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(54) **ANTIBODIES TO TIGIT**

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(58) **Field of Classification Search**

None

See application file for complete search history.

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(57) **ABSTRACT**

The invention provides monoclonal antibodies that specifically bind to TIGIT. The monoclonal antibodies have the capacity for substantial activation of T cells and natural killer cells by inhibiting binding of TIGIT to CD155. The monoclonal antibodies can be used for treatment of cancer and infectious disease, among other applications.

9 Claims, 34 Drawing Sheets

Specification includes a Sequence Listing.

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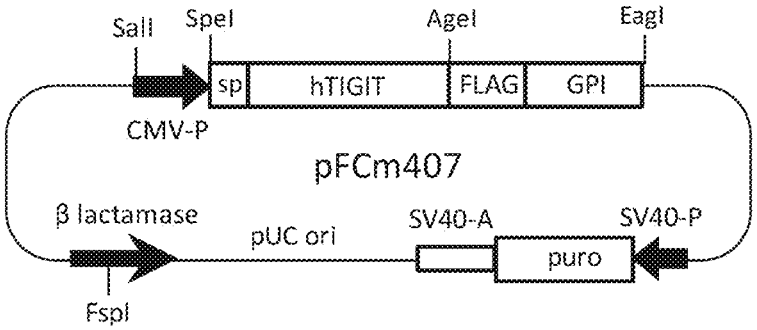
FIG. 1


SalI
SpeI
AgeI
EagI
sp
hTIGIT
FLAG
GPI
CMV-P
pFCm407
β lactamase
pUC ori
SV40-A
SV40-P
puro
FspI

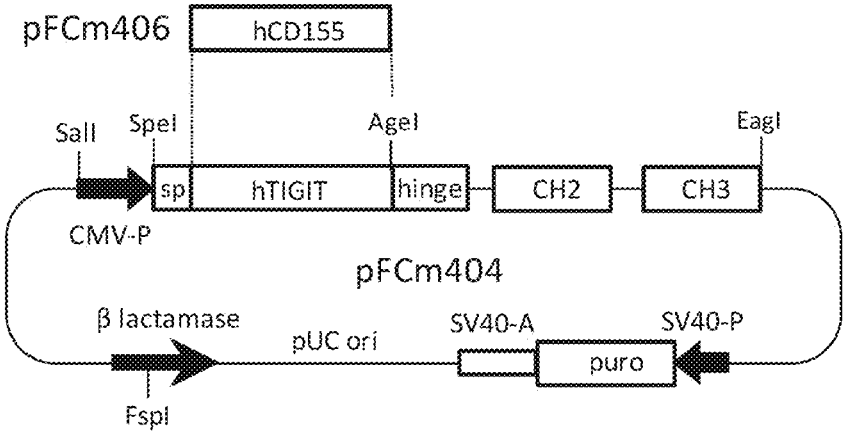

pFCm406
hCD155
SalI
SpeI
AgeI
EagI
sp
hTIGIT
hinge
CH2
CH3
CMV-P
pFCm404
β lactamase
pUC ori
SV40-A
SV40-P
puro
FspI

FIG. 2

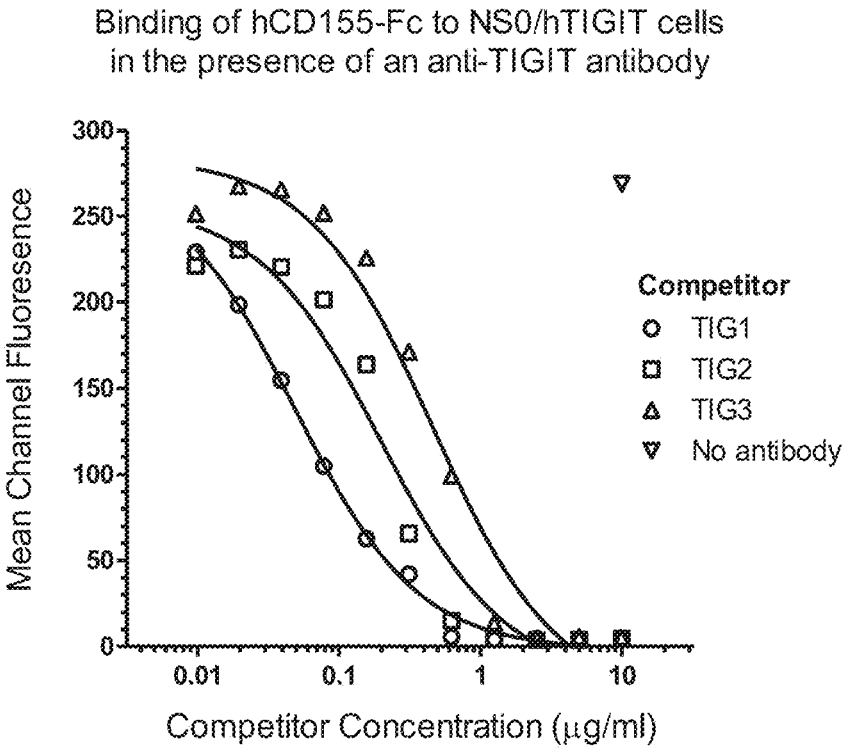

Binding of hCD155-Fc to NS0/hTIGIT cells
in the presence of an anti-TIGIT antibody
Mean Channel Fluoresence
300
250
200
150
100
50
0
0.01
0.1
1
10
Competitor Concentration (μg/ml)
Competitor
TIG1
TIG2
TIG3
No antibody

FIG. 3

TIG1 VH

```
          1           2           3
123456789 0123456789 0123456789 0123456789
DVQLVESGG GLVQPGGSRK LSCAASGFTF SNFGMHWVRQ
                                  CDR1

4          5           6          7
0123456789 01223456789 0123456789 0123456789
              a
APEKGLEWVA FISSGSSSIYY ADTVKGRFTI SRDNPKNTLF
                    CDR2

                                1           1
8              9                0           1
0122223456789 0123456789 000123456789 0123
   abc                      ab
LQMTSLRSEDTAM YYCARMRLDY YAMDYWGQGTSV TVSS (SEQ ID NO: 10)
                          CDR3
```

FIG. 4

TIG1 VL

```
          1           2           3
123456789 0123456789 0123456789 0123456789
DVQITQSPS YLAASPGETI TINCRASKSI SKYLAWYQEK
                                CDR1

4          5           6           7
0123456789 0123456789 0123456789 0123456789
PGKTNKLLIY SGSTLQSGIP SRFSGSGSGT DFTLTISSLE
             CDR2

                       1
8          9           0
0123456789 0123456789 01234567
PEDFAMYYCQ QHNEYPWTFG GGTKLEIK (SEQ ID NO: 14)
             CDR3
```

FIG. 5

TIG2 VH

```
           1           2           3
123456789 0123456789 0123456789 0123456789
EVQLQQSGP ELVKPGASVK ISCKTSGYTF TEYTMHWVKQ
                                  CDR1

4           5            6           7
0123456789 01223456789 0123456789 0123456789
              a
SHGKNLEWIG GINPNNGGTSY NQKFKGRATL TVDKSSSTAY
                  CDR2

                              1            1
8             9               0            1
0122223456789 0123456789 000123456789 0123
   abc                      ab
MELRSLTSDDSAV YYCARPGWYN YAMDYWGQGTSV TVSS (SEQ ID NO: 18)
                        CDR3
```

FIG. 6

TIG2 VL

```
          1           2           3
123456789 0123456789 0123456789 0123456789
DIVMTQSHK FMSTSVGDRV NITCKASQGV STAVAWYQQK
                               CDR1

4          5          6          7
0123456789 0123456789 0123456789 0123456789
PGQSPKLLIY SASYRYTGVP DRFTGSGSGT DFTFTISSVQ
             CDR2
                      1
8          9          0
0123456789 0123456789 01234567
AEDLAVYHCQ QHYITPWTFG GGTKLEIK (SEQ ID NO: 22)
            CDR3
```

FIG. 7

TIG3 VH

```
           1           2           3
123456789 0123456789 0123456789 0123456789
EVQLVESGG GLVKPGGSLK LSCAASGFAF SDYDMSWVRQ
                                  CDR1

4           5            6           7
0123456789 01223456789 0123456789 0123456789
              a
TPEKRLEWVA YISDGGYNTYY PDTVKGRFTI SRDNAKNTLY
                  CDR2

                              1           1
8             9               0           1
0122223456789 0123456789 000123456789 0123
   abc                       ab
LQMSSLKSEDTAI YYCARQILLR YYFDYWGQGTTL TVSS (SEQ ID NO: 26)
                        CDR3
```

FIG. 8

TIG3 VL

```
          1           2                   3
123456789 0123456789 01234567777777789 0123456789
                              abcdef
DIVMSQSPS SLAVSVGEKV TMTCKSSQSLLYSSNQ KNYLAWYQQK
                                  CDR1

4          5          6          7
0123456789 0123456789 0123456789 0123456789
PGQSPKLLIY WASTRESGVP DRFTGSGSGT DFTLTISSVK
             CDR2

                      1
8          9          0
0123456789 0123456789 01234567
AEDLAVYYCQ QYHSYPWTFG GGTKLEIK (SEQ ID NO: 30)
             CDR3
```