

FIG. 1A

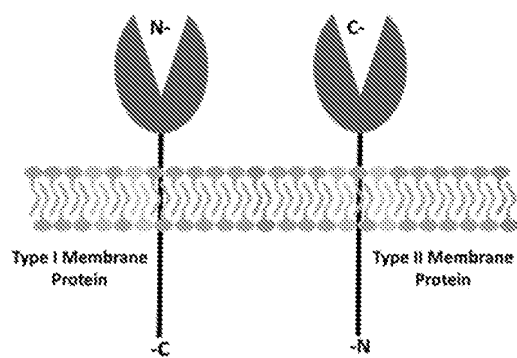


FIG. 1B

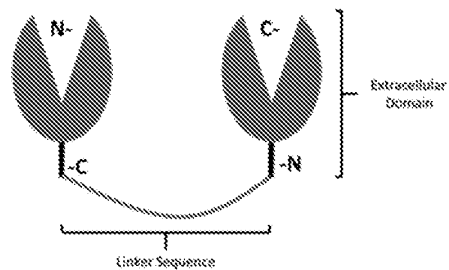


FIG. 1C

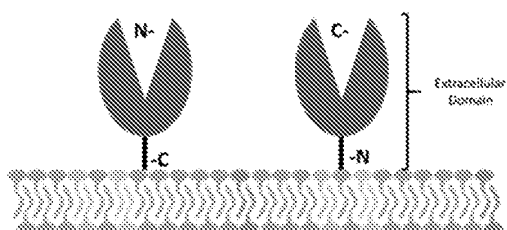


FIG. 1D

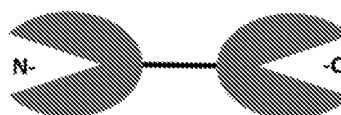


FIG. 2A

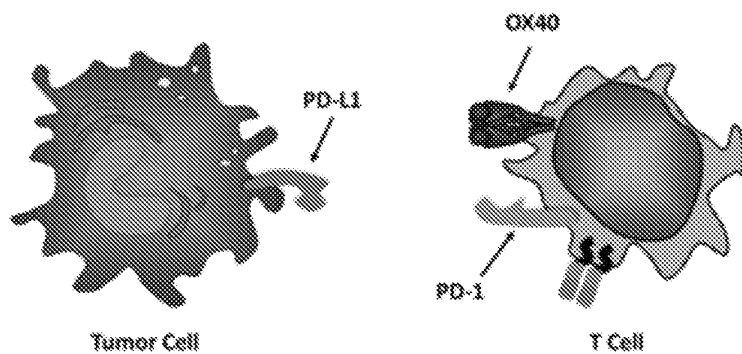


FIG. 2B

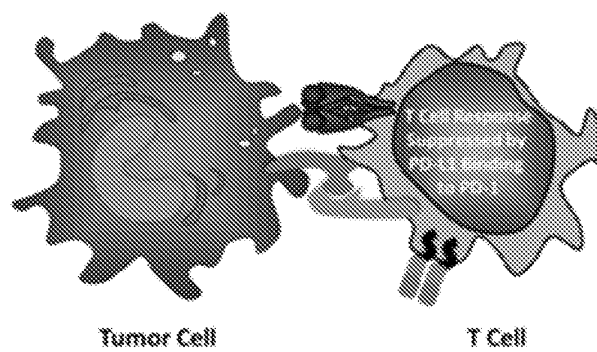


FIG. 2C

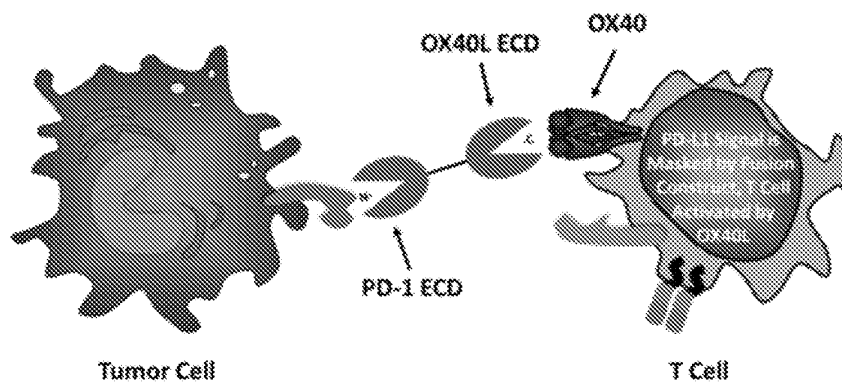


FIG. 2D

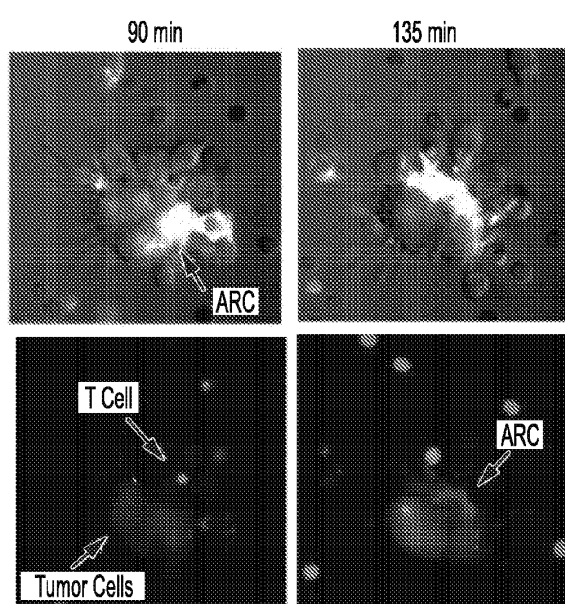


FIG. 3A

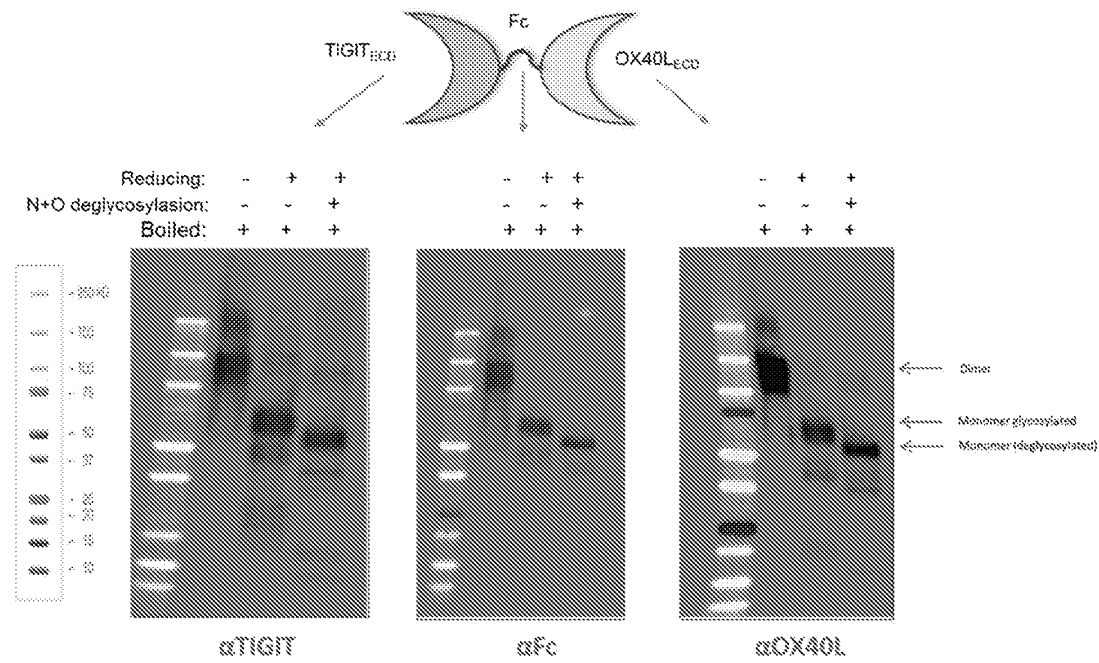


FIG. 3B

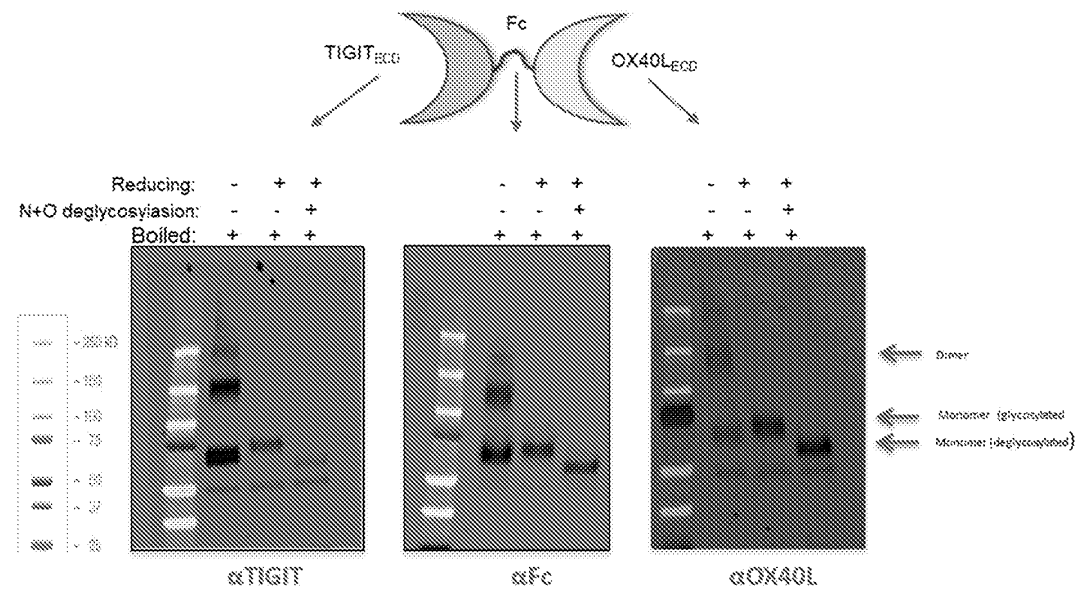
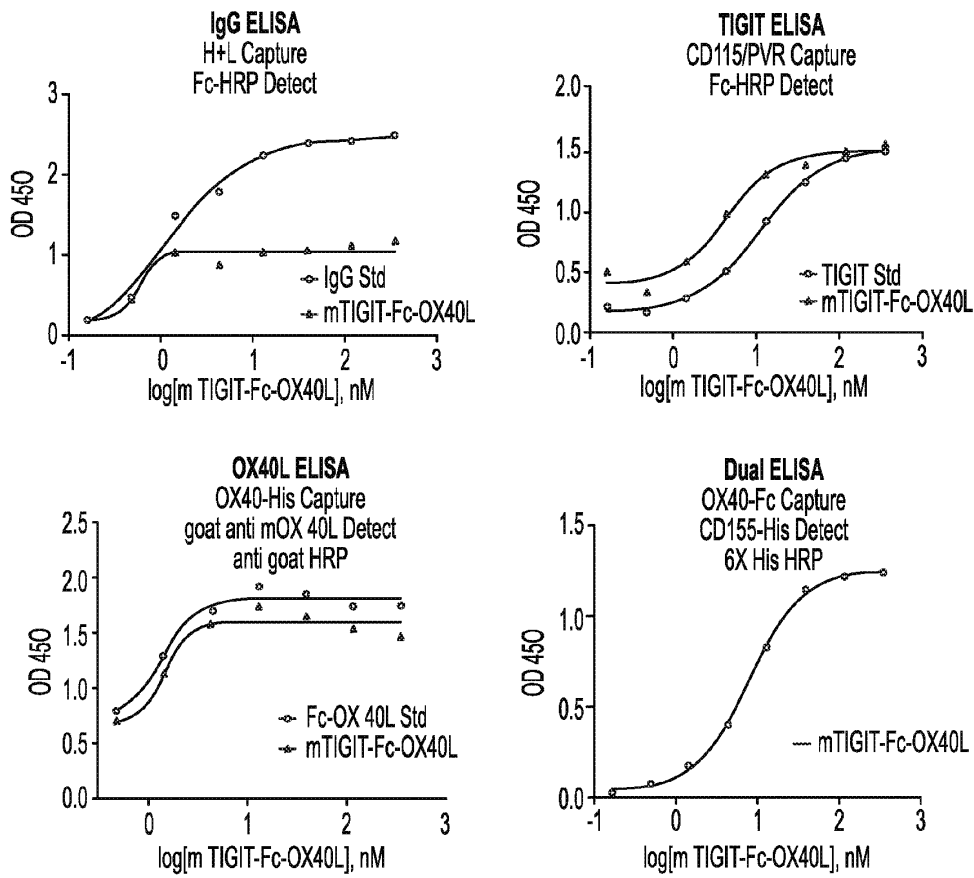
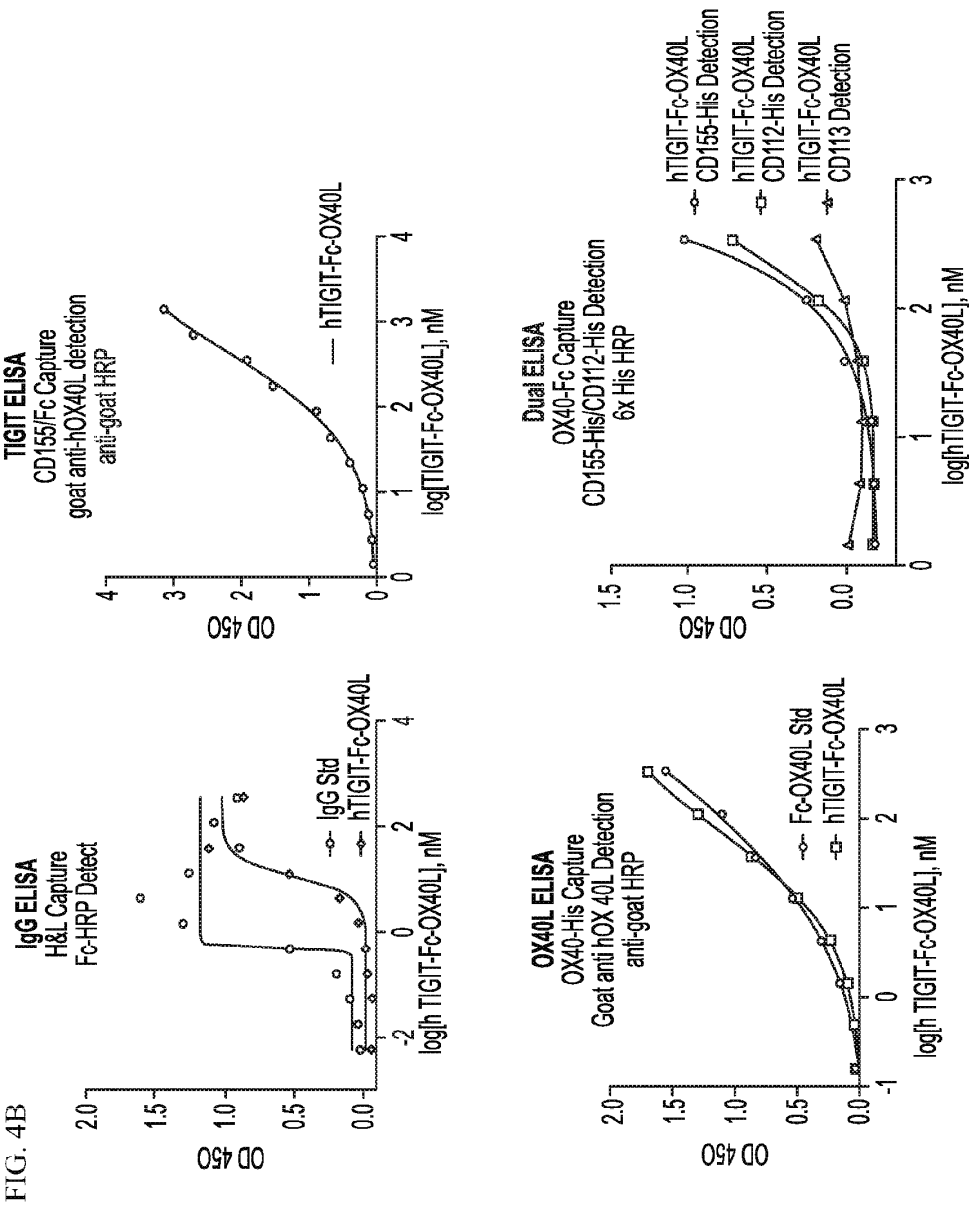


FIG. 4A





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FIG. 5A

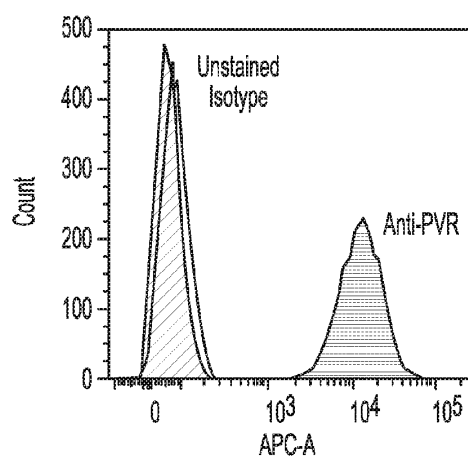
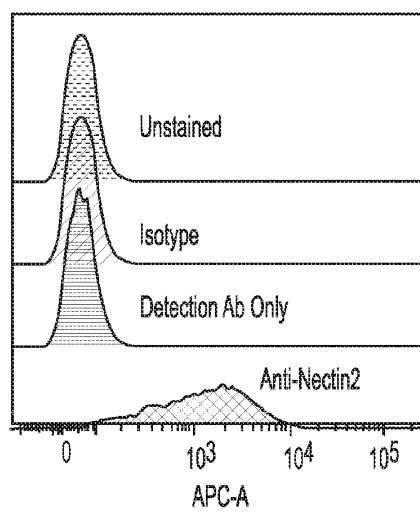


FIG. 5B



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FIG. 5C

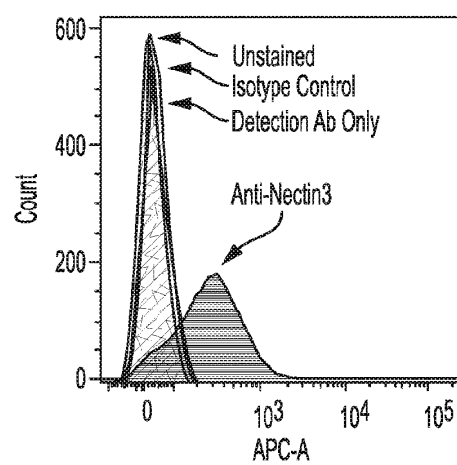


FIG. 6

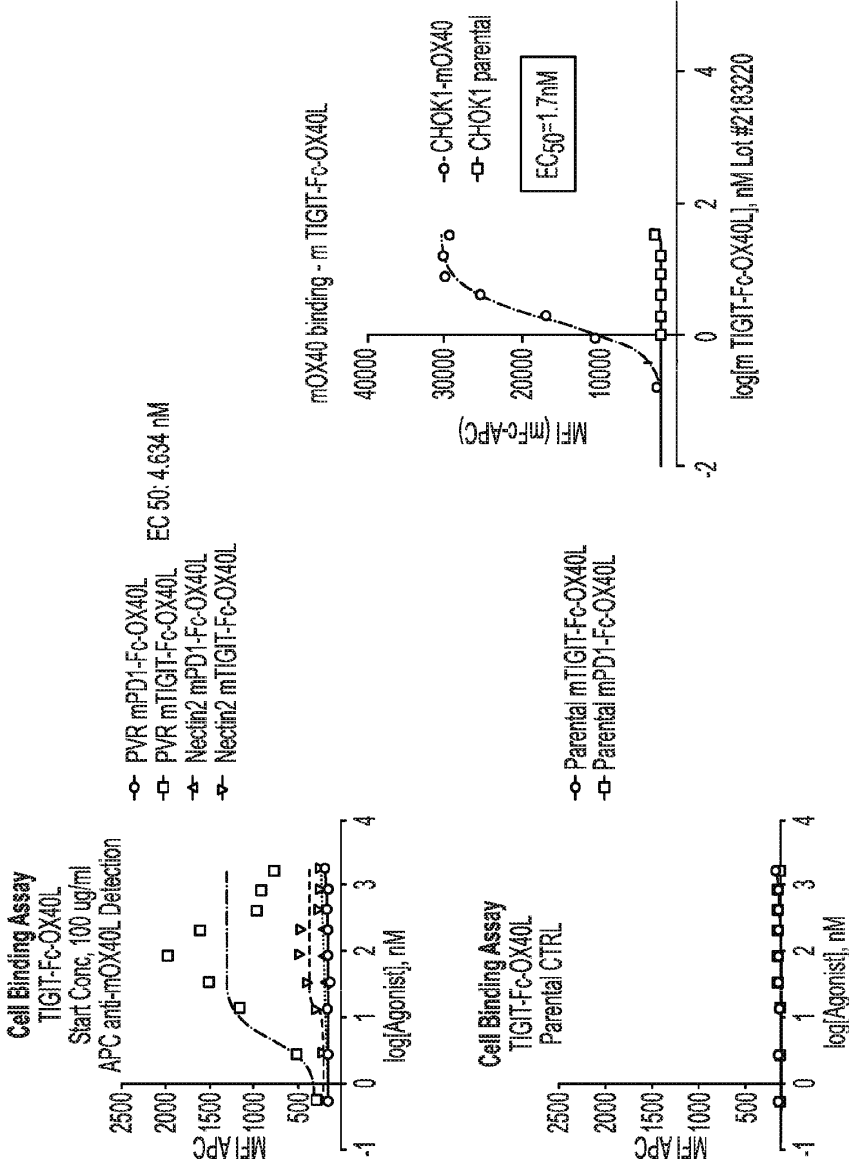


FIG. 7

| TIGIT-Fc-OX40L | Gene Id | Protein Name                      | Accession   | Primary Screen |            | Confirmation Screen |            | Comment                                     |
|----------------|---------|-----------------------------------|-------------|----------------|------------|---------------------|------------|---------------------------------------------|
|                | NECTIN4 | Nectin Cell Adhesion Molecule 4   | BC010293    | v. weak        | v. weak    | weak                | weak       |                                             |
|                | PVR     | Poliovirus Receptor               | BC015529    | strong         | strong     | strong              | strong     |                                             |
|                | OX40    | TNF Receptor Superfamily Member 4 |             | n/a            | n/a        | strong              | strong     |                                             |
|                | TNFRSF4 | TNF Receptor Superfamily Member 4 | NM_003327.3 | n/a            | n/a        | medium              | med/strong | canonical isoform                           |
|                | LGALS1  | Galectin 1                        | BC001693    | med/strong     | med/strong | weak                | weak       | soluble; seen with other Fc fusion proteins |

FIG. 8A

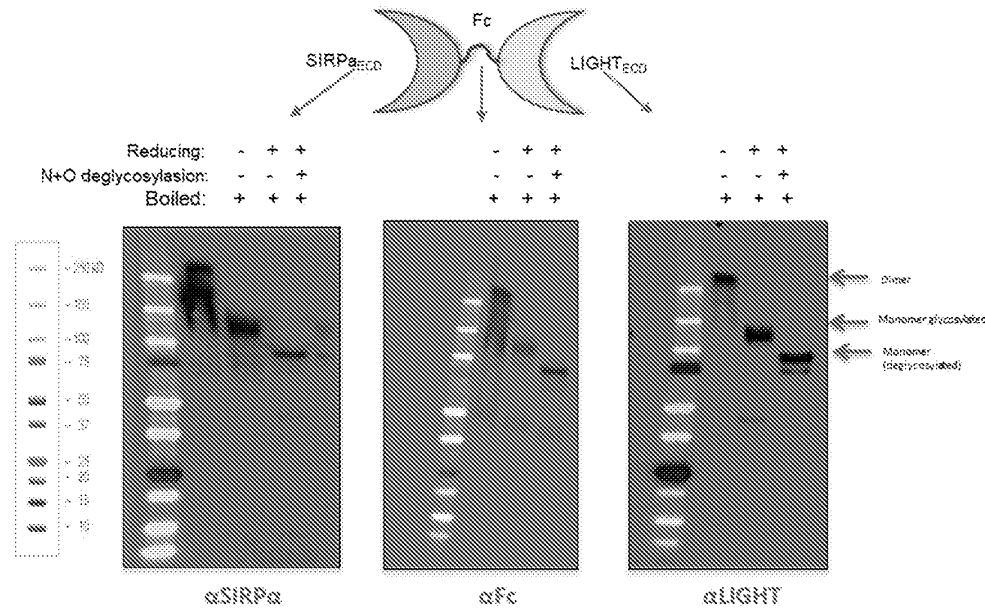
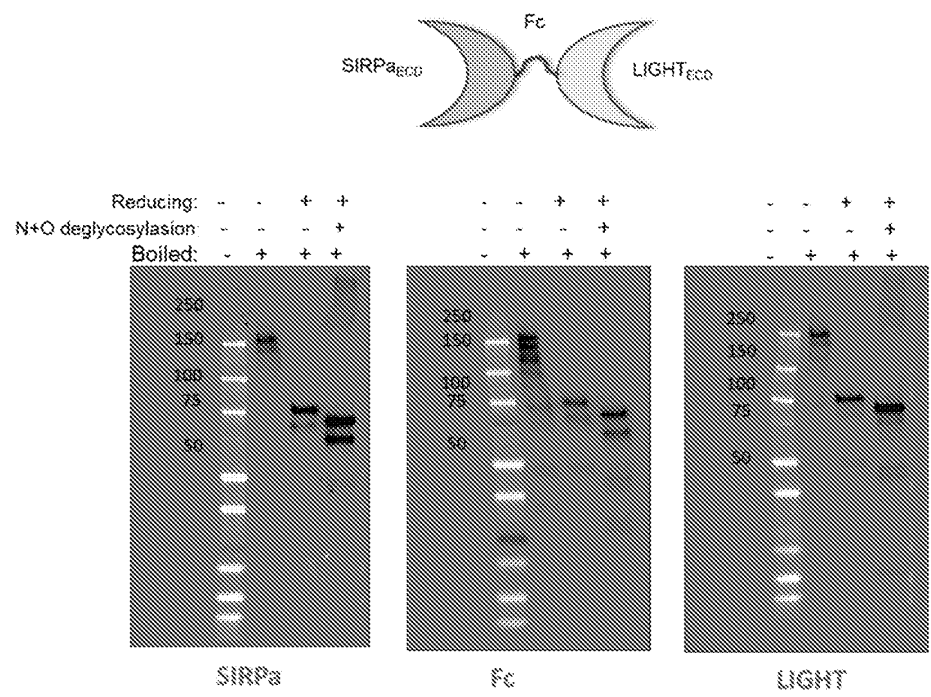
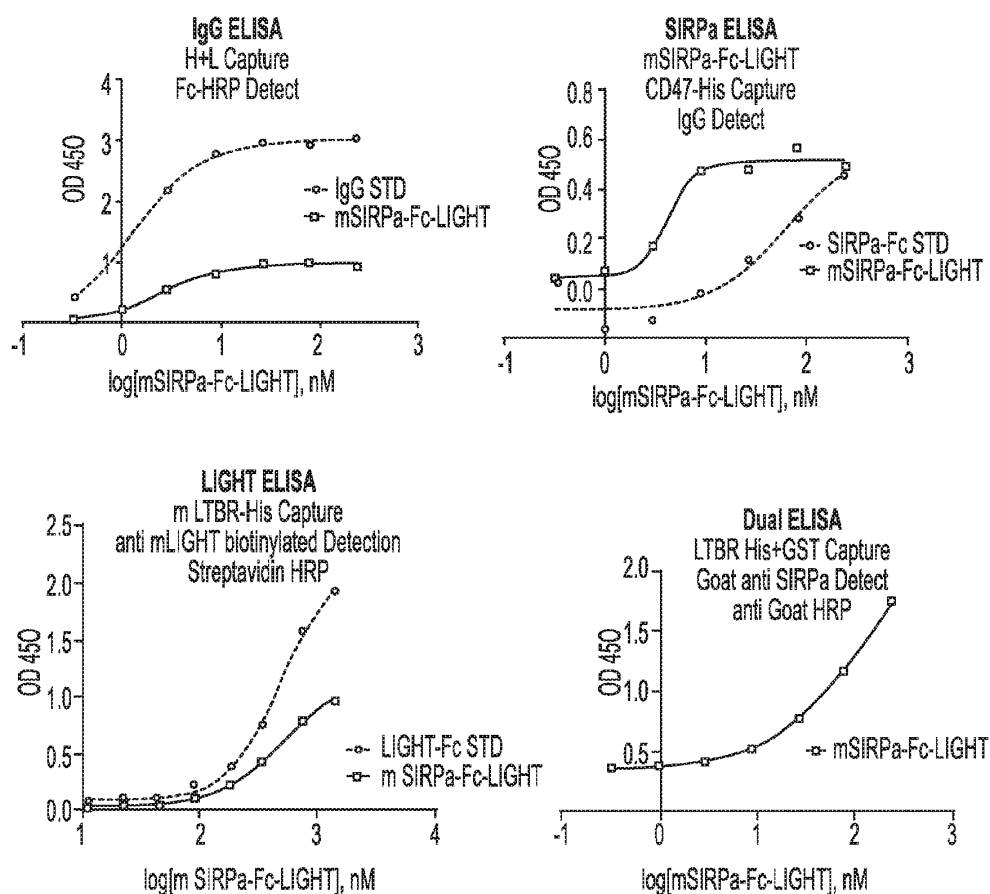


FIG. 8B



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FIG. 9A



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FIG. 9B

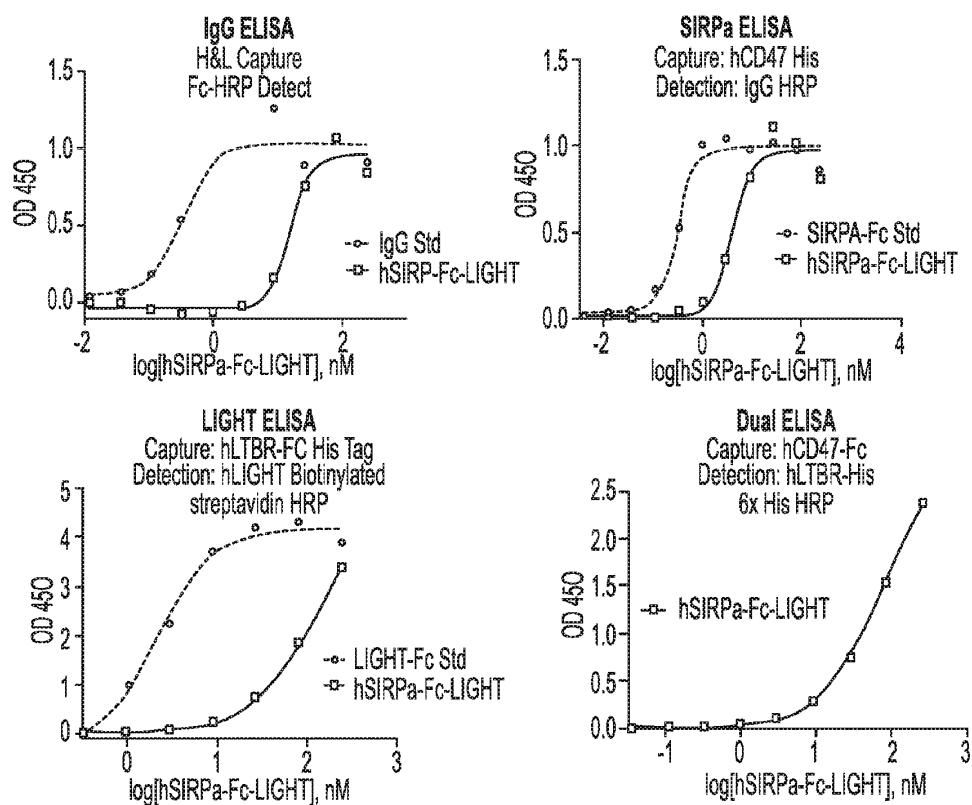
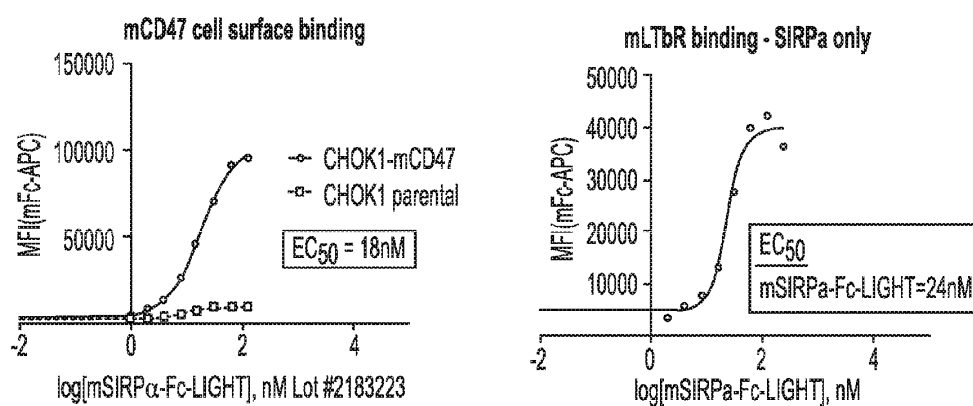
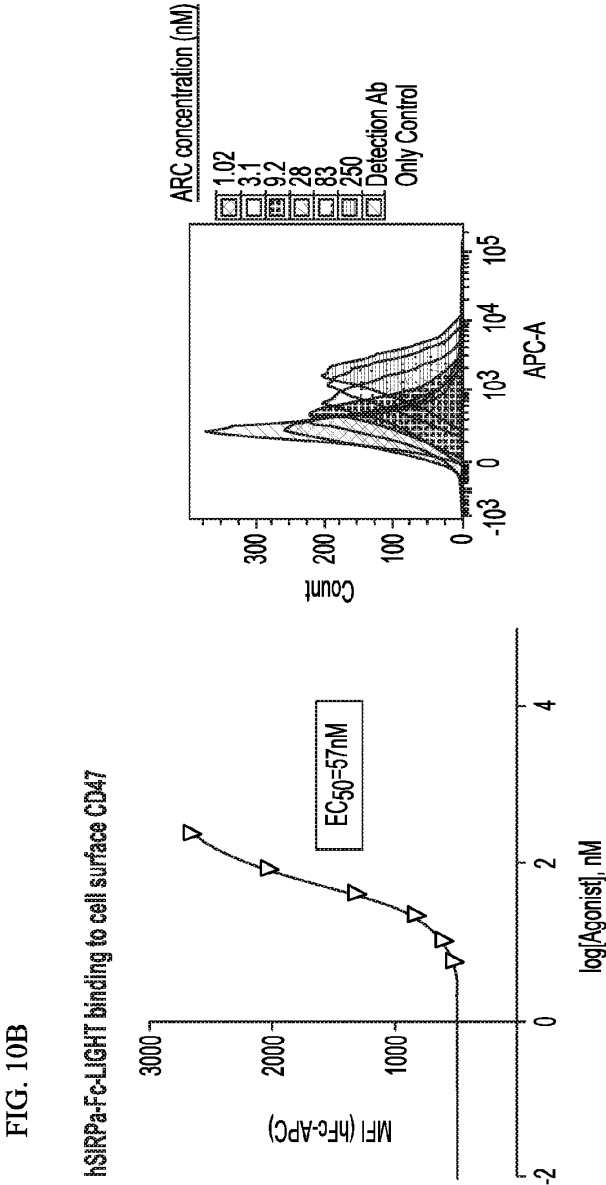
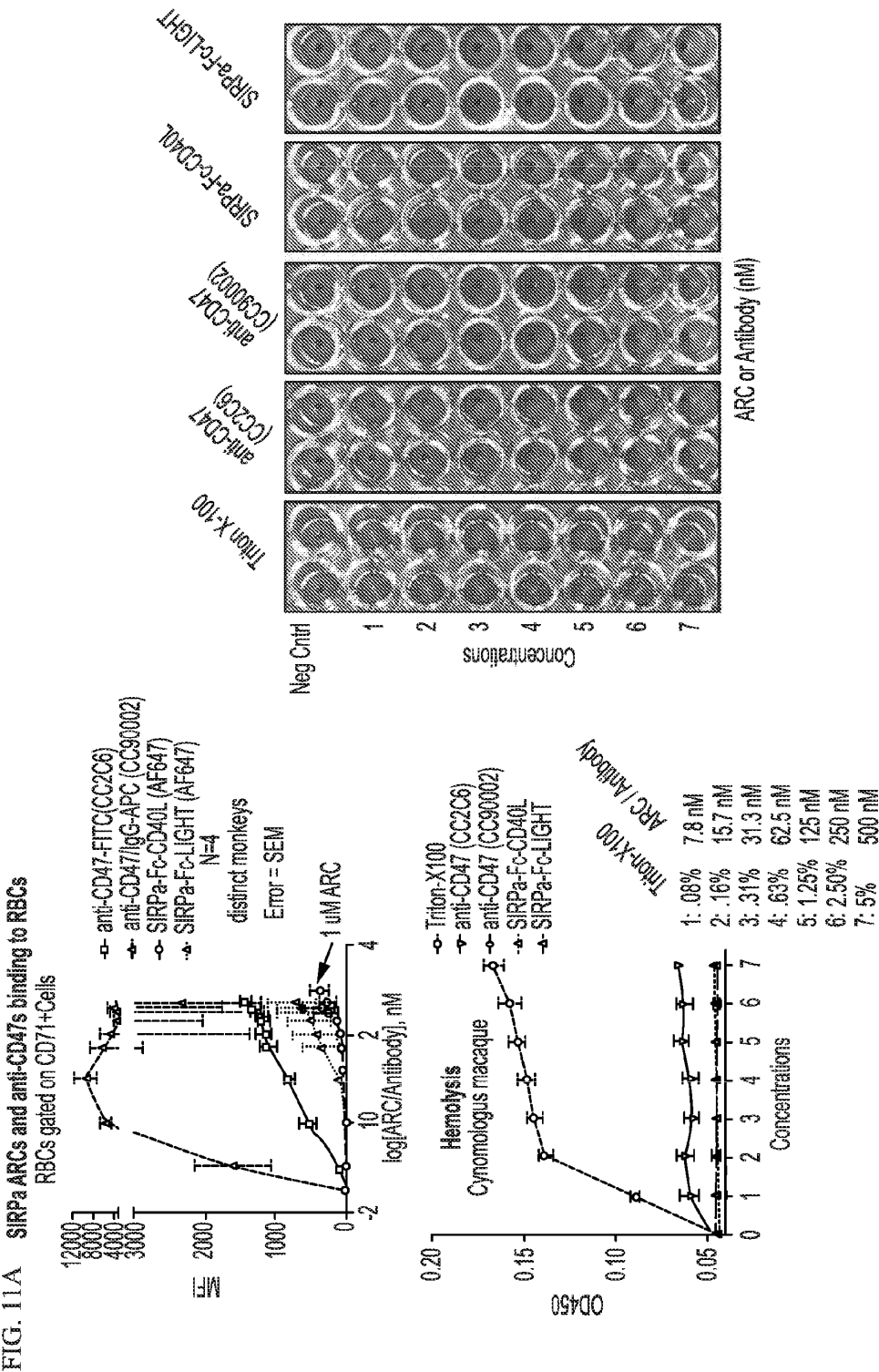
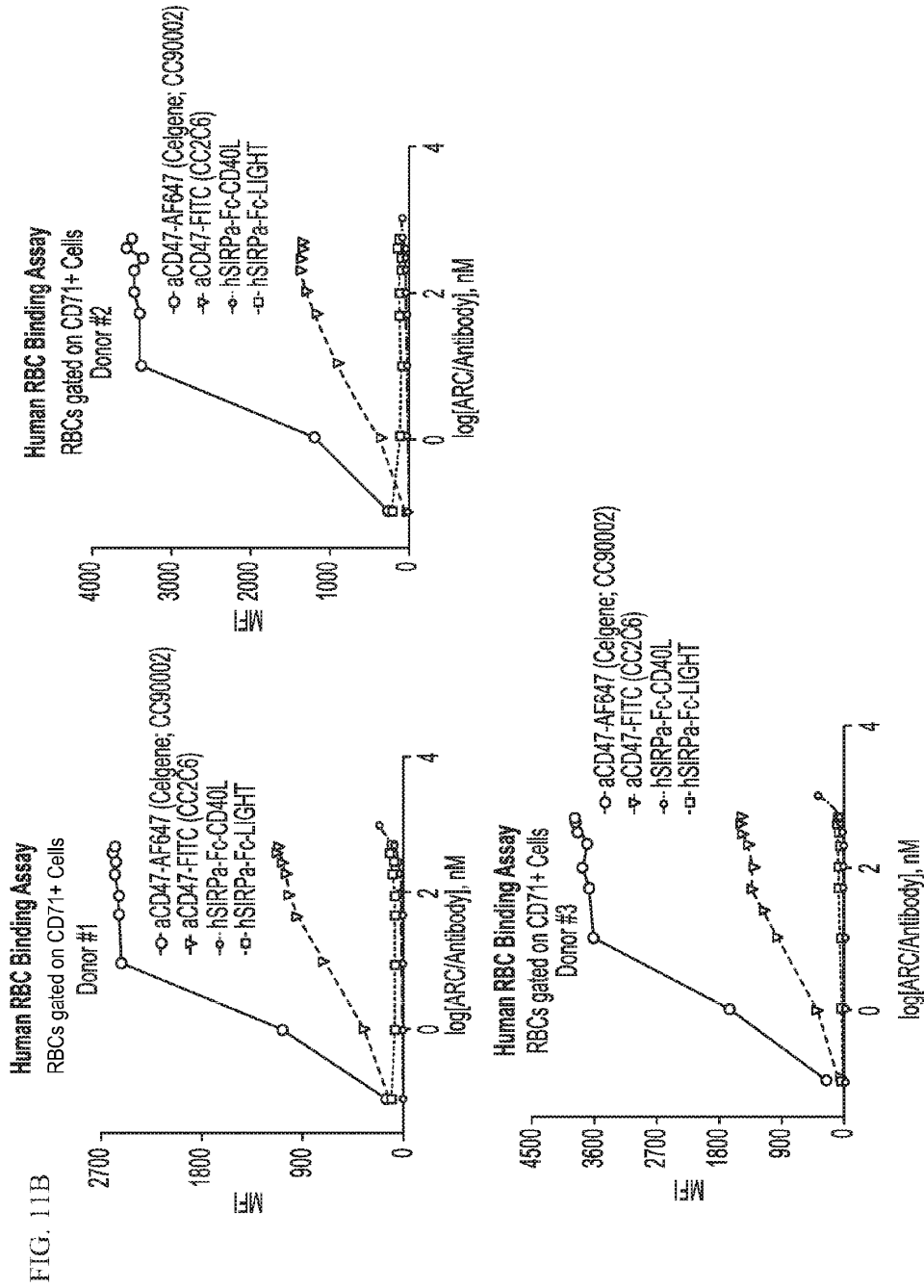


FIG. 10A









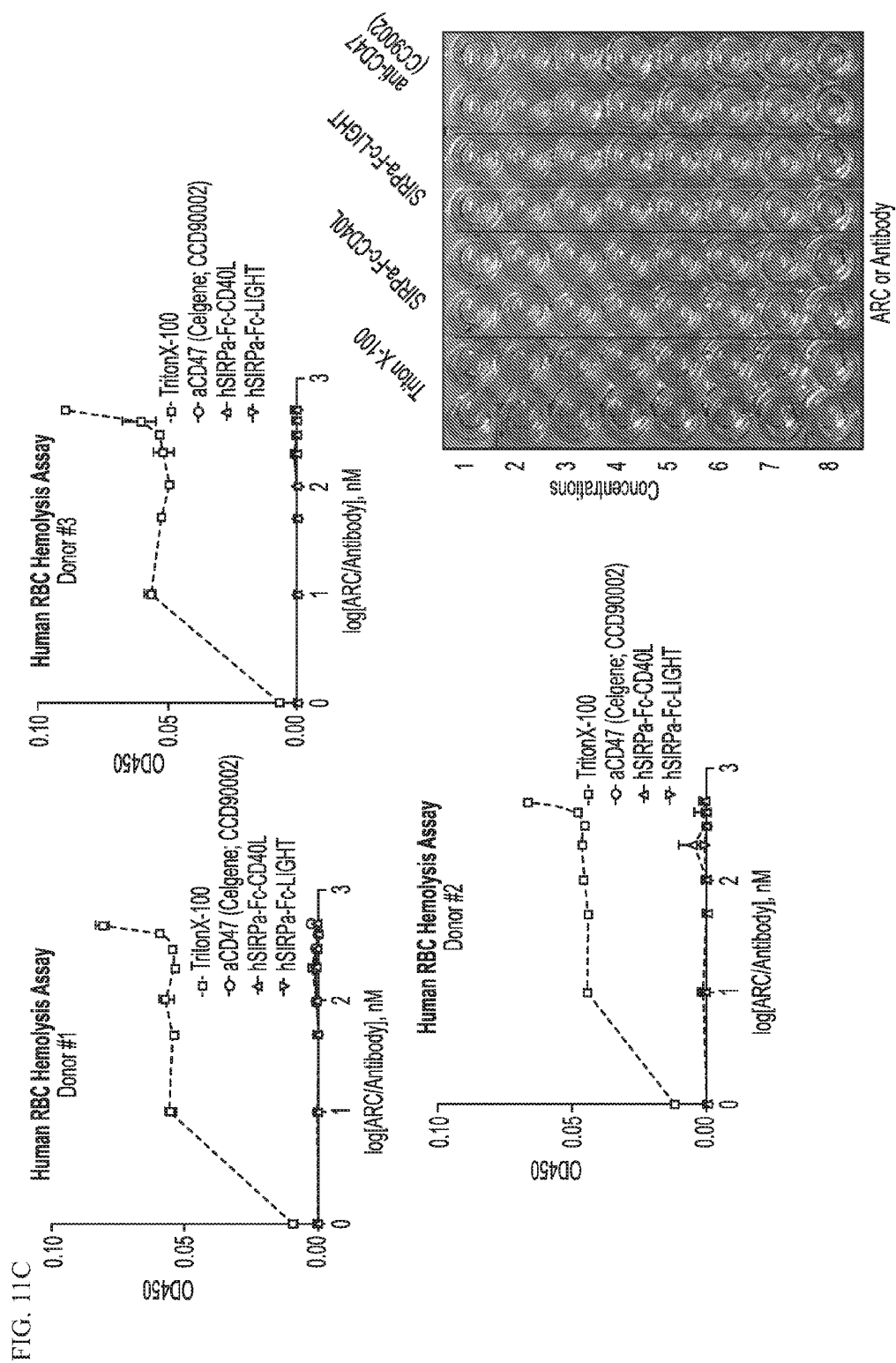


FIG. 12A

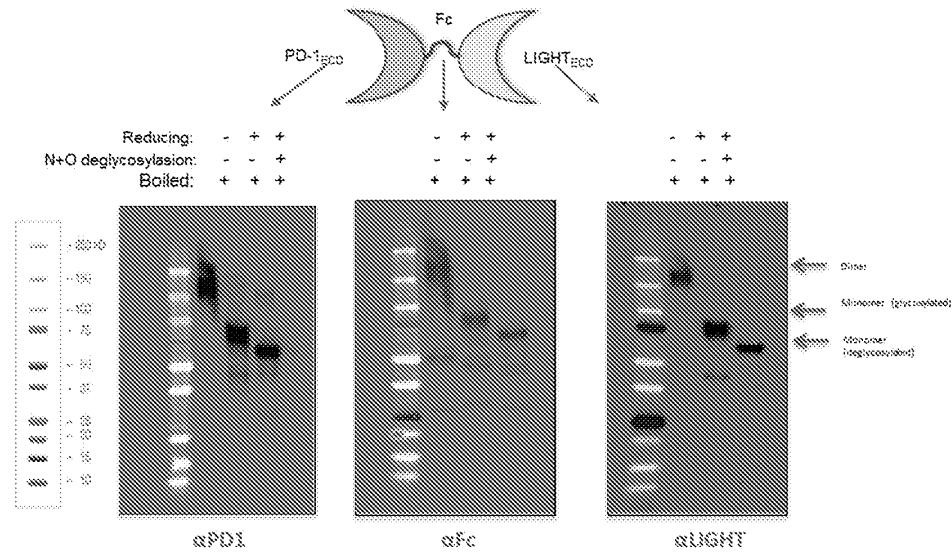
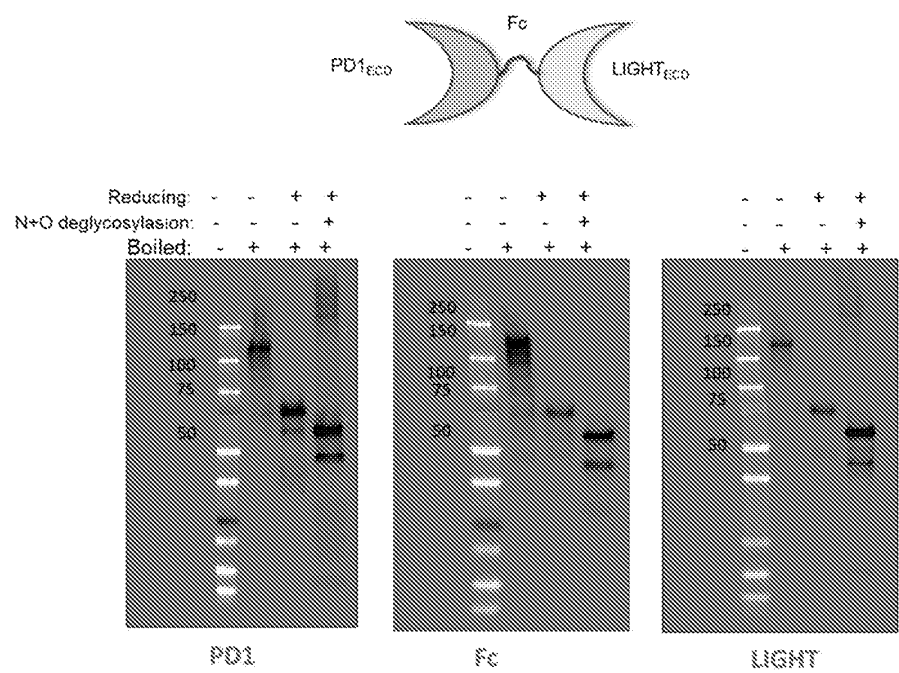
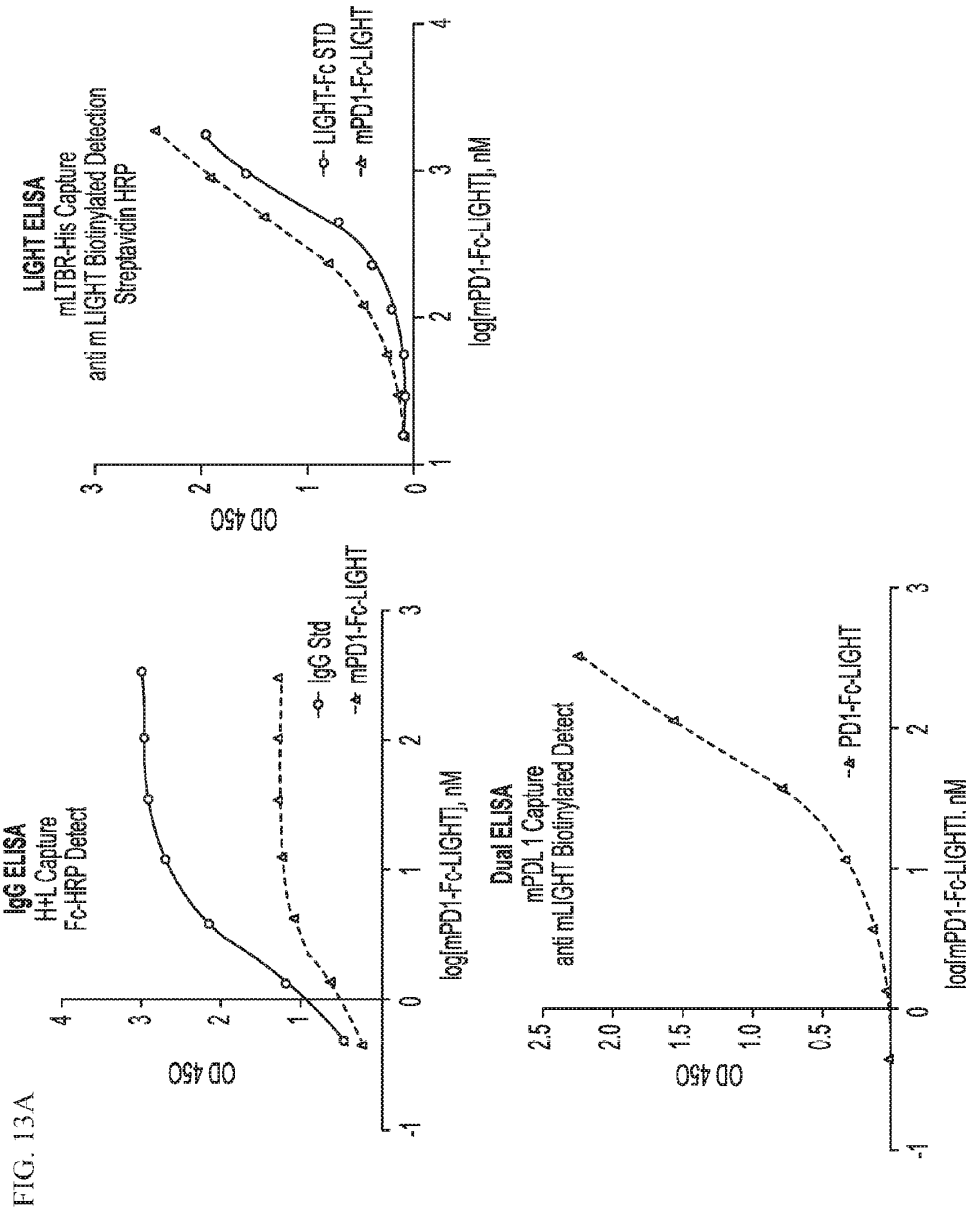
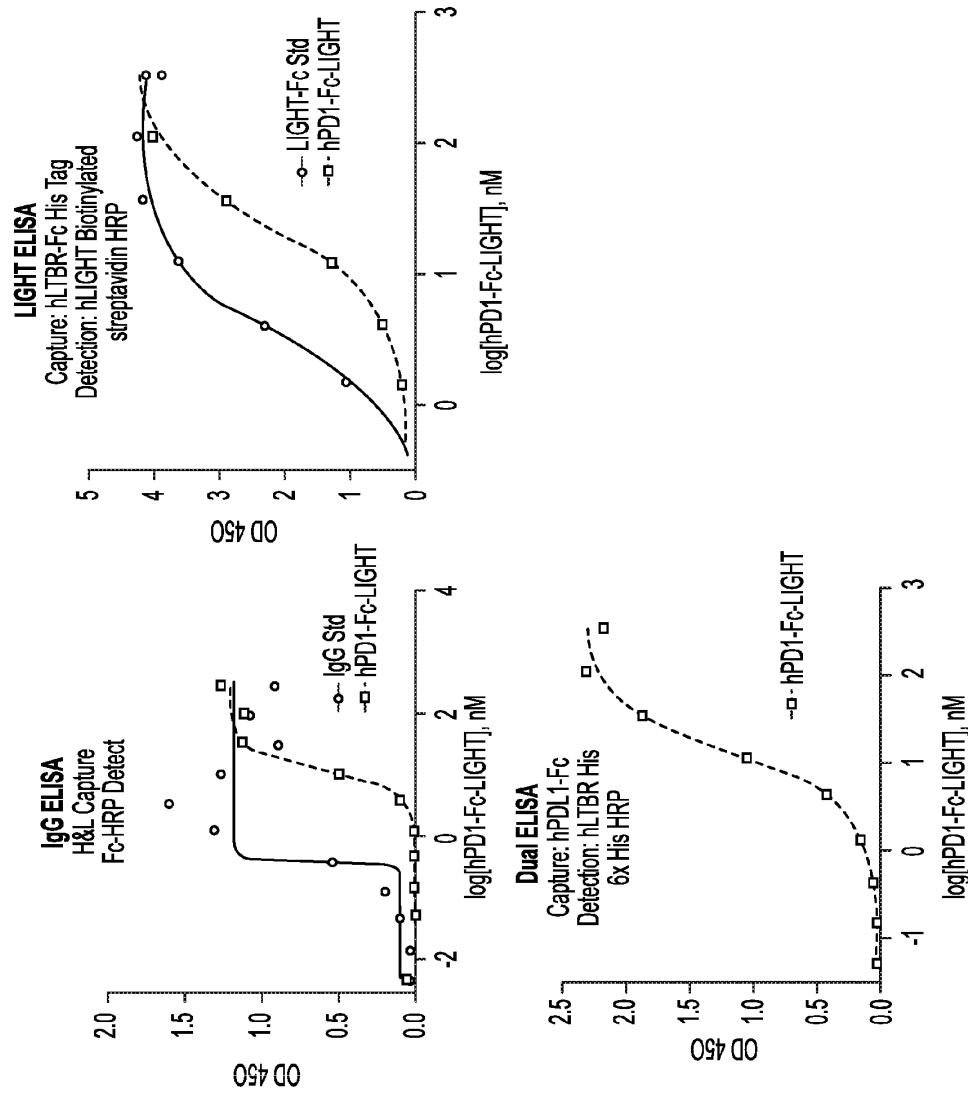


FIG. 12B







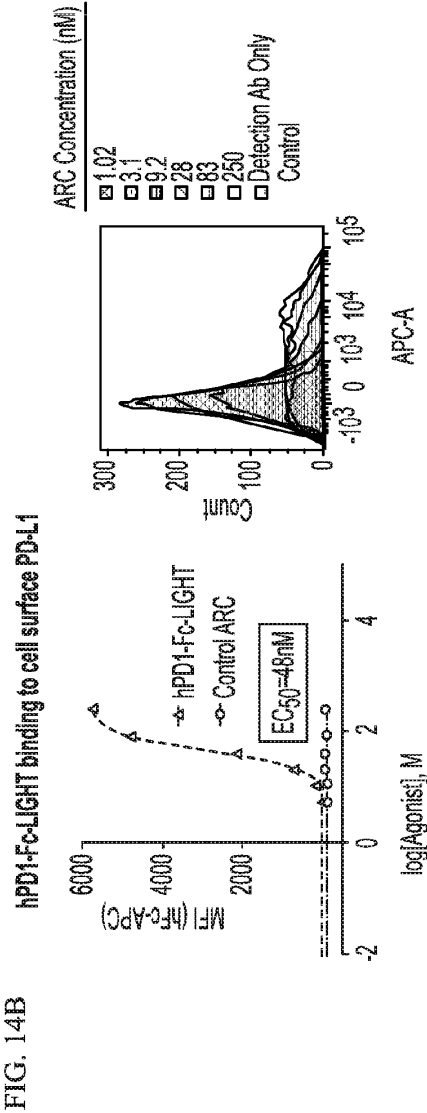
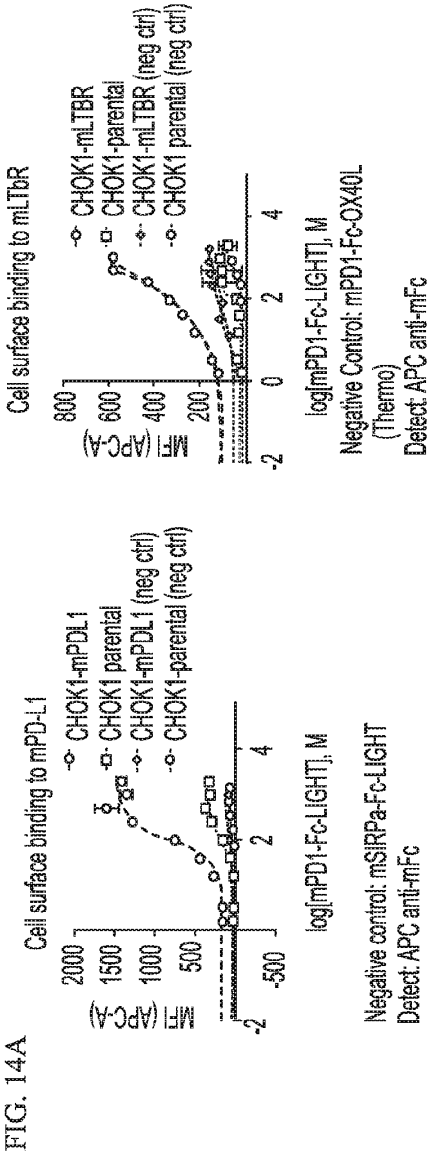


FIG. 15A

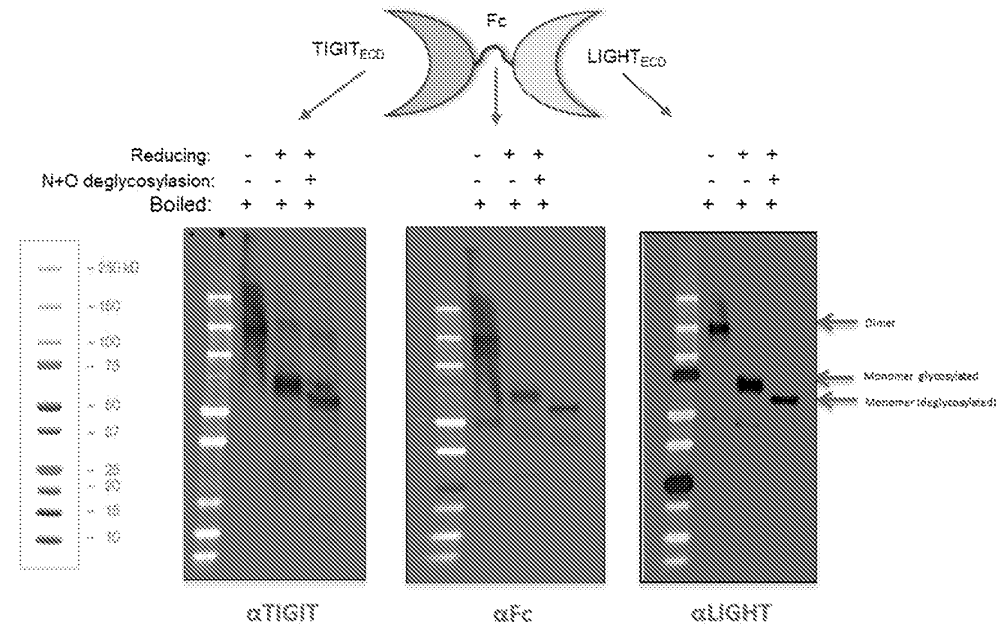
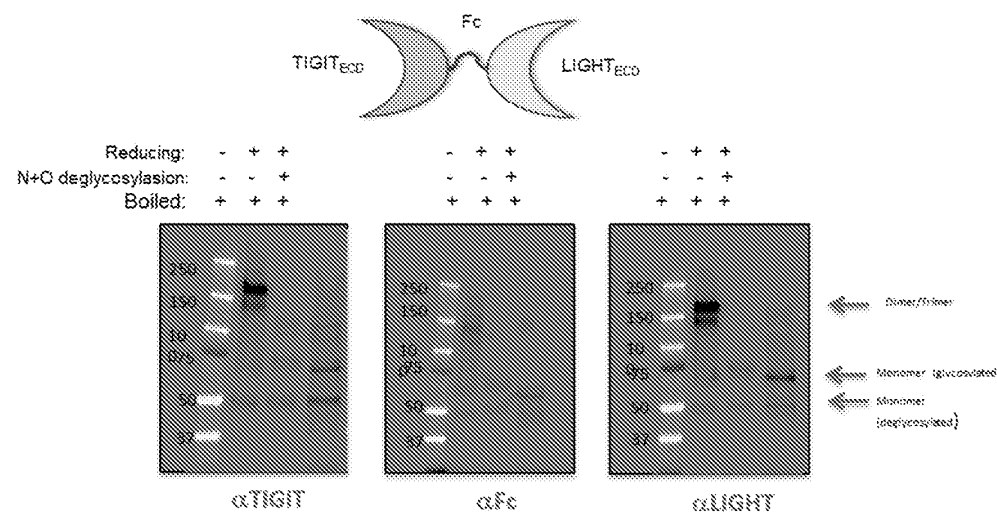


FIG. 15B



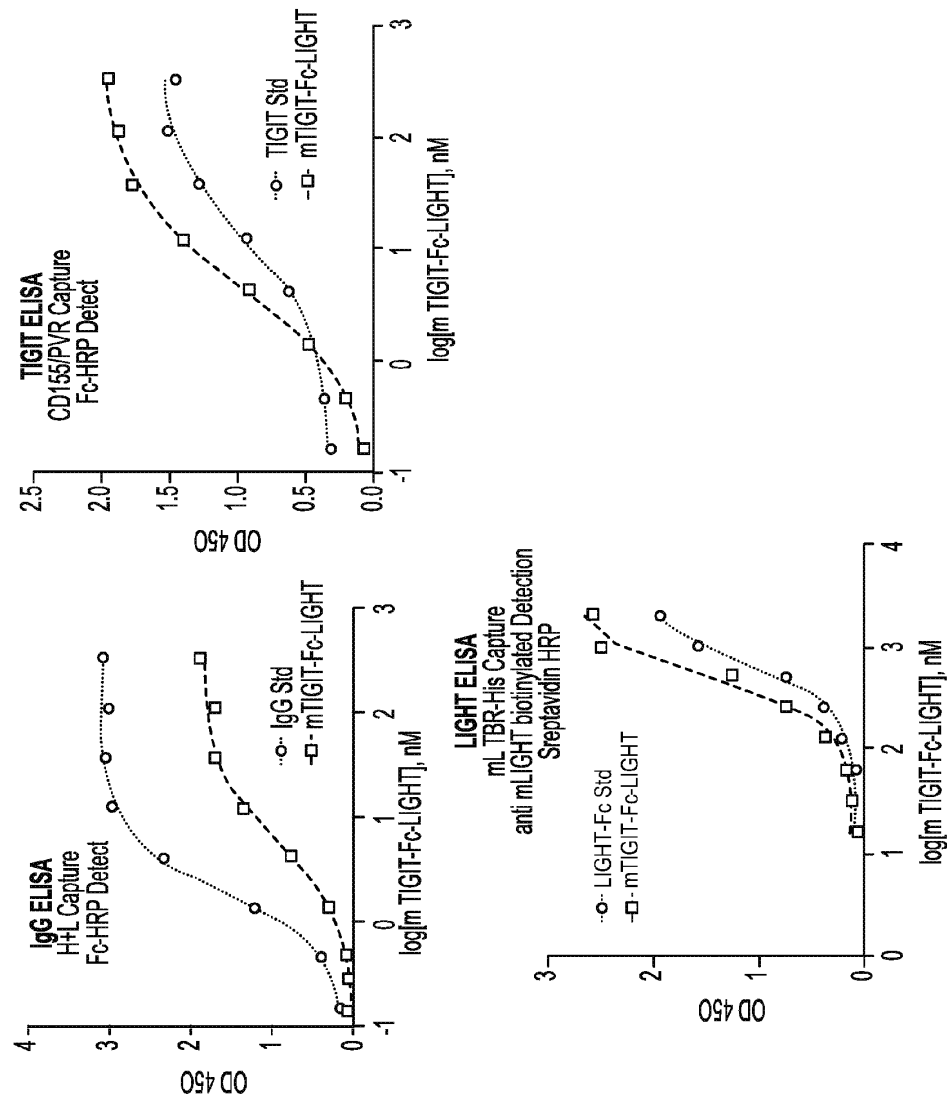
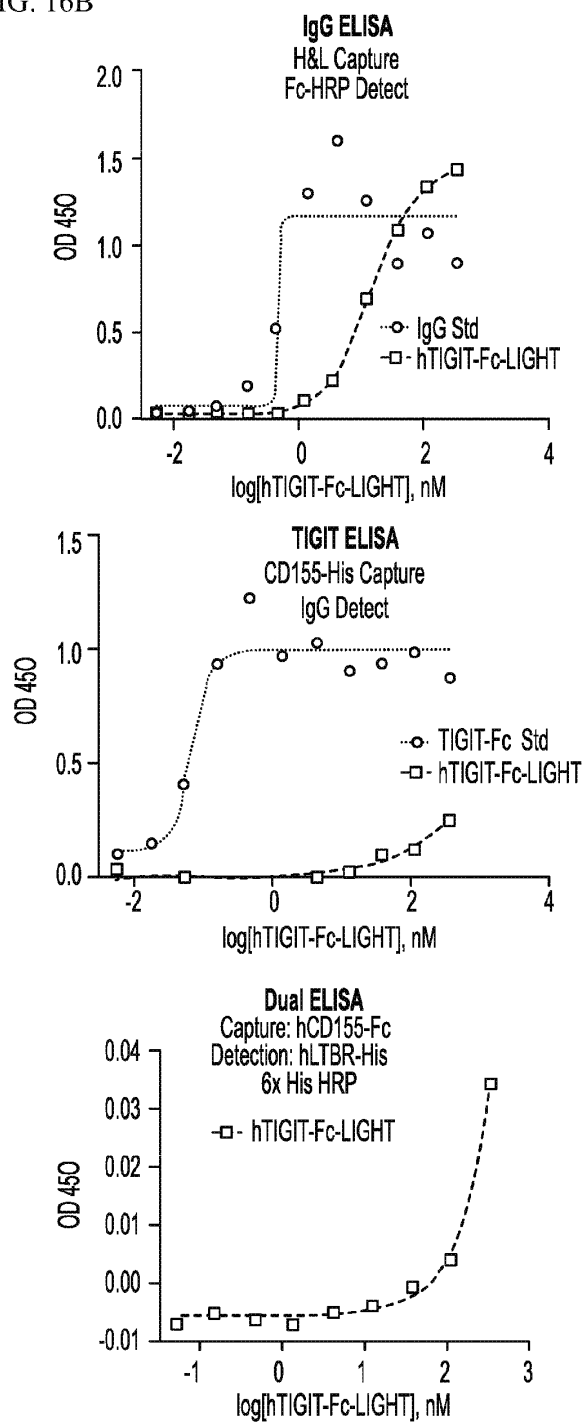


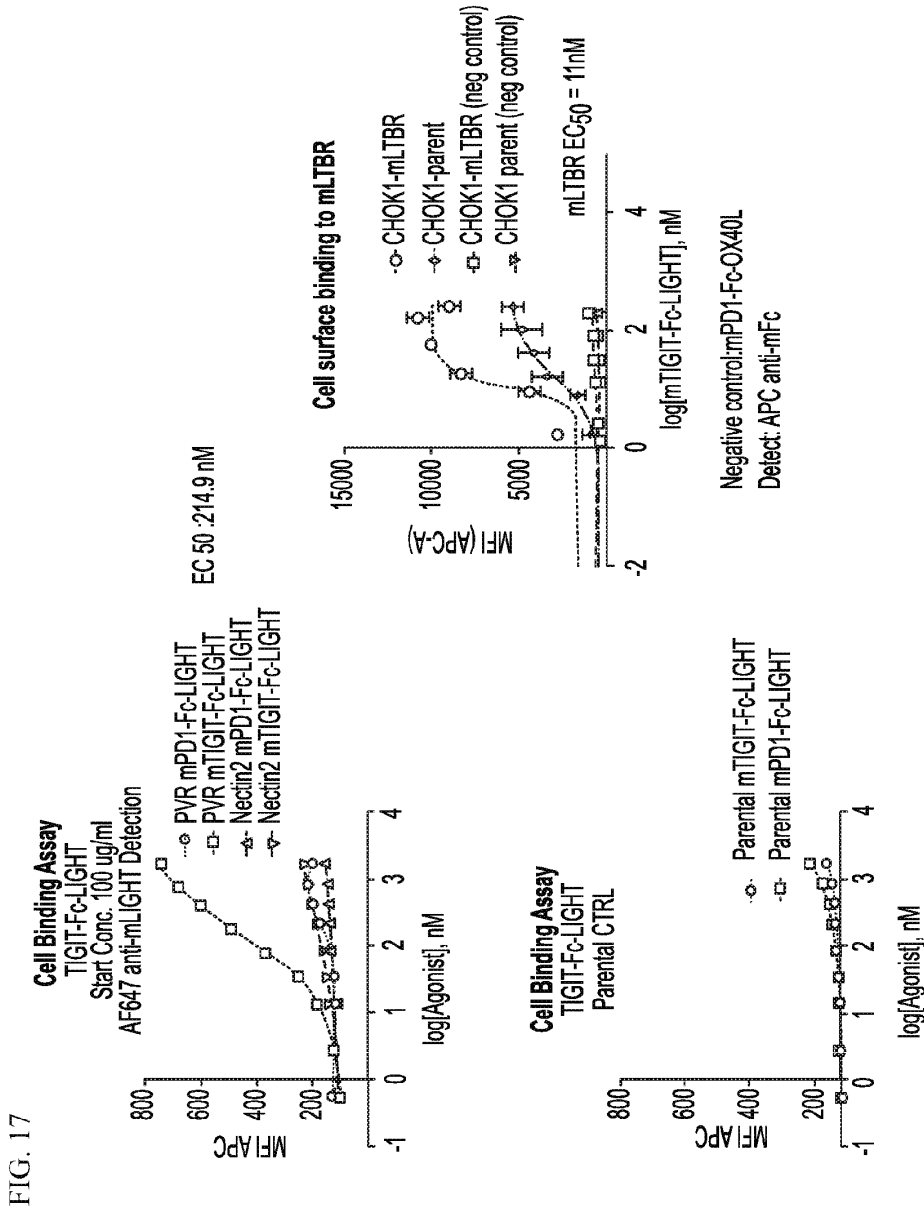
FIG. 16A

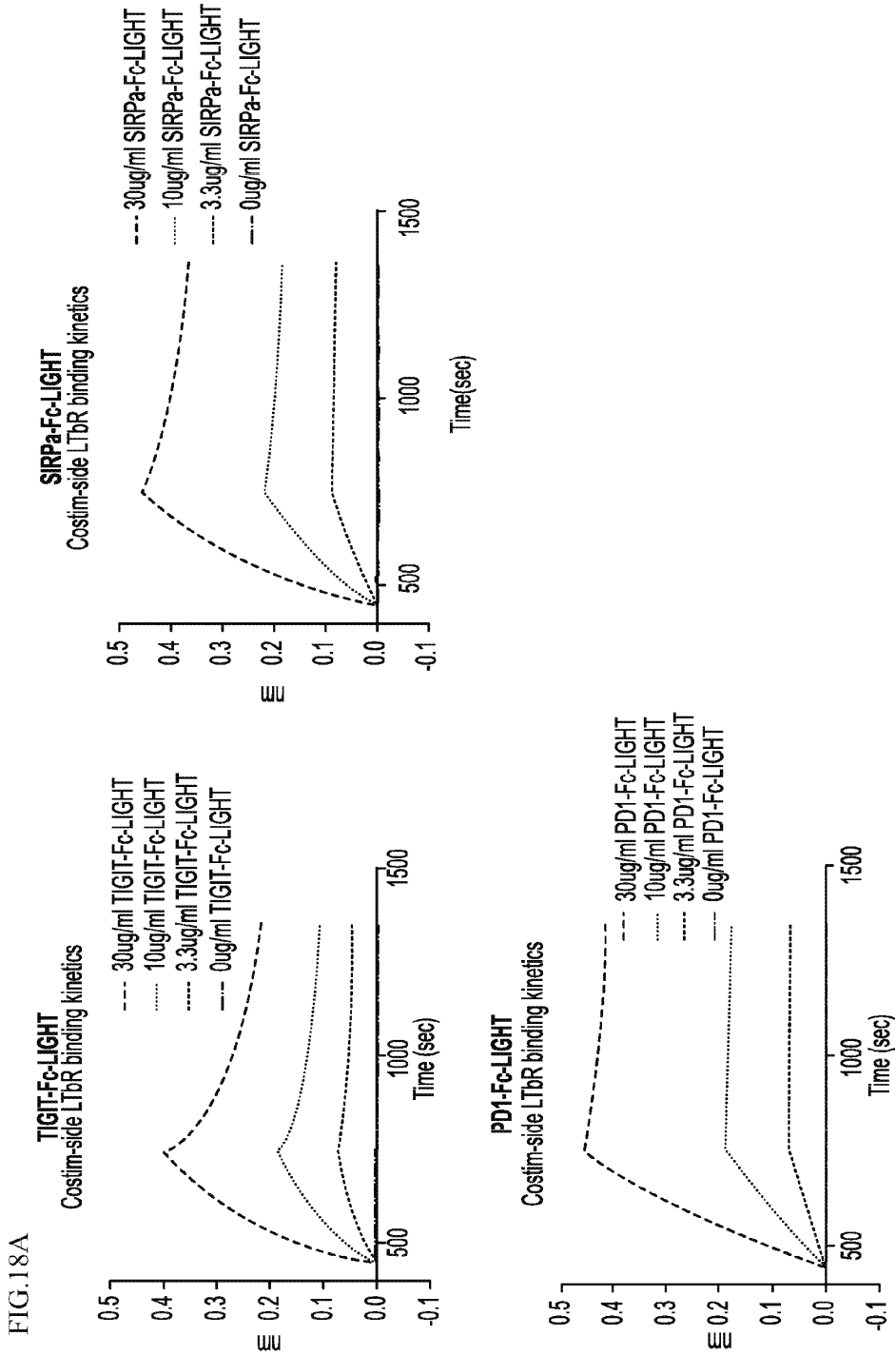
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FIG. 16B



SUBSTITUTE SHEET (RULE 26)





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FIG. 18B

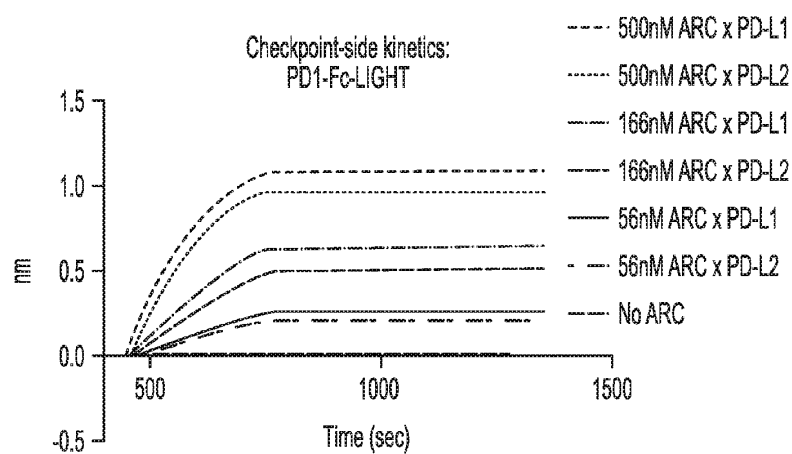
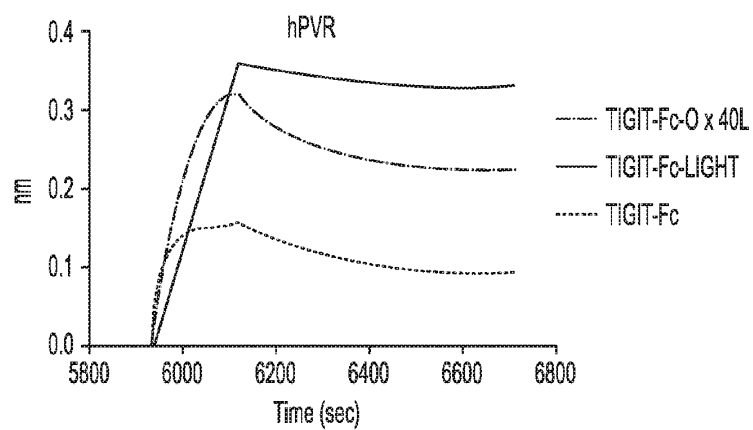


FIG. 19A



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FIG. 19B

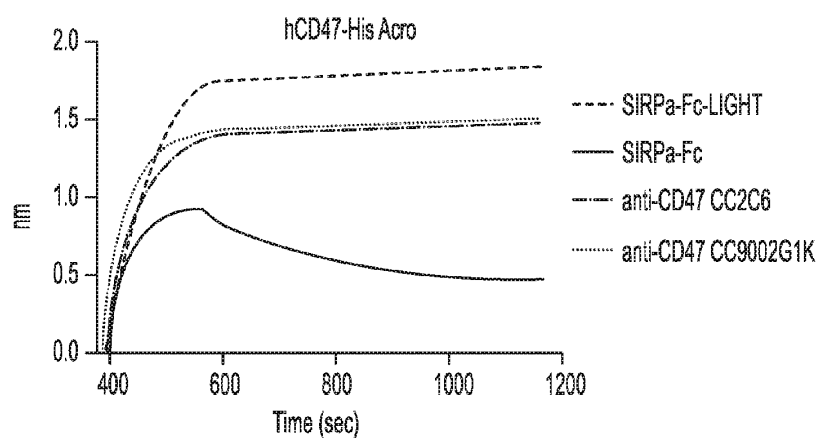


FIG. 19C

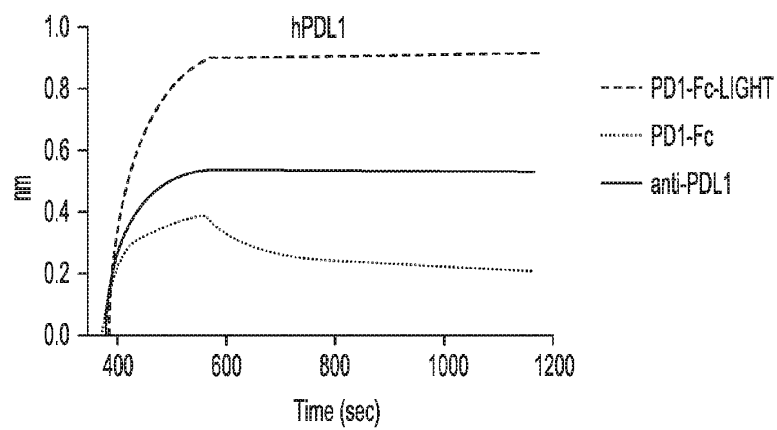
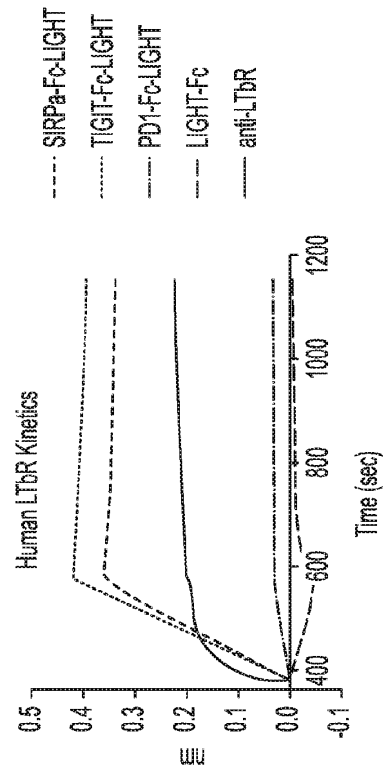
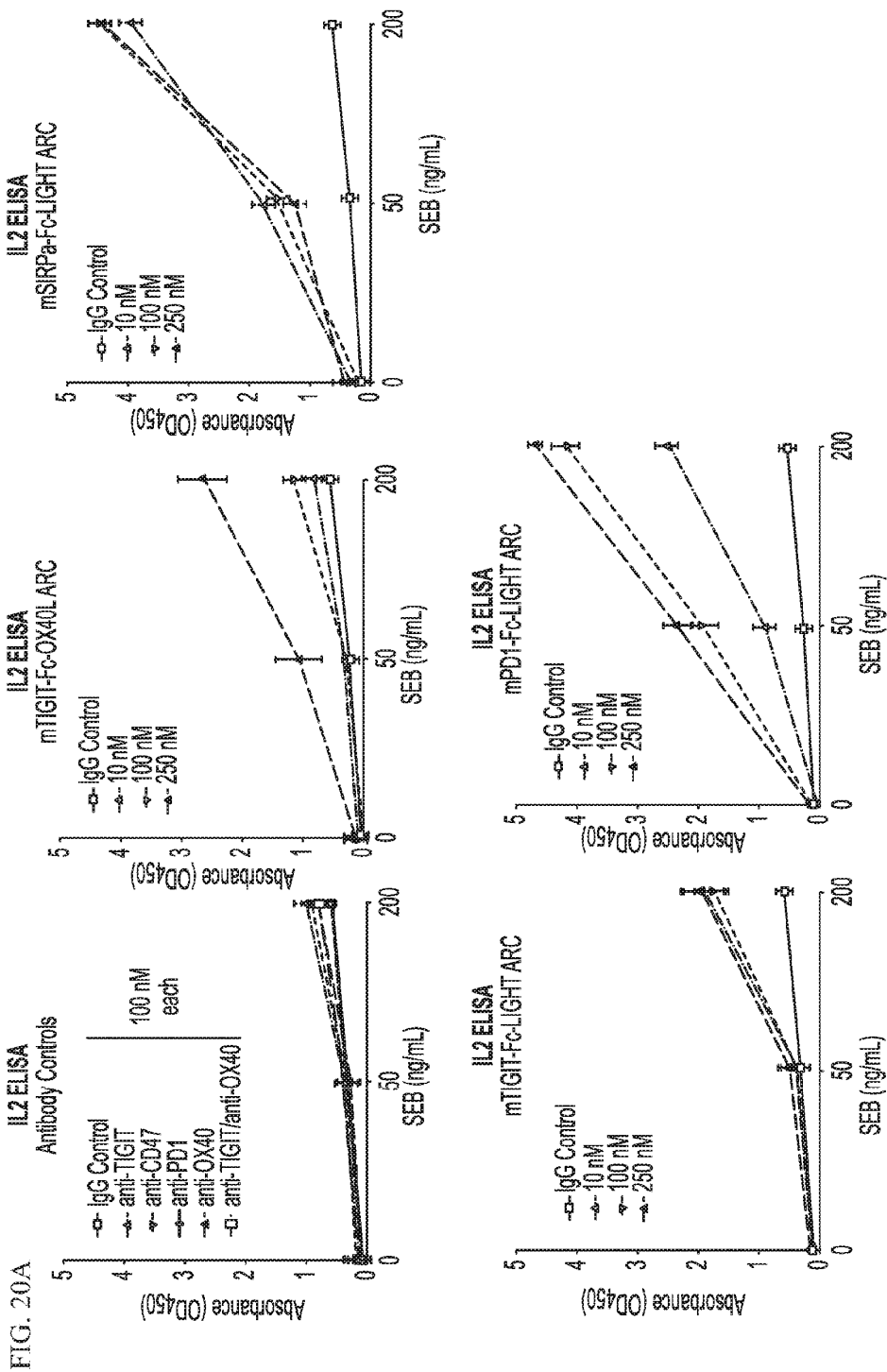
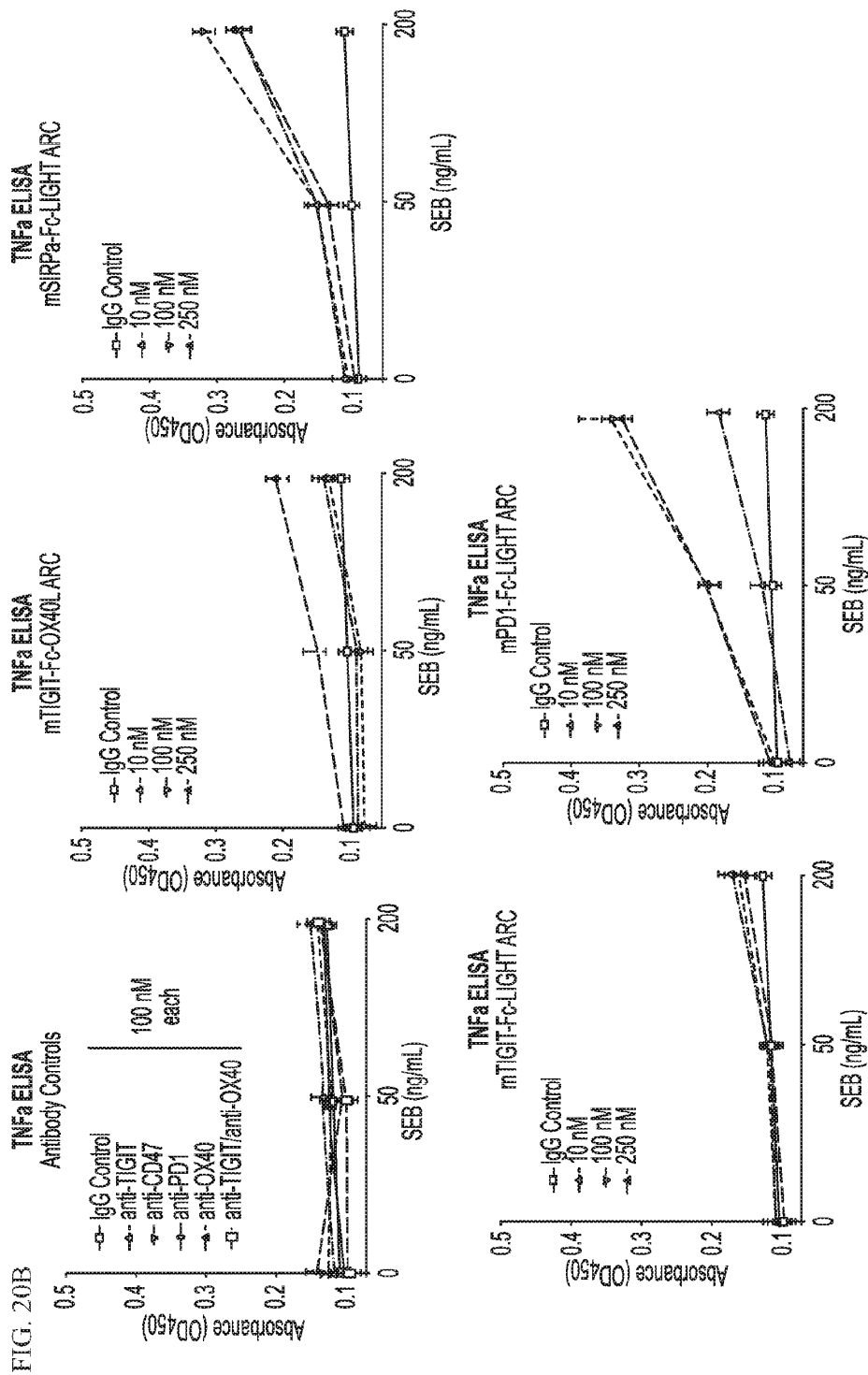
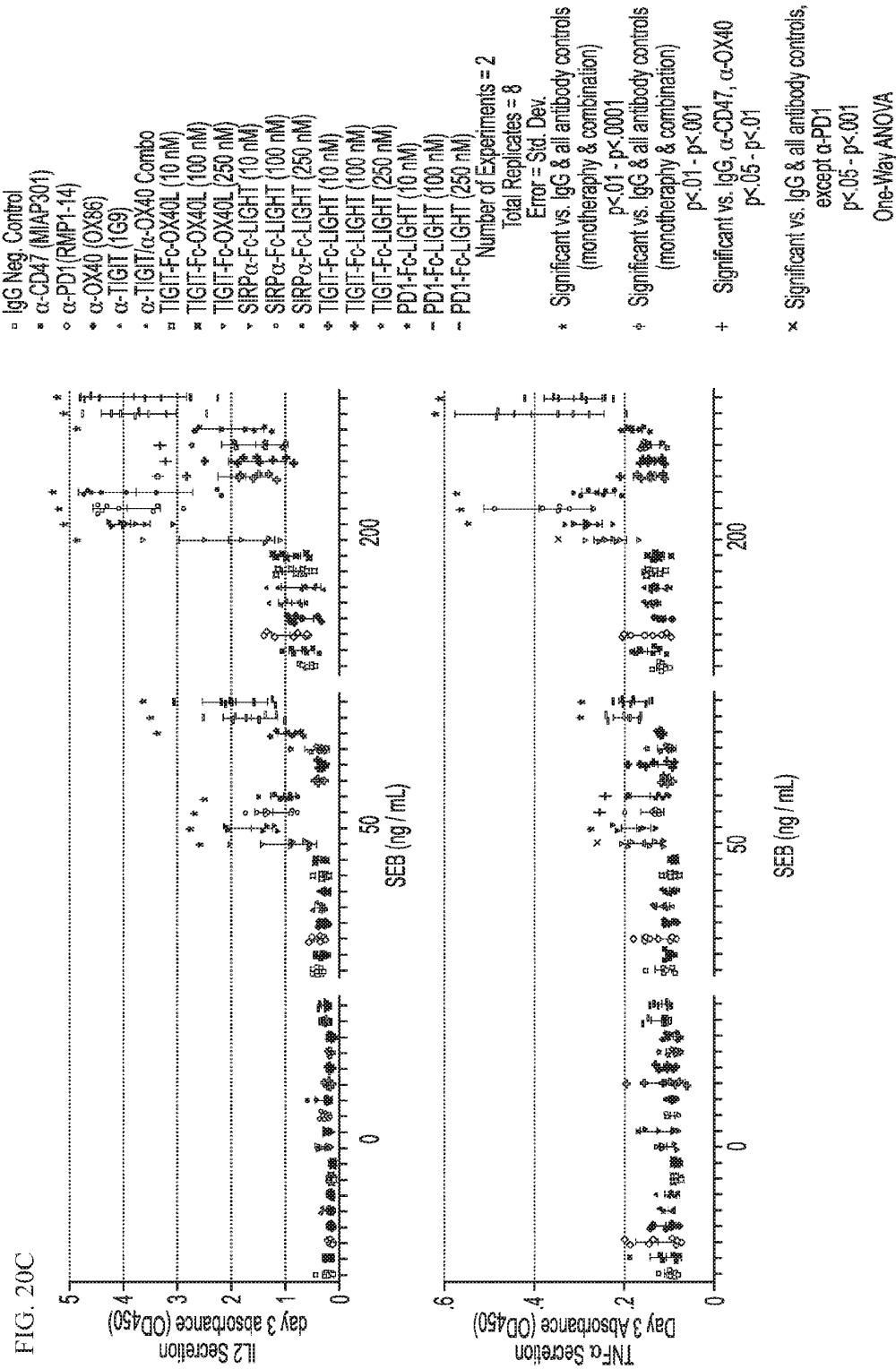


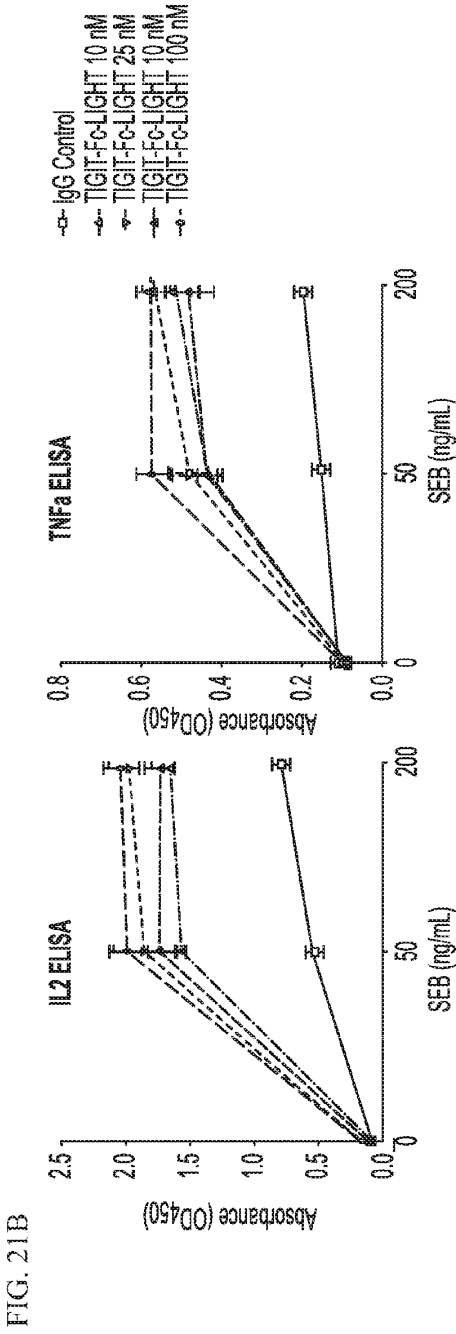
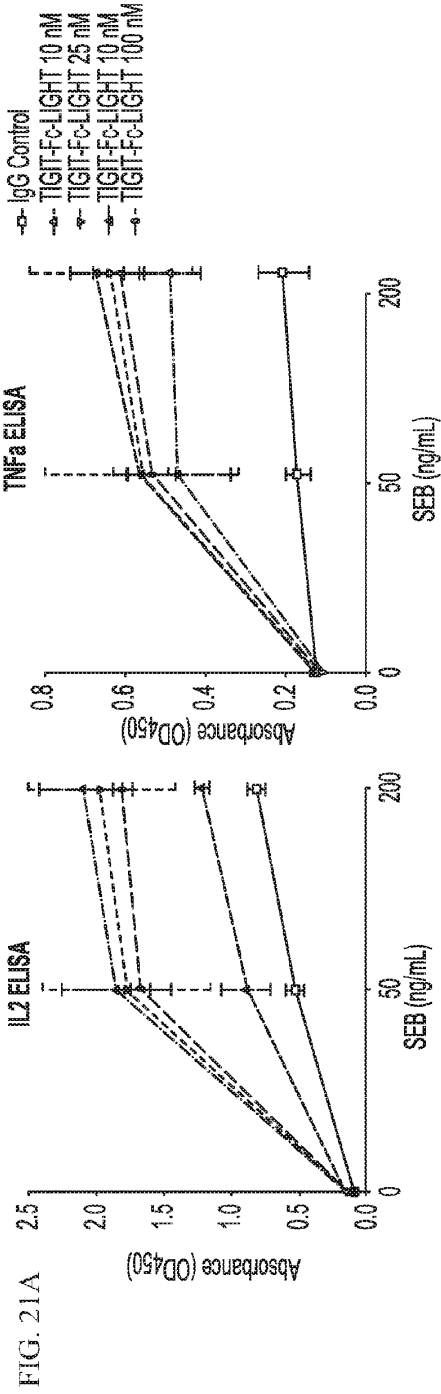
FIG. 19D

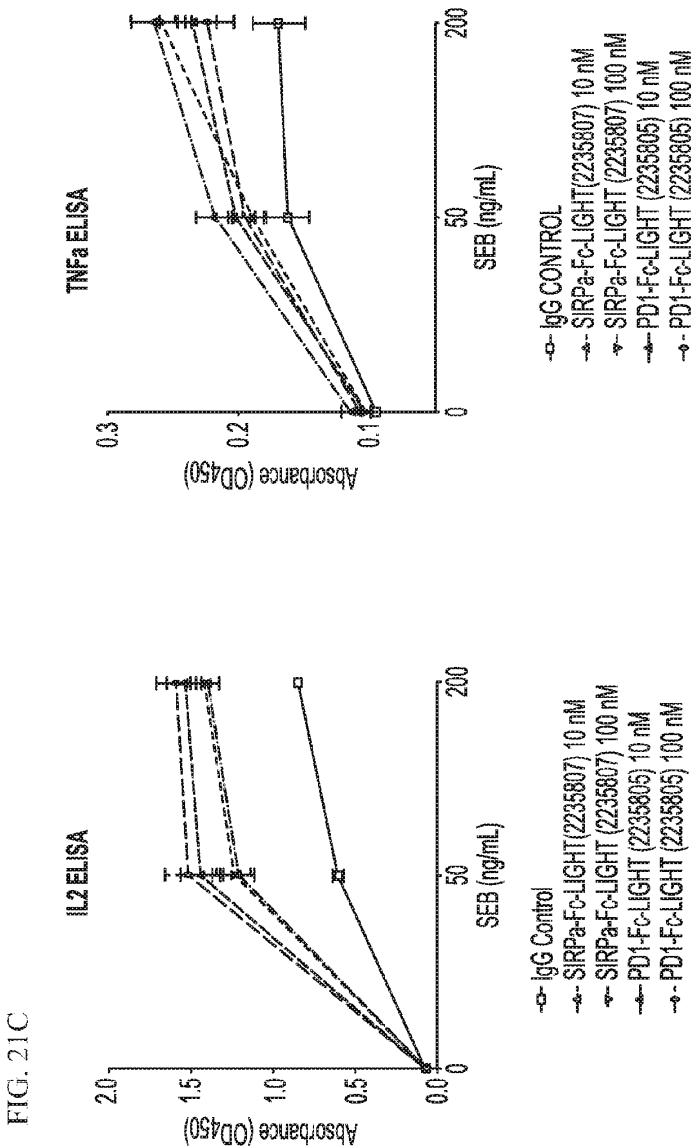












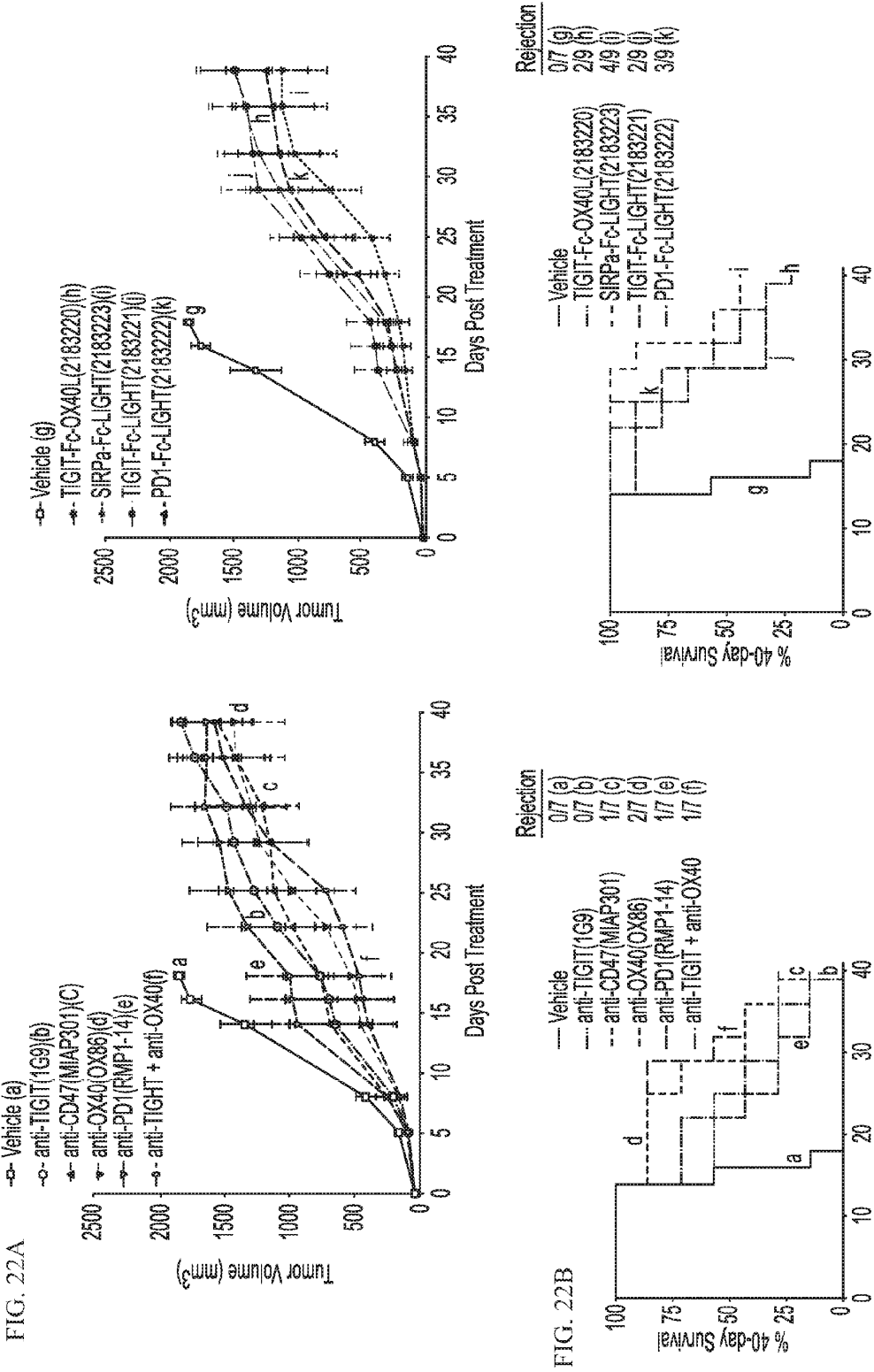


FIG. 23

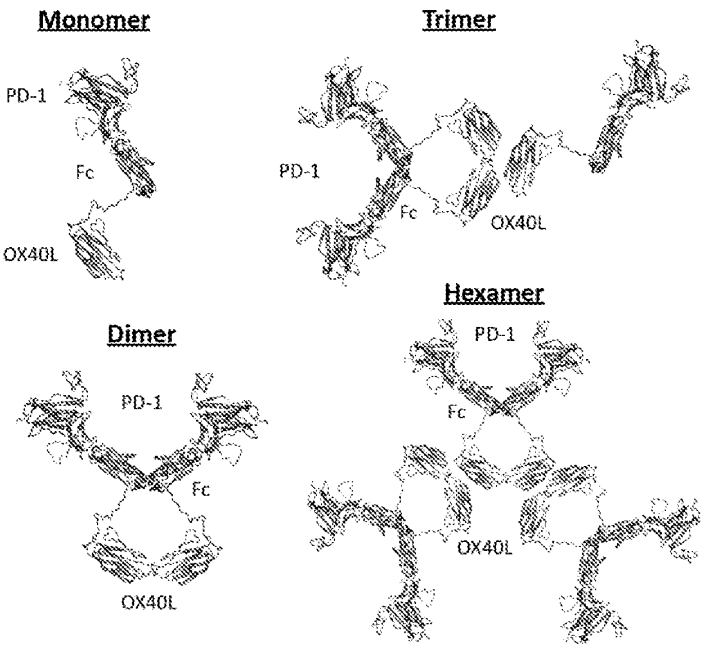


FIG. 24

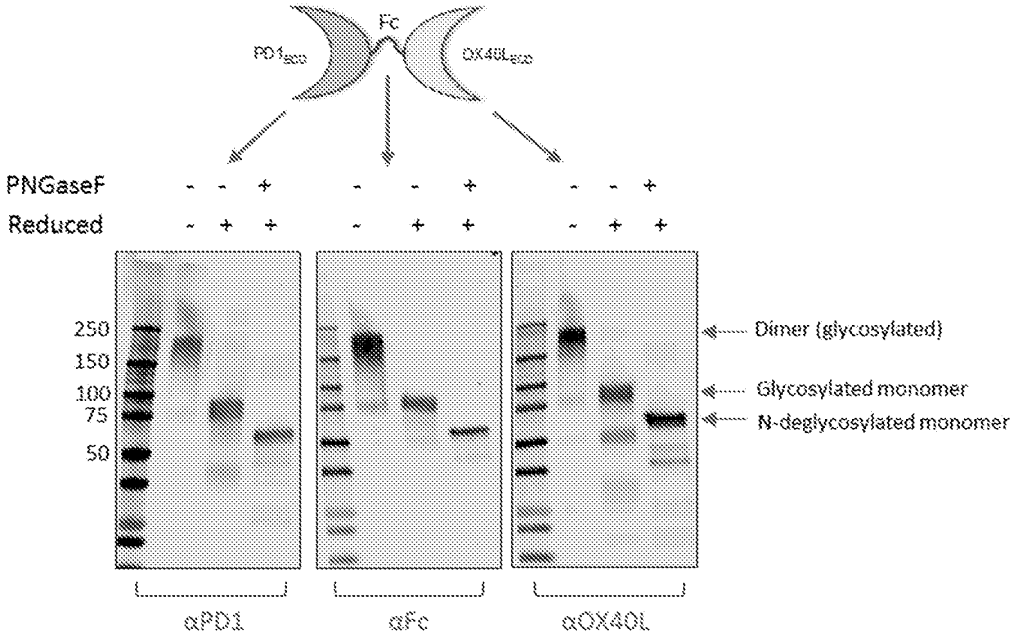


FIG. 25

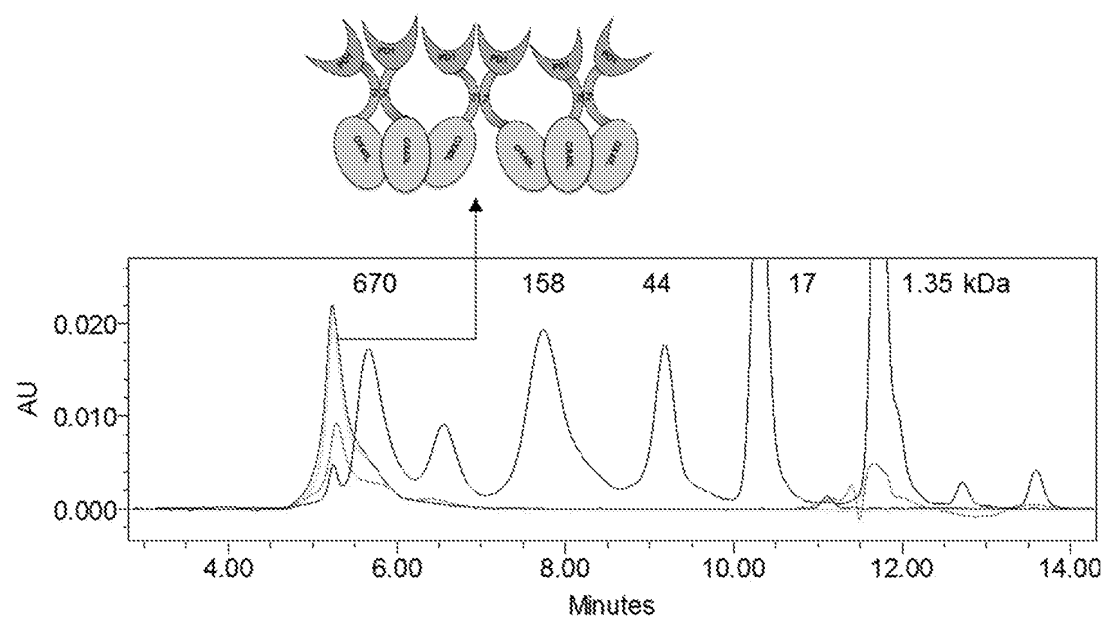
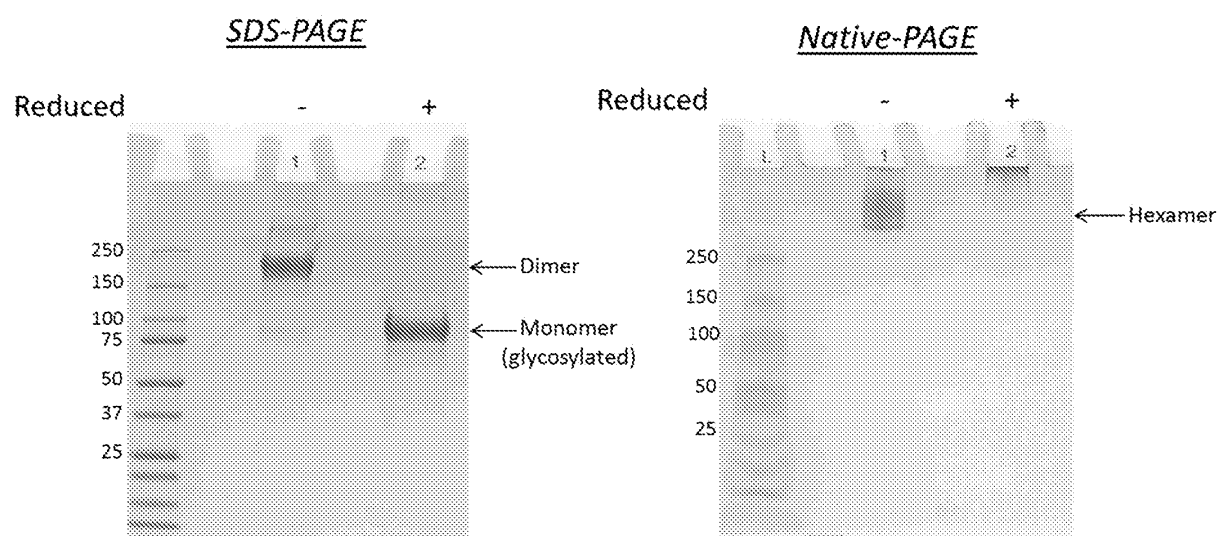


FIG. 26



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FIG. 27

Native-Page

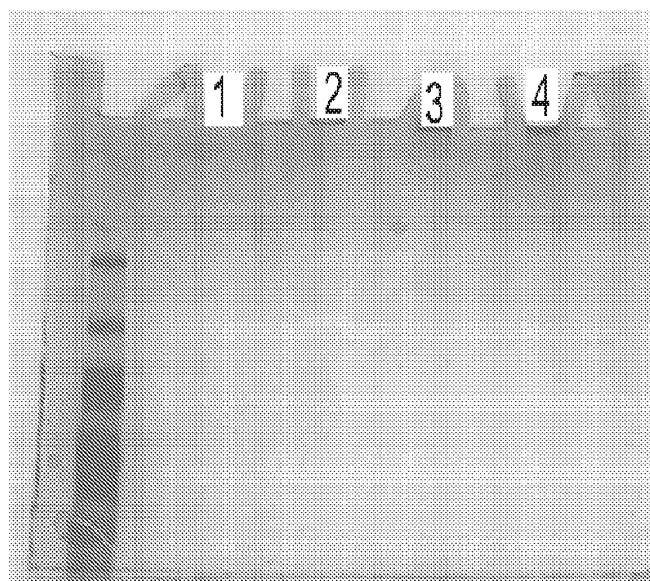
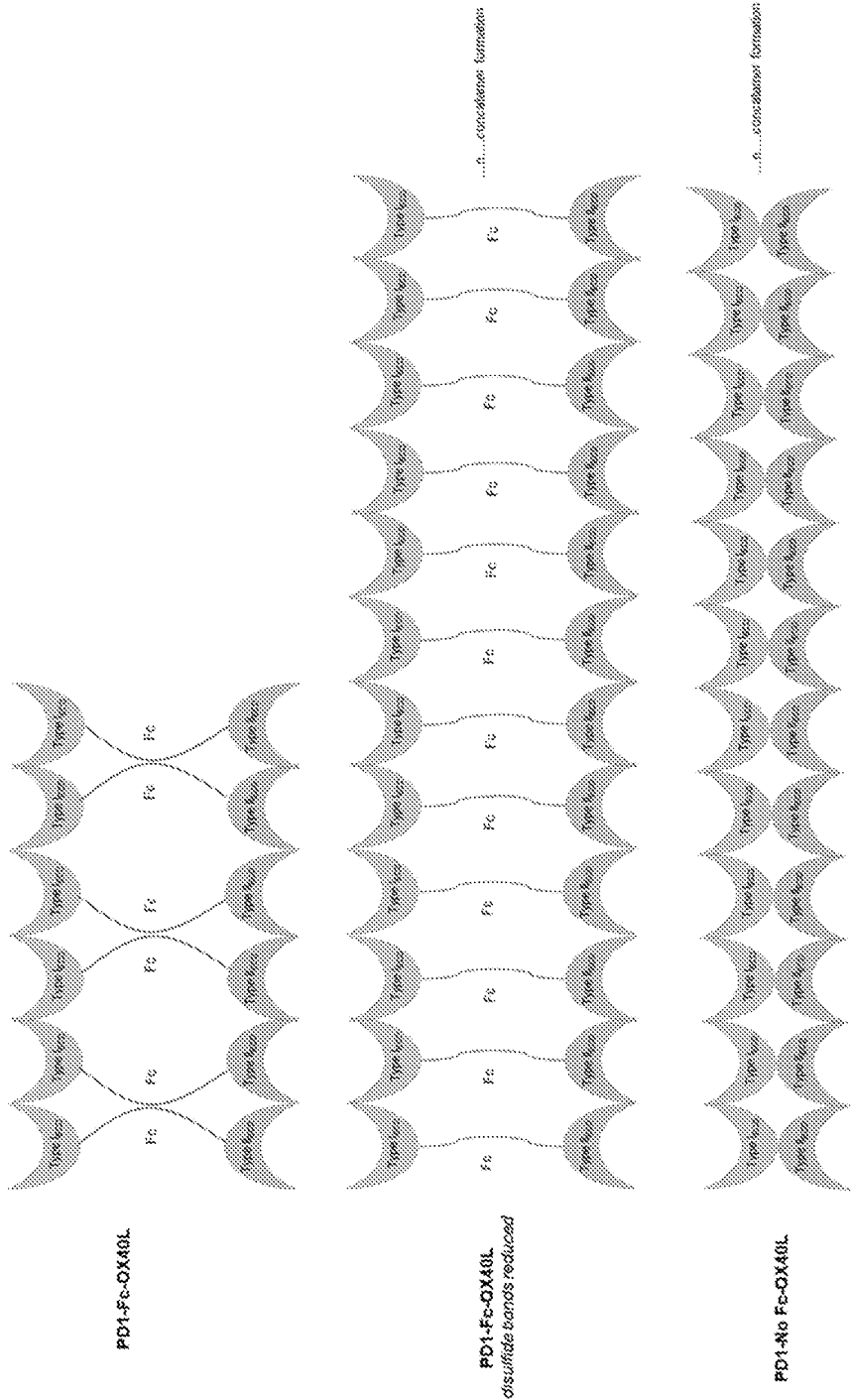


FIG. 28



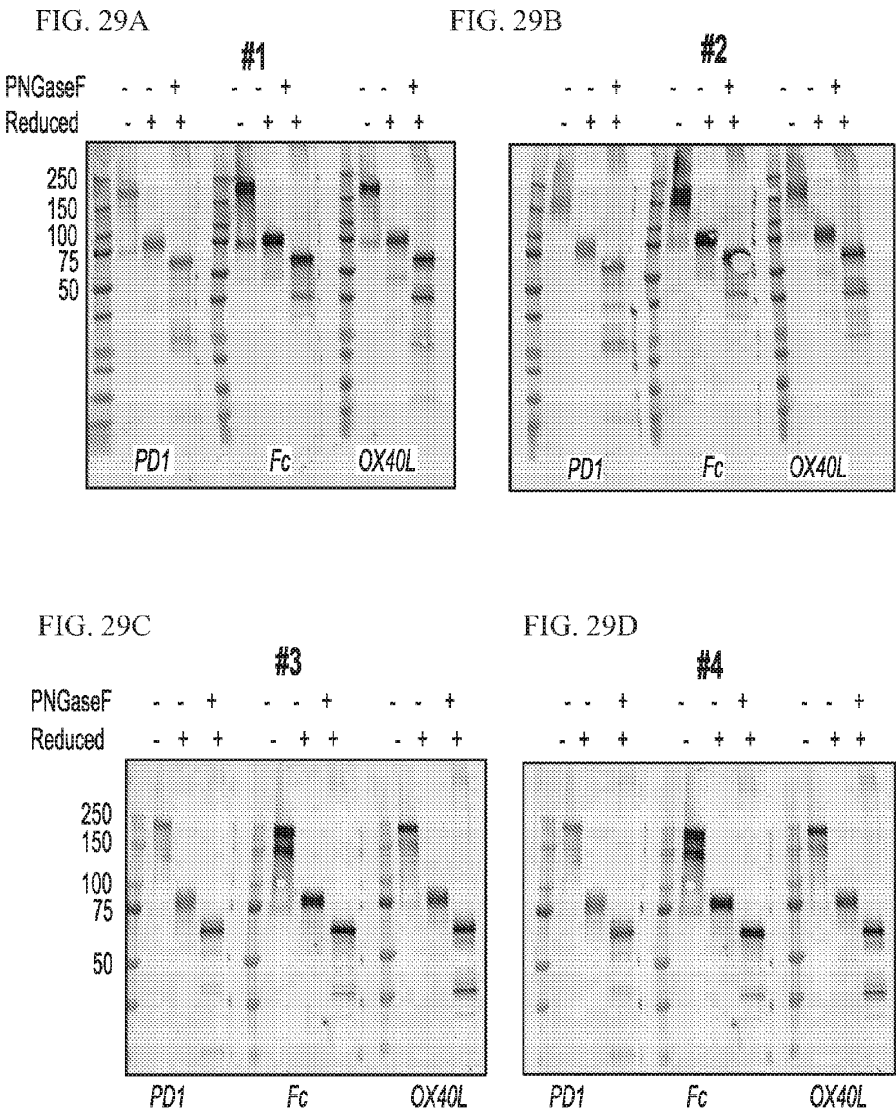


FIG. 29B

#2

PNGaseF

Reduced

-

-

+

-

-

+

-

-

+

-

+

+

-

+

+

-

+

+

250

150

100

75

50

PD1

Fc

OX40L

FIG. 29C

#3

PNGaseF

Reduced

-

-

+

-

-

+

-

-

+

-

+

+

-

+

+

-

+

+

250

150

100

75

50

PD1

Fc

OX40L

FIG. 29D

#4

PNGaseF

Reduced

-

-

+

-

-

+

-

-

+

-

+

+

-

+

+

-

+

+

250

150

100

75

50

PD1

Fc

OX40L

FIG. 29E

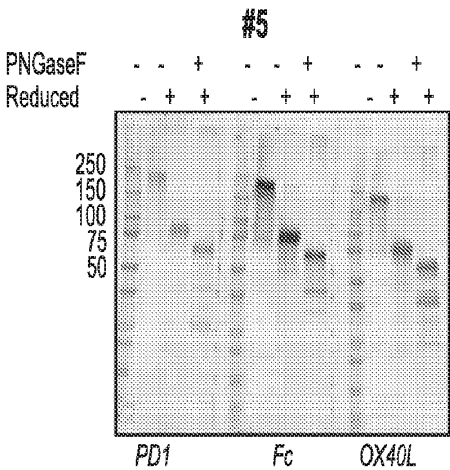


FIG. 29F

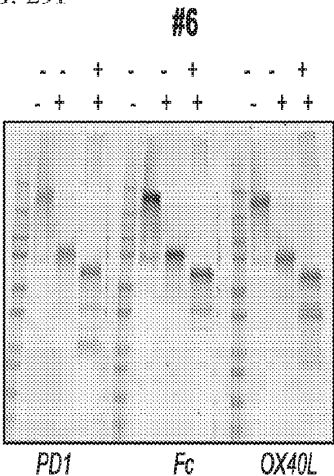


FIG. 29G

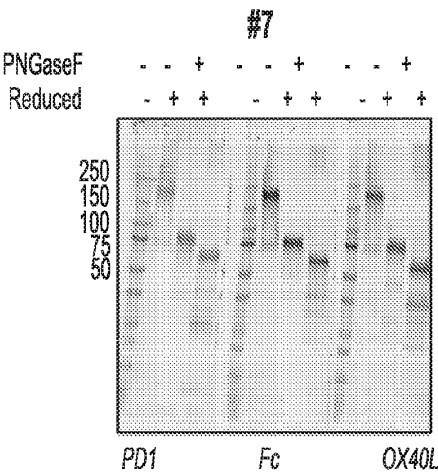


FIG. 29H

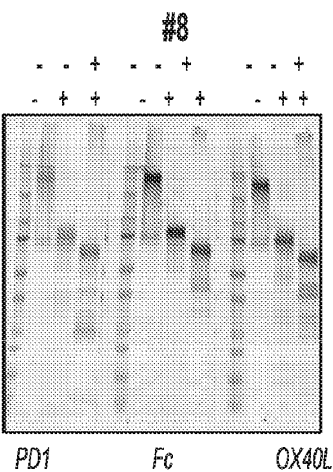


FIG. 29I

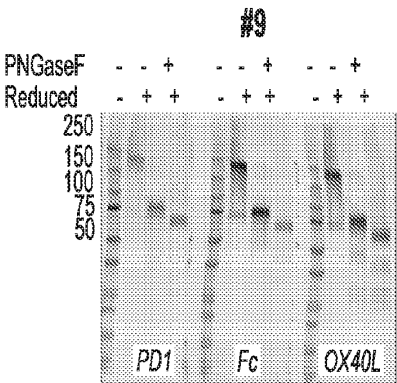


FIG. 29J

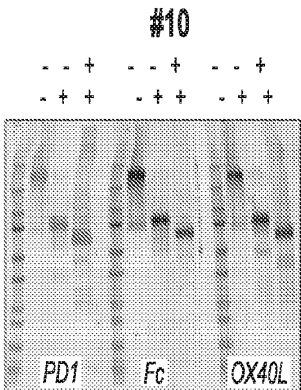


FIG. 29K

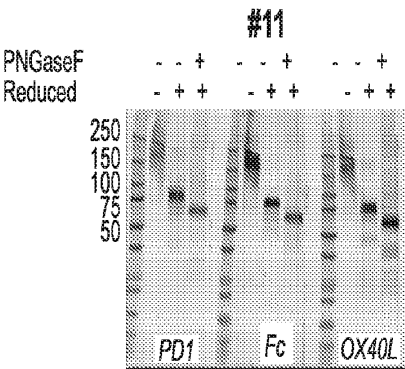


FIG. 29L

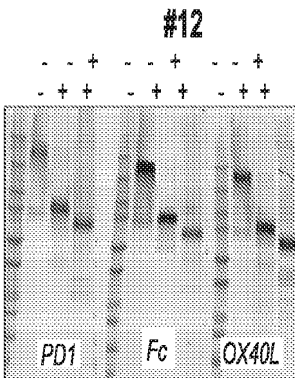


FIG. 29M

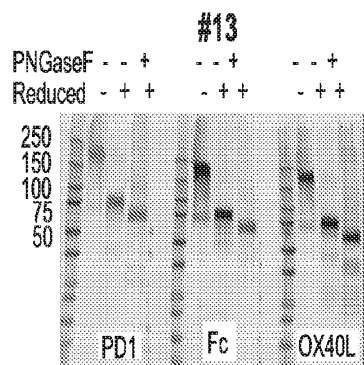


FIG. 29N

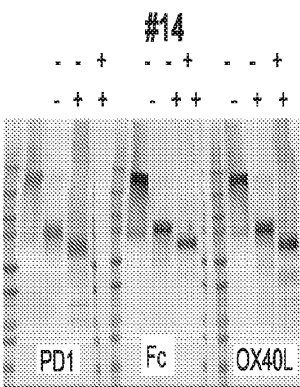


FIG. 29O

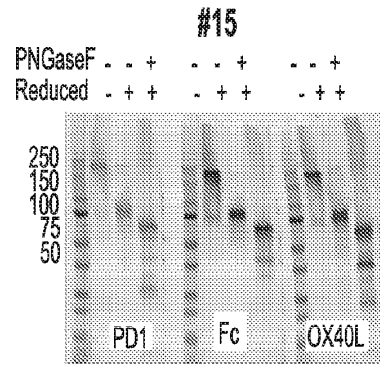


FIG. 29P

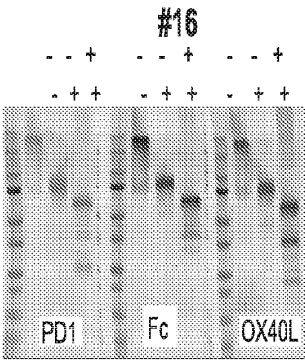


FIG. 29Q

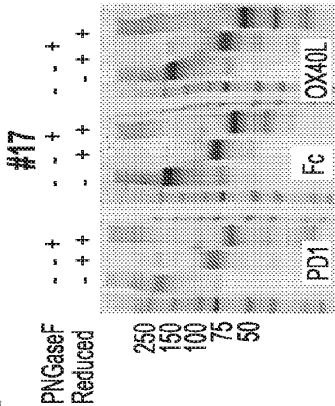


FIG. 30

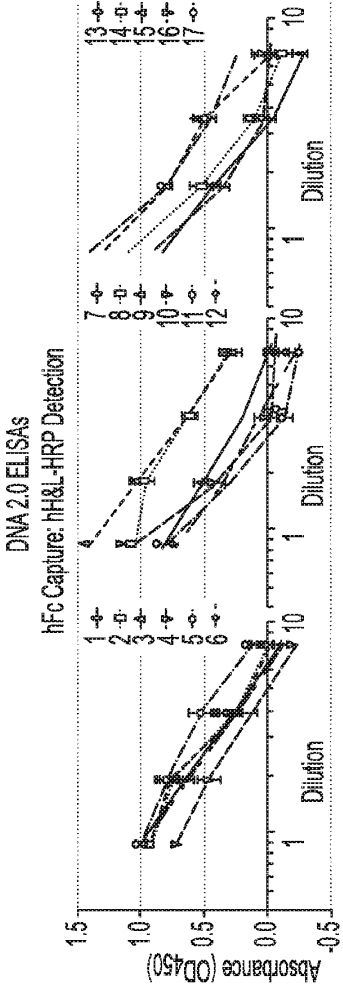


FIG. 31A

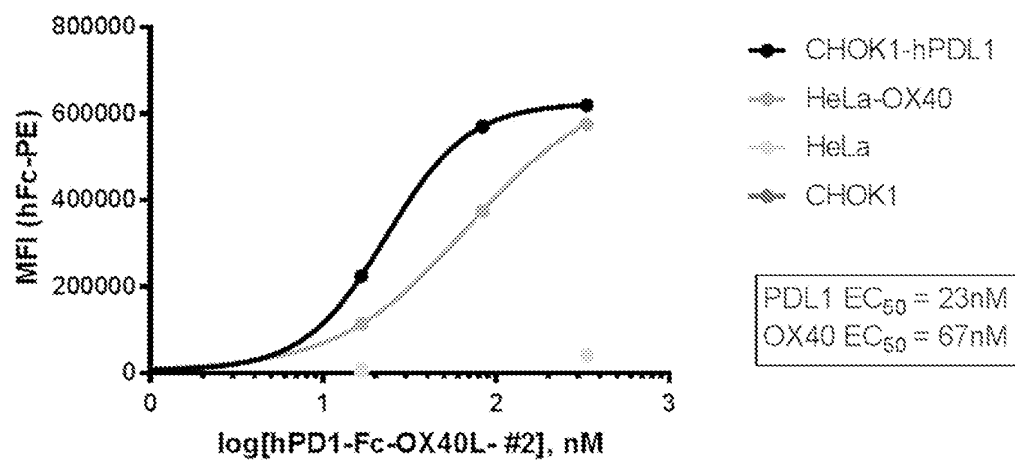


FIG. 31B

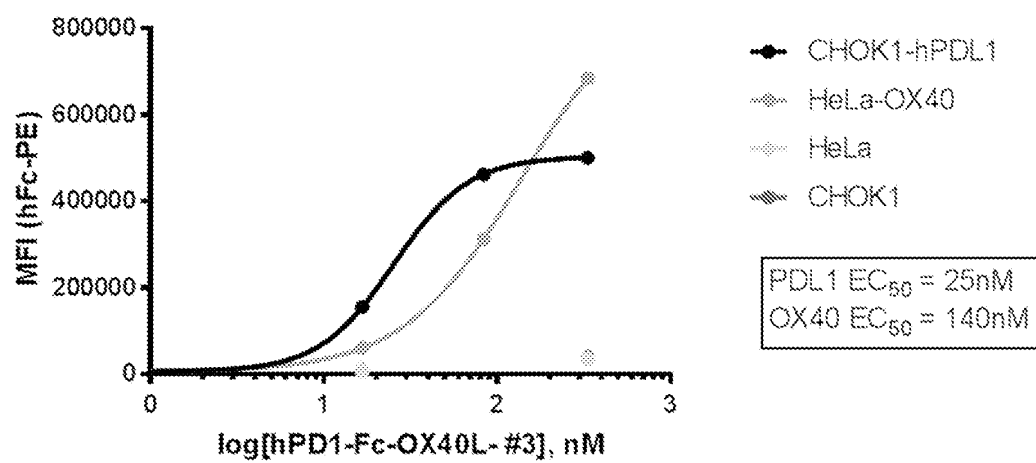


FIG. 31C

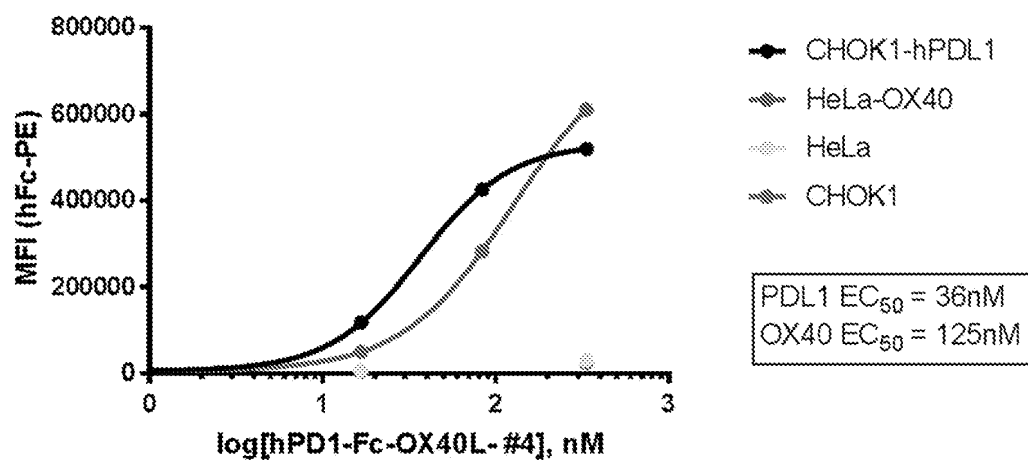


FIG. 31D

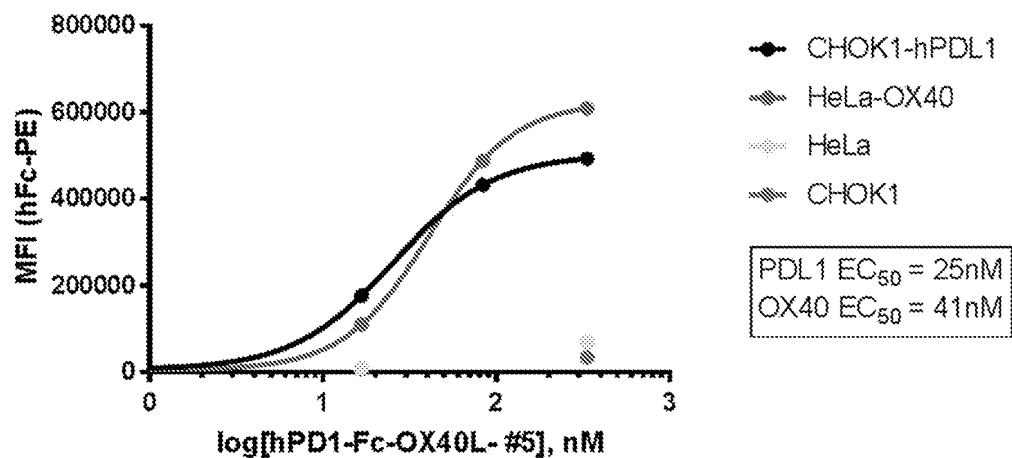


FIG. 31E

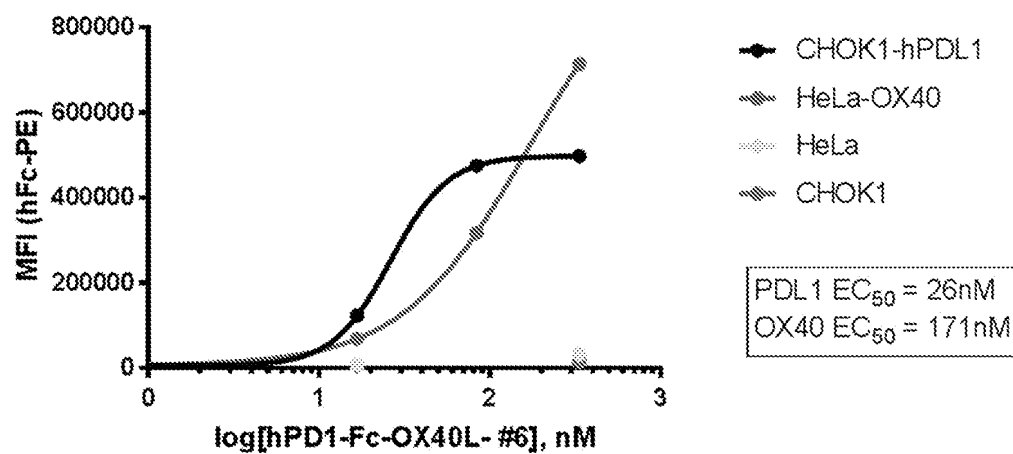


FIG. 31F

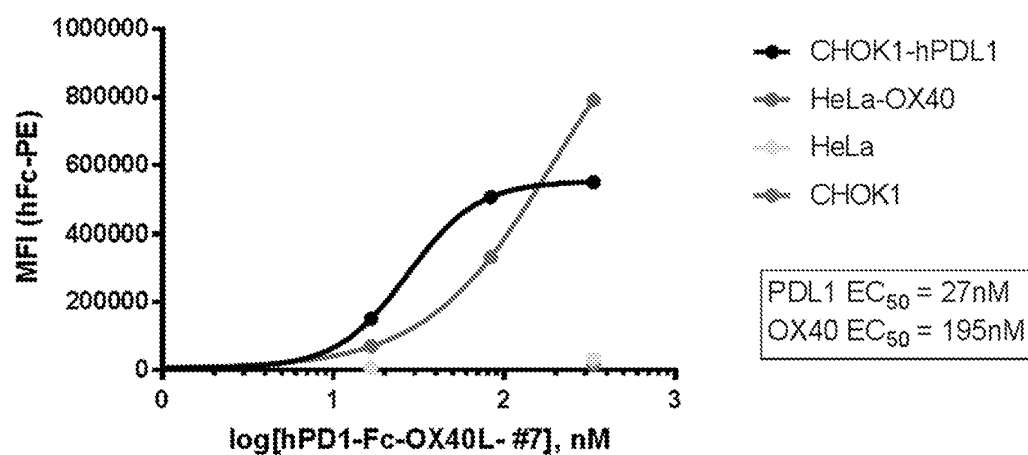


FIG. 31G

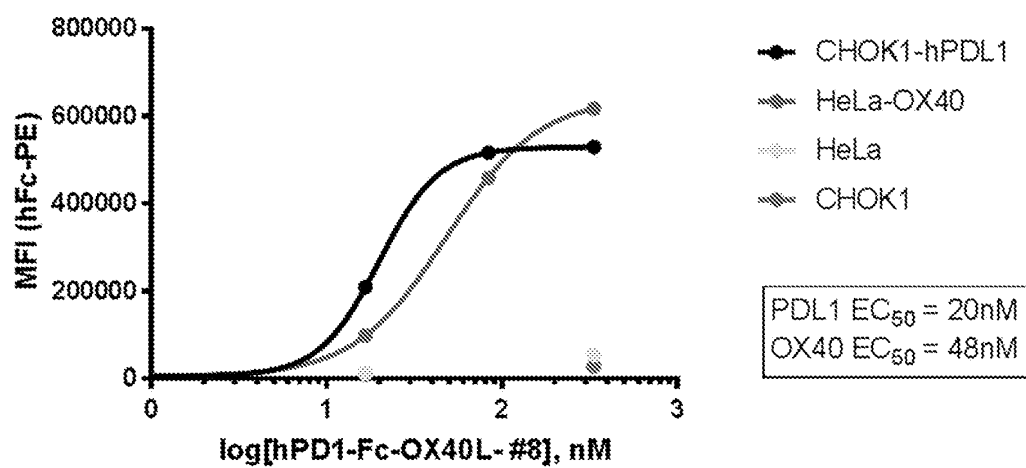


FIG. 31H

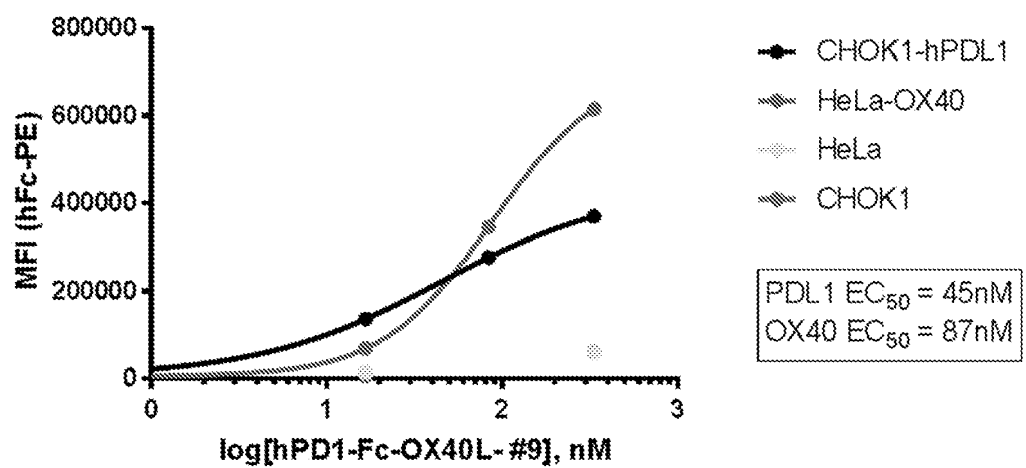


FIG. 31I

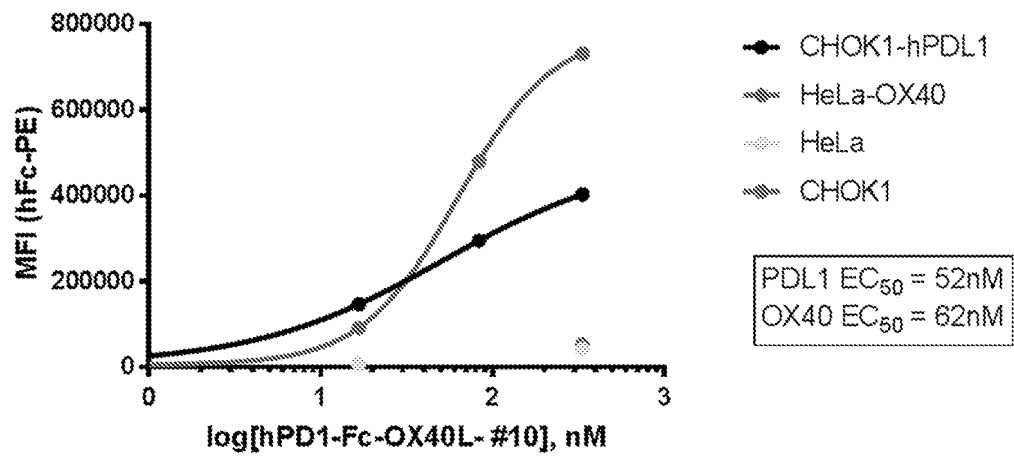


FIG. 31J

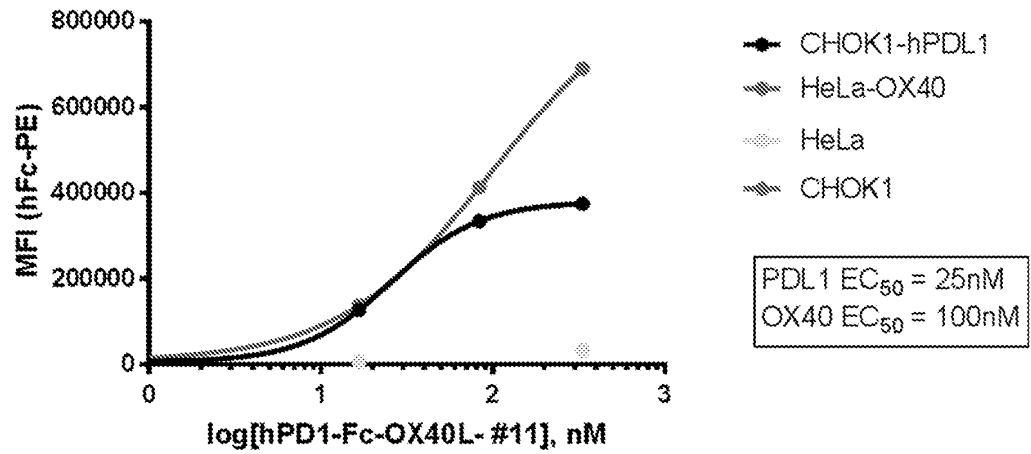


FIG. 31K

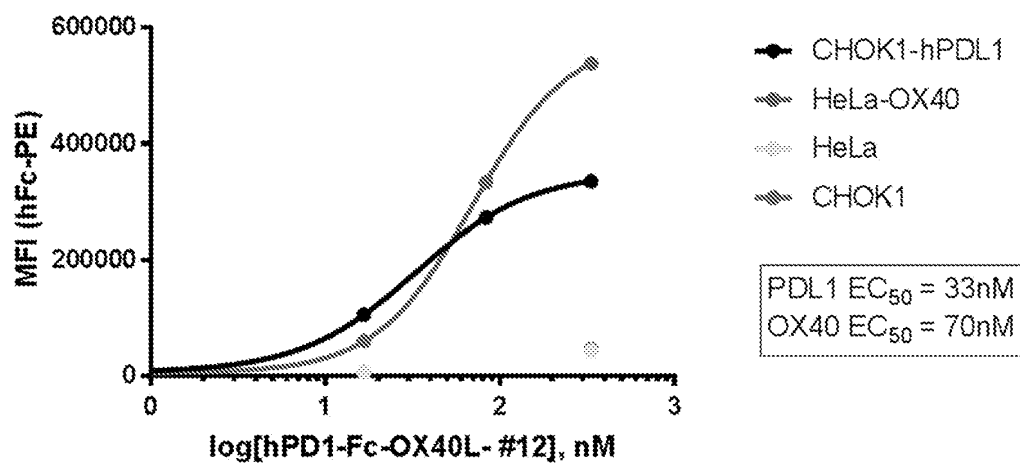


FIG. 31L

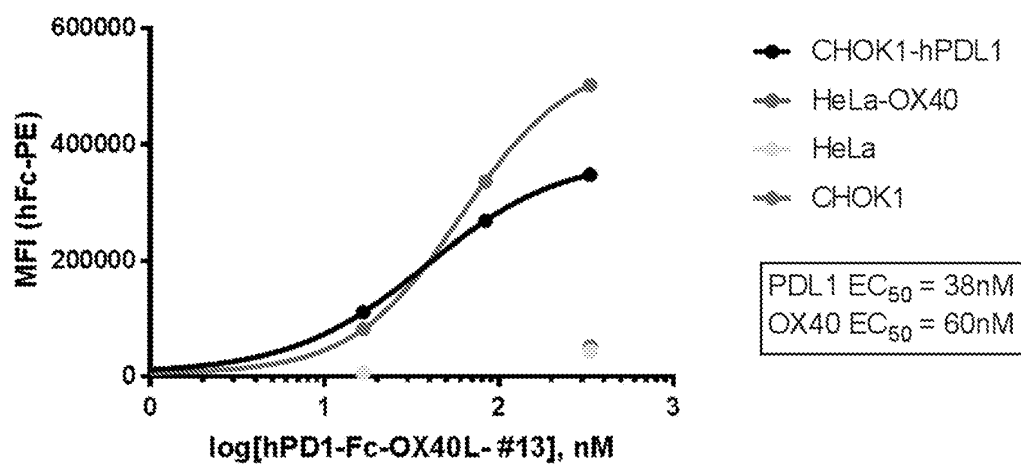


FIG. 31M

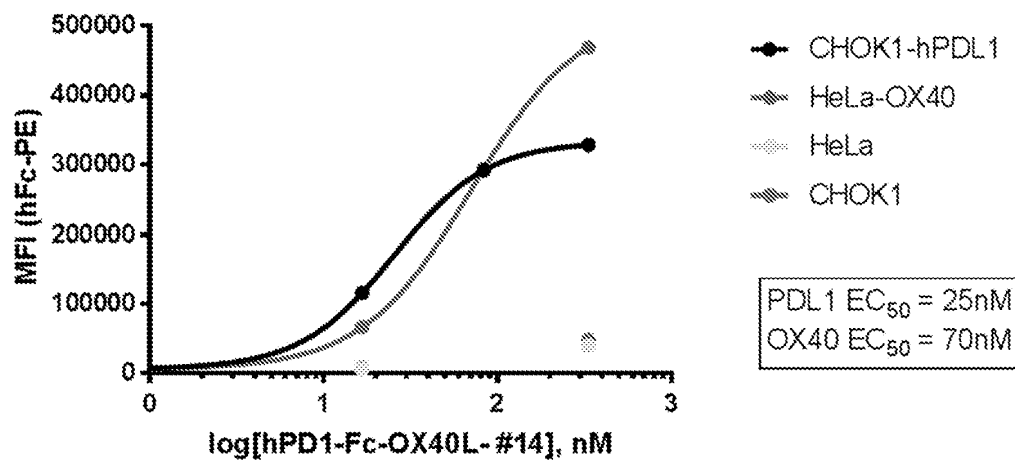


FIG. 31N

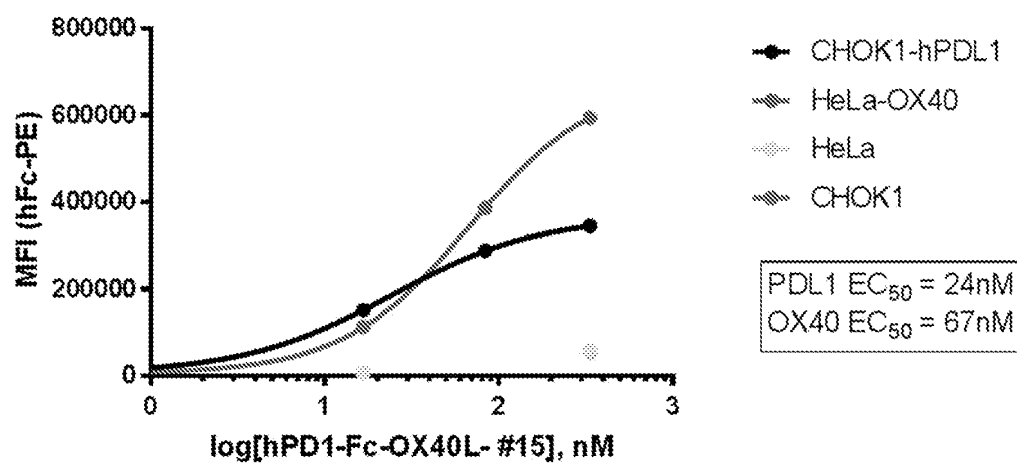


FIG. 31O

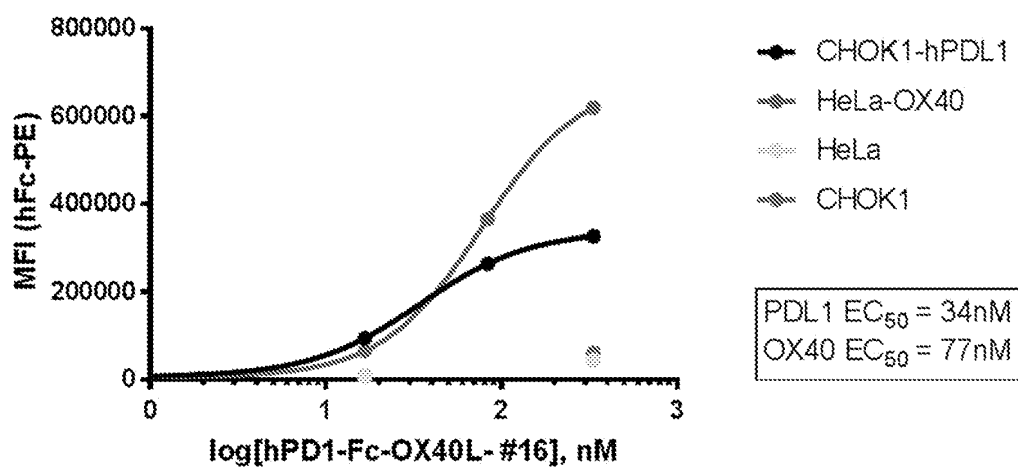
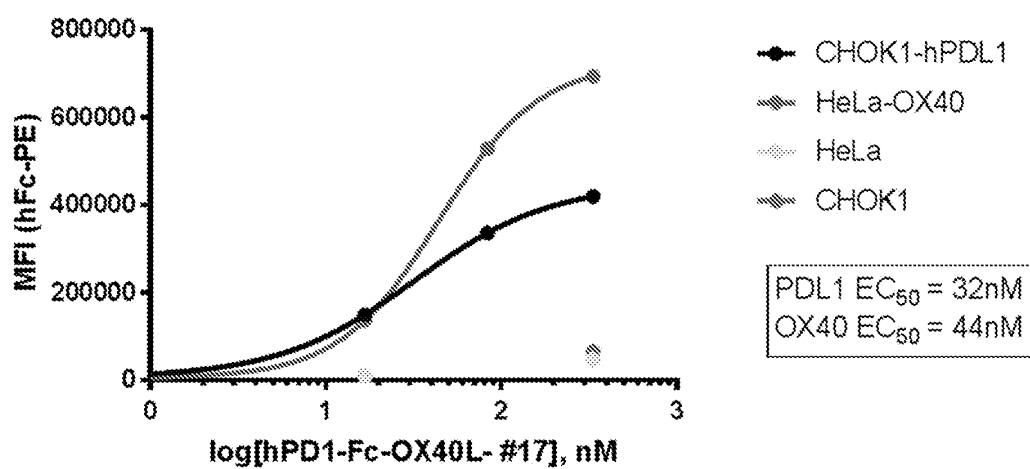


FIG. 31P



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FIG. 32

| Joining Linker 1              | Fc                                                                                                                                                                                                                                                        | Joining Linker 2          | Linker Module = Joining Linker 1 + Fc + Joining Linker 2                                                                                                                                                                                                                 |
|-------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| SKYGPCCPCP<br>(SEQ ID NO: 49) | APEFLGGPSVFLFPKPKDQIMISRTPEVTCVVDVSOE<br>DPEVQFNWYVDGVEVHNATKPREEQFNSTYRVSVLTV<br>LHODWLSGKEYCKVSSKGLPSSIEKTI SNATGQPREPQ<br>VYTLPPSQEEMTKNQVSLTCLVKGFPSPDI AVEWESNGQ<br>PENNYKTTTPVLDSDGSFFLYSRLTVDKSSWQEGNVFSC<br>SVLHEALHNHYTQKSLSLGLK (SEQ ID NO: 46) | IEGRMD<br>(SEQ ID NO: 52) | SKYGPCCPCPAPEFLGGPSVFLFPKPKDQIMISRTPEVTCVVDVSOE<br>DPEVQFNWYVDGVEVHNATKPREEQFNSTYRVSVLTVLHODWLS<br>GKEYCKVSSKGLPSSIEKTI SNATGQPREPQVYTLPPSQEEMTKNQV<br>SLTCLVKGFPSPDI AVEWESNGQPNNYKTTTPVLDSDGSFFLYSRLT<br>VDKSSWQEGNVFSCSVLHEALHNHYTQKSLSLGLKIEGRMD (SEQ<br>ID NO: 96)  |
| SKYGPCCPCP<br>(SEQ ID NO: 49) | APEFLGGPSVFLFPKPKDQIMISRTPEVTCVVDVSOE<br>DPEVQFNWYVDGVEVHNATKPREEQFNSTYRVSVLTV<br>PHSDWLSGKEYCKVSSKGLPSSIEKTI SNATGQPREPQ<br>VYTLPPSQEEMTKNQVSLTCLVKGFPSPDI AVEWESNGQ<br>PENNYKTTTPVLDSDGSFFLYSRLTVDKSSWQEGNVFSC<br>SVLHEALHNHYTQKSLSLGLK (SEQ ID NO: 47) | IEGRMD<br>(SEQ ID NO: 52) | SKYGPCCPCPAPEFLGGPSVFLFPKPKDQIMISRTPEVTCVVDVSOE<br>DPEVQFNWYVDGVEVHNATKPREEQFNSTYRVSVLTVPHSDWLS<br>GKEYCKVSSKGLPSSIEKTI SNATGQPREPQVYTLPPSQEEMTKNQV<br>SLTCLVKGFPSPDI AVEWESNGQPNNYKTTTPVLDSDGSFFLYSRLT<br>VDKSSWQEGNVFSCSVLHEALHNHYTQKSLSLGLKIEGRMD (SEQ<br>ID NO: 97)  |
| SKYGPCCPCP<br>(SEQ ID NO: 49) | APEFLGGPSVFLFPKPKDQIMISRTPEVTCVVDVSOE<br>DPEVQFNWYVDGVEVHNATKPREEQFNSTYRVSVLTV<br>LHODWLSGKEYCKVSSKGLPSSIEKTI SNATGQPREPQ<br>VYTLPPSQEEMTKNQVSLTCLVKGFPSPDI AVEWESNGQ<br>PENNYKTTTPVLDSDGSFFLYSRLTVDKSSWQEGNVFSC<br>SVLHEALHNHYTQKSLSLGLK (SEQ ID NO: 48) | IEGRMD<br>(SEQ ID NO: 52) | SKYGPCCPCPAPEFLGGPSVFLFPKPKDQIMISRTPEVTCVVDVSOE<br>DPEVQFNWYVDGVEVHNATKPREEQFNSTYRVSVLTVLHODWLS<br>GKEYCKVSSKGLPSSIEKTI SNATGQPREPQVYTLPPSQEEMTKNQV<br>SLTCLVKGFPSPDI AVEWESNGQPNNYKTTTPVLDSDGSFFLYSRLT<br>VDKSSWQEGNVFSCSVLHEALHNHYTQKSLSLGLKIEGRMD (SEQ<br>ID NO: 98)  |
| SKYGPCCPCP<br>(SEQ ID NO: 50) | APEFLGGPSVFLFPKPKDQIMISRTPEVTCVVDVSOE<br>DPEVQFNWYVDGVEVHNATKPREEQFNSTYRVSVLTV<br>LHODWLSGKEYCKVSSKGLPSSIEKTI SNATGQPREPQ<br>VYTLPPSQEEMTKNQVSLTCLVKGFPSPDI AVEWESNGQ<br>PENNYKTTTPVLDSDGSFFLYSRLTVDKSSWQEGNVFSC<br>SVLHEALHNHYTQKSLSLGLK (SEQ ID NO: 46) | IEGRMD<br>(SEQ ID NO: 52) | SKYGPCCPCPAPEFLGGPSVFLFPKPKDQIMISRTPEVTCVVDVSOE<br>DPEVQFNWYVDGVEVHNATKPREEQFNSTYRVSVLTVLHODWLS<br>GKEYCKVSSKGLPSSIEKTI SNATGQPREPQVYTLPPSQEEMTKNQV<br>SLTCLVKGFPSPDI AVEWESNGQPNNYKTTTPVLDSDGSFFLYSRLT<br>VDKSSWQEGNVFSCSVLHEALHNHYTQKSLSLGLKIEGRMD (SEQ<br>ID NO: 99)  |
| SKYGPCCPCP<br>(SEQ ID NO: 50) | APEFLGGPSVFLFPKPKDQIMISRTPEVTCVVDVSOE<br>DPEVQFNWYVDGVEVHNATKPREEQFNSTYRVSVLTV<br>PHSDWLSGKEYCKVSSKGLPSSIEKTI SNATGQPREPQ<br>VYTLPPSQEEMTKNQVSLTCLVKGFPSPDI AVEWESNGQ<br>PENNYKTTTPVLDSDGSFFLYSRLTVDKSSWQEGNVFSC<br>SVLHEALHNHYTQKSLSLGLK (SEQ ID NO: 47) | IEGRMD<br>(SEQ ID NO: 52) | SKYGPCCPCPAPEFLGGPSVFLFPKPKDQIMISRTPEVTCVVDVSOE<br>DPEVQFNWYVDGVEVHNATKPREEQFNSTYRVSVLTVPHSDWLS<br>GKEYCKVSSKGLPSSIEKTI SNATGQPREPQVYTLPPSQEEMTKNQV<br>SLTCLVKGFPSPDI AVEWESNGQPNNYKTTTPVLDSDGSFFLYSRLT<br>VDKSSWQEGNVFSCSVLHEALHNHYTQKSLSLGLKIEGRMD (SEQ<br>ID NO: 100) |
| SKYGPCCPCP<br>(SEQ ID NO: 50) | APEFLGGPSVFLFPKPKDQIMISRTPEVTCVVDVSOE<br>DPEVQFNWYVDGVEVHNATKPREEQFNSTYRVSVLTV<br>LHODWLSGKEYCKVSSKGLPSSIEKTI SNATGQPREPQ<br>VYTLPPSQEEMTKNQVSLTCLVKGFPSPDI AVEWESNGQ<br>PENNYKTTTPVLDSDGSFFLYSRLTVDKSSWQEGNVFSC<br>SVLHEALHNHYTQKSLSLGLK (SEQ ID NO: 48) | IEGRMD<br>(SEQ ID NO: 52) | SKYGPCCPCPAPEFLGGPSVFLFPKPKDQIMISRTPEVTCVVDVSOE<br>DPEVQFNWYVDGVEVHNATKPREEQFNSTYRVSVLTVLHODWLS<br>GKEYCKVSSKGLPSSIEKTI SNATGQPREPQVYTLPPSQEEMTKNQV<br>SLTCLVKGFPSPDI AVEWESNGQPNNYKTTTPVLDSDGSFFLYSRLT<br>VDKSSWQEGNVFSCSVLHEALHNHYTQKSLSLGLKIEGRMD (SEQ<br>ID NO: 101) |