SEQ ID NO:11、SEQ ID NO:13、SEQ ID NO:15、SEQ ID NO:24、SEQ ID NO:25、SEQ ID NO:47、SEQ ID NO:48、SEQ ID NO:66、SEQ ID NO:67、SEQ ID NO:76、SEQ ID NO:78、SEQ ID NO:87、SEQ ID NO:88、SEQ ID NO:108、SEQ ID NO:109、SEQ ID NO:110、SEQ ID NO:165、SEQ ID NO:166、SEQ ID NO:167、SEQ ID NO:176、SEQ ID NO:178和SEQ ID NO:192的氨基酸序列的多肽。

32. 一种向患者施用双特异性抗体构建体的方法,该方法包括:

a) 在容器中制备水性药物组合物,其中该水性药物组合物包含浓度介于约0.001 μ g/ml与约100 μ g/ml之间的该双特异性抗体构建体以及浓度为表面活性剂的CMC的至少约0.25倍的该表面活性剂,以及

b) 向该患者施用该水性药物组合物,

其中该双特异性抗体构建体包含具有选自SEQ ID NO:11、SEQ ID NO:13、SEQ ID NO:15、SEQ ID NO:24、SEQ ID NO:25、SEQ ID NO:47、SEQ ID NO:48、SEQ ID NO:66、SEQ ID

NO:67、SEQ ID NO:76、SEQ ID NO:78、SEQ ID NO:87、SEQ ID NO:88、SEQ ID NO:108、SEQ ID NO:109、SEQ ID NO:110、SEQ ID NO:165、SEQ ID NO:166、SEQ ID NO:167、SEQ ID NO:176、SEQ ID NO:178和SEQ ID NO:192的氨基酸序列的多肽。

33. 如权利要求32所述的方法,其中该水性药物组合物包含浓度介于约0.001 μ g/ml与约50 μ g/ml之间的该双特异性抗体构建体。

34. 如权利要求32或33所述的方法,其中该水性药物组合物包含浓度介于该表面活性剂的该CMC的约0.25倍与约20倍之间、或介于该CMC的约0.25倍与约10倍之间的该表面活性剂。

35. 如权利要求32-34中任一项所述的方法,其中该表面活性剂是聚山梨醇酯80、聚山梨醇酯60、聚山梨醇酯40、聚山梨醇酯20、泊洛沙姆188、泊洛沙姆407或曲拉通X-100。

36. 如权利要求32-35中任一项所述的方法,其中该水性药物组合物进一步包含选自盐、缓冲剂、氨基酸、糖类和防腐剂中的一种或多种。

37. 如权利要求32-36中任一项所述的方法,其中该水性药物组合物具有介于约4.2与约7.0之间的pH。

38. 如权利要求32-37中任一项所述的方法,其中该容器由包含聚烯烃、PVC、EVA或聚氨酯的材料制成。

39. 如权利要求32-38中任一项所述的方法,其中该表面活性剂是聚山梨醇酯80、聚山梨醇酯60、聚山梨醇酯40或聚山梨醇酯20,并且其中该容器由包含基本上不含DEHP或TOTM的PVC的材料制成。

40. 如权利要求32-39中任一项所述的方法,其中该水性药物组合物通过用合适的水性溶液稀释包含该双特异性抗体构建体的第一组合物来制备。

41. 如权利要求40所述的方法,其中该第一组合物是包含该双特异性抗体构建体的液体组合物。

42. 如权利要求40所述的方法,其中该第一组合物是由包含该双特异性抗体构建体的冻干组合物重构的液体组合物。

43. 如权利要求41-42中任一项所述的方法,其中该合适的溶液包含浓度为该表面活性剂的CMC的至少约0.25倍的该表面活性剂。

44. 如权利要求40-43中任一项所述的方法,其中该水性药物组合物通过将该合适的水性溶液添加到该容器中,然后将适当量的该第一组合物添加到该容器中来制备。

45. 如权利要求32-44中任一项所述的方法,其中该患者是癌症患者。

46. 如权利要求32-45中任一项所述的方法,其中该施用是IV施用。

47. 如权利要求25-31中任一项所述的药物制剂,其中该表面活性剂是泊洛沙姆188或泊洛沙姆407。

48. 如权利要求19所述的组合物、如权利要求31所述的药物制剂或如权利要求32所述的方法,其中该双特异性抗体构建体包含具有SEQ ID NO:13、SEQ ID NO:15、SEQ ID NO:25、SEQ ID NO:48、SEQ ID NO:67、SEQ ID NO:78、SEQ ID NO:88、SEQ ID NO:109、SEQ ID NO:110、SEQ ID NO:165、SEQ ID NO:166、SEQ ID NO:167、SEQ ID NO:178或SEQ ID NO:192的氨基酸序列的多肽。

用于在低蛋白浓度下使蛋白损失最小化的组合物和方法

[0001] 相关申请的交叉引用

[0002] 本申请要求2019年10月25日提交的美国临时申请号62/926,089的权益,该临时申请通过援引以其全文并入本文。

[0003] 以ASCII文本文件提交序列列表

[0004] 以下以ASCII文本文件提交的内容通过援引以其全文并入本文:序列列表的计算机可读形式(CRF)(文件名:A-2429-WO-PCT_ST25,创建日期:2020年10月23日,大小:451,608字节)。

技术领域

[0005] 本文披露的发明总体上涉及包含蛋白的组合物、特别是包含低蛋白浓度的治疗性蛋白的药物组合物的领域。本文披露的发明还涉及向有需要的受试者施用该组合物的方法。

背景技术

[0006] 治疗性蛋白是用于治疗患者的一类重要疗法。蛋白分子具有表面活性,可能会吸附到固体表面。药物组合物中的治疗性蛋白可被吸附到蛋白所接触的固体表面(例如,容纳药物组合物的容器的表面),这可能导致在储存和使用期间蛋白损失。通常,这些组合物中治疗性蛋白的浓度较高(例如,1mg/mL或更高),以使蛋白吸附到固体表面不会导致可用于向患者施用的药物量不足。然而,当组合物中蛋白的浓度较低时(例如,低于0.1mg/mL,诸如当在向患者施用之前稀释组合物时),蛋白损失的风险可能更明显,这可能导致可用于患者施用的药物量不足。

[0007] 表面活性剂通常用于包含治疗性蛋白的药物组合物中,例如以防止蛋白聚集和稳定蛋白。尚不清楚当蛋白在药物组合物中以低浓度(例如,0.1mg/mL或更低)存在时,表面活性剂是否可以用于有效防止由于表面吸附而引起的蛋白损失。

[0008] 需要最小化由于吸附到固体表面而引起的蛋白损失的蛋白组合物和方法,特别是当组合物包含低蛋白浓度的蛋白时。

发明内容

[0009] 本文披露了包含低蛋白浓度的蛋白的组合物以及向有需要的受试者施用这些组合物的方法。本文披露的组合物和方法具有最小化或消除由于蛋白吸附到固体表面而引起的蛋白损失的优点,并确保向患者准确给药治疗性蛋白。

[0010] 在某些实施例中,本文披露了一种包含蛋白和表面活性剂的水性组合物,其中蛋白以介于约0.001 μ g/mL与约100 μ g/mL之间的浓度存在于组合物中,并且表面活性剂以表面活性剂的临界胶束浓度(CMC)的至少约0.25倍的浓度存在于组合物中。

[0011] 在某些实施例中,蛋白是双特异性抗体构建体,该双特异性抗体构建体包含与靶细胞表面抗原结合的第一结合结构域、与T细胞表面上的人CD3结合的第二结合结构域,以

及任选地按氨基到羧基的顺序包含铰链-CH₂结构域-CH₃结构域-接头-铰链-CH₂结构域-CH₃结构域的第三结构域。在某些实施例中,第二结合结构域包含具有SEQ ID NO:201的序列的多肽。在某些实施例中,双特异性抗体构建体以介于约0.001μg/ml与约50μg/ml之间、或介于约0.01μg/ml至约50μg/ml、或0.1μg/ml至约50μg/ml、或0.1μg/ml至约10μg/ml、或1μg/ml至约10μg/ml之间的浓度存在。

[0012] 在某些实施例中,表面活性剂是聚山梨醇酯、泊洛沙姆或曲拉通(triton) x-100。在某些实施例中,表面活性剂是聚山梨醇酯80、聚山梨醇酯60、聚山梨醇酯40、聚山梨醇酯20或曲拉通X-100。在某些实施例中,表面活性剂是泊洛沙姆188或泊洛沙姆407。在某些实施例中,表面活性剂以介于表面活性剂的CMC的约0.25倍与约20倍之间、或介于CMC的约0.25倍与约10倍之间的浓度存在。

[0013] 在某些实施例中,其中组合物进一步包含盐、氨基酸、糖类或糖类衍生物或它们的组合。在某些实施例中,盐是NaCl。在某些实施例中,糖类或糖类衍生物是单糖、二糖、环状多糖或糖醇。在某些实施例中,糖类是蔗糖、海藻糖、甘露糖醇或山梨糖醇。在某些实施例中,氨基酸是赖氨酸。

[0014] 在某些实施例中,其中组合物的pH介于约3.5与约7.5之间。在某些实施例中,组合物的pH介于约4.2与约7.0之间。

[0015] 在某些实施例中,组合物进一步包含缓冲剂或防腐剂。在某些实施例中,缓冲剂是乙酸盐缓冲剂、谷氨酸盐缓冲剂、柠檬酸盐缓冲剂、琥珀酸盐缓冲剂、酒石酸盐缓冲剂、富马酸盐缓冲剂、马来酸盐缓冲剂、组氨酸缓冲剂或磷酸盐缓冲剂。

[0016] 在某些实施例中,双特异性抗体构建体的第一结合结构域和第二结合结构域中的每一者包含VH区和VL区。在某些实施例中,双特异性抗体构建体是单链抗体构建体。在某些实施例中,双特异性抗体构建体包含具有选自SEQ ID NO:11、SEQ ID NO:13、SEQ ID NO:15、SEQ ID NO:24、SEQ ID NO:25、SEQ ID NO:47、SEQ ID NO:48、SEQ ID NO:66、SEQ ID NO:67、SEQ ID NO:76、SEQ ID NO:78、SEQ ID NO:87、SEQ ID NO:88、SEQ ID NO:108、SEQ ID NO:109、SEQ ID NO:110、SEQ ID NO:165、SEQ ID NO:166、SEQ ID NO:167、SEQ ID NO:176、SEQ ID NO:178和SEQ ID NO:192的氨基酸序列的多肽。在某些实施例中,双特异性抗体构建体包含具有SEQ ID NO:13、SEQ ID NO:15、SEQ ID NO:25、SEQ ID NO:48、SEQ ID NO:67、SEQ ID NO:78、SEQ ID NO:88、SEQ ID NO:109、SEQ ID NO:110、SEQ ID NO:165、SEQ ID NO:166、SEQ ID NO:167、SEQ ID NO:178或SEQ ID NO:192的氨基酸序列的多肽。

[0017] 在某些实施例中,组合物容纳在塑料容器诸如IV袋或IV管中。在某些实施例中,容器由包含聚烯烃、聚氯乙烯(PVC)、乙酸乙烯酯(EVA)或聚氨酯的材料制成。在某些实施例中,容器由包含PVC的材料制成,并且其中PVC基本上不含邻苯二甲酸二-2-乙基己酯(DEHP)或偏苯三酸三-2-乙基己酯(TOTM)。

[0018] 在某些实施例中,本文披露了一种包含容纳在容器内的水性药物组合物的药物制剂,其中水性药物组合物包含:浓度介于约0.001μg/ml与约100μg/ml之间的双特异性抗体构建体,以及浓度为表面活性剂的CMC的至少约0.25倍表面活性剂,其中表面活性剂具有至少20的HLB值。在某些实施例中,表面活性剂是泊洛沙姆188或泊洛沙姆407。在某些实施例中,水性药物组合物包含浓度介于约0.001μg/ml与约50μg/ml之间的双特异性抗体构建体。在某些实施例中,水性药物组合物包含浓度介于表面活性剂的CMC的约0.25倍与约20倍

之间、或介于CMC的约0.25倍与约10倍之间的表面活性剂。

[0019] 在某些实施例中,水性药物组合物进一步包含盐、缓冲剂、氨基酸、糖类或糖类衍生物或它们的组合。在某些实施例中,水性药物组合物具有介于约4.2与约7.0之间的pH。

[0020] 在某些实施例中,容器由包含聚烯烃、PVC、EVA或聚氨酯(例如,聚酯和聚醚)的材料制成。

[0021] 在某些实施例中,双特异性抗体构建体包含具有选自SEQ ID NO:11、SEQ ID NO:13、SEQ ID NO:15、SEQ ID NO:24、SEQ ID NO:25、SEQ ID NO:47、SEQ ID NO:48、SEQ ID NO:66、SEQ ID NO:67、SEQ ID NO:76、SEQ ID NO:78、SEQ ID NO:87、SEQ ID NO:88、SEQ ID NO:108、SEQ ID NO:109、SEQ ID NO:110、SEQ ID NO:165、SEQ ID NO:166、SEQ ID NO:167、SEQ ID NO:176、SEQ ID NO:178和SEQ ID NO:192的氨基酸序列的多肽。在某些实施例中,双特异性抗体构建体包含具有SEQ ID NO:13、SEQ ID NO:15、SEQ ID NO:25、SEQ ID NO:48、SEQ ID NO:67、SEQ ID NO:78、SEQ ID NO:88、SEQ ID NO:109、SEQ ID NO:110、SEQ ID NO:165、SEQ ID NO:166、SEQ ID NO:167、SEQ ID NO:178或SEQ ID NO:192的氨基酸序列的多肽。

[0022] 本文还披露了一种向患者施用双特异性抗体构建体的方法,该方法包括:在容器中制备水性药物组合物,其中水性药物组合物包含浓度介于约0.001 μ g/ml与约100 μ g/ml之间的双特异性抗体构建体以及浓度为表面活性剂的CMC的至少约0.25倍的表面活性剂,以及向患者施用水性药物组合物,其中双特异性抗体构建体包含具有选自SEQ ID NO:11、SEQ ID NO:13、SEQ ID NO:15、SEQ ID NO:24、SEQ ID NO:25、SEQ ID NO:47、SEQ ID NO:48、SEQ ID NO:66、SEQ ID NO:67、SEQ ID NO:76、SEQ ID NO:78、SEQ ID NO:87、SEQ ID NO:88、SEQ ID NO:108、SEQ ID NO:109、SEQ ID NO:110、SEQ ID NO:165、SEQ ID NO:166、SEQ ID NO:167、SEQ ID NO:176、SEQ ID NO:178和SEQ ID NO:192的氨基酸序列的多肽。在某些实施例中,双特异性抗体构建体包含具有SEQ ID NO:13、SEQ ID NO:15、SEQ ID NO:25、SEQ ID NO:48、SEQ ID NO:67、SEQ ID NO:78、SEQ ID NO:88、SEQ ID NO:109、SEQ ID NO:110、SEQ ID NO:165、SEQ ID NO:166、SEQ ID NO:167、SEQ ID NO:178或SEQ ID NO:192的氨基酸序列的多肽。在某些实施例中,水性药物组合物包含浓度介于约0.001 μ g/ml与约50 μ g/ml之间的双特异性抗体构建体。

[0023] 在某些实施例中,水性药物组合物包含浓度介于表面活性剂的CMC的约0.25倍与约20倍之间、或介于CMC的约0.25倍与约10倍之间的表面活性剂。在某些实施例中,表面活性剂是聚山梨醇酯80、聚山梨醇酯60、聚山梨醇酯40、聚山梨醇酯20、泊洛沙姆188、泊洛沙姆407或曲拉通X-100。

[0024] 在某些实施例中,水性药物组合物进一步包含选自盐、缓冲剂、氨基酸、糖类或糖类衍生物和防腐剂中的一种或多种。在某些实施例中,水性药物组合物具有介于约4.2与约7.0之间的pH。

[0025] 在某些实施例中,容器由包含聚烯烃、PVC、EVA、聚氨酯的材料制成。在某些实施例中,表面活性剂是聚山梨醇酯80、聚山梨醇酯60、聚山梨醇酯40或聚山梨醇酯20,并且其中容器由基本上不含DEHP或TOTM的PVC的材料制成。

[0026] 在某些实施例中,水性药物组合物通过用合适的水性溶液稀释包含双特异性抗体构建体的第一组合物来制备。在某些实施例中,第一组合物是包含双特异性抗体构建体的

液体组合物。在某些实施例中，第一组合物是由包含双特异性抗体构建体的冻干组合物重构的液体组合物。在某些实施例中，合适的溶液包含浓度为表面活性剂的CMC的至少约0.25倍的表面活性剂。在某些实施例中，水性药物组合物通过将合适的水性溶液添加到容器中，然后将适当量的第一组合物添加到容器中来制备。

[0027] 在某些实施例中，患者是癌症患者。在某些实施例中，施用是IV施用。

附图说明

[0028] 图1示出了用于测量与固体表面结合的蛋白的测定的示意图。

[0029] 图2示出了在不存在表面活性剂的情况下蛋白与固体表面的结合。

[0030] 图3示出了不同地添加各种表面活性剂防止蛋白与固体表面结合。

[0031] 图4示出了在添加蛋白之前向固体表面添加表面活性剂更有效地防止蛋白与表面结合。

[0032] 图5示出了相同浓度的不同表面活性剂对邻苯二甲酸二-2-乙基己酯 (DEHP) 从含DEHP的PVC中浸出的影响。

[0033] 图6示出了在相同CMC倍数的不同表面活性剂对DEHP从含DEHP的PVC中浸出的影响。

具体实施方式

[0034] 本文披露的发明基于以下令人惊讶的发现：当表面活性剂以低于其临界胶束浓度的浓度使用时，可以稳定液体组合物中低浓度的蛋白，并有效地防止由于吸附到固体表面而引起的蛋白损失。

[0035] 在一些实施例中，本文披露了一种包含蛋白和表面活性剂的水性组合物，其中蛋白以介于约0.001 $\mu\text{g}/\text{ml}$ 与约100 $\mu\text{g}/\text{ml}$ 之间的浓度存在于组合物中，并且表面活性剂以表面活性剂的临界胶束浓度 (CMC) 的至少约0.25倍的浓度存在于组合物中。

[0036] 可以用于组合物中的表面活性剂可以是通常用于药物组合物中的任何表面活性剂。在一些实施例中，表面活性剂是非离子表面活性剂。在一些实施例中，表面活性剂是聚山梨醇酯，诸如聚山梨醇酯20、聚山梨醇酯40、聚山梨醇酯60、聚山梨醇酯65、聚山梨醇酯80或聚山梨醇酯85。在一些实施例中，表面活性剂是聚山梨醇酯20，在其他实施例中，表面活性剂是聚山梨醇酯80。在一些实施例中，表面活性剂是泊洛沙姆，诸如泊洛沙姆124、泊洛沙姆188、泊洛沙姆237、泊洛沙姆338和泊洛沙姆407。在一些实施例中，表面活性剂是曲拉通X-100。各种表面活性剂可商购获得（例如，吐温20、吐温80、普朗尼克F68和普朗尼克F127等）。

[0037] 表面活性剂可以以该表面活性剂的临界胶束浓度 (CMC) 的至少约0.25倍 (0.25x) 的浓度存在于组合物中。在一些实施例中，表面活性剂以介于表面活性剂的CMC的约0.25倍与约20倍之间的浓度存在于组合物中。在一些实施例中，表面活性剂以介于表面活性剂的CMC的约0.25倍与约15倍之间、或介于约0.25倍与约10倍之间、或介于约0.25倍与约8倍之间、或介于约0.25倍与约6倍之间、或介于约0.25倍与约4倍之间、或介于约0.25倍与约2倍之间、或介于约0.25倍与约1倍之间的浓度存在于组合物中。

[0038] 在一些实施例中，表面活性剂以介于表面活性剂的CMC的约0.5倍与约20倍之间的

浓度存在于组合物中。在一些实施例中,表面活性剂以介于表面活性剂的CMC的约0.5倍与约15倍之间、或介于约0.5倍与约10倍之间、或介于约0.5倍与约8倍之间、或介于约0.5倍与约6倍之间、或介于约0.5倍与约4倍之间、或介于约0.5倍与约2倍之间、或介于约0.5倍与约1倍之间的浓度存在于组合物中。

[0039] 在一些实施例中,表面活性剂以表面活性剂的CMC的约0.25倍、约0.5倍、约1倍、约2倍、约3倍、约4倍、约5倍、约6倍、约7倍、约8倍、约9倍、约10倍、约12倍、约14倍、约16倍、约18倍或约20倍的浓度存在于组合物中。在一些实施例中,表面活性剂以表面活性剂的CMC的约1.25倍、约2.5倍、约3.5倍、约4.5倍、约5.5倍、约6.5倍、约7.5倍、约8.5或约9.5倍的浓度存在于组合物中。

[0040] 如本文所用,术语“约”在用于修饰特定值或范围时,应理解是指给定值或范围内可以存在变化,包括规定值或范围的20%以内(例如,10%、5%、4%、3%、2%或1%以内)。

[0041] 临界胶束浓度是指表面活性剂的浓度,高于该浓度时会形成胶束,它是表面活性剂的一种性质。表面活性剂的CMC值可以通过本领域公知的实验方法(诸如荧光测定法、表面张力、电导测定法和动态光散射)来测量。参见例如Norman Scholz,Thomas Behnke,Ute Resch-Genger.Journal of Fluorescence[荧光杂志]28:465-476(2018)以及Önder Topel, Burçin Acar Çakır, Leyla Budama, Numan Hoda.Journal of Molecular Liquids[分子液体杂志]177 40-43(2013)。表面活性剂的CMC值也可以使用诸如Attention®Sigma 700或701的装置来自动测量。

[0042] 在一些实施例中,每种表面活性剂的CMC值在下表1中列出。

[0043] 表1.常用表面活性剂的CMC

表面活性剂	CMC* (w/v %)
聚山梨醇酯20	0.007
聚山梨醇酯80	0.002
泊洛沙姆188	0.4
泊洛沙姆407	0.004
曲拉通X-100	0.014

[0045] *对于表中列出的CMC值,参见例如le Maire M,Champeil P,Moller JV.2000.Interaction of membrane proteins and lipids with solubilizing detergents[膜蛋白和脂质与增溶洗涤剂的相互作用].Biochim Biophys Acta[生物化学生物物理学报]1508:86-111;Suksiriworapong J,Rungvimolsin T,A-gomol A,Junyaprasert VB,Chantasart D.Development and characterization of lyophilized diazepam-loaded polymeric micelles[载有地西泮的冻干聚合物胶束的开发和表征].2014.AAPS PharmSciTech[AAPS药学科技].15(1):52-64;https://www.sigmaaldrich.com/content/dam/sigma-aldrich/docs/Sigma/Product_Information_Sheet/1/t8532pis.pdf

[0046] 蛋白可以以介于约0.001μg/ml与约100μg/ml之间的浓度存在于组合物中。在一些实施例中,蛋白以介于约0.001μg/ml与约90μg/ml、或介于约0.001μg/ml与约80μg/ml之间、

或介于约0.001 $\mu\text{g}/\text{ml}$ 与约70 $\mu\text{g}/\text{ml}$ 之间、或介于约0.001 $\mu\text{g}/\text{ml}$ 与约60 $\mu\text{g}/\text{ml}$ 之间、或介于约0.001 $\mu\text{g}/\text{ml}$ 与约50 $\mu\text{g}/\text{ml}$ 之间、或介于约0.001 $\mu\text{g}/\text{ml}$ 与约40 $\mu\text{g}/\text{ml}$ 之间、介于约0.001 $\mu\text{g}/\text{ml}$ 与约30 $\mu\text{g}/\text{ml}$ 之间、或介于约0.001 $\mu\text{g}/\text{ml}$ 与约20 $\mu\text{g}/\text{ml}$ 之间、或介于约0.001 $\mu\text{g}/\text{ml}$ 与约10 $\mu\text{g}/\text{ml}$ 之间、或介于约0.001 $\mu\text{g}/\text{ml}$ 与约5 $\mu\text{g}/\text{ml}$ 之间、或介于约0.001 $\mu\text{g}/\text{ml}$ 与约1 $\mu\text{g}/\text{ml}$ 之间、或介于约0.001 $\mu\text{g}/\text{ml}$ 与约0.01 $\mu\text{g}/\text{ml}$ 之间的浓度存在于组合物中。

[0047] 在一些实施例中,蛋白以介于约0.01 $\mu\text{g}/\text{ml}$ 与约100 $\mu\text{g}/\text{ml}$ 、或介于约0.01 $\mu\text{g}/\text{ml}$ 与约80 $\mu\text{g}/\text{ml}$ 之间、或介于约0.01 $\mu\text{g}/\text{ml}$ 与约70 $\mu\text{g}/\text{ml}$ 之间、或介于约0.01 $\mu\text{g}/\text{ml}$ 与约60 $\mu\text{g}/\text{ml}$ 之间、或介于约0.01 $\mu\text{g}/\text{ml}$ 与约50 $\mu\text{g}/\text{ml}$ 之间、或介于约0.01 $\mu\text{g}/\text{ml}$ 与约40 $\mu\text{g}/\text{ml}$ 之间、介于约0.01 $\mu\text{g}/\text{ml}$ 与约30 $\mu\text{g}/\text{ml}$ 之间、或介于约0.01 $\mu\text{g}/\text{ml}$ 与约20 $\mu\text{g}/\text{ml}$ 之间、或介于约0.01 $\mu\text{g}/\text{ml}$ 与约10 $\mu\text{g}/\text{ml}$ 之间、或介于约0.01 $\mu\text{g}/\text{ml}$ 与约5 $\mu\text{g}/\text{ml}$ 之间、或介于约0.01 $\mu\text{g}/\text{ml}$ 与约1 $\mu\text{g}/\text{ml}$ 之间、或介于约0.01 $\mu\text{g}/\text{ml}$ 与约0.1 $\mu\text{g}/\text{ml}$ 之间、或介于约0.1 $\mu\text{g}/\text{ml}$ 与约1 $\mu\text{g}/\text{ml}$ 之间、或介于约0.1 $\mu\text{g}/\text{ml}$ 与约5 1 $\mu\text{g}/\text{ml}$ 之间的浓度存在于组合物中。

[0048] 在一些实施例中,蛋白以约0.001 $\mu\text{g}/\text{ml}$ 、约0.005 $\mu\text{g}/\text{ml}$ 、约0.01 $\mu\text{g}/\text{ml}$ 、约0.05 $\mu\text{g}/\text{ml}$ 、约0.1 $\mu\text{g}/\text{ml}$ 、约1 $\mu\text{g}/\text{ml}$ 、约4 $\mu\text{g}/\text{ml}$ 、约8 $\mu\text{g}/\text{ml}$ 、约10 $\mu\text{g}/\text{ml}$ 、约15 $\mu\text{g}/\text{ml}$ 、约20 $\mu\text{g}/\text{ml}$ 、约25 $\mu\text{g}/\text{ml}$ 、约30 $\mu\text{g}/\text{ml}$ 、约35 $\mu\text{g}/\text{ml}$ 、约40 $\mu\text{g}/\text{ml}$ 、约45 $\mu\text{g}/\text{ml}$ 、约50 $\mu\text{g}/\text{ml}$ 、约55 $\mu\text{g}/\text{ml}$ 、约60 $\mu\text{g}/\text{ml}$ 、约65 $\mu\text{g}/\text{ml}$ 、约70 $\mu\text{g}/\text{ml}$ 、约75 $\mu\text{g}/\text{ml}$ 、约80 $\mu\text{g}/\text{ml}$ 、约85 $\mu\text{g}/\text{ml}$ 、约90 $\mu\text{g}/\text{ml}$ 、约95 $\mu\text{g}/\text{ml}$ 或约100 $\mu\text{g}/\text{ml}$ 的浓度存在于组合物中。

[0049] 在本文披露的组合物中,可以将蛋白的任何浓度或浓度范围与表面活性剂的任何浓度或浓度范围组合。

[0050] 任何蛋白可以是组合物中的蛋白。在一些实施例中,组合物中的蛋白是治疗性蛋白,诸如抗原结合蛋白或融合蛋白。

[0051] 如本文所用,术语“抗原结合蛋白”是指特异性结合一种或多种靶抗原的蛋白。抗原结合蛋白包括但不限于抗体(例如,单克隆抗体)。抗原结合蛋白典型地包含特异性结合至抗原的抗原结合片段,且任选地包含使该抗原结合片段呈现促进该抗原结合蛋白结合至抗原的构型的支架或构架部分。“抗原结合片段”是指抗体中缺少全长重链和/或轻链中存在的至少一些氨基酸但仍能够特异性结合抗原的部分。抗原结合片段包括但不限于单链可变片段(scFv)、纳米抗体(例如,骆驼科重链抗体的VH结构域;VHH片段,参见Cortez-Retamozo等人,Cancer Research[癌症研究],第64卷:2853-57,2004)、Fab片段、Fab'片段、F(ab')₂片段、Fv片段、Fd片段和互补决定区(CDR)片段,并且可以衍生自任何哺乳动物来源,诸如人、小鼠、大鼠、兔或骆驼科动物。抗原结合片段可与完整抗体竞争结合靶抗原,并且这些片段可通过修饰完整抗体(例如,酶促或化学裂解)或者使用本领域已知的重组DNA技术或肽合成从头合成来产生。

[0052] 在一些实施例中,蛋白是双特异性的抗原结合蛋白。如本文所用,术语“双特异性”是指能够与两种不同抗原或靶标或表位特异性结合的抗原结合蛋白。如本文所用,“表位”是指能够被抗原结合蛋白诸如抗体或其片段特异性结合的任何决定簇。在一些实施例中,双特异性抗原结合蛋白包含与一种抗原或靶标特异性结合的第一结构域以及另一种抗原或靶标特异性结合的第二结构域。在一些实施例中,双特异性抗原结合蛋白的第一结构域与靶细胞表面抗原特异性结合,并且双特异性抗原结合蛋白的第二结合结构域与人CD3(T细胞上的T细胞受体复合物的亚基)特异性结合。在一些优选的实施例中,双特异性抗原

结合蛋白是如例如WO 2008119567和WO2017134140中所述的双特异性T细胞衔接(BiTE®)抗体构建体。

[0053] 如本文所用,术语“抗体构建体”是指其中结构和/或功能基于抗体(例如,全长或完整免疫球蛋白分子)的结构和/或功能并且/或者从抗体或其片段的可变重链(VH)和/或可变轻链(VL)结构域中提取的分子。因此,抗体构建体能够与其特异性靶标或抗原结合。抗体构建体还包括修饰的抗体片段,诸如scFv、二scFv或双(s)-scFv、scFv-Fc、scFv-拉链、scFab、Fab₂、Fab₃、双抗体、单链双抗体、串联双抗体(Tandab)、串联二scFv、串联三scFv、“多抗体”(诸如三抗体或四抗体)和单结构域抗体(诸如仅包含一个可变结构域(它可能是独立于其他V区或结构域特异性结合抗原或表位的VHH、VH或VL)的纳米抗体或单可变结构域抗体)。

[0054] 在一些实施例中,双特异性抗体构建体包含第一结合结构域和第二结合结构域,其中第一结合结构域与第一细胞表面抗原特异性结合,并且第二结合结构域与人CD3特异性结合。在一些实施例中,双特异性抗体构建体的第一结构域和第二结构域是“双特异性单链抗体构建体”、更优选双特异性“单链Fv”(scFv)。在scFv中,抗体的VL和VH例如通过合成接头连接为其中VL和VH区配对形成单价分子的单条蛋白链;参见例如Huston等人(1988) Proc.Natl.Acad.Sci USA[美国国家科学院院刊]85:5879-5883。接头可以是约10至约25个氨基酸、优选约15至20个氨基酸的短肽。接头通常富含甘氨酸以获得柔韧性,以及丝氨酸或苏氨酸以获得溶解性,并且可以将VH的N-末端与VL的C-末端连接起来,反之亦然。尽管去除了恒定区并引入了接头,但scFv保留了原始免疫球蛋白的特异性。VH和VL区以VH-VL或VL-VH的顺序排列。优选的是,VH区位于接头序列的N末端,并且VL区位于接头序列的C末端。在某些实施例中,双特异性抗体构建体的第一结构域和第二结构域是选自(scFv)₂、scFv单结构域mAb、双抗体的形式以及这些形式中任一种的低聚体。

[0055] 在一些实施例中,双特异性抗体构建体进一步包含第三结构域。在一些实施例中,第三结构域是单链Fc(scFc)结构域。在一些实施例中,scFc结构域是scFc半衰期延长(HLE)结构域。在一些优选的实施例中,双特异性抗体构建体的第三结构域是氨基至羧基顺序如下的HLE结构域:铰链-CH2-CH3-接头-铰链-CH2-CH3。

[0056] 在一些实施例中,双特异性抗体构建体的第一结合结构域与第一细胞表面抗原结合。在一些实施例中,第一细胞表面抗原是CD70。CD70(也称为CD27L或TNFSF7)是一种II型整合膜蛋白,其正常表达限于活化的T细胞和B细胞、成熟的树突细胞和胸腺髓样上皮细胞的亚群。

[0057] 在一些实施例中,第一细胞表面抗原是肿瘤抗原。如本文所用的术语“肿瘤抗原”应理解为是指呈递在肿瘤细胞上的那些抗原。这些抗原可以呈递在具有细胞外部分的细胞表面上,该细胞外部分通常与分子的跨膜和细胞质部分结合。这些抗原有时只能由肿瘤细胞呈递,而不能由正常细胞呈递。与正常细胞相比,肿瘤抗原可以只在肿瘤细胞上表达或者可能代表肿瘤特异性突变。在这种情况下,它们被称为肿瘤特异性抗原。更常见的是由肿瘤细胞和正常细胞呈递的抗原,并且它们被称为肿瘤相关抗原。与正常细胞相比,这些肿瘤相关抗原可以过表达,或者由于肿瘤组织的结构与正常组织相比不太紧密,因此是肿瘤细胞中的抗体结合可接近的。在一些实施例中,第一结合结构域与选自以下项的肿瘤抗原结合: CD19、CD33、表皮生长因子受体变体iii(EGFRvIII)、间皮素(MSLN)、钙粘素19(CDH19)、FMS

样酪氨酸激酶3 (FLT3)、δ样配体3 (DLL3)、胎盘钙粘素 (CDH3)、B细胞成熟抗原 (BCMA)、前列腺特异性膜抗原 (PSMA)、人粘蛋白17 (MUC17) 和闭合蛋白 (claudin)-18同种型2 (CLDN18.2)。在一些实施例中,肿瘤抗原是人肿瘤抗原。

[0058] 在一些优选的实施例中,双特异性抗体构建体包含第一结构域、第二结构域和任选的第三结构域,其中第一结构域与CD70结合,并且第二结构域与人CD3结合,并且第三结构域(如果存在)是氨基至羧基顺序如下的HLE结构域:铰链-CH₂-CH₃-接头-铰链-CH₂-CH₃。在其他优选的实施例中,双特异性抗体构建体包含第一结构域、第二结构域和任选的第三结构域,其中第一结构域与选自以下项的肿瘤抗原结合:CD19、CD33、EGFRvIII、MSLN、CDH19、FLT3、DLL3、CDH3、BCMA、PSMA、MUC17和CLDN18.2,并且第二结构域与人CD3结合,并且第三结构域(如果存在)是氨基至羧基顺序如下的HLE结构域:铰链-CH₂-CH₃-接头-铰链-CH₂-CH₃。在优选的实施例中,第一结构域和第二结构域经由肽接头连接在一起,并经由肽接头连接到第三结构域(如果存在)。优选的肽接头已经在上文描述并且其特征具有氨基酸序列Gly-Gly-Gly-Gly-Ser(即Gly₄Ser)或其聚合物(即(Gly₄Ser)_x),其中x为1或更大的整数(例如,2、3、4、5、6或7)。在一些优选的实施例中,第二结合结构域包含具有SEQ ID NO:201的氨基酸序列的多肽。

[0059] 在一些实施例中,第一结合结构域与CD33特异性结合。在一些实施例中,第一结合结构域包含具有SEQ ID NO:1-15中任一个的氨基酸序列的多肽。

[0060] 在一些实施例中,第一结合结构域与EGFRvIII特异性结合。在一些实施例中,第一结合结构域包含具有SEQ ID NO:16-26中任一个的氨基酸序列的多肽。

[0061] 在一些实施例中,第一结合结构域与MSLN特异性结合。在一些实施例中,第一结合结构域包含具有SEQ ID NO:27-38和165中任一个的氨基酸序列的多肽。

[0062] 在一些实施例中,第一结合结构域与CDH19特异性结合。在一些实施例中,第一结合结构域包含具有SEQ ID NO:39-56中任一个的氨基酸序列的多肽。

[0063] 在一些实施例中,第一结合结构域与DLL3特异性结合。在一些实施例中,第一结合结构域包含具有SEQ ID NO:68-78的氨基酸序列的多肽。

[0064] 在一些实施例中,第一结合结构域与CD19特异性结合。在一些实施例中,第一结合结构域包含具有SEQ ID NO:79-88中任一个的氨基酸序列的多肽。

[0065] 在一些实施例中,第一结合结构域与FLT3特异性结合。在一些实施例中,第一结合结构域包含具有SEQ ID NO:57-67中任一个的氨基酸序列的多肽。

[0066] 在一些实施例中,第一结合结构域与CDH3特异性结合。在一些实施例中,第一结合结构域包含具有SEQ ID NO:89-99中任一个的氨基酸序列的多肽。

[0067] 在一些实施例中,第一结合结构域与BCMA特异性结合。在一些实施例中,第一结合结构域包含具有SEQ ID NO:100-110中任一个的氨基酸序列的多肽。

[0068] 在一些实施例中,第一结合结构域与PSMA特异性结合。在一些实施例中,第一结合结构域包含具有SEQ ID NO:111-155、166和167中任一个的氨基酸序列的多肽。

[0069] 在一些实施例中,第一结合结构域与CD70特异性结合。在一些实施例中,第一结合结构域包含具有SEQ ID NO:156-164中任一个的氨基酸序列的多肽。

[0070] 在一些实施例中,双特异性抗体构建体的第二结合结构域与T细胞表面上的人CD3 ϵ 特异性结合。在一些实施例中,双特异性抗体构建体的第二结构域与人CD3 ϵ 链的细胞外表

位特异性结合。在一些实施例中,与人CD3特异性结合的双特异性抗体构建体的第二结构域包含VL区和VH区,该VL区包含具有SEQ ID NO:193的氨基酸序列的CDR-L1、具有SEQ ID NO:194的氨基酸序列的CDR-L2和具有SEQ ID NO:195的氨基酸序列的CDR-L3,该VH区包含具有SEQ ID NO:196的氨基酸序列的CDR-H1、具有SEQ ID NO:197的氨基酸序列的CDR-H2和具有SEQ ID NO:198的氨基酸序列的CDR-H3。

[0071] 在一些实施例中,双特异性抗体构建体的第二结构域包含具有SEQ ID NO:199的氨基酸序列的VH和具有SEQ ID NO:200的氨基酸的VL。在一些实施例中,双特异性抗体构建体的第二结构域包含具有SEQ ID NO:201的氨基酸序列的多肽。

[0072] 在一些实施例中,蛋白是CD70xCD3双特异性抗体构建体,其包含与CD70特异性结合的第一结构域和与CD3特异性结合的第二结构域。在一个实施例中,第一结构域与CD70特异性结合并且包含如SEQ ID NO:156-161所示的CDR,第二结构域与CD3特异性结合并且具有如SEQ ID NO:193-198所示的CDR。在一些实施例中,双特异性抗体构建体进一步包含HLE结构域(第三结构域)。在一个实施例中,双特异性抗体构建体包含VH和VL,其中该VH包含含有SEQ ID NO:162的氨基酸序列或者基本上由该氨基酸序列组成或由该氨基酸序列组成的多肽,并且该VL包含含有SEQ ID NO:163的氨基酸序列或者基本上由该氨基酸序列组成或由该氨基酸序列组成的多肽。在一个实施例中,CD70xCD3双特异性抗体构建体包含含有SEQ ID NO:164的氨基酸序列或者基本上由该氨基酸序列组成或由该氨基酸序列组成的多肽。

[0073] 在一些实施例中,蛋白是BCMAxCD3双特异性抗体构建体,其包含与BCMA特异性结合的第一结构域和与CD3特异性结合的第二结构域。在一些实施例中,双特异性抗体进一步包含HLE结构域(第三结构域)。在一个实施例中,第一结构域与BCMA特异性结合并且具有如SEQ ID NO:100-105所示的CDR,第二结构域与CD3特异性结合并且具有如SEQ ID NO:193-198所示的CDR。在一个实施例中,BCMAxCD3双特异性抗体构建体包含VH和VL,其中该VH包含含有SEQ ID NO:106的氨基酸序列或者基本上由该氨基酸序列组成或由该氨基酸序列组成的多肽,并且该VL包含含有SEQ ID NO:107的氨基酸序列或者基本上由该氨基酸序列组成或由该氨基酸序列组成的多肽。在一个实施例中,BCMAxCD3双特异性抗体构建体包含含有SEQ ID NO:108的氨基酸序列或者基本上由该氨基酸序列组成或由该氨基酸序列组成的多肽。在一个实施例中,BCMAxCD3双特异性抗体构建体包含含有SEQ ID NO:109的氨基酸序列或者基本上由该氨基酸序列组成或由该氨基酸序列组成的多肽。在另一个实施例中,BCMAxCD3双特异性抗体构建体包含含有SEQ ID NO:110的氨基酸序列或者基本上由该氨基酸序列组成或由该氨基酸序列组成的多肽。

[0074] 在一些实施例中,双特异性抗体是CD33xCD3双特异性抗体构建体,其包含与CD33特异性结合的第一结构域和与CD3特异性结合的第二结构域。在一些实施例中,双特异性抗体构建体进一步包含HLE结构域(第三结构域)。在一个实施例中,第一结构域与CD33特异性结合并且具有如SEQ ID NO:3-5和8-10所示的CDR,第二结构域与CD3特异性结合并且具有如SEQ ID NO:193-198所示的CDR。在一个实施例中,CD33xCD3双特异性抗体构建体包含VH和VL,其中该VH包含含有SEQ ID NO:1或2的氨基酸序列或者基本上由该氨基酸序列组成或由该氨基酸序列组成的多肽,并且该VL包含含有SEQ ID NO:6或7的氨基酸序列或者基本上由该氨基酸序列组成或由该氨基酸序列组成的多肽。在另一个实施例中,CD33xCD3双特异性抗体构建体包含含有SEQ ID NO:11或12中任一个的氨基酸序列或者基本上由该氨基酸

序列组成或由该氨基酸序列组成的多肽。在另一个实施例中,BCMAxCD3双特异性抗体构建体包含含有SEQ ID NO:13或15的氨基酸序列或者基本上由该氨基酸序列组成或由该氨基酸序列组成的多肽。

[0075] 在一些实施例中,蛋白是EGFRvIIIxCD3双特异性抗体构建体,其包含与EGFRvIII特异性结合的第一结构域和与CD3特异性结合的第二结构域。在一些实施例中,双特异性抗体进一步包含HLE结构域(第三结构域)。在一个实施例中,第一结构域与EGFRvIII特异性结合并且具有如SEQ ID NO:16-21所示的CDR,第二结构域与CD3特异性结合并且具有如SEQ ID NO:193-198所示的CDR。在一个实施例中,EGFRvIIIxCD3双特异性抗体构建体包含VH和VL,其中该VH包含含有SEQ ID NO:22的氨基酸序列或者基本上由该氨基酸序列组成或由该氨基酸序列组成的多肽,并且该VL包含含有SEQ ID NO:23的氨基酸序列或者基本上由该氨基酸序列组成或由该氨基酸序列组成的多肽。在一个实施例中,EGFRvIIIxCD3双特异性抗体构建体包含含有SEQ ID NO:24或25的氨基酸序列或者基本上由该氨基酸序列组成或由该氨基酸序列组成的多肽。在一个实施例中,EGFRvIIIxCD3双特异性抗体构建体包含含有SEQ ID NO:24或26的氨基酸序列或者基本上由该氨基酸序列组成或由该氨基酸序列组成的多肽。

[0076] 在一些实施例中,蛋白是MSLNxCD3双特异性抗体构建体,其包含与MSLN特异性结合的第一结构域和与CD3特异性结合的第二结构域。在一些实施例中,双特异性抗体构建体进一步包含HLE结构域(第三结构域)。在一个实施例中,第一结构域与MSLN特异性结合并且具有如SEQ ID NO:27-32所示的CDR,第二结构域与CD3特异性结合并且具有如SEQ ID NO:193-198所示的CDR。在一个实施例中,MSLNxCD3双特异性抗体构建体包含VH和VL,其中该VH包含含有SEQ ID NO:33的氨基酸序列或者基本上由该氨基酸序列组成或由该氨基酸序列组成的多肽,并且该VL包含含有SEQ ID NO:34的氨基酸序列或者基本上由该氨基酸序列组成或由该氨基酸序列组成的多肽。在一个实施例中,MSLNxCD3双特异性抗体构建体包含含有SEQ ID NO:35-38中任一个的氨基酸序列或者基本上由该氨基酸序列组成或由该氨基酸序列组成的多肽。在一个实施例中,MSLNxCD3双特异性抗体构建体包含含有SEQ ID NO:165的氨基酸序列或者基本上由该氨基酸序列组成或由该氨基酸序列组成的多肽。

[0077] 在一些实施例中,蛋白是CDH19xCD3双特异性抗体构建体,其包含与CDH19特异性结合的第一结构域和与CD3特异性结合的第二结构域。在一些实施例中,双特异性抗体进一步包含HLE结构域(第三结构域)。在一个实施例中,第一结构域与CDH19特异性结合并且具有如SEQ ID NO:39-44所示的CDR,第二结构域与CD3特异性结合并且具有如SEQ ID NO:193-198所示的CDR。在一个实施例中,CDH19xCD3双特异性抗体构建体包含VH和VL,其中该VH包含含有SEQ ID NO:45或51的氨基酸序列或者基本上由该氨基酸序列组成或由该氨基酸序列组成的多肽,并且该VL包含含有SEQ ID NO:46或52的氨基酸序列或者基本上由该氨基酸序列组成或由该氨基酸序列组成的多肽。在一个实施例中,CDH19xCD3双特异性抗体构建体包含含有SEQ ID NO:47、48-50和53-56中任一个的氨基酸序列或者基本上由该氨基酸序列组成或由该氨基酸序列组成的多肽。在一个实施例中,CDH19xCD3双特异性抗体构建体包含含有SEQ ID NO:48的氨基酸序列或者基本上由该氨基酸序列组成或由该氨基酸序列组成的多肽。

[0078] 在一些实施例中,蛋白是DLL3xCD3双特异性抗体,其包含与DLL3特异性结合的第

一结构域和与CD3特异性结合的第二结构域。在一些实施例中,双特异性抗体进一步包含HLE结构域(第三结构域)。在一个实施例中,第一结构域与DLL3特异性结合并且具有如SEQ ID NO:68-73所示的CDR,第二结构域与CD3特异性结合并且具有如SEQ ID NO:193-198所示的CDR。在一个实施例中,DLL3xCD3双特异性抗体构建体包含VH和VL,其中该VH包含含有SEQ ID NO:74的氨基酸序列或者基本上由该氨基酸序列组成或由该氨基酸序列组成的多肽,并且该VL包含含有SEQ ID NO:75的氨基酸序列或者基本上由该氨基酸序列组成或由该氨基酸序列组成的多肽。在一个实施例中,DLL3xCD3双特异性抗体构建体包含含有SEQ ID NO:76-78的氨基酸序列或者基本上由该氨基酸序列组成或由该氨基酸序列组成的多肽。在一个实施例中,DLL3xCD3双特异性抗体构建体包含含有SEQ ID NO:78的氨基酸序列或者基本上由该氨基酸序列组成或由该氨基酸序列组成的多肽。

[0079] 在一些实施例中,蛋白是FLT3xCD3双特异性抗体构建体,其包含与FLT3特异性结合的第一结构域和与CD3特异性结合的第二结构域。在一些实施例中,双特异性抗体进一步包含HLE结构域(第三结构域)。在一个实施例中,第一结构域与FLT3特异性结合并且具有如SEQ ID NO:57-62所示的CDR,第二结构域与CD3特异性结合并且具有如SEQ ID NO:193-198所示的CDR。在一个实施例中,FLT3xCD3双特异性抗体构建体包含VH和VL,其中该VH包含含有SEQ ID NO:63的氨基酸序列或者基本上由该氨基酸序列组成或由该氨基酸序列组成的多肽,并且该VL包含含有SEQ ID NO:64的氨基酸序列或者基本上由该氨基酸序列组成或由该氨基酸序列组成的多肽。在一个实施例中,FLT3xCD3双特异性抗体构建体包含含有SEQ ID NO:65-67中任一个的氨基酸序列或者基本上由该氨基酸序列组成或由该氨基酸序列组成的多肽。在一个实施例中,FLT3xCD3双特异性抗体构建体包含含有SEQ ID NO:67的氨基酸序列或者基本上由该氨基酸序列组成或由该氨基酸序列组成的多肽。

[0080] 在一些实施例中,蛋白是CDH3xCD3双特异性抗体构建体,其包含与CDH3特异性结合的第一结构域和与CD3特异性结合的第二结构域。在一些实施例中,双特异性抗体构建体进一步包含HLE结构域(第三结构域)。在一个实施例中,第一结构域与CDH3特异性结合并且具有如SEQ ID NO:89-94所示的CDR,第二结构域与CD3特异性结合并且具有如SEQ ID NO:193-198所示的CDR。在一个实施例中,CDH3xCD3双特异性抗体构建体包含VH和VL,其中该VH包含含有SEQ ID NO:95的氨基酸序列或者基本上由该氨基酸序列组成或由该氨基酸序列组成的多肽,并且该VL包含含有SEQ ID NO:96的氨基酸序列或者基本上由该氨基酸序列组成或由该氨基酸序列组成的多肽。在一个实施例中,CDH3xCD3双特异性抗体构建体包含含有SEQ ID NO:97-99中任一个的氨基酸序列或者基本上由该氨基酸序列组成或由该氨基酸序列组成的多肽。在一个实施例中,CDH3xCD3双特异性抗体构建体包含含有SEQ ID NO:99的氨基酸序列或者基本上由该氨基酸序列组成或由该氨基酸序列组成的多肽。

[0081] 在一些实施例中,蛋白是PSMAxCD3双特异性抗体构建体,其包含与PSMA特异性结合的第一结构域和与CD3特异性结合的第二结构域。在一些实施例中,双特异性抗体构建体进一步包含HLE结构域(第三结构域)。在一个实施例中,第一结构域与PSMA特异性结合并且具有如SEQ ID NO:111-116中任一个所示的CDR,第二结构域与CD3特异性结合并且具有如SEQ ID NO:193-198所示的CDR。在一个实施例中,第一结构域与PSMA结合并且具有如SEQ ID NO:126-131和141-146中任一个所示的CDR,第二结构域与CD3结合并且具有SEQ ID NO:193-198所示的CDR。在一个实施例中,PSMAxCD3双特异性抗体包含VH和VL,其中该VH包含含

有SEQ ID NO:117、132或147的氨基酸序列或者基本上由该氨基酸序列组成或由该氨基酸序列组成的多肽,并且该VL包含含有SEQ ID NO:118、133或148的氨基酸序列或者基本上由该氨基酸序列组成或由该氨基酸序列组成的多肽。在一个实施例中,PSMAxCD3双特异性抗体构建体包含含有SEQ ID NO:119-125、134-140和149-155中任一个的氨基酸序列或者基本上由该氨基酸序列组成或由该氨基酸序列组成的多肽。在一个实施例中,PSMAxCD3双特异性抗体构建体包含含有SEQ ID NO:121、122、124、125、136、137、139、140、151、152、154和155中任一个的氨基酸序列或者基本上由该氨基酸序列组成或由该氨基酸序列组成的多肽。在一个实施例中,PSMAxCD3双特异性抗体构建体包含含有SEQ ID NO:166或167的氨基酸序列或者基本上由该氨基酸序列组成或由该氨基酸序列组成的多肽。

[0082] 在一些实施例中,蛋白是C1dn18.2xCD3双特异性抗体构建体,其包含与C1dn18.2特异性结合的第一结构域和与CD3特异性结合的第二结构域。在一些实施例中,双特异性抗体进一步包含HLE结构域(第三结构域)。在一个实施例中,第一结构域与C1dn18.2特异性结合并且具有如SEQ ID NO:168-173所示的CDR,第二结构域与CD3特异性结合并且具有如SEQ ID NO:193-198所示的CDR。在一个实施例中,C1dn18.2xCD3双特异性抗体构建体包含VH和VL,其中该VH包含含有SEQ ID NO:174的氨基酸序列或者基本上由该氨基酸序列组成或由该氨基酸序列组成的多肽,并且该VL包含含有SEQ ID NO:175的氨基酸序列或者基本上由该氨基酸序列组成或由该氨基酸序列组成的多肽。在一个实施例中,C1dn18.2xCD3双特异性抗体构建体包含含有SEQ ID NO:176或178的氨基酸序列或者基本上由该氨基酸序列组成或由该氨基酸序列组成的多肽。在一个实施例中,C1dn18.2xCD3双特异性抗体构建体包含含有SEQ ID NO:178的氨基酸序列或者基本上由该氨基酸序列组成或由该氨基酸序列组成的多肽。

[0083] 在一些实施例中,蛋白是MUC17xCD3双特异性抗体构建体,其包含与MUC17特异性结合的第一结构域和与CD3特异性结合的第二结构域。在一些实施例中,双特异性抗体进一步包含HLE结构域(第三结构域)。在一个实施例中,第一结构域与MUC17特异性结合并且具有如SEQ ID NO:184-189所示的CDR,第二结构域与CD3特异性结合并且具有如SEQ ID NO:193-198所示的CDR。在一个实施例中,MUC17xCD3双特异性抗体构建体包含VH和VL,其中该VH包含含有SEQ ID NO:190的氨基酸序列或者基本上由该氨基酸序列组成或由该氨基酸序列组成的多肽,并且该VL包含含有SEQ ID NO:191的氨基酸序列或者基本上由该氨基酸序列组成或由该氨基酸序列组成的多肽。在一个实施例中,MUC17xCD3双特异性抗体构建体包含含有SEQ ID NO:192的氨基酸序列或者基本上由该氨基酸序列组成或由该氨基酸序列组成的多肽。

[0084] 在某些实施例中,双特异性抗体构建体包含含有SEQ ID NO:13、SEQ ID NO:15、SEQ ID NO:25、SEQ ID NO:48、SEQ ID NO:67、SEQ ID NO:78、SEQ ID NO:88、SEQ ID NO:109、SEQ ID NO:110、SEQ ID NO:165、SEQ ID NO:166、SEQ ID NO:167、SEQ ID NO:178或SEQ ID NO:192的氨基酸序列或者基本上由该氨基酸序列组成或由该氨基酸序列组成的多肽。

[0085] 本文披露的双特异性抗体可以通过本领域已知的方法制备。例如,双特异性抗体可以通过WO 2008/119657和WO 2017/134140中披露的方法制备。

[0086] 可用于组合物中的附加赋形剂

[0087] 在一些实施例中,组合物进一步包含一种或多种适用于药物组合物的赋形剂。在一些实施例中,组合物进一步包含盐、缓冲剂、糖类或糖类衍生物、氨基酸或防腐剂或者两种或更多种前述物质的组合。在一些实施例中,组合物进一步包含盐、糖类或糖类衍生物、氨基酸和任选的防腐剂。在一些实施例中,组合物进一步包含盐、缓冲剂、糖类或糖类衍生物和氨基酸。在一些实施例中,组合物进一步包含盐、缓冲剂、糖类或糖类衍生物、氨基酸和防腐剂。

[0088] 可用于组合物中的示例性盐包括适合用于药物组合物中的盐(例如,NaCl)。可用于组合物中的示例性缓冲剂包括乙酸盐缓冲剂、谷氨酸盐缓冲剂、柠檬酸盐缓冲剂、琥珀酸盐缓冲剂、酒石酸盐缓冲剂、富马酸盐缓冲剂、马来酸盐缓冲剂、组氨酸缓冲剂和磷酸盐缓冲剂。示例性糖类或糖类衍生物包括单糖、二糖、环状多糖和糖醇,诸如糖(例如,蔗糖和海藻糖)和糖醇(例如,甘露糖醇或山梨糖醇)。示例性氨基酸包括赖氨酸、组氨酸、精氨酸、甘氨酸、甲硫氨酸和丙氨酸。示例性防腐剂包括苯甲酸盐(例如,苯甲醇和苯甲酸钠)和山梨酸盐(例如,山梨酸钾)。

[0089] 组合物的pH可以在约3.5至7.5的范围内。在一些实施例中,组合物具有约4.0至约7.0的pH。在一些实施例中,组合物具有约4.2至约7.0、或约5.0至约7.0、或约5.5至约7.0、或约6.0至约7.0、或约6.5至约7.0、或约4.2至约6.5、或约4.2至约6.0、或约4.2至约5.5、或约4.2至约5.0、或约5.0至约6.0、或约5.0至约6.5、或约5.0至约6.0、或约5.0至约5.5、或约5.5至约6.0、或约5.5至约6.5、或约5.5至约6.0、或约6.0至约6.5的pH。在一些实施例中,组合物的pH为约3.5、约4.0、约4.5、约5.0、约5.5、约6.0、约6.5、约7.0或约7.5。

[0090] 组合物的pH可通过使用上文列出的一种或多种缓冲剂来实现。在一些实施例中,组合物包含选自乙酸盐缓冲剂、谷氨酸盐缓冲剂、柠檬酸盐缓冲剂、琥珀酸盐缓冲剂、酒石酸盐缓冲剂、富马酸盐缓冲剂、马来酸盐缓冲剂、组氨酸缓冲剂和磷酸盐缓冲剂的缓冲剂。在一些实施例中,组合物包含选自上述缓冲剂列表的两种缓冲剂(例如,谷氨酸盐缓冲剂和柠檬酸盐缓冲剂)的组合。

[0091] 在一些实施例中,组合物基本上不包含附加缓冲剂。如本文所用,短语“基本上不包含附加缓冲剂”是指组合物中不含为了调节和/或维持组合物的pH而添加的缓冲剂。例如,盐水溶液(0.9%NaCl溶液)不含附加缓冲剂并且具有约5.5的pH。据信盐水溶液的pH部分地通过溶解在水中的大气CO₂来实现和维持。参见例如Reddi, B.AJ Int.J.Med.Sci[国际医学科学杂志].10:747-750(2013)。这种组合物可含有对组合物的缓冲能力没有贡献的残余缓冲剂。

[0092] 在一些实施例中,组合物包含上文披露的任何浓度的蛋白、上文披露的任何浓度的表面活性剂,并且进一步包含盐(例如,NaCl)、糖(例如,蔗糖)、氨基酸(例如,赖氨酸)和任选的防腐剂(例如,苯甲醇)。在一些实施例中,组合物包含上文披露的任何浓度的蛋白、上文披露的任何浓度的表面活性剂,并且进一步包含盐(例如,NaCl)、糖(例如,蔗糖)、氨基酸(例如,赖氨酸)、缓冲剂(例如,谷氨酸盐和/或柠檬酸盐缓冲剂)和任选的防腐剂(例如,苯甲醇)。组合物的pH可以是上文披露的任何pH值。在一些实施例中,组合物的pH为约5.5。

[0093] 在一些实施例中,本文披露的组合物是药物组合物。如本文所用,术语“药物组合物”应理解为是指包含适合注射和/或施用到有需要的患者(例如,人)体内的蛋白(例如,双特异性抗体构建体)的配制品。更具体地,药物组合物是基本上无菌的并且不含对接受者具

有过度毒性或感染性的任何药剂。

[0094] 用于组合物的容器

[0095] 在一些实施例中,本文披露的组合物容纳在容器中。可用于本文的容器包括适用于药物用途的那些,例如由无毒且保持物理完整性的材料制成的容器。在一些实施例中,容器是用于静脉内(IV)施用的部件。如本文所用,短语“用于IV施用的部件”应理解为是指在IV施用期间可接触组合物的容器或系统的一部分。在一些实施例中,容器是IV袋或IV管。

[0096] 可用于制造容器的材料包括通常用于制造药物容器的那些,诸如玻璃和塑料。

[0097] 在一些实施例中,容器是塑料容器。在一些实施例中,容器由包含聚烯烃(例如,聚丙烯(PP)和聚乙烯(PE))、聚氯乙烯(PVC)、乙酸乙烯酯(EVA)或聚氨酯(例如,聚酯和聚醚)的材料制成。在一些实施例中,容器由包含PVC的材料制成。在一些实施例中,PVC基本上不含邻苯二甲酸二-2-乙基己酯(DEHP)或偏苯三酸三-2-乙基己酯(TOTM)。如本文所用,术语“基本上不含”应理解为是指其中未使用和/或未检测到DEHP或TOTM的PVC。DEHP和TOTM是可用于使PVC更软因此可以制成不同的形状的增塑剂。在一些实施例中,容器由不包含PVC的材料制成。

[0098] 在一些实施例中,容器由包含聚烯烃、EVA或聚氨酯(例如,聚酯和聚醚)的材料制成。在一些实施例中,容器由包含PP和/或PE的材料制成。

[0099] 在某些条件下,某些类型的PVC塑料中含有的DEHP或TOTM可以在某些浓度的某些表面活性剂(例如,聚山梨醇酯,参见实例3)存在下从塑料中浸出。不希望受任何特定理论的束缚,据信表面活性剂的亲脂性越高,DEHP或TOTM在表面活性剂存在下就可以更容易地浸出。表面活性剂的亲水-亲脂平衡(HLB)是其亲水或亲脂程度的量度,并且可以通过本领域已知的方法来计算。参见例如Griffin, William C. Calculation of HLB Values of Non-Ionic Surfactants[非离子表面活性剂的HLB值的计算], Journal of the Society of Cosmetic Chemists[化妆品化学家协会志], 5(4):249-56(1954)。HLB值可以用于预测表面活性剂的性质,例如,HLB>10表示表面活性剂更易溶于水(不溶于脂质),而HLB<10表示表面活性剂更易溶于脂质(不溶于水)。可以用于本文披露的组合物中的示例性表面活性剂的HLB值包括17(聚山梨醇酯20)、15(聚山梨醇酯80) (<https://pharmlabs.unc.edu/labs/emulsions/hlb.htm>) 和29(泊洛沙姆188) (http://www.rumapel.com.ar/cosmetica/miscelaneos/ficha_tecnica/Pluracare%20L-%20F%20Grades.pdf)。在容器由包含DEHP或TOTM的PVC塑料制成的实施例中,组合物中的表面活性剂优选地具有至少20的HLB值(例如,泊洛沙姆,参见实例3)、更优选介于20与30之间的HLB值。

[0100] 由上文列出的材料制成的容器诸如IV部件(例如,用于IV施用的IV袋和管)可商购获得。例如,各种合适的容器可从诸如百特医疗用品公司(Baxter Healthcare Corporation)和布劳恩医疗公司(B. Braun Medical Inc.)的制造商获得。

[0101] 药物制剂

[0102] 本文还披露了包含上文披露的水性组合物的药物制剂。如本文所用,术语“药物制剂”应理解为是指在向患者(例如,人)施用之前在合适的药物容器中包含本文披露的水性组合物的制剂。在一些实施例中,本文披露了一种在容器中包含水性药物组合物的药物制剂,其中水性药物组合物包含:a)浓度介于约0.001 μ g/ml与约100 μ g/ml之间的蛋白,以及b)浓度为表面活性剂的CMC的至少约0.25倍的表面活性剂,并且其中蛋白不是博纳吐单抗

(blinatumomab)。

[0103] 在一些实施例中,包含在组合物中的表面活性剂是聚山梨醇酯。在一些实施例中,表面活性剂是选自聚山梨醇酯20、聚山梨醇酯40、聚山梨醇酯60、聚山梨醇酯65、聚山梨醇酯80和聚山梨醇酯85的聚山梨醇酯。在一些实施例中,表面活性剂是聚山梨醇酯20或聚山梨醇酯80。在一些实施例中,表面活性剂是泊洛沙姆。在一些实施例中,表面活性剂是泊洛沙姆188或泊洛沙姆407。在一些实施例中,表面活性剂是曲拉通X-100。

[0104] 在一些实施例中,本文披露了一种在容器中包含水性药物组合物的药物制剂,其中水性药物组合物包含:a)浓度介于约0.001 $\mu\text{g}/\text{ml}$ 与约100 $\mu\text{g}/\text{ml}$ 之间的双特异性抗体构建体,以及b)浓度为表面活性剂的CMC的至少约0.25倍的表面活性剂,其中表面活性剂是泊洛沙姆。在一些实施例中,泊洛沙姆是泊洛沙姆188或泊洛沙姆407。

[0105] 在一些实施例中,表面活性剂以介于表面活性剂的CMC的约0.25倍与约20倍之间的浓度存在于组合物中。在一些实施例中,表面活性剂以介于表面活性剂的CMC的约0.25倍与约10倍之间的浓度存在于组合物中。在一些实施例中,表面活性剂以在上文披露的任何浓度范围内的浓度存在于组合物中。在一些实施例中,表面活性剂以作为上文披露的任何浓度的浓度存在于组合物中。表面活性剂的CMC值可以通过上文披露的方法测定。在一些实施例中,某些常用表面活性剂的CMC值在表1中列出。

[0106] 在一些实施例中,水性药物组合物包含浓度介于约0.001 $\mu\text{g}/\text{ml}$ 与约50 $\mu\text{g}/\text{ml}$ 之间的蛋白。在一些实施例中,组合物包含浓度在上文披露的任何范围内的蛋白(例如,双特异性抗体构建体)。在一些实施例中,蛋白(例如,双特异性抗体构建体)以上文披露的任何浓度存在于组合物中。可以将上文披露的蛋白的任何浓度或浓度范围与上文披露的表面活性剂的任何浓度或浓度范围组合。

[0107] 如上所披露,蛋白可以是治疗性蛋白,诸如抗原结合蛋白和融合蛋白。在一些实施例中,蛋白是双特异性抗原结合蛋白。在一些实施例中,蛋白是上文披露的双特异性抗体构建体。在一些实施例中,蛋白是CD70xCD3双特异性抗体构建体。在一些实施例中,蛋白是BCMAxCD3双特异性抗体构建体。在一些实施例中,蛋白是CD33xCD3双特异性抗体构建体。在一些实施例中,蛋白是EGFRvIIIxCD3双特异性抗体构建体。在一些实施例中,蛋白是MSLNxCD3双特异性抗体构建体。在一些实施例中,蛋白是CDH19xCD3双特异性抗体构建体。在一些实施例中,蛋白是DLL3xCD3双特异性抗体构建体。在一些实施例中,蛋白是FLT3xCD3双特异性抗体构建体。在一些实施例中,蛋白是CDH3xCD3双特异性抗体构建体。在一些实施例中,蛋白是PSMAxCD3双特异性抗体构建体。在一些实施例中,蛋白是Clon18.2xCD3双特异性抗体构建体。在一些实施例中,蛋白是MUC17xCD3双特异性抗体构建体。这些双特异性抗体构建体中的每一种在上文披露。在某些实施例中,蛋白包含SEQ ID NO:13、SEQ ID NO:15、SEQ ID NO:25、SEQ ID NO:48、SEQ ID NO:67、SEQ ID NO:78、SEQ ID NO:88、SEQ ID NO:109、SEQ ID NO:110、SEQ ID NO:165、SEQ ID NO:166、SEQ ID NO:167、SEQ ID NO:178或SEQ ID NO:192的氨基酸序列,基本上由这些氨基酸序列组成或由这些氨基酸序列组成。

[0108] 组合物的pH可以在上文披露的任何pH范围内。在一些实施例中,组合物的pH可以是上文披露的任何pH。

[0109] 在一些实施例中,水性药物组合物进一步包含一种或多种适用于药物组合物的赋形剂。在一些实施例中,水性药物组合物进一步包含盐、缓冲剂、氨基酸、糖类或糖类衍生

物、防腐剂或它们的组合。在一些实施例中，水性药物组合物进一步包含盐、氨基酸、糖类或糖类衍生物、防腐剂或它们的组合。可用于组合物中的示例性盐、缓冲剂、氨基酸、糖类或其衍生物和防腐剂在上文披露。

[0110] 在一些实施例中，容器是塑料容器。在一些实施例中，容器由包含聚烯烃（例如，PP和PE）、PVC、EVA或聚氨酯（例如，聚酯和聚醚）的材料制成。在一些实施例中，容器由包含PVC的材料制成。在一些实施例中，PVC基本上不含DEHP或TOTM。在一些实施例中，容器由不包含PVC的材料制成。

[0111] 在一些实施例中，包含在组合物中的表面活性剂是泊洛沙姆，并且容器可以由包含聚烯烃、PVC、EVA或聚氨酯（例如，聚酯和聚醚）的材料制成。在一些实施例中，包含在组合物中的表面活性剂是聚山梨醇酯或曲拉通X-100，并且容器可以由包含聚烯烃、基本上不含DEHP或TOTM的PVC、EVA或聚氨酯（例如，聚酯和聚醚）的材料制成。

[0112] 在一些实施例中，容器是用于静脉内（IV）施用的部件。在一些实施例中，容器是IV袋或IV管。

[0113] 在一些实施例中，药物制剂包含容器中的水性药物组合物，其中水性药物组合物包含双特异性抗体构建体（例如，本文披露的任何双特异性抗体构建体）、表面活性剂（例如，本文披露的任何表面活性剂），并且进一步包含盐（例如，NaCl）、氨基酸（例如，赖氨酸）、糖类或糖类衍生物（例如，蔗糖或甘露醇）、任选的防腐剂（例如，苯甲醇），并且其中容器由包含聚烯烃、PVC、EVA或聚氨酯（例如，聚酯和聚醚）的材料制成。在一些实施例中，药物制剂包含容器中的水性药物组合物，其中水性药物组合物包含双特异性抗体构建体（例如，本文披露的任何双特异性抗体构建体）、表面活性剂（例如，本文披露的任何表面活性剂），并且进一步包含盐（例如，NaCl）、缓冲剂（例如，谷氨酸盐缓冲剂和/或柠檬酸盐缓冲剂）、氨基酸（例如，赖氨酸）、糖类或糖类衍生物（例如，蔗糖或甘露醇）、任选的防腐剂（例如，苯甲醇），并且其中容器由包含聚烯烃、PVC、EVA或聚氨酯（例如，聚酯和聚醚）的材料制成。双特异性抗体构建体的浓度可以是上文针对蛋白披露的任何浓度。表面活性剂的浓度可以是上文披露的任何浓度。组合物的pH在介于约3.5与约7.0之间的范围内。在一些实施例中，组合物的pH为约5.5。在一些实施例中，容器是IV袋。

[0114] 施用组合物的方法

[0115] 本文还披露了向患者施用本文披露的组合物的方法。在一些实施例中，本文披露了一种向患者施用蛋白的方法，该方法包括a) 在容器中制备水性药物组合物，其中该水性药物组合物包含浓度介于约0.001 μ g/ml与约100 μ g/ml之间的蛋白（例如，本文披露的双特异性抗体构建体）以及浓度为表面活性剂的CMC的至少约0.25倍的表面活性剂，以及b) 向患者施用该水性药物组合物，其中蛋白不是博纳吐单抗。

[0116] 在一些实施例中，水性药物组合物通过用合适的水性溶液稀释包含蛋白（例如，双特异性抗体构建体）的第一组合物来制备。在一些实施例中，水性药物组合物通过将合适的溶液添加到容器中，然后将适当量的第一组合物添加到容器中，从而稀释包含蛋白的第一组合物来制备。

[0117] 在一些实施例中，第一组合物是包含蛋白的液体组合物。在一些实施例中，第一组合物是由包含蛋白的冻干组合物重构的液体组合物。在一些实施例中，第一组合物是使用无菌水由包含蛋白的冻干组合物重构的液体组合物。

[0118] 在一些实施例中,用于稀释第一组合物的合适水性溶液包含浓度为表面活性剂的CMC的至少约0.25倍的表面活性剂。在一些实施例中,用于稀释第一组合物的合适水性溶液包含浓度介于表面活性剂的CMC的约0.25倍与20倍之间、或介于约0.25倍与约10倍之间的表面活性剂。在一些实施例中,用于稀释第一组合物的合适水性溶液包含浓度为表面活性剂的CMC的0.25倍、约0.5倍、约1倍、约2倍、约3倍、约4倍、约5倍、约6倍、约7倍、约8倍、约9倍、约10倍、约15倍或约20倍的表面活性剂。在一些实施例中,用于稀释第一组合物的合适水性溶液进一步包含NaCl。在一些实施例中,用于稀释第一组合物的合适水性溶液具有介于约3.5与约7.0之间、或介于约4.0与约6.5之间的pH。在一些实施例中,用于稀释第一组合物的合适水性溶液具有约5.5的pH。在一些实施例中,该方法进一步包括在制备步骤之前用用于稀释第一组合物的合适水性溶液冲洗容器。

[0119] 在一些实施例中,水性药物组合物中的表面活性剂是聚山梨醇酯。在一些实施例中,表面活性剂是选自聚山梨醇酯20、聚山梨醇酯40、聚山梨醇酯60、聚山梨醇酯65、聚山梨醇酯80和聚山梨醇酯85的聚山梨醇酯。在一些实施例中,表面活性剂是聚山梨醇酯20或聚山梨醇酯80。在一些实施例中,表面活性剂是泊洛沙姆。在一些实施例中,表面活性剂是泊洛沙姆188或泊洛沙姆407。在一些实施例中,表面活性剂是曲拉通X-100。

[0120] 在一些实施例中,水性药物组合物中的表面活性剂以介于表面活性剂的CMC的约0.25倍与约20倍之间的浓度存在于组合物中。在一些实施例中,表面活性剂以介于表面活性剂的CMC的约0.25倍与约10倍之间的浓度存在于水性药物组合物中。在一些实施例中,表面活性剂以在上文披露的任何浓度范围内的浓度存在于水性药物组合物中。在一些实施例中,表面活性剂以作为上文披露的任何浓度的浓度存在于水性药物组合物中。表面活性剂的CMC值可以通过上文披露的方法测定。在一些实施例中,某些常用表面活性剂的CMC值在表1中列出。

[0121] 在一些实施例中,水性药物组合物包含浓度介于约0.001 μ g/ml与约50 μ g/ml之间的蛋白。在一些实施例中,水性药物组合物包含浓度在上文披露的任何范围内的蛋白。在一些实施例中,蛋白以上文披露的任何浓度存在于组合物中。

[0122] 如上所披露,蛋白可以是治疗性蛋白,诸如抗原结合蛋白、mAb或融合蛋白。在一些实施例中,蛋白是双特异性抗原结合蛋白。在一些实施例中,蛋白是上文披露的双特异性抗体构建体。在一些实施例中,蛋白是CD70xCD3双特异性抗体构建体。在一些实施例中,蛋白是BCMAxCD3双特异性抗体构建体。在一些实施例中,蛋白是CD33xCD3双特异性抗体构建体。在一些实施例中,蛋白是EGFRvIIIxCD3双特异性抗体构建体。在一些实施例中,蛋白是MSLNxCD3双特异性抗体构建体。在一些实施例中,蛋白是CDH19xCD3双特异性抗体构建体。在一些实施例中,蛋白是DLL3xCD3双特异性抗体构建体。在一些实施例中,蛋白是FLT3xCD3双特异性抗体构建体。在一些实施例中,蛋白是CDH3xCD3双特异性抗体构建体。在一些实施例中,蛋白是PSMAxCD3双特异性抗体构建体。在一些实施例中,蛋白是C1dn18.2xCD3双特异性抗体构建体。在一些实施例中,蛋白是MUC17xCD3双特异性抗体构建体。这些双特异性抗体构建体中的每一种在上文披露。在某些实施例中,蛋白包含SEQ ID NO:13、SEQ ID NO:15、SEQ ID NO:25、SEQ ID NO:48、SEQ ID NO:67、SEQ ID NO:78、SEQ ID NO:88、SEQ ID NO:109、SEQ ID NO:110、SEQ ID NO:165、SEQ ID NO:166、SEQ ID NO:167、SEQ ID NO:178或SEQ ID NO:192的氨基酸序列,基本上由这些氨基酸序列组成或由这些氨基酸序列组成。

[0123] 组合物的pH可以在上文披露的任何pH范围内。在一些实施例中,组合物的pH可以是上文披露的任何pH。

[0124] 在一些实施例中,水性药物组合物进一步包含一种或多种适用于药物组合物的赋形剂。在一些实施例中,水性药物组合物进一步包含盐、缓冲剂、氨基酸、糖类或糖类衍生物、任选的防腐剂或者两种或更多种前述物质的组合。在一些实施例中,水性药物组合物进一步包含盐、氨基酸、糖类或糖类衍生物、任选的防腐剂或者两种或更多种前述物质的组合。可用于组合物中的示例性盐、缓冲剂、氨基酸、糖类或其衍生物和防腐剂在上文披露。

[0125] 在一些实施例中,容器是塑料容器或部件。在一些实施例中,容器由包含聚烯烃(例如,PP和PE)、PVC、EVA或聚氨酯(例如,聚酯和聚醚)的材料制成。在一些实施例中,容器由包含PVC的材料制成。在一些实施例中,PVC基本上不含DEHP或TOTM。在一些实施例中,容器由不包含PVC的材料制成。在一些实施例中,容器是IV袋或IV管。

[0126] 在一些实施例中,水性药物组合物经由IV施用向患者施用。在一些实施例中,患者是癌症患者。在一些实施例中,患者是人。

[0127] 使蛋白与固体表面结合的方法

[0128] 本文还披露开了一种使蛋白与固体表面结合的方法。在一些实施例中,本文披露了使蛋白与固体表面结合的方法,该方法包括:a)将包含蛋白的水性溶液与固体表面一起孵育,其中将蛋白用荧光团标记,b)从固体表面除去水性溶液并冲洗表面,以及c)使用共聚焦显微镜对固体表面进行成像。

[0129] 下表2列出了本文披露的序列。

[0130]

	名称			氨基酸序列
1.	CD33 ccVH E11	人工的	aa	QVQLVQSGAEVKKPGESVKVSKASGYFTNYGM NWVKQAPGQCLEWMGWINTYTGEPTYADKFQG RVTMTTDTSTSTAYMEIRNLGGDDTAVYYCARWS WSDGYVYFDYWGQGTSVTVSS
2.	CD33 VH E11	人工的	aa	QVQLVQSGAEVKKPGESVKVSKASGYFTNYGM NWVKQAPGQGLEWMGWINTYTGEPTYADKFQG RVTMTTDTSTSTAYMEIRNLGGDDTAVYYCARWS WSDGYVYFDYWGQGTSVTVSS
3.	CD33 HCDR1 E11	人工的	aa	NYGMN
4.	CD33 HCDR2 E11	人工的	aa	WINTYTGEPTYADKFQG
5.	CD33 HCDR3	人工的	aa	WSWSDGYVYFDY

[0131]

	E11			
6.	CD33 CC VL E11	人工的	aa	DIVMTQSPDSLTVSLGERTTINCKSSQSVLDSSTNK NSLAWYQQKPGQPPKLLSWASTRESGIPDRFSGS GSGTDFTLTIDSPQPEDSATYYCQQSAHFPITFGCG TRLEIK
7.	CD33 VL E11	人工的	aa	DIVMTQSPDSLTVSLGERTTINCKSSQSVLDSSTNK NSLAWYQQKPGQPPKLLSWASTRESGIPDRFSGS GSGTDFTLTIDSPQPEDSATYYCQQSAHFPITFGQG TRLEIK
8.	CD33 LCDR1 E11	人工的	aa	KSSQSVLDSSTNKNSLA
9.	CD33 LCDR2 E11	人工的	aa	WASTRES
10.	CD33 LCDR3 E11	人工的	aa	QQSAHFPIT
11.	CD33 HL CC E11	人工的	aa	QVQLVQSGAEVKKPGESVKVSKASGYFTFTNYGM NWVKQAPGQCLEWMGWINTYTGEPTYADKFQG RVTMTTDTSTSTAYMEIRNLGGDDTAVYYCARWS WSDGYVYFDYWGGQTSVTVSSGGGGSGGGGSG GGGSDIVMTQSPDSLTVSLGERTTINCKSSQSVLDS STNKNSLAWYQQKPGQPPKLLSWASTRESGIPDR FSGSGSGTDFTLTIDSPQPEDSATYYCQQSAHFPITF GCGTRLEIK
12.	CD33 HL E11	人工的	aa	QVQLVQSGAEVKKPGESVKVSKASGYFTFTNYGM NWVKQAPGQGLEWMGWINTYTGEPTYADKFQG RVTMTTDTSTSTAYMEIRNLGGDDTAVYYCARWS WSDGYVYFDYWGGQTSVTVSSGGGGSGGGGSG GGGSDIVMTQSPDSLTVSLGERTTINCKSSQSVLDS STNKNSLAWYQQKPGQPPKLLSWASTRESGIPDR FSGSGSGTDFTLTIDSPQPEDSATYYCQQSAHFPITF GQGTRLEIK
13.	CD33 CC E11	人工的	aa	QVQLVQSGAEVKKPGESVKVSKASGYFTFTNYGM

[0132]

	HL x I2C HL 双特异性分子			NWVKQAPGQCLEWMGWINTYTGEPTYADKFQG RVTMTTDTSTSTAYMEIRNLGGDDTAVYYCARWS WSDGYVYFDYWGQGSTVTVSSGGGGSGGGGSG GGGSDIVMTQSPDSLTVSLGERTTINCKSSQSVLDS STNKNSLAWYQQKPGQPPKLLSWASTRESGIPDR FSGSGSGTDFTLTIDSPQPEDSATYYCQQSAHPITF GCGTRLEIKSGGGGSEVQLVESGGGLVQPGGSLKL SCAASGFTFNKYAMNWVRQAPGKGLEWVARIRSK YNNYATYYADSVKDRFTISRDDSKNTAYLQMNNLK TEDTAVYYCVRHGNFGNSYISYWAYWGQGLTVTV SSGGGGSGGGGSGGGGSGTQVTVTQEPSLTVSPGGT VTLTCGSSTGAVTSGNYPNWVQKPGQAPRGLIG GTKFLAPGTPARFSGSLLGGKAALTLSGVQPEDEAE YYCVLWYSNRWVFGGGTKLTVL
14.	CD33 E11 HL x I2C HL	人工的	aa	MGWSCIIFLVATATGVHSQVQLVQSGAEVKKPGE SVKVSCASGYTFTNYGMNWVKQAPGQGLEWM GWINTYTGEPTYADKFQGRVTMTTDTSTSTAYMEI RNLGGDDTAVYYCARWSWSDGYVYFDYWGQG TSVTVSSGGGGSGGGGSGGGGSDIVMTQSPDSL VSLGERTTINCKSSQSVLDSSTNKNSLAWYQQKPG QPPKLLSWASTRESGIPDRFSGSGSGTDFTLTIDSP QPEDSATYYCQQSAHPITFGGQTRLEIKSGGGGSE VQLVESGGGLVQPGGSLKLSAASGFTFNKYAMN WVRQAPGKGLEWVARIRSKYNNYATYYADSVKDR FTISRDDSKNTAYLQMNNLKTEDTAVYYCVRHGNF GNSYISYWAYWGQGLTVTVSSGGGGSGGGGSGG GGSGTQVTVTQEPSLTVSPGGTVTLTCGSSTGAVTSG NYPNWVQKPGQAPRGLIGGTKFLAPGTPARFSG SLLGGKAALTLSGVQPEDEAEYYCVLWYSNRWVFG GGTKLTVLHHHHHH
15.	CD33 CC x I2C-scFc 双特异	人工的	aa	QVQLVQSGAEVKKPGESVKVSCASGYTFTNYGMN WVKQAPGQCLEWMGWINTYTGEPTYADKFQGRVT

[0133]

	性 HLE 分子			MTTDTSTSTAYMEIRNLGGDDTAVYYCARWSWSDG YVYFDYWGQGTSTVTVSSGGGGSGGGGSGGGGSDI VMTQSPDSLTVSLGERTTINCKSSQSVLDSSTNKNL AWYQQKPGQPPLKLLSWASTRESGIPDRFSGSGSGT DFTLTIDSPQPEDSATYYCQSAHFPIFGCGTRLEIKS GGGGSEVQLVESGGGLVQPGGSLKLSAASGFTFNK YAMNWVRQAPGKGLEWVARIRSKYNNYATYYADS VKDRFTISRDDSKNTAYLQMNNLKTEDTAVYYCVRH GNFGNSYISYWAYWGQGLTVTVSSGGGGSGGGGS GGGGSQTVVTQEPSTVSPGGTVTLTCSSTGAVTS GNYPNWVQQKPGQAPRGLIGGTFKFLAPGTPARFSG SLLGGKAALTLSGVQPEDEAEYYCVLWYSNRWVFGG GTKLTVLGGGGDKHTHTCPPCPAPELLGGPSVFLFPPK PKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGV EVHNAKTKPCEEQYGSTYRCVSVLTVLHQDWLNGKE YKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRE EMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYK TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSVM HEALHNHYTQKSLSLSPGKGGGGSGGGGSGGGGSG GGGSGGGGSGGGGSDKHTHTCPPCPAPELLGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWY VDGVEVHNAKTKPCEEQYGSTYRCVSVLTVLHQDWL NGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTL PSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPE NNYKTTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFS CSVMHEALHNHYTQKSLSLSPGK
16.	EGFRvIIIxCD3-scFc VH CDR1	人工的	aa	NYGMH
17.	EGFRvIIIxCD3-scFc VH CDR2	人工的	aa	VIWYDGSDKYYADSVRG
18.	EGFRvIIIxCD3-scFc VH CDR3	人工的	aa	DGYDILTGNPRDFDY

[0134]

19.	EGFRvIIIxCD3-scFc VL CDR1	人工的	aa	RSSQSLVHSDGNTYLS
20.	EGFRvIIIxCD3-scFc VL CDR2	人工的	aa	RISRRFS
21.	EGFRvIIIxCD3-scFc VL CDR3	人工的	aa	MQSTHVPRT
22.	EGFRvIII_CCxC D3-scFc VH	人工的	aa	QVQLVESGGGVVQSGRSLRLSCAASGFTFRNYGMH WVRQAPGKCLEWVAVIWDGSDKYADSVRGRFTI SRDNSKNTLYLQMNSLRAEDTAVYYCARDGYDILT NPRDFDYWGQGTLLTVSS
23.	EGFRvIII_CCxC D3-scFc VL	人工的	aa	DTVMTQTPLSSHVTLGQPASISCRSSQSLVHSDGNTY LSWLQQRPGQPPRLIYRISRRFSGVPDRFSGSGAGT DFTLEISRVEAEDVGVYYCMQSTHVPRTFGCGTKVEI K
24.	EGFRvIII_CCxC D3-scFc scFv	人工的	aa	QVQLVESGGGVVQSGRSLRLSCAASGFTFRNYGMH WVRQAPGKCLEWVAVIWDGSDKYADSVRGRFTI SRDNSKNTLYLQMNSLRAEDTAVYYCARDGYDILT NPRDFDYWGQGTLLTVSSGGGGSGGGGSGGGGSD TVMTQTPLSSHVTLGQPASISCRSSQSLVHSDGNTYL SWLQQRPGQPPRLIYRISRRFSGVPDRFSGSGAGTD FTLEISRVEAEDVGVYYCMQSTHVPRTFGCGTKVEIK
25.	EGFRvIII_CCxC D3-scFc 双特异性分子	人工的	aa	QVQLVESGGGVVQSGRSLRLSCAASGFTFRNYGMH WVRQAPGKCLEWVAVIWDGSDKYADSVRGRFTI SRDNSKNTLYLQMNSLRAEDTAVYYCARDGYDILT NPRDFDYWGQGTLLTVSSGGGGSGGGGSGGGGSD TVMTQTPLSSHVTLGQPASISCRSSQSLVHSDGNTYL SWLQQRPGQPPRLIYRISRRFSGVPDRFSGSGAGTD FTLEISRVEAEDVGVYYCMQSTHVPRTFGCGTKVEIK SGGGGSEVQLVESGGGLVQPGGSLKLSAASGFTFN KYAMNWVRQAPGKGLEWVARIRSKYNNYATYYAD SVKDRFTISRDDSKNTAYLQMNNLKTEDTAVYYCVR HGNFGNSYISYWAYWGQGTLLTVSSGGGGSGGGG

[0135]

				SGGGGSQTVVTQEPSLTVSPGGTVTLTCGSSTGAVTS GNYPNWVQQKPGQAPRGLIGGTKFLAPGTPARFSG SLLGGKAALTLSGVQPEDEAEYYCVLWYSNRWVFGG GTKLTVL
26.	EGFRvIII_CCxC D3-scFc 双特异 性 HLE 分子	人工的	aa	QVQLVESGGGVVQSGRSLRLSCAASGFTFRNYGMH WVRQAPGKCLEWVAVIWDGSDKYADSVRGRFTI SRDNSKNTLYLQMNSLRAEDTAVYYCARDGYDILT NPRDFDYWGQGLTVTVSSGGGSGGGGSGGGGSD TVMTQTPLSSHVTLGQPASISCRSSQSLVHSDGNTYL SWLQQRPGQPPRLIYRISRRFSGVPDRFSGSGAGTD FTLEISRVEAEDVGVYYCMQSTHVPRTFGCGTKVEIK SGGGGSEVQLVESGGGLVQPGGSLKLSAASGFTFN KYAMNWVRQAPGKGLEWVARIRSKYNNYATYYAD SVKDRFTISRDDSKNTAYLQMNNLKTEDTAVYYCVR HGNFGNSYISYWAYWGQGLTVTVSSGGGSGGGG SGGGGSQTVVTQEPSLTVSPGGTVTLTCGSSTGAVTS GNYPNWVQQKPGQAPRGLIGGTKFLAPGTPARFSG SLLGGKAALTLSGVQPEDEAEYYCVLWYSNRWVFGG GTKLTVLGGGGDKHTHTCPPCPAPELLGGPSVFLFPPK PKDTLMISRTPEVTCVVDVSHEDPEVKFNWYVDGV EVHNAKTKPCEEQYGSTYRCVSVLTVLHQDWLNGKE YKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRE EMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYK TTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVM HEALHNHYTQKSLSLSPGKGGGGSGGGGSGGGGSG GGGSGGGGSGGGGSDKHTHTCPPCPAPELLGGPSVFL FPPKPKDTLMISRTPEVTCVVDVSHEDPEVKFNWY VDGVEVHNAKTKPCEEQYGSTYRCVSVLTVLHQDW LNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTL PPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQP ENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVF SCSVMHEALHNHYTQKSLSLSPGK

[0136]

27.	MSLN_5 VH CDR1	人工的	aa	DYYMT
28.	MSLN_5 VH CDR2	人工的	aa	YISSSGSTIYYADSVKG
29.	MSLN_5 VH CDR3	人工的	aa	DRNSHFDY
30.	MSLN_5 VL CDR1	人工的	aa	RASQGINTWLA
31.	MSLN_5 VL CDR2	人工的	aa	GASGLQS
32.	MSLN_5 VL CDR3	人工的	aa	QQAQSFPR
33.	MSLN_5 VH	人工的	aa	QVQLVESGGGLVKPGGSLRLSCAASGFTFSDYYMT WIRQAPGKGLEWLSYISSSGSTIYYADSVKGRFTISR DNAKNSLFLQMNSLRAEDTAVYYCARDNRNSHFDY WGQGTLLTVSS
34.	MSLN_5 VL	人工的	aa	DIQMTQSPSSVSASVGDRVITTCRASQGINTWLA WYQQKPGKAPKLLIYGASGLQSGVPSRFSGSGSGT DFTLTISLQPEDFATYYCQQAQSFPRTFGQGTKVEI K
35.	MSLN_5 scFv	人工的	aa	QVQLVESGGGLVKPGGSLRLSCAASGFTFSDYYMT WIRQAPGKGLEWLSYISSSGSTIYYADSVKGRFTISR DNAKNSLFLQMNSLRAEDTAVYYCARDNRNSHFDY WGQGTLLTVSSGGGGSGGGSGGGGSDIQMTQ SPSSVSASVGDRVITTCRASQGINTWLAWYQQK GKAPKLLIYGASGLQSGVPSRFSGSGSGTDFTLTIS LQPEDFATYYCQQAQSFPRTFGQGTKVEIK
36.	MSLN_5xI2C 0 双特异性 分子	人工的	aa	QVQLVESGGGLVKPGGSLRLSCAASGFTFSDYYMT WIRQAPGKGLEWLSYISSSGSTIYYADSVKGRFTISR DNAKNSLFLQMNSLRAEDTAVYYCARDNRNSHFDY WGQGTLLTVSSGGGGSGGGSGGGGSDIQMTQ SPSSVSASVGDRVITTCRASQGINTWLAWYQQK GKAPKLLIYGASGLQSGVPSRFSGSGSGTDFTLTIS

[0137]

				LQPEDFATYYCQQAQSFPRFTFGQGTKVEIKSGGGG SEVQLVESGGGLVQPGGSLKLSAASGFTFNKYAM NWVRQAPGKGLEWVARIRSKYNNYATYYADSVKD RFTISRDDSKNTAYLQMNNLKTEDTAVYYCVRHGN FGNSYISYWAYWGQGLTVTVSSGGGGSGGGGSG GGGSQTVVTQEPSLTVSPGGTVTLTCGSSTGAVTS GNYPNWVQQKPGQAPRGLIGGTKFLAPGTPARFS GSLLGGKAALTLSGVQPEDEAEYYCVLWYSNRWVF GGGTKLTVL
37.	MSLN_5xCD3 -scFc 双特异 性 HLE 分子	人工的	aa	QVQLVESGGGLVKPGGSLRLSCAASGFTFSDYYMT WIRQAPGKGLEWLSYISSSGSTIYYADSVKGRFTISR DNAKNSLFLQMNSLRAEDTAVYYCARDNRNSHFDY WGQGLTVTVSSGGGGSGGGGSGGGGSDIQMTQ SPSSVSASVGDRVITICRASQGINTWLAWYQQKP GKAPKLLIYGASGLQSGVPSRFSGSGSGTDFTLTISS LQPEDFATYYCQQAQSFPRFTFGQGTKVEIKSGGGG SEVQLVESGGGLVQPGGSLKLSAASGFTFNKYAM NWVRQAPGKGLEWVARIRSKYNNYATYYADSVKD RFTISRDDSKNTAYLQMNNLKTEDTAVYYCVRHGN FGNSYISYWAYWGQGLTVTVSSGGGGSGGGGSG GGGSQTVVTQEPSLTVSPGGTVTLTCGSSTGAVTS GNYPNWVQQKPGQAPRGLIGGTKFLAPGTPARFS GSLLGGKAALTLSGVQPEDEAEYYCVLWYSNRWVF GGGTKLTVLGGGGDKTHTCPPCPAPELLGGPSVFL FPPKPKDTLMISRTPEVTCVVDVSHEDPEVKFNW YVDGVEVHNAKTKPCEEQYGSTYRCVSVLTVLHQD WLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQV YTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESN GQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQ GNVFSCSVMHEALHNHYTQKSLSLSPGKGGGGSG GGGSGGGGSGGGGSGGGGSGGGGSDKTHTCPPC PAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVD

[0138]

				VSHEDPEVKFNWYVDGVEVHNAKTKPCEEQYGST YRCVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKT ISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKG FYPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLY SKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSL SLSPGK
38.	MSLN_5_CCx CD3-scFc 双特 异性 HLE 分 子	人工的	aa	QVQLVESGGGLVKPGGSLRLSCAASGFTFSDHYMS WIRQAPGKCLEWFSYISSGGIYYADSVKGRFTISR DNAKNSLYLQMNSLRAEDTAVYYCARDVGSFHDY WGQGTLLTVSSGGGGSGGGGSGGGGSDIQMTQ SPSSVSASVGDRVITCRASQDISRWLAWYQQKPG KAPKLLISAASRLQSGVPSRFSGSGSGTDFTLTISLQ PEDFAIYYCQAKSFPRTFGCGTKVEIKSGGGGSEV QLVESGGGLVQPGGSLKLSAASGFTFNKYAMNW VRQAPGKGLEWVARIRSKYNNYATYYADSVKDRFT ISRDDSKNTAYLQMNNLKTEDTAVYYCVRHGNFG NSYISYWAYWGQGTLLTVSSGGGGSGGGGSGGG GSQTVVTQEPSTVSPGGTVTLTCSSTGAVTSGN YPNWVQQKPGQAPRGLIGGKFLAPGTPARFSGSL LGGKAALTSGVQPEDEAEYYCVLWYSNRWVFGG GTKLTVLGGGGDKTHTCPPCPAPELLGGPSVFLFPP KPKDTLMISRTPEVTCVVDVSHEDPEVKFNWYVD GVEVHNAKTKPCEEQYGSTYRCVSVLTVLHQDWL NGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYT LPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTPPVLDSDGSFFLYSKLTVDKSRWQQG NVFSCFSVMHEALHNHYTQKSLSLSPGKGGGGSGG GGGGGGSGGGGSGGGGSGGGGSDKTHTCPPCP APELLGGPSVFLFPPKPKDTLMISRTPEVTCVVDV SHEDPEVKFNWYVDGVEVHNAKTKPCEEQYGSTY RCVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTI SKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKG

[0139]

				FYPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLY SKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSL SLSPGK
39.	CDR-H1 CDH19 65254.007	人工的	aa	SYGMH
40.	CDR-H2 CDH19 65254.007	人工的	aa	FIWYEGSNKYAESVKD
41.	CDR-H3 CDH19 65254.007	人工的	aa	RAGIIGTIGYYYGMDV
42.	CDR-L1 CDH19 65254.007	人工的	aa	SGDRLGEKYTS
43.	CDR-L2 CDH19 65254.007	人工的	aa	QDTRPS
44.	CDR-L3 CDH19 65254.007	人工的	aa	QAWESSTVV
45.	VH CDH19 65254.007	人工的	aa	QVQLVESGGGVVQPGGSLRLSCAASGFTFSSYGM HWVRQAPGKGLEWVAFIWIWYEGSNKYAESVKDRF TISRDNKNTLYLQMNSLRAEDTAVYYCARRAGIIG TIGYYYGMDVWGQGTITVTVSS
46.	VL CDH19 65254.007	人工的	aa	SYELTQPPSVSVSPGQTASITCSGDRLGEKYTSWYQ QRPQGSPLLVIYQDTRPSGIPERFSGSNSGNTATL TISGTQAMDEADYYCQAWESSTVVFSGGKTLTVLS
47.	VH-VL CDH19 65254.007	人工的	aa	QVQLVESGGGVVQPGGSLRLSCAASGFTFSSYGM HWVRQAPGKGLEWVAFIWIWYEGSNKYAESVKDRF TISRDNKNTLYLQMNSLRAEDTAVYYCARRAGIIG TIGYYYGMDVWGQGTITVTVSSGGGGSGGGSGG GGSSYELTQPPSVSVSPGQTASITCSGDRLGEKYTS

[0140]

				WYQQRPGQSPLLVIYQDTKRPSGIPERFSGSNSGN TATLTISGTQAMDEADYYCQAWESSTVVFGGGTKL TVLS
48.	CDH19 65254.007 x I2C	人工的	aa	QVQLVESGGGVVQPGGSLRLSCAASGFTFSSYGM HWVRQAPGKGLEWVAFIWEYSNKKYAESVKDRF TISRDN SKNTLYLQMNSLRAEDTAVYYCARRAGIIG TIGYYYGMDVWGQGTITVTVSSGGGGSGGGGSGG GGSSYELTQPPSVSVSPGQTASITCSGDRLEGEKYS WYQQRPGQSPLLVIYQDTKRPSGIPERFSGSNSGN TATLTISGTQAMDEADYYCQAWESSTVVFGGGTKL TVLSGGGGSEVQLVESGGGLVQPGGSLKLSAASG FTFNKYAMNWRQAPGKGLEWVARIRSKYNNYA TYYADSVKDRFTISRDDSKNTAYLQMNNLKTEDTA VYYCVRHGNFGNSYISYWAYWGQGLTVTVSSGGG GSGGGGSGGGGSQTVVTQEPLTVSPGGTVTLTC GSSTGAVTSGNYPNWWVQKPGQAPRGLIGGKFL APGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCVL WYSNRWVFGGGKLTVLHHHHHH
49.	CDH19 65254.007 x I2C -scFc 双特 异性 HLE 分子	人工的	aa	QVQLVESGGGVVQPGGSLRLSCAASGFTFSSYGMH WVRQAPGKGLEWVAFIWEYSNKKYAESVKDRFTIS RDN SKNTLYLQMNSLRAEDTAVYYCARRAGIIGTIGY YYGMDVWGQGTITVTVSSGGGGSGGGGSGGGGSS YELTQPPSVSVSPGQTASITCSGDRLEGEKYSWYQQR PGQSPLLVIYQDTKRPSGIPERFSGSNSGNTATLTISG TQAMDEADYYCQAWESSTVVFGGGKLTVLSSGGG SEVQLVESGGGLVQPGGSLKLSAASGFTFNKYAMN WVRQAPGKGLEWVARIRSKYNNYATYYADSVKDRF TISRDDSKNTAYLQMNNLKTEDTAVYYCVRHGNFGN SYISYWAYWGQGLTVTVSSGGGGSGGGGSGGGGS QTVVTQEPLTVSPGGTVTLTCGSSTGAVTSGNYPN WVQKPGQAPRGLIGGKFLAPGTPARFSGSLLGGK AALTLSGVQPEDEAEYYCVLWYSNRWVFGGGKLTV

[0141]

				LGGGGDKTHTCPPCPAPELLGGPSVFLFPPKPKDTL MISRTPEVTCVVDVSHEDPEVKFNWYVDGVEVHN AKTKPCEEQYGSTYRCVSVLTVLHQDWLNGKEYKCK VSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK NQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPP VLDSGDSFFLYSKLTVDKSRWQQGNVFCFSVMHEAL HNHYTQKSLSLSPGKGGGGSGGGGSGGGGSGGGG SGGGGSGGGGSDKTHTCPPCPAPELLGGPSVFLFPP KPKDTLMISRTPEVTCVVDVSHEDPEVKFNWYVDG VEVHNAKTKPCEEQYGSTYRCVSVLTVLHQDWLNG KEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPS REEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENN YKTTTPVLDSGDSFFLYSKLTVDKSRWQQGNVFCFSV MHEALHNHYTQKSLSLSPGK
50.	CDH19 65254.007 x I2C -scFc_delGK 双 特异性 HLE 分 子	人工的	aa	QVQLVESGGGVVQPGGSLRLSCAASGFTFSSYGMH WVRQAPGKGLEWVAFIWEYSNKKYAESVKDRFTIS RDNSKNTLYLQMNSLRAEDTAVYYCARRAGIIGTIGY YYGMDVWGQGTTVTVSSGGGGSGGGGSGGGGSS YELTQPPSVSVSPGQTASITCSGDRLEKEYTSWYQQR PGQSPLLVIYQDTRKPSGIPERFSGSNSGNTATLTISG TQAMDEADYYCQAWESSTVVFGGGKTLTVLSSGGG SEVQLVESGGGLVQPGGSLKLSAASGFTFNKYAMN WVRQAPGKGLEWVARIRSKYNNYATYYADSVKDRF TISRDDSKNTAYLQMNNLKTEDTAVYYCVRHGNFGN SYISYWAYWGQGLTVTVSSGGGGSGGGGSGGGGSS QTVVTQEPSLTVSPGGTVTLTCSSTGAVTSGNYPN WVQQKPGQAPRGLIGGKFLAPGTPARFSGSLLGGK AALTSGVQPEDEAEYYCVLWYSNRWVFGGGKTLTV LGGGGDKTHTCPPCPAPELLGGPSVFLFPPKPKDTL MISRTPEVTCVVDVSHEDPEVKFNWYVDGVEVHN AKTKPCEEQYGSTYRCVSVLTVLHQDWLNGKEYKCK VSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK

[0142]

				NQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPP VLDSGDGSFFLYSKLTVDKSRWQQGNVFCSSVMHEAL HNHYTQKSLSLSPGGGSGGGGSGGGGSGGGGSG GGGSGGGGSDKHTCPPCPAPELLGGPSVFLFPPKP KDTLMISRTPEVTCVVDVSHEDPEVKFNWYVDGVE VHNAKTKPCEEQYGSTYRCVSVLTVLHQDWLNGKEY KCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREE MTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKT TPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSSVMH EALHNHYTQKSLSLSPGK
51.	CDH19 65254.007_CC x I2C -scFc VH	人工的	aa	QVQLVESGGGVVQPGGSLRLSCAASGFTFSSYGMH WVRQAPGKCLEWVAFIWEYSNKKYAESVKDRFTIS RDNSKNTLYLQMNSLRAEDTAVYYCARRAGIIGTIGY YYGMDVWGQGTITVTVSS
52.	CDH19 65254.007_CC x I2C -scFc VL	人工的	aa	SYELTQPPSVSVSPGQTASITCSGDRLEGEYTSWYQQ RPGQSPLLVIYQDTRPSGIPERFSGSNSGNTATLTIS GTQAMDEADYYCQAWESSTVVFSGCGTKLTVL
53.	CDH19 65254.007_CC x I2C -scFc scFv	人工的	aa	QVQLVESGGGVVQPGGSLRLSCAASGFTFSSYGMH WVRQAPGKCLEWVAFIWEYSNKKYAESVKDRFTIS RDNSKNTLYLQMNSLRAEDTAVYYCARRAGIIGTIGY YYGMDVWGQGTITVTVSSGGGSGGGGSGGGGSS YELTQPPSVSVSPGQTASITCSGDRLEGEYTSWYQQR PGQSPLLVIYQDTRPSGIPERFSGSNSGNTATLTISG TQAMDEADYYCQAWESSTVVFSGCGTKLTVL
54.	CDH19 65254.007_CC x I2C -scFc 双 特异性分子	人工的	aa	QVQLVESGGGVVQPGGSLRLSCAASGFTFSSYGMH WVRQAPGKCLEWVAFIWEYSNKKYAESVKDRFTIS RDNSKNTLYLQMNSLRAEDTAVYYCARRAGIIGTIGY YYGMDVWGQGTITVTVSSGGGSGGGGSGGGGSS YELTQPPSVSVSPGQTASITCSGDRLEGEYTSWYQQR PGQSPLLVIYQDTRPSGIPERFSGSNSGNTATLTISG TQAMDEADYYCQAWESSTVVFSGCGTKLTVLSSGGG SEVQLVESGGGLVQPGGSLKLSCAASGFTFNKYAMN

[0143]

				WVRQAPGKGLEWVARIRSKYNNYATYYADSVKDRF TISRDDSKNTAYLQMNNLKTEDTAVYYCVRHGNFGN SYISYWAYWGQGLTVTVSSGGGSGGGGSGGGGS QTVVTQEPLTVSPGGTVTLTCGSSTGAVTSGNYPN WVQQKPGQAPRGLIGGTKFLAPGTPARFSGSLLGGK AALTLSGVQPEDEAEYYCVLWYSNRWVFGGGTKLTV L
55.	CDH19 65254.007_CC x I2C -scFc 双 特异性 HLE 分 子	人工的	aa	QVQLVESGGGVVQPGGSLRLSCAASGFTFSSYGMH WVRQAPGKCLEWVAFIWEYSNKKYAESVKDRFTIS RDNSKNTLYLQMNSLRAEDTAVYYCARRAGIIGTIGY YYGMDVWGQGTTVTVSSGGGSGGGGSGGGGSS YELTQPPSVSVSPGQTASITCSGDRLEKEYTSWYQQR PGQSPLLVIYQDTKRPSGIPERFSGSNSGNTATLTISG TQAMDEADYYCQAWESSTVFGCGTKLTVLSGGGG SEVQLVESGGGLVQPGGSLKLSCAASGFTFNKYAMN WVRQAPGKGLEWVARIRSKYNNYATYYADSVKDRF TISRDDSKNTAYLQMNNLKTEDTAVYYCVRHGNFGN SYISYWAYWGQGLTVTVSSGGGSGGGGSGGGGS QTVVTQEPLTVSPGGTVTLTCGSSTGAVTSGNYPN WVQQKPGQAPRGLIGGTKFLAPGTPARFSGSLLGGK AALTLSGVQPEDEAEYYCVLWYSNRWVFGGGTKLTV LGGGGDKTHTCPPCPAPPELLGGPSVFLFPPKPKDTL MISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHN AKTKPCEEQYGSTYRCVSVLTVLHQDWLNGKEYKCK VSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK NQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPP VLDSGDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEAL HNHYTQKSLSLSPGKGGGSGGGGSGGGGSGGGG SGGGSGGGGSDKTHTCPPCPAPPELLGGPSVFLFPP KPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDG VEVHNAKTKPCEEQYGSTYRCVSVLTVLHQDWLNG KEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPS

[0144]

				REEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENN YKTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSV MHEALHNHYTQKSLSLSPGK
56.	CDH19 65254.007_CC x I2C -scFc_delGK 双 特异性 HLE 分 子	人工的	aa	QVQLVESGGGVVQPGGSLRLSCAASGFTFSSYGMH WVRQAPGKCLEWVAFIWIYEGSNKYAESVKDRFTIS RDNSKNTLYLQMNSLRAEDTAVYYCARRAGIIGTIGY YYGMDVWGQGTITVTVSSGGGGSGGGGSGGGGSS YELTQPPSVSVSPGQTASITCSGDRLEKYTSWYQQR PGQSPLLVIYQDTRPSGIPERFSGSNSGNTATLTISG TQAMDEADYYCQAWESSTVVFVCGTKLTVLSGGGG SEVQLVESGGGLVQPGGSLKLSCAASGFTFNKYAMN WVRQAPGKLEWVARIRSKYNNYATYYADSVKDRF TISRDDSKNTAYLQMNNLKTEDTAVYYCVRHGNFGN SYISYWAYWGQGLTVTVSSGGGGSGGGGSGGGGS QTVVTQEPSLTVSPGGTVTLTCSSTGAVTSGNYPN WVQQKPGQAPRGLIGGKFLAPGTPARFSGSLLGGK AALTLSGVQPEDEAEYYCVLWYSNRWVFGGKTLTV LGGGGDKHTHTCPPCPAPELLGGPSVFLFPPKPKDTL MISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHN AKTKPCEEQYGSTYRCVSVLTVLHQDWLNGKEYKCK VSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK NQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPP VLSDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMH EALHNHYTQKSLSLSPGK
57.	FLT3_7	人工的	aa	NARMGV

[0145]

	A8xCD3-scFc VH CDR1			
58.	FLT3_7 A8xCD3-scFc VH CDR2	人工的	aa	HIFSNDEKSYSTSLKN
59.	FLT3_7 A8xCD3-scFc VH CDR3	人工的	aa	IVGYGSGWYGFFDY
60.	FLT3_7 A8xCD3-scFc VL CDR1	人工的	aa	RASQGIRNDLG
61.	FLT3_7 A8xCD3-scFc VL CDR2	人工的	aa	AASTLQS
62.	FLT3_7 A8xCD3-scFc VL CDR3	人工的	aa	LQHNSYPLT
63.	FLT3_7 A8xCD3-scFc VH	人工的	aa	QVTLKESGPTLVKPTETLTCTLSGFSLNNARMGVS WIRQPPGKCLEWLAHIFSNDEKSYSTSLKNRLTISKDS SKTQVVLTMNVDPVDTATYYCARIVGYGSGWYGF FDYWGQGTLTVSS
64.	FLT3_ A8-scFc VL	人工的	aa	DIQMTQSPSSLSASVGDRVITICRASQGIRNDLGWY QQKPGKAPKRLIYAASTLQSGVPSRFSGSGSGTEFTLT ISSLQPEDFATYYCLQHNSYPLTFGCGTKVEIK
65.	FLT3_7 A8xCD3- scFv	人工的	aa	QVTLKESGPTLVKPTETLTCTLSGFSLNNARMGVS WIRQPPGKCLEWLAHIFSNDEKSYSTSLKNRLTISKDS SKTQVVLTMNVDPVDTATYYCARIVGYGSGWYGF FDYWGQGTLTVSSGGGGSGGGGSGGGGSDIQMT QSPSSLSASVGDRVITICRASQGIRNDLGWYQQKPG KAPKRLIYAASTLQSGVPSRFSGSGSGTEFTLTISLQPE DFATYYCLQHNSYPLTFGCGTKVEIK
66.	FLT3_7 A8xCD3 双特异	人工的	aa	QVTLKESGPTLVKPTETLTCTLSGFSLNNARMGVS WIRQPPGKCLEWLAHIFSNDEKSYSTSLKNRLTISKDS

[0146]

	性分子			SKTQVVLMTNVPVDTATYYCARIVGYGSGWYGFF DYWGQGT LVT VSSGGGSGGGGSGGGGSDIQMT QSPSSLSASVGDRVTITCRASQGIRNDLGWYQQKPG KAPKRLIYAASLTQSGVPSRFSGSGSGTEFTLTISLQP EDFATYYCLQHNSYPLTFGCGTKVEIKSGGGGSEVQL VESGGGLVQPGGSLKLSAASGFTFNKYAMNWVRQ APGKGLEWVARIRSKYNNYATYYADSVKDRFTISRDD SKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYISY WAYWGQGT LVT VSSGGGSGGGGSGGGGSGTQVV TQEPSLTVSPGGTVTLTCSSTGAVTSGNYPNWVQQ KPGQAPRGLIGGTKFLAPGTPARFSGSLLGGKAALT LSGVQPEDEAEYCVLWYSNRWVFGGGTKLTVL
67.	FLT3_7 A8xCD3-scFc 双特异性 HLE 分子	人工的	aa	QVTLKESGPTLVKPTETLTCTLSGFSLNNARMGVS WIRQPPGKCLEWLAHIFSNDEKSYSTSLKNRLTISKDS SKTQVVLMTNVPVDTATYYCARIVGYGSGWYGFF DYWGQGT LVT VSSGGGSGGGGSGGGGSDIQMT QSPSSLSASVGDRVTITCRASQGIRNDLGWYQQKPG KAPKRLIYAASLTQSGVPSRFSGSGSGTEFTLTISLQP EDFATYYCLQHNSYPLTFGCGTKVEIKSGGGGSEVQL VESGGGLVQPGGSLKLSAASGFTFNKYAMNWVRQ APGKGLEWVARIRSKYNNYATYYADSVKDRFTISRDD SKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYISY WAYWGQGT LVT VSSGGGSGGGGSGGGGSGTQVV TQEPSLTVSPGGTVTLTCSSTGAVTSGNYPNWVQQ KPGQAPRGLIGGTKFLAPGTPARFSGSLLGGKAALT LSGVQPEDEAEYCVLWYSNRWVFGGGTKLTVLGGG GDKHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRT PEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPC EEQYGSTYRCVSVLTVLHQDWLNGKEYKCKVSNKAL PAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLT CLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDG SFFLYSKLTVDKSRWQQGNVFSQSVMSHEALHNHYT

[0147]

				QKSLSLSPGKGGGGSGGGGSGGGGSGGGGSGGGG SGGGGSDKTHTCPPCPAPELLGGPSVFLFPPKPKDTL MISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHN AKTKPCEEQYGSTYRCVSVLTVLHQDWLNGKEYKCK VSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK NQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPP VLDSGDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEAL HNHYTQKSLSLSPGK
68	VH CDR1 DLL3_1_CC_de IGK	人工的	aa	SYWWS
69	VH CDR2 DLL3_1_CC_de IGK	人工的	aa	YVYSGTTNYPNPSLKS
70	VH CDR3 DLL3_1_CC_de IGK	人工的	aa	IAVTGFYFDY
71	VL CDR1 DLL3_1_CC_de IGK	人工的	aa	RASQRVNNNYLA
72	VL CDR2 DLL3_1_CC_de IGK	人工的	aa	GASSRAT
73	VL CDR3 DLL3_1_CC_de IGK	人工的	aa	QQYDRSPLT
74.	VH DLL3_1_CC_de IGK	人工的	aa	QVQLQESGPGLVKPSSETLSLTCTVSGGSISSYYWSWI RQPPGKCLEWIGYVYVYSGTTNYPNPSLKSRTISVDTS KNQFSLKLSSVTAADTAVYYCASIATGFIYFDYWGQ GTLVTVSS
75.	VL DLL3_1_CC_de IGK	人工的	aa	EIVLTQSPGTLSPGERVTLSRASQRVNNNYLAWY QQRPGQAPRLIYGASSRATGIPDRFSGSGSGTDFTL TISRLEPEDFAVYYCQQYDRSPLTFGCGTKLEIK

[0148]

76.	DLL3_1_CC_de IGK	人工的	aa	QVQLQESGPGLVKPSSETLSLTCTVSGGSISSYYWSWI RQPPGKCLEWIGYVYVYSGTTNYPNPSLKSRTISVDTSK NQFSLKLSSVTAADTAVYYCASIATGIFYFDYWGQG TLVTVSSGGGGSGGGSGGGGSEIVLTQSPGTLSP GERVTLSRASQRVNNNYLAWYQQRPGQAPRLIY GASSRATGIPDRFSGSGSGTDFTLTISRLEPEDFAVYY CQYDRSPLTFGCGTKLEIK
77.	DLL3_1_CCxC D3_delIGK 双特 异性分子	人工的	aa	QVQLQESGPGLVKPSSETLSLTCTVSGGSISSYYWSWI RQPPGKCLEWIGYVYVYSGTTNYPNPSLKSRTISVDTSK NQFSLKLSSVTAADTAVYYCASIATGIFYFDYWGQG TLVTVSSGGGGSGGGSGGGGSEIVLTQSPGTLSP GERVTLSRASQRVNNNYLAWYQQRPGQAPRLIY GASSRATGIPDRFSGSGSGTDFTLTISRLEPEDFAVYY CQYDRSPLTFGCGTKLEIKSGGGGSEVQLVESGGGL VQPGGSLKLSAASGFTFNKYAMNWRQAPGKGLE WVARIRSKYNNYATYYADSVKDRFTISRDDSKNTAYL QMNNLKTEDTAVYYCVRHGNFGNSYISYWAYWGQ GTLVTVSSGGGGSGGGSGGGGSQTVVTQEPSLTV SPGGTVTLTCSSTGAVTSGNYPNWWQKPGQAPR GLIGGTKFLAPGTPARFSGSLLGGKAALTLSGVQPED EAHYCVLWYSNRWVFGGGTKLTVL
78.	DLL3_1_CCxC D3-scFc_delIGK 双特异性 HLE 分子	人工的	aa	QVQLQESGPGLVKPSSETLSLTCTVSGGSISSYYWSWI RQPPGKCLEWIGYVYVYSGTTNYPNPSLKSRTISVDTSK NQFSLKLSSVTAADTAVYYCASIATGIFYFDYWGQG TLVTVSSGGGGSGGGSGGGGSEIVLTQSPGTLSP GERVTLSRASQRVNNNYLAWYQQRPGQAPRLIY GASSRATGIPDRFSGSGSGTDFTLTISRLEPEDFAVYY CQYDRSPLTFGCGTKLEIKSGGGGSEVQLVESGGGL VQPGGSLKLSAASGFTFNKYAMNWRQAPGKGLE WVARIRSKYNNYATYYADSVKDRFTISRDDSKNTAYL QMNNLKTEDTAVYYCVRHGNFGNSYISYWAYWGQ GTLVTVSSGGGGSGGGSGGGGSQTVVTQEPSLTV

[0149]

				SPGGTVTLTCGSSTGAVTSGNYPNWWVQQKPGQAPR GLIGGTKFLAPGTPARFSGSLLGGKAALTLSGVQPED EAEYYCVLWYSNRWVFGGGTKLTVLGGGGDKHTC PPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVV DVSHEDPEVKFNWYVDGVEVHNAKTKPCEEQYGST YRCVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTI SKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGF YPSDIAVEWESNGQPENNYKTTPVLDSDGSFFLYSK LTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLS PGGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGDK THTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVT CVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPCEEQ YGSTYRCVSVLTVLHQDWLNGKEYKCKVSNKALPAPI EKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLV KGFYPSDIAVEWESNGQPENNYKTTPVLDSDGSFFL YSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSL SLSPGK
79.	VH CDR1 CD19 97-G1RE-C2	人工的	aa	SYGMH
80.	VH CDR2 CD19 97-G1RE-C2	人工的	aa	VISYEGSNKYAESVKG
81.	VH CDR3 CD19 97-G1RE-C2	人工的	aa	DRGTIFGNYGLEV
82.	VH CD19 97-G1RE-C2 CC	人工的	aa	QVQLVESGGGVVQPGRSLRLSCAASGFTFSSYGMH WVRQAPGKCLEWVAVISYEGSNKYAESVKGRFTIS RDNSKNTLYLQMNSLRDEDTAVYYCARDRTIFGNY GLEVWGQGTITVTVSS
83.	VL CDR1 CD19 97-G1RE-C2	人工的	aa	RSSQSLHKNAFNYLD

[0150]

84.	VL CDR2 CD19 97-G1RE-C2	人工的	aa	LGSNRAS
85.	VL CDR3 CD19 97-G1RE-C2	人工的	aa	MQALQTPFT
86.	VL CD19 97-G1RE-C2 CC	人工的	aa	DIVMTQSPLSLPVISGEPASISCRSSQSLHKNFNYL DWYLQKPGQSPQLLIYLGSNRASGVPDRFSGSGSGT DFTLKISRVEAEDVGVYYCMQALQTPFTFGCGTKVDI K
87.	CD19 97-G1RE-C2 CC x I2C0	人工的	aa	MDMRVPAQLLGLLLLWLRGARCDIVMTQSPLSLPVI SGEPASISCRSSQSLHKNFNYLDWYLQKPGQSPQL LIYLGSNRASGVPDRFSGSGSGTDFTLKISRVEAEDVG VYYCMQALQTPFTFGCGTKVDIKGGGSGGGGSGG GGSQVLVESGGGVVQPGRSLRLSCAASGFTFSSYG MHWVRQAPGKCLEWVAVISYEGSNKYAESVKGRF TISRDN SKNTLYLQMNSLRDEDTAVYYCARDRTIFG NYGLEWVGQGTTVTVSSGGGGSEVQLVESGGGLVQ PGGSLKLSAASGFTFNKYAMNWRQAPGKGLEW VARIRSKYNNYATYYADSVKDRFTISRDDSKNTAYLQ MNNLKTEDTAVYYCVRHGNFGNSYISYWAYWGQG TLTVSSGGGGSGGGSGGGGSQTVVTQEPSTVSP GGTVTLTCGSSTGAVTSGNYPNWVQKPGQAPRGL IGGTKFLAPGTPARFSGSLLGGKAALTLSGVQPEDEA EYYCVLWYSNRWVFVGGGKLTVL
88.	CD19 97-G1RE-C2 CC x I2C0-scFc	人工的	aa	MDMRVPAQLLGLLLLWLRGARCDIVMTQSPLSLPVI SGEPASISCRSSQSLHKNFNYLDWYLQKPGQSPQL LIYLGSNRASGVPDRFSGSGSGTDFTLKISRVEAEDVG VYYCMQALQTPFTFGCGTKVDIKGGGSGGGGSGG GGSQVLVESGGGVVQPGRSLRLSCAASGFTFSSYG MHWVRQAPGKCLEWVAVISYEGSNKYAESVKGRF TISRDN SKNTLYLQMNSLRDEDTAVYYCARDRTIFG

[0151]

				NYGLEVWGQGTTVTVSSGGGGSEVQLVESGGGLVQ PGGSLKLSCAASGFTFNKYAMNWVRQAPGKGLEW VARIRSKYNNYATYYADSVKDRFTISRDDSKNTAYLQ MNNLKTEDTAVYYCVRHGNFGNSYISYWAYWGQG TLVTVSSGGGGSGGGGSGGGGSQTVVTQEPSLTVSP GGTVTLTCGSSTGAVTSGNYPNWVQKPGQAPRGL IGGTKFLAPGTPARFSGSLLGGKAALTLSGVQPEDEA EYYCVLWYSNRWVFVGGGTKLTVLGGGGDKHTCPP CPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDV SHEDPEVKFNWYVDGVEVHNAKTKPCEEQYGSTYR CVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISK AKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYP SDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSKLT VDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPG KGGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGDK THTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVT CVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPCEEQ YGSTYRCVSVLTVLHQDWLNGKEYKCKVSNKALPAPI EKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLV KGFYP SDIAVEWESNGQPENNYKTPPVLDSDGSFFL YSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSL SLSPGK
89.	VH CDR1 CDH3 G8A 6-B12	人工的	aa	SYPIN
90.	VH CDR2 CDH3 G8A 6-B12	人工的	aa	VIWTGGGTNYASSVKG
91.	VH CDR3 CDH3 G8A 6-B12	人工的	aa	SRGVYDFDGRGAMDY
92.	VL CDR1 CDH3 G8A	人工的	aa	KSSQSLLYSSNQKNYFA

[0152]

	6-B12			
93.	VL CDR2 CDH3 G8A 6-B12	人工的	aa	WASTRES
94.	VL CDR3 CDH3 G8A 6-B12	人工的	aa	QQYYSYPYT
95.	VH CDH3 G8A 6-B12	人工的	aa	EVQLLESGGGLVQPGGSLRLSCAASGFSSYPINWV RQAPGKGLEWVGVIWTGGGTNYASSVKGRFTISRD NSKNTVYLQMNSLRAEDTAVYYCAKSRGVYDFDGR GAMDYWGQGTLLTVSS
96.	VL CDH3 G8A 6-B12	人工的	aa	DIVMTQSPDSLAVSLGERATINCKSSQLLYSSNQKN YFAWYQQKPGQPPKLLIYWASTRESGVPDRFSGSGS GTDFTLTISSLQAEDVAVYYCQQYYSYPYTFGQGTKL EIK
97.	CDH3 G8A 6-B12 scFv	人工的	aa	EVQLLESGGGLVQPGGSLRLSCAASGFSSYPINWV RQAPGKGLEWVGVIWTGGGTNYASSVKGRFTISRD NSKNTVYLQMNSLRAEDTAVYYCAKSRGVYDFDGR GAMDYWGQGTLLTVSSGGGGSGGGSGGGGSDI VMTQSPDSLAVSLGERATINCKSSQLLYSSNQKNYF AWYQQKPGQPPKLLIYWASTRESGVPDRFSGSGSGT DFTLTISLQAEDVAVYYCQQYYSYPYTFGQGTKLEIK
98.	CDH3 G8A 6-B12 x I2C0 双 特异性分子	人工的	aa	EVQLLESGGGLVQPGGSLRLSCAASGFSSYPINWV RQAPGKGLEWVGVIWTGGGTNYASSVKGRFTISRD NSKNTVYLQMNSLRAEDTAVYYCAKSRGVYDFDGR GAMDYWGQGTLLTVSSGGGGSGGGSGGGGSDI VMTQSPDSLAVSLGERATINCKSSQLLYSSNQKNYF AWYQQKPGQPPKLLIYWASTRESGVPDRFSGSGSGT DFTLTISLQAEDVAVYYCQQYYSYPYTFGQGTKLEIK SGGGGSEVQLVESGGGLVQPGGSLKLSCAASGFTFN KYAMNWRQAPGKGLEWVARIRSKYNNYATYYAD SVKDRFTISRDDSKNTAYLQMNNLKTEDTAVYYCVR

[0153]

				HGNFGNSYISYWAYWGQGLTVTVSSGGGGSGGGG SGGGGSQTVVTQEPLTVSPGGTVTLTCSSTGAVTS GNYPNWVQQKPGQAPRGLIGGTKFLAPGTPARFSG SLLGGKAALTLSGVQPEDEAEYYCVLWYSNRWVFGG GTKLTVL
99.	CDH3 G8A 6-B12 x I2C0 双 特异性分子 HLE	人工的	aa	EVQLLESGGGLVQPGGSLRLSCAASGFSFSSYPINWV RQAPGKGLEWVGVIWTGGGTNYASSVKGRFTISR NSKNTVYLQMNSLRAEDTAVYYCAKSRGVYDFDGR GAMDYWGQGLTVTVSSGGGGSGGGGSGGGGSDI VMTQSPDSLAVSLGERATINCKSSQSLYSSNQKNYF AWYQQKPGQPPKLLIYWASTRESGVPDRFSGSGSGT DFTLTISSLQAEDVAVYYCQQYSSYPYTFGQGTKLEIK SGGGGSEVQLVESGGGLVQPGGSLKLSCAASGFTFN KYAMNWVRQAPGKGLEWVARIRSKYNNYATYYAD SVKDRFTISRDDSKNTAYLQMNNLKTEDTAVYYCVR HGNFGNSYISYWAYWGQGLTVTVSSGGGGSGGGG SGGGGSQTVVTQEPLTVSPGGTVTLTCSSTGAVTS GNYPNWVQQKPGQAPRGLIGGTKFLAPGTPARFSG SLLGGKAALTLSGVQPEDEAEYYCVLWYSNRWVFGG GTKLTVLGGGGDKTHTCPPCPAPELLGGPSVFLFPPK PKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGV EVHNAKTKPCEEQYGSTYRCVSVLTVLHQDWLNGKE YKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRE EMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYK TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSVM HEALHNHYTQKSLSLSPGKGGGGSGGGGSGGGGSG GGGSGGGGSGGGGSDKTHTCPPCPAPELLGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWY VDGVEVHNAKTKPCEEQYGSTYRCVSVLTVLHQDW LNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTL PPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQP ENNYKTTTPPVLDSDGSFFLYSKLTVDKSRWQQGNV

[0154]

				SCSVMHEALHNHYTQKSLSLSPGK
100.	BCMA A7 27-C4-G7 CDR1 VH	人工的	aa	NHIIH
101.	BCMA A7 27-C4-G7 CDR2 VH	人工的	aa	YINPYPGYHAYNEKFQG
102.	BCMA A7 27-C4-G7 CDR3 VH	人工的	aa	DGYRDTDVLDY
103.	BCMA A7 27-C4-G7 CDR1 VL	人工的	aa	QASQDISNYLN
104.	BCMA A7 27-C4-G7 CDR2 VL	人工的	aa	YTSRLHT
105.	BCMA A7 27-C4-G7 CDR3 VL	人工的	aa	QQGNTLPWT
106.	BCMA A7 27-C4-G7 CC (44/100) VH	人工的	aa	QVQLVQSGAEVKKPGASVKVSCKASGYTFTNHIIHW VRQAPGQCLEWMGYINPYPGYHAYNEKFQGRATM TSDTSTSTVYMESSLRSEDTAVYYCARDGYRDTDV LDYWGQGTLVTVSS
107.	BCMA A7 27-C4-G7 CC (44/100) VL	人工的	aa	DIQMTQSPSSLSASVGDRVTITCQASQDISNYLNWY QQKPGKAPKLLIYTSRLHTGVPSRFSGSGSGTDFTFT ISSLEPEDIATYYCQQGNTLPWTFGCGTKLEIK
108.	BCMA A7 27-C4-G7 CC (44/100) scFv	人工的	aa	QVQLVQSGAEVKKPGASVKVSCKASGYTFTNHIIHW VRQAPGQCLEWMGYINPYPGYHAYNEKFQGRATM TSDTSTSTVYMESSLRSEDTAVYYCARDGYRDTDV LDYWGQGTLVTVSSGGGGSGGGSGGGGSDIQMT QSPSSLSASVGDRVTITCQASQDISNYLNWYQQKPG KAPKLLIYTSRLHTGVPSRFSGSGSGTDFTFTISSLEPE DIATYYCQQGNTLPWTFGCGTKLEIK

[0155]

109.	BCMA A7 27-C4-G7 CC (44/100) x I2C0 双特异性分子	人工的	aa	QVQLVQSGAEVKKPGASVKVSCKASGYFTFNHIIHW VRQAPGQCLEWMGYINPYPGYHAYNEKFQGRATM TSDTSTSTVYMELSSLRSEDTAVYYCARDGYRDTDV LDYWGQGTLVTVSSGGGGSGGGGSGGGGSDIQMT QSPSSLSASVGDRTITCQASQDISNYLNWYQQKPG KAPKLLIYYTSRLHTGVPSRFSGSGSGTDFTFTISSLEPE DIATYYCQQGNTLPWTFGCGTKLEIKSGGGGSEVQL VESGGGLVQPGGSLKLSCAASGFTFNKYAMNWVRQ APGKGLEWVARIRSKYNNYATYYADSVKDRFTISRDD SKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYISY WAYWGQGTLVTVSSGGGGSGGGGSGGGGSQTVV TQEPSLTVSPGGTVTLTCSSTGAVTSGNYPNWVQQ KPGQAPRGLIGGTKFLAPGTPARFSGSLLGGKAALT SGVQPEDEAEYCVLWYSNRWVFGGGTKLTVL
110.	BCMA A7 27-C4-G7 CC (44/100) x I2C0-scFc 双特 异性分子 HLE	人工的	aa	QVQLVQSGAEVKKPGASVKVSCKASGYFTFNHIIHW VRQAPGQCLEWMGYINPYPGYHAYNEKFQGRATM TSDTSTSTVYMELSSLRSEDTAVYYCARDGYRDTDV LDYWGQGTLVTVSSGGGGSGGGGSGGGGSDIQMT QSPSSLSASVGDRTITCQASQDISNYLNWYQQKPG KAPKLLIYYTSRLHTGVPSRFSGSGSGTDFTFTISSLEPE DIATYYCQQGNTLPWTFGCGTKVEIKSGGGGSEVQL VESGGGLVQPGGSLKLSCAASGFTFNKYAMNWVRQ APGKGLEWVARIRSKYNNYATYYADSVKDRFTISRDD SKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYISY WAYWGQGTLVTVSSGGGGSGGGGSGGGGSQTVV TQEPSLTVSPGGTVTLTCSSTGAVTSGNYPNWVQQ KPGQAPRGLIGGTKFLAPGTPARFSGSLLGGKAALT SGVQPEDEAEYCVLWYSNRWVFGGGTKLTVLGGG GDKHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRT P EVTCTVVDVSHEDPEVKFNWYVDGVEVHNAKTKPC EEQYGSTYRCVSVLTVLHQDWLNGKEYKCKVSNKAL PAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLT

[0156]

				CLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDG SFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYT QKSLSLSPGKGGGGSGGGGSGGGGSGGGGSGGGG SGGGGSDKTHTCPPELGGPSVFLFPPKPKDTL MISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHN AKTKPCEEQYGSTYRCVSVLTVLHQDWLNGKEYKCK VSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK NQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPP VLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEAL HNHYTQKSLSLSPGK
111.	PM 76-B10.17 CC VH CDR1	人工的	aa	DYYMY
112.	PM 76-B10.17 CC VH CDR2	人工的	aa	IISDAGYYTYYSDIKKG
113.	PM 76-B10.17 CC VH CDR3	人工的	aa	GFPLLRHGAMDY
114.	PM 76-B10.17 CC VL CDR1	人工的	aa	KASQNV DANVA
145.	PM 76-B10.17 CC VL CDR2	人工的	aa	SASYVYW
116.	PM 76-B10.17 CC VL CDR3	人工的	aa	QQYDQQLIT
117.	PM 76-B10.17 CC VH	人工的	aa	QVQLVESGGGLVKPGESLRLSCAASGFTFSYYMYW VRQAPGKCLEWVAIISDAGYYTYYSDIKGRFTISRDN AKNSLYLQMNSLKAEDTAVYYCARGFPLLRHGAMD YWGQGTLLTVSS
118.	PM 76-B10.17 CC VL	人工的	aa	DIQMTQSPSSLSASVGDRVTITCKASQNV DANVAW YQQKPGQAPKSLIYSASYVYWDVPSRFGSGASGTDFT LTISSVQSEDFATYYCQQYDQQLITFGCGTKLEIK
119.	PM 76-B10.17 CC scFv	人工的	aa	QVQLVESGGGLVKPGESLRLSCAASGFTFSYYMYW VRQAPGKCLEWVAIISDAGYYTYYSDIKGRFTISRDN AKNSLYLQMNSLKAEDTAVYYCARGFPLLRHGAMD

[0157]

				YWGQGTLLTVSSGGGSGGGGSGGGGSDIQMTQS PSSLSASVGDRVITITCKASQNV DANVAWYQQKPGQ APKSLIYSASYVYWDVPSRFSGSASGTDFTLTISVQS EDFATYYCQQYDQQLITFGCGTKLEIK
120.	PM 76-B10.17 CC x I2C0 双特 异性分子	人工的	aa	QVQLVESGGGLVKPGESLR LSCAASGFTFSDYYMYW VRQAPGKCLEWVAIISDAGYYTYSDIIKGRFTISRDN AKNSLYLQMNSLKAEDTAVYYCARGFLLRHGAMD YWGQGTLLTVSSGGGSGGGGSGGGGSDIQMTQS PSSLSASVGDRVITITCKASQNV DANVAWYQQKPGQ APKSLIYSASYVYWDVPSRFSGSASGTDFTLTISVQS EDFATYYCQQYDQQLITFGCGTKLEIKSGGGGSEVQL VESGGGLVQPGGSLK LSCAASGFTFNKYAMNWVRQ APGKGLEWVARIRSKYNNYATYYADSVKDRFTISRDD SKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYISY WAYWGQGTLLTVSSGGGSGGGGSGGGGSQTVV TQEPSLTVSPGGTVTLTCSSTGAVTSGNYPNWVQQ KPGQAPRGLIGGTKFLAPGTPARFSGSLLGGKAALT SGVQPEDEAEYYCVLWYSNRWVFGGGTKLTVL
121.	PM 76-B10.17 CC x I2C0-scFc 双特异性 HLE 分子	人工的	aa	QVQLVESGGGLVKPGESLR LSCAASGFTFSDYYMYW VRQAPGKCLEWVAIISDAGYYTYSDIIKGRFTISRDN AKNSLYLQMNSLKAEDTAVYYCARGFLLRHGAMD YWGQGTLLTVSSGGGSGGGGSGGGGSDIQMTQS PSSLSASVGDRVITITCKASQNV DANVAWYQQKPGQ APKSLIYSASYVYWDVPSRFSGSASGTDFTLTISVQS EDFATYYCQQYDQQLITFGCGTKLEIKSGGGGSEVQL VESGGGLVQPGGSLK LSCAASGFTFNKYAMNWVRQ APGKGLEWVARIRSKYNNYATYYADSVKDRFTISRDD SKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYISY WAYWGQGTLLTVSSGGGSGGGGSGGGGSQTVV TQEPSLTVSPGGTVTLTCSSTGAVTSGNYPNWVQQ KPGQAPRGLIGGTKFLAPGTPARFSGSLLGGKAALT SGVQPEDEAEYYCVLWYSNRWVFGGGTKLTVLGGG

[0158]

				GDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVDVSHEDPEVKFNWYVDGVEVHNAKTKPCEEQYGSTYRCVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK
122.	PM 76-B10.17 CC x I2C0-scFc_delG K 双特异性 HLE 分子	人工的	aa	QVQLVESGGGLVKGESLRLSCAASGFTFSDYYMYWVRQAPGKCLEWVAISDAGYYTYSDIIKGRFTISRDNAKNSLYLQMNSLKAEDTAVYYCARGFLLRHGAMYWGQGTLLTVSSGGGGSGGGSGGGGSDIQMTQSPSSLSASVGDRTITCKASQNVNANVAWYQQKPGQAPKSLIYSASYVYWDVPSRFSGSASGTDFLTISVQSEDFATYYCQYDQQLITFGCGTKLEIKSGGGGSEVQLVESGGGLVQPGGSLKLSCAASGFTFNKYAMNWVRQAPGKGLEWVARIRSKYNNYATYYADSVKDRFTISRDDSKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYISYWAYWGQGTLLTVSSGGGGSGGGSGGGGSQTVVTQEPSLTVSPGGTVTLTCSSTGAVTSGNYPNWVQQKPGQAPRGLIGGTKFLAPGTPARFSGSLLGGKAALTLSGVQPEDEAEYCVLWYSNRWVFGGGTKLTVLGGGDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVDVSHEDPEVKFNWYVDGVEVHNAKTKPCEEQYGSTYRCVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLT

[0159]

				CLVKGFPSPDIAVEWESNGQPENNYKTPPVLDSDG SFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYT QKSLSLSPGGGSGGGGSGGGGSGGGGSGGGGSG GGGSDKTHTCPPELLGGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAK TKPCEEQYGSTYRCVSVLTVLHQDWLNGKEYKCKVS NKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKN QVSLTCLVKGFPSPDIAVEWESNGQPENNYKTPPVL DSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALH NHYTQKSLSLSPGK
123.	PM 76-B10.17 CC x I2C0 CC (103/43)-scFc 双 特异性分子	人工的	aa	QVQLVESGGGLVKPGESLRLSCAASGFTFSDYYMYW VRQAPGKCLEWVAIISDAGYYTYSDIIKGRFTISRDN AKNSLYLQMNSLKAEDTAVYYCARGFPLLRHGAMD YWGQGTLLTVSSGGGSGGGGSGGGGSDIQMTQS PSSLSASVGDRTITCKASQNV DANVAWYQKPGQ APKSLIYSASYVYWDVPSRFGSASGTDFTLTSSVQS EDFATYYCQYDQQLITFGCGTKLEIKSGGGGSEVQL VESGGGLVQPGGSLKLSAASGFTFNKYAMNWVRQ APGKGLEWVARIRSKYNNYATYYADSVKDRFTISRDD SKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYISY WAYCGQGTLLTVSSGGGSGGGGSGGGGSGTQTVVT QEPSTLVSPGGTVTLTCSSTGAVTSGNYPNWVQQ KPGQCPRGLIGGTKFLAPGTPARFSGSLLGGKAALTLS GVQPDEAEYYCVLWYSNRWVFGGGTKLTVL
124.	PM 76-B10.17 CC x I2C0 CC (103/43)-scFc 双 特异性 HLE 分子	人工的	aa	QVQLVESGGGLVKPGESLRLSCAASGFTFSDYYMYW VRQAPGKCLEWVAIISDAGYYTYSDIIKGRFTISRDN AKNSLYLQMNSLKAEDTAVYYCARGFPLLRHGAMD YWGQGTLLTVSSGGGSGGGGSGGGGSDIQMTQS PSSLSASVGDRTITCKASQNV DANVAWYQKPGQ APKSLIYSASYVYWDVPSRFGSASGTDFTLTSSVQS EDFATYYCQYDQQLITFGCGTKLEIKSGGGGSEVQL VESGGGLVQPGGSLKLSAASGFTFNKYAMNWVRQ

[0160]

				APGKGLEWVARIRSKYNNYATYYADSVKDRFTISRDD SKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYISY WAYCGQGTLVTVSSGGGSGGGGSGGGGSQTVVT QEPSLTVSPGGTVTLTCSSTGAVTSGNYPNWWQQ KPGQCPRGLIGGTKFLAPGTPARFSGSLLGGKAALTS GVQPEDEAEYYCVLWYSNRWVFGGGTKLTVLGGGG DKTHTCPPELGGPSVFLFPPKPKDTLMISRTPE VTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPCE EQYGSTYRCVSVLTVLHQDWLNGKEYKCKVSNKALP APIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLT CLVKGFYPSDIAVEWESNGQPENNYKTTPVLDSGD SFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYT QKSLSLSPGKGGGSGGGGSGGGGSGGGGSGGGG SGGGSDKTHTCPPELGGPSVFLFPPKPKDTL MISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHN AKTKPCEEQYGSTYRCVSVLTVLHQDWLNGKEYKCK VSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK NQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPP VLDSGDSFFLYSKLTVDKSRWQQGNVFCFSVMHEAL HNHYTQKSLSLSPGK
125.	PM 76-B10.17 CC x I2C0 CC (103/43)-scFc_d eIGK 双特异性 HLE 分子	人工的	aa	QVQLVESGGGLVKPGESLRLSAASGFTFSDYYMYW VRQAPGKCLEWVAIISDAGYYTYSDIIKGRFTISRDN AKNSLYLQMNSLKAEDTAVYYCARGFPLLRHGAMD YWGQGTLVTVSSGGGSGGGGSGGGGSDIQMTQS PSSLSASVGDRVITCKASQNV DANVAWYQQKPGQ APKSLIYSASYVYWDVPSRFSGSASGTDFLTISVQS EDFATYYCQYDQQLITFGCGTKLEIKSGGGGSEVQL VESGGGLVQPGGSLKLSAASGFTFNKYAMNWVRQ APGKGLEWVARIRSKYNNYATYYADSVKDRFTISRDD SKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYISY WAYCGQGTLVTVSSGGGSGGGGSGGGGSQTVVT QEPSLTVSPGGTVTLTCSSTGAVTSGNYPNWWQQ

[0161]

				KPGQCPRGLIGGTKFLAPGTPARFSGSLLGGKAALTS GVQPEDEAEYYCVLWYSNRWVFGGGTKLTVLGGGG DKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPE VTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPCE EQYGSTYRCVSVLTVLHQDWLNGKEYKCKVSNKALP APIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLT CLVKGFPYPSDIAVEWESNGQPENNYKTTPVLDSDG SFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYT QKSLSLSPGGGGSGGGGSGGGGSGGGGSGGGGSG GGGSDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAK TKPCEEQYGSTYRCVSVLTVLHQDWLNGKEYKCKVS NKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKN QVSLTCLVKGFPYPSDIAVEWESNGQPENNYKTTPVL DSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALH NHYTQKSLSLSPGK
126.	PM 76-B10.11 CC VH CDR1	人工的	aa	DYYMY
127.	PM 76-B10.11 CC VH CDR2	人工的	aa	IISDGGYYTYYSDIKIG
128.	PM 76-B10.11 CC VH CDR3	人工的	aa	GFPLLRHGAMDY
129.	PM 76-B10.11 CC VL CDR1	人工的	aa	KASQNVDTNVA
130.	PM 76-B10.11 CC VL CDR2	人工的	aa	SASYVYW
131.	PM 76-B10.11 CC VL CDR3	人工的	aa	QQYDQQLIT
132.	PM 76-B10.11 CC VH	人工的	aa	QVQLVESGGGLVKPGESLRLSAASGFTFSDYYMYW VRQAPGKGLEWVAIISDGGYYTYYSDIKGRFTISRDN AKNSLYLQMNSLKAEDTAVYYCARGFPLLRHGAMD YWGQGTLLTVSS

[0162]

133.	PM 76-B10.11 CC VL	人工的	aa	DIQMTQSPSSLSASVGDRVTITCKASQNVDTNVAWY QQKPGQAPKSLIYSASYVYWDVPSRFGSGSASGTDFTL TISSVQSEDFATYYCQYDQQLITFGGGTKLEIK
134.	PM 76-B10.11 CC scFv	人工的	aa	QVQLVESGGGLVKPGESLRLSCAASGFTFSDYYMYW VRQAPGKGLEWVAIISDGGYYTYYSDIKGRFTISRDN AKNSLYLQMNSLKAEDTAVYYCARGFPLLRHGAMD YWGQGTLLTVSSGGGGSGGGGSGGGGSDIQMTQS PSSLSASVGDRVTITCKASQNVDTNVAWYQQKPGQ APKSLIYSASYVYWDVPSRFGSGSASGTDFTLTISSVQS EDFATYYCQYDQQLITFGGGTKLEIK
135.	PM 76-B10.11 CC x I2C0 双特 异性分子	人工的	aa	QVQLVESGGGLVKPGESLRLSCAASGFTFSDYYMYW VRQAPGKGLEWVAIISDGGYYTYYSDIKGRFTISRDN AKNSLYLQMNSLKAEDTAVYYCARGFPLLRHGAMD YWGQGTLLTVSSGGGGSGGGGSGGGGSDIQMTQS PSSLSASVGDRVTITCKASQNVDTNVAWYQQKPGQ APKSLIYSASYVYWDVPSRFGSGSASGTDFTLTISSVQS EDFATYYCQYDQQLITFGGGTKLEIKSGGGGSEVQL VESGGGLVQPGGSLKLSCAASGFTFNKYAMNWVRQ APGKGLEWVARIRSKYNNYATYYADSVKDRFTISRDD SKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYISY WAYWGQGTLLTVSSGGGGSGGGGSGGGGSQTVV TQEPSLTVSPGGTVTLTCGSSTGAVTSGNYPNWVQQ KPGQAPRGLIGGTKFLAPGTPARFSGSLLGGKAALT SGVQPEDEAEYCVLWYSNRWVFGGGTKLTVL
136.	PM 76-B10.11 CC x I2C0-scFc 双特异性 HLE 分子	人工的	aa	QVQLVESGGGLVKPGESLRLSCAASGFTFSDYYMYW VRQAPGKGLEWVAIISDGGYYTYYSDIKGRFTISRDN AKNSLYLQMNSLKAEDTAVYYCARGFPLLRHGAMD YWGQGTLLTVSSGGGGSGGGGSGGGGSDIQMTQS PSSLSASVGDRVTITCKASQNVDTNVAWYQQKPGQ APKSLIYSASYVYWDVPSRFGSGSASGTDFTLTISSVQS EDFATYYCQYDQQLITFGGGTKLEIKSGGGGSEVQL VESGGGLVQPGGSLKLSCAASGFTFNKYAMNWVRQ

[0163]

				APGKGLEWVARIRSKYNNYATYYADSVKDRFTISRDD SKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYISY WAYWGQGTTLTVSSGGGSGGGGSGGGGSQTVV TQEPSLTVSPGGTVTLTCGSSTGAVTSGNYPNWWQQ KPGQAPRGLIGGTKFLAPGTPARFSGSLLGGKAALT SGVQPEDEAEYYCVLWYSNRWVFGGGTKTLVLGGG GDKTHTCPPCPAPELLGGPSVFLFPPKPKDLMISRTP EVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPC EEQYGSTYRCVSVLTVLHQDWLNGKEYKCKVSNKAL PAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLT CLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDG SFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYT QKSLSLSPGKGGGSGGGGSGGGGSGGGGSGGGG SGGGSGDKTHTCPPCPAPELLGGPSVFLFPPKPKD TLISRTPVTCVVVDVSHEDPEVKFNWYVDGVEVHN AKTKPCEEQYGSTYRCVSVLTVLHQDWLNGKEYKCK VSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK NQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPP VLDSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEAL HNHYTQKSLSLSPGK
137.	PM 76-B10.11 CC x I2C0-scFc_delG K 双特异性 HLE 分子	人工的	aa	QVQLVESGGGLVKPGESLRLSCAASGFTFSDYYMYW VRQAPGKGLEWVAIISDGGYYTYSDIIKGRFTISRDN AKNSLYLQMNSLKAEDTAVYYCARGFPLLRHGAMD YWGQGTTLTVSSGGGSGGGGSGGGGSDIQMTQS PSSLSASVGDRTITCKASQNVDTNVAWYQKPGQ APKSLIYSASYVYWDVPSRFSGSASGTDFLTISVQS EDFATYYCQYDQQLITFGGGTKLEIKSGGGGSEVQL VESGGGLVQPGGSLKLSCAASGFTFNKYAMNWVRQ APGKGLEWVARIRSKYNNYATYYADSVKDRFTISRDD SKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYISY WAYWGQGTTLTVSSGGGSGGGGSGGGGSQTVV TQEPSLTVSPGGTVTLTCGSSTGAVTSGNYPNWWQQ

[0164]

				KPGQAPRGLIGGTKFLAPGTPARFSGSLLGGKAALT SGVQPEDEAEYYCVLWYSNRWVFGGGTKLTVLGGG GDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMIS RTP EVT CVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPC EEQYGSTYRCVSVLTVLHQDWLNGKEYKCKVSNKAL PAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLT CLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDS DG SFFLYSKLTVDKSRWQQGNV FSCSVMHEALHNHYT QKSLSLSPGGGGSGGGGSGGGGSGGGGSGGGGSG GGGSDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAK TKPCEEQYGSTYRCVSVLTVLHQDWLNGKEYKCKVS NKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKN QVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVL DSDGSFFLYSKLTVDKSRWQQGNV FSCSVMHEALH NHYTQKSLSLSPGK
138.	PM 76-B10.11 CC x I2C0 CC (103/43)-scFc 双 特异性分子	人工的	aa	QVQLVESGGGLVKPGESLRLS CAASGFTFSDYYMYW VRQAPGKGLEWVAIISDGGYYTYSDIIGRFTISRDN AKNSLYLQMNSLKAEDTAVYYCARGFLLRHGAMD YWGQGT LTVSSGGGGSGGGGSGGGGSDIQMTQS PSSLSASVGDRTITCKASQNVDTNVAWYQQKPGQ APKSLIYSASYVYWDVPSRFSGSASGTDFTLTISVQS EDFATYYCQYDQQLITFGGGTKLEIKSGGGGSEVQL VESGGGLVQPGGSLKLS CAASGFTFNKYAMNWVRQ APGKGLEWVARIRSKYNNYATYYADSVKDRFTISRDD SKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYISY WAYCGQGT LTVSSGGGGSGGGGSGGGGSQTVVT QEPSLTVSPGGTVTLTCSSTGAVTSGNYPNWWQQ KPGQCPRGLIGGTKFLAPGTPARFSGSLLGGKAALTLS GVQPEDEAEYYCVLWYSNRWVFGGGTKLTVL
139.	PM 76-B10.11 CC x I2C0 CC	人工的	aa	QVQLVESGGGLVKPGESLRLS CAASGFTFSDYYMYW VRQAPGKGLEWVAIISDGGYYTYSDIIGRFTISRDN

[0165]

	(103/43)-scFc 双 特异性 HLE 分子			AKNSLYLQMNSLKAEDTAVYYCARGFLLRHGAMD YWGQGTLLTVSSGGGGSGGGGSGGGGSDIQMTQS PSSLSASVGDRVITITCKASQNVDTNVAWYQQKPGQ APKSLIYSASYVYWDVPSRFSGSASGTDFLTISVQS EDFATYYCQYDQQLITFGGGTKLEIKSGGGGSEVQL VESGGGLVQPGGSLKLSCAASGFTFNKYAMNWVRQ APGKGLEWVARIRSKYNNYATYYADSVKDRFTISRDD SKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYISY WAYCGQGTLLTVSSGGGGSGGGGSGGGGSGTQTVVT QEPSTVSPGGTVTLTCSSTGAVTSGNYPNWWQQ KPGQCPRGLIGGTKFLAPGTPARFSGSLLGGKAALTLS GVQPDEAEYYCVLWYSNRWVFGGGTKLTVLGGGG DKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPE VTCVVDVSHEDPEVKFNWYVDGVEVHNAKTKPCE EQYGSTYRCVSVLTVLHQDWLNGKEYKCKVSNKALP APIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLT CLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSGD SFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYT QKSLSLSPGKGGGGSGGGGSGGGGSGGGGSGGGG SGGGGSDKTHTCPPCPAPELLGGPSVFLFPPKPKDTL MISRTPEVTCVVDVSHEDPEVKFNWYVDGVEVHN AKTKPCEEQYGSTYRCVSVLTVLHQDWLNGKEYKCK VSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK NQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTP VLDSGDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEAL HNHYTQKSLSLSPGK
140.	PM 76-B10.11 CC x I2C0 CC (103/43)-scFc_d eIGK 双特异性 HLE 分子	人工的	aa	QVQLVESGGGLVKPGESLRLSCAASGFTFSDYYMYW VRQAPGKGLEWVAIISDGGYYTYSDIIKGRFTISRDN AKNSLYLQMNSLKAEDTAVYYCARGFLLRHGAMD YWGQGTLLTVSSGGGGSGGGGSGGGGSDIQMTQS PSSLSASVGDRVITITCKASQNVDTNVAWYQQKPGQ APKSLIYSASYVYWDVPSRFSGSASGTDFLTISVQS

[0166]

				EDFATYYCQYDQQLITFGGGTKLEIKSGGGGSEVQL VESGGGLVQPGGSLKLSAASGFTFNKYAMNWVRQ APGKGLEWVARIRSKYNNYATYYADSVKDRFTISRDD SKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYISY WAYCGQGT LVT VSSGGGSGGGGSGGGGSQTVVT QEPSLTVSPGGTVTLTCSSTGAVTSGNYPNWVQQ KPGQCPRGLIGGTKFLAPGTPARFSGSLLGGKAALTLS GVQPEDEAEYYCVLWYSNRWVFGGGTKLTVLGGGG DKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPE VTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPCE EQYGSTYRCVSVLTVLHQDWLNGKEYKCKVSNKALP APIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLT CLVKGFPYPSDIAVEWESNGQPENNYKTTTPVLDSDG SFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYT QKSLSLSPGGGSGGGGSGGGGSGGGGSGGGGSG GGGSDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAK TKPCEEQYGSTYRCVSVLTVLHQDWLNGKEYKCKVS NKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKN QVSLTCLVKGFPYPSDIAVEWESNGQPENNYKTTTPVL DSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALH NHYTQKSLSLSPGK
141.	PM 76-B10.11 CC x I2C0-scFc VH CDR1	人工的	aa	DYYMY
142.	PM 76-B10.11 CC x I2C0-scFc VH CDR2	人工的	aa	IISDGGYYTYSDIIGK
143.	PM 76-B10.11 CC x I2C0-scFc VH CDR3	人工的	aa	GFPLL RHGAMDY
144.	PM 76-B10.11 CC x I2C0-scFc	人工的	aa	KASQNVDTNVA

[0167]

	VL CDR1			
145.	PM 76-B10.11 CC x I2C0-scFc VL CDR2	人工的	aa	SASYVYW
146.	PM 76-B10.11 CC x I2C0-scFc VL CDR3	人工的	aa	QQYDQQLIT
147.	PM 76-B10.11 CC x I2C0-scFc VH	人工的	aa	QVQLVESGGGLVKPGESLRLSCAASGFTFSDYYMYW VRQAPGKCLEWVAIISDGGYYTYSDIIKGRFTISRDN AKNSLYLQMNSLKAEDTAVYYCARGFPLLRHGAMD YWGQGTLVTVSS
148.	PM 76-B10.11 CC x I2C0-scFc VL	人工的	aa	DIQMTQSPSSLSASVGDRVTITCKASQNVDTNVAWY QQKPGQAPKSLIYSASYVYWDVPSRFGSASGTDFTL TISSVQSEDFATYYCQQYDQQLITFGCGTKLEIK
149.	PM 76-B10.11 CC x I2C0-scFc scFv	人工的	aa	QVQLVESGGGLVKPGESLRLSCAASGFTFSDYYMYW VRQAPGKCLEWVAIISDGGYYTYSDIIKGRFTISRDN AKNSLYLQMNSLKAEDTAVYYCARGFPLLRHGAMD YWGQGTLVTVSSGGGGSGGGGSGGGGSDIQMTQS PSSLSASVGDRVTITCKASQNVDTNVAWYQQKPGQ APKSLIYSASYVYWDVPSRFGSASGTDFTLTISSVQS EDFATYYCQQYDQQLITFGCGTKLEIK
150.	PM 76-B10.11 CC x I2C0-scFc 双特异性分子	人工的	aa	QVQLVESGGGLVKPGESLRLSCAASGFTFSDYYMYW VRQAPGKCLEWVAIISDGGYYTYSDIIKGRFTISRDN AKNSLYLQMNSLKAEDTAVYYCARGFPLLRHGAMD YWGQGTLVTVSSGGGGSGGGGSGGGGSDIQMTQS PSSLSASVGDRVTITCKASQNVDTNVAWYQQKPGQ APKSLIYSASYVYWDVPSRFGSASGTDFTLTISSVQS EDFATYYCQQYDQQLITFGCGTKLEIKSGGGGSEVQL VESGGGLVQPGGSLKLSAASGFTFNKYAMNWVRQ APGKGLEWVARIRSKYNNYATYYADSVKDRFTISRDD SKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYISY WAYWGQGTLVTVSSGGGGSGGGGSGGGGSQTIVV

[0168]

				TQEPSLTVSPGGTVTLTCGSSTGAVTSGNYPNWWQQ KPGQAPRGLIGGTKFLAPGTPARFSGSLLGGKAALT SGVQPEDEAEYCVLWYSNRWVFGGGTKLTVL
151.	PM 76-B10.11 CC x I2C0-scFc 双特异性 HLE 分子	人工的	aa	QVQLVESGGGLVKPGESLRLSCAASGFTFSDYYMYW VRQAPGKCLEWVAIISDGGYYTYSDIIKGRFTISRDN AKNSLYLQMNSLKAEDTAVYYCARGFPLLRHGAMD YWGQGTLLTVSSGGGGSGGGGSGGGGSDIQMTQS PSSLSASVGDRTITCKASQNVDTNVAWYQQKPGQ APKSLIYSASYVYWDVPSRFSGSASGTDFTLTISVSQS EDFATYYCQYDQQLITFGCGTKLEIKSGGGGSEVQL VESGGGLVQPGGSLKLSAASGFTFNKYAMNWVRQ APGKGLEWVARIRSKYNNYATYYADSVKDRFTISRDD SKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYISY WAYWGQGTLLTVSSGGGGSGGGGSGGGGSQTVV TQEPSLTVSPGGTVTLTCGSSTGAVTSGNYPNWWQQ KPGQAPRGLIGGTKFLAPGTPARFSGSLLGGKAALT SGVQPEDEAEYCVLWYSNRWVFGGGTKLTVLGGG GDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRT P EVTCTVVDVSHEDPEVKFNWYVDGVEVHNAKTKPC EEQYGSTYRCVSVLTVLHQDWLNGKEYKCKVSNKAL PAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLT CLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDG SFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYT QKSLSLSPGKGGGGSGGGGSGGGGSGGGGSGGGG SGGGGSDKTHTCPPCPAPELLGGPSVFLFPPKPKDTL MISRTPEVTCVVDVSHEDPEVKFNWYVDGVEVHN AKTKPCEEQYGSTYRCVSVLTVLHQDWLNGKEYKCK VSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK NQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPP VLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEAL HNHYTQKSLSLSPGK
152.	PM 76-B10.11	人工的	aa	QVQLVESGGGLVKPGESLRLSCAASGFTFSDYYMYW

[0169]

	CC x I2C0-scFc_delG K 双特异性 HLE 分子			VRQAPGKCLEWVAIISDGGYYTYYSDIKGRFTISRDN AKNSLYLQMNSLKAEDTAVYYCARGFLLRHGAMD YWGQGTLLTVSSGGGSGGGGSGGGGSDIQMTQS PSSLSASVGDRVITITCKASQNVDTNVAWYQQKPGQ APKSLIYSASYVYWDVPSRFSGSASGTDFLTITSSVQS EDFATYYCQQYDQQLITFGCGTKLEIKSGGGGSEVQL VESGGGLVQPGGSLKLSCAASGFTFNKYAMNWVRQ APGKGLEWVARIRSKYNNYATYYADSVKDRFTISRDD SKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYISY WAYWGQGTLLTVSSGGGSGGGGSGGGGSGQTVV TQEPSLTVSPGGTVTLTCGSSTGAVTSGNYPNWVQQ KPGQAPRGLIGGTKFLAPGTPARFSGSLLGGKAALT SGVQPEDEAEYCVLWYSNRWVFGGGTKLTVLGGG GDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRT EVTCTVVDVSHEDPEVKFNWYVDGVEVHNAKTKPC EEQYGSTYRCVSVLTVLHQDWLNGKEYKCKVSNKAL PAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLT CLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDG SFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYT QKSLSLSPGGGSGGGGSGGGGSGGGGSGGGGSGG GGGSDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMI SRTPEVTCVVDVSHEDPEVKFNWYVDGVEVHNAK TKPCEEQYGSTYRCVSVLTVLHQDWLNGKEYKCKVS NKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKN QVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVL DSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALH NHYTQKSLSLSPGK
153.	PM 76-B10.11 CC x I2C0 CC (103/43)-scFc 双 特异性分子	人工的	aa	QVQLVESGGGLVKPGESLRSLCAASGFTFSDYYMYW VRQAPGKCLEWVAIISDGGYYTYYSDIKGRFTISRDN AKNSLYLQMNSLKAEDTAVYYCARGFLLRHGAMD YWGQGTLLTVSSGGGSGGGGSGGGGSDIQMTQS PSSLSASVGDRVITITCKASQNVDTNVAWYQQKPGQ

[0170]

				APKSLIYSASYVYWDVPSRFSGSASGTDFTLTISVQS EDFATYYCQYDQQLITFGCGTKLEIKSGGGGSEVQL VESGGGLVQPGGSLKLSCAASGFTFNKYAMNWVRQ APGKGLEWVARIRSKYNNYATYYADSVKDRFTISRDD SKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYISY WAYCGQGTLTVSSGGGSGGGGSGGGGSQTVVT QEPSLTVSPGGTVTLTCSSTGAVTSGNYPNWWQQ KPGQCPRGLIGGTKFLAPGTPARFSGSLLGGKAALTLS GVQPEDEAEYYCVLWYSNRWVFGGGTKLTVL
154.	PM 76-B10.11 CC x I2C0 CC (103/43)-scFc 双 特异性 HLE 分子	人工的	aa	QVQLVESGGGLVKPGESLRLSCAASGFTFSDYYMYW VRQAPGKCLEWVAIISDGGYYTYYSDIKGRFTISRDN AKNSLYLQMNSLKAEDTAVYYCARGFLLRHGAMD YWGQGTLLTVSSGGGSGGGGSGGGGSDIQMTQS PSSLSASVGDRTITCKASQNVDTNVAWYQKPGQ APKSLIYSASYVYWDVPSRFSGSASGTDFTLTISVQS EDFATYYCQYDQQLITFGCGTKLEIKSGGGGSEVQL VESGGGLVQPGGSLKLSCAASGFTFNKYAMNWVRQ APGKGLEWVARIRSKYNNYATYYADSVKDRFTISRDD SKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYISY WAYCGQGTLTVSSGGGSGGGGSGGGGSQTVVT QEPSLTVSPGGTVTLTCSSTGAVTSGNYPNWWQQ KPGQCPRGLIGGTKFLAPGTPARFSGSLLGGKAALTLS GVQPEDEAEYYCVLWYSNRWVFGGGTKLTVLGGGG DKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPE VTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPCE EQYGSTYRCVSVLTVLHQDWLNGKEYKCKVSNKALP APIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLT CLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDG SFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYT QKSLSLSPGKGGGSGGGGSGGGGSGGGGSGGGG SGGGSGDKTHTCPPCPAPELLGGPSVFLFPPKPKDTL MISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHN

[0171]

				AKTKPCEEQYGSTYRCVSVLTVLHQDWLNGKEYKCK VSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK NQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPP VLDSGDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEAL HNHYTQKSLSLSPGK
155.	PM 76-B10.11 CC x I2C0 CC (103/43)-scFc_d elGK 双特异性 HLE 分子	人工的	aa	QVQLVESGGGLVKGESLRLSCAASGFTFSDYYMYW VRQAPGKCLEWVAIISDGGYYTYSDIIKGRFTISRDN AKNSLYLQMNSLKAEDTAVYYCARGFLLRHGAMD YWGQGTLLTVSSGGGSGGGGSGGGGSDIQMTQS PSSLSASVGDRTITCKASQNVDTNVAWYQQKPGQ APKSLIYSASYVYWDVPSRFSGSASGTDFTLTISVQS EDFATYYCQYDQQLITFGCGTKLEIKSGGGGSEVQL VESGGGLVQPGGSLKLSCAASGFTFNKYAMNWVRQ APGKGLEWVARIRSKYNNYATYYADSVKDRFTISRDD SKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYISY WAYCGQGTLLTVSSGGGSGGGGSGGGGSQTVVT QEPSLTVSPGGTVTLTCSSTGAVTSGNYPNWVQQ KPGQCPRGLIGGTKFLAPGTPARFSGSLLGGKAALTS GVQPEDEAEYYCVLWYSNRWVFGGGTKLTVLGGGG DKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPE VTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPCE EQYGSTYRCVSVLTVLHQDWLNGKEYKCKVSNKALP APIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLT CLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDG SFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYT QKSLSLSPGGGSGGGGSGGGGSGGGGSGGGGSGG GGGSDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAK TKPCEEQYGSTYRCVSVLTVLHQDWLNGKEYKCKVS NKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKN QVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPV DSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALH

[0172]

				NHYTQKSLSLSPGK
156.	CD70_21D_CC VH CDR1	人工的	aa	TYAMS
157.	CD70_21D_CC VH CDR2	人工的	aa	AISGSGGRTFYAESVEG
158.	CD70_21D_CC VH CDR3	人工的	aa	HDYSNYPYFDY
1659.	CD70_21D_CC VL CDR1	人工的	aa	RASQSVRSTYLA
160.	CD70_21D_CC VL CDR2	人工的	aa	GASSRAT
161.	CD70_21D_CC VL CDR3	人工的	aa	QQYGDLPFT
162.	CD70_21D_CC VH	人工的	aa	EVQLLESGGGMVQPGGSLRLSCAASGFTFSTYAMS WVRQAPGKCLEWVSAISGSGGRTFYAESVEGRFTIS RDNSKNTLYLQMNSLRAEDTAVYYCAKHDYSNYPYF DYWGQGTLVTVSS
163.	CD70_21D_CC VL	人工的	aa	EIVLTQSPGTLSLSPGERATLSCRASQSVRSTYLAWYQ QK PGQAPRLIYGASSRATGIPDRFSGSGSGTDFTLTISRLE E PEDFAVYSCQQYGDLPFTFGCGTKLEIK
164.	CD70_21D_CC x12C scFc	人工的	aa	EVQLLESGGGMVQPGGSLRLSCAASGFTFSTYAMS WVRQAPGKCLEWVSAISGSGGRTFYAESVEGRFTIS RDNSKNTLYLQMNSLRAEDTAVYYCAKHDYSNYPYF DYWGQGTLVTVSSGGGGSGGGSGGGGSEIVLTQS PGTSLSPGERATLSCRASQSVRSTYLAWYQQKPGQ APRLIYGASSRATGIPDRFSGSGSGTDFTLTISRLEPE DFAVYSCQQYGDLPFTFGCGTKLEIKSGGGGSEVQLV ESGGGLVQPGGSLKLSAASGFTFNKYAMNWVRQA PGKGLEWVARIRSKYNNYATYYADSVKDRFTISRDDS KNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYISYW

[0173]

			AYWGQGT ₁ LVTVSSGGGGSGGGGSGGGGSQTVVTQ EPSLTVSPGGTVTLT ₂ CGSSTGAVTSGNYPNWWVQKP GQAPRGLIGGTKFLAPGTPARFSGSLLGGKAALTLSG VQPEDEAEYYCVLWYSNRWVFGGGTKLTVLGGGGD KTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEV TCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPCEE QYGSTYRCVSVLTVLHQDWLNGKEYKCKVSNKALPA PIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCL VKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSF FLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQK SLSLSPGKGGGGSGGGGSGGGGSGGGGSGGGGSG GGGSDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAK TKPCEEQYGSTYRCVSVLTVLHQDWLNGKEYKCKVS NKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKN QVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPVL DSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALH NHYTQKSLSLSPGK
165	MSLN_5_CCx CD3-scFc 双特 异性 HLE 分子		MGWSCII ₁ FLVATATGVHSQVQLVESGGGLVPGGGS LRLSCAASGFTFSDYYMTWIRQAPGKGLEWLSYISS GSTIYYADSVKGRFTISRDNAKNSLFLQMNSLRAEDT AVYYCARD ₂ RNSHFDYWGGT ₃ LVTVSSGGGGSGGG GSGGGGSDIQMTQSPSSVSASVGDRVITICRASQGI NTWLAWYQQKPGKAPKLLIYGASGLQSGVPSRFSGS GSGTDFTLT ₄ ISSLQPEDFATYYCQAKSFPRTFGQGT KVEIKSGGGGSEVQLVESGGGLVQPGGSLKLSCAAS GFTFNKYAMNWVRQAPGKGLEWVARIRSKYNNYA TYYADSVKDRFTISRDDSKNTAYLQMNNLKTEDTAV YYCVRHGNFGNSYISYWAYWGQGT ₅ LVTVSSGGGG GGGGSGGGGSQTVVTQEP ₆ SLTVSPGGTVTLT ₇ CGSST GAVTSGNYPNWWVQKPGQAPRGLIGGTKFLAPGTP ARFSGSLLGGKAALTLSGVQPEDEAEYYCVLWYSNR

[0174]

			WVFGGGTKLTVLGGGGDKTHTCPPCPAPELLGGPSV FLFPPKPKDTLMISRTPEVTCVVDVSHEDPEVKFNW YVDGVEVHNAKTKPCEEQYGSTYRCVSVLTVLHQD WLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVY TLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGN VFSCSVMHEALHNHYTQKSLSLSPGKGGGGSGGGG SGGGGSGGGGSGGGGSGGGGSDKTHTCPPCPAPELL LGGPSVFLFPPKPKDTLMISRTPEVTCVVDVSHEDP EVKFNWYVDGVEVHNAKTKPCEEQYGSTYRCVSVLT VLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPR EPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEW ESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
166	具有 cys-夹的 抗 PSMA xI2C0, scFc 双特异性分子 HLE PM76-B10.11		QVQLVESGGGLVKGESLRLSCAASGFTFSDYYMYW VRQAPGKCLEWVAISDGGYYTYSDIIKGRFTISRDN AKNSLYLQMNSLKAEDTAVYYCARGFLLRHGAMD YWGQGTLLTVSSGGGGSGGGGSGGGGSDIQMTQS PSSLSASVGDRTITCKASQNVDTNVAWYQQKPGQ APKSLIYSASYVYWDVPSRFGSGASGTDFTLTISVQS EDFATYYCQYDQQLITFGCGTKLEIKSGGGGSEVQL VESGGGLVQPGGSLKLSAASGFTFNKYAMNWVRQ APGKGLEWVARIRSKYNNYATYYADSVKDRFTISRDD SKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYISY WAYWGQGTLLTVSSGGGGSGGGGSGGGGSGTQVW TQEPSLTVSPGGTVTLTCSSTGAVTSGNYPNWVQQ KPGQAPRGLIGGTKFLAPGTPARFSGSLLGGKAALT SGVQPEDEAEYCVLWYSNRWVFGGGTKLTVLGGG GDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRT PEVTCVVDVSHEDPEVKFNWYVDGVEVHNAKTKPC EEQYGSTYRCVSVLTVLHQDWLNGKEYKCKVSNKAL PAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSL

[0175]

				TCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDG SFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYT QKSLSLSPGKGGGSGGGSGGGSGGGSGGGSGGGG SGGGGSDKTHTCPPCPAPELLGGPSVFLFPPKPKDTL MISRTPEVTCVVDVSHEDPEVKFNWYVDGVEVHN AKTKPCEEQYGSTYRCVSVLTVLHQDWLNGKEYKCK VSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK NQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPP VLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEAL HNHYTQKSLSLSPGK
167	抗 PSMA IC20 双特异性分子 PM76-B10.17			QVQLVESGGGLVKPGESLRLSCAASGFTFSDYYMYW VRQAPGKGLEWVAIISDGGYYTYSDIIGRFTISRDN AKNSLYLQMNSLKAEDTAVYYCARGFPLLRHGAMD YWGQGTLLTVSSGGGSGGGGSGGGGSDIQMTQS PSSLSASVGDRVTITCKASQNVDTNVAWYQQKPGQ APKSLIYSASYRSDVPSRFGSGASGDTFTLTISVQSE DFATYYCQQYDSYPYTFGGGKLEIKSGGGGSEVQLV ESGGGLVQPGGSLKLSAASGFTFNKYAMNWVRQA PGKGLEWVARIRSKYNNYATYYADSVKDRFTISRDDS KNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYISYW AYWGQGTLLTVSSGGGSGGGGSGGGGSQTVVTQ EPSLTVSPGGTVTLTCSSTGAVTSGNYPNWVQQKP GQAPRGLIGGTKFLAPGTPARFSGSLLGGKAALTLSG VQPEDEAEYYCVLWYSNRWVFGGGTKLTVL
168	抗 Cldn 18.2 VH CDR1 CL-1 和 CL-2	人工的	aa	GYMH
169	抗 Cldn18.2 VH CDR2	人工的	aa	WINPNSGGTKYAQKFQG
170	抗 Cldn18.2 VH CDR3	人工的	aa	DRITVAGTYYYGMDV
171	抗 Cldn18.2 VL	人工的	aa	RASQGVNNWLA

[0176]

	CDR1			
172	抗 Cldn18.2 VL CDR2	人工的	aa	TASSLQS
173	抗 Cldn18.2 VL CDR3	人工的	aa	QQANSFPIT
174	抗 Cldn18.2 VH 抗 CL-1	人工的	aa	QVQLVQSGAEVKKPGASVKVCKASGYTFTGYMHWVR QAPGQCLEWMGWINPNSGGTKYAQKFQGRVTMTRDT SISTAYMELSRLRSDDTAVYYCARDRITVAGTYYYGMDV WGQGTTVTVSS
175	抗 Cldn18.2 VL CL-1	人工的	aa	DIQMTQSPSSVSASVGDRTITCRASQGVNNWLAWYQQ KPGKAPKLLIYTASSLQSGVPSRFSGSGSGTDFTLTIRSLQP EDFATYYCQQANSFPITFGCGTRLEIK
176	抗 Cldn18.2 scFv CL-1	人工的	aa	QVQLVQSGAEVKKPGASVKVCKASGYTFTGYMHWVR QAPGQCLEWMGWINPNSGGTKYAQKFQGRVTMTRDT SISTAYMELSRLRSDDTAVYYCARDRITVAGTYYYGMDV WGQGTTVTVSSGGGGSGGGSGGGGSDIQMTQSPSSV SASVGDRTITCRASQGVNNWLAWYQQKPGKAPKLLIYT ASSLQSGVPSRFSGSGSGTDFTLTIRSLQPEDFATYYCQQA NSFPITFGCGTRLEIK
177	抗 Cldn 18.2xCD3 双特 异性 分子 CL-1 x12C	人工的	aa	QVQLVQSGAEVKKPGASVKVCKASGYTFTGYMHWVR QAPGQCLEWMGWINPNSGGTKYAQKFQGRVTMTRDT SISTAYMELSRLRSDDTAVYYCARDRITVAGTYYYGMDV WGQGTTVTVSSGGGGSGGGSGGGGSDIQMTQSPSSV SASVGDRTITCRASQGVNNWLAWYQQKPGKAPKLLIYT ASSLQSGVPSRFSGSGSGTDFTLTIRSLQPEDFATYYCQQA NSFPITFGCGTRLEIKSGGGGSEVQLVESGGGLVQPGGSLK LSCAASGFTFNKYAMNWVRQAPGKGLEWVARIRSKYNN YATYYADSVKDRFTISRDDSKNTAYLQMNNLKTEDAVYY CVRHGNFGNSYISYWAYWGQGLTVTVSSGGGGSGGGGS GGGGSTVTVTQEPSLTVSPGGTVTLTCSSTGAVTSGNY PNWVQQKPGQAPRGLIGGTKFLAPGTPARFSGSLLGGKA ALTLSGVQPEDEAEYYCVLWYSNRWVFGGGTKLTVL
178	抗 Cldn 18.2xCD3 双特	人工的	aa	QVQLVQSGAEVKKPGASVKVCKASGYTFTGYMHWVR QAPGQCLEWMGWINPNSGGTKYAQKFQGRVTMTRDT

[0177]

	异性 scFc 分子 CL-1 xI2C-scFc			SISTAYMELSRLSDDTAVYYCARDRITVAGTYYYYGMDV WGQGTTVTVSSGGGGSGGGSGGGGSDIQMTQSPSSV SASVGDRVTITCRASQGVNNWLAWYQQKPGKAPKLLIYT ASSLQSGVPSRFSGSGSGTDFTLTIRSLQPEDFATYYCQQA NSFPITFGCGTRLEIKSGGGGSEVQLVESGGGLVQPGGSLK LSCAASGFTFNKYAMNWRQAPGKGLEWVARIRSKYNN YATYYADSVKDRFTISRDDSKNTAYLQMNNLKTEDTAVYY CVRHGNFGNSYISYWAYWGQGTLLTVSSGGGGSGGGGS GGGGSQTVVTQEPSLTVSPGGTVTLTCSSTGAVTSGNY PNWVQQKPGQAPRGLIGGTFKFLAPGTPARFSGSLLGGKA ALTLSGVQPEDEAEYYCVLWYSNRWVFGGGTKLTVLGGG GDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVT CVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPCEEQYGS TYRCVSVLTVLHQDWLNGKEYCKVSNKALPAPIEKTISKA KGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAV EWESNGQPENNYKTPPVLDSDGSFFLYSKLTVDKSRWQ QGNVFSCSVMHEALHNHYTQKSLSLSPGKGGGGSGGGG SGGGSGGGSGGGSGGGSGDKTHTCPPCPAPELLGG PSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPCEEQYGSTYRCVSVLTVLHQDWLNG KEYCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREE MTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPP VLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNH YTQKSLSLSPGK
179	抗 Cldn18.2 VH CL-2	人工的	aa	QVQMVQSGAEVKKHGASVKVSKASGYTFTGYMHVW RQAPGQCLEWMGWINPNSGGTKYAQKFQGRVTMTRD TSISTAYMELSRLSDDTAVYYCARDRITVAGTYYYYGMD VWGQGTTVTVSS
180	抗 Cldn18.2 VL CL-2	人工的	aa	DIQMTQSPSSVSASVGDRVTITCRASQGVNNWLAWYQQ KPGKAPKLLIYTASSLQSGVPSRFSGSGSGTDFTLTIRSLQ EDFATYYCQQA NSFPITFGCGTRLEIK
181	抗 Cldn18.2 scFv CL-2	人工的	aa	QVQMVQSGAEVKKHGASVKVSKASGYTFTGYMHVW RQAPGQCLEWMGWINPNSGGTKYAQKFQGRVTMTRD TSISTAYMELSRLSDDTAVYYCARDRITVAGTYYYYGMD VWGQGTTVTVSSGGGGSGGGSGGGGSDIQMTQSPSS

[0178]

				VSASVGDRVTITCRASQGVNNWLAWYQQKPGKAPKLLIY TASSLQSGVPSRFSGSGSGTDFTLTIRSLQPEDFATYYCQQ ANSFPITFGCGTRLEIK
182	抗 Cldn18.2xCD3 双特异性 分子 CL-2xI2C	人工的	aa	QVQMVQSGAEVKKHGASVKVSCKASGYTFTGYMHVW RQAPGQCLEWMGWINPNSGGTKYAQKFQGRVTMTRD TSISTAYMELSRLRSDDTAVYYCARDRITVAGTYYYYGMD VWVGQTTVTVSSGGGSGGGGSGGGGSDIQMTQSPSS VSASVGDRVTITCRASQGVNNWLAWYQQKPGKAPKLLIY TASSLQSGVPSRFSGSGSGTDFTLTIRSLQPEDFATYYCQQ ANSFPITFGCGTRLEIKSGGGGSEVQLVESGGGLVQPGGS LKLSCAASGFTFNKYAMNWVRQAPGKGLEWVARIRSKY NNYATYYADSVKDRFTISRDDSKNTAYLQMNNLKTEDTA VYYCVRHGNFGNSYISYWAYWGQGLTVTVSSGGGSGSGG GGSGGGGSQTVVTQEPSLTVSPGGTVTLTCGSSTGAVTS GNYPNWVQKPGQAPRGLIGGTKFLAPGTPARFSGSLLG GKAALTLSGVQPEDEAEYCVLWYSNRWVFGGGTKLTVL
183	抗 Cldn18.2xCD3 双特异性 scFc 分子 CL-2xI2C-scFc	人工的	aa	QVQMVQSGAEVKKHGASVKVSCKASGYTFTGYMHVW RQAPGQCLEWMGWINPNSGGTKYAQKFQGRVTMTRD TSISTAYMELSRLRSDDTAVYYCARDRITVAGTYYYYGMD VWVGQTTVTVSSGGGSGGGGSGGGGSDIQMTQSPSS VSASVGDRVTITCRASQGVNNWLAWYQQKPGKAPKLLIY TASSLQSGVPSRFSGSGSGTDFTLTIRSLQPEDFATYYCQQ ANSFPITFGCGTRLEIKSGGGGSEVQLVESGGGLVQPGGS LKLSCAASGFTFNKYAMNWVRQAPGKGLEWVARIRSKY NNYATYYADSVKDRFTISRDDSKNTAYLQMNNLKTEDTA VYYCVRHGNFGNSYISYWAYWGQGLTVTVSSGGGSGSGG GGSGGGGSQTVVTQEPSLTVSPGGTVTLTCGSSTGAVTS GNYPNWVQKPGQAPRGLIGGTKFLAPGTPARFSGSLLG GKAALTLSGVQPEDEAEYCVLWYSNRWVFGGGTKLTVL GGGGDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRT PEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPCEE QYGSTYRCVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEK TISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKS RWQQGNVFSCSVMHEALHNHYTQKSLSLSPGKGGGGS

[0179]

				GGGGSGGGGSGGGGSGGGGSGGGGSDKTHTCPPCPAP ELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEV KFNWYVDGVEVHNAKTKPCEEQYGSTYRCVSVLTVLHQD WLNKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPP SREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYK TTPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEA LHNHYTQKSLSLSPGK
184	抗 MUC17 VH CDR1 MU 8-B7	人工的	aa	GYYS
185	抗 MUC17 VH CDR2 MU 8-B7	人工的	aa	DIDASGSTKYNPSLKS
186	抗 MUC17 VH CDR3 MU 8-B7	人工的	aa	KKYSTVWSYFDN
187	抗 MUC17 VL CDR1 MU 8-B7	人工的	aa	SGDKLGDKYAS
188	抗 MUC17 VL CDR2 MU 8-B7	人工的	aa	QDRKRPS
189	抗 MUC17 VL CDR3 MU 8-B7	人工的	aa	QAWGSSTAV
190	抗 MUC17 VH MU 8-B7	人工的	aa	QVQLQQWGAGLLKPSETLSLTCAVYGGSFSGYYWSWIRQPPG KCLEWIGDIDASGSTKYNPSLKSRTISLDTSKNQFSKLNSVTAA DTAVYFCARKKYSTVWSYFDNWGQGLTVTVSS
191	抗 MUC17 VL MU 8-B7	人工的	aa	SYELTQPSSVSPPGQTASITCSGDKLGDKYASWYQQKPG QSPVLVIYQDRKRPSGVPERFSGNSGNTATLTISGTQAM DEADYYCQAWGSSTAVFGCGTKLTVL
192	双特异性 分子	人工的	aa	QVQLQQWGAGLLKPSETLSLTCAVYGGSFSGYYWSWIR QPPGKCLEWIGDIDASGSTKYNPSLKSRTISLDTSKNQFS

[0180]

	MU 8-B7 x I2C0scFc			LKLNSVTAADTAVYFCARKKYSTVWSYFDNWGQGLTVTV SSGGGGSGGGGSGGGGSSYELTQPSSVSVPPGQTASITCS GDKLGDKYASWYQQKPGQSPVLVIYQDRKRPSGVPERFS GSNSGNTATLTISGTQAMDEADYYCQAWGSSTAVFGCG TKLTVLSGGGGSEVQLVESGGGLVQPGGSLKLSCAASGFT FNKYAMNWVRQAPGKGLEWVARIRSKYNNYATYYADSV KDRFTISRDDSKNTAYLQMNNLKTEDTAVYYCVRHGNFG NSYISYWAYWGQGLTVTVSSGGGGSGGGGSGGGGSQT VVTQEPSLTVSPGGTVTLTCGSSTGAVTSGNYPNWWVQK PGQAPRGLIGGTKFLAPGTPARFSGSLLGGKAAALTLSGVQ PEDEAEYYCVLWYSNRWVFGGGTKLTVLGGGGDKTHC PPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVS HEDPEVKFNWYVDGVEVHNAKTKPCEEQYGSTYRCVSVL TVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREP QVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFS CSVMHEALHNHYTQKSLSLSPGKGGGGSGGGGSGGGGS GGGGSGGGGSGGGGSDKTHCPCPAPELLGGPSVFLFP PKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVE VHNAKTKPCEEQYGSTYRCVSVLTVLHQDWLNGKEYKCK VSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQ VSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDG SFFLYSKLTVDKSRWQQGNVFS CSVMHEALHNHYTQKSLSLSPGK
193	I2C 的 CDR-L1	人工的	aa	GSSTGAVTSGNYPN
194	I2C 的 CDR-L2	人工的	aa	GTKFLAP
195	I2C 的 CDR-L3	人工的	aa	VLWYSNRWV
196	I2C 的 CDR-H1	人工的	aa	KYAMN
197	I2C 的 CDR-H2	人工的	aa	RIRSKYNNYATYYADSVKD
198	I2C 的 CDR-H3	人工的	aa	HGNFGNSYISYWAY
199	I2C 的 VH	人工的	aa	EVQLVESGGGLVQPGGSLKLSCAASGFTFNKYAMNWVR QAPGKGLEWVARIRSKYNNYATYYADSVKDRFTISRDDSK NTAYLQMNNLKTEDTAVYYCVRHGNFGNSYISYWAYWG QGTLTVTVSS

[0181]	200	I2C 的 VL	人工的	aa	QTVVTQEPSTLVSPGGTVTLTCGSSTGAVTSGNYPNWWVQ QKPGQAPRGLIGGTKFLAPGTPARFSGSLLGGKAALTLSG VQPEDEAEYYCVLWYSNRWVFGGGTKLTVL
	201	I2C 的 VH-VL	人工的	aa	EVQLVESGGGLVQPGGSLKLSKAASGFTFNKYAMNWVR QAPGKGLEWVARIRSKYNNYATYYADSVKDRFTISRDDSK NTAYLQMNNLKTEDTAVYYCVRHGNFGNSYISYWAYWG QGTLVTVSSGGGGSGGGGSGGGGSQTVVTQEPSTLVSP GGTVTLTCGSSTGAVTSGNYPNWWVQKPGQAPRGLIGG TKFLAPGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCVL WYSNRWVFGGGTKLTVL

[0182] 通过参考以下实例将更充分地理解本发明。然而,这些实例不应被解释为限制本发明的范围。

[0183] 实例

[0184] 实例1. 测量蛋白与固体表面结合的方法

[0185] 双特异性抗体构建体是内部来源的。将它们用荧光团标记并在标记程序后纯化。

[0186] 每个测量室包含塑料盖片。为了测量蛋白与固体表面的结合,首先将底部具有塑料盖片的测量室与含有荧光团-蛋白(例如,荧光团标记的抗体构建体)的溶液一起孵育。然后吸出样品溶液,冲洗盖片并用缓冲剂填充,以稍后在共聚焦显微镜上成像。通过共聚焦显微镜测量的荧光强度显示双特异性抗体构建体与盖片结合。图1示出了实验装置的图。

[0187] 图2示出了在不存在表面活性剂的情况下分别与固体表面(例如,盖片)结合的两种荧光团标记的抗体构建体的滴定。通过对表面进行共聚焦xy扫描来测量结合的荧光团标记的抗体构建体的荧光强度。

[0188] 实例2. 用表面活性剂处理固体表面防止蛋白与表面结合

[0189] 几种表面活性剂以其各自CMC的不同倍数使用,以确定每种表面活性剂防止双特异性抗体构建体与固体表面结合的有效性。在该研究中,首先将含有表面活性剂的溶液与表面一起孵育,然后添加荧光团标记的抗体构建体并孵育。之后,吸出溶液,冲洗表面并用缓冲剂填充,以在共聚焦显微镜上成像。结果在图3中示出。在该图中,第一组条是没有任何表面活性剂的情况下与表面结合的双特异性抗体。这些用作基准,并将所有以下数据组与这些数据进行比较。从第2组到最后一组是与用不同CMC的不同倍数的不同表面活性剂预处理的表面结合的蛋白的相对百分比。插入部分是该图的下部区域的放大。研究了PS 80、PS 20、P188、P407和曲拉通X-100。

[0190] 测试了向表面添加表面活性剂和抗体的顺序。对于双特异性抗体1和2,测试了两种顺序:在第一种顺序中,在将抗体添加到表面之前,将含表面活性剂的溶液添加到表面;而另一种顺序反过来。结果在图4中示出(左边是抗体1,右边是抗体2)。对于这两个图,第一组条是没有任何表面活性剂的情况下与表面结合的双特异性抗体。这些用作基准,并将所有以下数据组与这些数据进行比较。从第2组到最后一组是与用其CMC的不同倍数的PS 80预处理的表面结合的抗体的相对百分比。表面活性剂有效地防止蛋白与表面结合。

[0191] 实例3. 某些表面活性剂与塑料IV部件中使用的增塑剂的不相容性

[0192] 将用盐水稀释剂预填充的Baxter Viaflex PVC-DEHP IV袋用于本研究。在研究中

使用表面活性剂聚山梨醇酯80 (PS80)、聚山梨醇酯20 (PS20)、泊洛沙姆188 (P188)、泊洛沙姆407 (P407) 和曲拉通X-100。将不同量的不同表面活性剂与袋在25℃下孵育24小时或48小时。然后对袋进行取样,并通过反相超高压液相色谱 (RP-UHPLC) 分析,并通过UV检测器检测。流动相A和B是0.1%三氟乙酸 (TFA) 的DI水溶液和0.1%TFA的乙腈溶液。梯度在下表3中列出。流速为0.6ml/min。为了定量,在相同条件下建立DEHP的标准曲线。

[0193] 表3.RP-UPLC梯度

时间 (min)	流量 (mL/min)	%A	%B
0.0	0.6	95	5
1.5	0.6	5	95
3.1	0.6	5	95
3.2	0.6	95	5
4.0	0.6	95	5

[0195] 比较25℃下、24小时和48小时、PVC-DEHP IV袋中0.3重量%的盐水溶液中的PS 80、PS 20和P188。结果在图5中示出。PS80和PS20导致DEHP从PVC-DEHP IV袋中大量浸出,而P188没有引起任何浸出(图5)。使用仅盐水,作为对照。

[0196] 通过在25℃下在PVC-DEHP IV袋中的盐水中孵育24小时,比较各自CMC的不同倍数的PS 80、PS 20、P188、P407和曲拉通X-100。将浸出的DEHP的量在图6中根据CMC的倍数绘图。显然,聚山梨醇酯提取了一定量的DEHP,而泊洛沙姆则没有。浸出的DEHP量与所使用的表面活性剂的量相关。

序列表

<110> 安进公司

<120> 用于在低蛋白浓度下使蛋白损失最小化的组合物和方法

<130> A-2429-W0-PCT

<150> 62/926,089

<151> 2019-10-25

<160> 201

<170> PatentIn 3.5版

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

Glu Arg Thr Thr Ile Asn Cys Lys Ser Ser Gln Ser Val Leu Asp Ser

20 25 30

Ser Thr Asn Lys Asn Ser Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln

35 40 45

Pro Pro Lys Leu Leu Leu Ser Trp Ala Ser Thr Arg Glu Ser Gly Ile

50 55 60

Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr

65 70 75 80

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Lys

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1 5 10 15

Glu Arg Thr Thr Ile Asn Cys Lys Ser Ser Gln Ser Val Leu Asp Ser

20 25 30

Ser Thr Asn Lys Asn Ser Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln

35	40	45
Pro Pro Lys Leu Leu Leu Ser Trp Ala Ser Thr Arg Glu Ser Gly Ile		
50	55	60
Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr		
65	70	75
Ile Asp Ser Pro Gln Pro Glu Asp Ser Ala Thr Tyr Tyr Cys Gln Gln		80
85	90	95
Ser Ala His Phe Pro Ile Thr Phe Gly Gln Gly Thr Arg Leu Glu Ile		
100	105	110

Lys

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Ser	Val	Lys	Val	Ser	Cys	Lys	Ala	Ser	Gly	Tyr	Thr	Phe	Thr	Asn	Tyr
			20					25					30		
Gly	Met	Asn	Trp	Val	Lys	Gln	Ala	Pro	Gly	Gln	Cys	Leu	Glu	Trp	Met
		35					40					45			
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Gln	Gly	Arg	Val	Thr	Met	Thr	Thr	Asp	Thr	Ser	Thr	Ser	Thr	Ala	Tyr
65					70					75					80
Met	Glu	Ile	Arg	Asn	Leu	Gly	Gly	Asp	Asp	Thr	Ala	Val	Tyr	Tyr	Cys
				85					90					95	
Ala	Arg	Trp	Ser	Trp	Ser	Asp	Gly	Tyr	Tyr	Val	Tyr	Phe	Asp	Tyr	Trp
			100					105					110		
Gly	Gln	Gly	Thr	Ser	Val	Thr	Val	Ser	Ser	Gly	Gly	Gly	Gly	Ser	Gly
		115					120					125			
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	130					135					140				
Pro	Asp	Ser	Leu	Thr	Val	Ser	Leu	Gly	Glu	Arg	Thr	Thr	Ile	Asn	Cys
145					150					155					160
Lys	Ser	Ser	Gln	Ser	Val	Leu	Asp	Ser	Ser	Thr	Asn	Lys	Asn	Ser	Leu
			165						170					175	
Ala	Trp	Tyr	Gln	Gln	Lys	Pro	Gly	Gln	Pro	Pro	Lys	Leu	Leu	Leu	Ser
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Gly	Ser	Gly	Thr	Asp	Phe	Thr	Leu	Thr	Ile	Asp	Ser	Pro	Gln	Pro	Glu
	210					215				220					
Asp	Ser	Ala	Thr	Tyr	Tyr	Cys	Gln	Gln	Ser	Ala	His	Phe	Pro	Ile	Thr
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Phe	Gly	Cys	Gly	Thr	Arg	Leu	Glu	Ile	Lys						
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<213> 人工序列

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

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

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Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val		
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Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp		
305	310	315
Ser Val Lys Asp Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr		
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Ala Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr		
340	345	350
Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Ile Ser Tyr Trp		
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Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly		
370	375	380
Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Thr Val Val		
385	390	395
Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly Thr Val Thr Leu		
405	410	415
Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Ser Gly Asn Tyr Pro Asn		
420	425	430
Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly Leu Ile Gly Gly		
435	440	445
Thr Lys Phe Leu Ala Pro Gly Thr Pro Ala Arg Phe Ser Gly Ser Leu		
450	455	460
Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val Gln Pro Glu Asp		
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Glu Trp Met Gly Trp Ile Asn Thr Tyr Thr Gly Glu Pro Thr Tyr Ala			
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Asp Lys Phe Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser			
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Thr Ala Tyr Met Glu Ile Arg Asn Leu Gly Gly Asp Asp Thr Ala Val			
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Tyr Tyr Cys Ala Arg Trp Ser Trp Ser Asp Gly Tyr Tyr Val Tyr Phe			
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Asp Tyr Trp Gly Gln Gly Thr Ser Val Thr Val Ser Ser Gly Gly Gly			
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Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Val Met			
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Thr Gln Ser Pro Asp Ser Leu Thr Val Ser Leu Gly Glu Arg Thr Thr			
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Ile Asn Cys Lys Ser Ser Gln Ser Val Leu Asp Ser Ser Thr Asn Lys			
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Asn Ser Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu			
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Leu Leu Ser Trp Ala Ser Thr Arg Glu Ser Gly Ile Pro Asp Arg Phe			
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Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Asp Ser Pro			
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Gln Pro Glu Asp Ser Ala Thr Tyr Tyr Cys Gln Gln Ser Ala His Phe			
245	250	255	
Pro Ile Thr Phe Gly Gln Gly Thr Arg Leu Glu Ile Lys Ser Gly Gly			
260	265	270	
Gly Gly Ser Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln			
275	280	285	
Pro Gly Gly Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe			
290	295	300	
Asn Lys Tyr Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu			
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Glu Trp Val Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr
 325 330 335
 Tyr Ala Asp Ser Val Lys Asp Arg Phe Thr Ile Ser Arg Asp Asp Ser
 340 345 350
 Lys Asn Thr Ala Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr
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 Ala Val Tyr Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Ile
 370 375 380
 Ser Tyr Trp Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
 385 390 395 400
 Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln
 405 410 415
 Thr Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly Thr
 420 425 430
 Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Ser Gly Asn
 435 440 445
 Tyr Pro Asn Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly Leu
 450 455 460
 Ile Gly Gly Thr Lys Phe Leu Ala Pro Gly Thr Pro Ala Arg Phe Ser
 465 470 475 480
 Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val Gln
 485 490 495
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His His

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Gly	Trp	Ile	Asn	Thr	Tyr	Thr	Gly	Glu	Pro	Thr	Tyr	Ala	Asp	Lys	Phe
	50						55					60			
Gln	Gly	Arg	Val	Thr	Met	Thr	Thr	Asp	Thr	Ser	Thr	Ser	Thr	Ala	Tyr
65					70					75					80
Met	Glu	Ile	Arg	Asn	Leu	Gly	Gly	Asp	Asp	Thr	Ala	Val	Tyr	Tyr	Cys
				85					90						95
Ala	Arg	Trp	Ser	Trp	Ser	Asp	Gly	Tyr	Tyr	Val	Tyr	Phe	Asp	Tyr	Trp
			100						105					110	
Gly	Gln	Gly	Thr	Ser	Val	Thr	Val	Ser	Ser	Gly	Gly	Gly	Gly	Ser	Gly
			115												125
Gly	Gly	Gly	Ser	Gly	Gly	Gly	Gly	Ser	Asp	Ile	Val	Met	Thr	Gln	Ser
							135								140
Pro	Asp	Ser	Leu	Thr	Val	Ser	Leu	Gly	Glu	Arg	Thr	Thr	Ile	Asn	Cys
145					150					155					160
Lys	Ser	Ser	Gln	Ser	Val	Leu	Asp	Ser	Ser	Thr	Asn	Lys	Asn	Ser	Leu
					165					170					175
Ala	Trp	Tyr	Gln	Gln	Lys	Pro	Gly	Gln	Pro	Pro	Lys	Leu	Leu	Leu	Ser
			180						185						190
Trp	Ala	Ser	Thr	Arg	Glu	Ser	Gly	Ile	Pro	Asp	Arg	Phe	Ser	Gly	Ser
			195						200						205
Gly	Ser	Gly	Thr	Asp	Phe	Thr	Leu	Thr	Ile	Asp	Ser	Pro	Gln	Pro	Glu
			210						215						220
Asp	Ser	Ala	Thr	Tyr	Tyr	Cys	Gln	Gln	Ser	Ala	His	Phe	Pro	Ile	Thr
225						230				235					240
Phe	Gly	Cys	Gly	Thr	Arg	Leu	Glu	Ile	Lys	Ser	Gly	Gly	Gly	Gly	Ser
					245					250					255
Glu	Val	Gln	Leu	Val	Glu	Ser	Gly	Gly	Gly	Leu	Val	Gln	Pro	Gly	Gly
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Ser	Leu	Lys	Leu	Ser	Cys	Ala	Ala	Ser	Gly	Phe	Thr	Phe	Asn	Lys	Tyr
			275						280						285
Ala	Met	Asn	Trp	Val	Arg	Gln	Ala	Pro	Gly	Lys	Gly	Leu	Glu	Trp	Val
			290						295						300
Ala	Arg	Ile	Arg	Ser	Lys	Tyr	Asn	Asn	Tyr	Ala	Thr	Tyr	Tyr	Ala	Asp
305						310				315					320
Ser	Val	Lys	Asp	Arg	Phe	Thr	Ile	Ser	Arg	Asp	Asp	Ser	Lys	Asn	Thr
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Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Ile Ser Tyr Trp					
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Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly					
	370		375		380
Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Thr Val Val					
385			390		395
Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly Thr Val Thr Leu					
	405		410		415
Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Ser Gly Asn Tyr Pro Asn					
	420		425		430
Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly Leu Ile Gly Gly					
	435		440		445
Thr Lys Phe Leu Ala Pro Gly Thr Pro Ala Arg Phe Ser Gly Ser Leu					
	450		455		460
Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val Gln Pro Glu Asp					
465			470		475
Glu Ala Glu Tyr Tyr Cys Val Leu Trp Tyr Ser Asn Arg Trp Val Phe					
	485		490		495
Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Gly Gly Gly Asp Lys Thr					
	500		505		510
His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser					
	515		520		525
Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg					
	530		535		540
Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro					
545			550		555
Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala					
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Lys Thr Lys Pro Cys Glu Glu Gln Tyr Gly Ser Thr Tyr Arg Cys Val					
	580		585		590
Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr					
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Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr					
	610		615		620
Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu					
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Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys					
	645		650		655

Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser		
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Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp		
675	680	685
Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser		
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Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala		
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Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys		
725	730	735
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740	745	750
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755	760	765
Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro		
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Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser		
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Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp		
805	810	815
Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn		
820	825	830
Ala Lys Thr Lys Pro Cys Glu Glu Gln Tyr Gly Ser Thr Tyr Arg Cys		
835	840	845
Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu		
850	855	860
Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys		
865	870	875
Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr		
885	890	895
Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr		
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Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu		
915	920	925
Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu		
930	935	940
Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys		
945	950	955
Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu		

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 Arg Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
 65 70 75 80
 Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
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Pro Arg Leu Leu Ile Tyr Arg Ile Ser Arg Arg Phe Ser Gly Val Pro
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Asp Arg Phe Ser Gly Ser Gly Ala Gly Thr Asp Phe Thr Leu Glu Ile
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 1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Arg Asn Tyr
 20 25 30

Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Cys Leu Glu Trp Val
 35 40 45

Ala Val Ile Trp Tyr Asp Gly Ser Asp Lys Tyr Tyr Ala Asp Ser Val

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

Trp Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly
 370 375 380
 Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Ser Gln Thr Val
 385 390 395 400
 Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly Thr Val Thr
 405 410 415
 Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Ser Gly Asn Tyr Pro
 420 425 430
 Asn Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly Leu Ile Gly
 435 440 445
 Gly Thr Lys Phe Leu Ala Pro Gly Thr Pro Ala Arg Phe Ser Gly Ser
 450 455 460
 Leu Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val Gln Pro Glu
 465 470 475 480
 Asp Glu Ala Glu Tyr Tyr Cys Val Leu Trp Tyr Ser Asn Arg Trp Val
 485 490 495
 Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
 500 505

<210> 26

<211> 994

<212> PRT

<213> 人工序列

<220>

<223> EGFRvIII_CCxCD3-scFc双特异性HLE分子

<400> 26

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

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

420	425	430
Asn Trp Val Gln Gln Lys Pro Gly	Gln Ala Pro Arg Gly	Leu Ile Gly
435	440	445
Gly Thr Lys Phe Leu Ala Pro Gly	Thr Pro Ala Arg Phe	Ser Gly Ser
450	455	460
Leu Leu Gly Gly Lys Ala Ala Leu	Thr Leu Ser Gly Val	Gln Pro Glu
465	470	475
Asp Glu Ala Glu Tyr Tyr Cys Val	Leu Trp Tyr Ser Asn Arg	Trp Val
485	490	495
Phe Gly Gly Gly Thr Lys Leu Thr	Val Leu Gly Gly Gly Gly	Asp Lys
500	505	510
Thr His Thr Cys Pro Pro Cys Pro	Ala Pro Glu Leu Leu Gly	Gly Pro
515	520	525
Ser Val Phe Leu Phe Pro Pro Lys	Pro Lys Asp Thr Leu Met	Ile Ser
530	535	540
Arg Thr Pro Glu Val Thr Cys Val	Val Val Asp Val Ser His	Glu Asp
545	550	555
Pro Glu Val Lys Phe Asn Trp Tyr	Val Asp Gly Val Glu Val	His Asn
565	570	575
Ala Lys Thr Lys Pro Cys Glu Glu	Gln Tyr Gly Ser Thr Tyr	Arg Cys
580	585	590
Val Ser Val Leu Thr Val Leu His	Gln Asp Trp Leu Asn Gly	Lys Glu
595	600	605
Tyr Lys Cys Lys Val Ser Asn Lys	Ala Leu Pro Ala Pro Ile	Glu Lys
610	615	620
Thr Ile Ser Lys Ala Lys Gly Gln	Pro Arg Glu Pro Gln Val	Tyr Thr
625	630	635
Leu Pro Pro Ser Arg Glu Glu Met	Thr Lys Asn Gln Val Ser	Leu Thr
645	650	655
Cys Leu Val Lys Gly Phe Tyr Pro	Ser Asp Ile Ala Val Glu	Trp Glu
660	665	670
Ser Asn Gly Gln Pro Glu Asn Asn	Tyr Lys Thr Thr Pro Pro	Val Leu
675	680	685
Asp Ser Asp Gly Ser Phe Phe Leu	Tyr Ser Lys Leu Thr Val	Asp Lys
690	695	700
Ser Arg Trp Gln Gln Gly Asn Val	Phe Ser Cys Ser Val Met	His Glu
705	710	715
Ala Leu His Asn His Tyr Thr Gln	Lys Ser Leu Ser Leu Ser	Pro Gly
725	730	735

Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser		
740	745	750
Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp		
755	760	765
Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly		
770	775	780
Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile		
785	790	795
Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu		
805	810	815
Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His		
820	825	830
Asn Ala Lys Thr Lys Pro Cys Glu Glu Gln Tyr Gly Ser Thr Tyr Arg		
835	840	845
Cys Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys		
850	855	860
Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu		
865	870	875
Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr		
885	890	895
Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu		
900	905	910
Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp		
915	920	925
Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val		
930	935	940
Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp		
945	950	955
Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His		
965	970	975
Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro		
980	985	990

Gly Lys

<210> 27

<211> 5

<212> PRT

<213> 人工序列

<220>

<223> MSLN_5 VH CDR1

<400> 27

Asp Tyr Tyr Met Thr

1 5

<210> 28

<211> 17

<212> PRT

<213> 人工序列

<220>

<223> MSLN_5 VH CDR2

<400> 28

Tyr Ile Ser Ser Ser Gly Ser Thr Ile Tyr Tyr Ala Asp Ser Val Lys

1 5 10 15

Gly

<210> 29

<211> 16

<212> PRT

<213> 人工序列

<220>

<223> MSLN_5 VH CDR3

<400> 29

Asp Arg Asn Ser His Phe Asp Tyr Asp Arg Asn Ser His Phe Asp Tyr

1 5 10 15

<210> 30

<211> 11

<212> PRT

<213> 人工序列

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<223> MSLN_5 VL CDR1

<400> 30

Arg Ala Ser Gln Gly Ile Asn Thr Trp Leu Ala

1 5 10

<210> 31

<211> 7

<212> PRT

<213> 人工序列

<220>

<223> MSLN_5 VL CDR2

<400> 31

Gly Ala Ser Gly Leu Gln Ser

1 5
 <210> 32
 <211> 9
 <212> PRT
 <213> 人工序列
 <220>
 <223> MSLN_5 VL CDR3
 <400> 32
 Gln Gln Ala Lys Ser Phe Pro Arg Thr
 1 5
 <210> 33
 <211> 117
 <212> PRT
 <213> 人工序列
 <220>
 <223> MSLN _5 VH
 <400> 33
 Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
 1 5 10 15
 Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr
 20 25 30
 Tyr Met Thr Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Leu
 35 40 45
 Ser Tyr Ile Ser Ser Ser Gly Ser Thr Ile Tyr Tyr Ala Asp Ser Val
 50 55 60
 Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Phe
 65 70 75 80
 Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
 85 90 95
 Ala Arg Asp Arg Asn Ser His Phe Asp Tyr Trp Gly Gln Gly Thr Leu
 100 105 110
 Val Thr Val Ser Ser
 115
 <210> 34
 <211> 107
 <212> PRT
 <213> 人工序列
 <220>
 <223> MSLN_5 VL

<400> 34

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

<210> 35

<211> 239

<212> PRT

<213> 人工序列

<220>

<223> MSLN_5 scFv

<400> 35

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

130	135	140
Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly		
145	150	155
Ile Asn Thr Trp Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro		
165	170	175
Lys Leu Leu Ile Tyr Gly Ala Ser Gly Leu Gln Ser Gly Val Pro Ser		
180	185	190
Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser		
195	200	205
Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ala Lys		
210	215	220
Ser Phe Pro Arg Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys		
225	230	235
<210> 36		
<211> 494		
<212> PRT		
<213> 人工序列		
<220>		
<223> MSLN_5xI2C0双特异性分子		
<400> 36		
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly		
1	5	10
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr		
20	25	30
Tyr Met Thr Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Leu		
35	40	45
Ser Tyr Ile Ser Ser Ser Gly Ser Thr Ile Tyr Tyr Ala Asp Ser Val		
50	55	60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Phe		
65	70	75
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys		
85	90	95
Ala Arg Asp Arg Asn Ser His Phe Asp Tyr Trp Gly Gln Gly Thr Leu		
100	105	110
Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly		
115	120	125
Gly Gly Gly Ser Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Val Ser		
130	135	140
Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly		

145	150	155	160
Ile Asn Thr Trp Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro			
	165	170	175
Lys Leu Leu Ile Tyr Gly Ala Ser Gly Leu Gln Ser Gly Val Pro Ser			
	180	185	190
Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser			
	195	200	205
Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ala Lys			
	210	215	220
Ser Phe Pro Arg Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Ser			
225	230	235	240
Gly Gly Gly Gly Ser Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu			
	245	250	255
Val Gln Pro Gly Gly Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe			
	260	265	270
Thr Phe Asn Lys Tyr Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys			
	275	280	285
Gly Leu Glu Trp Val Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala			
	290	295	300
Thr Tyr Tyr Ala Asp Ser Val Lys Asp Arg Phe Thr Ile Ser Arg Asp			
305	310	315	320
Asp Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu			
	325	330	335
Asp Thr Ala Val Tyr Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser			
	340	345	350
Tyr Ile Ser Tyr Trp Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val			
	355	360	365
Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly			
	370	375	380
Ser Gln Thr Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly			
385	390	395	400
Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Ser			
	405	410	415
Gly Asn Tyr Pro Asn Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg			
	420	425	430
Gly Leu Ile Gly Gly Thr Lys Phe Leu Ala Pro Gly Thr Pro Ala Arg			
	435	440	445
Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly			
	450	455	460

Val Gln Pro Glu Asp Glu Ala Glu Tyr Tyr Cys Val Leu Trp Tyr Ser
 465 470 475 480
 Asn Arg Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
 485 490
 <210> 37
 <211> 982
 <212> PRT
 <213> 人工序列
 <220>
 <223> MSLN_5xCD3-scFc双特异性HLE分子
 <400> 37
 Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
 1 5 10 15
 Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr
 20 25 30
 Tyr Met Thr Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Leu
 35 40 45
 Ser Tyr Ile Ser Ser Ser Gly Ser Thr Ile Tyr Tyr Ala Asp Ser Val
 50 55 60
 Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Phe
 65 70 75 80
 Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
 85 90 95
 Ala Arg Asp Arg Asn Ser His Phe Asp Tyr Trp Gly Gln Gly Thr Leu
 100 105 110
 Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Ser Gly
 115 120 125
 Gly Gly Gly Ser Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Val Ser
 130 135 140
 Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly
 145 150 155 160
 Ile Asn Thr Trp Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro
 165 170 175
 Lys Leu Leu Ile Tyr Gly Ala Ser Gly Leu Gln Ser Gly Val Pro Ser
 180 185 190
 Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser
 195 200 205
 Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ala Lys
 210 215 220

Ser	Phe	Pro	Arg	Thr	Phe	Gly	Gln	Gly	Thr	Lys	Val	Glu	Ile	Lys	Ser
225					230					235					240
Gly	Gly	Gly	Gly	Ser	Glu	Val	Gln	Leu	Val	Glu	Ser	Gly	Gly	Gly	Leu
				245						250					255
Val	Gln	Pro	Gly	Gly	Ser	Leu	Lys	Leu	Ser	Cys	Ala	Ala	Ser	Gly	Phe
			260							265					270
Thr	Phe	Asn	Lys	Tyr	Ala	Met	Asn	Trp	Val	Arg	Gln	Ala	Pro	Gly	Lys
			275												285
Gly	Leu	Glu	Trp	Val	Ala	Arg	Ile	Arg	Ser	Lys	Tyr	Asn	Asn	Tyr	Ala
			290												300
Thr	Tyr	Tyr	Ala	Asp	Ser	Val	Lys	Asp	Arg	Phe	Thr	Ile	Ser	Arg	Asp
305					310										320
Asp	Ser	Lys	Asn	Thr	Ala	Tyr	Leu	Gln	Met	Asn	Asn	Leu	Lys	Thr	Glu
					325										335
Asp	Thr	Ala	Val	Tyr	Tyr	Cys	Val	Arg	His	Gly	Asn	Phe	Gly	Asn	Ser
			340												350
Tyr	Ile	Ser	Tyr	Trp	Ala	Tyr	Trp	Gly	Gln	Gly	Thr	Leu	Val	Thr	Val
			355												365
Ser	Ser	Gly	Gly	Gly	Gly	Ser	Gly	Gly	Gly	Gly	Ser	Gly	Gly	Gly	Gly
			370												380
Ser	Gln	Thr	Val	Val	Thr	Gln	Glu	Pro	Ser	Leu	Thr	Val	Ser	Pro	Gly
385						390									400
Gly	Thr	Val	Thr	Leu	Thr	Cys	Gly	Ser	Ser	Thr	Gly	Ala	Val	Thr	Ser
						405									415
Gly	Asn	Tyr	Pro	Asn	Trp	Val	Gln	Gln	Lys	Pro	Gly	Gln	Ala	Pro	Arg
						420									430
Gly	Leu	Ile	Gly	Gly	Thr	Lys	Phe	Leu	Ala	Pro	Gly	Thr	Pro	Ala	Arg
						435									445
Phe	Ser	Gly	Ser	Leu	Leu	Gly	Gly	Lys	Ala	Ala	Leu	Thr	Leu	Ser	Gly
						450									460
Val	Gln	Pro	Glu	Asp	Glu	Ala	Glu	Tyr	Tyr	Cys	Val	Leu	Trp	Tyr	Ser
465						470									480
Asn	Arg	Trp	Val	Phe	Gly	Gly	Gly	Thr	Lys	Leu	Thr	Val	Leu	Gly	Gly
						485									495
Gly	Gly	Asp	Lys	Thr	His	Thr	Cys	Pro	Pro	Cys	Pro	Ala	Pro	Glu	Leu
						500									510
Leu	Gly	Gly	Pro	Ser	Val	Phe	Leu	Phe	Pro	Pro	Lys	Pro	Lys	Asp	Thr
						515									525
Leu	Met	Ile	Ser	Arg	Thr	Pro	Glu	Val	Thr	Cys	Val	Val	Val	Asp	Val

530	535	540
Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val		
545	550	555
Glu Val His Asn Ala Lys Thr Lys Pro Cys Glu Glu Gln Tyr Gly Ser		560
	565	570
Thr Tyr Arg Cys Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu		575
	580	585
Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala		590
	595	600
Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro		605
610	615	620
Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln		
625	630	635
Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala		640
	645	650
Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr		655
	660	665
Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu		670
675	680	685
Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser		
690	695	700
Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser		
705	710	715
Leu Ser Pro Gly Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly		720
	725	730
Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly		735
	740	745
Gly Gly Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu		750
755	760	765
Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp		
770	775	780
Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp		
785	790	795
Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly		800
	805	810
Val Glu Val His Asn Ala Lys Thr Lys Pro Cys Glu Glu Gln Tyr Gly		815
	820	825
Ser Thr Tyr Arg Cys Val Ser Val Leu Thr Val Leu His Gln Asp Trp		830
835	840	845

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
 850 855 860
 Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
 865 870 875 880
 Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn
 885 890 895
 Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
 900 905 910
 Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
 915 920 925
 Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys
 930 935 940
 Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
 945 950 955 960
 Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
 965 970 975
 Ser Leu Ser Pro Gly Lys
 980

<210> 38

<211> 982

<212> PRT

<213> 人工序列

<220>

<223> MSLN_5_CCxCD3-scFc双特异性HLE分子

<400> 38

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

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

420	425	430
Gly Leu Ile Gly Gly Thr Lys Phe	Leu Ala Pro Gly Thr Pro Ala Arg	
435	440	445
Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala	Leu Thr Leu Ser Gly	
450	455	460
Val Gln Pro Glu Asp Glu Ala Glu Tyr Tyr Cys	Val Leu Trp Tyr Ser	
465	470	475
Asn Arg Trp Val Phe Gly Gly Gly Thr Lys Leu Thr	Val Leu Gly Gly	
485	490	495
Gly Gly Asp Lys Thr His Thr Cys Pro Pro Cys	Pro Ala Pro Glu Leu	
500	505	510
Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys	Pro Lys Asp Thr	
515	520	525
Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val	Val Val Asp Val	
530	535	540
Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr	Val Asp Gly Val	
545	550	555
Glu Val His Asn Ala Lys Thr Lys Pro Cys Glu Glu	Gln Tyr Gly Ser	
565	570	575
Thr Tyr Arg Cys Val Ser Val Leu Thr Val Leu His	Gln Asp Trp Leu	
580	585	590
Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys	Ala Leu Pro Ala	
595	600	605
Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln	Pro Arg Glu Pro	
610	615	620
Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met	Thr Lys Asn Gln	
625	630	635
Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro	Ser Asp Ile Ala	
645	650	655
Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn	Tyr Lys Thr Thr	
660	665	670
Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu	Tyr Ser Lys Leu	
675	680	685
Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val	Phe Ser Cys Ser	
690	695	700
Val Met His Glu Ala Leu His Asn His Tyr Thr Gln	Lys Ser Leu Ser	
705	710	715
Leu Ser Pro Gly Lys Gly Gly Gly Gly Ser Gly Gly	Gly Gly Ser Gly	
725	730	735

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly		
740	745	750
Gly Gly Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu		
755	760	765
Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp		
770	775	780
Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp		
785	790	795
Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly		
805	810	815
Val Glu Val His Asn Ala Lys Thr Lys Pro Cys Glu Glu Gln Tyr Gly		
820	825	830
Ser Thr Tyr Arg Cys Val Ser Val Leu Thr Val Leu His Gln Asp Trp		
835	840	845
Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro		
850	855	860
Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu		
865	870	875
Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn		
885	890	895
Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile		
900	905	910
Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr		
915	920	925
Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys		
930	935	940
Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys		
945	950	955
Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu		
965	970	975
Ser Leu Ser Pro Gly Lys		
980		

<210> 39

<211> 5

<212> PRT

<213> 人工序列

<220>

<223> CDR-H1 CDH19 65254.007

<400> 39

Ser Tyr Gly Met His

1 5

<210> 40

<211> 17

<212> PRT

<213> 人工序列

<220>

<223> CDR-H2 CDH19 65254.007

<400> 40

Phe Ile Trp Tyr Glu Gly Ser Asn Lys Tyr Tyr Ala Glu Ser Val Lys

1 5 10 15

Asp

<210> 41

<211> 16

<212> PRT

<213> 人工序列

<220>

<223> CDR-H3 CDH19 65254.007

<400> 41

Arg Ala Gly Ile Ile Gly Thr Ile Gly Tyr Tyr Tyr Gly Met Asp Val

1 5 10 15

<210> 42

<211> 11

<212> PRT

<213> 人工序列

<220>

<223> CDR-L1 CDH19 65254.007

<400> 42

Ser Gly Asp Arg Leu Gly Glu Lys Tyr Thr Ser

1 5 10

<210> 43

<211> 7

<212> PRT

<213> 人工序列

<220>

<223> CDR-L2 CDH19 65254.007

<400> 43

Gln Asp Thr Lys Arg Pro Ser

1 5

<210> 44

<211> 9

<212> PRT

<213> 人工序列

<220>

<223> CDR-L3 CDH19 65254.007

<400> 44

Gln Ala Trp Glu Ser Ser Thr Val Val

1 5

<210> 45

<211> 125

<212> PRT

<213> 人工序列

<220>

<223> VH CDH19 65254.007

<400> 45

Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Gly

1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr

20 25 30

Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val

35 40 45

Ala Phe Ile Trp Tyr Glu Gly Ser Asn Lys Tyr Tyr Ala Glu Ser Val

50 55 60

Lys Asp Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr

65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys

85 90 95

Ala Arg Arg Ala Gly Ile Ile Gly Thr Ile Gly Tyr Tyr Tyr Gly Met

100 105 110

Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser

115 120 125

<210> 46

<211> 107

<212> PRT

<213> 人工序列

<220>

<223> VL CDH19 65254.007

<400> 46

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

<210> 47

<211> 247

<212> PRT

<213> 人工序列

<220>

<223> VH-VL CDH19 65254.007

<400> 47

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

Thr Gln Pro Pro Ser Val Ser Val Ser Pro Gly Gln Thr Ala Ser Ile
 145 150 155 160
 Thr Cys Ser Gly Asp Arg Leu Gly Glu Lys Tyr Thr Ser Trp Tyr Gln
 165 170 175
 Gln Arg Pro Gly Gln Ser Pro Leu Leu Val Ile Tyr Gln Asp Thr Lys
 180 185 190
 Arg Pro Ser Gly Ile Pro Glu Arg Phe Ser Gly Ser Asn Ser Gly Asn
 195 200 205
 Thr Ala Thr Leu Thr Ile Ser Gly Thr Gln Ala Met Asp Glu Ala Asp
 210 215 220
 Tyr Tyr Cys Gln Ala Trp Glu Ser Ser Thr Val Val Phe Gly Gly Gly
 225 230 235 240
 Thr Lys Leu Thr Val Leu Ser
 245

<210> 48

<211> 507

<212> PRT

<213> 人工序列

<220>

<223> CDH19 65254.007 x I2C

<400> 48

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

Thr	Gln	Pro	Pro	Ser	Val	Ser	Val	Ser	Pro	Gly	Gln	Thr	Ala	Ser	Ile
145					150					155					160
Thr	Cys	Ser	Gly	Asp	Arg	Leu	Gly	Glu	Lys	Tyr	Thr	Ser	Trp	Tyr	Gln
				165					170					175	
Gln	Arg	Pro	Gly	Gln	Ser	Pro	Leu	Leu	Val	Ile	Tyr	Gln	Asp	Thr	Lys
			180					185					190		
Arg	Pro	Ser	Gly	Ile	Pro	Glu	Arg	Phe	Ser	Gly	Ser	Asn	Ser	Gly	Asn
		195					200					205			
Thr	Ala	Thr	Leu	Thr	Ile	Ser	Gly	Thr	Gln	Ala	Met	Asp	Glu	Ala	Asp
	210					215					220				
Tyr	Tyr	Cys	Gln	Ala	Trp	Glu	Ser	Ser	Thr	Val	Val	Phe	Gly	Gly	Gly
225					230					235					240
Thr	Lys	Leu	Thr	Val	Leu	Ser	Gly	Gly	Gly	Gly	Ser	Glu	Val	Gln	Leu
				245					250					255	
Val	Glu	Ser	Gly	Gly	Gly	Leu	Val	Gln	Pro	Gly	Gly	Ser	Leu	Lys	Leu
			260					265					270		
Ser	Cys	Ala	Ala	Ser	Gly	Phe	Thr	Phe	Asn	Lys	Tyr	Ala	Met	Asn	Trp
		275					280					285			
Val	Arg	Gln	Ala	Pro	Gly	Lys	Gly	Leu	Glu	Trp	Val	Ala	Arg	Ile	Arg
	290					295					300				
Ser	Lys	Tyr	Asn	Asn	Tyr	Ala	Thr	Tyr	Tyr	Ala	Asp	Ser	Val	Lys	Asp
305					310					315					320
Arg	Phe	Thr	Ile	Ser	Arg	Asp	Asp	Ser	Lys	Asn	Thr	Ala	Tyr	Leu	Gln
				325					330					335	
Met	Asn	Asn	Leu	Lys	Thr	Glu	Asp	Thr	Ala	Val	Tyr	Tyr	Cys	Val	Arg
			340					345					350		
His	Gly	Asn	Phe	Gly	Asn	Ser	Tyr	Ile	Ser	Tyr	Trp	Ala	Tyr	Trp	Gly
		355					360					365			
Gln	Gly	Thr	Leu	Val	Thr	Val	Ser	Ser	Gly	Gly	Gly	Gly	Ser	Gly	Gly
	370					375					380				
Gly	Gly	Ser	Gly	Gly	Gly	Gly	Ser	Gln	Thr	Val	Val	Thr	Gln	Glu	Pro
385					390					395					400
Ser	Leu	Thr	Val	Ser	Pro	Gly	Gly	Thr	Val	Thr	Leu	Thr	Cys	Gly	Ser
				405					410				415		
Ser	Thr	Gly	Ala	Val	Thr	Ser	Gly	Asn	Tyr	Pro	Asn	Trp	Val	Gln	Gln
			420					425				430			
Lys	Pro	Gly	Gln	Ala	Pro	Arg	Gly	Leu	Ile	Gly	Gly	Thr	Lys	Phe	Leu
	435						440					445			
Ala	Pro	Gly	Thr	Pro	Ala	Arg	Phe	Ser	Gly	Ser	Leu	Leu	Gly	Gly	Lys

450	455	460
Ala Ala Leu Thr Leu Ser Gly Val Gln Pro Glu Asp Glu Ala Glu Tyr		
465	470	475
Tyr Cys Val Leu Trp Tyr Ser Asn Arg Trp Val Phe Gly Gly Gly Thr		480
	485	490
Lys Leu Thr Val Leu His His His His His His		495
500	505	
<210> 49		
<211> 989		
<212> PRT		
<213> 人工序列		
<220>		
<223> CDH19 65254.007 x I2C -scFc双特异性HLE分子		
<400> 49		
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Gly		
1	5	10
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr		
	20	25
Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val		
	35	40
Ala Phe Ile Trp Tyr Glu Gly Ser Asn Lys Tyr Tyr Ala Glu Ser Val		
50	55	60
Lys Asp Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr		
65	70	75
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys		
	85	90
Ala Arg Arg Ala Gly Ile Ile Gly Thr Ile Gly Tyr Tyr Tyr Gly Met		
	100	105
Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly		
	115	120
Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Ser Tyr Glu Leu		
130	135	140
Thr Gln Pro Pro Ser Val Ser Val Ser Pro Gly Gln Thr Ala Ser Ile		
145	150	155
Thr Cys Ser Gly Asp Arg Leu Gly Glu Lys Tyr Thr Ser Trp Tyr Gln		
	165	170
Gln Arg Pro Gly Gln Ser Pro Leu Leu Val Ile Tyr Gln Asp Thr Lys		
	180	185
Arg Pro Ser Gly Ile Pro Glu Arg Phe Ser Gly Ser Asn Ser Gly Asn		

195	200	205
Thr Ala Thr Leu Thr Ile Ser Gly Thr Gln Ala Met Asp Glu Ala Asp		
210	215	220
Tyr Tyr Cys Gln Ala Trp Glu Ser Ser Thr Val Val Phe Gly Gly Gly		
225	230	235
Thr Lys Leu Thr Val Leu Ser Gly Gly Gly Gly Ser Glu Val Gln Leu		240
	245	250
Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Lys Leu		255
	260	265
Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Lys Tyr Ala Met Asn Trp		270
	275	280
Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Arg Ile Arg		285
	290	295
Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp Ser Val Lys Asp		300
305	310	315
Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr Ala Tyr Leu Gln		320
	325	330
Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr Tyr Cys Val Arg		335
	340	345
His Gly Asn Phe Gly Asn Ser Tyr Ile Ser Tyr Trp Ala Tyr Trp Gly		350
	355	360
Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly		365
	370	375
Gly Gly Ser Gly Gly Gly Gly Ser Gln Thr Val Val Thr Gln Glu Pro		380
385	390	395
Ser Leu Thr Val Ser Pro Gly Gly Thr Val Thr Leu Thr Cys Gly Ser		400
	405	410
Ser Thr Gly Ala Val Thr Ser Gly Asn Tyr Pro Asn Trp Val Gln Gln		415
	420	425
Lys Pro Gly Gln Ala Pro Arg Gly Leu Ile Gly Gly Thr Lys Phe Leu		430
	435	440
Ala Pro Gly Thr Pro Ala Arg Phe Ser Gly Ser Leu Leu Gly Gly Lys		445
	450	455
Ala Ala Leu Thr Leu Ser Gly Val Gln Pro Glu Asp Glu Ala Glu Tyr		460
465	470	475
Tyr Cys Val Leu Trp Tyr Ser Asn Arg Trp Val Phe Gly Gly Gly Thr		480
	485	490
Lys Leu Thr Val Leu Gly Gly Gly Gly Asp Lys Thr His Thr Cys Pro		495
	500	505
		510

Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe		
515	520	525
Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val		
530	535	540
Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe		
545	550	555
Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro		
565	570	575
Cys Glu Glu Gln Tyr Gly Ser Thr Tyr Arg Cys Val Ser Val Leu Thr		
580	585	590
Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val		
595	600	605
Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala		
610	615	620
Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg		
625	630	635
Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly		
645	650	655
Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro		
660	665	670
Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser		
675	680	685
Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln		
690	695	700
Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His		
705	710	715
Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys Gly Gly Gly Gly		
725	730	735
Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser		
740	745	750
Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Lys Thr His Thr Cys		
755	760	765
Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu		
770	775	780
Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu		
785	790	795
Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys		
805	810	815
Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys		

820	825	830
Pro Cys Glu Glu Gln Tyr Gly Ser Thr Tyr Arg Cys Val Ser Val Leu		
835	840	845
Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys		
850	855	860
Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys		
865	870	875
Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser		
885	890	895
Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys		
900	905	910
Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln		
915	920	925
Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly		
930	935	940
Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln		
945	950	955
Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn		
965	970	975
His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys		
980	985	

<210> 50

<211> 987

<212> PRT

<213> 人工序列

<220>

<223> CDH19 65254.007 x I2C -scFc_delGK双特异性HLE分子

<400> 50

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

			85					90					95				
Ala	Arg	Arg	Ala	Gly	Ile	Ile	Gly	Thr	Ile	Gly	Tyr	Tyr	Tyr	Gly	Met		
			100					105					110				
Asp	Val	Trp	Gly	Gln	Gly	Thr	Thr	Val	Thr	Val	Ser	Ser	Gly	Gly	Gly		
			115					120					125				
Gly	Ser	Gly	Gly	Gly	Gly	Ser	Gly	Gly	Gly	Gly	Ser	Ser	Tyr	Glu	Leu		
			130					135					140				
Thr	Gln	Pro	Pro	Ser	Val	Ser	Val	Ser	Pro	Gly	Gln	Thr	Ala	Ser	Ile		
145			150					155					160				
Thr	Cys	Ser	Gly	Asp	Arg	Leu	Gly	Glu	Lys	Tyr	Thr	Ser	Trp	Tyr	Gln		
			165					170					175				
Gln	Arg	Pro	Gly	Gln	Ser	Pro	Leu	Leu	Val	Ile	Tyr	Gln	Asp	Thr	Lys		
			180					185					190				
Arg	Pro	Ser	Gly	Ile	Pro	Glu	Arg	Phe	Ser	Gly	Ser	Asn	Ser	Gly	Asn		
			195					200					205				
Thr	Ala	Thr	Leu	Thr	Ile	Ser	Gly	Thr	Gln	Ala	Met	Asp	Glu	Ala	Asp		
210			215					220									
Tyr	Tyr	Cys	Gln	Ala	Trp	Glu	Ser	Ser	Thr	Val	Val	Phe	Gly	Gly	Gly		
225			230					235					240				
Thr	Lys	Leu	Thr	Val	Leu	Ser	Gly	Gly	Gly	Gly	Ser	Glu	Val	Gln	Leu		
			245					250					255				
Val	Glu	Ser	Gly	Gly	Gly	Leu	Val	Gln	Pro	Gly	Gly	Ser	Leu	Lys	Leu		
			260					265					270				
Ser	Cys	Ala	Ala	Ser	Gly	Phe	Thr	Phe	Asn	Lys	Tyr	Ala	Met	Asn	Trp		
			275					280					285				
Val	Arg	Gln	Ala	Pro	Gly	Lys	Gly	Leu	Glu	Trp	Val	Ala	Arg	Ile	Arg		
290			295					300									
Ser	Lys	Tyr	Asn	Asn	Tyr	Ala	Thr	Tyr	Tyr	Ala	Asp	Ser	Val	Lys	Asp		
305			310					315					320				
Arg	Phe	Thr	Ile	Ser	Arg	Asp	Asp	Ser	Lys	Asn	Thr	Ala	Tyr	Leu	Gln		
			325					330					335				
Met	Asn	Asn	Leu	Lys	Thr	Glu	Asp	Thr	Ala	Val	Tyr	Tyr	Cys	Val	Arg		
			340					345					350				
His	Gly	Asn	Phe	Gly	Asn	Ser	Tyr	Ile	Ser	Tyr	Trp	Ala	Tyr	Trp	Gly		
			355					360					365				
Gln	Gly	Thr	Leu	Val	Thr	Val	Ser	Ser	Gly	Gly	Gly	Gly	Ser	Gly	Gly		
370			375					380									
Gly	Gly	Ser	Gly	Gly	Gly	Gly	Ser	Gln	Thr	Val	Val	Thr	Gln	Glu	Pro		
385			390					395					400				

Ser	Leu	Thr	Val	Ser	Pro	Gly	Gly	Thr	Val	Thr	Leu	Thr	Cys	Gly	Ser	
				405					410					415		
Ser	Thr	Gly	Ala	Val	Thr	Ser	Gly	Asn	Tyr	Pro	Asn	Trp	Val	Gln	Gln	
				420					425					430		
Lys	Pro	Gly	Gln	Ala	Pro	Arg	Gly	Leu	Ile	Gly	Gly	Thr	Lys	Phe	Leu	
				435					440					445		
Ala	Pro	Gly	Thr	Pro	Ala	Arg	Phe	Ser	Gly	Ser	Leu	Leu	Gly	Gly	Lys	
				450					455					460		
Ala	Ala	Leu	Thr	Leu	Ser	Gly	Val	Gln	Pro	Glu	Asp	Glu	Ala	Glu	Tyr	
465					470					475					480	
Tyr	Cys	Val	Leu	Trp	Tyr	Ser	Asn	Arg	Trp	Val	Phe	Gly	Gly	Gly	Thr	
				485					490					495		
Lys	Leu	Thr	Val	Leu	Gly	Gly	Gly	Gly	Asp	Lys	Thr	His	Thr	Cys	Pro	
				500					505					510		
Pro	Cys	Pro	Ala	Pro	Glu	Leu	Leu	Gly	Gly	Pro	Ser	Val	Phe	Leu	Phe	
				515					520					525		
Pro	Pro	Lys	Pro	Lys	Asp	Thr	Leu	Met	Ile	Ser	Arg	Thr	Pro	Glu	Val	
				530					535					540		
Thr	Cys	Val	Val	Val	Asp	Val	Ser	His	Glu	Asp	Pro	Glu	Val	Lys	Phe	
545					550					555					560	
Asn	Trp	Tyr	Val	Asp	Gly	Val	Glu	Val	His	Asn	Ala	Lys	Thr	Lys	Pro	
				565					570					575		
Cys	Glu	Glu	Gln	Tyr	Gly	Ser	Thr	Tyr	Arg	Cys	Val	Ser	Val	Leu	Thr	
				580					585					590		
Val	Leu	His	Gln	Asp	Trp	Leu	Asn	Gly	Lys	Glu	Tyr	Lys	Cys	Lys	Val	
				595					600					605		
Ser	Asn	Lys	Ala	Leu	Pro	Ala	Pro	Ile	Glu	Lys	Thr	Ile	Ser	Lys	Ala	
				610					615					620		
Lys	Gly	Gln	Pro	Arg	Glu	Pro	Gln	Val	Tyr	Thr	Leu	Pro	Pro	Ser	Arg	
625					630					635					640	
Glu	Glu	Met	Thr	Lys	Asn	Gln	Val	Ser	Leu	Thr	Cys	Leu	Val	Lys	Gly	
				645					650					655		
Phe	Tyr	Pro	Ser	Asp	Ile	Ala	Val	Glu	Trp	Glu	Ser	Asn	Gly	Gln	Pro	
				660					665					670		
Glu	Asn	Asn	Tyr	Lys	Thr	Thr	Pro	Pro	Val	Leu	Asp	Ser	Asp	Gly	Ser	
				675					680					685		
Phe	Phe	Leu	Tyr	Ser	Lys	Leu	Thr	Val	Asp	Lys	Ser	Arg	Trp	Gln	Gln	
				690					695					700		
Gly	Asn	Val	Phe	Ser	Cys	Ser	Val	Met	His	Glu	Ala	Leu	His	Asn	His	

705	710	715	720
Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Gly Gly Gly Ser Gly			
	725	730	735
Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly			
	740	745	750
Gly Gly Ser Gly Gly Gly Gly Ser Asp Lys Thr His Thr Cys Pro Pro			
	755	760	765
Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro			
	770	775	780
Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr			
785	790	795	800
Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn			
	805	810	815
Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Cys			
	820	825	830
Glu Glu Gln Tyr Gly Ser Thr Tyr Arg Cys Val Ser Val Leu Thr Val			
	835	840	845
Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser			
	850	855	860
Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys			
865	870	875	880
Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu			
	885	890	895
Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe			
	900	905	910
Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu			
	915	920	925
Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe			
	930	935	940
Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly			
945	950	955	960
Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr			
	965	970	975
Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys			
	980	985	

<210> 51

<211> 125

<212> PRT

<213> 人工序列

<220>

<223> CDH19 65254.007_CC x I2C -scFc VH

<400> 51

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

<210> 52

<211> 106

<212> PRT

<213> 人工序列

<220>

<223> CDH19 65254.007_CC x I2C -scFc VL

<400> 52

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

122

245

<210> 54

<211> 501

<212> PRT

<213> 人工序列

<220>

<223> CDH19 65254.007_CC x I2C -scFc双特异性分子

<400> 54

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

	245	250	255
Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Lys Leu			
	260	265	270
Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Lys Tyr Ala Met Asn Trp			
	275	280	285
Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Arg Ile Arg			
	290	295	300
Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp Ser Val Lys Asp			
305	310	315	320
Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr Ala Tyr Leu Gln			
	325	330	335
Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr Tyr Cys Val Arg			
	340	345	350
His Gly Asn Phe Gly Asn Ser Tyr Ile Ser Tyr Trp Ala Tyr Trp Gly			
	355	360	365
Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly			
	370	375	380
Gly Gly Ser Gly Gly Gly Gly Ser Gln Thr Val Val Thr Gln Glu Pro			
385	390	395	400
Ser Leu Thr Val Ser Pro Gly Gly Thr Val Thr Leu Thr Cys Gly Ser			
	405	410	415
Ser Thr Gly Ala Val Thr Ser Gly Asn Tyr Pro Asn Trp Val Gln Gln			
	420	425	430
Lys Pro Gly Gln Ala Pro Arg Gly Leu Ile Gly Gly Thr Lys Phe Leu			
	435	440	445
Ala Pro Gly Thr Pro Ala Arg Phe Ser Gly Ser Leu Leu Gly Gly Lys			
	450	455	460
Ala Ala Leu Thr Leu Ser Gly Val Gln Pro Glu Asp Glu Ala Glu Tyr			
465	470	475	480
Tyr Cys Val Leu Trp Tyr Ser Asn Arg Trp Val Phe Gly Gly Gly Thr			
	485	490	495
Lys Leu Thr Val Leu			
	500		

<210> 55

<211> 989

<212> PRT

<213> 人工序列

<220>

<223> CDH19 65254.007_CC x I2C -scFc双特异性HLE分子

<400> 55

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

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

610	615	620
Lys Gly Gln Pro Arg	Glu Pro Gln Val Tyr Thr	Leu Pro Pro Ser Arg
625	630	635
Glu Glu Met Thr Lys	Asn Gln Val Ser Leu Thr	Cys Leu Val Lys Gly
645	650	655
Phe Tyr Pro Ser Asp	Ile Ala Val Glu Trp Glu Ser	Asn Gly Gln Pro
660	665	670
Glu Asn Asn Tyr Lys	Thr Thr Pro Pro Val	Leu Asp Ser Asp Gly Ser
675	680	685
Phe Phe Leu Tyr Ser	Lys Leu Thr Val Asp	Lys Ser Arg Trp Gln Gln
690	695	700
Gly Asn Val Phe Ser	Cys Ser Val Met His	Glu Ala Leu His Asn His
705	710	715
Tyr Thr Gln Lys Ser	Leu Ser Leu Ser Pro	Gly Lys Gly Gly Gly Gly
725	730	735
Ser Gly Gly Gly Gly	Ser Gly Gly Gly Gly	Ser Gly Gly Gly Gly Ser
740	745	750
Gly Gly Gly Gly Ser	Gly Gly Gly Gly Ser	Asp Lys Thr His Thr Cys
755	760	765
Pro Pro Cys Pro Ala	Pro Glu Leu Leu Gly	Gly Pro Ser Val Phe Leu
770	775	780
Phe Pro Pro Lys Pro	Lys Asp Thr Leu Met	Ile Ser Arg Thr Pro Glu
785	790	795
Val Thr Cys Val Val	Val Asp Val Ser His	Glu Asp Pro Glu Val Lys
805	810	815
Phe Asn Trp Tyr Val	Asp Gly Val Glu Val	His Asn Ala Lys Thr Lys
820	825	830
Pro Cys Glu Glu Gln	Tyr Gly Ser Thr Tyr	Arg Cys Val Ser Val Leu
835	840	845
Thr Val Leu His Gln	Asp Trp Leu Asn Gly	Lys Glu Tyr Lys Cys Lys
850	855	860
Val Ser Asn Lys Ala	Leu Pro Ala Pro Ile	Glu Lys Thr Ile Ser Lys
865	870	875
Ala Lys Gly Gln Pro	Arg Glu Pro Gln Val	Tyr Thr Leu Pro Pro Ser
885	890	895
Arg Glu Glu Met Thr	Lys Asn Gln Val Ser	Leu Thr Cys Leu Val Lys
900	905	910
Gly Phe Tyr Pro Ser	Asp Ile Ala Val Glu	Trp Glu Ser Asn Gly Gln
915	920	925

Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly
 930 935 940
 Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln
 945 950 955 960
 Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
 965 970 975
 His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
 980 985
 <210> 56
 <211> 987
 <212> PRT
 <213> 人工序列
 <220>
 <223> CDH19 65254.007_CC x I2C -scFc_delGK双特异性HLE分子
 <400> 56
 Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Gly
 1 5 10 15
 Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
 20 25 30
 Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Cys Leu Glu Trp Val
 35 40 45
 Ala Phe Ile Trp Tyr Glu Gly Ser Asn Lys Tyr Tyr Ala Glu Ser Val
 50 55 60
 Lys Asp Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
 65 70 75 80
 Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
 85 90 95
 Ala Arg Arg Ala Gly Ile Ile Gly Thr Ile Gly Tyr Tyr Tyr Gly Met
 100 105 110
 Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly
 115 120 125
 Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Ser Tyr Glu Leu
 130 135 140
 Thr Gln Pro Pro Ser Val Ser Val Ser Pro Gly Gln Thr Ala Ser Ile
 145 150 155 160
 Thr Cys Ser Gly Asp Arg Leu Gly Glu Lys Tyr Thr Ser Trp Tyr Gln
 165 170 175
 Gln Arg Pro Gly Gln Ser Pro Leu Leu Val Ile Tyr Gln Asp Thr Lys
 180 185 190

Arg	Pro	Ser	Gly	Ile	Pro	Glu	Arg	Phe	Ser	Gly	Ser	Asn	Ser	Gly	Asn	
195						200				205						
Thr	Ala	Thr	Leu	Thr	Ile	Ser	Gly	Thr	Gln	Ala	Met	Asp	Glu	Ala	Asp	
210						215				220						
Tyr	Tyr	Cys	Gln	Ala	Trp	Glu	Ser	Ser	Thr	Val	Val	Phe	Gly	Cys	Gly	
225						230				235					240	
Thr	Lys	Leu	Thr	Val	Leu	Ser	Gly	Gly	Gly	Gly	Ser	Glu	Val	Gln	Leu	
245						250				255						
Val	Glu	Ser	Gly	Gly	Gly	Leu	Val	Gln	Pro	Gly	Gly	Ser	Leu	Lys	Leu	
260						265				270						
Ser	Cys	Ala	Ala	Ser	Gly	Phe	Thr	Phe	Asn	Lys	Tyr	Ala	Met	Asn	Trp	
275						280				285						
Val	Arg	Gln	Ala	Pro	Gly	Lys	Gly	Leu	Glu	Trp	Val	Ala	Arg	Ile	Arg	
290						295				300						
Ser	Lys	Tyr	Asn	Asn	Tyr	Ala	Thr	Tyr	Tyr	Ala	Asp	Ser	Val	Lys	Asp	
305						310				315					320	
Arg	Phe	Thr	Ile	Ser	Arg	Asp	Asp	Ser	Lys	Asn	Thr	Ala	Tyr	Leu	Gln	
325						330				335						
Met	Asn	Asn	Leu	Lys	Thr	Glu	Asp	Thr	Ala	Val	Tyr	Tyr	Cys	Val	Arg	
340						345				350						
His	Gly	Asn	Phe	Gly	Asn	Ser	Tyr	Ile	Ser	Tyr	Trp	Ala	Tyr	Trp	Gly	
355						360				365						
Gln	Gly	Thr	Leu	Val	Thr	Val	Ser	Ser	Gly	Gly	Gly	Gly	Ser	Gly	Gly	
370						375				380						
Gly	Gly	Ser	Gly	Gly	Gly	Gly	Ser	Gln	Thr	Val	Val	Thr	Gln	Glu	Pro	
385						390				395					400	
Ser	Leu	Thr	Val	Ser	Pro	Gly	Gly	Thr	Val	Thr	Leu	Thr	Cys	Gly	Ser	
405						410				415						
Ser	Thr	Gly	Ala	Val	Thr	Ser	Gly	Asn	Tyr	Pro	Asn	Trp	Val	Gln	Gln	
420						425				430						
Lys	Pro	Gly	Gln	Ala	Pro	Arg	Gly	Leu	Ile	Gly	Gly	Thr	Lys	Phe	Leu	
435						440				445						
Ala	Pro	Gly	Thr	Pro	Ala	Arg	Phe	Ser	Gly	Ser	Leu	Leu	Gly	Gly	Lys	
450						455				460						
Ala	Ala	Leu	Thr	Leu	Ser	Gly	Val	Gln	Pro	Glu	Asp	Glu	Ala	Glu	Tyr	
465						470				475					480	
Tyr	Cys	Val	Leu	Trp	Tyr	Ser	Asn	Arg	Trp	Val	Phe	Gly	Gly	Gly	Thr	
485						490				495						
Lys	Leu	Thr	Val	Leu	Gly	Gly	Gly	Gly	Asp	Lys	Thr	His	Thr	Cys	Pro	

	500		505		510
Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe					
515		520		525	
Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val					
530		535		540	
Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe					
545		550		555	560
Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro					
565		570		575	
Cys Glu Glu Gln Tyr Gly Ser Thr Tyr Arg Cys Val Ser Val Leu Thr					
580		585		590	
Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val					
595		600		605	
Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala					
610		615		620	
Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg					
625		630		635	640
Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly					
645		650		655	
Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro					
660		665		670	
Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser					
675		680		685	
Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln					
690		695		700	
Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His					
705		710		715	720
Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Gly Gly Gly Ser Gly					
725		730		735	
Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly					
740		745		750	
Gly Gly Ser Gly Gly Gly Gly Ser Asp Lys Thr His Thr Cys Pro Pro					
755		760		765	
Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro					
770		775		780	
Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr					
785		790		795	800
Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn					
805		810		815	

Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Cys
 820 825 830
 Glu Glu Gln Tyr Gly Ser Thr Tyr Arg Cys Val Ser Val Leu Thr Val
 835 840 845
 Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser
 850 855 860
 Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys
 865 870 875 880
 Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu
 885 890 895
 Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe
 900 905 910
 Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu
 915 920 925
 Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe
 930 935 940
 Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly
 945 950 955 960
 Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr
 965 970 975
 Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
 980 985

<210> 57

<211> 7

<212> PRT

<213> 人工序列

<220>

<223> FLT3_7 A8xCD3-scFc VH CDR1

<400> 57

Asn Ala Arg Met Gly Val Ser

1 5

<210> 58

<211> 32

<212> PRT

<213> 人工序列

<220>

<223> FLT3_7 A8xCD3-scFc VH CDR2

<400> 58

His Ile Phe Ser Asn Asp Glu Lys Ser Tyr Ser Thr Ser Leu Lys Asn

1	5	10	15
His Ile Phe Ser Asn Asp Glu Lys Ser Tyr Ser Thr Ser Leu Lys Asn			
	20	25	30

<210> 59

<211> 28

<212> PRT

<213> 人工序列

<220>

<223> FLT3_7 A8xCD3-scFc VH CDR3

<400> 59

Ile Val Gly Tyr Gly Ser Gly Trp Tyr Gly Phe Phe Asp Tyr Ile Val

1	5	10	15
---	---	----	----

Gly Tyr Gly Ser Gly Trp Tyr Gly Phe Phe Asp Tyr

20	25
----	----

<210> 60

<211> 11

<212> PRT

<213> 人工序列

<220>

<223> FLT3_7 A8xCD3-scFc VL CDR1

<400> 60

Arg Ala Ser Gln Gly Ile Arg Asn Asp Leu Gly

1	5	10
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<210> 61

<211> 7

<212> PRT

<213> 人工序列

<220>

<223> FLT3_7 A8xCD3-scFc VL CDR2

<400> 61

Ala Ala Ser Thr Leu Gln Ser

1	5
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<210> 62

<211> 9

<212> PRT

<213> 人工序列

<220>

<223> FLT3_7 A8xCD3-scFc VL CDR3

<400> 62

Leu Gln His Asn Ser Tyr Pro Leu Thr

1 5

<210> 63

<211> 124

<212> PRT

<213> 人工序列

<220>

<223> FLT3_7 A8xCD3-scFc VH

<400> 63

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

1 5 10 15

Thr Leu Thr Leu Thr Cys Thr Leu Ser Gly Phe Ser Leu Asn Asn Ala

20 25 30

Arg Met Gly Val Ser Trp Ile Arg Gln Pro Pro Gly Lys Cys Leu Glu

35 40 45

Trp Leu Ala His Ile Phe Ser Asn Asp Glu Lys Ser Tyr Ser Thr Ser

50 55 60

Leu Lys Asn Arg Leu Thr Ile Ser Lys Asp Ser Ser Lys Thr Gln Val

65 70 75 80

Val Leu Thr Met Thr Asn Val Asp Pro Val Asp Thr Ala Thr Tyr Tyr

85 90 95

Cys Ala Arg Ile Val Gly Tyr Gly Ser Gly Trp Tyr Gly Phe Phe Asp

100 105 110

Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser

115 120

<210> 64

<211> 107

<212> PRT

<213> 人工序列

<220>

<223> FLT3_ A8-scFc VL

<400> 64

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly

1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Arg Asn Asp

20 25 30

Leu Gly Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Leu Ile

35 40 45

Tyr Ala Ala Ser Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly

50	55	60																	
Ser	Gly	Ser	Gly	Thr	Glu	Phe	Thr	Leu	Thr	Ile	Ser	Ser	Leu	Gln	Pro				
65					70					75					80				
Glu	Asp	Phe	Ala	Thr	Tyr	Tyr	Cys	Leu	Gln	His	Asn	Ser	Tyr	Pro	Leu				
				85					90						95				
Thr	Phe	Gly	Cys	Gly	Thr	Lys	Val	Glu	Ile	Lys									
			100					105											
<210>	65																		
<211>	246																		
<212>	PRT																		
<213>	人工序列																		
<220>																			
<223>	FLT3_7 A8xCD3- scFv																		
<400>	65																		
Gln	Val	Thr	Leu	Lys	Glu	Ser	Gly	Pro	Thr	Leu	Val	Lys	Pro	Thr	Glu				
1				5					10					15					
Thr	Leu	Thr	Leu	Thr	Cys	Thr	Leu	Ser	Gly	Phe	Ser	Leu	Asn	Asn	Ala				
				20					25					30					
Arg	Met	Gly	Val	Ser	Trp	Ile	Arg	Gln	Pro	Pro	Gly	Lys	Cys	Leu	Glu				
				35				40					45						
Trp	Leu	Ala	His	Ile	Phe	Ser	Asn	Asp	Glu	Lys	Ser	Tyr	Ser	Thr	Ser				
				50				55					60						
Leu	Lys	Asn	Arg	Leu	Thr	Ile	Ser	Lys	Asp	Ser	Ser	Lys	Thr	Gln	Val				
65					70					75					80				
Val	Leu	Thr	Met	Thr	Asn	Val	Asp	Pro	Val	Asp	Thr	Ala	Thr	Tyr	Tyr				
				85					90						95				
Cys	Ala	Arg	Ile	Val	Gly	Tyr	Gly	Ser	Gly	Trp	Tyr	Gly	Phe	Phe	Asp				
				100					105					110					
Tyr	Trp	Gly	Gln	Gly	Thr	Leu	Val	Thr	Val	Ser	Ser	Gly	Gly	Gly	Gly				
				115					120					125					
Ser	Gly	Gly	Gly	Gly	Ser	Gly	Gly	Gly	Gly	Ser	Asp	Ile	Gln	Met	Thr				
				130					135					140					
Gln	Ser	Pro	Ser	Ser	Leu	Ser	Ala	Ser	Val	Gly	Asp	Arg	Val	Thr	Ile				
145					150					155					160				
Thr	Cys	Arg	Ala	Ser	Gln	Gly	Ile	Arg	Asn	Asp	Leu	Gly	Trp	Tyr	Gln				
				165						170					175				
Gln	Lys	Pro	Gly	Lys	Ala	Pro	Lys	Arg	Leu	Ile	Tyr	Ala	Ala	Ser	Thr				
				180						185					190				
Leu	Gln	Ser	Gly	Val	Pro	Ser	Arg	Phe	Ser	Gly	Ser	Gly	Ser	Gly	Thr				

195	200	205
Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr		
210	215	220
Tyr Tyr Cys Leu Gln His Asn Ser Tyr Pro Leu Thr Phe Gly Cys Gly		
225	230	235
Thr Lys Val Glu Ile Lys		240
	245	
<210> 66		
<211> 501		
<212> PRT		
<213> 人工序列		
<220>		
<223> FLT3_7 A8xCD3双特异性分子		
<400> 66		
Gln Val Thr Leu Lys Glu Ser Gly Pro Thr Leu Val Lys Pro Thr Glu		
1	5	10
Thr Leu Thr Leu Thr Cys Thr Leu Ser Gly Phe Ser Leu Asn Asn Ala		
	20	25
Arg Met Gly Val Ser Trp Ile Arg Gln Pro Pro Gly Lys Cys Leu Glu		30
	35	40
Trp Leu Ala His Ile Phe Ser Asn Asp Glu Lys Ser Tyr Ser Thr Ser		45
50	55	60
Leu Lys Asn Arg Leu Thr Ile Ser Lys Asp Ser Ser Lys Thr Gln Val		
65	70	75
Val Leu Thr Met Thr Asn Val Asp Pro Val Asp Thr Ala Thr Tyr Tyr		
	85	90
Cys Ala Arg Ile Val Gly Tyr Gly Ser Gly Trp Tyr Gly Phe Phe Asp		95
	100	105
Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly		110
	115	120
Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Gln Met Thr		125
130	135	140
Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile		
145	150	155
Thr Cys Arg Ala Ser Gln Gly Ile Arg Asn Asp Leu Gly Trp Tyr Gln		
	165	170
Gln Lys Pro Gly Lys Ala Pro Lys Arg Leu Ile Tyr Ala Ala Ser Thr		175
	180	185
Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr		190

195	200	205
Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr		
210	215	220
Tyr Tyr Cys Leu Gln His Asn Ser Tyr Pro Leu Thr Phe Gly Cys Gly		
225	230	235
Thr Lys Val Glu Ile Lys Ser Gly Gly Gly Ser Glu Val Gln Leu		
245	250	255
Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Lys Leu		
260	265	270
Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Lys Tyr Ala Met Asn Trp		
275	280	285
Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Arg Ile Arg		
290	295	300
Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp Ser Val Lys Asp		
305	310	315
Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr Ala Tyr Leu Gln		
325	330	335
Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr Tyr Cys Val Arg		
340	345	350
His Gly Asn Phe Gly Asn Ser Tyr Ile Ser Tyr Trp Ala Tyr Trp Gly		
355	360	365
Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Ser Gly Gly		
370	375	380
Gly Gly Ser Gly Gly Gly Gly Ser Gln Thr Val Val Thr Gln Glu Pro		
385	390	395
Ser Leu Thr Val Ser Pro Gly Gly Thr Val Thr Leu Thr Cys Gly Ser		
405	410	415
Ser Thr Gly Ala Val Thr Ser Gly Asn Tyr Pro Asn Trp Val Gln Gln		
420	425	430
Lys Pro Gly Gln Ala Pro Arg Gly Leu Ile Gly Gly Thr Lys Phe Leu		
435	440	445
Ala Pro Gly Thr Pro Ala Arg Phe Ser Gly Ser Leu Leu Gly Gly Lys		
450	455	460
Ala Ala Leu Thr Leu Ser Gly Val Gln Pro Glu Asp Glu Ala Glu Tyr		
465	470	475
Tyr Cys Val Leu Trp Tyr Ser Asn Arg Trp Val Phe Gly Gly Gly Thr		
485	490	495
Lys Leu Thr Val Leu		
500		

<210> 67

<211> 989

<212> PRT

<213> 人工序列

<220>

<223> FLT3_7 A8xCD3-scFc双特异性HLE分子

<400> 67

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

Val	Glu	Ser	Gly	Gly	Gly	Leu	Val	Gln	Pro	Gly	Gly	Ser	Leu	Lys	Leu			
			260					265					270					
Ser	Cys	Ala	Ala	Ser	Gly	Phe	Thr	Phe	Asn	Lys	Tyr	Ala	Met	Asn	Trp			
			275					280					285					
Val	Arg	Gln	Ala	Pro	Gly	Lys	Gly	Leu	Glu	Trp	Val	Ala	Arg	Ile	Arg			
			290					295					300					
Ser	Lys	Tyr	Asn	Asn	Tyr	Ala	Thr	Tyr	Tyr	Ala	Asp	Ser	Val	Lys	Asp			
305						310					315				320			
Arg	Phe	Thr	Ile	Ser	Arg	Asp	Asp	Ser	Lys	Asn	Thr	Ala	Tyr	Leu	Gln			
						325				330					335			
Met	Asn	Asn	Leu	Lys	Thr	Glu	Asp	Thr	Ala	Val	Tyr	Tyr	Cys	Val	Arg			
						340				345					350			
His	Gly	Asn	Phe	Gly	Asn	Ser	Tyr	Ile	Ser	Tyr	Trp	Ala	Tyr	Trp	Gly			
			355					360							365			
Gln	Gly	Thr	Leu	Val	Thr	Val	Ser	Ser	Gly	Gly	Gly	Gly	Ser	Gly	Gly			
			370					375							380			
Gly	Gly	Ser	Gly	Gly	Gly	Gly	Ser	Gln	Thr	Val	Val	Thr	Gln	Glu	Pro			
385						390						395			400			
Ser	Leu	Thr	Val	Ser	Pro	Gly	Gly	Thr	Val	Thr	Leu	Thr	Cys	Gly	Ser			
						405									415			
Ser	Thr	Gly	Ala	Val	Thr	Ser	Gly	Asn	Tyr	Pro	Asn	Trp	Val	Gln	Gln			
			420					425							430			
Lys	Pro	Gly	Gln	Ala	Pro	Arg	Gly	Leu	Ile	Gly	Gly	Thr	Lys	Phe	Leu			
			435					440							445			
Ala	Pro	Gly	Thr	Pro	Ala	Arg	Phe	Ser	Gly	Ser	Leu	Leu	Gly	Gly	Lys			
			450					455							460			
Ala	Ala	Leu	Thr	Leu	Ser	Gly	Val	Gln	Pro	Glu	Asp	Glu	Ala	Glu	Tyr			
465						470									480			
Tyr	Cys	Val	Leu	Trp	Tyr	Ser	Asn	Arg	Trp	Val	Phe	Gly	Gly	Gly	Thr			
						485									495			
Lys	Leu	Thr	Val	Leu	Gly	Gly	Gly	Gly	Asp	Lys	Thr	His	Thr	Cys	Pro			
			500					505							510			
Pro	Cys	Pro	Ala	Pro	Glu	Leu	Leu	Gly	Gly	Pro	Ser	Val	Phe	Leu	Phe			
			515					520							525			
Pro	Pro	Lys	Pro	Lys	Asp	Thr	Leu	Met	Ile	Ser	Arg	Thr	Pro	Glu	Val			
			530					535							540			
Thr	Cys	Val	Val	Val	Asp	Val	Ser	His	Glu	Asp	Pro	Glu	Val	Lys	Phe			
545						550									560			
Asn	Trp	Tyr	Val	Asp	Gly	Val	Glu	Val	His	Asn	Ala	Lys	Thr	Lys	Pro			

					565					570					575		
Cys	Glu	Glu	Gln	Tyr	Gly	Ser	Thr	Tyr	Arg	Cys	Val	Ser	Val	Leu	Thr		
					580					585					590		
Val	Leu	His	Gln	Asp	Trp	Leu	Asn	Gly	Lys	Glu	Tyr	Lys	Cys	Lys	Val		
					595					600					605		
Ser	Asn	Lys	Ala	Leu	Pro	Ala	Pro	Ile	Glu	Lys	Thr	Ile	Ser	Lys	Ala		
					610					615					620		
Lys	Gly	Gln	Pro	Arg	Glu	Pro	Gln	Val	Tyr	Thr	Leu	Pro	Pro	Ser	Arg		
625										630					635		
Glu	Glu	Met	Thr	Lys	Asn	Gln	Val	Ser	Leu	Thr	Cys	Leu	Val	Lys	Gly		
					645					650					655		
Phe	Tyr	Pro	Ser	Asp	Ile	Ala	Val	Glu	Trp	Glu	Ser	Asn	Gly	Gln	Pro		
					660					665					670		
Glu	Asn	Asn	Tyr	Lys	Thr	Thr	Pro	Pro	Val	Leu	Asp	Ser	Asp	Gly	Ser		
					675					680					685		
Phe	Phe	Leu	Tyr	Ser	Lys	Leu	Thr	Val	Asp	Lys	Ser	Arg	Trp	Gln	Gln		
					690					695					700		
Gly	Asn	Val	Phe	Ser	Cys	Ser	Val	Met	His	Glu	Ala	Leu	His	Asn	His		
705										710					715		
Tyr	Thr	Gln	Lys	Ser	Leu	Ser	Leu	Ser	Pro	Gly	Lys	Gly	Gly	Gly	Gly		
					725					730					735		
Ser	Gly	Gly	Gly	Gly	Ser	Gly	Gly	Gly	Gly	Ser	Gly	Gly	Gly	Gly	Ser		
					740					745					750		
Gly	Gly	Gly	Gly	Ser	Gly	Gly	Gly	Gly	Ser	Asp	Lys	Thr	His	Thr	Cys		
					755					760					765		
Pro	Pro	Cys	Pro	Ala	Pro	Glu	Leu	Leu	Gly	Gly	Pro	Ser	Val	Phe	Leu		
					770					775					780		
Phe	Pro	Pro	Lys	Pro	Lys	Asp	Thr	Leu	Met	Ile	Ser	Arg	Thr	Pro	Glu		
785										790					795		
Val	Thr	Cys	Val	Val	Val	Asp	Val	Ser	His	Glu	Asp	Pro	Glu	Val	Lys		
					805					810					815		
Phe	Asn	Trp	Tyr	Val	Asp	Gly	Val	Glu	Val	His	Asn	Ala	Lys	Thr	Lys		
					820					825					830		
Pro	Cys	Glu	Glu	Gln	Tyr	Gly	Ser	Thr	Tyr	Arg	Cys	Val	Ser	Val	Leu		
					835					840					845		
Thr	Val	Leu	His	Gln	Asp	Trp	Leu	Asn	Gly	Lys	Glu	Tyr	Lys	Cys	Lys		
					850					855					860		
Val	Ser	Asn	Lys	Ala	Leu	Pro	Ala	Pro	Ile	Glu	Lys	Thr	Ile	Ser	Lys		
865										870					875		
																	880

Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser
885 890 895
Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys
900 905 910
Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln
915 920 925
Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly
930 935 940
Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln
945 950 955 960
Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
965 970 975
His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
980 985

<210> 68

<211> 5

<212> PRT

<213> 人工序列

<220>

<223> VH CDR1 DLL3_1_CC_delGK

<400> 68

Ser Tyr Tyr Trp Ser

1 5

<210> 69

<211> 16

<212> PRT

<213> 人工序列

<220>

<223> VH CDR2 DLL3_1_CC_delGK

<400> 69

Tyr Val Tyr Tyr Ser Gly Thr Thr Asn Tyr Asn Pro Ser Leu Lys Ser

1 5 10 15

<210> 70

<211> 10

<212> PRT

<213> 人工序列

<220>

<223> VH CDR3 DLL3_1_CC_delGK

<400> 70

Ile Ala Val Thr Gly Phe Tyr Phe Asp Tyr

1 5 10

<210> 71

<211> 12

<212> PRT

<213> 人工序列

<220>

<223> VL CDR1 DLL3_1_CC_delGK

<400> 71

Arg Ala Ser Gln Arg Val Asn Asn Asn Tyr Leu Ala

1 5 10

<210> 72

<211> 7

<212> PRT

<213> 人工序列

<220>

<223> VL CDR2 DLL3_1_CC_delGK

<400> 72

Gly Ala Ser Ser Arg Ala Thr

1 5

<210> 73

<211> 9

<212> PRT

<213> 人工序列

<220>

<223> VL CDR3 DLL3_1_CC_delGK

<400> 73

Gln Gln Tyr Asp Arg Ser Pro Leu Thr

1 5

<210> 74

<211> 118

<212> PRT

<213> 人工序列

<220>

<223> VH DLL3_1_CC_delGK

<400> 74

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu

1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Tyr

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

<210> 75

<211> 108

<212> PRT

<213> 人工序列

<220>

<223> VL DLL3_1_CC_delGK

<400> 75

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

<210> 76

<211> 241

<212> PRT

<213> 人工序列

<220>

<223> DLL3_1_CC_delGK

<400> 76

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

Lys

<210> 77

<211> 496

<212> PRT

<213> 人工序列

<220>

<223> DLL3_1_CCxCD3_delGK双特异性分子

<400> 77

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

Tyr Ala Thr Tyr Tyr Ala Asp Ser Val Lys Asp Arg Phe Thr Ile Ser
 305 310 315 320
 Arg Asp Asp Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn Asn Leu Lys
 325 330 335
 Thr Glu Asp Thr Ala Val Tyr Tyr Cys Val Arg His Gly Asn Phe Gly
 340 345 350
 Asn Ser Tyr Ile Ser Tyr Trp Ala Tyr Trp Gly Gln Gly Thr Leu Val
 355 360 365
 Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly
 370 375 380
 Gly Gly Ser Gln Thr Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser
 385 390 395 400
 Pro Gly Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val
 405 410 415
 Thr Ser Gly Asn Tyr Pro Asn Trp Val Gln Gln Lys Pro Gly Gln Ala
 420 425 430
 Pro Arg Gly Leu Ile Gly Gly Thr Lys Phe Leu Ala Pro Gly Thr Pro
 435 440 445
 Ala Arg Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Leu
 450 455 460
 Ser Gly Val Gln Pro Glu Asp Glu Ala Glu Tyr Tyr Cys Val Leu Trp
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 Tyr Ser Asn Arg Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
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 Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Tyr
 20 25 30
 Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Cys Leu Glu Trp Ile
 35 40 45
 Gly Tyr Val Tyr Tyr Ser Gly Thr Thr Asn Tyr Asn Pro Ser Leu Lys
 50 55 60

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

370	375	380
Gly Gly Ser Gln Thr Val	Val Thr Gln Glu Pro	Ser Leu Thr Val Ser
385	390	395
Pro Gly Gly Thr Val Thr	Leu Thr Cys Gly Ser	Ser Thr Gly Ala Val
405	410	415
Thr Ser Gly Asn Tyr Pro	Asn Trp Val Gln Gln Lys	Pro Gly Gln Ala
420	425	430
Pro Arg Gly Leu Ile Gly	Gly Thr Lys Phe Leu Ala	Pro Gly Thr Pro
435	440	445
Ala Arg Phe Ser Gly Ser	Leu Leu Gly Gly Lys Ala	Ala Leu Thr Leu
450	455	460
Ser Gly Val Gln Pro Glu	Asp Glu Ala Glu Tyr Tyr	Cys Val Leu Trp
465	470	475
Tyr Ser Asn Arg Trp Val	Phe Gly Gly Gly Thr Lys	Leu Thr Val Leu
485	490	495
Gly Gly Gly Gly Asp Lys	Thr His Thr Cys Pro Pro	Cys Pro Ala Pro
500	505	510
Glu Leu Leu Gly Gly Pro	Ser Val Phe Leu Phe Pro	Pro Lys Pro Lys
515	520	525
Asp Thr Leu Met Ile Ser	Arg Thr Pro Glu Val Thr	Cys Val Val Val
530	535	540
Asp Val Ser His Glu Asp	Pro Glu Val Lys Phe Asn	Trp Tyr Val Asp
545	550	555
Gly Val Glu Val His Asn	Ala Lys Thr Lys Pro Cys	Glu Glu Gln Tyr
565	570	575
Gly Ser Thr Tyr Arg Cys	Val Ser Val Leu Thr Val	Leu His Gln Asp
580	585	590
Trp Leu Asn Gly Lys Glu	Tyr Lys Cys Lys Val Ser	Asn Lys Ala Leu
595	600	605
Pro Ala Pro Ile Glu Lys	Thr Ile Ser Lys Ala Lys	Gly Gln Pro Arg
610	615	620
Glu Pro Gln Val Tyr Thr	Leu Pro Pro Ser Arg Glu	Glu Glu Met Thr Lys
625	630	635
Asn Gln Val Ser Leu Thr	Cys Leu Val Lys Gly Phe	Tyr Pro Ser Asp
645	650	655
Ile Ala Val Glu Trp Glu	Ser Asn Gly Gln Pro Glu	Asn Asn Tyr Lys
660	665	670
Thr Thr Pro Pro Val Leu	Asp Ser Asp Gly Ser Phe	Phe Leu Tyr Ser
675	680	685

Lys	Leu	Thr	Val	Asp	Lys	Ser	Arg	Trp	Gln	Gln	Gly	Asn	Val	Phe	Ser
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Cys	Ser	Val	Met	His	Glu	Ala	Leu	His	Asn	His	Tyr	Thr	Gln	Lys	Ser
705															
Leu	Ser	Leu	Ser	Pro	Gly	Gly	Gly	Gly	Ser	Gly	Gly	Gly	Gly	Ser	Gly
Gly	Gly	Gly	Ser	Gly	Gly	Gly	Gly	Ser	Gly	Gly	Gly	Gly	Ser	Gly	Gly
Gly	Gly	Ser	Asp	Lys	Thr	His	Thr	Cys	Pro	Pro	Cys	Pro	Ala	Pro	Glu
Leu	Leu	Gly	Gly	Pro	Ser	Val	Phe	Leu	Phe	Pro	Pro	Lys	Pro	Lys	Asp
Thr	Leu	Met	Ile	Ser	Arg	Thr	Pro	Glu	Val	Thr	Cys	Val	Val	Val	Asp
Val	Ser	His	Glu	Asp	Pro	Glu	Val	Lys	Phe	Asn	Trp	Tyr	Val	Asp	Gly
Val	Glu	Val	His	Asn	Ala	Lys	Thr	Lys	Pro	Cys	Glu	Glu	Gln	Tyr	Gly
Ser	Thr	Tyr	Arg	Cys	Val	Ser	Val	Leu	Thr	Val	Leu	His	Gln	Asp	Trp
Leu	Asn	Gly	Lys	Glu	Tyr	Lys	Cys	Lys	Val	Ser	Asn	Lys	Ala	Leu	Pro
Ala	Pro	Ile	Glu	Lys	Thr	Ile	Ser	Lys	Ala	Lys	Gly	Gln	Pro	Arg	Glu
Pro	Gln	Val	Tyr	Thr	Leu	Pro	Pro	Ser	Arg	Glu	Glu	Met	Thr	Lys	Asn
Gln	Val	Ser	Leu	Thr	Cys	Leu	Val	Lys	Gly	Phe	Tyr	Pro	Ser	Asp	Ile
Ala	Val	Glu	Trp	Glu	Ser	Asn	Gly	Gln	Pro	Glu	Asn	Asn	Tyr	Lys	Thr
Thr	Pro	Pro	Val	Leu	Asp	Ser	Asp	Gly	Ser	Phe	Phe	Leu	Tyr	Ser	Lys
Leu	Thr	Val	Asp	Lys	Ser	Arg	Trp	Gln	Gln	Gly	Asn	Val	Phe	Ser	Cys
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Gly
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Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30
Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Cys Leu Glu Trp Val

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

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Leu Gly Ser Asn Arg Ala Ser
1 5

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

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

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

				405					410					415			
Gln	Thr	Val	Val	Thr	Gln	Glu	Pro	Ser	Leu	Thr	Val	Ser	Pro	Gly	Gly		
				420					425					430			
Thr	Val	Thr	Leu	Thr	Cys	Gly	Ser	Ser	Thr	Gly	Ala	Val	Thr	Ser	Gly		
				435					440					445			
Asn	Tyr	Pro	Asn	Trp	Val	Gln	Gln	Lys	Pro	Gly	Gln	Ala	Pro	Arg	Gly		
				450					455					460			
Leu	Ile	Gly	Gly	Thr	Lys	Phe	Leu	Ala	Pro	Gly	Thr	Pro	Ala	Arg	Phe		
465									470					475			480
Ser	Gly	Ser	Leu	Leu	Gly	Gly	Lys	Ala	Ala	Leu	Thr	Leu	Ser	Gly	Val		
				485					490					495			
Gln	Pro	Glu	Asp	Glu	Ala	Glu	Tyr	Tyr	Cys	Val	Leu	Trp	Tyr	Ser	Asn		
				500					505					510			
Arg	Trp	Val	Phe	Gly	Gly	Gly	Thr	Lys	Leu	Thr	Val	Leu					
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Leu	Arg	Gly	Ala	Arg	Cys	Asp	Ile	Val	Met	Thr	Gln	Ser	Pro	Leu	Ser		
				20					25					30			
Leu	Pro	Val	Ile	Ser	Gly	Glu	Pro	Ala	Ser	Ile	Ser	Cys	Arg	Ser	Ser		
				35					40					45			
Gln	Ser	Leu	Leu	His	Lys	Asn	Ala	Phe	Asn	Tyr	Leu	Asp	Trp	Tyr	Leu		
				50					55					60			
Gln	Lys	Pro	Gly	Gln	Ser	Pro	Gln	Leu	Leu	Ile	Tyr	Leu	Gly	Ser	Asn		
65									70					75			80
Arg	Ala	Ser	Gly	Val	Pro	Asp	Arg	Phe	Ser	Gly	Ser	Gly	Ser	Gly	Thr		
				85					90					95			
Asp	Phe	Thr	Leu	Lys	Ile	Ser	Arg	Val	Glu	Ala	Glu	Asp	Val	Gly	Val		
				100					105					110			
Tyr	Tyr	Cys	Met	Gln	Ala	Leu	Gln	Thr	Pro	Phe	Thr	Phe	Gly	Cys	Gly		
				115					120					125			
Thr	Lys	Val	Asp	Ile	Lys	Gly	Gly	Gly	Gly	Ser	Gly	Gly	Gly	Gly	Ser		

130	135	140
Gly Gly Gly Gly Ser Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val		
145	150	155
Val Gln Pro Gly Arg Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe		
165	170	175
Thr Phe Ser Ser Tyr Gly Met His Trp Val Arg Gln Ala Pro Gly Lys		
180	185	190
Cys Leu Glu Trp Val Ala Val Ile Ser Tyr Glu Gly Ser Asn Lys Tyr		
195	200	205
Tyr Ala Glu Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser		
210	215	220
Lys Asn Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Asp Glu Asp Thr		
225	230	235
Ala Val Tyr Tyr Cys Ala Arg Asp Arg Gly Thr Ile Phe Gly Asn Tyr		
245	250	255
Gly Leu Glu Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly		
260	265	270
Gly Gly Gly Ser Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val		
275	280	285
Gln Pro Gly Gly Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr		
290	295	300
Phe Asn Lys Tyr Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly		
305	310	315
Leu Glu Trp Val Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr		
325	330	335
Tyr Tyr Ala Asp Ser Val Lys Asp Arg Phe Thr Ile Ser Arg Asp Asp		
340	345	350
Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu Asp		
355	360	365
Thr Ala Val Tyr Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr		
370	375	380
Ile Ser Tyr Trp Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser		
385	390	395
Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser		
405	410	415
Gln Thr Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly		
420	425	430
Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Ser Gly		
435	440	445

Asn Tyr Pro Asn Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly			
450	455	460	
Leu Ile Gly Gly Thr Lys Phe Leu Ala Pro Gly Thr Pro Ala Arg Phe			
465	470	475	480
Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val			
	485	490	495
Gln Pro Glu Asp Glu Ala Glu Tyr Tyr Cys Val Leu Trp Tyr Ser Asn			
	500	505	510
Arg Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Gly Gly			
	515	520	525
Gly Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu			
	530	535	540
Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu			
545	550	555	560
Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser			
	565	570	575
His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu			
	580	585	590
Val His Asn Ala Lys Thr Lys Pro Cys Glu Glu Gln Tyr Gly Ser Thr			
	595	600	605
Tyr Arg Cys Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn			
610	615	620	
Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro			
625	630	635	640
Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln			
	645	650	655
Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val			
	660	665	670
Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val			
	675	680	685
Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro			
690	695	700	
Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr			
705	710	715	720
Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val			
	725	730	735
Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu			
	740	745	750
Ser Pro Gly Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly			

755	760	765
Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly		
770	775	780
Gly Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu		
785	790	795
Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr		
805	810	815
Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val		
820	825	830
Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val		
835	840	845
Glu Val His Asn Ala Lys Thr Lys Pro Cys Glu Glu Gln Tyr Gly Ser		
850	855	860
Thr Tyr Arg Cys Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu		
865	870	875
Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala		
885	890	895
Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro		
900	905	910
Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln		
915	920	925
Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala		
930	935	940
Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr		
945	950	955
Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu		
965	970	975
Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser		
980	985	990
Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser		
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Leu Ser Pro Gly Lys

1010

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Ser Tyr Pro Ile Asn

1 5

<210> 90

<211> 16

<212> PRT

<213> 人工序列

<220>

<223> VH CDR2 CDH3 G8A 6-B12

<400> 90

Val Ile Trp Thr Gly Gly Gly Thr Asn Tyr Ala Ser Ser Val Lys Gly

1 5 10 15

<210> 91

<211> 15

<212> PRT

<213> 人工序列

<220>

<223> VH CDR3 CDH3 G8A 6-B12

<400> 91

Ser Arg Gly Val Tyr Asp Phe Asp Gly Arg Gly Ala Met Asp Tyr

1 5 10 15

<210> 92

<211> 17

<212> PRT

<213> 人工序列

<220>

<223> VL CDR1 CDH3 G8A 6-B12

<400> 92

Lys Ser Ser Gln Ser Leu Leu Tyr Ser Ser Asn Gln Lys Asn Tyr Phe

1 5 10 15

Ala

<210> 93

<211> 7

<212> PRT

<213> 人工序列

<220>

<223> VL CDR2 CDH3 G8A 6-B12

<400> 93

Trp Ala Ser Thr Arg Glu Ser

1 5
 <210> 94
 <211> 9
 <212> PRT
 <213> 人工序列
 <220>
 <223> VL CDR3 CDH3 G8A 6-B12
 <400> 94
 Gln Gln Tyr Tyr Ser Tyr Pro Tyr Thr
 1 5
 <210> 95
 <211> 123
 <212> PRT
 <213> 人工序列
 <220>
 <223> VH CDH3 G8A 6-B12
 <400> 95
 Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
 1 5 10 15
 Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Ser Phe Ser Ser Tyr
 20 25 30
 Pro Ile Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
 35 40 45
 Gly Val Ile Trp Thr Gly Gly Gly Thr Asn Tyr Ala Ser Ser Val Lys
 50 55 60
 Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Val Tyr Leu
 65 70 75 80
 Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala
 85 90 95
 Lys Ser Arg Gly Val Tyr Asp Phe Asp Gly Arg Gly Ala Met Asp Tyr
 100 105 110
 Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
 115 120
 <210> 96
 <211> 113
 <212> PRT
 <213> 人工序列
 <220>
 <223> VL CDH3 G8A 6-B12

<400> 96

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

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Lys

<210> 97

<211> 251

<212> PRT

<213> 人工序列

<220>

<223> CDH3 G8A 6-B12 scFv

<400> 97

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

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Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Val Met Thr Gln
 130 135 140
 Ser Pro Asp Ser Leu Ala Val Ser Leu Gly Glu Arg Ala Thr Ile Asn
 145 150 155 160
 Cys Lys Ser Ser Gln Ser Leu Leu Tyr Ser Ser Asn Gln Lys Asn Tyr
 165 170 175
 Phe Ala Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu Leu Ile
 180 185 190
 Tyr Trp Ala Ser Thr Arg Glu Ser Gly Val Pro Asp Arg Phe Ser Gly
 195 200 205
 Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Ala
 210 215 220
 Glu Asp Val Ala Val Tyr Tyr Cys Gln Gln Tyr Tyr Ser Tyr Pro Tyr
 225 230 235 240
 Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
 245 250

<210> 98

<211> 506

<212> PRT

<213> 人工序列

<220>

<223> CDH3 G8A 6-B12 x I2C0双特异性分子

<400> 98

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

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

435	440	445
Gly Thr Lys Phe Leu Ala Pro	Gly Thr Pro Ala Arg Phe Ser Gly Ser	
450	455	460
Leu Leu Gly Gly Lys Ala Ala	Leu Thr Leu Ser Gly Val Gln Pro Glu	
465	470	475
Asp Glu Ala Glu Tyr Tyr Cys	Val Leu Trp Tyr Ser Asn Arg Trp Val	
485	490	495
Phe Gly Gly Gly Thr Lys Leu	Thr Val Leu	
500	505	
<210> 99		
<211> 994		
<212> PRT		
<213> 人工序列		
<220>		
<223> CDH3 G8A 6-B12 x I2C0双特异性分子HLE		
<400> 99		
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly		
1	5	10
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Ser Phe Ser Ser Tyr		
20	25	30
Pro Ile Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val		
35	40	45
Gly Val Ile Trp Thr Gly Gly Gly Thr Asn Tyr Ala Ser Ser Val Lys		
50	55	60
Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Val Tyr Leu		
65	70	75
Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala		
85	90	95
Lys Ser Arg Gly Val Tyr Asp Phe Asp Gly Arg Gly Ala Met Asp Tyr		
100	105	110
Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser		
115	120	125
Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Val Met Thr Gln		
130	135	140
Ser Pro Asp Ser Leu Ala Val Ser Leu Gly Glu Arg Ala Thr Ile Asn		
145	150	155
Cys Lys Ser Ser Gln Ser Leu Leu Tyr Ser Ser Asn Gln Lys Asn Tyr		
165	170	175
Phe Ala Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu Leu Ile		

	180		185		190
Tyr Trp Ala Ser Thr Arg Glu Ser Gly Val Pro Asp Arg Phe Ser Gly					
195		200		205	
Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Ala					
210		215		220	
Glu Asp Val Ala Val Tyr Tyr Cys Gln Gln Tyr Tyr Ser Tyr Pro Tyr					
225		230		235	240
Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Ser Gly Gly Gly Gly					
245		250		255	
Ser Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly					
260		265		270	
Gly Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Lys					
275		280		285	
Tyr Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp					
290		295		300	
Val Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala					
305		310		315	320
Asp Ser Val Lys Asp Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn					
325		330		335	
Thr Ala Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val					
340		345		350	
Tyr Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Ile Ser Tyr					
355		360		365	
Trp Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly					
370		375		380	
Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Thr Val					
385		390		395	400
Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly Thr Val Thr					
405		410		415	
Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Ser Gly Asn Tyr Pro					
420		425		430	
Asn Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly Leu Ile Gly					
435		440		445	
Gly Thr Lys Phe Leu Ala Pro Gly Thr Pro Ala Arg Phe Ser Gly Ser					
450		455		460	
Leu Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val Gln Pro Glu					
465		470		475	480
Asp Glu Ala Glu Tyr Tyr Cys Val Leu Trp Tyr Ser Asn Arg Trp Val					
485		490		495	

Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Gly Gly Gly Asp Lys		
500	505	510
Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro		
515	520	525
Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser		
530	535	540
Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp		
545	550	555
Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn		
565	570	575
Ala Lys Thr Lys Pro Cys Glu Glu Gln Tyr Gly Ser Thr Tyr Arg Cys		
580	585	590
Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu		
595	600	605
Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys		
610	615	620
Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr		
625	630	635
Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr		
645	650	655
Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu		
660	665	670
Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu		
675	680	685
Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys		
690	695	700
Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu		
705	710	715
Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly		
725	730	735
Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser		
740	745	750
Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp		
755	760	765
Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly		
770	775	780
Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile		
785	790	795
Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu		

805	810	815
Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His		
820	825	830
Asn Ala Lys Thr Lys Pro Cys Glu Glu Gln Tyr Gly Ser Thr Tyr Arg		
835	840	845
Cys Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys		
850	855	860
Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu		
865	870	875
Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr		
885	890	895
Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu		
900	905	910
Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp		
915	920	925
Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val		
930	935	940
Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp		
945	950	955
Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His		
965	970	975
Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro		
980	985	990

Gly Lys

<210> 100

<211> 5

<212> PRT

<213> 人工序列

<220>

<223> BCMA A7 27-C4-G7 CDR1 VH

<400> 100

Asn His Ile Ile His

1

5

<210> 101

<211> 17

<212> PRT

<213> 人工序列

<220>

<223> BCMA A7 27-C4-G7 CDR2 VH

<400> 101

Tyr Ile Asn Pro Tyr Pro Gly Tyr His Ala Tyr Asn Glu Lys Phe Gln

1 5 10 15

Gly

<210> 102

<211> 12

<212> PRT

<213> 人工序列

<220>

<223> BCMA A7 27-C4-G7 CDR3 VH

<400> 102

Asp Gly Tyr Tyr Arg Asp Thr Asp Val Leu Asp Tyr

1 5 10

<210> 103

<211> 11

<212> PRT

<213> 人工序列

<220>

<223> BCMA A7 27-C4-G7 CDR1 VL

<400> 103

Gln Ala Ser Gln Asp Ile Ser Asn Tyr Leu Asn

1 5 10

<210> 104

<211> 7

<212> PRT

<213> 人工序列

<220>

<223> BCMA A7 27-C4-G7 CDR2 VL

<400> 104

Tyr Thr Ser Arg Leu His Thr

1 5

<210> 105

<211> 9

<212> PRT

<213> 人工序列

<220>

<223> BCMA A7 27-C4-G7 CDR3 VL

<400> 105

Gln Gln Gly Asn Thr Leu Pro Trp Thr

1 5
 <210> 106
 <211> 121
 <212> PRT
 <213> 人工序列
 <220>
 <223> BCMA A7 27-C4-G7 CC (44/100) VH
 <400> 106
 Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
 1 5 10 15
 Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn His
 20 25 30
 Ile Ile His Trp Val Arg Gln Ala Pro Gly Gln Cys Leu Glu Trp Met
 35 40 45
 Gly Tyr Ile Asn Pro Tyr Pro Gly Tyr His Ala Tyr Asn Glu Lys Phe
 50 55 60
 Gln Gly Arg Ala Thr Met Thr Ser Asp Thr Ser Thr Ser Thr Val Tyr
 65 70 75 80
 Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
 85 90 95
 Ala Arg Asp Gly Tyr Tyr Arg Asp Thr Asp Val Leu Asp Tyr Trp Gly
 100 105 110
 Gln Gly Thr Leu Val Thr Val Ser Ser
 115 120
 <210> 107
 <211> 107
 <212> PRT
 <213> 人工序列
 <220>
 <223> BCMA A7 27-C4-G7 CC (44/100) VL
 <400> 107
 Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
 1 5 10 15
 Asp Arg Val Thr Ile Thr Cys Gln Ala Ser Gln Asp Ile Ser Asn Tyr
 20 25 30
 Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
 35 40 45
 Tyr Tyr Thr Ser Arg Leu His Thr Gly Val Pro Ser Arg Phe Ser Gly
 50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Glu Pro
 65 70 75 80
 Glu Asp Ile Ala Thr Tyr Tyr Cys Gln Gln Gly Asn Thr Leu Pro Trp
 85 90 95
 Thr Phe Gly Cys Gly Thr Lys Leu Glu Ile Lys
 100 105
 <210> 108
 <211> 243
 <212> PRT
 <213> 人工序列
 <220>
 <223> BCMA A7 27-C4-G7 CC (44/100) scFv
 <400> 108
 Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
 1 5 10 15
 Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn His
 20 25 30
 Ile Ile His Trp Val Arg Gln Ala Pro Gly Gln Cys Leu Glu Trp Met
 35 40 45
 Gly Tyr Ile Asn Pro Tyr Pro Gly Tyr His Ala Tyr Asn Glu Lys Phe
 50 55 60
 Gln Gly Arg Ala Thr Met Thr Ser Asp Thr Ser Thr Ser Thr Val Tyr
 65 70 75 80
 Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
 85 90 95
 Ala Arg Asp Gly Tyr Tyr Arg Asp Thr Asp Val Leu Asp Tyr Trp Gly
 100 105 110
 Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly
 115 120 125
 Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Gln Met Thr Gln Ser Pro
 130 135 140
 Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Gln
 145 150 155 160
 Ala Ser Gln Asp Ile Ser Asn Tyr Leu Asn Trp Tyr Gln Gln Lys Pro
 165 170 175
 Gly Lys Ala Pro Lys Leu Leu Ile Tyr Tyr Thr Ser Arg Leu His Thr
 180 185 190
 Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr
 195 200 205

Phe Thr Ile Ser Ser Leu Glu Pro Glu Asp Ile Ala Thr Tyr Tyr Cys
 210 215 220
 Gln Gln Gly Asn Thr Leu Pro Trp Thr Phe Gly Cys Gly Thr Lys Leu
 225 230 235 240
 Glu Ile Lys
 <210> 109
 <211> 498
 <212> PRT
 <213> 人工序列
 <220>
 <223> BCMA A7 27-C4-G7 CC (44/100) x I2C0双特异性分子
 <400> 109
 Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
 1 5 10 15
 Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn His
 20 25 30
 Ile Ile His Trp Val Arg Gln Ala Pro Gly Gln Cys Leu Glu Trp Met
 35 40 45
 Gly Tyr Ile Asn Pro Tyr Pro Gly Tyr His Ala Tyr Asn Glu Lys Phe
 50 55 60
 Gln Gly Arg Ala Thr Met Thr Ser Asp Thr Ser Thr Ser Thr Val Tyr
 65 70 75 80
 Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
 85 90 95
 Ala Arg Asp Gly Tyr Tyr Arg Asp Thr Asp Val Leu Asp Tyr Trp Gly
 100 105 110
 Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly
 115 120 125
 Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Gln Met Thr Gln Ser Pro
 130 135 140
 Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Gln
 145 150 155 160
 Ala Ser Gln Asp Ile Ser Asn Tyr Leu Asn Trp Tyr Gln Gln Lys Pro
 165 170 175
 Gly Lys Ala Pro Lys Leu Leu Ile Tyr Tyr Thr Ser Arg Leu His Thr
 180 185 190
 Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr
 195 200 205
 Phe Thr Ile Ser Ser Leu Glu Pro Glu Asp Ile Ala Thr Tyr Tyr Cys

210	215	220
Gln Gln Gly Asn Thr Leu Pro Trp Thr Phe Gly Cys Gly Thr Lys Leu		
225	230	235
Glu Ile Lys Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Val Glu Ser		240
	245	250
Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Lys Leu Ser Cys Ala		255
	260	265
Ala Ser Gly Phe Thr Phe Asn Lys Tyr Ala Met Asn Trp Val Arg Gln		270
	275	280
Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Arg Ile Arg Ser Lys Tyr		285
290	295	300
Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp Ser Val Lys Asp Arg Phe Thr		
305	310	315
Ile Ser Arg Asp Asp Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn Asn		320
	325	330
Leu Lys Thr Glu Asp Thr Ala Val Tyr Tyr Cys Val Arg His Gly Asn		335
	340	345
Phe Gly Asn Ser Tyr Ile Ser Tyr Trp Ala Tyr Trp Gly Gln Gly Thr		350
355	360	365
Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser		
370	375	380
Gly Gly Gly Gly Ser Gln Thr Val Val Thr Gln Glu Pro Ser Leu Thr		
385	390	395
Val Ser Pro Gly Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly		400
	405	410
Ala Val Thr Ser Gly Asn Tyr Pro Asn Trp Val Gln Gln Lys Pro Gly		415
	420	425
Gln Ala Pro Arg Gly Leu Ile Gly Gly Thr Lys Phe Leu Ala Pro Gly		
435	440	445
Thr Pro Ala Arg Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu		
450	455	460
Thr Leu Ser Gly Val Gln Pro Glu Asp Glu Ala Glu Tyr Tyr Cys Val		
465	470	475
Leu Trp Tyr Ser Asn Arg Trp Val Phe Gly Gly Gly Thr Lys Leu Thr		480
	485	490
		495
Val Leu		
<210> 110		
<211> 986		
<212> PRT		

<213> 人工序列

<220>

<223> BCMA A7 27-C4-G7 CC (44/100) x I2C0-scFc双特异性分子HLE

<400> 110

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

275	280	285
Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Arg Ile Arg Ser Lys Tyr		
290	295	300
Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp Ser Val Lys Asp Arg Phe Thr		
305	310	315
Ile Ser Arg Asp Asp Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn Asn		
325	330	335
Leu Lys Thr Glu Asp Thr Ala Val Tyr Tyr Cys Val Arg His Gly Asn		
340	345	350
Phe Gly Asn Ser Tyr Ile Ser Tyr Trp Ala Tyr Trp Gly Gln Gly Thr		
355	360	365
Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser		
370	375	380
Gly Gly Gly Gly Ser Gln Thr Val Val Thr Gln Glu Pro Ser Leu Thr		
385	390	395
Val Ser Pro Gly Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly		
405	410	415
Ala Val Thr Ser Gly Asn Tyr Pro Asn Trp Val Gln Gln Lys Pro Gly		
420	425	430
Gln Ala Pro Arg Gly Leu Ile Gly Gly Thr Lys Phe Leu Ala Pro Gly		
435	440	445
Thr Pro Ala Arg Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu		
450	455	460
Thr Leu Ser Gly Val Gln Pro Glu Asp Glu Ala Glu Tyr Tyr Cys Val		
465	470	475
Leu Trp Tyr Ser Asn Arg Trp Val Phe Gly Gly Gly Thr Lys Leu Thr		
485	490	495
Val Leu Gly Gly Gly Gly Asp Lys Thr His Thr Cys Pro Pro Cys Pro		
500	505	510
Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys		
515	520	525
Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val		
530	535	540
Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr		
545	550	555
Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Cys Glu Glu		
565	570	575
Gln Tyr Gly Ser Thr Tyr Arg Cys Val Ser Val Leu Thr Val Leu His		
580	585	590

Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys																	
595								600							605		
Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln																	
610								615							620		
Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met																	
625								630							635		640
Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro																	
Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn																	
660																	
Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu																	
675																	
Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val																	
690																	
Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln																	
705																	
Lys Ser Leu Ser Leu Ser Pro Gly Lys Gly Gly Gly Gly Ser Gly Gly																	
Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly																	
740																	
Gly Ser Gly Gly Gly Gly Ser Asp Lys Thr His Thr Cys Pro Pro Cys																	
755																	
Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro																	
770																	
Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys																	
785																	
Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp																	
Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Cys Glu																	
820																	
Glu Gln Tyr Gly Ser Thr Tyr Arg Cys Val Ser Val Leu Thr Val Leu																	
835																	
His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn																	
850																	
Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly																	
865																	
Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu																	
Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr																	

900	905	910
Pro Ser Asp Ile Ala Val Glu Trp	Glu Ser Asn Gly Gln Pro Glu Asn	
915	920	925
Asn Tyr Lys Thr Thr Pro Pro Val Leu	Asp Ser Asp Gly Ser Phe Phe	
930	935	940
Leu Tyr Ser Lys Leu Thr Val Asp Lys	Ser Arg Trp Gln Gln Gly Asn	
945	950	955
Val Phe Ser Cys Ser Val Met His Glu	Ala Leu His Asn His Tyr Thr	
965	970	975
Gln Lys Ser Leu Ser Leu Ser Pro Gly	Lys	

980	985
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<210> 111

<211> 5

<212> PRT

<213> 人工序列

<220>

<223> PM 76-B10.17 CC VH CDR1

<400> 111

Asp Tyr Tyr Met Tyr

1 5

<210> 112

<211> 17

<212> PRT

<213> 人工序列

<220>

<223> PM 76-B10.17 CC VH CDR2

<400> 112

Ile Ile Ser Asp Ala Gly Tyr Tyr Thr Tyr Tyr Ser Asp Ile Ile Lys

1 5 10 15

Gly

<210> 113

<211> 12

<212> PRT

<213> 人工序列

<220>

<223> PM 76-B10.17 CC VH CDR3

<400> 113

Gly Phe Pro Leu Leu Arg His Gly Ala Met Asp Tyr

1 5 10

<210> 114

<211> 11

<212> PRT

<213> 人工序列

<220>

<223> PM 76-B10.17 CC VL CDR1

<400> 114

Lys Ala Ser Gln Asn Val Asp Ala Asn Val Ala

1 5 10

<210> 115

<211> 7

<212> PRT

<213> 人工序列

<220>

<223> PM 76-B10.17 CC VL CDR2

<400> 115

Ser Ala Ser Tyr Val Tyr Trp

1 5

<210> 116

<211> 9

<212> PRT

<213> 人工序列

<220>

<223> PM 76-B10.17 CC VL CDR3

<400> 116

Gln Gln Tyr Asp Gln Gln Leu Ile Thr

1 5

<210> 117

<211> 121

<212> PRT

<213> 人工序列

<220>

<223> PM 76-B10.17 CC VH

<400> 117

Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Glu

1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr

20 25 30

Tyr Met Tyr Trp Val Arg Gln Ala Pro Gly Lys Cys Leu Glu Trp Val

35	40	45
Ala Ile Ile Ser Asp Ala Gly Tyr Tyr Thr Tyr Tyr Ser Asp Ile Ile		
50	55	60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr		
65	70	75
Leu Gln Met Asn Ser Leu Lys Ala Glu Asp Thr Ala Val Tyr Tyr Cys		
85	90	95
Ala Arg Gly Phe Pro Leu Leu Arg His Gly Ala Met Asp Tyr Trp Gly		
100	105	110
Gln Gly Thr Leu Val Thr Val Ser Ser		
115	120	
<210> 118		
<211> 107		
<212> PRT		
<213> 人工序列		
<220>		
<223> PM 76-B10.17 CC VL		
<400> 118		
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly		
1	5	10
Asp Arg Val Thr Ile Thr Cys Lys Ala Ser Gln Asn Val Asp Ala Asn		
20	25	30
Val Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Lys Ser Leu Ile		
35	40	45
Tyr Ser Ala Ser Tyr Val Tyr Trp Asp Val Pro Ser Arg Phe Ser Gly		
50	55	60
Ser Ala Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Val Gln Ser		
65	70	75
Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Asp Gln Gln Leu Ile		
85	90	95
Thr Phe Gly Cys Gly Thr Lys Leu Glu Ile Lys		
100	105	
<210> 119		
<211> 243		
<212> PRT		
<213> 人工序列		
<220>		
<223> PM 76-B10.17 CC scFv		
<400> 119		

Gln	Val	Gln	Leu	Val	Glu	Ser	Gly	Gly	Gly	Leu	Val	Lys	Pro	Gly	Glu
1				5					10					15	
Ser	Leu	Arg	Leu	Ser	Cys	Ala	Ala	Ser	Gly	Phe	Thr	Phe	Ser	Asp	Tyr
			20						25					30	
Tyr	Met	Tyr	Trp	Val	Arg	Gln	Ala	Pro	Gly	Lys	Cys	Leu	Glu	Trp	Val
			35						40					45	
Ala	Ile	Ile	Ser	Asp	Ala	Gly	Tyr	Tyr	Thr	Tyr	Tyr	Ser	Asp	Ile	Ile
			50						55					60	
Lys	Gly	Arg	Phe	Thr	Ile	Ser	Arg	Asp	Asn	Ala	Lys	Asn	Ser	Leu	Tyr
65									70					75	80
Leu	Gln	Met	Asn	Ser	Leu	Lys	Ala	Glu	Asp	Thr	Ala	Val	Tyr	Tyr	Cys
									85					90	95
Ala	Arg	Gly	Phe	Pro	Leu	Leu	Arg	His	Gly	Ala	Met	Asp	Tyr	Trp	Gly
									100					105	110
Gln	Gly	Thr	Leu	Val	Thr	Val	Ser	Ser	Gly	Gly	Gly	Gly	Ser	Gly	Gly
									115					120	125
Gly	Gly	Ser	Gly	Gly	Gly	Gly	Ser	Asp	Ile	Gln	Met	Thr	Gln	Ser	Pro
									130					135	140
Ser	Ser	Leu	Ser	Ala	Ser	Val	Gly	Asp	Arg	Val	Thr	Ile	Thr	Cys	Lys
145									150					155	160
Ala	Ser	Gln	Asn	Val	Asp	Ala	Asn	Val	Ala	Trp	Tyr	Gln	Gln	Lys	Pro
									165					170	175
Gly	Gln	Ala	Pro	Lys	Ser	Leu	Ile	Tyr	Ser	Ala	Ser	Tyr	Val	Tyr	Trp
									180					185	190
Asp	Val	Pro	Ser	Arg	Phe	Ser	Gly	Ser	Ala	Ser	Gly	Thr	Asp	Phe	Thr
									195					200	205
Leu	Thr	Ile	Ser	Ser	Val	Gln	Ser	Glu	Asp	Phe	Ala	Thr	Tyr	Tyr	Cys
									210					215	220
Gln	Gln	Tyr	Asp	Gln	Gln	Leu	Ile	Thr	Phe	Gly	Cys	Gly	Thr	Lys	Leu
225									230					235	240
Glu	Ile	Lys													
<210>	120														
<211>	498														
<212>	PRT														
<213>	人工序列														
<220>															
<223>	PM 76-B10.17 CC x I2C0双特异性分子														
<400>	120														
Gln	Val	Gln	Leu	Val	Glu	Ser	Gly	Gly	Gly	Leu	Val	Lys	Pro	Gly	Glu

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

Ile Ser Arg Asp Asp Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn Asn
 325 330 335
 Leu Lys Thr Glu Asp Thr Ala Val Tyr Tyr Cys Val Arg His Gly Asn
 340 345 350
 Phe Gly Asn Ser Tyr Ile Ser Tyr Trp Ala Tyr Trp Gly Gln Gly Thr
 355 360 365
 Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
 370 375 380
 Gly Gly Gly Gly Ser Gln Thr Val Val Thr Gln Glu Pro Ser Leu Thr
 385 390 395 400
 Val Ser Pro Gly Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly
 405 410 415
 Ala Val Thr Ser Gly Asn Tyr Pro Asn Trp Val Gln Gln Lys Pro Gly
 420 425 430
 Gln Ala Pro Arg Gly Leu Ile Gly Gly Thr Lys Phe Leu Ala Pro Gly
 435 440 445
 Thr Pro Ala Arg Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu
 450 455 460
 Thr Leu Ser Gly Val Gln Pro Glu Asp Glu Ala Glu Tyr Tyr Cys Val
 465 470 475 480
 Leu Trp Tyr Ser Asn Arg Trp Val Phe Gly Gly Gly Thr Lys Leu Thr
 485 490 495
 Val Leu
 <210> 121
 <211> 986
 <212> PRT
 <213> 人工序列
 <220>
 <223> PM 76-B10.17 CC x I2C0-scFc双特异性HLE分子
 <400> 121
 Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Glu
 1 5 10 15
 Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr
 20 25 30
 Tyr Met Tyr Trp Val Arg Gln Ala Pro Gly Lys Cys Leu Glu Trp Val
 35 40 45
 Ala Ile Ile Ser Asp Ala Gly Tyr Tyr Thr Tyr Tyr Ser Asp Ile Ile
 50 55 60
 Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr

65	70	75	80
Leu Gln Met Asn Ser	Leu Lys Ala Glu Asp Thr	Ala Val Tyr Tyr Cys	
	85	90	95
Ala Arg Gly Phe Pro	Leu Leu Arg His Gly Ala Met Asp Tyr Trp Gly		
	100	105	110
Gln Gly Thr Leu Val Thr	Val Ser Ser Gly Gly Gly Gly Ser Gly Gly		
	115	120	125
Gly Gly Ser Gly Gly Gly	Gly Ser Asp Ile Gln Met Thr Gln Ser Pro		
	130	135	140
Ser Ser Leu Ser Ala Ser	Val Gly Asp Arg Val Thr Ile Thr Cys Lys		
145	150	155	160
Ala Ser Gln Asn Val Asp	Ala Asn Val Ala Trp Tyr Gln Gln Lys Pro		
	165	170	175
Gly Gln Ala Pro Lys Ser	Leu Ile Tyr Ser Ala Ser Tyr Val Tyr Trp		
	180	185	190
Asp Val Pro Ser Arg Phe	Ser Gly Ser Ala Ser Gly Thr Asp Phe Thr		
	195	200	205
Leu Thr Ile Ser Ser Val	Gln Ser Glu Asp Phe Ala Thr Tyr Tyr Cys		
	210	215	220
Gln Gln Tyr Asp Gln Gln	Leu Ile Thr Phe Gly Cys Gly Thr Lys Leu		
225	230	235	240
Glu Ile Lys Ser Gly Gly	Gly Gly Ser Glu Val Gln Leu Val Glu Ser		
	245	250	255
Gly Gly Gly Leu Val Gln	Pro Gly Gly Ser Leu Lys Leu Ser Cys Ala		
	260	265	270
Ala Ser Gly Phe Thr Phe	Asn Lys Tyr Ala Met Asn Trp Val Arg Gln		
	275	280	285
Ala Pro Gly Lys Gly Leu	Glu Trp Val Ala Arg Ile Arg Ser Lys Tyr		
	290	295	300
Asn Asn Tyr Ala Thr Tyr	Tyr Ala Asp Ser Val Lys Asp Arg Phe Thr		
305	310	315	320
Ile Ser Arg Asp Asp Ser	Lys Asn Thr Ala Tyr Leu Gln Met Asn Asn		
	325	330	335
Leu Lys Thr Glu Asp Thr	Ala Val Tyr Tyr Cys Val Arg His Gly Asn		
	340	345	350
Phe Gly Asn Ser Tyr Ile	Ser Tyr Trp Ala Tyr Trp Gly Gln Gly Thr		
	355	360	365
Leu Val Thr Val Ser Ser	Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser		
	370	375	380

Gly Gly Gly Gly Ser Gln Thr Val Val Thr Gln Glu Pro Ser Leu Thr			
385	390	395	400
Val Ser Pro Gly Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly			
	405	410	415
Ala Val Thr Ser Gly Asn Tyr Pro Asn Trp Val Gln Gln Lys Pro Gly			
	420	425	430
Gln Ala Pro Arg Gly Leu Ile Gly Gly Thr Lys Phe Leu Ala Pro Gly			
	435	440	445
Thr Pro Ala Arg Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu			
	450	455	460
Thr Leu Ser Gly Val Gln Pro Glu Asp Glu Ala Glu Tyr Tyr Cys Val			
465	470	475	480
Leu Trp Tyr Ser Asn Arg Trp Val Phe Gly Gly Gly Thr Lys Leu Thr			
	485	490	495
Val Leu Gly Gly Gly Gly Asp Lys Thr His Thr Cys Pro Pro Cys Pro			
	500	505	510
Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys			
	515	520	525
Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val			
	530	535	540
Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr			
545	550	555	560
Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Cys Glu Glu			
	565	570	575
Gln Tyr Gly Ser Thr Tyr Arg Cys Val Ser Val Leu Thr Val Leu His			
	580	585	590
Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys			
	595	600	605
Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln			
	610	615	620
Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met			
625	630	635	640
Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro			
	645	650	655
Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn			
	660	665	670
Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu			
	675	680	685
Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val			

690	695	700
Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln		
705	710	715
Lys Ser Leu Ser Leu Ser Pro Gly Lys Gly Gly Gly Gly Ser Gly Gly		
725	730	735
Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly		
740	745	750
Gly Ser Gly Gly Gly Gly Ser Asp Lys Thr His Thr Cys Pro Pro Cys		
755	760	765
Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro		
770	775	780
Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys		
785	790	795
Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp		
805	810	815
Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Cys Glu		
820	825	830
Glu Gln Tyr Gly Ser Thr Tyr Arg Cys Val Ser Val Leu Thr Val Leu		
835	840	845
His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn		
850	855	860
Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly		
865	870	875
Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu		
885	890	895
Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr		
900	905	910
Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn		
915	920	925
Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe		
930	935	940
Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn		
945	950	955
Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr		
965	970	975
Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys		
980	985	
<210> 122		
<211> 984		

<212> PRT

<213> 人工序列

<220>

<223> PM 76-B10.17 CC x I2C0-scFc_delGK双特异性HLE分子

<400> 122

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

Ala Ser Gly Phe Thr Phe Asn Lys Tyr Ala Met Asn Trp Val Arg Gln		
275	280	285
Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Arg Ile Arg Ser Lys Tyr		
290	295	300
Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp Ser Val Lys Asp Arg Phe Thr		
305	310	315
Ile Ser Arg Asp Asp Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn Asn		
	325	330
Leu Lys Thr Glu Asp Thr Ala Val Tyr Tyr Cys Val Arg His Gly Asn		
	340	350
Phe Gly Asn Ser Tyr Ile Ser Tyr Trp Ala Tyr Trp Gly Gln Gly Thr		
	355	365
Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser		
	370	380
Gly Gly Gly Gly Ser Gln Thr Val Val Thr Gln Glu Pro Ser Leu Thr		
385	390	400
Val Ser Pro Gly Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly		
	405	415
Ala Val Thr Ser Gly Asn Tyr Pro Asn Trp Val Gln Gln Lys Pro Gly		
	420	430
Gln Ala Pro Arg Gly Leu Ile Gly Gly Thr Lys Phe Leu Ala Pro Gly		
	435	445
Thr Pro Ala Arg Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu		
450	455	460
Thr Leu Ser Gly Val Gln Pro Glu Asp Glu Ala Glu Tyr Tyr Cys Val		
465	470	480
Leu Trp Tyr Ser Asn Arg Trp Val Phe Gly Gly Gly Thr Lys Leu Thr		
	485	495
Val Leu Gly Gly Gly Gly Asp Lys Thr His Thr Cys Pro Pro Cys Pro		
	500	510
Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys		
	515	525
Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val		
	530	540
Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr		
545	550	560
Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Cys Glu Glu		
	565	575
Gln Tyr Gly Ser Thr Tyr Arg Cys Val Ser Val Leu Thr Val Leu His		

580	585	590
Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys		
595	600	605
Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln		
610	615	620
Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met		
625	630	635
Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro		
645	650	655
Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn		
660	665	670
Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu		
675	680	685
Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val		
690	695	700
Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln		
705	710	715
Lys Ser Leu Ser Leu Ser Pro Gly Gly Gly Gly Ser Gly Gly Gly Gly		
725	730	735
Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser		
740	745	750
Gly Gly Gly Gly Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala		
755	760	765
Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro		
770	775	780
Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val		
785	790	795
Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val		
805	810	815
Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Cys Glu Glu Gln		
820	825	830
Tyr Gly Ser Thr Tyr Arg Cys Val Ser Val Leu Thr Val Leu His Gln		
835	840	845
Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala		
850	855	860
Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro		
865	870	875
Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr		
885	890	895

Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser
 900 905 910
 Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr
 915 920 925
 Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr
 930 935 940
 Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe
 945 950 955 960
 Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys
 965 970 975
 Ser Leu Ser Leu Ser Pro Gly Lys
 980

<210> 123

<211> 498

<212> PRT

<213> 人工序列

<220>

<223> PM 76-B10.17 CC x I2C0 CC (103/43) -scFc双特异性分子

<400> 123

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

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

465	470	475	480
Leu Trp Tyr Ser Asn Arg Trp Val Phe Gly Gly Gly Thr Lys Leu Thr			
	485	490	495
Val Leu			
<210> 124			
<211> 986			
<212> PRT			
<213> 人工序列			
<220>			
<223> PM 76-B10.17 CC x I2C0 CC (103/43) -scFc双特异性HLE分子			
<400> 124			
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Glu			
1 5 10 15			
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr			
20 25 30			
Tyr Met Tyr Trp Val Arg Gln Ala Pro Gly Lys Cys Leu Glu Trp Val			
35 40 45			
Ala Ile Ile Ser Asp Ala Gly Tyr Tyr Thr Tyr Tyr Ser Asp Ile Ile			
50 55 60			
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr			
65 70 75 80			
Leu Gln Met Asn Ser Leu Lys Ala Glu Asp Thr Ala Val Tyr Tyr Cys			
85 90 95			
Ala Arg Gly Phe Pro Leu Leu Arg His Gly Ala Met Asp Tyr Trp Gly			
100 105 110			
Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Ser Gly Gly			
115 120 125			
Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Gln Met Thr Gln Ser Pro			
130 135 140			
Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Lys			
145 150 155 160			
Ala Ser Gln Asn Val Asp Ala Asn Val Ala Trp Tyr Gln Gln Lys Pro			
165 170 175			
Gly Gln Ala Pro Lys Ser Leu Ile Tyr Ser Ala Ser Tyr Val Tyr Trp			
180 185 190			
Asp Val Pro Ser Arg Phe Ser Gly Ser Ala Ser Gly Thr Asp Phe Thr			
195 200 205			
Leu Thr Ile Ser Ser Val Gln Ser Glu Asp Phe Ala Thr Tyr Tyr Cys			
210 215 220			

Gln	Gln	Tyr	Asp	Gln	Gln	Leu	Ile	Thr	Phe	Gly	Cys	Gly	Thr	Lys	Leu
225						230				235					240
Glu	Ile	Lys	Ser	Gly	Gly	Gly	Gly	Ser	Glu	Val	Gln	Leu	Val	Glu	Ser
				245						250					255
Gly	Gly	Gly	Leu	Val	Gln	Pro	Gly	Gly	Ser	Leu	Lys	Leu	Ser	Cys	Ala
				260						265					270
Ala	Ser	Gly	Phe	Thr	Phe	Asn	Lys	Tyr	Ala	Met	Asn	Trp	Val	Arg	Gln
				275						280					285
Ala	Pro	Gly	Lys	Gly	Leu	Glu	Trp	Val	Ala	Arg	Ile	Arg	Ser	Lys	Tyr
				290											300
Asn	Asn	Tyr	Ala	Thr	Tyr	Tyr	Ala	Asp	Ser	Val	Lys	Asp	Arg	Phe	Thr
305															320
Ile	Ser	Arg	Asp	Asp	Ser	Lys	Asn	Thr	Ala	Tyr	Leu	Gln	Met	Asn	Asn
				325						330					335
Leu	Lys	Thr	Glu	Asp	Thr	Ala	Val	Tyr	Tyr	Cys	Val	Arg	His	Gly	Asn
				340						345					350
Phe	Gly	Asn	Ser	Tyr	Ile	Ser	Tyr	Trp	Ala	Tyr	Cys	Gly	Gln	Gly	Thr
				355											365
Leu	Val	Thr	Val	Ser	Ser	Gly	Gly	Gly	Gly	Ser	Gly	Gly	Gly	Gly	Ser
				370											380
Gly	Gly	Gly	Gly	Ser	Gln	Thr	Val	Val	Thr	Gln	Glu	Pro	Ser	Leu	Thr
385															400
Val	Ser	Pro	Gly	Gly	Thr	Val	Thr	Leu	Thr	Cys	Gly	Ser	Ser	Thr	Gly
				405											415
Ala	Val	Thr	Ser	Gly	Asn	Tyr	Pro	Asn	Trp	Val	Gln	Gln	Lys	Pro	Gly
				420											430
Gln	Cys	Pro	Arg	Gly	Leu	Ile	Gly	Gly	Thr	Lys	Phe	Leu	Ala	Pro	Gly
				435											445
Thr	Pro	Ala	Arg	Phe	Ser	Gly	Ser	Leu	Leu	Gly	Gly	Lys	Ala	Ala	Leu
				450											460
Thr	Leu	Ser	Gly	Val	Gln	Pro	Glu	Asp	Glu	Ala	Glu	Tyr	Tyr	Cys	Val
465															480
Leu	Trp	Tyr	Ser	Asn	Arg	Trp	Val	Phe	Gly	Gly	Gly	Thr	Lys	Leu	Thr
				485											495
Val	Leu	Gly	Gly	Gly	Gly	Asp	Lys	Thr	His	Thr	Cys	Pro	Pro	Cys	Pro
				500											510
Ala	Pro	Glu	Leu	Leu	Gly	Gly	Pro	Ser	Val	Phe	Leu	Phe	Pro	Pro	Lys
				515											525
Pro	Lys	Asp	Thr	Leu	Met	Ile	Ser	Arg	Thr	Pro	Glu	Val	Thr	Cys	Val

530	535	540
Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr		
545	550	555
Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Cys Glu Glu		560
	565	570
Gln Tyr Gly Ser Thr Tyr Arg Cys Val Ser Val Leu Thr Val Leu His		575
	580	585
Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys		590
	595	600
Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln		605
	610	620
Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met		
625	630	635
Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro		640
	645	650
Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn		655
	660	665
Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu		670
	675	680
Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val		685
	690	700
Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln		
705	710	715
Lys Ser Leu Ser Leu Ser Pro Gly Lys Gly Gly Gly Gly Ser Gly Gly		720
	725	730
Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly		735
	740	745
Gly Ser Gly Gly Gly Gly Ser Asp Lys Thr His Thr Cys Pro Pro Cys		750
	755	760
Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro		765
	770	780
Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys		
785	790	795
Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp		800
	805	810
Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Cys Glu		815
	820	825
Glu Gln Tyr Gly Ser Thr Tyr Arg Cys Val Ser Val Leu Thr Val Leu		830
	835	840
		845

His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn
 850 855 860
 Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly
 865 870 875 880
 Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu
 885 890 895
 Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr
 900 905 910
 Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn
 915 920 925
 Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe
 930 935 940
 Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn
 945 950 955 960
 Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr
 965 970 975
 Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
 980 985

<210> 125

<211> 984

<212> PRT

<213> 人工序列

<220>

<223> PM 76-B10.17 CC x I2C0 CC (103/43) -scFc_delGK双特异性HLE分子

<400> 125

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

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

Ala Val Thr Ser Gly Asn Tyr Pro Asn Trp Val Gln Gln Lys Pro Gly		
420	425	430
Gln Cys Pro Arg Gly Leu Ile Gly Gly Thr Lys Phe Leu Ala Pro Gly		
435	440	445
Thr Pro Ala Arg Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu		
450	455	460
Thr Leu Ser Gly Val Gln Pro Glu Asp Glu Ala Glu Tyr Tyr Cys Val		
465	470	475
Leu Trp Tyr Ser Asn Arg Trp Val Phe Gly Gly Gly Thr Lys Leu Thr		
485	490	495
Val Leu Gly Gly Gly Gly Asp Lys Thr His Thr Cys Pro Pro Cys Pro		
500	505	510
Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys		
515	520	525
Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val		
530	535	540
Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr		
545	550	555
Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Cys Glu Glu		
565	570	575
Gln Tyr Gly Ser Thr Tyr Arg Cys Val Ser Val Leu Thr Val Leu His		
580	585	590
Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys		
595	600	605
Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln		
610	615	620
Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met		
625	630	635
Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro		
645	650	655
Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn		
660	665	670
Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu		
675	680	685
Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val		
690	695	700
Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln		
705	710	715
Lys Ser Leu Ser Leu Ser Pro Gly Gly Gly Gly Ser Gly Gly Gly Gly		

	725		730		735
Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser					
	740		745		750
Gly Gly Gly Gly Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala					
	755		760		765
Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro					
	770		775		780
Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val					
785		790		795	800
Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val					
	805		810		815
Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Cys Glu Glu Gln					
	820		825		830
Tyr Gly Ser Thr Tyr Arg Cys Val Ser Val Leu Thr Val Leu His Gln					
	835		840		845
Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala					
	850		855		860
Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro					
865		870		875	880
Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr					
	885		890		895
Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser					
	900		905		910
Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr					
	915		920		925
Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr					
	930		935		940
Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe					
945		950		955	960
Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys					
	965		970		975
Ser Leu Ser Leu Ser Pro Gly Lys					
	980				

<210> 126

<211> 5

<212> PRT

<213> 人工序列

<220>

<223> PM 76-B10.11 CC VH CDR1

<400> 126

Asp Tyr Tyr Met Tyr

1 5

<210> 127

<211> 17

<212> PRT

<213> 人工序列

<220>

<223> PM 76-B10.11 CC VH CDR2

<400> 127

Ile Ile Ser Asp Gly Gly Tyr Tyr Thr Tyr Tyr Ser Asp Ile Ile Lys

1 5 10 15

Gly

<210> 128

<211> 12

<212> PRT

<213> 人工序列

<220>

<223> PM 76-B10.11 CC VH CDR3

<400> 128

Gly Phe Pro Leu Leu Arg His Gly Ala Met Asp Tyr

1 5 10

<210> 129

<211> 11

<212> PRT

<213> 人工序列

<220>

<223> PM 76-B10.11 CC VL CDR1

<400> 129

Lys Ala Ser Gln Asn Val Asp Thr Asn Val Ala

1 5 10

<210> 130

<211> 7

<212> PRT

<213> 人工序列

<220>

<223> PM 76-B10.11 CC VL CDR2

<400> 130

Ser Ala Ser Tyr Val Tyr Trp

1 5
 <210> 131
 <211> 9
 <212> PRT
 <213> 人工序列
 <220>
 <223> PM 76-B10.11 CC VL CDR3
 <400> 131
 Gln Gln Tyr Asp Gln Gln Leu Ile Thr
 1 5
 <210> 132
 <211> 121
 <212> PRT
 <213> 人工序列
 <220>
 <223> PM 76-B10.11 CC VH
 <400> 132
 Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Glu
 1 5 10 15
 Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr
 20 25 30
 Tyr Met Tyr Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
 35 40 45
 Ala Ile Ile Ser Asp Gly Gly Tyr Tyr Thr Tyr Tyr Ser Asp Ile Ile
 50 55 60
 Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
 65 70 75 80
 Leu Gln Met Asn Ser Leu Lys Ala Glu Asp Thr Ala Val Tyr Tyr Cys
 85 90 95
 Ala Arg Gly Phe Pro Leu Leu Arg His Gly Ala Met Asp Tyr Trp Gly
 100 105 110
 Gln Gly Thr Leu Val Thr Val Ser Ser
 115 120
 <210> 133
 <211> 107
 <212> PRT
 <213> 人工序列
 <220>
 <223> PM 76-B10.11 CC VL

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

130	135	140
Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Lys		
145	150	155
Ala Ser Gln Asn Val Asp Thr Asn Val Ala Trp Tyr Gln Gln Lys Pro		
165	170	175
Gly Gln Ala Pro Lys Ser Leu Ile Tyr Ser Ala Ser Tyr Val Tyr Trp		
180	185	190
Asp Val Pro Ser Arg Phe Ser Gly Ser Ala Ser Gly Thr Asp Phe Thr		
195	200	205
Leu Thr Ile Ser Ser Val Gln Ser Glu Asp Phe Ala Thr Tyr Tyr Cys		
210	215	220
Gln Gln Tyr Asp Gln Gln Leu Ile Thr Phe Gly Gly Gly Thr Lys Leu		
225	230	235
Glu Ile Lys		
<210> 135		
<211> 498		
<212> PRT		
<213> 人工序列		
<220>		
<223> PM 76-B10.11 CC x I2C0双特异性分子		
<400> 135		
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Glu		
1	5	10
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr		
20	25	30
Tyr Met Tyr Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val		
35	40	45
Ala Ile Ile Ser Asp Gly Gly Tyr Tyr Thr Tyr Tyr Ser Asp Ile Ile		
50	55	60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr		
65	70	75
Leu Gln Met Asn Ser Leu Lys Ala Glu Asp Thr Ala Val Tyr Tyr Cys		
85	90	95
Ala Arg Gly Phe Pro Leu Leu Arg His Gly Ala Met Asp Tyr Trp Gly		
100	105	110
Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly		
115	120	125
Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Gln Met Thr Gln Ser Pro		
130	135	140

Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Lys			
145	150	155	160
Ala Ser Gln Asn Val Asp Thr Asn Val Ala Trp Tyr Gln Gln Lys Pro			
	165	170	175
Gly Gln Ala Pro Lys Ser Leu Ile Tyr Ser Ala Ser Tyr Val Tyr Trp			
	180	185	190
Asp Val Pro Ser Arg Phe Ser Gly Ser Ala Ser Gly Thr Asp Phe Thr			
	195	200	205
Leu Thr Ile Ser Ser Val Gln Ser Glu Asp Phe Ala Thr Tyr Tyr Cys			
	210	215	220
Gln Gln Tyr Asp Gln Gln Leu Ile Thr Phe Gly Gly Gly Thr Lys Leu			
225	230	235	240
Glu Ile Lys Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Val Glu Ser			
	245	250	255
Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Lys Leu Ser Cys Ala			
	260	265	270
Ala Ser Gly Phe Thr Phe Asn Lys Tyr Ala Met Asn Trp Val Arg Gln			
	275	280	285
Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Arg Ile Arg Ser Lys Tyr			
	290	295	300
Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp Ser Val Lys Asp Arg Phe Thr			
305	310	315	320
Ile Ser Arg Asp Asp Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn Asn			
	325	330	335
Leu Lys Thr Glu Asp Thr Ala Val Tyr Tyr Cys Val Arg His Gly Asn			
	340	345	350
Phe Gly Asn Ser Tyr Ile Ser Tyr Trp Ala Tyr Trp Gly Gln Gly Thr			
	355	360	365
Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser			
	370	375	380
Gly Gly Gly Gly Ser Gln Thr Val Val Thr Gln Glu Pro Ser Leu Thr			
385	390	395	400
Val Ser Pro Gly Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly			
	405	410	415
Ala Val Thr Ser Gly Asn Tyr Pro Asn Trp Val Gln Gln Lys Pro Gly			
	420	425	430
Gln Ala Pro Arg Gly Leu Ile Gly Gly Thr Lys Phe Leu Ala Pro Gly			
	435	440	445
Thr Pro Ala Arg Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu			

450	455	460
Thr Leu Ser Gly Val Gln Pro Glu Asp Glu Ala Glu Tyr Tyr Cys Val		
465	470	475
Leu Trp Tyr Ser Asn Arg Trp Val Phe Gly Gly Gly Thr Lys Leu Thr		480
	485	490
		495
Val Leu		
<210> 136		
<211> 986		
<212> PRT		
<213> 人工序列		
<220>		
<223> PM 76-B10.11 CC x I2C0-scFc双特异性HLE分子		
<400> 136		
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Glu		
1	5	10
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr		
	20	25
		30
Tyr Met Tyr Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val		
	35	40
		45
Ala Ile Ile Ser Asp Gly Gly Tyr Tyr Thr Tyr Tyr Ser Asp Ile Ile		
	50	55
		60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr		
65	70	75
		80
Leu Gln Met Asn Ser Leu Lys Ala Glu Asp Thr Ala Val Tyr Tyr Cys		
	85	90
		95
Ala Arg Gly Phe Pro Leu Leu Arg His Gly Ala Met Asp Tyr Trp Gly		
	100	105
		110
Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Ser Gly Gly		
	115	120
		125
Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Gln Met Thr Gln Ser Pro		
	130	135
		140
Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Lys		
145	150	155
		160
Ala Ser Gln Asn Val Asp Thr Asn Val Ala Trp Tyr Gln Gln Lys Pro		
	165	170
		175
Gly Gln Ala Pro Lys Ser Leu Ile Tyr Ser Ala Ser Tyr Val Tyr Trp		
	180	185
		190
Asp Val Pro Ser Arg Phe Ser Gly Ser Ala Ser Gly Thr Asp Phe Thr		
	195	200
		205

Leu Thr Ile Ser Ser Val Gln Ser Glu Asp Phe Ala Thr Tyr Tyr Cys			
210	215	220	
Gln Gln Tyr Asp Gln Gln Leu Ile Thr Phe Gly Gly Gly Thr Lys Leu			
225	230	235	240
Glu Ile Lys Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Val Glu Ser			
	245	250	255
Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Lys Leu Ser Cys Ala			
	260	265	270
Ala Ser Gly Phe Thr Phe Asn Lys Tyr Ala Met Asn Trp Val Arg Gln			
	275	280	285
Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Arg Ile Arg Ser Lys Tyr			
	290	295	300
Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp Ser Val Lys Asp Arg Phe Thr			
305	310	315	320
Ile Ser Arg Asp Asp Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn Asn			
	325	330	335
Leu Lys Thr Glu Asp Thr Ala Val Tyr Tyr Cys Val Arg His Gly Asn			
	340	345	350
Phe Gly Asn Ser Tyr Ile Ser Tyr Trp Ala Tyr Trp Gly Gln Gly Thr			
	355	360	365
Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser			
	370	375	380
Gly Gly Gly Gly Ser Gln Thr Val Val Thr Gln Glu Pro Ser Leu Thr			
385	390	395	400
Val Ser Pro Gly Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly			
	405	410	415
Ala Val Thr Ser Gly Asn Tyr Pro Asn Trp Val Gln Gln Lys Pro Gly			
	420	425	430
Gln Ala Pro Arg Gly Leu Ile Gly Gly Thr Lys Phe Leu Ala Pro Gly			
	435	440	445
Thr Pro Ala Arg Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu			
	450	455	460
Thr Leu Ser Gly Val Gln Pro Glu Asp Glu Ala Glu Tyr Tyr Cys Val			
465	470	475	480
Leu Trp Tyr Ser Asn Arg Trp Val Phe Gly Gly Gly Thr Lys Leu Thr			
	485	490	495
Val Leu Gly Gly Gly Gly Asp Lys Thr His Thr Cys Pro Pro Cys Pro			
	500	505	510
Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys			

515	520	525
Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val		
530	535	540
Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr		
545	550	555
Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Cys Glu Glu		
565	570	575
Gln Tyr Gly Ser Thr Tyr Arg Cys Val Ser Val Leu Thr Val Leu His		
580	585	590
Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys		
595	600	605
Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln		
610	615	620
Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met		
625	630	635
Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro		
645	650	655
Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn		
660	665	670
Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu		
675	680	685
Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val		
690	695	700
Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln		
705	710	715
Lys Ser Leu Ser Leu Ser Pro Gly Lys Gly Gly Gly Gly Ser Gly Gly		
725	730	735
Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly		
740	745	750
Gly Ser Gly Gly Gly Gly Ser Asp Lys Thr His Thr Cys Pro Pro Cys		
755	760	765
Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro		
770	775	780
Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys		
785	790	795
Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp		
805	810	815
Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Cys Glu		
820	825	830

Glu Gln Tyr Gly Ser Thr Tyr Arg Cys Val Ser Val Leu Thr Val Leu
 835 840 845
 His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn
 850 855 860
 Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly
 865 870 875 880
 Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu
 885 890 895
 Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr
 900 905 910
 Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn
 915 920 925
 Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe
 930 935 940
 Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn
 945 950 955 960
 Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr
 965 970 975
 Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
 980 985

<210> 137

<211> 984

<212> PRT

<213> 人工序列

<220>

<223> PM 76-B10.11 CC x I2C0-scFc_delGK双特异性HLE分子

<400> 137

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

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

	405		410		415
Ala Val Thr Ser Gly Asn Tyr Pro Asn Trp Val Gln Gln Lys Pro Gly					
	420		425		430
Gln Ala Pro Arg Gly Leu Ile Gly Gly Thr Lys Phe Leu Ala Pro Gly					
	435		440		445
Thr Pro Ala Arg Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu					
	450		455		460
Thr Leu Ser Gly Val Gln Pro Glu Asp Glu Ala Glu Tyr Tyr Cys Val					
465		470		475	480
Leu Trp Tyr Ser Asn Arg Trp Val Phe Gly Gly Gly Thr Lys Leu Thr					
	485		490		495
Val Leu Gly Gly Gly Gly Asp Lys Thr His Thr Cys Pro Pro Cys Pro					
	500		505		510
Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys					
	515		520		525
Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val					
	530		535		540
Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr					
545		550		555	560
Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Cys Glu Glu					
	565		570		575
Gln Tyr Gly Ser Thr Tyr Arg Cys Val Ser Val Leu Thr Val Leu His					
	580		585		590
Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys					
	595		600		605
Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln					
	610		615		620
Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met					
625		630		635	640
Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro					
	645		650		655
Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn					
	660		665		670
Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu					
	675		680		685
Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val					
	690		695		700
Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln					
705		710		715	720

Lys Ser Leu Ser Leu Ser Pro Gly Gly Gly Gly Ser Gly Gly Gly Gly		
725	730	735
Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser		
740	745	750
Gly Gly Gly Gly Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala		
755	760	765
Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro		
770	775	780
Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val		
785	790	795
Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val		
805	810	815
Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Cys Glu Glu Gln		
820	825	830
Tyr Gly Ser Thr Tyr Arg Cys Val Ser Val Leu Thr Val Leu His Gln		
835	840	845
Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala		
850	855	860
Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro		
865	870	875
Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr		
885	890	895
Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser		
900	905	910
Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr		
915	920	925
Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr		
930	935	940
Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe		
945	950	955
Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys		
965	970	975
Ser Leu Ser Leu Ser Pro Gly Lys		
980		

<210> 138

<211> 498

<212> PRT

<213> 人工序列

<220>

<223> PM 76-B10.11 CC x I2C0 CC (103/43) -scFc双特异性分子

<400> 138

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

290	295	300
Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp Ser Val Lys Asp Arg Phe Thr		
305	310	315
Ile Ser Arg Asp Asp Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn Asn		320
	325	330
Leu Lys Thr Glu Asp Thr Ala Val Tyr Tyr Cys Val Arg His Gly Asn		335
	340	345
Phe Gly Asn Ser Tyr Ile Ser Tyr Trp Ala Tyr Cys Gly Gln Gly Thr		350
	355	360
Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser		365
370	375	380
Gly Gly Gly Gly Ser Gln Thr Val Val Thr Gln Glu Pro Ser Leu Thr		
385	390	395
Val Ser Pro Gly Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly		
	405	410
Ala Val Thr Ser Gly Asn Tyr Pro Asn Trp Val Gln Gln Lys Pro Gly		415
	420	425
Gln Cys Pro Arg Gly Leu Ile Gly Gly Thr Lys Phe Leu Ala Pro Gly		
435	440	445
Thr Pro Ala Arg Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu		
450	455	460
Thr Leu Ser Gly Val Gln Pro Glu Asp Glu Ala Glu Tyr Tyr Cys Val		
465	470	475
Leu Trp Tyr Ser Asn Arg Trp Val Phe Gly Gly Gly Thr Lys Leu Thr		
	485	490
		495
Val Leu		
<210> 139		
<211> 986		
<212> PRT		
<213> 人工序列		
<220>		
<223> PM 76-B10.11 CC x I2C0 CC (103/43) -scFc双特异性HLE分子		
<400> 139		
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Glu		
1	5	10
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr		15
	20	25
		30
Tyr Met Tyr Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val		
35	40	45

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

355	360	365
Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser		
370	375	380
Gly Gly Gly Gly Ser Gln Thr Val Val Thr Gln Glu Pro Ser Leu Thr		
385	390	395
Val Ser Pro Gly Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly		400
405	410	415
Ala Val Thr Ser Gly Asn Tyr Pro Asn Trp Val Gln Gln Lys Pro Gly		
420	425	430
Gln Cys Pro Arg Gly Leu Ile Gly Gly Thr Lys Phe Leu Ala Pro Gly		
435	440	445
Thr Pro Ala Arg Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu		
450	455	460
Thr Leu Ser Gly Val Gln Pro Glu Asp Glu Ala Glu Tyr Tyr Cys Val		
465	470	475
Leu Trp Tyr Ser Asn Arg Trp Val Phe Gly Gly Gly Thr Lys Leu Thr		
485	490	495
Val Leu Gly Gly Gly Gly Asp Lys Thr His Thr Cys Pro Pro Cys Pro		
500	505	510
Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys		
515	520	525
Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val		
530	535	540
Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr		
545	550	555
Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Cys Glu Glu		
565	570	575
Gln Tyr Gly Ser Thr Tyr Arg Cys Val Ser Val Leu Thr Val Leu His		
580	585	590
Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys		
595	600	605
Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln		
610	615	620
Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met		
625	630	635
Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro		
645	650	655
Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn		
660	665	670

Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu		
675	680	685
Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val		
690	695	700
Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln		
705	710	715
Lys Ser Leu Ser Leu Ser Pro Gly Lys Gly Gly Gly Gly Ser Gly Gly		
	725	730
Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly		
	740	745
Gly Ser Gly Gly Gly Gly Ser Asp Lys Thr His Thr Cys Pro Pro Cys		
	755	760
Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro		
	770	775
Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys		
785	790	795
Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp		
	805	810
Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Cys Glu		
	820	825
Glu Gln Tyr Gly Ser Thr Tyr Arg Cys Val Ser Val Leu Thr Val Leu		
	835	840
His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn		
	850	855
Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly		
865	870	875
Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu		
	885	890
Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr		
	900	905
Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn		
	915	920
Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe		
	930	935
Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn		
945	950	955
Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr		
	965	970
Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys		

Glu Ile Lys Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Val Glu Ser		
245	250	255
Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Lys Leu Ser Cys Ala		
260	265	270
Ala Ser Gly Phe Thr Phe Asn Lys Tyr Ala Met Asn Trp Val Arg Gln		
275	280	285
Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Arg Ile Arg Ser Lys Tyr		
290	295	300
Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp Ser Val Lys Asp Arg Phe Thr		
305	310	315
Ile Ser Arg Asp Asp Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn Asn		
325	330	335
Leu Lys Thr Glu Asp Thr Ala Val Tyr Tyr Cys Val Arg His Gly Asn		
340	345	350
Phe Gly Asn Ser Tyr Ile Ser Tyr Trp Ala Tyr Cys Gly Gln Gly Thr		
355	360	365
Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser		
370	375	380
Gly Gly Gly Gly Ser Gln Thr Val Val Thr Gln Glu Pro Ser Leu Thr		
385	390	395
Val Ser Pro Gly Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly		
405	410	415
Ala Val Thr Ser Gly Asn Tyr Pro Asn Trp Val Gln Gln Lys Pro Gly		
420	425	430
Gln Cys Pro Arg Gly Leu Ile Gly Gly Thr Lys Phe Leu Ala Pro Gly		
435	440	445
Thr Pro Ala Arg Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu		
450	455	460
Thr Leu Ser Gly Val Gln Pro Glu Asp Glu Ala Glu Tyr Tyr Cys Val		
465	470	475
Leu Trp Tyr Ser Asn Arg Trp Val Phe Gly Gly Gly Thr Lys Leu Thr		
485	490	495
Val Leu Gly Gly Gly Gly Asp Lys Thr His Thr Cys Pro Pro Cys Pro		
500	505	510
Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys		
515	520	525
Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val		
530	535	540
Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr		

545	550	555	560
Val Asp Gly Val Glu	Val His Asn Ala Lys Thr Lys Pro Cys Glu Glu		
	565	570	575
Gln Tyr Gly Ser Thr Tyr Arg Cys Val Ser Val Leu Thr Val Leu His			
	580	585	590
Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys			
	595	600	605
Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln			
	610	615	620
Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met			
625	630	635	640
Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro			
	645	650	655
Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn			
	660	665	670
Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu			
	675	680	685
Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val			
	690	695	700
Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln			
705	710	715	720
Lys Ser Leu Ser Leu Ser Pro Gly Gly Gly Gly Ser Gly Gly Gly Gly			
	725	730	735
Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser			
	740	745	750
Gly Gly Gly Gly Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala			
	755	760	765
Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro			
	770	775	780
Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val			
785	790	795	800
Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val			
	805	810	815
Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Cys Glu Glu Gln			
	820	825	830
Tyr Gly Ser Thr Tyr Arg Cys Val Ser Val Leu Thr Val Leu His Gln			
	835	840	845
Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala			
	850	855	860

Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro
865 870 875 880
Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr
885 890 895
Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser
900 905 910
Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr
915 920 925
Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr
930 935 940
Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe
945 950 955 960
Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys
965 970 975
Ser Leu Ser Leu Ser Pro Gly Lys
980

<210> 141

<211> 5

<212> PRT

<213> 人工序列

<220>

<223> PM 76-B10.11 CC x I2C0-scFc VH CDR1

<400> 141

Asp Tyr Tyr Met Tyr

1 5

<210> 142

<211> 17

<212> PRT

<213> 人工序列

<220>

<223> PM 76-B10.11 CC x I2C0-scFc VH CDR2

<400> 142

Ile Ile Ser Asp Gly Gly Tyr Tyr Thr Tyr Tyr Ser Asp Ile Ile Lys

1 5 10 15

Gly

<210> 143

<211> 12

<212> PRT

<213> 人工序列

<220>

<223> PM 76-B10.11 CC x I2C0-scFc VH CDR3

<400> 143

Gly Phe Pro Leu Leu Arg His Gly Ala Met Asp Tyr

1 5 10

<210> 144

<211> 11

<212> PRT

<213> 人工序列

<220>

<223> PM 76-B10.11 CC x I2C0-scFc VL CDR1

<400> 144

Lys Ala Ser Gln Asn Val Asp Thr Asn Val Ala

1 5 10

<210> 145

<211> 7

<212> PRT

<213> 人工序列

<220>

<223> PM 76-B10.11 CC x I2C0-scFc VL CDR2

<400> 145

Ser Ala Ser Tyr Val Tyr Trp

1 5

<210> 146

<211> 9

<212> PRT

<213> 人工序列

<220>

<223> PM 76-B10.11 CC x I2C0-scFc VL CDR3

<400> 146

Gln Gln Tyr Asp Gln Gln Leu Ile Thr

1 5

<210> 147

<211> 121

<212> PRT

<213> 人工序列

<220>

<223> PM 76-B10.11 CC x I2C0-scFc VH

<400> 147

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

<210> 148

<211> 107

<212> PRT

<213> 人工序列

<220>

<223> PM 76-B10.11 CC x I2C0-scFc VL

<400> 148

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

<210> 149

<211> 243

<212> PRT

<213> 人工序列

<220>

<223> PM 76-B10.11 CC x I2C0-scFc scFv

<400> 149

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

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<210> 150

<211> 498

<212> PRT

<213> 人工序列

<220>

<223> PM 76-B10.11 CC x I2C0-scFc双特异性分子

<400> 150

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

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

Val Leu

<210> 151

<211> 986

<212> PRT

<213> 人工序列

<220>

<223> PM 76-B10.11 CC x I2C0-scFc双特异性HLE分子

<400> 151

Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Glu		
1	5	10
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr		
20	25	30

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

340	345	350
Phe Gly Asn Ser Tyr Ile Ser Tyr Trp Ala Tyr Trp Gly Gln Gly Thr		
355	360	365
Leu Val Thr Val Ser Ser Gly Gly Gly Ser Gly Gly Gly Ser		
370	375	380
Gly Gly Gly Gly Ser Gln Thr Val Val Thr Gln Glu Pro Ser Leu Thr		
385	390	395
Val Ser Pro Gly Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly		
405	410	415
Ala Val Thr Ser Gly Asn Tyr Pro Asn Trp Val Gln Gln Lys Pro Gly		
420	425	430
Gln Ala Pro Arg Gly Leu Ile Gly Gly Thr Lys Phe Leu Ala Pro Gly		
435	440	445
Thr Pro Ala Arg Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu		
450	455	460
Thr Leu Ser Gly Val Gln Pro Glu Asp Glu Ala Glu Tyr Tyr Cys Val		
465	470	475
Leu Trp Tyr Ser Asn Arg Trp Val Phe Gly Gly Gly Thr Lys Leu Thr		
485	490	495
Val Leu Gly Gly Gly Gly Asp Lys Thr His Thr Cys Pro Pro Cys Pro		
500	505	510
Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys		
515	520	525
Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val		
530	535	540
Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr		
545	550	555
Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Cys Glu Glu		
565	570	575
Gln Tyr Gly Ser Thr Tyr Arg Cys Val Ser Val Leu Thr Val Leu His		
580	585	590
Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys		
595	600	605
Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln		
610	615	620
Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met		
625	630	635
Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro		
645	650	655

Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn		
660	665	670
Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu		
675	680	685
Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val		
690	695	700
Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln		
705	710	715
Lys Ser Leu Ser Leu Ser Pro Gly Lys Gly Gly Gly Gly Ser Gly Gly		
725	730	735
Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly		
740	745	750
Gly Ser Gly Gly Gly Gly Ser Asp Lys Thr His Thr Cys Pro Pro Cys		
755	760	765
Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro		
770	775	780
Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys		
785	790	795
Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp		
805	810	815
Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Cys Glu		
820	825	830
Glu Gln Tyr Gly Ser Thr Tyr Arg Cys Val Ser Val Leu Thr Val Leu		
835	840	845
His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn		
850	855	860
Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly		
865	870	875
Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu		
885	890	895
Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr		
900	905	910
Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn		
915	920	925
Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe		
930	935	940
Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn		
945	950	955
Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr		

	965		970		975
Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys					
	980		985		
<210> 152					
<211> 984					
<212> PRT					
<213> 人工序列					
<220>					
<223> PM 76-B10.11 CC x I2C0-scFc_delGK双特异性HLE分子					
<400> 152					
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Glu					
1	5		10		15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr					
	20		25		30
Tyr Met Tyr Trp Val Arg Gln Ala Pro Gly Lys Cys Leu Glu Trp Val					
	35		40		45
Ala Ile Ile Ser Asp Gly Gly Tyr Tyr Thr Tyr Tyr Ser Asp Ile Ile					
	50		55		60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr					
65	70		75		80
Leu Gln Met Asn Ser Leu Lys Ala Glu Asp Thr Ala Val Tyr Tyr Cys					
	85		90		95
Ala Arg Gly Phe Pro Leu Leu Arg His Gly Ala Met Asp Tyr Trp Gly					
	100		105		110
Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly					
	115		120		125
Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Gln Met Thr Gln Ser Pro					
	130		135		140
Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Lys					
145	150		155		160
Ala Ser Gln Asn Val Asp Thr Asn Val Ala Trp Tyr Gln Gln Lys Pro					
	165		170		175
Gly Gln Ala Pro Lys Ser Leu Ile Tyr Ser Ala Ser Tyr Val Tyr Trp					
	180		185		190
Asp Val Pro Ser Arg Phe Ser Gly Ser Ala Ser Gly Thr Asp Phe Thr					
	195		200		205
Leu Thr Ile Ser Ser Val Gln Ser Glu Asp Phe Ala Thr Tyr Tyr Cys					
	210		215		220
Gln Gln Tyr Asp Gln Gln Leu Ile Thr Phe Gly Cys Gly Thr Lys Leu					

225	230	235	240
Glu Ile Lys Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Val Glu Ser			
	245	250	255
Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Lys Leu Ser Cys Ala			
	260	265	270
Ala Ser Gly Phe Thr Phe Asn Lys Tyr Ala Met Asn Trp Val Arg Gln			
	275	280	285
Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Arg Ile Arg Ser Lys Tyr			
	290	295	300
Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp Ser Val Lys Asp Arg Phe Thr			
305	310	315	320
Ile Ser Arg Asp Asp Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn Asn			
	325	330	335
Leu Lys Thr Glu Asp Thr Ala Val Tyr Tyr Cys Val Arg His Gly Asn			
	340	345	350
Phe Gly Asn Ser Tyr Ile Ser Tyr Trp Ala Tyr Trp Gly Gln Gly Thr			
	355	360	365
Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser			
	370	375	380
Gly Gly Gly Gly Ser Gln Thr Val Val Thr Gln Glu Pro Ser Leu Thr			
385	390	395	400
Val Ser Pro Gly Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly			
	405	410	415
Ala Val Thr Ser Gly Asn Tyr Pro Asn Trp Val Gln Gln Lys Pro Gly			
	420	425	430
Gln Ala Pro Arg Gly Leu Ile Gly Gly Thr Lys Phe Leu Ala Pro Gly			
	435	440	445
Thr Pro Ala Arg Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu			
	450	455	460
Thr Leu Ser Gly Val Gln Pro Glu Asp Glu Ala Glu Tyr Tyr Cys Val			
465	470	475	480
Leu Trp Tyr Ser Asn Arg Trp Val Phe Gly Gly Gly Thr Lys Leu Thr			
	485	490	495
Val Leu Gly Gly Gly Gly Asp Lys Thr His Thr Cys Pro Pro Cys Pro			
	500	505	510
Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys			
	515	520	525
Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val			
	530	535	540

Val	Val	Asp	Val	Ser	His	Glu	Asp	Pro	Glu	Val	Lys	Phe	Asn	Trp	Tyr
545					550					555					560
Val	Asp	Gly	Val	Glu	Val	His	Asn	Ala	Lys	Thr	Lys	Pro	Cys	Glu	Glu
				565					570					575	
Gln	Tyr	Gly	Ser	Thr	Tyr	Arg	Cys	Val	Ser	Val	Leu	Thr	Val	Leu	His
			580					585					590		
Gln	Asp	Trp	Leu	Asn	Gly	Lys	Glu	Tyr	Lys	Cys	Lys	Val	Ser	Asn	Lys
	595						600					605			
Ala	Leu	Pro	Ala	Pro	Ile	Glu	Lys	Thr	Ile	Ser	Lys	Ala	Lys	Gly	Gln
	610					615					620				
Pro	Arg	Glu	Pro	Gln	Val	Tyr	Thr	Leu	Pro	Pro	Ser	Arg	Glu	Glu	Met
625				630					635						640
Thr	Lys	Asn	Gln	Val	Ser	Leu	Thr	Cys	Leu	Val	Lys	Gly	Phe	Tyr	Pro
			645					650					655		
Ser	Asp	Ile	Ala	Val	Glu	Trp	Glu	Ser	Asn	Gly	Gln	Pro	Glu	Asn	Asn
			660					665					670		
Tyr	Lys	Thr	Thr	Pro	Pro	Val	Leu	Asp	Ser	Asp	Gly	Ser	Phe	Phe	Leu
	675						680					685			
Tyr	Ser	Lys	Leu	Thr	Val	Asp	Lys	Ser	Arg	Trp	Gln	Gln	Gly	Asn	Val
	690					695					700				
Phe	Ser	Cys	Ser	Val	Met	His	Glu	Ala	Leu	His	Asn	His	Tyr	Thr	Gln
705					710					715					720
Lys	Ser	Leu	Ser	Leu	Ser	Pro	Gly	Gly	Gly	Gly	Ser	Gly	Gly	Gly	Gly
				725				730					735		
Ser	Gly	Gly	Gly	Gly	Ser	Gly	Gly	Gly	Gly	Ser	Gly	Gly	Gly	Gly	Ser
			740					745					750		
Gly	Gly	Gly	Gly	Ser	Asp	Lys	Thr	His	Thr	Cys	Pro	Pro	Cys	Pro	Ala
			755					760					765		
Pro	Glu	Leu	Leu	Gly	Gly	Pro	Ser	Val	Phe	Leu	Phe	Pro	Pro	Lys	Pro
	770					775					780				
Lys	Asp	Thr	Leu	Met	Ile	Ser	Arg	Thr	Pro	Glu	Val	Thr	Cys	Val	Val
785					790					795					800
Val	Asp	Val	Ser	His	Glu	Asp	Pro	Glu	Val	Lys	Phe	Asn	Trp	Tyr	Val
				805					810					815	
Asp	Gly	Val	Glu	Val	His	Asn	Ala	Lys	Thr	Lys	Pro	Cys	Glu	Glu	Gln
			820					825					830		
Tyr	Gly	Ser	Thr	Tyr	Arg	Cys	Val	Ser	Val	Leu	Thr	Val	Leu	His	Gln
	835					840							845		
Asp	Trp	Leu	Asn	Gly	Lys	Glu	Tyr	Lys	Cys	Lys	Val	Ser	Asn	Lys	Ala

850	855	860
Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro		
865	870	875
Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr		
	885	890
Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser		
	900	905
Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr		
	915	920
Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr		
	930	935
Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe		
945	950	955
Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys		
	965	970
Ser Leu Ser Leu Ser Pro Gly Lys		
	980	

<210> 153

<211> 498

<212> PRT

<213> 人工序列

<220>

<223> PM 76-B10.11 CC x I2C0 CC (103/43) -scFc双特异性分子

<400> 153

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

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

Gln Cys Pro Arg Gly Leu Ile Gly Gly Thr Lys Phe Leu Ala Pro Gly
 435 440 445
 Thr Pro Ala Arg Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu
 450 455 460
 Thr Leu Ser Gly Val Gln Pro Glu Asp Glu Ala Glu Tyr Tyr Cys Val
 465 470 475 480
 Leu Trp Tyr Ser Asn Arg Trp Val Phe Gly Gly Gly Thr Lys Leu Thr
 485 490 495
 Val Leu
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 Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr
 20 25 30
 Tyr Met Tyr Trp Val Arg Gln Ala Pro Gly Lys Cys Leu Glu Trp Val
 35 40 45
 Ala Ile Ile Ser Asp Gly Gly Tyr Tyr Thr Tyr Tyr Ser Asp Ile Ile
 50 55 60
 Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
 65 70 75 80
 Leu Gln Met Asn Ser Leu Lys Ala Glu Asp Thr Ala Val Tyr Tyr Cys
 85 90 95
 Ala Arg Gly Phe Pro Leu Leu Arg His Gly Ala Met Asp Tyr Trp Gly
 100 105 110
 Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly
 115 120 125
 Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Gln Met Thr Gln Ser Pro
 130 135 140
 Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Lys
 145 150 155 160
 Ala Ser Gln Asn Val Asp Thr Asn Val Ala Trp Tyr Gln Gln Lys Pro
 165 170 175
 Gly Gln Ala Pro Lys Ser Leu Ile Tyr Ser Ala Ser Tyr Val Tyr Trp

	180		185		190
Asp Val Pro Ser Arg Phe Ser Gly Ser Ala Ser Gly Thr Asp Phe Thr					
195		200		205	
Leu Thr Ile Ser Ser Val Gln Ser Glu Asp Phe Ala Thr Tyr Tyr Cys					
210		215		220	
Gln Gln Tyr Asp Gln Gln Leu Ile Thr Phe Gly Cys Gly Thr Lys Leu					
225		230		235	240
Glu Ile Lys Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Val Glu Ser					
245		250		255	
Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Lys Leu Ser Cys Ala					
260		265		270	
Ala Ser Gly Phe Thr Phe Asn Lys Tyr Ala Met Asn Trp Val Arg Gln					
275		280		285	
Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Arg Ile Arg Ser Lys Tyr					
290		295		300	
Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp Ser Val Lys Asp Arg Phe Thr					
305		310		315	320
Ile Ser Arg Asp Asp Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn Asn					
325		330		335	
Leu Lys Thr Glu Asp Thr Ala Val Tyr Tyr Cys Val Arg His Gly Asn					
340		345		350	
Phe Gly Asn Ser Tyr Ile Ser Tyr Trp Ala Tyr Cys Gly Gln Gly Thr					
355		360		365	
Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser					
370		375		380	
Gly Gly Gly Gly Ser Gln Thr Val Val Thr Gln Glu Pro Ser Leu Thr					
385		390		395	400
Val Ser Pro Gly Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly					
405		410		415	
Ala Val Thr Ser Gly Asn Tyr Pro Asn Trp Val Gln Gln Lys Pro Gly					
420		425		430	
Gln Cys Pro Arg Gly Leu Ile Gly Gly Thr Lys Phe Leu Ala Pro Gly					
435		440		445	
Thr Pro Ala Arg Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu					
450		455		460	
Thr Leu Ser Gly Val Gln Pro Glu Asp Glu Ala Glu Tyr Tyr Cys Val					
465		470		475	480
Leu Trp Tyr Ser Asn Arg Trp Val Phe Gly Gly Gly Thr Lys Leu Thr					
485		490		495	

Val Leu Gly Gly Gly Gly Asp Lys Thr His Thr Cys Pro Pro Cys Pro		
500	505	510
Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys		
515	520	525
Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val		
530	535	540
Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr		
545	550	555
Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Cys Glu Glu		
565	570	575
Gln Tyr Gly Ser Thr Tyr Arg Cys Val Ser Val Leu Thr Val Leu His		
580	585	590
Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys		
595	600	605
Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln		
610	615	620
Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met		
625	630	635
Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro		
645	650	655
Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn		
660	665	670
Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu		
675	680	685
Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val		
690	695	700
Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln		
705	710	715
Lys Ser Leu Ser Leu Ser Pro Gly Lys Gly Gly Gly Gly Ser Gly Gly		
725	730	735
Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly		
740	745	750
Gly Ser Gly Gly Gly Gly Ser Asp Lys Thr His Thr Cys Pro Pro Cys		
755	760	765
Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro		
770	775	780
Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys		
785	790	795
Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp		

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

370	375	380
Gly Gly Gly Gly Ser Gln Thr Val Val Thr Gln Glu Pro Ser Leu Thr		
385	390	395
Val Ser Pro Gly Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly		400
405	410	415
Ala Val Thr Ser Gly Asn Tyr Pro Asn Trp Val Gln Gln Lys Pro Gly		
420	425	430
Gln Cys Pro Arg Gly Leu Ile Gly Gly Thr Lys Phe Leu Ala Pro Gly		
435	440	445
Thr Pro Ala Arg Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu		
450	455	460
Thr Leu Ser Gly Val Gln Pro Glu Asp Glu Ala Glu Tyr Tyr Cys Val		
465	470	475
Leu Trp Tyr Ser Asn Arg Trp Val Phe Gly Gly Gly Thr Lys Leu Thr		
485	490	495
Val Leu Gly Gly Gly Gly Asp Lys Thr His Thr Cys Pro Pro Cys Pro		
500	505	510
Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys		
515	520	525
Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val		
530	535	540
Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr		
545	550	555
Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Cys Glu Glu		
565	570	575
Gln Tyr Gly Ser Thr Tyr Arg Cys Val Ser Val Leu Thr Val Leu His		
580	585	590
Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys		
595	600	605
Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln		
610	615	620
Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met		
625	630	635
Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro		
645	650	655
Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn		
660	665	670
Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu		
675	680	685

Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val			
690	695	700	
Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln			
705	710	715	720
Lys Ser Leu Ser Leu Ser Pro Gly Gly Gly Gly Ser Gly Gly Gly Gly			
	725	730	735
Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser			
	740	745	750
Gly Gly Gly Gly Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala			
	755	760	765
Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro			
	770	775	780
Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val			
785	790	795	800
Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val			
	805	810	815
Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Cys Glu Glu Gln			
	820	825	830
Tyr Gly Ser Thr Tyr Arg Cys Val Ser Val Leu Thr Val Leu His Gln			
	835	840	845
Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala			
850	855	860	
Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro			
865	870	875	880
Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr			
	885	890	895
Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser			
	900	905	910
Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr			
	915	920	925
Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr			
	930	935	940
Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe			
945	950	955	960
Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys			
	965	970	975
Ser Leu Ser Leu Ser Pro Gly Lys			
	980		

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<223> CD70_21D_CC VH CDR1

<400> 156

Thr Tyr Ala Met Ser

1 5

<210> 157

<211> 17

<212> PRT

<213> 人工序列

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<223> CD70_21D_CC VH CDR2

<400> 157

Ala Ile Ser Gly Ser Gly Gly Arg Thr Phe Tyr Ala Glu Ser Val Glu

1 5 10 15

Gly

<210> 158

<211> 11

<212> PRT

<213> 人工序列

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<223> CD70_21D_CC VH CDR3

<400> 158

His Asp Tyr Ser Asn Tyr Pro Tyr Phe Asp Tyr

1 5 10

<210> 159

<211> 12

<212> PRT

<213> 人工序列

<220>

<223> CD70_21D_CC VL CDR1

<400> 159

Arg Ala Ser Gln Ser Val Arg Ser Thr Tyr Leu Ala

1 5 10

<210> 160

<211> 7

<212> PRT

<213> 人工序列

<220>

<223> CD70_21D_CC VL CDR2

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Gly Ala Ser Ser Arg Ala Thr

1 5

<210> 161

<211> 9

<212> PRT

<213> 人工序列

<220>

<223> CD70_21D_CC VL CDR3

<400> 161

Gln Gln Tyr Gly Asp Leu Pro Phe Thr

1 5

<210> 162

<211> 120

<212> PRT

<213> 人工序列

<220>

<223> CD70_21D_CC VH

<400> 162

Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Met Val Gln Pro Gly Gly

1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Thr Tyr

20 25 30

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Cys Leu Glu Trp Val

35 40 45

Ser Ala Ile Ser Gly Ser Gly Gly Arg Thr Phe Tyr Ala Glu Ser Val

50 55 60

Glu Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr

65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys

85 90 95

Ala Lys His Asp Tyr Ser Asn Tyr Pro Tyr Phe Asp Tyr Trp Gly Gln

100 105 110

Gly Thr Leu Val Thr Val Ser Ser

115 120

<210> 163

<211> 108

<212> PRT

<213> 人工序列

<220>

<223> CD70_21D_CC VL

<400> 163

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

<210> 164

<211> 986

<212> PRT

<213> 人工序列

<220>

<223> CD70_21D_CCx12C scFc

<400> 164

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

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

				405					410					415			
Ala	Val	Thr	Ser	Gly	Asn	Tyr	Pro	Asn	Trp	Val	Gln	Gln	Lys	Pro	Gly		
				420					425					430			
Gln	Ala	Pro	Arg	Gly	Leu	Ile	Gly	Gly	Thr	Lys	Phe	Leu	Ala	Pro	Gly		
				435					440					445			
Thr	Pro	Ala	Arg	Phe	Ser	Gly	Ser	Leu	Leu	Gly	Gly	Lys	Ala	Ala	Leu		
				450					455					460			
Thr	Leu	Ser	Gly	Val	Gln	Pro	Glu	Asp	Glu	Ala	Glu	Tyr	Tyr	Cys	Val		
465					470					475				480			
Leu	Trp	Tyr	Ser	Asn	Arg	Trp	Val	Phe	Gly	Gly	Gly	Thr	Lys	Leu	Thr		
				485					490					495			
Val	Leu	Gly	Gly	Gly	Gly	Asp	Lys	Thr	His	Thr	Cys	Pro	Pro	Cys	Pro		
				500					505					510			
Ala	Pro	Glu	Leu	Leu	Gly	Gly	Pro	Ser	Val	Phe	Leu	Phe	Pro	Pro	Lys		
				515					520					525			
Pro	Lys	Asp	Thr	Leu	Met	Ile	Ser	Arg	Thr	Pro	Glu	Val	Thr	Cys	Val		
				530					535					540			
Val	Val	Asp	Val	Ser	His	Glu	Asp	Pro	Glu	Val	Lys	Phe	Asn	Trp	Tyr		
545					550					555				560			
Val	Asp	Gly	Val	Glu	Val	His	Asn	Ala	Lys	Thr	Lys	Pro	Cys	Glu	Glu		
				565					570					575			
Gln	Tyr	Gly	Ser	Thr	Tyr	Arg	Cys	Val	Ser	Val	Leu	Thr	Val	Leu	His		
				580					585					590			
Gln	Asp	Trp	Leu	Asn	Gly	Lys	Glu	Tyr	Lys	Cys	Lys	Val	Ser	Asn	Lys		
				595					600					605			
Ala	Leu	Pro	Ala	Pro	Ile	Glu	Lys	Thr	Ile	Ser	Lys	Ala	Lys	Gly	Gln		
				610					615					620			
Pro	Arg	Glu	Pro	Gln	Val	Tyr	Thr	Leu	Pro	Pro	Ser	Arg	Glu	Glu	Met		
625					630					635				640			
Thr	Lys	Asn	Gln	Val	Ser	Leu	Thr	Cys	Leu	Val	Lys	Gly	Phe	Tyr	Pro		
				645					650					655			
Ser	Asp	Ile	Ala	Val	Glu	Trp	Glu	Ser	Asn	Gly	Gln	Pro	Glu	Asn	Asn		
				660					665					670			
Tyr	Lys	Thr	Thr	Pro	Pro	Val	Leu	Asp	Ser	Asp	Gly	Ser	Phe	Phe	Leu		
				675					680					685			
Tyr	Ser	Lys	Leu	Thr	Val	Asp	Lys	Ser	Arg	Trp	Gln	Gln	Gly	Asn	Val		
				690					695					700			
Phe	Ser	Cys	Ser	Val	Met	His	Glu	Ala	Leu	His	Asn	His	Tyr	Thr	Gln		
705					710					715				720			

Lys Ser Leu Ser Leu Ser Pro Gly Lys Gly Gly Gly Gly Ser Gly Gly		
725	730	735
Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly		
740	745	750
Gly Ser Gly Gly Gly Gly Ser Asp Lys Thr His Thr Cys Pro Pro Cys		
755	760	765
Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro		
770	775	780
Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys		
785	790	800
Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp		
805	810	815
Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Cys Glu		
820	825	830
Glu Gln Tyr Gly Ser Thr Tyr Arg Cys Val Ser Val Leu Thr Val Leu		
835	840	845
His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn		
850	855	860
Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly		
865	870	880
Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu		
885	890	895
Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr		
900	905	910
Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn		
915	920	925
Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe		
930	935	940
Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn		
945	950	960
Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr		
965	970	975
Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys		
980	985	

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<211> 1001

<212> PRT

<213> 人工序列

<220>

<223> MSLN_5_CCxCD3-scFc双特异性HLE分子

<400> 165

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

290	295	300
Pro Gly Lys Gly Leu Glu Trp Val Ala Arg Ile Arg Ser Lys Tyr Asn		
305	310	315
Asn Tyr Ala Thr Tyr Tyr Ala Asp Ser Val Lys Asp Arg Phe Thr Ile		320
	325	330
Ser Arg Asp Asp Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn Asn Leu		335
	340	345
Lys Thr Glu Asp Thr Ala Val Tyr Tyr Cys Val Arg His Gly Asn Phe		350
	355	360
Gly Asn Ser Tyr Ile Ser Tyr Trp Ala Tyr Trp Gly Gln Gly Thr Leu		365
370	375	380
Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly		
385	390	395
Gly Gly Gly Ser Gln Thr Val Val Thr Gln Glu Pro Ser Leu Thr Val		
	405	410
Ser Pro Gly Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala		415
	420	425
Val Thr Ser Gly Asn Tyr Pro Asn Trp Val Gln Gln Lys Pro Gly Gln		
435	440	445
Ala Pro Arg Gly Leu Ile Gly Gly Thr Lys Phe Leu Ala Pro Gly Thr		
450	455	460
Pro Ala Arg Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr		
465	470	475
Leu Ser Gly Val Gln Pro Glu Asp Glu Ala Glu Tyr Tyr Cys Val Leu		
	485	490
Trp Tyr Ser Asn Arg Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val		495
	500	505
Leu Gly Gly Gly Gly Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala		510
	515	520
Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro		525
530	535	540
Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val		
545	550	555
Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val		
	565	570
Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Cys Glu Glu Gln		575
	580	585
Tyr Gly Ser Thr Tyr Arg Cys Val Ser Val Leu Thr Val Leu His Gln		590
595	600	605

Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala		
610	615	620
Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro		
625	630	635 640
Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr		
	645	650 655
Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser		
	660	665 670
Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr		
	675	680 685
Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr		
	690	695 700
Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe		
705	710	715 720
Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys		
	725	730 735
Ser Leu Ser Leu Ser Pro Gly Lys Gly Gly Gly Ser Gly Gly Gly		
	740	745 750
Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Gly		
	755	760 765
Ser Gly Gly Gly Gly Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro		
770	775	780
Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys		
785	790	795 800
Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val		
	805	810 815
Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr		
	820	825 830
Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Cys Glu Glu		
	835	840 845
Gln Tyr Gly Ser Thr Tyr Arg Cys Val Ser Val Leu Thr Val Leu His		
850	855	860
Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys		
865	870	875 880
Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln		
	885	890 895
Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met		
	900	905 910
Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro		

915	920	925
Ser Asp Ile Ala Val Glu Trp	Glu Ser Asn Gly Gln Pro Glu Asn Asn	
930	935	940
Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu		
945	950	955
Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val		
965	970	975
Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln		
980	985	990
Lys Ser Leu Ser Leu Ser Pro Gly Lys		
995	1000	
<210> 166		
<211> 986		
<212> PRT		
<213> 人工序列		
<220>		
<223> 具有cys钳的抗PSMA xI2C0,scFc双特异性分子HLE		
PM76-B10.11		
<400> 166		
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Glu		
1	5	10
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr		
20	25	30
Tyr Met Tyr Trp Val Arg Gln Ala Pro Gly Lys Cys Leu Glu Trp Val		
35	40	45
Ala Ile Ile Ser Asp Gly Gly Tyr Tyr Thr Tyr Tyr Ser Asp Ile Ile		
50	55	60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr		
65	70	75
Leu Gln Met Asn Ser Leu Lys Ala Glu Asp Thr Ala Val Tyr Tyr Cys		
85	90	95
Ala Arg Gly Phe Pro Leu Leu Arg His Gly Ala Met Asp Tyr Trp Gly		
100	105	110
Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly		
115	120	125
Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Gln Met Thr Gln Ser Pro		
130	135	140
Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Lys		
145	150	155
		160

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

465	470	475	480
Leu Trp Tyr Ser Asn Arg Trp Val Phe Gly Gly Gly Thr Lys Leu Thr			
	485	490	495
Val Leu Gly Gly Gly Gly Asp Lys Thr His Thr Cys Pro Pro Cys Pro			
500	505	510	
Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys			
515	520	525	
Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val			
530	535	540	
Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr			
545	550	555	560
Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Cys Glu Glu			
	565	570	575
Gln Tyr Gly Ser Thr Tyr Arg Cys Val Ser Val Leu Thr Val Leu His			
580	585	590	
Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys			
595	600	605	
Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln			
610	615	620	
Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met			
625	630	635	640
Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro			
	645	650	655
Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn			
660	665	670	
Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu			
675	680	685	
Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val			
690	695	700	
Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln			
705	710	715	720
Lys Ser Leu Ser Leu Ser Pro Gly Lys Gly Gly Gly Gly Ser Gly Gly			
	725	730	735
Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly			
740	745	750	
Gly Ser Gly Gly Gly Gly Ser Asp Lys Thr His Thr Cys Pro Pro Cys			
755	760	765	
Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro			
770	775	780	

Lys	Pro	Lys	Asp	Thr	Leu	Met	Ile	Ser	Arg	Thr	Pro	Glu	Val	Thr	Cys
785						790				795					800
Val	Val	Val	Asp	Val	Ser	His	Glu	Asp	Pro	Glu	Val	Lys	Phe	Asn	Trp
						805				810					815
Tyr	Val	Asp	Gly	Val	Glu	Val	His	Asn	Ala	Lys	Thr	Lys	Pro	Cys	Glu
						820				825					830
Glu	Gln	Tyr	Gly	Ser	Thr	Tyr	Arg	Cys	Val	Ser	Val	Leu	Thr	Val	Leu
						835									840
His	Gln	Asp	Trp	Leu	Asn	Gly	Lys	Glu	Tyr	Lys	Cys	Lys	Val	Ser	Asn
						850									855
Lys	Ala	Leu	Pro	Ala	Pro	Ile	Glu	Lys	Thr	Ile	Ser	Lys	Ala	Lys	Gly
865						870									875
Gln	Pro	Arg	Glu	Pro	Gln	Val	Tyr	Thr	Leu	Pro	Pro	Ser	Arg	Glu	Glu
						885									890
Met	Thr	Lys	Asn	Gln	Val	Ser	Leu	Thr	Cys	Leu	Val	Lys	Gly	Phe	Tyr
						900									905
Pro	Ser	Asp	Ile	Ala	Val	Glu	Trp	Glu	Ser	Asn	Gly	Gln	Pro	Glu	Asn
						915									920
Asn	Tyr	Lys	Thr	Thr	Pro	Pro	Val	Leu	Asp	Ser	Asp	Gly	Ser	Phe	Phe
						930									935
Leu	Tyr	Ser	Lys	Leu	Thr	Val	Asp	Lys	Ser	Arg	Trp	Gln	Gln	Gly	Asn
945						950									955
Val	Phe	Ser	Cys	Ser	Val	Met	His	Glu	Ala	Leu	His	Asn	His	Tyr	Thr
						965									970
Gln	Lys	Ser	Leu	Ser	Leu	Ser	Pro	Gly	Lys						
						980									985

<210> 167

<211> 498

<212> PRT

<213> 人工序列

<220>

<223> 抗PSMA IC20双特异性分子PM76-B10.17

<400> 167

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

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

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

Val Leu

<210> 168

<211> 5

<212> PRT

<213> 人工序列

<220>

<223> 抗C1dn 18.2 VH CDR1 CL-1和CL-2

<400> 168

Gly Tyr Tyr Met His

1

5

<210> 169

<211> 17

<212> PRT

<213> 人工序列

<220>

<223> 抗C1dn18.2 VH CDR2

<400> 169

Trp Ile Asn Pro Asn Ser Gly Gly Thr Lys Tyr Ala Gln Lys Phe Gln

1

5

10

15

Gly

<210> 170

<211> 16

<212> PRT

<213> 人工序列

<220>

<223> 抗C1dn18.2 VH CDR3

<400> 170

Asp Arg Ile Thr Val Ala Gly Thr Tyr Tyr Tyr Tyr Gly Met Asp Val

1

5

10

15

<210> 171

<211> 11

<212> PRT

<213> 人工序列

<220>

<223> 抗C1dn18.2 VL CDR1

<400> 171

Arg Ala Ser Gln Gly Val Asn Asn Trp Leu Ala

1

5

10

<210> 172

<211> 7

<212> PRT

<213> 人工序列

<220>

<223> 抗C1dn18.2 VL CDR2

<400> 172

Thr Ala Ser Ser Leu Gln Ser

1

5

<210> 173

<211> 9

<212> PRT

<213> 人工序列

<220>

<223> 抗C1dn18.2 VL CDR3

<400> 173

Gln Gln Ala Asn Ser Phe Pro Ile Thr

1

5

<210> 174

<211> 125

<212> PRT

<213> 人工序列

<220>

<223> 抗Cldn18.2 VH 抗CL-1

<400> 174

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

<210> 175

<211> 107

<212> PRT

<213> 人工序列

<220>

<223> 抗Cldn18.2 VL CL-1

<400> 175

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

<210> 176

<211> 247

<212> PRT

<213> 人工序列

<220>

<223> 抗Cldn18.2 scFv CL-1

<400> 176

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

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<210> 177

<211> 502

<212> PRT

<213> 人工序列

<220>

<223> 抗Clon 18.2xCD3双特异性分子CL-1 xI2C

<400> 177

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

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

<210> 178

<211> 990

<212> PRT

<213> 人工序列

<220>

<223> 抗Clon 18.2xCD3双特异性scFc分子CL-1 xI2C-scFc

<400> 178

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

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

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

930				935				940							
Gly	Ser	Phe	Phe	Leu	Tyr	Ser	Lys	Leu	Thr	Val	Asp	Lys	Ser	Arg	Trp
945				950				955				960			
Gln	Gln	Gly	Asn	Val	Phe	Ser	Cys	Ser	Val	Met	His	Glu	Ala	Leu	His
				965				970				975			
Asn	His	Tyr	Thr	Gln	Lys	Ser	Leu	Ser	Leu	Ser	Pro	Gly	Lys		
980								985				990			

<210> 179

<211> 125

<212> PRT

〈213〉 人工序列

 $\langle 220 \rangle$

〈223〉 抗C1dn18.2 VH CL-2

<400> 179

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

 $\langle 210 \rangle$ 180

<211> 107

<212> PRT

〈213〉 人工序列

 $\langle 220 \rangle$

〈223〉 抗C1dn18.2 VL CL-2

 $\langle 400 \rangle$ 180

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

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

<210> 181

<211> 247

<212> PRT

<213> 人工序列

<220>

<223> 抗Cldn18.2 scFv CL-2

<400> 181

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

Ile Thr Cys Arg Ala Ser Gln Gly Val Asn Asn Trp Leu Ala Trp Tyr
 165 170 175
 Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Thr Ala Ser
 180 185 190
 Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly
 195 200 205
 Thr Asp Phe Thr Leu Thr Ile Arg Ser Leu Gln Pro Glu Asp Phe Ala
 210 215 220
 Thr Tyr Tyr Cys Gln Gln Ala Asn Ser Phe Pro Ile Thr Phe Gly Cys
 225 230 235 240
 Gly Thr Arg Leu Glu Ile Lys
 245

<210> 182

<211> 502

<212> PRT

<213> 人工序列

<220>

<223> 抗C1dn18.2xCD3双特异性分子CL-2xI2C

<400> 182

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

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

465	470	475	480
Tyr Tyr Cys Val Leu Trp Tyr Ser Asn Arg Trp Val Phe Gly Gly Gly			
	485	490	495
Thr Lys Leu Thr Val Leu			
500			
<210> 183			
<211> 990			
<212> PRT			
<213> 人工序列			
<220>			
<223> 抗Clon18.2xCD3双特异性scFc分子CL-2xI2C-scFc			
<400> 183			
Gln Val Gln Met Val Gln Ser Gly Ala Glu Val Lys Lys His Gly Ala			
1 5 10 15			
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Gly Tyr			
20 25 30			
Tyr Met His Trp Val Arg Gln Ala Pro Gly Gln Cys Leu Glu Trp Met			
35 40 45			
Gly Trp Ile Asn Pro Asn Ser Gly Gly Thr Lys Tyr Ala Gln Lys Phe			
50 55 60			
Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr			
65 70 75 80			
Met Glu Leu Ser Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys			
85 90 95			
Ala Arg Asp Arg Ile Thr Val Ala Gly Thr Tyr Tyr Tyr Tyr Gly Met			
100 105 110			
Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly			
115 120 125			
Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Gln Met			
130 135 140			
Thr Gln Ser Pro Ser Ser Val Ser Ala Ser Val Gly Asp Arg Val Thr			
145 150 155 160			
Ile Thr Cys Arg Ala Ser Gln Gly Val Asn Asn Trp Leu Ala Trp Tyr			
165 170 175			
Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Thr Ala Ser			
180 185 190			
Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly			
195 200 205			
Thr Asp Phe Thr Leu Thr Ile Arg Ser Leu Gln Pro Glu Asp Phe Ala			

210	215	220
Thr Tyr Tyr Cys Gln Gln Ala Asn Ser Phe Pro Ile Thr Phe Gly Cys		
225	230	235
Gly Thr Arg Leu Glu Ile Lys Ser Gly Gly Gly Gly Ser Glu Val Gln		240
	245	250
Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Lys		255
	260	265
Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Lys Tyr Ala Met Asn		270
	275	280
Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Arg Ile		285
290	295	300
Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp Ser Val Lys		
305	310	315
Asp Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr Ala Tyr Leu		320
	325	330
Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr Tyr Cys Val		335
	340	345
Arg His Gly Asn Phe Gly Asn Ser Tyr Ile Ser Tyr Trp Ala Tyr Trp		
355	360	365
Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly		
370	375	380
Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Thr Val Val Thr Gln Glu		
385	390	395
Pro Ser Leu Thr Val Ser Pro Gly Gly Thr Val Thr Leu Thr Cys Gly		400
	405	410
Ser Ser Thr Gly Ala Val Thr Ser Gly Asn Tyr Pro Asn Trp Val Gln		415
	420	425
Gln Lys Pro Gly Gln Ala Pro Arg Gly Leu Ile Gly Gly Thr Lys Phe		
435	440	445
Leu Ala Pro Gly Thr Pro Ala Arg Phe Ser Gly Ser Leu Leu Gly Gly		
450	455	460
Lys Ala Ala Leu Thr Leu Ser Gly Val Gln Pro Glu Asp Glu Ala Glu		
465	470	475
Tyr Tyr Cys Val Leu Trp Tyr Ser Asn Arg Trp Val Phe Gly Gly Gly		480
	485	490
Thr Lys Leu Thr Val Leu Gly Gly Gly Gly Asp Lys Thr His Thr Cys		495
	500	505
Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu		510
515	520	525

Phe	Pro	Pro	Lys	Pro	Lys	Asp	Thr	Leu	Met	Ile	Ser	Arg	Thr	Pro	Glu
530						535					540				
Val	Thr	Cys	Val	Val	Val	Asp	Val	Ser	His	Glu	Asp	Pro	Glu	Val	Lys
545					550					555					560
Phe	Asn	Trp	Tyr	Val	Asp	Gly	Val	Glu	Val	His	Asn	Ala	Lys	Thr	Lys
				565					570					575	
Pro	Cys	Glu	Glu	Gln	Tyr	Gly	Ser	Thr	Tyr	Arg	Cys	Val	Ser	Val	Leu
			580					585					590		
Thr	Val	Leu	His	Gln	Asp	Trp	Leu	Asn	Gly	Lys	Glu	Tyr	Lys	Cys	Lys
	595						600					605			
Val	Ser	Asn	Lys	Ala	Leu	Pro	Ala	Pro	Ile	Glu	Lys	Thr	Ile	Ser	Lys
	610					615					620				
Ala	Lys	Gly	Gln	Pro	Arg	Glu	Pro	Gln	Val	Tyr	Thr	Leu	Pro	Pro	Ser
625					630					635					640
Arg	Glu	Glu	Met	Thr	Lys	Asn	Gln	Val	Ser	Leu	Thr	Cys	Leu	Val	Lys
				645					650					655	
Gly	Phe	Tyr	Pro	Ser	Asp	Ile	Ala	Val	Glu	Trp	Glu	Ser	Asn	Gly	Gln
			660					665					670		
Pro	Glu	Asn	Asn	Tyr	Lys	Thr	Thr	Pro	Pro	Val	Leu	Asp	Ser	Asp	Gly
	675						680					685			
Ser	Phe	Phe	Leu	Tyr	Ser	Lys	Leu	Thr	Val	Asp	Lys	Ser	Arg	Trp	Gln
	690					695					700				
Gln	Gly	Asn	Val	Phe	Ser	Cys	Ser	Val	Met	His	Glu	Ala	Leu	His	Asn
705					710					715					720
His	Tyr	Thr	Gln	Lys	Ser	Leu	Ser	Leu	Ser	Pro	Gly	Lys	Gly	Gly	Gly
			725						730				735		
Gly	Ser	Gly	Gly	Gly	Gly	Ser	Gly	Gly	Gly	Gly	Ser	Gly	Gly	Gly	Gly
			740					745				750			
Ser	Gly	Gly	Gly	Gly	Ser	Gly	Gly	Gly	Gly	Ser	Asp	Lys	Thr	His	Thr
	755						760				765				
Cys	Pro	Pro	Cys	Pro	Ala	Pro	Glu	Leu	Leu	Gly	Gly	Pro	Ser	Val	Phe
	770					775					780				
Leu	Phe	Pro	Pro	Lys	Pro	Lys	Asp	Thr	Leu	Met	Ile	Ser	Arg	Thr	Pro
785					790					795					800
Glu	Val	Thr	Cys	Val	Val	Val	Asp	Val	Ser	His	Glu	Asp	Pro	Glu	Val
				805						810				815	
Lys	Phe	Asn	Trp	Tyr	Val	Asp	Gly	Val	Glu	Val	His	Asn	Ala	Lys	Thr
			820						825				830		
Lys	Pro	Cys	Glu	Glu	Gln	Tyr	Gly	Ser	Thr	Tyr	Arg	Cys	Val	Ser	Val

835	840	845
Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys		
850	855	860
Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser		
865	870	875
Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro		
885	890	895
Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val		
900	905	910
Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly		
915	920	925
Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp		
930	935	940
Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp		
945	950	955
Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His		
965	970	975
Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys		
980	985	990

<210> 184

<211> 5

<212> PRT

<213> 人工序列

<220>

<223> 抗MUC17 VH CDR1 MU 8-B7

<400> 184

Gly Tyr Tyr Trp Ser

1 5

<210> 185

<211> 16

<212> PRT

<213> 人工序列

<220>

<223> 抗MUC17 VH CDR2 MU 8-B7

<400> 185

Asp Ile Asp Ala Ser Gly Ser Thr Lys Tyr Asn Pro Ser Leu Lys Ser

1 5 10 15

<210> 186

<211> 12

<212> PRT

<213> 人工序列

<220>

<223> 抗MUC17 VH CDR3 MU 8-B7

<400> 186

Lys Lys Tyr Ser Thr Val Trp Ser Tyr Phe Asp Asn

1 5 10

<210> 187

<211> 11

<212> PRT

<213> 人工序列

<220>

<223> 抗MUC17 VL CDR1 MU 8-B7

<400> 187

Ser Gly Asp Lys Leu Gly Asp Lys Tyr Ala Ser

1 5 10

<210> 188

<211> 7

<212> PRT

<213> 人工序列

<220>

<223> 抗MUC17 VL CDR2 MU 8-B7

<400> 188

Gln Asp Arg Lys Arg Pro Ser

1 5

<210> 189

<211> 9

<212> PRT

<213> 人工序列

<220>

<223> 抗MUC17 VL CDR3 MU 8-B7

<400> 189

Gln Ala Trp Gly Ser Ser Thr Ala Val

1 5

<210> 190

<211> 120

<212> PRT

<213> 人工序列

<220>

<223> 抗MUC17 VH MU 8-B7

<400> 190

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

<210> 191

<211> 106

<212> PRT

<213> 人工序列

<220>

<223> 抗MUC17 VL MU 8-B7

<400> 191

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

<210> 192

<211> 984

<212> PRT

<213> 人工序列

<220>

<223>双特异性分子MU 8-B7 x I2C0scFc

<400> 192

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

Gly Leu Val Gln Pro Gly Gly Ser Leu Lys Leu Ser Cys Ala Ala Ser		
260	265	270
Gly Phe Thr Phe Asn Lys Tyr Ala Met Asn Trp Val Arg Gln Ala Pro		
275	280	285
Gly Lys Gly Leu Glu Trp Val Ala Arg Ile Arg Ser Lys Tyr Asn Asn		
290	295	300
Tyr Ala Thr Tyr Tyr Ala Asp Ser Val Lys Asp Arg Phe Thr Ile Ser		
305	310	315
Arg Asp Asp Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn Asn Leu Lys		
325	330	335
Thr Glu Asp Thr Ala Val Tyr Tyr Cys Val Arg His Gly Asn Phe Gly		
340	345	350
Asn Ser Tyr Ile Ser Tyr Trp Ala Tyr Trp Gly Gln Gly Thr Leu Val		
355	360	365
Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly		
370	375	380
Gly Gly Ser Gln Thr Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser		
385	390	395
Pro Gly Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val		
405	410	415
Thr Ser Gly Asn Tyr Pro Asn Trp Val Gln Gln Lys Pro Gly Gln Ala		
420	425	430
Pro Arg Gly Leu Ile Gly Gly Thr Lys Phe Leu Ala Pro Gly Thr Pro		
435	440	445
Ala Arg Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Leu		
450	455	460
Ser Gly Val Gln Pro Glu Asp Glu Ala Glu Tyr Tyr Cys Val Leu Trp		
465	470	475
Tyr Ser Asn Arg Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu		
485	490	495
Gly Gly Gly Gly Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro		
500	505	510
Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys		
515	520	525
Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val		
530	535	540
Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp		
545	550	555
Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Cys Glu Glu Gln Tyr		

				565					570					575			
Gly	Ser	Thr	Tyr	Arg	Cys	Val	Ser	Val	Leu	Thr	Val	Leu	His	Gln	Asp		
				580					585					590			
Trp	Leu	Asn	Gly	Lys	Glu	Tyr	Lys	Cys	Lys	Val	Ser	Asn	Lys	Ala	Leu		
				595					600					605			
Pro	Ala	Pro	Ile	Glu	Lys	Thr	Ile	Ser	Lys	Ala	Lys	Gly	Gln	Pro	Arg		
				610					615					620			
Glu	Pro	Gln	Val	Tyr	Thr	Leu	Pro	Pro	Ser	Arg	Glu	Glu	Met	Thr	Lys		
625						630				635					640		
Asn	Gln	Val	Ser	Leu	Thr	Cys	Leu	Val	Lys	Gly	Phe	Tyr	Pro	Ser	Asp		
				645					650					655			
Ile	Ala	Val	Glu	Trp	Glu	Ser	Asn	Gly	Gln	Pro	Glu	Asn	Asn	Tyr	Lys		
				660					665					670			
Thr	Thr	Pro	Pro	Val	Leu	Asp	Ser	Asp	Gly	Ser	Phe	Phe	Leu	Tyr	Ser		
				675					680					685			
Lys	Leu	Thr	Val	Asp	Lys	Ser	Arg	Trp	Gln	Gln	Gly	Asn	Val	Phe	Ser		
				690					695					700			
Cys	Ser	Val	Met	His	Glu	Ala	Leu	His	Asn	His	Tyr	Thr	Gln	Lys	Ser		
705						710				715					720		
Leu	Ser	Leu	Ser	Pro	Gly	Lys	Gly	Gly	Gly	Gly	Ser	Gly	Gly	Gly	Gly		
				725					730					735			
Ser	Gly	Gly	Gly	Gly	Ser	Gly	Gly	Gly	Gly	Ser	Gly	Gly	Gly	Gly	Ser		
				740					745					750			
Gly	Gly	Gly	Gly	Ser	Asp	Lys	Thr	His	Thr	Cys	Pro	Pro	Cys	Pro	Ala		
				755					760					765			
Pro	Glu	Leu	Leu	Gly	Gly	Pro	Ser	Val	Phe	Leu	Phe	Pro	Pro	Lys	Pro		
				770					775					780			
Lys	Asp	Thr	Leu	Met	Ile	Ser	Arg	Thr	Pro	Glu	Val	Thr	Cys	Val	Val		
785						790				795					800		
Val	Asp	Val	Ser	His	Glu	Asp	Pro	Glu	Val	Lys	Phe	Asn	Trp	Tyr	Val		
				805					810					815			
Asp	Gly	Val	Glu	Val	His	Asn	Ala	Lys	Thr	Lys	Pro	Cys	Glu	Glu	Gln		
				820					825					830			
Tyr	Gly	Ser	Thr	Tyr	Arg	Cys	Val	Ser	Val	Leu	Thr	Val	Leu	His	Gln		
				835					840					845			
Asp	Trp	Leu	Asn	Gly	Lys	Glu	Tyr	Lys	Cys	Lys	Val	Ser	Asn	Lys	Ala		
				850					855					860			
Leu	Pro	Ala	Pro	Ile	Glu	Lys	Thr	Ile	Ser	Lys	Ala	Lys	Gly	Gln	Pro		
865						870				875					880		

Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr
 885 890 895
 Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser
 900 905 910
 Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr
 915 920 925
 Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr
 930 935 940
 Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe
 945 950 955 960
 Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys
 965 970 975
 Ser Leu Ser Leu Ser Pro Gly Lys
 980

<210> 193

<211> 14

<212> PRT

<213> 人工序列

<220>

<223> I2C的CDR-L1

<400> 193

Gly Ser Ser Thr Gly Ala Val Thr Ser Gly Asn Tyr Pro Asn
 1 5 10

<210> 194

<211> 7

<212> PRT

<213> 人工序列

<220>

<223> I2C的CDR-L2

<400> 194

Gly Thr Lys Phe Leu Ala Pro
 1 5

<210> 195

<211> 9

<212> PRT

<213> 人工序列

<220>

<223> I2C的CDR-L3

<400> 195

Val Leu Trp Tyr Ser Asn Arg Trp Val

1 5

<210> 196

<211> 5

<212> PRT

<213> 人工序列

<220>

<223> I2C的CDR-H1

<400> 196

Lys Tyr Ala Met Asn

1 5

<210> 197

<211> 19

<212> PRT

<213> 人工序列

<220>

<223> I2C的CDR-H2

<400> 197

Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp Ser

1 5 10 15

Val Lys Asp

<210> 198

<211> 14

<212> PRT

<213> 人工序列

<220>

<223> I2C的CDR-H3

<400> 198

His Gly Asn Phe Gly Asn Ser Tyr Ile Ser Tyr Trp Ala Tyr

1 5 10

<210> 199

<211> 125

<212> PRT

<213> 人工序列

<220>

<223> I2C的VH

<400> 199

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly

1 5 10 15

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

<210> 200

<211> 109

<212> PRT

<213> 人工序列

<220>

<223> I2C的VL

<400> 200

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

<210> 201

<211> 249

<212> PRT

<213> 人工序列

<220>

<223> I2C的VH-VL

<400> 201

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

用于测量蛋白与固体表面结合的测定的示意图
荧光团标记的双特异性抗体

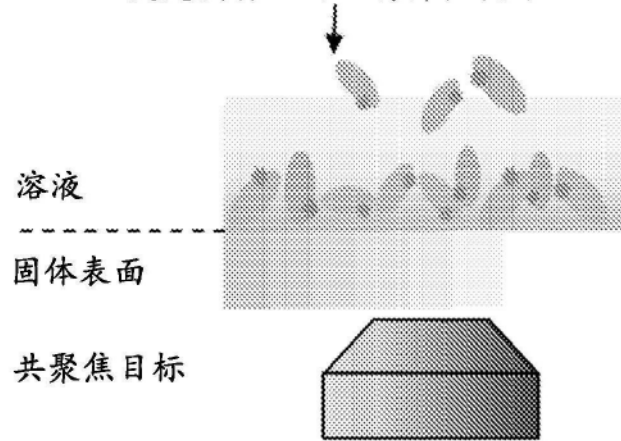


图1

在不存在表面活性剂的情况下蛋白与固体表面结合

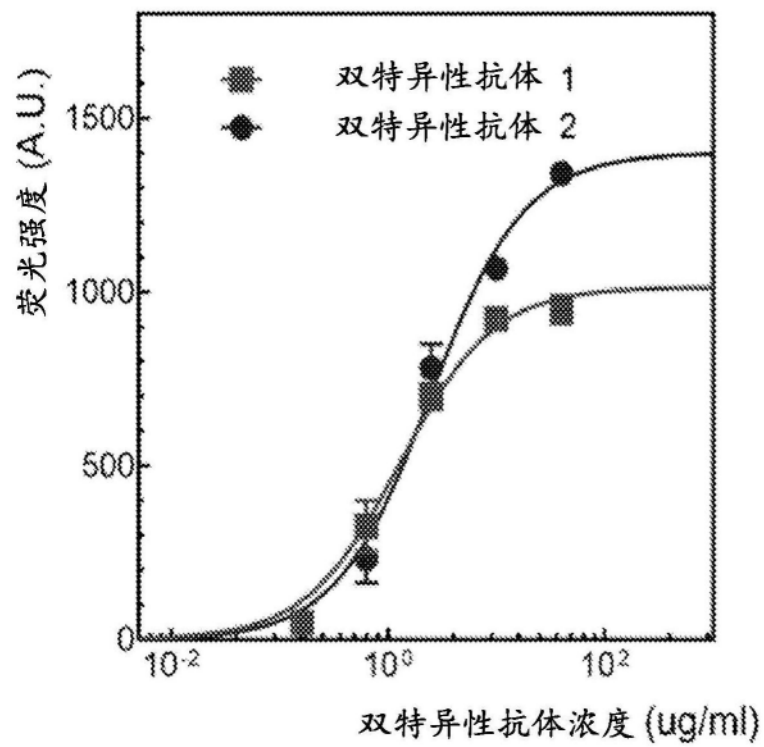
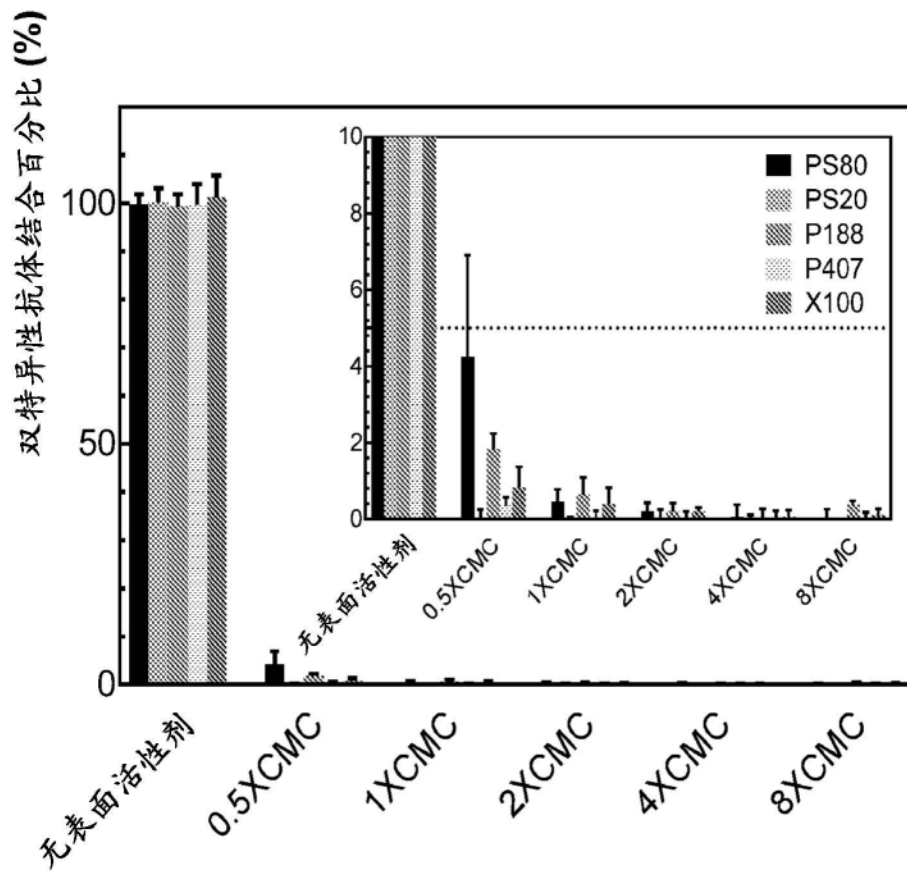


图2

不同表面活性剂的筛选



在添加蛋白之前向固体表面添加表面活性剂更有效地防止蛋白结合

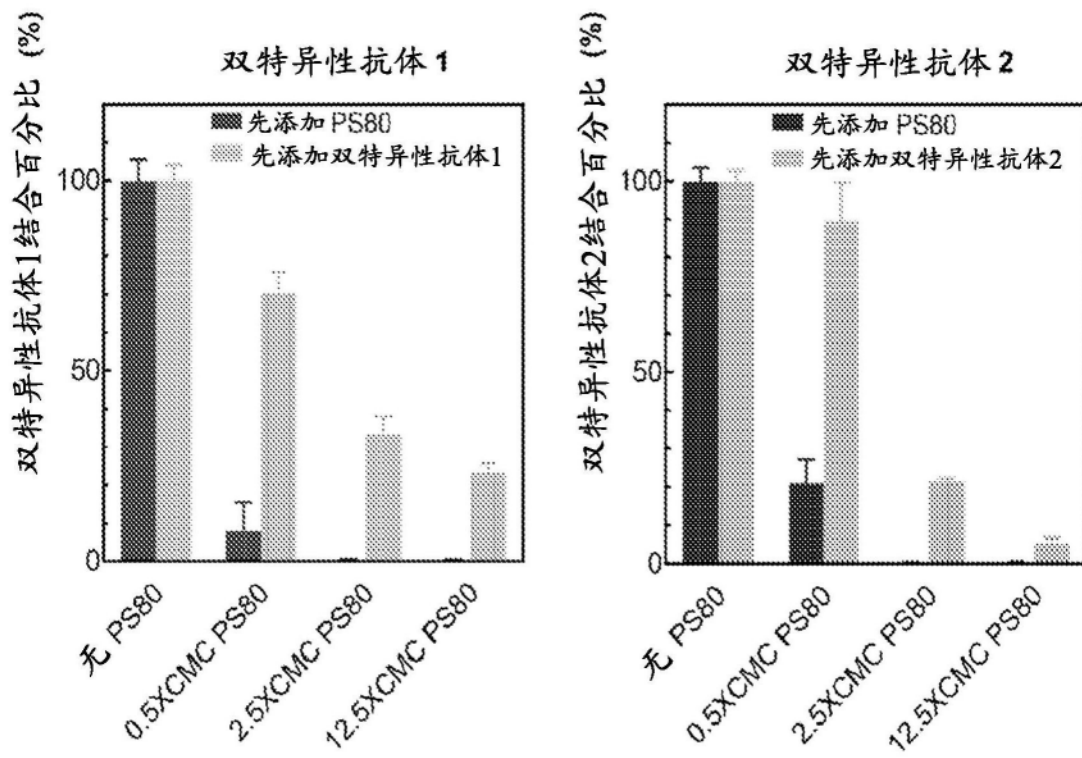


图4

相同浓度的不同表面活性剂对DEHP浸出的影响

0.3 wt%

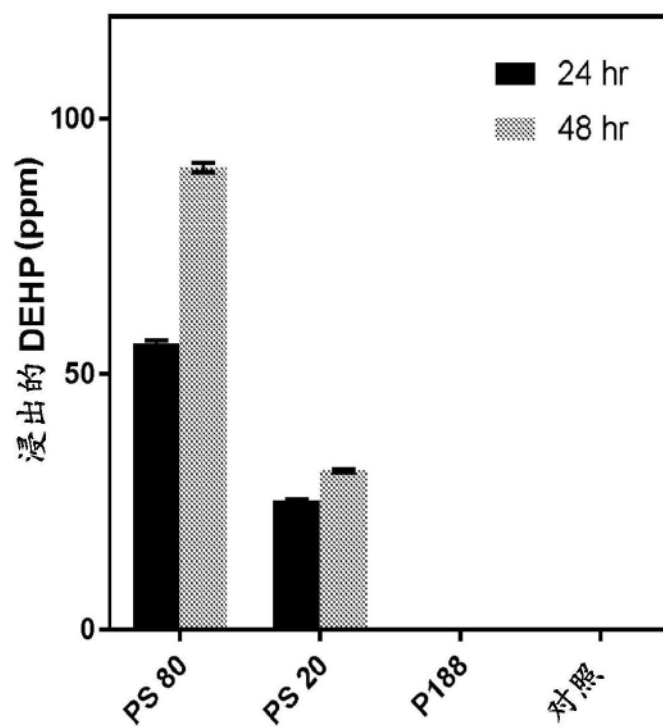


图5

比较CMC的相同倍数的不同表面活性剂在24小时内对DEHP浸出的影响

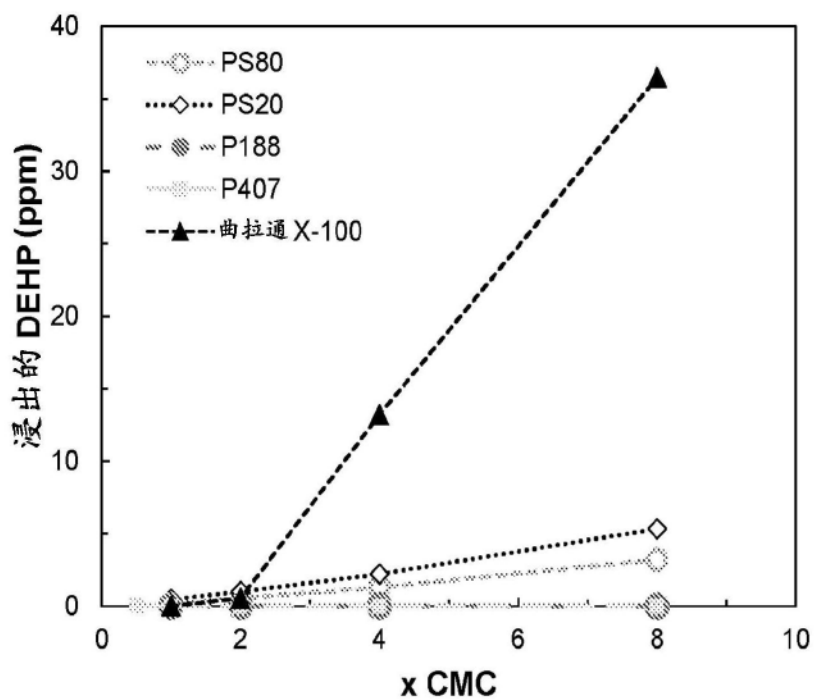


图6