

Figure 1. Ab650 humanisation alignments

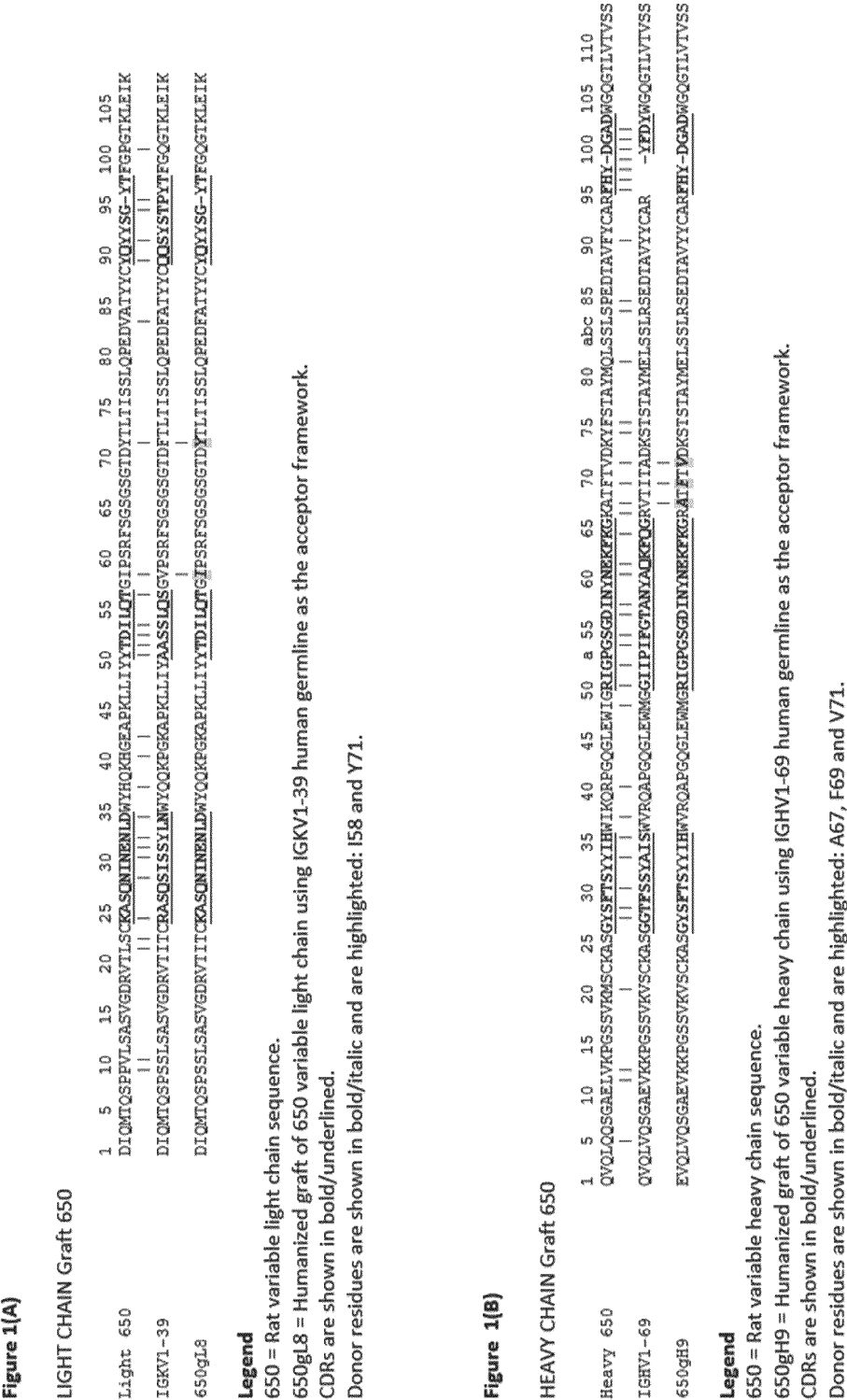


Figure 2: Amino acid and DNA sequencesAnti-IL-17A/FCDR sequences Ab 496.g3

SEQ ID NO:1 CDRL1 of 496.g3

RADESVRTLMMH

SEQ ID NO:2 CDRL2 of 496.g3

LVSNSEI

SEQ ID NO:3 CDRL3 of 496.g3

QQTWSDPWT

SEQ ID NO:4 CDRH1 of 496.g3

GFTFSDYNMA

SEQ ID NO:5 CDRH2 of 496.g3

TITYEGRNTYYRDSVKG

SEQ ID NO:6 CDRH3 of 496.g3

PPQYYEGSIYRLWFAH

SEQ ID NO:7 Light chain variable region of 496.g3

AIQLTQSPSSLSASVGDRTTITCRADESVRTLMMHWYQKPGKAPKLLIYLVSNSEIGVPDRFSGSGSG
TDFRLTISSLQPEDFATYYCQQTWSDPWTFGQGTKVEIK

SEQ ID NO:8 Light chain variable region of 496.g3

gcaatccagctcaccagagtcacaagcagtcctctccgccagcgtaggcgaccgtgtgactattacctg
tagagcggacgagtcggtcaggactctcatgcactggatcaacagaagcctggtaaagctcctaacc
tgctcatctatctgggtgtccaactcggagataggtgtgccagatcggtttagtgggtctgggttcaggc
actgatttcagactgaccatatcatctctacagccagaggacttcgccacatattactgtcagcaaac
ctggagtgaccgtggactttcggccagggcactaaagtagaaattaaa

SEQ ID NO:9 Heavy chain variable region of 496.g3

EVQLVESGGGLVQPGGSLRLSCAASGFTFSDYNMAWVRQAPGKGLEWVATITYEGRNTYYRDSVKGRF
TISRDNANKSLYLQMNSLR AEDTAVYYCASPPQYYEGSIYRLWFAHWGQGLTVTVSS

Fig. 2 cont'd

SEQ ID NO:10 Heavy chain variable region of 496.g3

gaagttcagctgggtcgagtcctggaggtggccttgtccaacctggagggagcctgcgtctctcttgtgc
agcaagcggattcacgttttctgattacaatatggcttgggttagacaggcaccgggtaagggccttg
aatgggttgcgacgattacatacgaaggcagaaatacctattacagggaactcagtaaaagggcggttt
accataagccgagataatgctaaaaacagtcctgtatttgcaaataaacagcctacgagctgaagacac
tgccgtgtattactgcgcgagtcacacctcagtcattatgaaggatcaatctatcgccctctgggttcgcac
attggggacaggggacccttgtgacagtcctcgagt

SEQ ID NO:11 Light chain (VL-CL) 496.g3

AIQLTQSPSSLSASVGDRTITCRADESVRTLHWHYQQKPGKAPKLLIYLVSNSEIGVDPDRFSGSGSG
TDFRLTISSLQPEDFATYYCQQTWSDPWTFGQGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLL
NNFYPREAKVQWKVDNALQSGNSQESVTEQDSKSTYLSSTLTLSKADYEKHKVYACEVTHQGLSSP
VTKSFNRGEC

SEQ ID NO:12 Light chain (VL-CL) 496.g3

gcaatccagctcaccagagtcgaagcagtcctctccgccagcgtaggcgaccgtgtgactattacctg
tagagcggacgagtcgggtcaggactctcatgcactgggtatcaacagaagcctggtaaagctcctaacc
tgctcatctatctgggtgtccaactcggagataggtgtgccagatcggtttagtgggtctgggtcaggc
actgatttcagactgaccatattcatctctacagccagaggacttcgccacatactactgtcagcaaac
ctggagtgaccctggactttcggccagggcactaaagtagaaattaaacgtacgggtggcgctccct
ccgtgttcattctccaccctccgacgagcagctgaagtcggcaccgcctccgtcgtgtgcctgctg
aacaacttctacccccgcgaggccaaggtgcagtggaaggtggacaacgccctgcagtcgggcaactc
ccaggaatccgtcaccgagcaggactccaaggacagcacctactccctgtcctccaccctgaccctgt
ccaaggccgactacgagaagcacaaggtgtacgcctgcgaagtgaccaccaggggcctgtccagcccc
gtgaccaagtccttcaaccggggcgagtcg

SEQ ID NO:13 Heavy chain (VH-CH1) 496.g3

EVQLVESGGGLVQPGGSLRLSCAASGFTFSDYNMAWVRQAPGKGLEWVATITYEGRNTYYRDSVKGRF
TISRDNAKNSLYLQMNSLRAEDTAVYYCASPPQYYEGSIYRLWFAHWGQGTLVTVSSASTKGPSVFPL
APSSKSTSGGTAALGCLVKDYFPEPTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVTPSSSLGTQ
TYICNVNHKPSNTKVDKKVEPKSC

SEQ ID NO:14 Heavy chain (VH-CH1) 496.g3

gaagttcagctgggtcgagtcctggaggtggccttgtccaacctggagggagcctgcgtctctcttgtgc
agcaagcggattcacgttttctgattacaatatggcttgggttagacaggcaccgggtaagggccttg
aatgggttgcgacgattacatacgaaggcagaaatacctattacagggaactcagtaaaagggcggttt
accataagccgagataatgctaaaaacagtcctgtatttgcaaataaacagcctacgagctgaagacac
tgccgtgtattactgcgcgagtcacacctcagtcattatgaaggatcaatctatcgccctctgggttcgcac
attggggacaggggacccttgtgacagtcctcgagtcgctccacaaagggcccatcggtcttccccctg
gcacctcctccaagagcacctctgggggcacagcgccctgggtcgctgggtcaaggactacttccc
cgaaccagtgacgggtgtcgtggaactcaggtgccttgaccagcgcggttcacaccttcccggctgtcc
tacagtcctcaggactctactccctgagcagcgtgggtgaccgtgcctccagcagcttgggacccag

Fig. 2 cont'd

acctacatctgcaacgtgaatcacaagcccagcaacaccaaggtcgataagaaagttgagcccaaattc
ttgt

Anti- IL-13**CDR sequences Ab 650 (1539)**

SEQ ID NO:15 CDR1 of Ab 650 (1539)

KASQNINENLD

SEQ ID NO:16 CDR2 of Ab 650 (1539)

YTDILQT

SEQ ID NO:17 CDR3 of Ab 650 (1539)

YQYYSGYT

SEQ ID NO:18 CDRH1 of Ab 650 (1539)

GYSFTSYI H

SEQ ID NO:19 CDRH2 of Ab 650 (1539)

RIGPGSGDINYNKFKG

SEQ ID NO:20 CDRH3 of Ab 650 (1539)

FHYDGAD

SEQ ID NO:21 Rat Ab 650 (1539) VL-region

DIQMTQSPPVLSASVGRVTLSCASQNINENLDWYHQKHGEAPKLLIYYTDILQTGIPSRFSGSGSG
TDYTLTISSLQPEDVATYYCYQYYSGYTFGPGTKLEIK

SEQ ID NO:22 Rat Ab 650 (1539) VL-region

gacatccagatgaccagtcctcctccagtcctgtctgcatctgtgggagacagagtcactctcagttg
caaagcaagtcagaatattaatgagaacttagactggatcatcaaaagcatggcgaagctccaaac
tcctgatataattatacagacatTTTgcaaacgggcatcccatcaaggttcagtggcagtggtatctggt
acagattacacactcaccatcagcagcctgcagcctgaagatggtgccacataattactgctatcagta
ttacagtggttacacgtttggacctgggaccaagctggaataaaa

Fig. 2 cont'd

SEQ ID NO:23 Rat Ab 650 (1539) VH-region

QVQLQQSGAELVKPGSSVKMSCKASGYSFTSYIHWIKQRPQGQLEWIGRIGPGSGDINYNKFKGKA
TFTVDKYFSTAYMQLSSLSPEDTAVFYCARFHYDGADWGQGTLLTVSS

SEQ ID NO:24 Rat Ab 650 (1539) VH-region

caggtaactgcagcagctctggagctgagttggtgaagcctgggtcttcagtgaagatgtcctgcaa
ggcttctggctacagtttcaccagctactacatacactggataaagcagaggcctggacagggccttg
agtggattggcgctattggctcctggaagtggagatattaattacaatgagaagttcaagggcaaggcc
acatttactgtggacaaatatttcagcacagcctacatgcaactcagcagcctgtcacctgaggacac
tgcggtctttactgtgcaagatttcactatgatggggctgactggggccaaggcactctggtcacag
tctcgagc

SEQ ID NO:25 Human IGKV1-39 IGKJ2 acceptor framework

DIQMTQSPSSLSASVGDRVTITCRASQSISSYLNWYQQKPGKAPKLLIYAASSLQSGVPSRFSGSGSG
TDFTLTISSLQPEDFATYYCQQSYSTPYTFGQGTKLEIK

SEQ ID NO:26 Human IGHV1-69 IGHJ4 acceptor framework

QVQLVQSGAEVKKPGSSVKVSKASGGTFSSYAISWVRQAPGQGLEWMGGIIPIFGTANYAQKFQGRV
TITADKSTSTAYMELSSLRSEDVAVYYCARYFDYWGQGTLLTVSS

SEQ ID NO:27 Ab 650 (1539) gL8 V-region (unmutated*)

DIQMTQSPSSLSASVGDRVTITCKASQNINENLDWYQQKPGKAPKLLIYYTDILQTGIPSRFSGSGSG
TDYTLTISSLQPEDFATYYCYQYYSGYTFGQGTKLEIK

SEQ ID NO:28 Ab 650 (1539) gH9 V-region (unmutated*)

EVQLVQSGAEVKKPGSSVKVSKASGYSFTSYIHWVRQAPGQGLEWMGRIGPGSGDINYNKFKGRA
TFTVDKSTSTAYMELSSLRSEDVAVYYCARFHYDGADWGQGTLLTVSS

SEQ ID NO:29 Ab 650 (1539) gL8 V-region (unmutated*)

gacatccagatgacccagtcctccctcctcctgtccgcctccgtggcgacagggtgaccatcacctg
caaggcctcccagaacatcaacgagaacctggactggtagcagcagaagcccggaaggcccccaagc
tgctgatctactacaccgacatcctgcagaccggcatccctccaggttctccggctccggctccggc
accgactacaccctgaccatctcctcctgcagcccaggacttcgccacctactactgctaccagta
ctactccggctacaccttcggccagggcaccaagctggagatcaag

SEQ ID NO:30 Ab 650 (1539) gH9 V-region (unmutated*)

gagggtgcagctgggtgcagtcggcgccgaggtgaagaagcccggtcctccgtgaagggtgtcctgcaa
ggcctccggctactccttcacctcctactacatccactgggtgaggcagggcccccgccaggggcctgg

Fig. 2 cont'd

agtggatgggcaggatcgccccggctccggcgacatcaactacaacgagaagttcaagggcagggcc
accttcaccgtggacaagtccacctccaccgcctacatggagctgtcctccctgaggtccgaggacac
cgccgtgtactactgcgccagggttccactacgacggcgccgactggggccagggcaccctggtgaccg
tctcgagc

SEQ ID NO:31 Ab 650 (1539) gL8 V-region (mutated**)

DIQMTQSPSSLSASVGDRVITITCKASQNINENLDWYQQKPGKAPKLLIYYTDILQTGIPSRFSGSGSG
TDYTLTISSLQPEDFATYYCYQYYSGYTFGCGTKLEIK

SEQ ID NO:32 Ab 650 (1539) gH9 V-region (mutated**)

EVQLVQSGAEVKKPGSSVKVSKASGYSFTSYIIHWVRQAPGQCLEWMGRIGPGSGDINYNKFKGRA
TFTVDKSTSTAYMELSSLRSEDTAVYYCARFHYDGADWGQGTITVTVSS

SEQ ID NO:33 Ab 650 (1539) gL8 V-region (mutated**)

gacatccagatgacccagtcctccctcctcctgtccgcctccgtggcgacagggtgaccatcacctg
caaggcctcccagaacatcaacgagaacctggactggtaggcagcagaagcccggaaggcccccaagc
tgctgatctactacaccgacatcctgcagaccggcatccctccaggttctccggctccggctccggc
accgactacacctgaccatctcctcctcctgcagcccaggacttcgccacctactactgctaccagta
ctactccggctacaccttcggctgcggcaccaagctggagatcaag

SEQ ID NO:34 Ab 650 (1539) gH9 V-region (mutated**)

gaggtgcagctggtgcagtcggcgccgaggtgaagaagcccggtcctccgtgaaggtgtcctgcaa
ggcctccggctactccttcacctcctactacatccactgggtgaggcagggcccccgccagtgacctg
agtggatgggcaggatcgccccggctccggcgacatcaactacaacgagaagttcaagggcagggcc
accttcaccgtggacaagtccacctccaccgcctacatggagctgtcctccctgaggtccgaggacac
cgccgtgtactactgcgccagggttccactacgacggcgccgactggggccagggcaccctggtgaccg
tgtcctcc

SEQ ID NO:35 650 (1539) scFv (VH/VL) gH9gL8 (unmutated*)

EVQLVQSGAEVKKPGSSVKVSKASGYSFTSYIIHWVRQAPGQGLEWMGRIGPGSGDINYNKFKGRA
TFTVDKSTSTAYMELSSLRSEDTAVYYCARFHYDGADWGQGTITVTVSSGGGGSGGGGSGGGGSGGGG
DIQMTQSPSSLSASVGDRVITITCKASQNINENLDWYQQKPGKAPKLLIYYTDILQTGIPSRFSGSGSG
TDYTLTISSLQPEDFATYYCYQYYSGYTFGQGTKLEIK

SEQ ID NO:36 650 (1539) scFv (VH/VL) gH9gL8 (unmutated*)

gaggtgcagctggtgcagtcggcgccgaggtgaagaagcccggtcctccgtgaaggtgtcctgcaa
ggcctccggctactccttcacctcctactacatccactgggtgaggcagggcccccgccagggcctgg
agtggatgggcaggatcgccccggctccggcgacatcaactacaacgagaagttcaagggcagggcc
accttcaccgtggacaagtccacctccaccgcctacatggagctgtcctccctgaggtccgaggacac
cgccgtgtactactgcgccagggttccactacgacggcgccgactggggccagggcaccctggtgaccg
tgtcctccggaggtggcggttctggcggtggcggttccggtggcggtggatcgggaggtggcggttct

Fig. 2 cont'd

gacatccagatgacccagtcctccctgtccgcctccgtggcgacagggtgaccatcacctg
 caaggcctcccagaacatcaacgagaacctggactggtaccagcagaagcccggaaggccccaagc
 tgctgatctactacaccgacatcctgcagaccggcatcccctccaggttctccggtccggctccggc
 accgactacaccctgaccatctcctcctgcagcccaggacttcgccacctactactgctaccagta
 ctactccggctacaccttcggccagggcaccaagctggagatcaag

SEQ ID NO:37 650 (1539) dsscFv (VH/VL) gH9gL8 (mutated**)

EVQLVQSGAEVKKPGSSVKVSKASGYSFTSYIHWVRQAPGQCLEWMGRIGPGSGDINYNEKFKGRA
 TFTVDKSTSTAYMELSSLRSEDTAVYYCARFHYDGADWGQGLVTVSSGGGSGGGGSGGGGSGGGG
 DIQMTQSPSSLSASVGDRVTITCKASQNINENLDWYQQKPGKAPKLLIYYTDILQTGIPSRFSGSGSG
 TDYTLTISSLQPEDFATYYCYQYYSGYTFGCGTKLEIK

SEQ ID NO:38 650 (1539) dsscFv (VH/VL) gH9gL8 (mutated**)

gaggtgcagctggtgcagtcggcgccgaggtgaagaagcccggtcctccgtgaaggtgtcctgcaa
 ggcctccggctactccttcacctcctactacatccactgggtgaggcagggcccgccagtgctgg
 agtggatgggcaggatcgccccgggtcggcgacatcaactacaacgagaagttcaagggcagggcc
 acctcacgtggacaagtccacctccaccgcctacatggagctgtcctcctgaggtccgaggacac
 cgccgtgtactactgcgccaggttccactacgacggcgccgactggggccagggcaccctggtgaccg
 tgtcctccggaggtggcggttctggcggtggcggttccggtggcggtggatcgggaggtggcggttct
 gacatccagatgacccagtcctccctgtccgcctccgtggcgacagggtgaccatcacctg
 caaggcctcccagaacatcaacgagaacctggactggtaccagcagaagcccggaaggccccaagc
 tgctgatctactacaccgacatcctgcagaccggcatcccctccaggttctccggtccggctccggc
 accgactacaccctgaccatctcctcctgcagcccaggacttcgccacctactactgctaccagta
 ctactccggctacaccttcggctgcggcaccaagctggagatcaag

* ie without cysteines engineered for a disulphide bond

** ie with cysteines engineered for a disulphide bond

Anti- HSA**CDR sequences Ab 645**

SEQ ID NO:39 CDRL1 of Ab 645

QSSPSVWSNFLS

SEQ ID NO:40 CDRL2 of Ab 645

EASKLTS

SEQ ID NO:41 CDRL3 of Ab 645

GGGYSSISDTT

Fig. 2 cont'd

SEQ ID NO:42 CDRH1 of Ab 645

GIDLSNYAIN

SEQ ID NO:43 CDRH2 of Ab 645

IIWASGTTFYATWAKG

SEQ ID NO:44 CDRH3 of Ab 645

TVPGYSTAPYFDL

SEQ ID NO:45 Ab 645 VL-region (unmutated*)

DIQMTQSPSSVSASVGDRVTITCQSSPSVWSNFLSWYQQKPGKAPKLLIYEASKLTSGVPSRFSGSGS
GTDFTLTISSLQPEDFATYYCGGGYSSISDITFGGGTKVEIK

SEQ ID NO:46 Ab 645 VH-region (unmutated*)

EVQLLESQGGGLVQPGGSLRLSCAIVSGIDLSNYAINWVRQAPGKLEWIGIIWASGTTFYATWAKGRFT
ISRDNKNTVYILQMNSLRAEDTAVYYCARTVPGYSTAPYFDLWGQGTLVTVSS

SEQ ID NO:47 Ab 645 VL-region (unmutated*)

gatattcagatgacgcaatcaccttcgagcgtatccgcctcgggtgggagacagggtgacaatcacttg
tcagtcatccccctcagtcctggagcaactttttgtcatgggtatcagcagaagcccgaaaggctccga
aattgctgatctacgagcatcgaagttgacgagcgggtgtaccaagcagattctccggttcggggctcg
ggaactgacttcacccttacgatctcatcgctgcagccggaggattttgcgacctactactgtggggg
tgggtattcgtcgatttccgacacaacattcggggggcggcacgaaagtggaaatcaag

SEQ ID NO:48 Ab 645 VH-region (unmutated*)

gaagtgcagttgctggagtcaggtggagggctggtgcagccccggaggatcgctgcggttgctcatgcgc
ggtgtccggtattgatttgccaattacgccatcaattgggtacgccaagcgccagggaagggccttg
agtggattggcatcatctgggcgtcggggacgaccttttatgctacttgggcaaaggaagattcaca
atctcccagacaactcgaagaacaccgtgtatcttcaaatgaactcgctcagggccgaggacacggc
ggtctactactgtgcacggacagtgccgggttattcaacggcaccttactttgatctttggggccagg
ggaccctcgtgactgtctcaagt

SEQ ID NO:49 Ab 645 VL-region (mutated**)

DIQMTQSPSSVSASVGDRVTITCQSSPSVWSNFLSWYQQKPGKAPKLLIYEASKLTSGVPSRFSGSGS
GTDFTLTISSLQPEDFATYYCGGGYSSISDITFGCGTKVEIK

Fig. 2 cont'd

SEQ ID NO:50 Ab 645 VH-region (mutated**)

EVQLLES^{SGGGLVQPGGSLRLSCA}VS^{GIDLSNYAINWVRQAPGK}CLEWIGIIWASGTTFYATWAKGRFT
ISRDN^{SKNTVYLQMNSLRAEDTAVYYCARTVPGYSTAPYFDLWGQGTLVTVSS}

SEQ ID NO:51 Ab 645 VL-region (mutated**)

gata^{ttcagatgacgcaatcaccttcgagcgtatccgcctcgg}tggagacaggg^{tgacaatcacttg}
tcagtcatccccctcag^{tctggagcaactttttgtcatggtatcagcagaagccc}ggaaggctccga
aattg^{tgatctacgag}gc^{atcgaagttgacgagcgg}tgtaccaagcagattctccg^{gttcgggg}tgcg
ggaactgacttcaccc^{ttacgatctcatcgctgcagccg}gaggat^{tttgcgac}tactactgtggggg
tgggtattcgtcgatttccgacacaacattcgggtgcggcacgaaagtggaaatcaag

SEQ ID NO:52 Ab 645 VH-region (mutated**)

gaagtgcagttgctggagtcaggtggagggctggtgcagcccggaggatcgctgcggttgtcatgcgc
ggtgtccggtattgatttgtccaattacgccatcaattgggtacgccaagcgccagggaagtgccttg
agtggattggcatcatctgggcgtcggggacgaccttttatgctacttgggccaaggaagattcaca
atctcccgagacaactcgaagaacaccgtgtatcttcaaatgaactcgctcagggccgaggacacggc
ggtctactactgtgcacggacagtgcgggttattcaacggcaccttactttgatctttggggccagg
ggaccctcgtgactgtctcaagt

SEQ ID NO:53 645 scFv (VH/VL) (unmutated*)

EVQLLES^{SGGGLVQPGGSLRLSCA}VS^{GIDLSNYAINWVRQAPGK}LEWIGIIWASGTTFYATWAKGRFT
ISRDN^{SKNTVYLQMNSLRAEDTAVYYCARTVPGYSTAPYFDLWGQGTLVTVSS}SGGGGSGGGGSGGGGS
GGGSDIQMTQSPSSVSASVGD^{RVTITCQSSPSVWSNFLSWYQQKPGKAPKLLIYEASKLTS}GVPSRF
SGSGSGTDFTLT^{ISSIQPEDFATYYCGGYS}SSISDTTFGGGTKVEIK

SEQ ID NO:54 645 scFv (VH/VL) (unmutated*)

gaagtgcagttgctggagtcaggtggagggctggtgcagcccggaggatcgctgcggttgtcatgcgc
ggtgtccggtattgatttgtccaattacgccatcaattgggtacgccaagcgccagggaagggccttg
agtggattggcatcatctgggcgtcggggacgaccttttatgctacttgggccaaggaagattcaca
atctcccgagacaactcgaagaacaccgtgtatcttcaaatgaactcgctcagggccgaggacacggc
ggtctactactgtgcacggacagtgcgggttattcaacggcaccttactttgatctttggggccagg
ggaccctcgtgactgtctcaagtggaggtggcgggttctggcgggtggcgggtccggtggcgggtggatcg
ggaggtggcgggttctgatattcagatgacgcaatcaccttcgagcgtatccgcctcgggtgggagacag
ggtgacaatcacttgtcagtcacccccctcagtcctggagcaactttttgtcatggtatcagcagaagc
ccggaaggctccgaaattgctgatctacgaggcatcgaagttgacgagcgggtgtaccaagcagattc
tccggttcggggtcgggaactgacttcaccc^{ttacgatctcatcgctgcagccg}gaggat^{tttgcgac}
ctactactgtgggggtgggtattcgtcgatttccgacacaacattcggggg^{cggcacgaa}agtg^{gaaa}
tcaag

Fig. 2 cont'd

SEQ ID NO:55 645 dsscFv (VH/VL) (mutated**)

EVQLLES⁵⁵GGGLVQPGGSLRLSCA⁵⁵VS⁵⁵GIDLSNYAINWVRQAPGKCLEWIGIIWASGTTFYATWAKGRFT
ISRDN⁵⁵SKNTVY⁵⁵LQMNSLRAEDTAVYYCARTVPGYSTAPYFDLWGQGT⁵⁵LVTVSSGGGGSGGGSGGGGS
GGGGSDIQMTQSPSSVSASV⁵⁵GDRVTITCQSSPSVWSN⁵⁵FLSWYQQKPGKAPKLLIYEASKLTSGVPSRF
SGSGSGTDFTLT⁵⁵ISS⁵⁵LQPEDFATYYCGGGYSSISD⁵⁵TFGCGTKVEIK

SEQ ID NO:56 645 dsscFv (VH/VL) (mutated**)

gaagtgcagttgctggagtcaggtggagggctggtgcagcccgaggatcgctgcggttgtcatgcgc
ggtgtccggtattgatttgtccaattacgccatcaattgggtacgccaagcgccagggaagtgccttg
agtggattggcatcatctggcgctcggggacgaccttttatgctacttgggccaaaggaagattcaca
atctcccagacaactcgaagaacaccgtgtatcttcaaatgaactcgctcagggccgaggacacggc
ggtctactactgtgcacggacagtgccgggttattcaacggcaccttactttgatctttggggccagg
ggacctcgtgactgtctcaagtggaggtggcggttctggcggtggcggttccggtggcggtggatcg
ggaggtggcggttctgatattcagatgacgcaatcaccttcgagcgtatccgcctcggtgggagacag
ggtgacaatcacttgtcagtcattccccctcagtcctggagcaacttttgtcatggtatcagcagaagc
ccggaaggtccgaaattgctgatctacgaggcatcgaagttgacgagcggtgtaccaagcagattc
tccggttcggggtcggaactgacttcacccttacgatctcatcgctgcagccggaggattttgcgac
ctactactgtgggggtgggtattcgtcgatttccgacacaacattcggtgctgggcacgaaagtggaaa
tcaag

Full-length chains

SEQ ID NO:57 496.g3 HC- 645 (VH/VL) scFv (unmutated*)

EVQLVESGGGLVQPGGSLRLSCAASGFTFSDYNMAWVRQAPGKGLEWVATITYEGRNTYYRDSVKGRF
TISRDN⁵⁷AKNSLYLQMNSLRAEDTAVYYCASPPQY⁵⁷EGSIYRLWFAHWGQGT⁵⁷LVTVSSASTKGPSVFPL
APSSKSTSGGTAALGCLVKDYFPEPVT⁵⁷SVNSGALTSGVHTFPAVLQSSGLYSLSSVTV⁵⁷PSSSLGTQ
TYICNVNHKPSNTKVDKKVEPKSCSGGGGTGGGGSEVQLLES⁵⁷GGGLVQPGGSLRLSCA⁵⁷VS⁵⁷GIDLSNYA
INWVRQAPGK⁵⁷GLEWIGIIWASGTTFYATWAKGRFTISRDN⁵⁷SKNTVY⁵⁷LQMNSLRAEDTAVYYCARTVPG
YSTAPYFDLWGQGT⁵⁷LVTVSSGGGGSGGGSGGGSGGGGSDIQMTQSPSSVSASV⁵⁷GDRVTITCQSSPS
VWSN⁵⁷FLSWYQQKPGKAPKLLIYEASKLTSGVPSRFSGSGSGTDFTLT⁵⁷ISS⁵⁷LQPEDFATYYCGGGYSSI
SDTTFGGG⁵⁷TKVEIKRT

SEQ ID NO:58 496.g3 HC- 645 (VH/VL) scFv (unmutated*)

gaagttcagctggtcgagtcctggaggtggccttgtccaacctggaggagcctgcgtctctcttgtgc
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aatgggttgcgacgattacatacgaaggcagaaatacctattacagggactcagtaaaagggcggttt
accataagccgagataaatgctaaaaacagtcgttatttgcaaatgaacagcctacgagctgaagacac
tgccgtgtattactgcgcgagtcacctcagtcattatgaaggatcaatctatcgccctctggttcgcac
attggggacaggggacccttgtgacagtcctcgagtcggtccacaaagggcccatcggtcttccccctg
gcacctcctccaagagcacctctgggggcacagcgccctgggctgctggtcaaggactacttccc
cgaaccagtgacggtgtcgtggaactcaggtgccctgaccagcggttcacacctccccggctgtcc
tacagtcctcaggactctactccctgagcagcgtggtgaccgtgccctccagcagcttgggacccag
acctacatctgcaacgtgaatcacaagcccagcaacaccaaggtcgataagaaagttgagcccaaatc
ttgtagcgggtggcggtggcaccggaggtggcggttcagaagtgcagttgctggagtcaggtggagggc

Fig. 2 cont'd

tggtgcagcccgaggatcgctgcggttgatgcgcggtgtccggtattgatttgtccaattacgcc
atcaattgggtacgccaagcgccaggggaagggccttgagtggattggcatcatctgggcgtcggggac
gaccttttatgctacttgggccaaggaagattcacaatctcccagacaactcgaagaacaccgtgt
atcttcaaatgaactcgctcagggccgaggacacggcggtctactactgtgcacggacagtgcgggt
tattcaacggcaccttactttgatctttggggccaggggaccctcgtgactgtctcaagtggaggtgg
cggttctggcggtggcggttccggtggcggtggatcgggaggtggcggttctgatattcagatgacgc
aatcaccttcgagcgtatccgcctcgggtgggagacagggtgacaatcacttgtcagtcacccccctca
gtctggagcaactttttgtcatggtatcagcagaagcccgaaaggctccgaaattgctgatctacga
ggcatcgaagttgacgagcggtgtaccaagcagattctccggttcggggtcgggaactgacttcaccc
ttacgatctcatcgctgcagccggaggattttgcgacctactactgtgggggtgggtattcgtcgatt
tccgacacaacattcgggggcggcacgaaagtggaaatcaagcgtacc

SEQ ID NO:59 496.g3 HC- 645 (VH/VL) dsscFv (mutated**)

EVQLVESGGGLVQPGGSLRLSCAASGFTFSDYNMAWVRQAPGKGLEWVATITYEGRNTYYRDSVKGRF
TISRDNAKNSLYLQMNSLRAEDTAVYYCASPPQYYEGSIYRLWFAHWGQGLTVTVSSASTKGPSVFPL
APSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVTPSSSLGTQ
TYICNVNHKPSNTKVDKKVEPKSCSGGGGTGGGGSEVQLLESVGGGLVQPGGSLRLSCAVSGIDL
SNYA INWVRQAPGKLEWIGIIWASGTFYATWAKGRFTISRDN SKNTVYLQMNSLRAEDTAVYYCARTVPG
YSTAPYFDLWGQGLTVTVSSGGGSGGGGSGGGGSGGGGSDIQMTQSPSSVSASVGDRTVITCQSSPS
VWSNFLSWYQQKPGKAPKLLIYEASKLTSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCGGGYSSI
SDTTFGCGTKVEIKRT

SEQ ID NO:60 496.g3 HC- 645 (VH/VL) dsscFv (mutated**)

gaagttcagctgggtcgagtctggaggtggccttgtccaacctggaggagcctgcgtctctcttgtgc
agcaagcggattcacgttttctgattacaatatggcttgggttagacaggcaccgggtaagggccttg
aatgggttgcgacgattacatacgaaggcagaaatacctattacagggactcagtaaaagggcggttt
accataagccgagataatgctaaaaacagtctgtatttgcaaatgaacagcctacgagctgaagacac
tgccgtgtattactgcgcgagtcacctcagttatgaaggatcaatctatcgctctggttcgcac
attggggacaggggacccttgtgacagtcctcgagtgcgtccacaaagggcccatcggtcttccccctg
gcaccctcctccaagagcacctctgggggcacagcgccctgggctgcctggtcaaggactacttccc
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tacagtcttcaggactctactccctgagcagcgtggtgaccgtgcctccagcagcttgggcacccag
acctacatctgcaacgtgaatcacaagcccagcaacaccaaggtcgataagaaagttgagcccaaac
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cggttctggcggtggcggttccggtggcggtggatcgggaggtggcggttctgatattcagatgacgc
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gtctggagcaactttttgtcatggtatcagcagaagcccgaaaggctccgaaattgctgatctacga
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Fig. 2 cont'd

SEQ ID NO:61 496.g3 LC- 650 (1539) scFv (unmutated*)

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NNFYPREAKVQWKVDNALQSGNSQESVTEQDSKSTYLSSTLTLSKADYEKHKVYACEVTHQGLSSP
VTKSFNRGECSSGGGSGGGGSEVQLVQSGAEVKKPGSSVKVSKASGYSTSYIHWVRQAPGQGLEW
MGRIGPGSGDINYNKFKGRATFTVDKSTSTAYMELSSLRSEDTAVYYCARFHYDGADWGQGTLLVTVS
SGGGGSGGGGSGGGGSDIQMTQSPSSLSASVGDRVITITCKASQNINENLDWYQQKPGKAPKLL
IYYTDILQGTGIPSRFSGSGSGTDYTLTISSLQPEDFATYYCYQYSGYTFGQGTKEIKRT

SEQ ID NO:62 496.g3 LC- 650 (1539) scFv (unmutated*)

gcaatccagctcaccagagtcgaagcagtcctcctccgccagcgtaggcgaccgtgtgactattacctg
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ctggagtgaccctggactttcggccagggcactaaagtagaaattaaacgtacgggtggcgctccct
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tccggaggtggcggttctggcggtggcggttccgggtggcggtggatcgggaggtggcggttctgacat
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cctcccagaacatcaacgagaacctggactggtaccagcagaagcccggaaggcccccaagctgctg
atctactacaccgacatcctgcagaccggcatccctccaggttctccggctccggctccggcaccga
ctacaccctgaccatctcctccctgcagcccaggacttcgccacctactactgctaccagtactact
ccggctacaccttcggccagggcaccaagctggagatcaagcgtacc

SEQ ID NO:63 496.g3 LC- 650 (1539) dsscFv (mutated**)

AIQLTQSPSSLSASVGDRVITITCRADESVRTLHWHYQQKPGKAPKLLIYLVSNSEIGVPDRFSGSGSG
TDFRLTISSLQPEDFATYYCQQTWSDPWTFGQGTKEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLL
NNFYPREAKVQWKVDNALQSGNSQESVTEQDSKSTYLSSTLTLSKADYEKHKVYACEVTHQGLSSP
VTKSFNRGECSSGGGSGGGGSEVQLVQSGAEVKKPGSSVKVSKASGYSTSYIHWVRQAPGQGLEW
MGRIGPGSGDINYNKFKGRATFTVDKSTSTAYMELSSLRSEDTAVYYCARFHYDGADWGQGTLLVTVS
SGGGGSGGGGSGGGGSDIQMTQSPSSLSASVGDRVITITCKASQNINENLDWYQQKPGKAPKLL
IYYTDILQGTGIPSRFSGSGSGTDYTLTISSLQPEDFATYYCYQYSGYTFGCGTKLEIKRT

SEQ ID NO:64 496.g3 LC- 650 (1539) dsscFv (mutated**)

gcaatccagctcaccagagtcgaagcagtcctcctccgccagcgtaggcgaccgtgtgactattacctg
tagagcggacgagtcgggtcaggactctcatgcactggatcaacagaagcctggtaaagctcctaaac

Fig. 2 cont'd

tgctcatctatctgggtgtccaactcggagataggtgtgccagatcggtttagtgggtctgggttcaggc
actgatttcagactgaccatatcatctctacagccagaggacttcgccacatattactgtcagcaaac
ctggagtgaccctggactttcggccagggcactaaagtagaaattaaacgtacgggtggccgctccct
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ctacacctgaccatctcctccctgcagccgaggacttcgccacctactactgctaccagtactact
ccggctacaccttcgggtgcgggcaccaagctggagatcaagcgtacc

* ie without cysteines engineered for a disulphide bond

** ie with cysteines engineered for a disulphide bond

Linkers

SEQ ID NO:65 Light chain linker between kappa constant region and 650 (1539) VH of scFv/dssFv
645 VH of scFv/dssFv

SGGGGSGGGGS

SEQ ID NO:66 Light chain linker between VH and VL of 650 (1539) scFv/dsscFv 645 scFv/dsscFv

GGGSGGGGSGGGGSGGGGS

SEQ ID NO:67 Heavy chain linker between CH1 constant region and 645 VH of scFv/dssFv

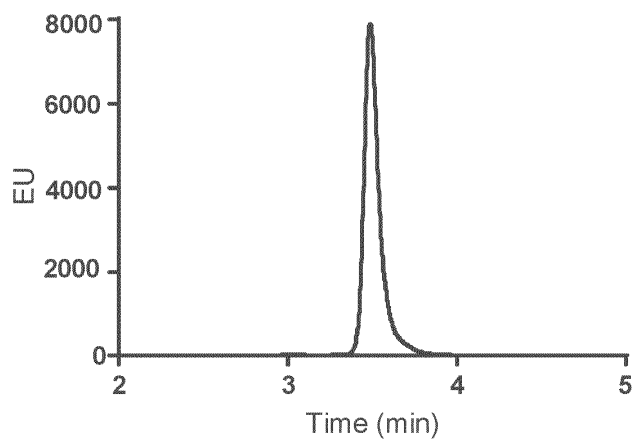
SGGGGTGGGGS

SEQ ID NO:68 Heavy chain linker between VH and VL of 645 scFv/dsscFv

GGGSGGGGSGGGGSGGGGS

Figure 3. Purification of IL-13/IL-17AF multi-specific antibody

(A) BEH200 SEC-UPLC analysis of final purified antibody, detection by FLR.



(B) SDS-PAGE under non-reducing (lane 1) or reducing (lane 2) conditions.

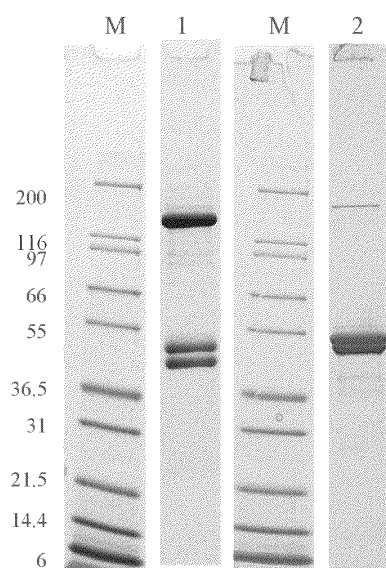


Figure 4. Inhibition of STAT6 signalling

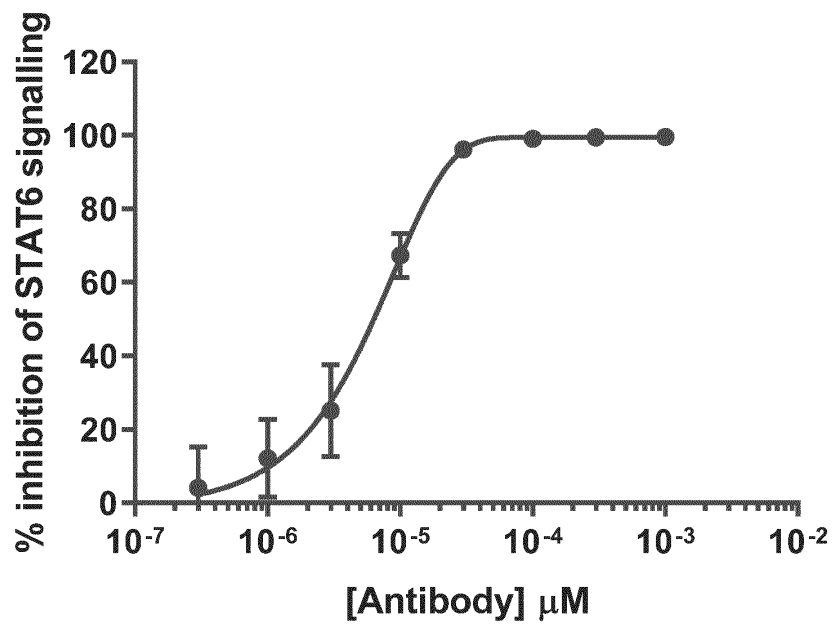
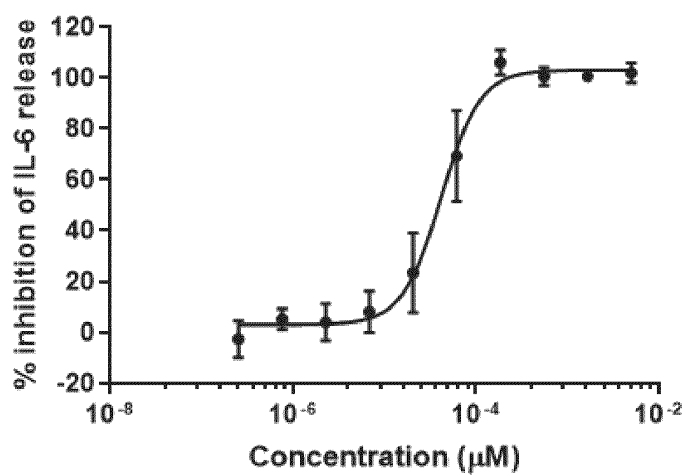


Figure 5(A) Inhibition of IL-6 production in response to human or cynomolgus IL-17A in combination with TNF- α .

(i) Human IL-17A.



(ii) Cynomolgus IL-17A.

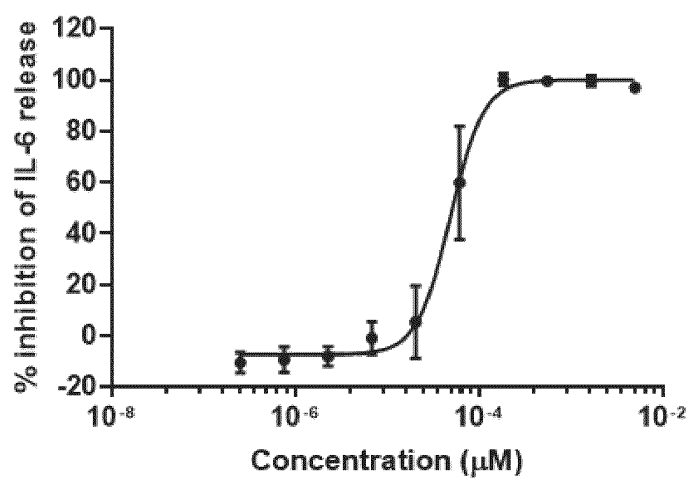
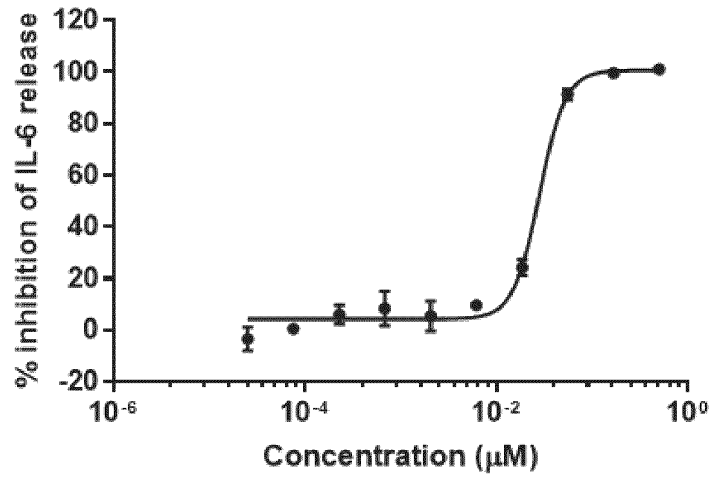


Figure 5(B) Inhibition of IL-6 production in response to human or cynomolgus IL-17F in combination with TNF- α .

(i) Human IL-17F.



(ii) Cynomolgus IL-17F.

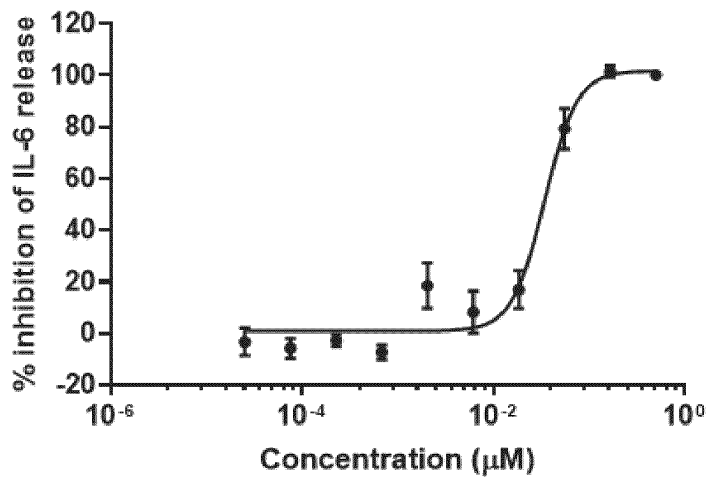


Figure 6. Simultaneous neutralisation of IL-13, IL-17A and IL-17F by IL-13/IL-17AF multi-specific antibody

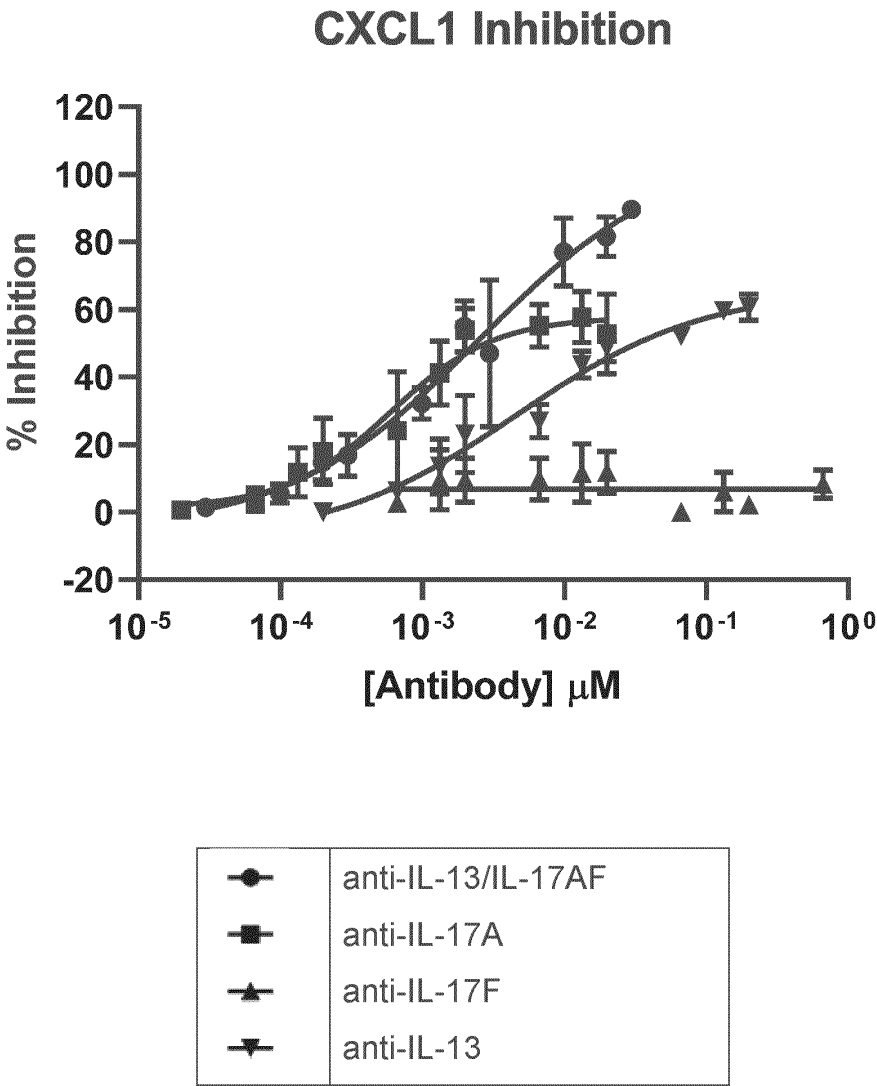


Figure 7.

