Fig. 1

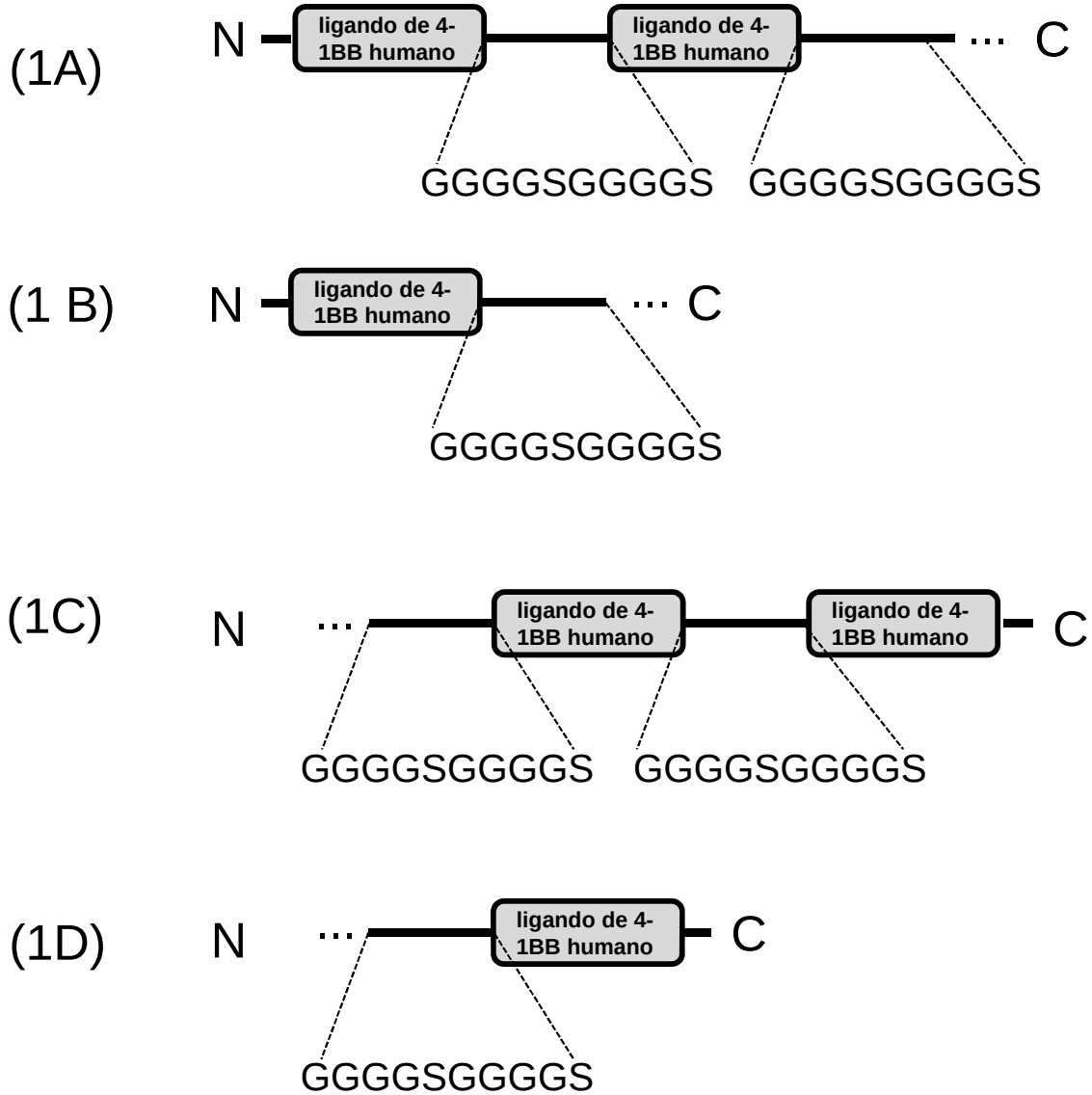
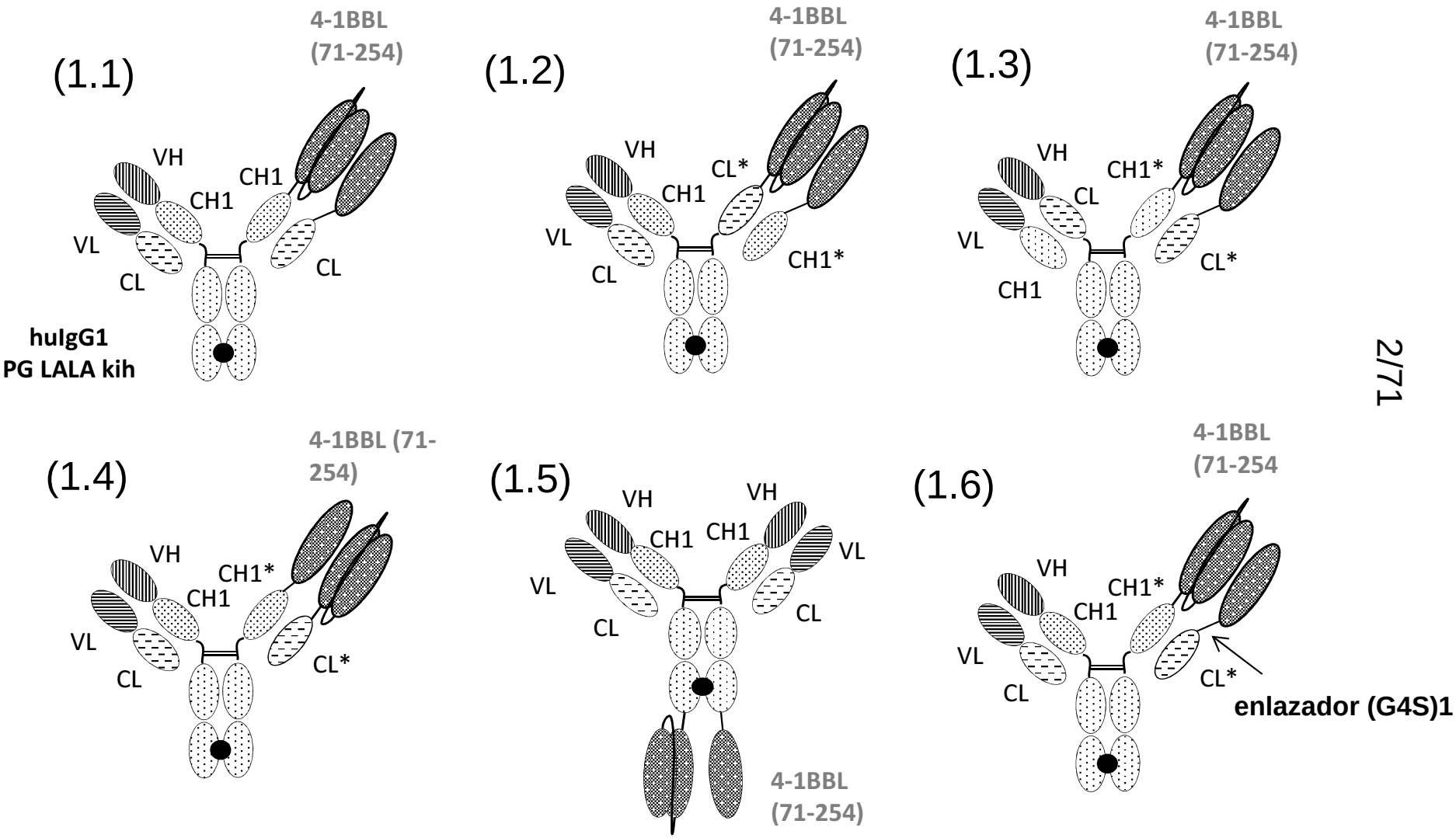
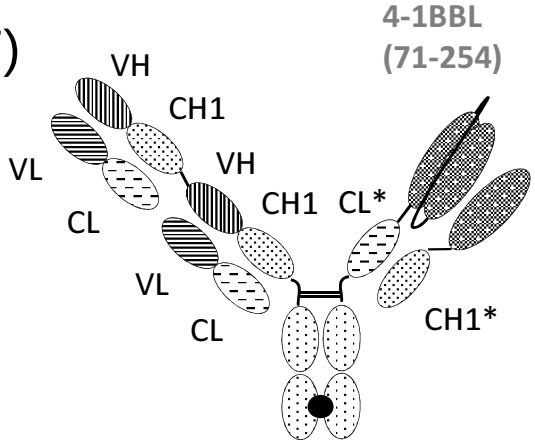

(1A)
N
ligando de 4-1BB humano
ligando de 4-1BB humano
... C
GGGGSGGGGS
GGGGSGGGGS
(1 B)
N
ligando de 4-1BB humano
... C
GGGGSGGGGS
(1C)
N
...
ligando de 4-1BB humano
ligando de 4-1BB humano
C
GGGGSGGGGS
GGGGSGGGGS
(1D)
N
...
ligando de 4-1BB humano
C
GGGGSGGGGS

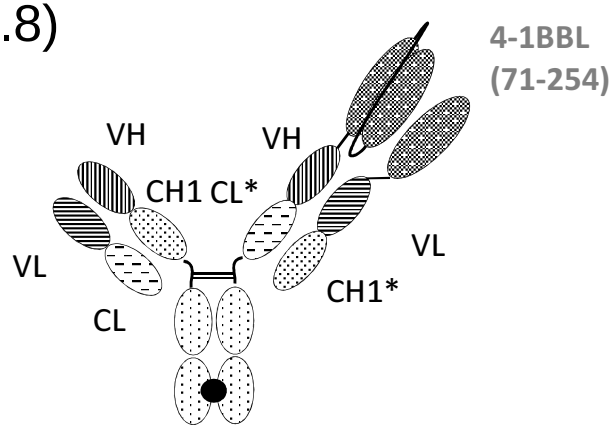
Fig. 2


(1.1)
4-1BBL
(71-254)
VH
CH1
CH1
VL
CL
CL
huIgG1
PG LALA kih
(1.2)
4-1BBL
(71-254)
VH
CL*
CH1
VL
CL
CH1*
(1.3)
4-1BBL
(71-254)
VH
CH1*
CL
VL
CH1
CL*
(1.4)
4-1BBL (71-
254)
VH
CH1*
CH1
VL
CL
CL*
(1.5)
VH
VH
CH1
CH1
VL
VL
CL
CL
4-1BBL
(71-254)
(1.6)
4-1BBL
(71-254
VH
CH1*
CH1
VL
CL
CL*
enlazador (G4S)1

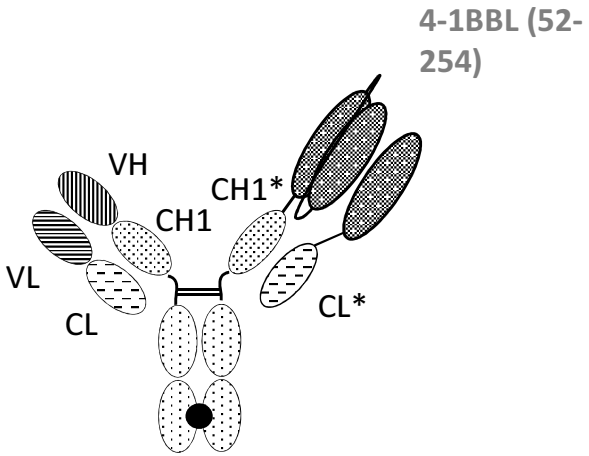
(1.7)



(1.8)



(1.9)



(1.10)

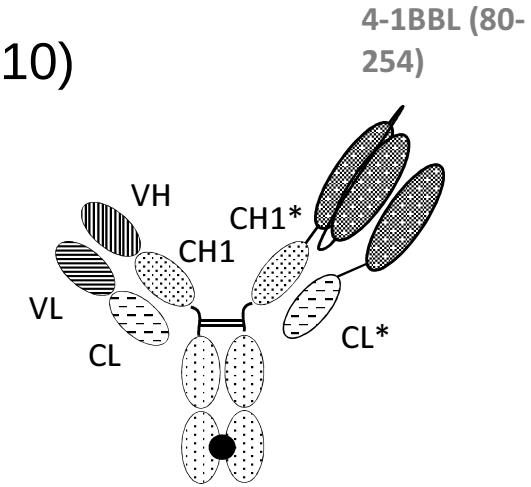


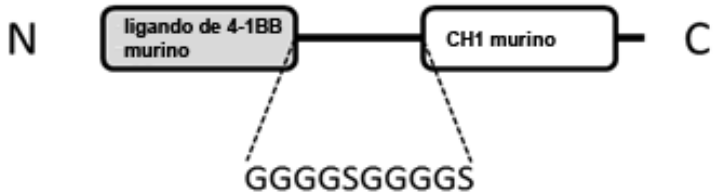
Fig. 2

Fig. 3

(3 A)

N
ligando de 4-1BB murino
ligando de 4-1BB murino
CL murino
C
GGGGSGGGGS
GGGGSGGGGS

(3 B)


N
ligando de 4-1BB murino
CH1 murino
C
GGGGSGGGGS

(3C)

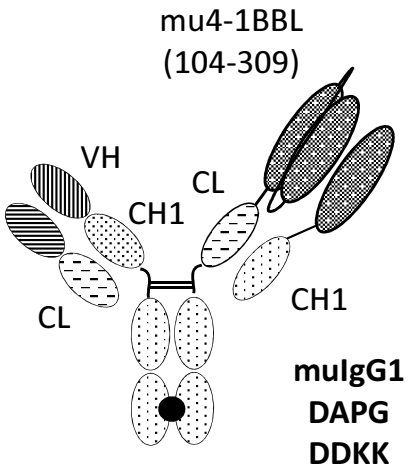
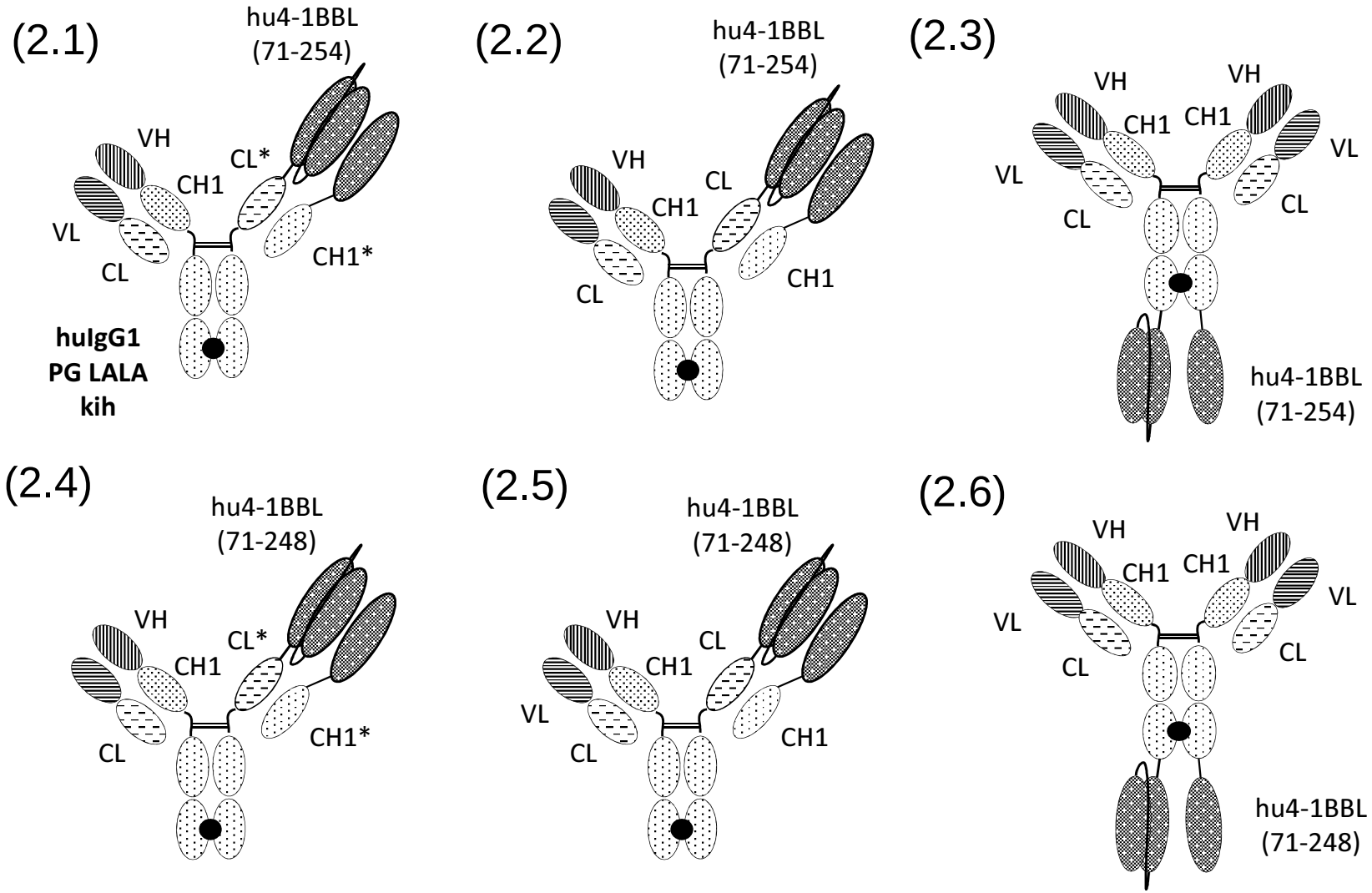
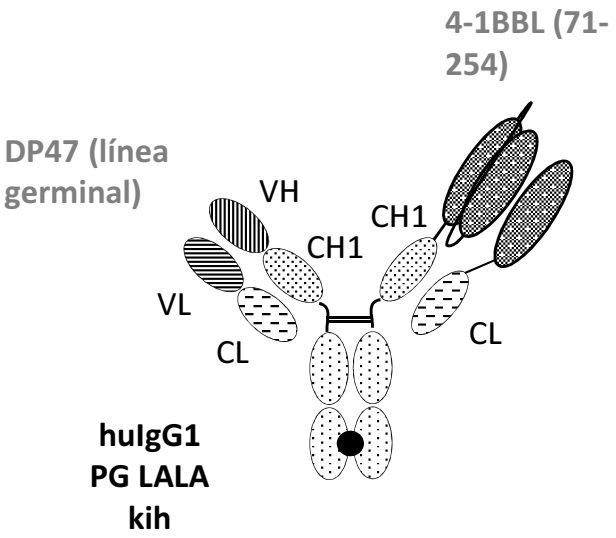

mu4-1BBL
(104-309)
VH
CL
CH1
CL
CH1
muIgG1
DAPG
DDKK

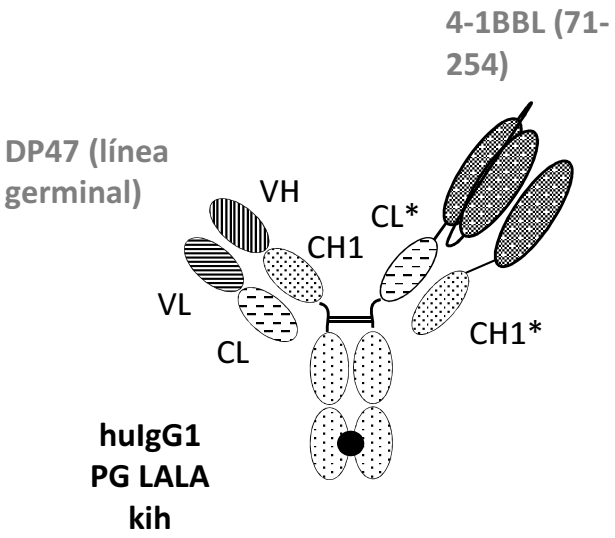
Fig. 4


(2.1)
hu4-1BBL
(71-254)
VH
CL*
CH1
VL
CL
CH1*
huIgG1
PG LALA
kih
(2.2)
hu4-1BBL
(71-254)
VH
CL
CH1
CL
CH1
(2.3)
VH
VH
CH1
CH1
VL
VL
CL
CL
hu4-1BBL
(71-254)
(2.4)
hu4-1BBL
(71-248)
VH
CL*
CH1
CL
CH1*
(2.5)
hu4-1BBL
(71-248)
VH
CL
CH1
VL
CL
CH1
(2.6)
VH
VH
CH1
CH1
VL
VL
CL
CL
hu4-1BBL
(71-248)

(5 A)


4-1BBL (71-254)
DP47 (línea germinal)
VH
CH1
CH1
VL
CL
CL
huIgG1
PG LALA
kih

(5 B)


4-1BBL (71-254)
DP47 (línea germinal)
VH
CL*
CH1
VL
CL
CH1*
huIgG1
PG LALA
kih

(5C)

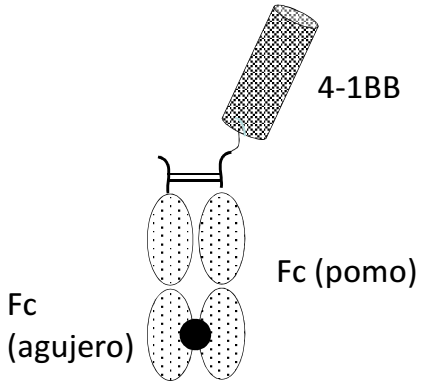
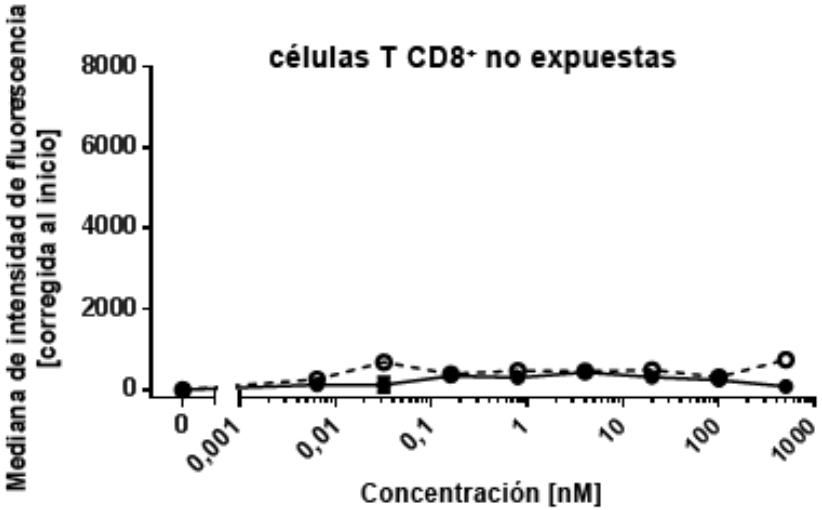
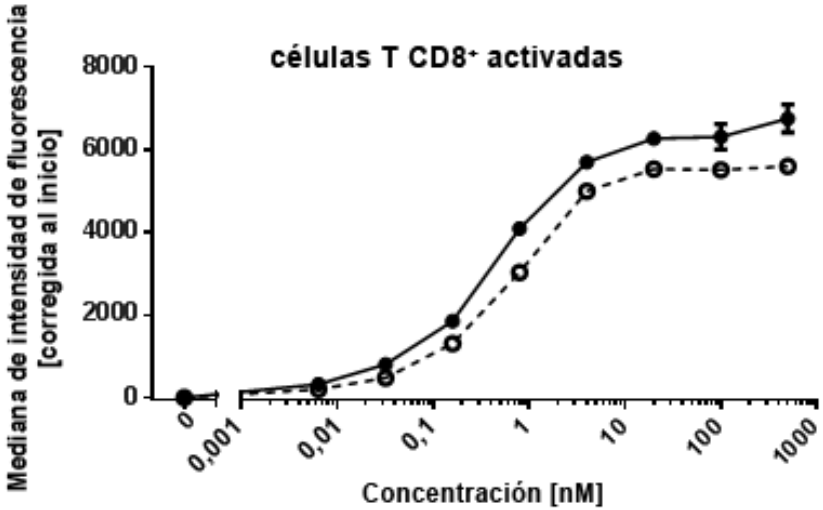

4-1BB
Fc (pomo)
Fc
(agujero)

Fig. 5

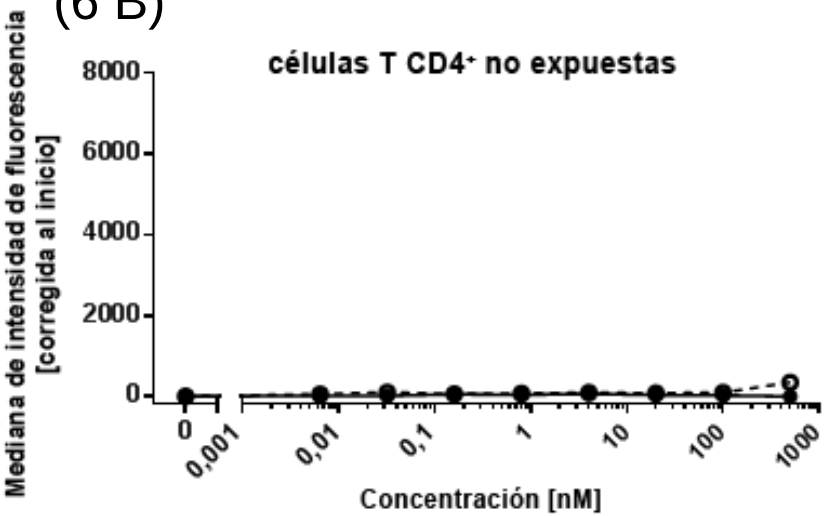
Fig. 6

(6 A)


células T CD8⁺ no expuestas
Mediana de intensidad de fluorescencia [corregida al inicio]
8000
6000
4000
2000
0
0
0,001
0,01
0,1
1
10
100
1000
Concentración [nM]


células T CD8⁺ activadas
Mediana de intensidad de fluorescencia [corregida al inicio]
8000
6000
4000
2000
0
0
0,001
0,01
0,1
1
10
100
1000
Concentración [nM]

(6 B)


células T CD4⁺ no expuestas
Mediana de intensidad de fluorescencia [corregida al inicio]
8000
6000
4000
2000
0
0
0,001
0,01
0,1
1
10
100
1000
Concentración [nM]

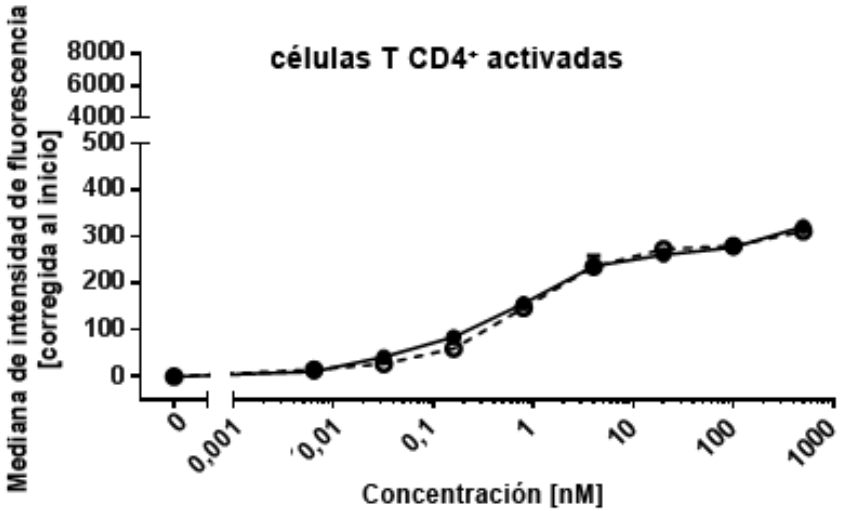
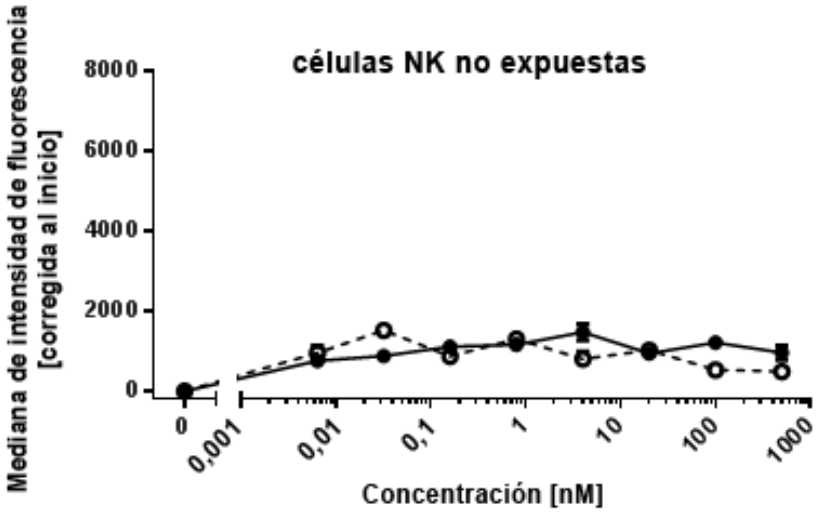

células T CD4⁺ activadas
Mediana de intensidad de fluorescencia [corregida al inicio]
8000
6000
4000
500
400
300
200
100
0
0
0,001
0,01
0,1
1
10
100
1000
Concentración [nM]

Fig. 6

(6C)


células NK no expuestas
Mediana de intensidad de fluorescencia [corregida al inicio]
8000
6000
4000
2000
0
0
0,001
0,01
0,1
1
10
100
1000
Concentración [nM]

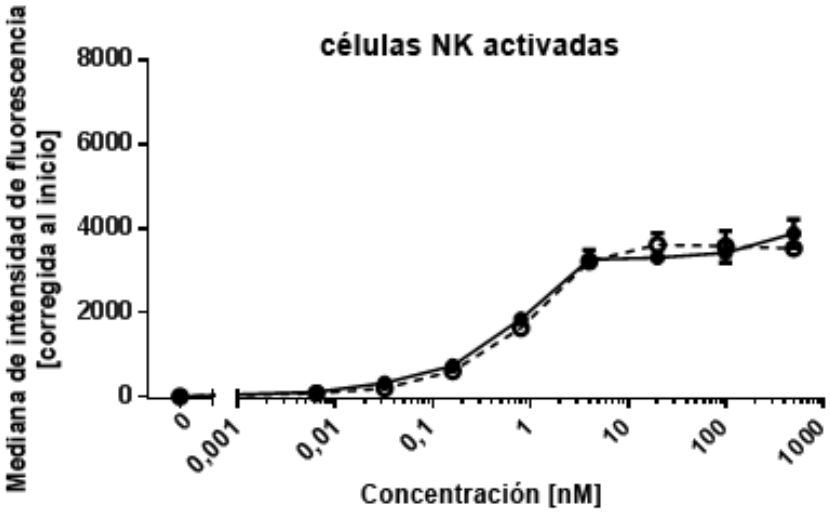

células NK activadas
Mediana de intensidad de fluorescencia [corregida al inicio]
8000
6000
4000
2000
0
0
0,001
0,01
0,1
1
10
100
1000
Concentración [nM]

Fig. 7 A

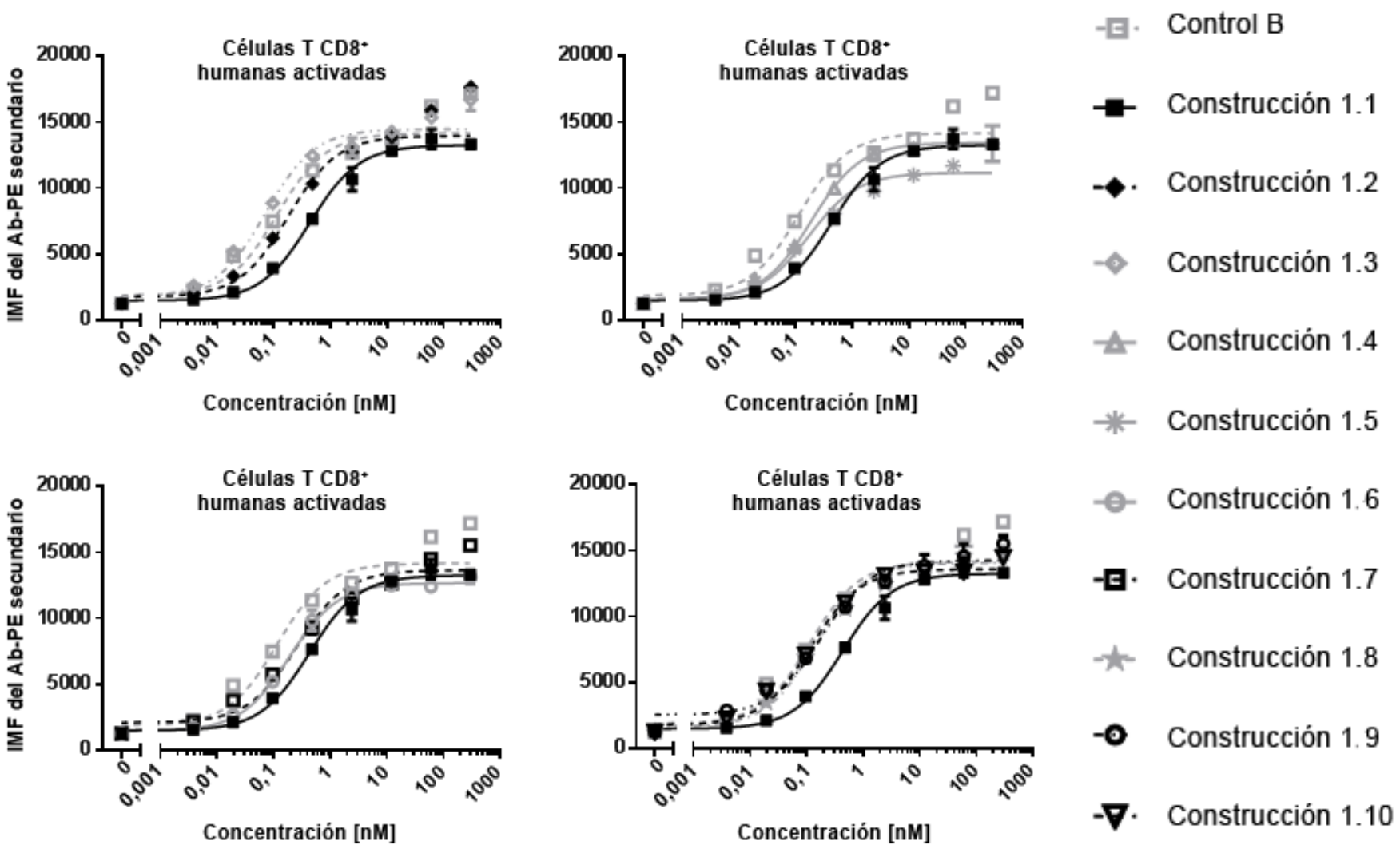

Células T CD8+ humanas activadas
IMF del Ab-PE secundario
20000
15000
10000
5000
0
0
0,001
0,01
0,1
1
10
100
1000
Concentración [nM]
Control B
Construcción 1.1
Construcción 1.2
Construcción 1.3
Construcción 1.4
Construcción 1.5
Construcción 1.6
Construcción 1.7
Construcción 1.8
Construcción 1.9
Construcción 1.10

Fig. 7 B

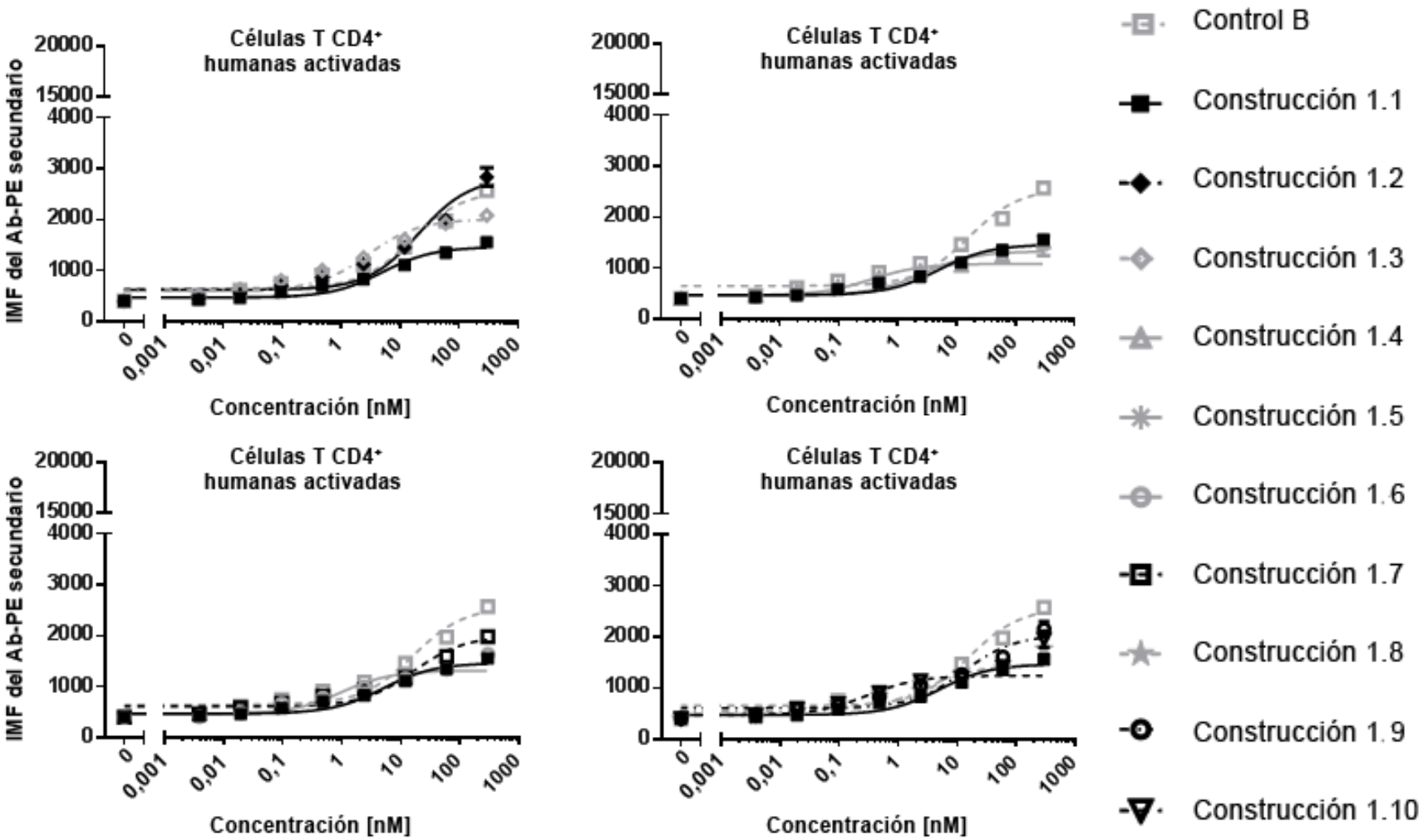

Células T CD4+
humanas activadas
IMF del Ab-PE secundario
20000
15000
4000
3000
2000
1000
0
0
0,001
0,01
0,1
1
10
100
1000
Concentración [nM]
Control B
Construcción 1.1
Construcción 1.2
Construcción 1.3
Construcción 1.4
Construcción 1.5
Construcción 1.6
Construcción 1.7
Construcción 1.8
Construcción 1.9
Construcción 1.10

Fig. 8A

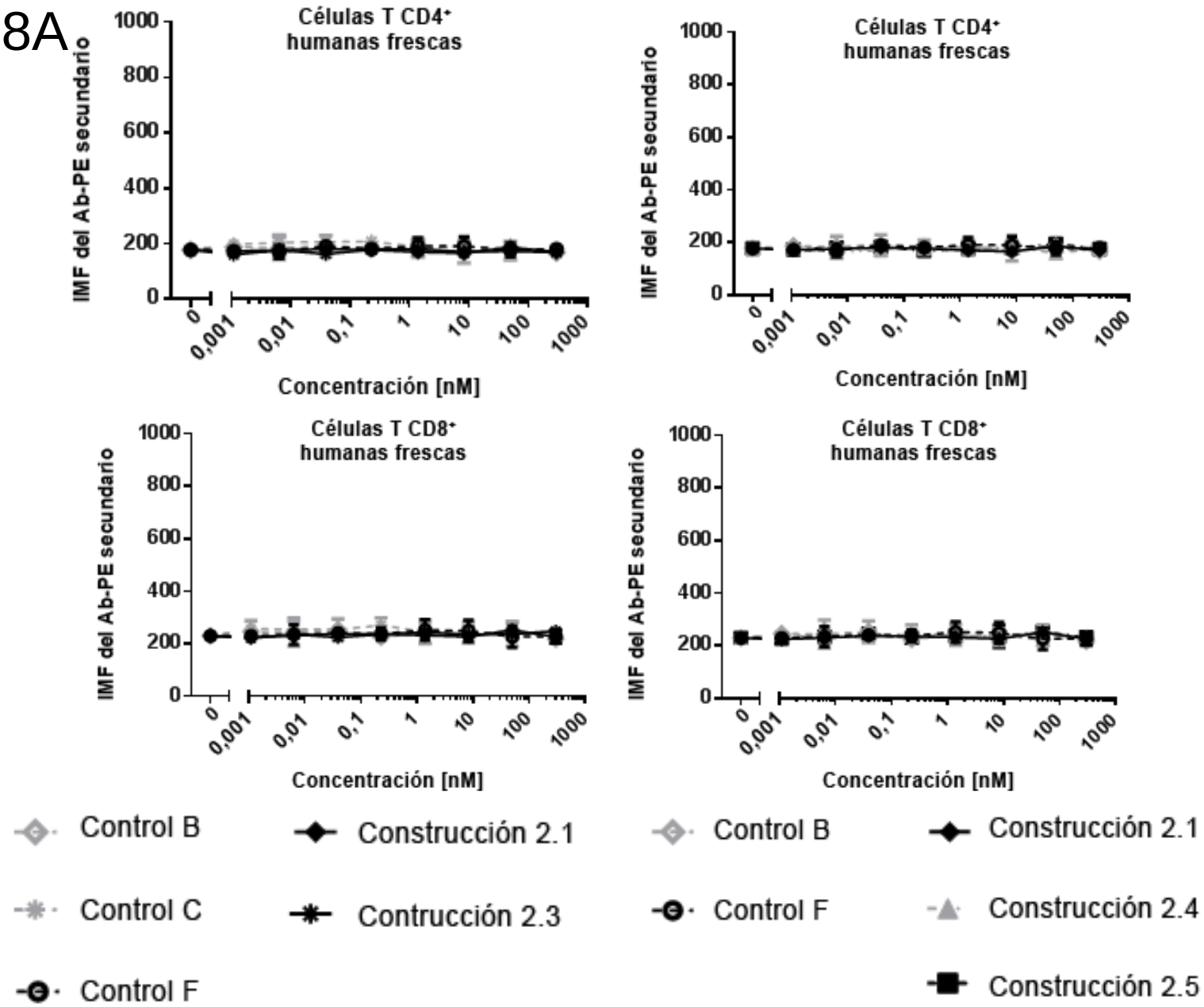

Células T CD4+ humanas frescas
Células T CD4+ humanas frescas
Células T CD8+ humanas frescas
Células T CD8+ humanas frescas
IMF del Ab-PE secundario
1000
800
600
400
200
0
0
0,001
0,01
0,1
1
10
100
1000
Concentración [nM]
Control B
Construcción 2.1
Control C
Contrucción 2.3
Control F
Control B
Construcción 2.1
Control F
Construcción 2.4
Construcción 2.5

Fig. 8 B

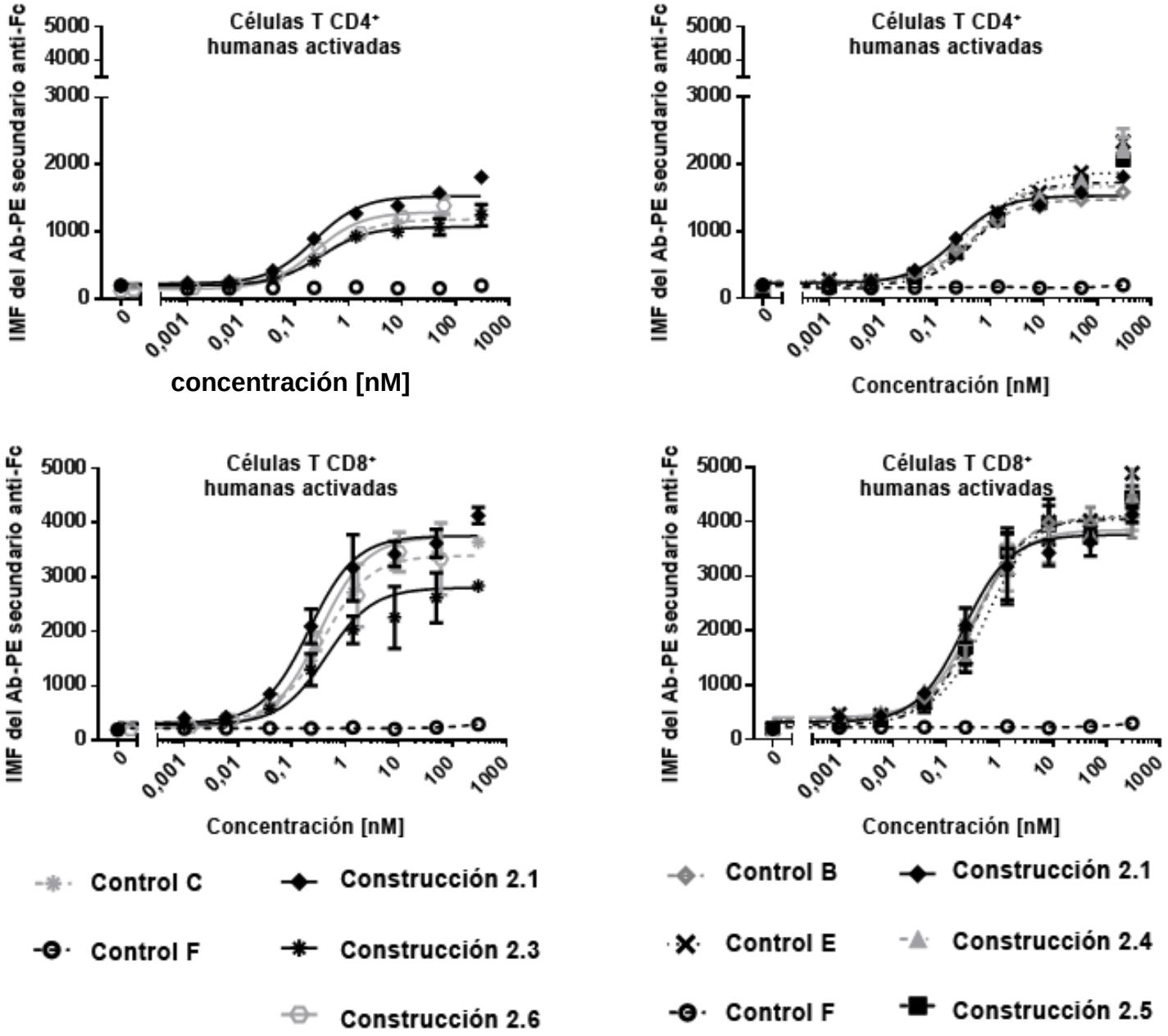
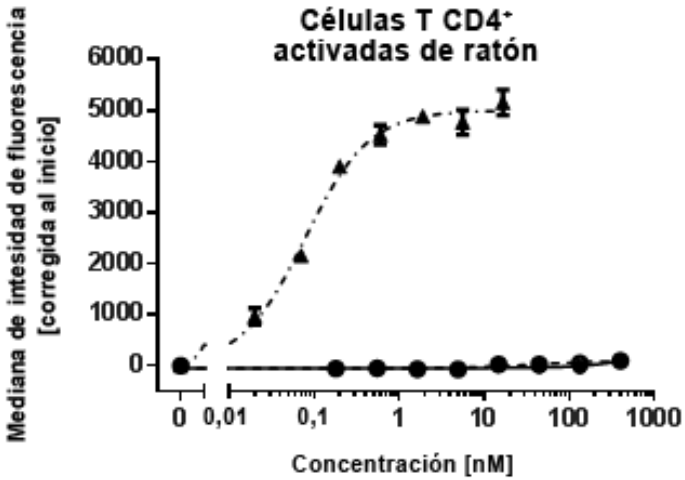

Células T CD4+ humanas activadas
IMF del Ab-PE secundario anti-Fc
5000
4000
3000
2000
1000
0
0
0,001
0,01
0,1
1
10
100
1000
concentración [nM]
Células T CD4+ humanas activadas
IMF del Ab-PE secundario anti-Fc
Concentración [nM]
Células T CD8+ humanas activadas
IMF del Ab-PE secundario anti-Fc
Concentración [nM]
Control C
Construcción 2.1
Control F
Construcción 2.3
Construcción 2.6
Células T CD8+ humanas activadas
IMF del Ab-PE secundario anti-Fc
Concentración [nM]
Control B
Construcción 2.1
Control E
Construcción 2.4
Control F
Construcción 2.5

Fig. 9

(9 A)


Células T CD4+
activadas de ratón
Mediana de intesidad de fluorescencia
[corregida al inicio]
6000
5000
4000
3000
2000
1000
0
0
0,01
0,1
1
10
100
1000
Concentración [nM]

(9 B)

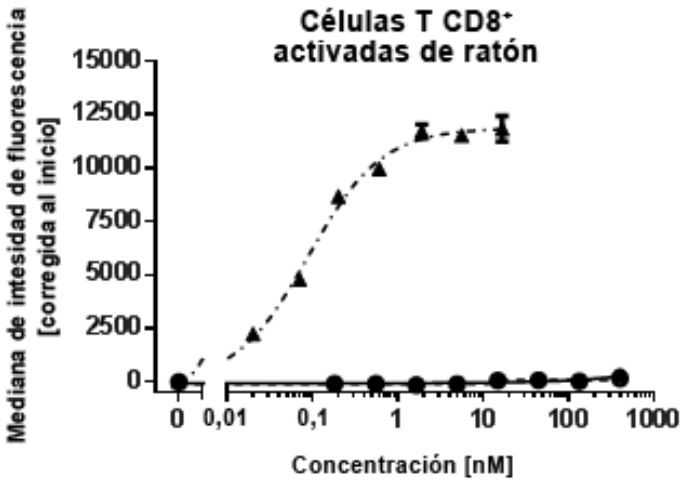
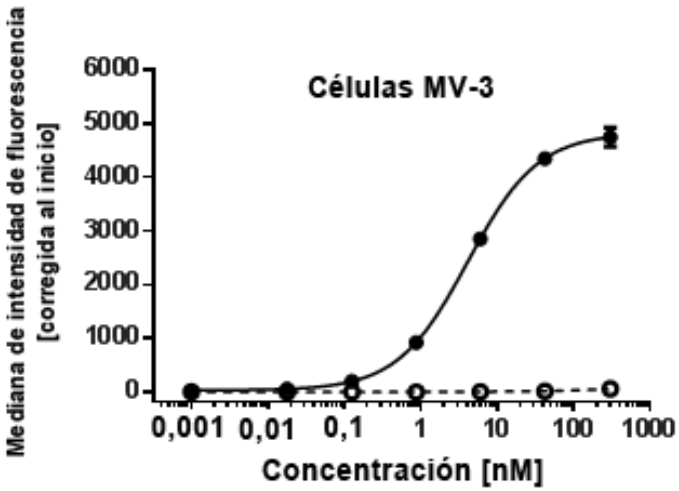

Células T CD8+
activadas de ratón
Mediana de intesidad de fluorescencia
[corregida al inicio]
15000
12500
10000
7500
5000
2500
0
0
0,01
0,1
1
10
100
1000
Concentración [nM]

Fig. 10

(10 A)



(10 B)

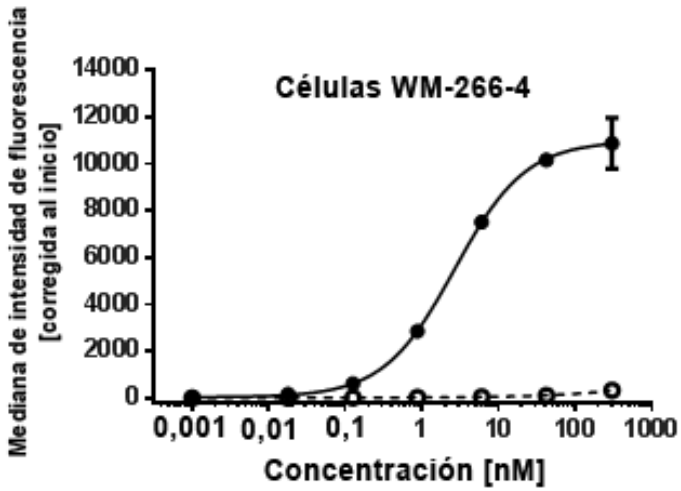


Fig. 11 A

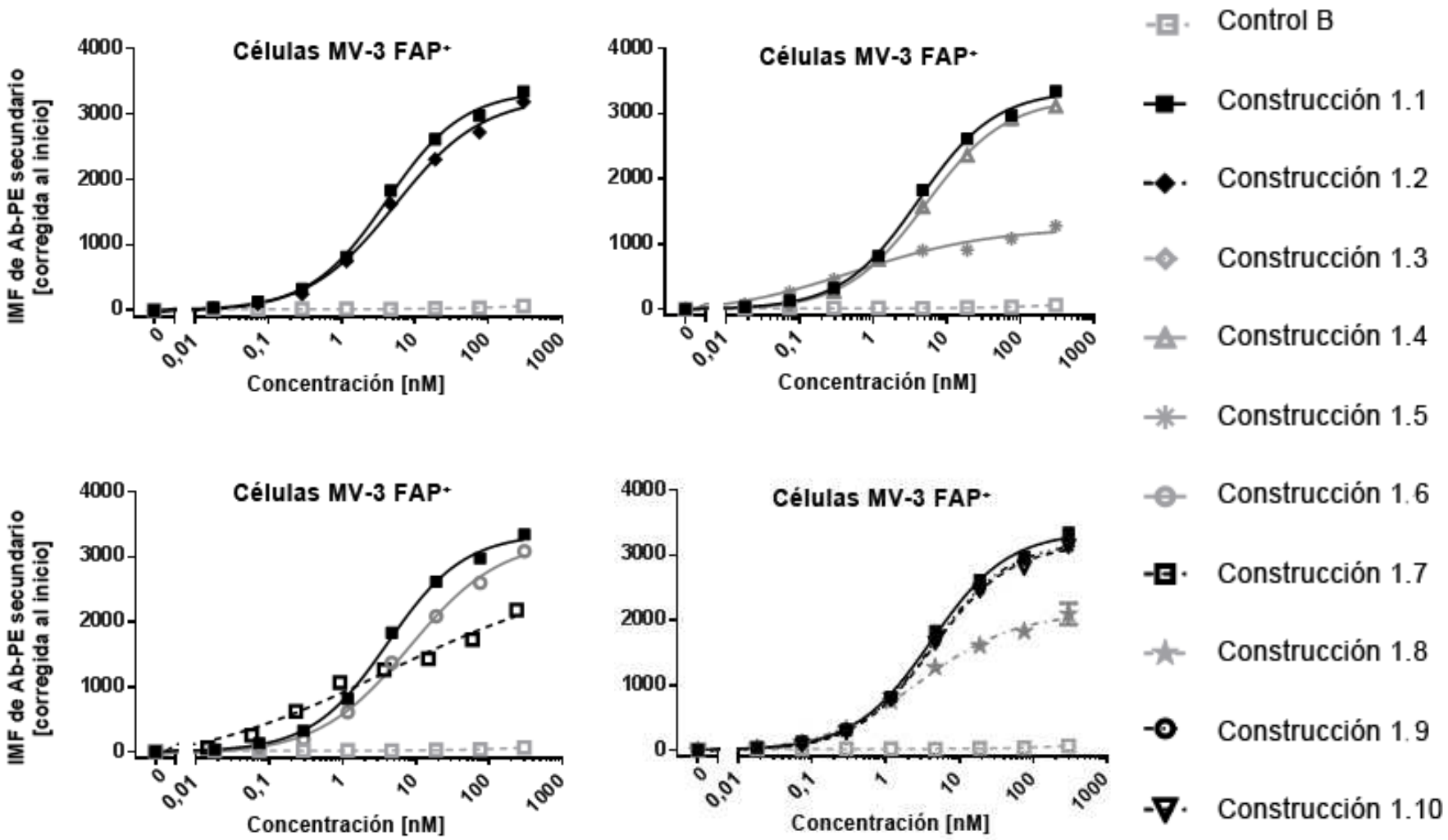

Células MV-3 FAP+
IMF de Ab-PE secundario [corregida al inicio]
Concentración [nM]
4000
3000
2000
1000
0
0
0,01
0,1
1
10
100
1000
Control B
Construcción 1.1
Construcción 1.2
Construcción 1.3
Construcción 1.4
Construcción 1.5
Construcción 1.6
Construcción 1.7
Construcción 1.8
Construcción 1.9
Construcción 1.10

Fig. 11 B

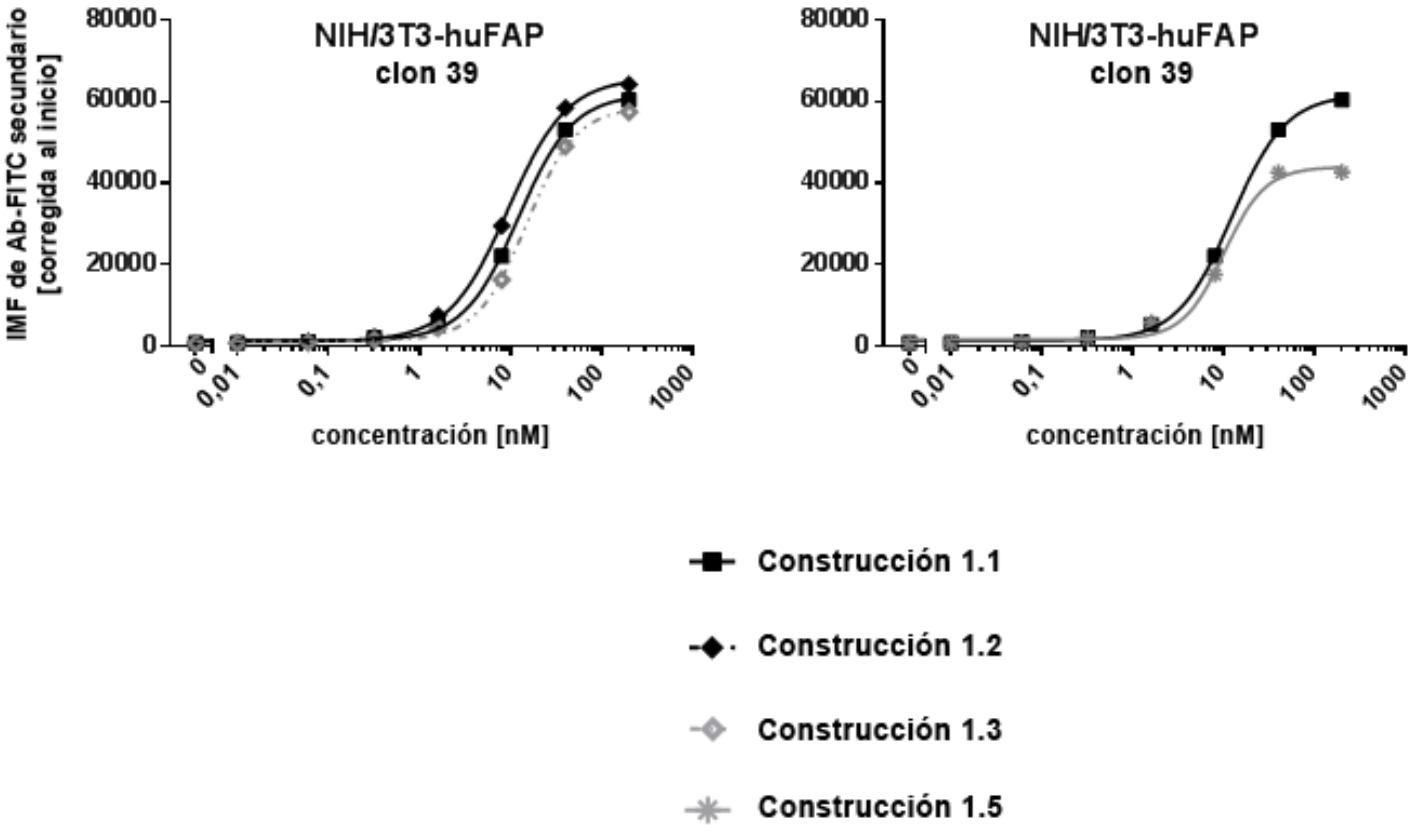

IMF de Ab-FITC secundario
[corregida al inicio]
80000
60000
40000
20000
0
NIH/3T3-huFAP
clon 39
0
0,01
0,1
1
10
100
1000
concentración [nM]
NIH/3T3-huFAP
clon 39
concentración [nM]
Construcción 1.1
Construcción 1.2
Construcción 1.3
Construcción 1.5

Fig. 12 A

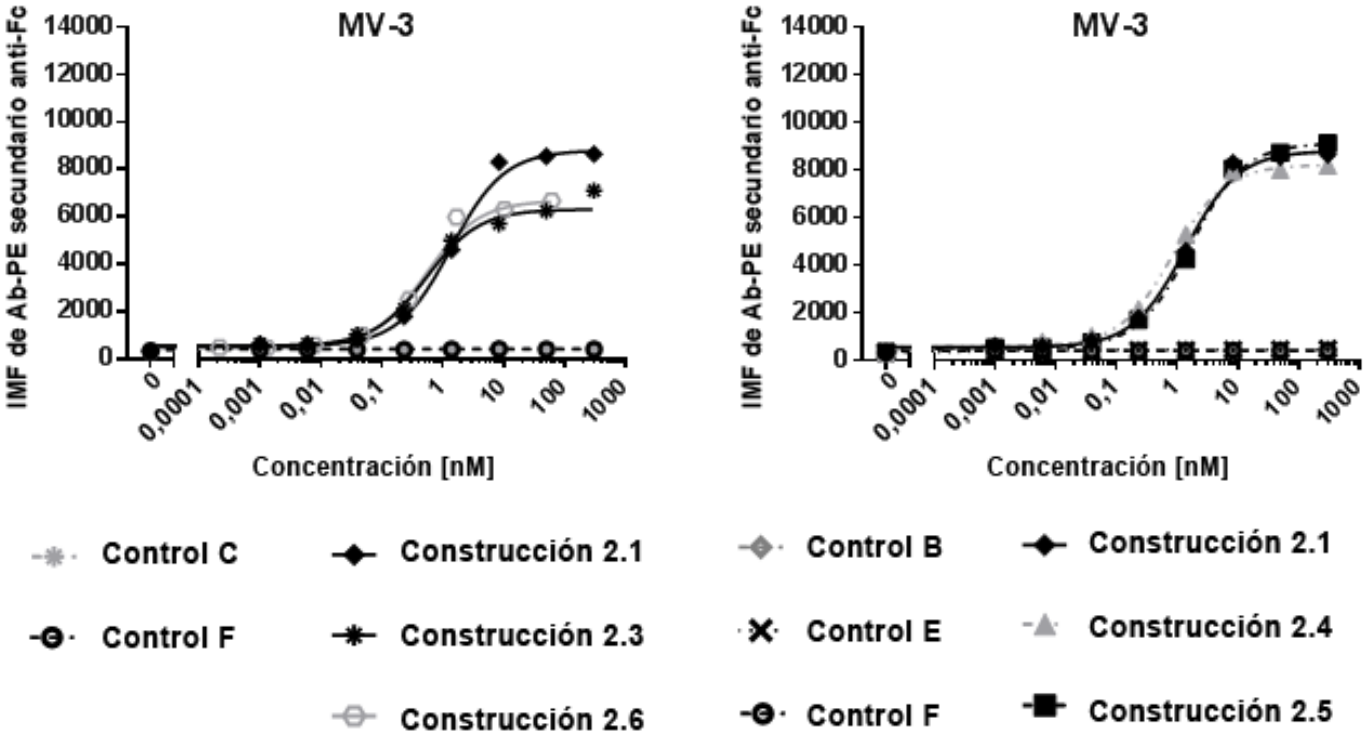
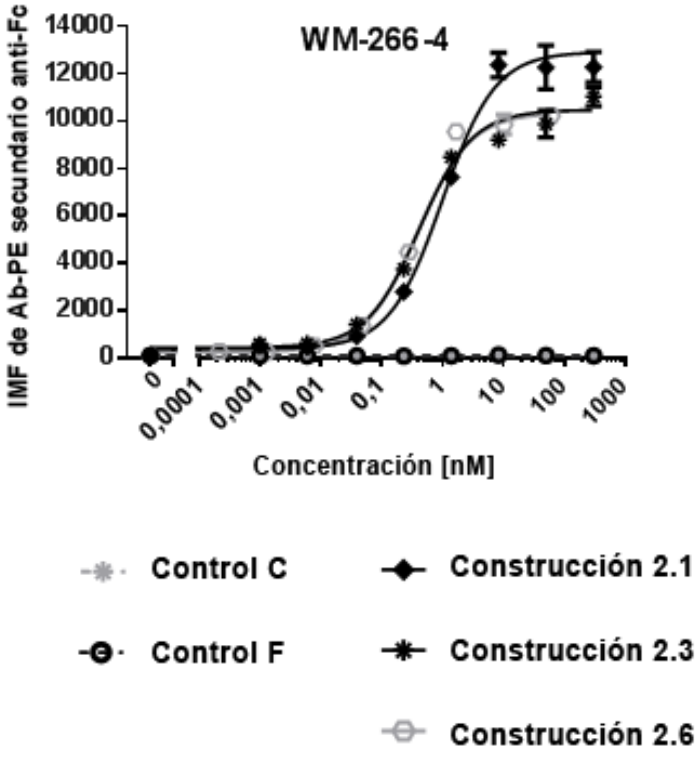

MV-3
IMF de Ab-PE secundario anti-Fc
14000
12000
10000
8000
6000
4000
2000
0
0
0,0001
0,001
0,01
0,1
1
10
100
1000
Concentración [nM]
Control C
Construcción 2.1
Control F
Construcción 2.3
Construcción 2.6
MV-3
IMF de Ab-PE secundario anti-Fc
14000
12000
10000
8000
6000
4000
2000
0
0
0,0001
0,001
0,01
0,1
1
10
100
1000
Concentración [nM]
Control B
Construcción 2.1
Control E
Construcción 2.4
Control F
Construcción 2.5

Fig. 12 B


WM-266-4
IMF de Ab-PE secundario anti-Fc
14000
12000
10000
8000
6000
4000
2000
0
0
0,0001
0,001
0,01
0,1
1
10
100
1000
Concentración [nM]
Control C
Construcción 2.1
Control F
Construcción 2.3
Construcción 2.6

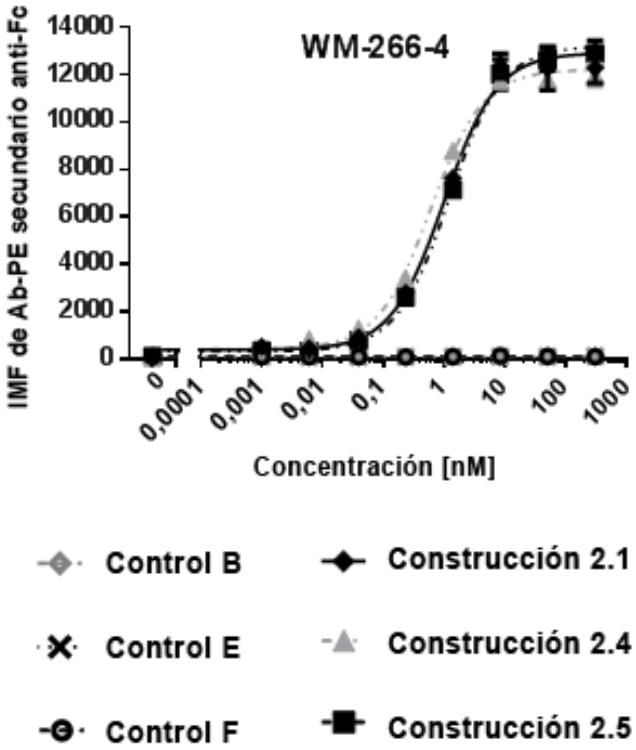
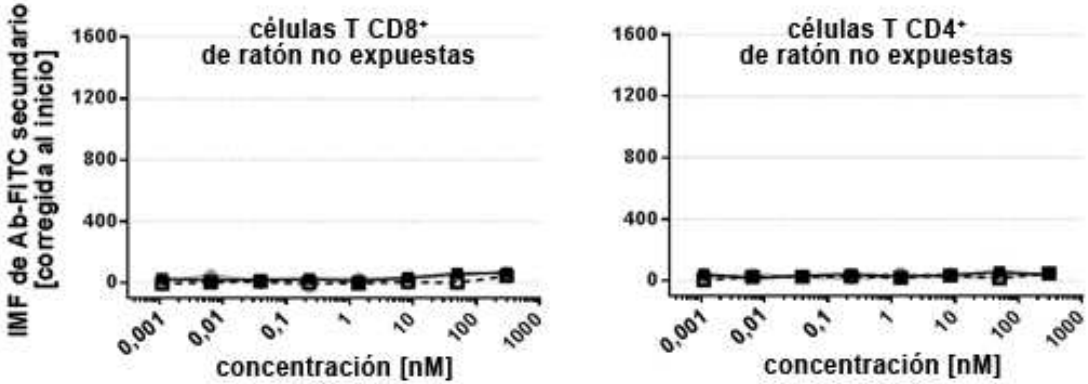

WM-266-4
IMF de Ab-PE secundario anti-Fc
14000
12000
10000
8000
6000
4000
2000
0
0
0,0001
0,001
0,01
0,1
1
10
100
1000
Concentración [nM]
Control B
Construcción 2.1
Control E
Construcción 2.4
Control F
Construcción 2.5

Fig. 13

(13 A)



(13 B)

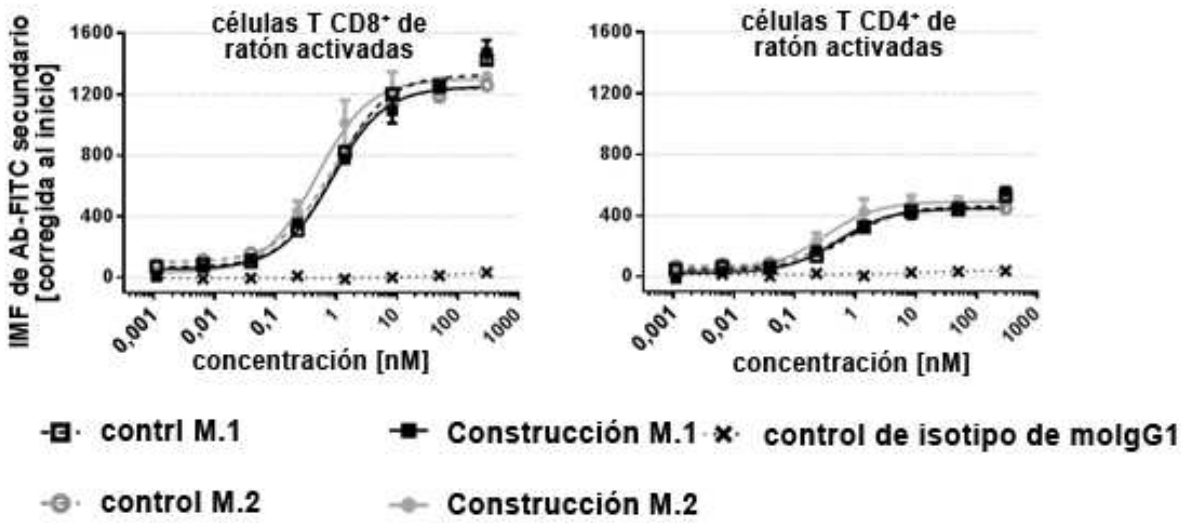
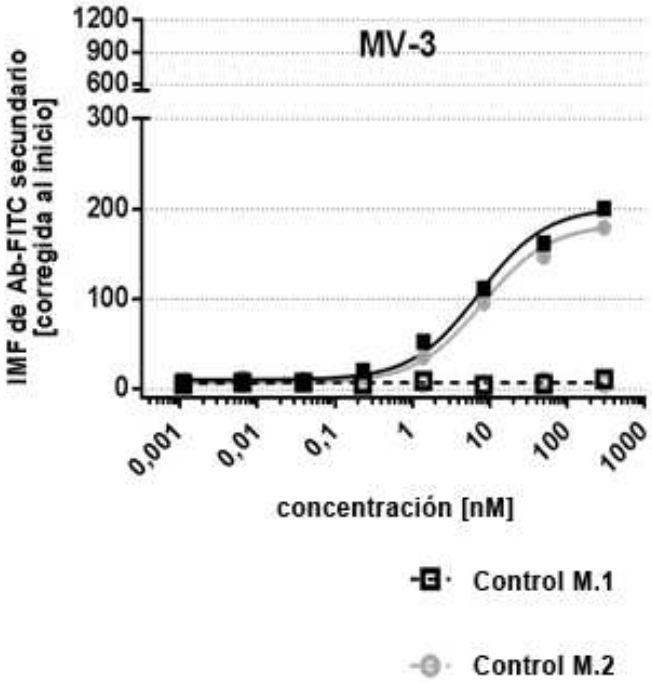
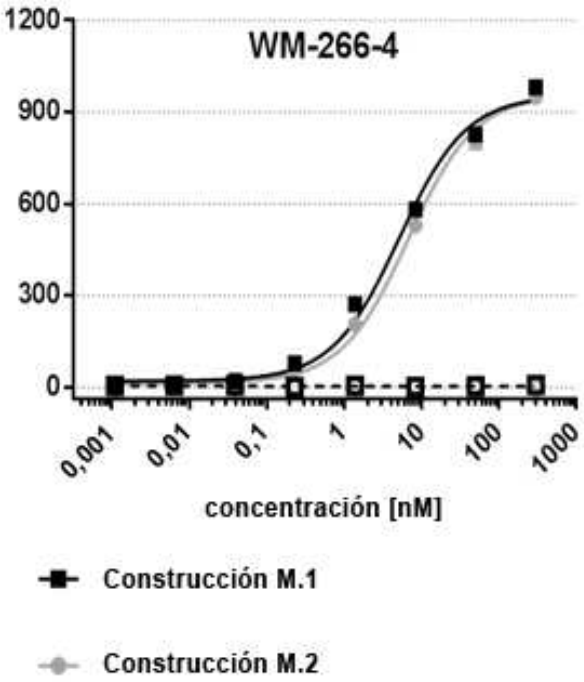


Fig. 14

(14 A)



(14 B)



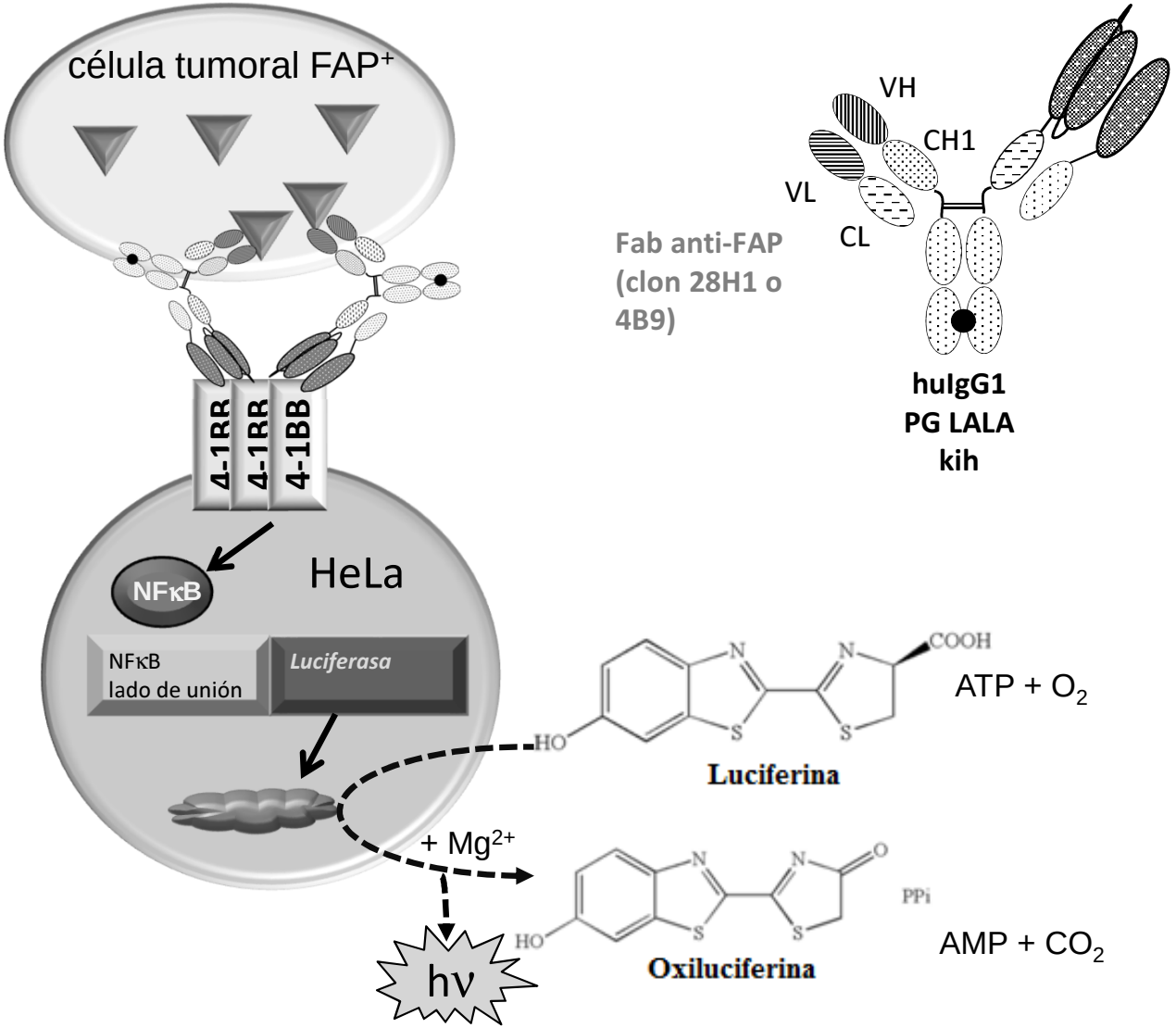
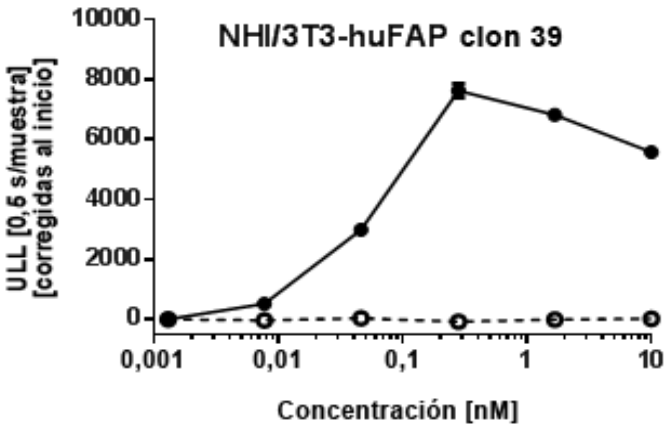
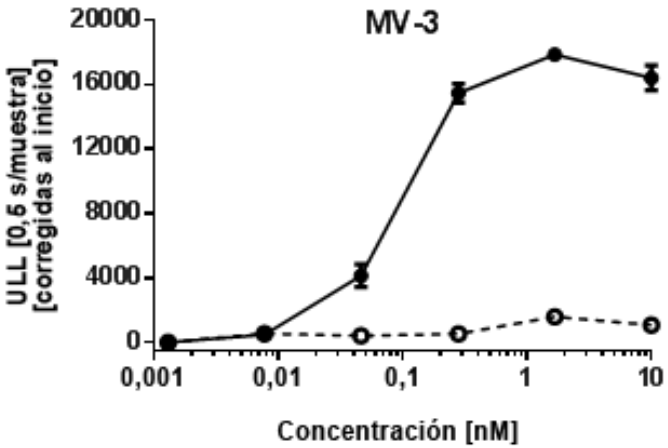

célula tumoral FAP+
4-1RR
4-1RR
4-1BB
NFκB
HeLa
NFκB
lado de unión
Luciferasa
+ Mg2+
hν
VH
CH1
VL
CL
Fab anti-FAP
(clon 28H1 o
4B9)
huIgG1
PG LALA
kih
COOH
ATP + O2
Luciferina
PPi
AMP + CO2
Oxiluciferina

Fig. 15

(16 A)



(16 B)



(16C)

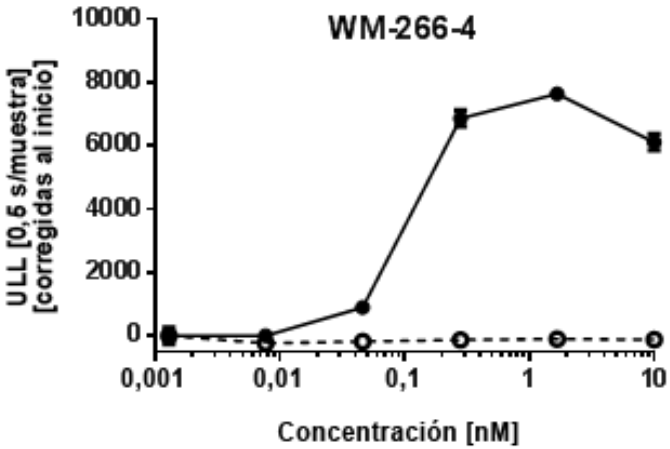


Fig. 16

Fig. 17 A

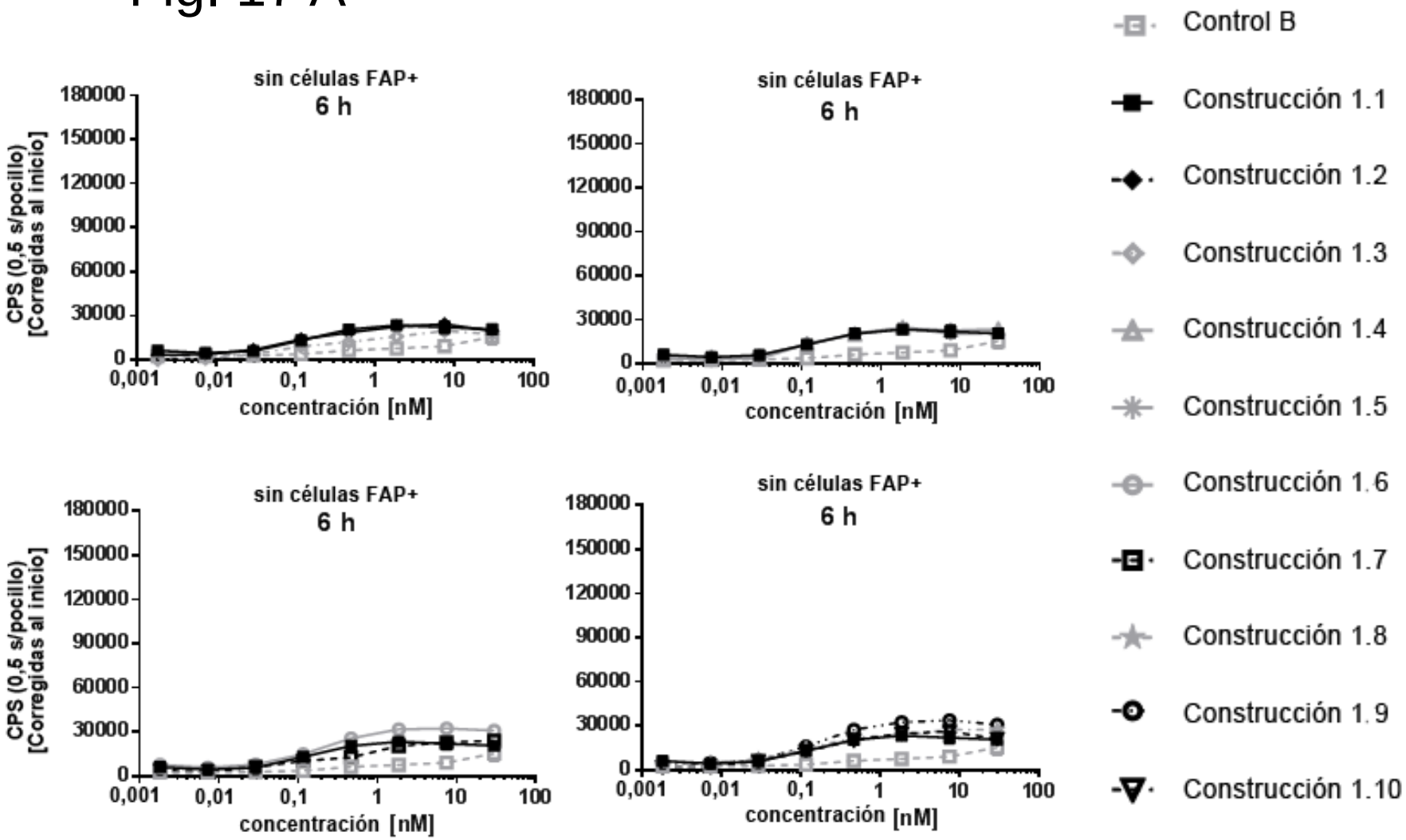

sin células FAP+
6 h
CPS (0,5 s/pocillo)
[Corregidas al inicio]
180000
150000
120000
90000
60000
30000
0
0,001
0,01
0,1
1
10
100
concentración [nM]
Control B
Construcción 1.1
Construcción 1.2
Construcción 1.3
Construcción 1.4
Construcción 1.5
Construcción 1.6
Construcción 1.7
Construcción 1.8
Construcción 1.9
Construcción 1.10

Fig. 17 B

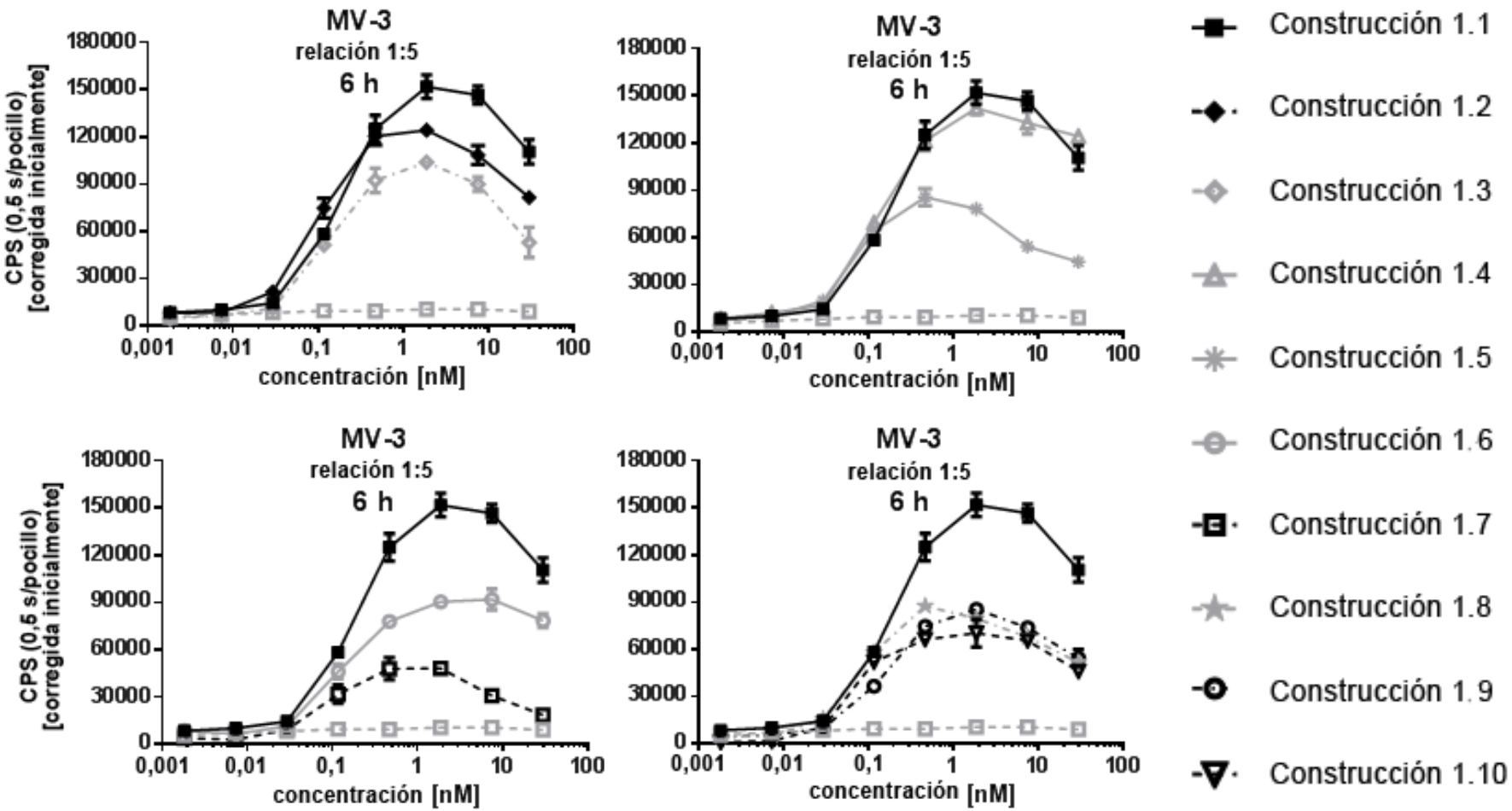

MV-3
relación 1:5
6 h
CPS (0,5 s/pocillo)
[corregida inicialmente]
concentración [nM]
0,001
0,01
0,1
1
10
100
0
30000
60000
90000
120000
150000
180000
Control B
Construcción 1.1
Construcción 1.2
Construcción 1.3
Construcción 1.4
Construcción 1.5
Construcción 1.6
Construcción 1.7
Construcción 1.8
Construcción 1.9
Construcción 1.10

Fig. 17C

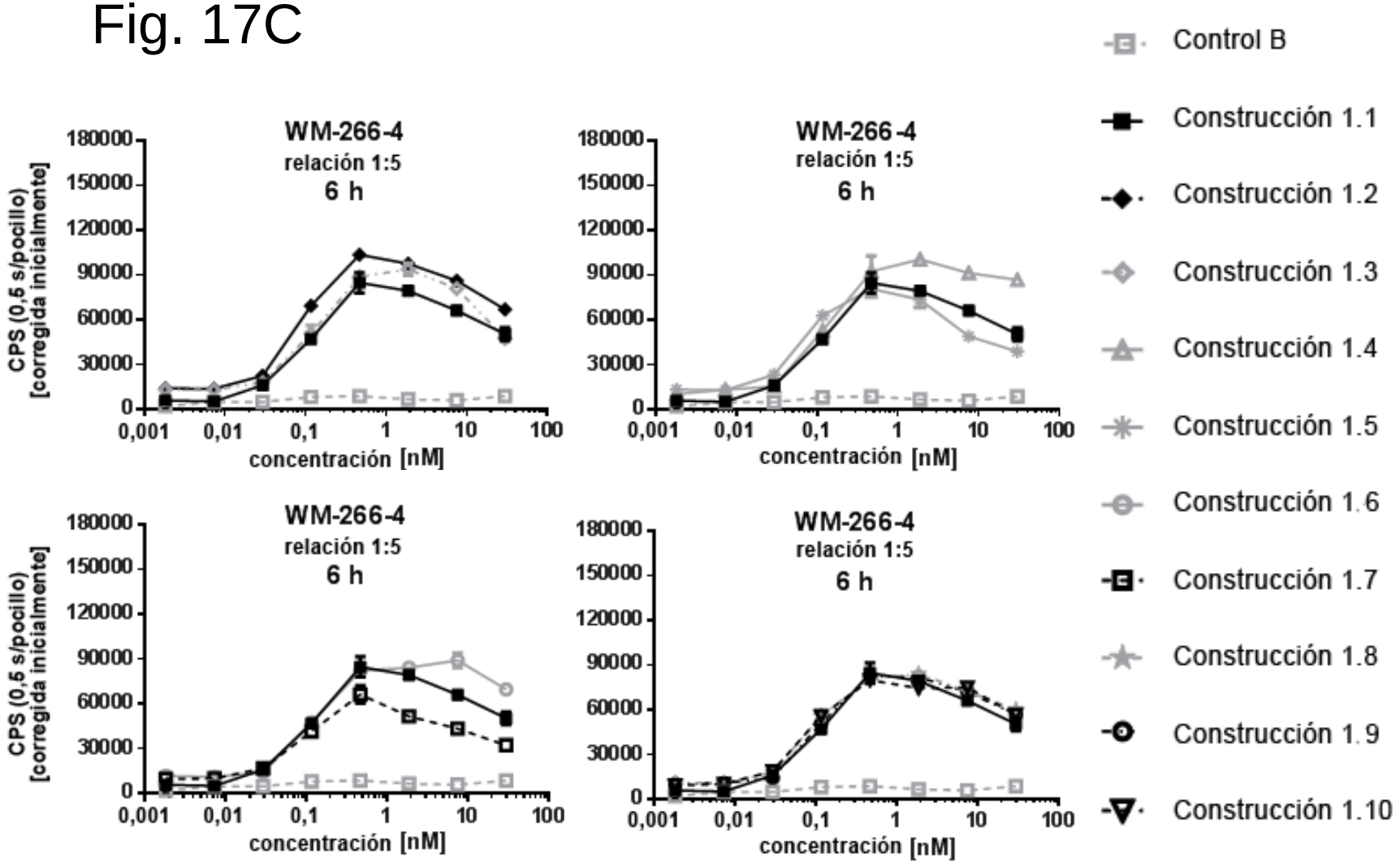
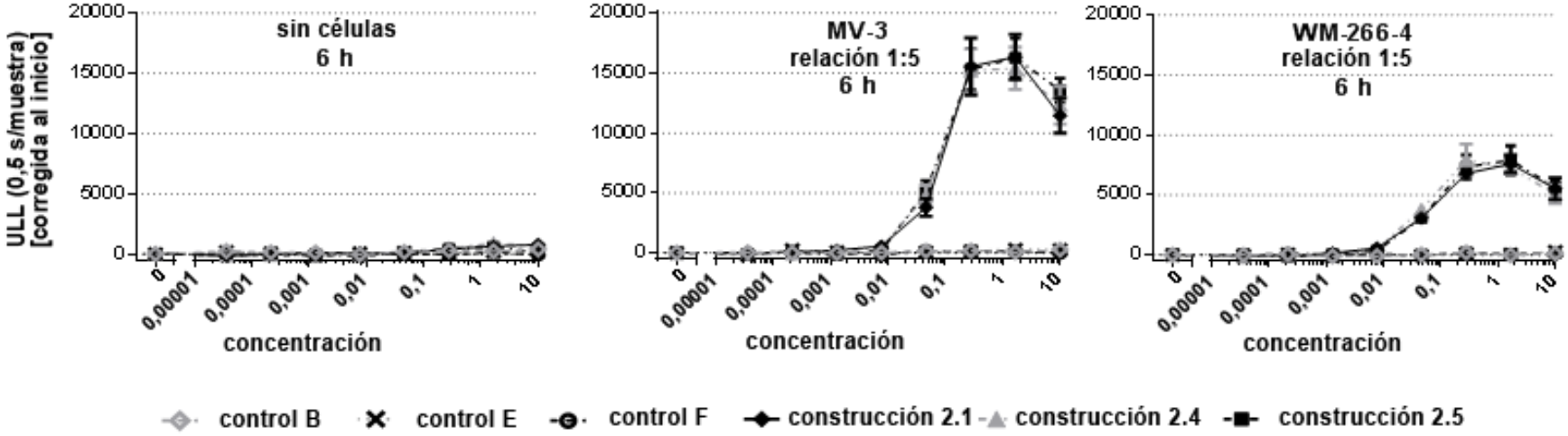

WM-266-4
relación 1:5
6 h
CPS (0,5 s/pocillo)
[corregida inicialmente]
concentración [nM]
180000
150000
120000
90000
60000
30000
0
0,001
0,01
0,1
1
10
100
Control B
Construcción 1.1
Construcción 1.2
Construcción 1.3
Construcción 1.4
Construcción 1.5
Construcción 1.6
Construcción 1.7
Construcción 1.8
Construcción 1.9
Construcción 1.10

Fig. 18


ULL (0,5 s/muestra) [corregida al inicio]
sin células
6 h
MV-3
relación 1:5
6 h
WM-266-4
relación 1:5
6 h
concentración
control B
control E
control F
construcción 2.1
construcción 2.4
construcción 2.5

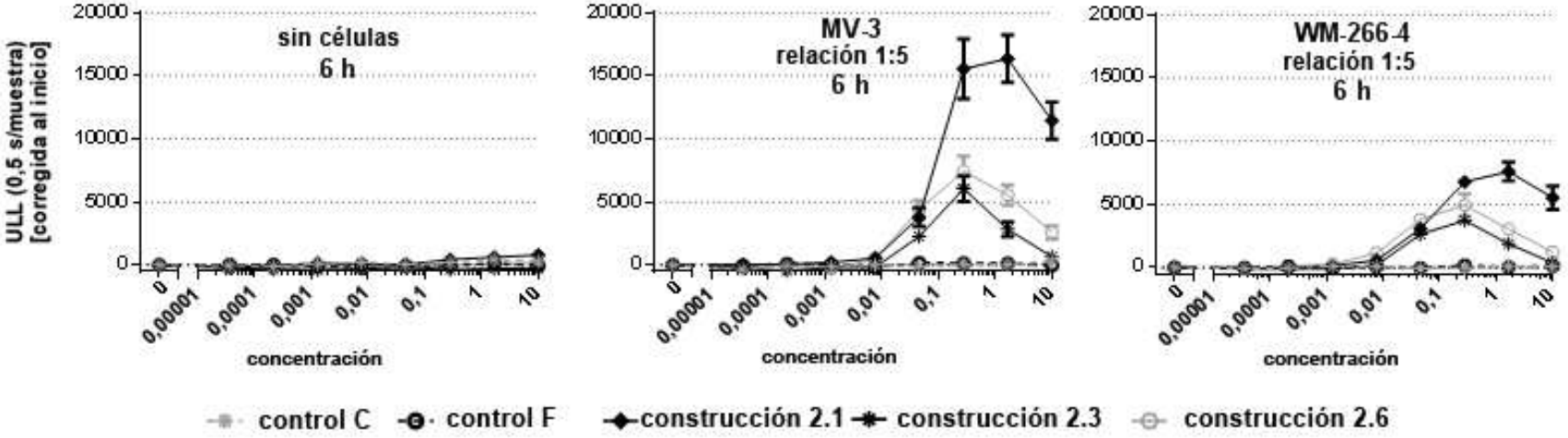

ULL (0,5 s/muestra) [corregida al inicio]
sin células
6 h
MV-3
relación 1:5
6 h
WM-266-4
relación 1:5
6 h
concentración
control C
control F
construcción 2.1
construcción 2.3
construcción 2.6

Fig. 19

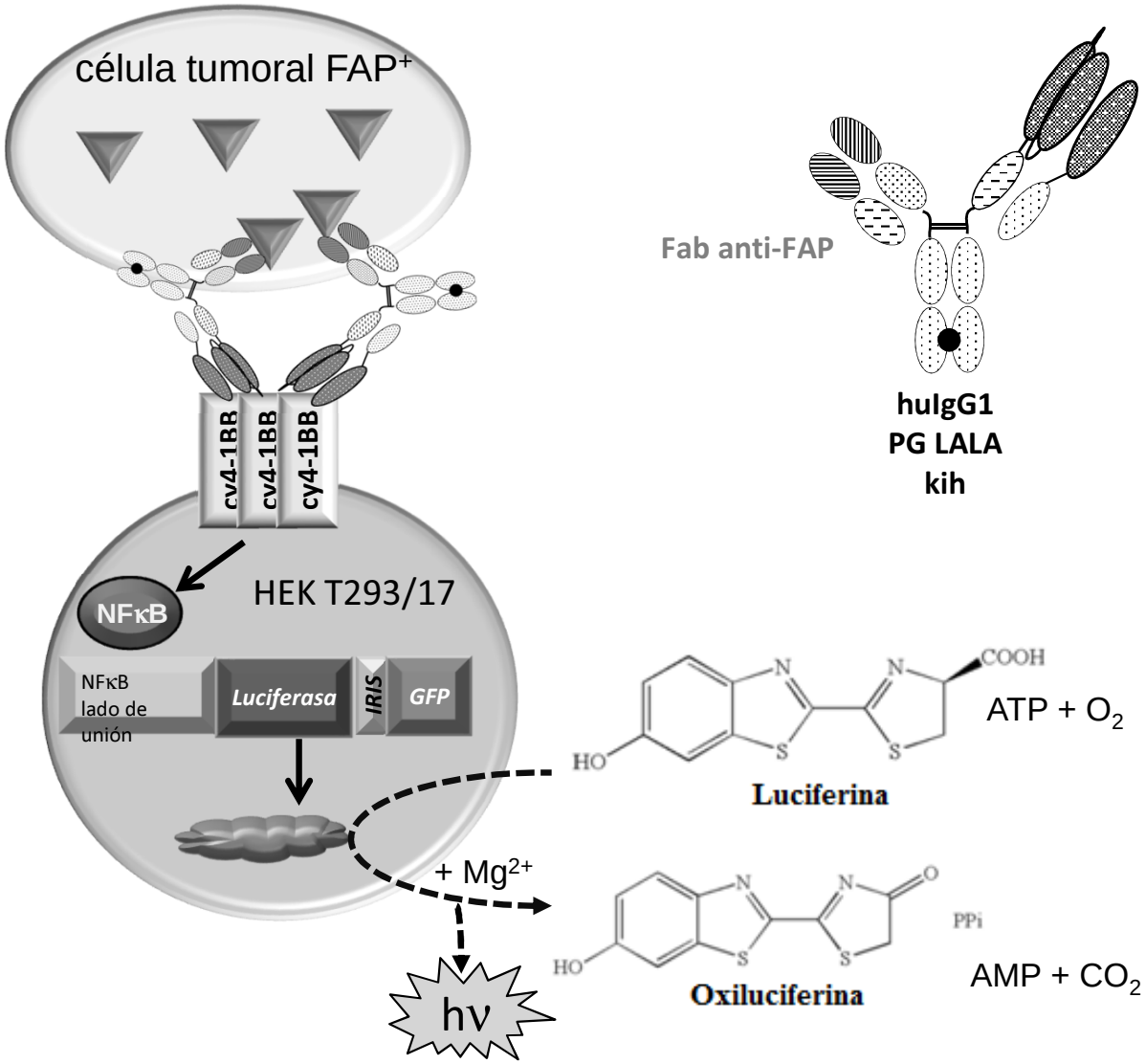
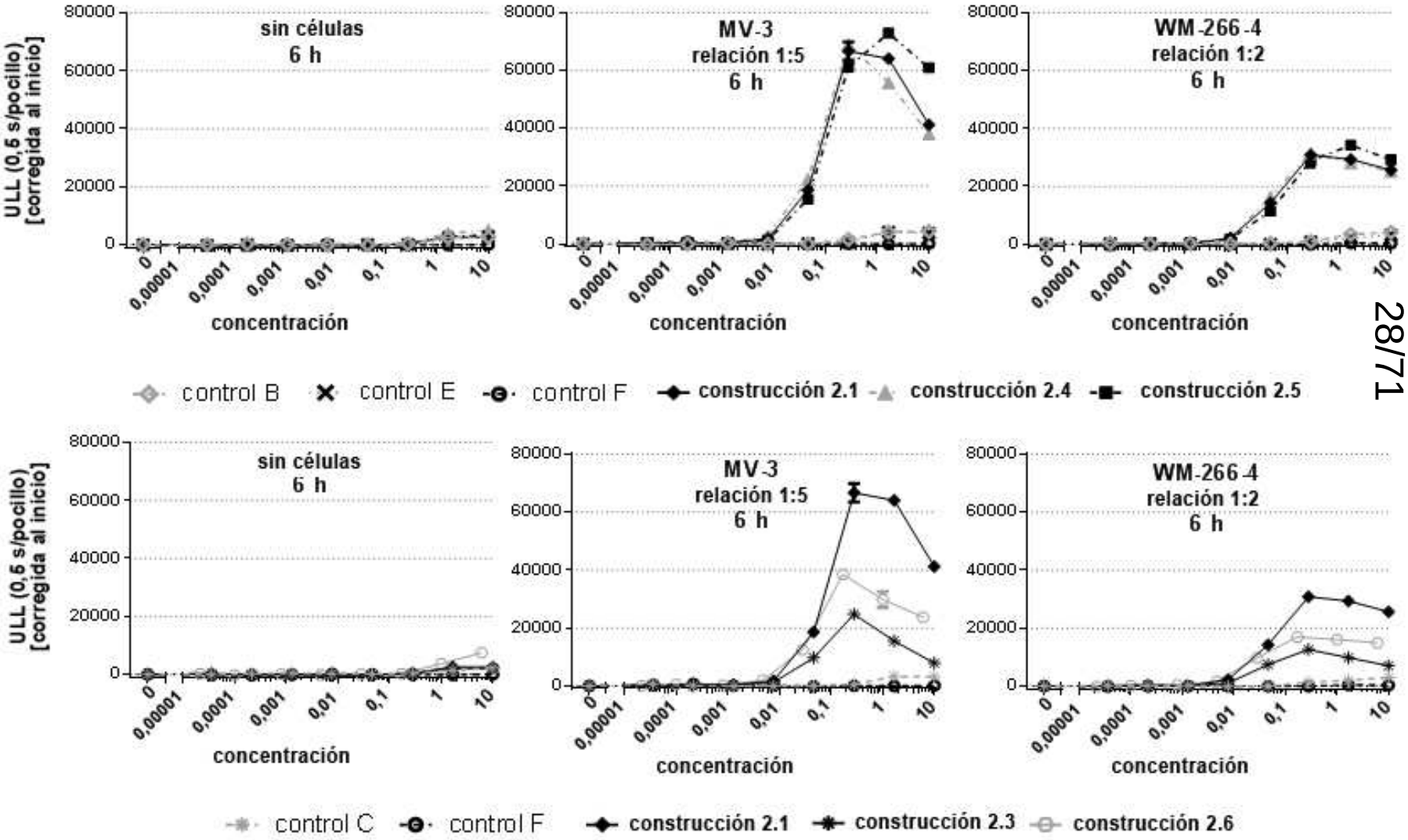

célula tumoral FAP+
cv4-1BB
cv4-1BB
cy4-1BB
NFκB
HEK T293/17
NFκB lado de unión
Luciferasa
IRIS
GFP
+ Mg2+
hν
Fab anti-FAP
huIgG1
PG LALA
kih
COOH
HO
Luciferina
ATP + O2
PPi
Oxiluciferina
AMP + CO2

Fig. 20


ULL (0,5 s/pocillo) [corregida al inicio]
80000
60000
40000
20000
0
sin células
6 h
MV-3
relación 1:5
6 h
WM-266-4
relación 1:2
6 h
0
0,00001
0,0001
0,001
0,01
0,1
1
10
concentración
control B
control E
control F
construcción 2.1
construcción 2.4
construcción 2.5
control C
construcción 2.3
construcción 2.6

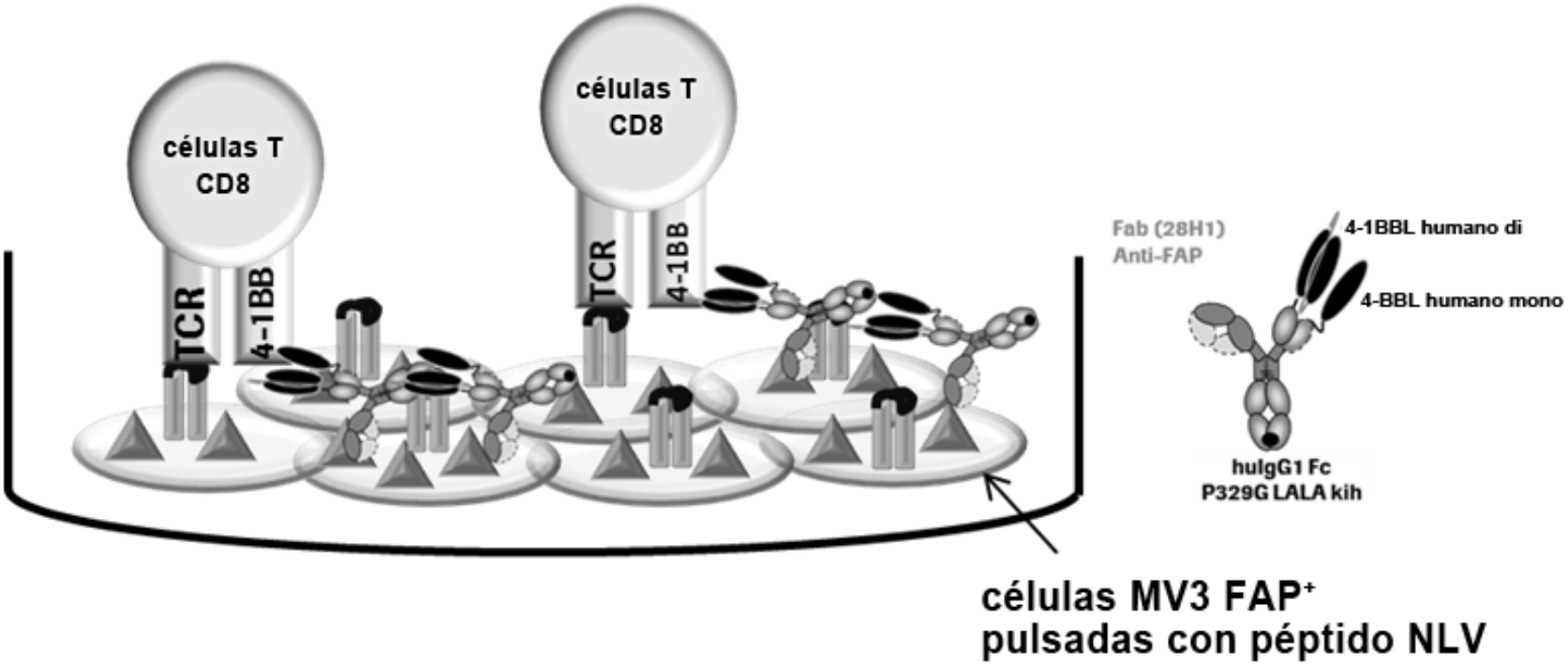
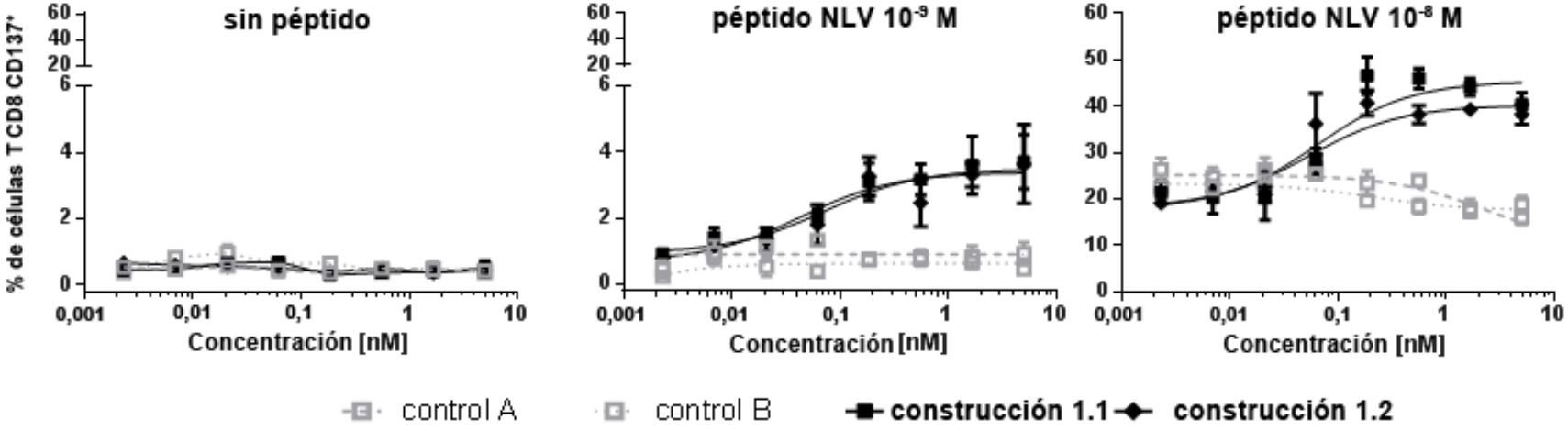

células T
CD8
TCR
4-1BB
células T
CD8
TCR
4-1BB
Fab (28H1)
Anti-FAP
4-1BBL humano di
4-BBL humano mono
huIgG1 Fc
P329G LALA kih
células MV3 FAP+
pulsadas con péptido NLV

Fig. 21

Fig. 22

(22 A)



(22 B)

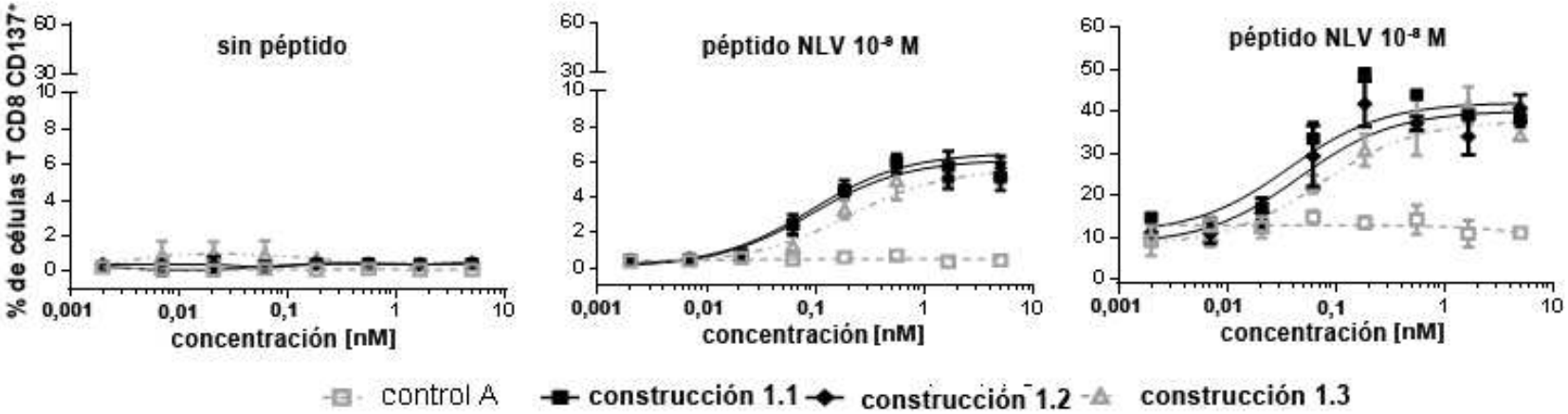
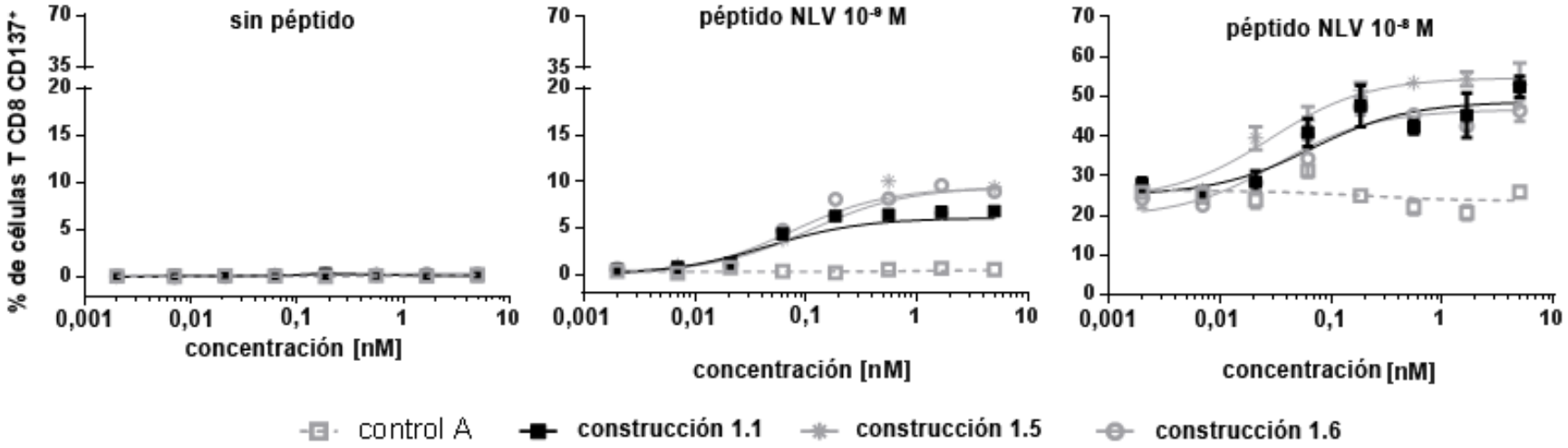


Fig. 22

(22C)



(22D)

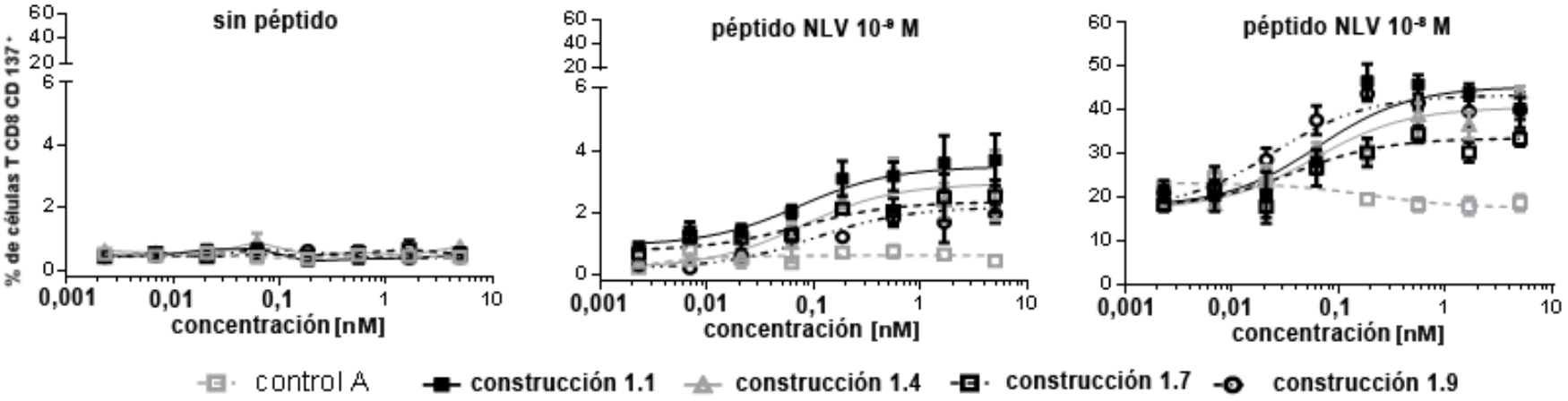


Fig. 22

(22E)

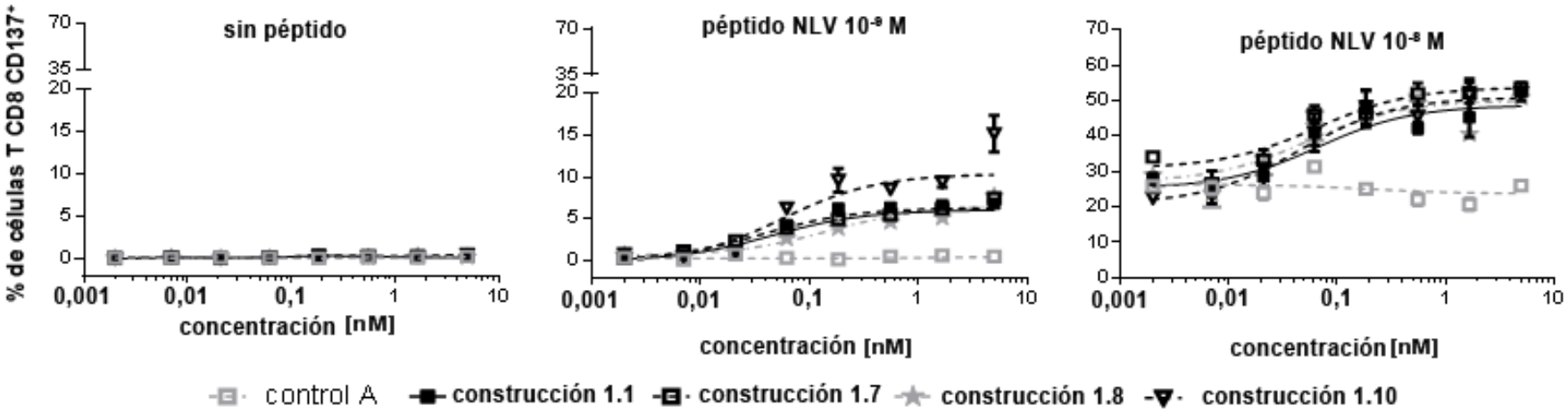
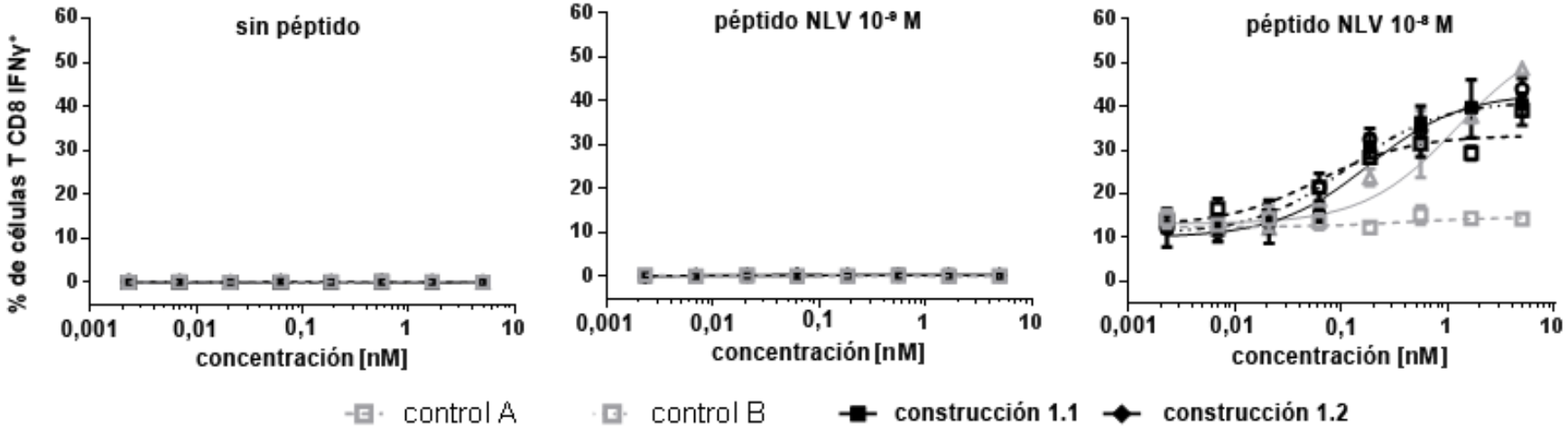

% de células T CD8 CD137+
sin péptido
péptido NLV 10-8 M
péptido NLV 10-8 M
concentración [nM]
concentración [nM]
concentración [nM]
control A
construcción 1.1
construcción 1.7
construcción 1.8
construcción 1.10

Fig. 23

(23 A)



(23 B)

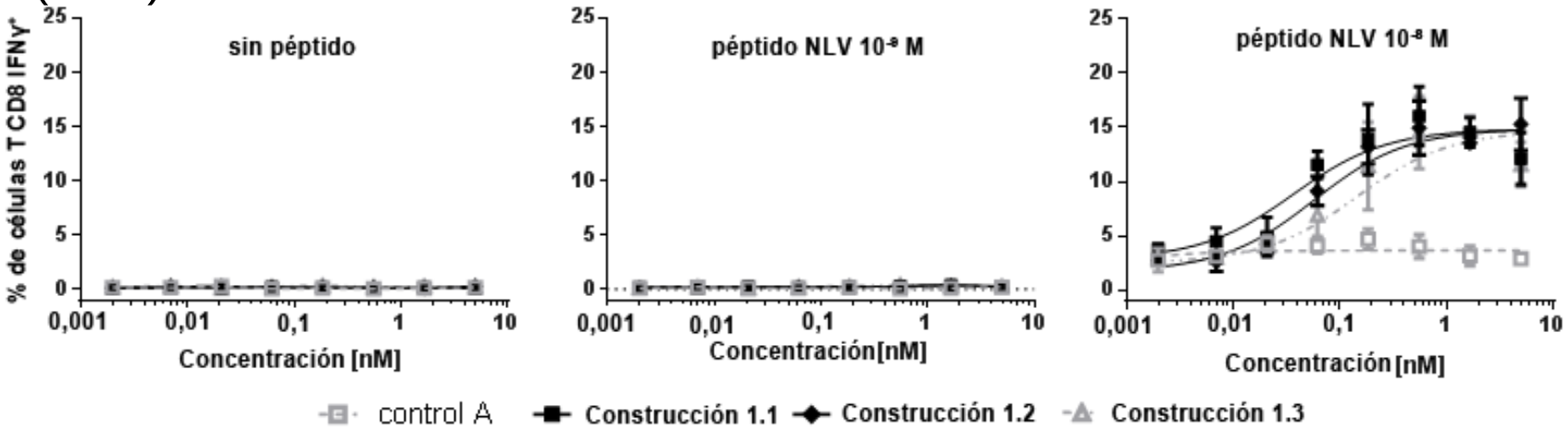
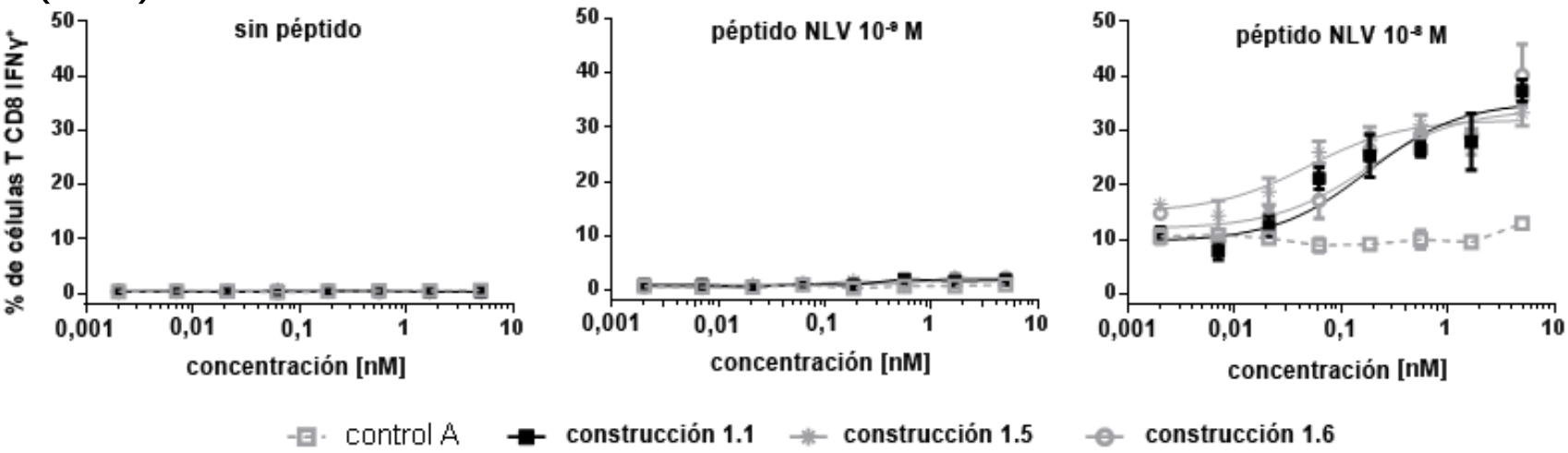


Fig. 23

(23C)



(23D)

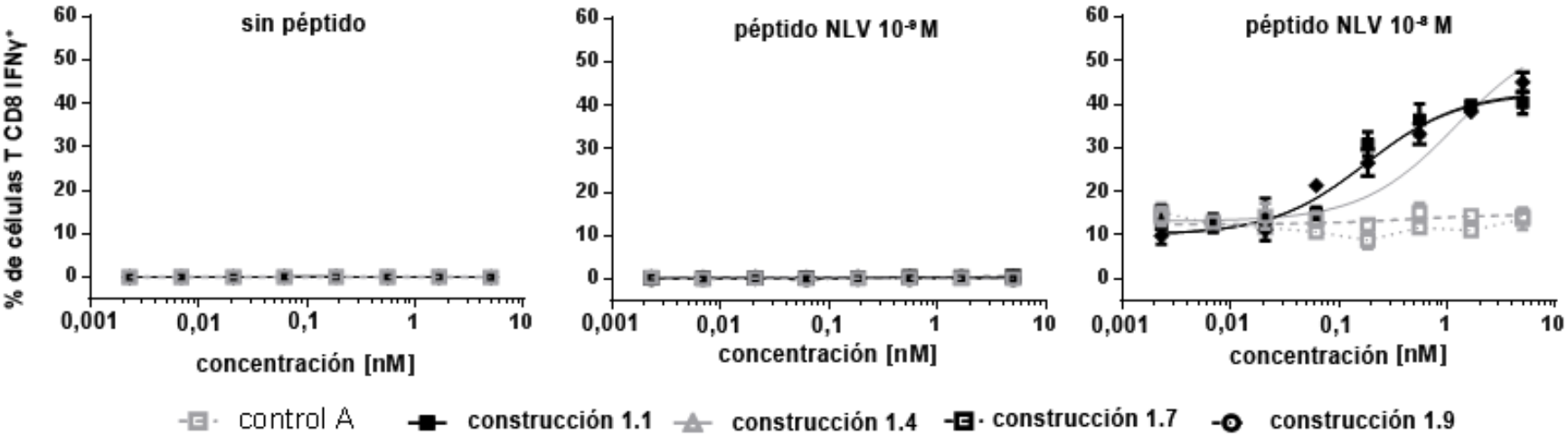


Fig. 23

(23E)

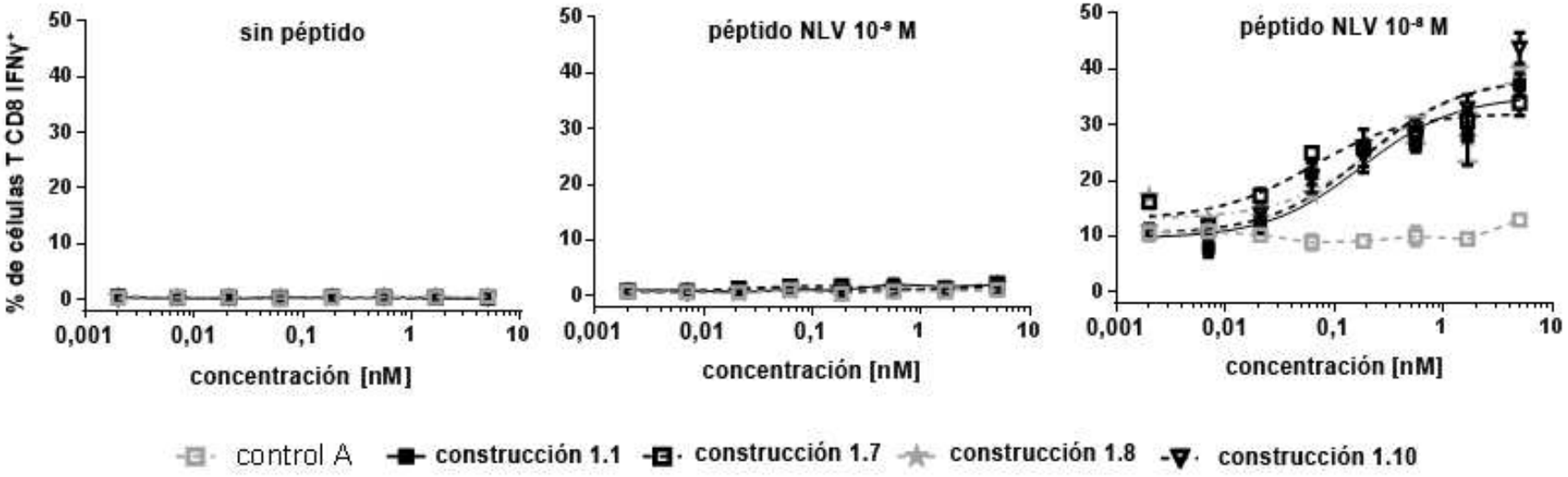
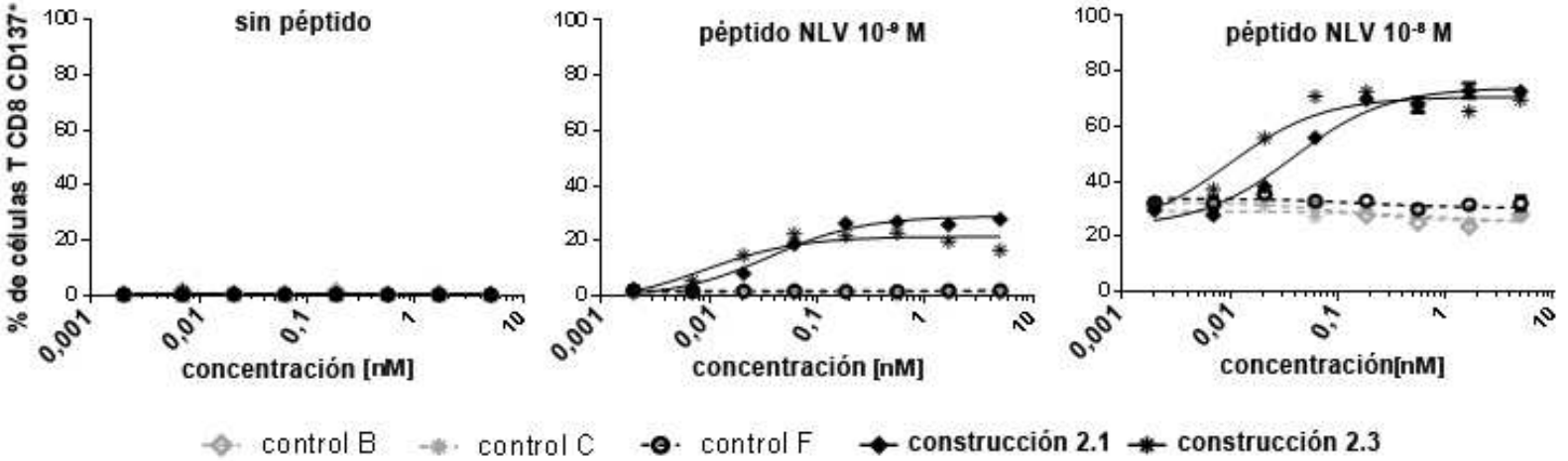

% de células T CD8 IFNγ+
sin péptido
péptido NLV 10-9 M
péptido NLV 10-8 M
concentración [nM]
0,001
0,01
0,1
1
10
0
10
20
30
40
50
control A
construcción 1.1
construcción 1.7
construcción 1.8
construcción 1.10

Fig. 24

(24 A)



(24 B)

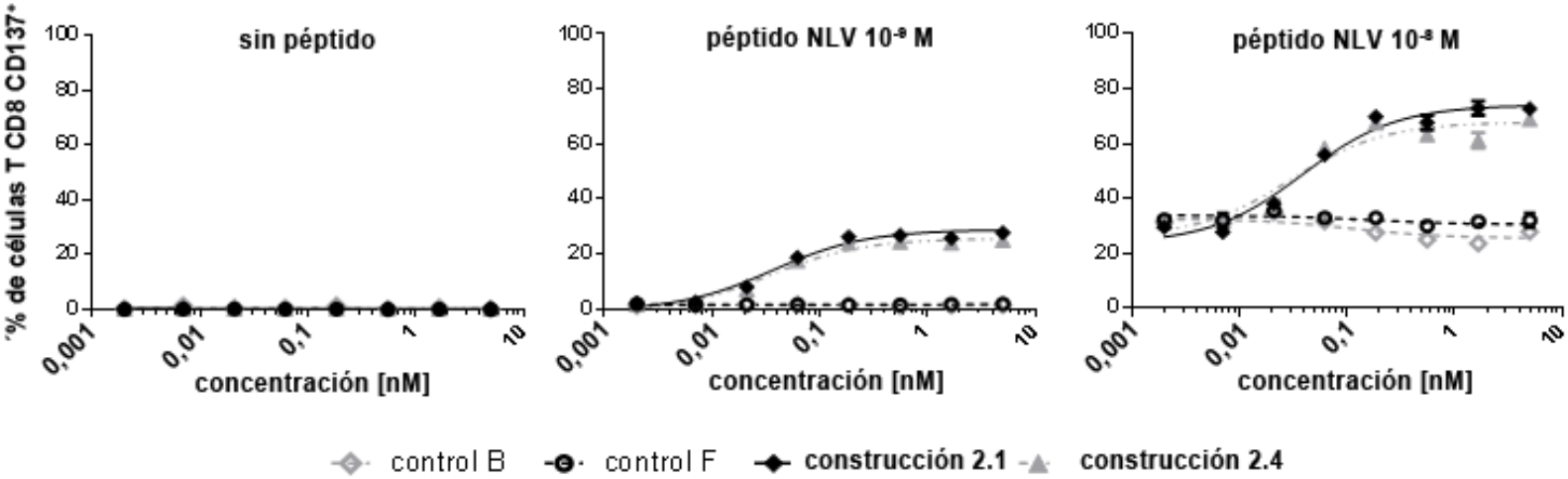
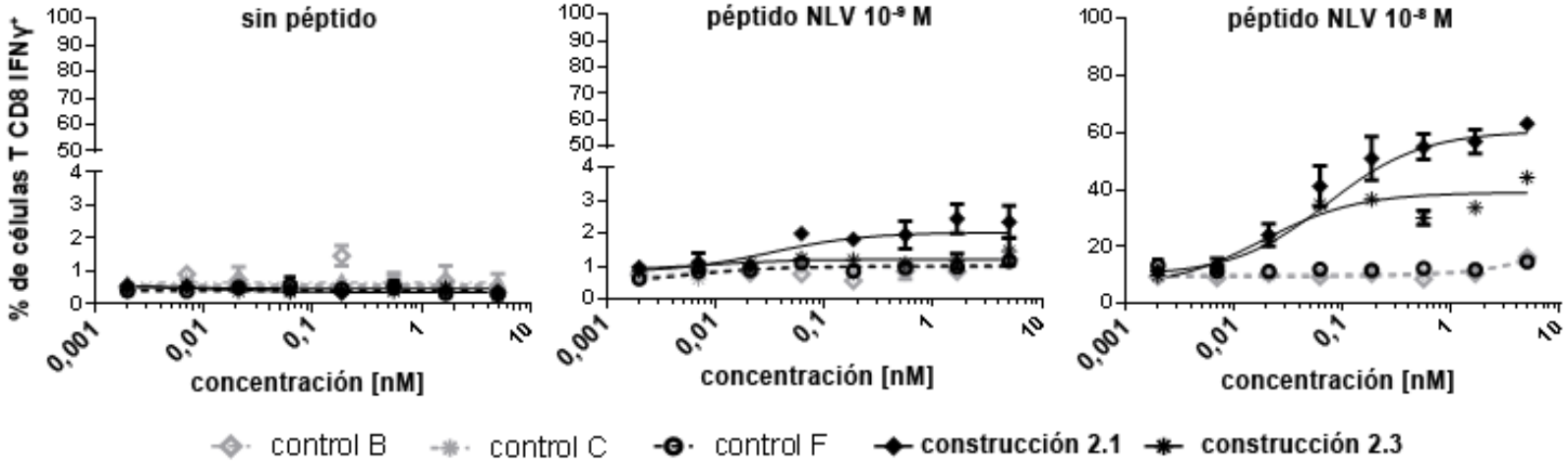
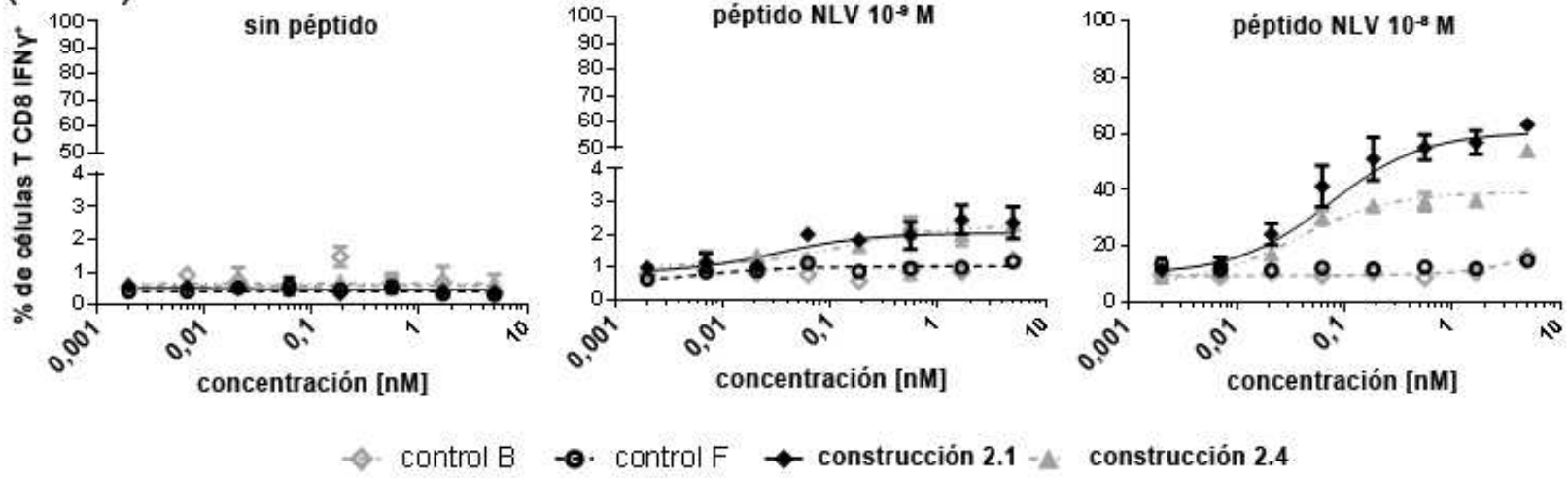


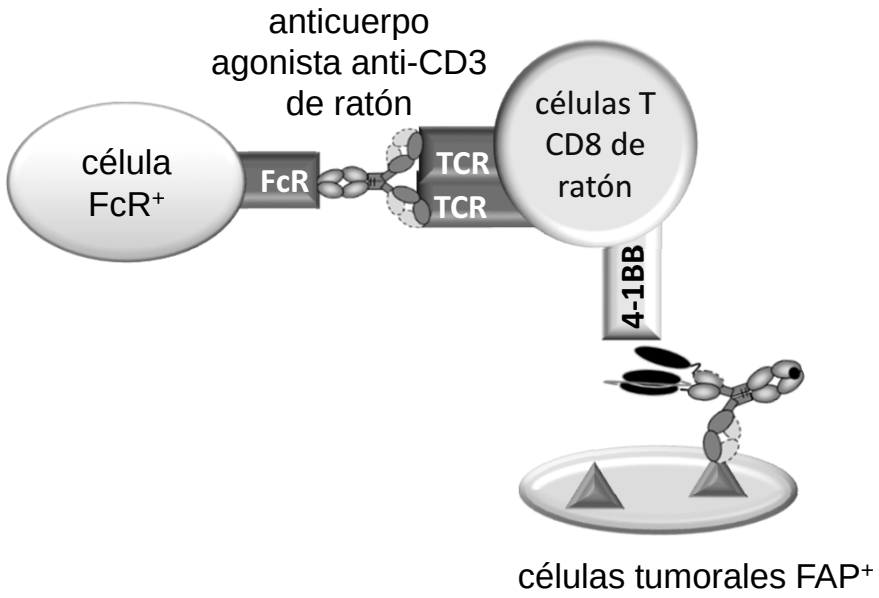
Fig. 25

(25 A)



(25 B)




anticuerpo
agonista anti-CD3
de ratón
célula
FcR+
FcR
TCR
TCR
células T
CD8 de
ratón
4-1BB
células tumorales FAP+

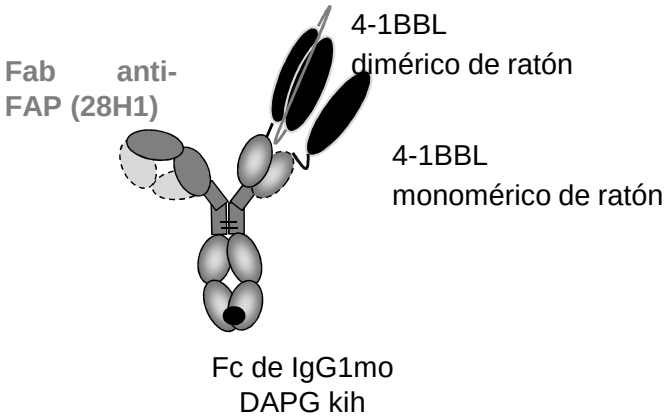

Fab anti-
FAP (28H1)
4-1BBL
dimérico de ratón
4-1BBL
monomérico de ratón
Fc de IgG1mo
DAPG kih

Fig. 26

Fig. 27

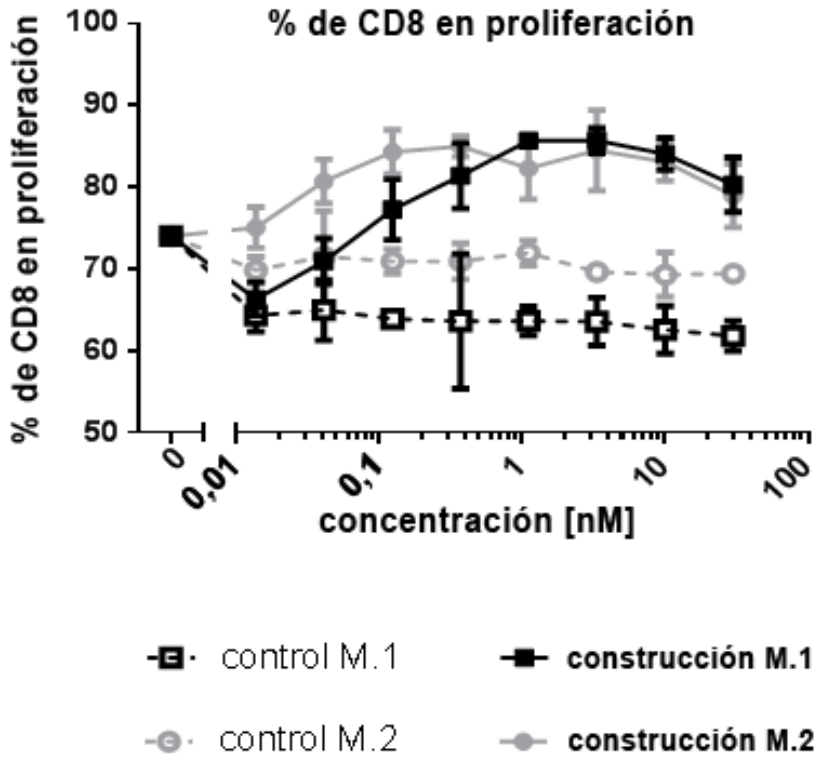

% de CD8 en proliferación
% de CD8 en proliferación
100
90
80
70
60
50
0
0,01
0,1
1
10
100
concentración [nM]
control M.1
construcción M.1
control M.2
construcción M.2

Fig. 28 A

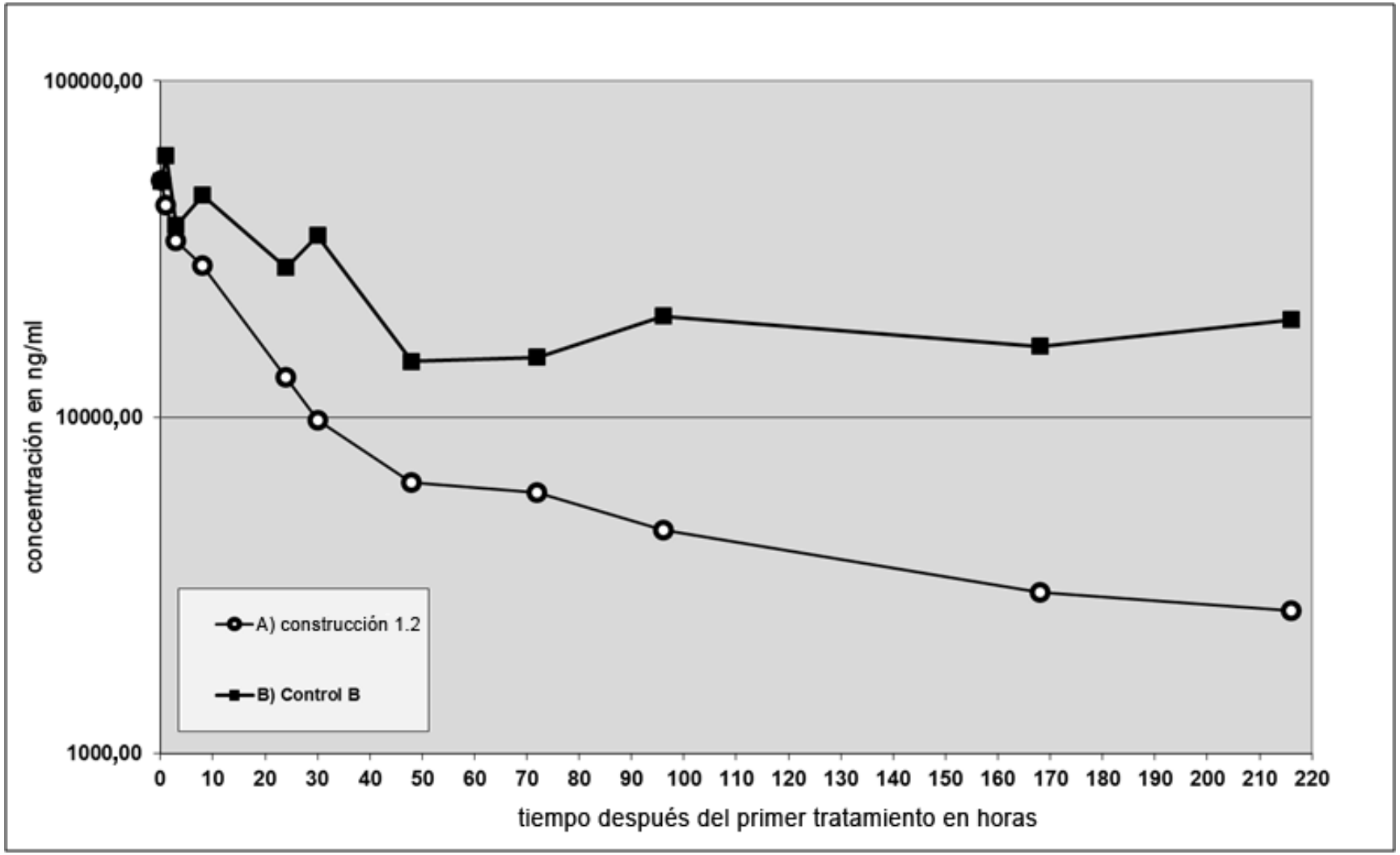

100000,00
10000,00
1000,00
concentración en ng/ml
0
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
190
200
210
220
tiempo después del primer tratamiento en horas
A) construcción 1.2
B) Control B

Fig. 28 B

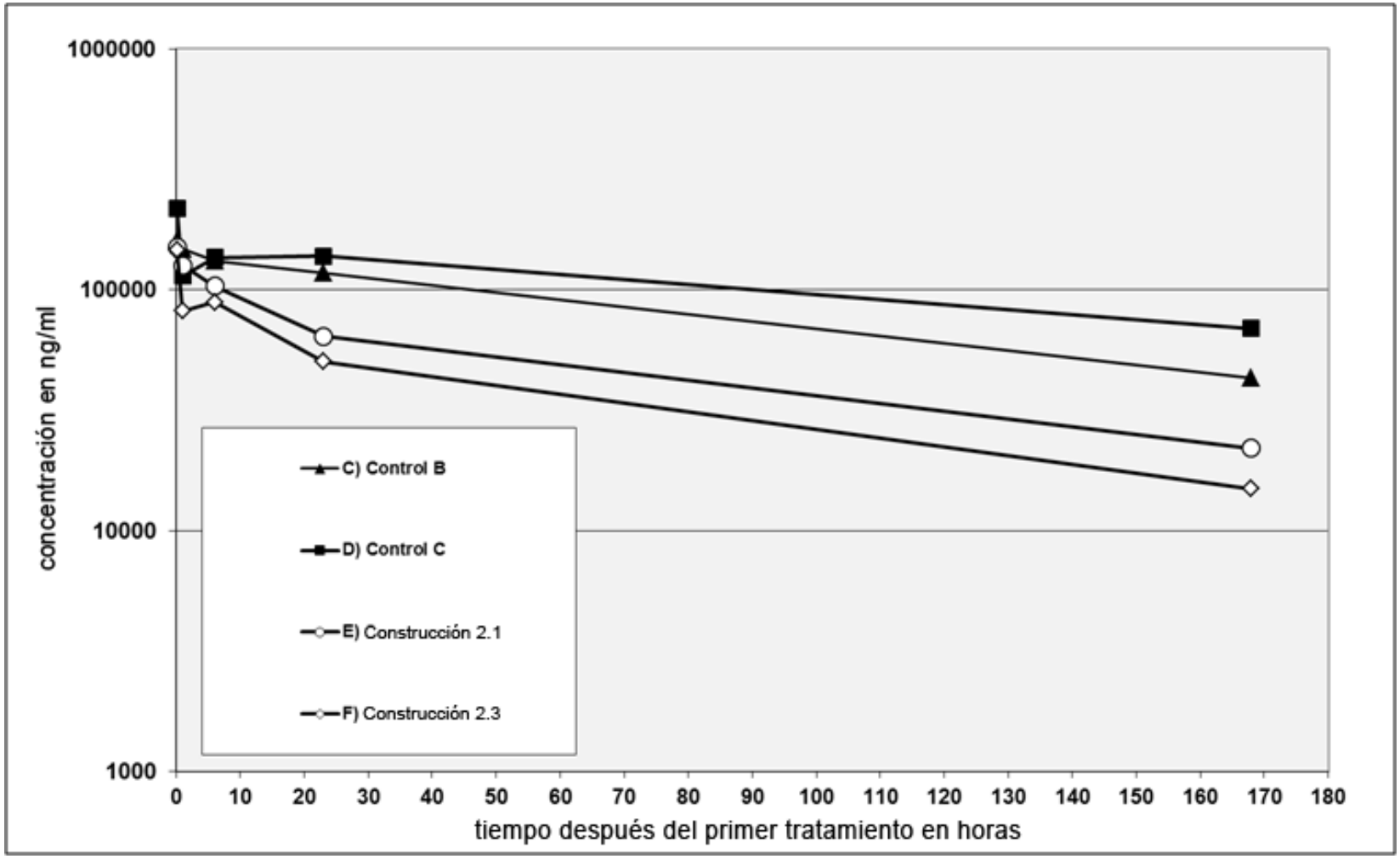

1000000
100000
10000
1000
concentración en ng/ml
0
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
tiempo después del primer tratamiento en horas
C) Control B
D) Control C
E) Construcción 2.1
F) Construcción 2.3

Fig. 28C

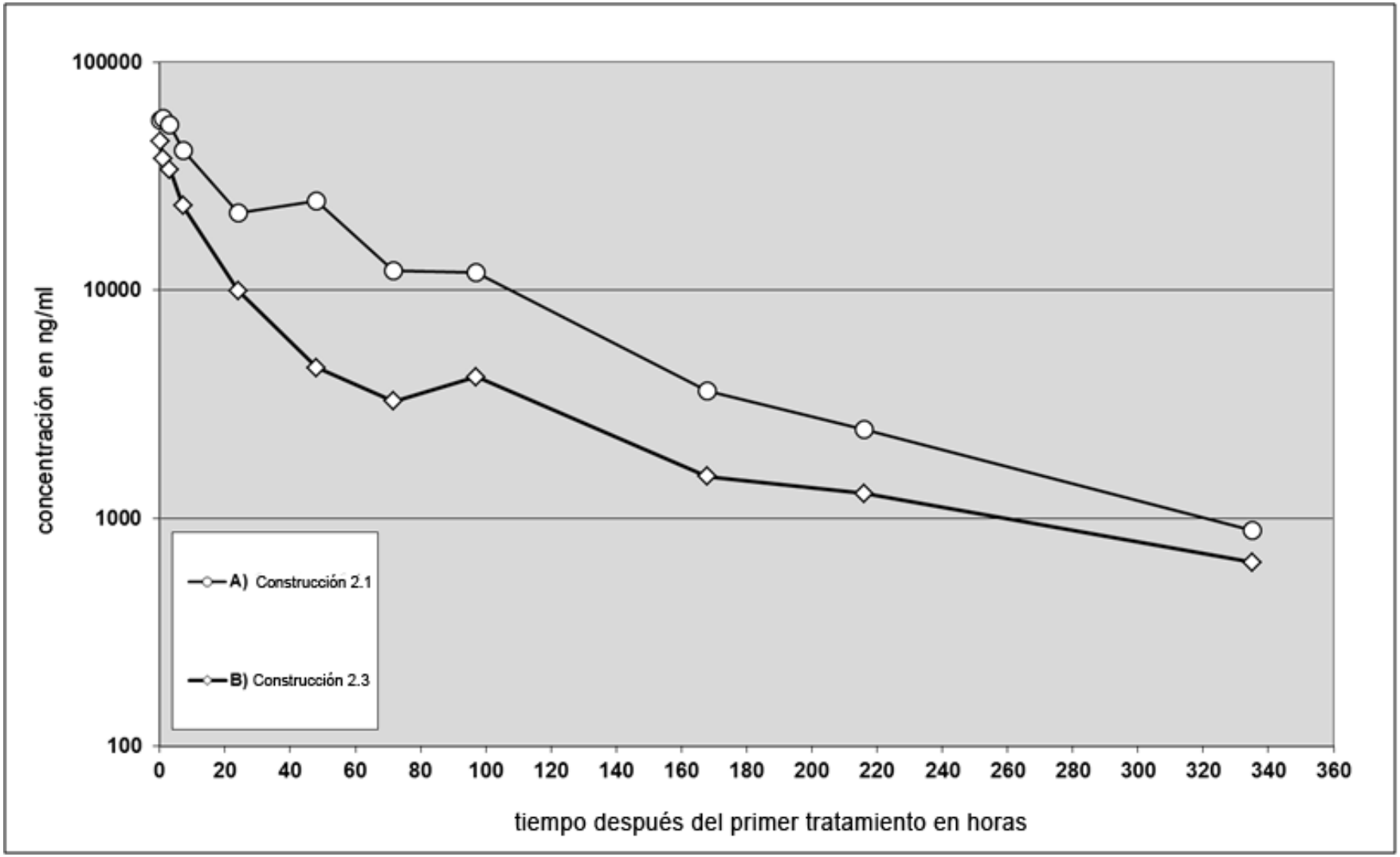
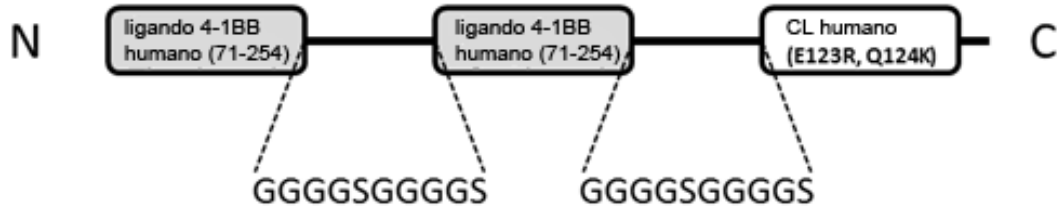
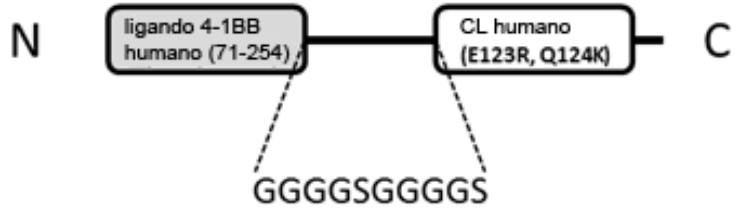

100000
10000
1000
100
concentración en ng/ml
0
20
40
60
80
100
120
140
160
180
200
220
240
260
280
300
320
340
360
tiempo después del primer tratamiento en horas
A) Construcción 2.1
B) Construcción 2.3

Fig. 29

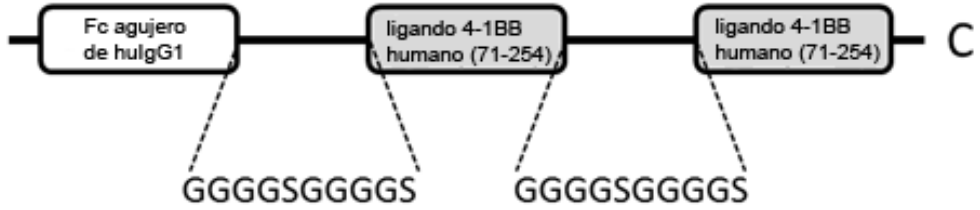
(29 A)



(29 B)



(29C)



(29D)

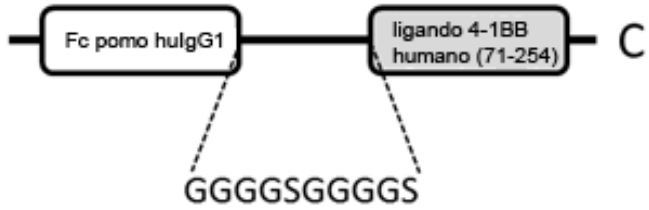


Fig. 30

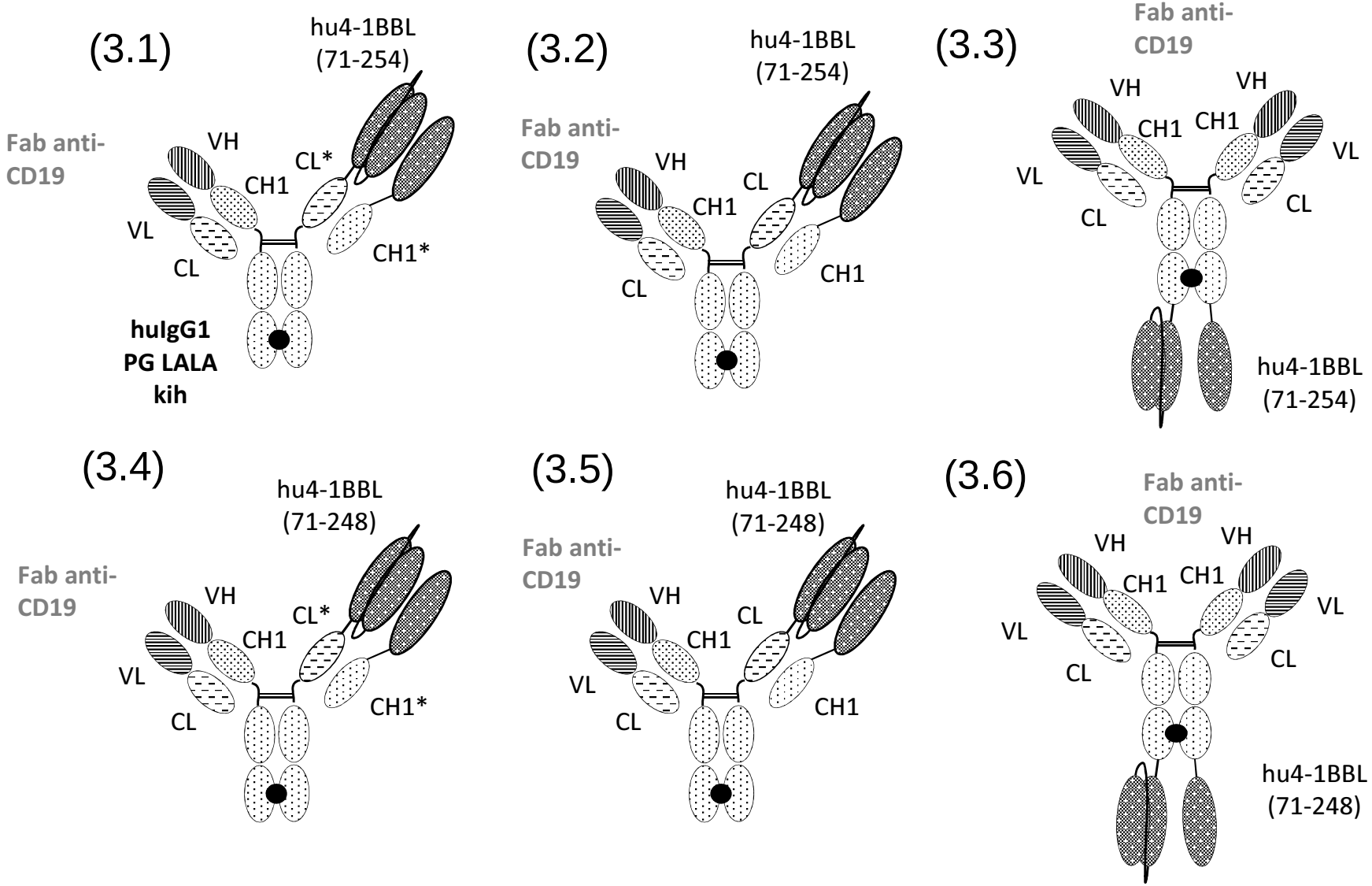
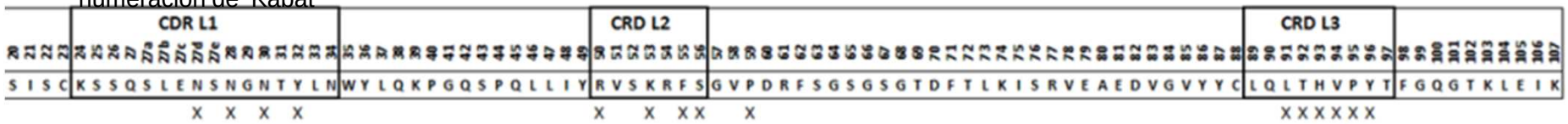

(3.1)
hu4-1BBL
(71-254)
Fab anti-
CD19
VH
CH1
CL*
VL
CL
CH1*
huIgG1
PG LALA
kih
(3.2)
hu4-1BBL
(71-254)
Fab anti-
CD19
VH
CH1
CL
CL
CH1
(3.3)
Fab anti-
CD19
VH
VH
CH1
CH1
VL
VL
CL
CL
hu4-1BBL
(71-254)
(3.4)
hu4-1BBL
(71-248)
Fab anti-
CD19
VH
CH1
CL*
VL
CL
CH1*
(3.5)
hu4-1BBL
(71-248)
Fab anti-
CD19
VH
CH1
CL
VL
CL
CH1
(3.6)
Fab anti-
CD19
VH
VH
CH1
CH1
VL
VL
CL
CL
hu4-1BBL
(71-248)

Fig. 31 A

CDRs de acuerdo con la numeración de Kabat



secuencia de VL de 8B8

secuencia de VH de 8B8

X = posiciones aleatorizadas

Fig. 31 B

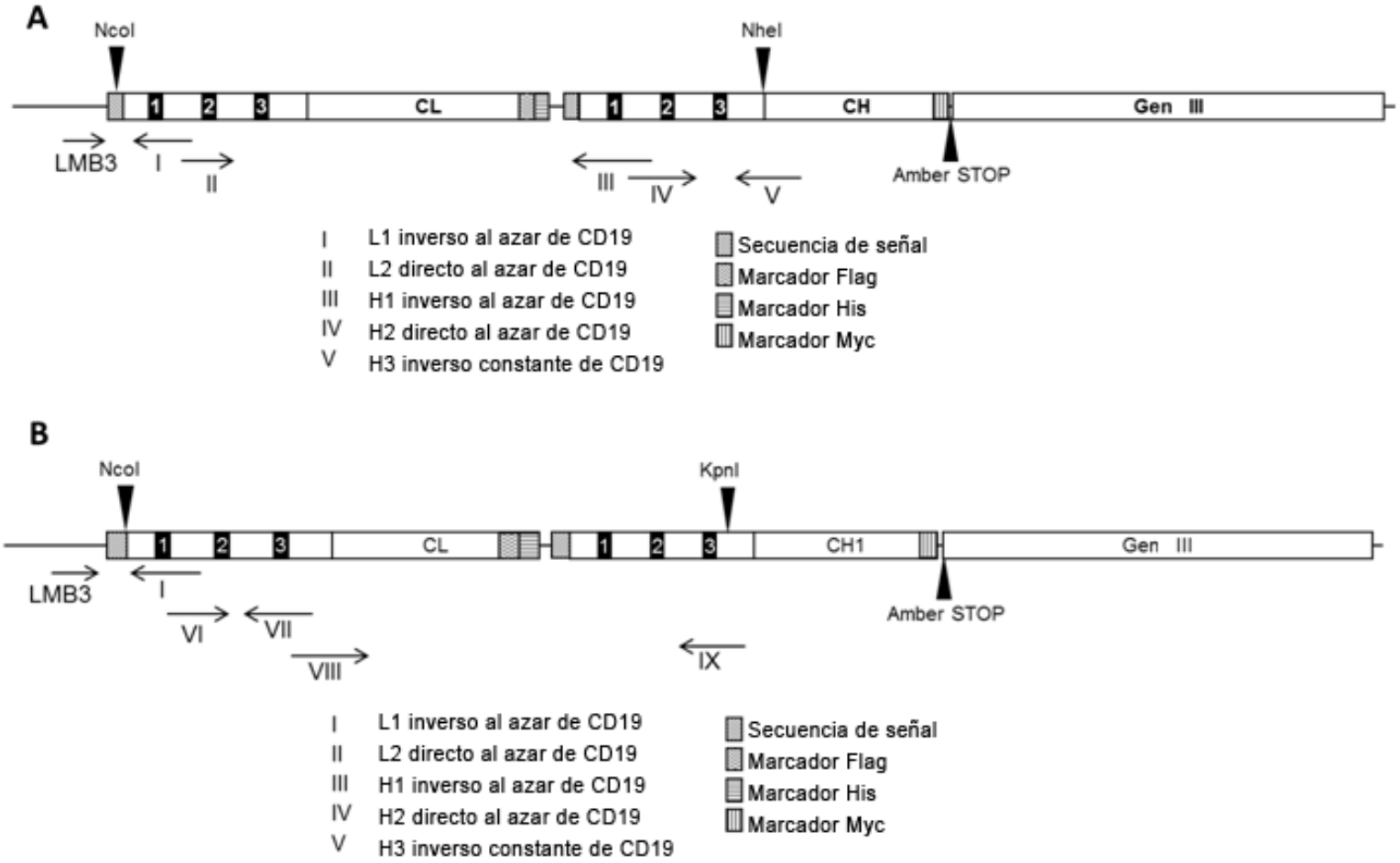

A
NcoI
NheI
1
2
3
CL
CH
Gen III
LMB3
I
II
III
IV
V
Amber STOP
I L1 inverso al azar de CD19
II L2 directo al azar de CD19
III H1 inverso al azar de CD19
IV H2 directo al azar de CD19
V H3 inverso constante de CD19
Secuencia de señal
Marcador Flag
Marcador His
Marcador Myc
B
NcoI
KpnI
CL
CH1
Gen III
LMB3
I
VI
VII
VIII
IX
Amber STOP
I L1 inverso al azar de CD19
II L2 directo al azar de CD19
III H1 inverso al azar de CD19
IV H2 directo al azar de CD19
V H3 inverso constante de CD19
Secuencia de señal
Marcador Flag
Marcador His
Marcador Myc

Fig. 32

```
                                LCDR1                                LCDR2                                LCDR3
CD19 LC   DIVMTQTPLSLSVTPGQPASISCKSSQSLENSNGNTYLNWYLQKPGQSPQLLIYRVSKRFSGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCLQLTHVPYTFGQGTKLEIK
5H09      ........................S.T.......................................................IDY.V..........
7H07      ........................T.T.......................................................A..I...........
2B03      ........................T.T.......................................................................
2B11      ........................T.T.T.....................................................LED............
5A07      ........................T.T.......................................................PG.Y.G..........
5B08      ........................T.T.......................................................DSY.N..........
5D08      ........................T.T.......................................................E...........

                                HCDR1                                HCDR2                                HCDR3
CD19 HC   QVQLVQSGAEVKKPGASVKVSCKASGYTFTDYIMHWVRQAPGQGLEWMGYINPYNDGSKYTEKFQGRVTMTSDTSISTAYMELSRLRSDDTAVYYCARGTYYYGSALFDYWGQGTTVTVSS
5H09      ..............................................................................................................
7H07      ..............................................................................................E...............
2B03      ...............................T..............................................................PD..............
2B11      ..............................................................................................PQ..............
5A07      ..............................................................................................................
5B08      ..............................................................................................PQ..............
5D08      ..............................................................................................E...............
```

Fig. 33

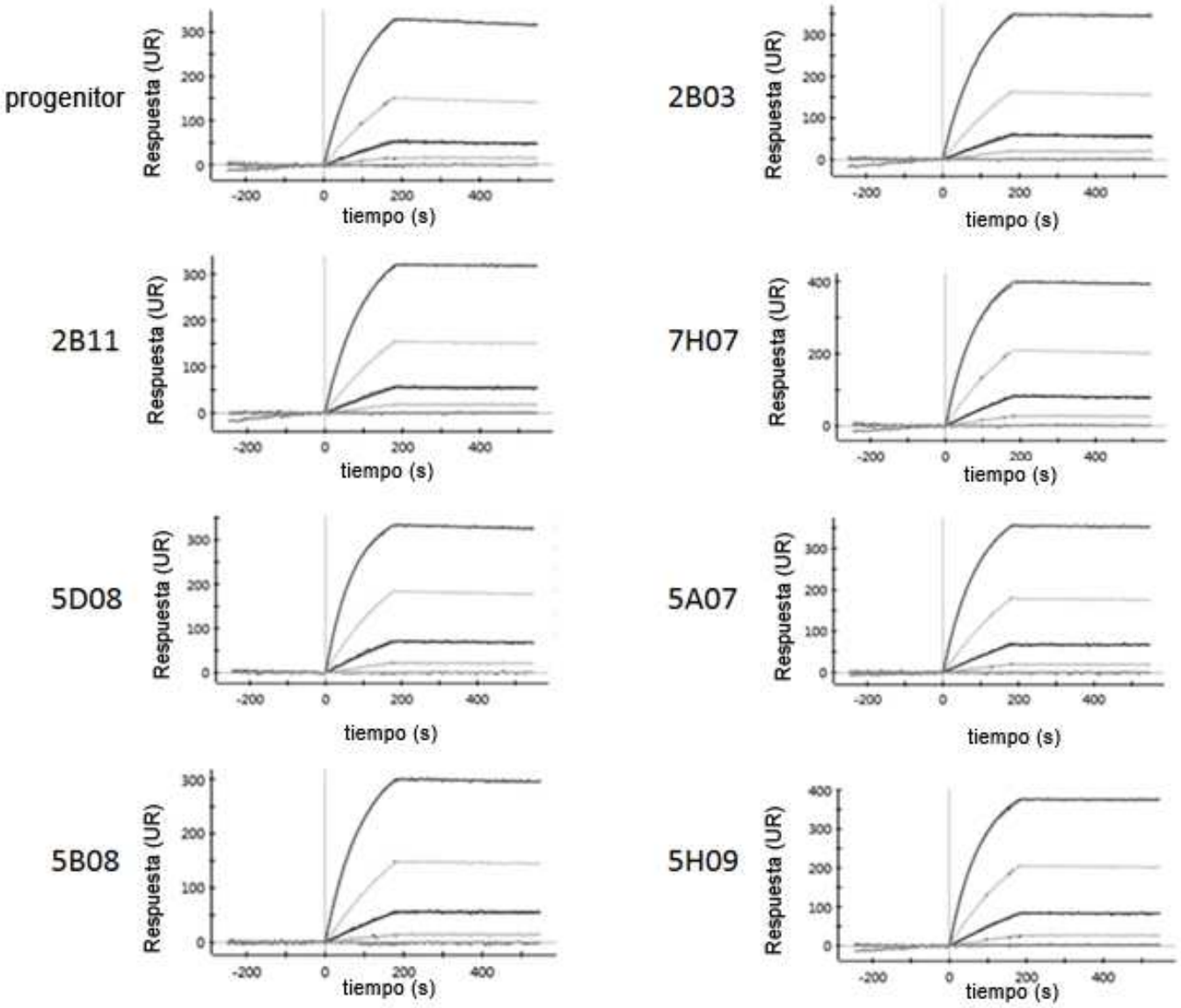

progenitor
2B03
2B11
7H07
5D08
5A07
5B08
5H09
Respuesta (UR)
tiempo (s)

Fig. 34

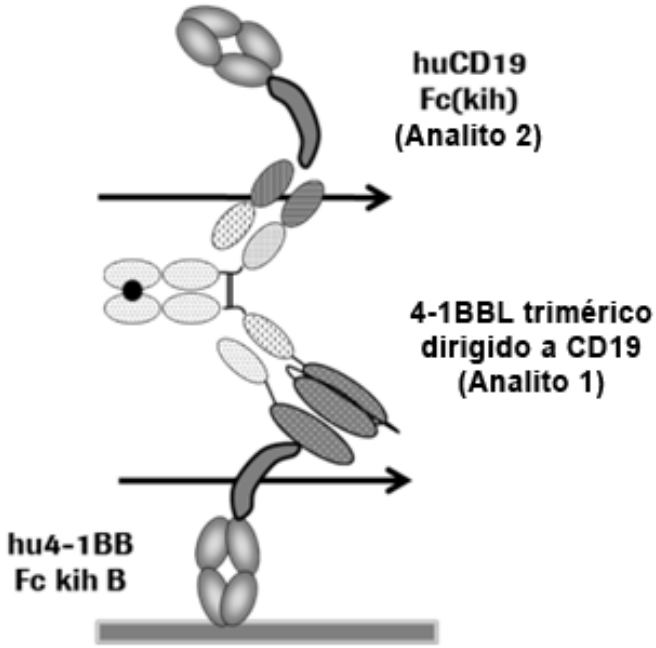

huCD19
Fc(kih)
(Analito 2)
4-1BBL trimérico
dirigido a CD19
(Analito 1)
hu4-1BB
Fc kih B

Fig. 35

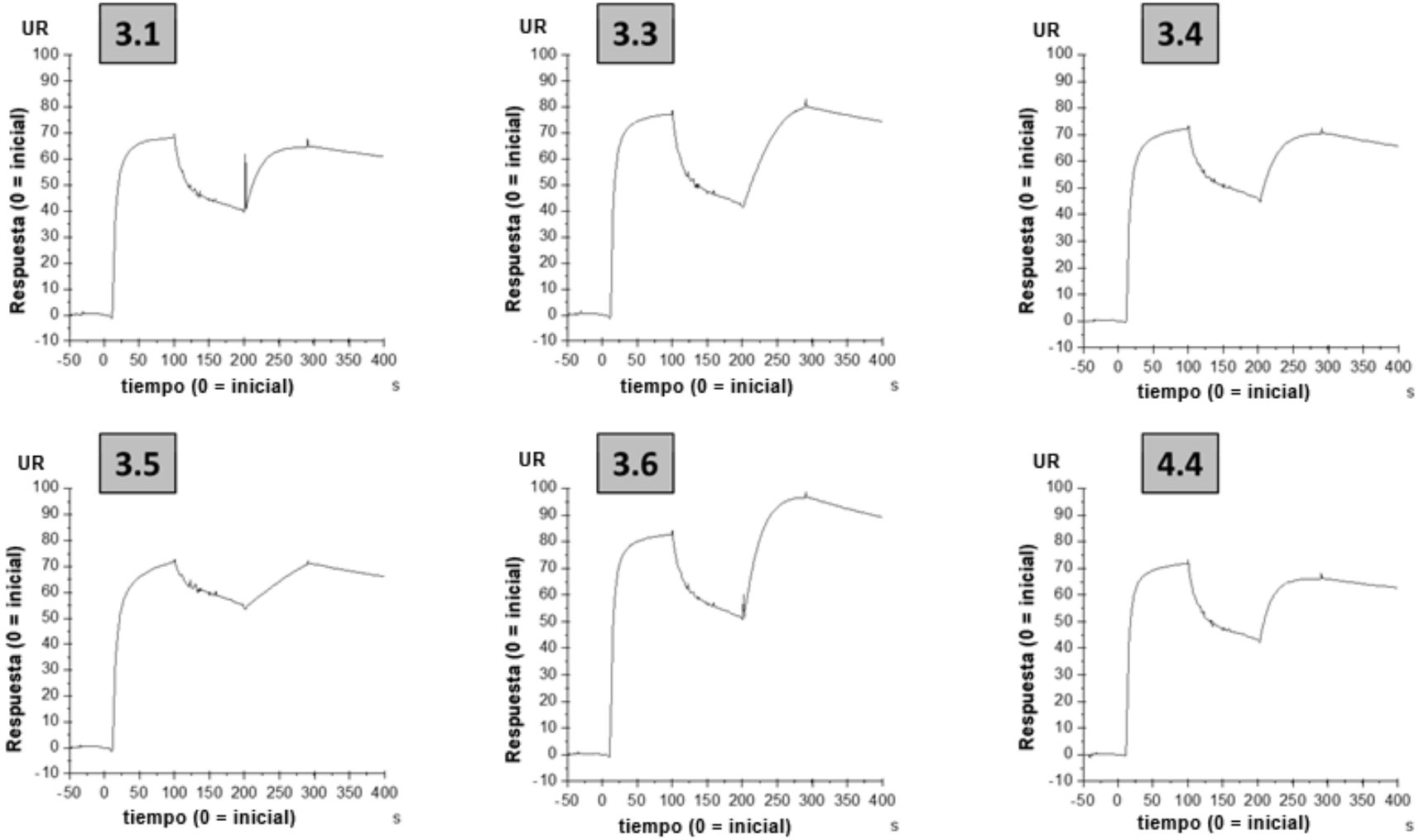


Fig. 36 A

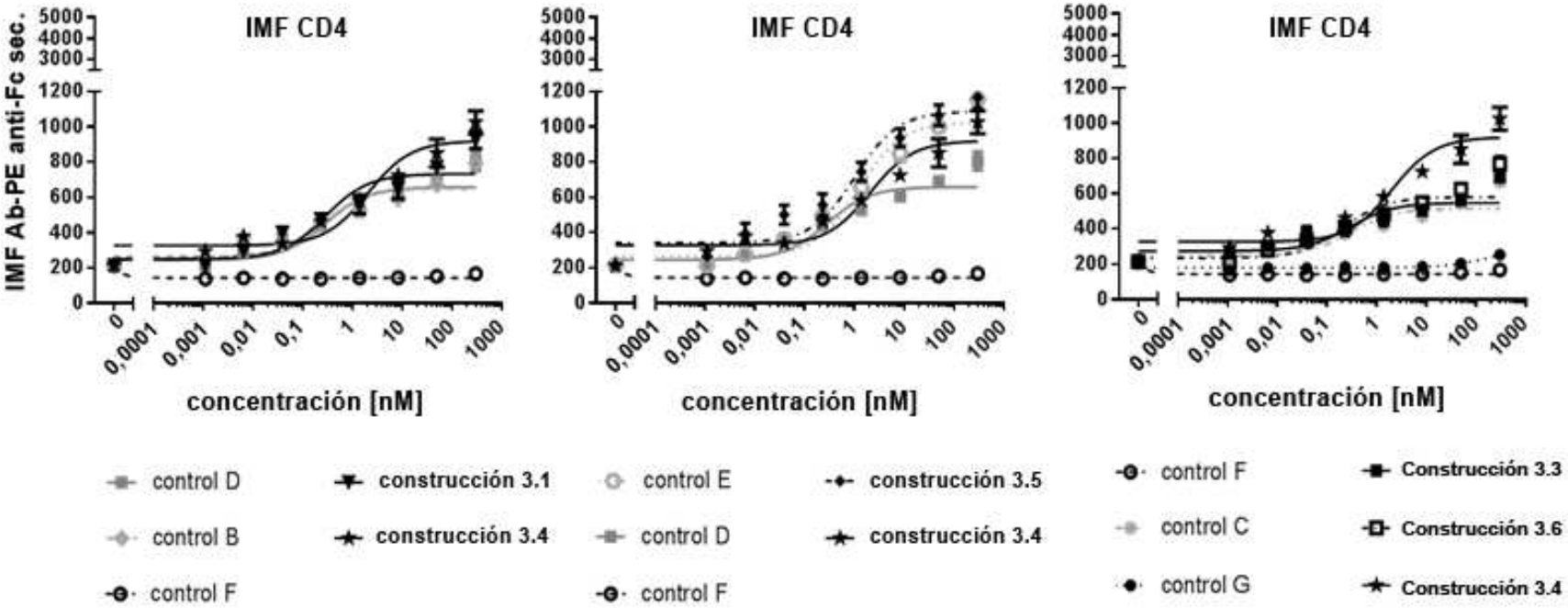

IMF CD4
IMF Ab-PE anti-Fc sec.
5000
4000
3000
1200
1000
800
600
400
200
0
0
0,0001
0,001
0,01
0,1
1
10
100
1000
concentración [nM]
control D
construcción 3.1
control B
construcción 3.4
control F
IMF CD4
concentración [nM]
control E
construcción 3.5
control D
construcción 3.4
control F
IMF CD4
concentración [nM]
control F
Construcción 3.3
control C
Construcción 3.6
control G
Construcción 3.4

Fig. 36B

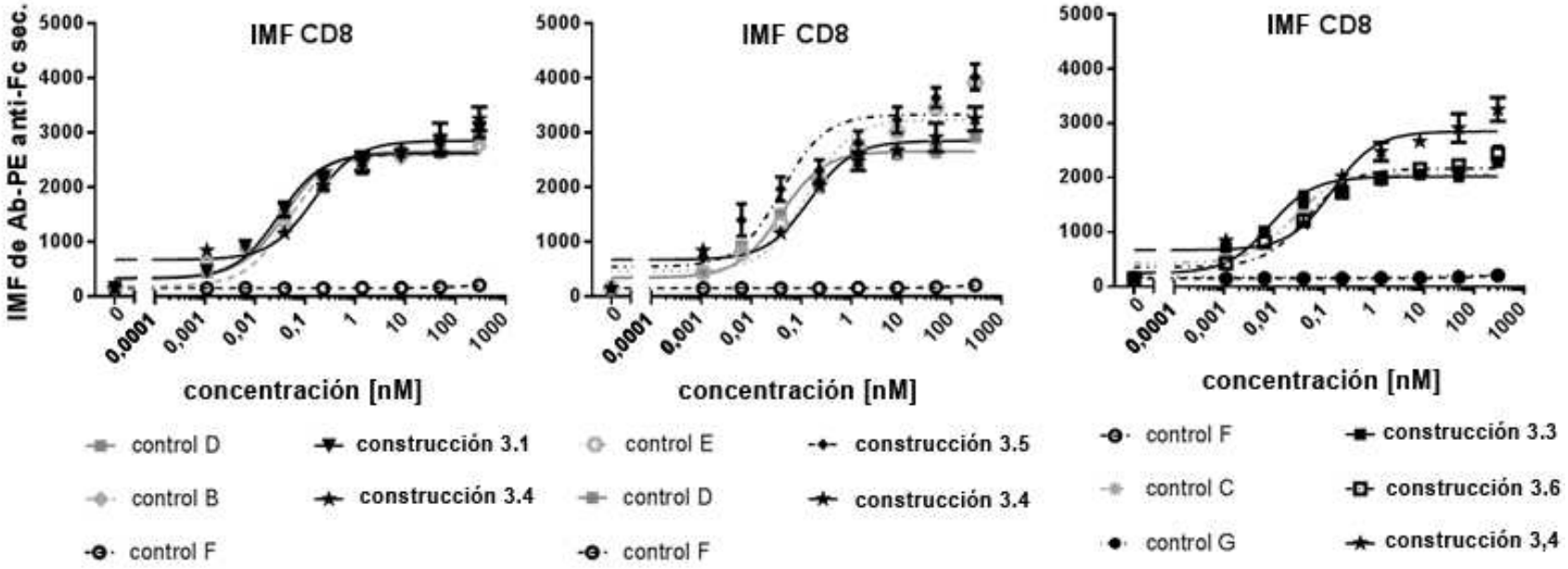

IMF de Ab-PE anti-Fc sec.
IMF CD8
5000
4000
3000
2000
1000
0
0
0,0001
0,001
0,01
0,1
1
10
100
1000
concentración [nM]
control D
construcción 3.1
control B
construcción 3.4
control F
IMF CD8
concentración [nM]
control E
construcción 3.5
control D
construcción 3.4
control F
IMF CD8
concentración [nM]
control F
construcción 3.3
control C
construcción 3.6
control G
construcción 3,4

Fig. 37A

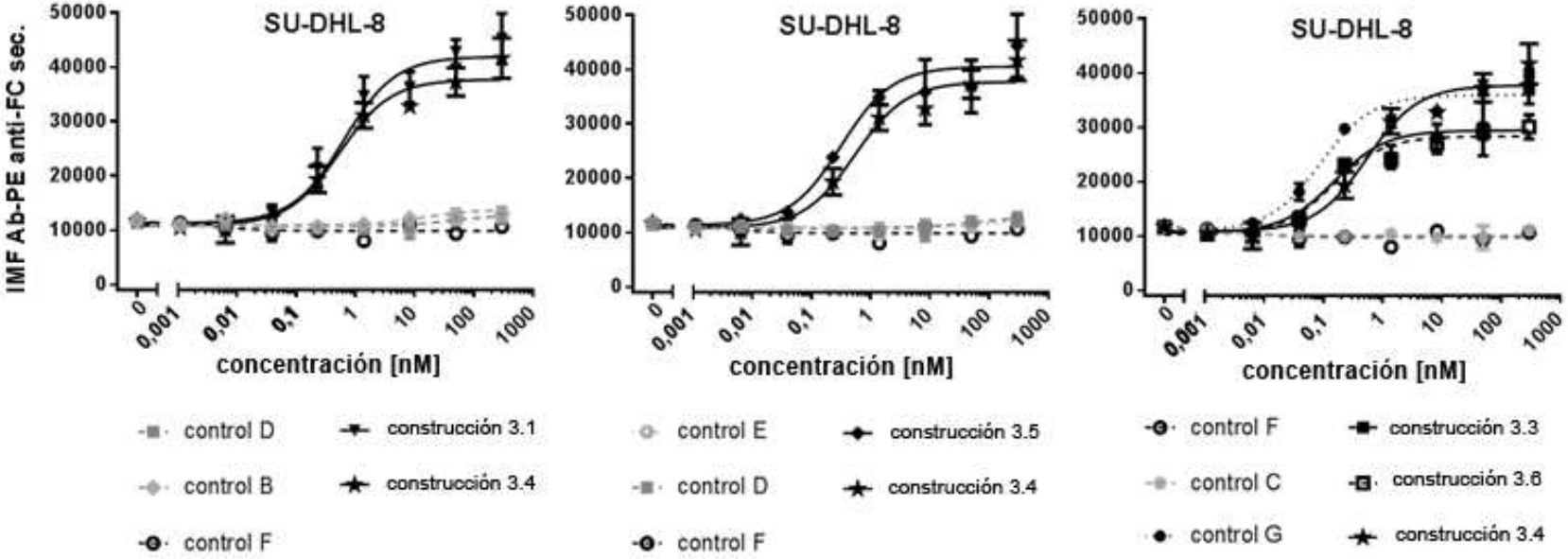

SU-DHL-8
IMF Ab-PE anti-FC sec.
50000
40000
30000
20000
10000
0
0
0,001
0,01
0,1
1
10
100
1000
concentración [nM]
control D
construcción 3.1
control B
construcción 3.4
control F
SU-DHL-8
concentración [nM]
control E
construcción 3.5
control D
construcción 3.4
control F
SU-DHL-8
concentración [nM]
control F
construcción 3.3
control C
construcción 3.6
control G
construcción 3.4

Fig. 37 B

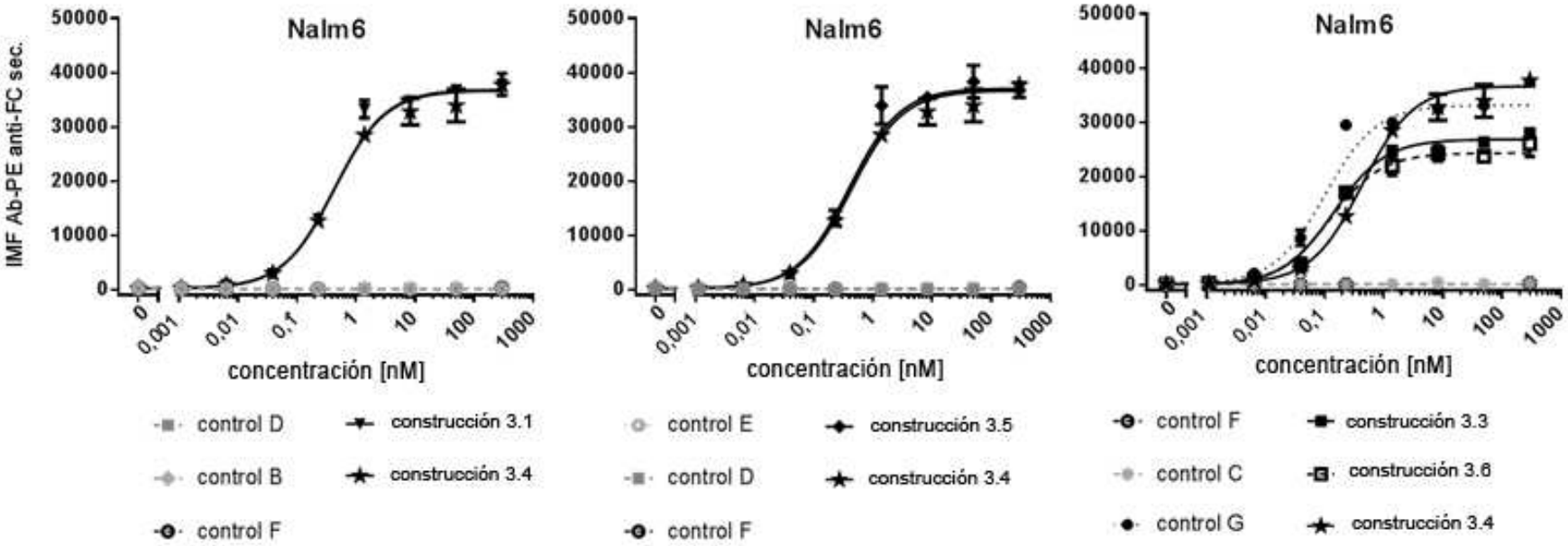

Nalm6
IMF Ab-PE anti-FC sec.
50000
40000
30000
20000
10000
0
0
0,001
0,01
0,1
1
10
100
1000
concentración [nM]
control D
construcción 3.1
control B
construcción 3.4
control F
Nalm6
concentración [nM]
control E
construcción 3.5
control D
construcción 3.4
control F
Nalm6
concentración [nM]
control F
construcción 3.3
control C
construcción 3.6
control G
construcción 3.4

Fig. 37C

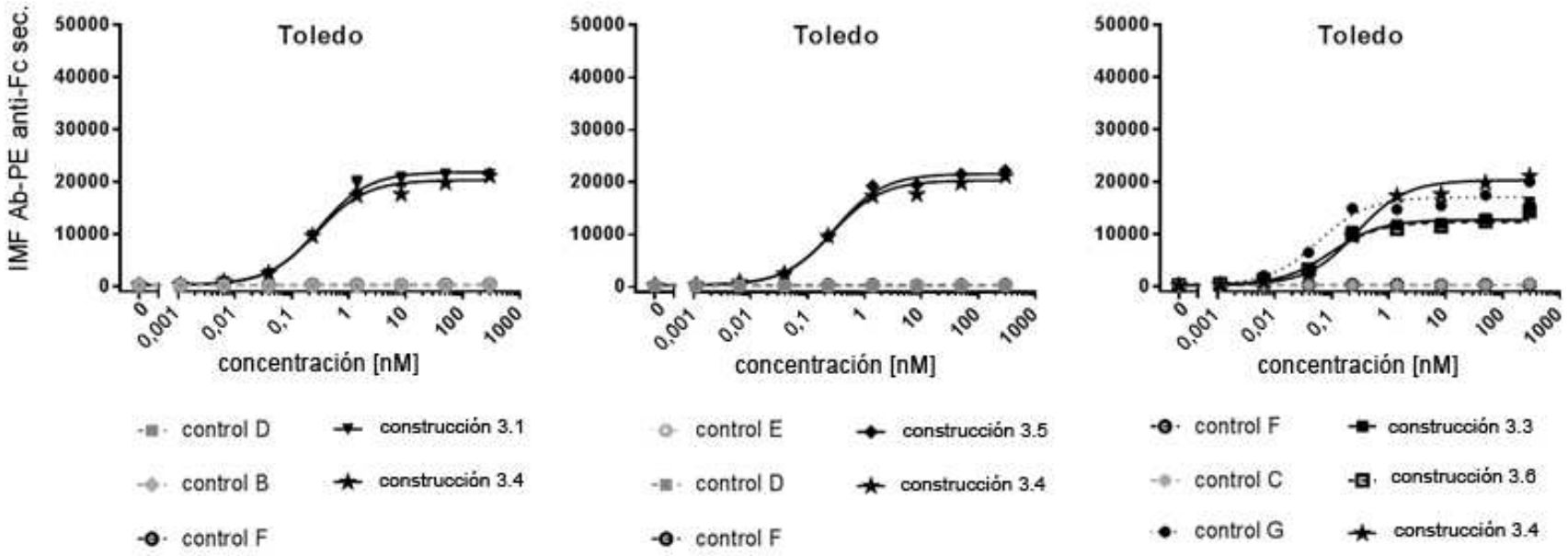

IMF Ab-PE anti-Fc sec.
Toledo
50000
40000
30000
20000
10000
0
0
0,001
0,01
0,1
1
10
100
1000
concentración [nM]
control D
construcción 3.1
control B
construcción 3.4
control F
Toledo
concentración [nM]
control E
construcción 3.5
control D
construcción 3.4
control F
Toledo
concentración [nM]
control F
construcción 3.3
control C
construcción 3.6
control G
construcción 3.4

Fig. 37D

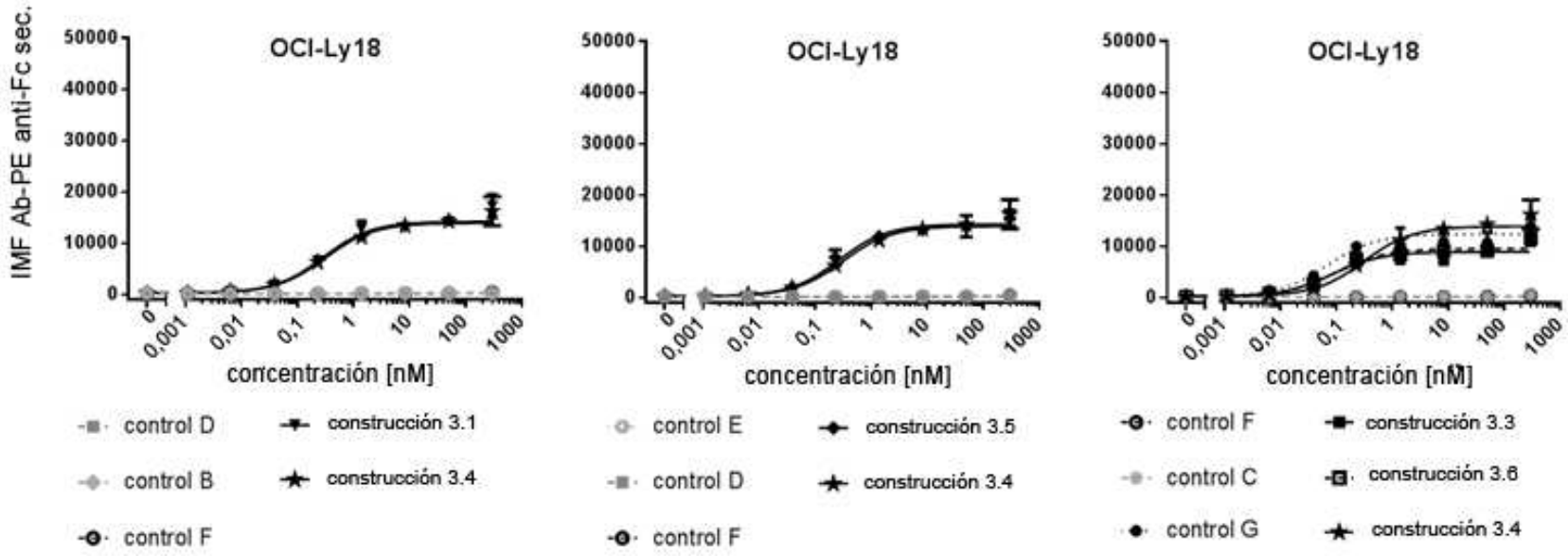

IMF Ab-PE anti-Fc sec.
OCI-Ly18
50000
40000
30000
20000
10000
0
0
0,001
0,01
0,1
1
10
100
1000
concentración [nM]
control D
construcción 3.1
control B
construcción 3.4
control F
OCI-Ly18
concentración [nM]
control E
construcción 3.5
control D
construcción 3.4
control F
OCI-Ly18
concentración [nM]
control F
construcción 3.3
control C
construcción 3.6
control G
construcción 3.4

Fig. 38

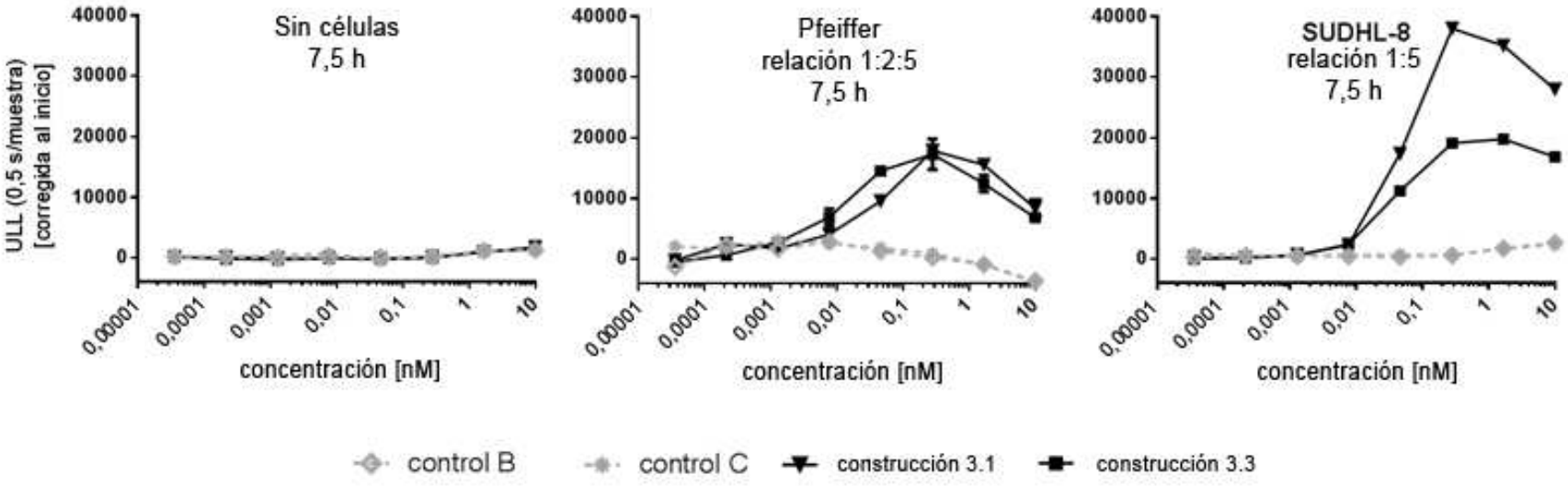

ULL (0,5 s/muestra)
[corregida al inicio]
Sin células
7,5 h
Pfeiffer
relación 1:2:5
7,5 h
SUDHL-8
relación 1:5
7,5 h
40000
30000
20000
10000
0
0,00001
0,0001
0,001
0,01
0,1
1
10
concentración [nM]
control B
control C
construcción 3.1
construcción 3.3

Fig. 39

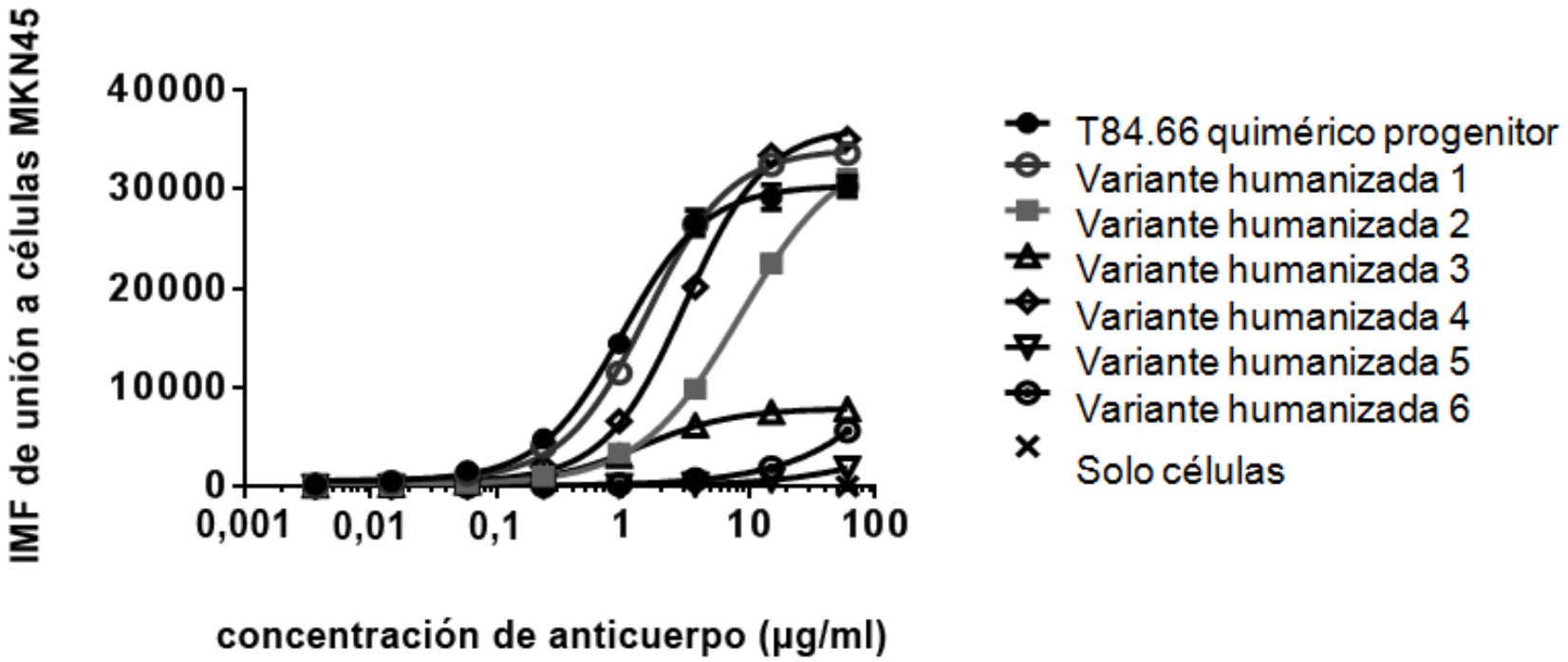

IMF de unión a células MKN45
40000
30000
20000
10000
0
0,001
0,01
0,1
1
10
100
concentración de anticuerpo (µg/ml)
T84.66 quimérico progenitor
Variante humanizada 1
Variante humanizada 2
Variante humanizada 3
Variante humanizada 4
Variante humanizada 5
Variante humanizada 6
Solo células

Fig. 40

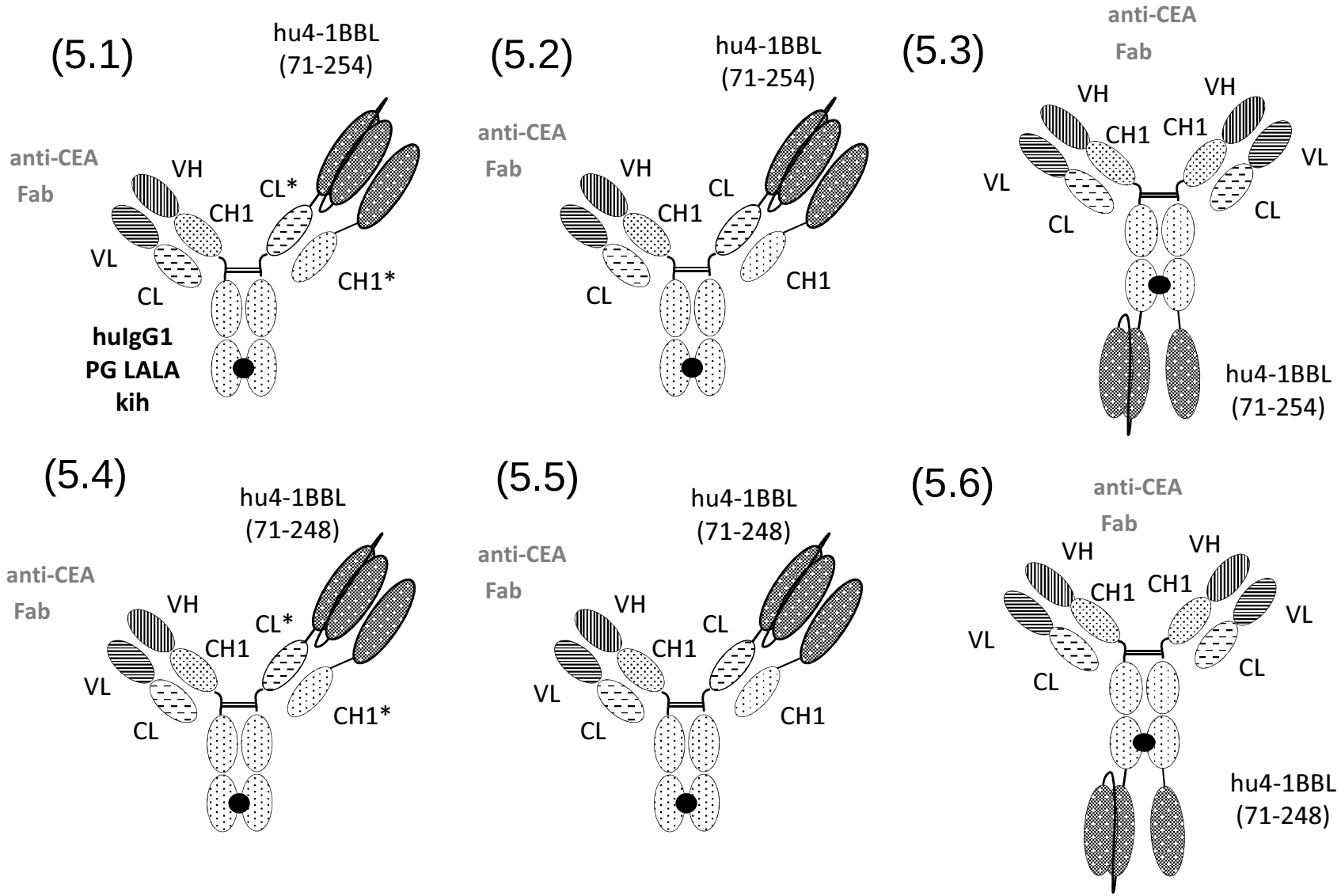
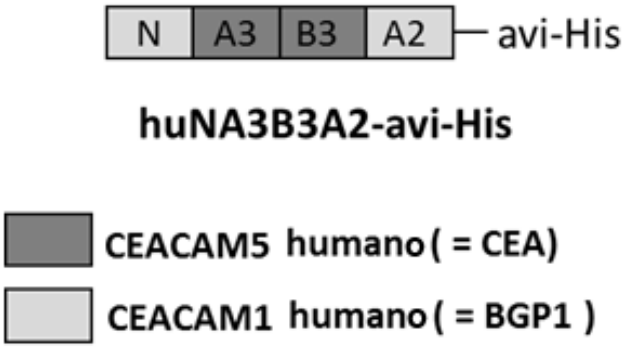

(5.1)
hu4-1BBL
(71-254)
anti-CEA
Fab
VH
CL*
CH1
VL
CL
CH1*
huIgG1
PG LALA
kih
(5.2)
hu4-1BBL
(71-254)
anti-CEA
Fab
VH
CL
CH1
CL
CH1
(5.3)
anti-CEA
Fab
VH
VH
CH1
CH1
VL
VL
CL
CL
hu4-1BBL
(71-254)
(5.4)
hu4-1BBL
(71-248)
anti-CEA
Fab
VH
CL*
CH1
VL
CL
CH1*
(5.5)
hu4-1BBL
(71-248)
anti-CEA
Fab
VH
CL
CH1
VL
CL
CH1
(5.6)
anti-CEA
Fab
VH
VH
CH1
CH1
VL
VL
CL
CL
hu4-1BBL
(71-248)

Fig. 41

(41 A)



(41 B)

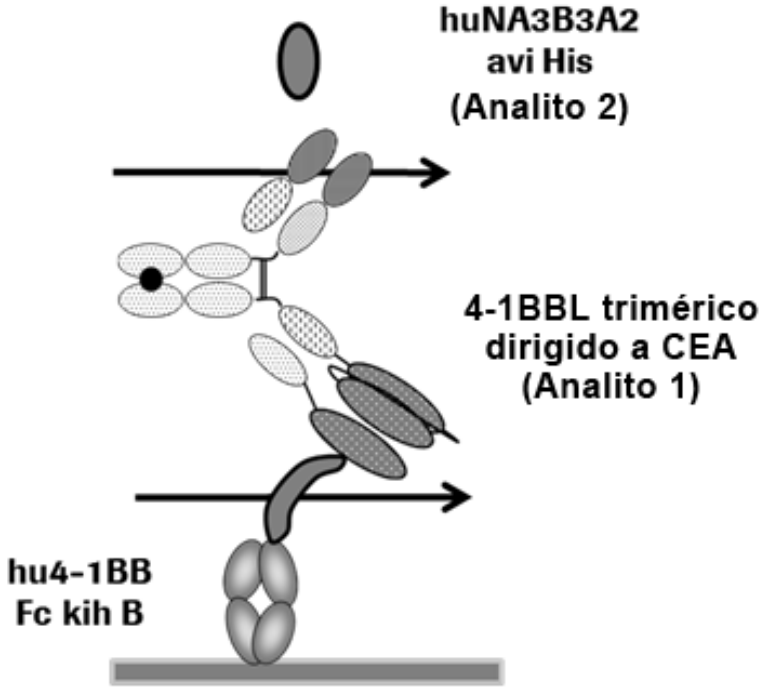
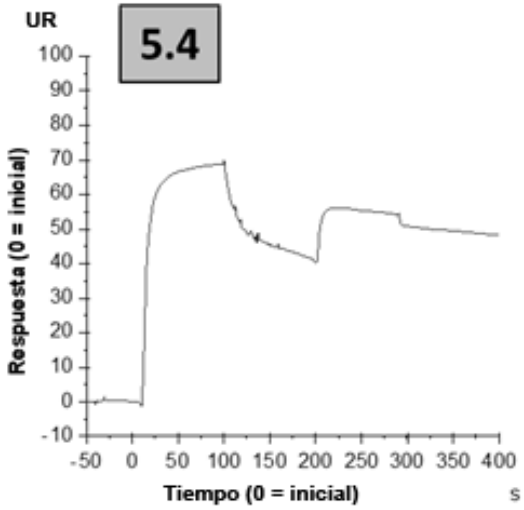
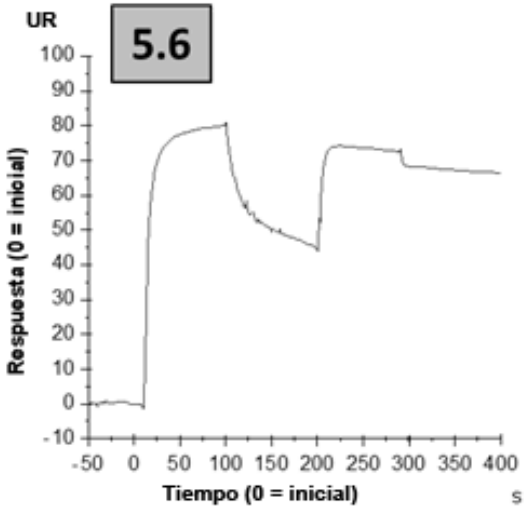
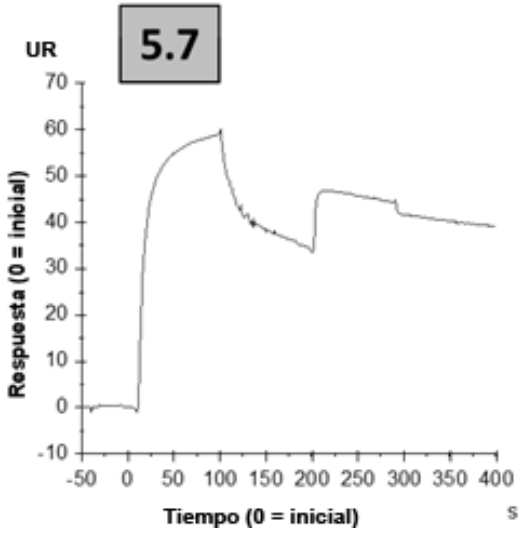


Fig. 42


5.4
UR
Respuesta (0 = inicial)
Tiempo (0 = inicial)
s


5.6
UR
Respuesta (0 = inicial)
Tiempo (0 = inicial)
s


5.7
UR
Respuesta (0 = inicial)
Tiempo (0 = inicial)
s

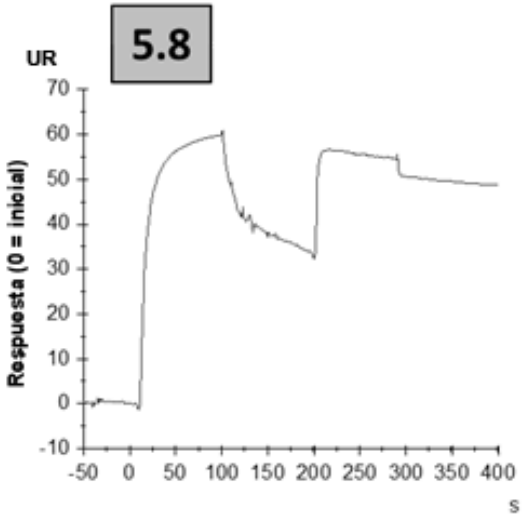

5.8
UR
Respuesta (0 = inicial)
s

Fig. 43

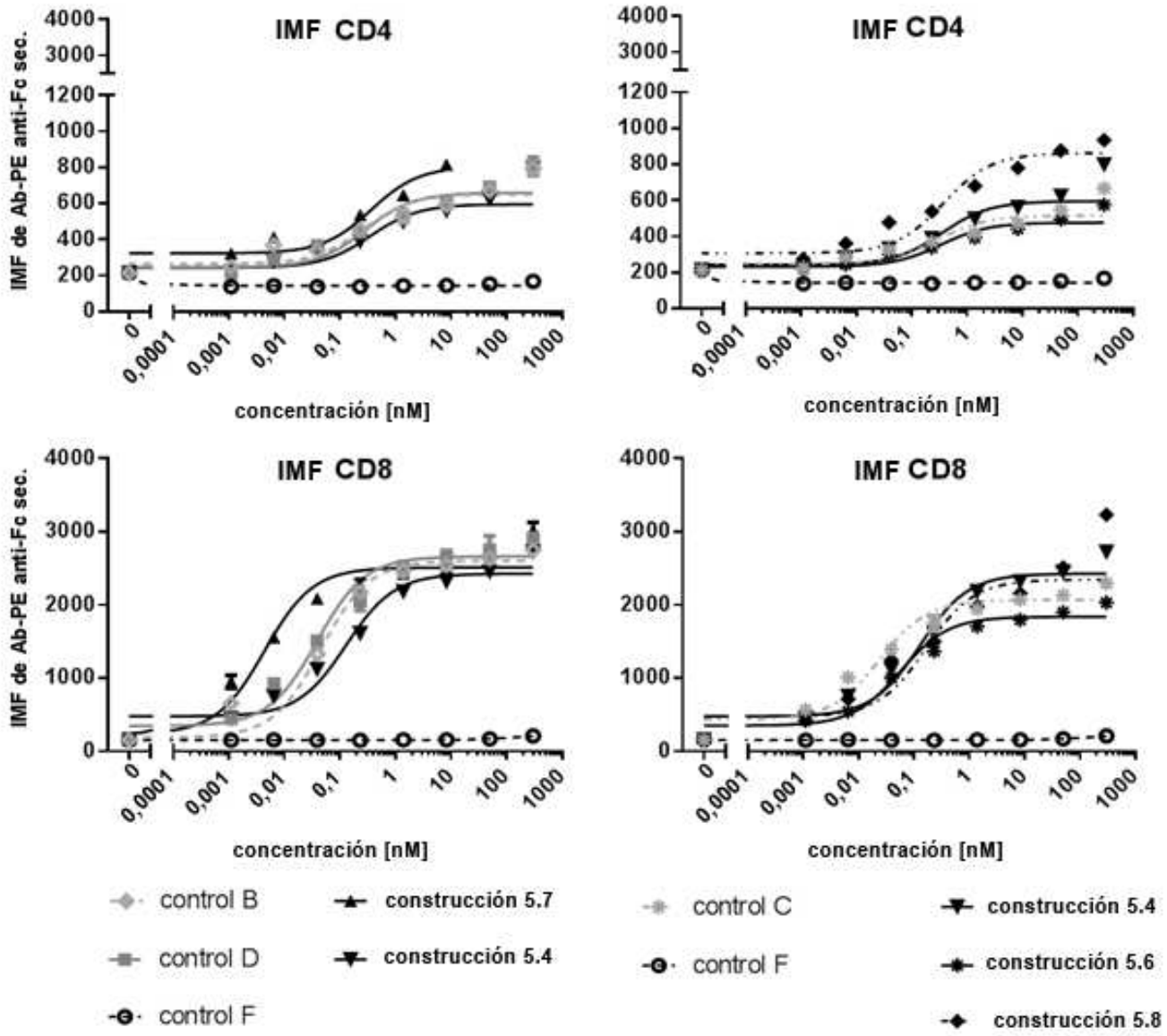

IMF CD4
IMF CD4
IMF CD8
IMF CD8
IMF de Ab-PE anti-Fc sec.
concentración [nM]
control B
control D
control F
construcción 5.7
construcción 5.4
control C
control F
construcción 5.4
construcción 5.6
construcción 5.8

Fig. 44

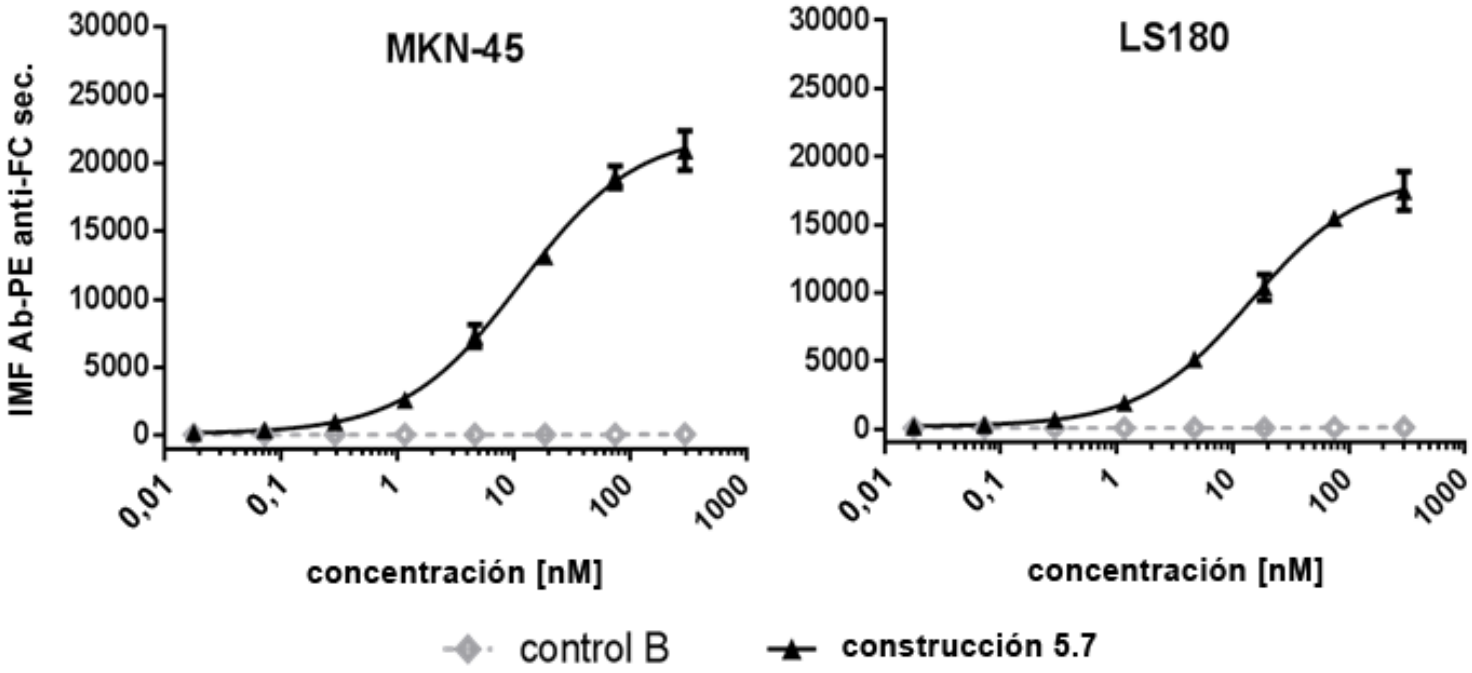

MKN-45
LS180
IMF Ab-PE anti-FC sec.
30000
25000
20000
15000
10000
5000
0
0,01
0,1
1
10
100
1000
concentración [nM]
control B
construcción 5.7

Fig. 45

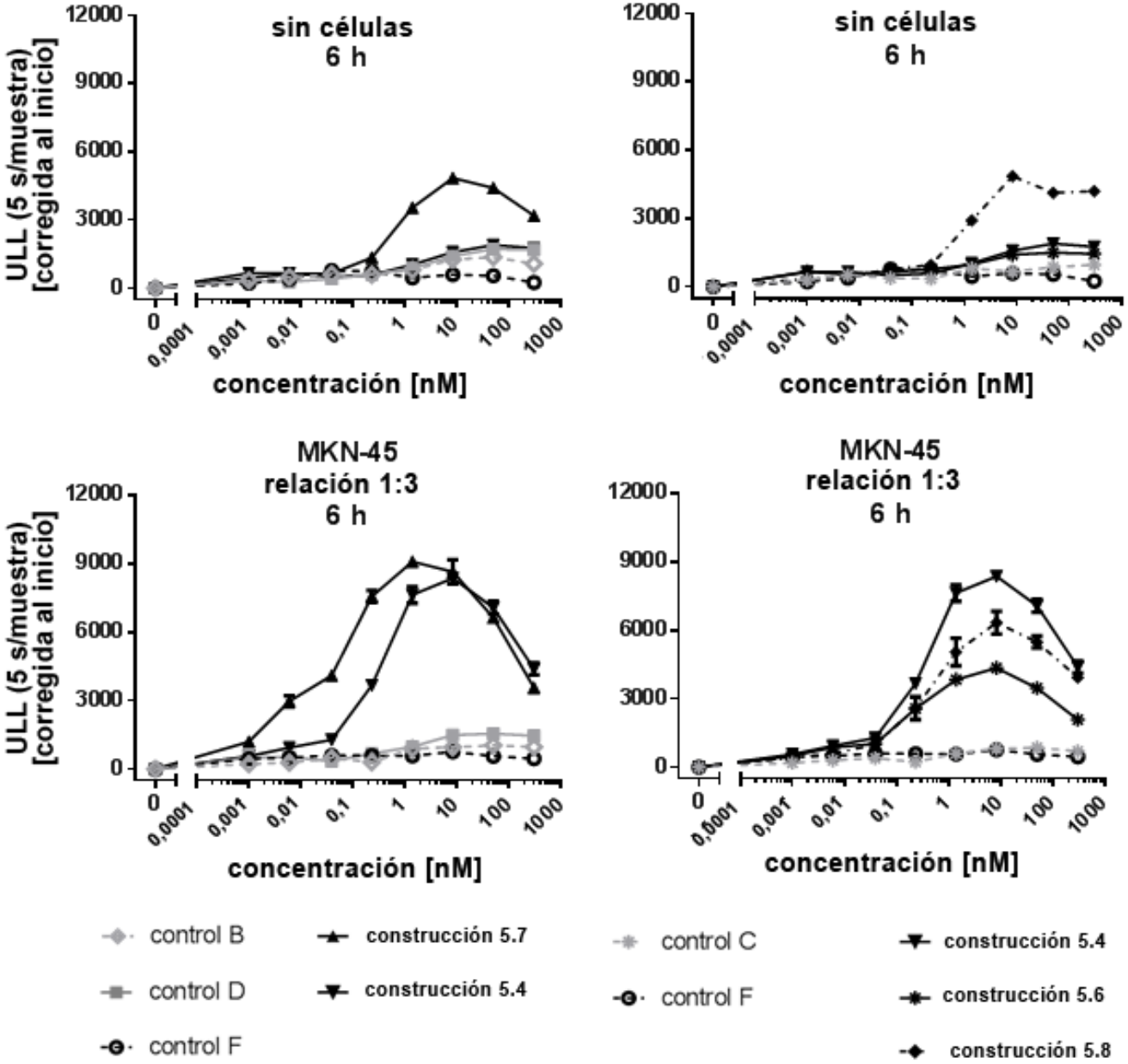
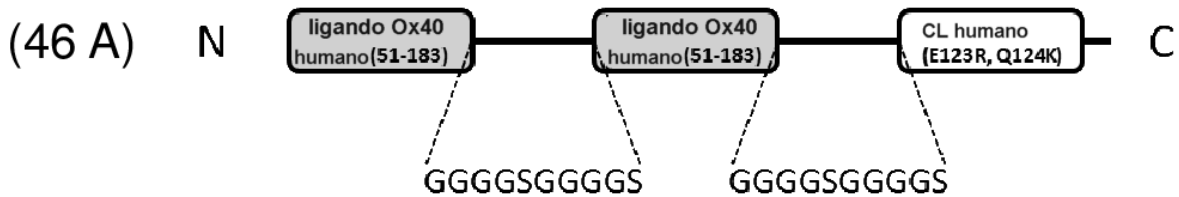
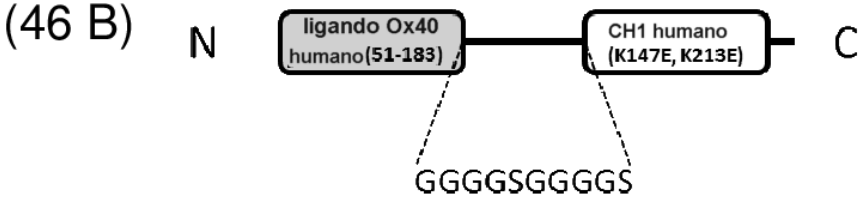
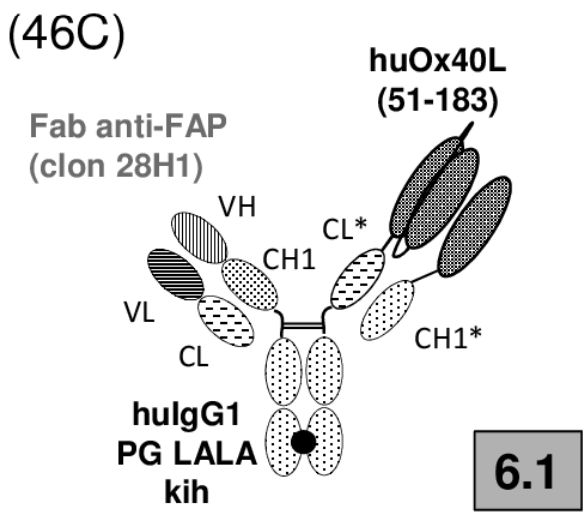

sin células
6 h
ULL (5 s/muestra)
[corregida al inicio]
12000
9000
6000
3000
0
0
0,0001
0,001
0,01
0,1
1
10
100
1000
concentración [nM]
sin células
6 h
MKN-45
relación 1:3
6 h
MKN-45
relación 1:3
6 h
control B
control D
control F
construcción 5.7
construcción 5.4
control C
control F
construcción 5.4
construcción 5.6
construcción 5.8

Fig. 46


(46 A)
N
ligando Ox40 humano(51-183)
ligando Ox40 humano(51-183)
CL humano (E123R, Q124K)
C
GGGGSGGGGS
GGGGSGGGGS


(46 B)
N
ligando Ox40 humano(51-183)
CH1 humano (K147E, K213E)
C
GGGGSGGGGS


(46C)
huOx40L (51-183)
Fab anti-FAP (clon 28H1)
VH
CH1
CL*
VL
CL
CH1*
hulgG1 PG LALA kih
6.1

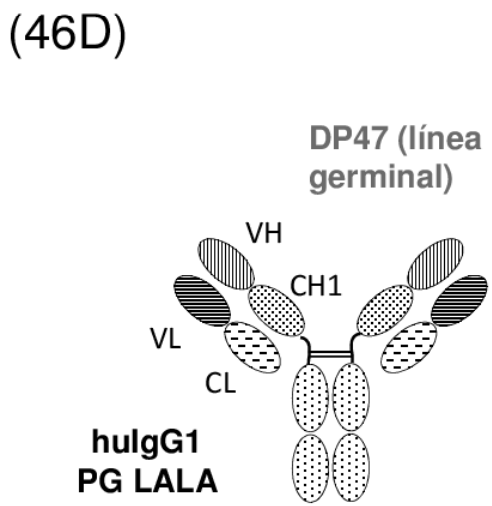
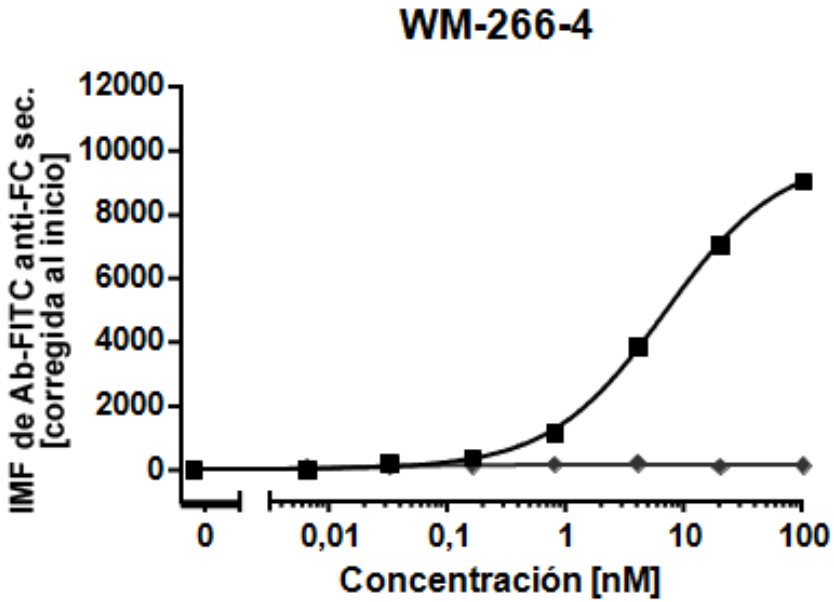
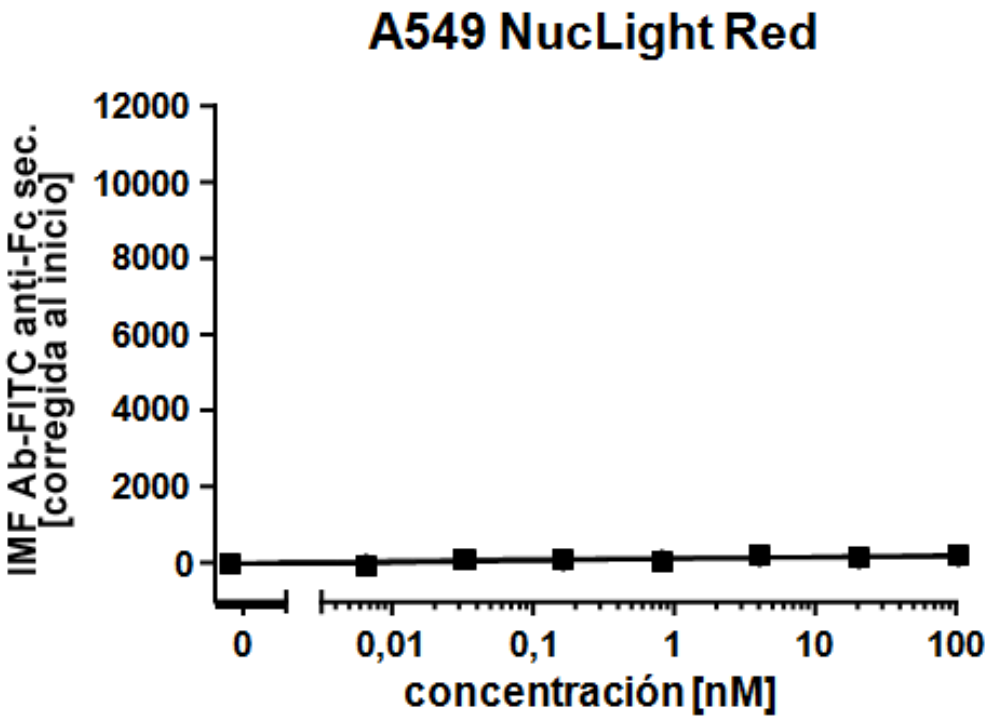

(46D)
DP47 (línea germinal)
VH
CH1
VL
CL
hulgG1 PG LALA

Fig. 47 A



Fusión de Fc (kih) de ligando Ox40 trimérico separado dirigido a FAP (28H1) monovalente
Control F

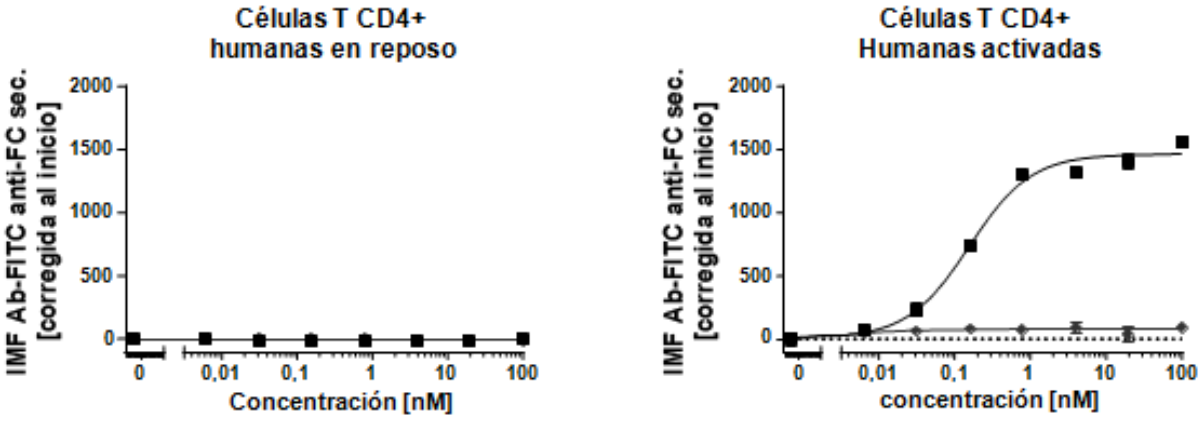
Fig. 47 B



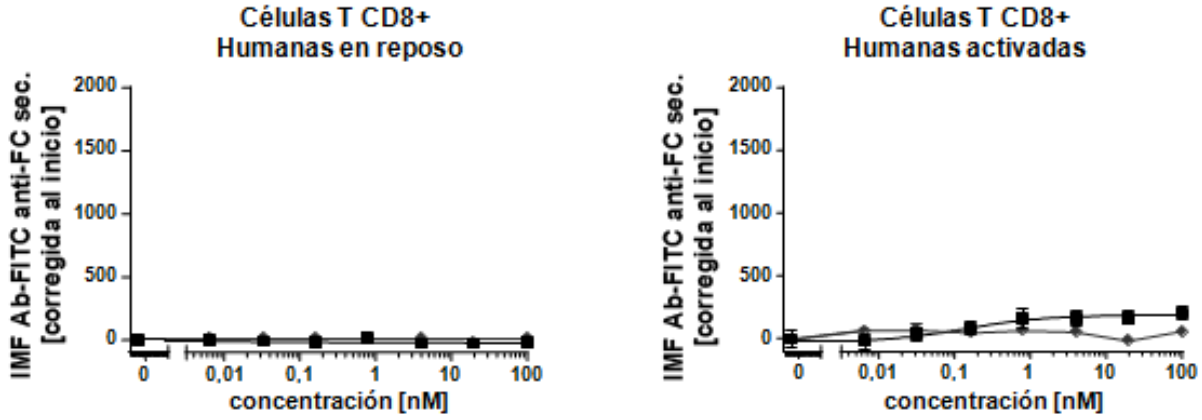
Fusión de Fc (kih) de ligando Ox40 trimérico separado dirigido a FAP (28H1) monovalente
Control F

Fig. 48

(48 A)



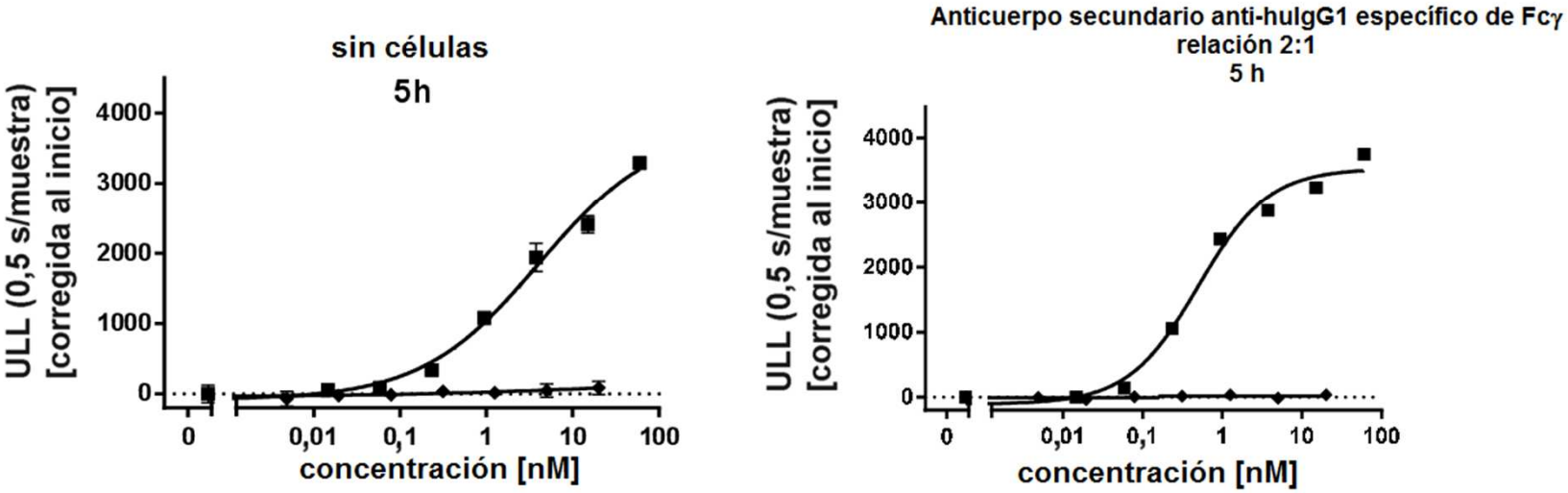
(48 B)



Fusión de Fc (kih) de ligando Ox40 trimérico separado dirigido a FAP (28H1) monovalente

Control F

Fig. 49

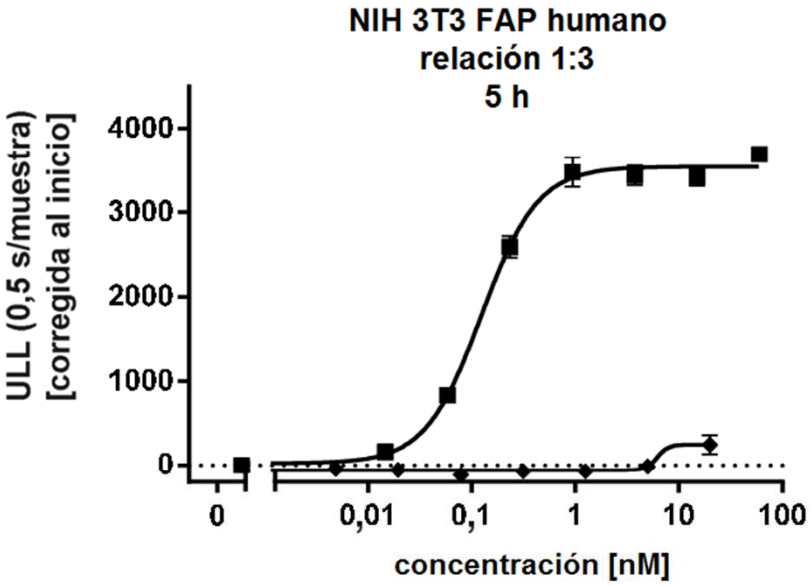


Fusión de Fc (kih) de ligando Ox40 trimérico separado dirigido a FAP (28H1) monovalente

Control F

Fig. 50

(50 A)



(50 B)

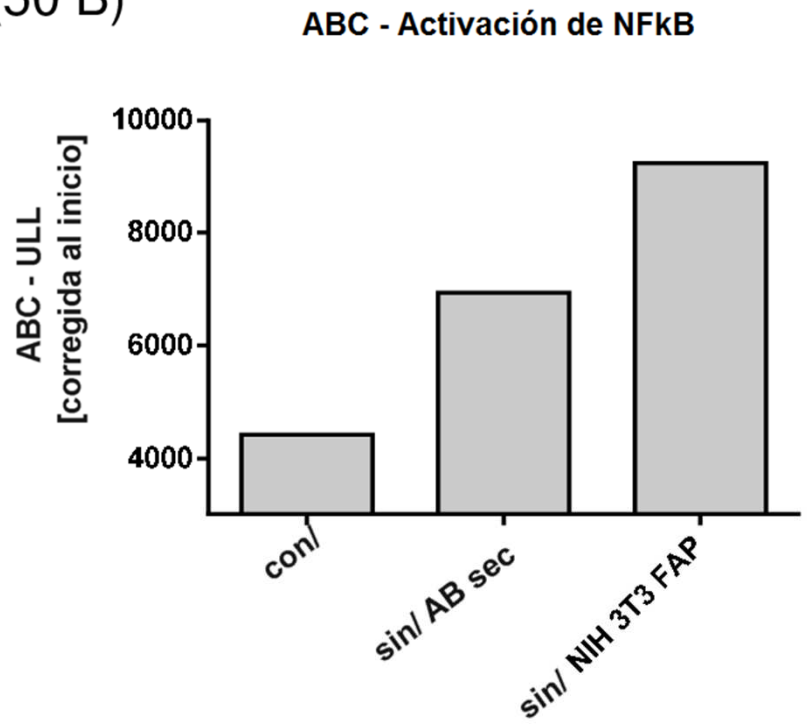
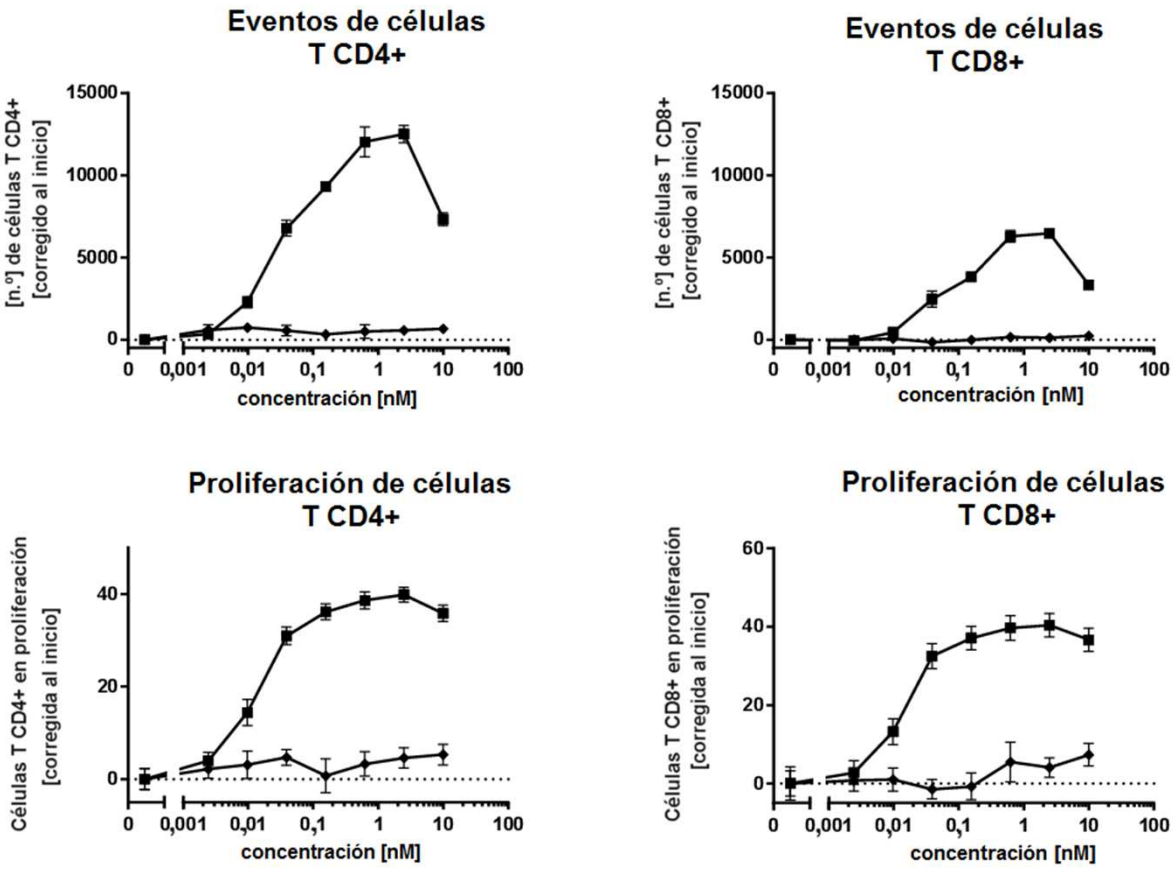


Fig. 51



Fusión de Fc (kih) de ligando Ox40 trimérico separado dirigido a FAP (28H1) monovalente

Control F