A3 clone

LPVLTQPPSASGTPGQRVTISCSGSSSNIKFNSVNWYQQLPGTAPKLLIYSNNQRPSGVPDRFSGSKSGTSASLAISGLQSEDEADY
FCASWDDVLYGSVFGGGTKLTVL (SEQ ID NO:1)

LC-CDR1:	SGSSSNIKFNSVN	(SEQ ID NO:25)
LC-CDR2:	SNNQRPS	(SEQ ID NO:26)
LC-CDR3:	ASWDDVLYGSV	(SEQ ID NO:27)

A10 clone

LPVLTQPPSASGTPGQRVTISCSGSSSNIKFNSVNWYQQLPGTAPKLLIYSNNQRPSGVPDRFSGSKSGTSASLAISGLQSEDEADY
FCASWDDYYYGTIFGGGTKLTVL (SEQ ID NO:2)

LC-CDR1:	SGSSSNIKFNSVN	(SEQ ID NO:25)
LC-CDR2:	SNNQRPS	(SEQ ID NO:26)
LC-CDR3:	ASWDDYYYGTI	(SEQ ID NO:28)

Figure 1

B6 clone

QSVLTQPPSASGTPGQRVTISCSGSSSNIKFNSVNWYQQLPGTAPKLLIYSNNQRPSGVPDRFSGSKSGTSASLAISGLQSEDEADY
YCASWDDYLRGTVFGGGTKLTVL (SEQ ID NO:3)

LC-CDR1:	SGSSSNIKFNSVN	(SEQ ID NO:25)
LC-CDR2:	SNNQRPS	(SEQ ID NO:26)
LC-CDR3:	ASWDDYLRGTV	(SEQ ID NO:29)

C4 clone

QSVLTQPPSASGTPGQRVTISCSGSSSNIKFNSVNWYQQLPGTAPKLLIYSNNQRPSGVPDRFSGSKSGTSASLAISGLQSEDEADY
YCSAWDDYLHGTVFGGGTKLTVL (SEQ ID NO:4)

LC-CDR1:	SGSSSNIKFNSVN	(SEQ ID NO:25)
LC-CDR2:	SNNQRPS	(SEQ ID NO:26)
LC-CDR3:	SAWDDYLHGTV	(SEQ ID NO:30)

Figure 1 (cont.)

D4 clone

QSVLTQPPSASGTPGQRVTISCSGSSSNIKFNSVNWYQQLPGTAPKLLIYSNNQRPSGVPDRFSGSKSGTSASLAISGLQSEDEADY
YCASWDDYVRGTMFGGGTKLTVL (SEQ ID NO:5)

LC-CDR1:	SGSSSNIKFNSVN	(SEQ ID NO:25)
LC-CDR2:	SNNQRPS	(SEQ ID NO:26)
LC-CDR3:	ASWDDYVRGTM	(SEQ ID NO:31)

E1 clone

QSVLTQPPSASGTPGQRVTISCSGSSSNIKFNSVNWYQQLPGTAPKLLIYSNNQRPSGVPDRFSGSKSGTSASLAISGLQSEDEADY
YCSSWDDFLRGTVFGGGTKLTVL (SEQ ID NO:6)

LC-CDR1:	SGSSSNIKFNSVN	(SEQ ID NO:25)
LC-CDR2:	SNNQRPS	(SEQ ID NO:26)
LC-CDR3:	SSWDDFLRGTV	(SEQ ID NO:32)

Figure 1 (cont.)

F2 clone

QSVLTQPPSASGTPGQRVTISCSGSSSNIKFNSVNWYQQLPGTAPKLLIYSNNQRPSGVPDRFSGSKSGTSASLAISGLQSEDEADY
YCSSWDDDARGTIFGGGTKLTVL (SEQ ID NO:7)

LC-CDR1:	SGSSSNIKFNSVN	(SEQ ID NO:25)
LC-CDR2:	SNNQRPS	(SEQ ID NO:26)
LC-CDR3:	SSWDDDARGTI	(SEQ ID NO:33)

G1 clone

QSVLTQPPSASGTPGQRVTISCSGSSSNIKFNSVNWYQQLPGTAPKLLIYSNNQRPSGVPDRFSGSKSGTSASLAISGLQSEDEADY
YCAAWDDVYYGTIFGGGTKLTVL (SEQ ID NO:8)

LC-CDR1:	SGSSSNIKFNSVN	(SEQ ID NO:25)
LC-CDR2:	SNNQRPS	(SEQ ID NO:26)
LC-CDR3:	AAWDDVYYGTI	(SEQ ID NO:34)

Figure 1 (cont.)

G2 clone

QSVLTQPPSASGTPGQRVTISCSGSSSNIKFNSVNWYQQLPGTAPKLLIYSNNQRPSGVPDRFSGSKSGTSASLAISGLQSEDEADY
YCASWDDSLYGTVFGGGTKLTVL (SEQ ID NO:9)

LC-CDR1: SGSSSNIKFNSVN (SEQ ID NO:25)

LC-CDR2: SNNQRPS (SEQ ID NO:26)

LC-CDR3: ASWDDSLYGTV (SEQ ID NO:35)

G10 clone

QSVLTQPPSASGTPGQRVTISCSGSSSNIKFNSVNWYQQLPGTAPKLLIYSNNQRPSGVPDRFSGSKSGTSASLAISGLQSEDEADY
YCAAWDDAYYGTIFGGGTKLTVL (SEQ ID NO:10)

LC-CDR1: SGSSSNIKFNSVN (SEQ ID NO:25)

LC-CDR2: SNNQRPS (SEQ ID NO:26)

LC-CDR3: AAWDDAYYGTI (SEQ ID NO:36)

Figure 1 (cont.)

H4 clone

QSVLTQPPSASGTPGQRVTISCSGSSSNIKFNSVNWYQQLPGTAPKLLIYSNNQRPSGVPDRFSGSKSGTSASLAISGLQSEDEADY
YCASWDDVYRGTVFGGGTKLTVL (SEQ ID NO:11)

LC-CDR1:	SGSSSNIKFNSVN	(SEQ ID NO:25)
LC-CDR2:	SNNQRPS	(SEQ ID NO:26)
LC-CDR3:	ASWDDVYRGTV	(SEQ ID NO:37)

H9 clone

QSVLTQPPSASGTPGQRVTISCSGSSSNIKFNSVNWYQQLPGTAPKLLIYSNNQRPSGVPDRFSGSKSGTSASLAISGLQSEDEADY
YCSSWDDSLYGTIFGGGTKLTVL (SEQ ID NO:12)

LC-CDR1:	SGSSSNIKFNSVN	(SEQ ID NO:25)
LC-CDR2:	SNNQRPS	(SEQ ID NO:26)
LC-CDR3:	SSWDDSLYGTI	(SEQ ID NO:38)

Figure 1 (cont.)

A3 clone

QVQLVQSGGGVVQPGRSLRLSCAASGFTFSSYGMHWVRQAPGKGLEWVAVISYDGSNKYYADSVKGRFTISRDNSKNTLYLQMN
SLRAEDTAVYYCASDLGAGPYYYGKDHWGQGTTVTVSS (SEQ ID NO:13)

HC-CDR1:	GFTFSSYGMH	(SEQ ID NO:39) or
	SYGMH	(SEQ ID NO:89)
HC-CDR2:	VISYDGSNKYYADSVKG	(SEQ ID NO:40)
HC-CDR3:	DLGAGPYYYGKDH	(SEQ ID NO:41)

A10 clone

QVQLVQSGGGVVQPGRSLRLSCAASGFTFSSYGMHWVRQAPGKGLEWVAVISYDGSNKYYADSVKGRFTISRDNSKNTLYLQMN
SLRAEDTAVYYCASDLGAGPYYYGKDVWGQGTTVTVSS (SEQ ID NO:14)

HC-CDR1:	GFTFSSYGMH	(SEQ ID NO:39) or
	SYGMH	(SEQ ID NO:89)
HC-CDR2:	VISYDGSNKYYADSVKG	(SEQ ID NO:40)
HC-CDR3:	DLGAGPYYYGKDV	(SEQ ID NO:42)

Figure 2

B6 clone

QVQLVESGGGVVQPGRSLRLSCAASGFTFSSYGMHWVRQAPGKGLEWVAVISYDGSNKYYADSVKGRFTISRDNSKNTLYLQMN
SLRAEDTAVYYCASDYGAGPYYYGMDVWGQGTTVTVSS (SEQ ID NO:15)

HC-CDR1:	GFTFSSYGMH	(SEQ ID NO:39) or
	SYGMH	(SEQ ID NO:89)
HC-CDR2:	VISYDGSNKYYADSVKG	(SEQ ID NO:40)
HC-CDR3:	DYGAGPYYYGMDV	(SEQ ID NO:43)

C4 clone

QVQLVESGGGVVQPGRSLRLSCAASGFTFSSYGMHWVRQAPGKGLEWVAVISYDGSNKYYADSVKGRFTISRDNSKNTLYLQMN
SLRAEDTAVYYCASDLGAGPYYYGLDVWGQGTTVTVSS (SEQ ID NO:16)

HC-CDR1:	GFTFSSYGMH	(SEQ ID NO:39) or
	SYGMH	(SEQ ID NO:89)
HC-CDR2:	VISYDGSNKYYADSVKG	(SEQ ID NO:40)
HC-CDR3:	DLGAGPYYYGLDV	(SEQ ID NO:44)

Figure 2 (cont.)

D4 clone

QVQLVESGGGVVQPGRSLRLSCAASGFTFSSYGMHWVRQAPGKGLEWVAVISYDGSNKYYADSVKGRFTISRDNSKNTLYLQMN
SLRAEDTAVYYCASDLGAGPYYYGMDVWGQGTTVTVSS (SEQ ID NO:17)

HC-CDR1:	GFTFSSYGMH	(SEQ ID NO:39) or
	SYGMH	(SEQ ID NO:89)
HC-CDR2:	VISYDGSNKYYADSVKG	(SEQ ID NO:40)
HC-CDR3:	DLGAGPYYYGMDV	(SEQ ID NO:45)

E1 clone

QVQLVESGGGVVQPGRSLRLSCAASGFTFSSYGMHWVRQAPGKGLEWVAVISYDGSNKYYADSVKGRFTISRDNSKNTLYLQMN
SLRAEDTAVYYCASDLGAGPYYYGMDVWGQGTTVTVSS (SEQ ID NO:18)

HC-CDR1:	GFTFSSYGMH	(SEQ ID NO:39) or
	SYGMH	(SEQ ID NO:89)
HC-CDR2:	VISYDGSNKYYADSVKG	(SEQ ID NO:40)
HC-CDR3:	DLGAGPYYYGMDV	(SEQ ID NO:46)

Figure 2 (cont.)

F2 clone

QVQLVESGGGVVQPGRSLRLSCAASGFTFSSYGMHWVRQAPGKGLEWVAVISYDGSNKYYADSVKGRFTISRDNSKNTLYLQMN
SLRAEDTAVYYCASDLGAGPYYYGMDVWGQGTTVTVSS (SEQ ID NO:19)

HC-CDR1:	GFTFSSYGMH	(SEQ ID NO:39) or
	SYGMH	(SEQ ID NO:89)
HC-CDR2:	VISYDGSNKYYADSVKG	(SEQ ID NO:40)
HC-CDR3:	DLGAGPYYYGMDV	(SEQ ID NO:47)

G1 clone

QVQLVESGGGVVQPGRSLRLSCAASGFTFSSYGMHWVRQAPGKGLEWVAVISYDGSNKYYADSVKGRFTISRDNSKNTLYLQMN
SLRAEDTAVYYCASDLGAGPYYYGMDVWGQGTTVTVSS (SEQ ID NO:20)

HC-CDR1:	GFTFSSYGMH	(SEQ ID NO:39) or
	SYGMH	(SEQ ID NO:89)
HC-CDR2:	VISYDGSNKYYADSVKG	(SEQ ID NO:40)
HC-CDR3:	DLGAGPYYYGMDV	(SEQ ID NO:48)

Figure 2 (cont.)

G2 clone

QVQLVESGGGVVQPGRSLRLSCAASGFTFSSYGMHWVRQAPGKGLEWVAVISYDGSNKYYADSVKGRFTISRDNSKNTLYLQMN
SLRAEDTAVYYCASDLGAGPYYYGMDVWGQGTTVTVSS (SEQ ID NO:21)

HC-CDR1:	GFTFSSYGMH	(SEQ ID NO:39) or
	SYGMH	(SEQ ID NO:89)
HC-CDR2:	VISYDGSNKYYADSVKG	(SEQ ID NO:40)
HC-CDR3:	DLGAGPYYYGMDV	(SEQ ID NO:49)

G10 clone

QVQLVESGGGVVQPGRSLRLSCAASGFTFSSYGMHWVRQAPGKGLEWVAVISYDGSNKYYADSVKGRFTISRDNSKNTLYLQMN
SLRAEDTAVYYCASDYGAGPYYYGMDVWGQGTTVTVSS (SEQ ID NO:22)

HC-CDR1:	GFTFSSYGMH	(SEQ ID NO:39) or
	SYGMH	(SEQ ID NO:89)
HC-CDR2:	VISYDGSNKYYADSVKG	(SEQ ID NO:40)
HC-CDR3:	DYGAGPYYYGMDV	(SEQ ID NO:50)

Figure 2 (cont.)

H4 clone

QVQLVESGGGVVQPGRSLRLSCAASGFTFSSYGMHWVRQAPGKGLEWVAVISYDGSNKYYADSVKGRFTISRDNSKNTLYLQMN
SLRAEDTAVYYCASDLGSGYYLYGMDVWGQGTTVTVSS (SEQ ID NO:23)

HC-CDR1:	GFTFSSYGMH	(SEQ ID NO:39) or
	SYGMH	(SEQ ID NO:89)
HC-CDR2:	VISYDGSNKYYADSVKG	(SEQ ID NO:40)
HC-CDR3:	DLGSGYYLYGMDV	(SEQ ID NO:51)

H9 clone

QVQLVESGGGVVQPGRSLRLSCAASGFTFSSYGMHWVRQAPGKGLEWVAVISYDGSNKYYADSVKGRFTISRDNSKNTLYLQMN
SLRAEDTAVYYCASDLGAGPYYYGMDVWGQGTTVTVSS (SEQ ID NO:24)

HC-CDR1:	GFTFSSYGMH	(SEQ ID NO:39) or
	SYGMH	(SEQ ID NO:89)
HC-CDR2:	VISYDGSNKYYADSVKG	(SEQ ID NO:40)
HC-CDR3:	DLGAGPYYYGMDV	(SEQ ID NO:52)

Figure 2 (cont.)

Clone	CDR L1	CDR L2	CDR L3
Light Chain			
A3	SGSSSNIKFNSVN (SEQ ID NO:25)	SNNQRPS (SEQ ID NO:26)	ASWDDVLYGSV (SEQ ID NO:27)
A10	SGSSSNIKFNSVN (SEQ ID NO:25)	SNNQRPS (SEQ ID NO:26)	ASWDDYYYGTI (SEQ ID NO:28)
B6	SGSSSNIKFNSVN (SEQ ID NO:25)	SNNQRPS (SEQ ID NO:26)	ASWDDYLRGTV (SEQ ID NO:29)
C4	SGSSSNIKFNSVN (SEQ ID NO:25)	SNNQRPS (SEQ ID NO:26)	SAWDDYLHGTV (SEQ ID NO:30)
D4	SGSSSNIKFNSVN (SEQ ID NO:25)	SNNQRPS (SEQ ID NO:26)	ASWDDYVRGTM (SEQ ID NO:31)
E1	SGSSSNIKFNSVN (SEQ ID NO:25)	SNNQRPS (SEQ ID NO:26)	SSWDDFLRGTV (SEQ ID NO:32)
F2	SGSSSNIKFNSVN (SEQ ID NO:25)	SNNQRPS (SEQ ID NO:26)	SSWDDDARGTI (SEQ ID NO:33)
G1	SGSSSNIKFNSVN (SEQ ID NO:25)	SNNQRPS (SEQ ID NO:26)	AAWDDVYYGTI (SEQ ID NO:34)
G2	SGSSSNIKFNSVN (SEQ ID NO:25)	SNNQRPS (SEQ ID NO:26)	ASWDDSLYGTV (SEQ ID NO:35)
G10	SGSSSNIKFNSVN (SEQ ID NO:25)	SNNQRPS (SEQ ID NO:26)	AAWDDAYYGTI (SEQ ID NO:36)
H4	SGSSSNIKFNSVN (SEQ ID NO:25)	SNNQRPS (SEQ ID NO:26)	ASWDDVYRGTV (SEQ ID NO:37)
H9	SGSSSNIKFNSVN (SEQ ID NO:25)	SNNQRPS (SEQ ID NO:26)	SSWDDSLYGTI (SEQ ID NO:38)
Consensus	SGSSSNIKFNSVN (SEQ ID NO:25)	SNNQRPS (SEQ ID NO:26)	X_1X_2WDD$X_3X_4X_5$GX_6X_7 X_1= A or S X_2= S or A X_3= V, Y, F, D, S or A X_4= L, Y, V or A X_5= Y, R or H X_6= S, or T X_7= V, I, or M (SEQ ID NO:53)

Figure 3

Clone	CDR L1	CDR L2	CDR L3
Heavy Chain			
A3	GFTFSSYGMH (SEQ ID NO:39) or SYGMH (SEQ ID NO:89)	VISYDGSNKYYADSVKG (SEQ ID NO:40)	DLGAGPYYYGKDH (SEQ ID NO:41)
A10	GFTFSSYGMH (SEQ ID NO:39) or SYGMH (SEQ ID NO:89)	VISYDGSNKYYADSVKG (SEQ ID NO:40)	DLGAGPYYYGKDV (SEQ ID NO:42)
B6	GFTFSSYGMH (SEQ ID NO:39) or SYGMH (SEQ ID NO:89)	VISYDGSNKYYADSVKG (SEQ ID NO:40)	DYGAGPYYYGMDV (SEQ ID NO:43)
C4	GFTFSSYGMH (SEQ ID NO:39) or SYGMH (SEQ ID NO:89)	VISYDGSNKYYADSVKG (SEQ ID NO:40)	DLGAGPYYYGLDV (SEQ ID NO:44)
D4	GFTFSSYGMH (SEQ ID NO:39) or SYGMH (SEQ ID NO:89)	VISYDGSNKYYADSVKG (SEQ ID NO:40)	DLGAGPYYYGMDV (SEQ ID NO:45)
E1	GFTFSSYGMH (SEQ ID NO:39) or SYGMH (SEQ ID NO:89)	VISYDGSNKYYADSVKG (SEQ ID NO:40)	DLGAGPYYYGMDV (SEQ ID NO:46)
F2	GFTFSSYGMH (SEQ ID NO:39) or SYGMH (SEQ ID NO:89)	VISYDGSNKYYADSVKG (SEQ ID NO:40)	DLGAGPYYYGMDV (SEQ ID NO:47)
G1	GFTFSSYGMH (SEQ ID NO:39) or SYGMH (SEQ ID NO:89)	VISYDGSNKYYADSVKG (SEQ ID NO:40)	DLGAGPYYYGMDV (SEQ ID NO:48)

Figure 3 (cont.)

G2	GFTFSSYGMH (SEQ ID NO:39) or SYGMH (SEQ ID NO:89)	VISYDGSNKYYADSVKG (SEQ ID NO:40)	DLGAGPYYYGMDV (SEQ ID NO:49)
G10	GFTFSSYGMH (SEQ ID NO:39) or SYGMH (SEQ ID NO:89)	VISYDGSNKYYADSVKG (SEQ ID NO:40)	DYGAGPYYYGMDV (SEQ ID NO:50)
H4	GFTFSSYGMH (SEQ ID NO:39) or SYGMH (SEQ ID NO:89)	VISYDGSNKYYADSVKG (SEQ ID NO:40)	DLGSGYYLYGMDV (SEQ ID NO:51)
H9	GFTFSSYGMH (SEQ ID NO:39) or SYGMH (SEQ ID NO:89)	VISYDGSNKYYADSVKG (SEQ ID NO:40)	DLGAGPYYYGMDV (SEQ ID NO:52)
Consensus	GFTFSSYGMH (SEQ ID NO:39) or SYGMH (SEQ ID NO:89)	VISYDGSNKYYADSVKG (SEQ ID NO:40)	$DZ_1GZ_2GZ_3YZ_4YGZ_5DZ_6$ Z_1= L or Y Z_2= A or S Z_3= P or Y Z_4= Y or L Z_5= K, M or L Z_6= H or V (SEQ ID NO:54)

Figure 3 (cont.)

Light chain variable domains

A3 clone

>A3_aa_L

LPVLTQPPSASGTPGQRVTISCSGSSSNIKFNSVNWYQQLPGTAPKLLIYSNNQRPSGVPD
RFSGSKSGTSASLAISGLQSEDEADYFCASWDDVLYGSVFGGGTKLTVL [SEQ ID NO.
1]

>A3_ntd_L

CTGCCTGTGCTGACTCAGCCCCCCTCAGCGTCCGGGACCCCCGGGCAGAGGGTCACCATCT
CTTGTTCTGGAAGCAGCTCCAACATCAAATTTAACAGTGTTAACTGGTATCAGCAACTCCC
AGGAACGGCCCCCAAACTCCTCATCTATAGTAATAATCAGCGACCCTCAGGGGTCCCTGAC
CGATTCTCTGGCTCCAAGTCTGGCACTTCAGCCTCCCTGGCCATCAGTGGGCTCCAGTCTG
AGGATGAGGCTGATTATTTCTGTGCTTCTTGGGATGATGTTCTTTATGGATCTGTGTTCGG
CGGAGGGACCAAGCTGACCGTCCTG [SEQ ID NO. 55]

A10 clone

>A10_aa_L

LPVLTQPPSASGTPGQRVTISCSGSSSNIKFNSVNWYQQLPGTAPKLLIYSNNQRPSGVPD
RFSGSKSGTSASLAISGLQSEDEADYFCASWDDYYYGTIFGGGTKLTVL [SEQ ID NO.
2]

>A10_ntd_L

CTGCCTGTGCTGACTCAGCCCCCCTCAGCGTCCGGGACCCCCGGGCAGAGGGTCACCATCT
CTTGTTCTGGAAGCAGCTCCAACATCAAATTTAACAGTGTTAACTGGTATCAGCAACTCCC
AGGAACGGCCCCCAAACTCCTCATCTATAGTAATAATCAGCGACCCTCAGGGGTCCCTGAC
CGATTCTCTGGCTCCAAGTCTGGCACTTCAGCCTCCCTGGCCATCAGTGGGCTCCAGTCTG
AGGATGAGGCTGATTATTTCTGTGCTTCTTGGGATGATTATTATTATGGAACTATTTTCGG
CGGAGGGACCAAGCTGACCGTCCTG [SEQ ID NO. 56]

Figure 4

A10 codon-optimised clone (induced modifications in the amino-acid sequence)

>A10_optimised_aa_L

QSVLTQPPSASGTPGQRVTISCSGSSSNIKFNSVNWYQQLPGTAPKLLIYSNNQRPSGVPD
RFSGSKSGTSASLAISGLQSEDEADYYCASWDDYYYGTIFGGGTKLTVL [SEQ ID NO. 57]

>A10_optimised_ntd_L

CAGAGCGTCCTGACACAGCCTCCTAGTGCAAGCGGAACCCCTGGGCAGAGAGTGACCATTT
CTTGTAGCGGCAGCAGCAGTAACATCAAGTTCAACTCCGTGAATTGGTATCAGCAGCTGCC
CGGAACTGCTCCTAAACTGCTGATCTACTCTAACAATCAGCGACCAAGTGGCGTCCCCGAC
CGGTTCAGCGGCTCCAAGTCTGGGACCAGTGCCTCACTGGCTATCAGCGGGCTCCAGTCCG
AGGACGAAGCAGATTACTATTGCGCCAGCTGGGACGATTACTATTACGGCACCATTTTCGG
CGGGGGAACAAAACTGACCGTCCTG [SEQ ID NO. 58]

B6 clone

>B6_aa_L

QSVLTQPPSASGTPGQRVTISCSGSSSNIKFNSVNWYQQLPGTAPKLLIYSNNQRPSGVPD
RFSGSKSGTSASLAISGLQSEDEADYYCASWDDYLRGTVFGGGTKLTVL [SEQ ID NO. 3]

>B6_ntd_L

CAGTCTGTGCTGACTCAGCCCCCCTCAGCGTCCGGGACCCCCGGGCAGAGGGTCACCATCT
CTTGTTCTGGAAGCAGCTCCAACATCAAATTTAACAGTGTTAACTGGTATCAGCAACTCCC
AGGAACGGCCCCCAAACTCCTCATCTATAGTAATAATCAGCGACCCTCAGGGGTCCCTGAC
CGATTCTCTGGCTCCAAGTCTGGCACTTCAGCCTCCCTGGCCATCAGTGGGCTCCAGTCTG
AGGATGAGGCTGATTATTACTGTGCTTCTTGGGATGATTATCTTCGTGGAACTGTTTTCGG
CGGAGGGACCAAGCTGACCGTCCTG [SEQ ID NO. 59]

B6 codon-optimised clone (no modifications of the amino-acid sequence)

>B6_optimised_ntd_L

CAGAGCGTGCTGACCCAGCCCCCCAGCGCCAGTGGAACACCCGGACAGAGAGTGACCATCA
GTTGCTCAGGCAGCTCCTCTAACATTAAGTTCAACTCTGTGAATTGGTATCAGCAGCTGCC
CGGAACTGCTCCTAAACTGCTGATCTATTCTAACAATCAGCGACCAAGTGGCGTCCCCGAC
CGGTTCAGCGGCTCCAAGTCTGGGACCAGTGCCTCACTGGCTATTAGCGGGCTCCAGTCCG
AGGACGAAGCAGATTACTATTGTGCCAGCTGGGACGATTACCTGAGGGGCACCGTGTTCGG
AGGAGGAACAAAACTGACCGTCCTG [SEQ ID NO. 60]

Figure 4 (cont.)

C4 clone

>C4_aa_L

QSVLTQPPSASGTPGQRVTISCSGSSSNIKFNSVNWYQQLPGTAPKLLIYSNNQRPSGVPD
RFSGSKSGTSASLAISGLQSEDEADYYCSAWDDYLHGTVFGGGTKLTVL [SEQ ID NO.
4]

>C4_ntd_L

CAGTCTGTGCTGACTCAGCCCCCCTCAGCGTCCGGGACCCCCGGGCAGAGGGTCACCATCT
CTTGTTCTGGAAGCAGCTCCAACATCAAATTTAACAGTGTTAACTGGTATCAGCAACTCCC
AGGAACGGCCCCCAAACTCCTCATCTATAGTAATAATCAGCGACCCTCAGGGGTCCCTGAC
CGATTCTCTGGCTCCAAGTCTGGCACTTCAGCCTCCCTGGCCATCAGTGGGCTCCAGTCTG
AGGATGAGGCTGATTATTACTGTTCTGCTTGGGATGATTATCTTCATGGAACTGTGTTCGG
CGGAGGGACCAAGCTGACCGTCCTG [SEQ ID NO. 61]

C4 codon-optimised clone (no modifications of the amino-acid sequence)

>C4_optimised_ntd_L

CAGAGCGTCCTGACACAGCCCCCTTCCGCAAGTGGAACCCCTGGGCAGCGAGTGACTATTT
CATGCAGTGGATCTTCATCTAACATCAAGTTCAACTCCGTGAATTGGTATCAGCAGCTGCC
CGGAACTGCTCCTAAACTGCTGATCTATTCTAACAATCAGCGACCAAGTGGCGTCCCCGAC
CGGTTCAGCGGCTCCAAGTCTGGGACCAGTGCCTCACTGGCTATTAGCGGGCTCCAGTCCG
AGGACGAAGCAGATTACTATTGCAGCGCCTGGGACGATTACCTGCACGGCACCGTGTTCGG
AGGAGGAACAAAACTGACCGTCCTG [SEQ ID NO. 62]

D4 clone

>D4_aa_L

QSVLTQPPSASGTPGQRVTISCSGSSSNIKFNSVNWYQQLPGTAPKLLIYSNNQRPSGVPD
RFSGSKSGTSASLAISGLQSEDEADYYCASWDDYVRGTMFGGGTKLTVL [SEQ ID NO.
5]

>D4_ntd_L

CAGTCTGTGCTGACTCAGCCCCCCTCAGCGTCCGGGACCCCCGGGCAGAGGGTCACCATCT
CTTGTTCTGGAAGCAGCTCCAACATCAAATTTAACAGTGTTAACTGGTATCAGCAACTCCC
AGGAACGGCCCCCAAACTCCTCATCTATAGTAATAATCAGCGACCCTCAGGGGTCCCTGAC
CGATTCTCTGGCTCCAAGTCTGGCACTTCAGCCTCCCTGGCCATCAGTGGGCTCCAGTCTG
AGGATGAGGCTGATTATTACTGTGCTTCTTGGGATGATTATGTTCGTGGAACTATGTTCGG
CGGAGGGACCAAGCTGACCGTCCTG [SEQ ID NO. 63]

Figure 4 (cont.)

E1 clone

>E1_aa_L

QSVLTQPPSASGTPGQRVTISCSGSSSNIKFNSVNWYQQLPGTAPKLLIYSNNQRPSGVPD
RFSGSKSGTSASLAISGLQSEDEADYYCSSWDDFLRGTVFGGGTKLTVL [SEQ ID NO.
6]

>E1_ntd_L

CAGTCTGTGCTGACTCAGCCCCCCTCAGCGTCCGGGACCCCCGGGCAGAGGGTCACCATCT
CTTGTTCTGGAAGCAGCTCCAACATCAAATTTAACAGTGTTAACTGGTATCAGCAACTCCC
AGGAACGGCCCCCAAACTCCTCATCTATAGTAATAATCAGCGACCCTCAGGGGTCCCTGAC
CGATTCTCTGGCTCCAAGTCTGGCACTTCAGCCTCCCTGGCCATCAGTGGGCTCCAGTCTG
AGGATGAGGCTGATTATTACTGTTCTTCTTGGGATGATTTTCTTCGTGGAACTGTTTTCGG
CGGAGGGACCAAGCTGACCGTCCTG [SEQ ID NO. 64]

F2 clone

>F2_aa_L

QSVLTQPPSASGTPGQRVTISCSGSSSNIKFNSVNWYQQLPGTAPKLLIYSNNQRPSGVPD
RFSGSKSGTSASLAISGLQSEDEADYYCSSWDDDARGTIFGGGTKLTVL [SEQ ID NO.
7]

>F2_ntd_L

CAGTCTGTGCTGACTCAGCCCCCCTCAGCGTCCGGGACCCCCGGGCAGAGGGTCACCATCT
CTTGTTCTGGAAGCAGCTCCAACATCAAATTTAACAGTGTTAACTGGTATCAGCAACTCCC
AGGAACGGCCCCCAAACTCCTCATCTATAGTAATAATCAGCGACCCTCAGGGGTCCCTGAC
CGATTCTCTGGCTCCAAGTCTGGCACTTCAGCCTCCCTGGCCATCAGTGGGCTCCAGTCTG
AGGATGAGGCTGATTATTACTGTTCTTCTTGGGATGATGATGCTCGTGGAACTATTTTCGG
CGGAGGGACCAAGCTGACCGTCCTG [SEQ ID NO. 65]

Figure 4 (cont.)

G1 clone

>G1_aa_L

QSVLTQPPSASGTPGQRVTISCSGSSSNIKFNSVNWYQQLPGTAPKLLIYSNNQRPSGVPD
RFSGSKSGTSASLAISGLQSEDEADYYCAAWDDVYYGTIFGGGTKLTVL [SEQ ID NO.
8]

>G1_ntd_L

CAGTCTGTGCTGACTCAGCCCCCCTCAGCGTCCGGGACCCCCGGGCAGAGGGTCACCATCT
CTTGTTCTGGAAGCAGCTCCAACATCAAATTTAACAGTGTTAACTGGTATCAGCAACTCCC
AGGAACGGCCCCCAAACTCCTCATCTATAGTAATAATCAGCGACCCTCAGGGGTCCCTGAC
CGATTCTCTGGCTCCAAGTCTGGCACTTCAGCCTCCCTGGCCATCAGTGGGCTCCAGTCTG
AGGATGAGGCTGATTATTACTGTGCTGCTTGGGATGATGTTTATTATGGAACTATTTTCGG
CGGAGGGACCAAGCTGACCGTCCTG [SEQ ID NO. 66]

G2 clone

>G2_aa_L

QSVLTQPPSASGTPGQRVTISCSGSSSNIKFNSVNWYQQLPGTAPKLLIYSNNQRPSGVPD
RFSGSKSGTSASLAISGLQSEDEADYYCASWDDSLYGTVFGGGTKLTVL [SEQ ID NO.
9]

>G2_ntd_L

CAGTCTGTGCTGACTCAGCCCCCCTCAGCGTCCGGGACCCCCGGGCAGAGGGTCACCATCT
CTTGTTCTGGAAGCAGCTCCAACATCAAATTTAACAGTGTTAACTGGTATCAGCAACTCCC
AGGAACGGCCCCCAAACTCCTCATCTATAGTAATAATCAGCGACCCTCAGGGGTCCCTGAC
CGATTCTCTGGCTCCAAGTCTGGCACTTCAGCCTCCCTGGCCATCAGTGGGCTCCAGTCTG
AGGATGAGGCTGATTATTACTGTGCTTCTTGGGATGATTCTCTTTATGGAACTGTTTTCGG
CGGAGGGACCAAGCTGACCGTCCTG [SEQ ID NO. 67]

Figure 4 (cont.)

G10 clone

>G10_aa_L

QSVLTQPPSASGTPGQRVTISCSGSSSNIKFNSVNWYQQLPGTAPKLLIYSNNQRPSGVPD
RFSGSKSGTSASLAISGLQSEDEADYYCAAWDDAYYGTIFGGGTKLTVL [SEQ ID NO.
10]

>G10_ntd_L

CAGTCTGTGCTGACTCAGCCCCCCTCAGCGTCCGGGACCCCCGGGCAGAGGGTCACCATCT
CTTGTTCTGGAAGCAGCTCCAACATCAAATTTAACAGTGTTAACTGGTATCAGCAACTCCC
AGGAACGGCCCCCAAACTCCTCATCTATAGTAATAATCAGCGACCCTCAGGGGTCCCTGAC
CGATTCTCTGGCTCCAAGTCTGGCACTTCAGCCTCCCTGGCCATCAGTGGGCTCCAGTCTG
AGGATGAGGCTGATTATTACTGTGCTGCTTGGGATGATGCTTATTATGGAACTATTTTCGG
CGGAGGGACCAAGCTGACCGTCCTG [SEQ ID NO. 68]

H4 clone

>H4_aa_L

QSVLTQPPSASGTPGQRVTISCSGSSSNIKFNSVNWYQQLPGTAPKLLIYSNNQRPSGVPD
RFSGSKSGTSASLAISGLQSEDEADYYCASWDDVYRGTVFGGGTKLTVL [SEQ ID NO.
11]

>H4_ntd_L

CAGTCTGTGCTGACTCAGCCCCCCTCAGCGTCCGGGACCCCCGGGCAGAGGGTCACCATCT
CTTGTTCTGGAAGCAGCTCCAACATCAAATTTAACAGTGTTAACTGGTATCAGCAACTCCC
AGGAACGGCCCCCAAACTCCTCATCTATAGTAATAATCAGCGACCCTCAGGGGTCCCTGAC
CGATTCTCTGGCTCCAAGTCTGGCACTTCAGCCTCCCTGGCCATCAGTGGGCTCCAGTCTG
AGGATGAGGCTGATTATTACTGTGCTTCTTGGGATGATGTTTATCGTGGAACTGTTTTCGG
CGGAGGGACCAAGCTGACCGTCCTG [SEQ ID NO. 69]

Figure 4 (cont.)

H4 codon-optimised clone (no modifications of the amino-acid sequence)

>H4_optimised_ntd_L

CAGAGCGTCCTGACACAGCCCCCAAGCGCAAGCGGAACCCCCGGCCAGCGAGTGACCATTA
GTTGTAGTGGAAGTAGTAGTAACATCAAGTTCAACTCCGTGAATTGGTATCAGCAGCTGCC
CGGAACTGCTCCTAAACTGCTGATCTATTCTAACAATCAGCGACCAAGTGGCGTCCCCGAC
CGGTTCAGCGGCTCCAAGTCTGGGACCAGTGCCTCACTGGCTATTAGCGGGCTCCAGTCCG
AGGACGAAGCAGATTACTATTGCGCCAGCTGGGACGATGTGTACAGGGGCACCGTCTTCGG
CGGGGGAACAAAACTGACCGTCCTG [SEQ ID NO. 70]

H9 clone

>H9_aa_L

QSVLTQPPSASGTPGQRVTISCSGSSSNIKFNSVNWYQQLPGTAPKLLIYSNNQRPSGVPD
RFSGSKSGTSASLAISGLQSEDEADYYCSSWDDSLYGTIFGGGTKLTVL [SEQ ID NO.
12]

>H9_ntd_L

CAGTCTGTGCTGACTCAGCCCCCCTCAGCGTCCGGGACCCCCGGGCAGAGGGTCACCATCT
CTTGTTCTGGAAGCAGCTCCAACATCAAATTTAACAGTGTTAACTGGTATCAGCAACTCCC
AGGAACGGCCCCCAAACTCCTCATCTATAGTAATAATCAGCGACCCTCAGGGGTCCCTGAC
CGATTCTCTGGCTCCAAGTCTGGCACTTCAGCCTCCCTGGCCATCAGTGGGCTCCAGTCTG
AGGATGAGGCTGATTATTACTGTTCTTCTTGGGATGATTCTCTTTATGGAACTATTTTCGG
CGGAGGGACCAAGCTGACCGTCCTG [SEQ ID NO. 71]

Figure 4 (cont.)

Heavy chain variable domains

A3 clone

>A3_aa_H

QVQLVQSGGGVVQPGRSLRLSCAASGFTFSSYGMHWVRQAPGKGLEWVAVISYDGSNKYYA
DSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCASDLGAGPYYYGKDHWGQGTTVTVSS
[SEQ ID NO. 13]

>A3_ntd_H

CAGGTCCAGCTGGTGCAGTCCGGGGGAGGCGTGGTCCAGCCTGGGCGGTCCCTGAGACTCT
CCTGTGCAGCCTCTGGATTCACCTTCAGTAGCTATGGCATGCACTGGGTCCGCCAGGCTCC
AGGCAAGGGGCTGGAGTGGGTGGCAGTTATATCATATGATGGAAGTAATAAATACTACGCA
GACTCCGTGAAGGGCCGATTCACCATCTCCAGAGACAATTCCAAGAACACGCTGTATCTGC
AAATGAACAGCCTGAGAGCCGAGGACACGGCTGTGTATTACTGTGCGAGTGATCTTGGTGC
TGGTCCTTATTATTATGGTAAGGATCATTGGGGCCAAGGGACCACGGTCACCGTCTCAAGC
[SEQ ID NO. 72]

A10 clone

>A10_aa_H

QVQLVQSGGGVVQPGRSLRLSCAASGFTFSSYGMHWVRQAPGKGLEWVAVISYDGSNKYYA
DSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCASDLGAGPYYYGKDVWGQGTTVTVSS
[SEQ ID NO. 14]

>A10_ntd_H

CAGGTCCAGCTGGTGCAGTCTGGGGGAGGCGTGGTCCAGCCTGGGCGGTCCCTGAGACTCT
CCTGTGCAGCCTCTGGATTCACCTTCAGTAGCTATGGCATGCACTGGGTCCGCCAGGCTCC
AGGCAAGGGGCTGGAGTGGGTGGCAGTTATATCATATGATGGAAGTAATAAATACTACGCA
GACTCCGTGAAGGGCCGATTCACCATCTCCAGAGACAATTCCAAGAACACGCTGTATCTGC
AAATGAACAGCCTGAGAGCCGAGGACACGGCTGTGTATTACTGTGCGAGTGATCTTGGTGC
TGGTCCTTATTATTATGGTAAGGATGTTTGGGGCCAAGGGACCACGGTCACCGTCTCAAGC
[SEQ ID NO. 73]

Figure 4 (cont.)

A10 codon-optimised clone (induced modifications in the amino-acid sequence)

>A10_optimised_aa_H

QVQLVESGGGVVQPGRSLRLSCAASGFTFSSYGMHWVRQAPGKGLEWVAVISYDGSNKYYA
DSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCASDLGAGPYYYGKDVWGQGTTVTVSS
[SEQ ID NO. 74]

>A10_optimised_ntd_H

CAGGTGCAGCTGGTCGAATCCGGGGGGGGGGTGGTGCAGCCTGGACGGTCACTGAGACTGA
GTTGTGCCGCCTCTGGGTTTACTTTCAGCTCCTATGGCATGCACTGGGTGAGGCAGGCTCC
CGGCAAGGGGCTGGAGTGGGTGGCAGTCATCTCTTACGACGGCAGTAACAAGTACTATGCC
GATAGCGTCAAAGGGCGGTTCACTATTTCAAGAGACAACAGCAAAAATACCCTGTACCTCC
AGATGAACAGCCTGCGGGCCGAAGACACAGCTGTGTACTATTGCGCATCTGATCTGGGAGC
CGGCCCTTACTATTACGGCAAGGATGTCTGGGGGCAGGGAACCACAGTCACCGTCTCAAGC
[SEQ ID NO. 75]

B6 clone

>B6_aa_H

QVQLVESGGGVVQPGRSLRLSCAASGFTFSSYGMHWVRQAPGKGLEWVAVISYDGSNKYYA
DSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCASDYGAGPYYYGMDVWGQGTTVTVSS
[SEQ ID NO. 15]

>B6_ntd_H

CAGGTCCAGCTGGTAGAGTCCGGGGGAGGCGTGGTCCAGCCTGGGCGGTCCCTGAGACTCT
CCTGTGCAGCCTCTGGATTCACCTTCAGTAGCTATGGCATGCACTGGGTCCGCCAGGCTCC
AGGCAAGGGGCTGGAGTGGGTGGCAGTTATATCATATGATGGAAGTAATAAATACTACGCA
GACTCCGTGAAGGGCCGATTCACCATCTCCAGAGACAATTCCAAGAACACGCTGTATCTGC
AAATGAACAGCCTGAGAGCCGAGGACACGGCTGTGTATTACTGTGCGAGTGATTATGGTGC
TGGTCCTTATTATTATGGTATGGATGTTTGGGGCCAAGGGACCACGGTCACCGTCTCAAGC
[SEQ ID NO. 76]

Figure 4 (cont.)

B6 codon-optimised clone (no modifications in the amino-acid sequence)

>B6_optimised_ntd_H

CAGGTGCAGCTGGTGGAAAGCGGGGGGGGCGTGGTGCAGCCTGGAAGGTCACTGAGACTGT
CTTGTGCCGCATCTGGGTTTACATTTAGCTCCTATGGCATGCACTGGGTGAGGCAGGCTCC
CGGCAAGGGGCTGGAGTGGGTGGCAGTCATCTCTTACGACGGCAGTAACAAGTACTATGCC
GATAGCGTCAAAGGGCGGTTCACTATTTCAAGAGACAACAGCAAAAATACCCTGTACCTCC
AGATGAACAGCCTGCGGGCCGAAGACACAGCTGTGTACTATTGCGCATCTGATTACGGAGC
CGGCCCTTACTATTACGGCATGGATGTCTGGGGGCAGGGAACCACAGTCACCGTCTCAAGC
[SEQ ID NO. 77]

C4 clone

>C4_aa_H

QVQLVESGGGVVQPGRSLRLSCAASGFTFSSYGMHWVRQAPGKGLEWVAVISYDGSNKYYA
DSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCASDLGAGPYYYGLDVWGQGTTVTVSS
[SEQ ID NO. 16]

>C4_ntd_H

CAGGTCCAGCTGGTAGAGTCCGGGGGAGGCGTGGTCCAGCCTGGGCGGTCCCTGAGACTCT
CCTGTGCAGCCTCTGGATTCACCTTCAGTAGCTATGGCATGCACTGGGTCCGCCAGGCTCC
AGGCAAGGGGCTGGAGTGGGTGGCAGTTATATCATATGATGGAAGTAATAAATACTACGCA
GACTCCGTGAAGGGCCGATTCACCATCTCCAGAGACAATTCCAAGAACACGCTGTATCTGC
AAATGAACAGCCTGAGAGCCGAGGACACGGCTGTGTATTACTGTGCGAGTGATCTTGGTGC
TGGTCCTTATTATTATGGTTTGGATGTTTGGGGCCAAGGGACCACGGTCACCGTCTCAAGC
[SEQ ID NO. 78]

C4 codon-optimised clone (no modifications in the amino-acid sequence)

>C4_optimised_ntd_H

CAGGTGCAGCTGGTGGAATCTGGGGGGGGGGTCGTGCAGCCCGGACGGTCACTGAGACTGT
CATGTGCCGCTTCAGGGTTTACTTTTAGCTCCTATGGCATGCACTGGGTGAGGCAGGCTCC
CGGCAAGGGGCTGGAGTGGGTGGCAGTCATCTCTTACGACGGCAGTAACAAGTACTATGCC
GATAGCGTCAAAGGGCGGTTCACTATTTCAAGAGACAACAGCAAAAATACCCTGTACCTCC
AGATGAACAGCCTGCGGGCCGAAGACACAGCTGTGTACTATTGCGCATCTGATCTGGGAGC
CGGCCCTTACTATTACGGCCTGGATGTCTGGGGGCAGGGAACCACAGTCACCGTCTCAAGC
[SEQ ID NO. 79]

Figure 4 (cont.)

D4 clone

>D4_aa_H

QVQLVESGGGVVQPGRSLRLSCAASGFTFSSYGMHWVRQAPGKGLEWVAVISYDGSNKYYA
DSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCASDLGAGPYYYGMDVWGQGTTVTVSS
[SEQ ID NO. 17]

>D4_ntd_H

CAGGTCCAGCTGGTAGAGTCCGGGGGAGGCGTGGTCCAGCCTGGGCGGTCCCTGAGACTCT
CCTGTGCAGCCTCTGGATTCACCTTCAGTAGCTATGGCATGCACTGGGTCCGCCAGGCTCC
AGGCAAGGGGCTGGAGTGGGTGGCAGTTATATCATATGATGGAAGTAATAAATACTACGCA
GACTCCGTGAAGGGCCGATTCACCATCTCCAGAGACAATTCCAAGAACACGCTGTATCTGC
AAATGAACAGCCTGAGAGCCGAGGACACGGCTGTGTATTACTGTGCGAGTGATCTTGGTGC
TGGTCCTTATTATTATGGTATGGATGTTTGGGGCCAAGGGACCACGGTCACCGTCTCAAGC
[SEQ ID NO. 80]

E1 clone

>E1_aa_H

QVQLVESGGGVVQPGRSLRLSCAASGFTFSSYGMHWVRQAPGKGLEWVAVISYDGSNKYYA
DSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCASDLGAGPYYYGMDVWGQGTTVTVSS
[SEQ ID NO. 18]

>E1_ntd_H

CAGGTCCAGCTGGTAGAGTCCGGGGGAGGCGTGGTCCAGCCTGGGCGGTCCCTGAGACTCT
CCTGTGCAGCCTCTGGATTCACCTTCAGTAGCTATGGCATGCACTGGGTCCGCCAGGCTCC
AGGCAAGGGGCTGGAGTGGGTGGCAGTTATATCATATGATGGAAGTAATAAATACTACGCA
GACTCCGTGAAGGGCCGATTCACCATCTCCAGAGACAATTCCAAGAACACGCTGTATCTGC
AAATGAACAGCCTGAGAGCCGAGGACACGGCTGTGTATTACTGTGCGAGTGATCTTGGTGC
TGGTCCTTATTATTATGGTATGGATGTTTGGGGCCAAGGGACCACGGTCACCGTCTCAAGC
[SEQ ID NO. 81]

Figure 4 (cont.)

F2 clone

>F2_aa_H

QVQLVESGGGVVQPGRSLRLSCAASGFTFSSYGMHWVRQAPGKGLEWVAVISYDGSNKYYA
DSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCASDLGAGPYYYGMDVWGQGTTVTVSS
[SEQ ID NO. 19]

>F2_ntd_H

CAGGTCCAGCTGGTAGAGTCCGGGGGAGGCGTGGTCCAGCCTGGGCGGTCCCTGAGACTCT
CCTGTGCAGCCTCTGGATTCACCTTCAGTAGCTATGGCATGCACTGGGTCCGCCAGGCTCC
AGGCAAGGGGCTGGAGTGGGTGGCAGTTATATCATATGATGGAAGTAATAAATACTACGCA
GACTCCGTGAAGGGCCGATTCACCATCTCCAGAGACAATTCCAAGAACACGCTGTATCTGC
AAATGAACAGCCTGAGAGCCGAGGACACGGCTGTGTATTACTGTGCGAGTGATCTTGGTGC
TGGTCCTTATTATTATGGTATGGATGTTTGGGGCCAAGGGACCACGGTCACCGTCTCAAGC
[SEQ ID NO. 82]

G1 clone

>G1_aa_H

QVQLVESGGGVVQPGRSLRLSCAASGFTFSSYGMHWVRQAPGKGLEWVAVISYDGSNKYYA
DSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCASDLGAGPYYYGMDVWGQGTTVTVSS
[SEQ ID NO. 20]

>G1_ntd_H

CAGGTCCAGCTGGTAGAGTCCGGGGGAGGCGTGGTCCAGCCTGGGCGGTCCCTGAGACTCT
CCTGTGCAGCCTCTGGATTCACCTTCAGTAGCTATGGCATGCACTGGGTCCGCCAGGCTCC
AGGCAAGGGGCTGGAGTGGGTGGCAGTTATATCATATGATGGAAGTAATAAATACTACGCA
GACTCCGTGAAGGGCCGATTCACCATCTCCAGAGACAATTCCAAGAACACGCTGTATCTGC
AAATGAACAGCCTGAGAGCCGAGGACACGGCTGTGTATTACTGTGCGAGTGATCTTGGTGC
TGGTCCTTATTATTATGGTATGGATGTTTGGGGCCAAGGGACCACGGTCACCGTCTCAAGC
[SEQ ID NO. 83]

Figure 4 (cont.)

G2 clone

>G2_aa_H

QVQLVESGGGVVQPGRSLRLSCAASGFTFSSYGMHWVRQAPGKGLEWVAVISYDGSNKYYA
DSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCASDLGAGPYYYGMDVWGQGTTVTVSS
[SEQ ID NO. 21]

>G2_ntd_H

CAGGTCCAGCTGGTAGAGTCCGGGGGAGGCGTGGTCCAGCCTGGGCGGTCCCTGAGACTCT
CCTGTGCAGCCTCTGGATTCACCTTCAGTAGCTATGGCATGCACTGGGTCCGCCAGGCTCC
AGGCAAGGGGCTGGAGTGGGTGGCAGTTATATCATATGATGGAAGTAATAAATACTACGCA
GACTCCGTGAAGGGCCGATTCACCATCTCCAGAGACAATTCCAAGAACACGCTGTATCTGC
AAATGAACAGCCTGAGAGCCGAGGACACGGCTGTGTATTACTGTGCGAGTGATCTTGGTGC
TGGTCCTTATTATTATGGTATGGATGTTTGGGGCCAAGGGACCACGGTCACCGTCTCAAGC
[SEQ ID NO. 84]

G10 clone

>G10_aa_H

QVQLVESGGGVVQPGRSLRLSCAASGFTFSSYGMHWVRQAPGKGLEWVAVISYDGSNKYYA
DSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCASDYGAGPYYYGMDVWGQGTTVTVSS
[SEQ ID NO. 22]

>G10_ntd_H

CAGGTCCAGCTGGTAGAGTCCGGGGGAGGCGTGGTCCAGCCTGGGCGGTCCCTGAGACTCT
CCTGTGCAGCCTCTGGATTCACCTTCAGTAGCTATGGCATGCACTGGGTCCGCCAGGCTCC
AGGCAAGGGGCTGGAGTGGGTGGCAGTTATATCATATGATGGAAGTAATAAATACTACGCA
GACTCCGTGAAGGGCCGATTCACCATCTCCAGAGACAATTCCAAGAACACGCTGTATCTGC
AAATGAACAGCCTGAGAGCCGAGGACACGGCTGTGTATTACTGTGCGAGTGATTATGGTGC
TGGTCCTTATTATTATGGTATGGATGTTTGGGGCCAAGGGACCACGGTCACCGTCTCAAGC
[SEQ ID NO. 85]

Figure 4 (cont.)

H4 clone

>H4_aa_H

QVQLVESGGGVVQPGRSLRLSCAASGFTFSSYGMHWVRQAPGKGLEWVAVISYDGSNKYYA
DSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCASDLGSGYYLYGMDVWGQGTTVTVSS
[SEQ ID NO. 23]

>H4_ntd_H

CAGGTCCAGCTGGTAGAGTCCGGGGGAGGCGTGGTCCAGCCTGGGCGGTCCCTGAGACTCT
CCTGTGCAGCCTCTGGATTCACCTTCAGTAGCTATGGCATGCACTGGGTCCGCCAGGCTCC
AGGCAAGGGGCTGGAGTGGGTGGCAGTTATATCATATGATGGAAGTAATAAATACTACGCA
GACTCCGTGAAGGGCCGATTCACCATCTCCAGAGACAATTCCAAGAACACGCTGTATCTGC
AAATGAACAGCCTGAGAGCCGAGGACACGGCTGTGTATTACTGTGCGAGTGATCTTGGTTC
TGGTTATTATCTTTATGGTATGGACGTCTGGGGCCAAGGGACCACGGTCACCGTCTCAAGC
[SEQ ID NO. 86]

H4 codon-optimised clone (no modifications in the amino-acid sequence)

>H4_optimised_ntd_H

CAGGTGCAGCTGGTGGAGAGCGGGGGGGGGGTGGTGCAGCCTGGACGGTCACTGAGACTGA
GTTGCGCCGCATCTGGATTCACATTTAGCTCCTACGGCATGCACTGGGTGAGGCAGGCACC
CGGCAAGGGGCTGGAGTGGGTGGCCGTCATCTCTTATGACGGCAGTAACAAGTACTATGCT
GATAGCGTCAAAGGGCGGTTCACTATTTCAAGAGACAACAGCAAAAATACCCTGTACCTCC
AGATGAATAGCCTGCGGGCCGAAGACACAGCTGTGTACTATTGCGCCTCCGATCTGGGATC
TGGCTACTATCTGTATGGCATGGATGTCTGGGGGCAGGGAACCACAGTCACCGTCTCAAGC
[SEQ ID NO. 87]

H9 clone

>H9_aa_H

QVQLVESGGGVVQPGRSLRLSCAASGFTFSSYGMHWVRQAPGKGLEWVAVISYDGSNKYYA
DSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCASDLGAGPYYYGMDVWGQGTTVTVSS
[SEQ ID NO. 24]

>H9_ntd_H

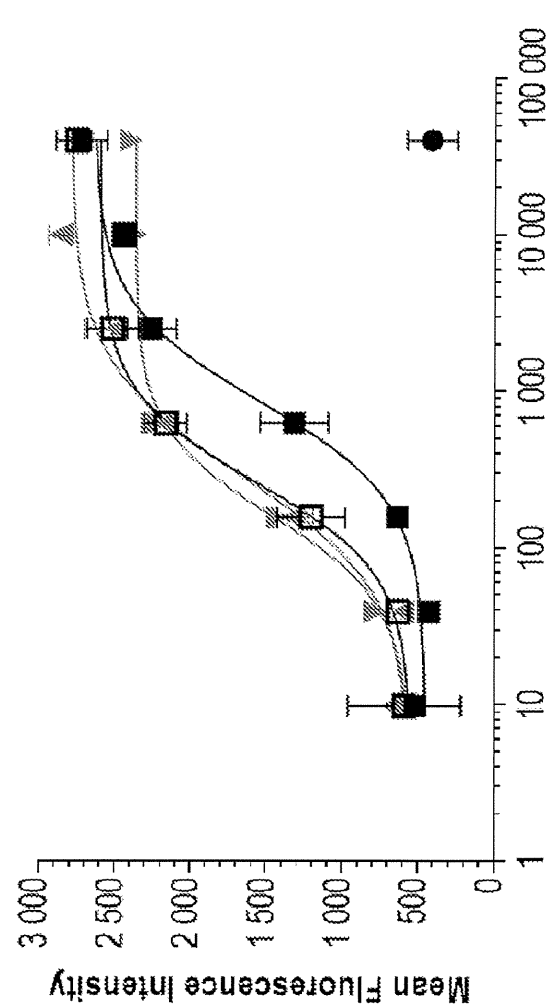
CAGGTCCAGCTGGTAGAGTCCGGGGGAGGCGTGGTCCAGCCTGGGCGGTCCCTGAGACTCT
CCTGTGCAGCCTCTGGATTCACCTTCAGTAGCTATGGCATGCACTGGGTCCGCCAGGCTCC
AGGCAAGGGGCTGGAGTGGGTGGCAGTTATATCATATGATGGAAGTAATAAATACTACGCA
GACTCCGTGAAGGGCCGATTCACCATCTCCAGAGACAATTCCAAGAACACGCTGTATCTGC
AAATGAACAGCCTGAGAGCCGAGGACACGGCTGTGTATTACTGTGCGAGTGATCTTGGTGC
TGGTCCTTATTATTATGGTATGGATGTTTGGGGCCAAGGGACCACGGTCACCGTCTCAAGC
[SEQ ID NO. 88]

Figure 4 (cont.)

Affinity

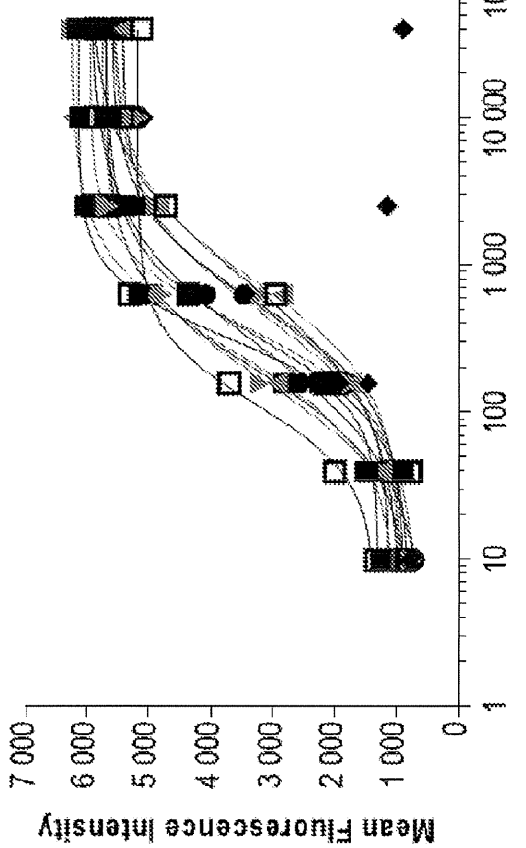
	K_D (nM)
A3	0.20
A10	0.08
B6	0.26
C4	0.40
D4	0.22
E1	0.21
F2	0.11
G1	0.10
G2	0.10
G10	0.27
H4	0.27
H9	ND
nivolumab	1.9
lambrolizumab	0.5

Figure 5



	A3-IgG4	A10-IgG4	nivolumab	lambrolizumab
EC50	854.5	262.3	287.0	160.1

Figure 6



Abs	nivolumab	lambrolizumab	A10	B6	C4	D4	E1
EC50	315.3	110	252.6	158.1	281.2	318.1	542.5

Abs	F2	G1	G2	G10	H4	H9
EC50	445.5	738.4	780	531.6	188.6	375.3

Figure 7

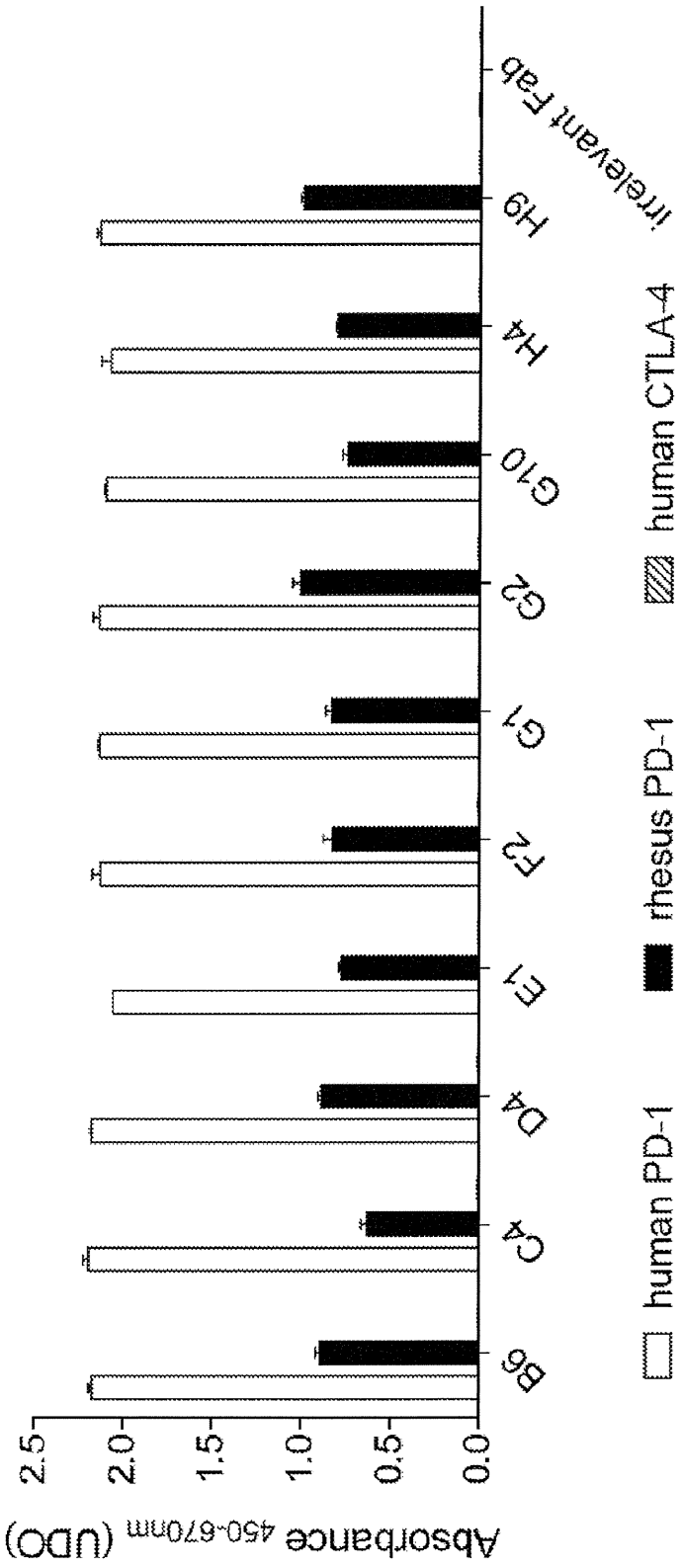

Absorbance 450-670nm (UDO)
2.5
2.0
1.5
1.0
0.5
0.0
B6
C4
D4
E1
F2
G1
G2
G10
H4
H9
irrelevant Fab
human PD-1
rhesus PD-1
human CTLA-4

Figure 8

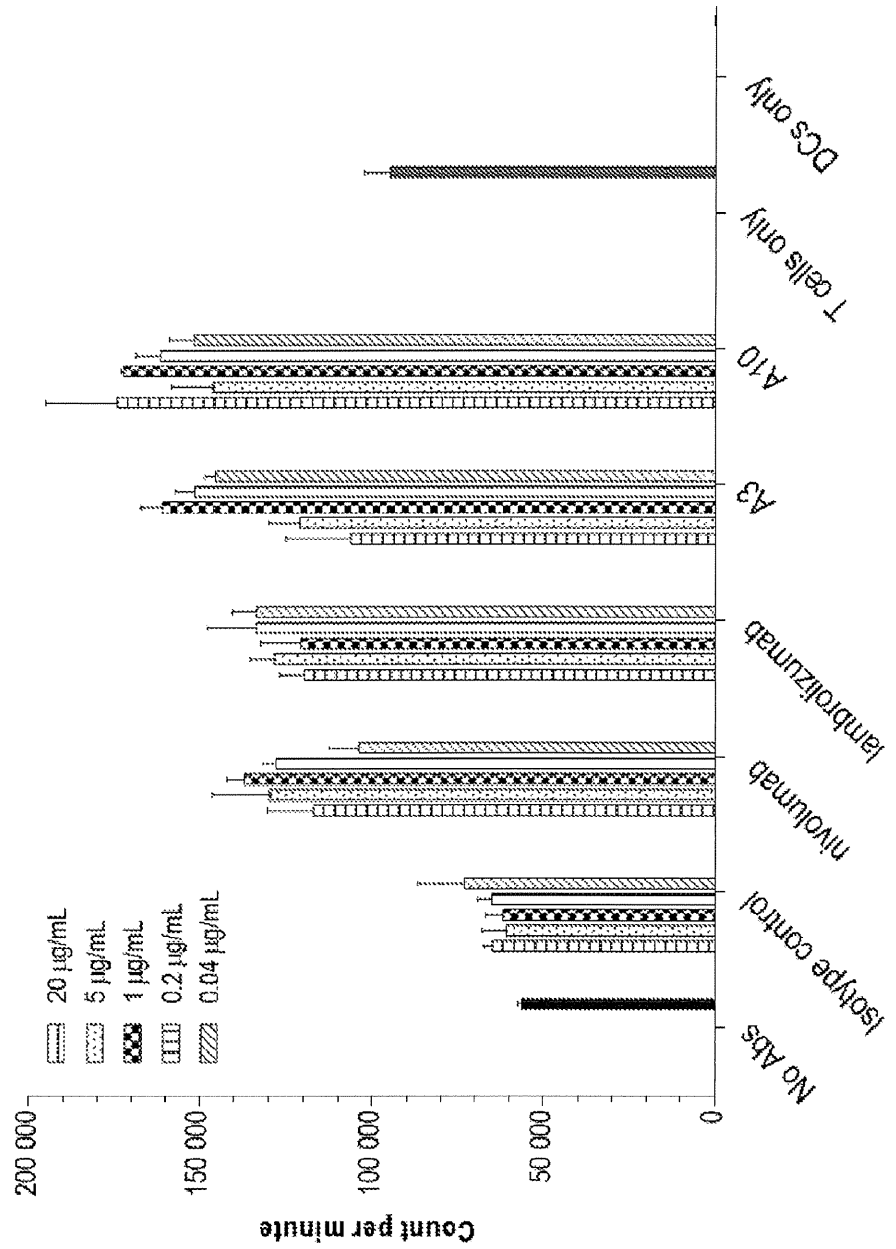

Count per minute
200 000
150 000
100 000
50 000
0
20 µg/mL
5 µg/mL
1 µg/mL
0.2 µg/mL
0.04 µg/mL
No Abs
Isotype control
nivolumab
lambrolizumab
A3
A10
T cells only
DCs only

Figure 9

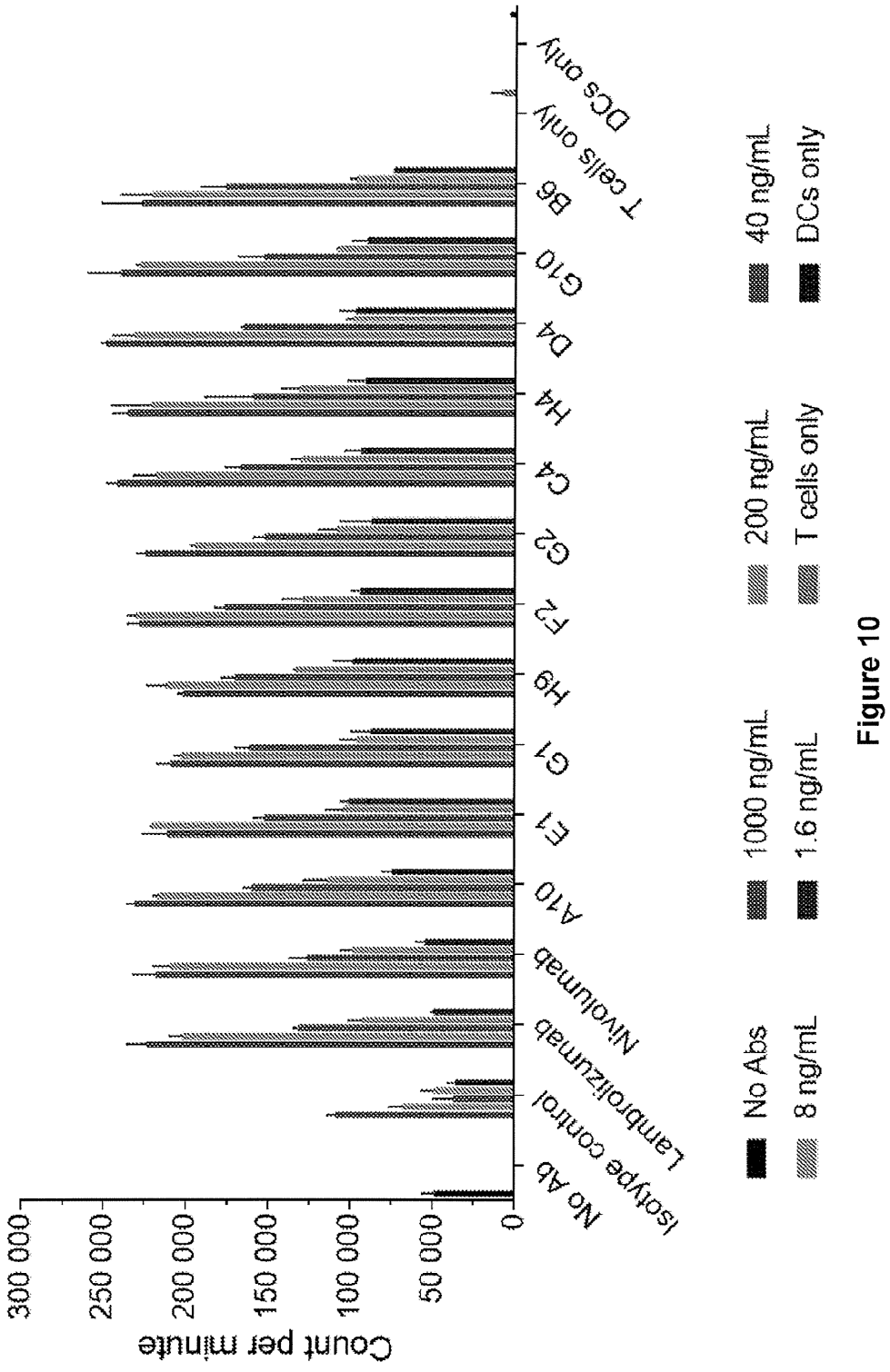
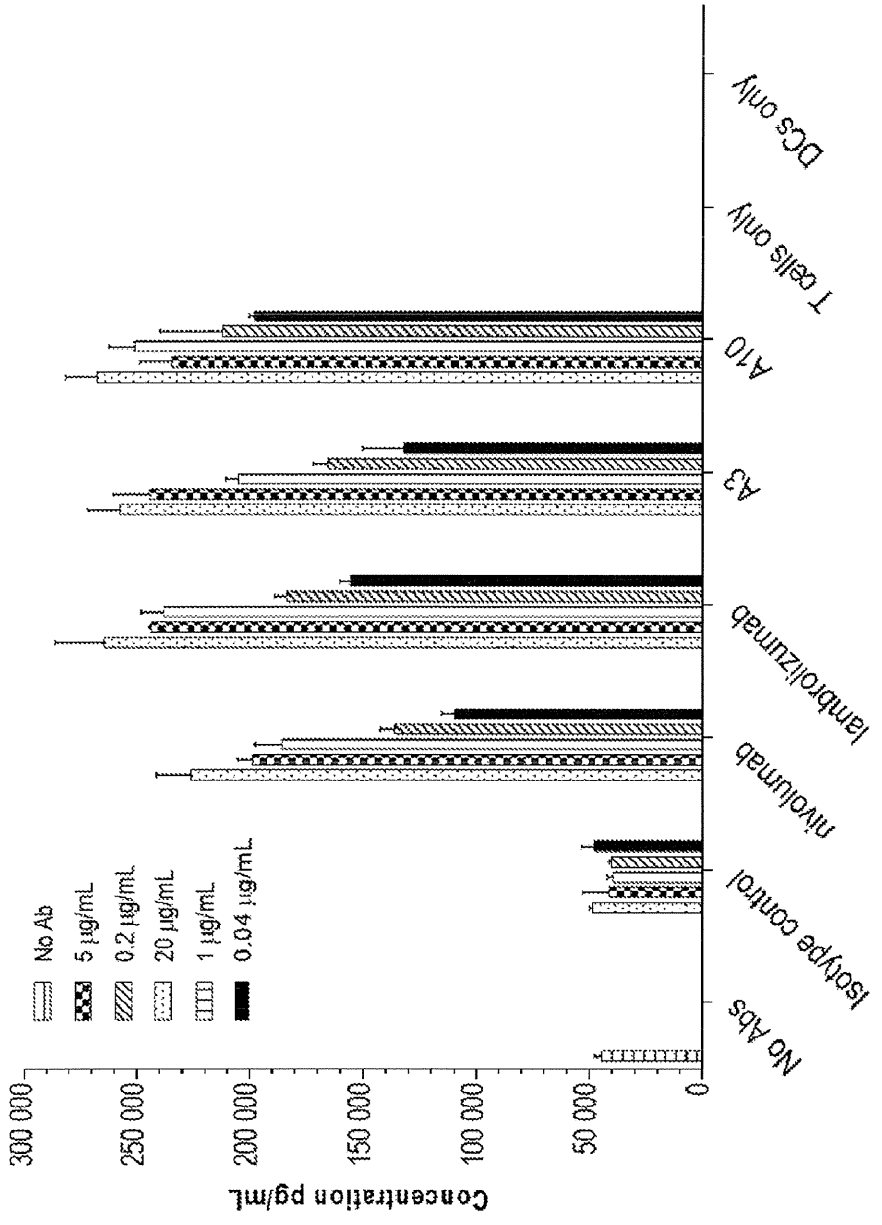

Count per minute
300 000
250 000
200 000
150 000
100 000
50 000
0
No Ab
Isotype control
Lambrolizumab
Nivolumab
A10
E1
G1
H9
F2
G2
C4
H4
D4
G10
B6
T cells only
DCs only
No Abs
8 ng/mL
1000 ng/mL
1.6 ng/mL
200 ng/mL
T cells only
40 ng/mL
DCs only

Figure 10


Concentration pg/mL
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250 000
200 000
150 000
100 000
50 000
0
No Ab
5 µg/mL
0.2 µg/mL
20 µg/mL
1 µg/mL
0.04 µg/mL
No Abs
Isotype control
nivolumab
lambrolizumab
A3
A10
T cells only
DCs only

Figure 11

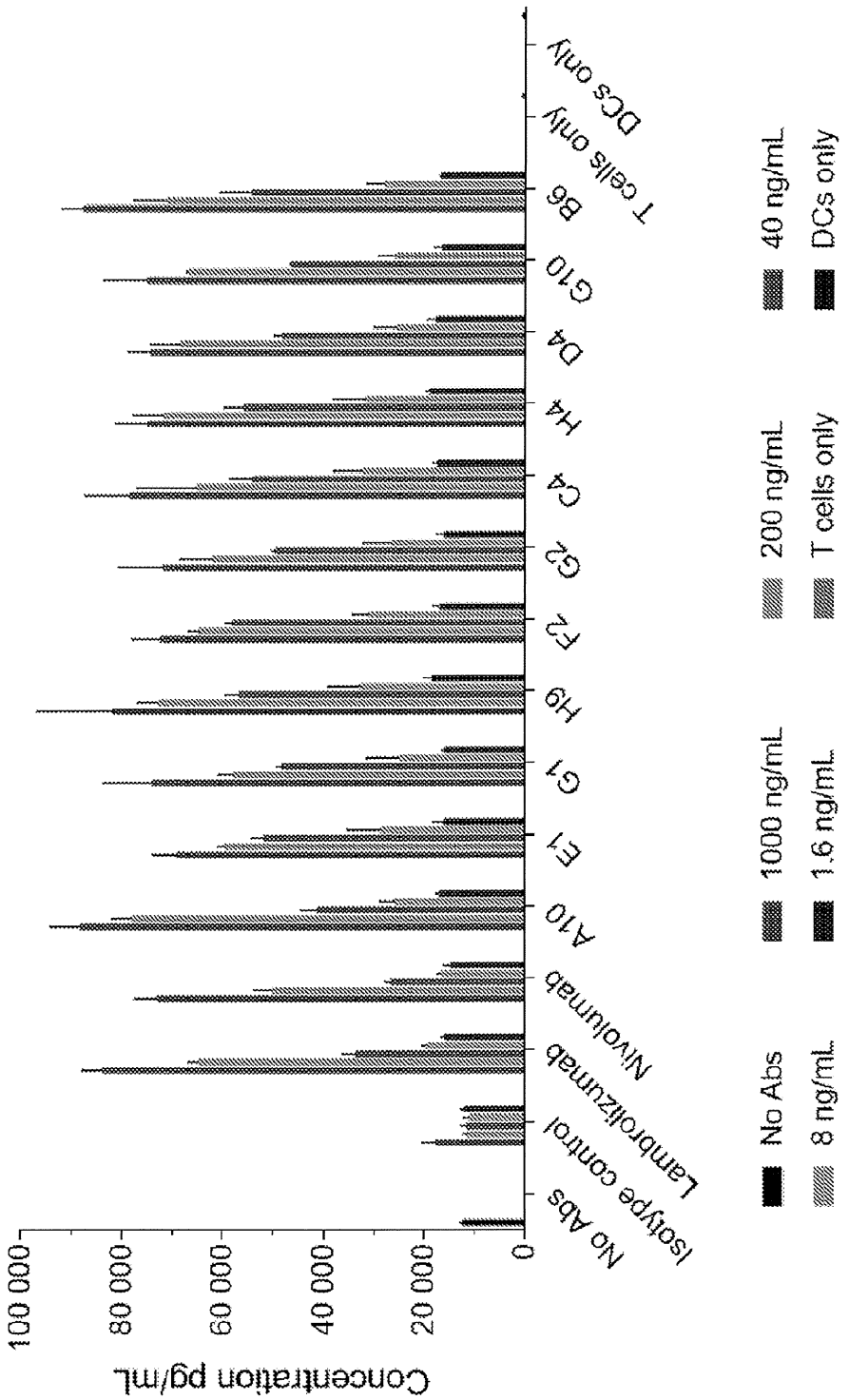
Concentration pg/mL
100 000
80 000
60 000
40 000
20 000
0
No Abs
Isotype control
Lambrolizumab
Nivolumab
A10
E1
G1
H9
F2
G2
C4
H4
D4
G10
B6
T cells only
DCs only
No Abs
8 ng/mL
1000 ng/mL
1.6 ng/mL
200 ng/mL
T cells only
40 ng/mL
DCs only

Figure 12

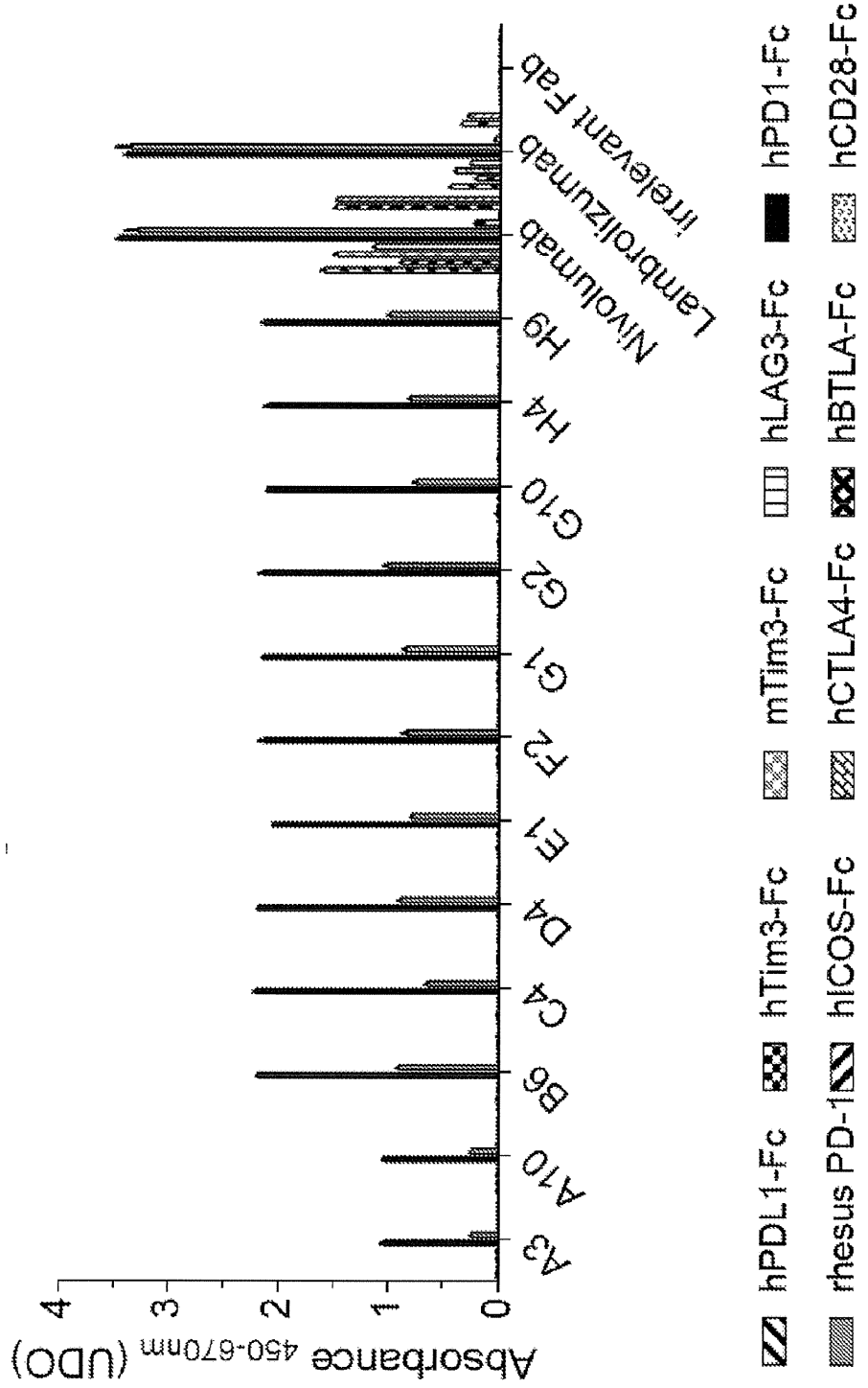
Absorbance 450-670nm (UDO)
0
1
2
3
4
A3
A10
B6
C4
D4
E1
F2
G1
G2
G10
H4
H9
Nivolumab
Lambrolizumab
Irrelevant Fab
hPDL1-Fc
hTim3-Fc
mTim3-Fc
hLAG3-Fc
hPD1-Fc
rhesus PD-1
hICOS-Fc
hCTLA4-Fc
hBTLA-Fc
hCD28-Fc

Figure 13

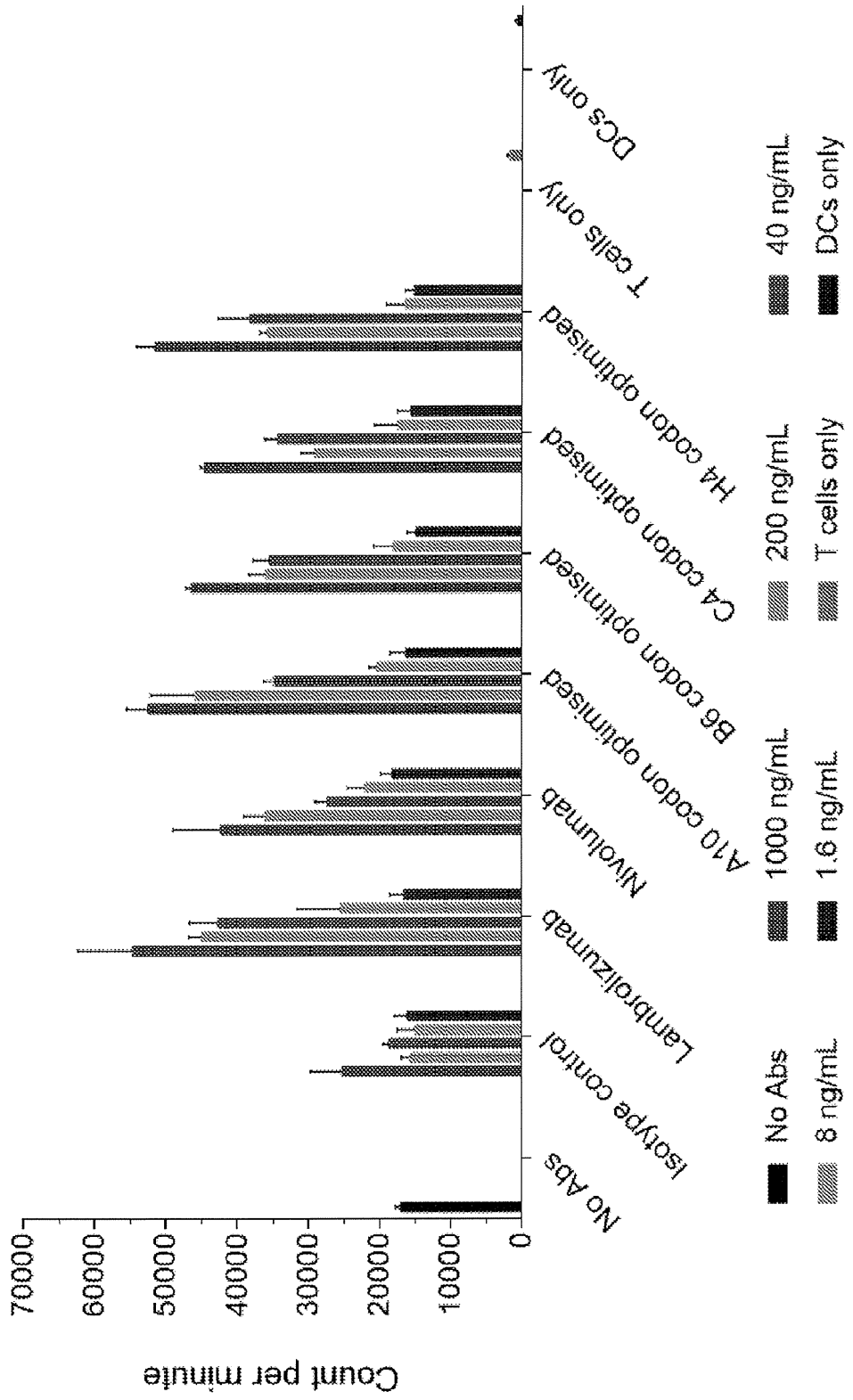
Count per minute
70000
60000
50000
40000
30000
20000
10000
0
No Abs
Isotype control
Lambrolizumab
Nivolumab
A10 codon optimised
B6 codon optimised
C4 codon optimised
H4 codon optimised
T cells only
DCs only
No Abs
8 ng/mL
1000 ng/mL
1.6 ng/mL
200 ng/mL
T cells only
40 ng/mL
DCs only

Figure 14

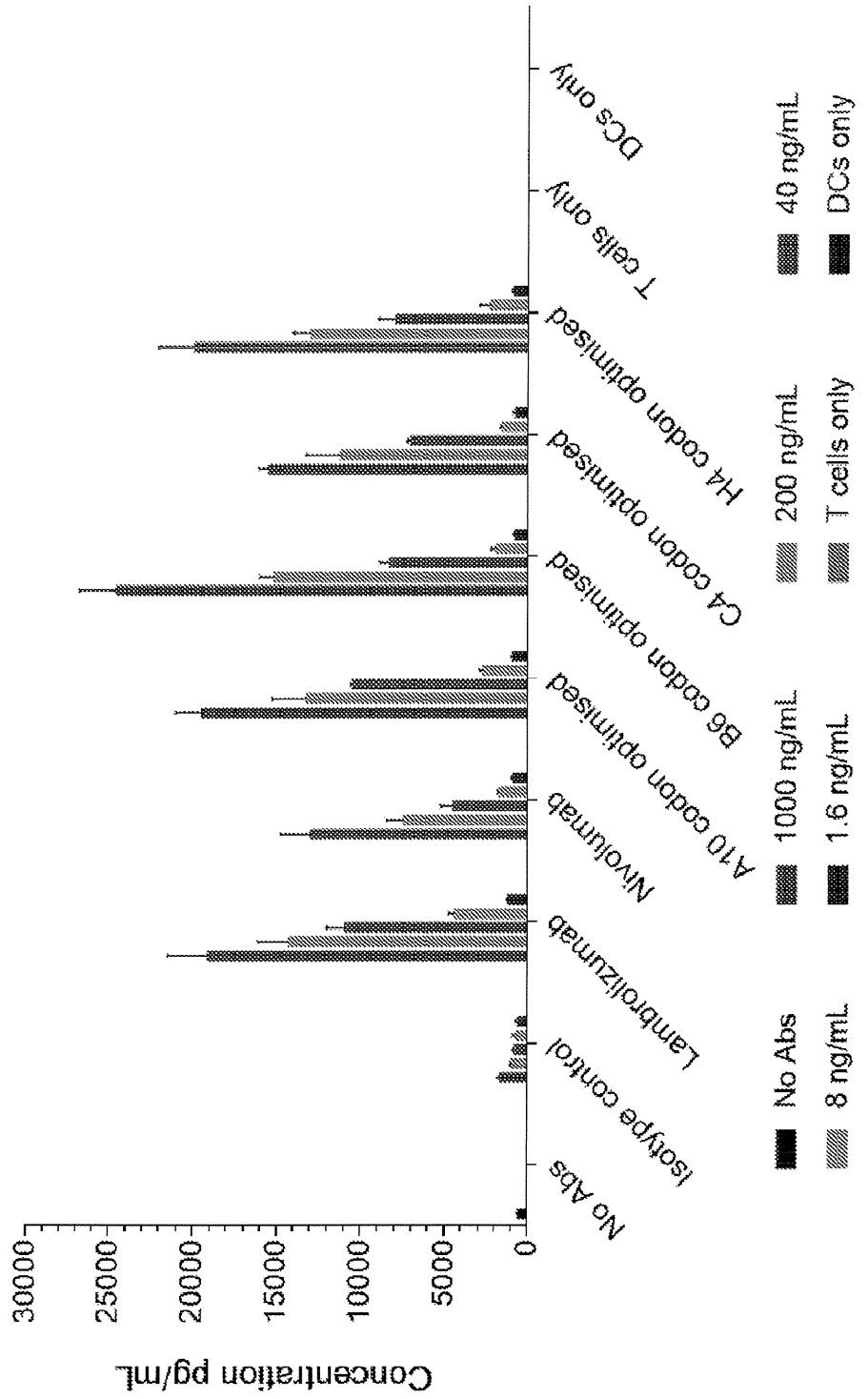
Concentration pg/mL
30000
25000
20000
15000
10000
5000
0
No Abs
Isotype control
Lambrolizumab
Nivolumab
A10 codon optimised
B6 codon optimised
C4 codon optimised
H4 codon optimised
T cells only
DCs only
No Abs
8 ng/mL
1000 ng/mL
1.6 ng/mL
200 ng/mL
T cells only
40 ng/mL
DCs only

Figure 15

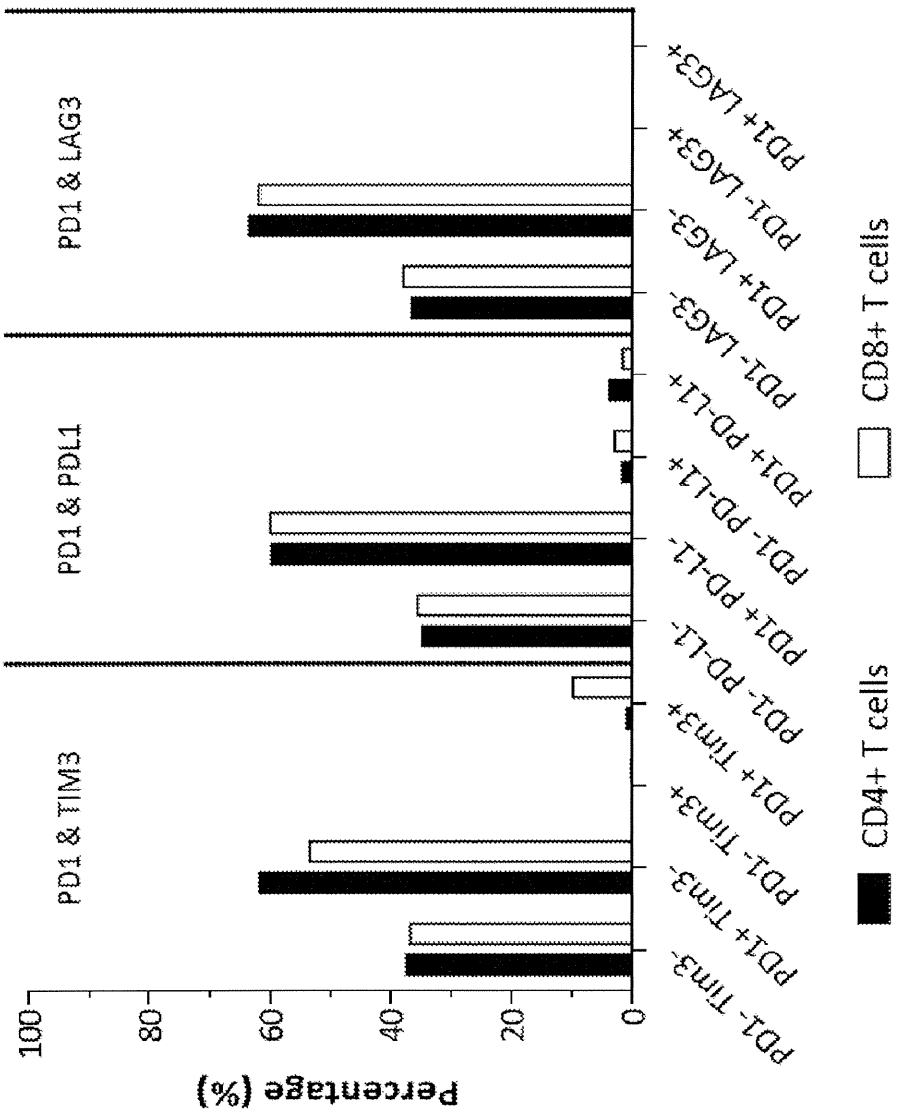
Percentage (%)
100
80
60
40
20
0
PD1 & TIM3
PD1 & PDL1
PD1 & LAG3
PD1- Tim3-
PD1+ Tim3-
PD1- Tim3+
PD1+ Tim3+
PD1- PD-L1-
PD1+ PD-L1-
PD1- PD-L1+
PD1+ PD-L1+
PD1- LAG3-
PD1+ LAG3-
PD1- LAG3+
PD1+ LAG3+
CD4+ T cells
CD8+ T cells

Figure 16

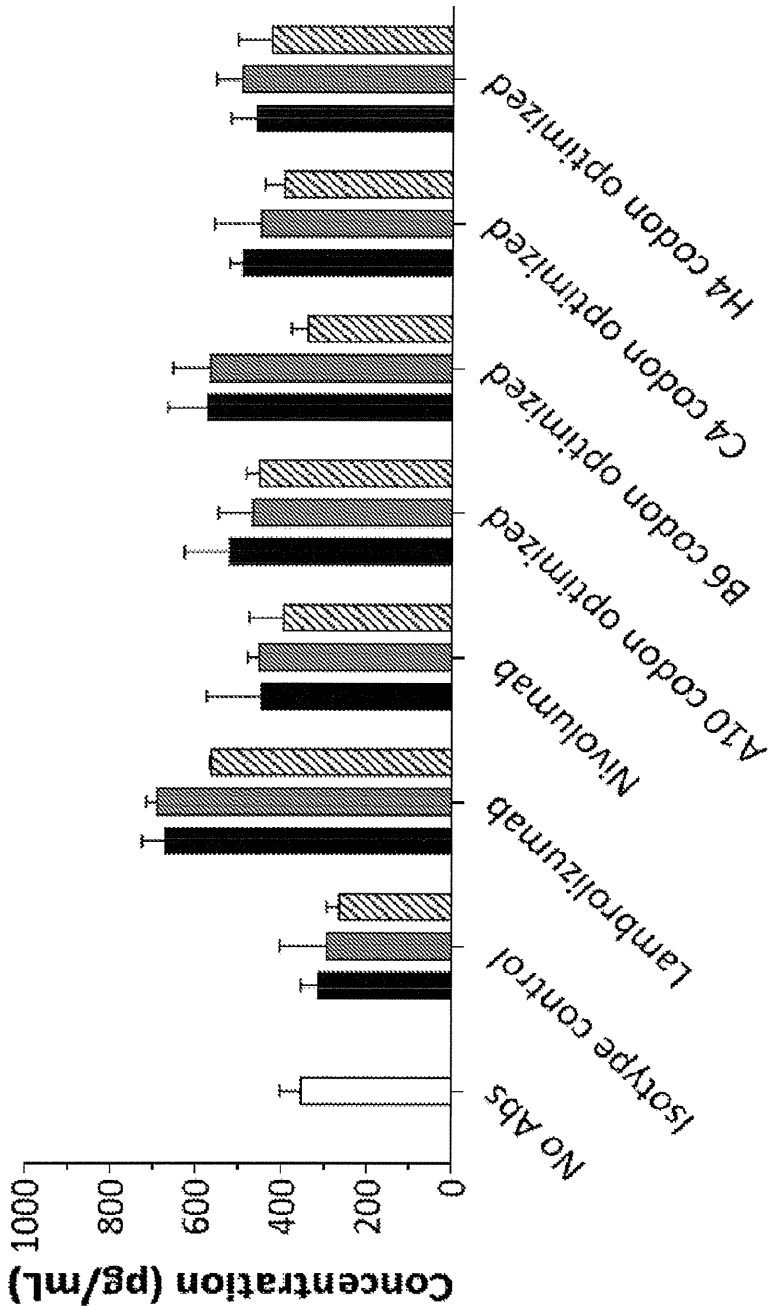
Concentration (pg/mL)
1000
800
600
400
200
0
No Abs
Isotype control
Lambrolizumab
Nivolumab
A10 codon optimized
B6 codon optimized
C4 codon optimized
H4 codon optimized
10 µg/mL
2 µg/mL
0.4 µg/mL
no Abs controls

Figure 17A

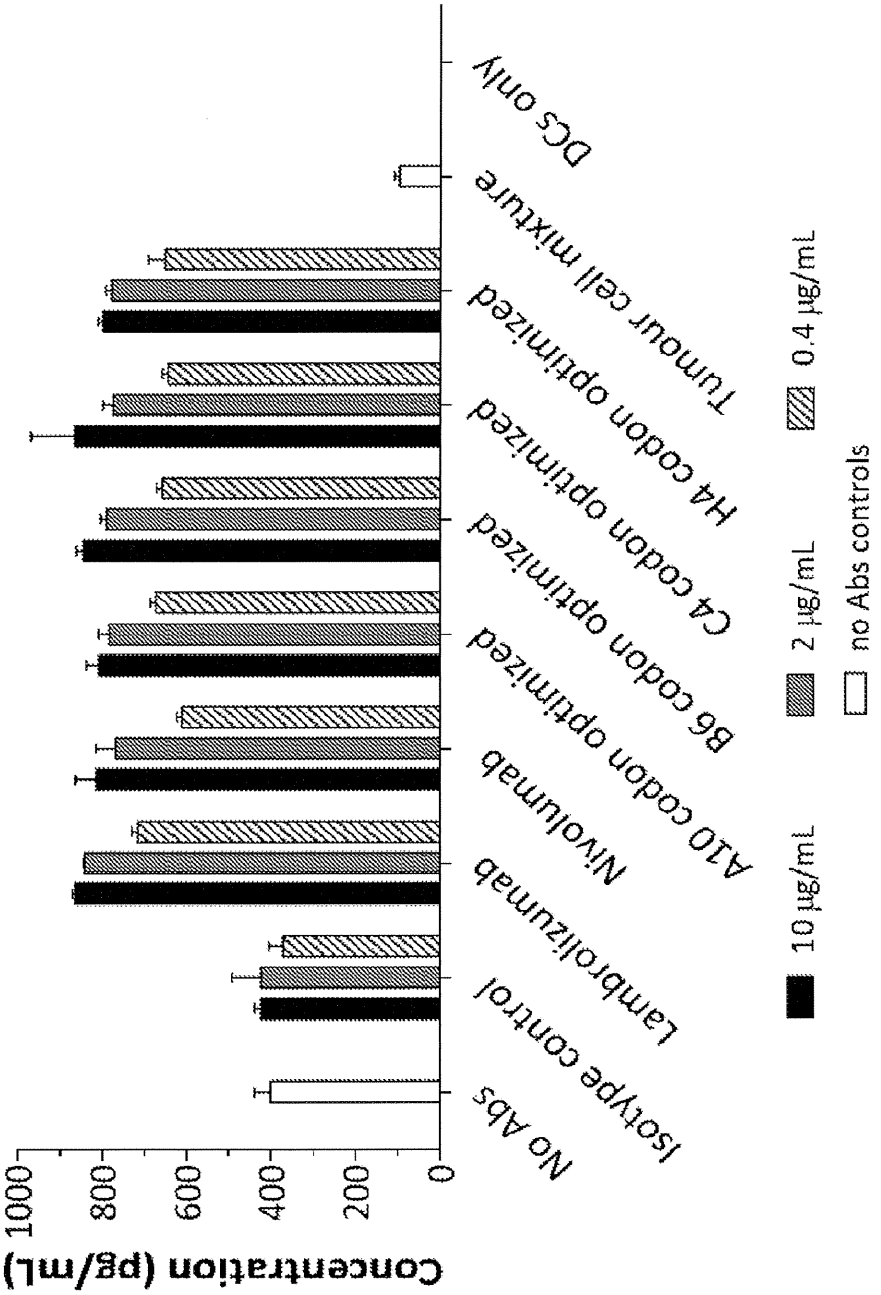
Concentration (pg/mL)
1000
800
600
400
200
0
No Abs
Isotype control
Lambrolizumab
Nivolumab
A10 codon optimized
B6 codon optimized
C4 codon optimized
H4 codon optimized
Tumour cell mixture
DCs only
10 µg/mL
2 µg/mL
0.4 µg/mL
no Abs controls

Figure 17B

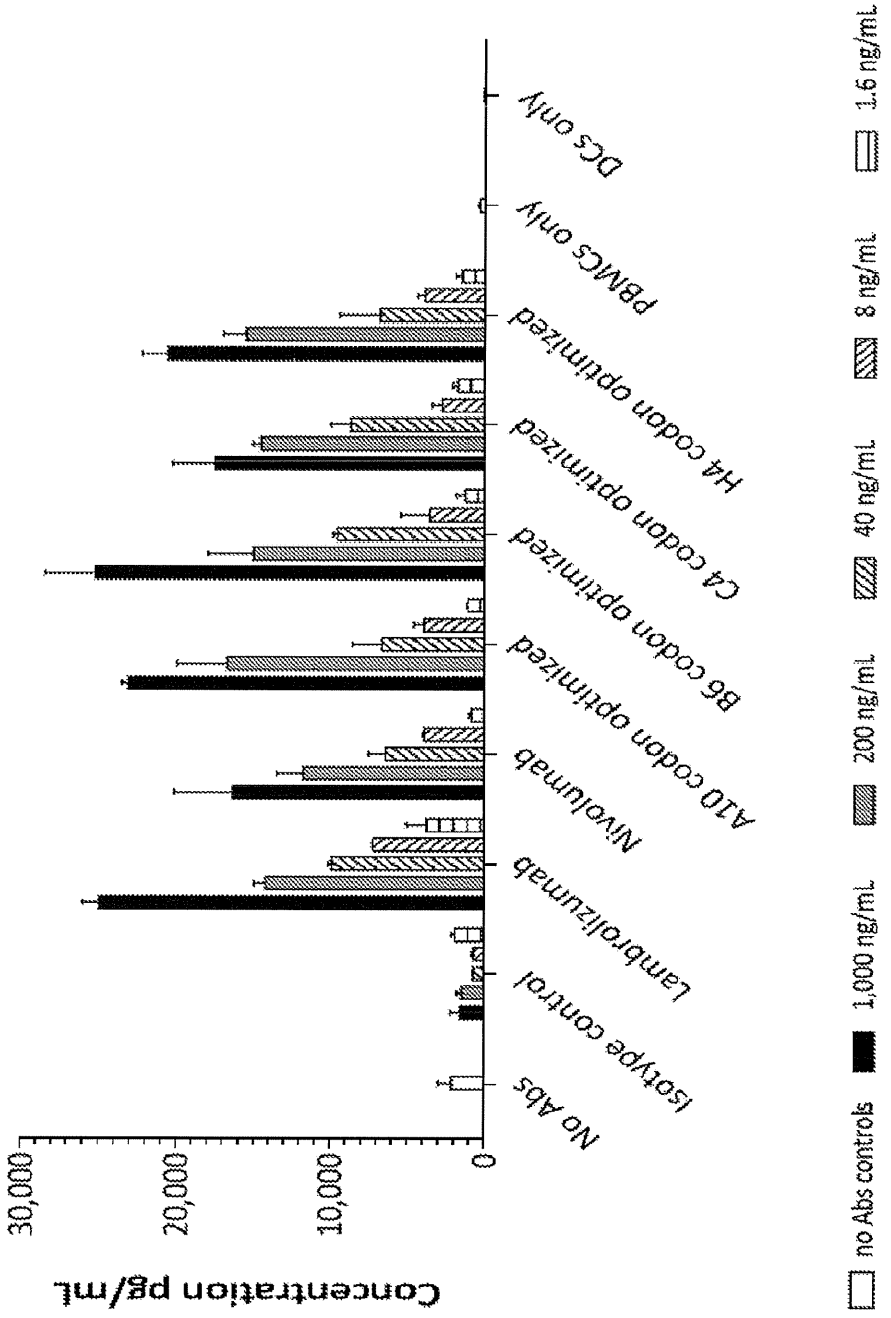
Concentration pg/mL
30,000
20,000
10,000
0
No Abs
Isotype control
Lambrolizumab
Nivolumab
A10 codon optimized
B6 codon optimized
C4 codon optimized
H4 codon optimized
pBMCs only
DCs only
no Abs controls
1,000 ng/mL
200 ng/mL
40 ng/mL
8 ng/mL
1.6 ng/mL

Figure 18

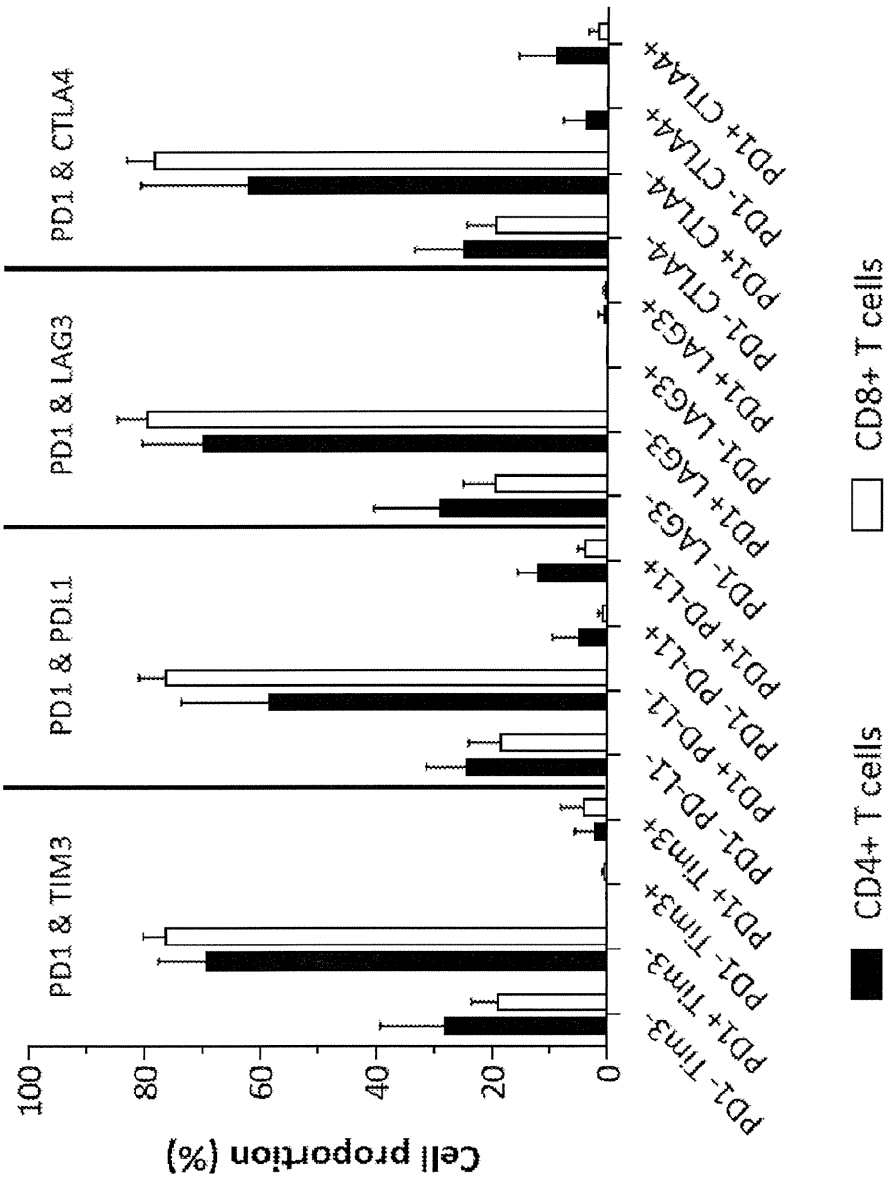
Cell proportion (%)
100
80
60
40
20
0
PD1 & TIM3
PD1 & PDL1
PD1 & LAG3
PD1 & CTLA4
PD1- Tim3-
PD1+ Tim3-
PD1- Tim3+
PD1+ Tim3+
PD1- PD-L1-
PD1+ PD-L1-
PD1- PD-L1+
PD1+ PD-L1+
PD1- LAG3-
PD1+ LAG3-
PD1- LAG3+
PD1+ LAG3+
PD1- CTLA4-
PD1+ CTLA4-
PD1- CTLA4+
PD1+ CTLA4+
CD4+ T cells
CD8+ T cells

Figure 19

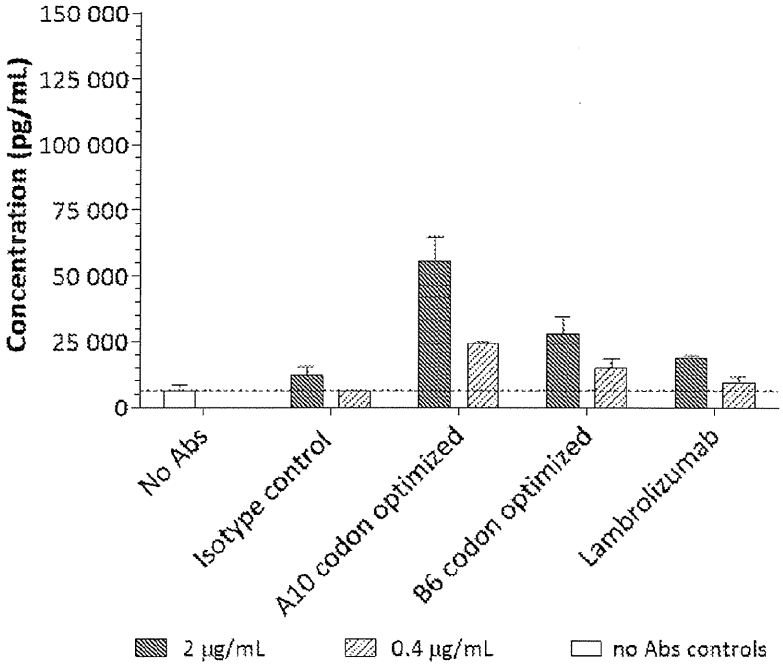

Figure 20A

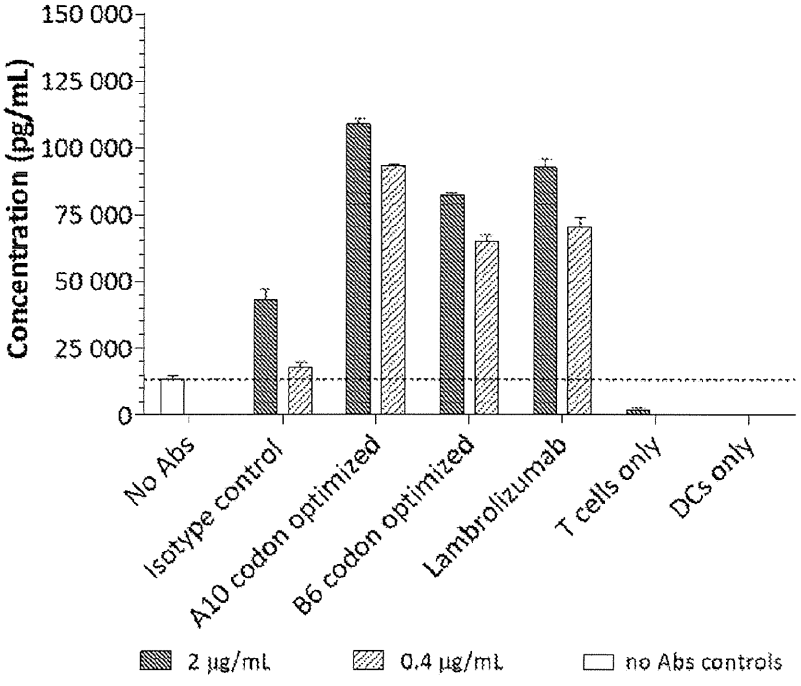

Figure 20B

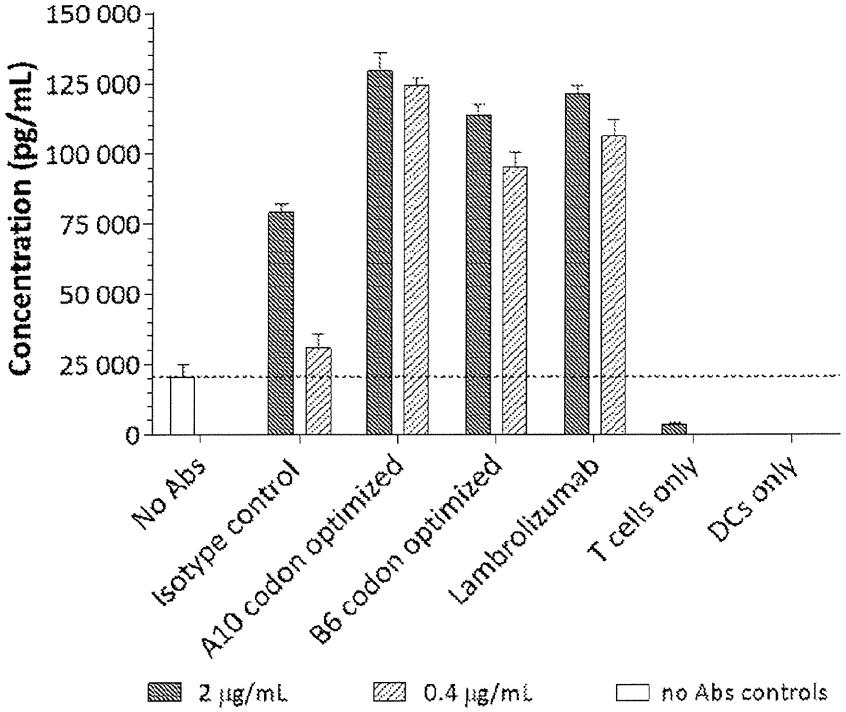
150 000
125 000
100 000
75 000
50 000
25 000
0
Concentration (pg/mL)
No Abs
Isotype control
A10 codon optimized
B6 codon optimized
Lambrolizumab
T cells only
DCs only
2 µg/mL
0.4 µg/mL
no Abs controls

Figure 20C

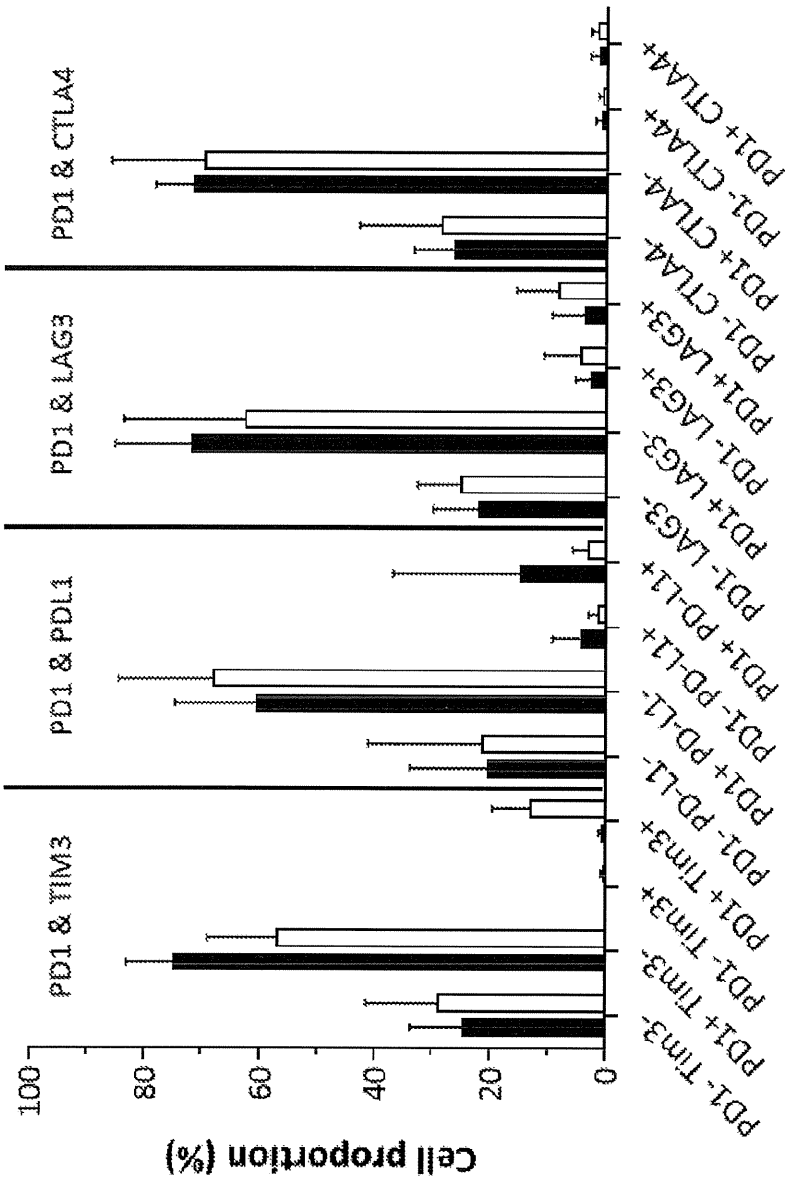
Cell proportion (%)
100
80
60
40
20
0
PD1 & TIM3
PD1 & PDL1
PD1 & LAG3
PD1 & CTLA4
PD1- Tim3-
PD1+ Tim3-
PD1- Tim3+
PD1+ Tim3+
PD1- PD-L1-
PD1+ PD-L1-
PD1- PD-L1+
PD1+ PD-L1+
PD1- LAG3-
PD1+ LAG3-
PD1- LAG3+
PD1+ LAG3+
PD1- CTLA-
PD1+ CTLA-
PD1- CTLA+
PD1+ CTLA+
CD4+ T cells
CD8+ T cells

Figure 21A

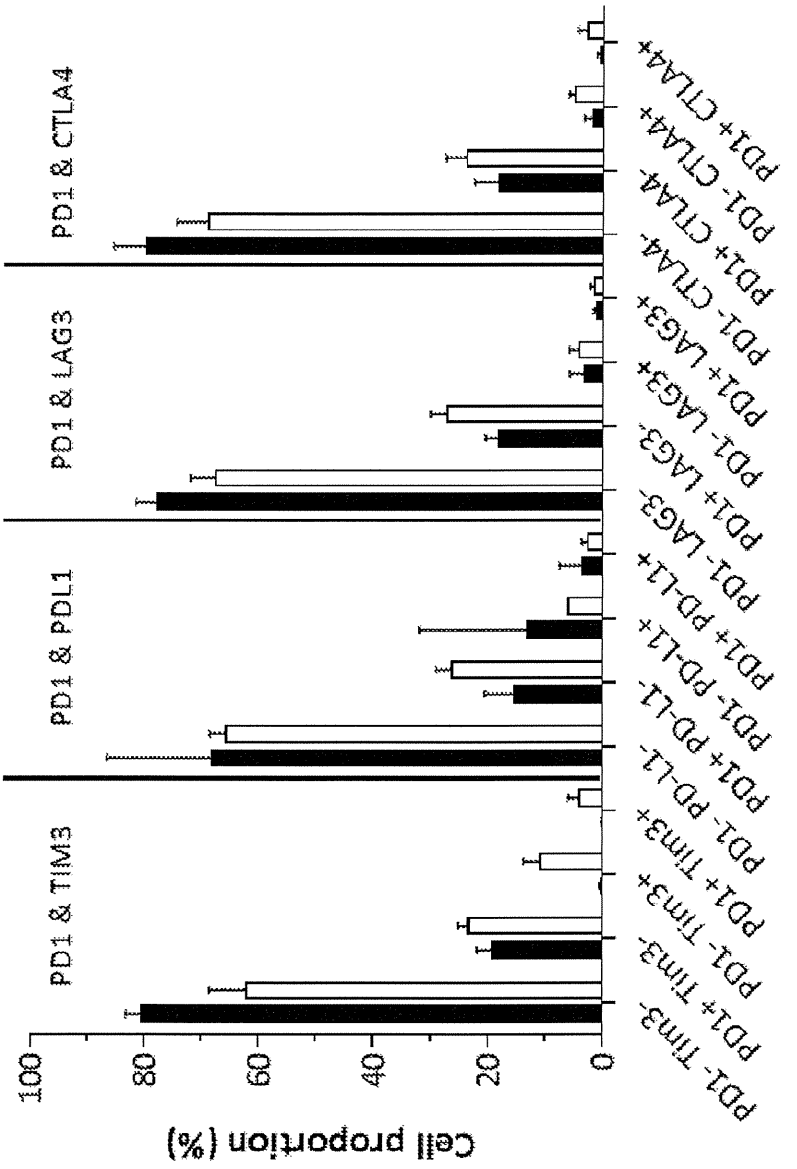
PD1 & TIM3
PD1 & PDL1
PD1 & LAG3
PD1 & CTLA4
PD1- Tim3-
PD1+ Tim3-
PD1- Tim3+
PD1+ Tim3+
PD1- PD-L1-
PD1+ PD-L1-
PD1- PD-L1+
PD1+ PD-L1+
PD1- LAG3-
PD1+ LAG3-
PD1- LAG3+
PD1+ LAG3+
PD1- CTLA4-
PD1+ CTLA4-
PD1- CTLA4+
PD1+ CTLA4+
Cell proportion (%)
100
80
60
40
20
0
CD4+ T cells
CD8+ T cells

Figure 21B

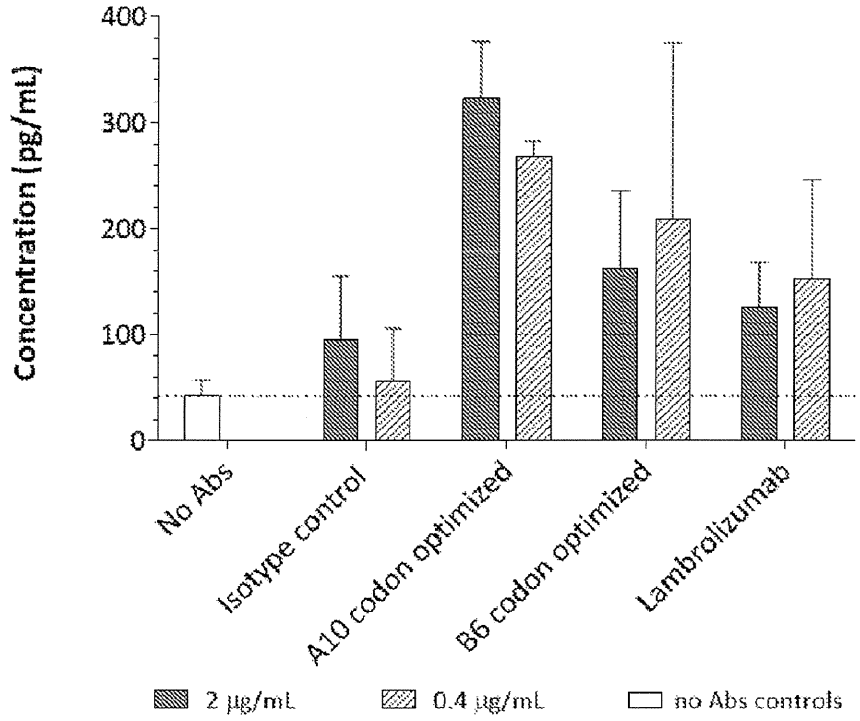

Figure 22A

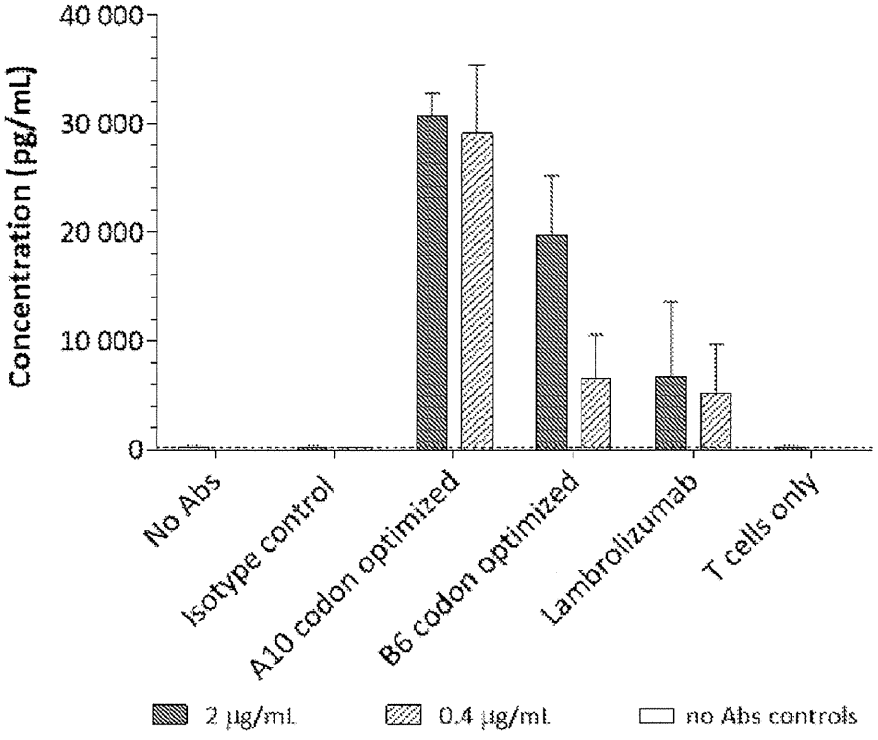

Figure 22B

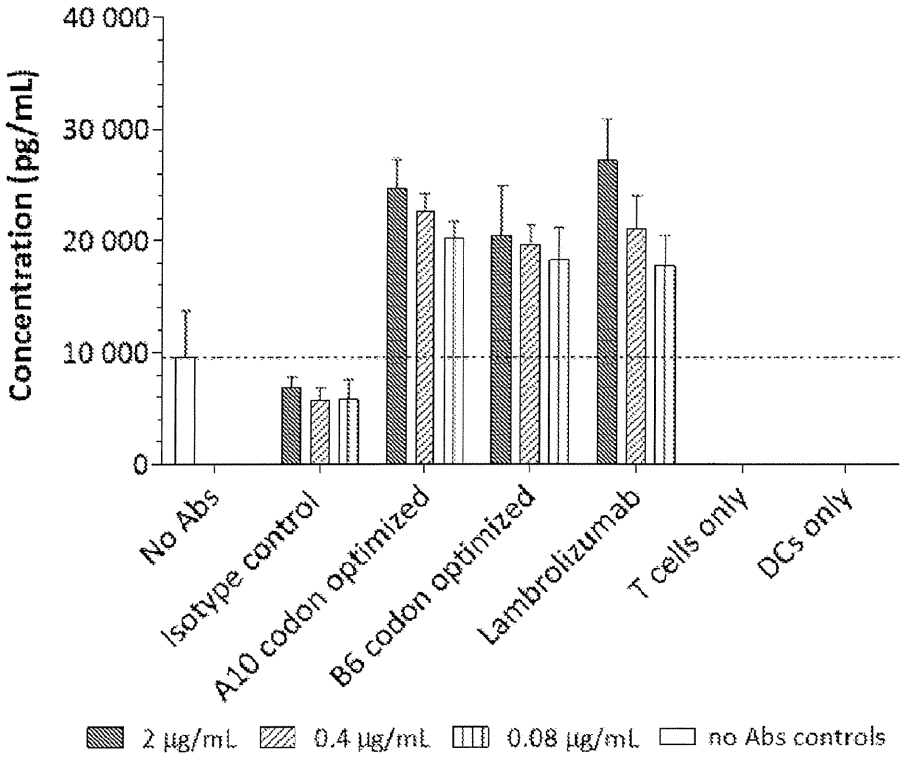
40 000
30 000
20 000
10 000
0
Concentration (pg/mL)
No Abs
Isotype control
A10 codon optimized
B6 codon optimized
Lambrolizumab
T cells only
DCs only
2 µg/mL
0.4 µg/mL
0.08 µg/mL
no Abs controls

Figure 22C

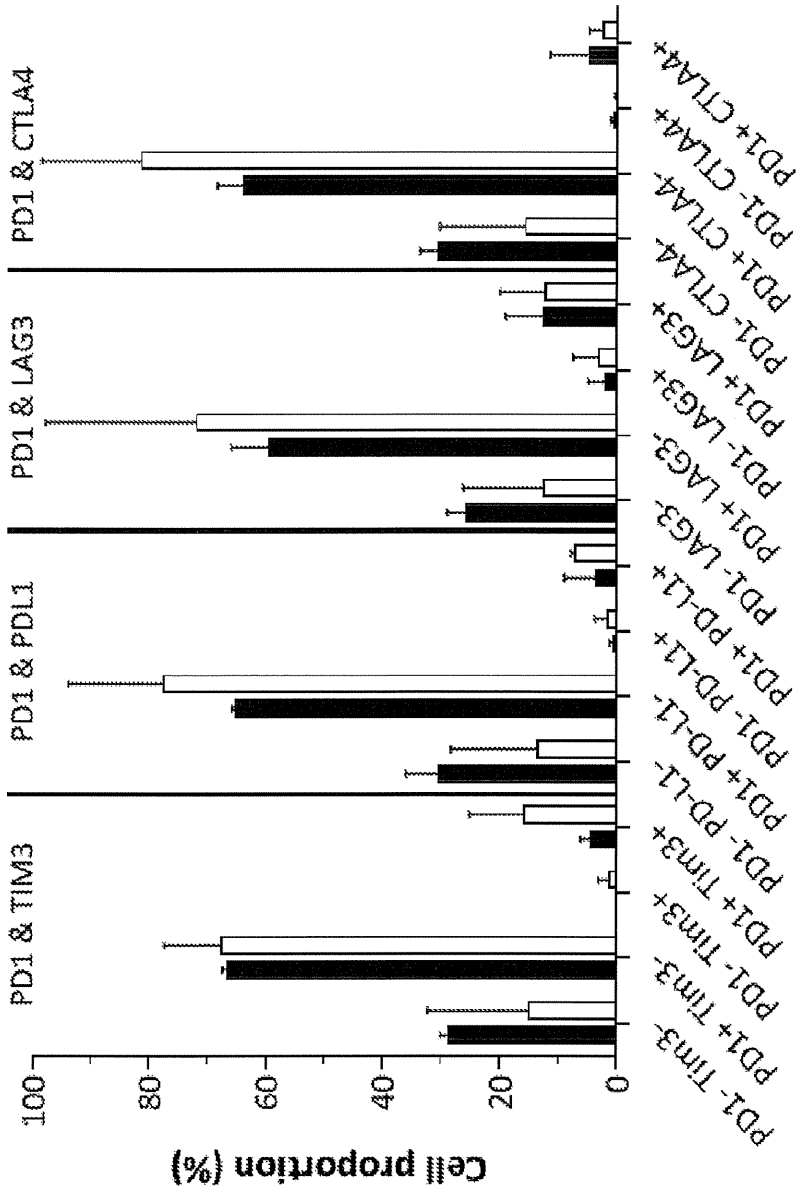
Cell proportion (%)
100
80
60
40
20
0
PD1 & TIM3
PD1 & PDL1
PD1 & LAG3
PD1 & CTLA4
PD1- Tim3-
PD1+ Tim3-
PD1- Tim3+
PD1+ Tim3+
PD1- PD-L1-
PD1+ PD-L1-
PD1- PD-L1+
PD1+ PD-L1+
PD1- LAG3-
PD1+ LAG3-
PD1- LAG3+
PD1+ LAG3+
PD1- CTLA-
PD1+ CTLA-
PD1- CTLA+
PD1+ CTLA+
CD4+ T cells
CD8+ T cells

Figure 23A

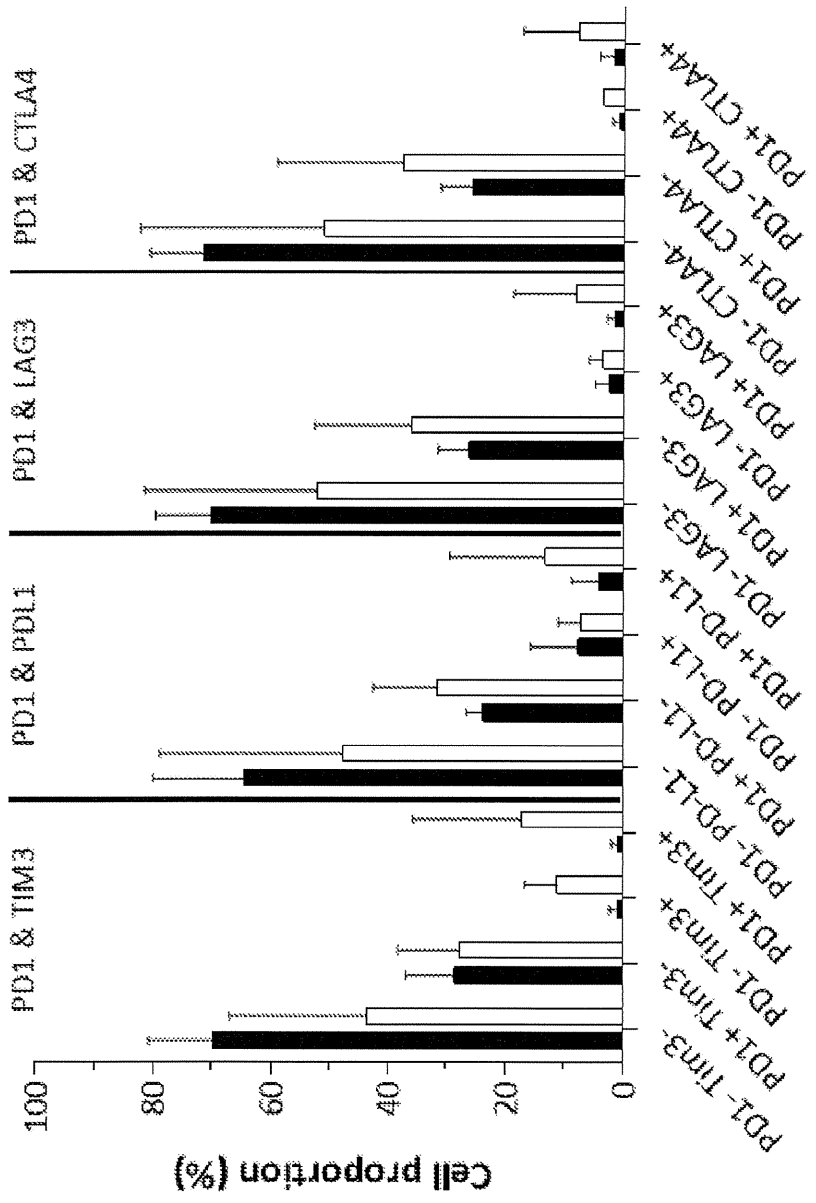
Cell proportion (%)
100
80
60
40
20
0
PD1 & TIM3
PD1 & PDL1
PD1 & LAG3
PD1 & CTLA4
PD1- Tim3-
PD1+ Tim3-
PD1- Tim3+
PD1+ Tim3+
PD1- PD-L1-
PD1+ PD-L1-
PD1- PD-L1+
PD1+ PD-L1+
PD1- LAG3-
PD1+ LAG3-
PD1- LAG3+
PD1+ LAG3+
PD1- CTLA4-
PD1+ CTLA4-
PD1- CTLA4+
PD1+ CTLA4+
CD4+ T cells
CD8+ T cells

Figure 23B

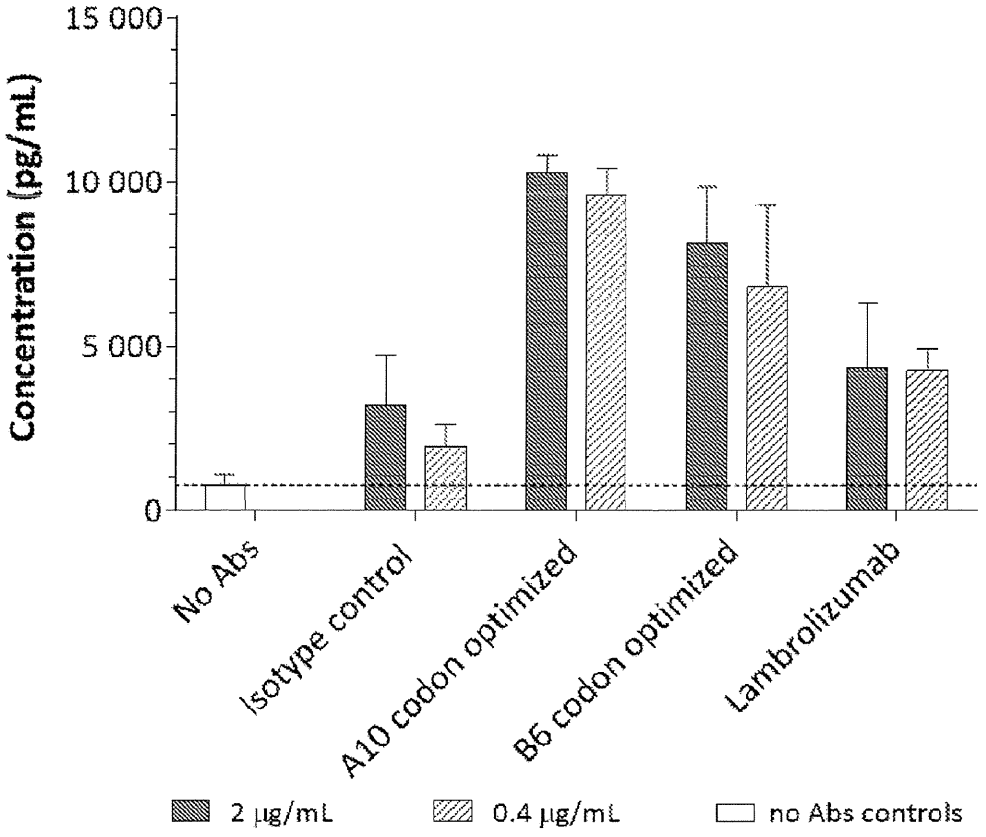
15 000
10 000
5 000
0
Concentration (pg/mL)
No Abs
Isotype control
A10 codon optimized
B6 codon optimized
Lambrolizumab
2 µg/mL
0.4 µg/mL
no Abs controls

Figure 24