

Figure 1A

Human IL-2 Sequence (SEQ ID NO: 1)

>sp | P60568
MYRMQLLSICIALSLALVTNSAPTSSSTKKTQLQLEHLLLDLQMI L N G I N N Y K N P K L T R M L T F K F Y M P K K A T E L K H L Q
C L E E E L K P L E E V L N L A Q S K N F H L R P R D L I S N I N V I V L E L K G S E T T F M C E Y A D E T A T I V E F L N R W I T F C Q S I I S T L T

Human IL-2 mature form sequence (SEQ ID NO: 2)

>sp | P60568 | 21-153
A P T S S T K K T Q L Q L E H L L L D L Q M I L N G I N N Y K N P K L T R M L T F K F Y M P K K A T E L K H L Q C L E E E L K P L E E V L N L A Q S K N
F H L R P R D L I S N I N V I V L E L K G S E T T F M C E Y A D E T A T I V E F L N R W I T F C Q S I I S T L T

Human IL-2R α (CD25) sequence (SEQ ID NO: 3)

>sp | P01589
M D S Y L L M W G L L T F I M V P G C Q A E L C D D D P P E I P H A T F K A M A Y K E G T M L N C E C K R G F R R I K S G S L Y M L C T G N S S H S S W D
N Q C Q C T S S A T R N T T K Q V T P Q P E E Q K E R K T T E M Q S P M Q P V D Q A S L P G H C R E P P P W E N E A T E R I Y H F V V G Q M V Y Y Q C V Q
G Y R A L H R G P A E S V C K M T H G K T R W T Q P Q L I C T G E M E T S Q F P G E E K P Q A S P E G R P E S E T S C L V T T T D F Q I Q T E M A A T M E
T S I F T T E Y Q V A V A G C V F L L I S V L L L S G L T W Q R R Q R K S R R T I

Human IL-2R α (CD25), extracellular domain (SEQ ID NO: 4)

>sp | P01589 | 22-240
E L C D D D P P E I P H A T F K A M A Y K E G T M L N C E C K R G F R R I K S G S L Y M L C T G N S S H S S W D N Q C Q C T S S A T R N T T K Q V T P Q P
E E Q K E R K T T E M Q S P M Q P V D Q A S L P G H C R E P P P W E N E A T E R I Y H F V V G Q M V Y Y Q C V Q G Y R A L H R G P A E S V C K M T H G K T
R W T Q P Q L I C T G E M E T S Q F P G E E K P Q A S P E G R P E S E T S C L V T T T D F Q I Q T E M A A T M E T S I F T T E Y Q

Human IL-2R β (CD122) sequence (SEQ ID NO: 5)

>sp | P14784
M A A P A L S W R L P L L I L L L P L A T S W A S A A V N G T S Q F T C F Y N S R A N I S C V W S Q D G A L Q D T S C Q V H A W P D R R R W N Q T C E L L
P V S Q A S W A C N L I L G A P D S Q K L T T V D I V T L R V L C R E G V R W R V M A I Q D F K P F E N L R L M A P I S L Q V V H V E T H R C N I S W E I
S Q A S H Y F E R H L E F E A R T L S P G H T W E E A P L L T L K Q K Q E W I C L E T L T P D T Q Y E F Q V R V K P L Q G E F T T W S P W S Q P L A F R T
K P A A L G K D T I P W L G H L L V G L S G A F G F I I L V Y L L I N C R N T G P W L K K V L K C N T P D P S K F F S Q L S S E H G G D V Q K W L S S P F
P S S S F S P G G L A P E I S P L E V L E R D K V T Q L L L Q D K V P E P A S L S S N H S L T S C F T N Q G Y F F F H L P D A L E I E A C Q V Y F T Y D
P Y S E E D P D E G V A G A P T G S S P Q P L Q P L S G E D D A Y C T F P S R D D L L L F S P S L L G G P S P P S T A P G G S G A G E E R M P P S L Q E R
V P R D W D P Q P L G P P T P G V P D L V D F Q P P P E L V L R E A G E E V P D A G P R E G V S F P W S R P P G Q G E F R A L N A R L P L N T D A Y L S L
Q E L Q G Q D P T H L V

Human IL-2R β (CD122), extracellular domain (SEQ ID NO: 6)

>sp | P14784 | 27-240
A V N G T S Q F T C F Y N S R A N I S C V W S Q D G A L Q D T S C Q V H A W P D R R R W N Q T C E L L P V S Q A S W A C N L I L G A P D S Q K L T T V D I
V T L R V L C R E G V R W R V M A I Q D F K P F E N L R L M A P I S L Q V V H V E T H R C N I S W E I S Q A S H Y F E R H L E F E A R T L S P G H T W E E
A P L L T L K Q K Q E W I C L E T L T P D T Q Y E F Q V R V K P L Q G E F T T W S P W S Q P L A F R T K P A A L G K D T

Human common gamma chain (CD132) sequence (SEQ ID NO: 7)

>sp | P31785
M L K P S L P F T S L L F L Q L P L L G V G L N T T I L T P N G N E D T T A D F F L T T M P T D S L S V S T L P L P E V Q C F V F N V E Y M N C T W N S S
S E P Q P T N L T L H Y W Y K N S D N D K V Q K C S H Y L F S E E I T S G C Q L Q K K E I H L Y Q T F V V Q L Q D P R E P R R Q A T Q M L K L Q N L V I P
W A P E N L T L H K L S E S Q L E L N W N N R F L N H C L E H L V Q Y R T D W D H S W T E Q S V D Y R H K F S L P S V D G Q K R Y T F R V R S R F N P L C
G S A Q H W S E W S H P I H W G S N T S K E N P F L F A L E A V V I S V G S M G L I I S L L C V Y F W L E R T M P R I P T L K N L E D L V T E Y H G N F S
A W S G V S K G L A E S L Q P D Y S E R L C L V S E I P P K G G A L G E G P G A S P C N Q H S P Y W A P P C Y T L K P E T

Figure 1B

Human common gamma chain (CD132), extracellular domain (SEQ ID NO: 8)

>sp|P31785|23-262

LNNTTILTPNGNEDTTADFFLTMTPTDSL SVSTLPLPEVQCFVFNVEYMNCTWNSSSEPQPTNLT
LHYWYKNSDNDKV
QKCSHYLFSEEITSGCQLQKKEIHLYQTFVVQLQDPREPRRQATQMLKLQNLVIPWAPENLT
LHKLSESOLELNWNN
RFLNHCLEHLVQYRTDWDHSWTEQSVDYRHKFSLPSVDGQKRYTFRVRSRFPNPLCGSAQ
HWSEWSHPIHWGSNTSKE
NPFLFALEA

Figure 2A

Monomer 1	Monomer 2
F405A	T394F
S364D	Y349K
S364E	L368K
S364E	Y349K
S364F	K370G
S364H	Y349K
S364H	Y349T
S364Y	K370G
T411K	K370E
V397S/F405A	T394F
K370R/T411K	K370E/T411E
L351E/S364D	Y349K/L351K
L351E/S364E	Y349K/L351K
L351E/T366D	L351K/T366K
P395T/V397S/F405A	T394F
S364D/K370G	S364Y/K370R
S364D/T394F	Y349K/F405A
S364E/F405A	Y349K/T394F
S364E/F405S	Y349K/T394Y
S364E/T411E	Y349K/D401K
S364H/D401K	Y349T/T411E
S364H/F405A	Y349T/T394F
S364H/T394F	Y349T/F405A
Y349C/S364E	Y349K/S354C
L351E/S364D/F405A	Y349K/L351K/T394F
L351K/S364H/D401K	Y349T/L351E/T411E
S364E/T411E/F405A	Y349K/T394F/D401K
S364H/D401K/F405A	Y349T/T394F/T411E
S364H/F405A/T411E	Y349T/T394F/D401K

Figure 2B

Monomer 1	Monomer 2
K370E/T411D	T411K
L368E/K409E	L368K
Y349T/T394F/S354C	S364H/F405A/Y349C
T411E	D401K
T411E	D401R/T411R
Q347E/K360E	Q347R
L368E	S364K/E357Q
L368E/K370S	S364K/E357Q
L368E/K370T	S364K/E357Q
L368E/D401R	S364K/E357Q
L368E/D401N	S364K/E357Q
L368E	E357S/S364K/E357Q
L368E	S364K/E357Q/K409E
L368E	S364K/E357Q/K409V
L368D	S364K/E357Q
L368D/K370S	S364K/E357Q
L368D/K370S	S364K/E357Q/E357L
L368D/K370S	S364K/E357Q
T411E/K360E/Q362E	D401K
K370S	S364K/E357Q
L368E/K370S	S364K/E357Q
K370S	S364K/E357Q
T411E/K360D	D401K
T411E/K360E	D401K
T411E/Q362E	D401K
T411E/N390D	D401K
T411E	D401K/Q347K
T411E	D401K/Q347R
T411E/K360D/Q362E	D401K

Figure 2C

Monomer 1	Monomer 2
T411E/K360E/N390D	D401K
T411E/Q362E/N390D	D401K
T411E/Q347R	D401K/K360D
T411E/Q347R	D401K/K360E
T411E/K360	D401K/Q347K
T411E/K360D	D401K/Q347R
T411E/K360E	D401K/Q347K
T411E/K360E	D401K/Q347R
T411E/S364K/E357Q	D401K/K370S
T411E/K370S	D401K/S364K/E357Q
Q347E	E357Q
Q347E	E357Q/Q362K
K360D/Q362E	Q347R
K360D/Q362E	D401K
K360D/Q362E	Q347R/D401K
K360E/Q362E	Q347R
K360E/Q362E	D401K
K360E/Q362E	Q347R/D401K
Q362E/N390D	D401K
Q347E/K360D	D401N
K360D	Q347R/N390K
K360D	N390K/D401N
K360E	Y349H
K370S/Q347E	S364K/E357Q
K370S/E357L	S364K/E357Q
K370S/E357Q	S364K/E357Q
K370S/Q347E/E357L	S364K/E357Q
K370S/Q347E/E357Q	S364K/E357Q

Figure 2D

Monomer 1	Monomer 2
L368D/K370S/Q347E	S364K/E357Q
L368D/K370S/E357L	S364K/E357Q
L368D/K370S/E357Q	S364K/E357Q
L368D/K370S/Q347E/E357L	S364K/E357Q
L368D/K370S/Q347E/E357Q	S364K/E357Q
L368E/K370S/Q347E	S364K/E357Q
L368E/K370S/E357L	S364K/E357Q
L368E/K370S/E357Q	S364K/E357Q
L368E/K370S/Q347E/E357L	S364K/E357Q
L368E/K370S/Q347E/E357Q	S364K/E357Q
L368D/K370T/Q347E	S364K/E357Q
L368D/K370T/E357L	S364K/E357Q
L368D/K370T/E357Q	S364K/E357Q
L368D/K370T/Q347E/E357L	S364K/E357Q
L368D/K370T/Q347E/E357Q	S364K/E357Q
L368E/K370T/Q347E	S364K/E357Q
L368E/K370T/E357L	S364K/E357Q
L368E/K370T/E357Q	S364K/E357Q
L368E/K370T/Q347E/E357L	S364K/E357Q
L368E/K370T/Q347E/E357Q	S364K/E357Q
T411E/Q362E	D401K/T411K
T411E/N390D	D401K/T411K
T411E/Q362E	D401R/T411R
T411E/N390D	D401R/T411R
Y407T	T366Y
F405A	T394W
T366Y/F405A	T394W/Y407T
Y407A	T366W
T366S/L368A/Y407V	T366W
T366S/L368A/Y407V/Y349C	T366W/S354C

Figure 2E

Monomer 1	Monomer 2
K392D/K409D	E356K/D399K
K370D/K392D/K409D	E356K/E357K/D399K
K247Q/R355Q/N384S/K392N/V397M/Q419E/K447_	P217R/P228R/N276K
K247Q/R355Q/N384S/K392N/V397M/Q419E/K447_	N276K
N384S/K392N/V397M/Q419E	N276K
D221E/P228E/L368E	D221R/P228R/K409R
C220E/P228E/L368E	C220R/E224R/P228R/K409R
F405L	K409R
T366I/K392M/T394W	F405A/Y407V
T366V/K409F	L351Y/Y407A
T366A/K392E/K409F/T411E	D399R/S400R/Y407A
L351K	L351E
K247Q/R355Q/Q419E/K447_	P217R/P228R/N276K
K247Q/R355Q/Q419E/K447_	N276K
K274Q/R355Q/N384S/K392N/V397M/Q419E/K447_	
Q295E/N384D/Q418E/N421D	
Q295E/Q418E/N421D	
P217R/P228R/N276K	
N276K	
E269Q/E272Q/E283Q/E357Q	
E269Q/E272Q/E283Q	
E269Q/E272Q	
E269Q/E283Q	
E272Q/E283Q	
E269Q	

Figure 3

<u>Variant constant region</u>	<u>Substitutions</u>
pl_ISO(-)-Fc only	K274Q/R355Q/N384S/K392N/V397M/Q419E/K447_
pl_(-)_isosteric_A-Fc only	Q295E/N384D/Q418E/N421D
pl_(-)_isosteric_B-Fc only	Q295E/Q418E/N421D
pl_ISO(+RR)-Fc only	P217R/P228R/N276K
pl_ISO(+)-Fc only	N276K
pl_(+)_isosteric_A	E269Q/E272Q/E283Q/E357Q
pl_(+)_isosteric_B	E269Q/E272Q/E283Q
pl_(+)_isosteric_E269Q/E272Q	E269Q/E272Q
pl_(+)_isosteric_E269Q/E283Q	E269Q/E283Q
pl_(+)_isosteric_E272Q/E283Q	E272Q/E283Q
pl_(+)_isosteric_E269Q	E269Q

Figure 4

Ablation Variants

G236R
S239G
S239K
S239Q
S239R
V266D
S267K
S267R
H268K
E269R
299R
299K
K322A
A327G
A327L
A327N
A327Q
L328E
P329K
A330L
A330S/P331S
I332K
I332R
V266D/A327Q
V266D/P329K
S267R/A327Q
S267R/P329K
G236R/L328R
E233P/L234V/L235A/G236_/S239K
E233P/L234V/L235A/G236_/S267K
E233P/L234V/L235A/G236_/S239K/A327G
E233P/L234V/L235A/G236_/S267K/A327G
E233P/L234V/L235A/G236_
S239K/S267K
267K/P329K

Figure 5A

Figure 5A	
empty-Fc monomer (-)	IL-2-Fc monomer (+)
C220S	C220S
Heterodimer skew variants L368D/K370S	Heterodimer skew variants S364K/E357Q
Isosteric pl substitutions Q295E/N384D/Q418E/N421D	
FcKO E233P/L234V/L235A/G236_/S267K	FcKO E233P/L234V/L235A/G236_/S267K
±M428L/N434S	±M428L/N434S

Figure 5B

Figure 5B	
IL-2-Fc monomer 1	IL-2-Fc monomer 2
C220S	C220S
FcKO E233P/L234V/L235A/G236_/S267K	FcKO E233P/L234V/L235A/G236_/S267K
±M428L/N434S	±M428L/N434S

Figure 6A

IL-2-Fc Backbone 1**>IL-2-Fc monomer 1 (SEQ ID NO: 9)**

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHN
AKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRE
QMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCS
VMHEALHNHYTQKSLSLSPGK

>IL-2-Fc monomer 2 (SEQ ID NO: 10)

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHN
AKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRE
EMTKNQVSLTCDVSGFYPSDIAVEWESDQGPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCS
VMHEALHNHYTQKSLSLSPGK

IL-2-Fc Backbone 2**>IL-2-Fc monomer 1 (SEQ ID NO: 11)**

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHN
AKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRE
EMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCS
VMHEALHNHYTQKSLSLSPGK

>IL-2-Fc monomer 2 (SEQ ID NO: 12)

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHN
AKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRE
EMTKNQVSLTCDVSGFYPSDIAVEWESDQGPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCS
VMHEALHNHYTQKSLSLSPGK

IL-2-Fc Backbone 3**>IL-2-Fc monomer 1 (SEQ ID NO: 13)**

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHN
AKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRE
EMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCS
VMHEALHNHYTQKSLSLSPGK

>IL-2-Fc monomer 2 (SEQ ID NO: 14)

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHN
AKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRE
EMTKNQVSLTCEVSGFYPSDIAVEWESDQGPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCS
VMHEALHNHYTQKSLSLSPGK

IL-2-Fc Backbone 4**>IL-2-Fc monomer 1 (SEQ ID NO: 15)**

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHN
AKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRE
EMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDKSGSFFLYSKLTVDKSRWQQGNVFSCS
VMHEALHNHYTQKSLSLSPGK

Figure 6B

>IL-2-Fc monomer 2 (SEQ ID NO: 16)

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHN
AKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRE
EMTENEVSLTCLVKGFYPSDIAVEWESDGGQPENNYKTTTPVLDSDGSFFLYSKLEVDKSRWEQGDVFSCS
VMHEALHNHYTQKSLSLSPGK

IL-2-Fc Backbone 5**>IL-2-Fc monomer 1 (SEQ ID NO: 17)**

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHN
AKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRD
QLTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSS
VMHEALHNHYTQKSLSLSPGK

>IL-2-Fc monomer 2 (SEQ ID NO: 18)

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHN
AKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRD
ELTKNQVSLTCDVSGFYPSDIAVEWESDGGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCS
VMHEALHNHYTQKSLSLSPGK

IL-2-Fc Backbone 6**>IL-2-Fc monomer 1 (SEQ ID NO: 19)**

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHN
AKTKPREEQYASTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRE
QMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSS
VMHEALHNHYTQKSLSLSPGK

>IL-2-Fc monomer 2 (SEQ ID NO: 20)

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHN
AKTKPREEEYASTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRE
EMTKNQVSLTCDVSGFYPSDIAVEWESDGGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCS
VMHEALHNHYTQKSLSLSPGK

IL-2-Fc Backbone 7**>IL-2-Fc monomer 1 (SEQ ID NO: 21)**

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHN
AKTKPREEQYSSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRE
QMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSS
VMHEALHNHYTQKSLSLSPGK

>IL-2-Fc monomer 2 (SEQ ID NO: 22)

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHN
AKTKPREEEYSSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRE
EMTKNQVSLTCDVSGFYPSDIAVEWESDGGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCS
VMHEALHNHYTQKSLSLSPGK

Figure 6C

IL-2-Fc Backbone 8**>IL-2-Fc monomer 1 (SEQ ID NO: 23)**

ESKYGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAK
TKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTIKAKGQPREPQVYTLPPSQEQM
TKNQVKLTCLVKGfYPSDIAVEWESNGQPENNYKTTPVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVM
HEALHNHYTQKSLSLGLGK

>IL-2-Fc monomer 2 (SEQ ID NO: 24)

ESKYGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAK
TKPREEEFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTIKAKGQPREPQVYTLPPSQEEM
TKNQVSLTCDVSGfYPSDIAVEWESDGQPENNYKTTPVLDSDGSFFLYSRLTVDKSRWEEGDVFSCSVM
HEALHNHYTQKSLSLGLGK

IL-2-Fc Backbone 9**>IL-2-Fc monomer 1 (SEQ ID NO: 25)**

ERKCCVECPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVQFNWYVDGVEVHNAKT
KPREEQFNSTFRVSVLTVVHQDWLNGKEYKCKVSNKGLPAPIEKTISKTKGQPREPQVYTLPPSREQMT
KNQVKLTCLVKGfYPSDIAVEWESNGQPENNYKTTPMLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMH
EALHNHYTQKSLSLSPGK

>IL-2-Fc monomer 2 (SEQ ID NO: 26)

ERKCCVECPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVQFNWYVDGVEVHNAKT
KPREEEFNSTFRVSVLTVVHQDWLNGKEYKCKVSNKGLPAPIEKTISKTKGQPREPQVYTLPPSREEMT
KNQVSLTCDVSGfYPSDIAVEWESDGQPENNYKTTPMLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMH
EALHNHYTQKSLSLSPGK

IL-2-Fc Backbone 10**>IL-2-Fc monomer 1 (SEQ ID NO: 27)**

ERKCCVECPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVQFNWYVDGVEVHNAKT
KPREEQFNSTFRVSVLTVVHQDWLNGKEYKCKVSNKGLPAPIEKTISKTKGQPREPQVYTLPPSREQMT
KNQVKLTCLVKGfYPSDIAVEWESNGQPENNYKTTPMLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMH
EALHNHYTQKSLSLSPGK

>IL-2-Fc monomer 2 (SEQ ID NO: 28)

ERKCCVECPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVQFNWYVDGVEVHNAKT
KPREEEFNSTFRVSVLTVVHQDWLNGKEYKCKVSNKGLPAPIEKTISKTKGQPREPQVYTLPPSREEMT
KNQVSLTCDVSGfYPSDIAVEWESDGQPENNYKTTPMLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMH
EALHNHYTQKSLSLSPGK

IL-2-Fc Backbone 11**>IL-2-Fc monomer 1 (SEQ ID NO: 29)**

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHN
AKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRE
QMTKNQVKLTCLVKGfYPSDIAVEWESNGQPENNYKTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCS
VLHEALHSHYTQKSLSLSPGK

Figure 6D

>IL-2-Fc monomer 2 (SEQ ID NO: 30)

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHN
AKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRE
EMTKNQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCS
VLHEALHSHYTQKSLSLSPGK

IL-2-Fc Backbone 12**>IL-2-Fc monomer 1 (SEQ ID NO: 31)**

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHN
AKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRE
EMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCS
VMHEALHNHYTQKSLSLSPGK

>IL-2-Fc monomer 2 (SEQ ID NO: 32)

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHN
AKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRE
EMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCS
VMHEALHNHYTQKSLSLSPGK

IL-2-Fc Backbone 13**>IL-2-Fc monomer 1 (SEQ ID NO: 33)**

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHN
AKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRE
EMTKNQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCS
VMHEALHNHYTQKSLSLSPGK

>IL-2-Fc monomer 2 (SEQ ID NO: 34)

ERKSSDKTHTCPRCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFKWYVDGVEVHN
AKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRE
QMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCS
VMHEALHNHYTQKSLSLSPGK

Figure 7

<u>Name</u>	<u>Sequence</u>	<u>SEQ ID NO:</u>
(GGGGS) ₁ or GGGGS	GGGGS	35
(GGGGS) ₂	GGGGSGGGGS	36
(GGGGS) ₃	GGGGSGGGGSGGGGS	37
(GGGGS) ₄	GGGGSGGGGSGGGGSGGGGS	38
(GGGES) ₁ or GGGES	GGGES	39

Figure 8A

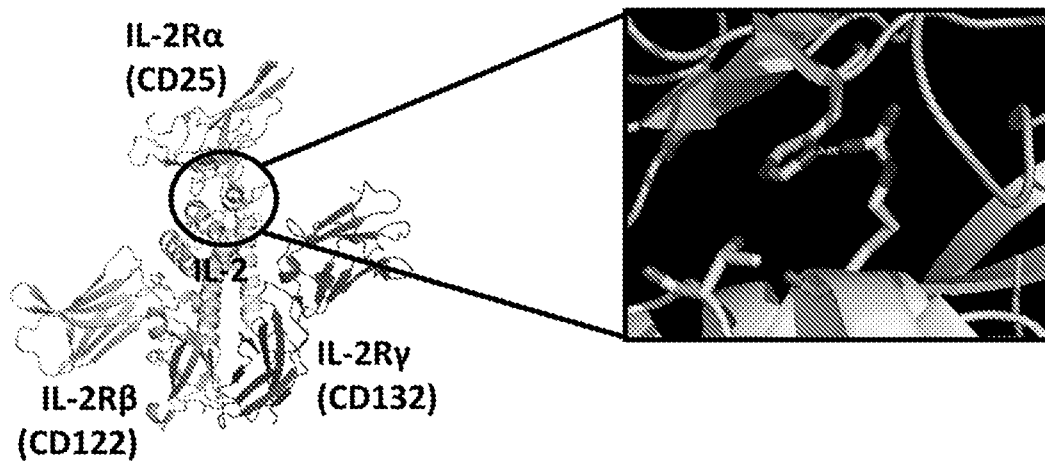


Figure 8B

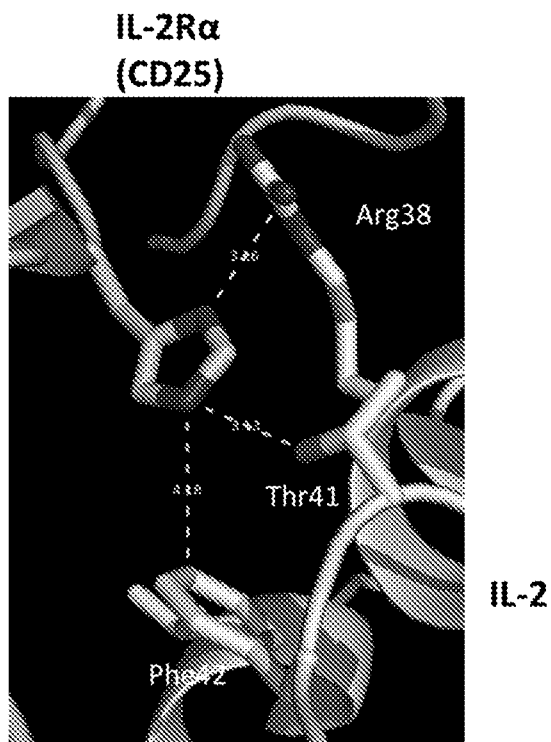


Figure 9A

>XENP014135 hIL2 0.1 (SEQ ID NO: 40)

APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTRMLTFKFYMPKKATELKHLQCLEEEELKPLEEVLNLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLTGS

>XENP014136 hIL2 0.9 (SEQ ID NO: 41)

APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTAMLTTFKFYMPKKATELKHLQCLEEEELKPLEEVLNLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLTGS

>XENP014137 hIL2 0.10 (SEQ ID NO: 42)

APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTDMLTFKFYMPKKATELKHLQCLEEEELKPLEEVLNLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT

>XENP014138 hIL2 0.11 (SEQ ID NO: 43)

APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTEMLTFKFYMPKKATELKHLQCLEEEELKPLEEVLNLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT

>XENP014139 hIL2 0.12 (SEQ ID NO: 44)

APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTFMLTFKFYMPKKATELKHLQCLEEEELKPLEEVLNLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT

>XENP014140 hIL2 0.13 (SEQ ID NO: 45)

APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTGMLTFKFYMPKKATELKHLQCLEEEELKPLEEVLNLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT

>XENP014141 hIL2 0.14 (SEQ ID NO: 46)

APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTHMLTFKFYMPKKATELKHLQCLEEEELKPLEEVLNLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT

>XENP014142 hIL2 0.15 (SEQ ID NO: 47)

APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTIMLTFKFYMPKKATELKHLQCLEEEELKPLEEVLNLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLTGS

>XENP014143 hIL2 0.16 (SEQ ID NO: 48)

APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTKMLTFKFYMPKKATELKHLQCLEEEELKPLEEVLNLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT

>XENP014144 hIL2 0.17 (SEQ ID NO: 49)

APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTLMLTFKFYMPKKATELKHLQCLEEEELKPLEEVLNLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLTGS

>XENP014145 hIL2 0.18 (SEQ ID NO: 50)

APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTMMLTFKFYMPKKATELKHLQCLEEEELKPLEEVLNLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT

>XENP014146 hIL2 0.19 (SEQ ID NO: 51)

APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTNMLTFKFYMPKKATELKHLQCLEEEELKPLEEVLNLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT

>XENP014147 hIL2 0.20 (SEQ ID NO: 52)

APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTPMLTFKFYMPKKATELKHLQCLEEEELKPLEEVLNLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT

Figure 9B

>XENP014148 hIL2 0.21 (SEQ ID NO: 53)

APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTQMLTFKFYMPKKATELKHLQCLEEEELKPLEEVLNLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT

>XENP014149 hIL2 0.22 (SEQ ID NO: 54)

APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTSMLTFKFYMPKKATELKHLQCLEEEELKPLEEVLNLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT

>XENP014150 hIL2 0.23 (SEQ ID NO: 55)

APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTTMLTFKFYMPKKATELKHLQCLEEEELKPLEEVLNLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT

>XENP014151 hIL2 0.24 (SEQ ID NO: 56)

APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTVMLTFKFYMPKKATELKHLQCLEEEELKPLEEVLNLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT

>XENP014152 hIL2 0.25 (SEQ ID NO: 57)

APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTWMLTFKFYMPKKATELKHLQCLEEEELKPLEEVLNLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT

>XENP014153 hIL2 0.26 (SEQ ID NO: 58)

APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTYMLTFKFYMPKKATELKHLQCLEEEELKPLEEVLNLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT

>XENP014154 hIL2 0.27 (SEQ ID NO: 59)

APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTRMLAFKFYMPKKATELKHLQCLEEEELKPLEEVLNLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT

>XENP014155 hIL2 0.28 (SEQ ID NO: 60)

APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTRMLDFKFYMPKKATELKHLQCLEEEELKPLEEVLNLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT

>XENP014156 hIL2 0.29 (SEQ ID NO: 61)

APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTRMLEFKFYMPKKATELKHLQCLEEEELKPLEEVLNLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT

>XENP014157 hIL2 0.30 (SEQ ID NO: 62)

APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTRMLFFKFYMPKKATELKHLQCLEEEELKPLEEVLNLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT

>XENP014158 hIL2 0.31 (SEQ ID NO: 63)

APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTRMLGFKFYMPKKATELKHLQCLEEEELKPLEEVLNLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT

>XENP014159 hIL2 0.32 (SEQ ID NO: 64)

APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTRMLHFKFYMPKKATELKHLQCLEEEELKPLEEVLNLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT

>XENP014160 hIL2 0.33 (SEQ ID NO: 65)

APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTRMLIFKFYMPKKATELKHLQCLEEEELKPLEEVLNLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT

Figure 9C

>XENP014161 hIL2 0.34 (SEQ ID NO: 66)

APTSSSTKKTQLQLEHLLLDLQMLNGINNYKNPKLTRMLKFKFYMPKKATELKHLQCLEEEELKPLEEVLNLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT

>XENP014162 hIL2 0.35 (SEQ ID NO: 67)

APTSSSTKKTQLQLEHLLLDLQMLNGINNYKNPKLTRMLLKFYMPKKATELKHLQCLEEEELKPLEEVLNLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT

>XENP014163 hIL2 0.36 (SEQ ID NO: 68)

APTSSSTKKTQLQLEHLLLDLQMLNGINNYKNPKLTRMLMFKFYMPKKATELKHLQCLEEEELKPLEEVLNLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT

>XENP014164 hIL2 0.37 (SEQ ID NO: 69)

APTSSSTKKTQLQLEHLLLDLQMLNGINNYKNPKLTRMLNFKFYMPKKATELKHLQCLEEEELKPLEEVLNLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT

>XENP014165 hIL2 0.38 (SEQ ID NO: 70)

APTSSSTKKTQLQLEHLLLDLQMLNGINNYKNPKLTRMLPFKFYMPKKATELKHLQCLEEEELKPLEEVLNLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT

>XENP014166 hIL2 0.39 (SEQ ID NO: 71)

APTSSSTKKTQLQLEHLLLDLQMLNGINNYKNPKLTRMLQFKFYMPKKATELKHLQCLEEEELKPLEEVLNLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT

>XENP014167 hIL2 0.40 (SEQ ID NO: 72)

APTSSSTKKTQLQLEHLLLDLQMLNGINNYKNPKLTRMLRKFYMPKKATELKHLQCLEEEELKPLEEVLNLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT

>XENP014168 hIL2 0.41 (SEQ ID NO: 73)

APTSSSTKKTQLQLEHLLLDLQMLNGINNYKNPKLTRMLSFKFYMPKKATELKHLQCLEEEELKPLEEVLNLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT

>XENP014169 hIL2 0.42 (SEQ ID NO: 74)

APTSSSTKKTQLQLEHLLLDLQMLNGINNYKNPKLTRMLVFKFYMPKKATELKHLQCLEEEELKPLEEVLNLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT

>XENP014170 hIL2 0.43 (SEQ ID NO: 75)

APTSSSTKKTQLQLEHLLLDLQMLNGINNYKNPKLTRMLWFKFYMPKKATELKHLQCLEEEELKPLEEVLNLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT

>XENP014171 hIL2 0.44 (SEQ ID NO: 76)

APTSSSTKKTQLQLEHLLLDLQMLNGINNYKNPKLTRMLYFKFYMPKKATELKHLQCLEEEELKPLEEVLNLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT

>XENP014172 hIL2 0.45 (SEQ ID NO: 77)

APTSSSTKKTQLQLEHLLLDLQMLNGINNYKNPKLTRMLTAKFYMPKKATELKHLQCLEEEELKPLEEVLNLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT

>XENP014173 hIL2 0.46 (SEQ ID NO: 78)

APTSSSTKKTQLQLEHLLLDLQMLNGINNYKNPKLTRMLTDKFYMPKKATELKHLQCLEEEELKPLEEVLNLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT

Figure 9D

>XENP014174 hIL2 0.47 (SEQ ID NO: 79)

APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTRMLTEKFYMPKKATELKHLQCLEEEELKPLEEVLNLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT

>XENP014175 hIL2 0.48 (SEQ ID NO: 80)

APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTRMLTGKFYMPKKATELKHLQCLEEEELKPLEEVLNLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT

>XENP014176 hIL2 0.49 (SEQ ID NO: 81)

APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTRMLTHKFYMPKKATELKHLQCLEEEELKPLEEVLNLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT

>XENP014177 hIL2 0.50 (SEQ ID NO: 82)

APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTRMLTIKFYMPKKATELKHLQCLEEEELKPLEEVLNLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT

>XENP014178 hIL2 0.51 (SEQ ID NO: 83)

APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTRMLTKKFYMPKKATELKHLQCLEEEELKPLEEVLNLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT

>XENP014179 hIL2 0.52 (SEQ ID NO: 84)

APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTRMLTLKFYMPKKATELKHLQCLEEEELKPLEEVLNLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT

>XENP014180 hIL2 0.53 (SEQ ID NO: 85)

APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTRMLTMKFYMPKKATELKHLQCLEEEELKPLEEVLNLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT

>XENP014181 hIL2 0.54 (SEQ ID NO: 86)

APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTRMLTNKFYMPKKATELKHLQCLEEEELKPLEEVLNLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT

>XENP014182 hIL2 0.55 (SEQ ID NO: 87)

APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTRMLTPKFYMPKKATELKHLQCLEEEELKPLEEVLNLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT

>XENP014183 hIL2 0.56 (SEQ ID NO: 88)

APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTRMLTQKFYMPKKATELKHLQCLEEEELKPLEEVLNLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT

>XENP014184 hIL2 0.57 (SEQ ID NO: 89)

APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTRMLTRKFYMPKKATELKHLQCLEEEELKPLEEVLNLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT

>XENP014185 hIL2 0.58 (SEQ ID NO: 90)

APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTRMLTSKFYMPKKATELKHLQCLEEEELKPLEEVLNLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT

>XENP014186 hIL2 0.59 (SEQ ID NO: 91)

APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTRMLTTKFYMPKKATELKHLQCLEEEELKPLEEVLNLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT

Figure 9E

>XENP014187 hIL2 0.60 (SEQ ID NO: 92)

APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTRMLTVKFYMPKKATELKHLQCLEEEELKPLEEVLNLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT

>XENP014188 hIL2 0.61 (SEQ ID NO: 93)

APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTRMLTWKFYMPKKATELKHLQCLEEEELKPLEEVLNLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT

>XENP014189 hIL2 0.62 (SEQ ID NO: 94)

APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTRMLTYKFYMPKKATELKHLQCLEEEELKPLEEVLNLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT

>XENP014190 hIL2 0.63 (SEQ ID NO: 95)

APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTQMLKFKFYMPKKATELKHLQCLEEEELKPLEEVLNLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT

>XENP014191 hIL2 0.64 (SEQ ID NO: 96)

APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTQMLQFKFYMPKKATELKHLQCLEEEELKPLEEVLNLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT

>XENP014192 hIL2 0.65 (SEQ ID NO: 97)

APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTEMLKFKFYMPKKATELKHLQCLEEEELKPLEEVLNLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT

>XENP014193 hIL2 0.66 (SEQ ID NO: 98)

APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTQMLRFKFYMPKKATELKHLQCLEEEELKPLEEVLNLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT

>XENP014194 hIL2 0.67 (SEQ ID NO: 99)

APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTNMLQFKFYMPKKATELKHLQCLEEEELKPLEEVLNLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT

>XENP014195 hIL2 0.68 (SEQ ID NO: 100)

APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTQMLVFKFYMPKKATELKHLQCLEEEELKPLEEVLNLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT

>XENP014196 hIL2 0.69 (SEQ ID NO: 101)

APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTNMLVFKFYMPKKATELKHLQCLEEEELKPLEEVLNLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT

>XENP014201 hIL2 0.70 (SEQ ID NO: 102)

APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTQMLMFKFYMPKKATELKHLQCLEEEELKPLEEVLNLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT

>XENP014202 hIL2 0.71 (SEQ ID NO: 103)

APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTQMLSFKFYMPKKATELKHLQCLEEEELKPLEEVLNLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT

>XENP014203 hIL2 0.72 (SEQ ID NO: 104)

APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTQMLLKFYMPKKATELKHLQCLEEEELKPLEEVLNLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT

Figure 9F

>XENP014204 hIL2 0.73 (SEQ ID NO: 105)

APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTNMLMFKFYMPKKATELKHLQCLEEEELKPLEEVLNLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT

>XENP014205 hIL2 0.74 (SEQ ID NO: 106)

APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTRMLIYKFYMPKKATELKHLQCLEEEELKPLEEVLNLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT

>XENP014206 hIL2 0.75 (SEQ ID NO: 107)

APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTRMLEYKFYMPKKATELKHLQCLEEEELKPLEEVLNLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT

>XENP014207 hIL2 0.76 (SEQ ID NO: 108)

APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTRMLDYKFYMPKKATELKHLQCLEEEELKPLEEVLNLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT

>XENP014208 hIL2 0.77 (SEQ ID NO: 109)

APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTRMLMYKFYMPKKATELKHLQCLEEEELKPLEEVLNLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT

>XENP014209 hIL2 0.78 (SEQ ID NO: 110)

APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTRMLQYKFYMPKKATELKHLQCLEEEELKPLEEVLNLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT

>XENP014210 hIL2 0.79 (SEQ ID NO: 111)

APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTRMLEHKFYMPKKATELKHLQCLEEEELKPLEEVLNLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT

>XENP014211 hIL2 0.80 (SEQ ID NO: 112)

APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTRMLELKFYMPKKATELKHLQCLEEEELKPLEEVLNLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT

>XENP014212 hIL2 0.81 (SEQ ID NO: 113)

APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTRMLEPKFYMPKKATELKHLQCLEEEELKPLEEVLNLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT

>XENP014213 hIL2 0.82 (SEQ ID NO: 114)

APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTQMLTYKFYMPKKATELKHLQCLEEEELKPLEEVLNLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT

>XENP014214 hIL2 0.83 (SEQ ID NO: 115)

APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTNMLRKFYMPKKATELKHLQCLEEEELKPLEEVLNLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT

>XENP014215 hIL2 0.84 (SEQ ID NO: 116)

APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTNMLKFKFYMPKKATELKHLQCLEEEELKPLEEVLNLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT

>XENP014216 hIL2 0.85 (SEQ ID NO: 117)

APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTVMLRKFYMPKKATELKHLQCLEEEELKPLEEVLNLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT

Figure 9G

>XENP014217 hIL2 0.86 (SEQ ID NO: 118)

APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLT PMLRKFYMPKKATELKHLQCLEEEELKPLEEVLNLAQSKN
FHLRPRLDISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT

>XENP014218 hIL2 0.87 (SEQ ID NO: 119)

APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTRMLEKKFYMPKKATELKHLQCLEEEELKPLEEVLNLAQSKN
FHLRPRLDISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT

>XENP014219 hIL2 0.88 (SEQ ID NO: 120)

APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTRMLDKKFYMPKKATELKHLQCLEEEELKPLEEVLNLAQSKN
FHLRPRLDISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT

>XENP014220 hIL2 0.89 (SEQ ID NO: 121)

APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTRMLMKKFYMPKKATELKHLQCLEEEELKPLEEVLNLAQSKN
FHLRPRLDISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT

>XENP014221 hIL2 0.90 (SEQ ID NO: 122)

APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTRMLQKKFYMPKKATELKHLQCLEEEELKPLEEVLNLAQSKN
FHLRPRLDISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT

>XENP014222 hIL2 0.91 (SEQ ID NO: 123)

APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTQMLTKKFYMPKKATELKHLQCLEEEELKPLEEVLNLAQSKN
FHLRPRLDISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT

>XENP014223 hIL2 0.92 (SEQ ID NO: 124)

APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTRMLIKKFYMPKKATELKHLQCLEEEELKPLEEVLNLAQSKN
FHLRPRLDISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT

>XENP014224 hIL2 0.93 (SEQ ID NO: 125)

APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTNMLTKKFYMPKKATELKHLQCLEEEELKPLEEVLNLAQSKN
FHLRPRLDISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT

>XENP014225 hIL2 0.94 (SEQ ID NO: 126)

APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTRMLHKKFYMPKKATELKHLQCLEEEELKPLEEVLNLAQSKN
FHLRPRLDISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT

>XENP014226 hIL2 0.95 (SEQ ID NO: 127)

APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTQMLKYKFYMPKKATELKHLQCLEEEELKPLEEVLNLAQSKN
FHLRPRLDISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT

>XENP014227 hIL2 0.96 (SEQ ID NO: 128)

APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTQMLRYKFYMPKKATELKHLQCLEEEELKPLEEVLNLAQSKN
FHLRPRLDISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT

>XENP014228 hIL2 0.97 (SEQ ID NO: 129)

APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTQMLQYKFYMPKKATELKHLQCLEEEELKPLEEVLNLAQSKN
FHLRPRLDISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT

>XENP014229 hIL2 0.98 (SEQ ID NO: 130)

APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTQMLVYKFYMPKKATELKHLQCLEEEELKPLEEVLNLAQSKN
FHLRPRLDISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT

Figure 9H

>XENP014230 hIL2 0.99 (SEQ ID NO: 131)

APTSSSTKKTQLQLEHLLLDLQMLNGINNYKNPKLTNMLKKKFYMPKKATELKHLQCLEEEELKPLEEVLNLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT

>XENP014231 hIL2 0.100 (SEQ ID NO: 132)

APTSSSTKKTQLQLEHLLLDLQMLNGINNYKNPKLTQMLHKKFYMPKKATELKHLQCLEEEELKPLEEVLNLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT

>XENP014232 hIL2 0.101 (SEQ ID NO: 133)

APTSSSTKKTQLQLEHLLLDLQMLNGINNYKNPKLTQMLKKKFYMPKKATELKHLQCLEEEELKPLEEVLNLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT

>XENP014233 hIL2 0.102 (SEQ ID NO: 134)

APTSSSTKKTQLQLEHLLLDLQMLNGINNYKNPKLTQMLQKKFYMPKKATELKHLQCLEEEELKPLEEVLNLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT

>XENP014234 hIL2 0.103 (SEQ ID NO: 135)

APTSSSTKKTQLQLEHLLLDLQMLNGINNYKNPKLTQMLVKKFYMPKKATELKHLQCLEEEELKPLEEVLNLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT

>XENP014235 hIL2 0.104 (SEQ ID NO: 136)

APTSSSTKKTQLQLEHLLLDLQMLNGINNYKNPKLTQMLRKKFYMPKKATELKHLQCLEEEELKPLEEVLNLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT

Figure 10A

XENP	Variant	k_a (1/Ms)	k_d (1/s)	K_D (M)	Fold k_d over XENP14135	Fold K_D over XENP14135
14135	C125S	5.44E+05	9.09E-02	1.67E-07	1.00	1.00
14136	R38A C125S	7.48E+05	6.24E-02	8.34E-08	1.46	2.00
14137	R38D C125S	3.43E+05	4.82E-01	1.40E-06	0.19	0.12
14138	R38E C125S	4.12E+06	1.08E+00	2.62E-07	0.08	0.64
14139	R38F C125S	1.01E+06	7.19E-02	7.10E-08	1.26	2.35
14140	R38G C125S	NB				
14141	R38H C125S	7.71E+05	5.22E-02	6.78E-08	1.74	2.46
14142	R38I C125S	8.82E+05	1.62E-02	1.83E-08	5.64	9.13
14143	R38K C125S	9.38E+05	1.73E-01	1.85E-07	0.53	0.90
14144	R38L C125S	9.76E+05	1.72E-02	1.77E-08	5.28	9.44
14145	R38M C125S	1.07E+06	3.49E-02	3.26E-08	2.60	5.12
14146	R38N C125S	3.14E+06	8.82E-02	2.81E-08	1.03	5.94
14147	R38P C125S	NB				
14148	R38Q C125S	8.52E+05	2.41E-01	2.83E-07	0.38	0.59
14149	R38S C125S	2.13E+06	9.46E-02	4.45E-08	0.96	3.75
14150	R38T C125S	5.96E+05	7.80E-02	1.31E-07	1.17	1.27
14151	R38V C125S	9.55E+05	2.77E-02	2.90E-08	3.28	5.76
14152	R38W C125S	6.14E+05	7.96E-02	1.30E-07	1.14	1.28
14153	R38Y C125S	6.97E+04	2.07E-01	2.96E-06	0.44	0.06
14154	T41A C125S	1.35E+05	2.08E-01	1.54E-06	0.44	0.11
14155	T41D C125S	1.68E+04	3.30E-01	1.96E-05	0.28	0.01
14156	T41E C125S	8.23E+05	2.44E-01	2.97E-07	0.37	0.56
14157	T41F C125S	2.30E+06	9.11E-02	3.97E-08	1.00	4.21
14158	T41G C125S	1.03E+06	1.05E-01	1.02E-07	0.87	1.64
14159	T41H C125S	1.26E+06	7.04E-02	5.59E-08	1.29	2.99
14160	T41I C125S	NB				
14161	T41K C125S	6.59E+05	3.54E-02	5.37E-08	2.57	3.11
14162	T41L C125S	1.67E+06	3.59E-02	2.15E-08	2.53	7.77
14163	T41M C125S	1.37E+06	8.14E-02	5.94E-08	1.12	2.81
14164	T41N C125S	4.88E+05	1.49E-01	3.06E-07	0.61	0.55
14165	T41P C125S	NB				

Figure 10B

XENP	Variant	k_a (1/Ms)	k_d (1/s)	K_D (M)	Fold k_d over XENP14135	Fold K_D over XENP14135
14166	T41Q C125S	1.51E+05	1.99E-01	1.32E-06	0.46	0.13
14167	T41R C125S	7.17E+05	5.25E-02	7.32E-08	1.73	2.28
14168	T41S C125S	6.77E+05	9.79E-02	1.44E-07	0.93	1.16
14169	T41V C125S	NB				
14170	T41W C125S	NB				
14171	T41Y C125S	NB				
14172	F42A C125S	NB				
14173	F42D C125S	NB				
14174	F42E C125S	NB				
14175	F42G C125S	NB				
14176	F42H C125S	NB				
14177	F42I C125S	NB				
14178	F42K C125S	NB				
14179	F42L C125S	NB				
14180	F42M C125S	2.62E+06	1.34E-01	5.12E-08	0.68	3.26
14181	F42N C125S	NB				
14182	F42P C125S	NB				
14183	F42Q C125S	NB				
14184	F42R C125S	NB				
14185	F42S C125S	NB				
14186	F42T C125S	NB				
14187	F42V C125S	NB				
14188	F42W C125S	1.36E+06	8.63E-02	6.35E-08	1.05	2.63
14189	F42Y C125S	4.46E+05	3.12E-01	7.00E-07	0.29	0.24
14190	R38Q T41K C125S	3.54E+05	1.73E-01	4.89E-07	0.53	0.34
14191	R38Q T41Q C125S	2.12E+05	5.25E-01	2.47E-06	0.17	0.07
14192	R38E T41K C125S	3.54E+06	1.10E-01	3.11E-08	0.83	5.37
14193	R38Q T41R C125S	4.34E+05	2.31E-01	5.33E-07	0.39	0.31
14194	R38N T41Q C125S	5.32E+06	4.50E-01	8.46E-08	0.20	1.97
14195	R38Q T41V C125S	NB				
14196	R38N T41V C125S	NB				
14201	R38Q T41M C125S	NB				
14202	R38Q T41S C125S	2.23E+05	3.82E-01	1.71E-06	0.24	0.10
14203	R38Q T41L C125S	NB				
14204	R38N T41M C125S	NB				
14205	T41I F42Y C125S	NB				

Figure 10C

XENP	Variant	k_a (1/Ms)	k_d (1/s)	K_D (M)	Fold k_d over XENP14135	Fold K_D over XENP14135
14206	T41E F42Y C125S	9.73E+03	2.95E-01	3.03E-05	0.31	0.01
14207	T41D F42Y C125S	1.15E+06	3.65E-01	3.19E-07	0.25	0.52
14208	T41M F42Y C125S	3.43E+06	2.85E-01	8.30E-08	0.32	2.01
14209	T41Q F42Y C125S	1.54E+05	4.06E-01	2.63E-06	0.22	0.06
14210	T41E F42H C125S	NB				
14211	T41E F42L C125S	NB				
14212	T41E F42P C125S	NB				
14213	R38Q F42Y C125S	2.94E+05	7.14E-01	2.43E-06	0.13	0.07
14214	R38N T41R C125S	5.95E+03	3.40E-01	5.72E-05	0.27	0.00
14215	R38N T41K C125S	NB				
14216	R38V T41R C125S	5.30E+05	6.80E-02	1.28E-07	1.34	1.30
14217	R38P T41R C125S	1.73E+05	2.97E-01	1.71E-06	0.31	0.10
14218	T41E F42K C125S	NB				
14219	T41D F42K C125S	NB				
14220	T41M F42K C125S	NB				
14221	T41Q F42K C125S	NB				
14222	R38Q F42K C125S	NB				
14223	T41I F42K C125S	NB				
14224	R38N F42K C125S	NB				
14225	T41H F42K C125S	NB				
14226	R38Q T41K F42Y C125S	NB				
14227	R38Q T41R F42Y C125S	NB				
14228	R38Q T41Q F42Y C125S	NB				
14229	R38Q T41V F42Y C125S	NB				
14230	R38N T41K F42K C125S	NB				
14231	R38Q T41H F42K C125S	NB				
14232	R38Q T41K F42K C125S	NB				
14233	R38Q T41Q F42K C125S	NB				
14234	R38Q T41V F42K C125S	NB				
14235	R38Q T41R F42K C125S	NB				

Figure 11A

XENP	Variant	k_a (1/Ms)	k_d (1/s)	K_D (M)	Fold k_d over XENP14135	Fold K_D over XENP14135
14135	C125S	1.05E+06	1.64E-02	1.56E-08	1.00	1.00
14136	R38A C125S	9.84E+05	7.03E-02	7.14E-08	0.23	0.22
14137	R38D C125S	NB				
14138	R38E C125S	NB				
14139	R38F C125S	1.54E+06	7.92E-02	5.13E-08	0.21	0.30
14140	R38G C125S	NB				
14141	R38H C125S	9.17E+05	7.24E-02	7.90E-08	0.23	0.20
14142	R38I C125S	4.48E+05	2.23E-02	4.98E-08	0.74	0.31
14143	R38K C125S	7.87E+05	5.30E-02	6.73E-08	0.31	0.23
14144	R38L C125S	7.61E+05	2.98E-02	3.91E-08	0.55	0.40
14145	R38M C125S	9.27E+05	4.64E-02	5.01E-08	0.35	0.31
14146	R38N C125S	4.62E+06	2.85E-01	6.17E-08	0.06	0.25
14147	R38P C125S	NB				
14148	R38Q C125S	4.13E+04	4.16E-01	1.01E-05	0.04	0.00
14149	R38S C125S	3.32E+06	1.02E-01	3.07E-08	0.16	0.51
14150	R38T C125S	6.61E+05	1.19E-01	1.80E-07	0.14	0.09
14151	R38V C125S	7.67E+05	3.67E-02	4.78E-08	0.45	0.33
14152	R38W C125S	1.12E+06	1.13E-01	1.01E-07	0.15	0.15
14153	R38Y C125S	3.05E+06	1.32E-01	4.34E-08	0.12	0.36
14154	T41A C125S	6.33E+05	7.46E-02	1.18E-07	0.22	0.13
14155	T41D C125S	5.07E+03	2.36E-01	4.65E-05	0.07	0.00
14156	T41E C125S	5.68E+05	2.91E-01	5.12E-07	0.06	0.03
14157	T41F C125S	2.24E+06	1.14E-01	5.10E-08	0.14	0.31
14158	T41G C125S	1.33E+06	3.47E-02	2.62E-08	0.47	0.60
14159	T41H C125S	1.43E+06	2.87E-02	2.00E-08	0.57	0.78
14160	T41I C125S	2.64E+05	1.02E-02	3.86E-08	1.61	0.40
14161	T41K C125S	1.07E+06	8.24E-03	7.71E-09	1.99	2.02
14162	T41L C125S	1.97E+05	9.81E-03	4.99E-08	1.67	0.31
14163	T41M C125S	2.42E+06	1.71E-02	7.04E-09	0.96	2.22
14164	T41N C125S	8.84E+05	5.68E-02	6.43E-08	0.29	0.24
14165	T41P C125S	NA				

Figure 11B

XENP	Variant	k_a (1/Ms)	k_d (1/s)	K_D (M)	Fold k_d over XENP14135	Fold K_D over XENP14135
14166	T41Q C125S	9.54E+05	6.75E-02	7.08E-08	0.24	0.22
14167	T41R C125S	1.15E+06	1.04E-02	9.05E-09	1.57	1.72
14168	T41S C125S	1.39E+06	2.48E-02	1.79E-08	0.66	0.87
14169	T41V C125S	9.11E+04	1.69E-02	1.85E-07	0.97	0.08
14170	T41W C125S	NB				
14171	T41Y C125S	NB				
14172	F42A C125S	NB				
14173	F42D C125S	NB				
14174	F42E C125S	NB				
14175	F42G C125S	NB				
14176	F42H C125S	NB				
14177	F42I C125S	NB				
14178	F42K C125S	NB				
14179	F42L C125S	4.52E+05	1.91E-02	4.23E-08	0.86	0.37
14180	F42M C125S	1.72E+06	3.18E-02	1.85E-08	0.52	0.84
14181	F42N C125S	NB				
14182	F42P C125S	NB				
14183	F42Q C125S	NB				
14184	F42R C125S	NB				
14185	F42S C125S	NB				
14186	F42T C125S	NB				
14187	F42V C125S	NB				
14188	F42W C125S	2.78E+05	3.92E-02	1.41E-07	0.42	0.11
14189	F42Y C125S	9.64E+05	2.21E-01	2.29E-07	0.07	0.07
14190	R38Q T41K C125S	1.46E+06	1.43E-01	9.83E-08	0.11	.16
14191	R38Q T41Q C125S	9.08E+05	1.78E-01	1.96E-07	0.09	0.08
14192	R38E T41K C125S	8.18E+05	1.41E-01	1.72E-07	0.12	0.09
14193	R38Q T41R C125S	4.06E+05	1.86E-01	4.58E-07	0.09	0.03
14194	R38N T41Q C125S	Weak				
14195	R38Q T41V C125S	NB				
14196	R38N T41V C125S	NB				
14201	R38Q T41M C125S	Weak				
14202	R38Q T41S C125S	2.17E+05	2.68E-01	1.24E-06	0.06	0.01
14203	R38Q T41L C125S	NB				
14204	R38N T41M C125S	NB				
14205	T41I F42Y C125S	NB				

Figure 11C

XENP	Variant	k_a (1/Ms)	k_d (1/s)	K_D (M)	Fold k_d over XENP14135	Fold K_D over XENP14135
14206	T41E F42Y C125S	8.99E+05	2.52E-01	2.80E-07	0.07	0.06
14207	T41D F42Y C125S	1.40E+06	1.94E-01	1.39E-07	0.08	0.11
14208	T41M F42Y C125S	1.71E+06	1.39E-01	8.10E-08	0.12	0.19
14209	T41Q F42Y C125S	4.41E+04	2.62E-01	5.95E-06	0.06	0.00
14210	T41E F42H C125S	NB				
14211	T41E F42L C125S	NB				
14212	T41E F42P C125S	NB				
14213	R38Q F42Y C125S	3.75E+05	4.16E-01	1.11E-06	0.04	0.01
14214	R38N T41R C125S	1.01E+06	1.50E-01	1.49E-07	0.11	0.10
14215	R38N T41K C125S	9.96E+05	7.51E-02	7.54E-08	0.22	0.21
14216	R38V T41R C125S	1.91E+05	4.08E-02	2.14E-07	0.40	0.07
14217	R38P T41R C125S	5.38E+05	1.75E-01	3.26E-07	0.09	0.05
14218	T41E F42K C125S	NB				
14219	T41D F42K C125S	NB				
14220	T41M F42K C125S	NB				
14221	T41Q F42K C125S	NB				
14222	R38Q F42K C125S	NB				
14223	T41I F42K C125S	NB				
14224	R38N F42K C125S	NB				
14225	T41H F42K C125S	NB				
14226	R38Q T41K F42Y C125S	NB				
14227	R38Q T41R F42Y C125S	NB				
14228	R38Q T41Q F42Y C125S	NB				
14229	R38Q T41V F42Y C125S	NB				
14230	R38N T41K F42K C125S	NB				
14231	R38Q T41H F42K C125S	NB				
14232	R38Q T41K F42K C125S	NB				
14233	R38Q T41Q F42K C125S	NB				
14234	R38Q T41V F42K C125S	NB				
14235	R38Q T41R F42K C125S	NB				

Figure 12

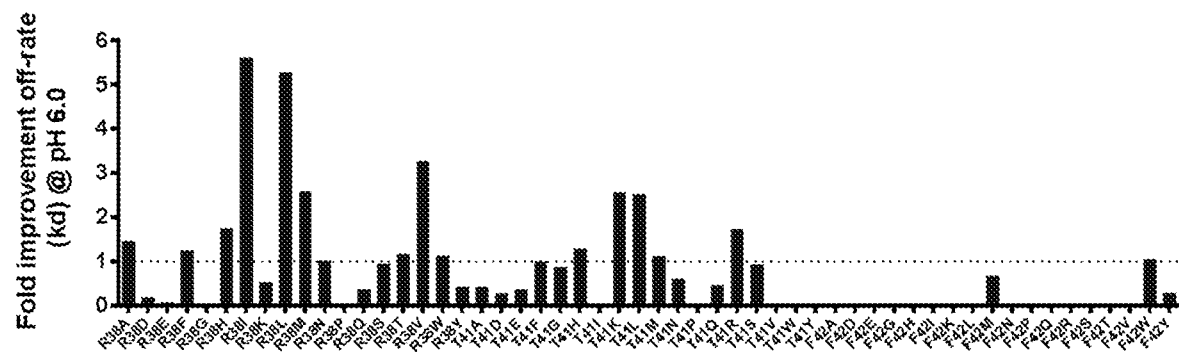


Figure 13

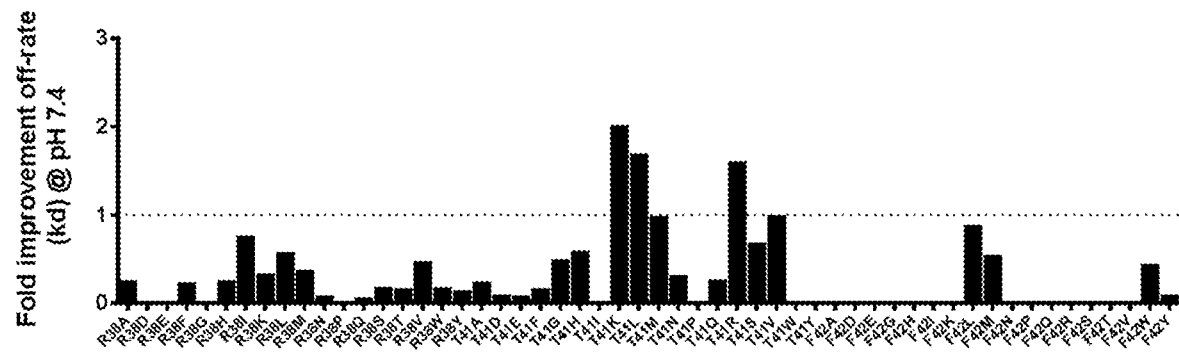


Figure 14

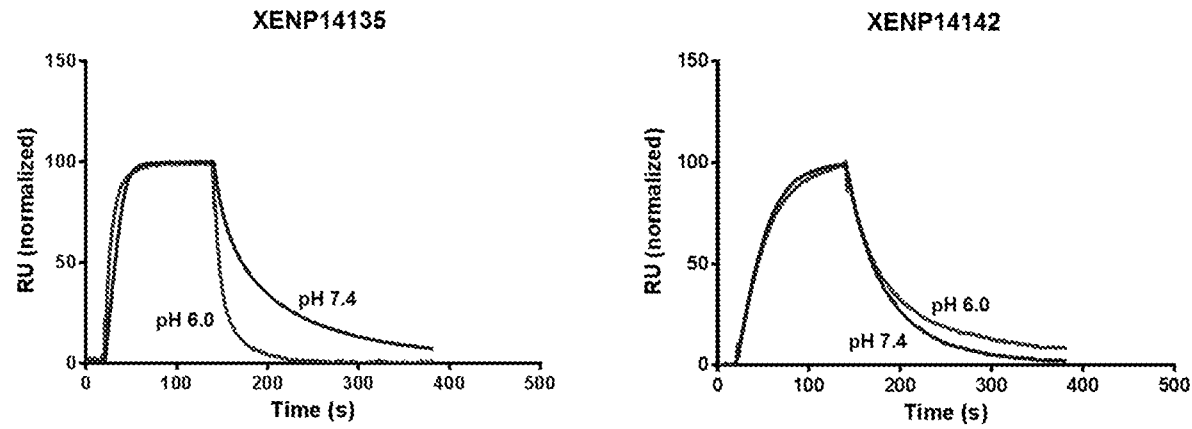


Figure 15

>XENP014277 hIL2 0.6 (SEQ ID NO: 137)

APTSSSTKKTQLQLEHLLLDLQMI LNGI SNHKNPRLARMLTFKFYMPEKATELKHLQCLEEEELKPLEEALRLAPSKN
FHLRPRDLISDVNVIVLELKGSETTFMCEYADETATIVEFLNRWITFSTSIISTLTGS

>XENP014381 hIL2 0.202 (SEQ ID NO: 138)

APTSSSTKKTQLQLEHLLLDLQMI LNGI SNHKNPRLALMLTFKFYMPEKATELKHLQCLEEEELKPLEEALRLAPSKN
FHLRPRDLISDVNVIVLELKGSETTFMCEYADETATIVEFLNRWITFSTSIISTLTGS

Figure 16

XENP	Substitutions	pH 7.4			pH 6.0			Ratio pH 7.4/pH 6.0
		k_a (1/Ms)	k_d (1/s)	K_D (M)	k_a (1/Ms)	k_d (1/s)	K_D (M)	
14277	N29S Y31H K35R T37A K48E V69A N71R Q74P N88D I89V C125S Q126T	4.7E+07	9.2E-02	2.0E-09	3.3E+05	6.2E-02	1.9E-07	0.01
14381	N29S Y31H K35R T37A R38L K48E V69A N71R Q74P N88D I89V C125S Q126T	4.2E+05	3.9E-03	9.4E-09	2.7E+5	4.2E-03	1.68E-08	0.59

Figure 17A

>XENP014135 hIL2 0.1 (SEQ ID NO: 139)

APTSSSTKKTQLQLEHLLLDLQMLNGINNYKNPKLTRMLTFKFYMPKKATELKHLQCLEEEELKPLEEVLNLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLTGS

>XENP014142 hIL2 0.15 (SEQ ID NO: 140)

APTSSSTKKTQLQLEHLLLDLQMLNGINNYKNPKLTIMLTTFKFYMPKKATELKHLQCLEEEELKPLEEVLNLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLTGS

>XENP014143 hIL2 0.16 (SEQ ID NO: 141)

APTSSSTKKTQLQLEHLLLDLQMLNGINNYKNPKLTKMLTFKFYMPKKATELKHLQCLEEEELKPLEEVLNLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT

>XENP014144 hIL2 0.17 (SEQ ID NO: 142)

APTSSSTKKTQLQLEHLLLDLQMLNGINNYKNPKLTMLTFKFYMPKKATELKHLQCLEEEELKPLEEVLNLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLTGS

>XENP014168 hIL2 0.41 (SEQ ID NO: 143)

APTSSSTKKTQLQLEHLLLDLQMLNGINNYKNPKLTRMLSFKFYMPKKATELKHLQCLEEEELKPLEEVLNLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT

>XENP014189 hIL2 0.62 (SEQ ID NO: 144)

APTSSSTKKTQLQLEHLLLDLQMLNGINNYKNPKLTRMLTYKFYMPKKATELKHLQCLEEEELKPLEEVLNLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT

>XENP023816 hIL2 0.205 (SEQ ID NO: 145)

APTSSSTKKTQLQLEHLLLDLQMLNGINNYKNPKLTRMLTFKFYMPKKATELKHLQCLEEEELKPLEEVLNLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLTGS

>XENP023817 hIL2 0.206 (SEQ ID NO: 146)

APTSSSTKKTQDQLEHLLLDLQMLNGINNYKNPKLTRMLTFKFYMPKKATELKHLQCLEEEELKPLEEVLNLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLTGS

>XENP023820 hIL2 0.209 (SEQ ID NO: 147)

APTSSSTKKTQLEHLLLDLQMLNGINNYKNPKLTRMLTFKFYMPKKATELKHLQCLEEEELKPLEEVLNLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLTGS

>XENP023824 hIL2 0.213 (SEQ ID NO: 148)

APTSSSTKKTQLQLEHLLLDLQMLNGINNYKNPKLTRMLTFKFYMPKKATELKHLQCLEEEELKPLEEVLNLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLTGS

>XENP023827 hIL2 0.216 (SEQ ID NO: 149)

APTSSSTKKTQLQLEYLLLDLQMLNGINNYKNPKLTRMLTFKFYMPKKATELKHLQCLEEEELKPLEEVLNLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLTGS

>XENP023830 hIL2 0.219 (SEQ ID NO: 150)

APTSSSTKKTQLQLEHLLDDLQMLNGINNYKNPKLTRMLTFKFYMPKKATELKHLQCLEEEELKPLEEVLNLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLTGS

>XENP023833 hIL2 0.222 (SEQ ID NO: 151)

APTSSSTKKTQLQLEHLLLDLQMLNGINNYKNPKLTRMLTFKFYMPKKATELKHLQCLEEEELKPLEEVLNLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLTGS

Figure 17B

>XENP023834 hIL2 0.223 (SEQ ID NO: 152)

APTSSSTKKTQLQLEHLLLDLQMLNGINNYKNPKLTRMLTFKFYMPKKATELKHLQCLEEEELKPLEEVLNLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLTGS

>XENP023836 hIL2 0.225 (SEQ ID NO: 153)

APTSSSTKKTQLQLEHLLLDLQMLNGINNYKNPRLTRMLTFKFYMPKKATELKHLQCLEEEELKPLEEVLNLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLTGS

>XENP023837 hIL2 0.226 (SEQ ID NO: 154)

APTSSSTKKTQLQLEHLLLDLQMLNGINNYKNPKLSRMLTFKFYMPKKATELKHLQCLEEEELKPLEEVLNLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLTGS

>XENP023838 hIL2 0.227 (SEQ ID NO: 155)

APTSSSTKKTQLQLEHLLLDLQMLNGINNYKNPKLTRMLTFRFYMPKKATELKHLQCLEEEELKPLEEVLNLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLTGS

>XENP023839 hIL2 0.228 (SEQ ID NO: 156)

APTSSSTKKTQLQLEHLLLDLQMLNGINNYKNPKLTRMLTFKYMPKKATELKHLQCLEEEELKPLEEVLNLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLTGS

>XENP023840 hIL2 0.229 (SEQ ID NO: 157)

APTSSSTKKTQLQLEHLLLDLQMLNGINNYKNPKLTRMLTFKFFMPKKATELKHLQCLEEEELKPLEEVLNLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLTGS

>XENP023842 hIL2 0.231 (SEQ ID NO: 158)

APTSSSTKKTQLQLEHLLLDLQMLNGINNYKNPKLTRMLTFKFYMPRKATELKHLQCLEEEELKPLEEVLNLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLTGS

>XENP023843 hIL2 0.232 (SEQ ID NO: 159)

APTSSSTKKTQLQLEHLLLDLQMLNGINNYKNPKLTRMLTFKFYMPKEATELKHLQCLEEEELKPLEEVLNLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLTGS

>XENP023846 hIL2 0.235 (SEQ ID NO: 160)

APTSSSTKKTQLQLEHLLLDLQMLNGINNYKNPKLTRMLTFKFYMPKKATELKHLQCLEQEELKPLEEVLNLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLTGS

>XENP023848 hIL2 0.237 (SEQ ID NO: 161)

APTSSSTKKTQLQLEHLLLDLQMLNGINNYKNPKLTRMLTFKFYMPKKATELKHLQCLEEEQLKPLEEVLNLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLTGS

>XENP023849 hIL2 0.238 (SEQ ID NO: 162)

APTSSSTKKTQLQLEHLLLDLQMLNGINNYKNPKLTRMLTFKFYMPKKATELKHLQCLEEEELRPLEEVLNLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLTGS

>XENP023851 hIL2 0.240 (SEQ ID NO: 163)

APTSSSTKKTQLQLEHLLLDLQMLNGINNYKNPKLTRMLTFKFYMPKKATELKHLQCLEEEELKPLEQVLNLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLTGS

>XENP023852 hIL2 0.241 (SEQ ID NO: 164)

APTSSSTKKTQLQLEHLLLDLQMLNGINNYKNPKLTRMLTFKFYMPKKATELKHLQCLEEEELKPLEELLNLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLTGS

Figure 17C

>XENP023853 hIL2 0.242 (SEQ ID NO: 165)

APTSSSTKKTQLQLEHLLLDLQMLNGINNYKNPKLTRMLTFKFYMPKKATELKHLQCLEEEELKPLEEVLNLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLTGS

>XENP023855 hIL2 0.244 (SEQ ID NO: 166)

APTSSSTKKTQLQLEHLLLDLQMLNGINNYKNPKLTRMLTFKFYMPKKATELKHLQCLEEEELKPLEEVLNLAQSKN
FHLDPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLTGS

>XENP023859 hIL2 0.248 (SEQ ID NO: 167)

APTSSSTKKTQLQLEHLLLDLQMLNGINNYKNPKLTRMLTFKFYMPKKATELKHLQCLEEEELKPLEEVLNLAQSKN
FHLRPRNLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLTGS

>XENP023861 hIL2 0.250 (SEQ ID NO: 168)

APTSSSTKKTQLQLEHLLLDLQMLNGINNYKNPKLTRMLTFKFYMPKKATELKHLQCLEEEELKPLEEVLNLAQSKN
FHLRPRDLITNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLTGS

>XENP023862 hIL2 0.251 (SEQ ID NO: 169)

APTSSSTKKTQLQLEHLLLDLQMLNGINNYKNPKLTRMLTFKFYMPKKATELKHLQCLEEEELKPLEEVLNLAQSKN
FHLRPRDLISDINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLTGS

>XENP023868 hIL2 0.257 (SEQ ID NO: 170)

APTSSSTKKTQLQLEHLLLDLQMLNGINNYKNPKLTRMLTFKFYMPKKATELKHLQCLEEEELKPLEEVLNLAQSKN
FHLRPRDLISNINLIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLTGS

>XENP023869 hIL2 0.258 (SEQ ID NO: 171)

APTSSSTKKTQLQLEHLLLDLQMLNGINNYKNPKLTRMLTFKFYMPKKATELKHLQCLEEEELKPLEEVLNLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLTGS

>XENP023871 hIL2 0.260 (SEQ ID NO: 172)

APTSSSTKKTQLQLEHLLLDLQMLNGINNYKNPKLTRMLTFKFYMPKKATELKHLQCLEEEELKPLEEVLNLAQSKN
FHLRPRDLISNINVIVLQLKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLTGS

>XENP023874 hIL2 0.263 (SEQ ID NO: 173)

APTSSSTKKTQLQLEHLLLDLQMLNGINNYKNPKLTRMLTFKFYMPKKATELKHLQCLEEEELKPLEEVLNLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEFADETATIVEFLNRWITFSQSIISTLTGS

>XENP023875 hIL2 0.264 (SEQ ID NO: 174)

APTSSSTKKTQLQLEHLLLDLQMLNGINNYKNPKLTRMLTFKFYMPKKATELKHLQCLEEEELKPLEEVLNLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVRFLNRWITFSQSIISTLTGS

>XENP023876 hIL2 0.265 (SEQ ID NO: 175)

APTSSSTKKTQLQLEHLLLDLQMLNGINNYKNPKLTRMLTFKFYMPKKATELKHLQCLEEEELKPLEEVLNLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLDRWITFSQSIISTLTGS

>XENP023878 hIL2 0.267 (SEQ ID NO: 176)

APTSSSTKKTQLQLEHLLLDLQMLNGINNYKNPKLTRMLTFKFYMPKKATELKHLQCLEEEELKPLEEVLNLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNDWITFSQSIISTLTGS

Figure 17D

>XENP023882 hIL2 0.271 (SEQ ID NO: 177)

APTSSSTKKTQLQLEHLLLDLQMI L N G I N N Y K N P K L T R M L T F K F Y M P K K A T E L K H L Q C L E E E L K P L E E V L N L A Q S K N
F H L R P R D L I S N I N V I V L E L K G S E T T F M C E Y A D E T A T I V E F L N R W I S F S Q S I I S T L T G S

>XENP023883 hIL2 0.272 (SEQ ID NO: 178)

APTSSSTKKTQLQLEHLLLDLQMI L N G I N N Y K N P K L T R M L T F K F Y M P K K A T E L K H L Q C L E E E L K P L E E V L N L A Q S K N
F H L R P R D L I S N I N V I V L E L K G S E T T F M C E Y A D E T A T I V E F L N R W I T F S E S I I S T L T G S

>XENP023885 hIL2 0.274 (SEQ ID NO: 179)

APTSSSTKKTQLQLEHLLLDLQMI L N G I N N Y K N P K L T R M L T F K F Y M P K K A T E L K H L Q C L E E E L K P L E E V L N L A Q S K N
F H L R P R D L I S N I N V I V L E L K G S E T T F M C E Y A D E T A T I V E F L N R W I T F S Q T I I S T L T G S

>XENP023886 hIL2 0.275 (SEQ ID NO: 180)

APTSSSTKKTQLQLEHLLLDLQMI L N G I N N Y K N P K L T R M L T F K F Y M P K K A T E L K H L Q C L E E E L K P L E E V L N L A Q S K N
F H L R P R D L I S N I N V I V L E L K G S E T T F M C E Y A D E T A T I V E F L N R W I T F S Q S I L S T L T G S

>XENP023888 hIL2 0.277 (SEQ ID NO: 181)

APTSSSTKKTQLQLEHLLLDLQMI L N G I N N Y K N P K L T R M L T F K F Y M P K K A T E L K H L Q C L E E E L K P L E E V L N L A Q S K N
F H L R P R D L I S N I N V I V L E L K G S E T T F M C E Y A D E T A T I V E F L N R W I T F S Q S I I T T L T G S

>XENP023889 hIL2 0.278 (SEQ ID NO: 182)

APTSSSTKKTQLQLEHLLLDLQMI L N G I N N Y K N P K L T R M L T F K F Y M P K K A T E L K H L Q C L E E E L K P L E E V L N L A Q S K N
F H L R P R D L I S N I N V I V L E L K G S E T T F M C E Y A D E T A T I V E F L N R W I T F S Q S I I S T L S G S

Figure 18A

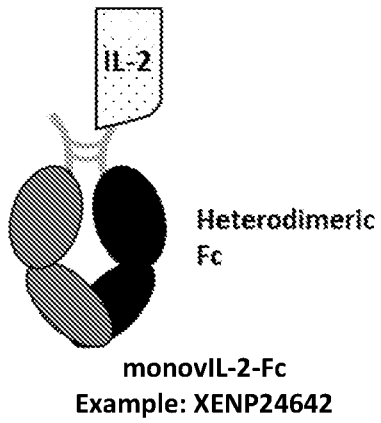
XENP	Substitution	Interface	IL-2Rα	IL-2Rβ	IL-2R$\beta\gamma$
14135	WT (C125S)		1.00	1.00	1.00
14142	R38I C125S	IL-2R α	0.96	0.33	0.81
14143	R38K C125S	IL-2R α	0.85	0.39	1.13
14144	R38L C125S	IL-2R α	0.92	0.31	0.83
14168	T41S C125S	IL-2R α	0.97	0.50	1.52
14189	F42Y C125S	IL-2R α	0.61	0.50	1.49
23816	Q11E C125S	γc	0.74	0.51	0.00
23817	L12D C125S	IL-2R $\beta\gamma$	1.06	0.16	0.33
23820	Q13E C125S	IL-2R β	1.03	0.28	1.10
23824	E15Q C125S	IL-2R $\beta\gamma$	1.08	0.59	2.01
23827	H16Y C125S	IL-2R β	1.09	0.27	0.34
23830	L19D C125S	IL-2R $\beta\gamma$	0.94	0.09	0.17
23833	D20N C125S	IL-2R β	1.16	0.00	0.41
23834	Q22E C125S	γc	1.03	0.31	1.12
23836	K35R C125S	IL-2R α	1.06	0.49	1.27
23837	T37S C125S	IL-2R α	1.02	0.47	1.53
23838	K43R C125S	IL-2R α	0.86	0.24	1.10
23839	F44Y C125S	IL-2R α	-0.05	0.05	0.00
23840	Y45F C125S	IL-2R α	0.90	0.20	0.97
23842	K48R C125S	γc	1.06	0.38	1.05
23843	K49E C125S	γc	1.01	0.23	1.18
23846	E61Q C125S	IL-2R α	0.43	0.17	0.96
23848	E62Q C125S	IL-2R α	0.40	0.45	1.29
23849	K64R C125S	IL-2R α	1.04	0.48	1.21
23851	E68Q C125S	IL-2R α	1.19	0.44	1.22
23852	V69L C125S	IL-2R α	1.12	0.12	0.86
23853	L72I C125S	IL-2R α	1.04	0.42	1.12
23855	R81D C125S	IL-2R α	1.07	0.77	2.45
23859	D84N C125S	IL-2R β	0.49	0.05	0.11
23861	S87T C125S	IL-2R β	1.07	0.43	0.77
23862	N88D C125S	IL-2R β	0.95	0.02	0.09
23868	V91L C125S	IL-2R β	1.08	0.11	1.06
23869	I92L C125S	IL-2R β	1.05	0.72	1.90
23871	E95Q C125S	IL-2R β	0.99	0.12	0.66
23874	Y107F C125S	IL-2R α	0.74	0.22	0.82
23875	E116R C125S	γc	-0.02	0.09	0.00
23876	N119D C125S	γc	0.91	0.52	0.59
23878	R120D C125S	γc	0.43	0.09	0.36

Figure 18B

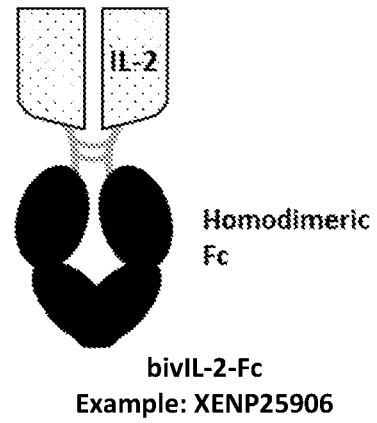
XENP	Substitution	Interface	IL-2R α	IL-2R β	IL-2R $\beta\gamma$
23882	T123S C125S	γc	0.89	0.53	0.69
23883	C125S Q126E	γc	0.91	0.75	1.09
23885	C125S S127T	γc	1.06	0.39	1.19
23886	C125S I129L	γc	0.94	0.05	1.04
23888	C125S S130T	γc	1.12	0.36	1.12
23889	C125S T133S	γc	0.99	0.62	0.36

Figure 19

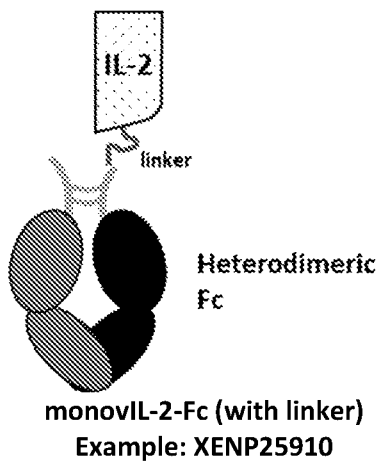
A)



B)



C)



D)

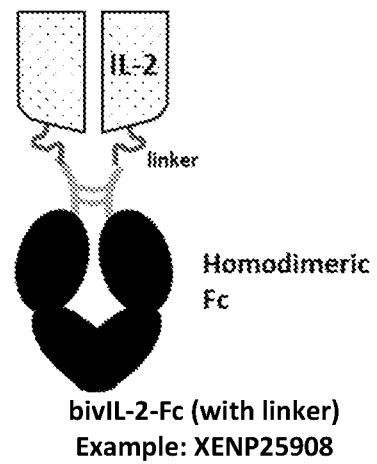


Figure 20A

> XENP024635 empty-Fc-hIL2 0.1 Fc(216) IgG1 pl(-)
) Isosteric A C220S/PVA /S267K/L368D/K370S IgG1 C220S/PVA /S267K/S364K/E357Q

Chain 1 – empty-Fc(216)_IgG1_pl(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S (SEQ ID NO: 183)

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPRE
EEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVS
GFYPSDIAVEWESDGPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEEQGDVFSFSVMHEALHNHYTQKSLSLSPGK

Chain 2 - hIL2_0.1_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q (SEQ ID NO: 184)

APTSSSTKKTQLQLEHLLLDLQMLNGINNYKNPKLTRMLTFKFYMPKKATELKHLCLEEEELKPLEEVLNLAQSKN
FHLRPRDLISNINIVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT/EPKSSDKTHTCPPCPAPPVA
GPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDW
LNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENN
YKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSFSVMHEALHNHYTQKSLSLSPGK

> XENP024636 empty-Fc-hIL2 0.2 Fc(216) IgG1 pl(-)
) Isosteric A C220S/PVA /S267K/L368D/K370S IgG1 C220S/PVA /S267K/S364K/E357Q

Chain 1 - empty_Fc(216)_IgG1_pl(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S (SEQ ID NO: 185)

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPRE
EEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVS
GFYPSDIAVEWESDGPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEEQGDVFSFSVMHEALHNHYTQKSLSLSPGK

Chain 2 - hIL2_0.2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q (SEQ ID NO: 186)

APASSSTKKTQLQLEHLLLDLQMLNGINNYKNPKLTRMLTFKFYMPKKATELKHLCLEEEELKPLEEVLNLAQSKN
FHLRPRDLISNINIVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT/EPKSSDKTHTCPPCPAPPVA
GPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDW
LNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENN
YKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSFSVMHEALHNHYTQKSLSLSPGK

> XENP024637 empty-Fc-hIL2 0.3 Fc(216) IgG1 pl(-)
) Isosteric A C220S/PVA /S267K/L368D/K370S IgG1 C220S/PVA /S267K/S364K/E357Q

Chain 1 - empty_Fc(216)_IgG1_pl(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S (SEQ ID NO: 187)

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPRE
EEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVS
GFYPSDIAVEWESDGPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEEQGDVFSFSVMHEALHNHYTQKSLSLSPGK

Chain 2 - hIL2_0.3_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q (SEQ ID NO: 188)

APASSSTKKTQLQLEHLLLDLQMLNGINNYKNPKLTRMLTAKFAMPKKATELKHLCLEEEELKPLEEVLNLAQSKN
FHLRPRDLISNINIVIVLELKGSETTFMCEYADETATIVEFLNRWITFAQSIISTLT/EPKSSDKTHTCPPCPAPPVA
GPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDW
LNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENN
YKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSFSVMHEALHNHYTQKSLSLSPGK

> XENP024638 empty-Fc-hIL2 0.4 Fc(216) IgG1 pl(-)
) Isosteric A C220S/PVA /S267K/L368D/K370S IgG1 C220S/PVA /S267K/S364K/E357Q

Chain 1 – empty_Fc(216)_IgG1_pl(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S (SEQ ID NO: 189)

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPRE
EEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVS
GFYPSDIAVEWESDGPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEEQGDVFSFSVMHEALHNHYTQKSLSLSPGK

Figure 20B

Chain 2 - hIL2_0.4_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q (SEQ ID NO: 190)

APTSSSTKKTQLQLEHLLLDLQMI LNGLSNHKNPRLARMLTFKFYMPKATELKHLCLEEEELKPLEEALRLAPSKN
 FHLRPRDLISDVNVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT/EPKSSDKTHTCPPCPAPPVA
 GPSVFLFPPKPKDITLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDW
 LNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVVKLTCLVKGFPYPSDIAVEWESNGQPENN
 YKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSVMSVMEALHNHYTQKSLSLSPGK

> XENP024639 empty-Fc-hIL2 0.5 Fc(216) IgG1 pl(-)

) Isosteric A C220S/PVA_/S267K/L368D/K370S IgG1 C220S/PVA_/S267K/S364K/E357Q

Chain 1 – empty_Fc(216)_IgG1_pl(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S (SEQ ID NO: 191)

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDITLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPRE
 EEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVS
 GFYPSDIAVEWESDGPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSVMSVMEALHNHYTQKSLSLSPGK

Chain 2 - hIL2_0.5_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q (SEQ ID NO: 192)

APTSSSTKKTQLQLEHLLLDLQMI LNGLINNYKNPKLTRMLTFKFYMPKATELKHLCLEEEELKPLEEALNLAPSKN
 FHLRPRDLISNINIVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSTISTLT/EPKSSDKTHTCPPCPAPPVA
 GPSVFLFPPKPKDITLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDW
 LNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVVKLTCLVKGFPYPSDIAVEWESNGQPENN
 YKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSVMSVMEALHNHYTQKSLSLSPGK

> XENP024640 empty-Fc-hIL2 0.6 Fc(216) IgG1 pl(-)

) Isosteric A C220S/PVA_/S267K/L368D/K370S IgG1 C220S/PVA_/S267K/S364K/E357Q

Chain 1 - empty_Fc(216)_IgG1_pl(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S (SEQ ID NO: 193)

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDITLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPRE
 EEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVS
 GFYPSDIAVEWESDGPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSVMSVMEALHNHYTQKSLSLSPGK

Chain 2 - hIL2_0.6_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q (SEQ ID NO: 194)

APTSSSTKKTQLQLEHLLLDLQMI LNGLSNHKNPRLARMLTFKFYMPKATELKHLCLEEEELKPLEEALRLAPSKN
 FHLRPRDLISDVNVIVLELKGSETTFMCEYADETATIVEFLNRWITFSTSIISTLT/EPKSSDKTHTCPPCPAPPVA
 GPSVFLFPPKPKDITLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDW
 LNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVVKLTCLVKGFPYPSDIAVEWESNGQPENN
 YKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSVMSVMEALHNHYTQKSLSLSPGK

> XENP024641 empty-Fc-hIL2 0.7 Fc(216) IgG1 pl(-)

) Isosteric A C220S/PVA_/S267K/L368D/K370S IgG1 C220S/PVA_/S267K/S364K/E357Q

Chain 1 – empty_Fc(216)_IgG1_pl(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S (SEQ ID NO: 195)

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDITLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPRE
 EEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVS
 GFYPSDIAVEWESDGPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSVMSVMEALHNHYTQKSLSLSPGK

Chain 2 - hIL2_0.7_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q (SEQ ID NO: 196)

APTSSSTKKTQLQLEHLLLDLQMI LNGLINNYKNPKLTRMLTFKFYMPKATELKHLCLEEEELKPLEEVLNLAQSKN
 FHLRPRDLISNINIVIVLELKGSETTFMCEYADETATIVEFLNRWITFSTSIISTLT/EPKSSDKTHTCPPCPAPPVA
 GPSVFLFPPKPKDITLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDW
 LNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVVKLTCLVKGFPYPSDIAVEWESNGQPENN
 YKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSVMSVMEALHNHYTQKSLSLSPGK

Figure 20C

> XENP024642 empty-Fc-hIL2 0.8 Fc(216) IgG1 pl(-)
) Isosteric A C220S/PVA /S267K/L368D/K370S IgG1 C220S/PVA /S267K/S364K/E357Q

Chain 1 – empty_Fc(216)_IgG1_pl(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S (SEQ ID NO: 197)

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPRE
EEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVS
GFYPSDIAVEWESDGPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVVFSCSVMEALHNHYTQKSLSLSPGK

Chain 2 - hIL2_0.8_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q (SEQ ID NO: 198)

APTSSSTKKTQLQLEHLLLDLQMLNGINNYKNPKLTRMLTFKFYMPKKATELKHLCLEELKPLEEVLNLAQSKN
ELKPLEEVLNLAQSKNFHLRPRDLISRINIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT/EPKS
SDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYN
STYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVS
SDIAVEWESNGQDENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVVFSCSVMEALHNHYTQKSLSLSPGK

> XENP024643 empty-Fc-hIL2 0.15 Fc(216) IgG1 pl(-)
) Isosteric A C220S/PVA /S267K/L368D/K370S IgG1 C220S/PVA /S267K/S364K/E357Q

Chain 1 – empty_Fc(216)_IgG1_pl(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S (SEQ ID NO: 199)

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPRE
EEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVS
GFYPSDIAVEWESDGPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVVFSCSVMEALHNHYTQKSLSLSPGK

Chain 2 - hIL2_0.15_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q (SEQ ID NO: 200)

APTSSSTKKTQLQLEHLLLDLQMLNGINNYKNPKLTIMLTFKFYMPKKATELKHLCLEELKPLEEVLNLAQSKN
FHLRPRDLISRINIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT/EPKSSDKTHTCPPCPAPPVA
GPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDW
LNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVS
GFYPSDIAVEWESNGQDENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVVFSCSVMEALHNHYTQKSLSLSPGK

> XENP024725 empty-Fc-hIL2 0.279 Fc(216) IgG1 pl(-)
) Isosteric A C220S/PVA /S267K/L368D/K370S IgG1 C220S/PVA /S267K/S364K/E357Q

Chain 1 – empty_Fc(216)_IgG1_pl(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S (SEQ ID NO: 201)

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPRE
EEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVS
GFYPSDIAVEWESDGPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVVFSCSVMEALHNHYTQKSLSLSPGK

Chain 2 - hIL2_0.279_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q (SEQ ID NO: 202)

APTSSSTKKTQLQLEHLLLDLQMLNGINNYKNPKLTRMLTFKFYMPKKATELKHLCLEELKPLEEVLNLAQSKN
FHFDPDVISININVFVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT/EPKSSDKTHTCPPCPAPPVA
GPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDW
LNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVS
GFYPSDIAVEWESNGQDENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVVFSCSVMEALHNHYTQKSLSLSPGK

> XENP024728 empty-Fc-hIL2 0.282 Fc(216) IgG1 pl(-)
) Isosteric A C220S/PVA /S267K/L368D/K370S IgG1 C220S/PVA /S267K/S364K/E357Q

Chain 1 – empty_Fc(216)_IgG1_pl(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S (SEQ ID NO: 203)

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPRE
EEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVS
GFYPSDIAVEWESDGPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVVFSCSVMEALHNHYTQKSLSLSPGK

Figure 20D

Chain 2 - hIL2_0.282_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q (SEQ ID NO: 204)

APTSSSTKKTQLQLEHLRLDLEMILNGINNYKNPKLTRMLTFKFYMPKKATELKHLCLEEEELKPLEEVLNLAQSKN
 FHFDPDVISNINVFVLELKGSETTFMCEYADETATIVEFLNRWITFSTSIISTLT/EPKSSDKTHTCPPCPAPPVA
 GPSVFLFPPKPKDITLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDW
 LNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVVKLTCLVKGFPYPSDIAVEWESNGQPENN
 YKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSVMSHEALHNHYTQKSLSLSPGK

> XENP024729 empty-Fc-hIL2_0.283_Fc(216)_IgG1_pl(-)

) Isosteric A C220S/PVA_/S267K/L368D/K370S IgG1 C220S/PVA_/S267K/S364K/E357Q

Chain 1 – empty_Fc(216)_IgG1_pl(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S (SEQ ID NO: 205)

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDITLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPRE
 EEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVS
 GFYPYPSDIAVEWESDGPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSVMSHEALHNHYTQKSLSLSPGK

Chain 2 - hIL2_0.283_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q (SEQ ID NO: 206)

APTSSSTKKTQLQLEHLRLDLEMILNGINNYKNPKLTRMLTFKFYMPKKATELKHLCLEEEELKPLEEVLNLAQSKN
 FHFDPDVISNINVFVLELKGSETTFMCEYADETATIVEFLNRWITFSTSIIRTLT/EPKSSDKTHTCPPCPAPPVA
 GPSVFLFPPKPKDITLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDW
 LNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVVKLTCLVKGFPYPSDIAVEWESNGQPENN
 YKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSVMSHEALHNHYTQKSLSLSPGK

> XENP024730 empty-Fc-hIL2_0.284_Fc(216)_IgG1_pl(-)

) Isosteric A C220S/PVA_/S267K/L368D/K370S IgG1 C220S/PVA_/S267K/S364K/E357Q

Chain 1 – empty_Fc(216)_IgG1_pl(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S (SEQ ID NO: 207)

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDITLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPRE
 EEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVS
 GFYPYPSDIAVEWESDGPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSVMSHEALHNHYTQKSLSLSPGK

Chain 2 - hIL2_0.284_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q (SEQ ID NO: 208)

APASSSTKKTQLQLEHLLLDLQMI LINGINNYKNPKLTRMLTAKFAMPKKATELKHLCLEEEELKPLEEVLNLAQSKN
 FHLRPDLISNINVFVLELKGSETTFMCEYADETATIVEFLNRWITFAQSIISTLT/EPKSSDKTHTCPPCPAPPVA
 GPSVFLFPPKPKDITLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDW
 LNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVVKLTCLVKGFPYPSDIAVEWESNGQPENN
 YKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSVMSHEALHNHYTQKSLSLSPGK

> XENP024731 empty-Fc-hIL2_0.285_Fc(216)_IgG1_pl(-)

) Isosteric A C220S/PVA_/S267K/L368D/K370S IgG1 C220S/PVA_/S267K/S364K/E357Q

Chain 1 – empty_Fc(216)_IgG1_pl(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S (SEQ ID NO: 209)

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDITLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPRE
 EEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVS
 GFYPYPSDIAVEWESDGPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSVMSHEALHNHYTQKSLSLSPGK

Chain 2 - hIL2_0.285_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q (SEQ ID NO: 210)

APASSSTKKTQLQLEHLLLDLQMI LINGINNYKNPKLTRMLTAKFAMPKKATELKHLCLEEEELKPLEEVLNLAQSKN
 FHLRPDLISNINVFVLELKGSETTFMCEYADETATIVEFLNRWITFATSIIISTLT/EPKSSDKTHTCPPCPAPPVA
 GPSVFLFPPKPKDITLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDW
 LNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVVKLTCLVKGFPYPSDIAVEWESNGQPENN
 YKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSVMSHEALHNHYTQKSLSLSPGK

Figure 20E

**> XENP024732 empty-Fc-hIL2 0.286 Fc(216) IgG1 pl(-)
) Isosteric A C220S/PVA /S267K/L368D/K370S IgG1 C220S/PVA /S267K/S364K/E357Q**

Chain 1 – empty_Fc(216)_IgG1_pl(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S (SEQ ID NO: 211)

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPRE
EEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVS
GFYPSDIAVEWESDGPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSQSVMEALHNHYTQKSLSLSPGK

Chain 2 - hIL2_0.286_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q (SEQ ID NO: 212)

APASSSTKKTQLQLEHLLLDLQMI LGINNYKNPKLTRMLTAKFAMPKKATELKHLQCLEEELKPLEEVLNGAQSKN
FHLRPRDLISRINVIVLELKGSETTFMCEYADETATIVEFLNRWITFATSIISTLT/EPKSSDKTHTCPPCPAPPVA
GPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDW
LNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVCLVKGFPYSDIAVEWESNGQPENN
YKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSQSVMEALHNHYTQKSLSLSPGK

Figure 21

	CD25			CD122			CD122:CD132		
XENP	K _D (M)	k _a (1/Ms)	k _d (1/s)	K _D (M)	k _a (1/Ms)	k _d (1/s)	K _D (M)	k _a (1/Ms)	k _d (1/s)
24635	1.74E-08	5.28E+05	9.20E-03	1.47E-08	2.66E+05	3.91E-03	1.28E-09	3.27E+05	4.20E-04
24636	1.45E-08	6.63E+05	9.63E-03	7.94E-09	7.89E+05	6.26E-03	1.24E-09	4.48E+05	5.54E-04
24637				9.97E-09*	8.73E+05	8.70E-03	1.46E-09	4.48E+05	6.54E-04
24638	1.33E-09	6.47E+05	8.59E-04				1.46E-07	1.49E+05	2.17E-02
24639	8.04E-09	3.57E+05	2.87E-03	9.15E-09	4.65E+05	4.25E-03	2.66E-09	2.34E+05	6.24E-04
24640	1.14E-09	9.26E+05	1.05E-03						
24641	1.27E-08	1.09E+06	1.39E-02	1.14E-08	1.21E+06	1.37E-02	1.92E-08	3.96E+05	7.62E-03
24642	1.37E-08	1.19E+06	1.63E-02				1.31E-07	1.28E+05	1.69E-02
24643	2.66E-08	7.54E+05	2.00E-02	1.01E-07	1.00E+06	1.01E-01	6.56E-10	5.52E+05	3.62E-04
24725	1.96E-08	8.76E+05	1.72E-02	7.56E-09	6.95E+05	5.25E-03	2.53E-09	6.84E+05	1.73E-03
24728	4.18E-08	4.13E+05	1.73E-02	8.86E-09	3.19E+05	2.83E-03	8.68E-09	2.93E+05	2.55E-03
24729	2.55E-08	1.01E+06	2.57E-02	2.74E-09	1.01E+06	2.77E-03	2.97E-09	9.81E+05	2.91E-03
24730							1.91E-08	1.49E+05	2.85E-03
24731				5.79E-09	5.07E+05	2.94E-03	8.65E-09	4.49E+05	3.88E-03
24732	9.12E-08	5.69E+03	5.19E-04						

Figure 22A

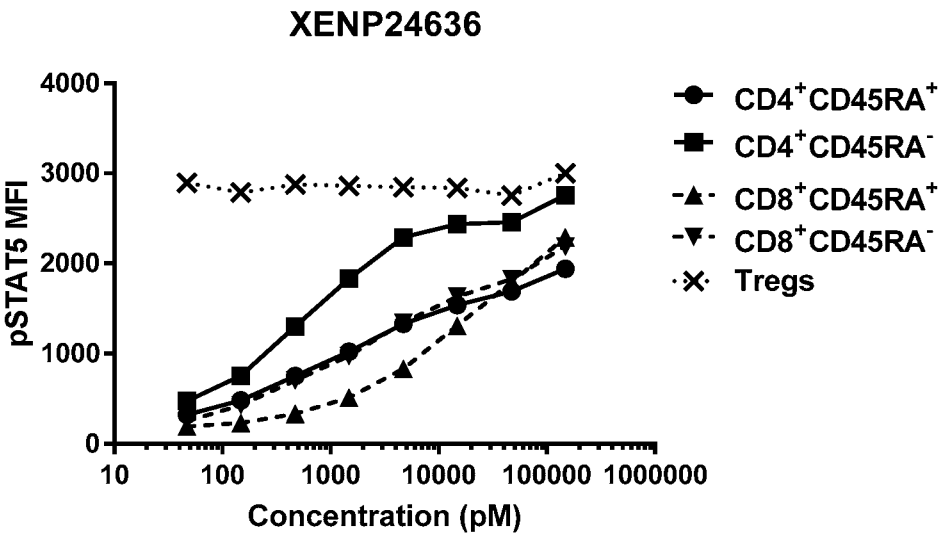


Figure 22B

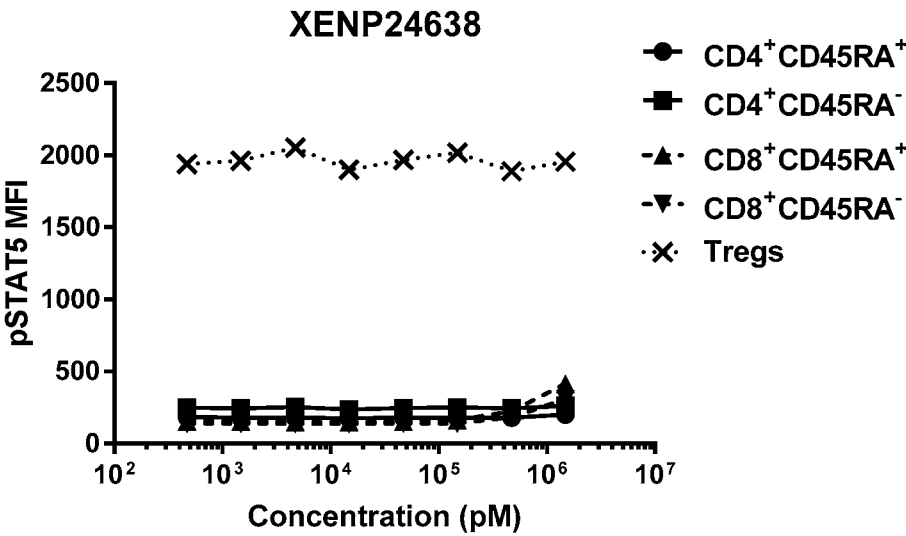


Figure 22C

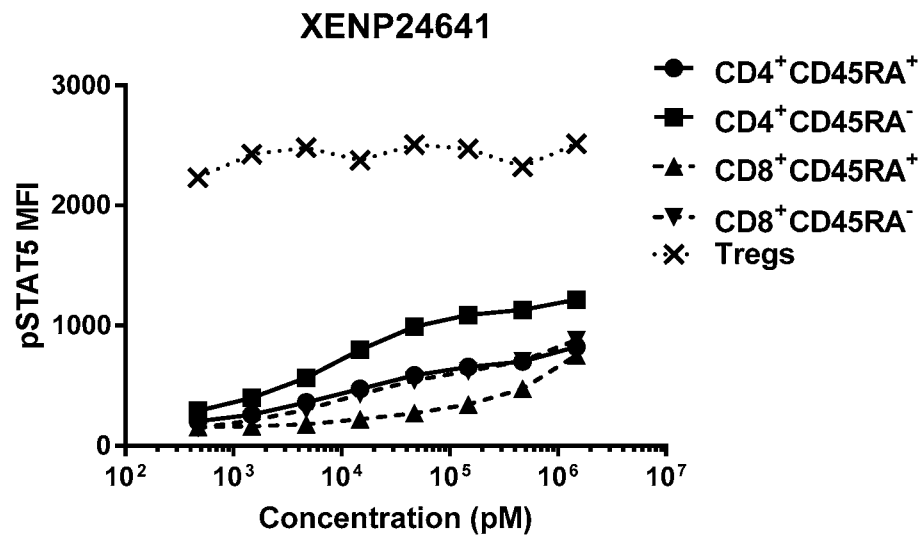


Figure 22D

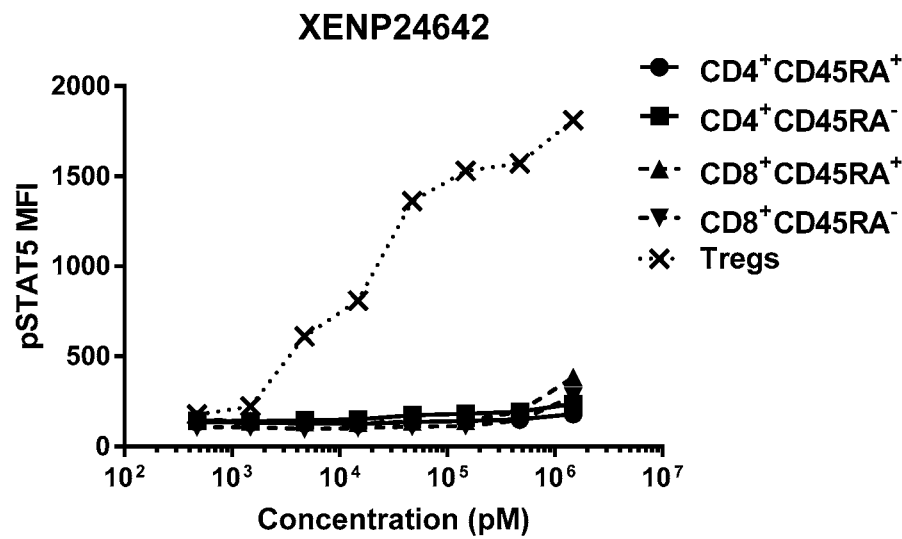


Figure 22E

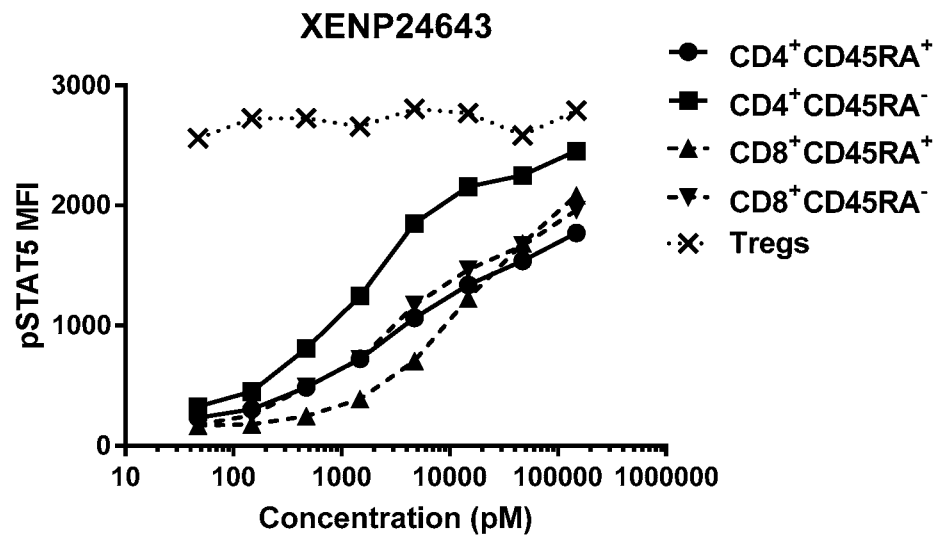


Figure 22F

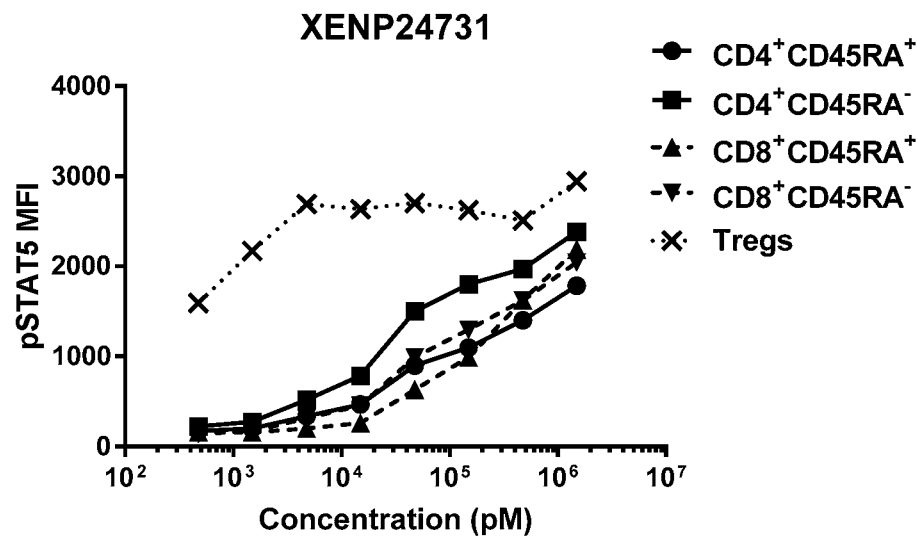


Figure 23

>XENP025906 hIL2 0.8 Fc(216) IgG1 C220S/PVA /S267K (SEQ ID NO: 213)

APTSSSTKKTQLQLEHLLLDLQMI L N G I N N Y K N P K L T R M L T F K F Y M P K K A T E L K H L Q C L E E E L K P L E E V L N L A Q S K N E H L R P R D L I S R I N V I V
L E L K G S E T T F M C E Y A D E T A T I V E F L N R W I T F S Q S I I S T L T / E P K S S D K T H T C P P C P A P P V A G P S V F L F P P K P K D T L M I S R T P E V T C V V V D V K H
E D P E V K F N W Y V D G V E V H N A K T K P R E E Q Y N S T Y R V V S V L T V L H Q D W L N G K E Y K C K V S N K A L P A P I E K T I S K A K G Q P R E P Q V Y T L P P S R E E M T K N
Q V S L T C L V K G F Y P S D I A V E W E S N G Q P E N N Y K T T P P V L D S D G S F F L Y S K L T V D K S R W Q Q G N V F S C S V M H E A L H N H Y T Q K S L S L S P G K

>XENP025907 hIL2 0.2 Fc(216) IgG1 C220S/PVA /S267K (SEQ ID NO: 214)

A P A S S S T K K T Q L Q L E H L L L D L Q M I L N G I N N Y K N P K L T R M L T F K F Y M P K K A T E L K H L Q C L E E E L K P L E E V L N L A Q S K N E H L R P R D L I S N I N V I V
L E L K G S E T T F M C E Y A D E T A T I V E F L N R W I T F S Q S I I S T L T / E P K S S D K T H T C P P C P A P P V A G P S V F L F P P K P K D T L M I S R T P E V T C
V V V D V K H E D P E V K F N W Y V D G V E V H N A K T K P R E E Q Y N S T Y R V V S V L T V L H Q D W L N G K E Y K C K V S N K A L P A P I E K T I S K A
K G Q P R E P Q V Y T L P P S R E E M T K N Q V S L T C L V K G F Y P S D I A V E W E S N G Q P E N N Y K T T P P V L D S D G S F F L Y S K L T V D K S R W
Q Q G N V F S C S V M H E A L H N H Y T Q K S L S L S P G K

Figure 24A

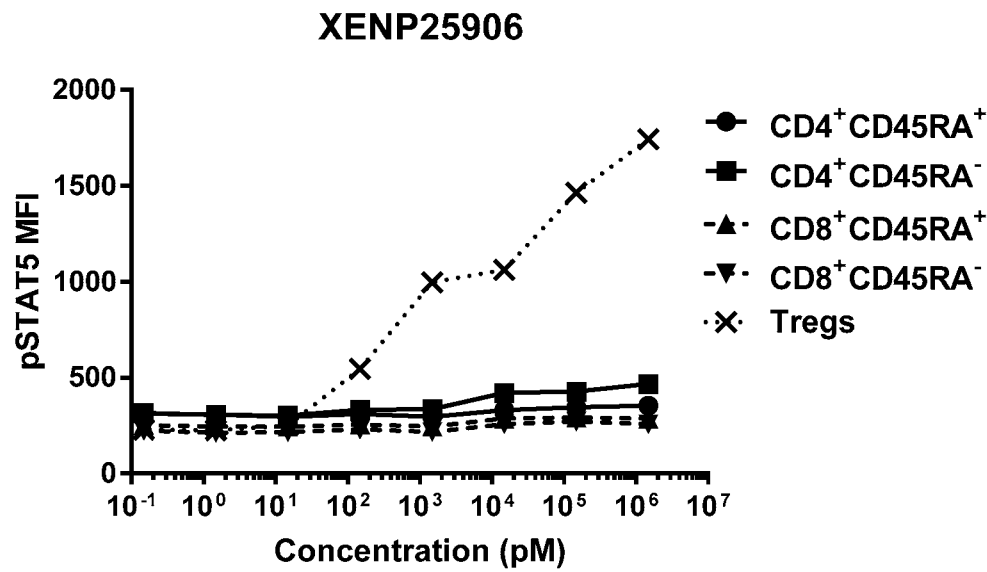


Figure 24B

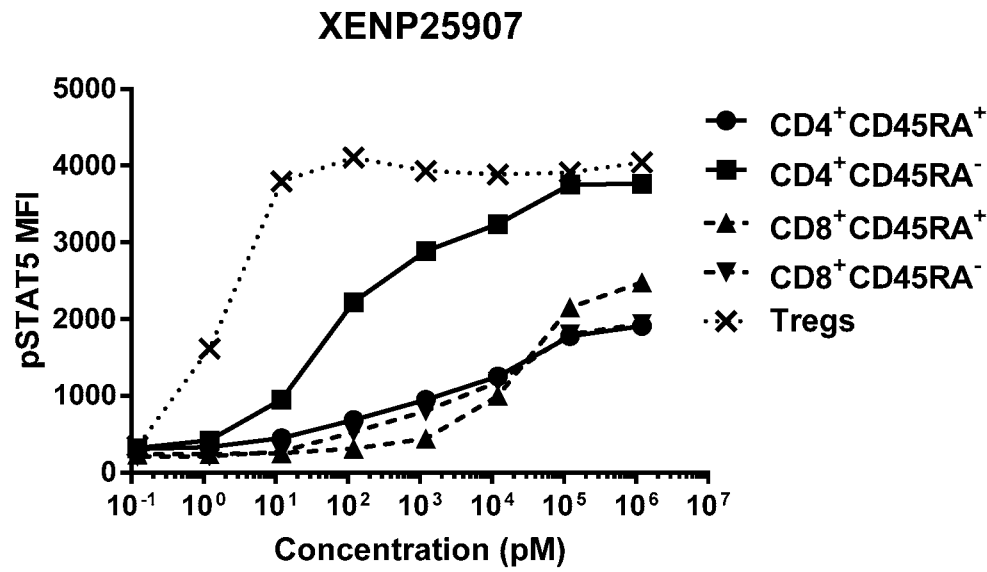


Figure 25A

>XENP025908 hIL2 0.8 (GGGGS)4 Fc(216) IgG1 C220S/PVA /S267K (SEQ ID NO: 215)

APTSSSTKKTQLQLEHLLLDLQMI LINGINNYKNPKLTRMLTFKFYMPKKATELKHLQCLEEEELKPLEEVNLNAQSKNFHLRPRDLISRINVTIV
LELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT/GGGSGGGSGGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKP
KDTLMI.SRTPEVTCVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAK
GQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALH
NHYTQKSLSLSPGK

>XENP025909 hIL2 0.2 (GGGGS)4 Fc(216) IgG1 C220S/PVA /S267K (SEQ ID NO: 216)

APASSSTKKTQLQLEHLLLDLQMI LINGINNYKNPKLTRMLTFKFYMPKKATELKHLQCLEEEELKPLEEVNLNAQSKNFHLRPRDLISRINVTIV
LELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT/GGGSGGGSGGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKP
KDTLMI.SRTPEVTCVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAK
GQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALH
NHYTQKSLSLSPGK

**>XENP025910 empty-Fc-hIL2 0.8 (GGGGS)4 Fc(216) IgG1 pl(-)
Isosteric A C220S/PVA /S267K/L368D/K370S IgG1 C220S/PVA /S267K/S364K/E357Q**
Chain 1 – empty_Fc(216)_IgG1_pl(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S (SEQ ID NO: 217)

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI.SRTPEVTCVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVL
HQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQFENNYKTTPPVLDSDG
SFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK

Chain 2 - hIL2_0.8_(GGGGS)4_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q (SEQ ID NO: 218)

APTSSSTKKTQLQLEHLLLDLQMI LINGINNYKNPKLTRMLTFKFYMPKKATELKHLQCLEEEELKPLEEVNLNAQSKNFHLRPRDLISRINVTIV
LELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT/GGGSGGGSGGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKP
KDTLMI.SRTPEVTCVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAK
GQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALH
NHYTQKSLSLSPGK

**>XENP025911 empty-Fc-hIL2 0.2 (GGGGS)4 Fc(216) IgG1 pl(-)
Isosteric A C220S/PVA /S267K/L368D/K370S IgG1 C220S/PVA /S267K/S364K/E357Q**
Chain 1 – empty_Fc(216)_IgG1_pl(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S (SEQ ID NO: 219)

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI.SRTPEVTCVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVL
HQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQFENNYKTTPPVLDSDG
SFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK

Chain 2 - hIL2_0.2_(GGGGS)4_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q (SEQ ID NO: 220)

APASSSTKKTQLQLEHLLLDLQMI LINGINNYKNPKLTRMLTFKFYMPKKATELKHLQCLEEEELKPLEEVNLNAQSKNFHLRPRDLISRINVTIV
LELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT/GGGSGGGSGGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKP
KDTLMI.SRTPEVTCVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAK
GQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALH
NHYTQKSLSLSPGK

Figure 26A

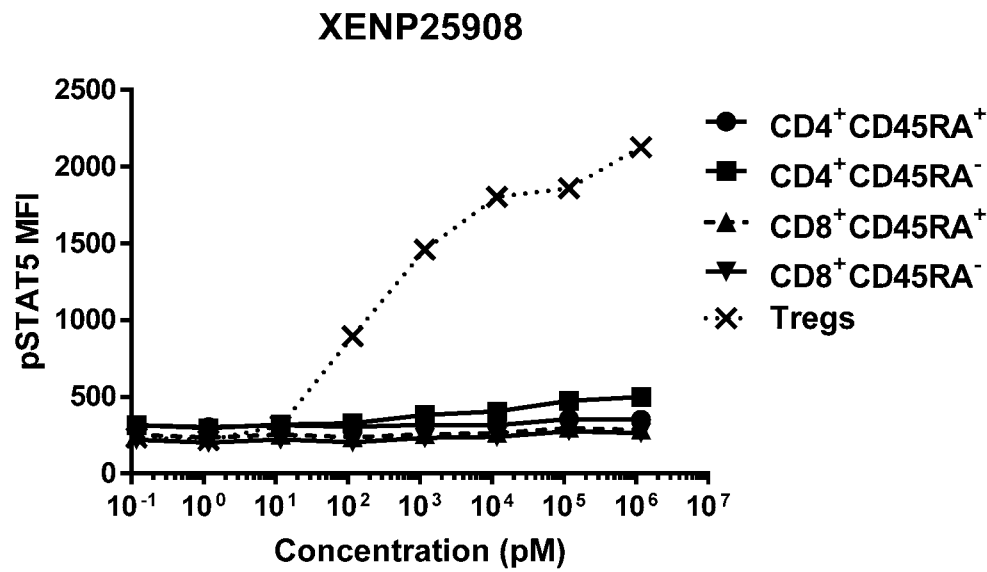


Figure 26B

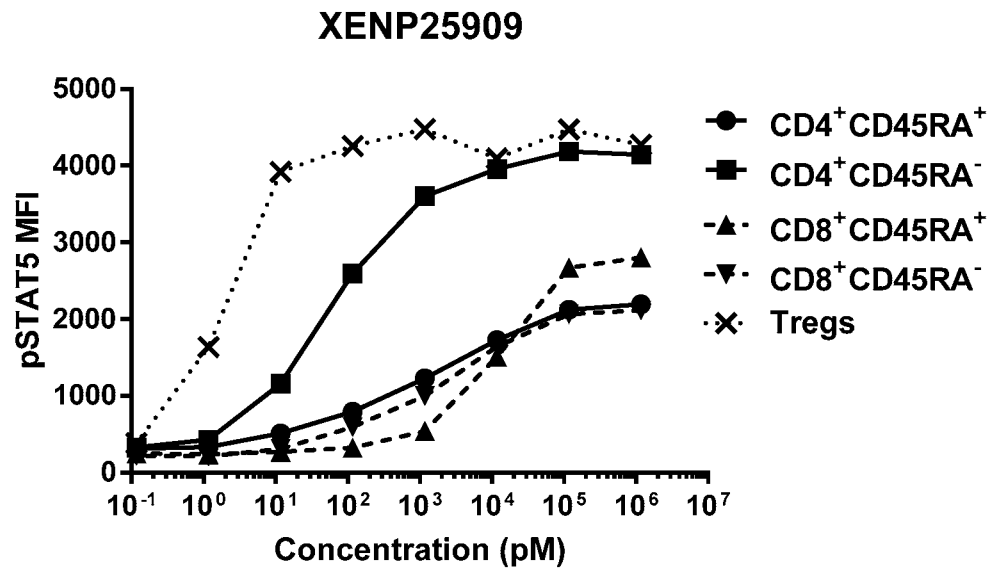


Figure 26C

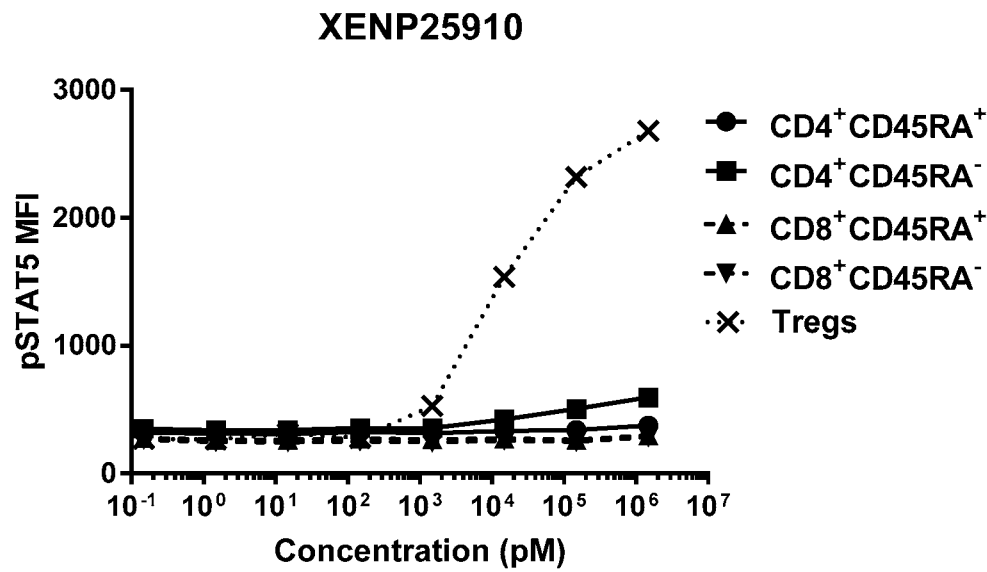


Figure 26D

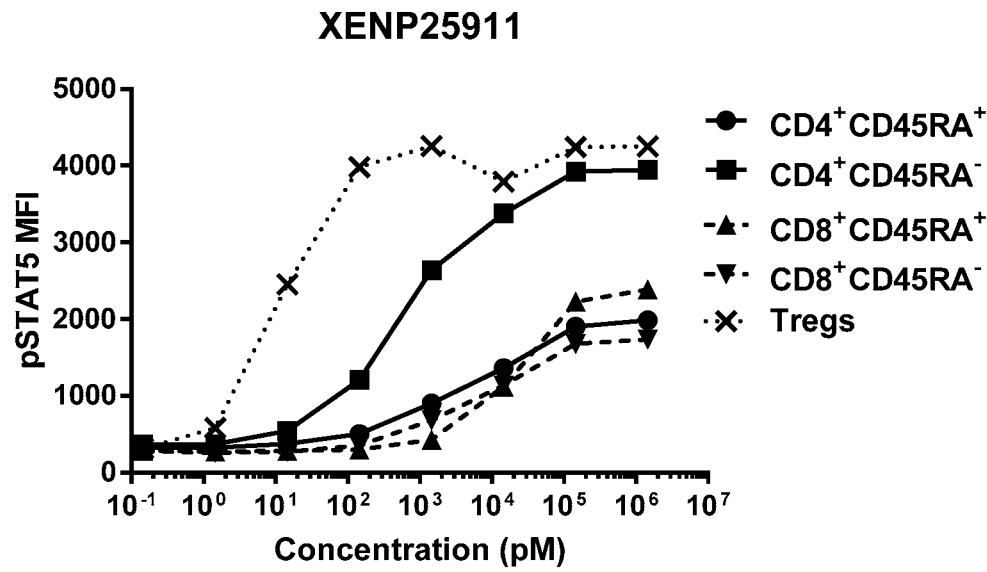


Figure 26E

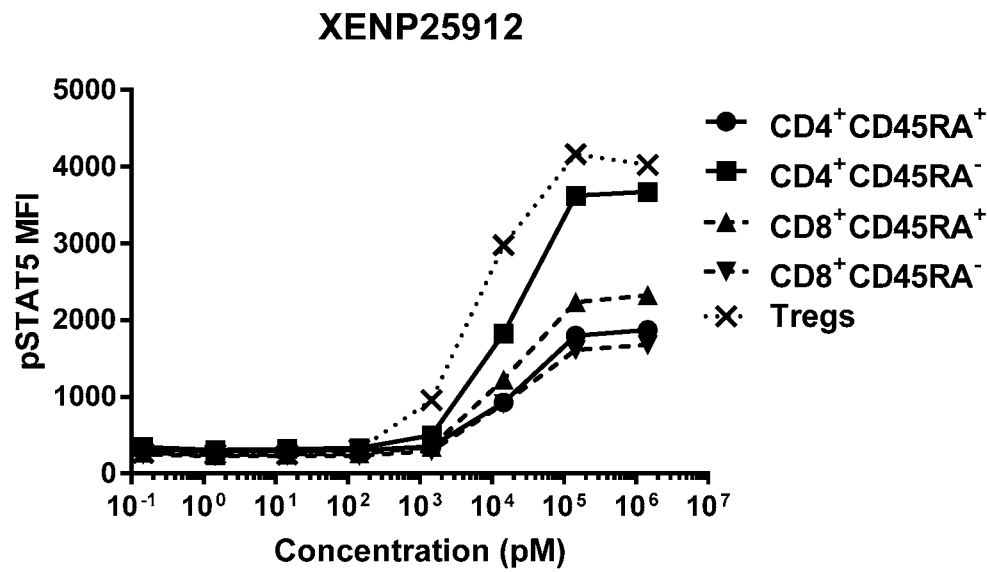


Figure 27A

>XENP025717 empty-Fc-hIL2 0.219 Fc(216) IgG1 pl(-)
) Isosteric A C220S/PVA /S267K/L368D/K370S IgG1 C220S/PVA /S267K/S364K/E357Q

Chain 1 – empty_Fc(216)_IgG1_pl(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S (SEQ ID NO: 223)

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPRE
EEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVS
GFYPDSIAVEWESDGPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSVMSHEALHNHYTQKSLSLSPGK

Chain 2 - hIL2_0.219_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q (SEQ ID NO: 224)

APASSSTKKTQLQLEHLLDDLQMI LINGINNYKNPKLTRMLTFKFYMPKKATELKHLQCLEEELKPLEEVLNLAQSKN
FHLRPRDLISNINIVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT/EPKSSDKTHTCPPCPAPPVA
GPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDW
LNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVS
GFYPDSIAVEWESDGPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSVMSHEALHNHYTQKSLSLSPGK

>XENP025720 empty-Fc-hIL2 0.222 Fc(216) IgG1 pl(-)
) Isosteric A C220S/PVA /S267K/L368D/K370S IgG1 C220S/PVA /S267K/S364K/E357Q

Chain 1 – empty_Fc(216)_IgG1_pl(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S (SEQ ID NO: 225)

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPRE
EEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVS
GFYPDSIAVEWESDGPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSVMSHEALHNHYTQKSLSLSPGK

Chain 2 - hIL2_0.222_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q (SEQ ID NO: 226)

APASSSTKKTQLQLEHLLLNQMI LINGINNYKNPKLTRMLTFKFYMPKKATELKHLQCLEEELKPLEEVLNLAQSKN
FHLRPRDLISNINIVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT/EPKSSDKTHTCPPCPAPPVA
GPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDW
LNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVS
GFYPDSIAVEWESDGPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSVMSHEALHNHYTQKSLSLSPGK

>XENP025725 empty-Fc-hIL2 0.251 Fc(216) IgG1 pl(-)
) Isosteric A C220S/PVA /S267K/L368D/K370S IgG1 C220S/PVA /S267K/S364K/E357Q

Chain 1 – empty_Fc(216)_IgG1_pl(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S (SEQ ID NO: 227)

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPRE
EEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVS
GFYPDSIAVEWESDGPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSVMSHEALHNHYTQKSLSLSPGK

Chain 2 - hIL2_0.251_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q (SEQ ID NO: 228)

APASSSTKKTQLQLEHLLLDLQMI LINGINNYKNPKLTRMLTFKFYMPKKATELKHLQCLEEELKPLEEVLNLAQSKN
FHLRPRDLISNINIVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT/EPKSSDKTHTCPPCPAPPVA
GPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDW
LNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVS
GFYPDSIAVEWESDGPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSVMSHEALHNHYTQKSLSLSPGK

Figure 27B

>XENP025727 empty-Fc-hIL2 0.253 Fc(216) IgG1 pl(-)
) Isosteric A C220S/PVA /S267K/L368D/K370S IgG1 C220S/PVA /S267K/S364K/E357Q

Chain 1 – empty_Fc(216)_IgG1_pl(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S (SEQ ID NO: 229)

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPRE
EEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPI EKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVS
GFYP S DIAVEWESDGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEEQGDV FSCSV MHEALHNHYTQKSLSLSPGK

Chain 2 - hIL2_0.253_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q (SEQ ID NO: 230)

APASSSTKKTQLQLEHLLLDLQMI L N G I N N Y K N P K L T R M L T F K F Y M P K K A T E L K H L Q C L E E E L K P L E E V L N L A Q S K N
FHLRPRDLISKINIVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT/EPKSSDKTHTCPPCPAPPVA
GPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDW
LNGKEYKCKVSNKALPAPI EKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVS
GFYP S DIAVEWESDGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEEQGDV FSCSV MHEALHNHYTQKSLSLSPGK

>XENP026086 empty-Fc-hIL2 0.289 Fc(216) IgG1 pl(-)
) Isosteric A C220S/PVA /S267K/L368D/K370S IgG1 C220S/PVA /S267K/S364K/E357Q

Chain 1 – empty_Fc(216)_IgG1_pl(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S (SEQ ID NO: 231)

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPRE
EEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPI EKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVS
GFYP S DIAVEWESDGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEEQGDV FSCSV MHEALHNHYTQKSLSLSPGK

Chain 2 - hIL2_0.289_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q (SEQ ID NO: 232)

APTSSSTKKTQLQLEHLLLDLQMI L N G I S N H K N P R L A R M L T F K F Y M P E K A T E L K H L Q C L E E E L K P L E E V L R L A Q S K N
FHLRPRDLISDVNVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT/EPKSSDKTHTCPPCPAPPVA
GPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDW
LNGKEYKCKVSNKALPAPI EKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVS
GFYP S DIAVEWESDGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEEQGDV FSCSV MHEALHNHYTQKSLSLSPGK

>XENP026088 empty-Fc-hIL2 0.291 Fc(216) IgG1 pl(-)
) Isosteric A C220S/PVA /S267K/L368D/K370S IgG1 C220S/PVA /S267K/S364K/E357Q

Chain 1 – empty_Fc(216)_IgG1_pl(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S (SEQ ID NO: 233)

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPRE
EEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPI EKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVS
GFYP S DIAVEWESDGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEEQGDV FSCSV MHEALHNHYTQKSLSLSPGK

Chain 2 - hIL2_0.291_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q (SEQ ID NO: 234)

APTSSSTKKTQLQLEHLLDDLQMI L N G I S N H K N P R L A R M L T F K F Y M P E K A T E L K H L Q C L E E E L K P L E E V L R L A Q S K N
FHLRPRDLISNINIVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT/EPKSSDKTHTCPPCPAPPVA
GPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDW
LNGKEYKCKVSNKALPAPI EKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVS
GFYP S DIAVEWESDGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEEQGDV FSCSV MHEALHNHYTQKSLSLSPGK

>XENP026089 empty-Fc-hIL2 0.292 Fc(216) IgG1 pl(-)
) Isosteric A C220S/PVA /S267K/L368D/K370S IgG1 C220S/PVA /S267K/S364K/E357Q

Chain 1 – empty_Fc(216)_IgG1_pl(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S (SEQ ID NO: 235)

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPRE
EEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPI EKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVS
GFYP S DIAVEWESDGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEEQGDV FSCSV MHEALHNHYTQKSLSLSPGK

Figure 27C

Chain 2 - hIL2_0.292_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q (SEQ ID NO: 236)

APTSSSTKKTQLQLEHLLLNLMILNGISNHKNPRLARMLTFKFYMPKATELKHLCLEEEELKPLEEVLRLAQSKN
 FHLRPRDLISNINIVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT/EPKSSDKTHTCPPCPAPPVA
 GPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDW
 LNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVVKLTCLVKGFPYPSDIAVEWESNGQPENN
 YKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSVMSVMEALHNHYTQKSLSLSPGK

>XENP026092 empty-Fc-hIL2_0.295_Fc(216)_IgG1_pl(-)

) Isosteric A C220S/PVA_/S267K/L368D/K370S_IgG1_C220S/PVA_/S267K/S364K/E357Q

Chain 1 – empty_Fc(216)_IgG1_pl(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S (SEQ ID NO: 237)

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPRE
 EEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVS
 GFYPYPSDIAVEWESDGPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSVMSVMEALHNHYTQKSLSLSPGK

Chain 2 - hIL2_0.295_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q (SEQ ID NO: 238)

APTSSSTKKTQLQLEHLLDDLMILNGISNHKNPRLARMLTFKFYMPKATELKHLCLEEEELKPLEEVLNLAQSKN
 FHLRPRDLISNINIVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT/EPKSSDKTHTCPPCPAPPVA
 GPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDW
 LNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVVKLTCLVKGFPYPSDIAVEWESNGQPENN
 YKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSVMSVMEALHNHYTQKSLSLSPGK

>XENP026093 empty-Fc-hIL2_0.296_Fc(216)_IgG1_pl(-)

) Isosteric A C220S/PVA_/S267K/L368D/K370S_IgG1_C220S/PVA_/S267K/S364K/E357Q

Chain 1 – empty_Fc(216)_IgG1_pl(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S (SEQ ID NO: 239)

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPRE
 EEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVS
 GFYPYPSDIAVEWESDGPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSVMSVMEALHNHYTQKSLSLSPGK

Chain 2 - hIL2_0.296_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q (SEQ ID NO: 240)

APTSSSTKKTQLQLEHLLLNLMILNGISNHKNPRLARMLTFKFYMPKATELKHLCLEEEELKPLEEVLNLAQSKN
 FHLRPRDLISNINIVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT/EPKSSDKTHTCPPCPAPPVA
 GPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDW
 LNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVVKLTCLVKGFPYPSDIAVEWESNGQPENN
 YKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSVMSVMEALHNHYTQKSLSLSPGK

>XENP026096 empty-Fc-hIL2_0.299_Fc(216)_IgG1_pl(-)

) Isosteric A C220S/PVA_/S267K/L368D/K370S_IgG1_C220S/PVA_/S267K/S364K/E357Q

Chain 1 – empty_Fc(216)_IgG1_pl(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S (SEQ ID NO: 241)

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPRE
 EEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVS
 GFYPYPSDIAVEWESDGPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSVMSVMEALHNHYTQKSLSLSPGK

Chain 2 - hIL2_0.299_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q (SEQ ID NO: 242)

APASSSTKKTQLQLEHLLDDLMILNGINNYKNPRLTRMLTFKFYMPKATELKHLCLEEEELKPLEEVLNLAQSKN
 FHLRPRDLISNINIVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT/EPKSSDKTHTCPPCPAPPVA
 GPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDW
 LNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVVKLTCLVKGFPYPSDIAVEWESNGQPENN
 YKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSVMSVMEALHNHYTQKSLSLSPGK

Figure 27D

>XENP026104 empty-Fc-hIL2 0.303 Fc(216) IgG1 pl(-)
) Isosteric A C220S/PVA /S267K/L368D/K370S IgG1 C220S/PVA /S267K/S364K/E357Q

Chain 1 – empty_Fc(216)_IgG1_pl(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S (SEQ ID NO: 243)

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPRE
EEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVS
GFYPSDIAVEWESDGPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEEQGDVVFSCSVMEALHNHYTQKSLSLSPGK

Chain 2 - hIL2_0.303_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q (SEQ ID NO: 244)

APASSSTKKTQLQLEHLLDDLQMLNGINNYKNPKLRRLMTFKFYMPKKATELKHLCLEEEELKPLEEVLNLAQSKN
FHLRPRDLISNINIVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT/EPKSSDKTHTCPPCPAPPVA
GPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDW
LNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENN
YKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVVFSCSVMEALHNHYTQKSLSLSPGK

>XENP026105 empty-Fc-hIL2 0.304 Fc(216) IgG1 pl(-)
) Isosteric A C220S/PVA /S267K/L368D/K370S IgG1 C220S/PVA /S267K/S364K/E357Q

Chain 1 – empty_Fc(216)_IgG1_pl(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S (SEQ ID NO: 245)

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPRE
EEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVS
GFYPSDIAVEWESDGPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEEQGDVVFSCSVMEALHNHYTQKSLSLSPGK

Chain 2 - hIL2_0.304_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q (SEQ ID NO: 246)

APASSSTKKTQLQLEHLLLNLMILNGINNYKNPKLRRLMTFKFYMPKKATELKHLCLEEEELKPLEEVLNLAQSKN
FHLRPRDLISNINIVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT/EPKSSDKTHTCPPCPAPPVA
GPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDW
LNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENN
YKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVVFSCSVMEALHNHYTQKSLSLSPGK

>XENP026108 empty-Fc-hIL2 0.307 Fc(216) IgG1 pl(-)
) Isosteric A C220S/PVA /S267K/L368D/K370S IgG1 C220S/PVA /S267K/S364K/E357Q

Chain 1 – empty_Fc(216)_IgG1_pl(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S (SEQ ID NO: 247)

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPRE
EEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVS
GFYPSDIAVEWESDGPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEEQGDVVFSCSVMEALHNHYTQKSLSLSPGK

Chain 2 - hIL2_0.307_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q (SEQ ID NO: 248)

APASSSTKKTQLQLEHLLDDLQMLNGINNYKNPKLRLMTFKFYMPKKATELKHLCLEEEELKPLEEVLKLAQSKN
FHLRPRDLISNINIVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT/EPKSSDKTHTCPPCPAPPVA
GPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDW
LNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENN
YKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVVFSCSVMEALHNHYTQKSLSLSPGK

>XENP026109 empty-Fc-hIL2 0.308 Fc(216) IgG1 pl(-)
) Isosteric A C220S/PVA /S267K/L368D/K370S IgG1 C220S/PVA /S267K/S364K/E357Q

Chain 1 – empty_Fc(216)_IgG1_pl(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S (SEQ ID NO: 249)

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPRE
EEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVS
GFYPSDIAVEWESDGPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEEQGDVVFSCSVMEALHNHYTQKSLSLSPGK

Figure 27E

Chain 2 - hIL2_0.308_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q (SEQ ID NO: 250)

APASSSTKKTQLQLEHLLLNLQMILNGINNYKNPKLTRMLTFKFYMPKKATELKHLQCLEEEELKPLEEVLKLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT/EPKSSDKTHTCPPCPAPPVA
GPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDW
LNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENN
YKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSVSMHEALHNHYTQKSLSLSPGK

Figure 28A

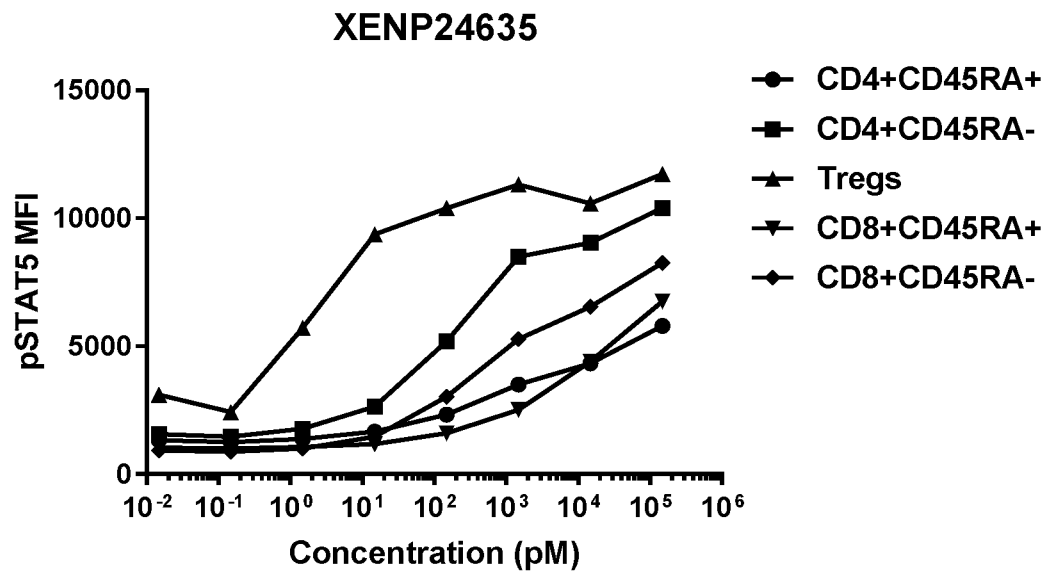


Figure 28B

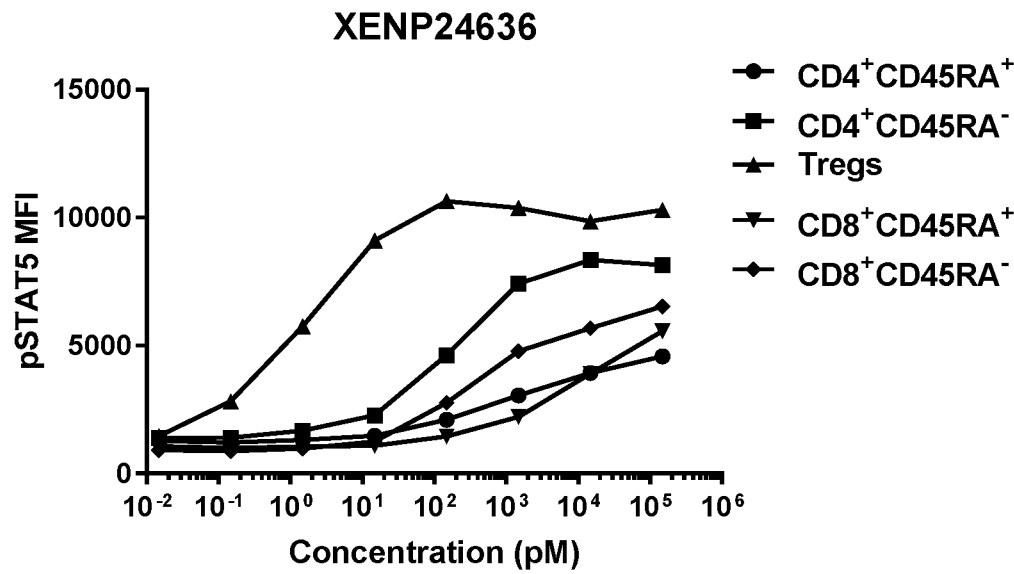


Figure 28C

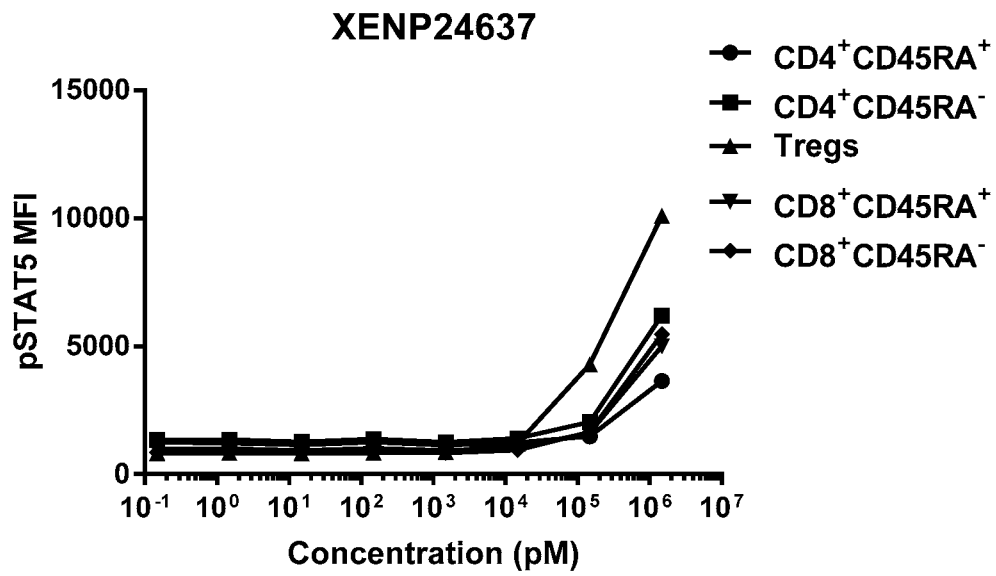


Figure 28D

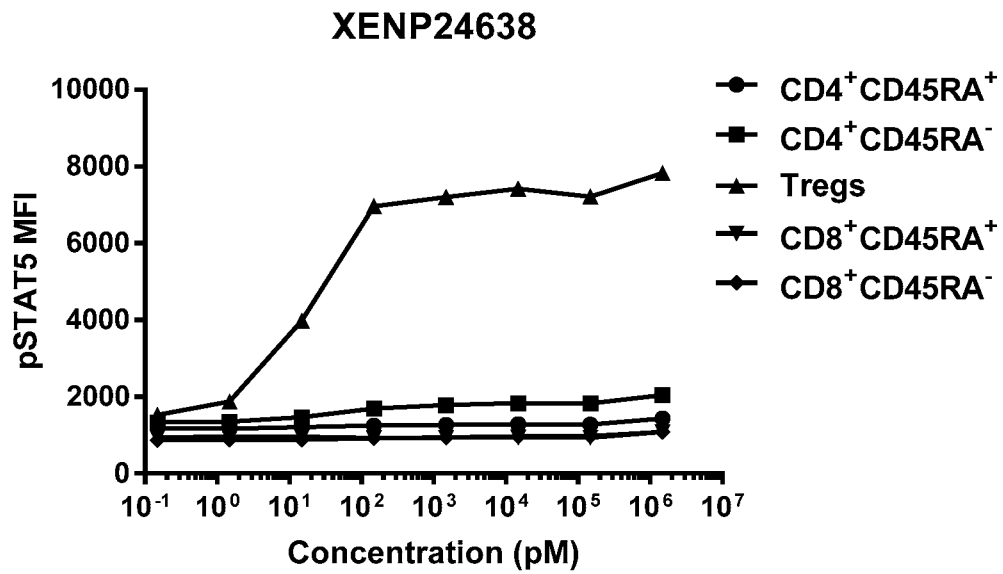


Figure 28E

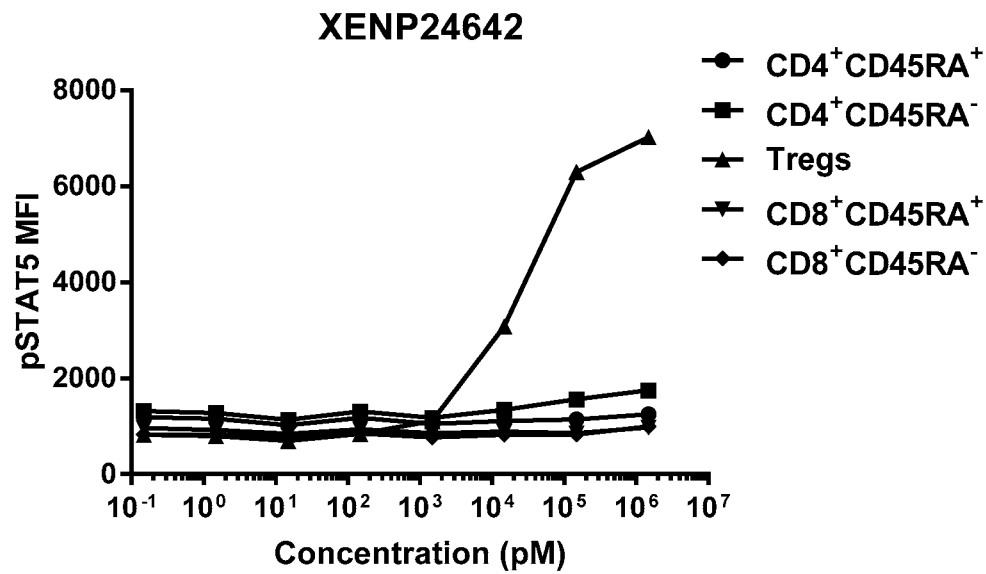


Figure 28F

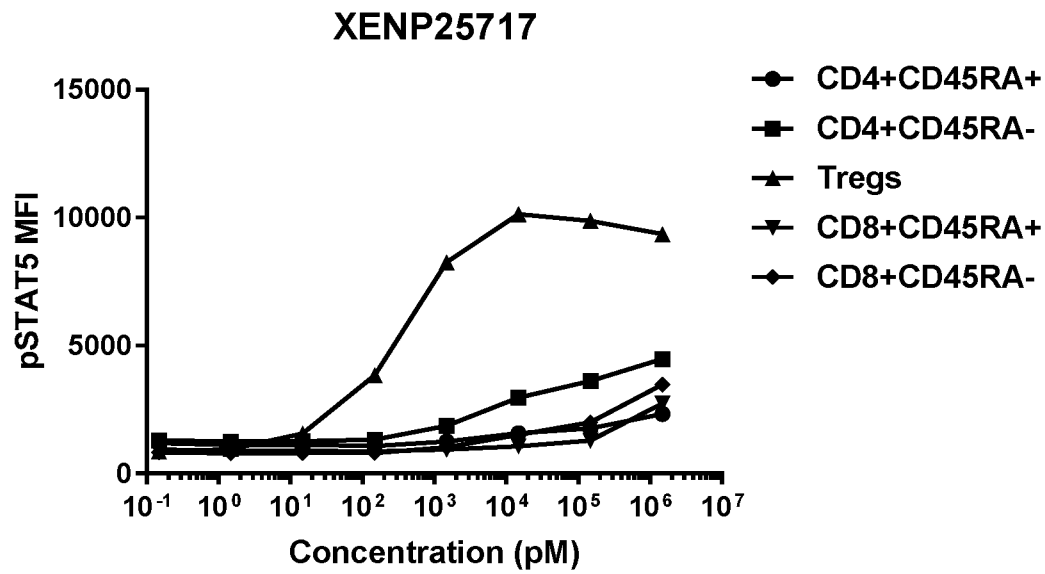


Figure 28G

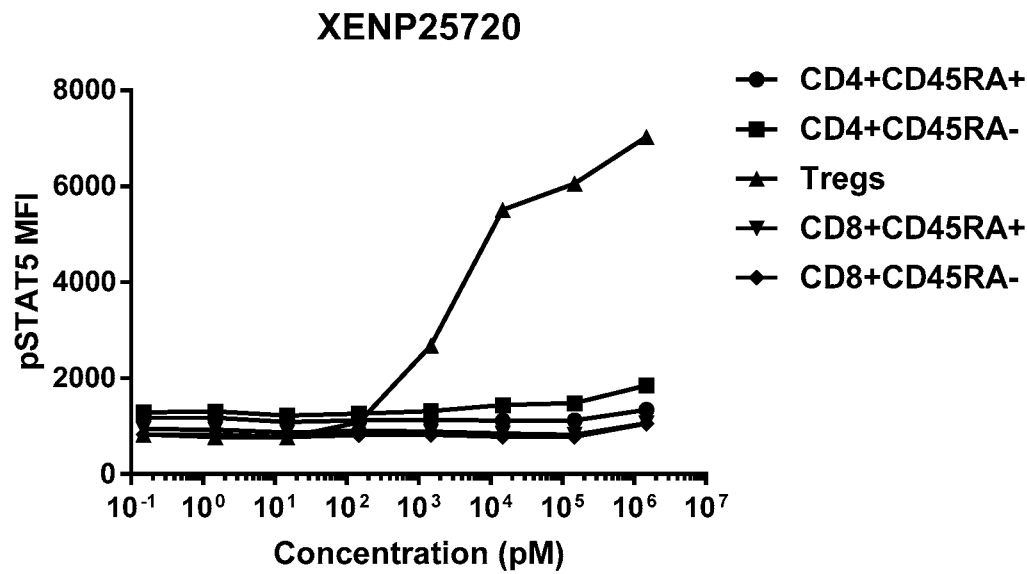


Figure 28H

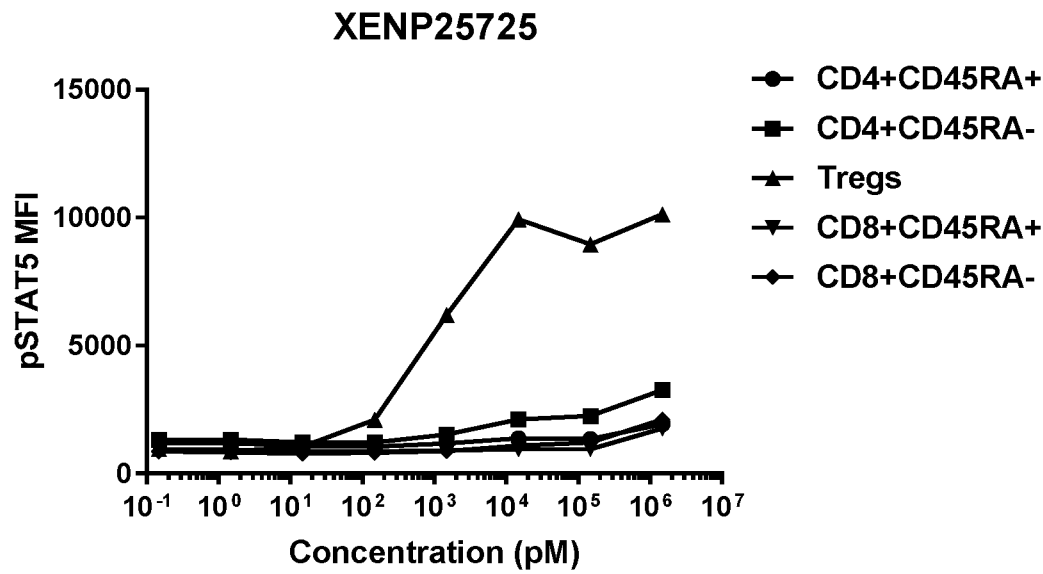


Figure 28I

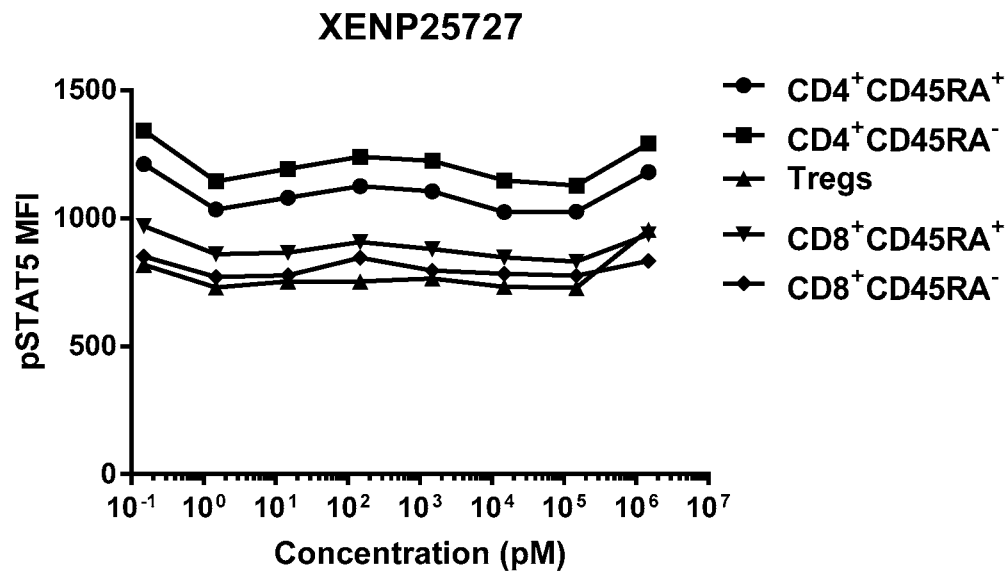


Figure 28J

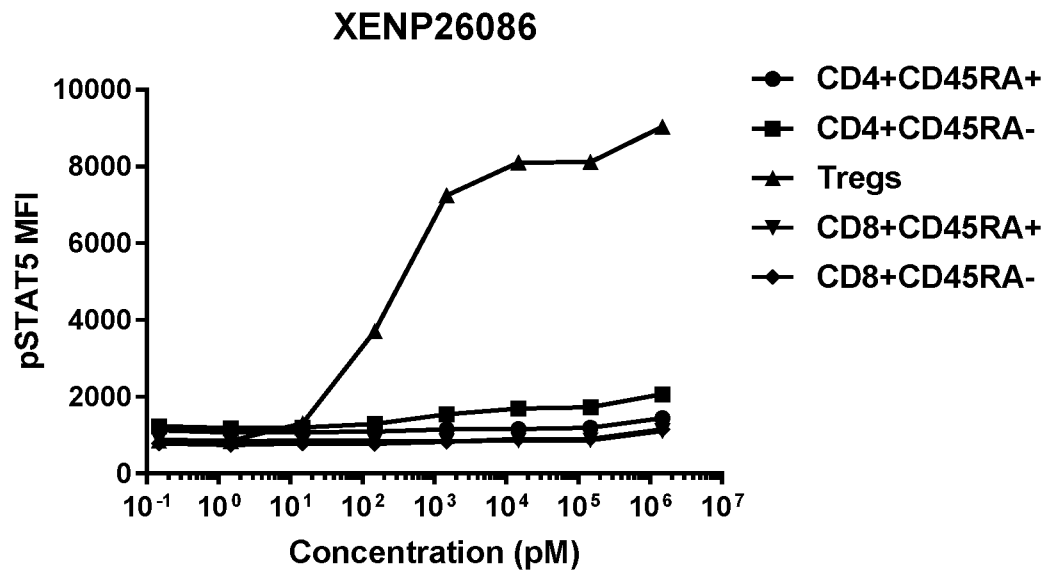


Figure 28K

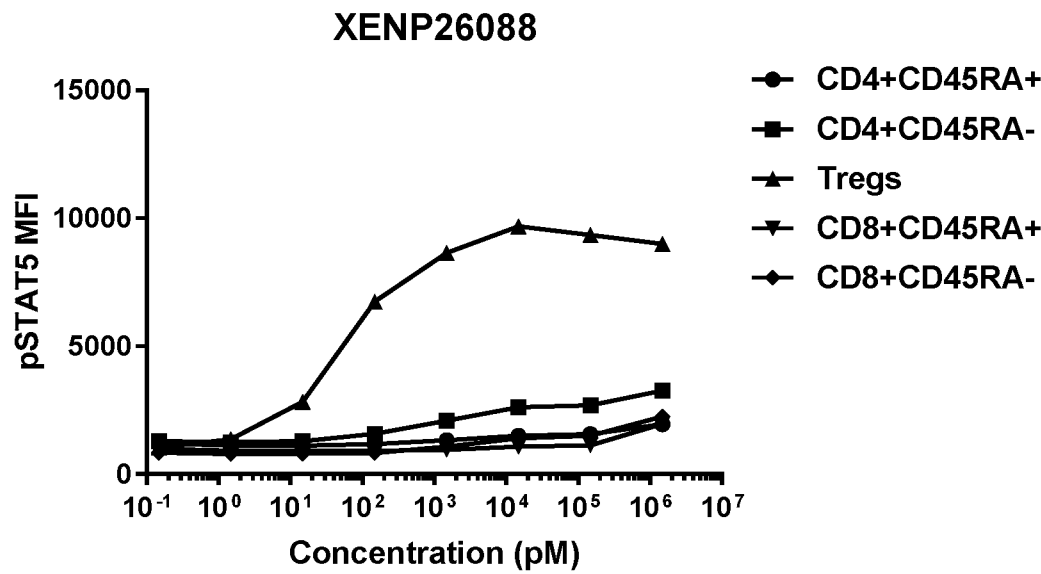


Figure 28L

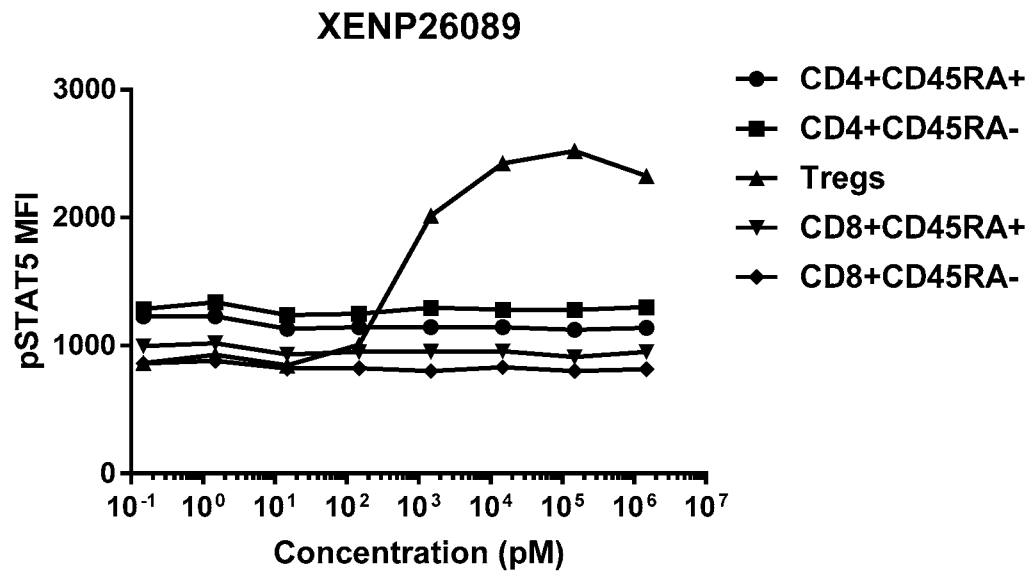


Figure 28M

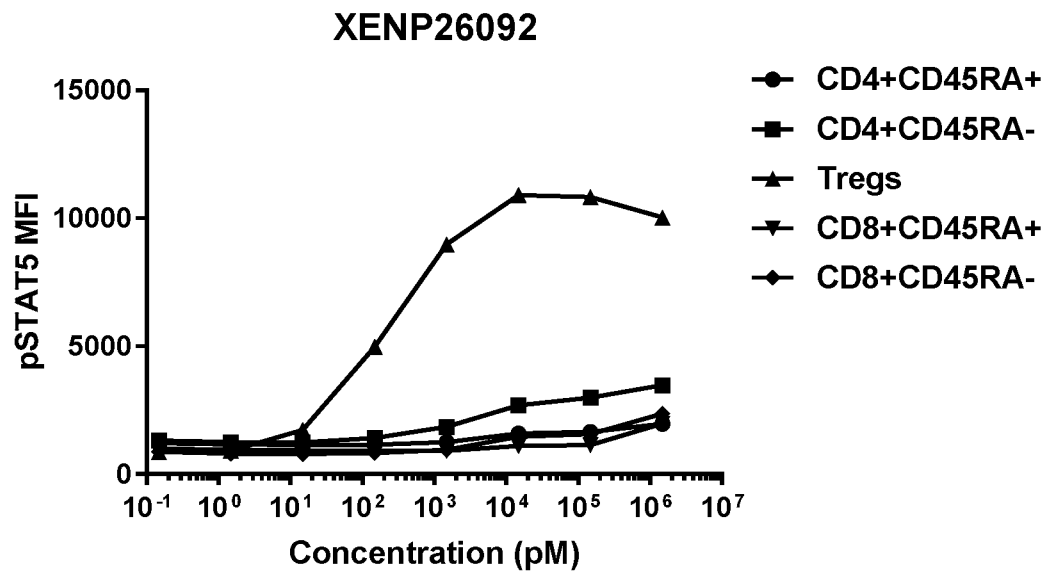


Figure 28N

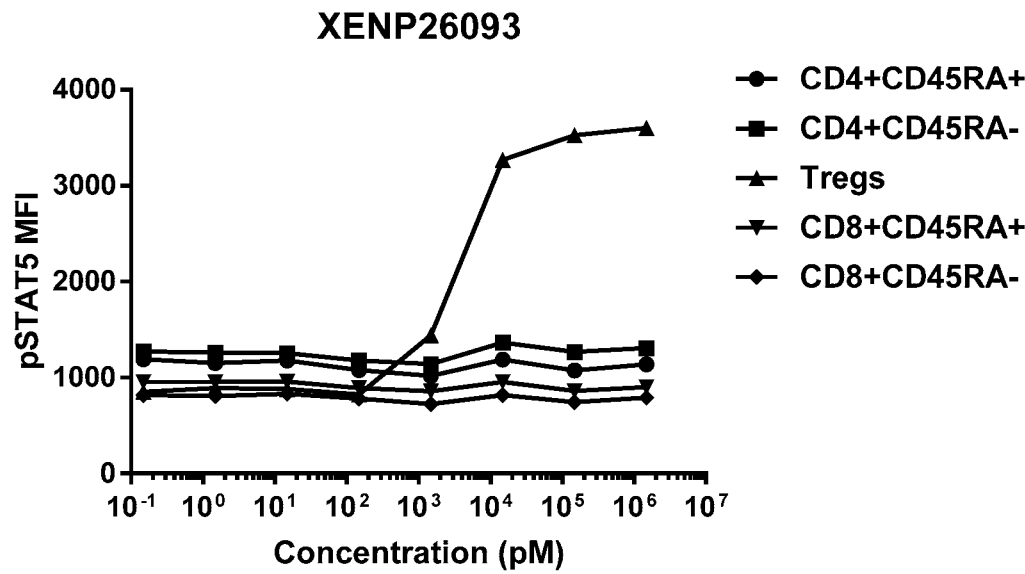


Figure 28O

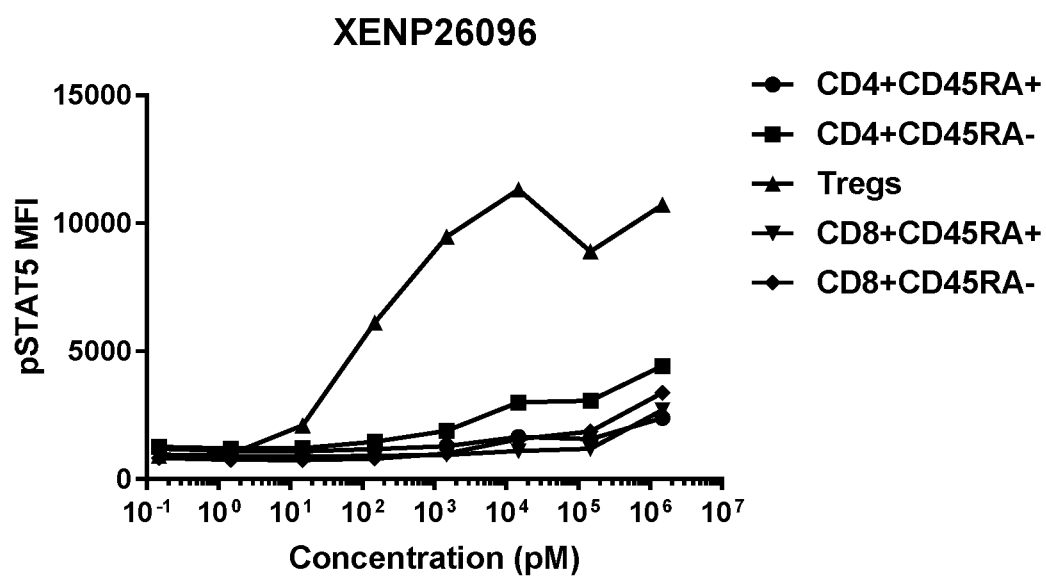


Figure 28P

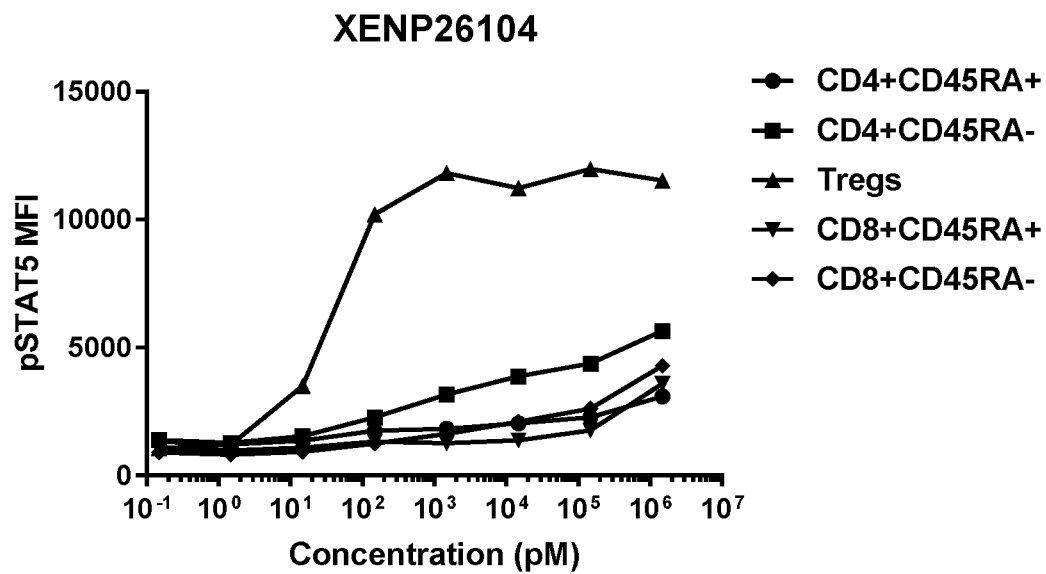


Figure 28Q

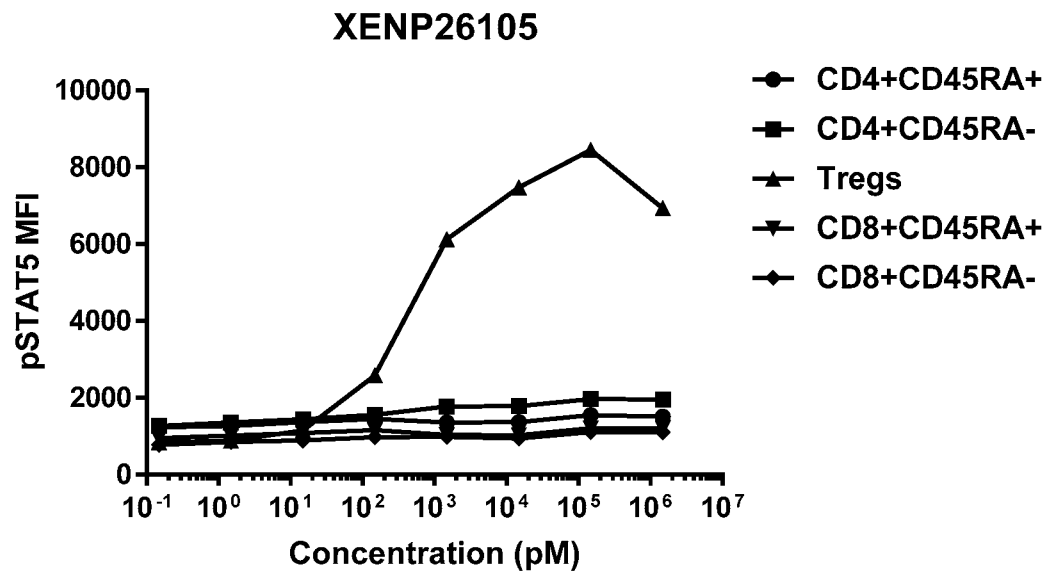


Figure 28R

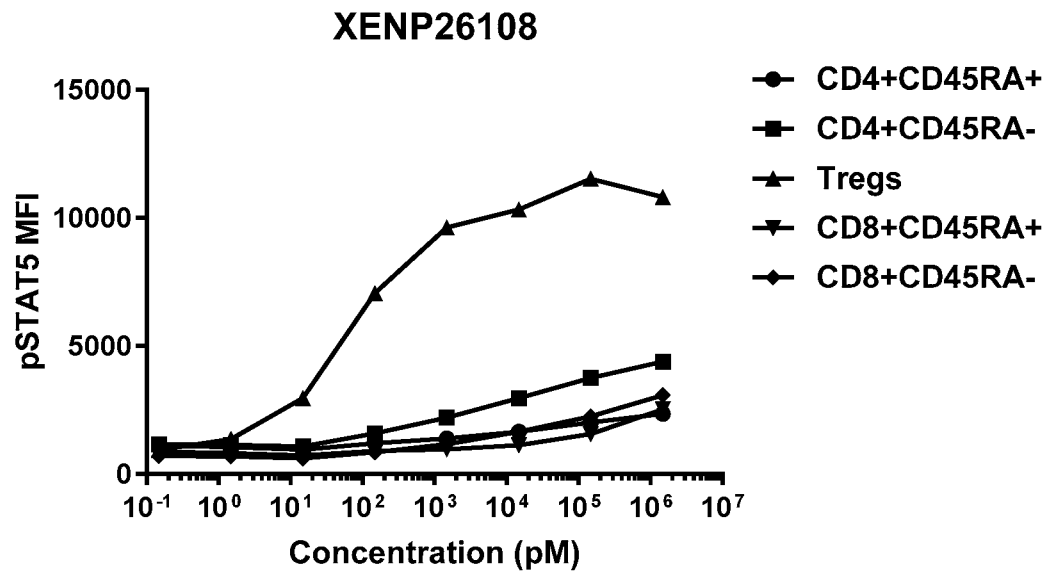


Figure 28S

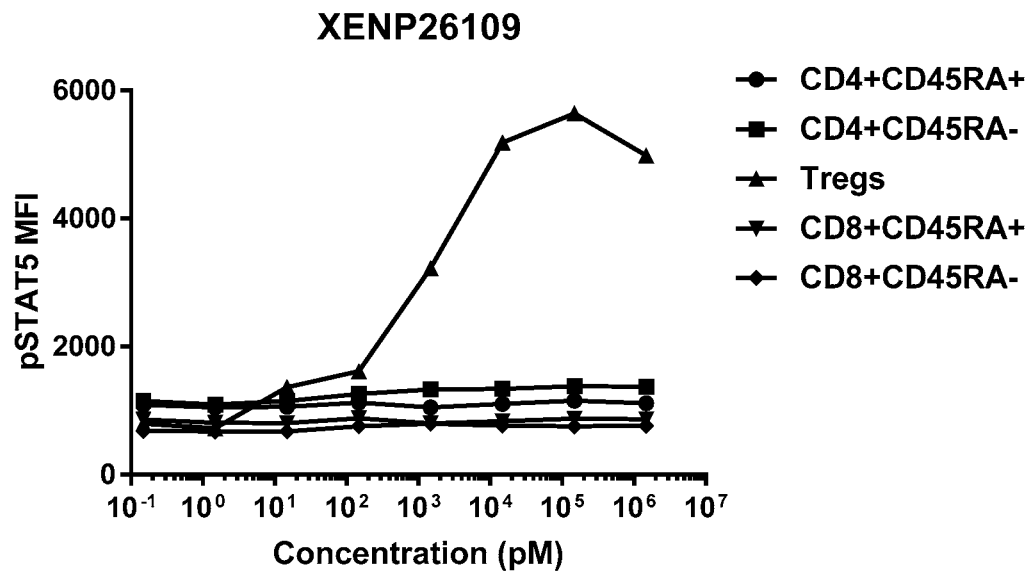
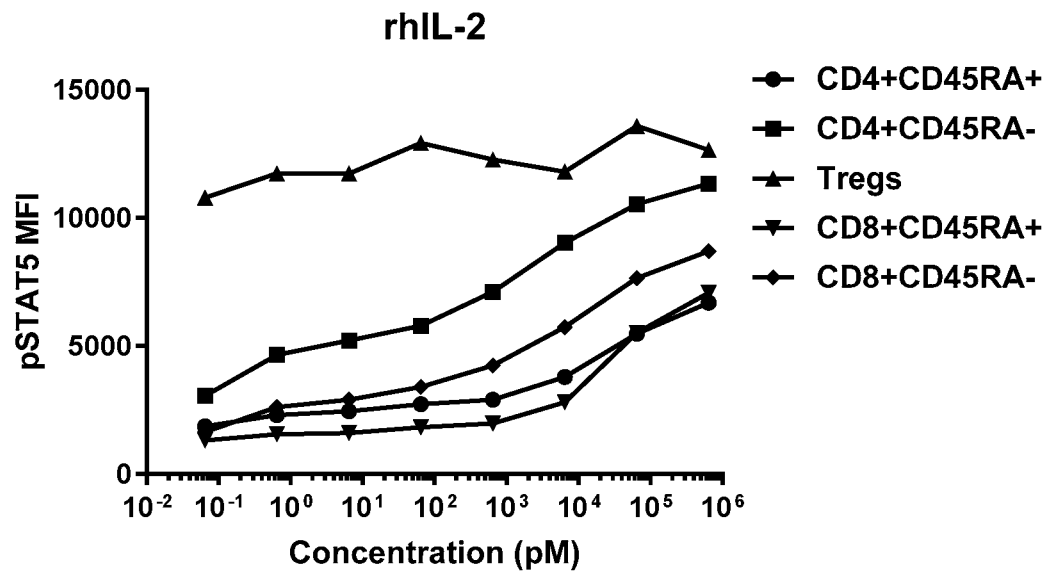


Figure 28T



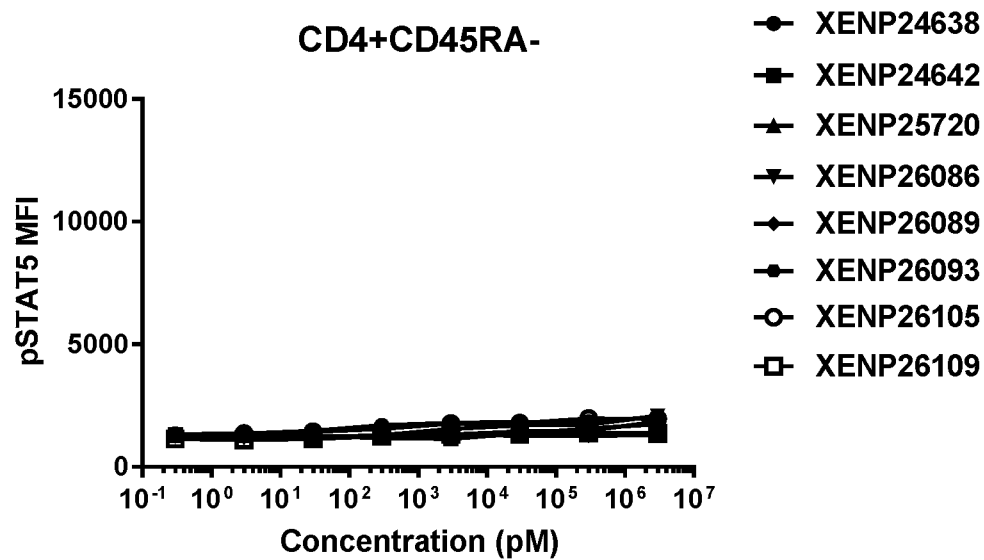
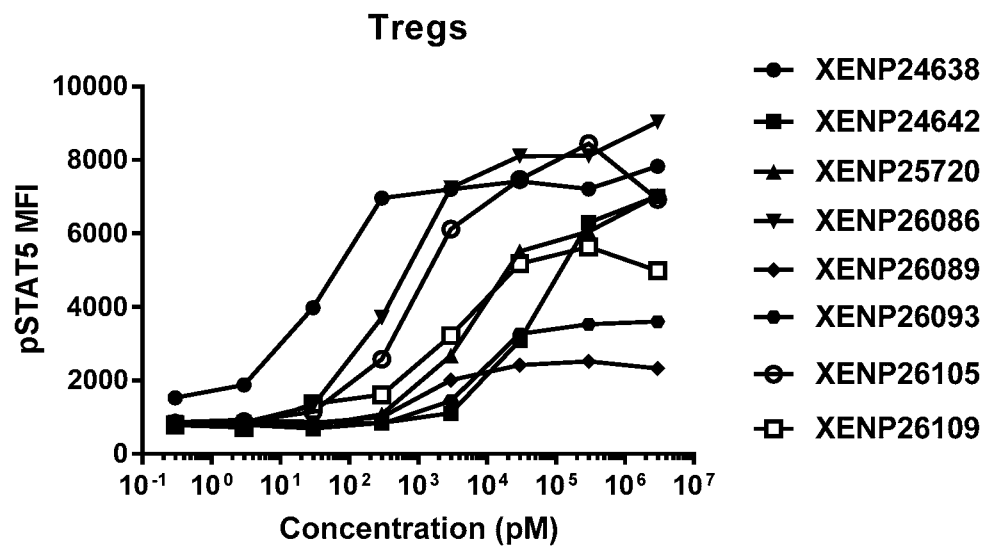


Figure 30A

>XENP026835 empty-Fc-hIL2 0.313 Fc(216) IgG1 pl(-)
) Isosteric A C220S/PVA /S267K/L368D/K370S IgG1 C220S/PVA /S267K/S364K/E357Q

Chain 1 – empty_Fc(216)_IgG1_pl(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S (SEQ ID NO: 251)

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVL
HQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTTPVLDSDG
SFFLYSKLTVDKSRWEGQDVFSCSVMEALHNHYTQKSLSLSPGK

Chain 2 – hIL2_0.313_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q (SEQ ID NO: 252)

APASSSTKKTQLQLEHLLLNLMILNGINNYKNPKLIMLTFFKFMPPKATELKHLLQCLEEELKPLEEVLNLAQSKNFHLRPRDLISNINVIV
LELKGSETTFMCEYADETATIVEEFLNRWITFSQSIISTLT/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKH
EDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKN
QVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSLSLSPGK

>XENP026839 empty-Fc-hIL2 0.317 Fc(216) IgG1 pl(-)
) Isosteric A C220S/PVA /S267K/L368D/K370S IgG1 C220S/PVA /S267K/S364K/E357Q

Chain 1 – empty_Fc(216)_IgG1_pl(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S (SEQ ID NO: 253)

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVL
HQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTTPVLDSDG
SFFLYSKLTVDKSRWEGQDVFSCSVMEALHNHYTQKSLSLSPGK

Chain 2 – hIL2_0.317_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q (SEQ ID NO: 254)

APASSSTKKTQLQLEHLLLNLMILNGINNYKNPKLRIMLTFFKFMPPKATELKHLLQCLEEELKPLEEVLNLAQSKNFHLRPRDLISNINVIV
LELKGSETTFMCEYADETATIVEEFLNRWITFSQSIISTLT/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKH
EDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKN
QVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSLSLSPGK

>XENP026840 empty-Fc-hIL2 0.318 Fc(216) IgG1 pl(-)
) Isosteric A C220S/PVA /S267K/L368D/K370S IgG1 C220S/PVA /S267K/S364K/E357Q

Chain 1 – empty_Fc(216)_IgG1_pl(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S (SEQ ID NO: 255)

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVL
HQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTTPVLDSDG
SFFLYSKLTVDKSRWEGQDVFSCSVMEALHNHYTQKSLSLSPGK

Chain 2 – hIL2_0.318_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q (SEQ ID NO: 256)

APASSSTKKTQLQLEHLLLNLMILNGINNYKNPKLIMLTFFKFMPPKATELKHLLQCLEEELKPLEEVLKLAQSKNFHLRPRDLISNINVIV
LELKGSETTFMCEYADETATIVEEFLNRWITFSQSIISTLT/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKH
EDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKN
QVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSLSLSPGK

>XENP026986 empty-Fc-hIL2 0.222 (GGGGS)2 Fc(216) IgG1 pl(-)
) Isosteric A C220S/PVA /S267K/L368D/K370S IgG1 C220S/PVA /S267K/S364K/E357Q

Chain 1 – empty_Fc(216)_IgG1_pl(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S (SEQ ID NO: 257)

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPRE
EEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVS
GFYPSDIAVEWESDGPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEGQDVFSCSVMEALHNHYTQKSLSLSPGK

Figure 30B

Chain 2 – hIL2_0.222_(GGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q (SEQ ID NO: 258)

APASSSTKKTQLQLEHLLLNLMILNGINNYKNPKLTRMLTFKFYMPKKATELKHLQCLEEELKPLEEVLNLAQSKN
 FHLRPRDLISNINIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT/____GGGSGGGGS____/EPKSSDKTH
 TCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRV
 VSVLTVLHQDWLNGKEYKCKVSNKALPAPI EKTISKAKGQPREPQVYTLPPSREQMTKNQVLTCLVKGFYPSDIAV
 EWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVMHEALHNHYTQKSLSLSPGK

**>XENP026987 empty-Fc-hIL2_0.304_(GGGGS)2_Fc(216)_IgG1_pl(-)
) Isosteric A C220S/PVA_/S267K/L368D/K370S_IgG1_C220S/PVA_/S267K/S364K/E357Q**

Chain 1 – empty_Fc(216)_IgG1_pl(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S (SEQ ID NO: 259)

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPRE
 EEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPI EKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVS
 GFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCSCVMHEALHNHYTQKSLSLSPGK

Chain 2 – hIL2_0.304_(GGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q (SEQ ID NO: 260)

APASSSTKKTQLQLEHLLLNLMILNGINNYKNPKLRMLTFKFYMPKKATELKHLQCLEEELKPLEEVLNLAQSKN
 FHLRPRDLISNINIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT/____GGGSGGGGS____/EPKSSDKTH
 TCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRV
 VSVLTVLHQDWLNGKEYKCKVSNKALPAPI EKTISKAKGQPREPQVYTLPPSREQMTKNQVLTCLVKGFYPSDIAV
 EWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVMHEALHNHYTQKSLSLSPGK

**>XENP026841 empty-Fc-hIL2_0.308_(GGGGS)2_Fc(216)_IgG1_pl(-)
) Isosteric A C220S/PVA_/S267K/L368D/K370S_IgG1_C220S/PVA_/S267K/S364K/E357Q**

Chain 1 – empty_Fc(216)_IgG1_pl(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S (SEQ ID NO: 261)

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVL
 HQDWLNGKEYKCKVSNKALPAPI EKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDG
 SFFLYSKLTVDKSRWEQGDVFCSCVMHEALHNHYTQKSLSLSPGK

Chain 2 – hIL2_0.308_(GGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q (SEQ ID NO: 262)

APASSSTKKTQLQLEHLLLNLMILNGINNYKNPKLTRMLTFKFYMPKKATELKHLQCLEEELKPLEEVLKLAQSKNFHLRPRDLISNINIV
 LELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT/____GGGSGGGGS____/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRT
 P EVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPI EKTISKAKGQPREPQVY
 TLPPSREQMTKNQVLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVMHEALHNHYTQKSLS
 SPGK

**>XENP026989 empty-Fc-hIL2_0.313_(GGGGS)2_Fc(216)_IgG1_pl(-)
) Isosteric A C220S/PVA_/S267K/L368D/K370S_IgG1_C220S/PVA_/S267K/S364K/E357Q**

Chain 1 – empty_Fc(216)_IgG1_pl(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S (SEQ ID NO: 263)

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPRE
 EEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPI EKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVS
 GFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCSCVMHEALHNHYTQKSLSLSPGK

Chain 2 – hIL2_0.313_(GGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q (SEQ ID NO: 264)

APASSSTKKTQLQLEHLLLNLMILNGINNYKNPKLTIMLTTFKFYMPKKATELKHLQCLEEELKPLEEVLNLAQSKN
 FHLRPRDLISNINIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT/____GGGSGGGGS____/EPKSSDKTH
 TCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRV
 VSVLTVLHQDWLNGKEYKCKVSNKALPAPI EKTISKAKGQPREPQVYTLPPSREQMTKNQVLTCLVKGFYPSDIAV
 EWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVMHEALHNHYTQKSLSLSPGK

Figure 30C

**>XENP026990 empty-Fc-hIL2 0.317 (GGGGS)2 Fc(216) IgG1 pl(-)
Isosteric A C220S/PVA /S267K/L368D/K370S IgG1 C220S/PVA /S267K/S364K/E357Q**

Chain 1 – empty_Fc(216)_IgG1_pl(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S (SEQ ID NO: 265)

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPRE
EEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVS
GFYPDSIAVEWESDGPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGDFVSCSVMEALHNHYTQKSLSLSPGK

Chain 2 – hIL2_0.317_(GGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q (SEQ ID NO: 266)

APASSSTKKTQLQLEHLLLNLMILNGINNYKNPKLRIMLTFFKFMPPKATLKHLCLEEEELKPLEEVLNLAQSKN
FHLRPRDLISNINIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT/GGGGSGGGGS/EPKSSDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRV
VSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPDSIAV
EWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSVMEALHNHYTQKSLSLSPGK

**>XENP026991 empty-Fc-hIL2 0.318 (GGGGS)2 Fc(216) IgG1 pl(-)
Isosteric A C220S/PVA /S267K/L368D/K370S IgG1 C220S/PVA /S267K/S364K/E357Q**

Chain 1 – empty_Fc(216)_IgG1_pl(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S (SEQ ID NO: 267)

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPRE
EEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVS
GFYPDSIAVEWESDGPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGDFVSCSVMEALHNHYTQKSLSLSPGK

Chain 2 – hIL2_0.318_(GGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q (SEQ ID NO: 268)

APASSSTKKTQLQLEHLLLNLMILNGINNYKNPKLTIMLTFFKFMPPKATLKHLCLEEEELKPLEEVLKLAQSKN
FHLRPRDLISNINIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT/GGGGSGGGGS/EPKSSDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRV
VSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPDSIAV
EWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSVMEALHNHYTQKSLSLSPGK

>XENP026992 hIL2 0.222 Fc(216) IgG1 C220S/PVA /S267K (SEQ ID NO: 269)

APASSSTKKTQLQLEHLLLNLMILNGINNYKNPKLTRMLTFFKFMPPKATLKHLCLEEEELKPLEEVLNLAQSKN
FHLRPRDLISNINIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT/EPKSSDKTHTCPPCPAPPVA
GPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDW
LNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPDSIAVEWESNGQPENN
YKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSVMEALHNHYTQKSLSLSPGK

>XENP026993 hIL2 0.304 Fc(216) IgG1 C220S/PVA /S267K (SEQ ID NO: 270)

APASSSTKKTQLQLEHLLLNLMILNGINNYKNPKLRMLTFFKFMPPKATLKHLCLEEEELKPLEEVLNLAQSKN
FHLRPRDLISNINIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT/EPKSSDKTHTCPPCPAPPVA
GPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDW
LNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPDSIAVEWESNGQPENN
YKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSVMEALHNHYTQKSLSLSPGK

>XENP026994 hIL2 0.308 Fc(216) IgG1 C220S/PVA /S267K (SEQ ID NO: 271)

APASSSTKKTQLQLEHLLLNLMILNGINNYKNPKLTRMLTFFKFMPPKATLKHLCLEEEELKPLEEVLKLAQSKN
FHLRPRDLISNINIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT/EPKSSDKTHTCPPCPAPPVA
GPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDW
LNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPDSIAVEWESNGQPENN
YKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSVMEALHNHYTQKSLSLSPGK

Figure 30D

>XENP026995 hIL2 0.313 Fc(216) IgG1 C220S/PVA /S267K (SEQ ID NO: 272)

APASSSTKKTQLQLEHLLLNLQMI L N G I N N Y K N P K L T I M L T F K F Y M P K K A T E L K H L Q C L E E E L K P L E E V L N L A Q S K N
F H L R P R D L I S N I N V I V L E L K G S E T T F M C E Y A D E T A T I V E F L N R W I T F S Q S I I S T L T / E P K S S D K T H T C P P C P A P P V A
G P S V F L F P P K P K D T L M I S R T P E V T C V V V D V K H E D P E V K F N W Y V D G V E V H N A K T K P R E E Q Y N S T Y R V V S V L T V L H Q D W
L N G K E Y K C K V S N K A L P A P I E K T I S K A K G Q P R E P Q V Y T L P P S R E E M T K N Q V S L T C L V K G F Y P S D I A V E W E S N G Q P E N N
Y K T T P P V L D S D G S F F L Y S K L T V D K S R W Q Q G N V F S C S V M H E A L H N H Y T Q K S L S L S P G K

>XENP026996 hIL2 0.317 Fc(216) IgG1 C220S/PVA /S267K (SEQ ID NO: 273)

APASSSTKKTQLQLEHLLLNLQMI L N G I N N Y K N P K L R I M L T F K F Y M P K K A T E L K H L Q C L E E E L K P L E E V L N L A Q S K N
F H L R P R D L I S N I N V I V L E L K G S E T T F M C E Y A D E T A T I V E F L N R W I T F S Q S I I S T L T / E P K S S D K T H T C P P C P A P P V A
G P S V F L F P P K P K D T L M I S R T P E V T C V V V D V K H E D P E V K F N W Y V D G V E V H N A K T K P R E E Q Y N S T Y R V V S V L T V L H Q D W
L N G K E Y K C K V S N K A L P A P I E K T I S K A K G Q P R E P Q V Y T L P P S R E E M T K N Q V S L T C L V K G F Y P S D I A V E W E S N G Q P E N N
Y K T T P P V L D S D G S F F L Y S K L T V D K S R W Q Q G N V F S C S V M H E A L H N H Y T Q K S L S L S P G K

>XENP027001 hIL2 0.318 Fc(216) IgG1 C220S/PVA /S267K (SEQ ID NO: 274)

APASSSTKKTQLQLEHLLLNLQMI L N G I N N Y K N P K L T I M L T F K F Y M P K K A T E L K H L Q C L E E E L K P L E E V L K L A Q S K N
F H L R P R D L I S N I N V I V L E L K G S E T T F M C E Y A D E T A T I V E F L N R W I T F S Q S I I S T L T / E P K S S D K T H T C P P C P A P P V A
G P S V F L F P P K P K D T L M I S R T P E V T C V V V D V K H E D P E V K F N W Y V D G V E V H N A K T K P R E E Q Y N S T Y R V V S V L T V L H Q D W
L N G K E Y K C K V S N K A L P A P I E K T I S K A K G Q P R E P Q V Y T L P P S R E E M T K N Q V S L T C L V K G F Y P S D I A V E W E S N G Q P E N N
Y K T T P P V L D S D G S F F L Y S K L T V D K S R W Q Q G N V F S C S V M H E A L H N H Y T Q K S L S L S P G K

>XENP027002 hIL2 0.222 (GGGGS)2 Fc(216) IgG1 C220S/PVA /S267K (SEQ ID NO: 275)

APASSSTKKTQLQLEHLLLNLQMI L N G I N N Y K N P K L T R M L T F K F Y M P K K A T E L K H L Q C L E E E L K P L E E V L N L A Q S K N
F H L R P R D L I S N I N V I V L E L K G S E T T F M C E Y A D E T A T I V E F L N R W I T F S Q S I I S T L T / G G G G S G G G G S / E P K S S D K T H
T C P P C P A P P V A G P S V F L F P P K P K D T L M I S R T P E V T C V V V D V K H E D P E V K F N W Y V D G V E V H N A K T K P R E E Q Y N S T Y R V
V S V L T V L H Q D W L N G K E Y K C K V S N K A L P A P I E K T I S K A K G Q P R E P Q V Y T L P P S R E E M T K N Q V S L T C L V K G F Y P S D I A V
E W E S N G Q P E N N Y K T T P P V L D S D G S F F L Y S K L T V D K S R W Q Q G N V F S C S V M H E A L H N H Y T Q K S L S L S P G K

>XENP027003 hIL2 0.304 (GGGGS)2 Fc(216) IgG1 C220S/PVA /S267K (SEQ ID NO: 276)

APASSSTKKTQLQLEHLLLNLQMI L N G I N N Y K N P K L R R M L T F K F Y M P K K A T E L K H L Q C L E E E L K P L E E V L N L A Q S K N
F H L R P R D L I S N I N V I V L E L K G S E T T F M C E Y A D E T A T I V E F L N R W I T F S Q S I I S T L T / G G G G S G G G G S / E P K S S D K T H
T C P P C P A P P V A G P S V F L F P P K P K D T L M I S R T P E V T C V V V D V K H E D P E V K F N W Y V D G V E V H N A K T K P R E E Q Y N S T Y R V
V S V L T V L H Q D W L N G K E Y K C K V S N K A L P A P I E K T I S K A K G Q P R E P Q V Y T L P P S R E E M T K N Q V S L T C L V K G F Y P S D I A V
E W E S N G Q P E N N Y K T T P P V L D S D G S F F L Y S K L T V D K S R W Q Q G N V F S C S V M H E A L H N H Y T Q K S L S L S P G K

>XENP027004 hIL2 0.308 (GGGGS)2 Fc(216) IgG1 C220S/PVA /S267K (SEQ ID NO: 277)

APASSSTKKTQLQLEHLLLNLQMI L N G I N N Y K N P K L T R M L T F K F Y M P K K A T E L K H L Q C L E E E L K P L E E V L K L A Q S K N
F H L R P R D L I S N I N V I V L E L K G S E T T F M C E Y A D E T A T I V E F L N R W I T F S Q S I I S T L T / G G G G S G G G G S / E P K S S D K T H
T C P P C P A P P V A G P S V F L F P P K P K D T L M I S R T P E V T C V V V D V K H E D P E V K F N W Y V D G V E V H N A K T K P R E E Q Y N S T Y R V
V S V L T V L H Q D W L N G K E Y K C K V S N K A L P A P I E K T I S K A K G Q P R E P Q V Y T L P P S R E E M T K N Q V S L T C L V K G F Y P S D I A V
E W E S N G Q P E N N Y K T T P P V L D S D G S F F L Y S K L T V D K S R W Q Q G N V F S C S V M H E A L H N H Y T Q K S L S L S P G K

>XENP027005 hIL2 0.313 (GGGGS)2 Fc(216) IgG1 C220S/PVA /S267K (SEQ ID NO: 278)

APASSSTKKTQLQLEHLLLNLQMI L N G I N N Y K N P K L T I M L T F K F Y M P K K A T E L K H L Q C L E E E L K P L E E V L N L A Q S K N
F H L R P R D L I S N I N V I V L E L K G S E T T F M C E Y A D E T A T I V E F L N R W I T F S Q S I I S T L T / G G G G S G G G G S / E P K S S D K T H
T C P P C P A P P V A G P S V F L F P P K P K D T L M I S R T P E V T C V V V D V K H E D P E V K F N W Y V D G V E V H N A K T K P R E E Q Y N S T Y R V
V S V L T V L H Q D W L N G K E Y K C K V S N K A L P A P I E K T I S K A K G Q P R E P Q V Y T L P P S R E E M T K N Q V S L T C L V K G F Y P S D I A V
E W E S N G Q P E N N Y K T T P P V L D S D G S F F L Y S K L T V D K S R W Q Q G N V F S C S V M H E A L H N H Y T Q K S L S L S P G K

Figure 30E

>XENP027006 hIL2 0.317 (GGGGS)2 Fc(216) IgG1 C220S/PVA /S267K (SEQ ID NO: 279)

APASSSTKKTQLQLEHLLLNLQMILNGINNYKNPKLRIMLTFFKFYMPKKATELKHLCLEEEELKPLEEVLNLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT/____GGGSGGGGS____/EPKSSDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRV
VSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAV
EWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSLSLSPGK

>XENP027007 hIL2 0.318 (GGGGS)2 Fc(216) IgG1 C220S/PVA /S267K (SEQ ID NO: 280)

APASSSTKKTQLQLEHLLLNLQMILNGINNYKNPKLTIMLTFFKFYMPKKATELKHLCLEEEELKPLEEVLKLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT/____GGGSGGGGS____/EPKSSDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRV
VSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAV
EWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSLSLSPGK

Figure 31A

<u>Variant</u>	<u>IL-2</u>	<u>monovIL-2-Fc</u> <u>(w/o linker)</u>	<u>monovIL-2-Fc</u> <u>(with linker)</u>	<u>bivIL-2-Fc</u> <u>(w/o linker)</u>	<u>bivIL-2-Fc</u> <u>(with linker)</u>
C125S	14135	24635	25911	25907	25909
R38A C125S	14136				
R38D C125S	14137				
R38E C125S	14138				
R38F C125S	14139				
R38G C125S	14140				
R38H C125S	14141				
R38I C125S	14142	24643			
R38K C125S	14143				
R38L C125S	14144				
R38M C125S	14145				
R38N C125S	14146				
R38P C125S	14147				
R38Q C125S	14148				
R38S C125S	14149				
R38T C125S	14150				
R38V C125S	14151				
R38W C125S	14152				
R38Y C125S	14153				
T41A C125S	14154				
T41D C125S	14155				
T41E C125S	14156				
T41F C125S	14157				
T41G C125S	14158				
T41H C125S	14159				
T41I C125S	14160				
T41K C125S	14161				
T41L C125S	14162				
T41M C125S	14163				
T41N C125S	14164				
T41P C125S	14165				
T41Q C125S	14166				
T41R C125S	14167				
T41S C125S	14168				
T41V C125S	14169				

Figure 31B

<u>Variant</u>	<u>IL-2</u>	<u>monovIL-2-Fc</u> <u>(w/o linker)</u>	<u>monovIL-2-Fc</u> <u>(with linker)</u>	<u>bivIL-2-Fc</u> <u>(w/o linker)</u>	<u>bivIL-2-Fc</u> <u>(with linker)</u>
T41W C125S	14170				
T41Y C125S	14171				
F42A C125S	14172				
F42D C125S	14173				
F42E C125S	14174				
F42G C125S	14175				
F42H C125S	14176				
F42I C125S	14177				
F42K C125S	14178				
F42L C125S	14179				
F42M C125S	14180				
F42N C125S	14181				
F42P C125S	14182				
F42Q C125S	14183				
F42R C125S	14184				
F42S C125S	14185				
F42T C125S	14186				
F42V C125S	14187				
F42W C125S	14188				
F42Y C125S	14189				
R38Q T41K C125S	14190				
R38Q T41Q C125S	14191				
R38E T41K C125S	14192				
R38Q T41R C125S	14193				
R38N T41Q C125S	14194				
R38Q T41V C125S	14195				
R38N T41V C125S	14196				
R38Q T41M C125S	14201				
R38Q T41S C125S	14202				
R38Q T41L C125S	14203				
R38N T41M C125S	14204				
T41I F42Y C125S	14205				
T41E F42Y C125S	14206				
T41D F42Y C125S	14207				
T41M F42Y C125S	14208				

Figure 31C

<u>Variant</u>	<u>IL-2</u>	<u>monovIL-2-Fc</u> <u>(w/o linker)</u>	<u>monovIL-2-Fc</u> <u>(with linker)</u>	<u>bivIL-2-Fc</u> <u>(w/o linker)</u>	<u>bivIL-2-Fc</u> <u>(with linker)</u>
T41Q F42Y C125S	14209				
T41E F42H C125S	14210				
T41E F42L C125S	14211				
T41E F42P C125S	14212				
R38Q F42Y C125S	14213				
R38N T41R C125S	14214				
R38N T41K C125S	14215				
R38V T41R C125S	14216				
R38P T41R C125S	14217				
T41E F42K C125S	14218				
T41D F42K C125S	14219				
T41M F42K C125S	14220				
T41Q F42K C125S	14221				
R38Q F42K C125S	14222				
T41I F42K C125S	14223				
R38N F42K C125S	14224				
T41H F42K C125S	14225				
R38Q T41K F42Y C125S	14226				
R38Q T41R F42Y C125S	14227				
R38Q T41Q F42Y C125S	14228				
R38Q T41V F42Y C125S	14229				
R38N T41K F42K C125S	14230				
R38Q T41H F42K C125S	14231				
R38Q T41K F42K C125S	14232				
R38Q T41Q F42K C125S	14233				
R38Q T41V F42K C125S	14234				
R38Q T41R F42K C125S	14235				
N29S Y31H K35R T37A K48E V69A N71R Q74P N88D I89V C125S Q126T	14277				
N29S Y31H K35R T37A R38L K48E V69A N71R Q74P N88D I89V C125S Q126T	14381	24640			
Q11E C125S	23816				
L12D C125S	23817				
Q13E C125S	23820				
E15Q C125S	23824				
H16Y C125S	23827				

Figure 31D

<u>Variant</u>	<u>IL-2</u>	<u>monovIL-2-Fc (w/o linker)</u>	<u>monovIL-2-Fc (with linker)</u>	<u>bivIL-2-Fc (w/o linker)</u>	<u>bivIL-2-Fc (with linker)</u>
L19D C125S	23830				
D20N C125S	23833				
Q22E C125S	23834				
K35R C125S	23836				
T37S C125S	23837				
K43R C125S	23838				
F44Y C125S	23839				
Y45F C125S	23840				
K48R C125S	23842				
K49E C125S	23843				
E61Q C125S	23846				
E62Q C125S	23848				
K64R C125S	23849				
E68Q C125S	23851				
V69L C125S	23852				
L72I C125S	23853				
R81D C125S	23855				
D84N C125S	23859				
S87T C125S	23861				
N88D C125S	23862				
V91L C125S	23868				
I92L C125S	23869				
E95Q C125S	23871				
Y107F C125S	23874				
E116R C125S	23875				
N119D C125S	23876				
R120D C125S	23878				
T123S C125S	23882				
C125S Q126E	23883				
C125S S127T	23885				
C125S I129L	23886				
C125S S130T	23888				
C125S T133S	23889				
T3A C125S		24636			
T3A F42A Y45A L72G C125A		24637	25912		
N29S Y31H K35R T37A K48E V69A N71R Q74P N88D I89V C125S		24638			

Figure 31E

<u>Variant</u>	<u>IL-2</u>	<u>monovIL-2-Fc</u> <u>(w/o linker)</u>	<u>monovIL-2-Fc</u> <u>(with linker)</u>	<u>bivIL-2-Fc</u> <u>(w/o linker)</u>	<u>bivIL-2-Fc</u> <u>(with linker)</u>
V69A Q74P I128T C125S		24639			
C125S Q126T		24641			
N88R C125S		24642	25910	25906	25908
L80F R81D L85V I92F C125S		24725			
L18R L80F R81D L85V I92F C125S Q126T		24728			
L18R L80F R81D L85V I92F C125S Q126T S130R		24729			
T3A F42A Y45A L72G N88R C125A		24730			
T3A F42A Y45A L72G C125A Q126T		24731			
T3A F42A Y45A L72G N88R C125A Q126T		24732			
T3A L19D C125S		25717			
T3A D20N C125S		25720	26986	26992	27002
T3A N88D C125S		25725			
T3A N88K C125S		25727			
N29S Y31H K35R T37A K48E N71R N88D I89V C125S		26086			
L19D N29S Y31H K35R T37A K48E N71R C125S		26088			
D20N N29S Y31H K35R T37A K48E N71R C125S		26089			
L19D N29S Y31H K35R T37A K48E C125S		26092			
D20N N29S Y31H K35R T37A K48E C125S		26093			
T3A L19D K35R C125S		26096			
T3A L19D T37R C125S		26104			
T3A D20N T37R C125S		26105	26987	26993	27003
T3A L19D N71K C125S		26108			
T3A D20N N71K C125S		26109	26841	26994	27004
T3A D20N R38I C125S		26835	26989	26995	27005
T3A D20N T37R R38I C125S		26839	26990	26996	27006
T3A D20N R38I N71K C125S		26840	26991	27001	27007

Figure 32

A) pH Switch

IL-2-His	XENP14142	XENP14144
Substitutions	R38I C125S	R38L C125S

B) Treg Selective

IL-2-His	XENP23833				
monovIL-2-Fc without Domain Linkers		XENP25720	XENP26086	XENP26105	XENP26109
bivIL-2-Fc without Domain Linkers		XENP26992		XENP26993	XENP26994
monovIL-2-Fc with Domain Linkers		XENP26896		XENP26987	XENP26841
bivIL-2-Fc with Domain Linkers		XENP27002		XENP27003	XENP27004
Substitutions	D20N C125S	T3A D20N C125S	N29S Y31H K35R T37A K48E N71R N88D I89V C125S	T3A D20N T37R C125S	T3A D20N N71K C125S

C) Treg Selective + pH Switch

monovIL-2-Fc without Domain Linkers	XENP26839	XENP26835	XENP26840
bivIL-2-Fc without Domain Linkers	XENP26996	XENP26995	XENP27001
monovIL-2-Fc with Domain Linkers	XENP26990	XENP26989	XENP26991
bivIL-2-Fc with Domain Linkers	XENP27006	XENP27005	XENP27007
Substitutions	T3A D20N T37R R38I C125S	T3A D20N R38I C125S	T3A D20N R38I N71K C125S

Figure 33

	CD25			CD122			CD122:CD132		
XENP	K _D (M)	k _a (1/Ms)	k _d (1/s)	K _D (M)	k _a (1/Ms)	k _d (1/s)	K _D (M)	k _a (1/Ms)	k _d (1/s)
26086	1.69E-08	5.30E+05	8.97E-03	N.B.			3.85E-08	9.24E+04	3.56E-03
26088	1.66E-08	5.15E+05	8.55E-03	N.B.			3.62E-08	1.43E+05	5.18E-03
26089	1.44E-08	5.40E+05	7.75E-03	N.B.			N.B.		
26092	2.64E-08	5.60E+05	1.48E-02	N.B.			2.38E-08	1.88E+05	4.47E-03
26093	2.13E-08	6.30E+05	1.34E-02	N.B.			N.B.		
26096	3.92E-08	6.12E+05	2.40E-02	N.B.			1.27E-08	2.56E+05	3.23E-03
26104	1.47E-08	6.85E+05	1.00E-02	N.B.			1.27E-08	2.49E+05	3.17E-03
26105	1.41E-08	6.71E+05	9.43E-03	N.B.			3.64E-08	2.27E+05	8.27E-03
26108	2.77E-08	7.03E+05	1.94E-02	N.B.			1.51E-08	2.87E+05	4.33E-03
26109	2.85E-08	5.63E+05	1.60E-02	N.B.			5.73E-08	3.02E+05	1.73E-02

Figure 34

XENP27193 empty-Fc(221;N297G) GGGGS hIL2(V91K) (SEQ ID NO: 281)

DKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTK
PREEQYGSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHE
ALHNHYTQKSLSLSPG/GGGGS/APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPKLTRMLTFKFYMP
KKATELKHLQCLEEELKPLEEVLNLAQSKNFHLRPRDLISNINKIVLELKGSETTFMCEYADETATIVEF
LNRWITFAQSIISTLT

Figure 35A

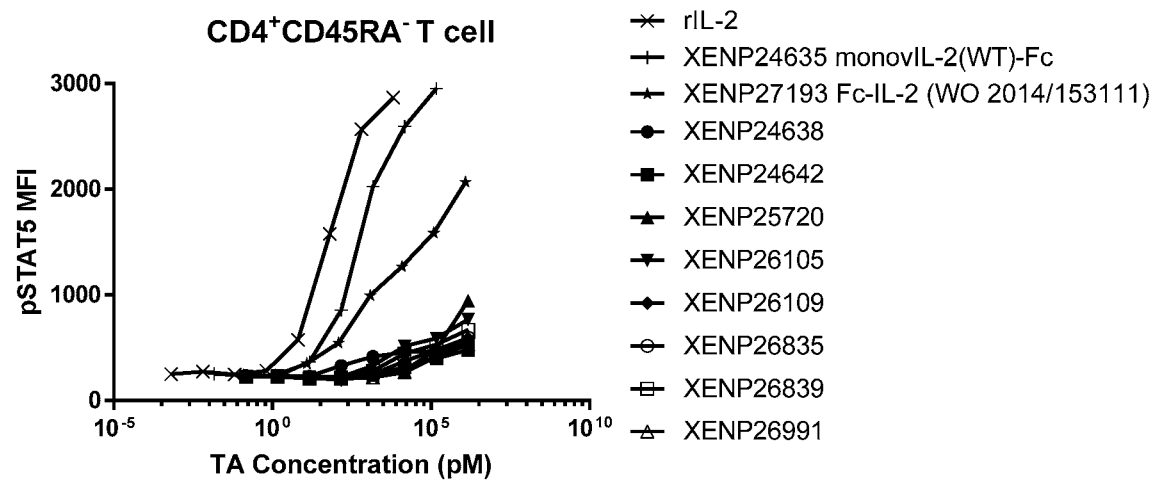


Figure 35B

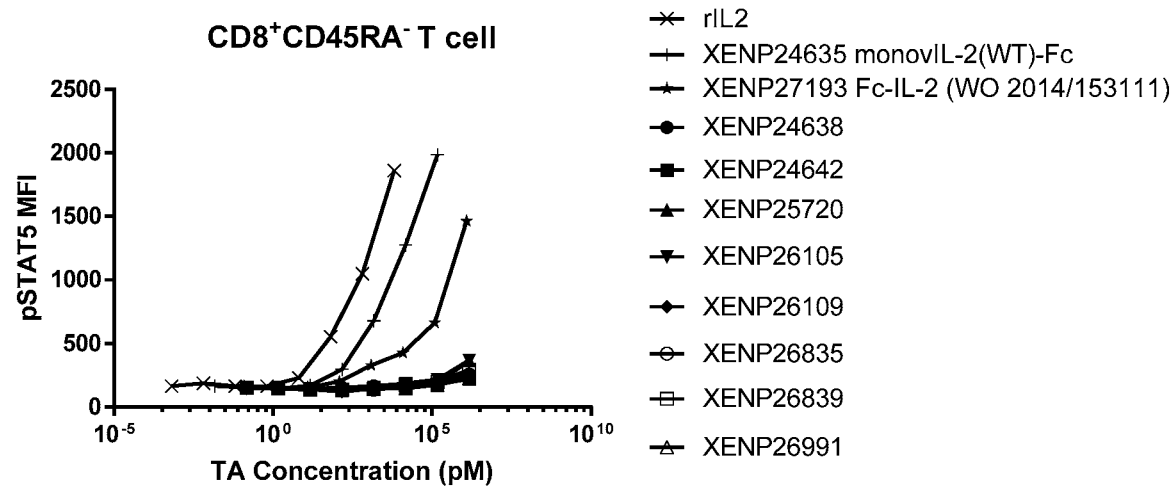


Figure 35C

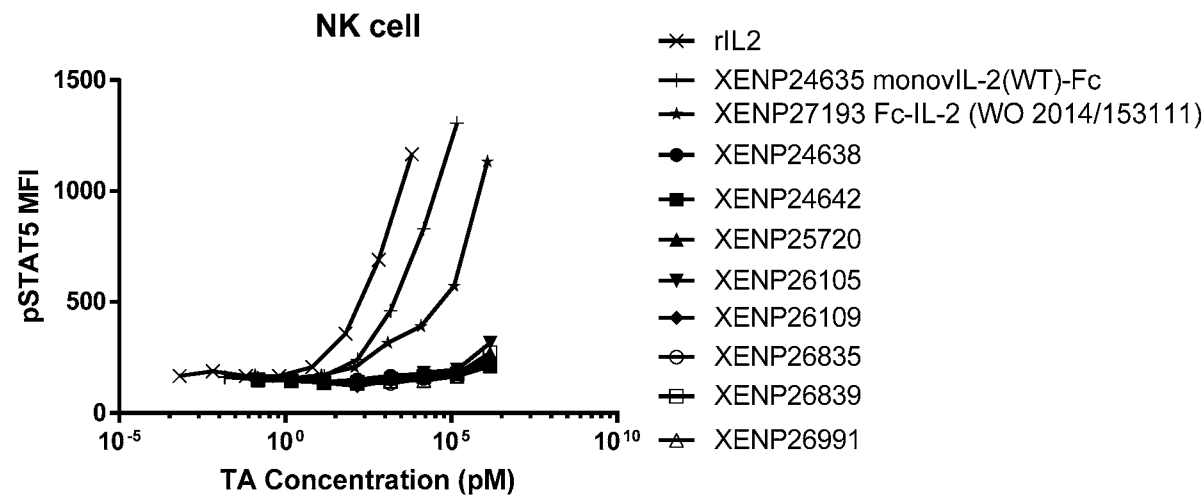


Figure 35D

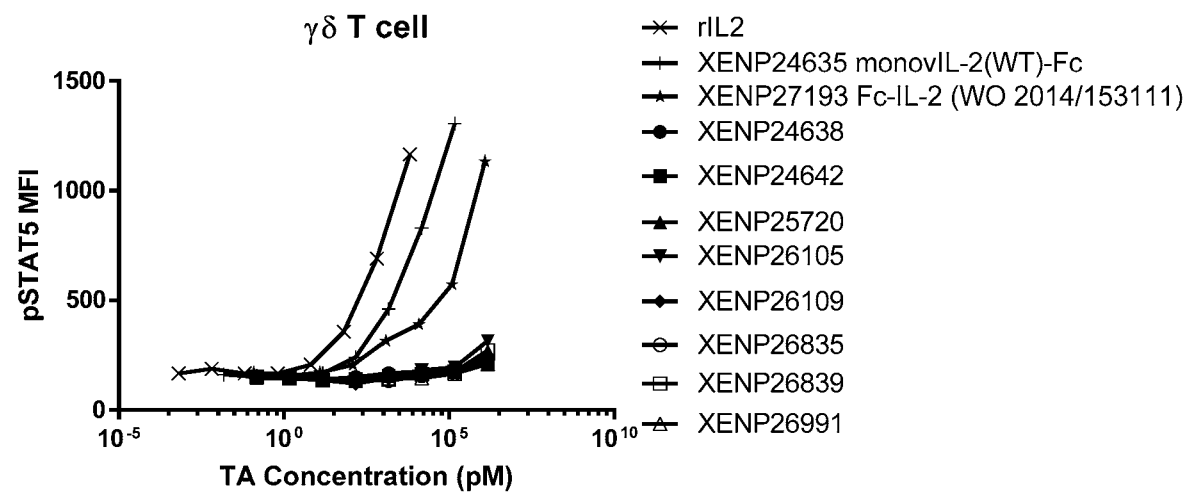


Figure 35E

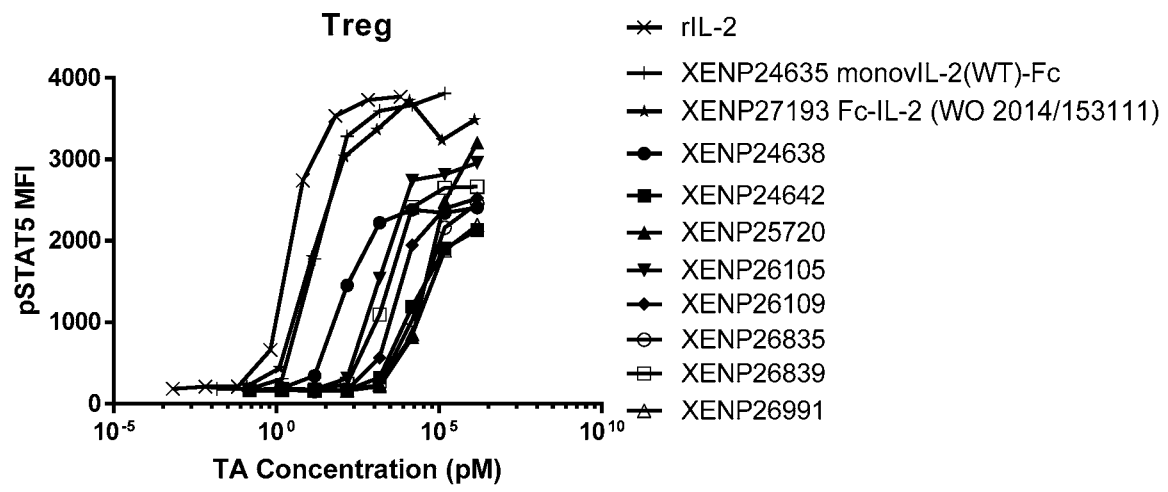


Figure 36

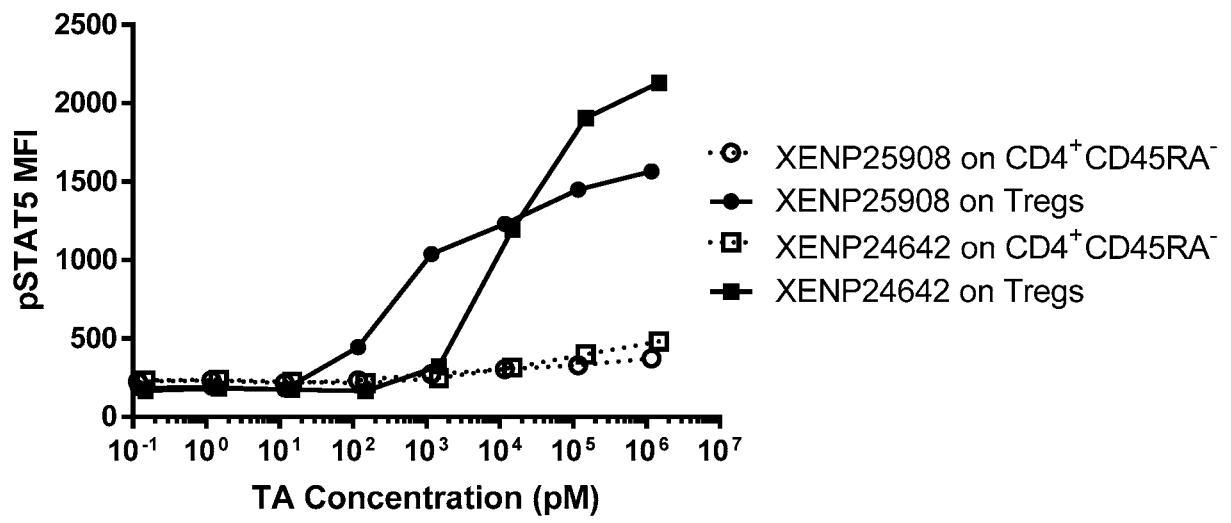


Figure 37

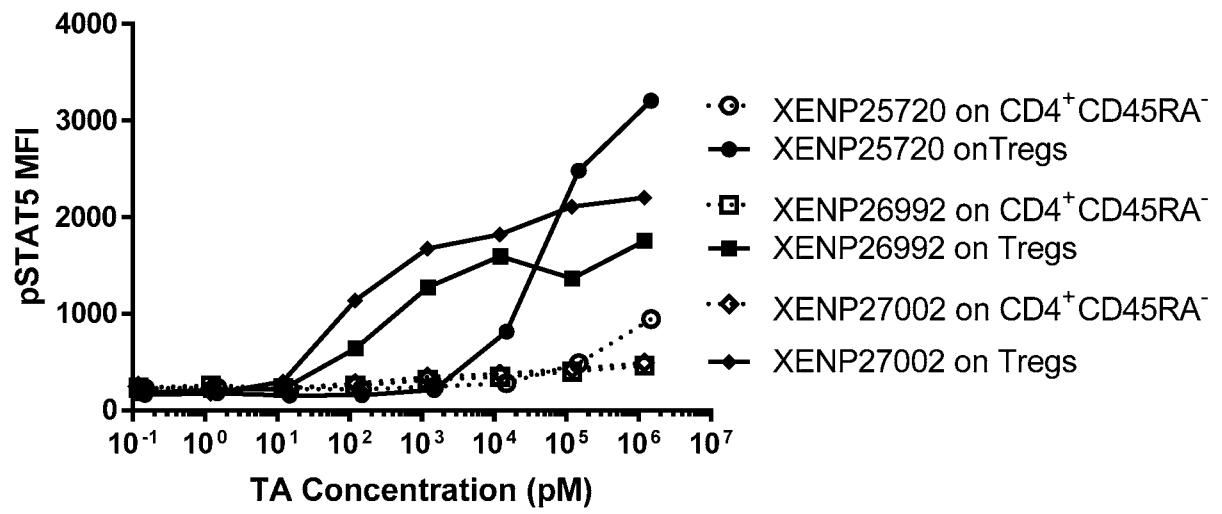


Figure 38

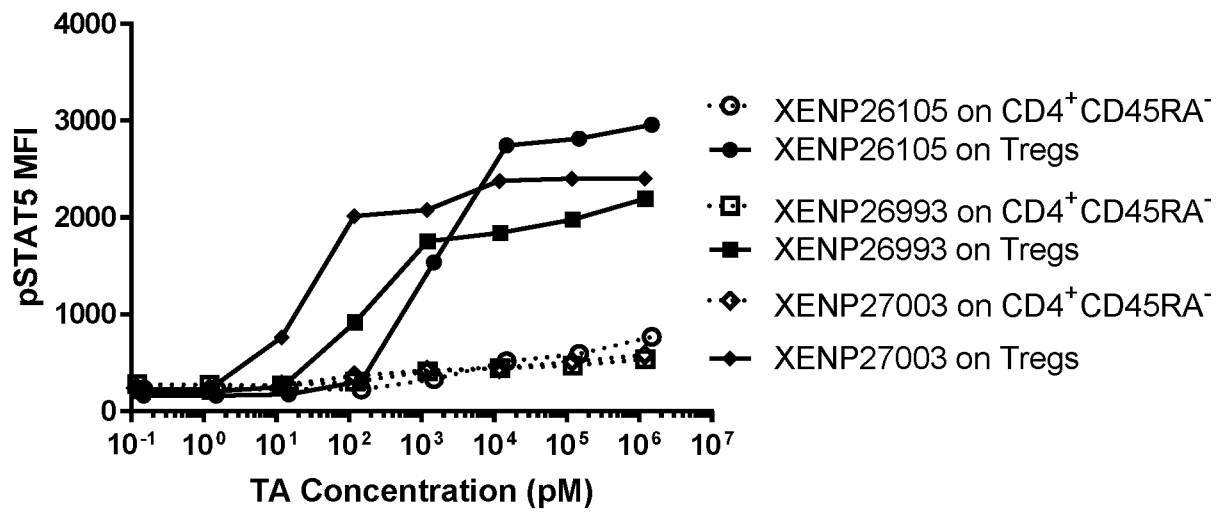


Figure 39

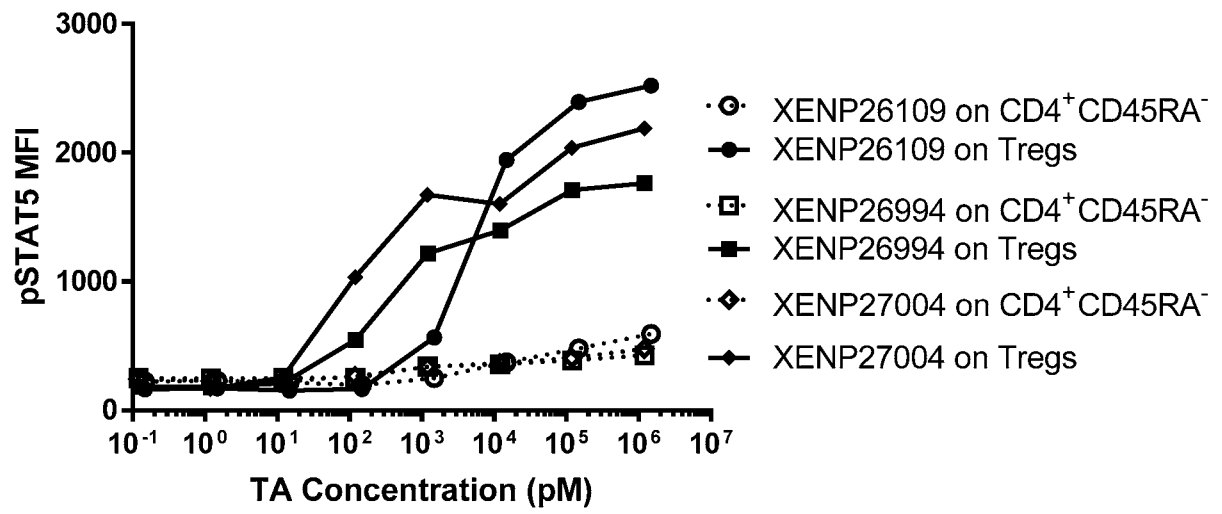


Figure 40

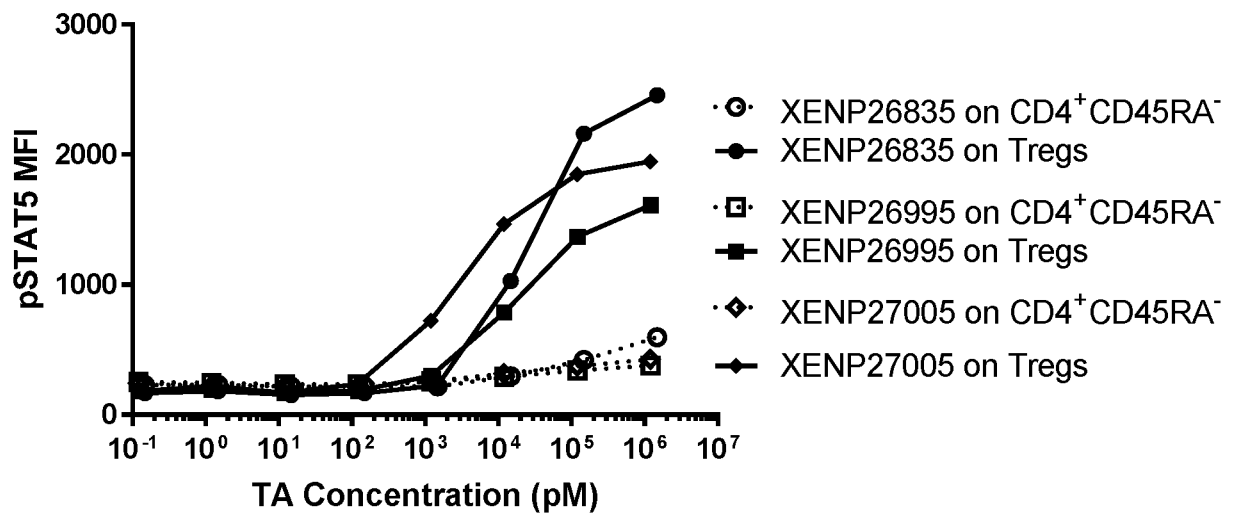


Figure 41

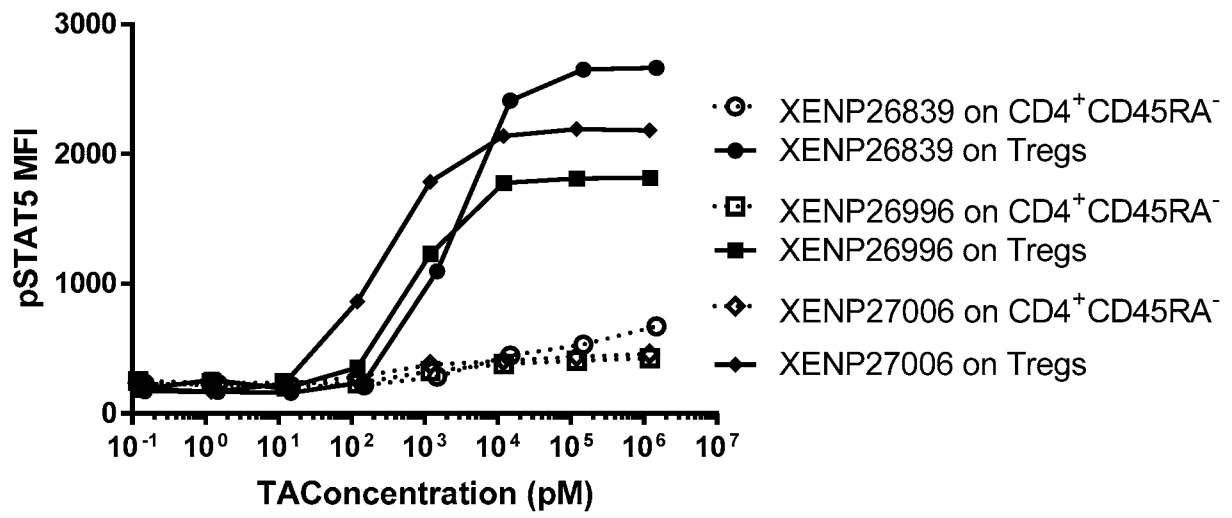


Figure 42

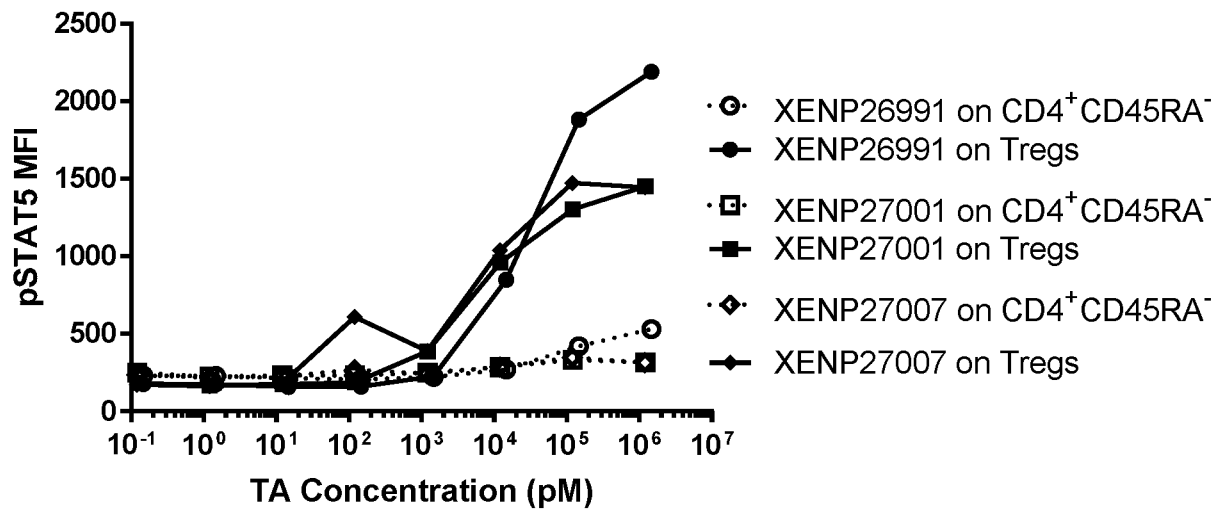


Figure 43A

>XENP27568 hIL2 0.222 Fc(216) IgG1 C220S/PVA /S267K/M428L/N434S (SEQ ID NO: 282)

APASSSTKKTQLQLEHLLLNLQMILNGINNYKNPKLTRMLTFKFYMPKKATELKHLQCLEEELKPLEEVLNLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT/EPKSSDKTHTCPPCPAPPVA
GPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDW
LNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENN
YKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVVFSCSVLHEALHSHYTQKSLSLSPGK

>XENP27569 hIL2 0.304 Fc(216) IgG1 C220S/PVA /S267K/M428L/N434S (SEQ ID NO: 283)

APASSSTKKTQLQLEHLLLNLQMILNGINNYKNPKLRRLTFKFYMPKKATELKHLQCLEEELKPLEEVLNLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT/EPKSSDKTHTCPPCPAPPVA
GPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDW
LNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENN
YKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVVFSCSVLHEALHSHYTQKSLSLSPGK

>XENP27570 hIL2 0.308 Fc(216) IgG1 C220S/PVA /S267K/M428L/N434S (SEQ ID NO: 284)

APASSSTKKTQLQLEHLLLNLQMILNGINNYKNPKLTRMLTFKFYMPKKATELKHLQCLEEELKPLEEVLKLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT/EPKSSDKTHTCPPCPAPPVA
GPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDW
LNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENN
YKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVVFSCSVLHEALHSHYTQKSLSLSPGK

>XENP27571 hIL2 0.313 Fc(216) IgG1 C220S/PVA /S267K/M428L/N434S (SEQ ID NO: 285)

APASSSTKKTQLQLEHLLLNLQMILNGINNYKNPKLTIMLTFKFYMPKKATELKHLQCLEEELKPLEEVLNLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT/EPKSSDKTHTCPPCPAPPVA
GPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDW
LNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENN
YKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVVFSCSVLHEALHSHYTQKSLSLSPGK

>XENP27572 hIL2 0.317 Fc(216) IgG1 C220S/PVA /S267K/M428L/N434S (SEQ ID NO: 286)

APASSSTKKTQLQLEHLLLNLQMILNGINNYKNPKLRIMLTFKFYMPKKATELKHLQCLEEELKPLEEVLNLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT/EPKSSDKTHTCPPCPAPPVA
GPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDW
LNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENN
YKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVVFSCSVLHEALHSHYTQKSLSLSPGK

>XENP27573 hIL2 0.318 Fc(216) IgG1 C220S/PVA /S267K/M428L/N434S (SEQ ID NO: 287)

APASSSTKKTQLQLEHLLLNLQMILNGINNYKNPKLTIMLTFKFYMPKKATELKHLQCLEEELKPLEEVLKLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT/EPKSSDKTHTCPPCPAPPVA
GPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDW
LNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENN
YKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVVFSCSVLHEALHSHYTQKSLSLSPGK

Figure 43B

>XENP27576 hIL2 0.1 Fc(216) IgG1 C220S/PVA /S267K/M428L/N434S (SEQ ID NO: 288)

APTSSSTKKTQLQLEHLLLDLQMLNGINNYKNPKLTRMLTFKFYMPKKATELKHLQCLEEELKPLEEVLNLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT/EPKSSDKTHTCPAPPPVA
GPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDW
LNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENN
YKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVVFSCSVLHEALHSHYTQKSLSLSPGK

>XENP27577 hIL2 0.2 Fc(216) IgG1 C220S/PVA /S267K/M428L/N434S (SEQ ID NO: 289)

APASSSTKKTQLQLEHLLLDLQMLNGINNYKNPKLTRMLTFKFYMPKKATELKHLQCLEEELKPLEEVLNLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT/EPKSSDKTHTCPAPPPVA
GPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDW
LNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENN
YKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVVFSCSVLHEALHSHYTQKSLSLSPGK

>XENP28668 hIL2 0.222 (GGGG)2 Fc(216) IgG1 C220S/PVA /S267K/M428L/N434S (SEQ ID NO: 290)

APASSSTKKTQLQLEHLLLDLQMLNGINNYKNPKLTRMLTFKFYMPKKATELKHLQCLEEELKPLEEVLNLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT/GGGGSGGGG/EPKSSDKTH
TCPAPPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRV
VSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAV
EWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVVFSCSVLHEALHSHYTQKSLSLSPGK

>XENP28669 hIL2 0.304 (GGGG)2 Fc(216) IgG1 C220S/PVA /S267K/M428L/N434S (SEQ ID NO: 291)

APASSSTKKTQLQLEHLLLDLQMLNGINNYKNPKLRMLTFKFYMPKKATELKHLQCLEEELKPLEEVLNLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT/GGGGSGGGG/EPKSSDKTH
TCPAPPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRV
VSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAV
EWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVVFSCSVLHEALHSHYTQKSLSLSPGK

>XENP28670 hIL2 0.308 (GGGG)2 Fc(216) IgG1 C220S/PVA /S267K/M428L/N434S (SEQ ID NO: 292)

APASSSTKKTQLQLEHLLLDLQMLNGINNYKNPKLTRMLTFKFYMPKKATELKHLQCLEEELKPLEEVLKLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT/GGGGSGGGG/EPKSSDKTH
TCPAPPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRV
VSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAV
EWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVVFSCSVLHEALHSHYTQKSLSLSPGK

Figure 44A

>XENP27562 empty-Fc-hIL2 0.222 Fc(216) IgG1 pl(-)

) Isosteric A C220S/PVA /S267K/L368D/K370S/M428L/N434S IgG1 C220S/PVA /S267K/S364K/E357Q/M428L/N434S

Chain 1 - empty_Fc(216)_IgG1_pl(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S/M428L/N434S (SEQ ID NO: 293)

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPRE
EEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVS
GFYPSDIAVEWESDGPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEEQGDVVFSCSVLHEALHSHYTQKSLSLSPGK

Chain 2 - hIL2_0.222_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q/M428L/N434S (SEQ ID NO: 294)

APASSSTKKTQLQLEHLLLNLMILNGINNYKNPKLTRMLTFKFYMPKKATELKHLCLEEEELKPLEEVLNLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT/EPKSSDKTHTCPPCPAPPVA
GPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDW
LNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENN
YKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVVFSCSVLHEALHSHYTQKSLSLSPGK

>XENP27563 empty-Fc-hIL2 0.304 Fc(216) IgG1 pl(-)

) Isosteric A C220S/PVA /S267K/L368D/K370S/M428L/N434S IgG1 C220S/PVA /S267K/S364K/E357Q/M428L/N434S

Chain 1 - empty_Fc(216)_IgG1_pl(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S/M428L/N434S (SEQ ID NO: 295)

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPRE
EEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVS
GFYPSDIAVEWESDGPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEEQGDVVFSCSVLHEALHSHYTQKSLSLSPGK

Chain 2 - hIL2_0.304_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q/M428L/N434S (SEQ ID NO: 296)

APASSSTKKTQLQLEHLLLNLMILNGINNYKNPKLRRMLTFKFYMPKKATELKHLCLEEEELKPLEEVLNLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT/EPKSSDKTHTCPPCPAPPVA
GPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDW
LNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENN
YKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVVFSCSVLHEALHSHYTQKSLSLSPGK

>XENP27564 empty-Fc-hIL2 0.308 Fc(216) IgG1 pl(-)

) Isosteric A C220S/PVA /S267K/L368D/K370S/M428L/N434S IgG1 C220S/PVA /S267K/S364K/E357Q/M428L/N434S

Chain 1 - empty_Fc(216)_IgG1_pl(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S/M428L/N434S (SEQ ID NO: 297)

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPRE
EEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVS
GFYPSDIAVEWESDGPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEEQGDVVFSCSVLHEALHSHYTQKSLSLSPGK

Figure 44B

Chain 2 - hIL2_0.308_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q/M428L/N434S (SEQ ID NO: 298)

APASSSTKKTQLQLEHLLLNLMILNGINNYKNPKLTRMLTFKFYMPKKATELKHLQCLEEELKPLEEVLKLAQSKN
 FHLRPRDLISNINIVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT/EPKSSDKTHTCPPCPAPPVA
 GPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDW
 LNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVCLTKLVKGFYPSDIAVEWESNGQPENN
 YKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVVFSCSVLHEALHSHYTQKSLSLSPGK

>XENP27565 empty-Fc-hIL2 0.313 Fc(216) IgG1 pl(-)

) Isosteric A C220S/PVA_/S267K/L368D/K370S/M428L/N434S IgG1 C220S/PVA_/S267K/S364K/E357Q/M428L/N434S

Chain 1 - empty_Fc(216)_IgG1_pl(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S/M428L/N434S (SEQ ID NO: 299)

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPRE
 EEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVS
 GFYPSDIAVEWESDGPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVVFSCSVLHEALHSHYTQKSLSLSPGK

Chain 2 - hIL2_0.313_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q/M428L/N434S (SEQ ID NO: 300)

APASSSTKKTQLQLEHLLLNLMILNGINNYKNPKLTIMLTFKFYMPKKATELKHLQCLEEELKPLEEVLNLAQSKN
 FHLRPRDLISNINIVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT/EPKSSDKTHTCPPCPAPPVA
 GPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDW
 LNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVCLTKLVKGFYPSDIAVEWESNGQPENN
 YKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVVFSCSVLHEALHSHYTQKSLSLSPGK

>XENP27566 empty-Fc-hIL2 0.317 Fc(216) IgG1 pl(-)

) Isosteric A C220S/PVA_/S267K/L368D/K370S/M428L/N434S IgG1 C220S/PVA_/S267K/S364K/E357Q/M428L/N434S

Chain 1 - empty_Fc(216)_IgG1_pl(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S/M428L/N434S (SEQ ID NO: 301)

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPRE
 EEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVS
 GFYPSDIAVEWESDGPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVVFSCSVLHEALHSHYTQKSLSLSPGK

Chain 2 - hIL2_0.317_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q/M428L/N434S (SEQ ID NO: 302)

APASSSTKKTQLQLEHLLLNLMILNGINNYKNPKLRIMLTFKFYMPKKATELKHLQCLEEELKPLEEVLNLAQSKN
 FHLRPRDLISNINIVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT/EPKSSDKTHTCPPCPAPPVA
 GPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDW
 LNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVCLTKLVKGFYPSDIAVEWESNGQPENN
 YKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVVFSCSVLHEALHSHYTQKSLSLSPGK

Figure 44C

>XENP27567 empty-Fc-hIL2 0.318 Fc(216) IgG1 pl(-)

) Isosteric A C220S/PVA /S267K/L368D/K370S/M428L/N434S IgG1 C220S/PVA /S267K/S364K/E357Q/M428L/N434S

Chain 1 - empty_Fc(216)_IgG1_pl(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S/M428L/N434S (SEQ ID NO: 303)

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPRE
EEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVS
GFYPSDIAVEWESDGPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEEQGDVFSQSVLHEALHSHYTQKSLSLSPGK

Chain 2 - hIL2_0.318_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q/M428L/N434S (SEQ ID NO: 304)

APASSSTKKTQLQLEHLLLNLMILNGINNYKNPKLTIMLTFKFYMPKKATELKHLQCLEEELKPLEEVLKLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT/EPKSSDKTHTCPPCPAPPVA
GPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDW
LNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENN
YKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSQSVLHEALHSHYTQKSLSLSPGK

>XENP27574 empty-Fc-hIL2 0.1 Fc(216) IgG1 pl(-)

) Isosteric A C220S/PVA /S267K/L368D/K370S/M428L/N434S IgG1 C220S/PVA /S267K/S364K/E357Q/M428L/N434S

Chain 1 - empty_Fc(216)_IgG1_pl(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S/M428L/N434S (SEQ ID NO: 305)

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPRE
EEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVS
GFYPSDIAVEWESDGPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEEQGDVFSQSVLHEALHSHYTQKSLSLSPGK

Chain 2 - hIL2_0.1_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q/M428L/N434S (SEQ ID NO: 306)

APTSSSTKKTQLQLEHLLLDLMILNGINNYKNPKLTRMLTFKFYMPKKATELKHLQCLEEELKPLEEVLNLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT/EPKSSDKTHTCPPCPAPPVA
GPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDW
LNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENN
YKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSQSVLHEALHSHYTQKSLSLSPGK

Figure 44D

>XENP27575 empty-Fc-hIL2 0.2 Fc(216) IgG1 pl(-)

) Isosteric A C220S/PVA /S267K/L368D/K370S/M428L/N434S IgG1 C220S/PVA /S267K/S364K/E357Q/M428L/N434S

Chain 1 - empty_Fc(216)_IgG1_pl(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S/M428L/N434S (SEQ ID NO: 307)

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPRE
EEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVS
GFYPSDIAVEWESDGPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSQSVLHEALHSHYTQKSLSLSPGK

Chain 2 - hIL2_0.2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q/M428L/N434S (SEQ ID NO: 308)

APASSSTKKTQLQLEHLLLDLQMLNGINNYKNPKLTRMLTFKFYMPKKATELKHLQCLEEELKPLEEVLNLAQSKN
FHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFSQSIISTLT/EPKSSDKTHTCPPCPAPPVA
GPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDW
LNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVCLTKLVKGFYPSPDIWESNGQPENN
YKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSQSVLHEALHSHYTQKSLSLSPGK

Figure 45A

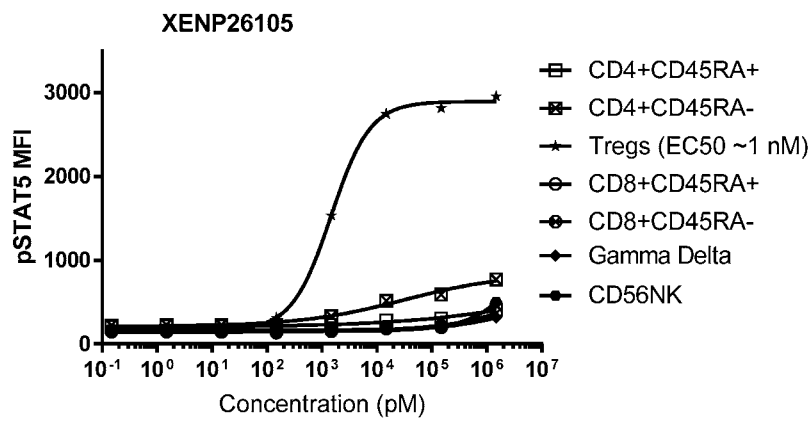


Figure 45B

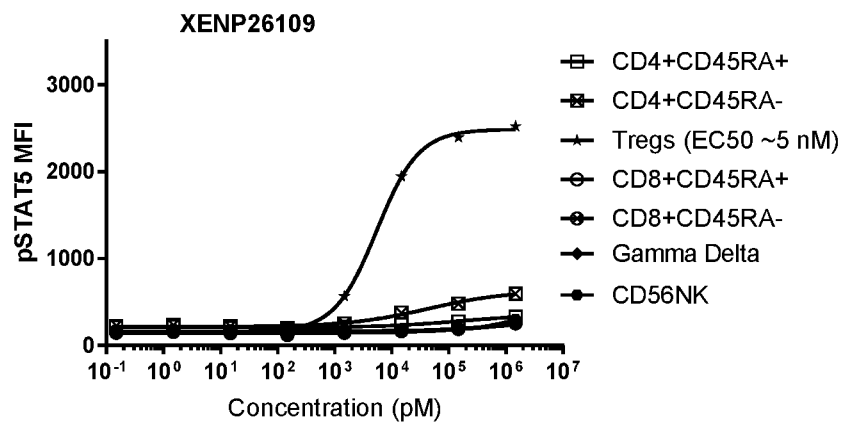


Figure 45C

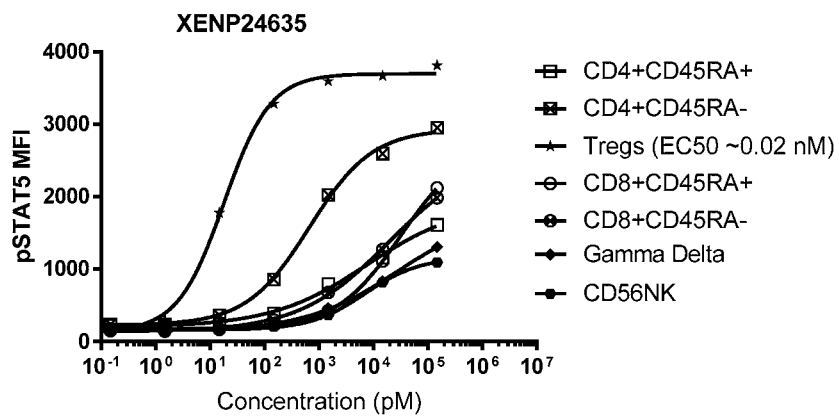


Figure 45D

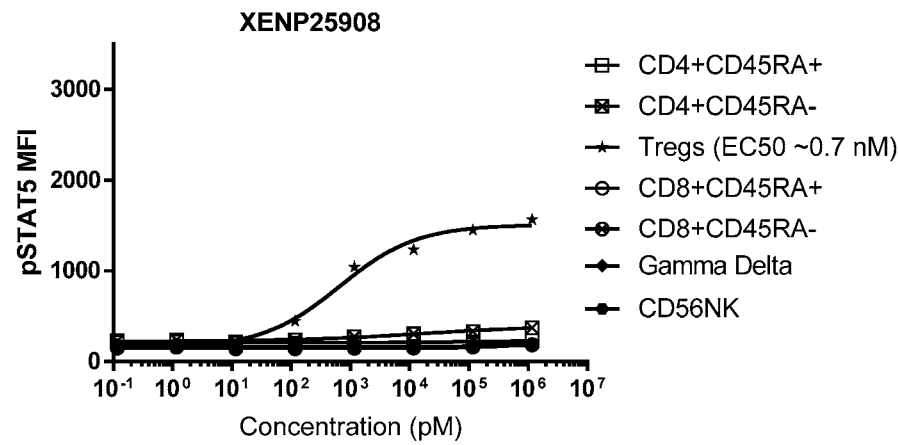


Figure 45E

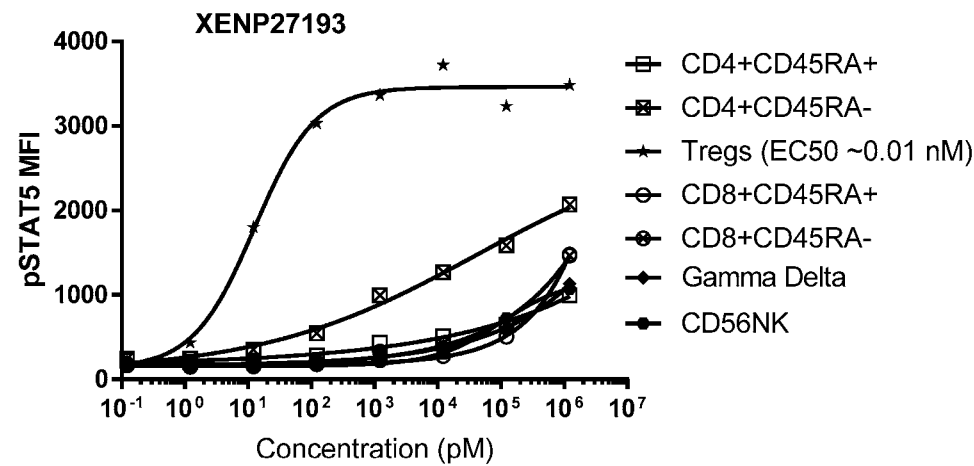


Figure 46

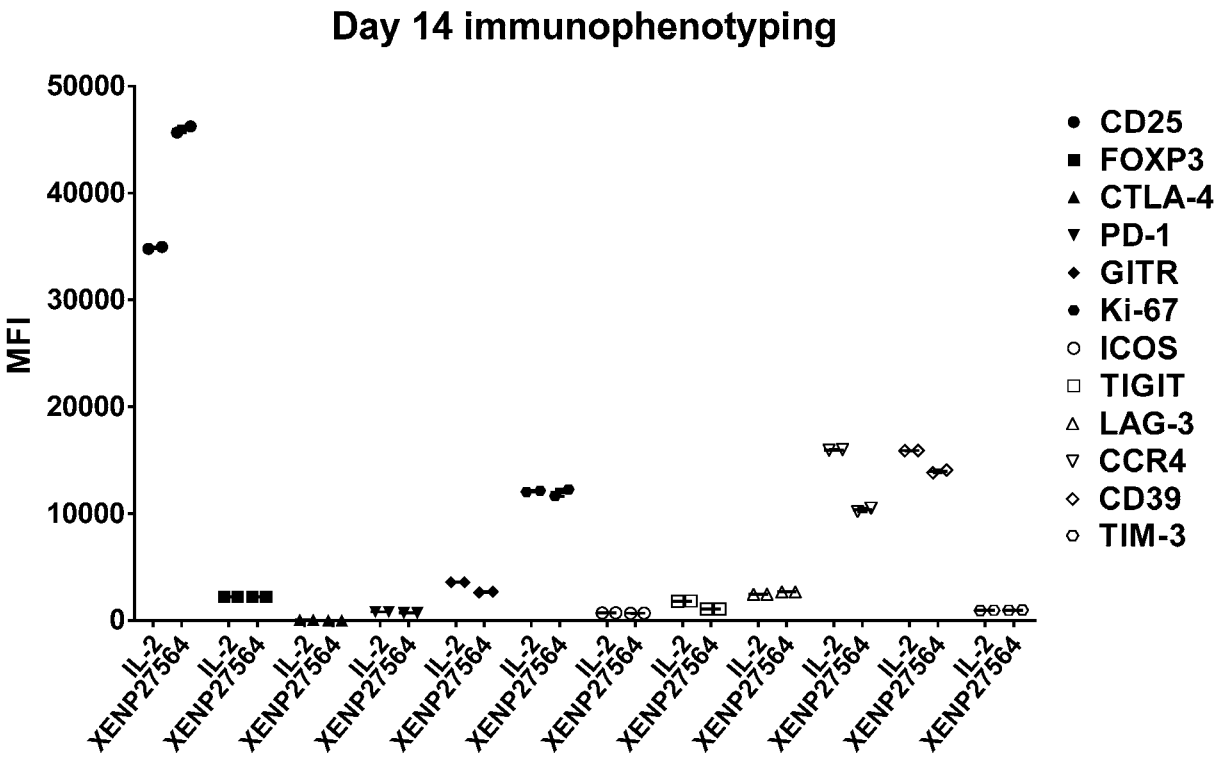
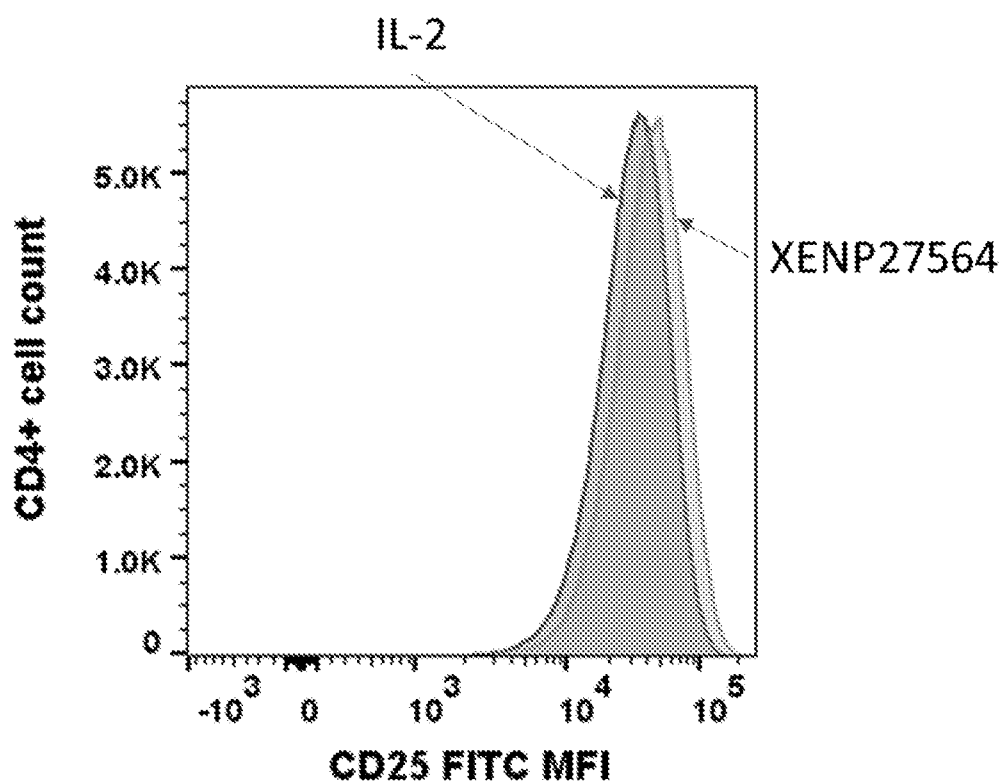


Figure 47



Test Article	Mean : CD25
XENP27564	45658
IL-2	34968

Figure 48

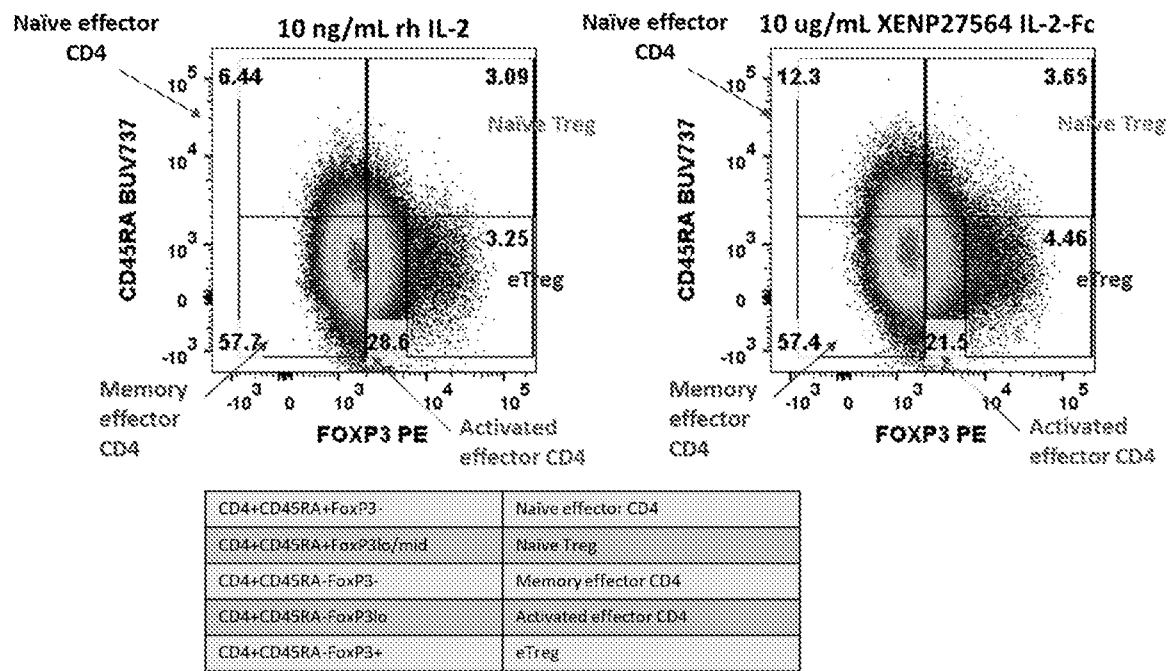


Figure 49A

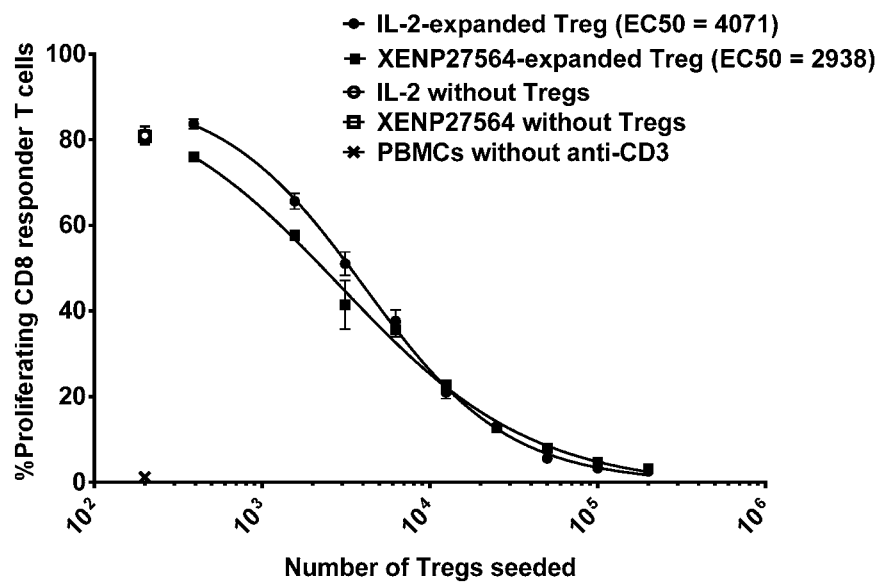


Figure 49B

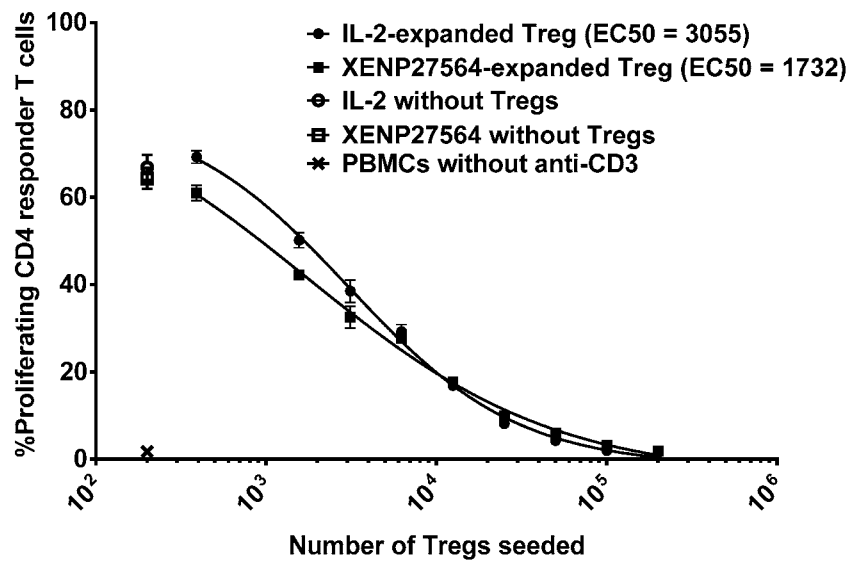


Figure 50A

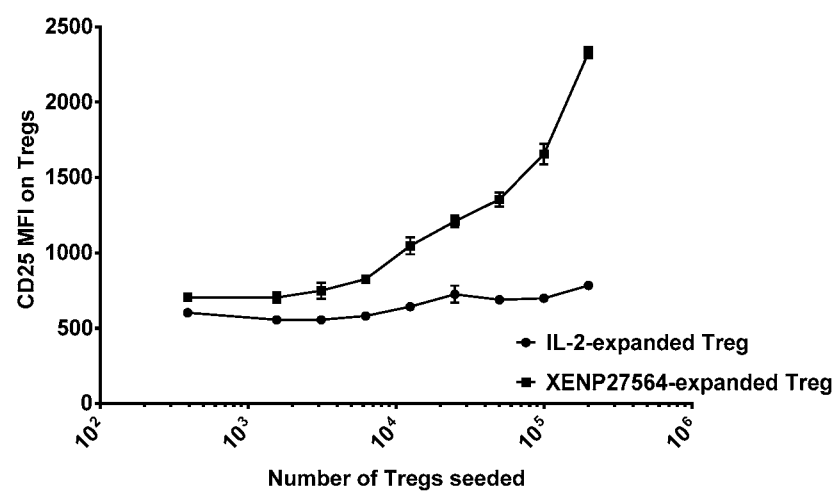


Figure 50B

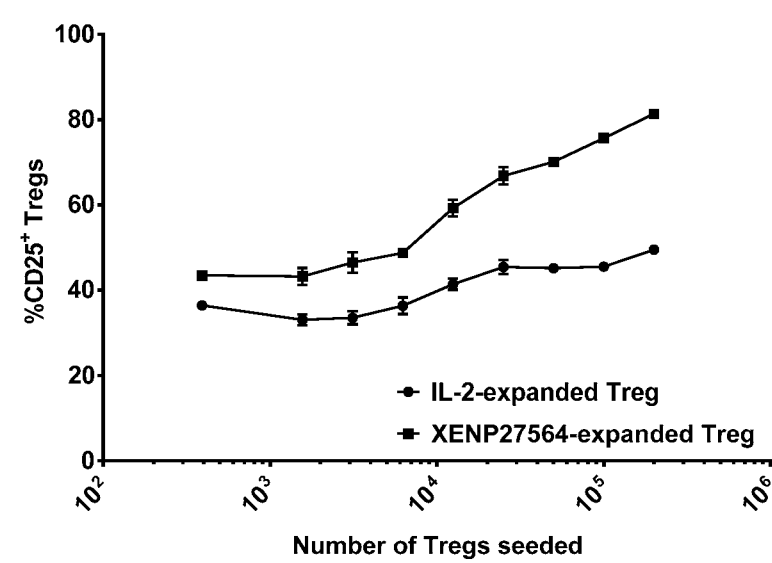


Figure 51A

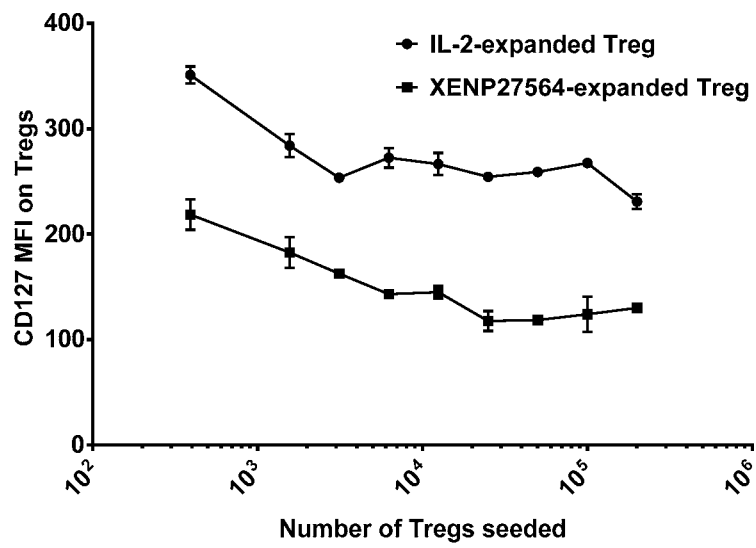


Figure 51B

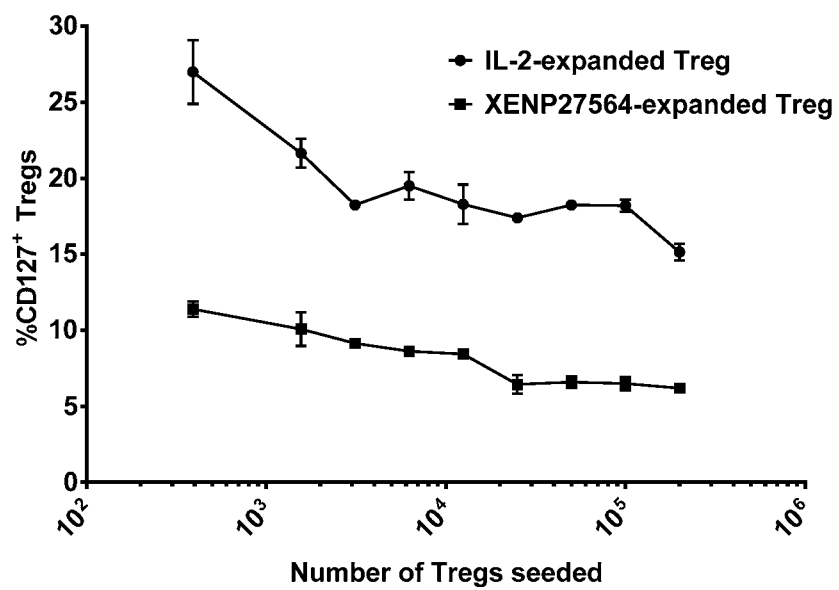


Figure 52A

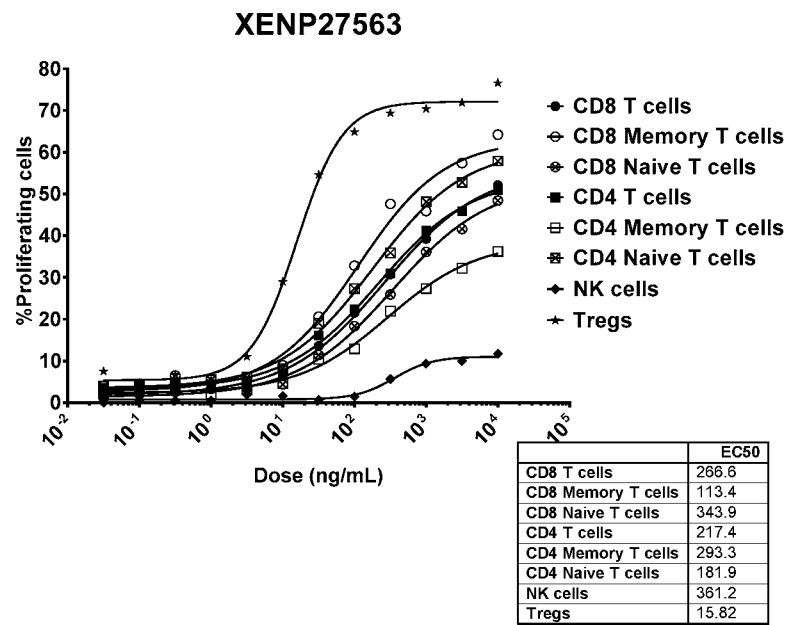


Figure 52B

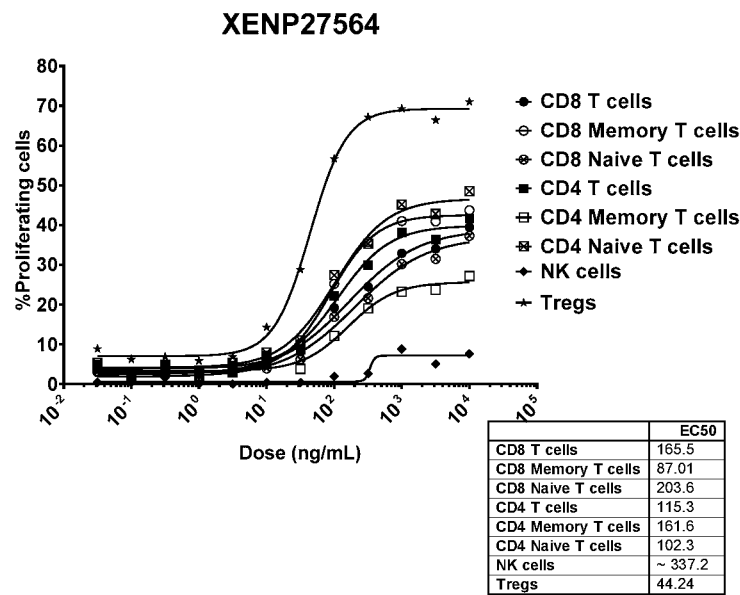


Figure 52C

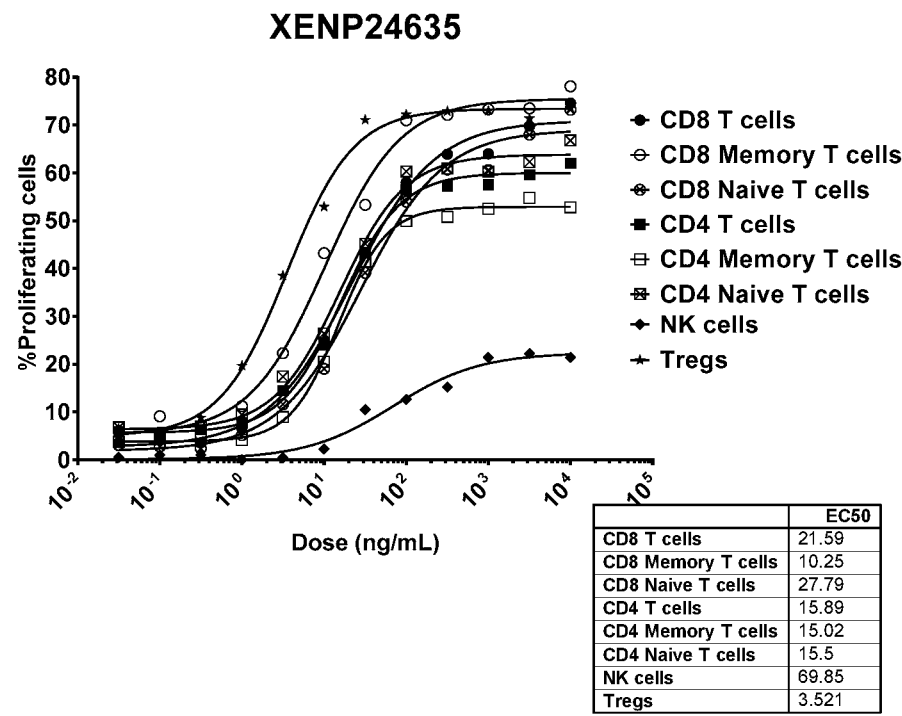


Figure 52D

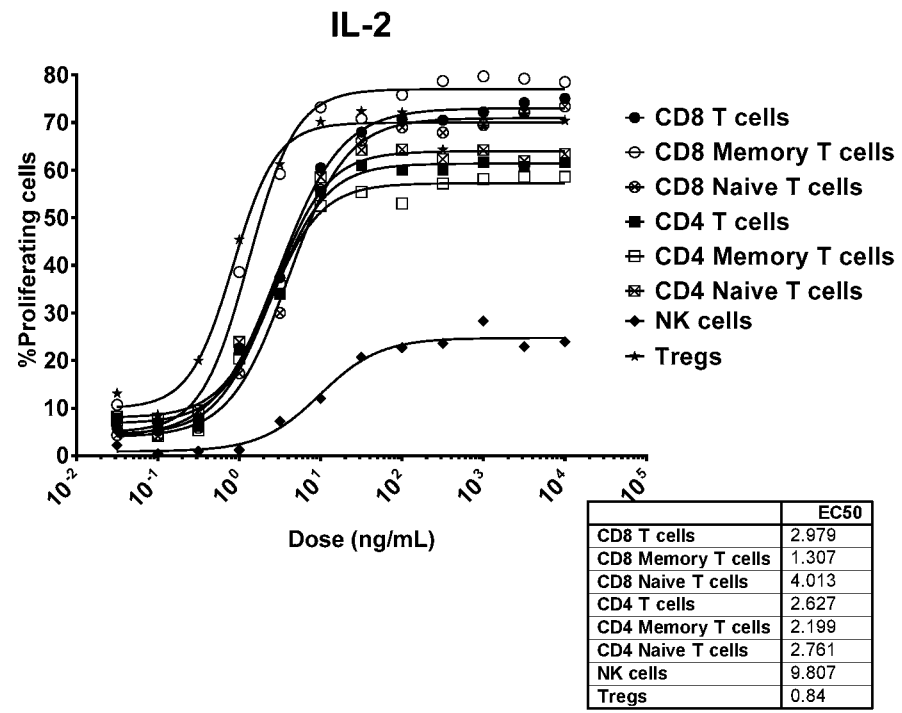


Figure 52E

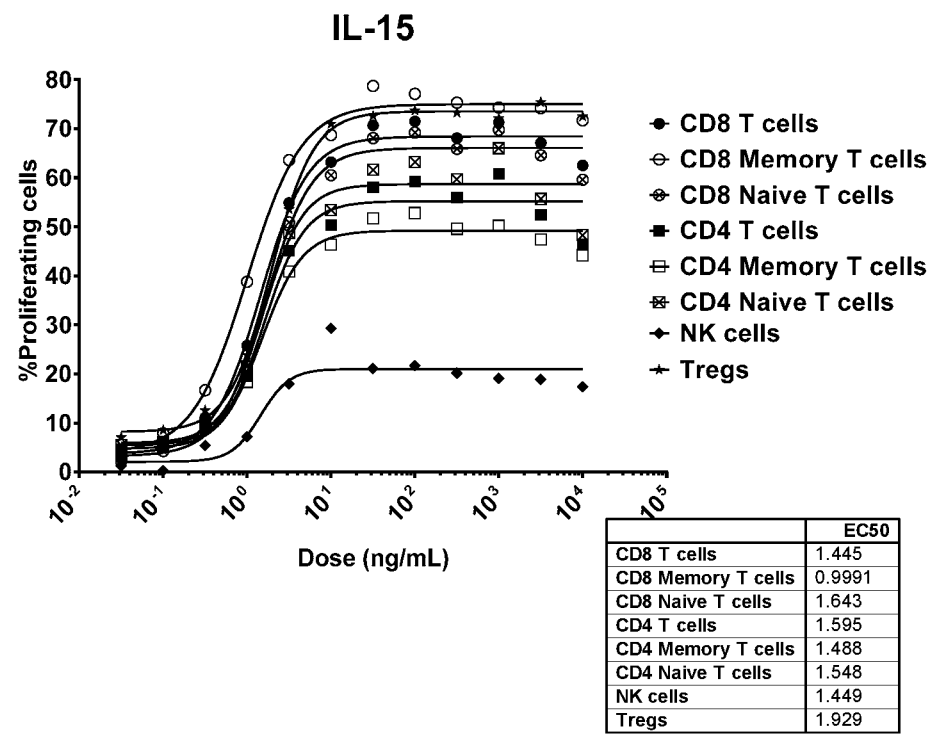


Figure 53A

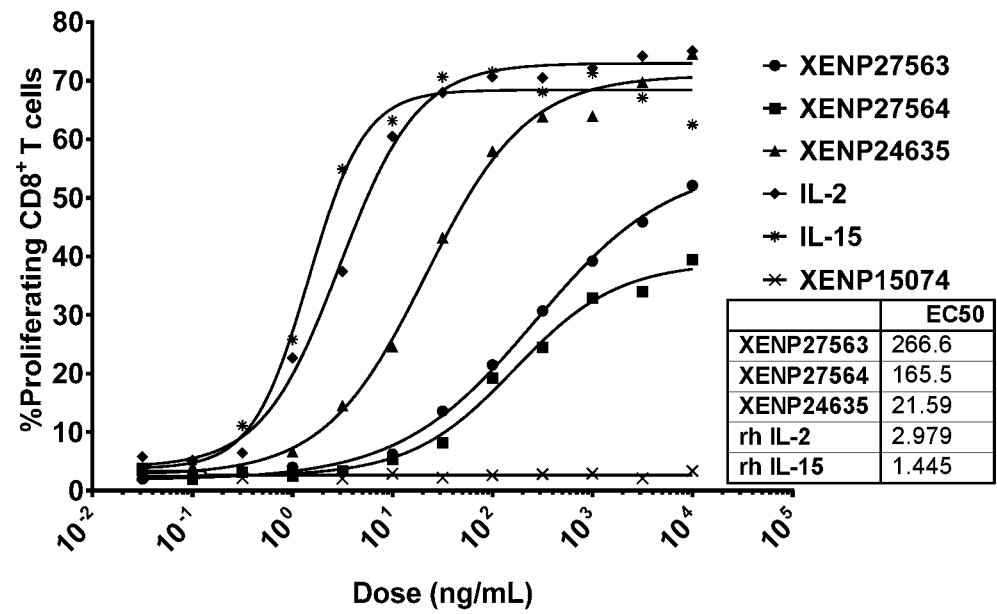


Figure 53B

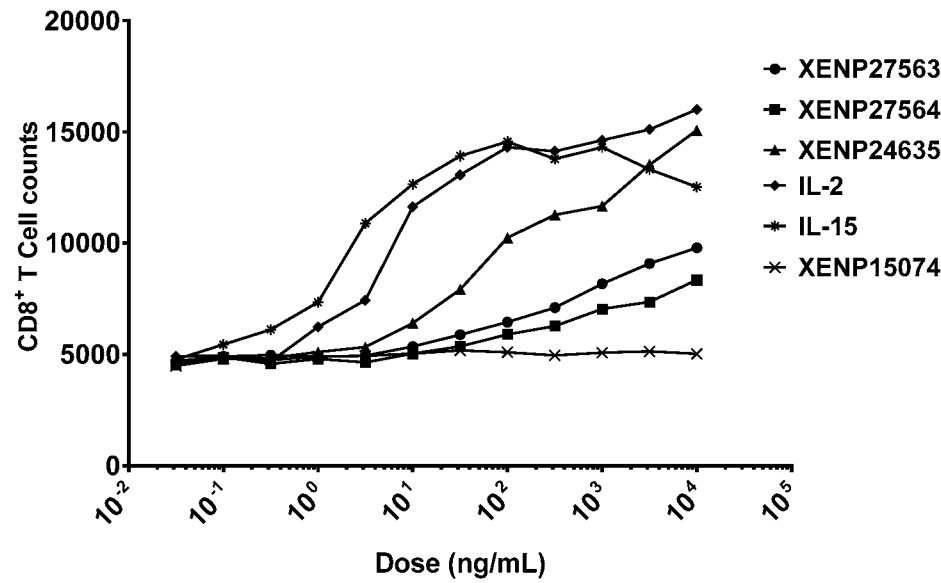


Figure 54A

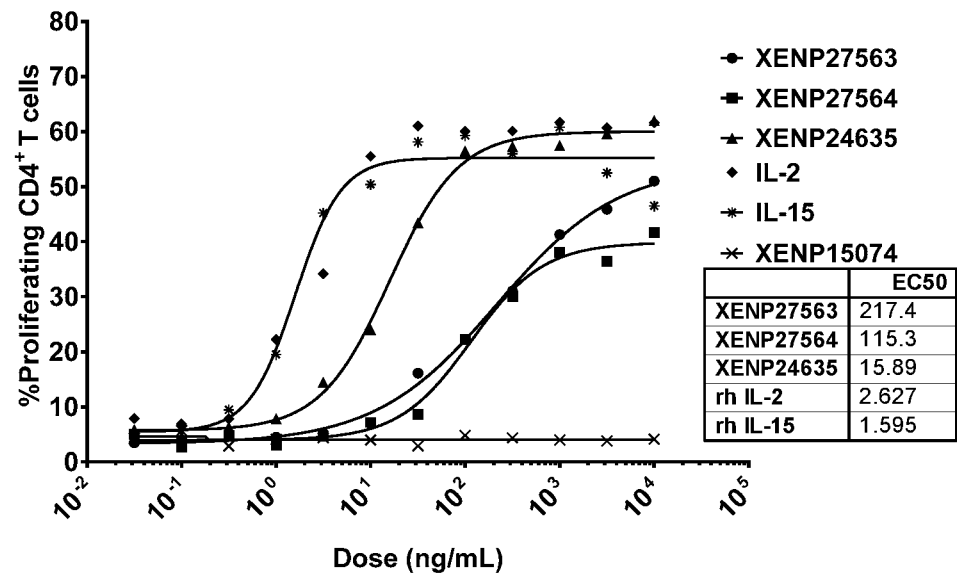


Figure 54B

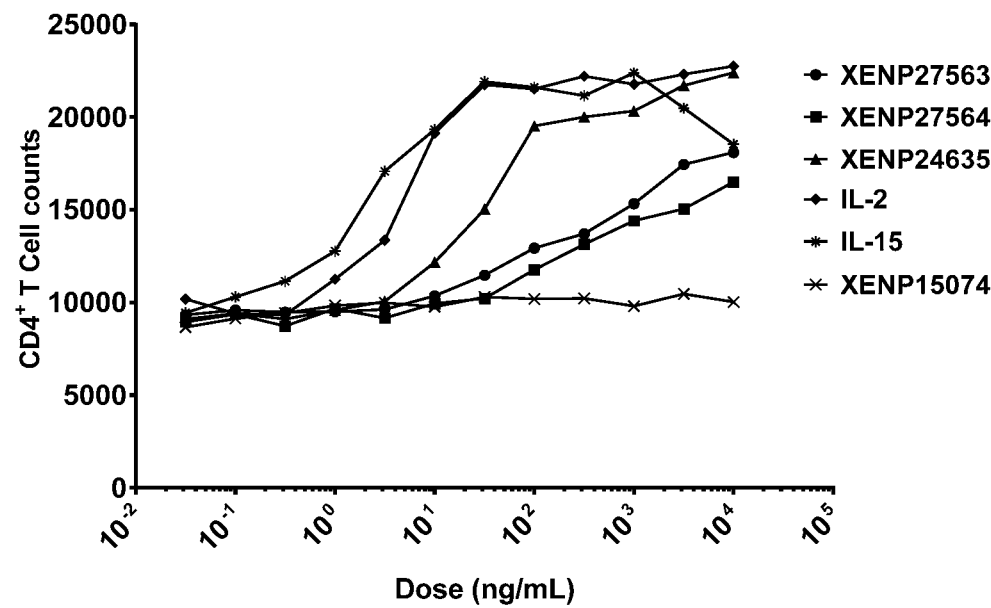


Figure 55

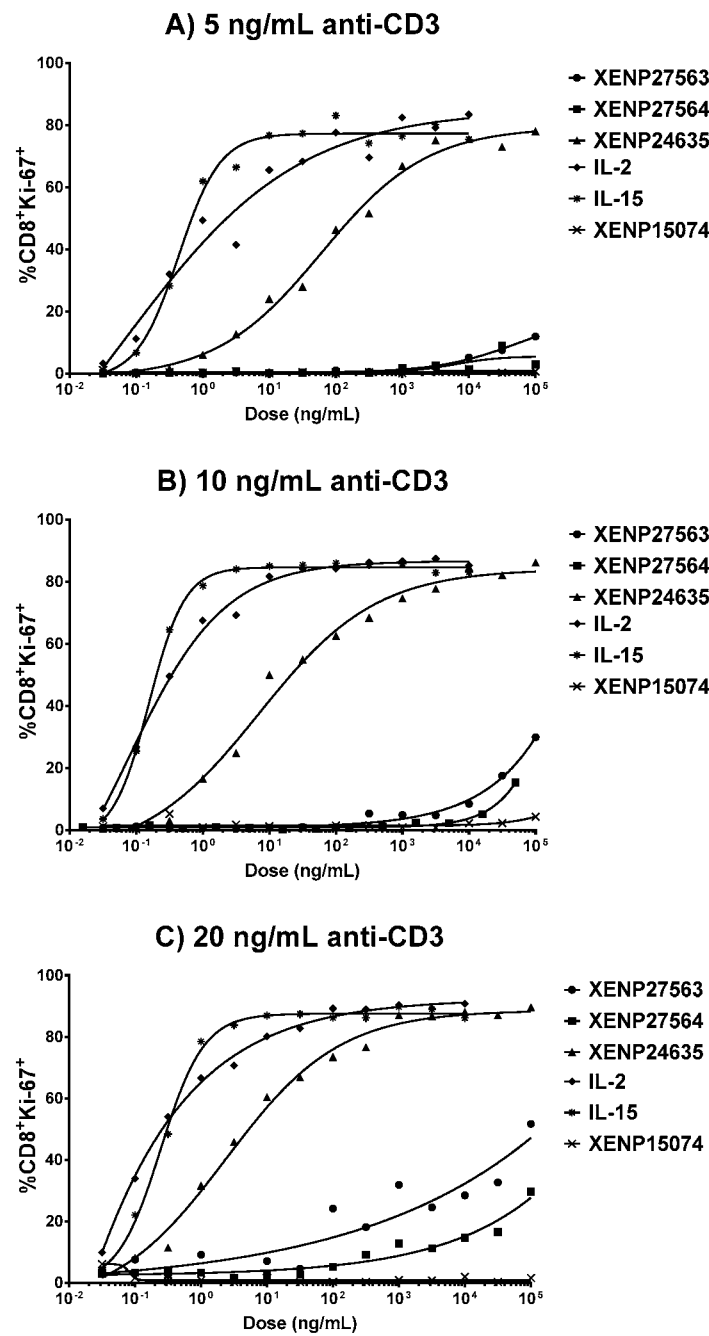


Figure 56

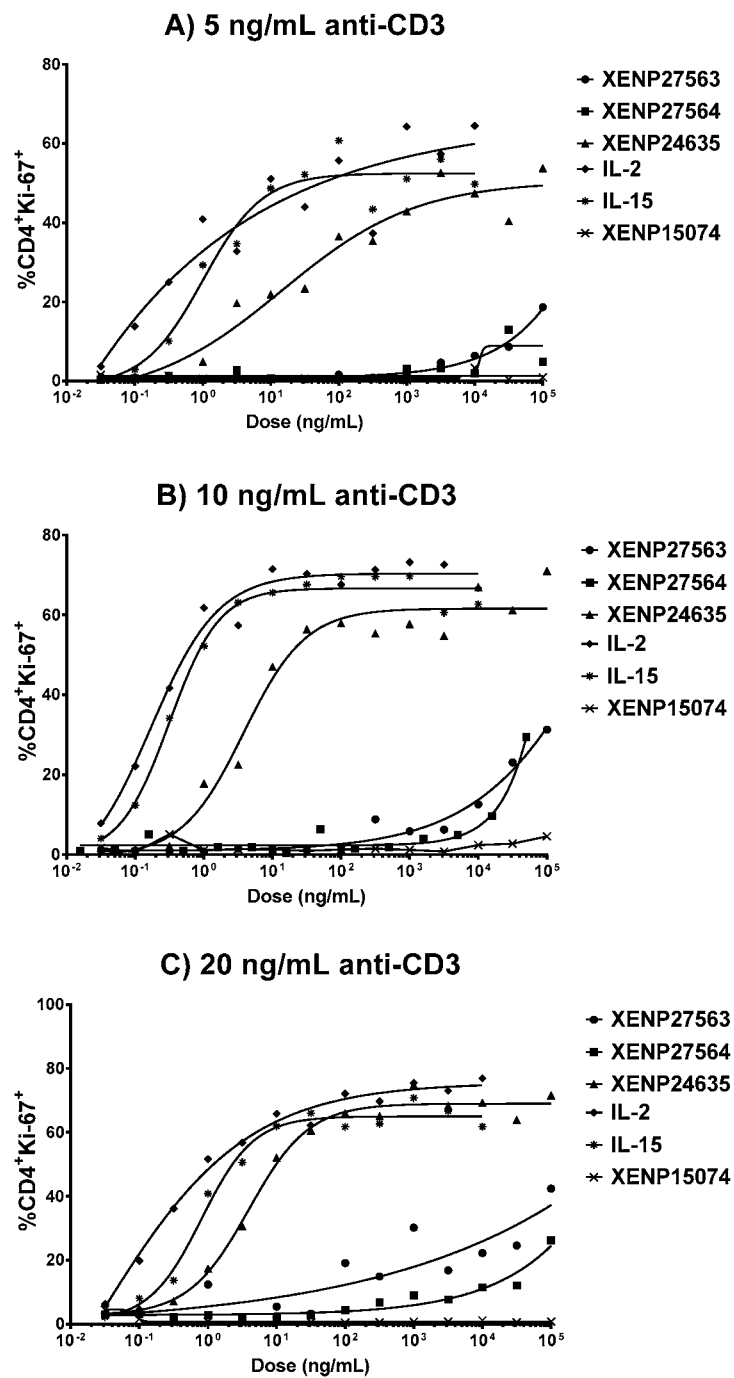


Figure 57

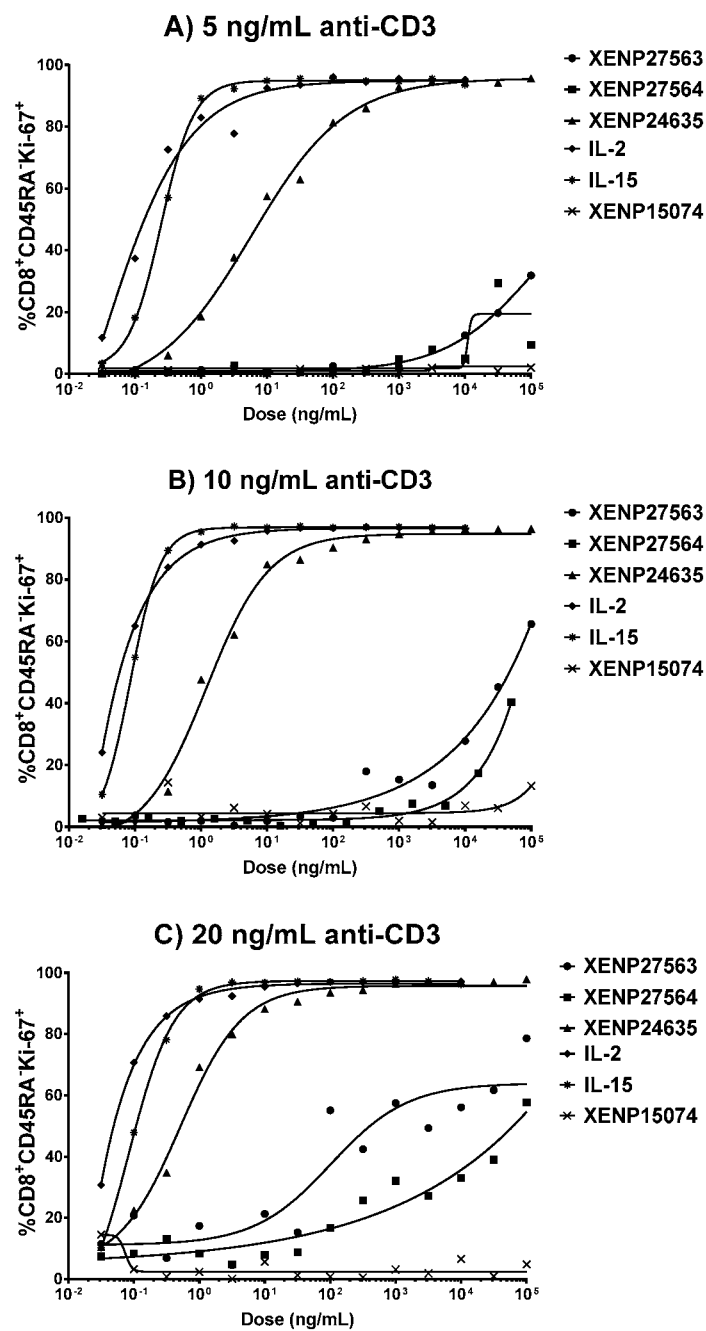


Figure 58

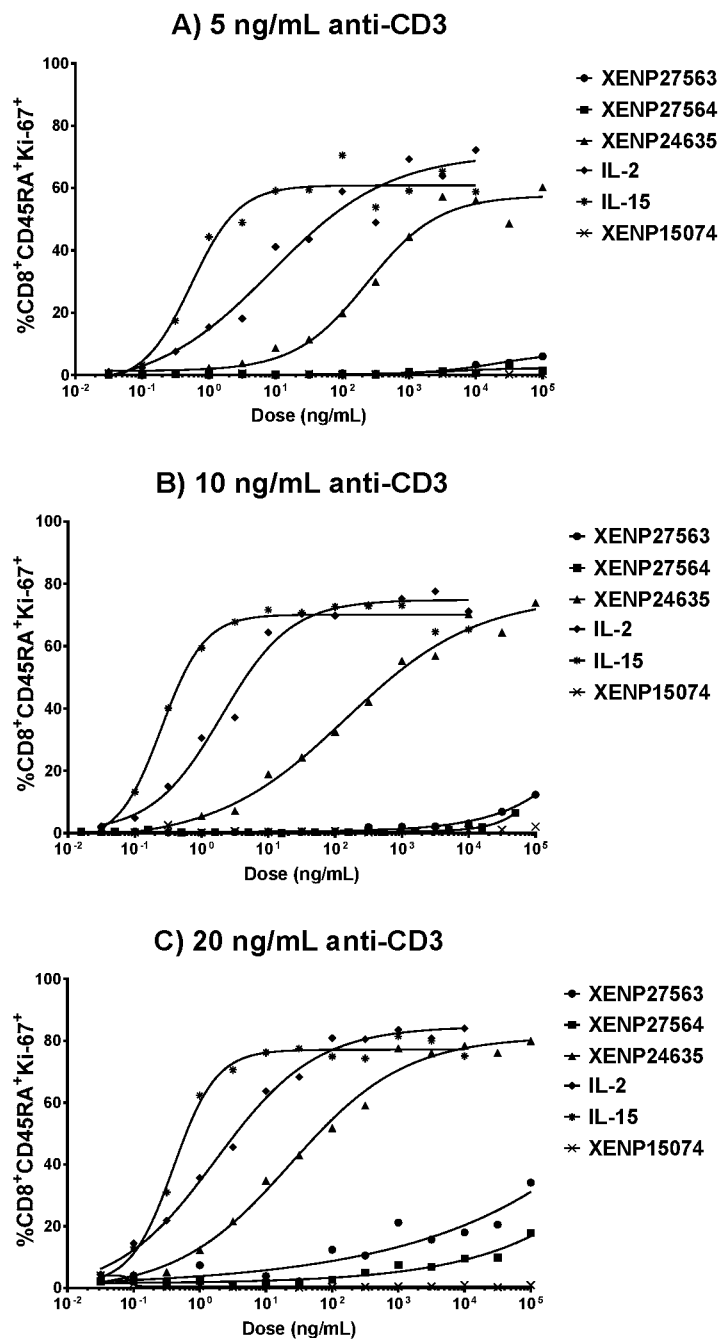


Figure 59

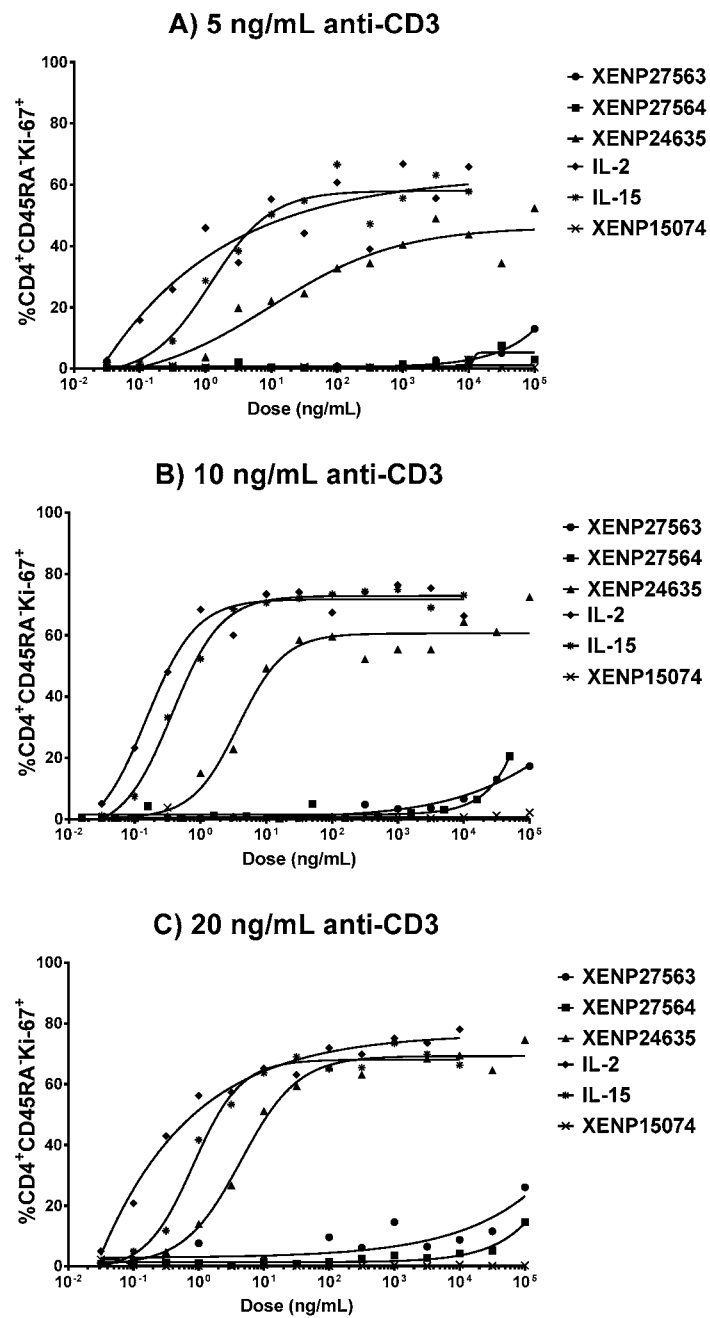


Figure 60

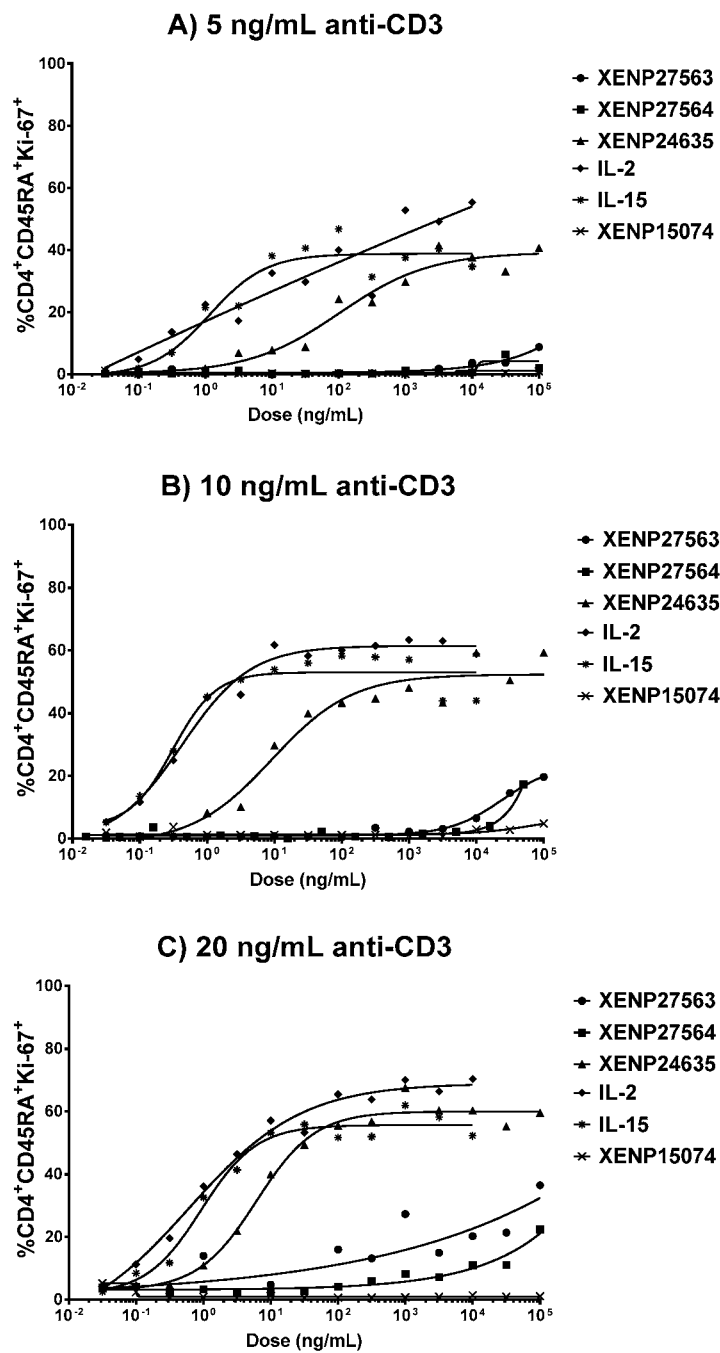


Figure 61

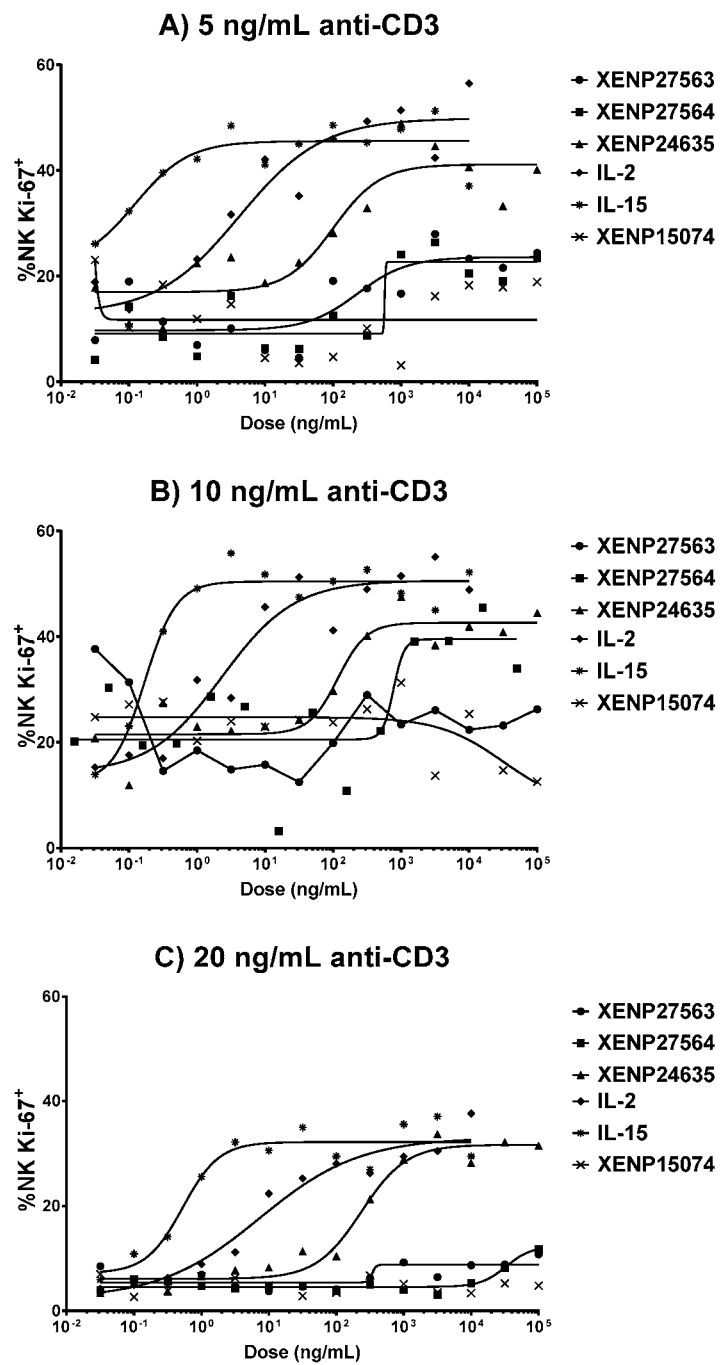


Figure 62

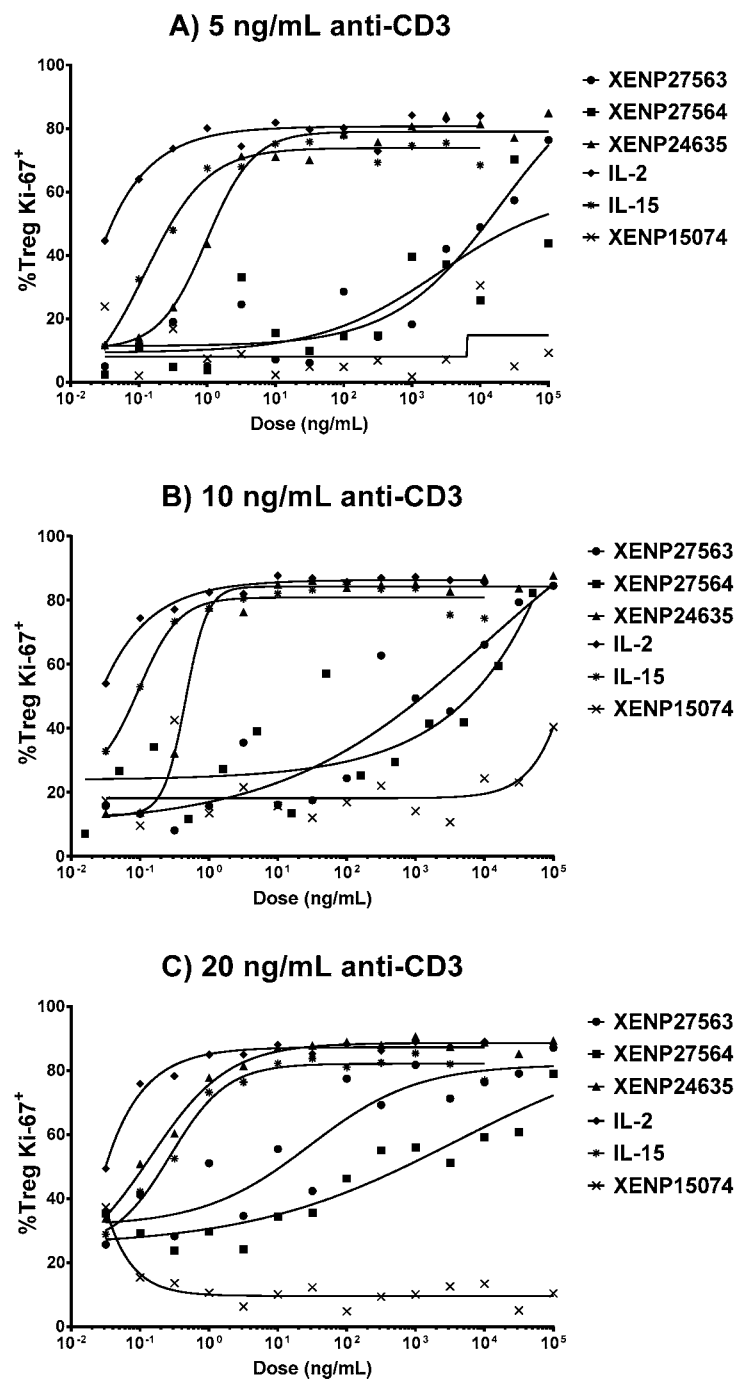


Figure 63

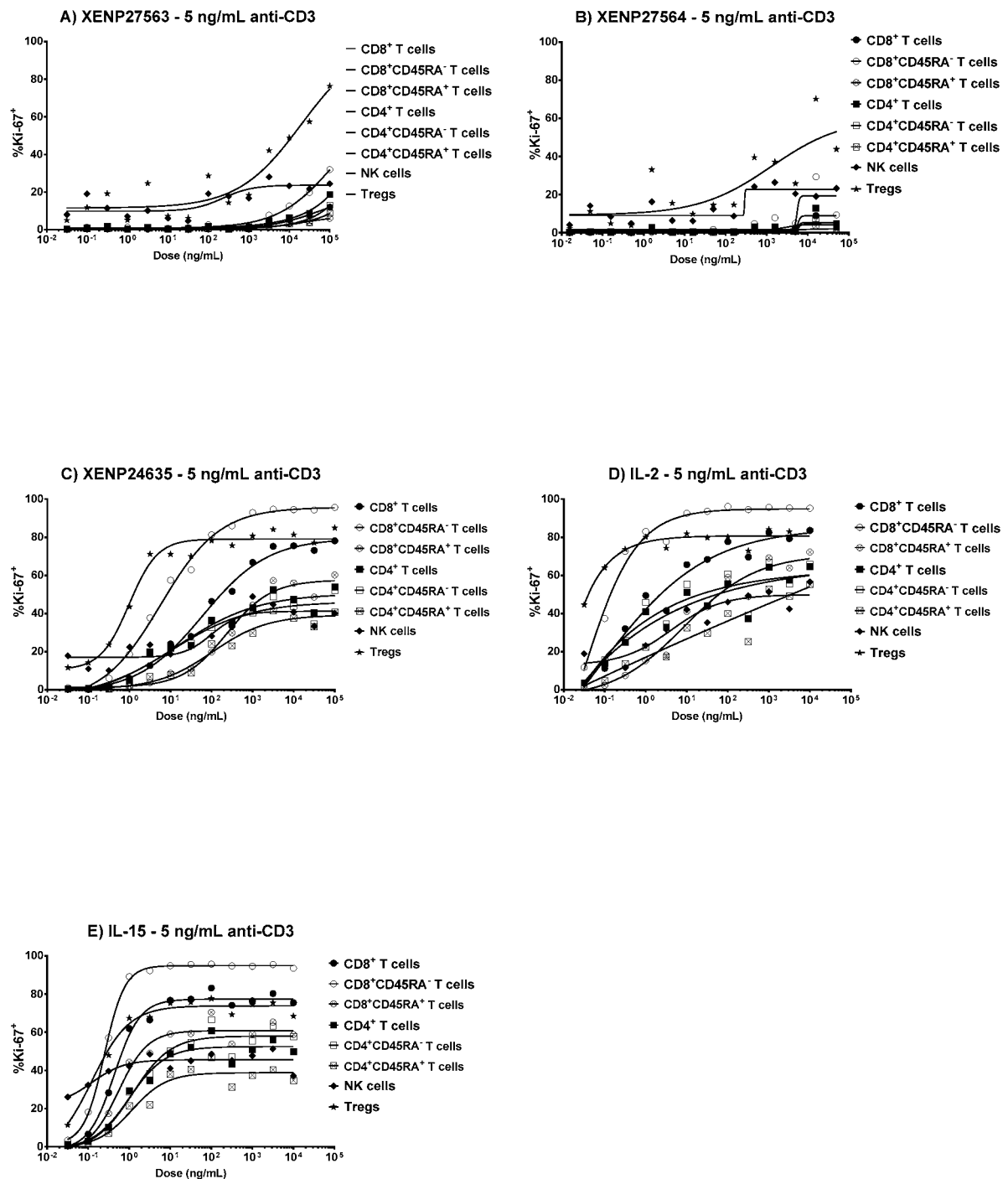


Figure 64

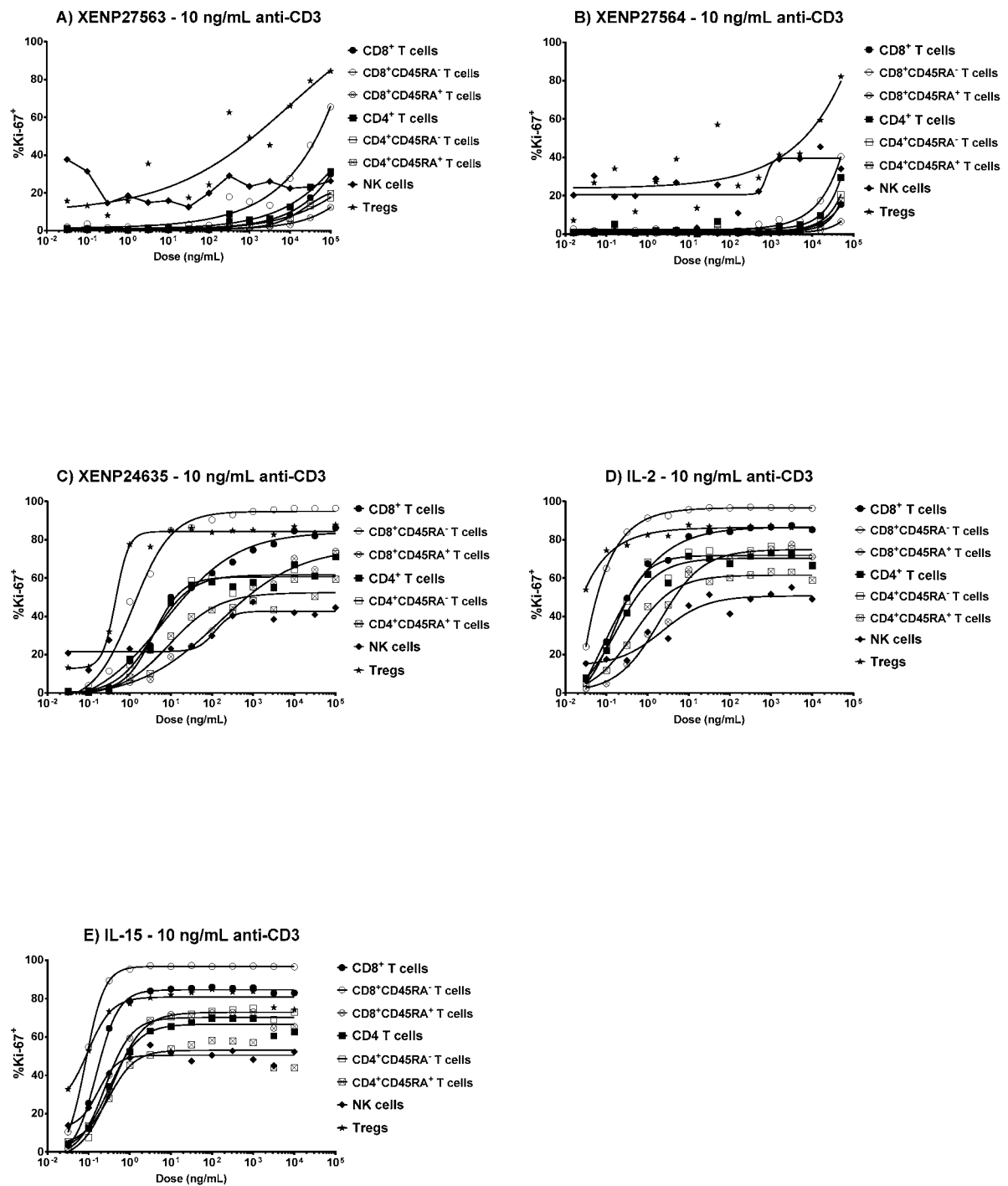


Figure 65

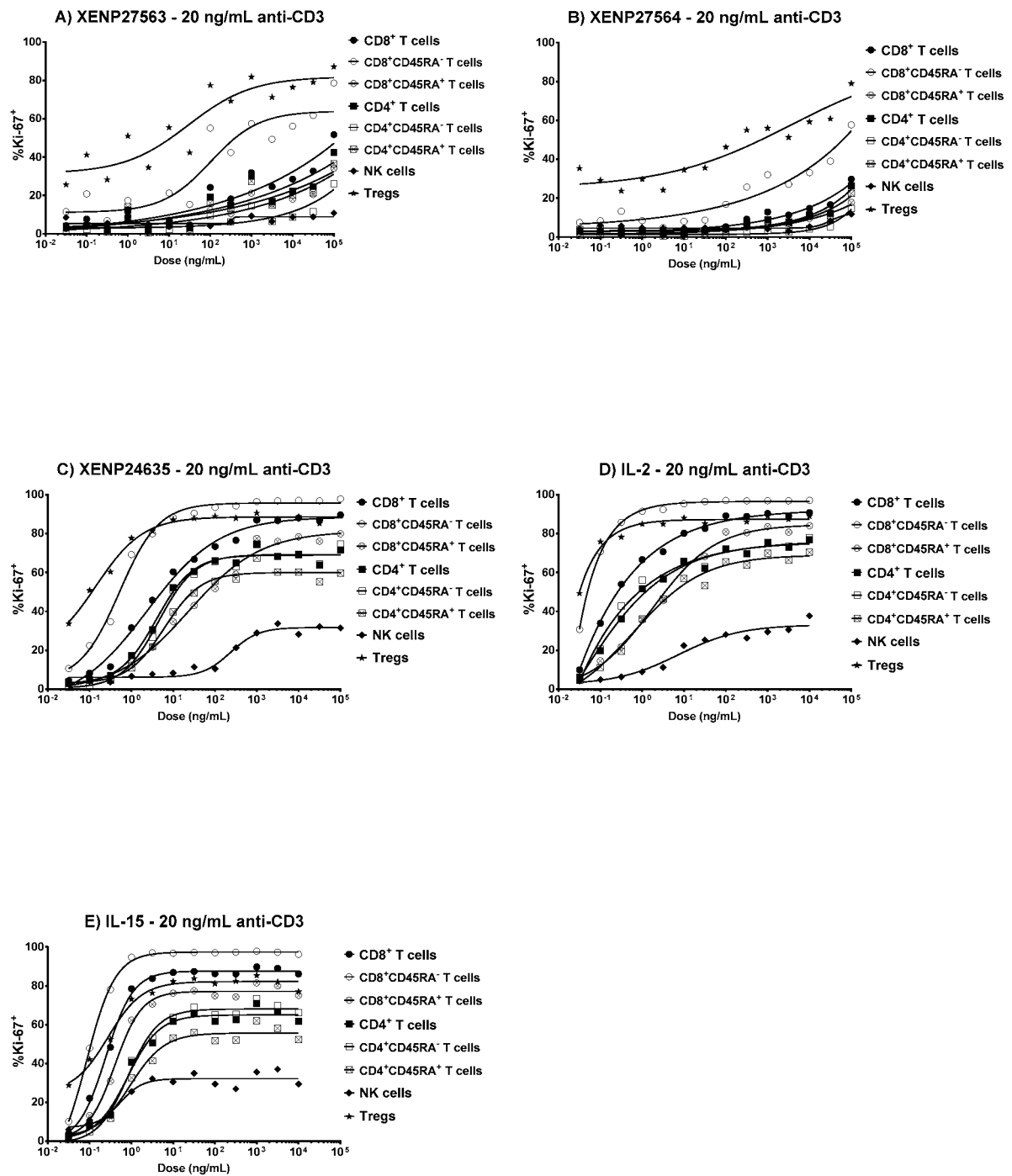


Figure 66A

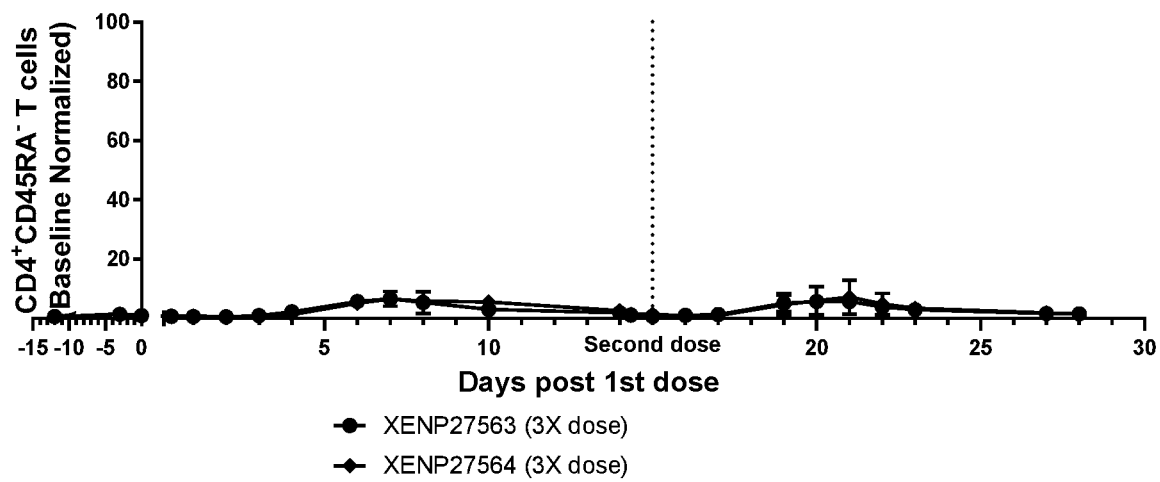


Figure 66B

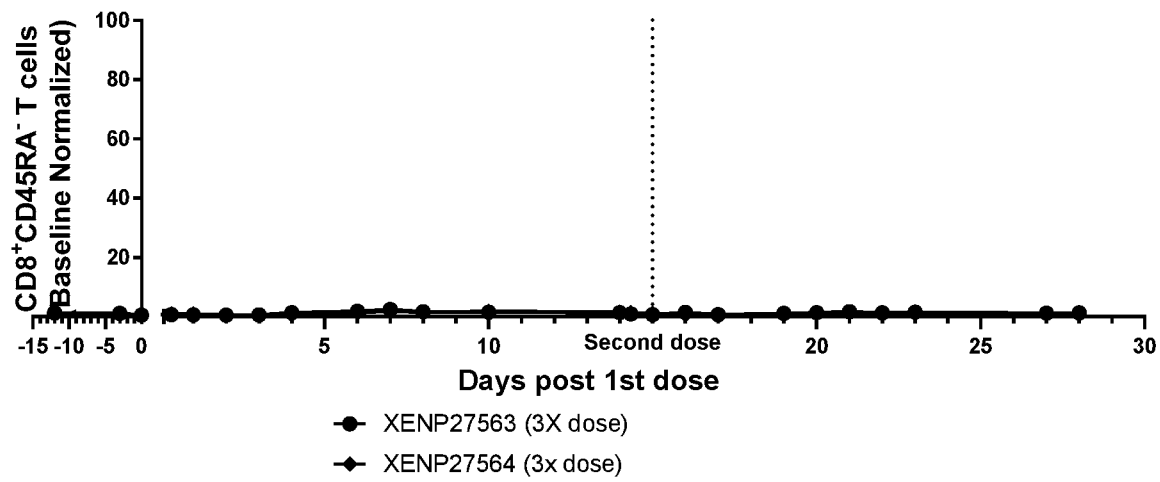


Figure 66C

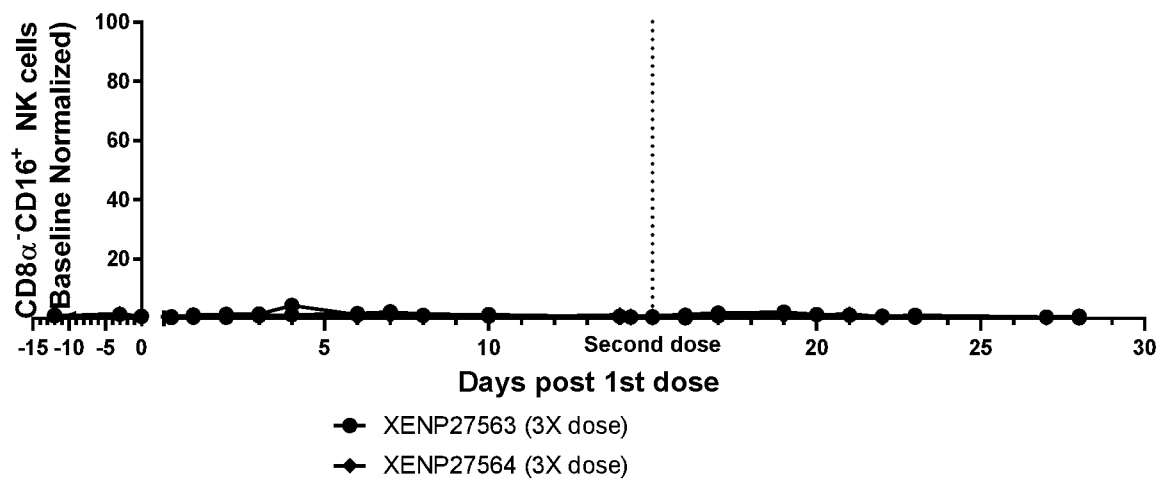


Figure 66D

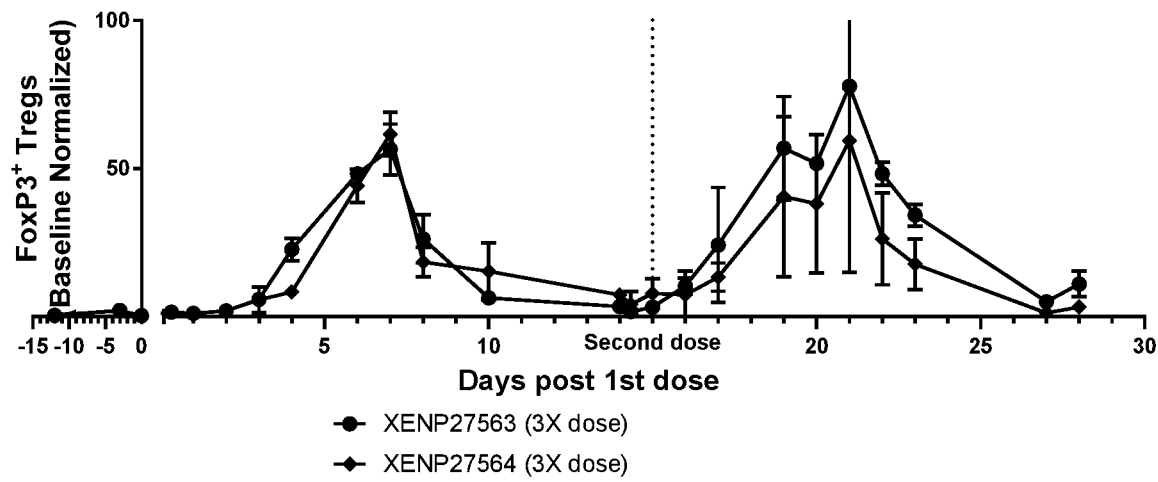


Figure 67A

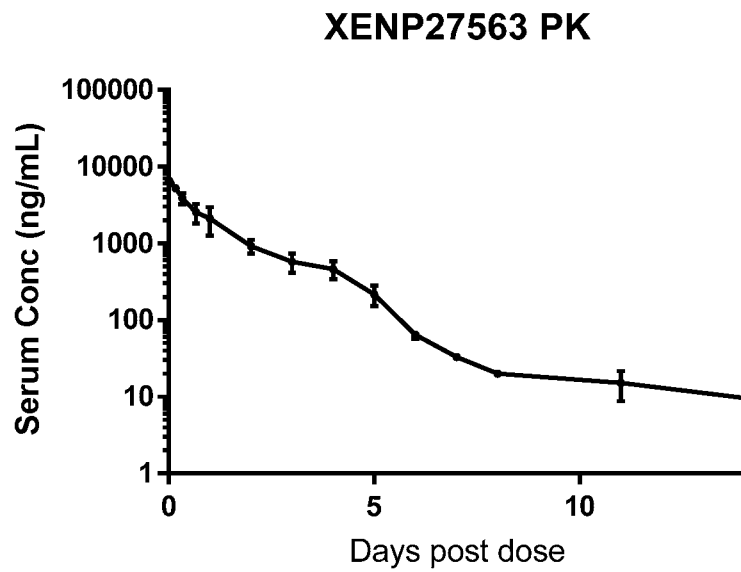


Figure 67B

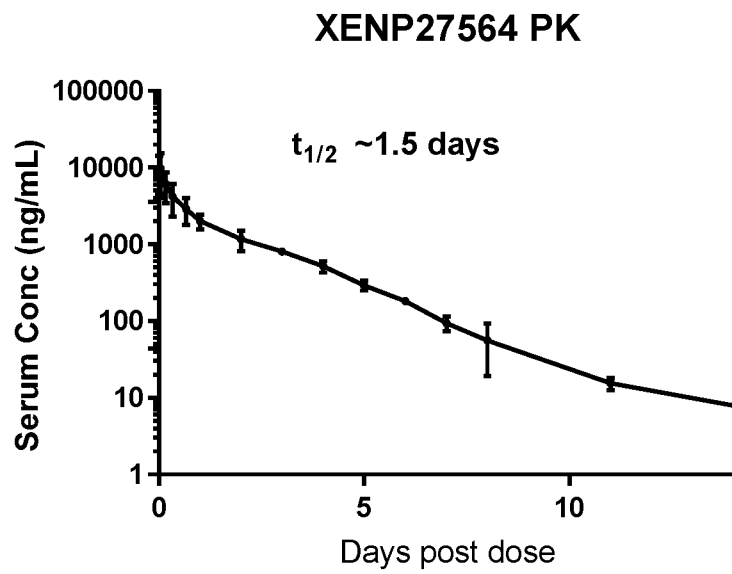


Figure 68

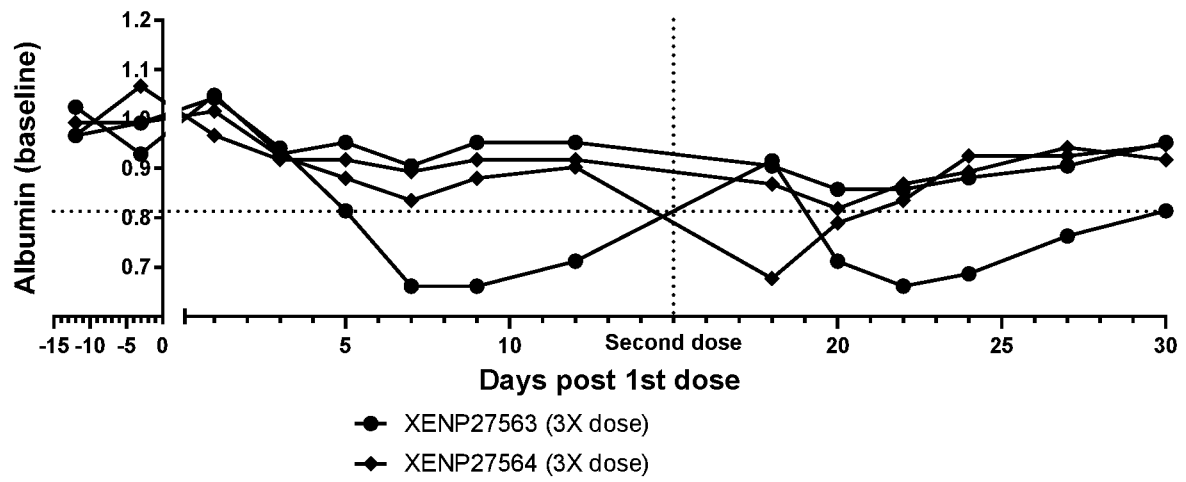


Figure 69A

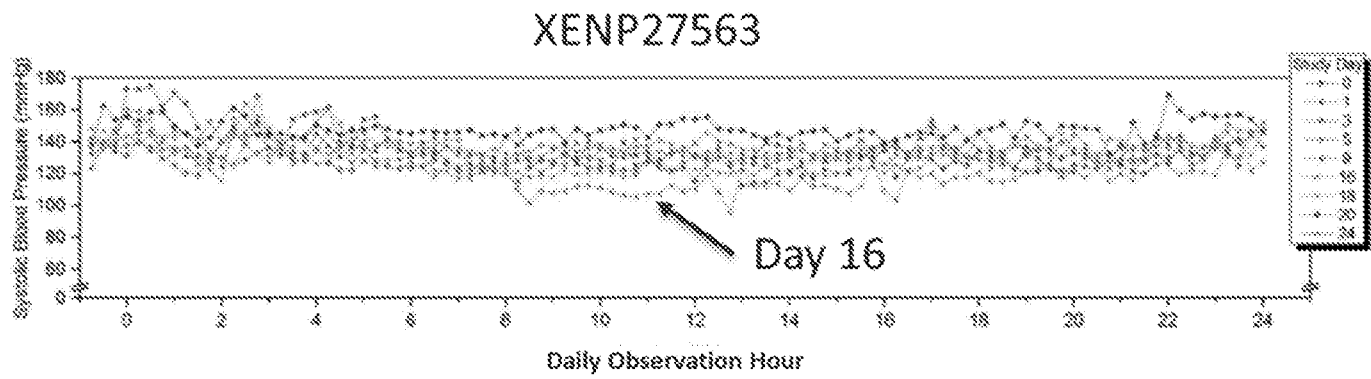


Figure 69B

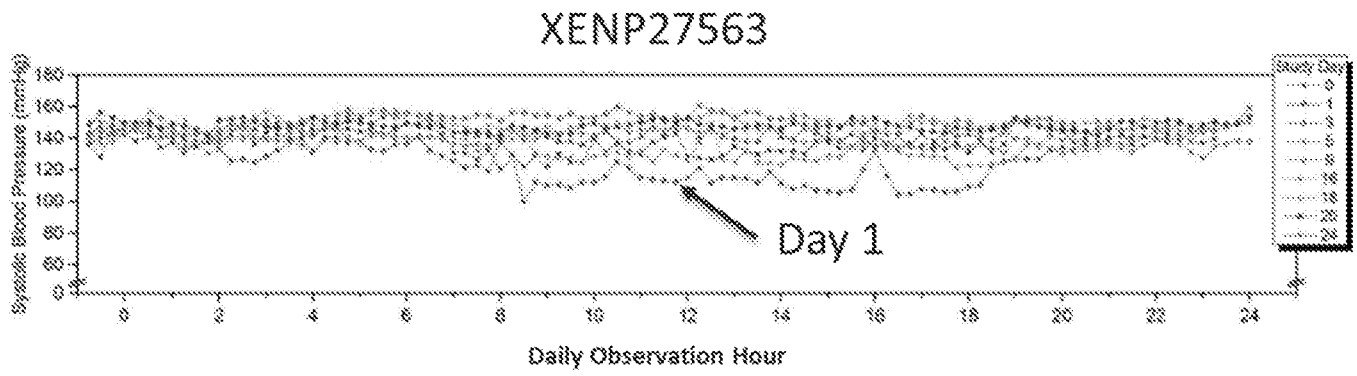


Figure 69C

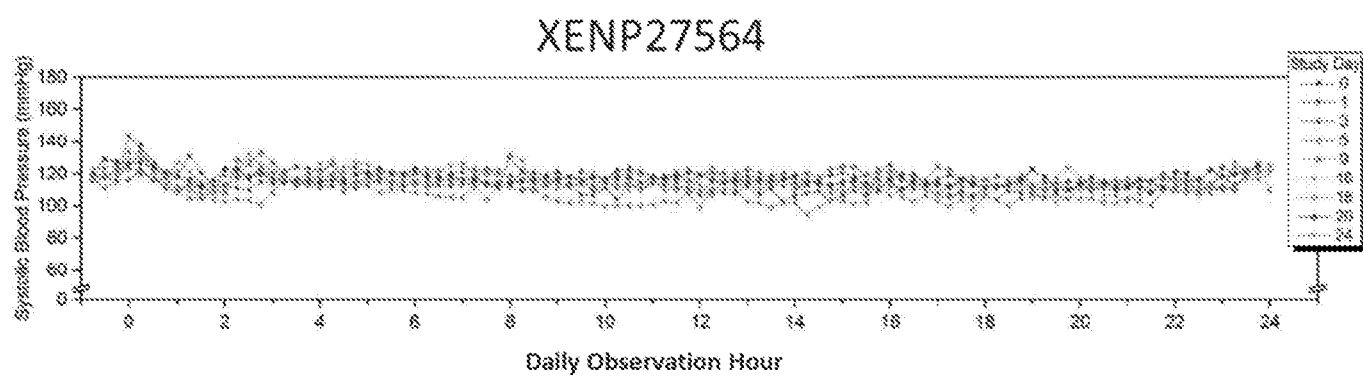


Figure 70A

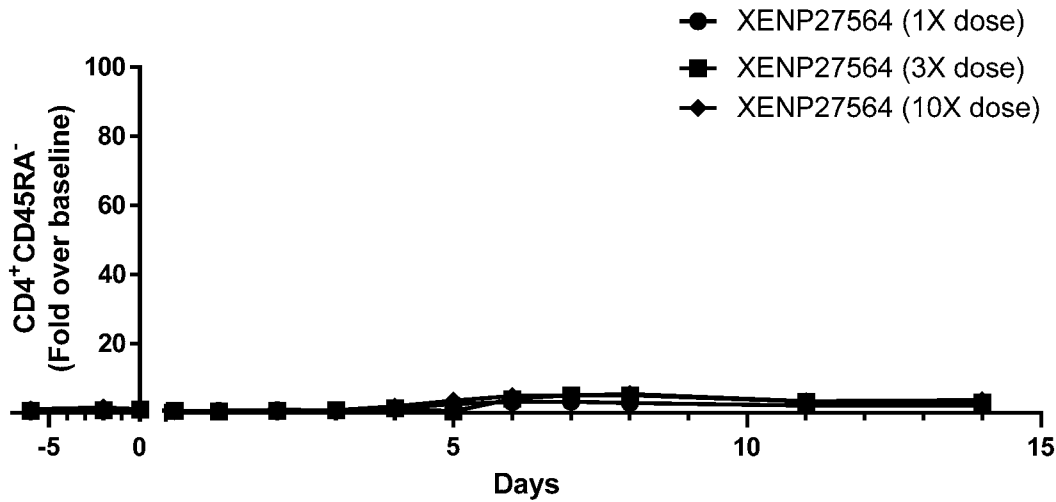


Figure 70B

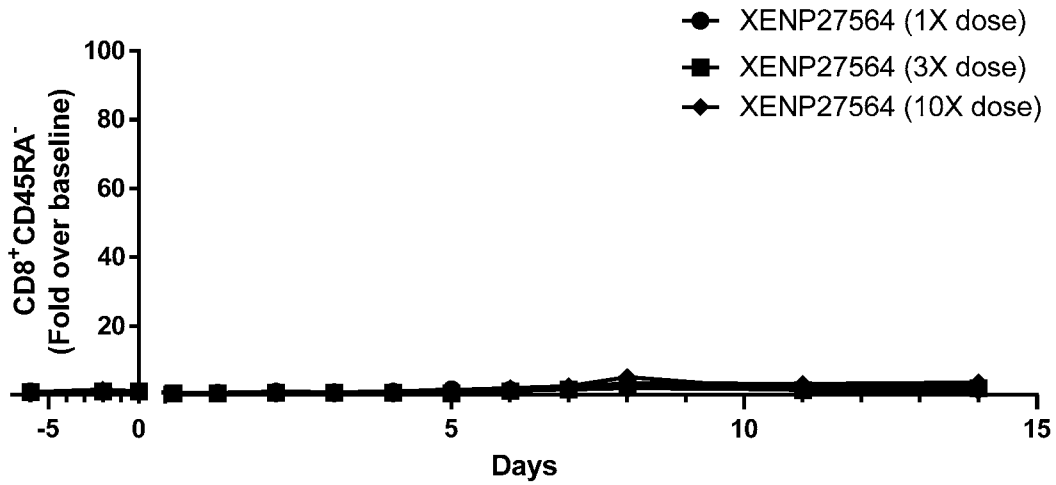


Figure 70C

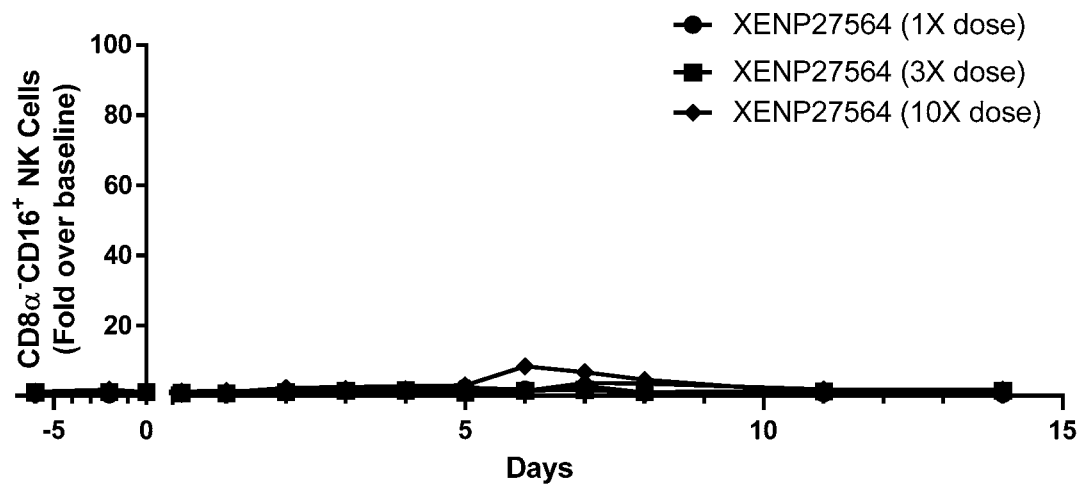


Figure 70D

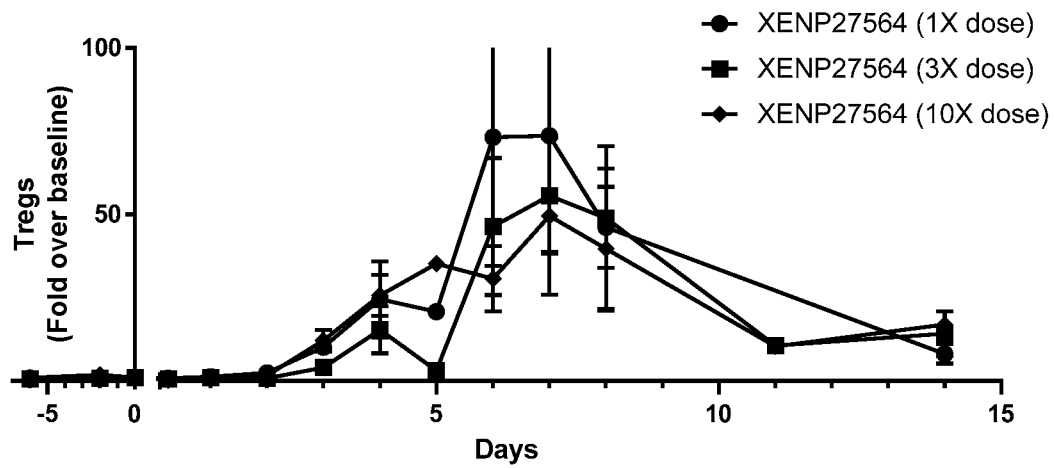


Figure 71

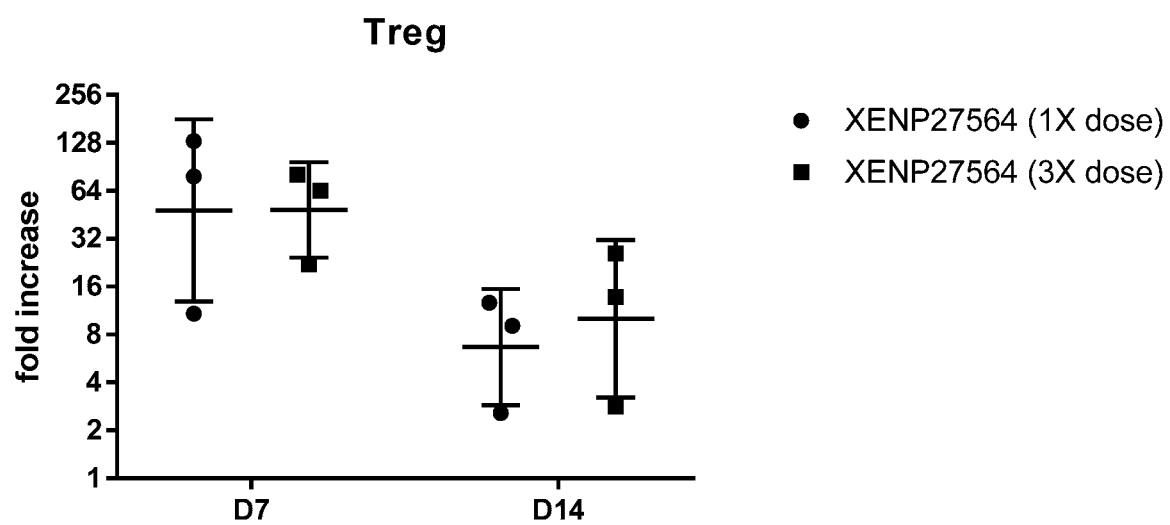


Figure 72

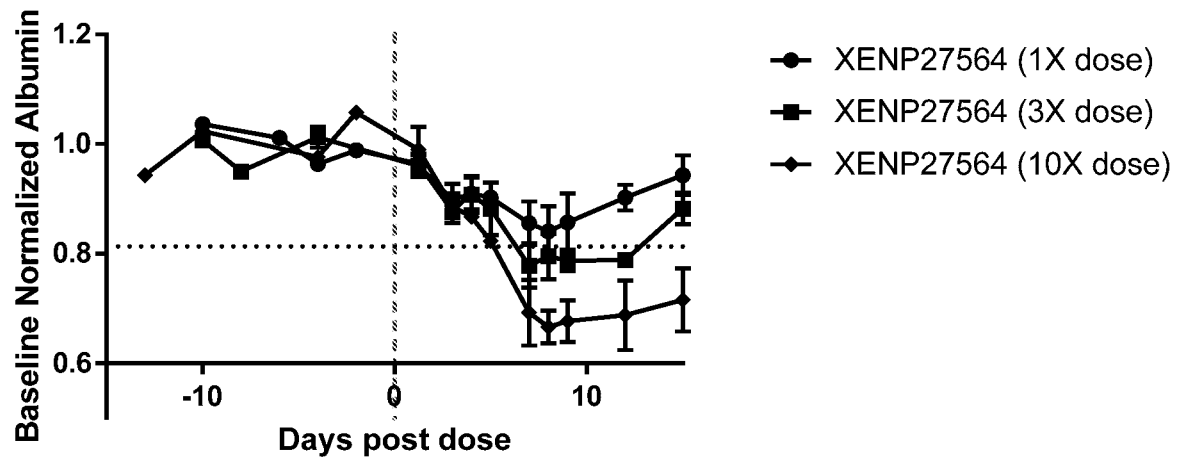


Figure 73

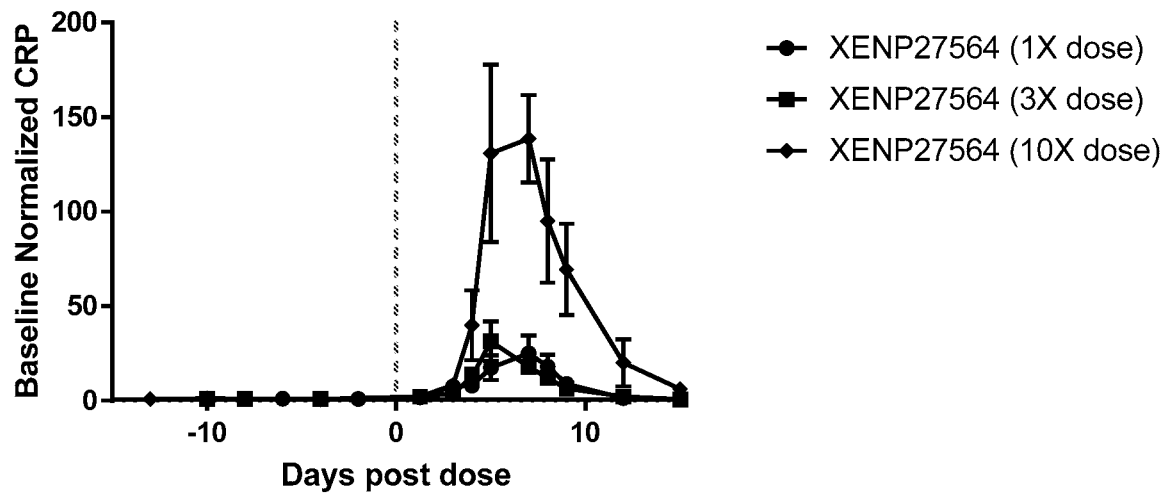


Figure 74A

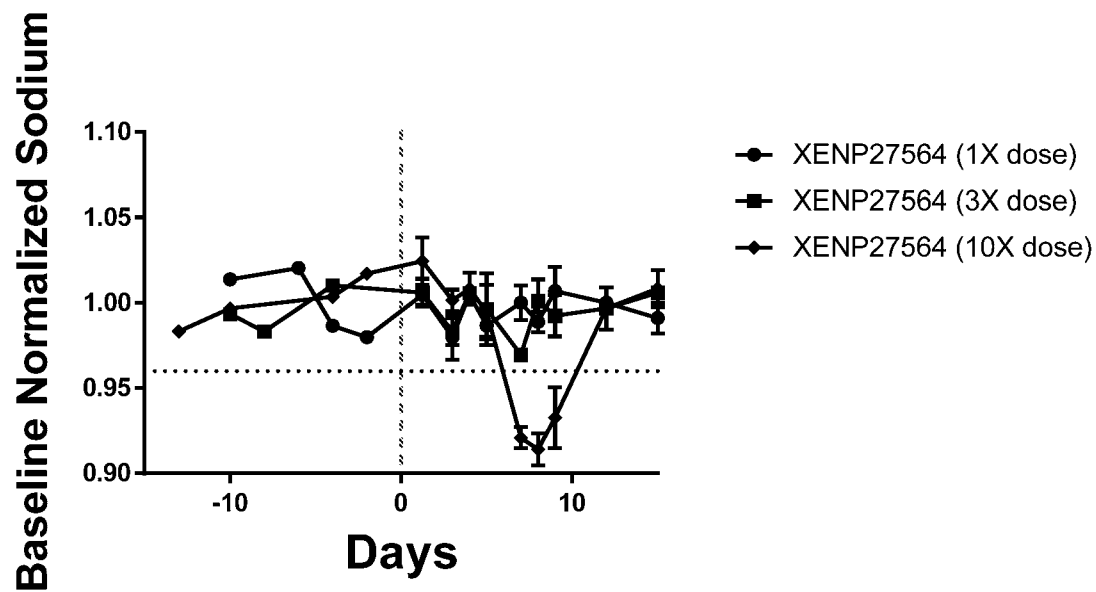


Figure 74B

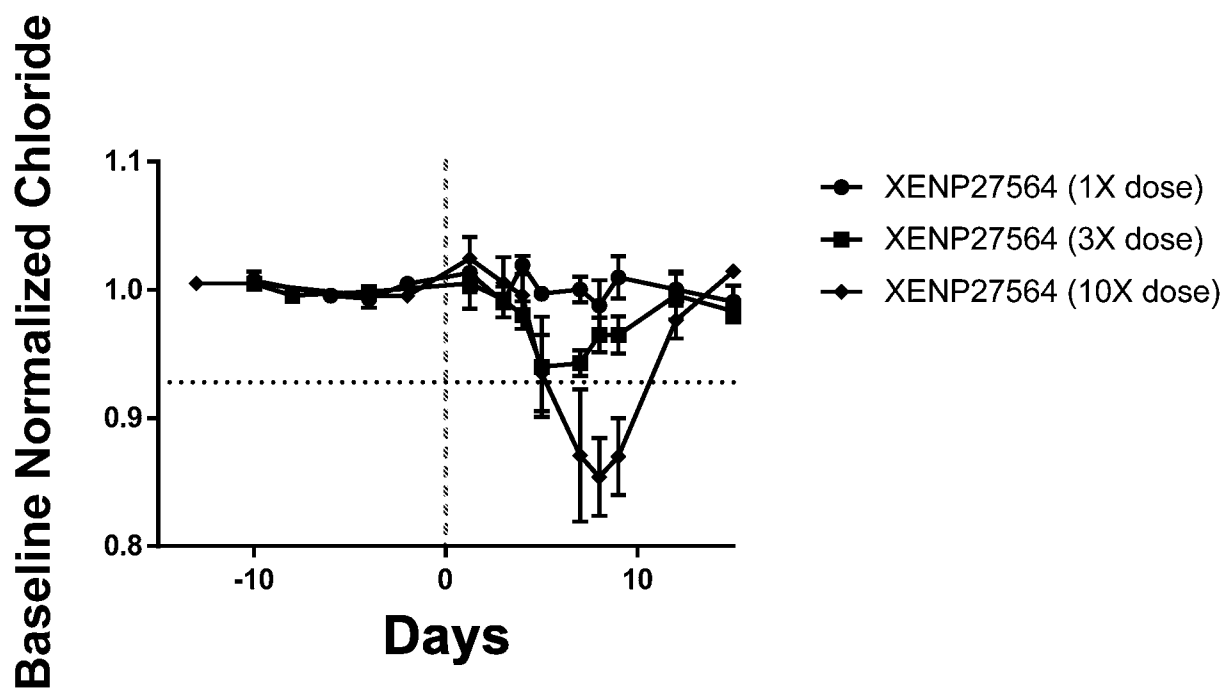


Figure 74C

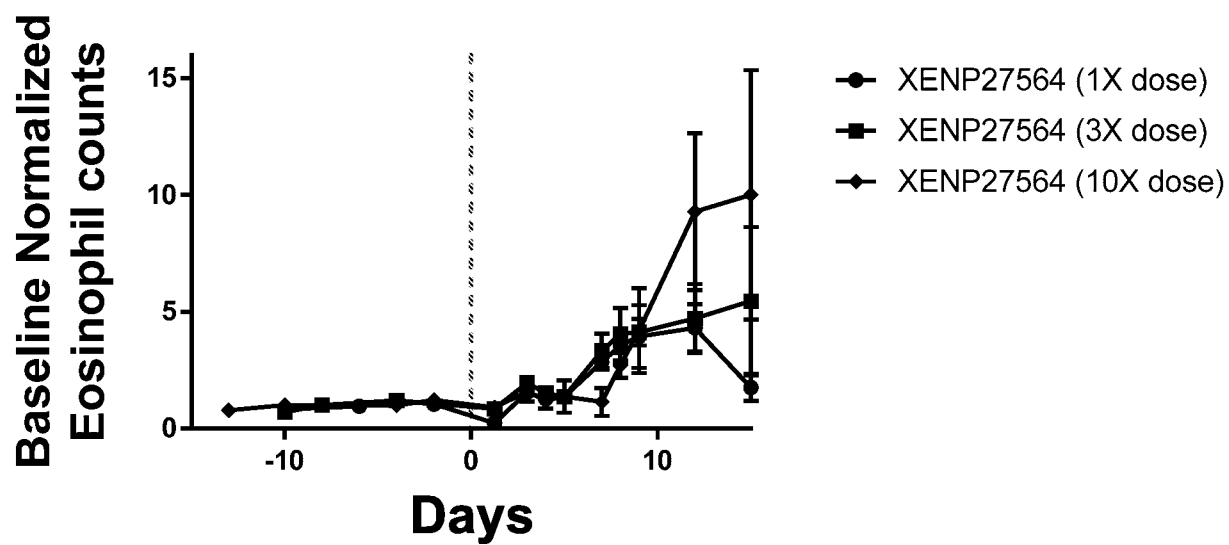


Figure 74D

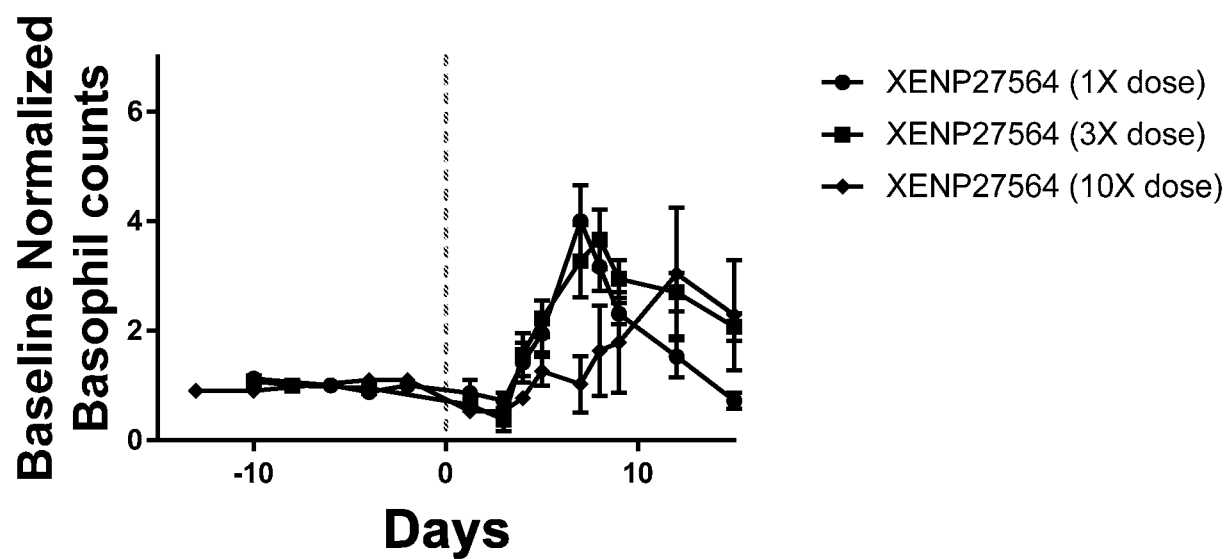


Figure 75

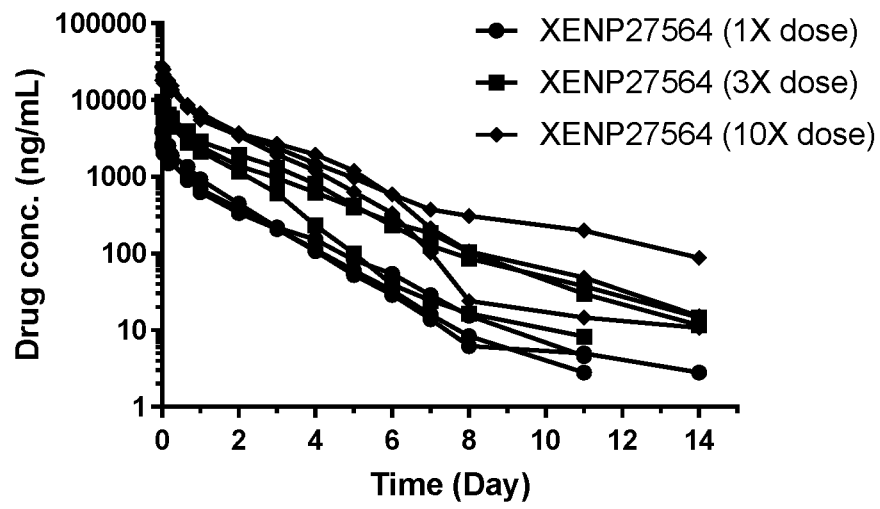


Figure 76A

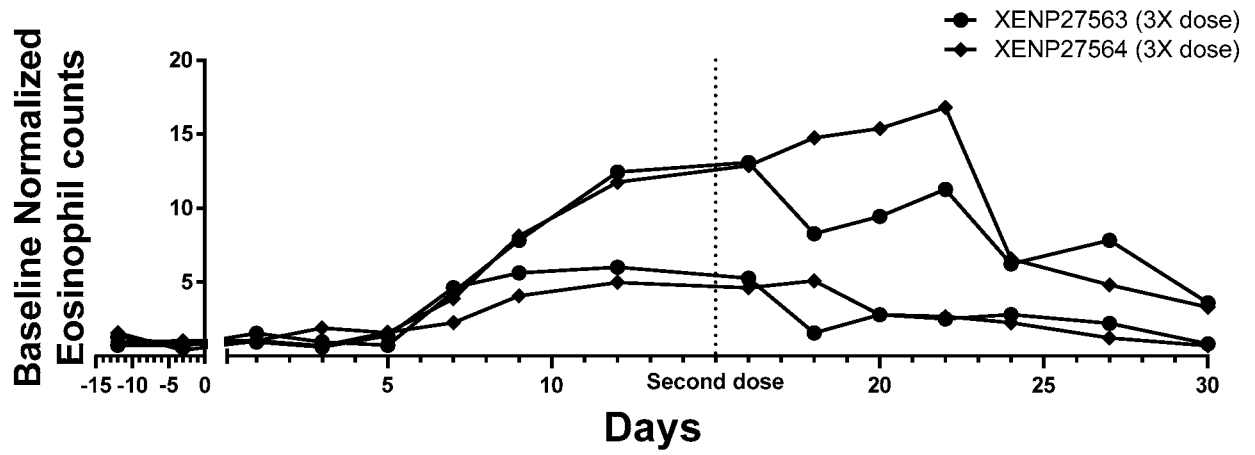


Figure 76B

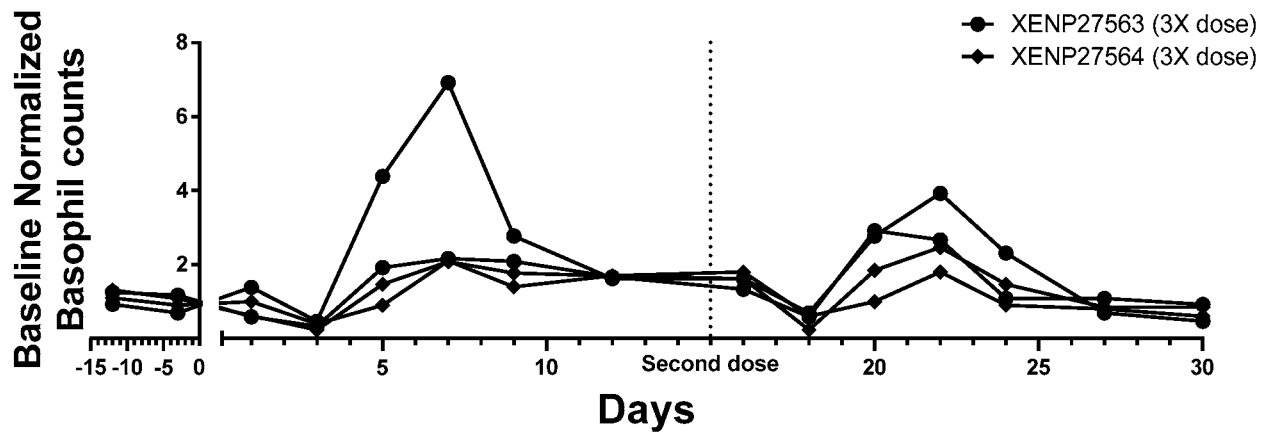


Figure 77A

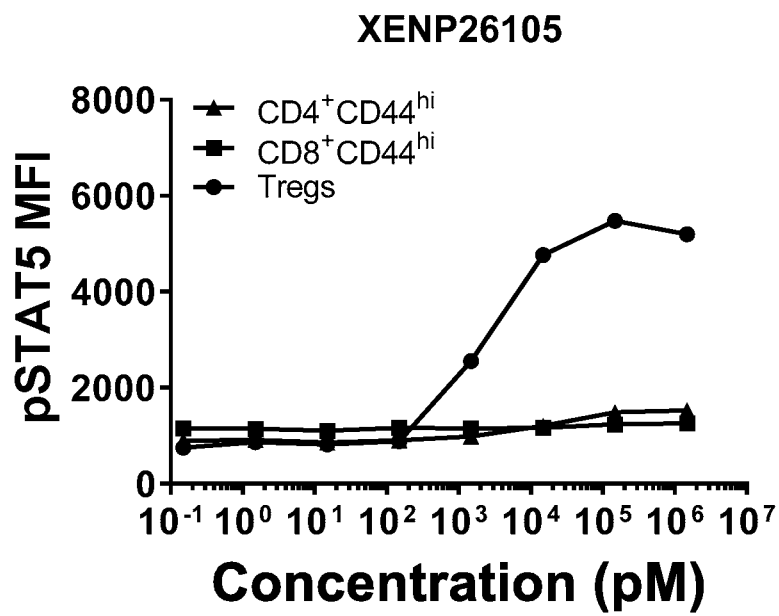


Figure 77B

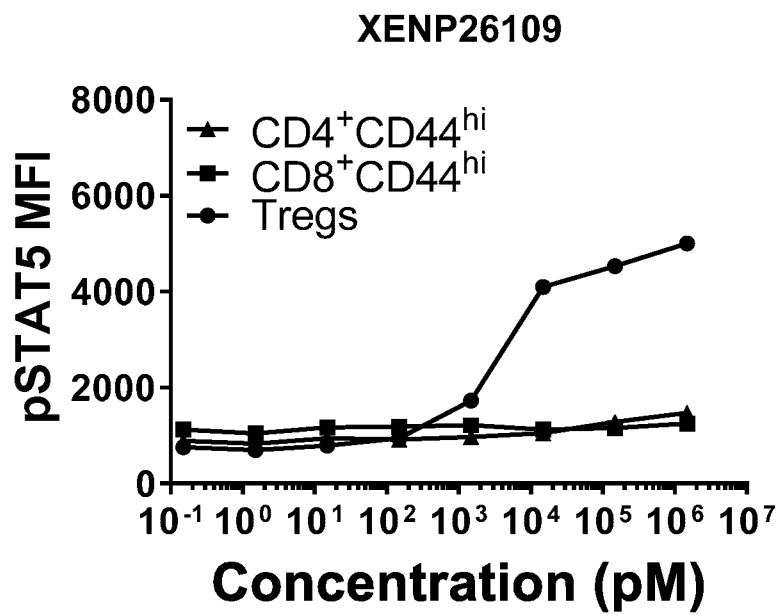


Figure 77C

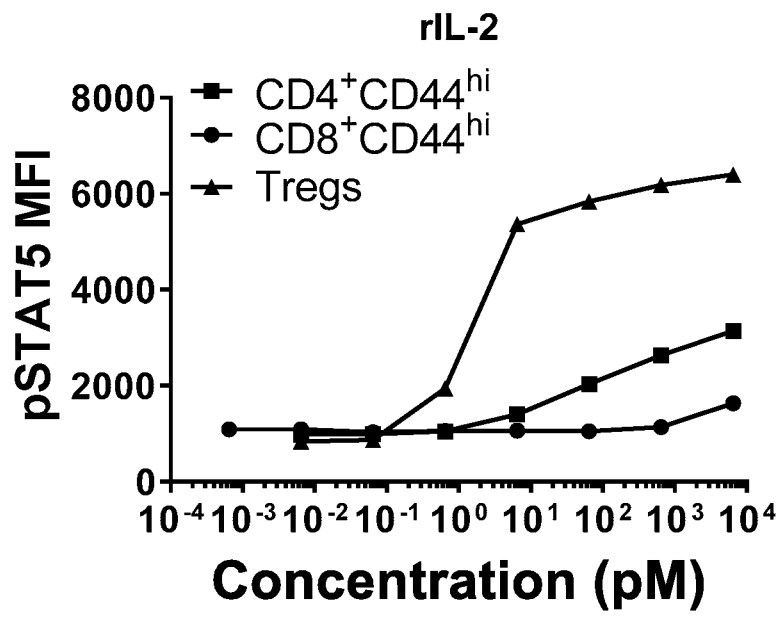


Figure 78

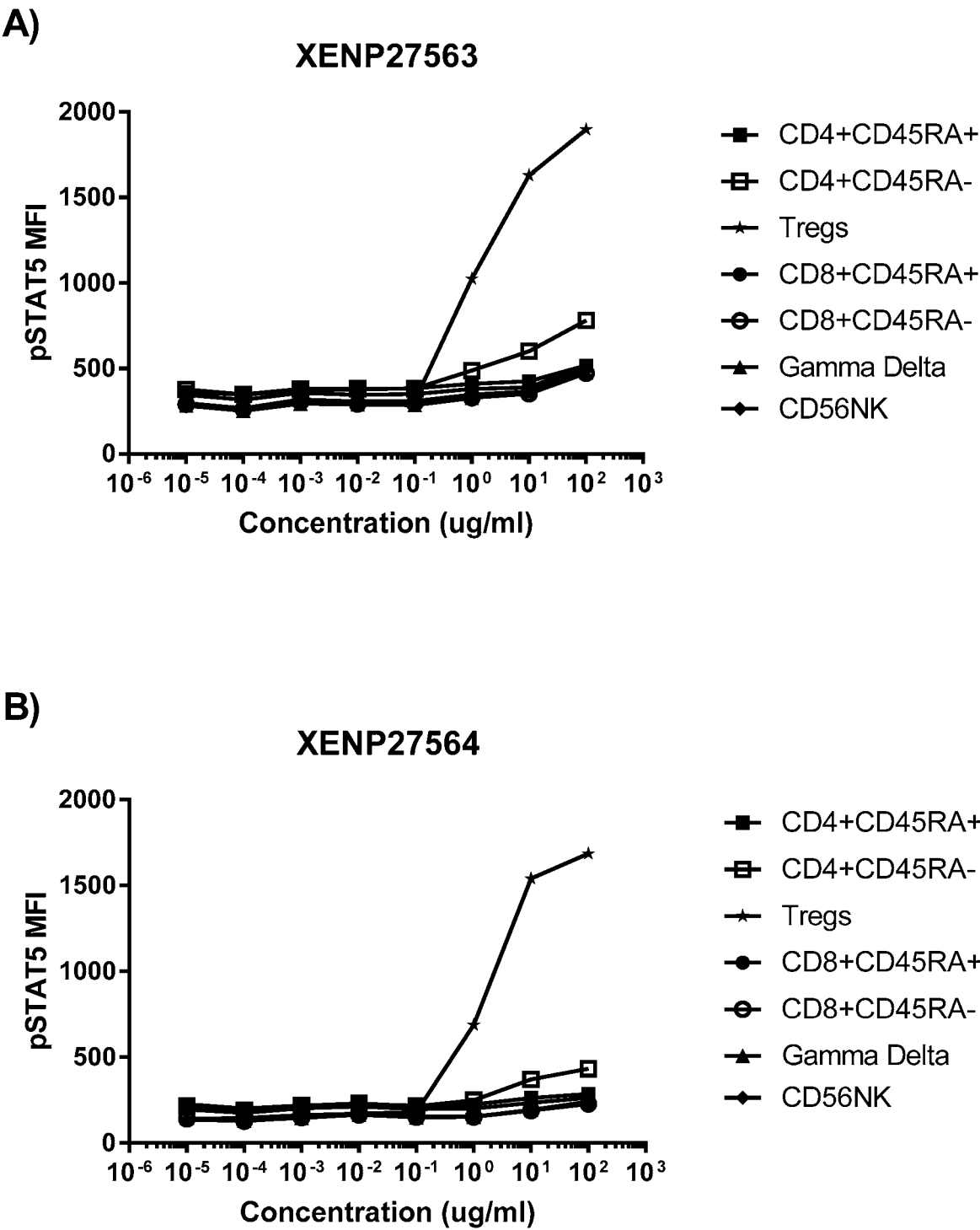


Figure 79

