

FIG. 1

PD1 WT 1 *MQIPQAPWPFVVWAVLQLGWRPGWFLDSPDRPWNPTTFSPALLVVTEGDNATFTCSFSNTS*
 PD1 V1 1 *MQIPQAPWPFVVWAVLQLGWRPGWFLDSPDRPWNPTTFSPALLVVTEGDNATFTCSFSNTS*
 PD1 V2 1 *MQIPQAPWPFVVWAVLQLGWRPGWFLDSPDRPWNPTTFSPALLVVTEGDNATFTCSFSNTS*

PD1 WT 61 *ESFVLNWYRMSPSNQTDKLAAFPEDRSQPGQDCRFRVTQLPNGRDFHMSVVRARRNDSGT*
 PD1 V1 61 *EGFVLNWYRMSPSNQTDKLAAFPEDR**QG**LGQDCRFRVTQLPNGRDFHMSVVRARR**S**DSGT*
 PD1 V2 61 *EGFVLNWYRMSPSNQTDKLAAFPEDR**QG**LGQDCRFRVTQLPNGRDFHMSVVRARRNDSGT*

PD1 WT 121 *YLCGAISLAPKAQIKESLRAELRVTERRAEVPTAHPSPSRPAGQFQTLVGGGGS*
 PD1 V1 121 *YLC**SA**IVLAPK**I**QIKESLRVELRVTERRAEVPTAHPSPSRPAGQFQTLVGGGGS*
 PD1 V2 121 *YLC**SA**IVLAPK**I**QIKESLRVELRVTERRAEVPTAHPSPSRPAGQFQTLVGGGGS*

Italic - the signaling peptide domain

Bold - mutated residue

Bold and underlining - mutated N-glycosylation site

Double underlining - Linker

IgG4 S228P 1 *ESKYGPPCP**P**CPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNWY*
 IgG4 S228P 61 *VDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTIK*
 IgG4 S228P 121 *AKGQPREPQVYITLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVL*
 IgG4 S228P 181 *DSDGSFFLYSRLTVDKSRWQEGNVFSCSVMEALHNHYTQKSLSLSLGK*

FIG. 2

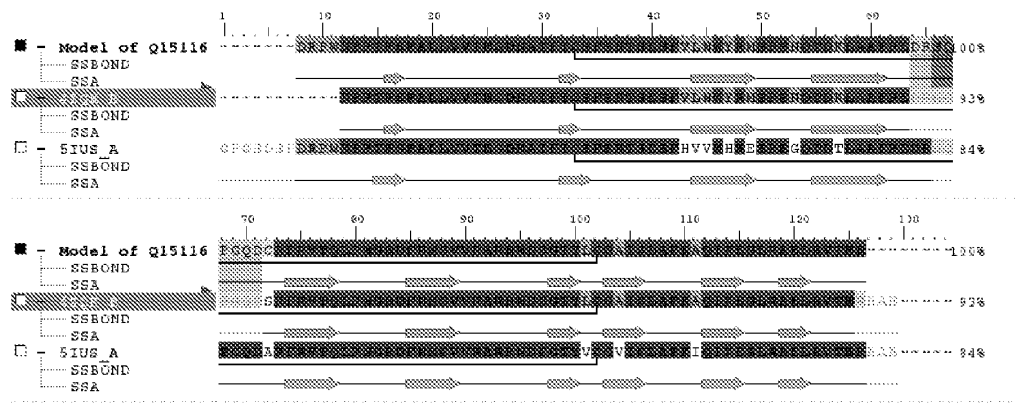


FIG. 3

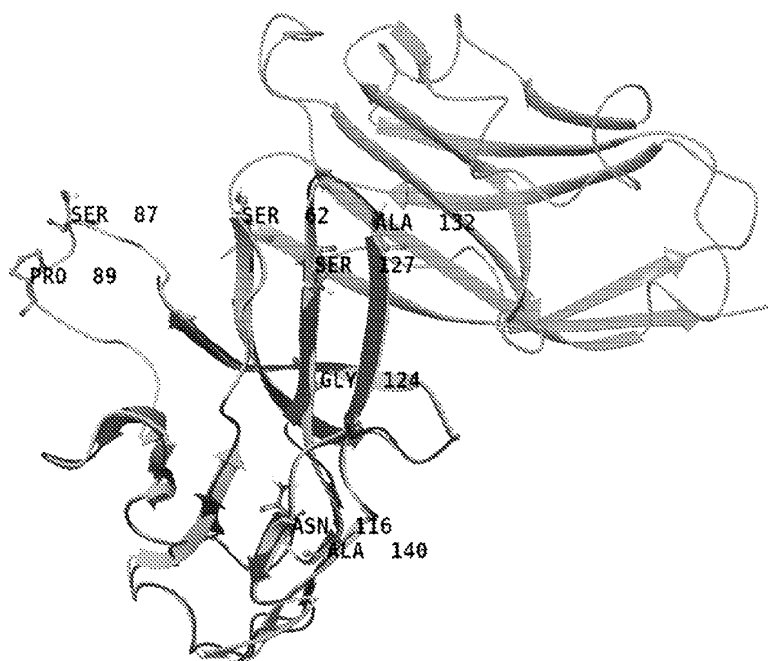


FIG. 4

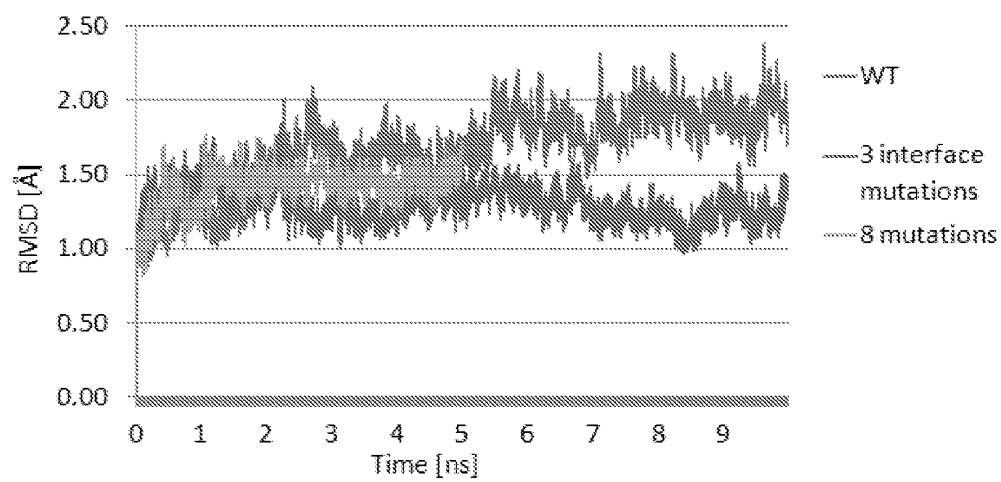


FIG. 5A

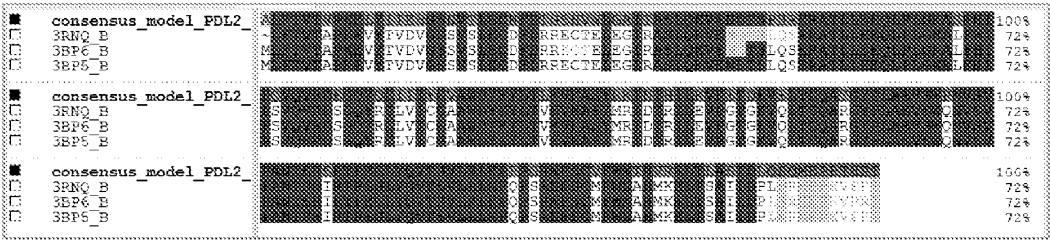


FIG. 5B

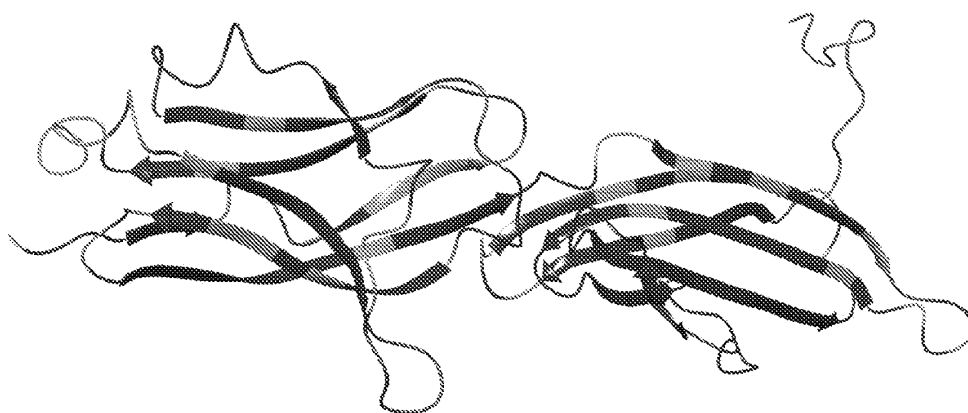


FIG. 6

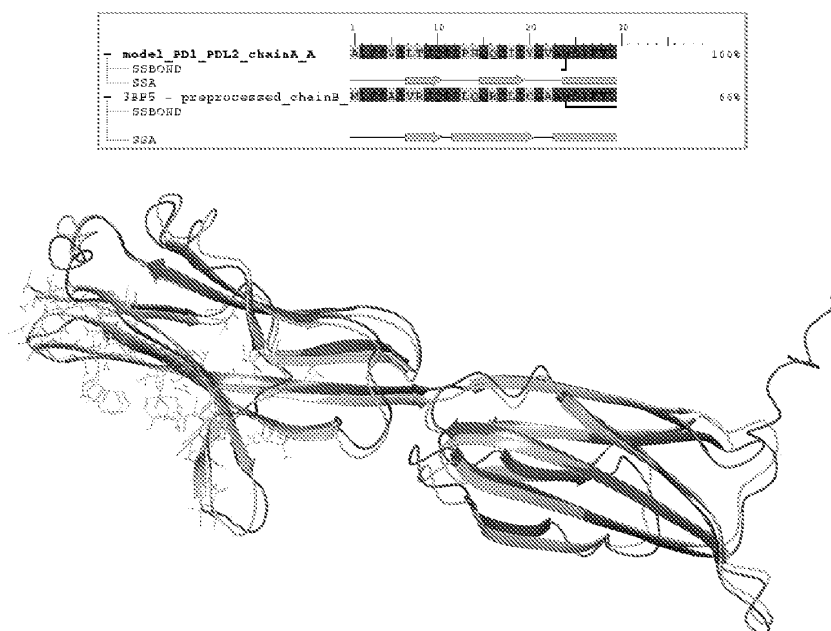


FIG. 7

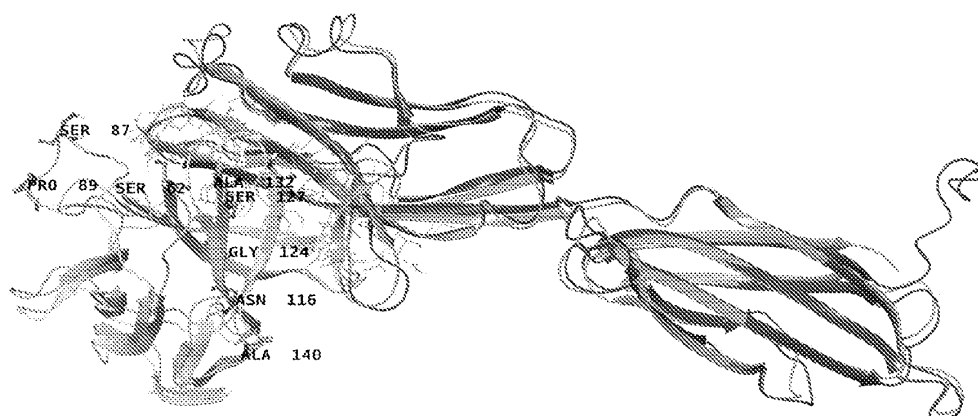


FIG. 8

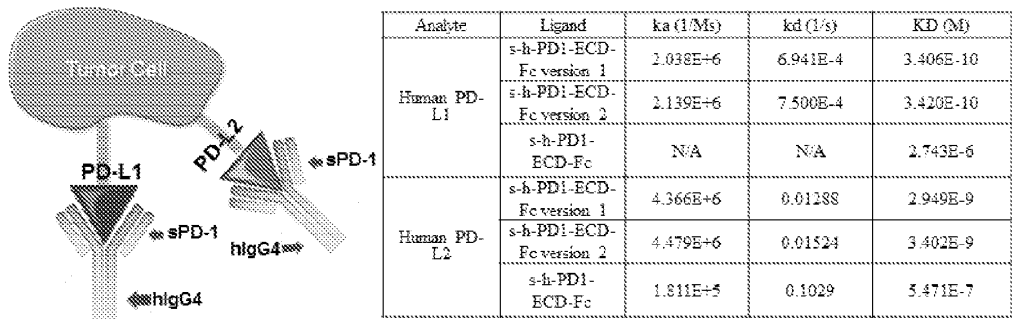


FIG. 9A

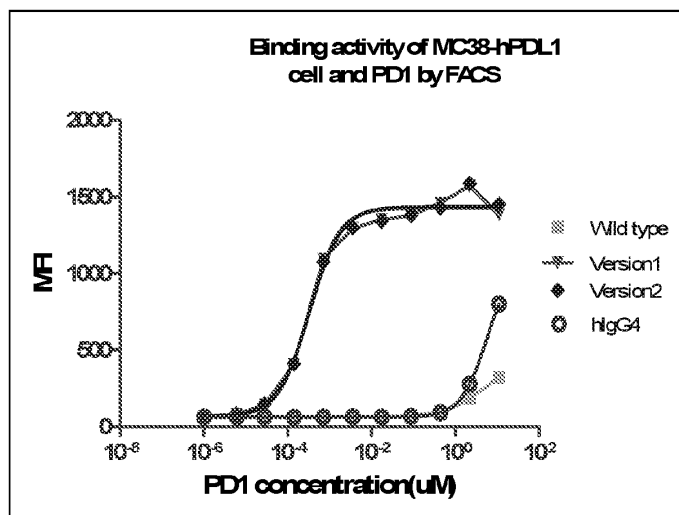


FIG. 9B

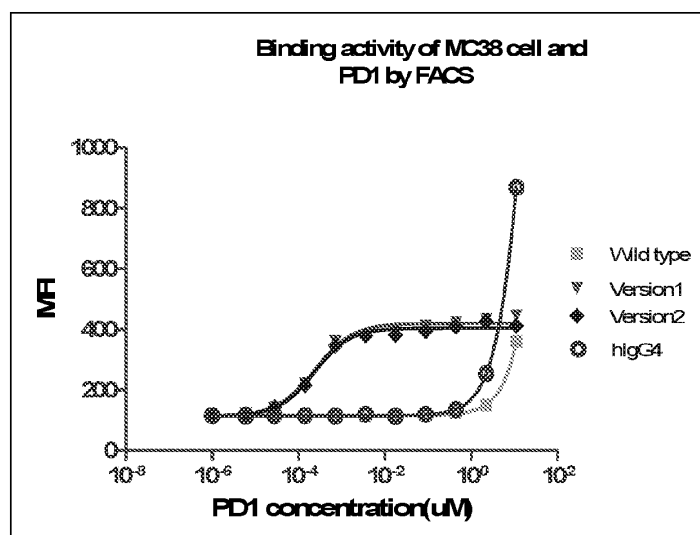


FIG. 10

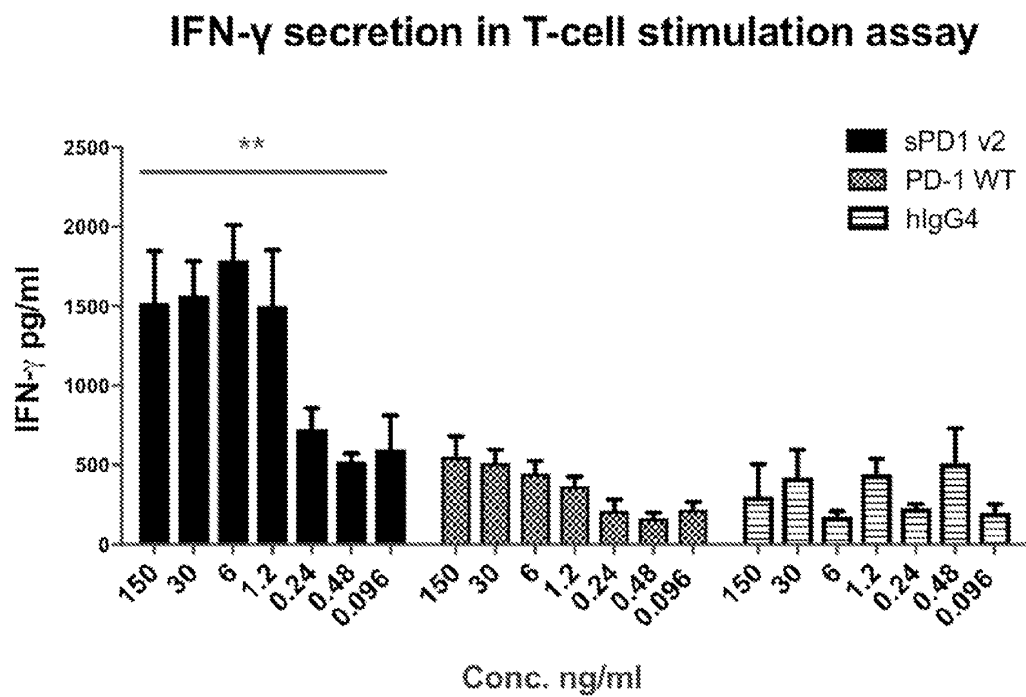


FIG. 11A

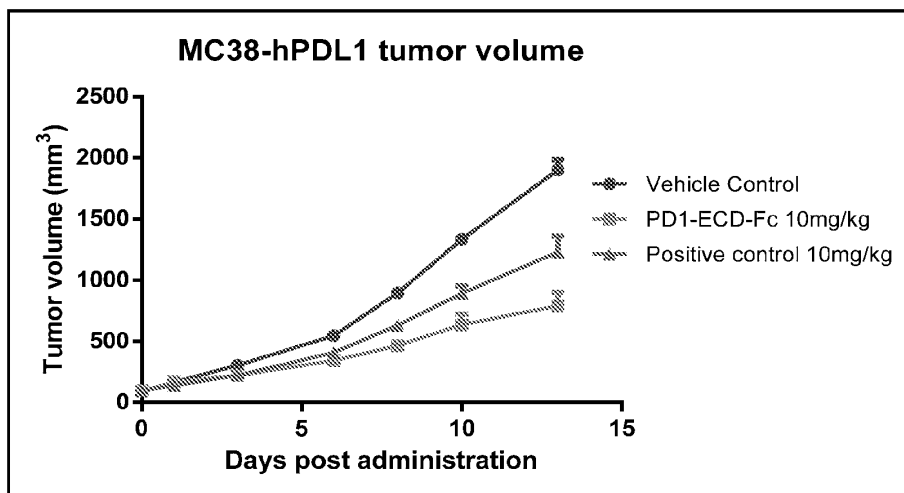


FIG. 11B

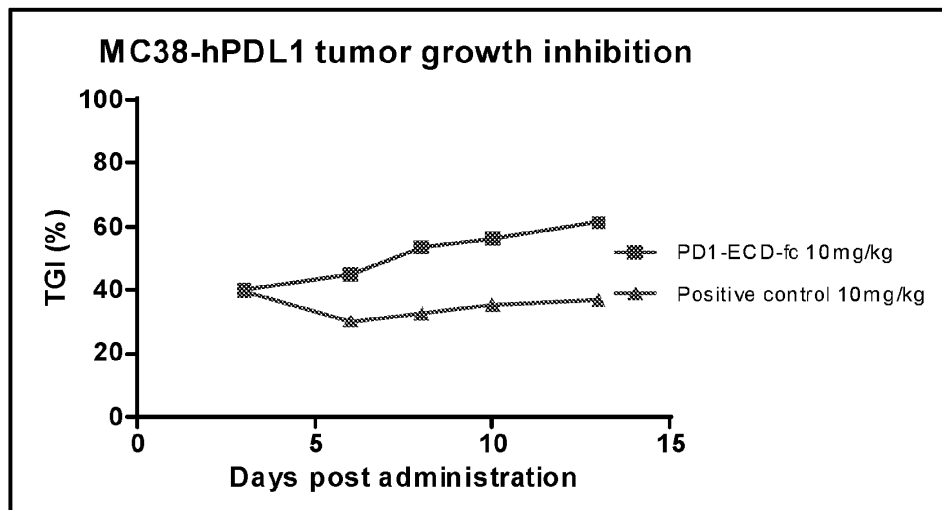


FIG. 11C

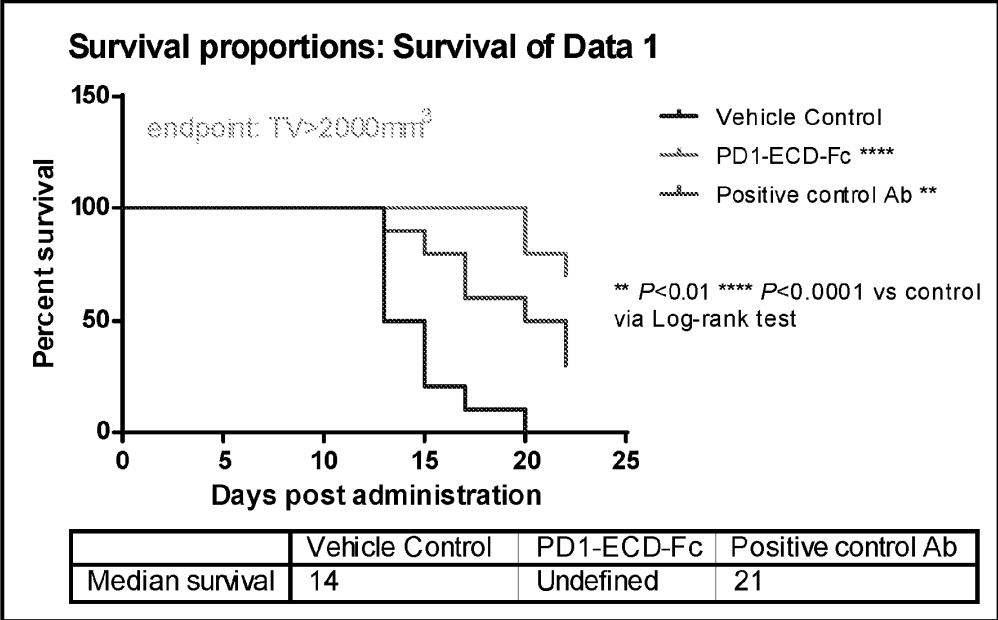


FIG. 11D

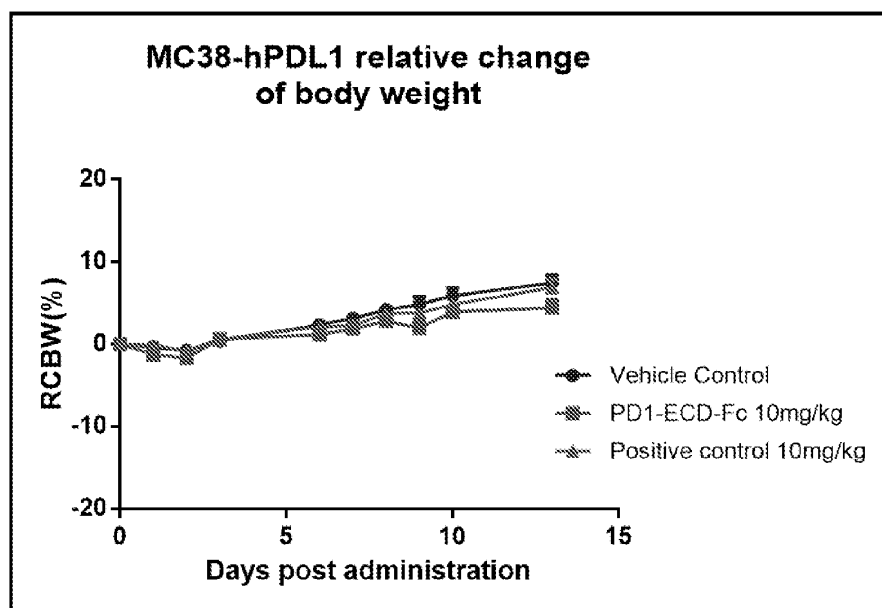


FIG. 12

Hinge sequence of Human IgG1:

EPKSCDKTHTCPPCPAPELLGGP

Hinge sequence of Human IgG2:

ERKCCVECPPCPAPPVAGP

Hinge sequence of Human IgG3:

ELKTPLGDTTHTCPRCPEPKSCDTPPPCPRCPEPKSCDTPPPCPRCPEPKSCDTPPPCPRCP
APEFLGGP

Hinge sequence of Human IgG4:

ESKYGPPCPSCPAPEFLGGP

FIG. 13

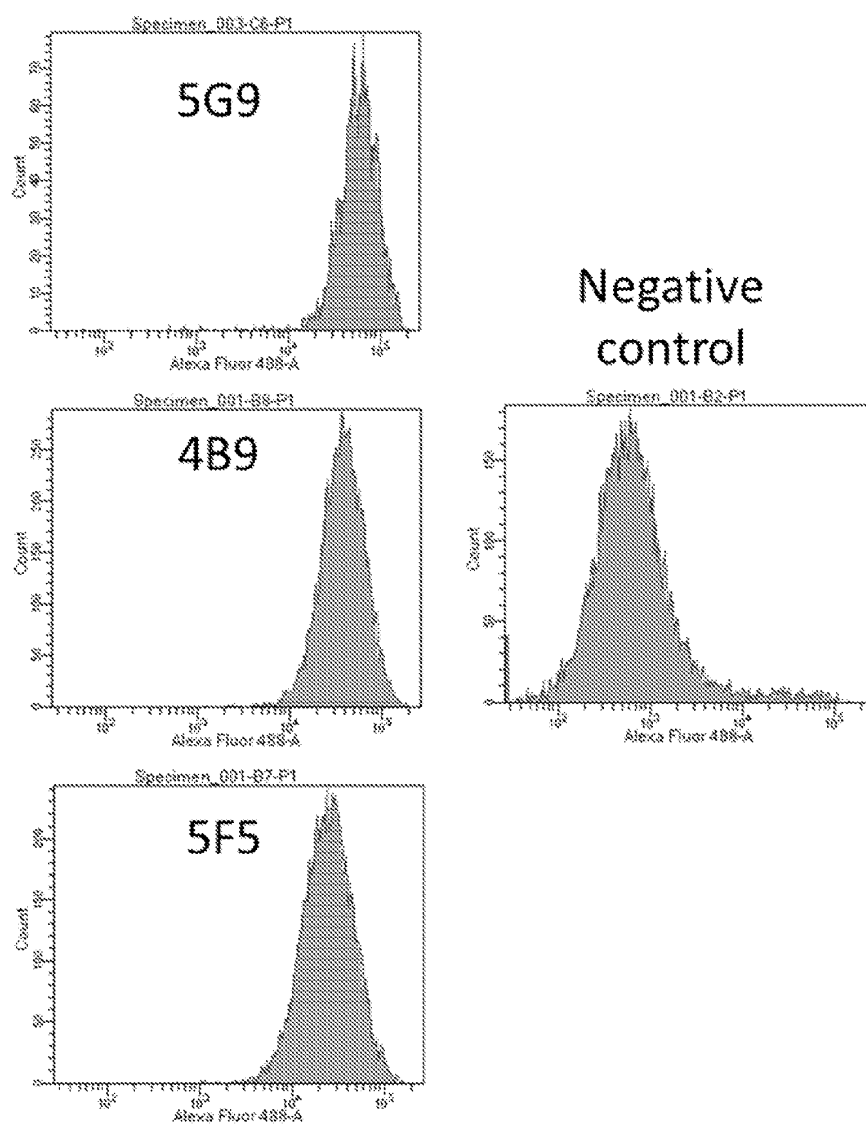


FIG. 14

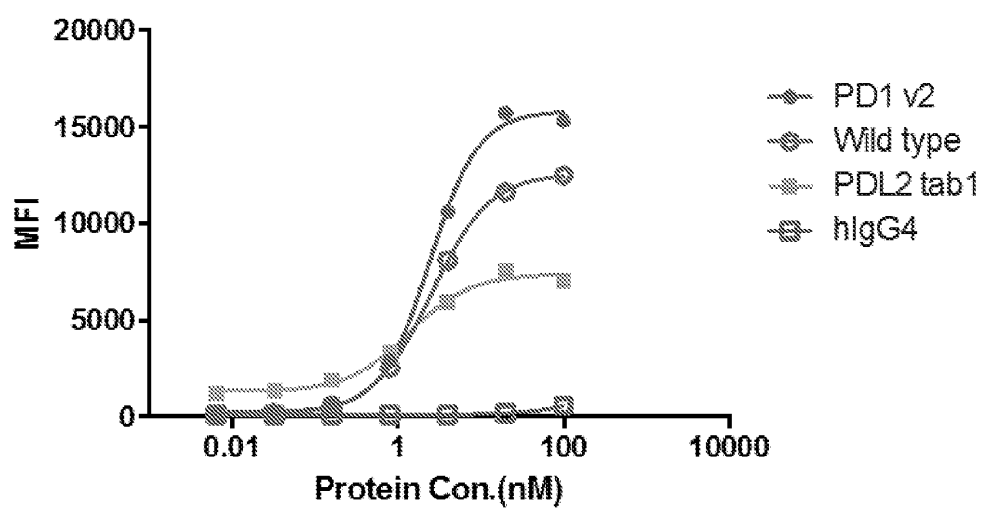


FIG. 15

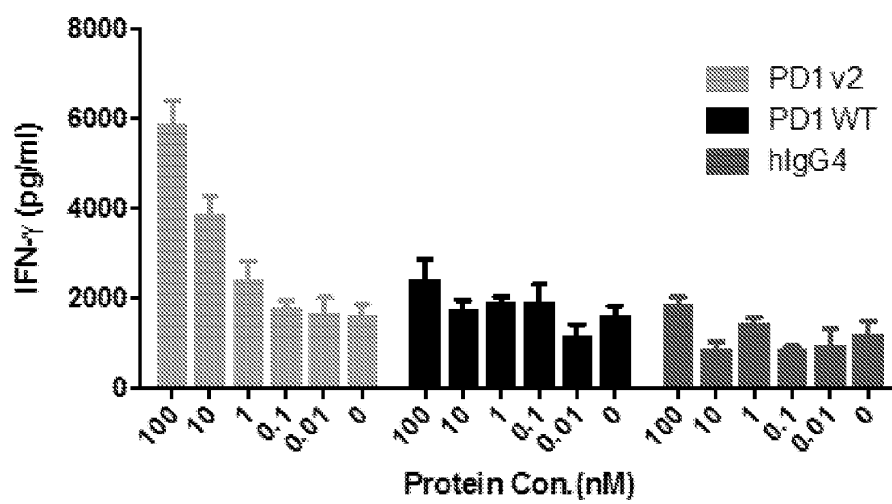


FIG. 16

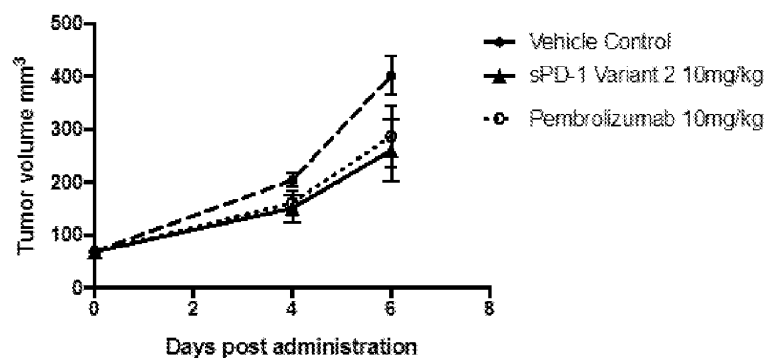


FIG. 17A**1-WT (SEQ ID NO: 11)**

PGWFLDSPDRPWNPPPTFSPALLVVTEGDNATFTCSFSNTSESFVLNWYRMSPSNQTDKLAAFPEDRSQPGQD
CRFRVTQLPNGRDFHMSVVRARRNDSGTYLCGAISLAPKAQIKESLRAELRVTERRAEVPTAHPSPSPRPAG
QFQTLV

2-7 mutations (SEQ ID NO:12)

PGWFLDSPDRPWNPPPTFSPALLVVTEGDNATFTCSFSNTSE**G**FVLNWYRMSPSNQTDKLAAFPEDR**GQLGQ**
DCRFRVTQLPNGRDFHMSVVRARRNDSGTYLC**SAIVLAPKIQIKESLRVELRV**TERRAEVPTAHPSPSPRPAG
QFQTLV

3-1 mutation (SEQ ID NO:13)

PGWFLDSPDRPWNPPPTFSPALLVVTEGDNATFTCSFSNTSE**G**FVLNWYRMSPSNQTDKLAAFPEDRSQPGQ
DCRFRVTQLPNGRDFHMSVVRARRNDSGTYLCGAISLAPKAQIKESLRAELRVTERRAEVPTAHPSPSPRPAG
QFQTLV

4-1 mutation (SEQ ID NO:14)

PGWFLDSPDRPWNPPPTFSPALLVVTEGDNATFTCSFSNTSESFVLNWYRMSPSNQTDKLAAFPEDR**GQPGQ**
DCRFRVTQLPNGRDFHMSVVRARRNDSGTYLCGAISLAPKAQIKESLRAELRVTERRAEVPTAHPSPSPRPAG
QFQTLV

5-1 mutation (SEQ ID NO:15)

PGWFLDSPDRPWNPPPTFSPALLVVTEGDNATFTCSFSNTSESFVLNWYRMSPSNQTDKLAAFPEDRS**QLGQ**
DCRFRVTQLPNGRDFHMSVVRARRNDSGTYLCGAISLAPKAQIKESLRAELRVTERRAEVPTAHPSPSPRPAG
QFQTLV

6-1 mutation (SEQ ID NO:16)

PGWFLDSPDRPWNPPPTFSPALLVVTEGDNATFTCSFSNTSESFVLNWYRMSPSNQTDKLAAFPEDRSQPGQD
CRFRVTQLPNGRDFHMSVVRARRNDSGTYLC**SAISLAPKAQIKESLR**AELRVTERRAEVPTAHPSPSPRPAG
QFQTLV

7-1 mutation (SEQ ID NO:17)

PGWFLDSPDRPWNPPPTFSPALLVVTEGDNATFTCSFSNTSESFVLNWYRMSPSNQTDKLAAFPEDRSQPGQD
CRFRVTQLPNGRDFHMSVVRARRNDSGTYLC**GAIVLAPKAQIKESLR**AELRVTERRAEVPTAHPSPSPRPAG
QFQTLV

8-1 mutation (SEQ ID NO:18)

PGWFLDSPDRPWNPPPTFSPALLVVTEGDNATFTCSFSNTSESFVLNWYRMSPSNQTDKLAAFPEDRSQPGQD
CRFRVTQLPNGRDFHMSVVRARRNDSGTYLCGAISLAPK**IQIKESLR**AELRVTERRAEVPTAHPSPSPRPAG
FQTLV

9-1 mutation (SEQ ID NO:19)

PGWFLDSPDRPWNPPPTFSPALLVVTEGDNATFTCSFSNTSESFVLNWYRMSPSNQTDKLAAFPEDRSQPGQD
CRFRVTQLPNGRDFHMSVVRARRNDSGTYLCGAISLAPKAQIKESL**RVELRV**TERRAEVPTAHPSPSPRPAG
QFQTLV

FIG. 17B**10-2 mutations (SEQ ID NO:20)**

PGWFLDSPDRPWNPTFSPALLVVTEGDNATFTCSFSNTSE**G**FVLNWYRMSPSNQTDKLAAFPEDRG**Q**PGQ
DCRFRVTQLPNGRDFHMSVVRARRNDSGYLCSAISLAPKAQIKESLRAELRVTERRAEVPTAHPSPSPRPA
GQFQTLV

11-2 mutations (SEQ ID NO:21)

PGWFLDSPDRPWNPTFSPALLVVTEGDNATFTCSFSNTSE**G**FVLNWYRMSPSNQTDKLAAFPEDRS**Q**LGG
DCRFRVTQLPNGRDFHMSVVRARRNDSGYLCSAISLAPKAQIKESLRAELRVTERRAEVPTAHPSPSPRPA
GQFQTLV

12-2 mutations (SEQ ID NO:22)

PGWFLDSPDRPWNPTFSPALLVVTEGDNATFTCSFSNTSE**G**FVLNWYRMSPSNQTDKLAAFPEDRS**Q**PGQ
DCRFRVTQLPNGRDFHMSVVRARRNDSGYLCSAISLAPKAQIKESLRAELRVTERRAEVPTAHPSPSPRPA
GQFQTLV

13-2 mutations (SEQ ID NO:23)

PGWFLDSPDRPWNPTFSPALLVVTEGDNATFTCSFSNTSE**G**FVLNWYRMSPSNQTDKLAAFPEDRS**Q**PGQ
DCRFRVTQLPNGRDFHMSVVRARRNDSGYLCSAIVLAPKAQIKESLRAELRVTERRAEVPTAHPSPSPRPA
GQFQTLV

14-2 mutations (SEQ ID NO:24)

PGWFLDSPDRPWNPTFSPALLVVTEGDNATFTCSFSNTSE**G**FVLNWYRMSPSNQTDKLAAFPEDRS**Q**PGQ
DCRFRVTQLPNGRDFHMSVVRARRNDSGYLCSAISLAPK**I**QIKESLRAELRVTERRAEVPTAHPSPSPRPA
GQFQTLV

15-2 mutations (SEQ ID NO:25)

PGWFLDSPDRPWNPTFSPALLVVTEGDNATFTCSFSNTSE**G**FVLNWYRMSPSNQTDKLAAFPEDRS**Q**PGQ
DCRFRVTQLPNGRDFHMSVVRARRNDSGYLCSAISLAPKAQIKESL**R**VELRVTERRAEVPTAHPSPSPRPA
GQFQTLV

16-2 mutations (SEQ ID NO:26)

PGWFLDSPDRPWNPTFSPALLVVTEGDNATFTCSFSNTSE**S**FVLNWYRMSPSNQTDKLAAFPEDR**G**QLGG
DCRFRVTQLPNGRDFHMSVVRARRNDSGYLCSAISLAPKAQIKESLRAELRVTERRAEVPTAHPSPSPRPA
GQFQTLV

17-2 mutations (SEQ ID NO:27)

PGWFLDSPDRPWNPTFSPALLVVTEGDNATFTCSFSNTSE**S**FVLNWYRMSPSNQTDKLAAFPEDR**G**QPGQ
DCRFRVTQLPNGRDFHMSVVRARRNDSGYLCSAISLAPKAQIKESLRAELRVTERRAEVPTAHPSPSPRPA
GQFQTLV

18-2 mutations (SEQ ID NO:28)

PGWFLDSPDRPWNPTFSPALLVVTEGDNATFTCSFSNTSE**S**FVLNWYRMSPSNQTDKLAAFPEDR**G**QPGQ
DCRFRVTQLPNGRDFHMSVVRARRNDSGYLCSAIVLAPKAQIKESLRAELRVTERRAEVPTAHPSPSPRPA
GQFQTLV

FIG. 17C

19-2 mutations (SEQ ID NO:29)

PGWFLDSPDRPWNPTTFSPALLVVTEGDNATFTCSFSNTSESFVLNWYRMSPSNQTDKLAAFPEDRGQPGQ
DCRFRVTQLPNGRDFHMSVVRARRNDSGTYLCSAISLAPKIQIKESLRAELRVTERRAEVPTAHPSPSPRPAG
QFQTLV

20-2 mutations (SEQ ID NO:30)

PGWFLDSPDRPWNPTTFSPALLVVTEGDNATFTCSFSNTSESFVLNWYRMSPSNQTDKLAAFPEDRGQPGQ
DCRFRVTQLPNGRDFHMSVVRARRNDSGTYLCSAISLAPKAQIKESLRVELRVTERRAEVPTAHPSPSPRPAG
QFQTLV

21-2 mutations (SEQ ID NO:31)

PGWFLDSPDRPWNPTTFSPALLVVTEGDNATFTCSFSNTSESFVLNWYRMSPSNQTDKLAAFPEDRSQLGQ
DCRFRVTQLPNGRDFHMSVVRARRNDSGTYLCSAISLAPKAQIKESLRAELRVTERRAEVPTAHPSPSPRPAG
QFQTLV

22-2 mutations (SEQ ID NO:32)

PGWFLDSPDRPWNPTTFSPALLVVTEGDNATFTCSFSNTSESFVLNWYRMSPSNQTDKLAAFPEDRSQLGQ
DCRFRVTQLPNGRDFHMSVVRARRNDSGTYLCSAIVLAPKAQIKESLRAELRVTERRAEVPTAHPSPSPRPAG
QFQTLV

23-2 mutations (SEQ ID NO:33)

PGWFLDSPDRPWNPTTFSPALLVVTEGDNATFTCSFSNTSESFVLNWYRMSPSNQTDKLAAFPEDRSQLGQ
DCRFRVTQLPNGRDFHMSVVRARRNDSGTYLCSAISLAPKIQIKESLRAELRVTERRAEVPTAHPSPSPRPAG
QFQTLV

24-2 mutations (SEQ ID NO:34)

PGWFLDSPDRPWNPTTFSPALLVVTEGDNATFTCSFSNTSESFVLNWYRMSPSNQTDKLAAFPEDRSQLGQ
DCRFRVTQLPNGRDFHMSVVRARRNDSGTYLCSAISLAPKAQIKESLRVELRVTERRAEVPTAHPSPSPRPAG
QFQTLV

25-2 mutations (SEQ ID NO:35)

PGWFLDSPDRPWNPTTFSPALLVVTEGDNATFTCSFSNTSESFVLNWYRMSPSNQTDKLAAFPEDRSQPGQD
CRFRVTQLPNGRDFHMSVVRARRNDSGTYLCSAIVLAPKAQIKESLRAELRVTERRAEVPTAHPSPSPRPAG
QFQTLV

26-2 mutations (SEQ ID NO:36)

PGWFLDSPDRPWNPTTFSPALLVVTEGDNATFTCSFSNTSESFVLNWYRMSPSNQTDKLAAFPEDRSQPGQD
CRFRVTQLPNGRDFHMSVVRARRNDSGTYLCSAISLAPKIQIKESLRAELRVTERRAEVPTAHPSPSPRPAG
QFQTLV

27-2 mutations (SEQ ID NO:37)

PGWFLDSPDRPWNPTTFSPALLVVTEGDNATFTCSFSNTSESFVLNWYRMSPSNQTDKLAAFPEDRSQPGQD
CRFRVTQLPNGRDFHMSVVRARRNDSGTYLCSAISLAPKAQIKESLRVELRVTERRAEVPTAHPSPSPRPAG
QFQTLV

FIG. 17D**28-2 mutations (SEQ ID NO:38)**

PGWFLDSPDRPWNPPPTFSPALLVVTEGDNATFTCSFSNTSESFVLNWYRMSPSNQTDKLAAFPEDRSQPGQD
CRFRVTQLPNGRDFHMSVVRARRNDSGTYLCGAI~~VL~~APKIQIKESLRAELRVTERRAEVPTAHPSPSPRPAG
QFQTLV

29-2 mutations (SEQ ID NO:39)

PGWFLDSPDRPWNPPPTFSPALLVVTEGDNATFTCSFSNTSESFVLNWYRMSPSNQTDKLAAFPEDRSQPGQD
CRFRVTQLPNGRDFHMSVVRARRNDSGTYLCGAI~~VL~~APKAQIKESLRVELRVTERRAEVPTAHPSPSPRPAG
QFQTLV

30-2 mutations (SEQ ID NO:40)

PGWFLDSPDRPWNPPPTFSPALLVVTEGDNATFTCSFSNTSESFVLNWYRMSPSNQTDKLAAFPEDRSQPGQD
CRFRVTQLPNGRDFHMSVVRARRNDSGTYLCGAISLAPKIQIKESLRVELRVTERRAEVPTAHPSPSPRPAG
FQTLV

31-3 mutations (SEQ ID NO:41)

PGWFLDSPDRPWNPPPTFSPALLVVTEGDNATFTCSFSNTSE~~G~~FVLNWYRMSPSNQTDKLAAFPEDRG~~QL~~GQ
DCRFRVTQLPNGRDFHMSVVRARRNDSGTYLCGAISLAPKAQIKESLRAELRVTERRAEVPTAHPSPSPRPA
GQFQTLV

32-3 mutations (SEQ ID NO:42)

PGWFLDSPDRPWNPPPTFSPALLVVTEGDNATFTCSFSNTSE~~G~~FVLNWYRMSPSNQTDKLAAFPEDRGQPGQ
DCRFRVTQLPNGRDFHMSVVRARRNDSGTYLCSAISLAPKAQIKESLRAELRVTERRAEVPTAHPSPSPRPA
GQFQTLV

33-3 mutations (SEQ ID NO:43)

PGWFLDSPDRPWNPPPTFSPALLVVTEGDNATFTCSFSNTSE~~G~~FVLNWYRMSPSNQTDKLAAFPEDRGQPGQ
DCRFRVTQLPNGRDFHMSVVRARRNDSGTYLCGAI~~VL~~APKAQIKESLRAELRVTERRAEVPTAHPSPSPRPA
GQFQTLV

34-3 mutations (SEQ ID NO:44)

PGWFLDSPDRPWNPPPTFSPALLVVTEGDNATFTCSFSNTSE~~G~~FVLNWYRMSPSNQTDKLAAFPEDRGQPGQ
DCRFRVTQLPNGRDFHMSVVRARRNDSGTYLCGAISLAPKIQIKESLRAELRVTERRAEVPTAHPSPSPRPAG
QFQTLV

35-3 mutations (SEQ ID NO:45)

PGWFLDSPDRPWNPPPTFSPALLVVTEGDNATFTCSFSNTSE~~G~~FVLNWYRMSPSNQTDKLAAFPEDRGQPGQ
DCRFRVTQLPNGRDFHMSVVRARRNDSGTYLCGAISLAPKAQIKESLRVELRVTERRAEVPTAHPSPSPRPA
GQFQTLV

36-3 mutations (SEQ ID NO:46)

PGWFLDSPDRPWNPPPTFSPALLVVTEGDNATFTCSFSNTSE~~G~~FVLNWYRMSPSNQTDKLAAFPEDRSQ~~LG~~Q
DCRFRVTQLPNGRDFHMSVVRARRNDSGTYLCSAISLAPKAQIKESLRAELRVTERRAEVPTAHPSPSPRPA
GQFQTLV

FIG. 17E

37-3 mutations (SEQ ID NO:47)

PGWFLDSPDRPWNPPPTFSPALLVVTEGDNATFTCSFSNTSEGFVLNWYRMSPSNQTDKLAAFPEDRSQ**L**GQ
DCRFRVTQLPNGRDFHMSVVRARRNDSGTYLCGAIVLAPKAQIKESLRAELRVTERRAEVPTAHPSPSPRPA
QGFQTLV

38-3 mutations (SEQ ID NO:48)

PGWFLDSPDRPWNPPPTFSPALLVVTEGDNATFTCSFSNTSEGFVLNWYRMSPSNQTDKLAAFPEDRSQ**L**GQ
DCRFRVTQLPNGRDFHMSVVRARRNDSGTYLCGAISLAPK**I**QIKESLRAELRVTERRAEVPTAHPSPSPRPA
QGFQTLV

39-3 mutations (SEQ ID NO:49)

PGWFLDSPDRPWNPPPTFSPALLVVTEGDNATFTCSFSNTSEGFVLNWYRMSPSNQTDKLAAFPEDRSQ**L**GQ
DCRFRVTQLPNGRDFHMSVVRARRNDSGTYLCGAISLAPKAQIKESL**R**VELRVTERRAEVPTAHPSPSPRPA
QGFQTLV

40-3 mutations (SEQ ID NO:50)

PGWFLDSPDRPWNPPPTFSPALLVVTEGDNATFTCSFSNTSEGFVLNWYRMSPSNQTDKLAAFPEDRSQ**P**GQ
DCRFRVTQLPNGRDFHMSVVRARRNDSGTYLC**S**AIVLAPKAQIKESLRAELRVTERRAEVPTAHPSPSPRPA
QGFQTLV

41-3 mutations (SEQ ID NO:51)

PGWFLDSPDRPWNPPPTFSPALLVVTEGDNATFTCSFSNTSEGFVLNWYRMSPSNQTDKLAAFPEDRSQ**P**GQ
DCRFRVTQLPNGRDFHMSVVRARRNDSGTYLC**S**AISLAPK**I**QIKESLRAELRVTERRAEVPTAHPSPSPRPA
QGFQTLV

42-3 mutations (SEQ ID NO:52)

PGWFLDSPDRPWNPPPTFSPALLVVTEGDNATFTCSFSNTSEGFVLNWYRMSPSNQTDKLAAFPEDRSQ**P**GQ
DCRFRVTQLPNGRDFHMSVVRARRNDSGTYLC**S**AISLAPKAQIKESL**R**VELRVTERRAEVPTAHPSPSPRPA
QGFQTLV

43-3 mutations (SEQ ID NO:53)

PGWFLDSPDRPWNPPPTFSPALLVVTEGDNATFTCSFSNTSEGFVLNWYRMSPSNQTDKLAAFPEDRSQ**P**GQ
DCRFRVTQLPNGRDFHMSVVRARRNDSGTYLCGAIVLAPK**I**QIKESLRAELRVTERRAEVPTAHPSPSPRPA
QGFQTLV

44-3 mutations (SEQ ID NO:54)

PGWFLDSPDRPWNPPPTFSPALLVVTEGDNATFTCSFSNTSEGFVLNWYRMSPSNQTDKLAAFPEDRSQ**P**GQ
DCRFRVTQLPNGRDFHMSVVRARRNDSGTYLCGAIVLAPKAQIKESL**R**VELRVTERRAEVPTAHPSPSPRPA
QGFQTLV

45-3 mutations (SEQ ID NO:55)

PGWFLDSPDRPWNPPPTFSPALLVVTEGDNATFTCSFSNTSEGFVLNWYRMSPSNQTDKLAAFPEDRSQ**P**GQ
DCRFRVTQLPNGRDFHMSVVRARRNDSGTYLCGAISLAPK**I**QIKESL**R**VELRVTERRAEVPTAHPSPSPRPA
QGFQTLV

FIG. 17F**46-3 mutations (SEQ ID NO:56)**

PGWFLDSPDRPWNPPPTFSPALLVVTEGDNATFTCSFSNTSESFVLNWYRMSPSNQTDKLAAPEDRGQLGQ
DCRFRVTQLPNGRDFHMSVVRARRNDSGTLYLCSAISLAPKAQIKESLRAELRVTERRAEVPTAHPSPSPRPA
GQFQTLV

47-3 mutations (SEQ ID NO:57)

PGWFLDSPDRPWNPPPTFSPALLVVTEGDNATFTCSFSNTSESFVLNWYRMSPSNQTDKLAAPEDRGQLGQ
DCRFRVTQLPNGRDFHMSVVRARRNDSGTLYLCSAISLAPKAQIKESLRAELRVTERRAEVPTAHPSPSPRPA
GQFQTLV

48-3 mutations (SEQ ID NO:58)

PGWFLDSPDRPWNPPPTFSPALLVVTEGDNATFTCSFSNTSESFVLNWYRMSPSNQTDKLAAPEDRGQLGQ
DCRFRVTQLPNGRDFHMSVVRARRNDSGTLYLCSAISLAPKAQIKESLRAELRVTERRAEVPTAHPSPSPRPA
GQFQTLV

49-3 mutations (SEQ ID NO:59)

PGWFLDSPDRPWNPPPTFSPALLVVTEGDNATFTCSFSNTSESFVLNWYRMSPSNQTDKLAAPEDRGQLGQ
DCRFRVTQLPNGRDFHMSVVRARRNDSGTLYLCSAISLAPKAQIKESLRAELRVTERRAEVPTAHPSPSPRPA
GQFQTLV

50-3 mutations (SEQ ID NO:60)

PGWFLDSPDRPWNPPPTFSPALLVVTEGDNATFTCSFSNTSESFVLNWYRMSPSNQTDKLAAPEDRGQPGQ
DCRFRVTQLPNGRDFHMSVVRARRNDSGTLYLCSAISLAPKAQIKESLRAELRVTERRAEVPTAHPSPSPRPA
GQFQTLV

51-3 mutations (SEQ ID NO:61)

PGWFLDSPDRPWNPPPTFSPALLVVTEGDNATFTCSFSNTSESFVLNWYRMSPSNQTDKLAAPEDRGQPGQ
DCRFRVTQLPNGRDFHMSVVRARRNDSGTLYLCSAISLAPKAQIKESLRAELRVTERRAEVPTAHPSPSPRPA
GQFQTLV

52-3 mutations (SEQ ID NO:62)

PGWFLDSPDRPWNPPPTFSPALLVVTEGDNATFTCSFSNTSESFVLNWYRMSPSNQTDKLAAPEDRGQPGQ
DCRFRVTQLPNGRDFHMSVVRARRNDSGTLYLCSAISLAPKAQIKESLRAELRVTERRAEVPTAHPSPSPRPA
GQFQTLV

53-3 mutations (SEQ ID NO:63)

PGWFLDSPDRPWNPPPTFSPALLVVTEGDNATFTCSFSNTSESFVLNWYRMSPSNQTDKLAAPEDRGQPGQ
DCRFRVTQLPNGRDFHMSVVRARRNDSGTLYLCSAISLAPKAQIKESLRAELRVTERRAEVPTAHPSPSPRPA
GQFQTLV

54-3 mutations (SEQ ID NO:64)

PGWFLDSPDRPWNPPPTFSPALLVVTEGDNATFTCSFSNTSESFVLNWYRMSPSNQTDKLAAPEDRGQPGQ
DCRFRVTQLPNGRDFHMSVVRARRNDSGTLYLCSAISLAPKAQIKESLRAELRVTERRAEVPTAHPSPSPRPA
GQFQTLV

FIG. 17G**55-3 mutations (SEQ ID NO:65)**

PGWFLDSPDRPWNPTTFSPALLVVTEGDNATFTCSFSNTSESFVLNWYRMSPSNQTDKLAAFPEDRGQPGQ
DCRFRVTQLPNGRDFHMSVVRARRNDSGTYLCSAISLAPKIQIKESLRVELRVTERRAEVPTAHPSPSPRPAG
QFQTLV

56-3 mutations (SEQ ID NO:66)

PGWFLDSPDRPWNPTTFSPALLVVTEGDNATFTCSFSNTSESFVLNWYRMSPSNQTDKLAAFPEDRSQLGQ
DCRFRVTQLPNGRDFHMSVVRARRNDSGTYLCSAIVLAPKAQIKESLRAELRVTERRAEVPTAHPSPSPRPAG
QFQTLV

57-3 mutations (SEQ ID NO:67)

PGWFLDSPDRPWNPTTFSPALLVVTEGDNATFTCSFSNTSESFVLNWYRMSPSNQTDKLAAFPEDRSQLGQ
DCRFRVTQLPNGRDFHMSVVRARRNDSGTYLCSAISLAPKIQIKESLRAELRVTERRAEVPTAHPSPSPRPAG
QFQTLV

58-3 mutations (SEQ ID NO:68)

PGWFLDSPDRPWNPTTFSPALLVVTEGDNATFTCSFSNTSESFVLNWYRMSPSNQTDKLAAFPEDRSQLGQ
DCRFRVTQLPNGRDFHMSVVRARRNDSGTYLCSAISLAPKAQIKESLRVELRVTERRAEVPTAHPSPSPRPAG
QFQTLV

59-3 mutations (SEQ ID NO:69)

PGWFLDSPDRPWNPTTFSPALLVVTEGDNATFTCSFSNTSESFVLNWYRMSPSNQTDKLAAFPEDRSQLGQ
DCRFRVTQLPNGRDFHMSVVRARRNDSGTYLCSAIVLAPKIQIKESLRAELRVTERRAEVPTAHPSPSPRPAG
QFQTLV

60-3 mutations (SEQ ID NO:70)

PGWFLDSPDRPWNPTTFSPALLVVTEGDNATFTCSFSNTSESFVLNWYRMSPSNQTDKLAAFPEDRSQLGQ
DCRFRVTQLPNGRDFHMSVVRARRNDSGTYLCSAIVLAPKAQIKESLRVELRVTERRAEVPTAHPSPSPRPAG
QFQTLV

61-3 mutations (SEQ ID NO:71)

PGWFLDSPDRPWNPTTFSPALLVVTEGDNATFTCSFSNTSESFVLNWYRMSPSNQTDKLAAFPEDRSQLGQ
DCRFRVTQLPNGRDFHMSVVRARRNDSGTYLCSAISLAPKIQIKESLRVELRVTERRAEVPTAHPSPSPRPAG
QFQTLV

62-3 mutations (SEQ ID NO:72)

PGWFLDSPDRPWNPTTFSPALLVVTEGDNATFTCSFSNTSESFVLNWYRMSPSNQTDKLAAFPEDRSQPGQD
CRFRVTQLPNGRDFHMSVVRARRNDSGTYLCSAIVLAPKIQIKESLRAELRVTERRAEVPTAHPSPSPRPAG
FQTLV

63-3 mutations (SEQ ID NO:73)

PGWFLDSPDRPWNPTTFSPALLVVTEGDNATFTCSFSNTSESFVLNWYRMSPSNQTDKLAAFPEDRSQPGQD
CRFRVTQLPNGRDFHMSVVRARRNDSGTYLCSAIVLAPKAQIKESLRVELRVTERRAEVPTAHPSPSPRPAG
QFQTLV

FIG. 17H**64-3 mutations (SEQ ID NO:74)**

PGWFLDSPDRPWNPTTFSPALLVVTEGDNATFTCSFSNTSESFVLNWYRMSPSNQTDKLAAFPEDRSQPGQD
DCRFRVTQLPNGRDFHMSVVRARRNDSGTYLCSAISLAPKIQIKESLRVELRVTERRAEVPTAHPSPSPRPAG
QFQTLV

65-3 mutations (SEQ ID NO:75)

PGWFLDSPDRPWNPTTFSPALLVVTEGDNATFTCSFSNTSESFVLNWYRMSPSNQTDKLAAFPEDRSQPGQD
DCRFRVTQLPNGRDFHMSVVRARRNDSGTYLCSAISLAPKIQIKESLRVELRVTERRAEVPTAHPSPSPRPAG
QFQTLV

66-4 mutations (SEQ ID NO:76)

PGWFLDSPDRPWNPTTFSPALLVVTEGDNATFTCSFSNTSEGFVLNWYRMSPSNQTDKLAAFPEDRGQLGQ
DCRFRVTQLPNGRDFHMSVVRARRNDSGTYLCSAISLAPKAQIKESLRAELRVTERRAEVPTAHPSPSPRPAG
QFQTLV

67-4 mutations (SEQ ID NO:77)

PGWFLDSPDRPWNPTTFSPALLVVTEGDNATFTCSFSNTSEGFVLNWYRMSPSNQTDKLAAFPEDRGQLGQ
DCRFRVTQLPNGRDFHMSVVRARRNDSGTYLCSAISLAPKAQIKESLRAELRVTERRAEVPTAHPSPSPRPAG
QFQTLV

68-4 mutations (SEQ ID NO:78)

PGWFLDSPDRPWNPTTFSPALLVVTEGDNATFTCSFSNTSEGFVLNWYRMSPSNQTDKLAAFPEDRGQLGQ
DCRFRVTQLPNGRDFHMSVVRARRNDSGTYLCSAISLAPKIQIKESLRAELRVTERRAEVPTAHPSPSPRPAG
QFQTLV

69-4 mutations (SEQ ID NO:79)

PGWFLDSPDRPWNPTTFSPALLVVTEGDNATFTCSFSNTSEGFVLNWYRMSPSNQTDKLAAFPEDRGQLGQ
DCRFRVTQLPNGRDFHMSVVRARRNDSGTYLCSAISLAPKAQIKESLRVELRVTERRAEVPTAHPSPSPRPAG
QFQTLV

70-4 mutations (SEQ ID NO:80)

PGWFLDSPDRPWNPTTFSPALLVVTEGDNATFTCSFSNTSEGFVLNWYRMSPSNQTDKLAAFPEDRGQPGQ
DCRFRVTQLPNGRDFHMSVVRARRNDSGTYLCSAISLAPKAQIKESLRAELRVTERRAEVPTAHPSPSPRPAG
QFQTLV

71-4 mutations (SEQ ID NO:81)

PGWFLDSPDRPWNPTTFSPALLVVTEGDNATFTCSFSNTSEGFVLNWYRMSPSNQTDKLAAFPEDRGQPGQ
DCRFRVTQLPNGRDFHMSVVRARRNDSGTYLCSAISLAPKIQIKESLRAELRVTERRAEVPTAHPSPSPRPAG
QFQTLV

72-4 mutations (SEQ ID NO:82)

PGWFLDSPDRPWNPTTFSPALLVVTEGDNATFTCSFSNTSEGFVLNWYRMSPSNQTDKLAAFPEDRGQPGQ
DCRFRVTQLPNGRDFHMSVVRARRNDSGTYLCSAISLAPKAQIKESLRVELRVTERRAEVPTAHPSPSPRPAG
QFQTLV

FIG. 17I

73-4 mutations (SEQ ID NO:83)

PGWFLDSPDRPWNPPPTFSPALLVVTEGDNATFTCSFSNTSEGFVLNWYRMSPSNQTDKLAAFPEDRGQPGQ
DCRFRVTQLPNGRDFHMSVVRARRNDSGTLYLCAIIVLAPKIQIKESLRAELRVTERRAEVPTAHPSPSPRPA
GQFQTLV

74-4 mutations (SEQ ID NO:84)

PGWFLDSPDRPWNPPPTFSPALLVVTEGDNATFTCSFSNTSEGFVLNWYRMSPSNQTDKLAAFPEDRGQPGQ
DCRFRVTQLPNGRDFHMSVVRARRNDSGTLYLCAIIVLAPKAQIKESLRVELRVTERRAEVPTAHPSPSPRPA
GQFQTLV

75-4 mutations (SEQ ID NO:85)

PGWFLDSPDRPWNPPPTFSPALLVVTEGDNATFTCSFSNTSEGFVLNWYRMSPSNQTDKLAAFPEDRGQPGQ
DCRFRVTQLPNGRDFHMSVVRARRNDSGTLYLCAISLAPKIQIKESLRVELRVTERRAEVPTAHPSPSPRPA
GQFQTLV

76-4 mutations (SEQ ID NO:86)

PGWFLDSPDRPWNPPPTFSPALLVVTEGDNATFTCSFSNTSEGFVLNWYRMSPSNQTDKLAAFPEDRSQLGQ
DCRFRVTQLPNGRDFHMSVVRARRNDSGTLYLCSAIVLAPKAQIKESLRAELRVTERRAEVPTAHPSPSPRPA
GQFQTLV

77-4 mutations (SEQ ID NO:87)

PGWFLDSPDRPWNPPPTFSPALLVVTEGDNATFTCSFSNTSEGFVLNWYRMSPSNQTDKLAAFPEDRSQLGQ
DCRFRVTQLPNGRDFHMSVVRARRNDSGTLYLCSAISLAPKIQIKESLRAELRVTERRAEVPTAHPSPSPRPA
GQFQTLV

78-4 mutations (SEQ ID NO:88)

PGWFLDSPDRPWNPPPTFSPALLVVTEGDNATFTCSFSNTSEGFVLNWYRMSPSNQTDKLAAFPEDRSQLGQ
DCRFRVTQLPNGRDFHMSVVRARRNDSGTLYLCSAISLAPKAQIKESLRVELRVTERRAEVPTAHPSPSPRPA
GQFQTLV

79-4 mutations (SEQ ID NO:89)

PGWFLDSPDRPWNPPPTFSPALLVVTEGDNATFTCSFSNTSEGFVLNWYRMSPSNQTDKLAAFPEDRSQLGQ
DCRFRVTQLPNGRDFHMSVVRARRNDSGTLYLCAIIVLAPKIQIKESLRAELRVTERRAEVPTAHPSPSPRPA
GQFQTLV

80-4 mutations (SEQ ID NO:90)

PGWFLDSPDRPWNPPPTFSPALLVVTEGDNATFTCSFSNTSEGFVLNWYRMSPSNQTDKLAAFPEDRSQLGQ
DCRFRVTQLPNGRDFHMSVVRARRNDSGTLYLCAIIVLAPKAQIKESLRVELRVTERRAEVPTAHPSPSPRPA
GQFQTLV

81-4 mutations (SEQ ID NO:91)

PGWFLDSPDRPWNPPPTFSPALLVVTEGDNATFTCSFSNTSEGFVLNWYRMSPSNQTDKLAAFPEDRSQLGQ
DCRFRVTQLPNGRDFHMSVVRARRNDSGTLYLCAISLAPKIQIKESLRVELRVTERRAEVPTAHPSPSPRPA
GQFQTLV

FIG. 17J

82-4 mutations (SEQ ID NO:92)

PGWFLDSPDRPWNPTTFSPALLVVTEGDNATFTCSFSNTSEGFVLNWYRMSPSNQTDKLAAFPEDRSQPGQ
DCRFRVTQLPNGRDFHMSVVRARRNDSGTYLCSAIVLAPKIQIKESLRAELRVTERRAEVPTAHPSPSPRPA
GQFQTLV

83-4 mutations (SEQ ID NO:93)

PGWFLDSPDRPWNPTTFSPALLVVTEGDNATFTCSFSNTSEGFVLNWYRMSPSNQTDKLAAFPEDRSQPGQ
DCRFRVTQLPNGRDFHMSVVRARRNDSGTYLCSAIVLAPKAQIKESLRVELRVTERRAEVPTAHPSPSPRPA
GQFQTLV

84-4 mutations (SEQ ID NO:94)

PGWFLDSPDRPWNPTTFSPALLVVTEGDNATFTCSFSNTSEGFVLNWYRMSPSNQTDKLAAFPEDRSQPGQ
DCRFRVTQLPNGRDFHMSVVRARRNDSGTYLCSAISLAPKIQIKESLRVELRVTERRAEVPTAHPSPSPRPA
GQFQTLV

85-4 mutations (SEQ ID NO:95)

PGWFLDSPDRPWNPTTFSPALLVVTEGDNATFTCSFSNTSEGFVLNWYRMSPSNQTDKLAAFPEDRSQPGQ
DCRFRVTQLPNGRDFHMSVVRARRNDSGTYLCSAIVLAPKIQIKESLRVELRVTERRAEVPTAHPSPSPRPA
GQFQTLV

86-4 mutations (SEQ ID NO:96)

PGWFLDSPDRPWNPTTFSPALLVVTEGDNATFTCSFSNTSESFVLNWYRMSPSNQTDKLAAFPEDRGQLGQ
DCRFRVTQLPNGRDFHMSVVRARRNDSGTYLCSAIVLAPKAQIKESLRAELRVTERRAEVPTAHPSPSPRPA
GQFQTLV

87-4 mutations (SEQ ID NO:97)

PGWFLDSPDRPWNPTTFSPALLVVTEGDNATFTCSFSNTSESFVLNWYRMSPSNQTDKLAAFPEDRGQLGQ
DCRFRVTQLPNGRDFHMSVVRARRNDSGTYLCSAISLAPKIQIKESLRAELRVTERRAEVPTAHPSPSPRPA
GQFQTLV

88-4 mutations (SEQ ID NO:98)

PGWFLDSPDRPWNPTTFSPALLVVTEGDNATFTCSFSNTSESFVLNWYRMSPSNQTDKLAAFPEDRGQLGQ
DCRFRVTQLPNGRDFHMSVVRARRNDSGTYLCSAISLAPKAQIKESLRVELRVTERRAEVPTAHPSPSPRPA
GQFQTLV

89-4 mutations (SEQ ID NO:99)

PGWFLDSPDRPWNPTTFSPALLVVTEGDNATFTCSFSNTSESFVLNWYRMSPSNQTDKLAAFPEDRGQLGQ
DCRFRVTQLPNGRDFHMSVVRARRNDSGTYLCSAIVLAPKIQIKESLRAELRVTERRAEVPTAHPSPSPRPA
GQFQTLV

90-4 mutations (SEQ ID NO:100)

PGWFLDSPDRPWNPTTFSPALLVVTEGDNATFTCSFSNTSESFVLNWYRMSPSNQTDKLAAFPEDRGQLGQ
DCRFRVTQLPNGRDFHMSVVRARRNDSGTYLCSAIVLAPKAQIKESLRVELRVTERRAEVPTAHPSPSPRPA
GQFQTLV

FIG. 17K**91-4 mutations (SEQ ID NO:101)**

PGWFLDSPDRPWNPTTFSPALLVVTEGDNATFTCSFSNTSESFVLNWYRMSPSNQTDKLAAPEDRGQLGQ
DCRFRVTQLPNGRDFHMSVVRARRNDSGTLYLCSAIVLAPKIQIKESLRVELRVTERRAEVPTAHPSPSPRPAG
QFQTLV

92-4 mutations (SEQ ID NO:102)

PGWFLDSPDRPWNPTTFSPALLVVTEGDNATFTCSFSNTSESFVLNWYRMSPSNQTDKLAAPEDRGQPGQ
DCRFRVTQLPNGRDFHMSVVRARRNDSGTLYLCSAIVLAPKIQIKESLRAELRVTERRAEVPTAHPSPSPRPAG
QFQTLV

93-4 mutations (SEQ ID NO:103)

PGWFLDSPDRPWNPTTFSPALLVVTEGDNATFTCSFSNTSESFVLNWYRMSPSNQTDKLAAPEDRGQPGQ
DCRFRVTQLPNGRDFHMSVVRARRNDSGTLYLCSAIVLAPKAQIKESLRVELRVTERRAEVPTAHPSPSPRPAG
QFQTLV

94-4 mutations (SEQ ID NO:104)

PGWFLDSPDRPWNPTTFSPALLVVTEGDNATFTCSFSNTSESFVLNWYRMSPSNQTDKLAAPEDRGQPGQ
DCRFRVTQLPNGRDFHMSVVRARRNDSGTLYLCSAIVLAPKIQIKESLRVELRVTERRAEVPTAHPSPSPRPAG
QFQTLV

95-4 mutations (SEQ ID NO:105)

PGWFLDSPDRPWNPTTFSPALLVVTEGDNATFTCSFSNTSESFVLNWYRMSPSNQTDKLAAPEDRGQPGQ
DCRFRVTQLPNGRDFHMSVVRARRNDSGTLYLCSAIVLAPKIQIKESLRVELRVTERRAEVPTAHPSPSPRPAG
QFQTLV

96-4 mutations (SEQ ID NO:106)

PGWFLDSPDRPWNPTTFSPALLVVTEGDNATFTCSFSNTSESFVLNWYRMSPSNQTDKLAAPEDRSQLGQ
DCRFRVTQLPNGRDFHMSVVRARRNDSGTLYLCSAIVLAPKIQIKESLRAELRVTERRAEVPTAHPSPSPRPAG
QFQTLV

97-4 mutations (SEQ ID NO:107)

PGWFLDSPDRPWNPTTFSPALLVVTEGDNATFTCSFSNTSESFVLNWYRMSPSNQTDKLAAPEDRSQLGQ
DCRFRVTQLPNGRDFHMSVVRARRNDSGTLYLCSAIVLAPKAQIKESLRVELRVTERRAEVPTAHPSPSPRPAG
QFQTLV

98-4 mutations (SEQ ID NO:108)

PGWFLDSPDRPWNPTTFSPALLVVTEGDNATFTCSFSNTSESFVLNWYRMSPSNQTDKLAAPEDRSQLGQ
DCRFRVTQLPNGRDFHMSVVRARRNDSGTLYLCSAIVLAPKIQIKESLRVELRVTERRAEVPTAHPSPSPRPAG
QFQTLV

99-4 mutations (SEQ ID NO:109)

PGWFLDSPDRPWNPTTFSPALLVVTEGDNATFTCSFSNTSESFVLNWYRMSPSNQTDKLAAPEDRSQLGQ
DCRFRVTQLPNGRDFHMSVVRARRNDSGTLYLCSAIVLAPKIQIKESLRVELRVTERRAEVPTAHPSPSPRPAG
QFQTLV

FIG. 17L**100-4 mutations (SEQ ID NO:110)**

PGWFLDSPDRPWNPTTFSPALLVVTEGDNATFTCSFSNTSESFVLNWYRMSPSNQTDKLAAFPEDRSQPGQD
DCRFRVTQLPNGRDFHMSVVRARRNDSGTYLCSAIVLAPKIQIKESLRVELRVTERRAEVPTAHPSPSPRPAG
QFQTLV

101-5 mutations (SEQ ID NO:111)

PGWFLDSPDRPWNPTTFSPALLVVTEGDNATFTCSFSNTSEGFVLNWYRMSPSNQTDKLAAFPEDRGQLGQ
DCRFRVTQLPNGRDFHMSVVRARRNDSGTYLCSAIVLAPKAQIKESLRAELRVTERRAEVPTAHPSPSPRPA
GQFQTLV

102-5 mutations (SEQ ID NO:112)

PGWFLDSPDRPWNPTTFSPALLVVTEGDNATFTCSFSNTSEGFVLNWYRMSPSNQTDKLAAFPEDRGQLGQ
DCRFRVTQLPNGRDFHMSVVRARRNDSGTYLCSAISLAPKIQIKESLRAELRVTERRAEVPTAHPSPSPRPAG
QFQTLV

103-5 mutations (SEQ ID NO:113)

PGWFLDSPDRPWNPTTFSPALLVVTEGDNATFTCSFSNTSEGFVLNWYRMSPSNQTDKLAAFPEDRGQLGQ
DCRFRVTQLPNGRDFHMSVVRARRNDSGTYLCSAISLAPKAQIKESLRVELRVTERRAEVPTAHPSPSPRPA
GQFQTLV

104-5 mutations (SEQ ID NO:114)

PGWFLDSPDRPWNPTTFSPALLVVTEGDNATFTCSFSNTSEGFVLNWYRMSPSNQTDKLAAFPEDRGQLGQ
DCRFRVTQLPNGRDFHMSVVRARRNDSGTYLCSAIVLAPKIQIKESLRAELRVTERRAEVPTAHPSPSPRPA
GQFQTLV

105-5 mutations (SEQ ID NO:115)

PGWFLDSPDRPWNPTTFSPALLVVTEGDNATFTCSFSNTSEGFVLNWYRMSPSNQTDKLAAFPEDRGQLGQ
DCRFRVTQLPNGRDFHMSVVRARRNDSGTYLCSAIVLAPKAQIKESLRVELRVTERRAEVPTAHPSPSPRPA
GQFQTLV

106-5 mutations (SEQ ID NO:116)

PGWFLDSPDRPWNPTTFSPALLVVTEGDNATFTCSFSNTSEGFVLNWYRMSPSNQTDKLAAFPEDRGQLGQ
DCRFRVTQLPNGRDFHMSVVRARRNDSGTYLCSAISLAPKIQIKESLRVELRVTERRAEVPTAHPSPSPRPAG
QFQTLV

107-5 mutations (SEQ ID NO:117)

PGWFLDSPDRPWNPTTFSPALLVVTEGDNATFTCSFSNTSEGFVLNWYRMSPSNQTDKLAAFPEDRGQPGQ
DCRFRVTQLPNGRDFHMSVVRARRNDSGTYLCSAIVLAPKIQIKESLRAELRVTERRAEVPTAHPSPSPRPAG
QFQTLV

108-5 mutations (SEQ ID NO:118)

PGWFLDSPDRPWNPTTFSPALLVVTEGDNATFTCSFSNTSEGFVLNWYRMSPSNQTDKLAAFPEDRGQPGQ
DCRFRVTQLPNGRDFHMSVVRARRNDSGTYLCSAIVLAPKAQIKESLRVELRVTERRAEVPTAHPSPSPRPA
GQFQTLV

FIG. 17M**109-5 mutations (SEQ ID NO:119)**

PGWFLDSPDRPWNPTFSPALLVVTEGDNATFTCSFSNTSEGFVLNWYRMSPSNQTDKLAAFPEDRGQPGQ
DCRFRVTQLPNGRDFHMSVVRARRNDSGTYLCSAISLAPKIQIKESLRVELRVTERRAEVPTAHPSPSPRPAG
QFQTLV

110-5 mutations (SEQ ID NO:120)

PGWFLDSPDRPWNPTFSPALLVVTEGDNATFTCSFSNTSEGFVLNWYRMSPSNQTDKLAAFPEDRGQPGQ
DCRFRVTQLPNGRDFHMSVVRARRNDSGTYLCSAIVLAPKIQIKESLRVELRVTERRAEVPTAHPSPSPRPA
GQFQTLV

111-5 mutations (SEQ ID NO:121)

PGWFLDSPDRPWNPTFSPALLVVTEGDNATFTCSFSNTSEGFVLNWYRMSPSNQTDKLAAFPEDRSQLGQ
DCRFRVTQLPNGRDFHMSVVRARRNDSGTYLCSAIVLAPKIQIKESLRAELRVTERRAEVPTAHPSPSPRPAG
QFQTLV

112-5 mutations (SEQ ID NO:122)

PGWFLDSPDRPWNPTFSPALLVVTEGDNATFTCSFSNTSEGFVLNWYRMSPSNQTDKLAAFPEDRSQLGQ
DCRFRVTQLPNGRDFHMSVVRARRNDSGTYLCSAIVLAPKAQIKESLRVELRVTERRAEVPTAHPSPSPRPA
GQFQTLV

113-5 mutations (SEQ ID NO:123)

PGWFLDSPDRPWNPTFSPALLVVTEGDNATFTCSFSNTSEGFVLNWYRMSPSNQTDKLAAFPEDRSQLGQ
DCRFRVTQLPNGRDFHMSVVRARRNDSGTYLCSAISLAPKIQIKESLRVELRVTERRAEVPTAHPSPSPRPAG
QFQTLV

114-5 mutations (SEQ ID NO:124)

PGWFLDSPDRPWNPTFSPALLVVTEGDNATFTCSFSNTSEGFVLNWYRMSPSNQTDKLAAFPEDRSQLGQ
DCRFRVTQLPNGRDFHMSVVRARRNDSGTYLCSAIVLAPKIQIKESLRVELRVTERRAEVPTAHPSPSPRPA
GQFQTLV

115-5 mutations (SEQ ID NO:125)

PGWFLDSPDRPWNPTFSPALLVVTEGDNATFTCSFSNTSEGFVLNWYRMSPSNQTDKLAAFPEDRSQPGQ
DCRFRVTQLPNGRDFHMSVVRARRNDSGTYLCSAIVLAPKIQIKESLRVELRVTERRAEVPTAHPSPSPRPAG
QFQTLV

116-5 mutations (SEQ ID NO:126)

PGWFLDSPDRPWNPTFSPALLVVTEGDNATFTCSFSNTSESFVLNWYRMSPSNQTDKLAAFPEDRGQLGQ
DCRFRVTQLPNGRDFHMSVVRARRNDSGTYLCSAIVLAPKIQIKESLRAELRVTERRAEVPTAHPSPSPRPAG
QFQTLV

117-5 mutations (SEQ ID NO:127)

PGWFLDSPDRPWNPTFSPALLVVTEGDNATFTCSFSNTSESFVLNWYRMSPSNQTDKLAAFPEDRGQLGQ
DCRFRVTQLPNGRDFHMSVVRARRNDSGTYLCSAIVLAPKAQIKESLRVELRVTERRAEVPTAHPSPSPRPA
GQFQTLV

FIG. 17N**118-5 mutations (SEQ ID NO:128)**

PGWFLDSPDRPWNPTTFSPALLVVTEGDNATFTCSFSNTSESFVLNWYRMSPSNQTDKLAAPEDRGQLGQ
DCRFRVTQLPNGRDFHMSVVRARRNDSGTYLCSAISLAPKIQIKESLRVELRVTERRAEVPTAHPSPSPRPAG
QFQTLV

119-5 mutations (SEQ ID NO:129)

PGWFLDSPDRPWNPTTFSPALLVVTEGDNATFTCSFSNTSESFVLNWYRMSPSNQTDKLAAPEDRGQLGQ
DCRFRVTQLPNGRDFHMSVVRARRNDSGTYLCSAIVLAPKIQIKESLRVELRVTERRAEVPTAHPSPSPRPA
QFQTLV

120-5 mutations (SEQ ID NO:130)

PGWFLDSPDRPWNPTTFSPALLVVTEGDNATFTCSFSNTSESFVLNWYRMSPSNQTDKLAAPEDRGQPGQ
DCRFRVTQLPNGRDFHMSVVRARRNDSGTYLCSAIVLAPKIQIKESLRVELRVTERRAEVPTAHPSPSPRPAG
QFQTLV

121-5 mutations (SEQ ID NO:131)

PGWFLDSPDRPWNPTTFSPALLVVTEGDNATFTCSFSNTSESFVLNWYRMSPSNQTDKLAAPEDRSQLGQ
DCRFRVTQLPNGRDFHMSVVRARRNDSGTYLCSAIVLAPKIQIKESLRVELRVTERRAEVPTAHPSPSPRPAG
QFQTLV

122-6 mutations (SEQ ID NO:132)

PGWFLDSPDRPWNPTTFSPALLVVTEGDNATFTCSFSNTSEGFVLNWYRMSPSNQTDKLAAPEDRGQLGQ
DCRFRVTQLPNGRDFHMSVVRARRNDSGTYLCSAIVLAPKIQIKESLRAELRVTERRAEVPTAHPSPSPRPAG
QFQTLV

123-6 mutations (SEQ ID NO:133)

PGWFLDSPDRPWNPTTFSPALLVVTEGDNATFTCSFSNTSEGFVLNWYRMSPSNQTDKLAAPEDRGQLGQ
DCRFRVTQLPNGRDFHMSVVRARRNDSGTYLCSAIVLAPKAQIKESLRVELRVTERRAEVPTAHPSPSPRPA
QFQTLV

124-6 mutations (SEQ ID NO:134)

PGWFLDSPDRPWNPTTFSPALLVVTEGDNATFTCSFSNTSEGFVLNWYRMSPSNQTDKLAAPEDRGQLGQ
DCRFRVTQLPNGRDFHMSVVRARRNDSGTYLCSAISLAPKIQIKESLRVELRVTERRAEVPTAHPSPSPRPAG
QFQTLV

125-6 mutations (SEQ ID NO:135)

PGWFLDSPDRPWNPTTFSPALLVVTEGDNATFTCSFSNTSEGFVLNWYRMSPSNQTDKLAAPEDRGQLGQ
DCRFRVTQLPNGRDFHMSVVRARRNDSGTYLCSAIVLAPKIQIKESLRVELRVTERRAEVPTAHPSPSPRPA
QFQTLV

126-6 mutations (SEQ ID NO:136)

PGWFLDSPDRPWNPTTFSPALLVVTEGDNATFTCSFSNTSEGFVLNWYRMSPSNQTDKLAAPEDRGQPGQ
DCRFRVTQLPNGRDFHMSVVRARRNDSGTYLCSAIVLAPKIQIKESLRVELRVTERRAEVPTAHPSPSPRPAG
QFQTLV

FIG. 170**127-6 mutations (SEQ ID NO:137)**

PGWFLDSPDRPWNPPPTFSPALLVVTEGDNATFTCSFSNTSE**G**FVLNWYRMSPSNQTDKLAAFPEDRSQ**L**GQ
DCRFRVTQLPNGRDFHMSVVRARRNDSGTYLCSAIVLAPK**I**QIKESLR**V**ELRVTERRAEVPTAHPSPSPRPAG
QFQTLV

128-6 mutations (SEQ ID NO:138)

PGWFLDSPDRPWNPPPTFSPALLVVTEGDNATFTCSFSNTSE**S**FVLNWYRMSPSNQTDKLAAFPEDR**G**Q**L**GQ
DCRFRVTQLPNGRDFHMSVVRARRNDSGTYLCSAIVLAPK**I**QIKESLR**V**ELRVTERRAEVPTAHPSPSPRPAG
QFQTLV

129-8 mutations (SEQ ID NO:139)

PGWFLDSPDRPWNPPPTFSPALLVVTEGDNATFTCSFSNTSE**G**FVLNWYRMSPSNQTDKLAAFPEDR**G**Q**L**GQ
DCRFRVTQLPNGRDFHMSVVRARR**S**DSGTYLCSAIVLAPK**I**QIKESLR**V**ELRVTERRAEVPTAHPSPSPRPAG
QFQTLV

FIG. 18A

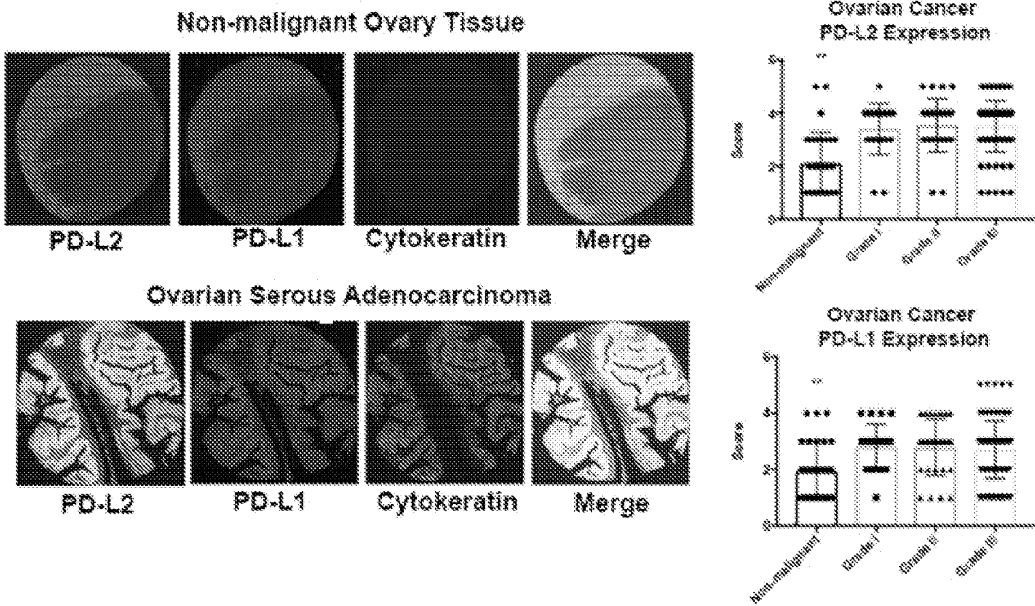


FIG. 18B

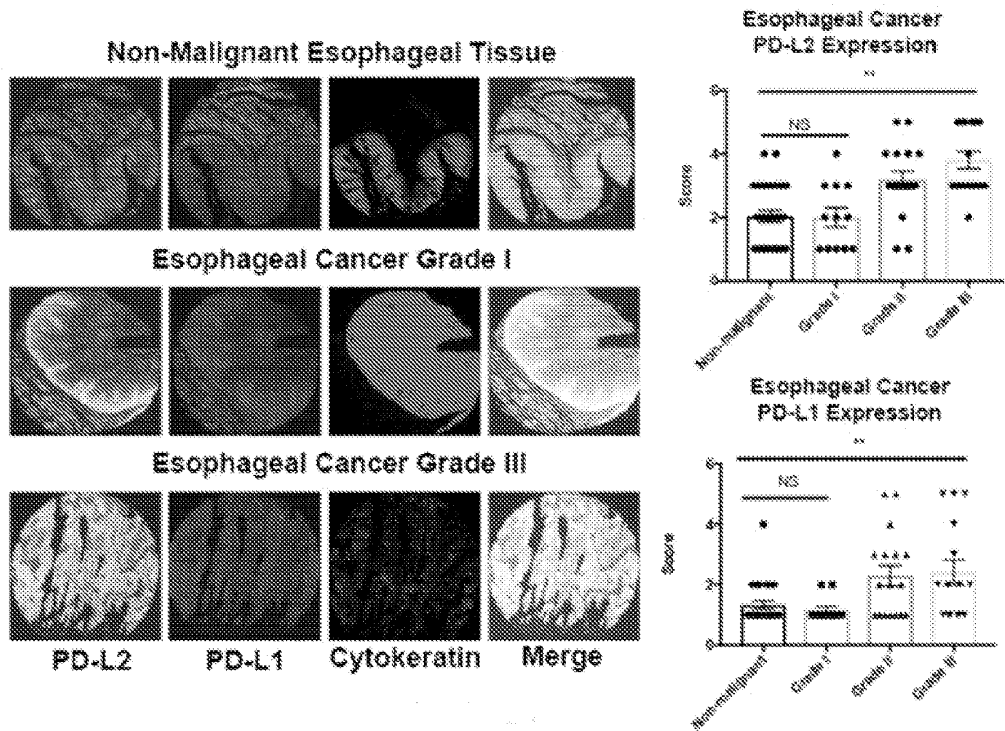


FIG. 18C

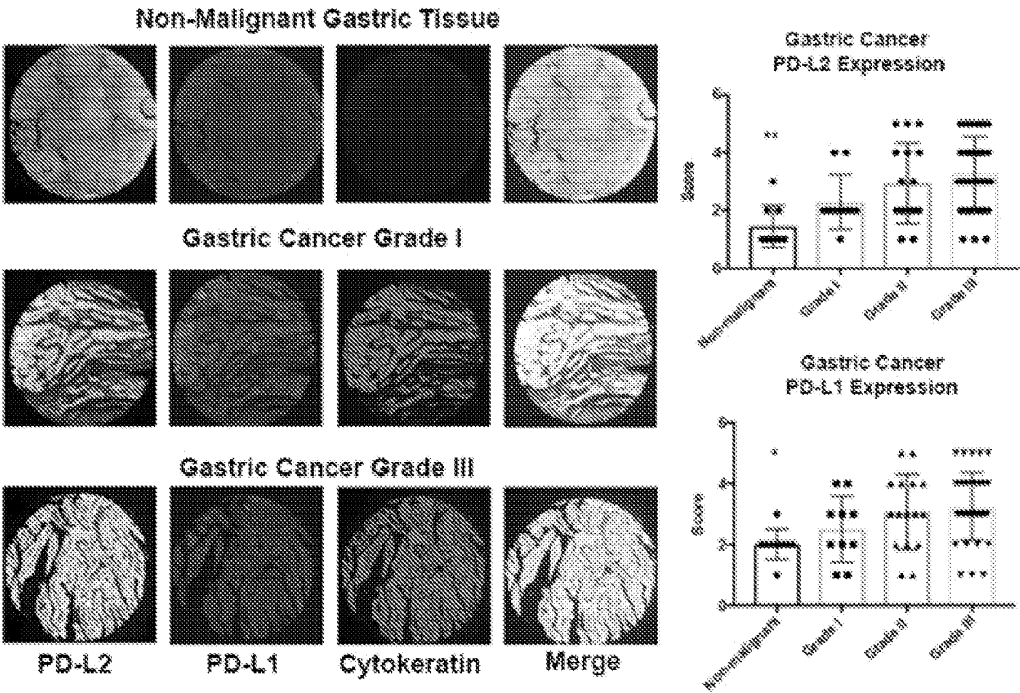


FIG. 18D

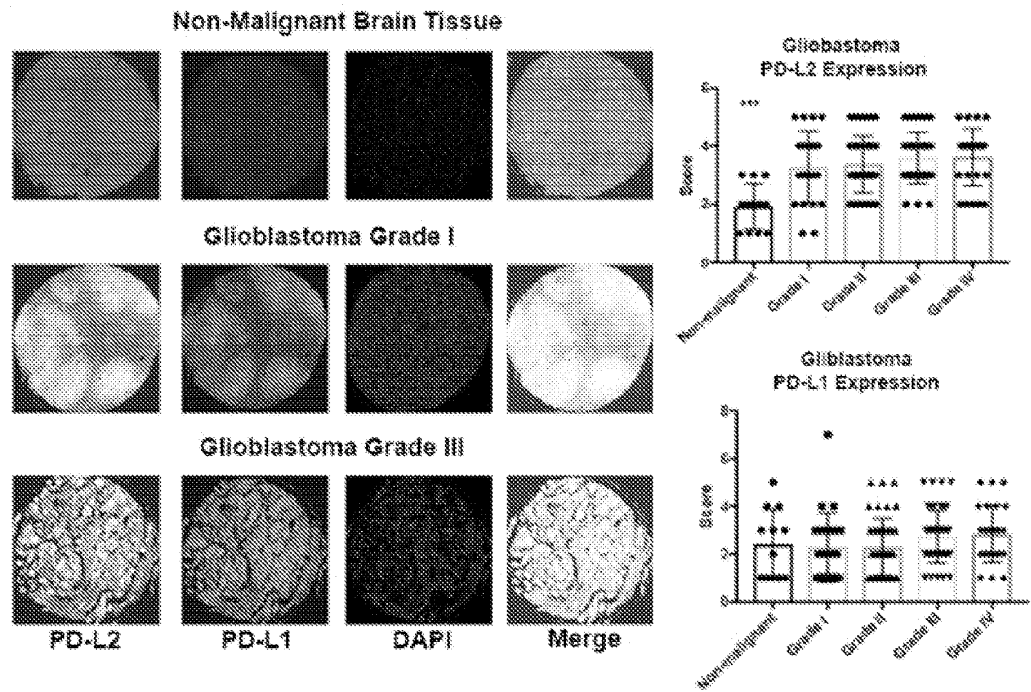


FIG. 18E

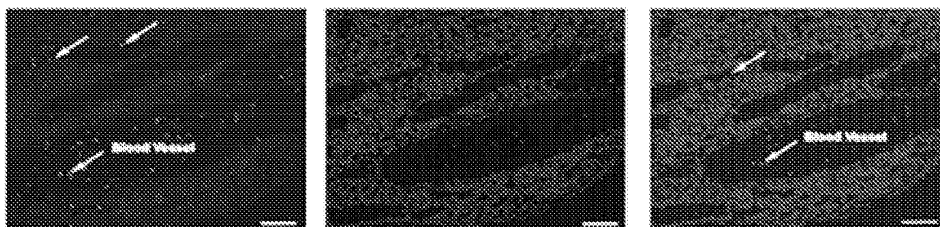
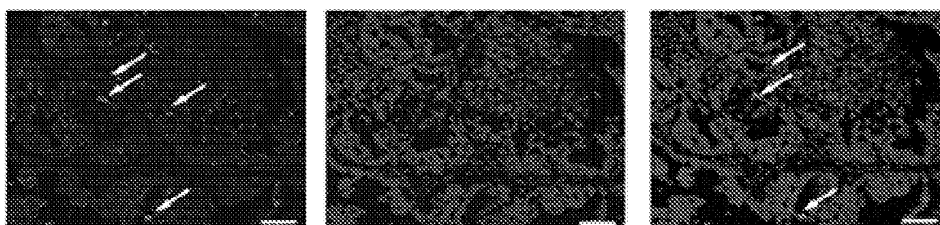
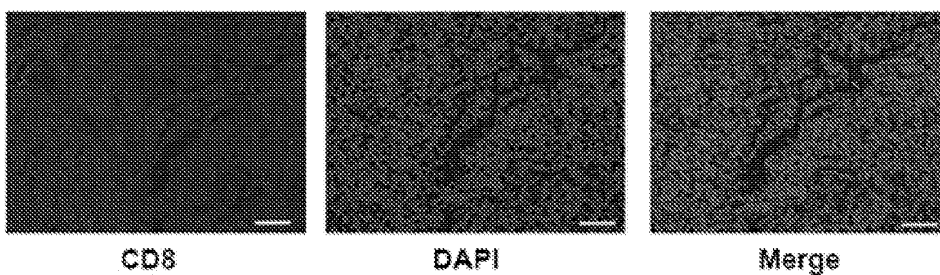
Non-Malignant Ovary Tissue with Blood Vessel**Ovarian Cancer Tissue CD8 Positive****Ovarian Cancer Tissue CD8 Negative**

FIG. 18F

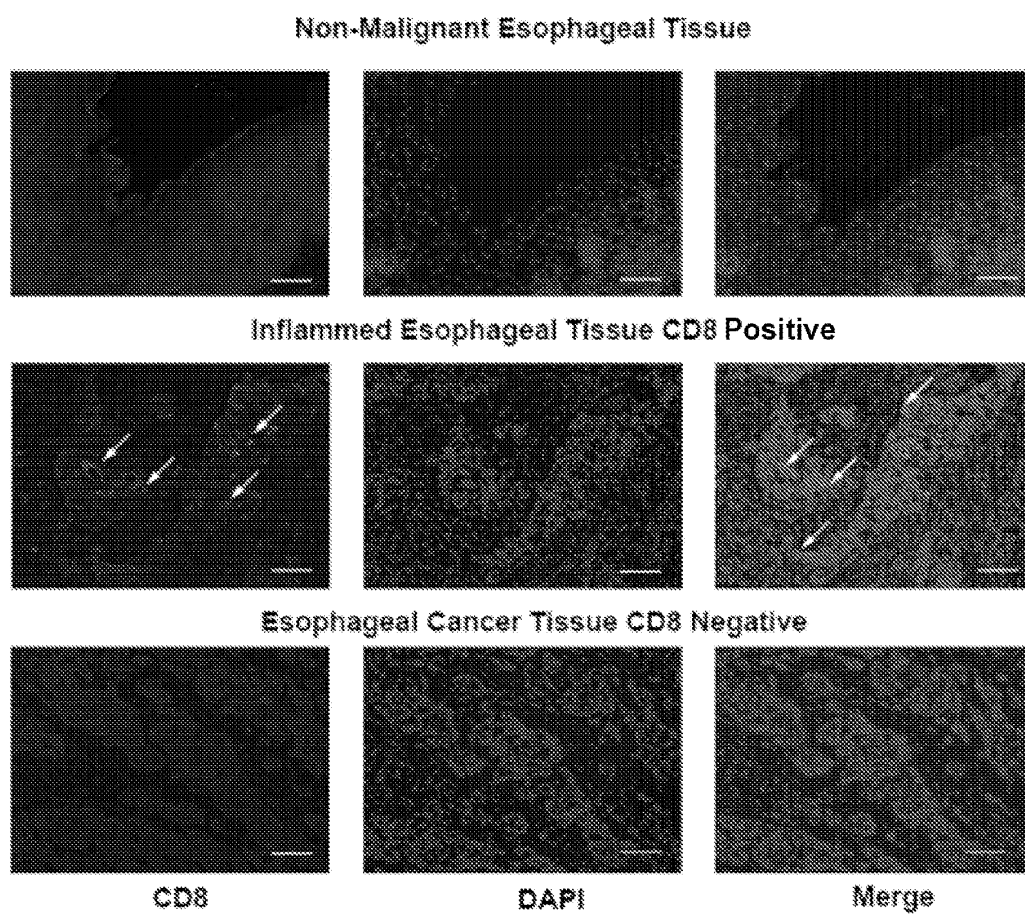


FIG. 19A

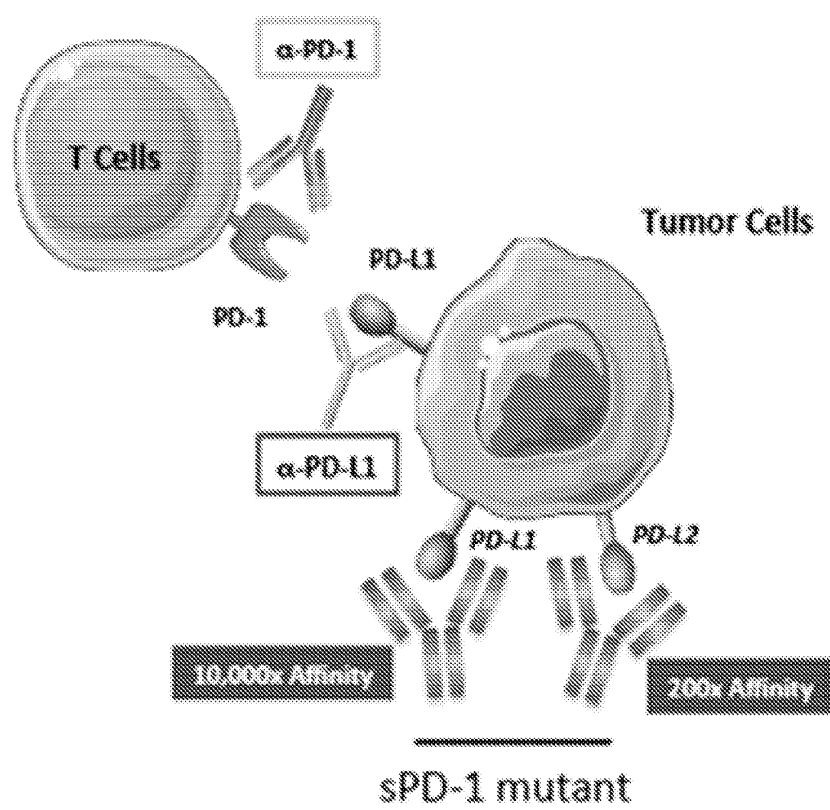


FIG. 19B

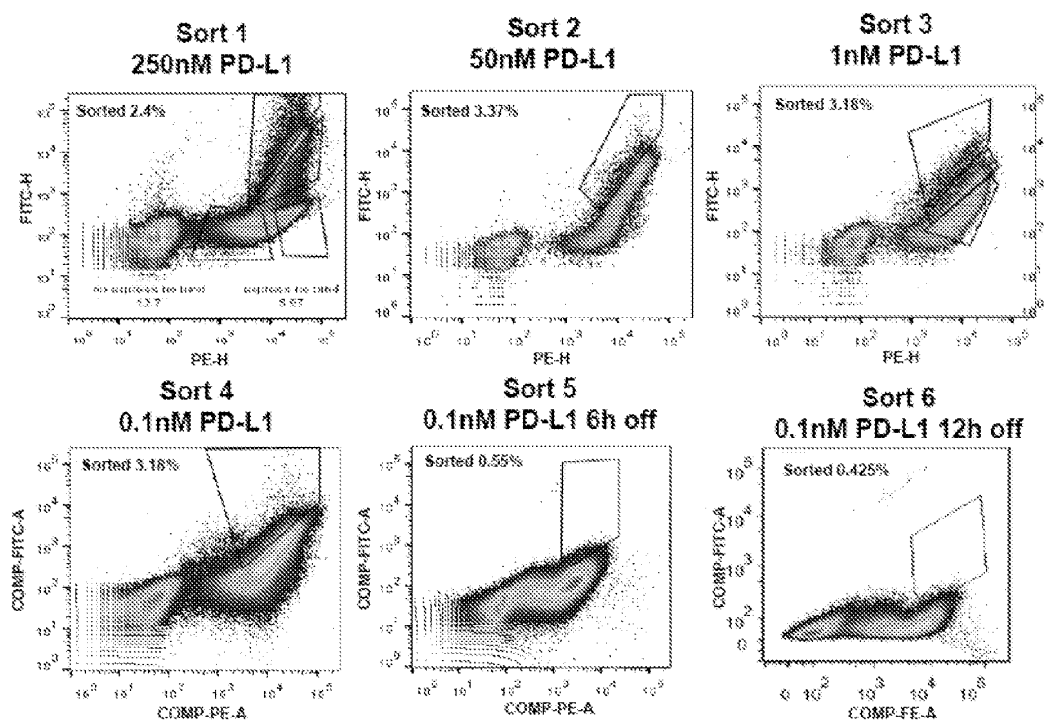


FIG. 19C

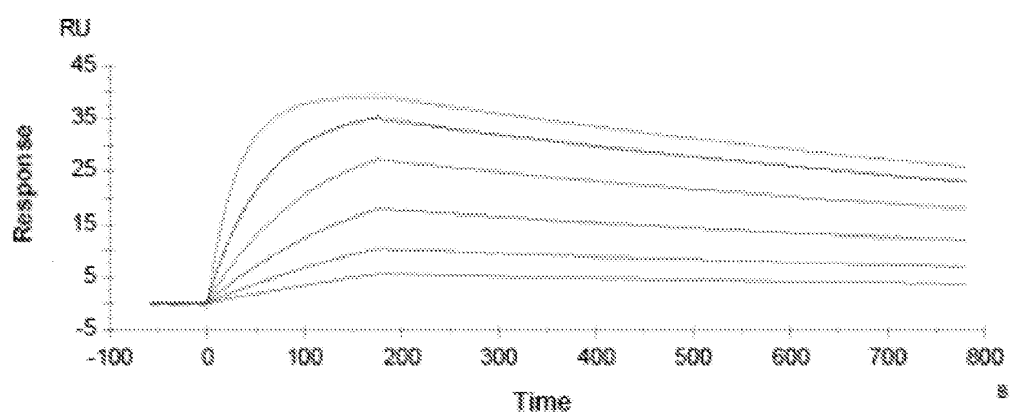
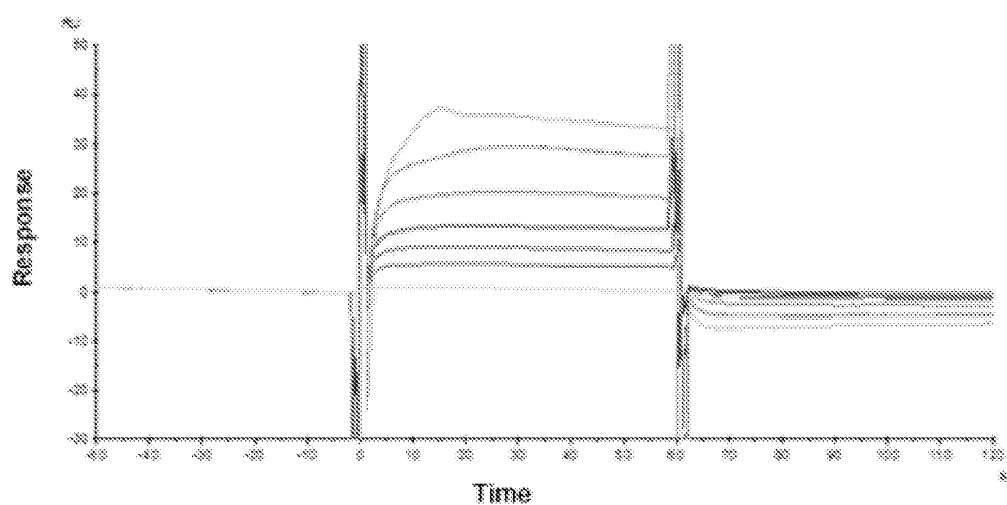
sPD-1 Mutant V1 Binding Kinetics to PD-L1**sPD-1 Wild Type Binding Kinetics to PD-L1**

FIG. 19D

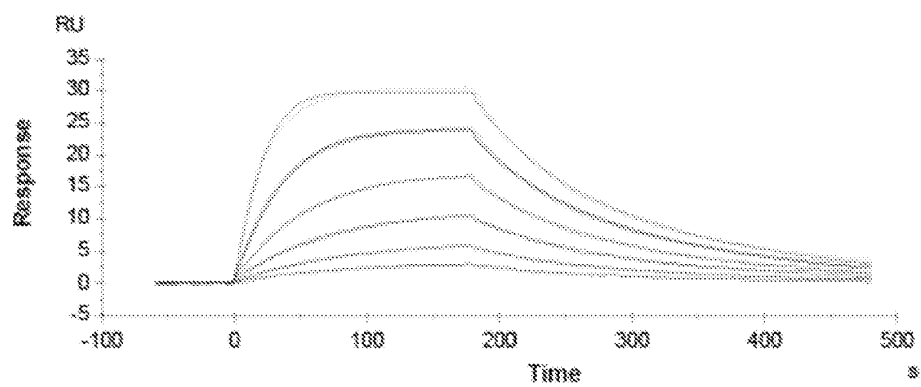
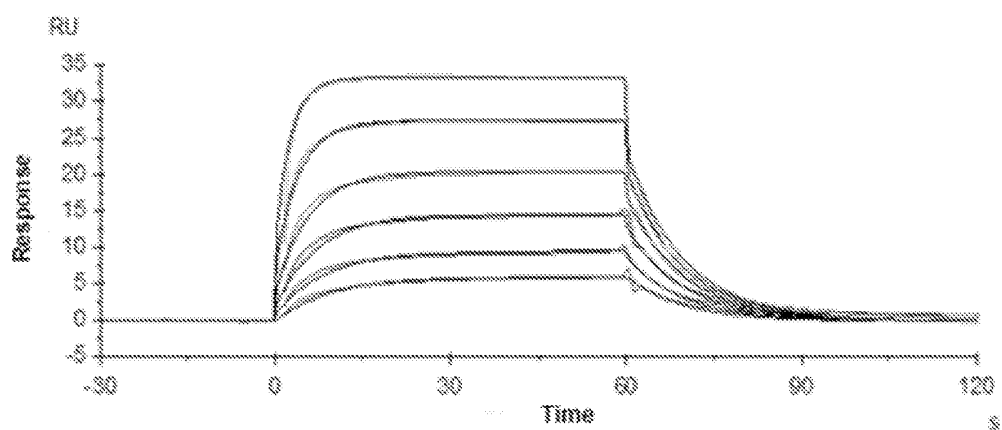
sPD-1 Mutant V1 Binding Kinetics to PD-L2**sPD-1 Wild Type Binding Kinetics to PD-L2**

FIG. 20A

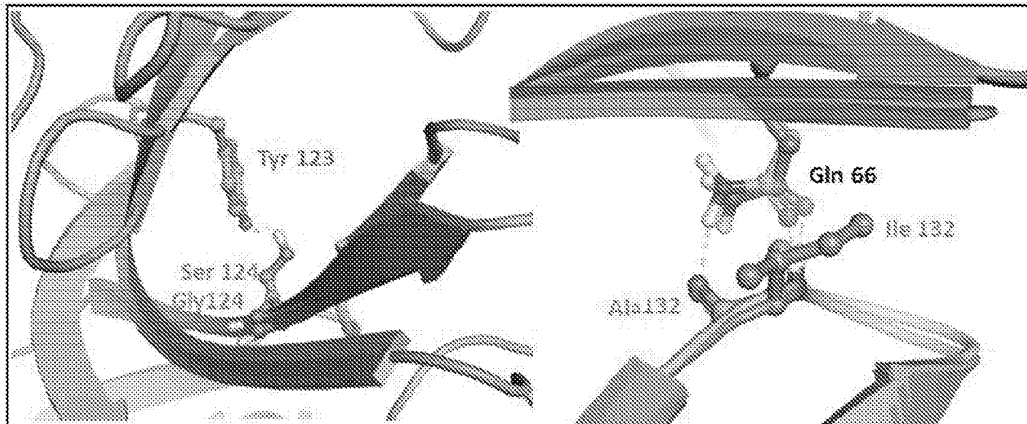


FIG. 20B

Surface Complementarity with PD-L1

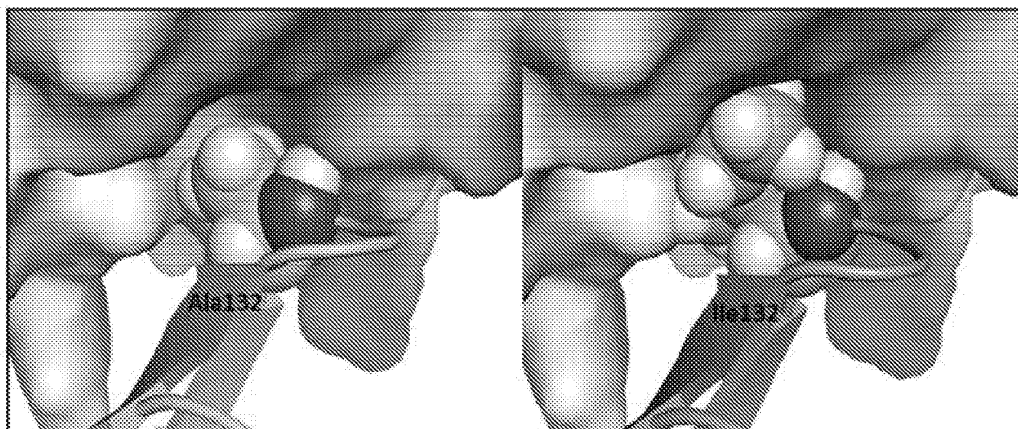


FIG. 20C

Surface Complementarity with PD-L2

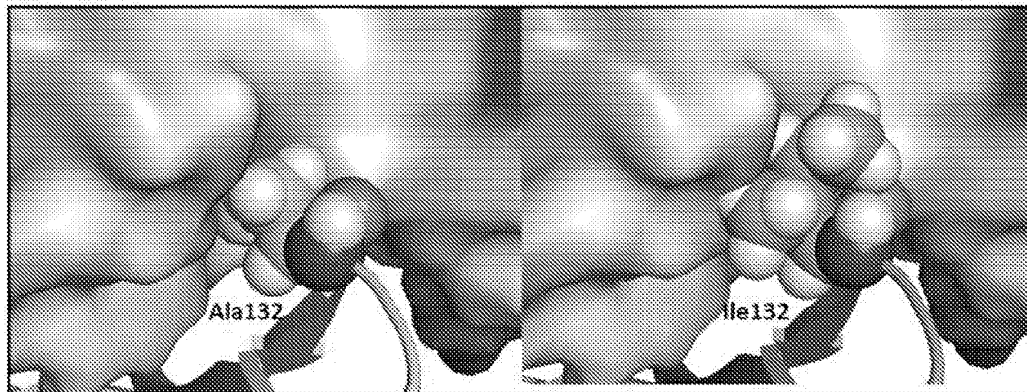


FIG. 21A

Blocking PD-L1 mediated binding

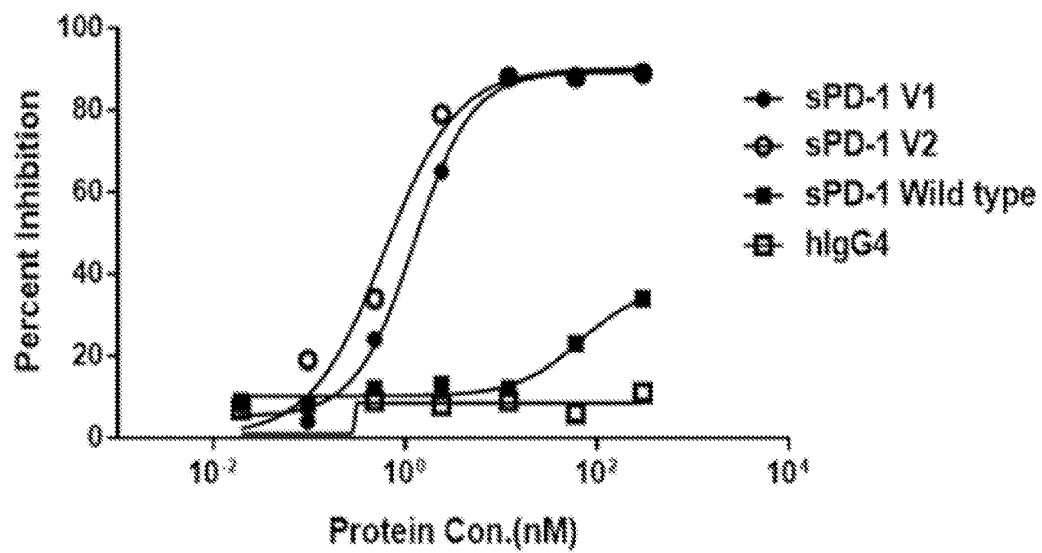


FIG. 21B

Blocking PD-L2 mediated binding

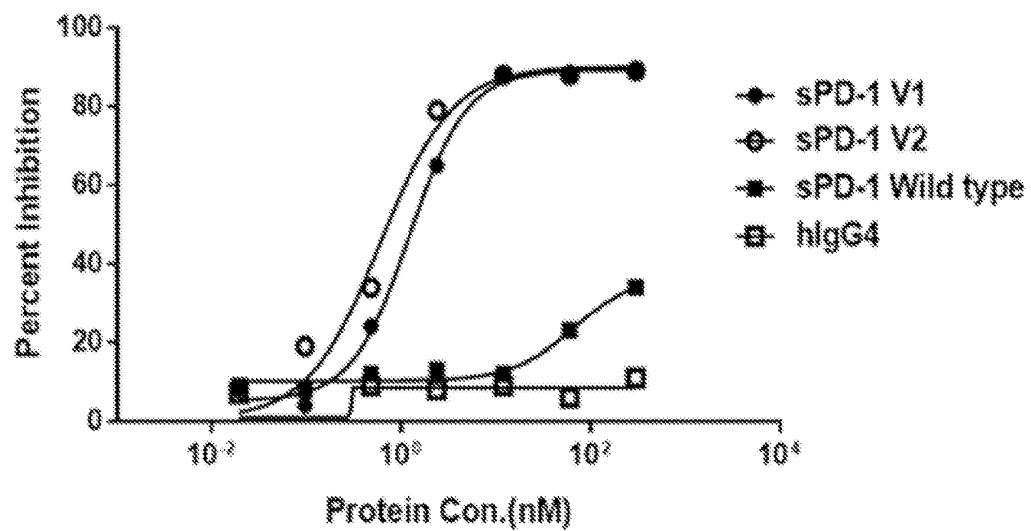


FIG. 21C

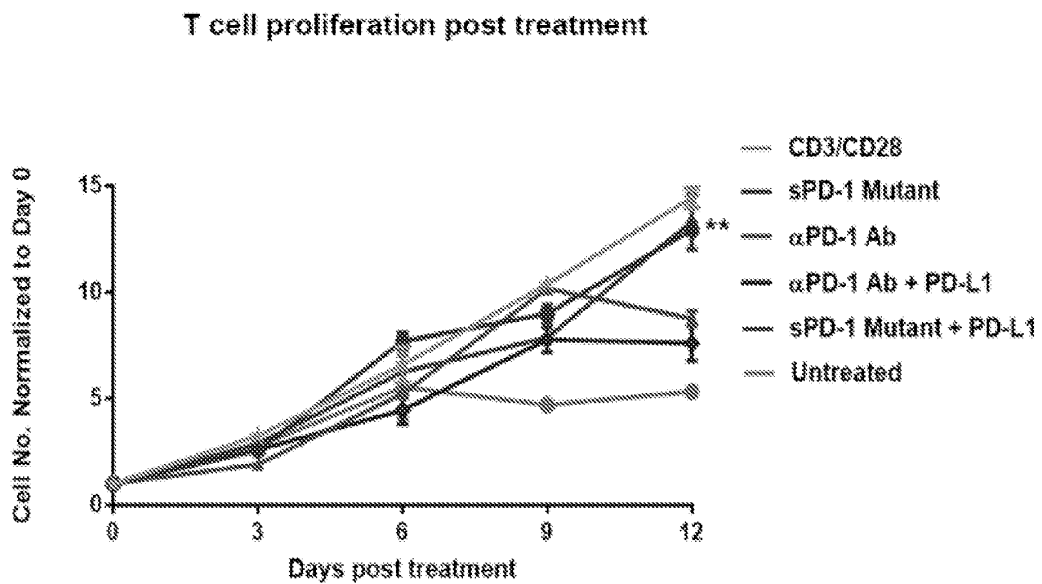


FIG. 22A

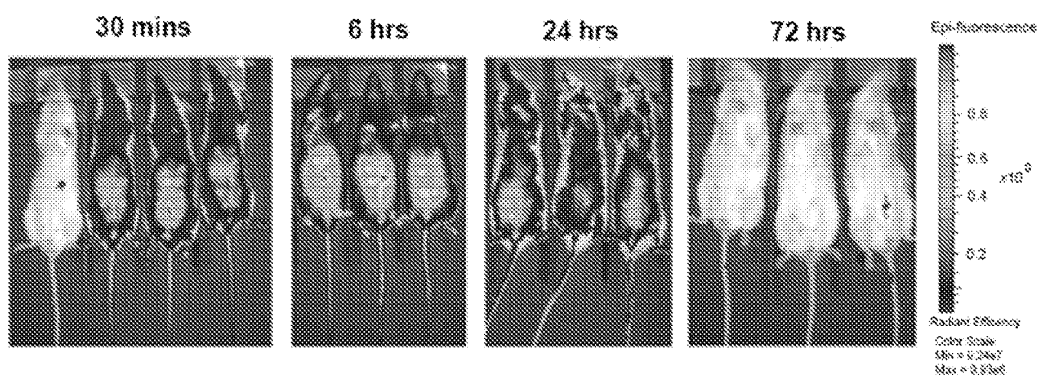


FIG. 22B

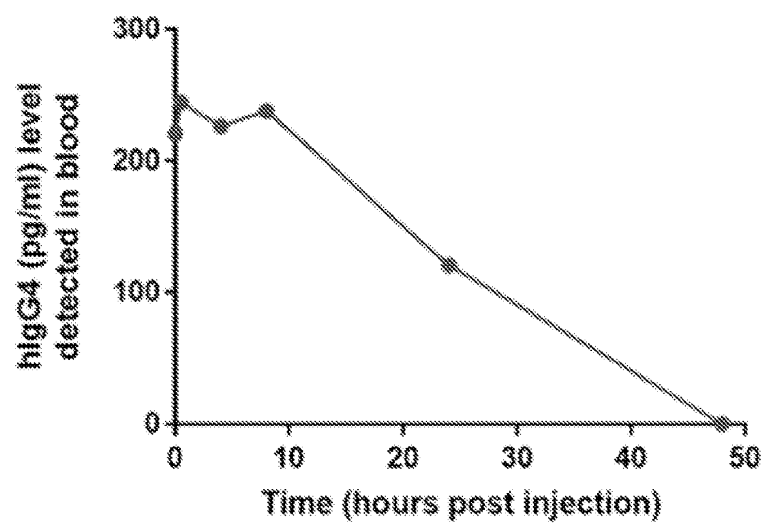


FIG. 22C

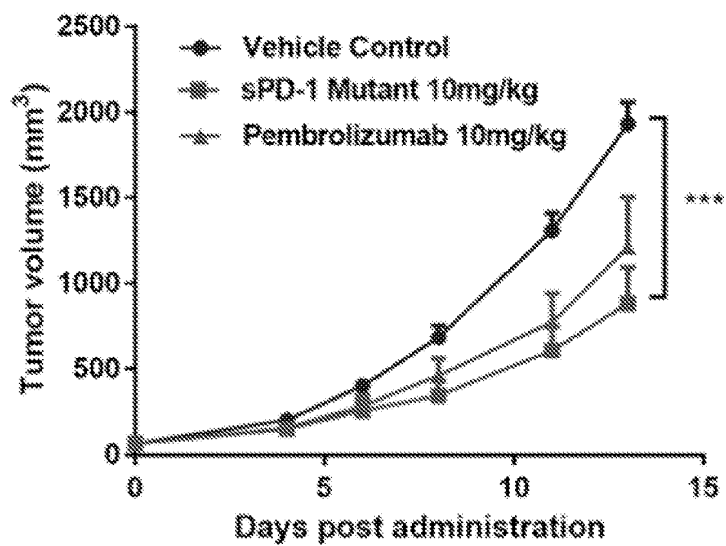


FIG. 22D

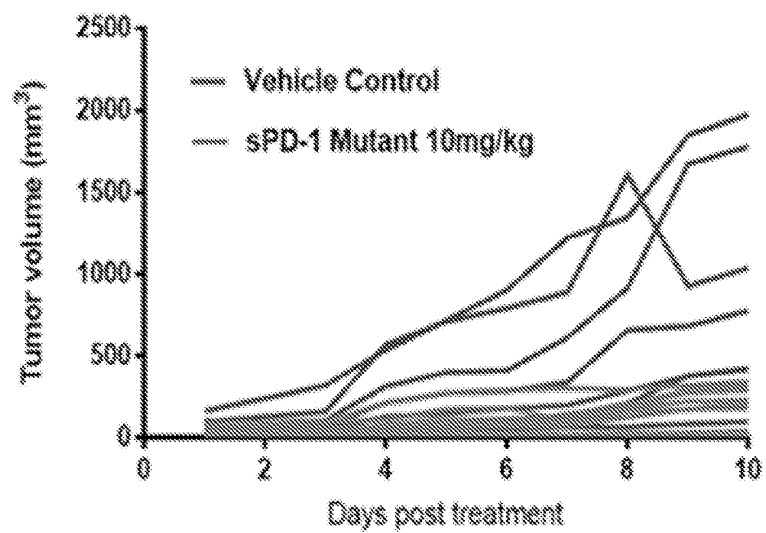
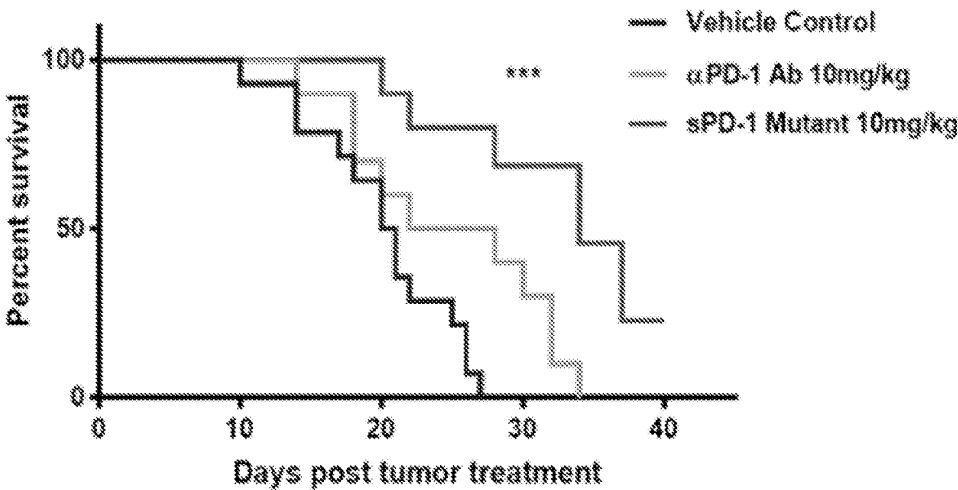


FIG. 22E



	Vehicle control	αPD-1 Ab	sPD-1 Mutant
Median survival	20.5	25	34

FIG. 22F

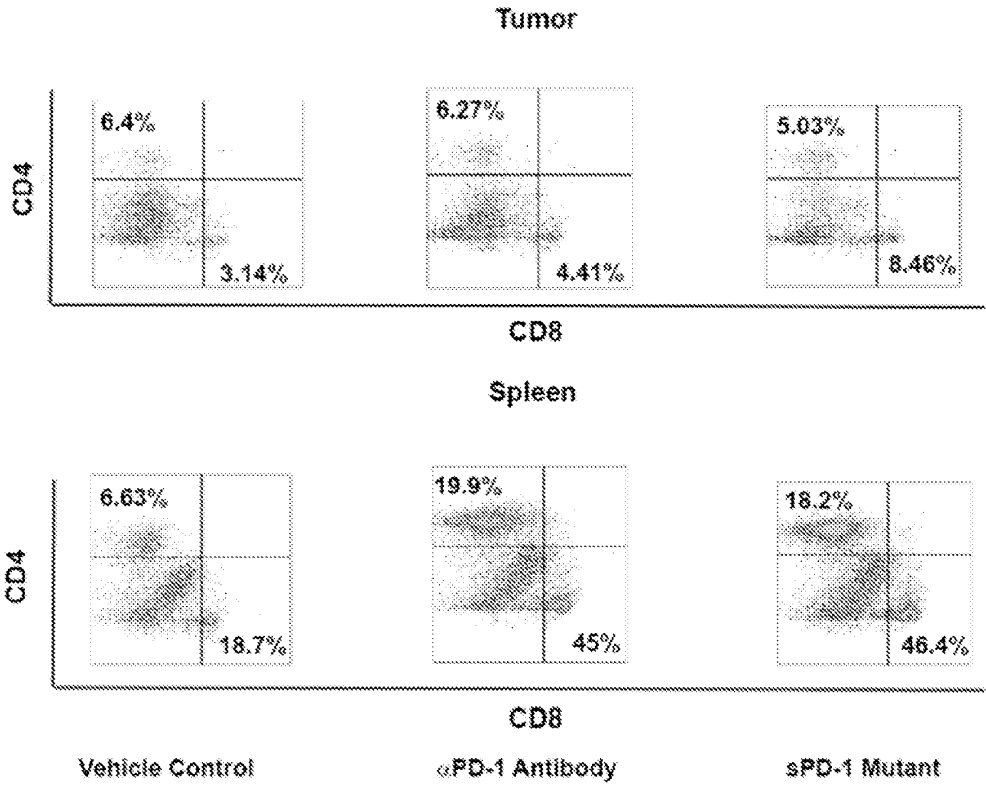


FIG. 22G

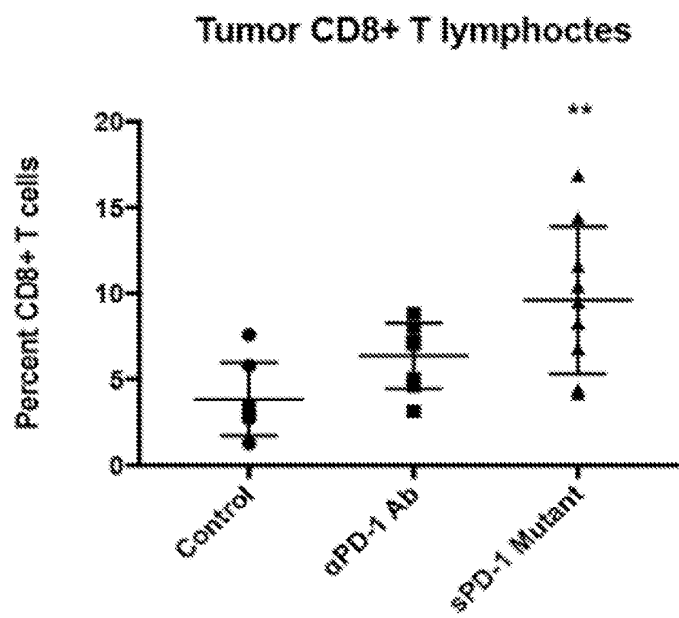


FIG. 22H

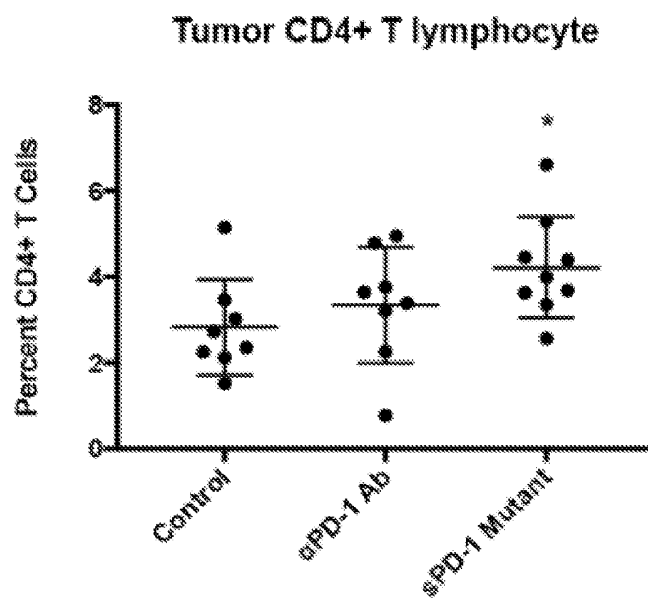


FIG. 23A

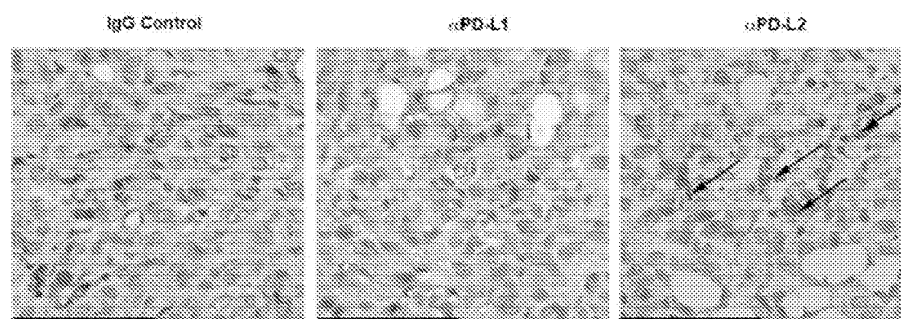


FIG. 23B

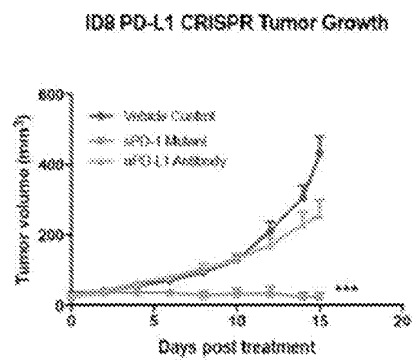


FIG. 23C

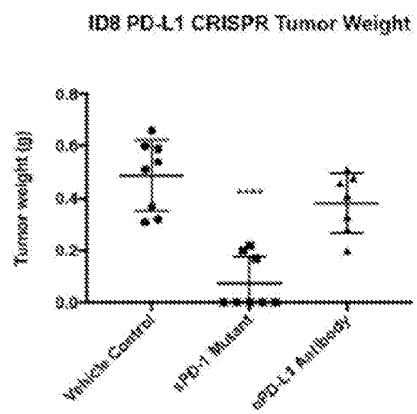


FIG. 23D

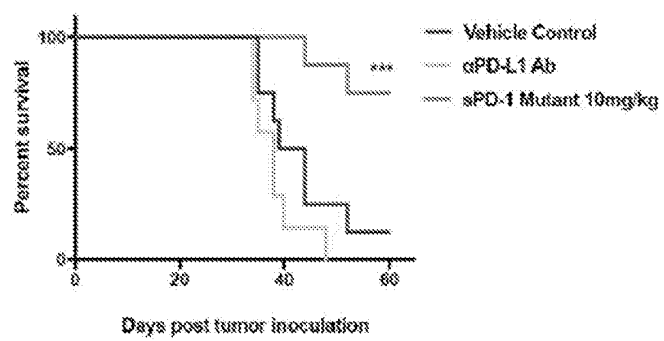


FIG. 23E

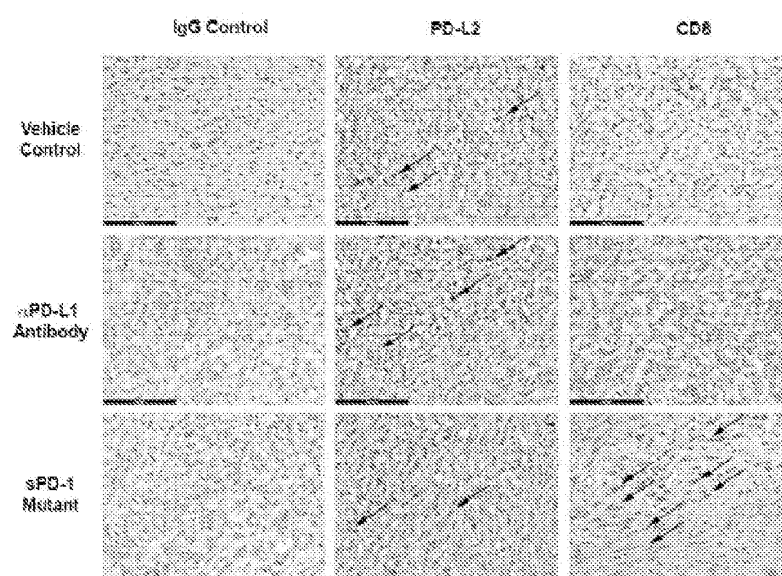


FIG. 24A

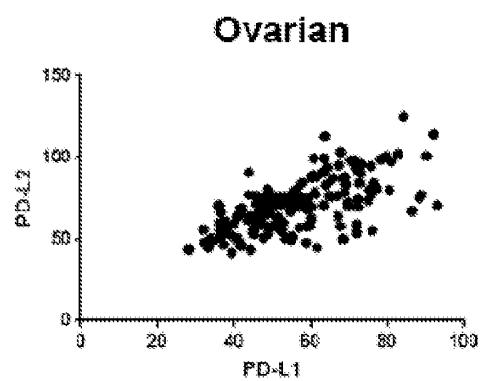


FIG. 24B

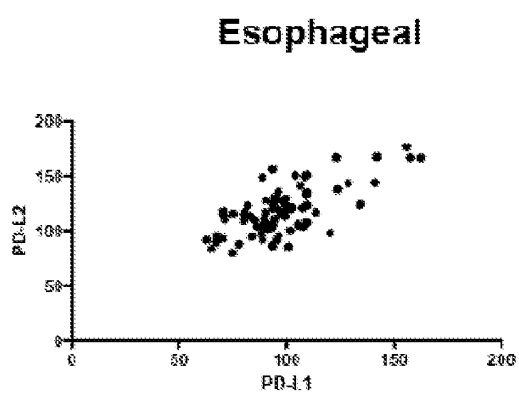


FIG. 24C

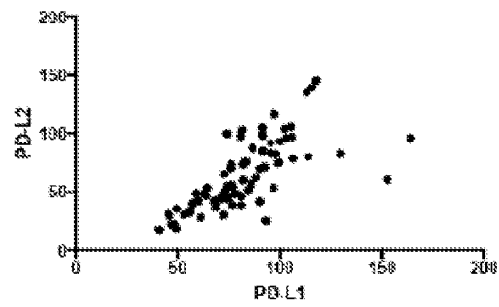
Gastric

FIG. 24D

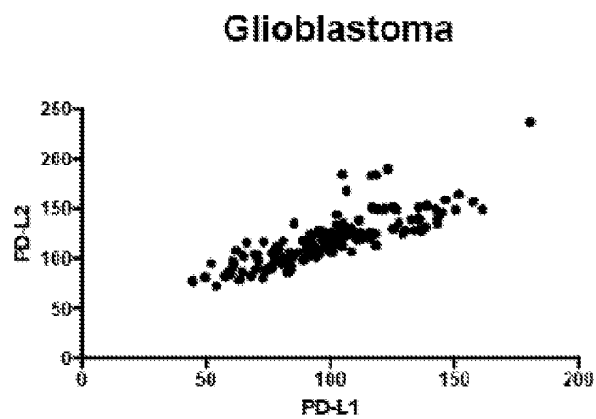


FIG. 24E

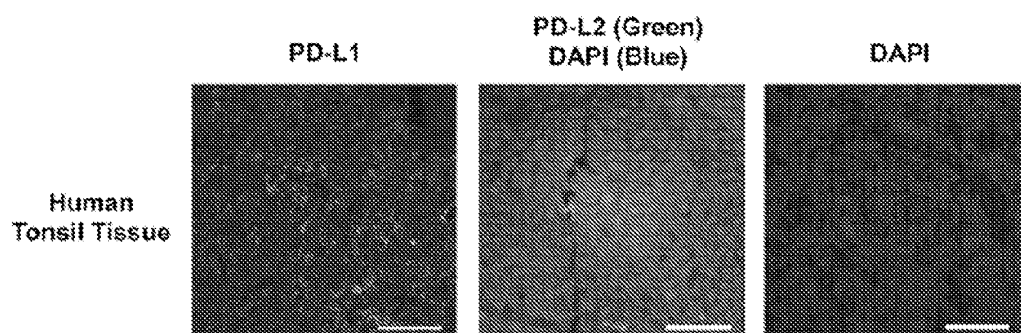


FIG. 25A

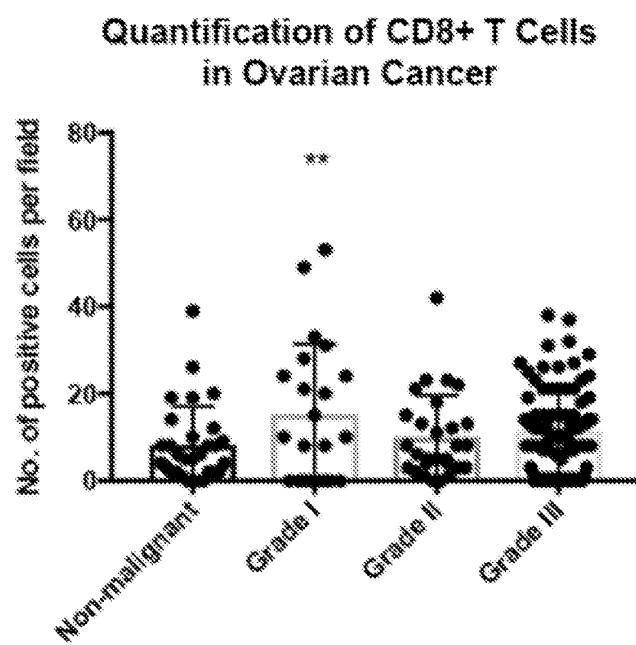


FIG. 25B

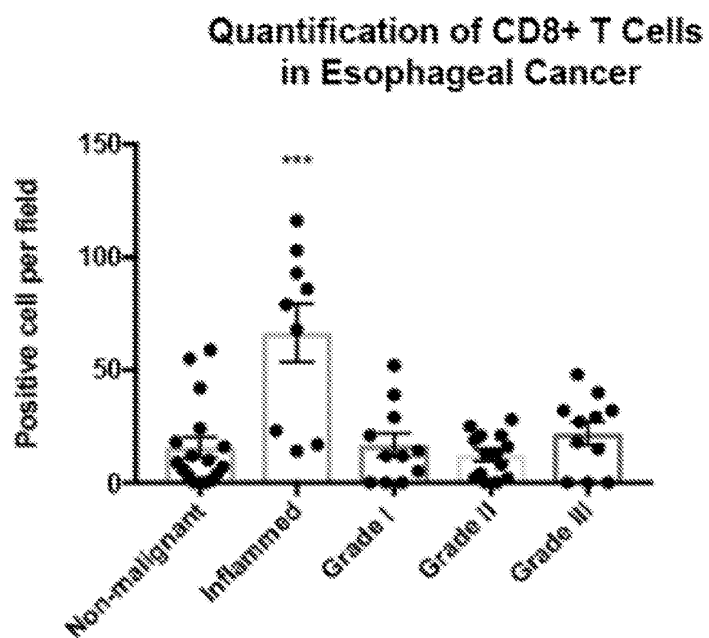


FIG. 26

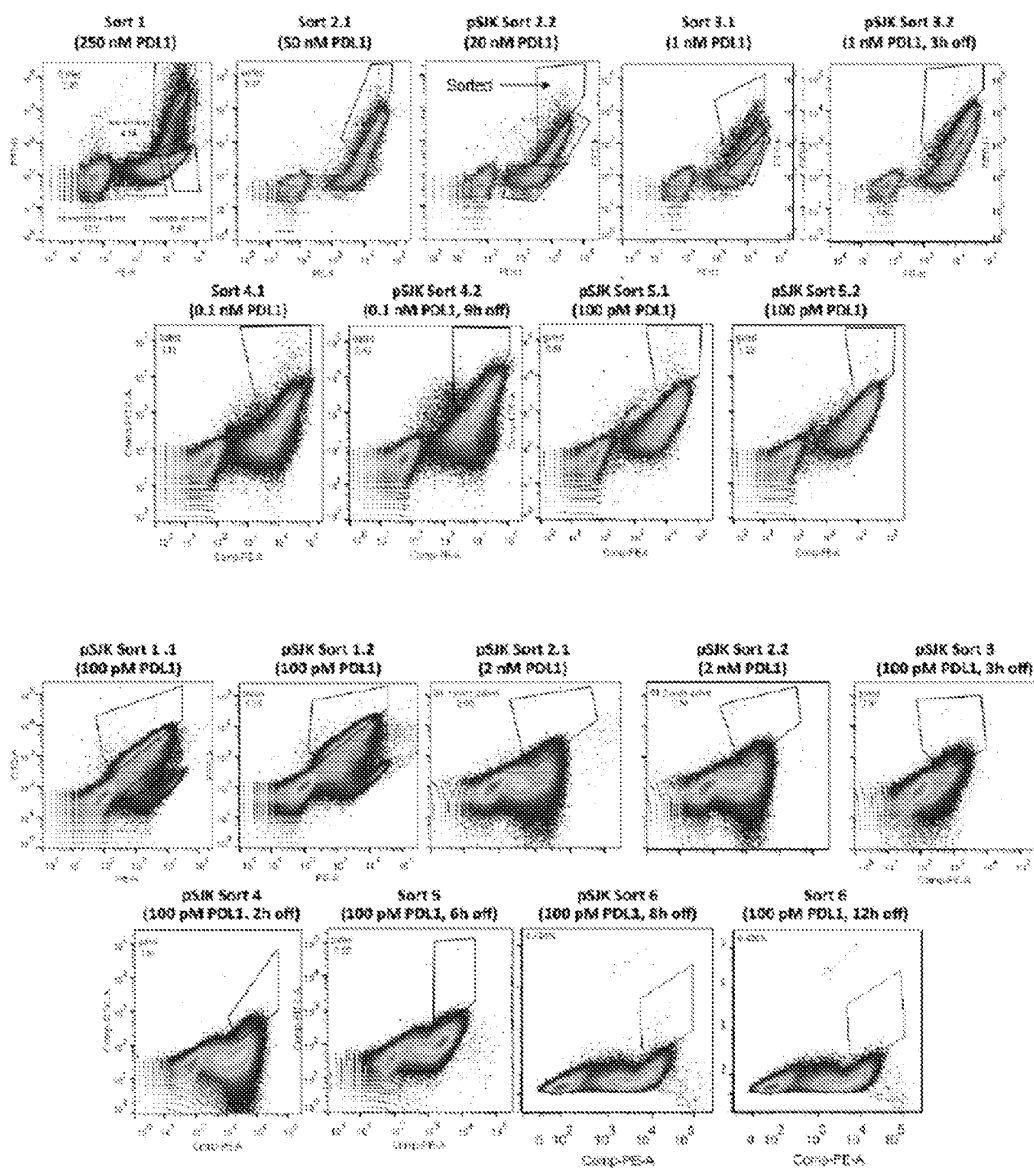


FIG. 27A

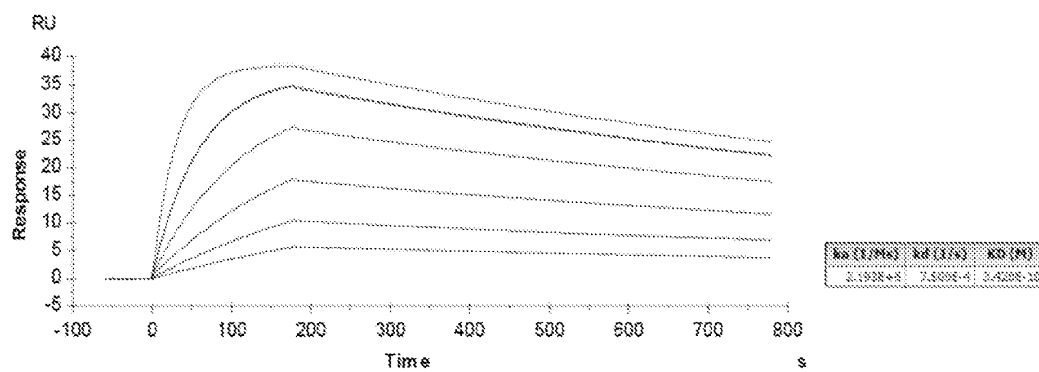


FIG. 27B

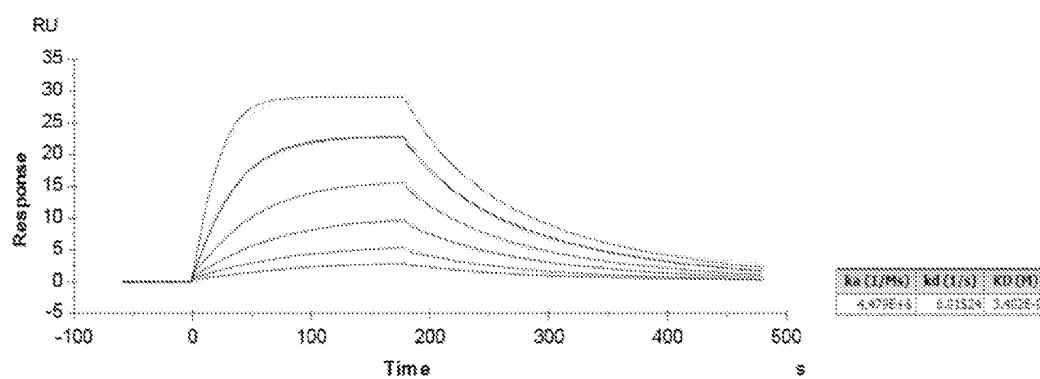
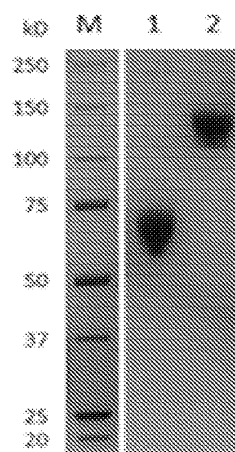


FIG. 28A



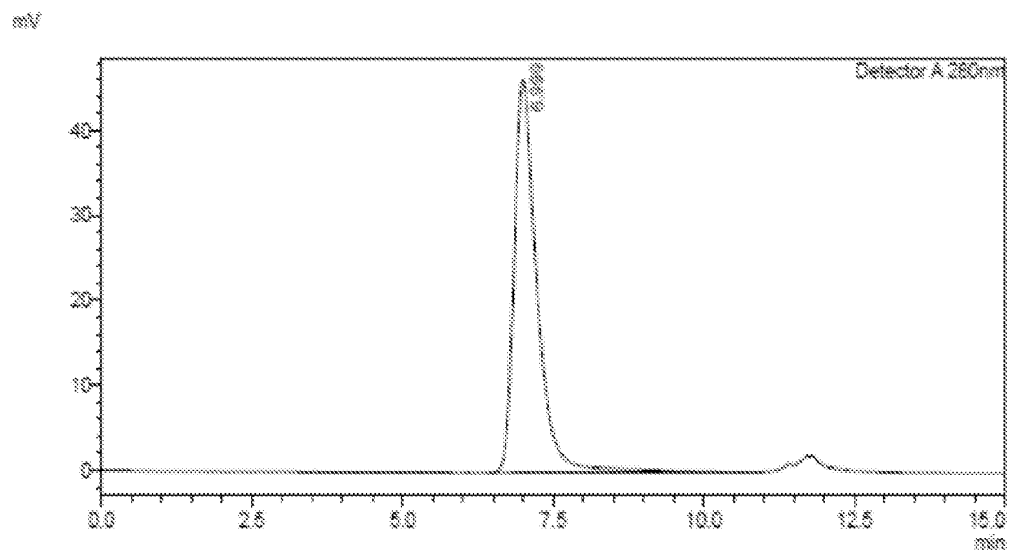
4-20% SDS-PAGE

M: Marker

1: Reduced (2ug)

2: Non-reduced (2ug)

FIG. 28B

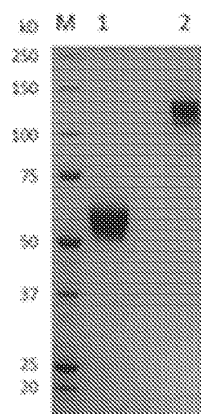


<Peak Table>

Detector A 280nm

Peak#	Ret. Time	Area	Area%	Height	Height%
1	6.999	1225529	100.000	46228	100.000
Total		1225529	100.000	46228	100.000

FIG. 28C



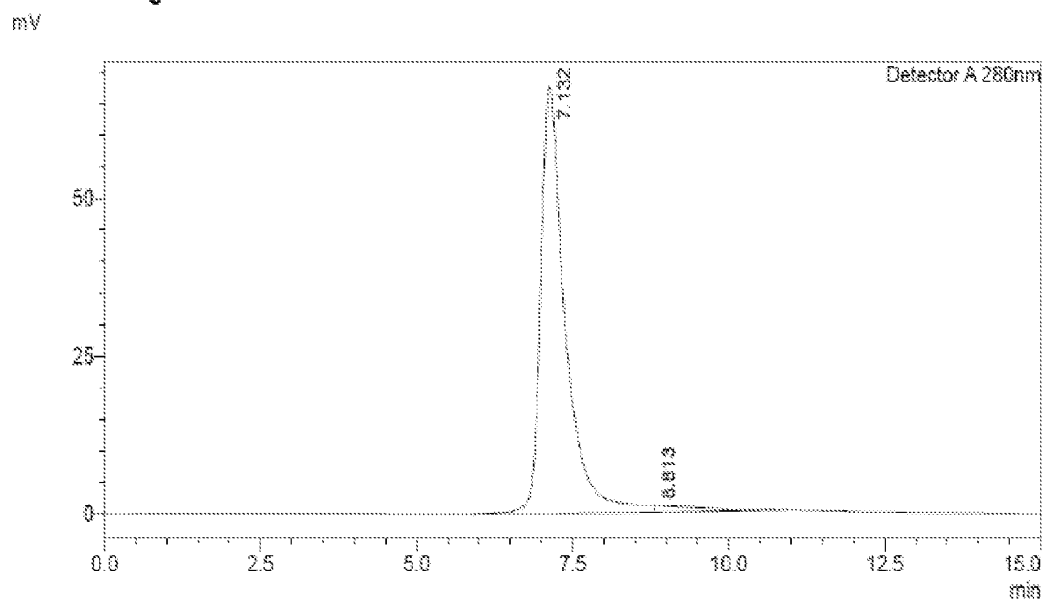
4-20% SDS-PAGE

M: Marker

1: Reduced (2ug)

2: Non-reduced (1ug)

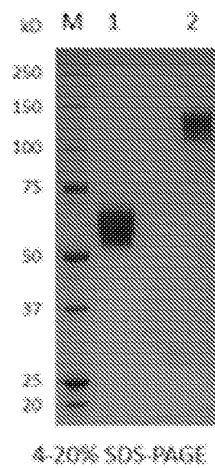
FIG. 28D



<Peak Table>

Detector A 280nm					
Peak#	Ret. Time	Area	Area%	Height	Height%
1	7.132	1864414	97.078	67727	98.505
2	8.813	58116	2.922	1028	1.495
Total		1920530	100.000	68755	100.000

FIG. 28E

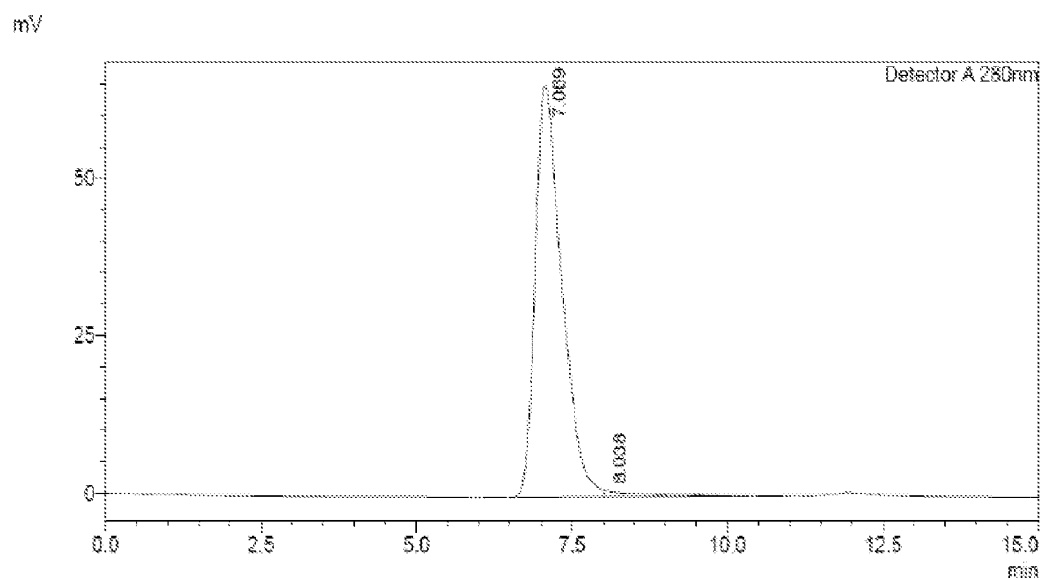


M: Marker

1: Reduced (2ug)

2: Non-reduced (1ug)

FIG. 28F



<Peak Table>

Detector A 280nm

Peak#	Ret. Time	Area	Area%	Height	Height%
1	7.089	1954452	97.756	65418	98.424
2	8.038	44872	2.244	1048	1.576
Total		1999324	100.000	66466	100.000

FIG. 29

Site in PD-1	Surface Complementarity		Hydrogen Bond with PD-L1	
	WT	Single mutation	WT	Single mutation
G124S	0.93	0.75	0	1 to Y123
S127V	0.89	0.64	0	0
A132I	0.72	0.85	1 to Q66	2 to Q66

FIG. 30

Site in PD1	Surface Complementarity		Hydrogen bond with PD-L2	
	WT	Single mutation	WT	Single mutation
G124S	0.80	0.85	0	0
A132I	0.83	0.86	1 to Q60	1 to Q60

FIG. 31

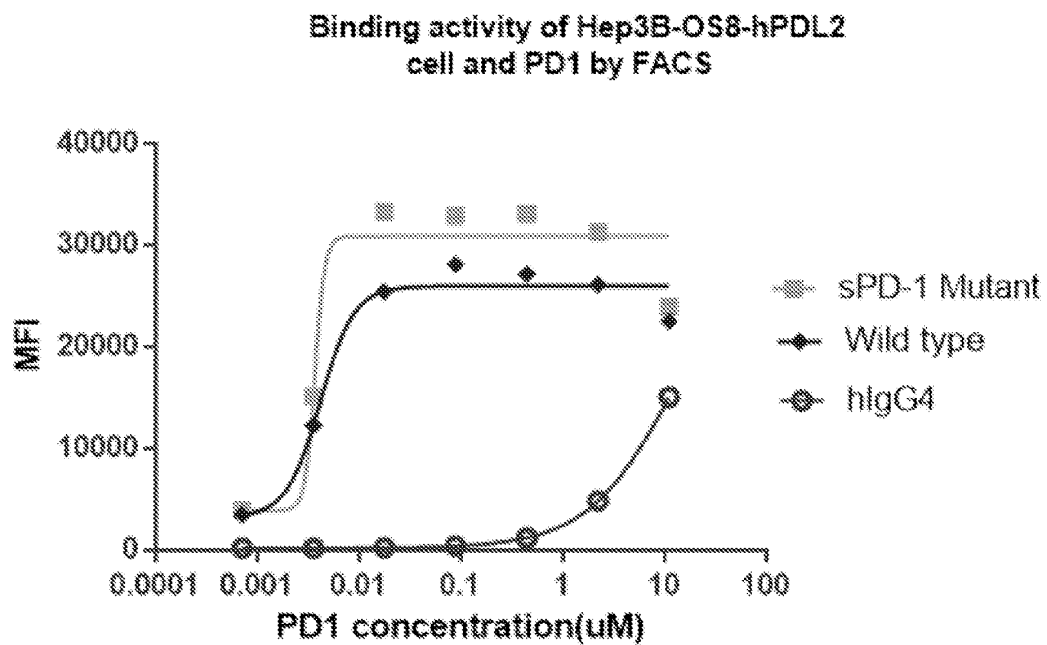


FIG. 32A

		cells	Freq. of Parent (%)	cells	Mean (Alexa Fluor 488-A)	corresponding specimen
166/well during transduction	4F3		86		4972.6	Specimen_001_A1_A01_001.fcs
	4G10		95.2		4730.4	Specimen_001_A2_A02_002.fcs
	4C3		94		4259.3	Specimen_001_A3_A03_003.fcs
	5E9		97.2		4322.7	Specimen_001_A4_A04_004.fcs
	4C7		99.2		5820.7	Specimen_001_A5_A05_005.fcs
	4F11		65		3711.2	Specimen_001_A6_A06_006.fcs
	4F12		95.2		7110.8	Specimen_001_A7_A07_007.fcs
	4E8		97.2		6691.2	Specimen_001_A8_A08_008.fcs
585/well during transduction	5B11		95.1		7515	Specimen_001_B1_B01_011.fcs
	5C10		97.9		6117.9	Specimen_001_B2_B02_012.fcs
	4H7		99.7		11616.6	Specimen_001_B3_B03_013.fcs
	4B6		95.7		5717.5	Specimen_001_B4_B04_014.fcs
	5A10		97.7		4869.3	Specimen_001_B5_B05_015.fcs
	5D4		99.5		12933.3	Specimen_001_B6_B06_016.fcs
	5D12		98.8		10138	Specimen_001_B7_B07_017.fcs
	5E2		99.1		9648.6	Specimen_001_B8_B08_018.fcs
	5E5		89.7		3820.5	Specimen_001_B9_B09_019.fcs
	5F5		96.9		5485.8	Specimen_001_B10_B10_020.fcs
	5A7		98.6		9980.6	Specimen_001_B11_B11_021.fcs
	5F8		99.3		7276	Specimen_001_B12_B12_022.fcs
	4G6		98.1		10644.7	Specimen_002_C1_C01_023.fcs
MAC38	stained		62.8		3405.6	Specimen_001_A11_A11_009.fcs
blank	unstained		0.5		351.8	Specimen_001_A12_A12_010.fcs

FIG. 32B

Sample set 1 (<30%) +ve cells

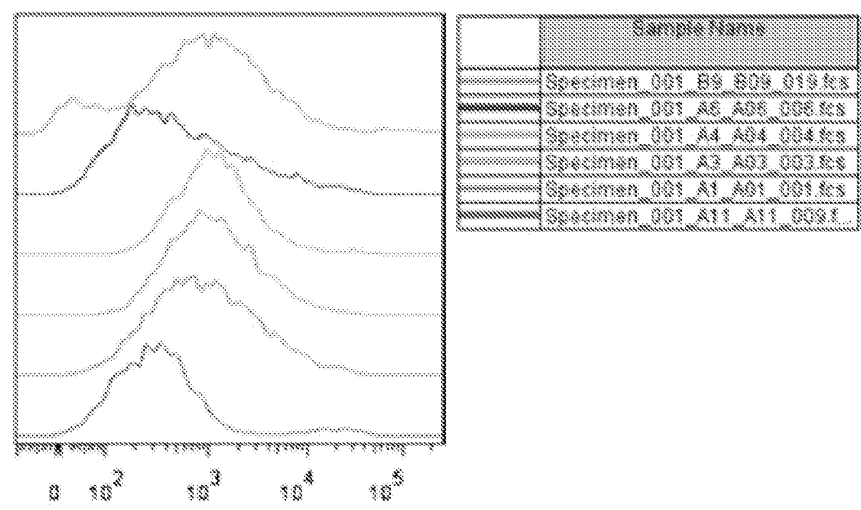


FIG. 32C

Sample set 2 (30-50%) +ve cells

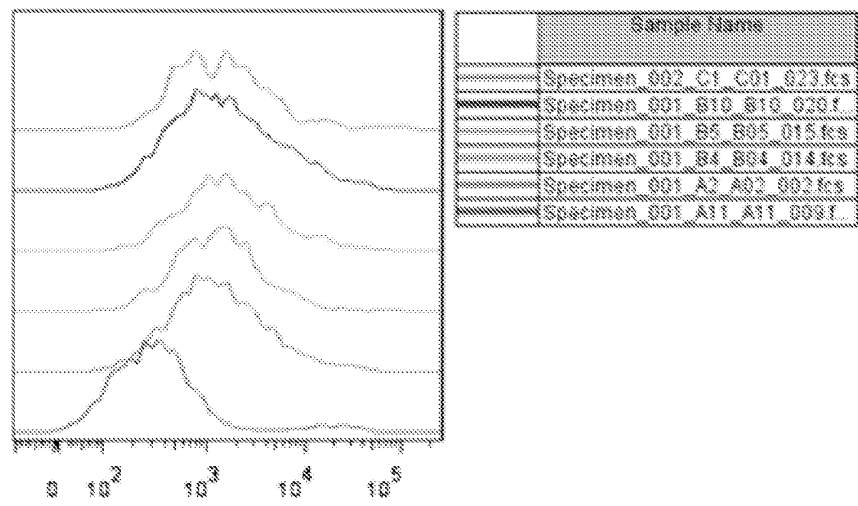
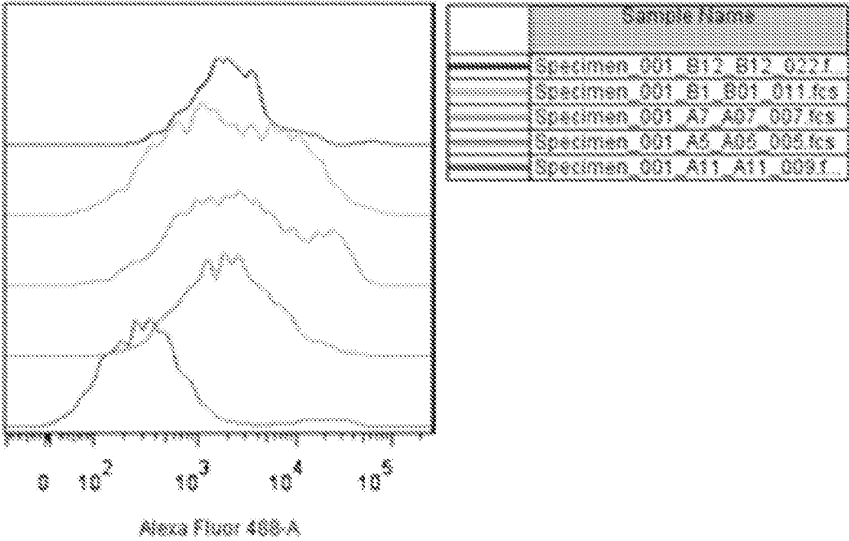
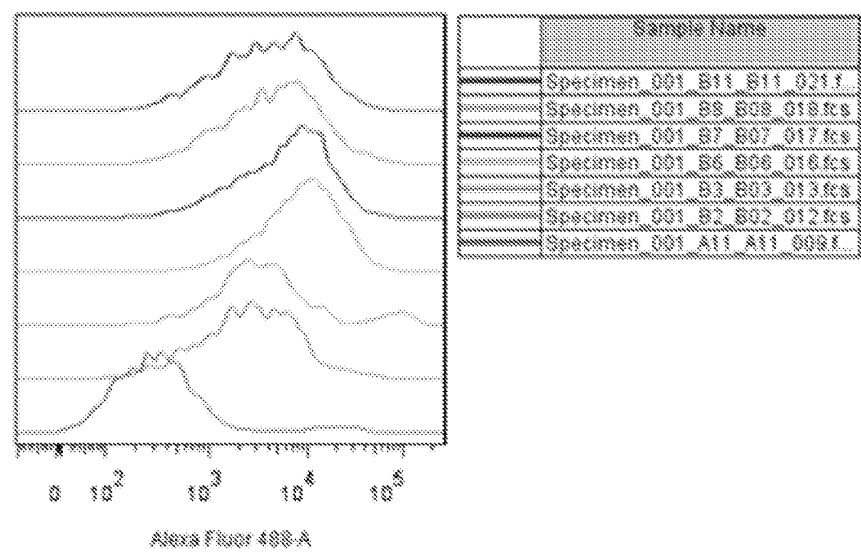


FIG. 32D



Sample set 3 (50%-60%) +ve cells

FIG. 32E



Sample set 4 (>60%) +ve cells

FIG. 33A

Clone	Alexa488 MFI	P2 %Parent	Peak number
Hep3B blank+Ab2	53.1	0.3	1
Hep3B blank+Ab1+Ab2	2699	75.7	1
SC5	34409	98.4	1
SD8	53268	95.9	1
SE8	50584.3	95.3	1
SF8	32883.8	98.8	1
SF5	28832.1	98.9	1
4B9	41703.5	98.5	1
4G6	34652.9	98.1	1
4E2	38126.1	99.1	1
4F2	46515.5	92.7	1
4E7	32394.5	98.7	1
SE7	50304.4	98.6	1
SF7	39739.9	97.1	1
4F9	42523.6	96.4	1
SG3	43873.9	98.4	1
SG6	33266.8	98.5	1
SG9	61274.1	97.8	1

Clone	Alexa488 MFI
SG9	61274.1
SD8	53268
SE8	50584.3
SE7	50304.4
4F2	46515.5
SG3	43873.9
4F9	42523.6
4B9	41703.5
SF7	39739.9
4E2	38126.1
4G6	34652.9
SC5	34409
SG6	33266.8
SF8	32883.8
4E7	32394.5
SF5	28832.1

FIG. 33B

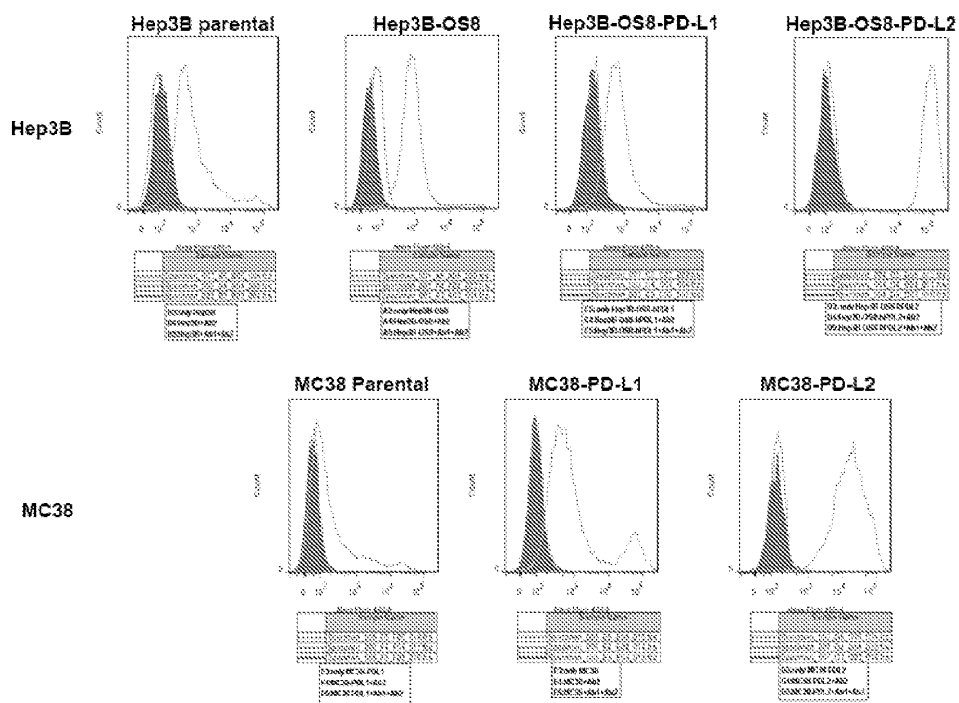


FIG. 34

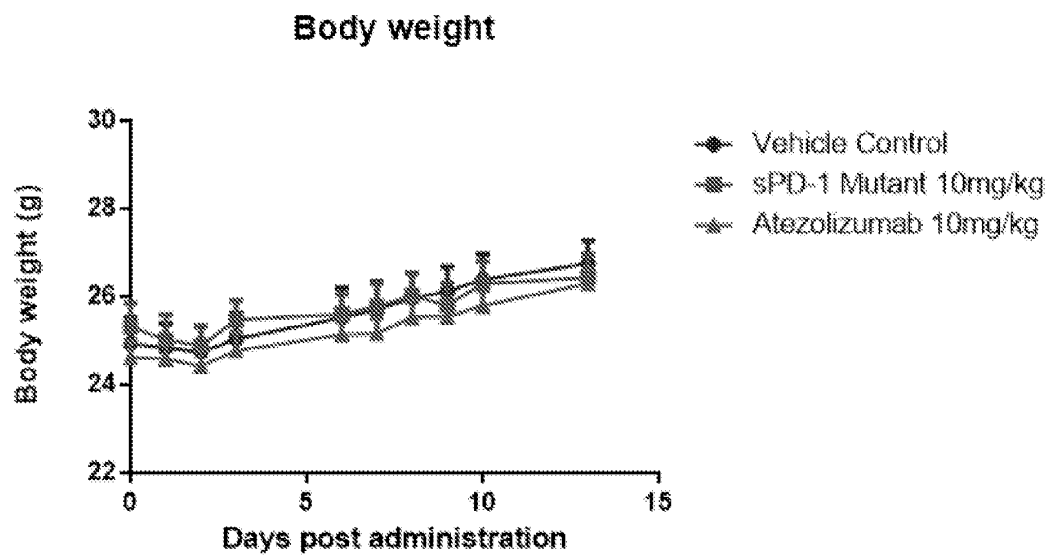


FIG. 35A

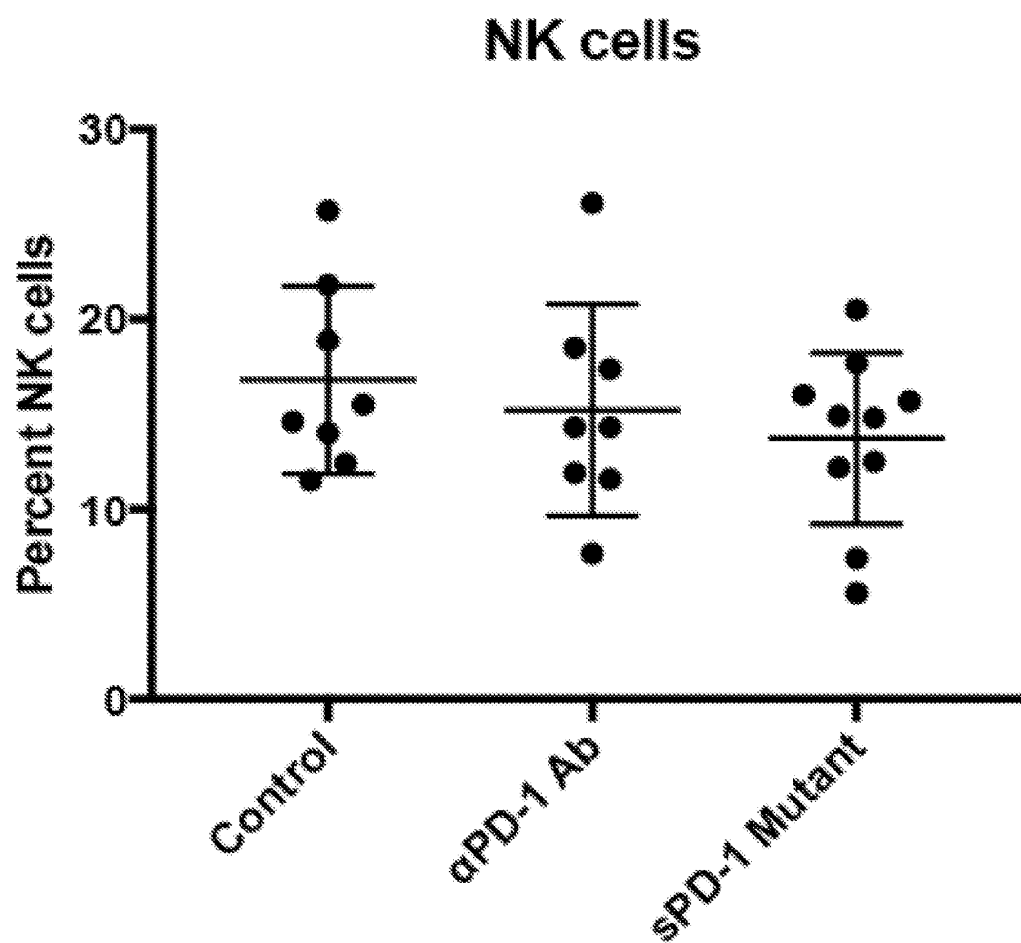


FIG. 35B

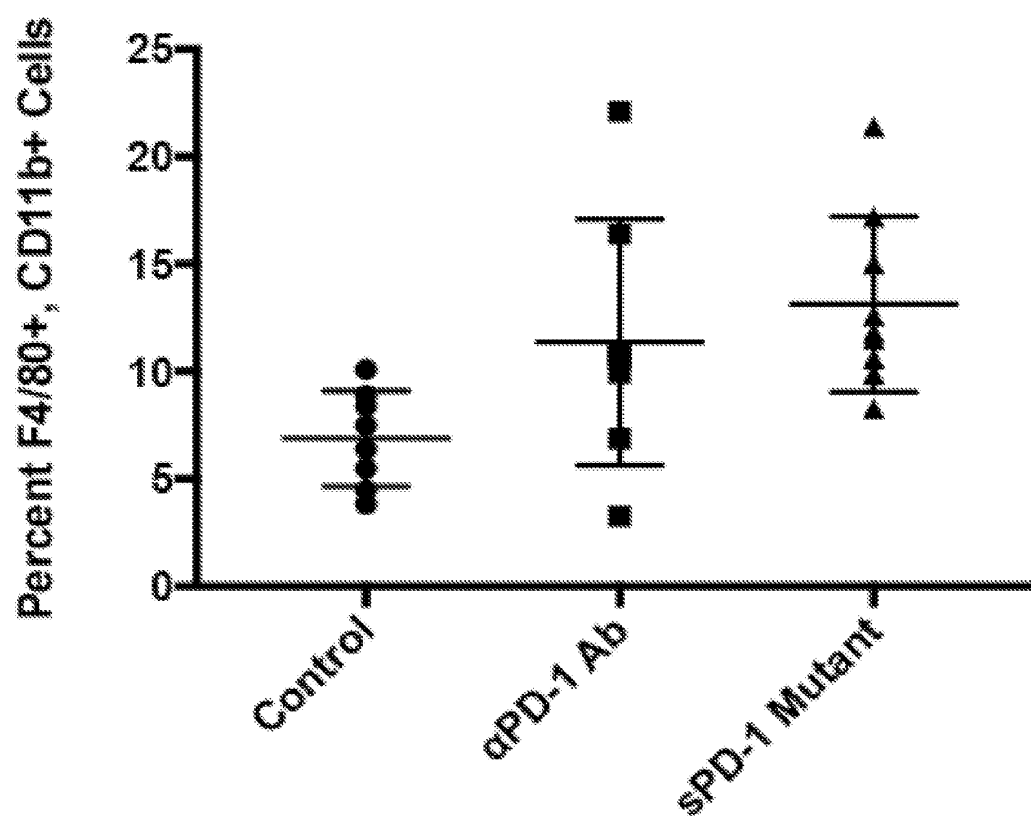
F4/80, CD11b Macrophage

FIG. 36A

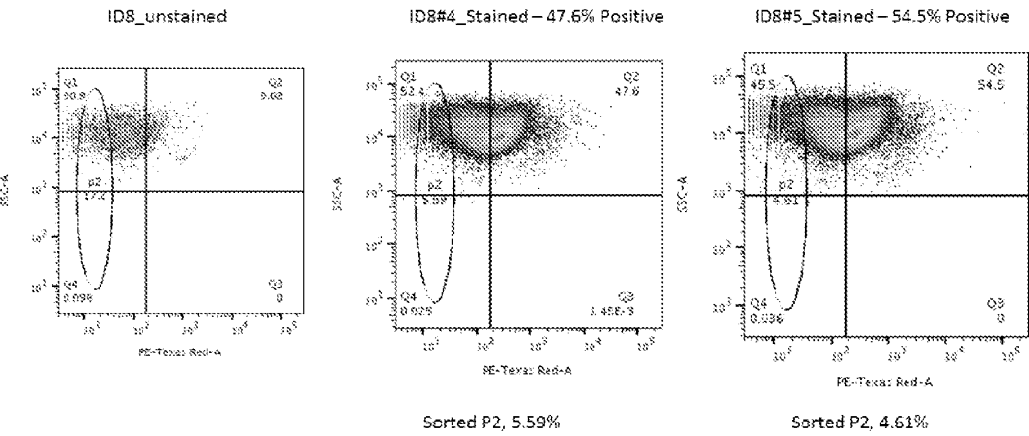


FIG. 36B

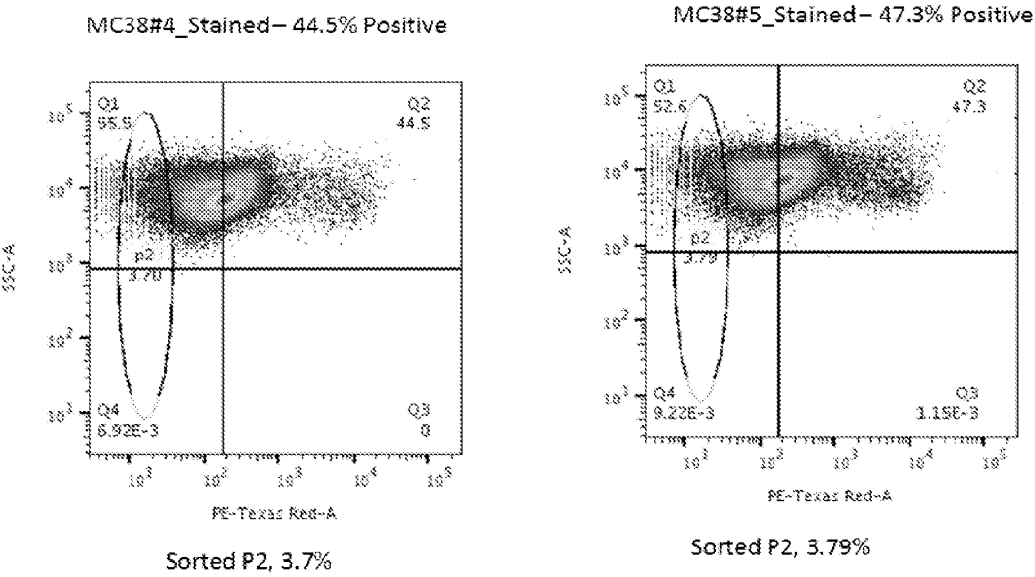


FIG. 37

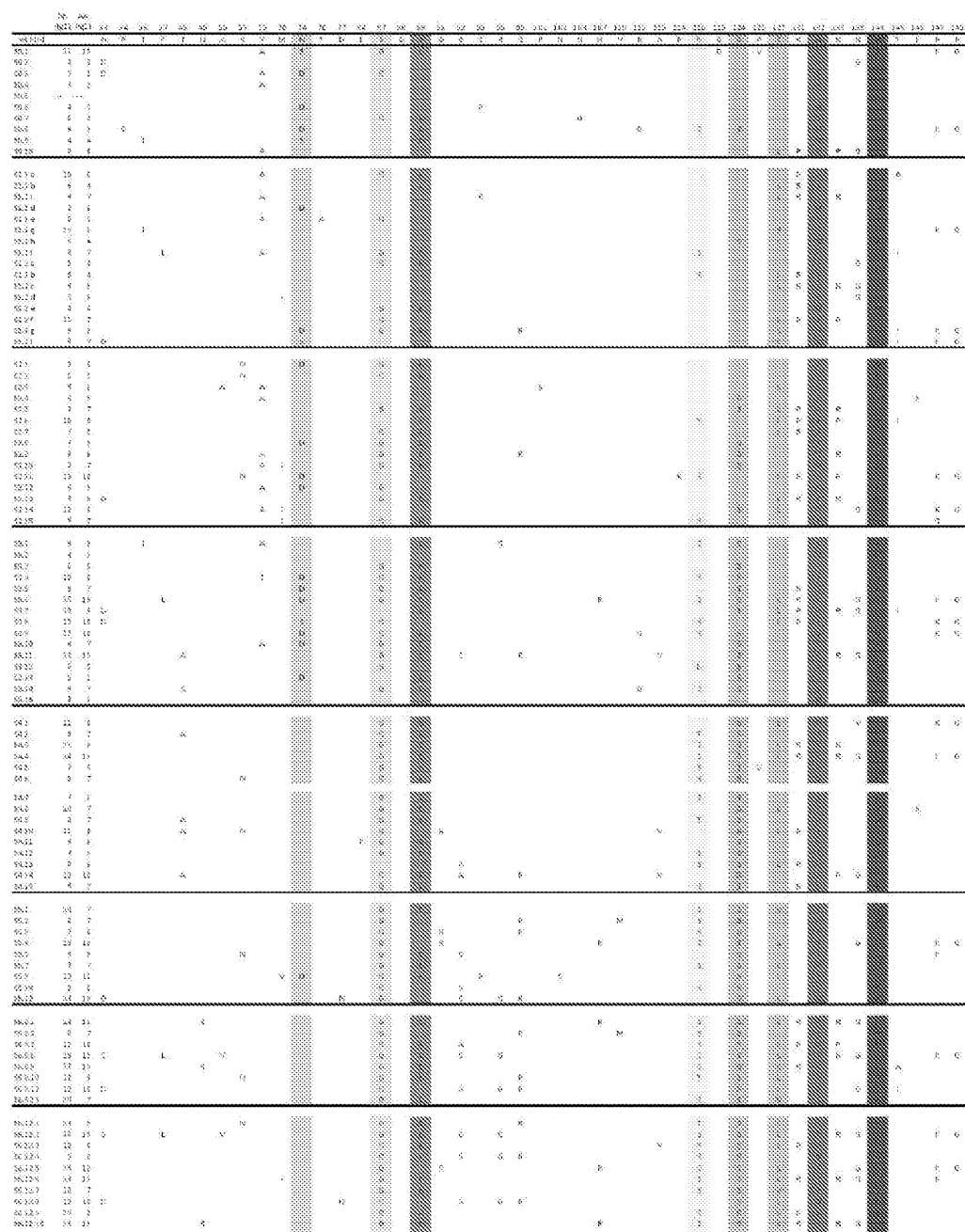


FIG. 38A

Refined clones to test in the binding assay

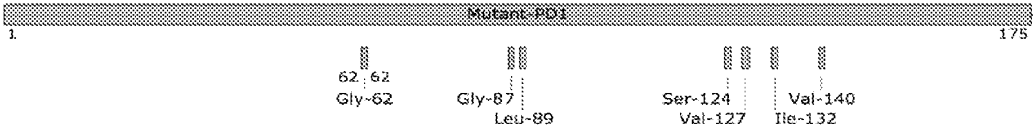
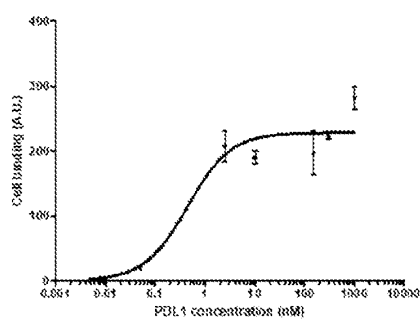


FIG. 38B

<u>Clone#1</u>	89-124-127-132-140
<u>Clone#2</u>	87-124-127-132-140
<u>Clone#3</u>	87-89-124-127-132-140
<u>Clone#4</u>	124-127-132-140
<u>Clone#5</u>	124-127-132

FIG. 39A

Original Mutant PD1
(62-87-89-124-127-132-140)



Kd = 0.44 nM

FIG. 39B

Clone#1

89-124-127-132-140

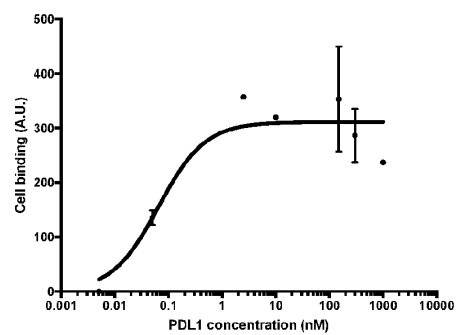
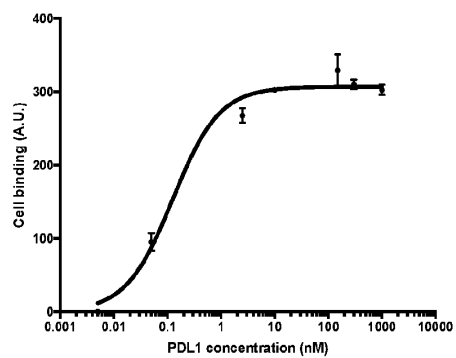
**Kd = 0.03 nM**

FIG. 39C

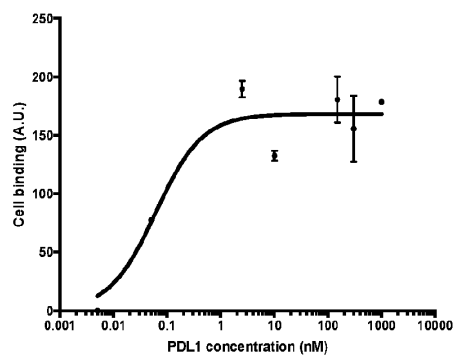
Clone#2
87-124-127-132-140



Kd = 0.12 nM

FIG. 39D

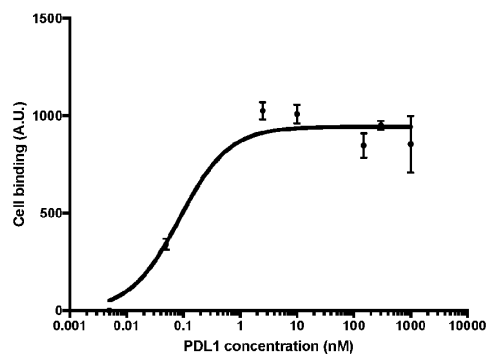
Clone#3
87-89-124-127-132-140



Kd = 0.06 nM

FIG. 39E

Clone#4
124-127-132-140



Kd = 0.08 nM

FIG. 39F

Clone#5
124-127-132

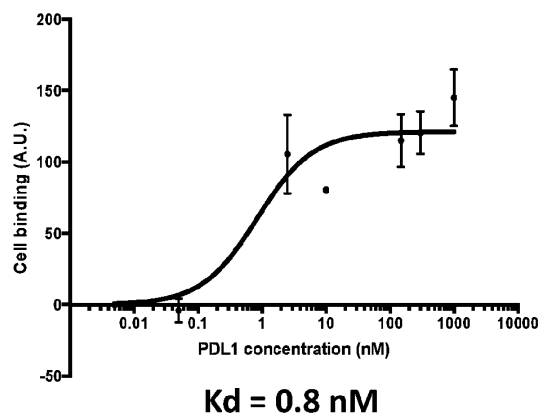


FIG. 40A

Refined clones to test in the binding assay for PDL1

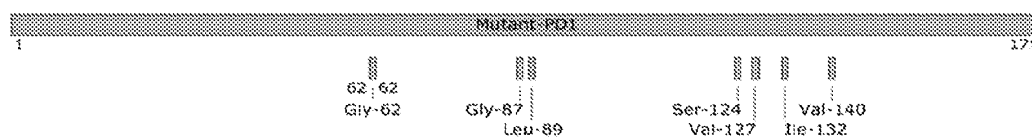
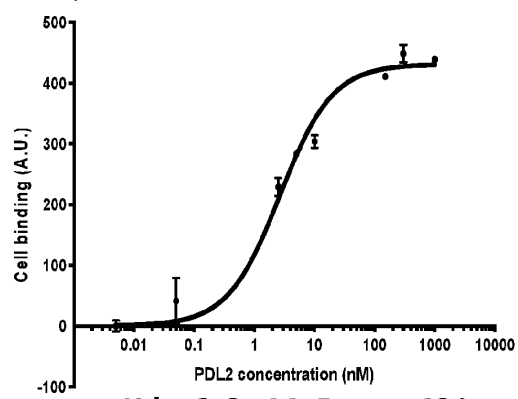


FIG. 40B

<u>Original Mutant</u>	62-87-89-124-127-132-140	Kd: 0.44 nM
<u>Clone#1</u>	89-124-127-132-140	Kd: 0.03 nM or 30 pM
<u>Clone#2</u>	87-124-127-132-140	Kd: 0.12 nM
<u>Clone#3</u>	87-89-124-127-132-140	Kd: 0.06 nM
<u>Clone#4</u>	124-127-132-140	Kd: 0.08 nM or 80 pM
<u>Clone#5</u>	124-127-132	Kd: 0.8 nM

FIG. 41A

Original Mutant PD1
(62-87-89-124-127-132-140)



Kd = 2.6 nM, Bmax: 431

FIG. 41B

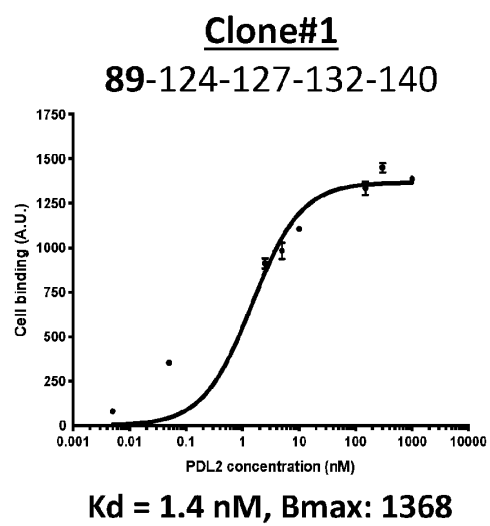


FIG. 41C

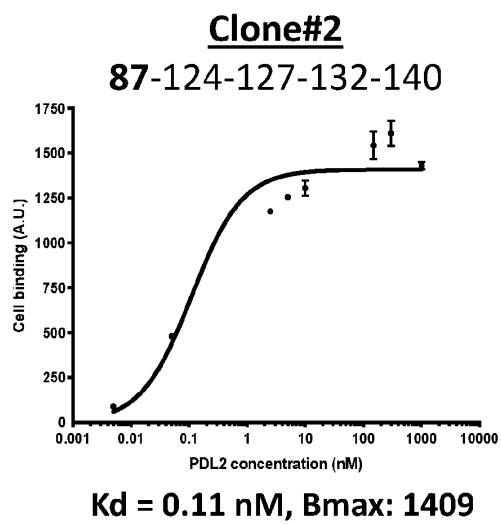
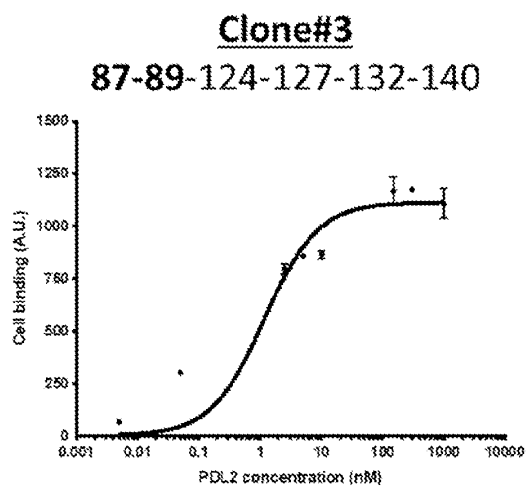


FIG. 41D



Kd = 1.1 nM, Bmax: 1116

FIG. 41E

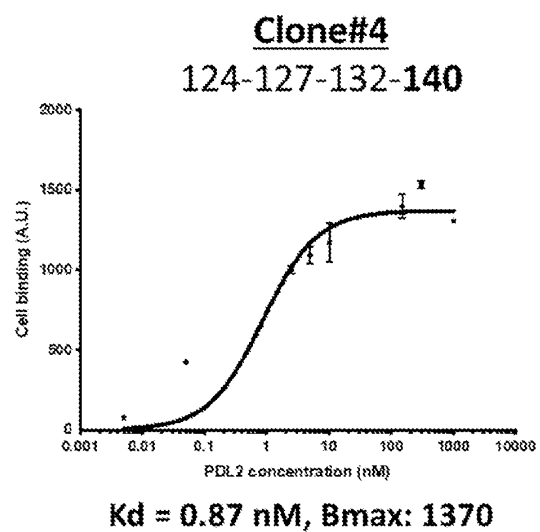


FIG. 41F

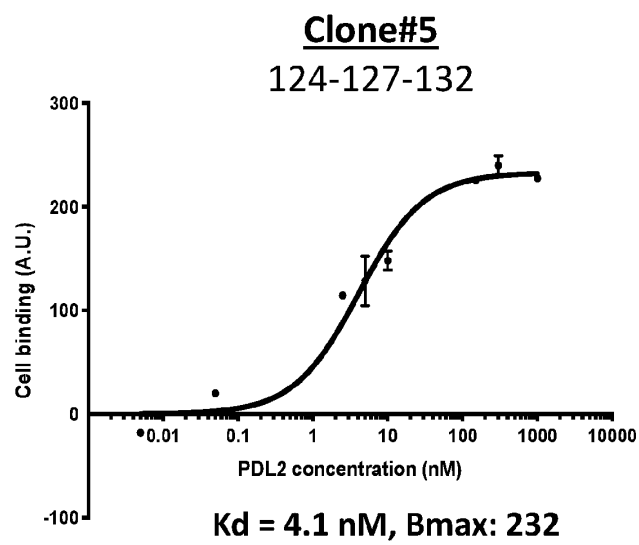


FIG. 42A

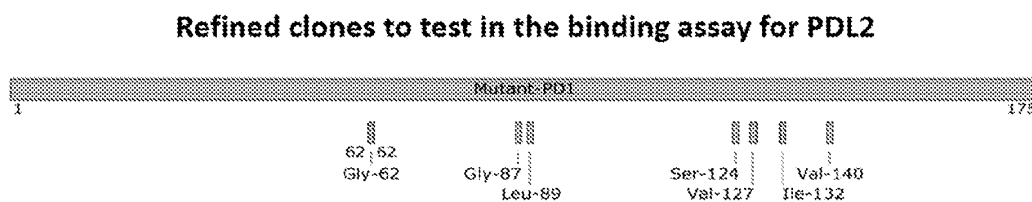


FIG. 42B

<u>Original Mutant</u>	62-87-89-124-127-132-140	Kd: 2.6 nM
<u>Clone#1</u>	89-124-127-132-140	Kd: 1.4 nM
<u>Clone#2</u>	87-124-127-132-140	Kd: 0.11 nM
<u>Clone#3</u>	87-89-124-127-132-140	Kd: 1.1 nM
<u>Clone#4</u>	124-127-132-140	Kd: 0.87 nM
<u>Clone#5</u>	124-127-132	Kd: 4.1 nM