FIGURE 1

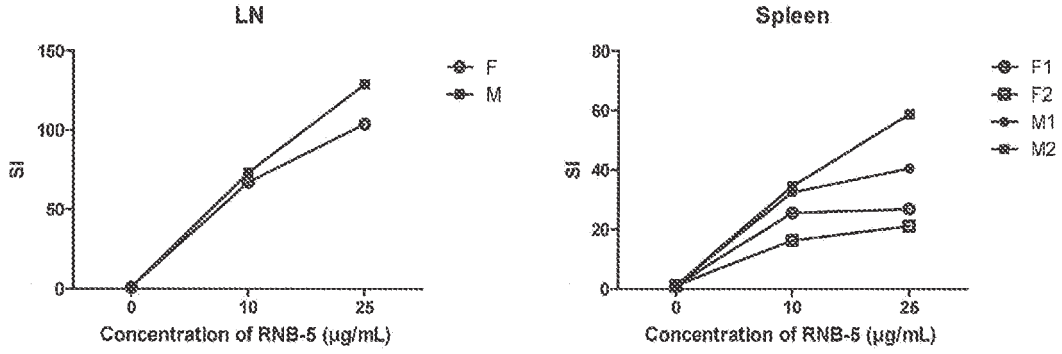

LN
SI
150
100
50
0
0
10
25
Concentration of RNB-5 (µg/mL)
F
M
Spleen
SI
80
60
40
20
0
0
10
25
Concentration of RNB-5 (µg/mL)
F1
F2
M1
M2

FIGURE 2

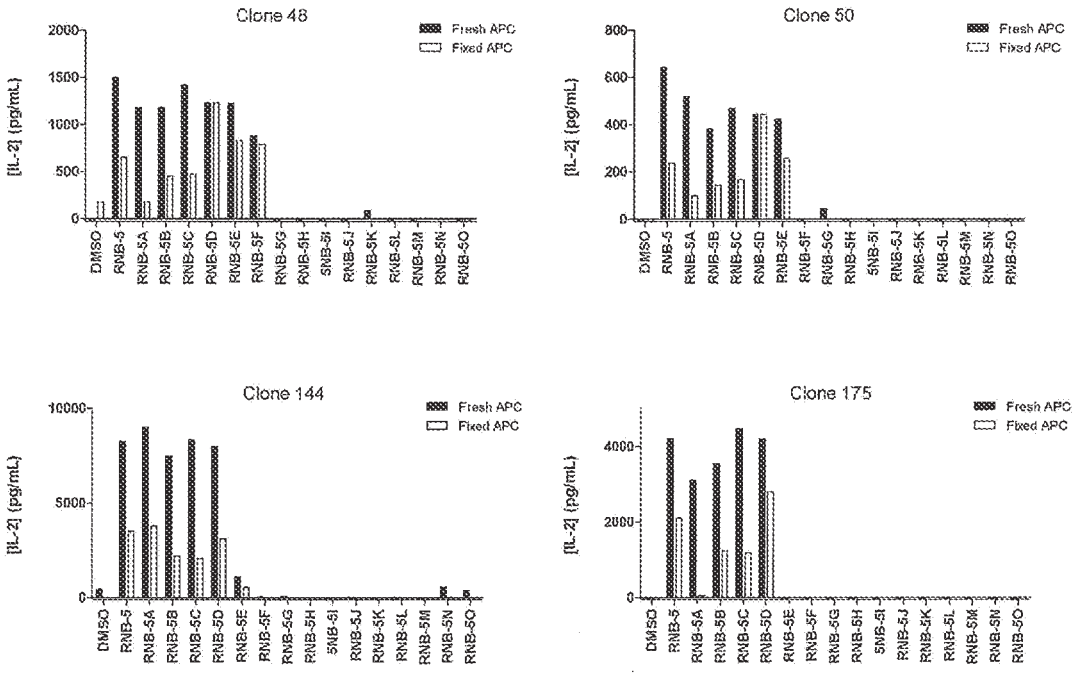

Clone 48
Fresh APC
Fixed APC
[IL-2] (pg/mL)
2000
1500
1000
500
0
DMSO
RNB-5
RNB-5A
RNB-5B
RNB-5C
RNB-5D
RNB-5E
RNB-5F
RNB-5G
RNB-5H
5NB-5I
RNB-5J
RNB-5K
RNB-5L
RNB-5M
RNB-5N
RNB-5O
Clone 50
Fresh APC
Fixed APC
[IL-2] (pg/mL)
800
600
400
200
0
DMSO
RNB-5
RNB-5A
RNB-5B
RNB-5C
RNB-5D
RNB-5E
RNB-5F
RNB-5G
RNB-5H
5NB-5I
RNB-5J
RNB-5K
RNB-5L
RNB-5M
RNB-5N
RNB-5O
Clone 144
Fresh APC
Fixed APC
[IL-2] (pg/mL)
10000
5000
0
DMSO
RNB-5
RNB-5A
RNB-5B
RNB-5C
RNB-5D
RNB-5E
RNB-5F
RNB-5G
RNB-5H
5NB-5I
RNB-5J
RNB-5K
RNB-5L
RNB-5M
RNB-5N
RNB-5O
Clone 175
Fresh APC
Fixed APC
[IL-2] (pg/mL)
4000
2000
0
DMSO
RNB-5
RNB-5A
RNB-5B
RNB-5C
RNB-5D
RNB-5E
RNB-5F
RNB-5G
RNB-5H
5NB-5I
RNB-5J
RNB-5K
RNB-5L
RNB-5M
RNB-5N
RNB-5O

FIGURE 3

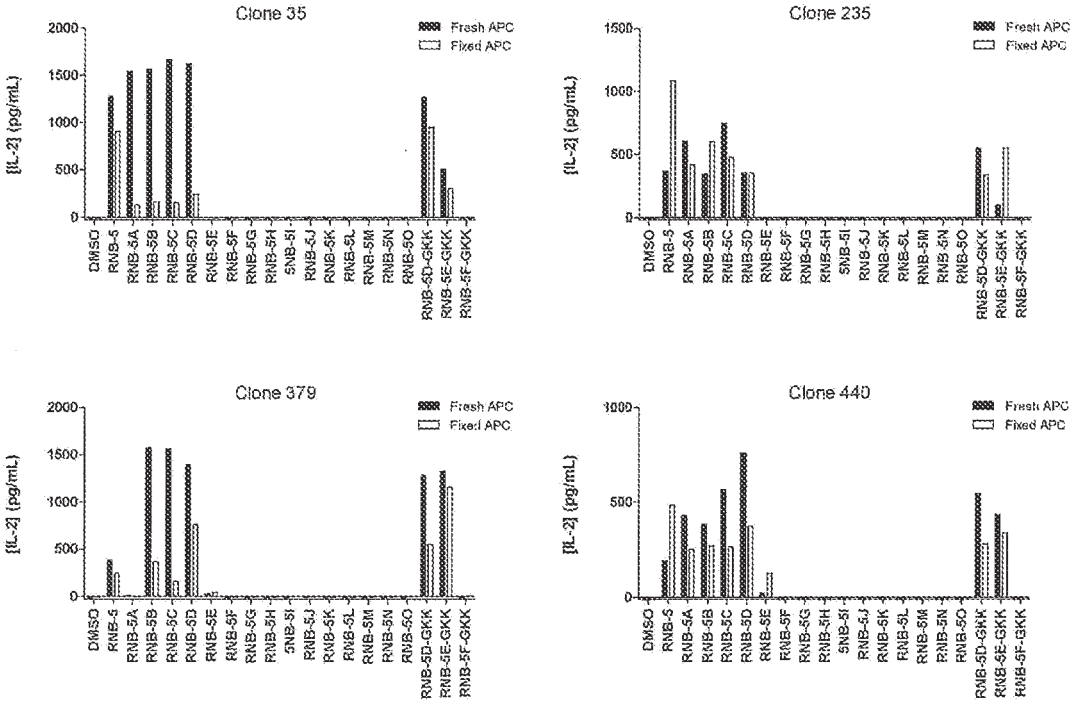
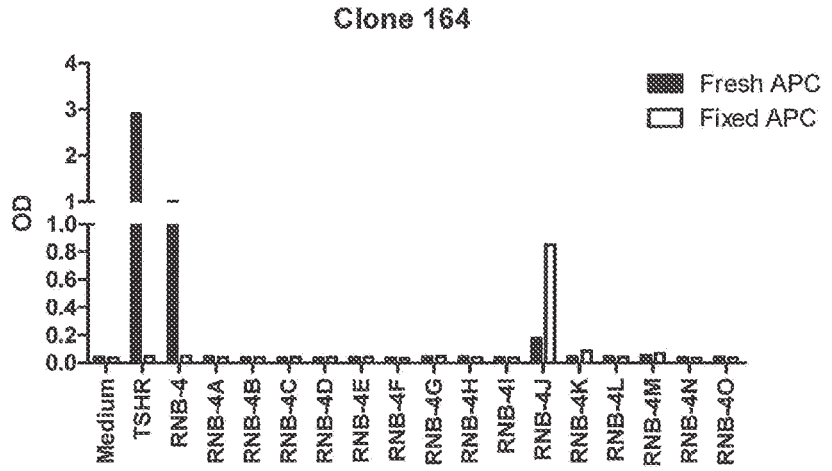

Clone 35
Fresh APC
Fixed APC
[IL-2] (pg/mL)
2000
1500
1000
500
0
DMSO
RNB-5
RNB-5A
RNB-5B
RNB-5C
RNB-5D
RNB-5E
RNB-5F
RNB-5G
RNB-5H
5NB-5I
RNB-5J
RNB-5K
RNB-5L
RNB-5M
RNB-5N
RNB-5O
RNB-5D-GKK
RNB-5E-GKK
RNB-5F-GKK
Clone 235
Fresh APC
Fixed APC
[IL-2] (pg/mL)
1500
1000
500
0
DMSO
RNB-5
RNB-5A
RNB-5B
RNB-5C
RNB-5D
RNB-5E
RNB-5F
RNB-5G
RNB-5H
5NB-5I
RNB-5J
RNB-5K
RNB-5L
RNB-5M
RNB-5N
RNB-5O
RNB-5D-GKK
RNB-5E-GKK
RNB-5F-GKK
Clone 379
Fresh APC
Fixed APC
[IL-2] (pg/mL)
2000
1500
1000
500
0
DMSO
RNB-5
RNB-5A
RNB-5B
RNB-5C
RNB-5D
RNB-5E
RNB-5F
RNB-5G
RNB-5H
5NB-5I
RNB-5J
RNB-5K
RNB-5L
RNB-5M
RNB-5N
RNB-5O
RNB-5D-GKK
RNB-5E-GKK
RNB-5F-GKK
Clone 440
Fresh APC
Fixed APC
[IL-2] (pg/mL)
1000
500
0
DMSO
RNB-5
RNB-5A
RNB-5B
RNB-5C
RNB-5D
RNB-5E
RNB-5F
RNB-5G
RNB-5H
5NB-5I
RNB-5J
RNB-5K
RNB-5L
RNB-5M
RNB-5N
RNB-5O
RNB-5D-GKK
RNB-5E-GKK
RNB-5F-GKK

FIGURE 4

A.


Clone 164
Fresh APC
Fixed APC
OD
4
3
2
1
1.0
0.8
0.6
0.4
0.2
0.0
Medium
TSHR
RNB-4
RNB-4A
RNB-4B
RNB-4C
RNB-4D
RNB-4E
RNB-4F
RNB-4G
RNB-4H
RNB-4I
RNB-4J
RNB-4K
RNB-4L
RNB-4M
RNB-4N
RNB-4O

B.

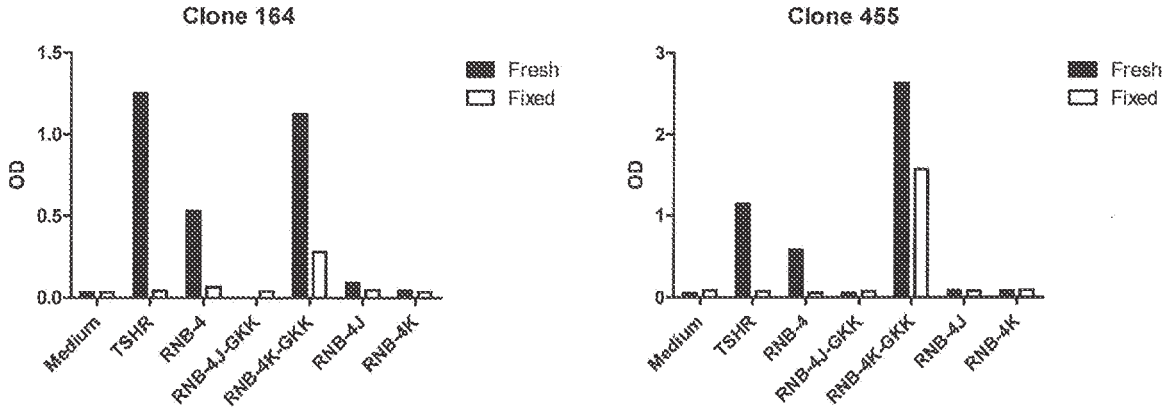

Clone 164
Fresh
Fixed
OD
1.5
1.0
0.5
0.0
Medium
TSHR
RNB-4
RNB-4J-GKK
RNB-4K-GKK
RNB-4J
RNB-4K
Clone 455
Fresh
Fixed
OD
3
2
1
0
Medium
TSHR
RNB-4
RNB-4J-GKK
RNB-4K-GKK
RNB-4J
RNB-4K

FIGURE 5

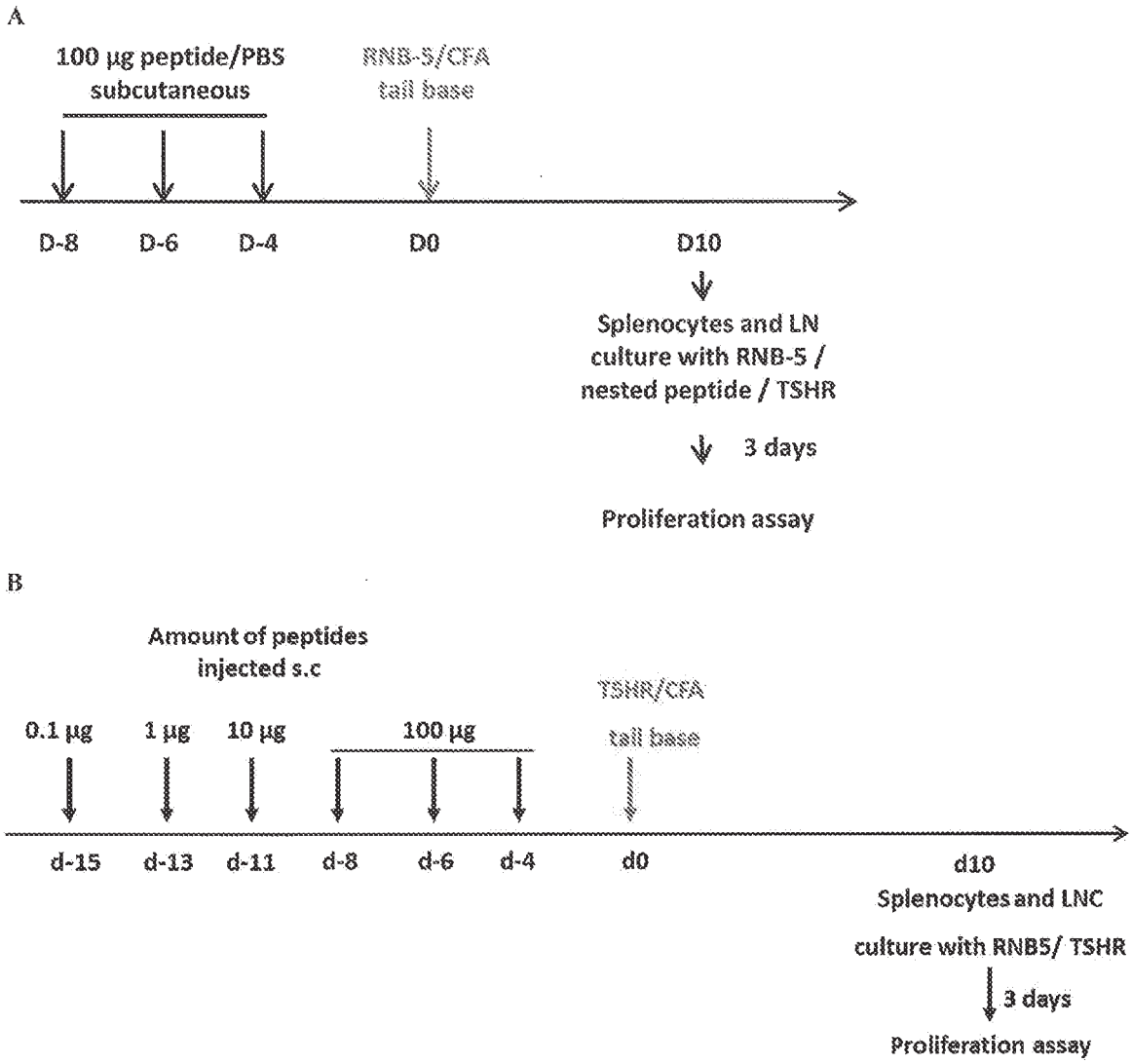

A
100 µg peptide/PBS
subcutaneous
RNB-5/CFA
tail base
D-8
D-6
D-4
D0
D10
Splenocytes and LN
culture with RNB-5 /
nested peptide / TSHR
3 days
Proliferation assay
B
Amount of peptides
injected s.c
TSHR/CFA
tail base
0.1 µg
1 µg
10 µg
100 µg
d-15
d-13
d-11
d-8
d-6
d-4
d0
d10
Splenocytes and LNC
culture with RNB5/ TSHR
3 days
Proliferation assay

FIGURE 6

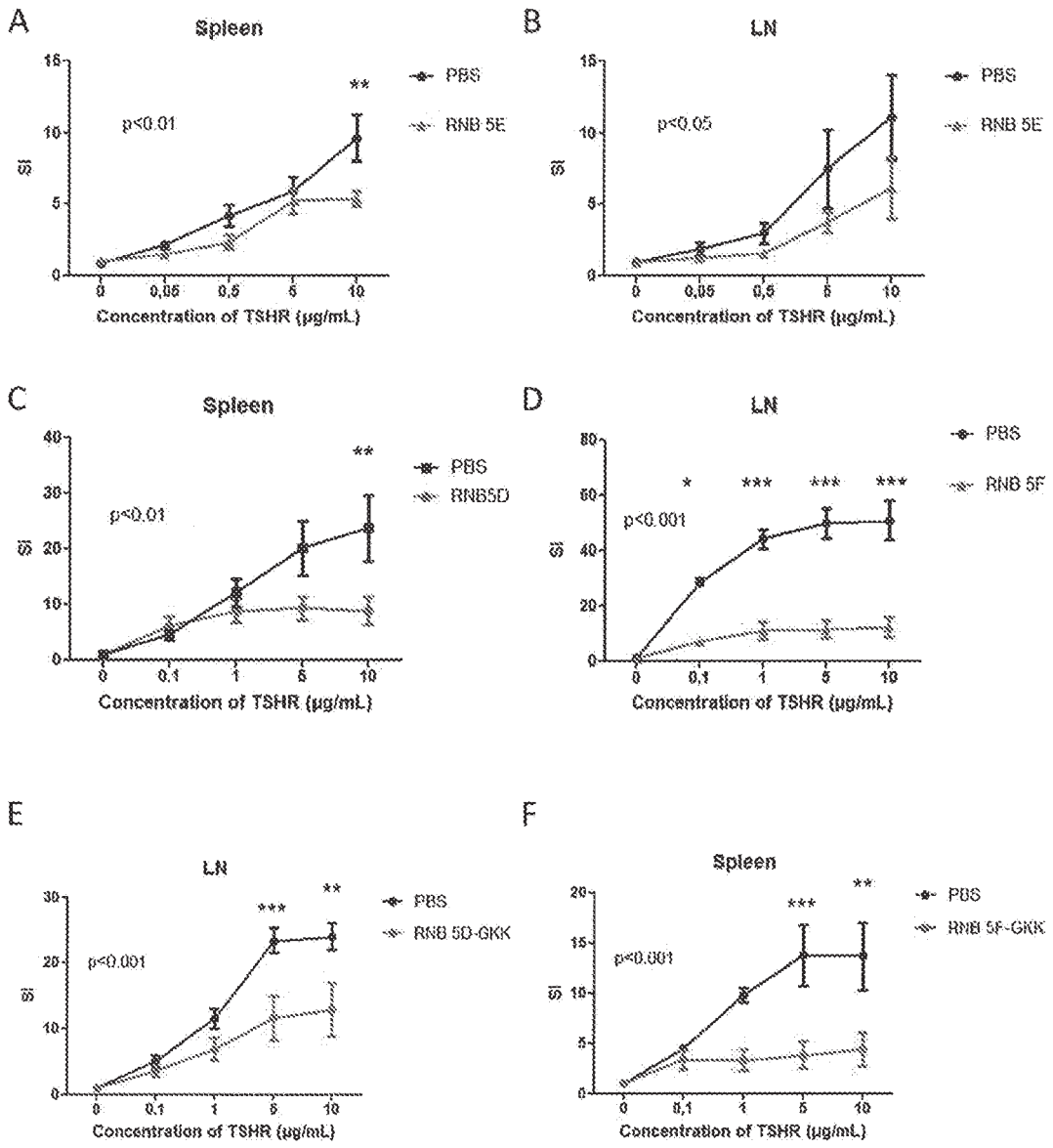

A
Spleen
p<0.01
**
PBS
RNB 5E
SI
Concentration of TSHR (µg/mL)
B
LN
p<0.05
PBS
RNB 5E
C
Spleen
p<0.01
**
PBS
RNB5D
D
LN
p<0.001
*
***
PBS
RNB 5F
E
LN
p<0.001
PBS
RNB 5D-GKK
F
Spleen
p<0.001
PBS
RNB 5F-GKK

FIGURE 7

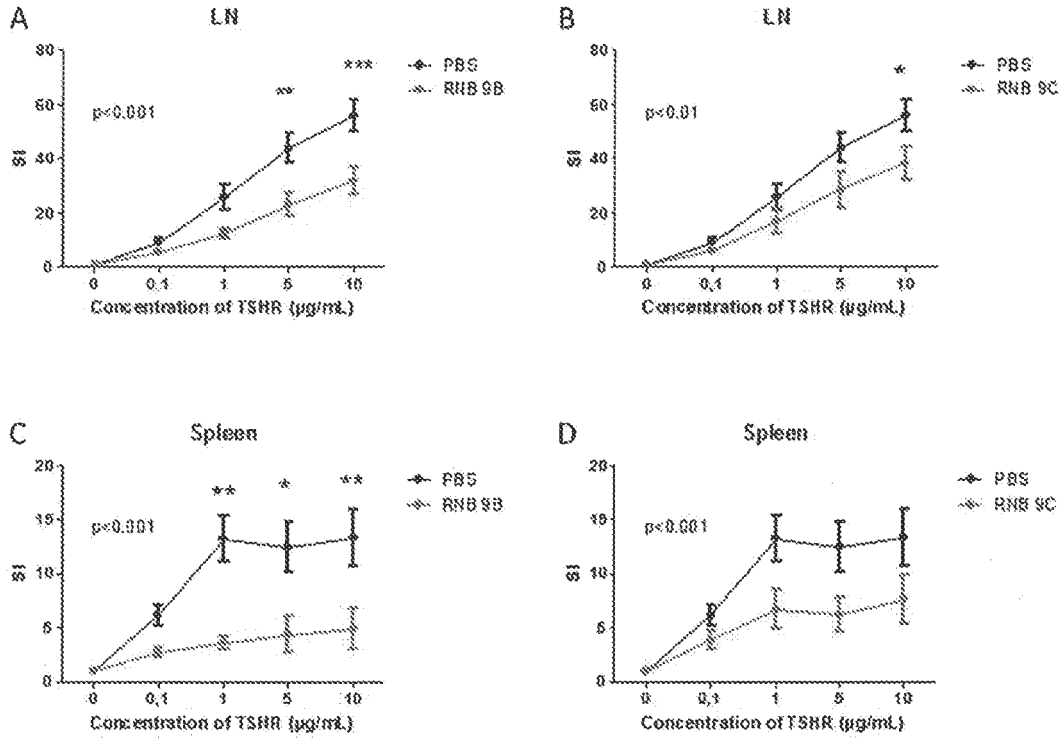

A
LN
p<0.001
SI
Concentration of TSHR (µg/mL)
PBS
RNB SB
B
LN
p<0.01
SI
Concentration of TSHR (µg/mL)
PBS
RNB SC
C
Spleen
p<0.001
SI
Concentration of TSHR (µg/mL)
PBS
RNB SB
D
Spleen
p<0.001
SI
Concentration of TSHR (µg/mL)
PBS
RNB SC

FIGURE 8

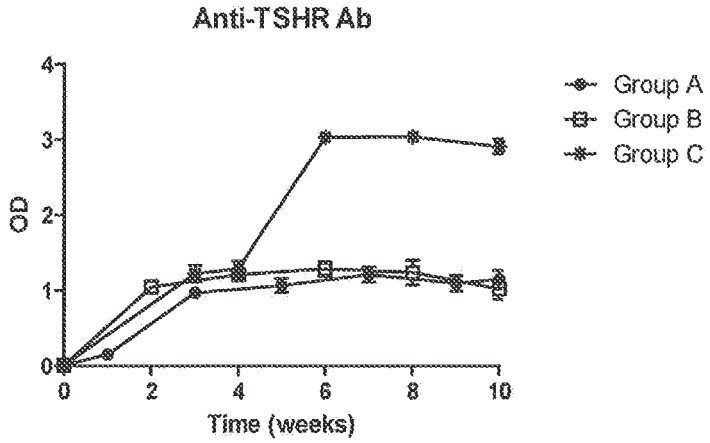

Anti-TSHR Ab
OD
Time (weeks)
0
1
2
3
4
0
2
4
6
8
10
Group A
Group B
Group C

FIGURE 9

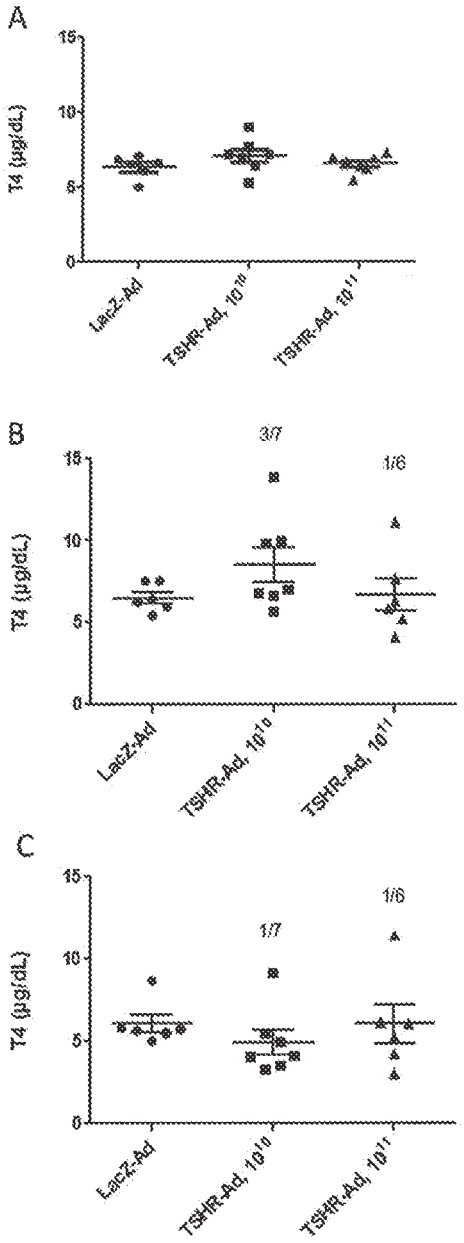

A
T4 (µg/dL)
15
10
5
0
LacZ-Ad
TSHR-Ad, 10^10
TSHR-Ad, 10^11
B
T4 (µg/dL)
3/7
1/6
LacZ-Ad
TSHR-Ad, 10^10
TSHR-Ad, 10^11
C
T4 (µg/dL)
1/7
1/6
LacZ-Ad
TSHR-Ad, 10^10
TSHR-Ad, 10^11

FIGURE 10

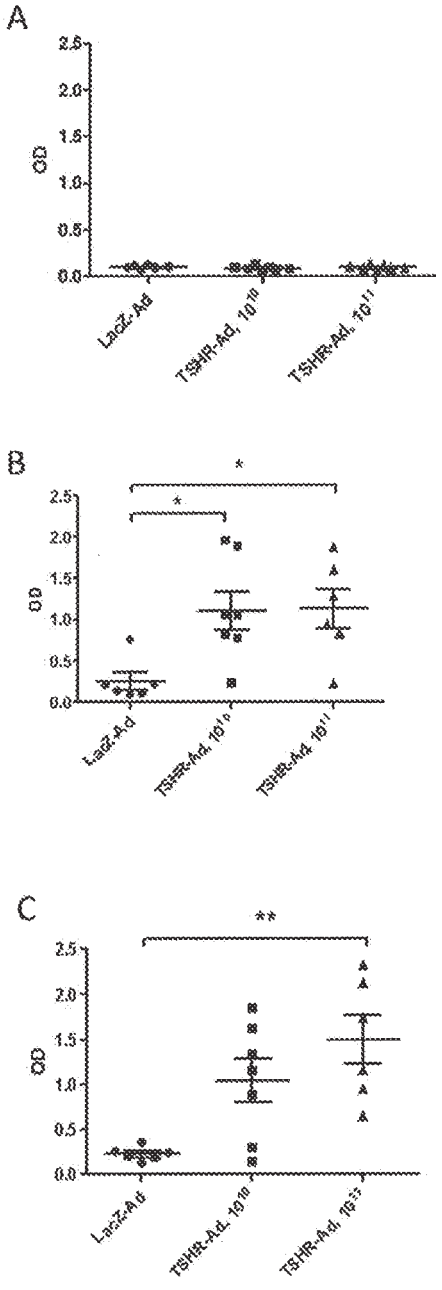

A
OD
2.5
2.0
1.5
1.0
0.5
0.0
LacZ-Ad
TSHR-Ad, 10^10
TSHR-Ad, 10^11
B
*
*
OD
2.5
2.0
1.5
1.0
0.5
0.0
LacZ-Ad
TSHR-Ad, 10^10
TSHR-Ad, 10^11
C
**
OD
2.5
2.0
1.5
1.0
0.5
0.0
LacZ-Ad
TSHR-Ad, 10^10
TSHR-Ad, 10^11

Figure 11

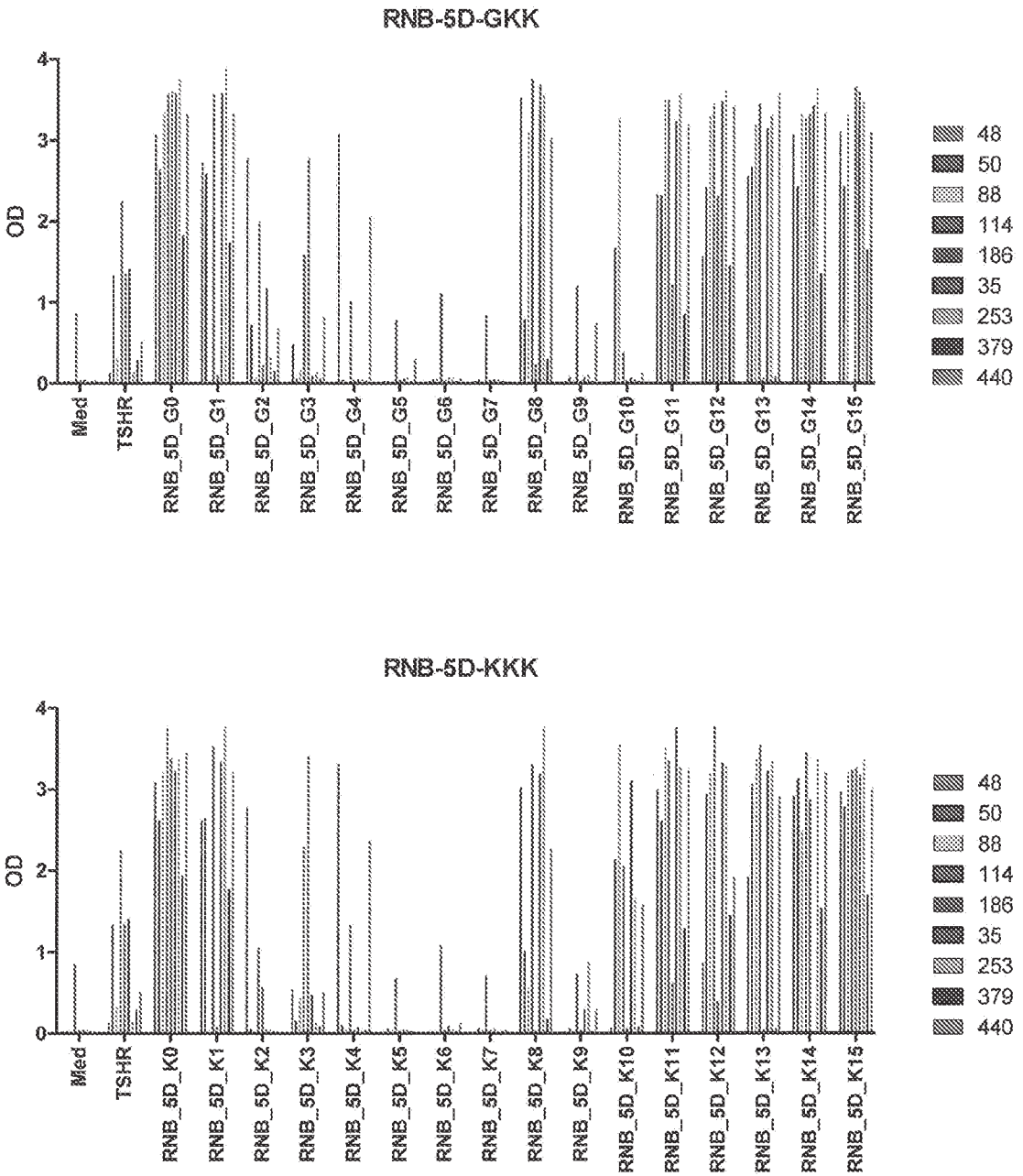

RNB-5D-GKK
OD
0
1
2
3
4
Med
TSHR
RNB_5D_G0
RNB_5D_G1
RNB_5D_G2
RNB_5D_G3
RNB_5D_G4
RNB_5D_G5
RNB_5D_G6
RNB_5D_G7
RNB_5D_G8
RNB_5D_G9
RNB_5D_G10
RNB_5D_G11
RNB_5D_G12
RNB_5D_G13
RNB_5D_G14
RNB_5D_G15
48
50
88
114
186
35
253
379
440
RNB-5D-KKK
OD
0
1
2
3
4
Med
TSHR
RNB_5D_K0
RNB_5D_K1
RNB_5D_K2
RNB_5D_K3
RNB_5D_K4
RNB_5D_K5
RNB_5D_K6
RNB_5D_K7
RNB_5D_K8
RNB_5D_K9
RNB_5D_K10
RNB_5D_K11
RNB_5D_K12
RNB_5D_K13
RNB_5D_K14
RNB_5D_K15
48
50
88
114
186
35
253
379
440

Figure 12

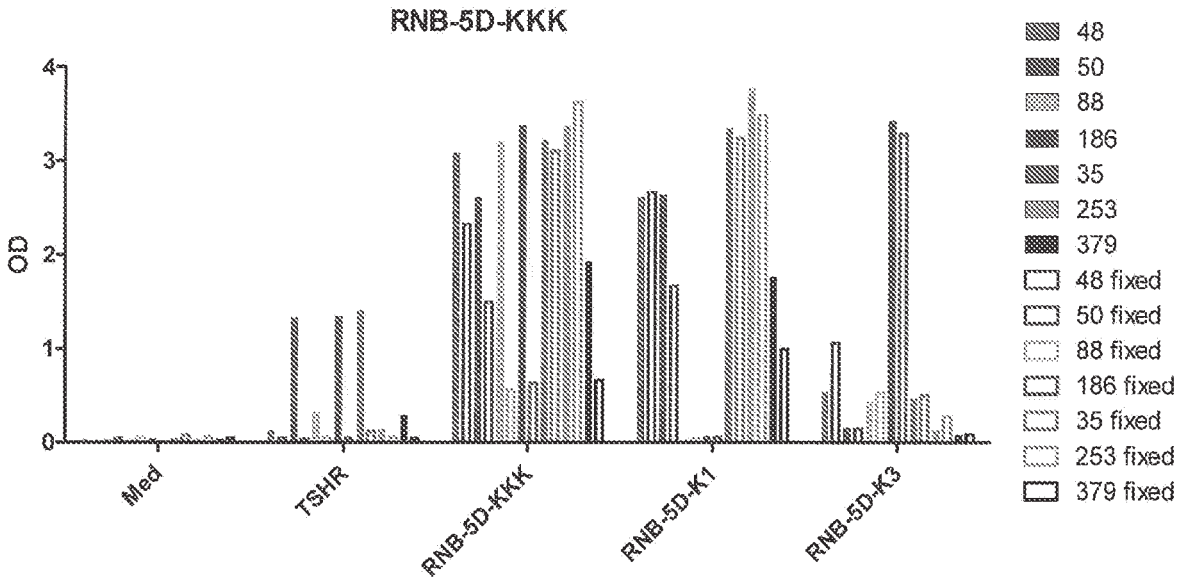

RNB-5D-KKK
OD
0
1
2
3
4
Med
TSHR
RNB-5D-KKK
RNB-5D-K1
RNB-5D-K3
48
50
88
186
35
253
379
48 fixed
50 fixed
88 fixed
186 fixed
35 fixed
253 fixed
379 fixed

Figure 13

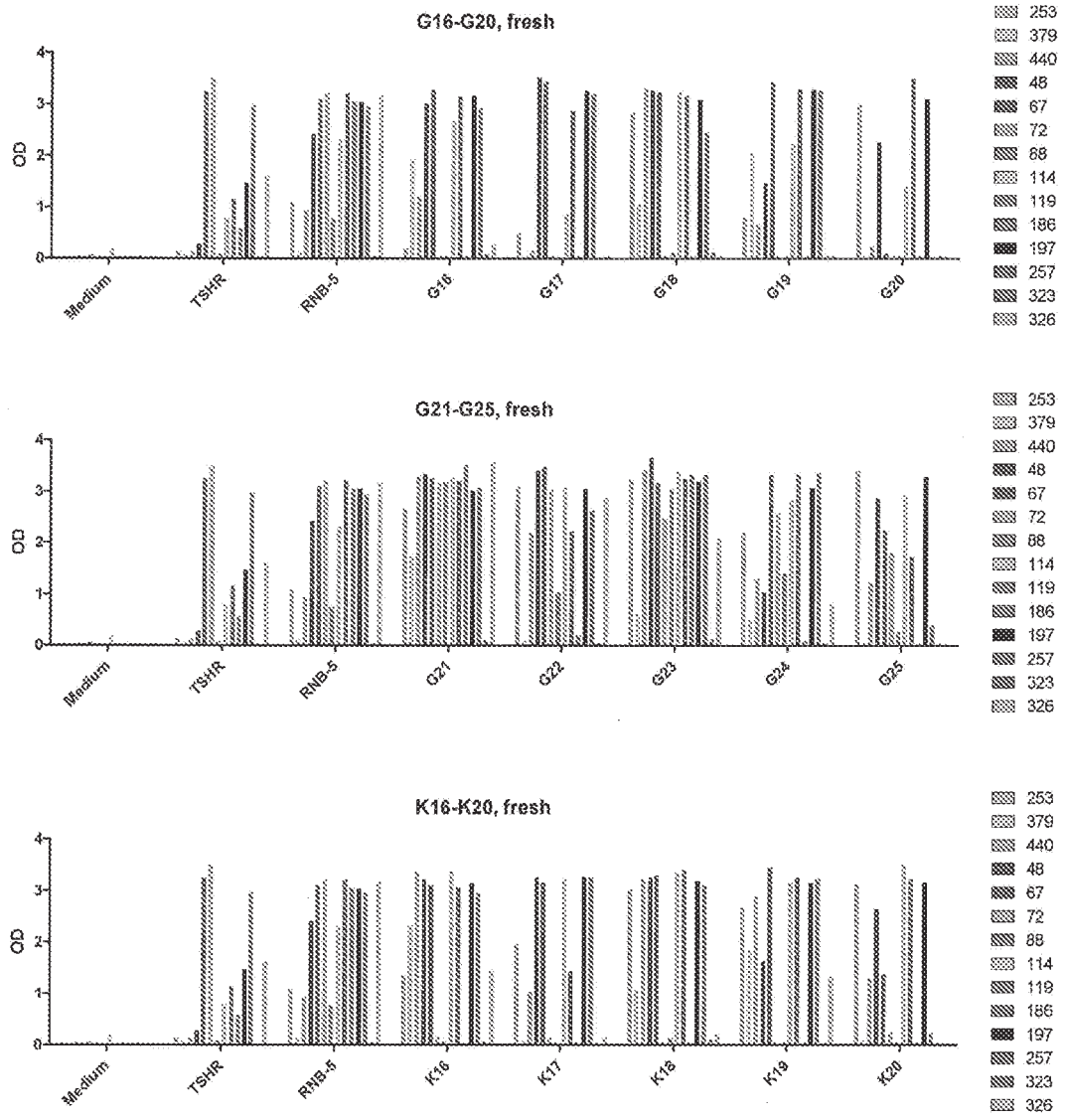

G16-G20, fresh
OD
0
1
2
3
4
Medium
TSHR
RNB-5
G16
G17
G18
G19
G20
253
379
440
48
67
72
88
114
119
186
197
257
323
326
G21-G25, fresh
OD
0
1
2
3
4
Medium
TSHR
RNB-5
G21
G22
G23
G24
G25
253
379
440
48
67
72
88
114
119
186
197
257
323
326
K16-K20, fresh
OD
0
1
2
3
4
Medium
TSHR
RNB-5
K16
K17
K18
K19
K20
253
379
440
48
67
72
88
114
119
186
197
257
323
326

Figure 14

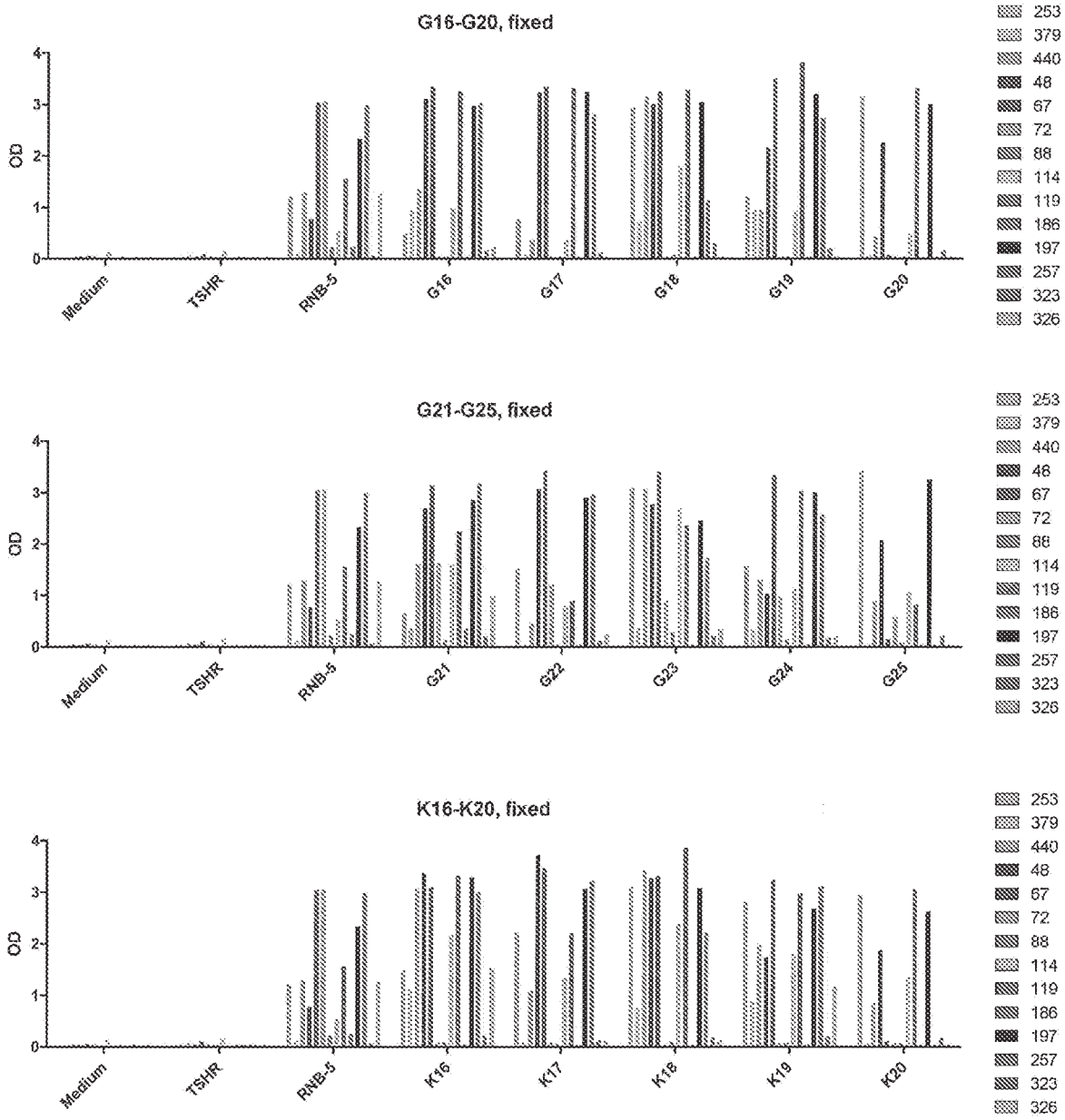

G16-G20, fixed
OD
0
1
2
3
4
Medium
TSHR
RNB-5
G16
G17
G18
G19
G20
253
379
440
48
67
72
88
114
119
186
197
257
323
326
G21-G25, fixed
OD
0
1
2
3
4
Medium
TSHR
RNB-5
G21
G22
G23
G24
G25
253
379
440
48
67
72
88
114
119
186
197
257
323
326
K16-K20, fixed
OD
0
1
2
3
4
Medium
TSHR
RNB-5
K16
K17
K18
K19
K20
253
379
440
48
67
72
88
114
119
186
197
257
323
326

Figure 15

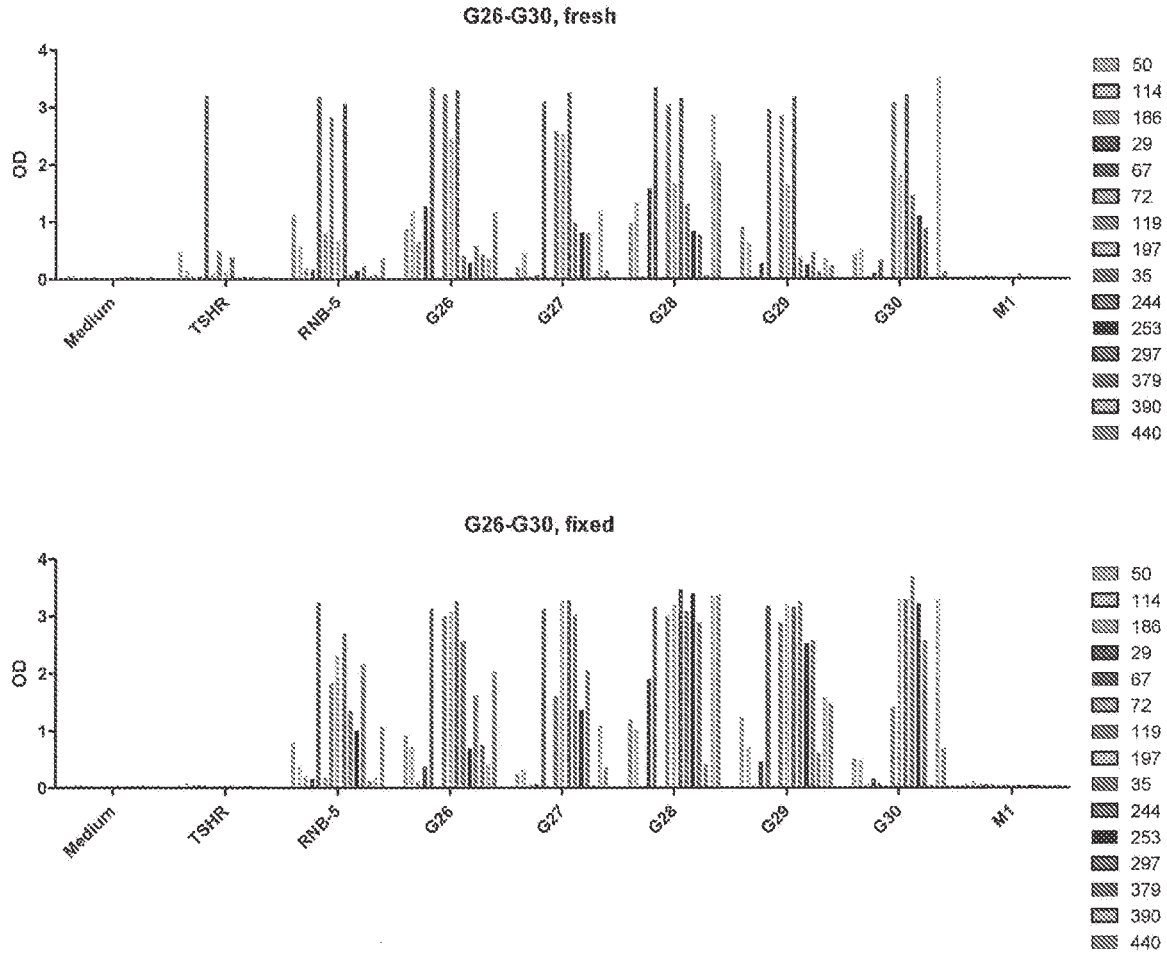

G26-G30, fresh
OD
0
1
2
3
4
Medium
TSHR
RNB-5
G26
G27
G28
G29
G30
M1
50
114
186
29
67
72
119
197
35
244
253
297
379
390
440
G26-G30, fixed
OD
0
1
2
3
4
Medium
TSHR
RNB-5
G26
G27
G28
G29
G30
M1
50
114
186
29
67
72
119
197
35
244
253
297
379
390
440

Figure 16

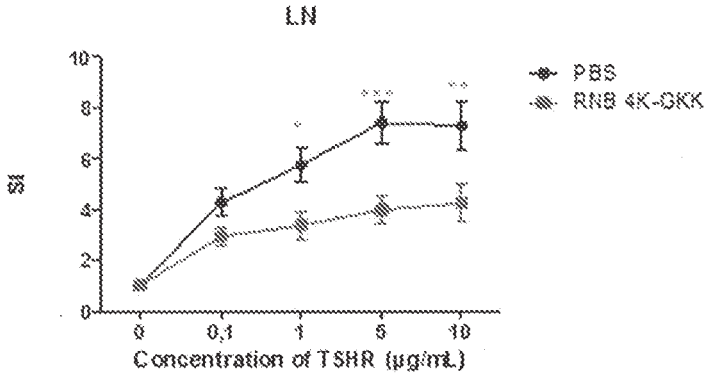


Figure 17

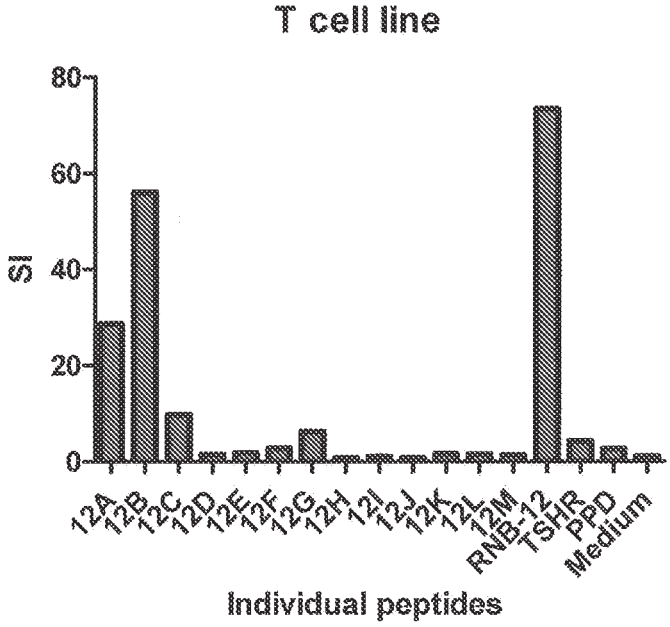


Figure 18

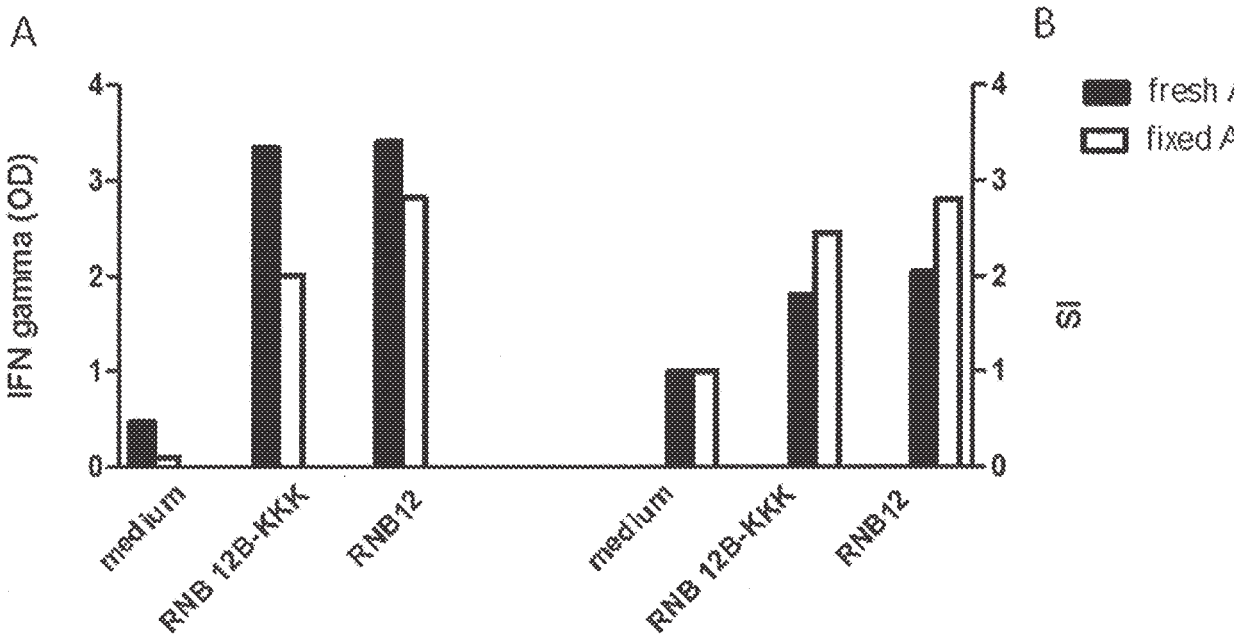


Figure 19

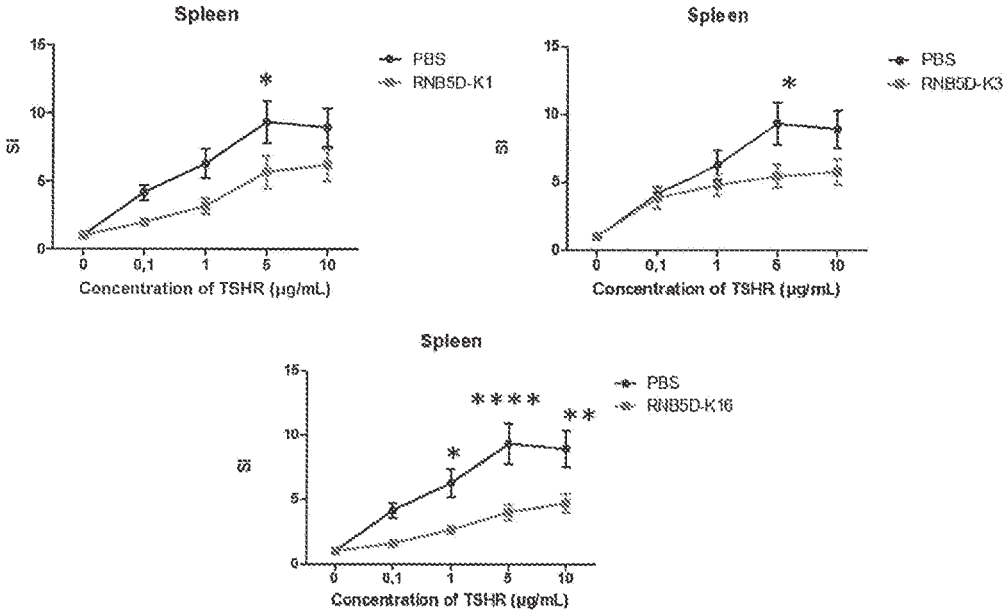
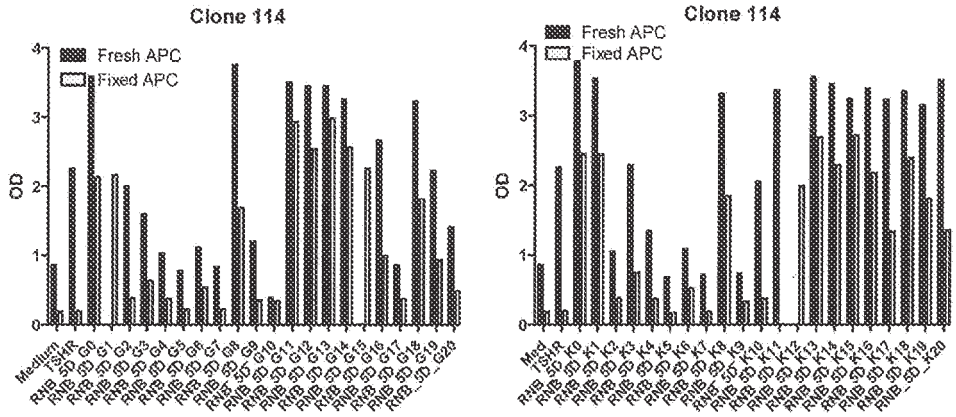

Spleen
SI
Concentration of TSHR (µg/mL)
PBS
RNB5D-K1
Spleen
SI
Concentration of TSHR (µg/mL)
PBS
RNB5D-K3
Spleen
SI
Concentration of TSHR (µg/mL)
PBS
RNB5D-K16

Figure 20


Clone 114
Fresh APC
Fixed APC
OD
0
1
2
3
4
Medium
TSHR
RNB_5D_G0
RNB_5D_G1
RNB_5D_G2
RNB_5D_G3
RNB_5D_G4
RNB_5D_G5
RNB_5D_G6
RNB_5D_G7
RNB_5D_G8
RNB_5D_G9
RNB_5D_G10
RNB_5D_G11
RNB_5D_G12
RNB_5D_G13
RNB_5D_G14
RNB_5D_G15
RNB_5D_G16
RNB_5D_G17
RNB_5D_G18
RNB_5D_G19
RNB_5D_G20
Clone 114
Fresh APC
Fixed APC
OD
0
1
2
3
4
Med
TSHR
RNB_5D_K0
RNB_5D_K1
RNB_5D_K2
RNB_5D_K3
RNB_5D_K4
RNB_5D_K5
RNB_5D_K6
RNB_5D_K7
RNB_5D_K8
RNB_5D_K9
RNB_5D_K10
RNB_5D_K11
RNB_5D_K12
RNB_5D_K13
RNB_5D_K14
RNB_5D_K15
RNB_5D_K16
RNB_5D_K17
RNB_5D_K18
RNB_5D_K19
RNB_5D_K20