

Antibody ID	KD (M)	Antibody ID	KD (M)
D2M008-A1C8	2.82E-09	D2M008-B2A8	2.59E-09
D2M008-A1C6	2.69E-09	D2M008-B2A1	5.58E-09
D2M008-A1A12	1.55E-08	D2M008-B2B10	1.26E-08
D2M008-A1E11	3.12E-08	D2M008-B2B1	2.15E-09
D2M008-A1E5	3.09E-09	D2M008-B2C1	2.65E-09
D2M008-A1A2	7.96E-09	D2M008-B2B6	1.07E-08
D2M008-A1E7	6.27E-09	D2M008-B2C6	1.64E-08
D2M008-A1G9	2.67E-09	D2M008-B2B12	9.62E-09
D2M008-A1D3	2.90E-09	D2M008-B2C3	6.14E-09
D2M008-A1A8	1.55E-10	D2M008-B2B7	1.36E-09
D2M008-A1A9	1.73E-10	D2M008-3A4	1.00E-09
D2M008-A1B4	3.72E-10	D2M008-3A8	8.31E-09
D2M008-A1E10	1.73E-10	D2M008-4A4	1.69E-10
D2M008-B2C4	O.R.	D2M008-4A5	1.01E-09
D2M008-B2A12	1.22E-08	D2M008-3A11	9.14E-10
D2M008-B2C5	6.53E-09	anti-hP40	2.75E-10

O.R.: out of range

FIG. 1

Antibody ID	KD (M)		
	Binding to human IL-12p70	Binding to Rhesus IL-12p70	Binding to Canine IL-12p70
D2M008-A1A8	5.44E-11	3.68E-09	N.D.
D2M008-A1A9	O.R.	8.36E-10	N.D.
27H28L	O.R.	4.93E-09	N.D.
D2M008-4A4	O.R.	1.60E-10	N.D.
27H28L YTE	O.R.	5.55E-09	N.D.
27H28L-hblb-YTE	O.R.	9.97E-10	O.R.
D2M-4A4 YTE	O.R.	1.45E-10	N.D.
4A4-hblb2-YTE	3.34E-11	2.36E-10	8.44E-09
anit-P40	4.74E-11	1.38E-10	N.D.

O.R.: out of range, due to high affinity; N.D.: not performed; N.B.: no binding was detected.

FIG. 2A

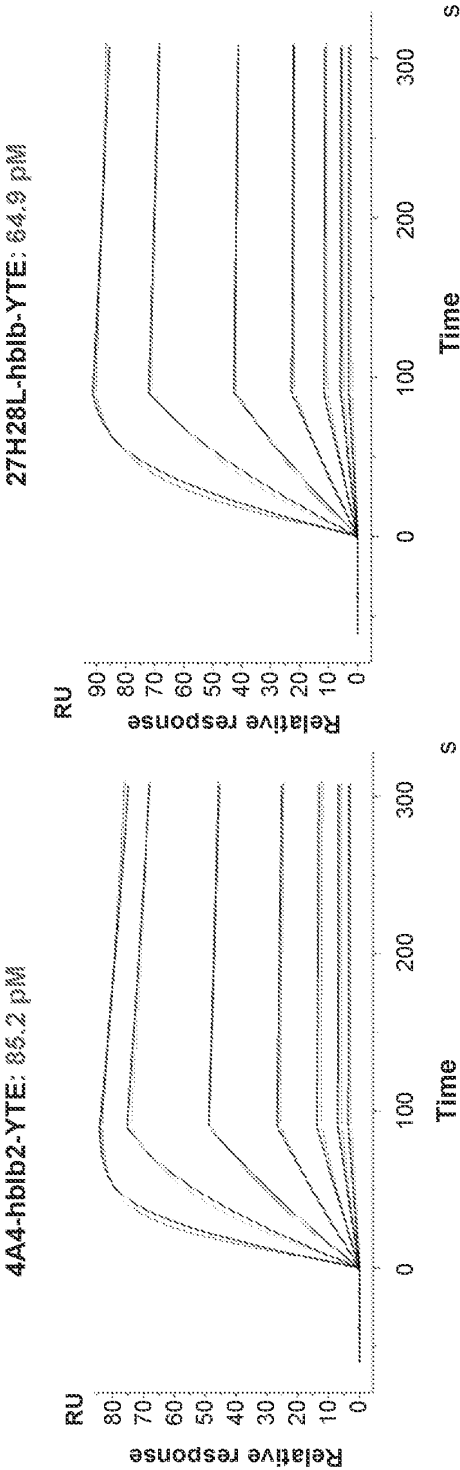


FIG. 2B

Method	Ligand	Capture Level (RU)	Analyte	Analyte Conc. (nM)	ka (1/Ms)	kd (1/s)	KD (M)	Rmax (RU)	Chi² (RU²)	Fit model
Protein A	4A4-hblb2-YTE	94.9	Human IL-12	0.195-12.5	7.23E+06	6.15E-04	8.52E-11	85.0	0.89	1:1 binding
Protein A	27H28L-hblb-YTE	101.5	Human IL-12	0.195-12.5	5.14E+06	3.34E-04	6.49E-11	93.5	0.82	1:1 binding

FIG. 2C

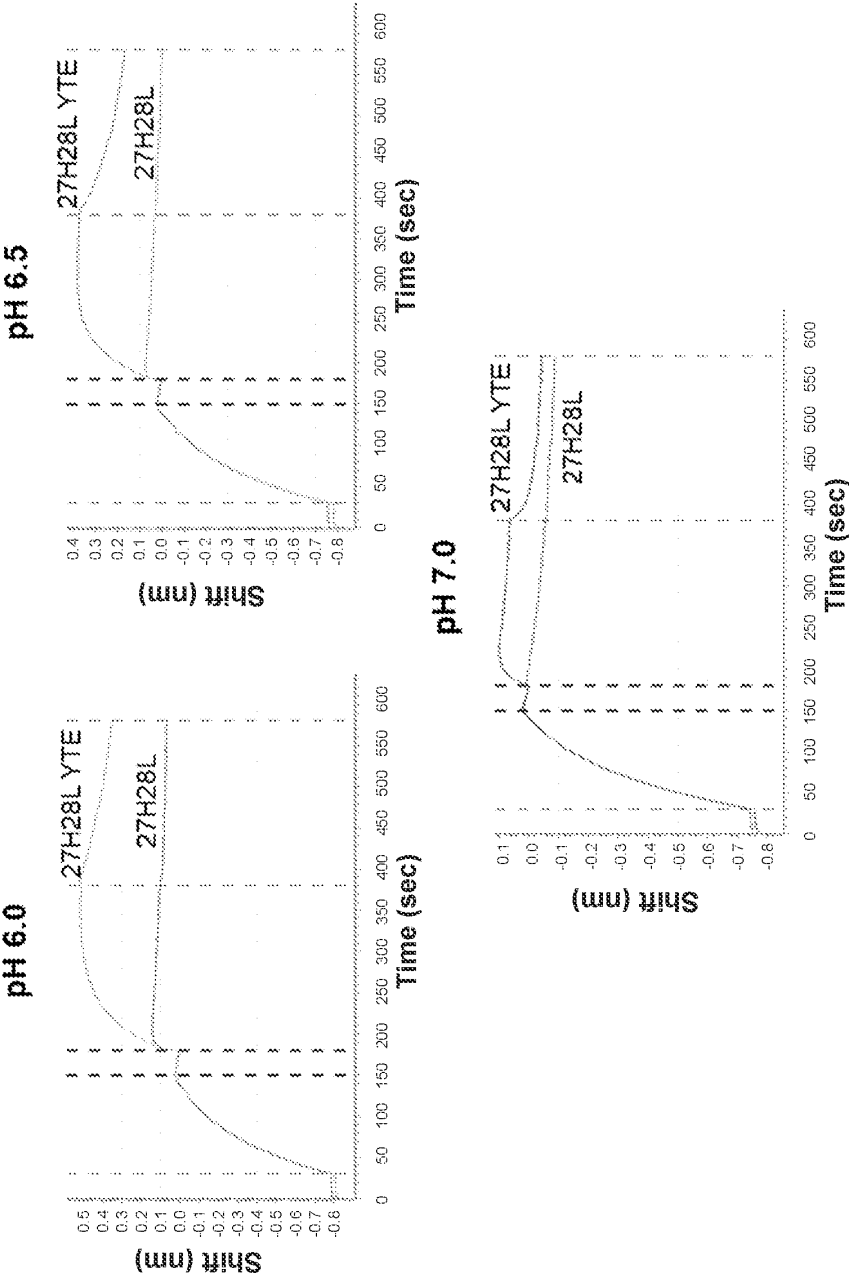


FIG. 3A

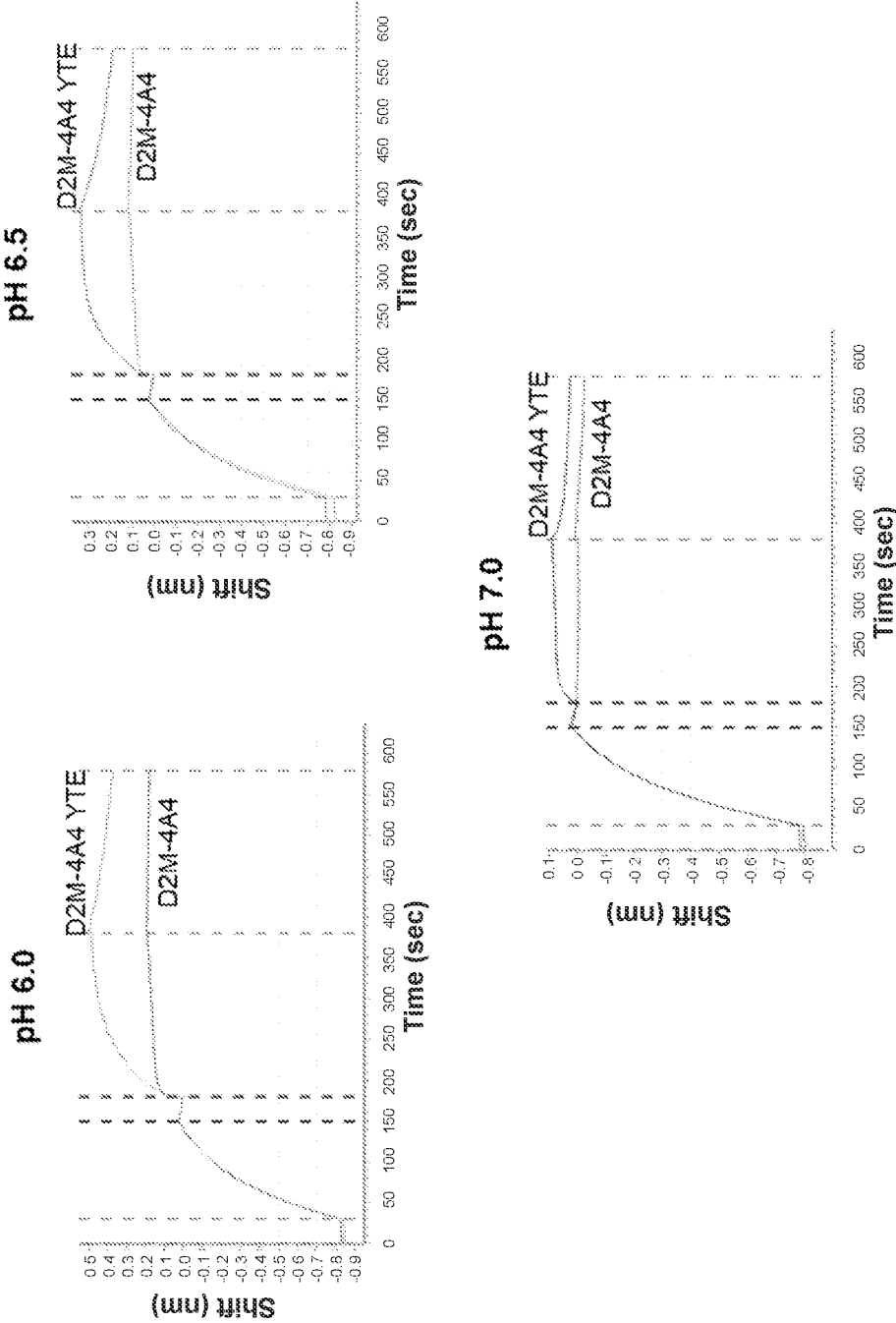


FIG. 3B

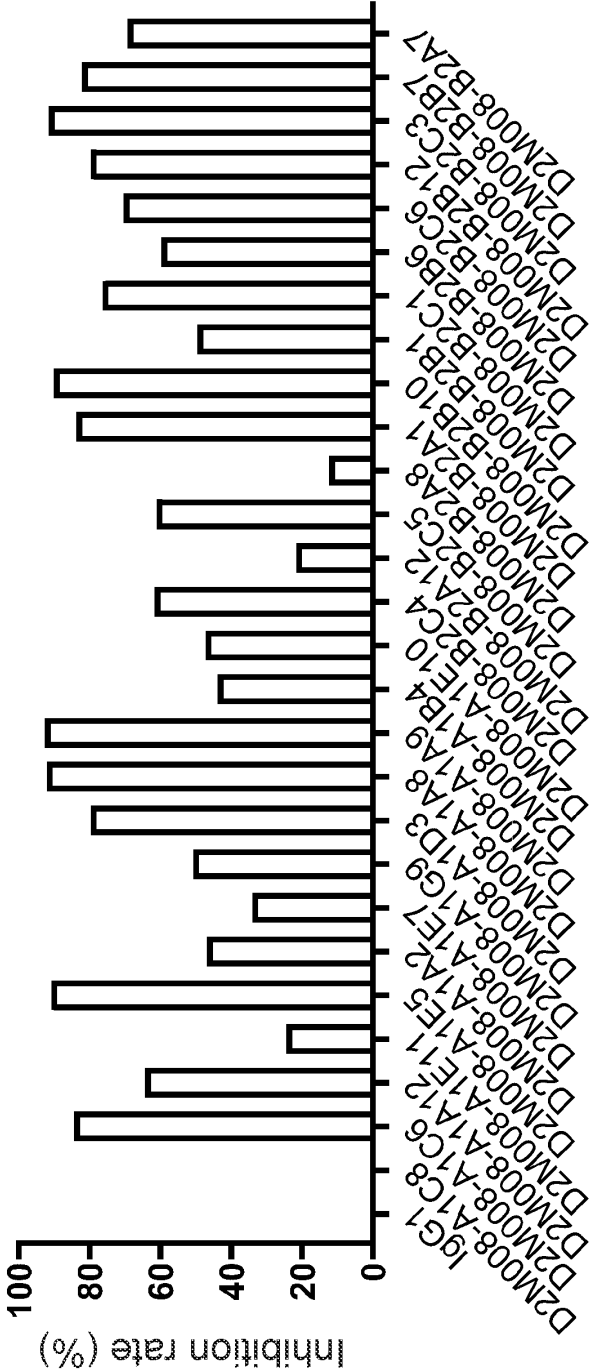


FIG. 4A

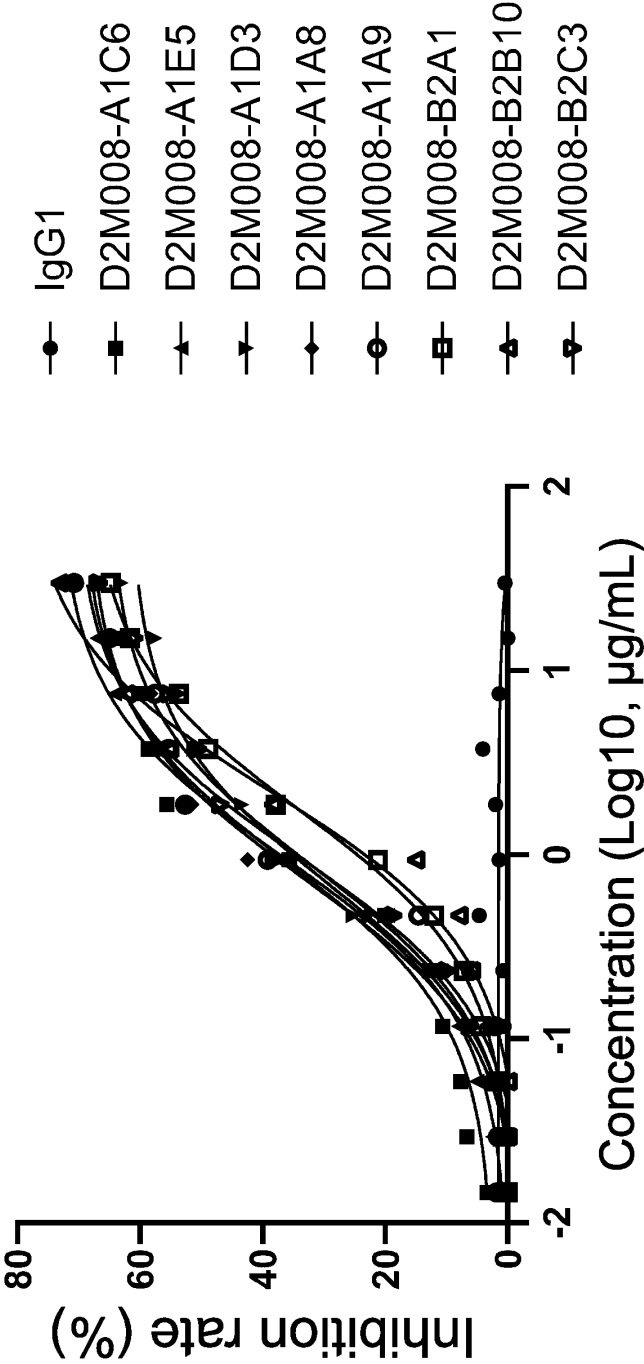


FIG. 4B

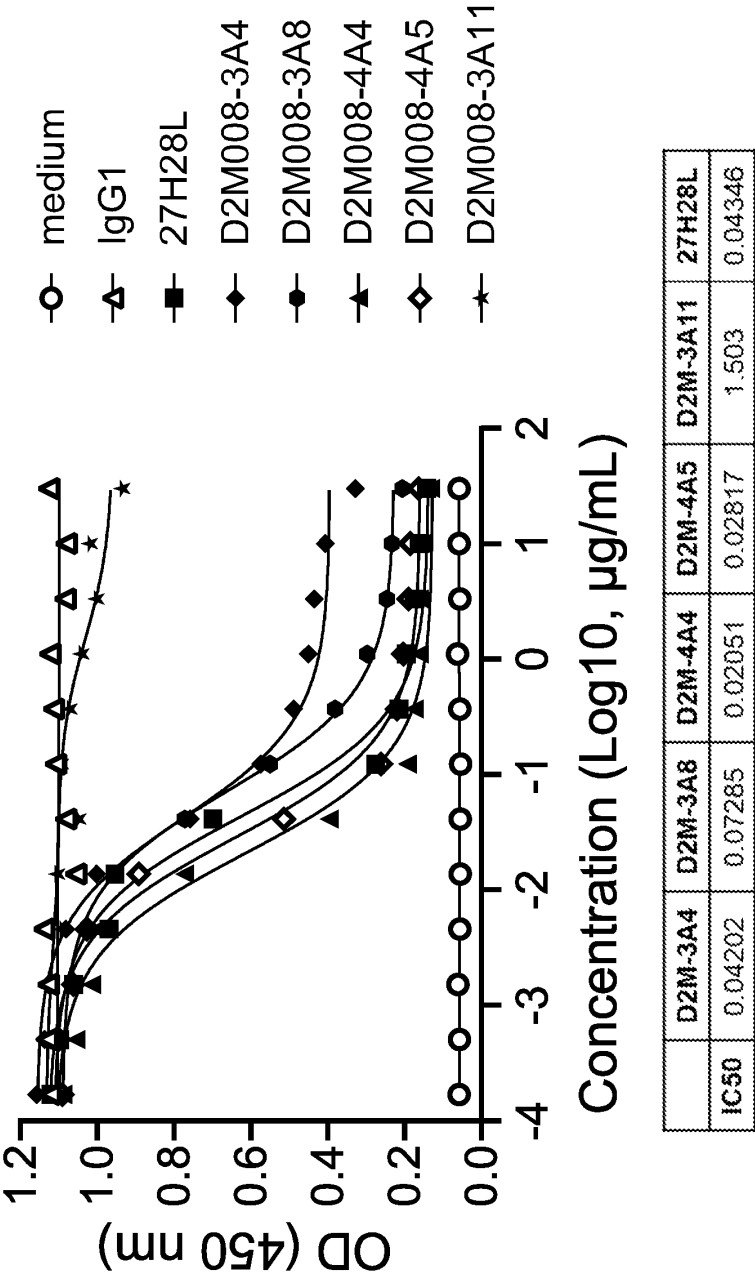


FIG. 4C

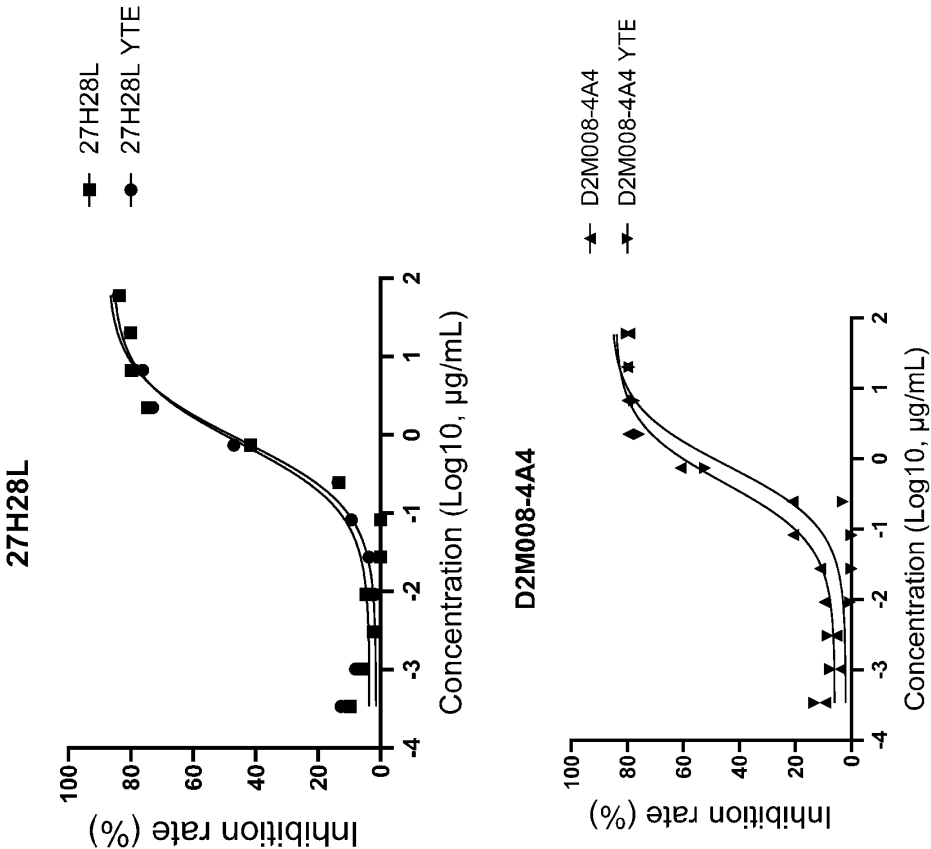


FIG. 4D

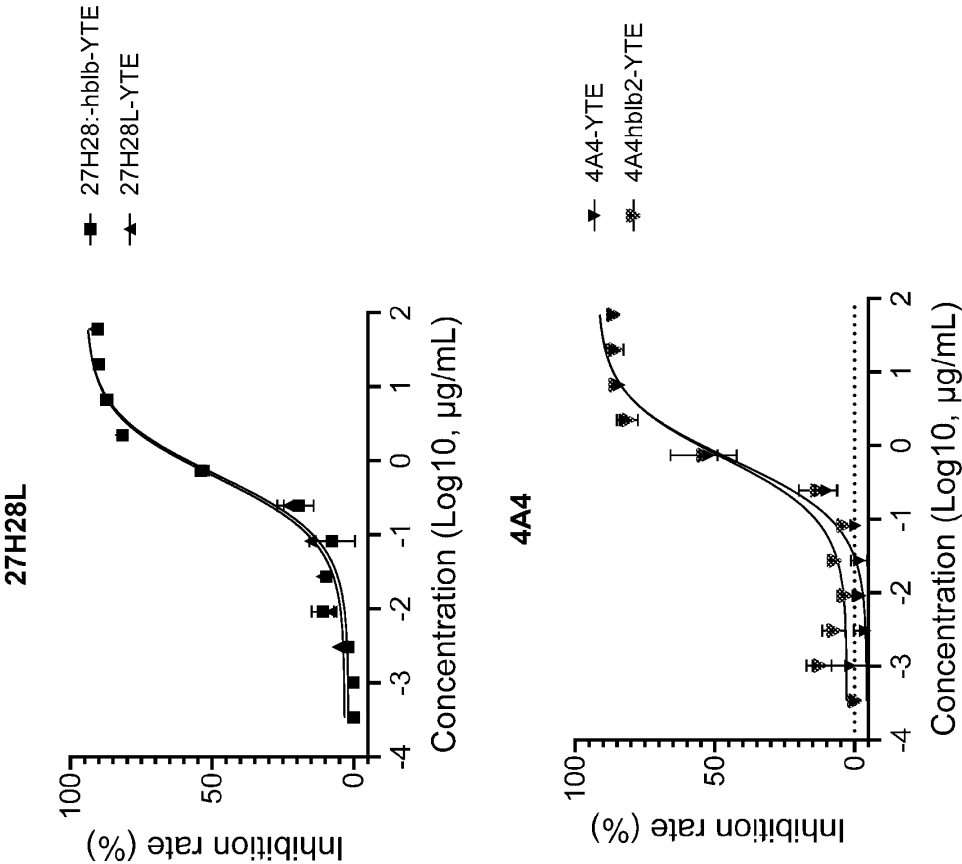


FIG. 4E

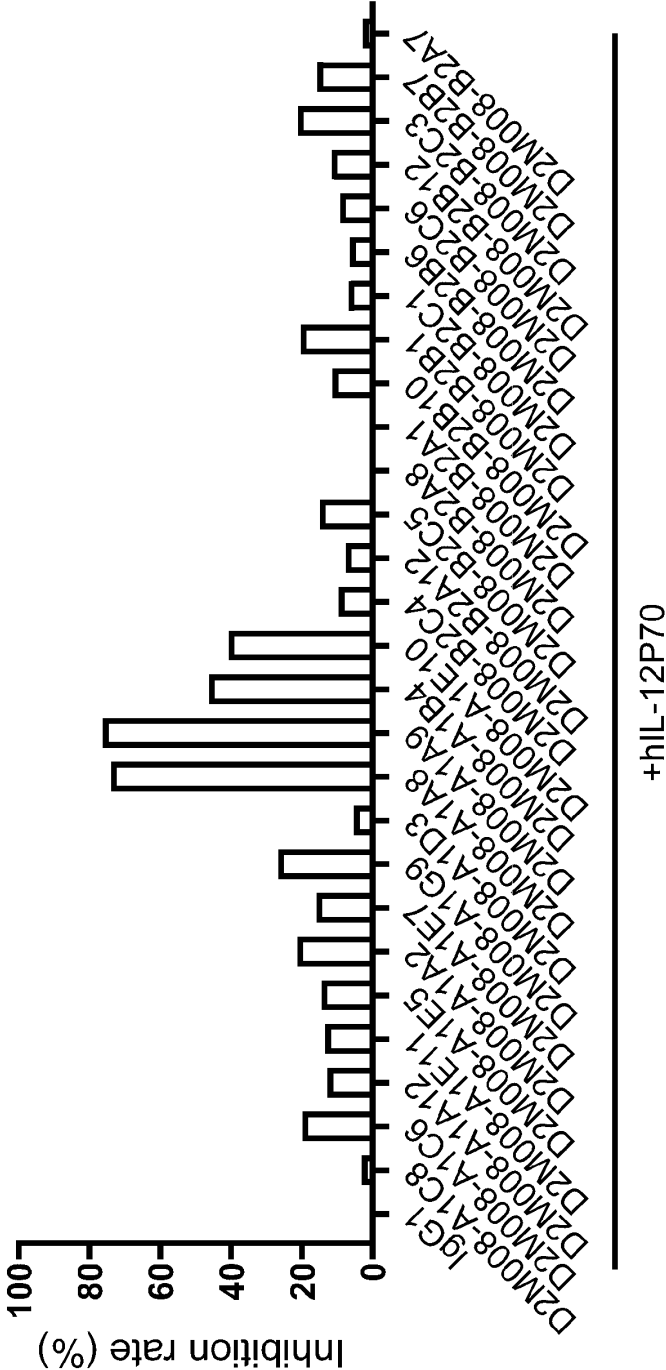


FIG. 5A

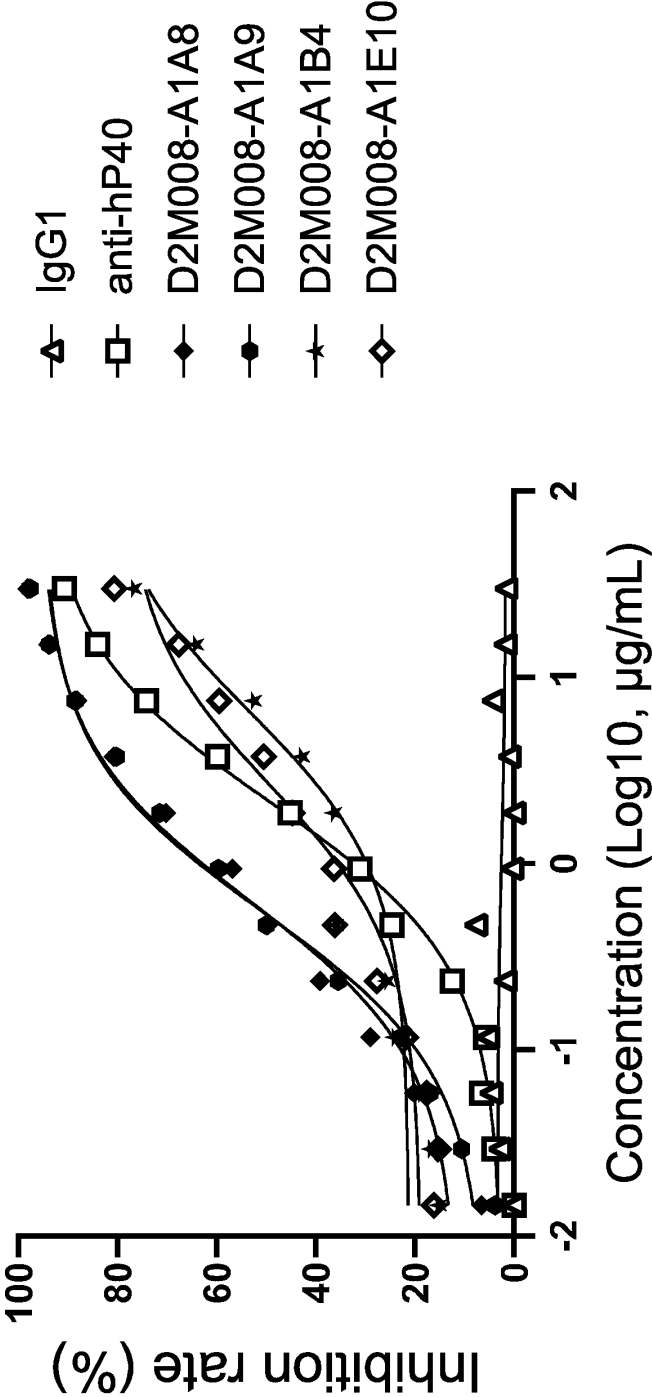


FIG. 5B

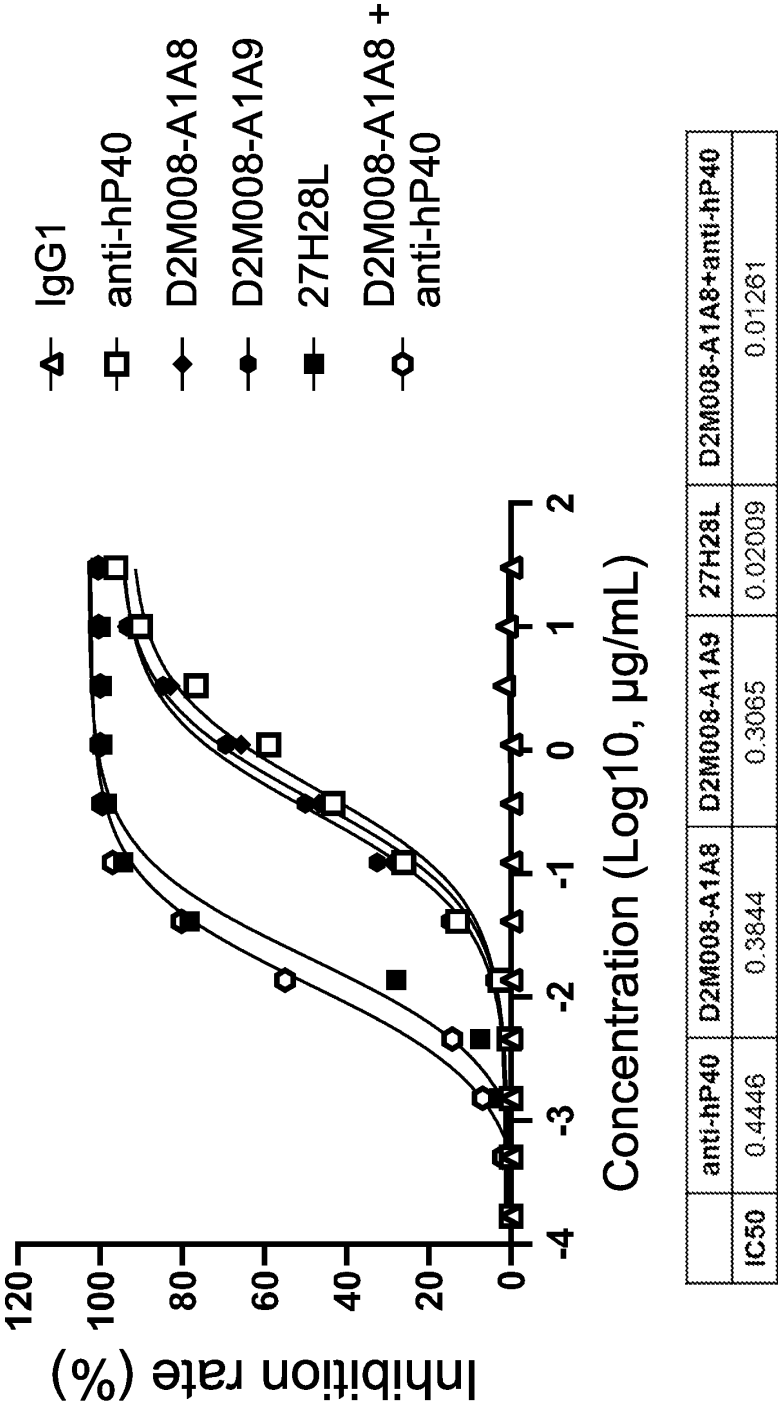
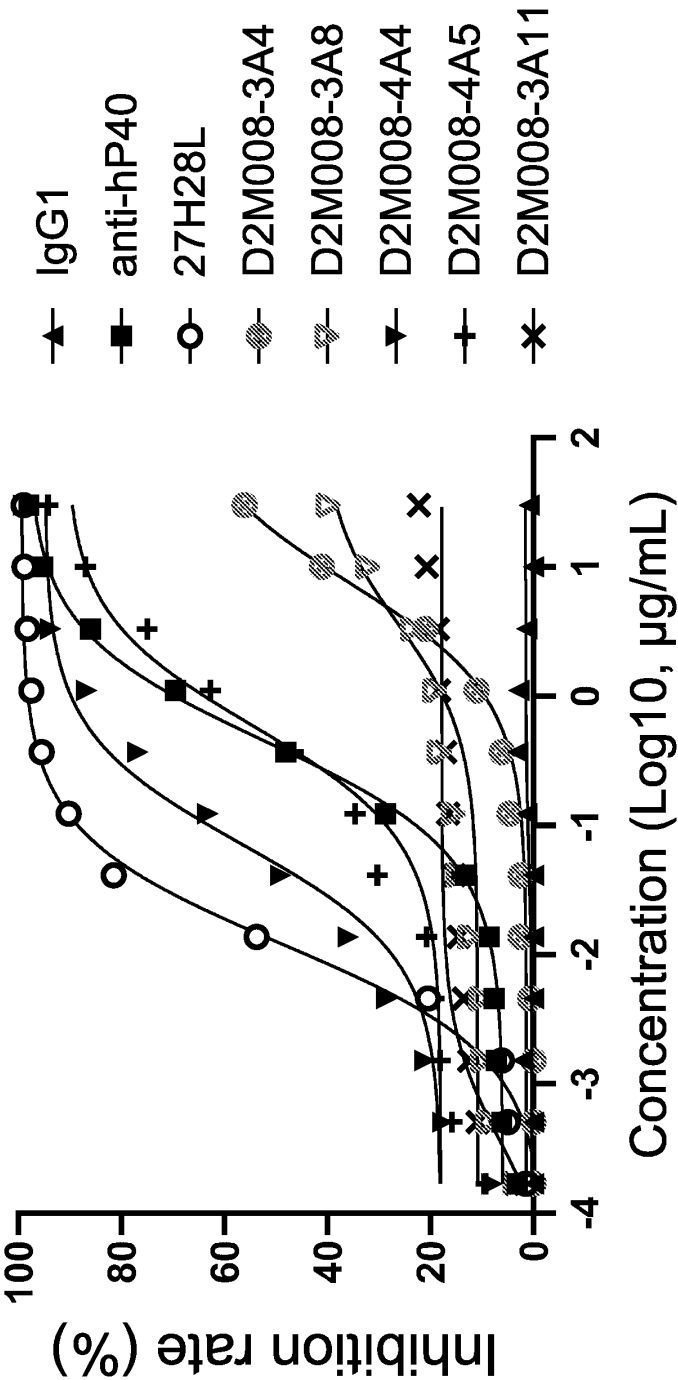


FIG. 5C



	D2M008-3A4	D2M008-3A8	D2M008-4A4	D2M009-4A5	D2M008-3A11	27H28L	anti-hP40
IC50	N.A.	N.A.	0.07114	0.5907	N.A.	0.01201	0.4485

FIG. 5D

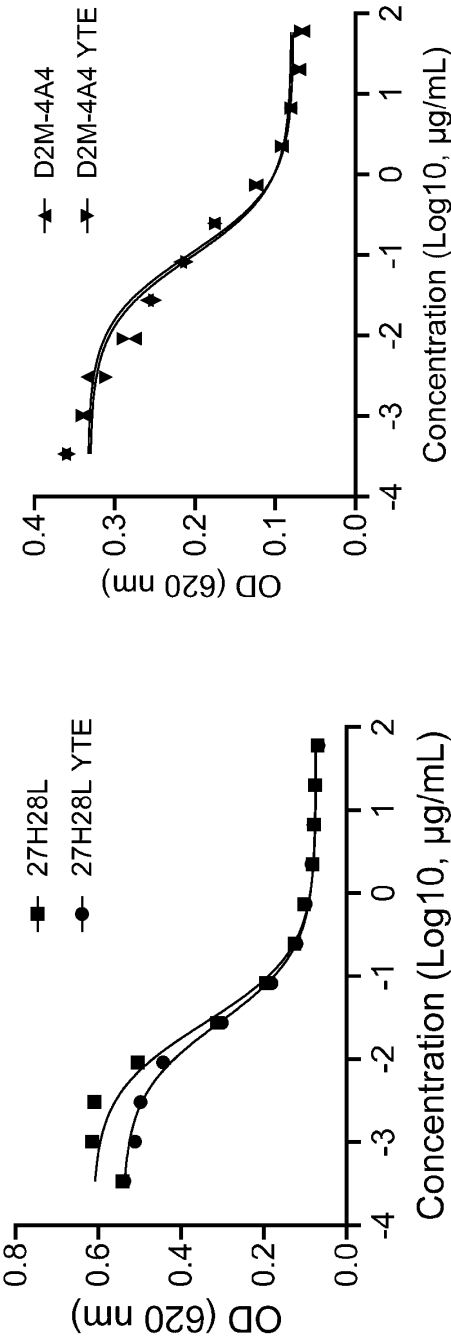


FIG. 5E

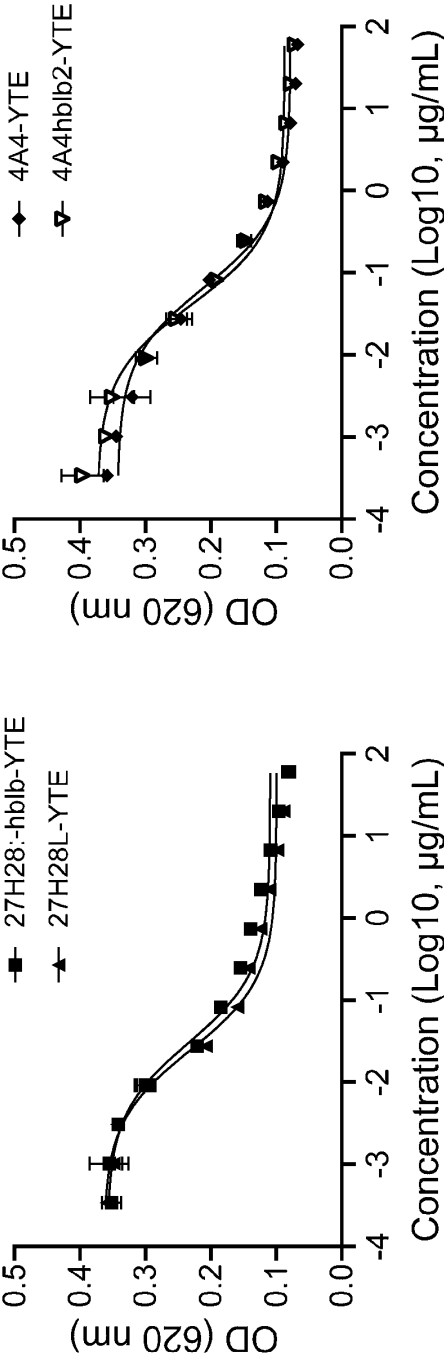


FIG. 5F

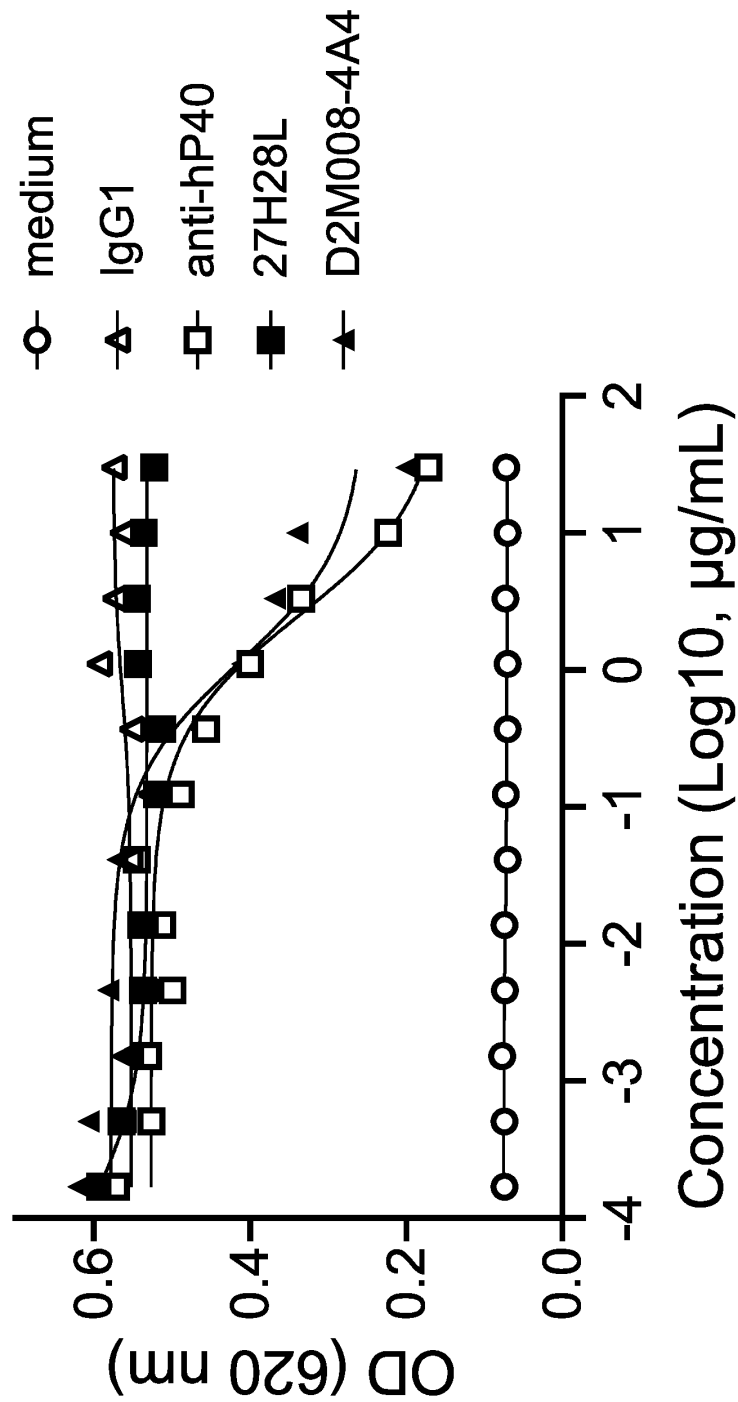


FIG. 6

#20 PBMC

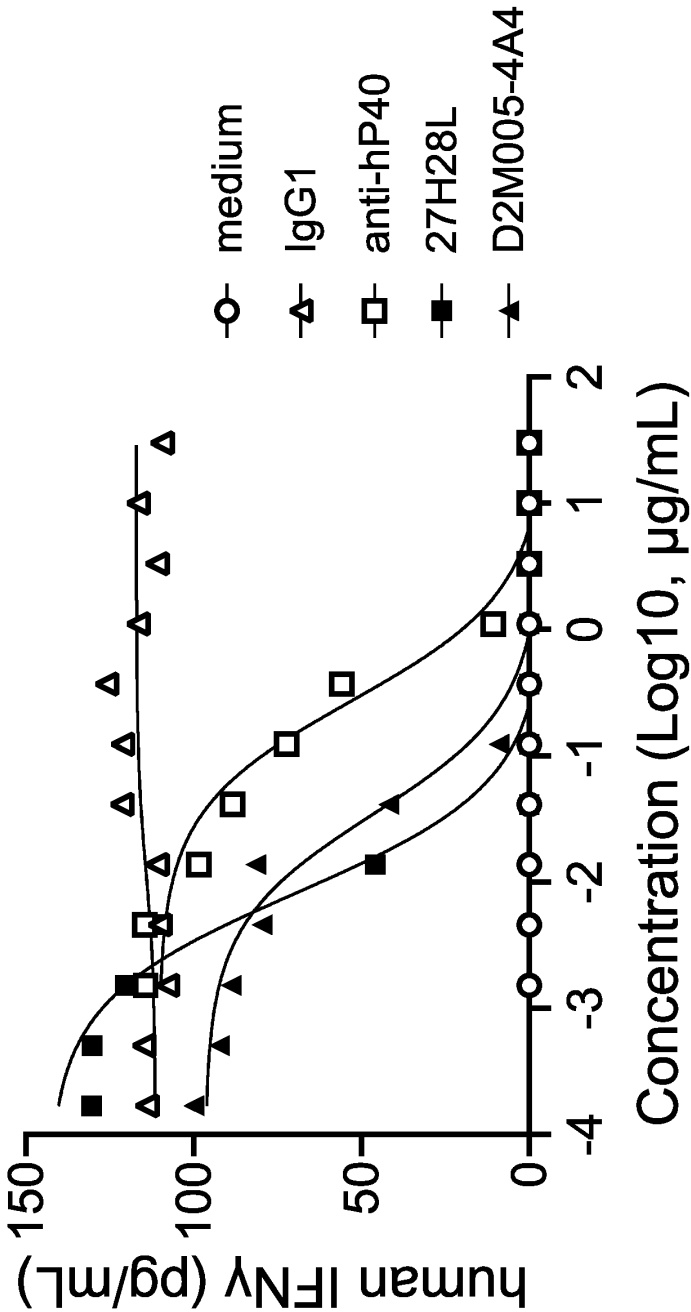


FIG. 7A

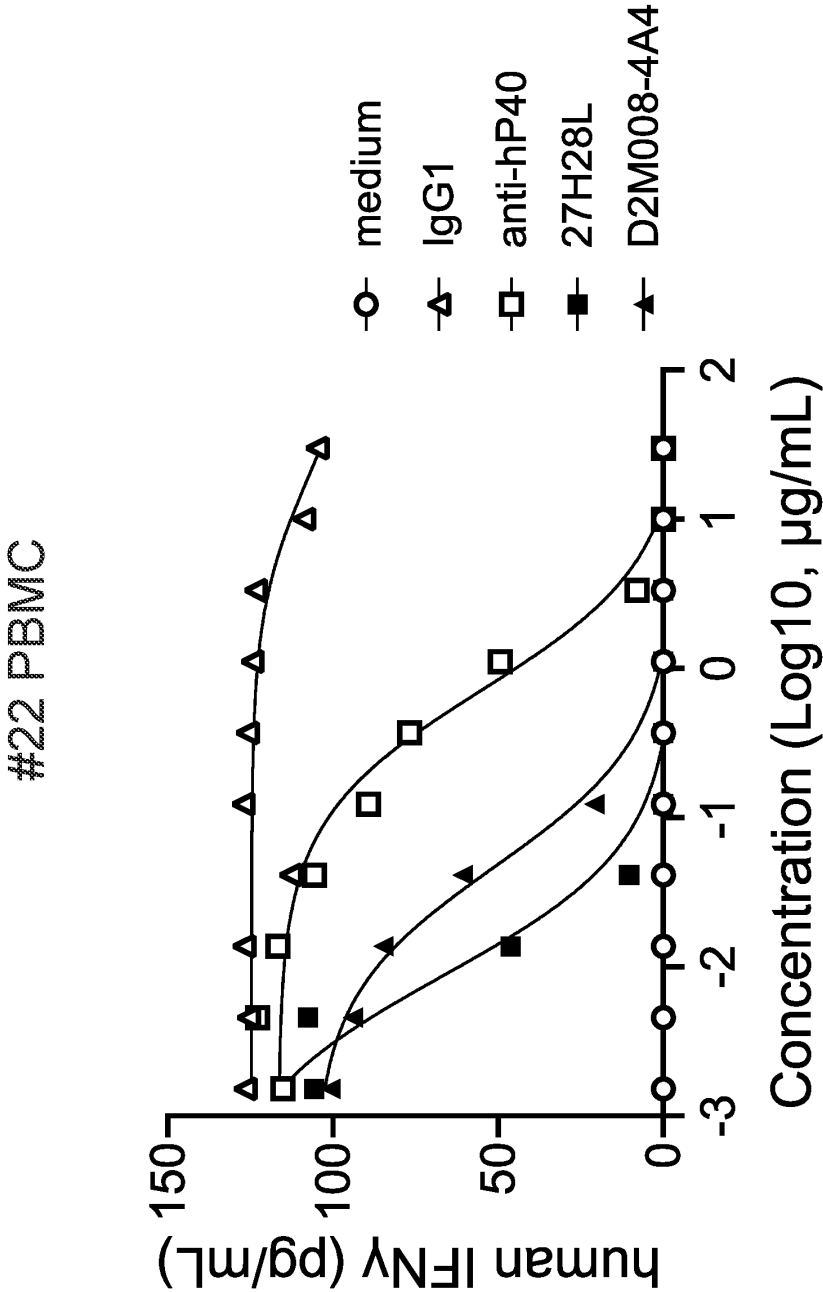


FIG. 7B

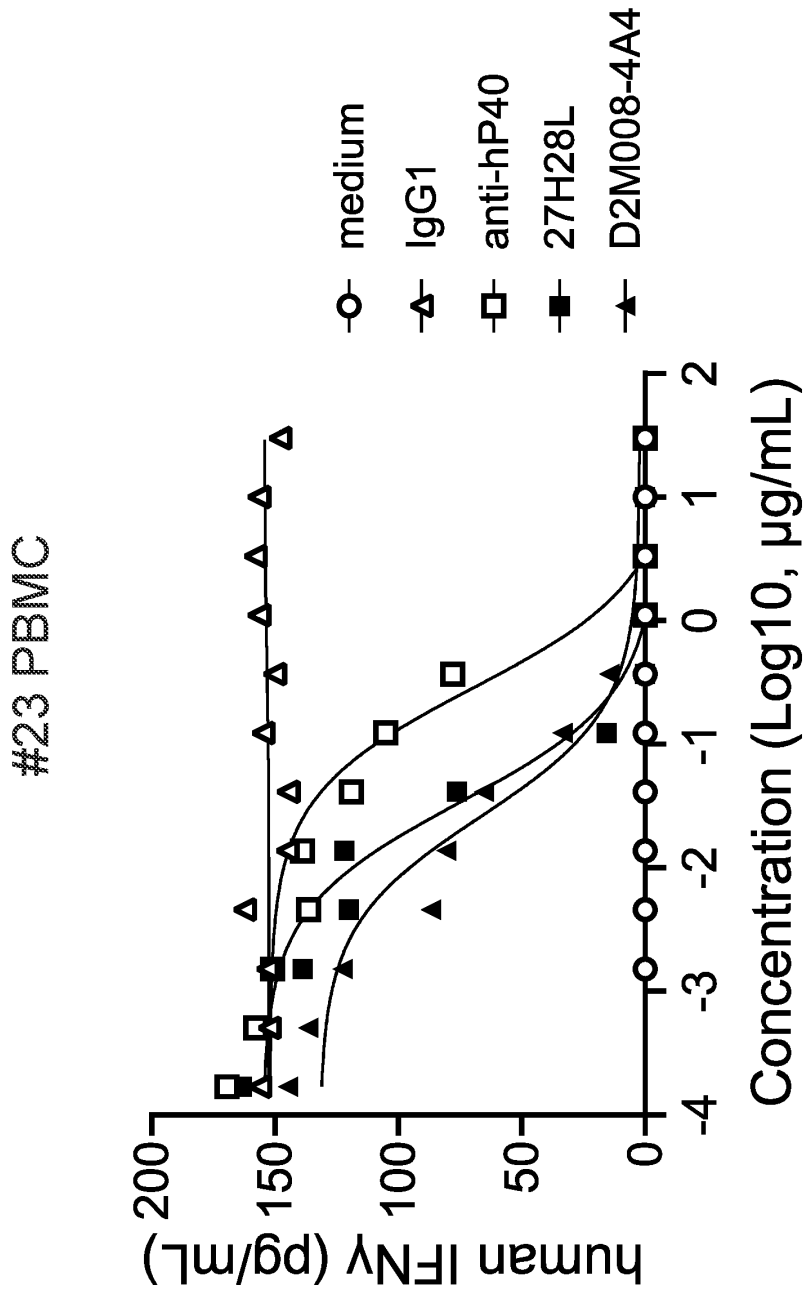


FIG. 7C

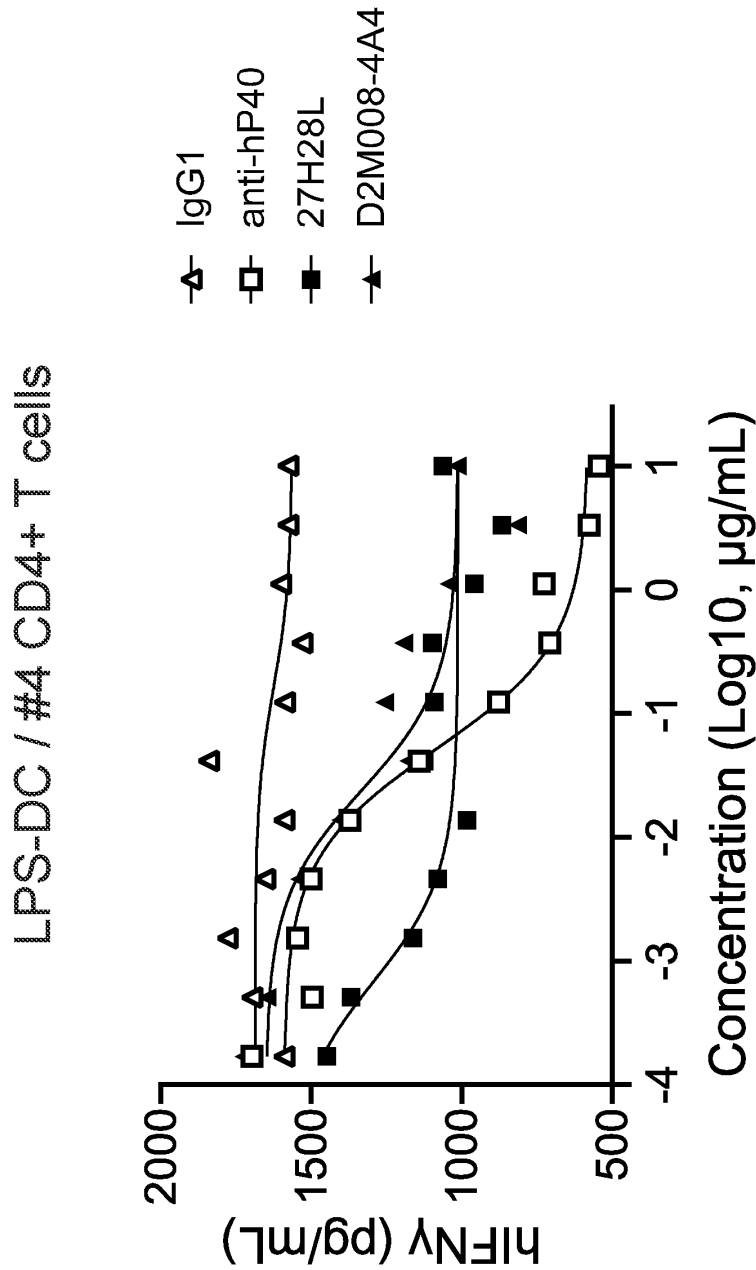


FIG. 8A

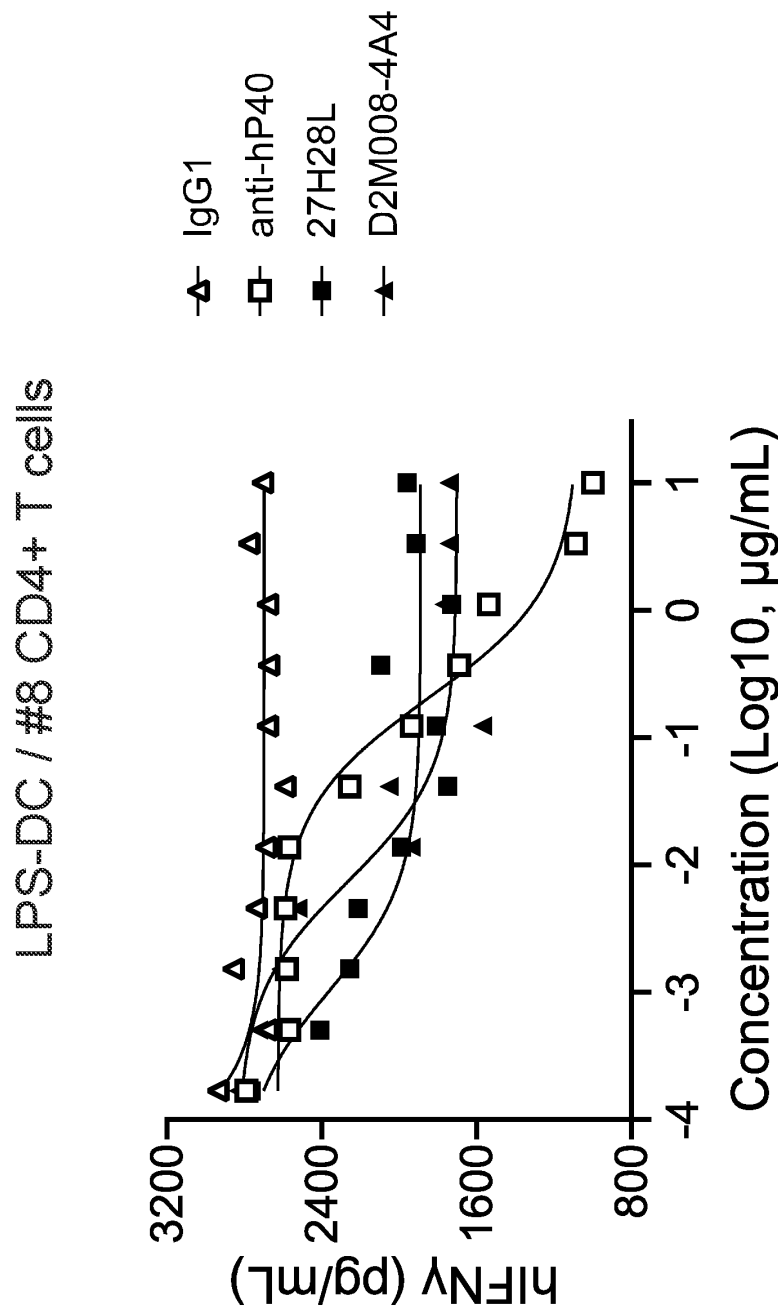


FIG. 8B

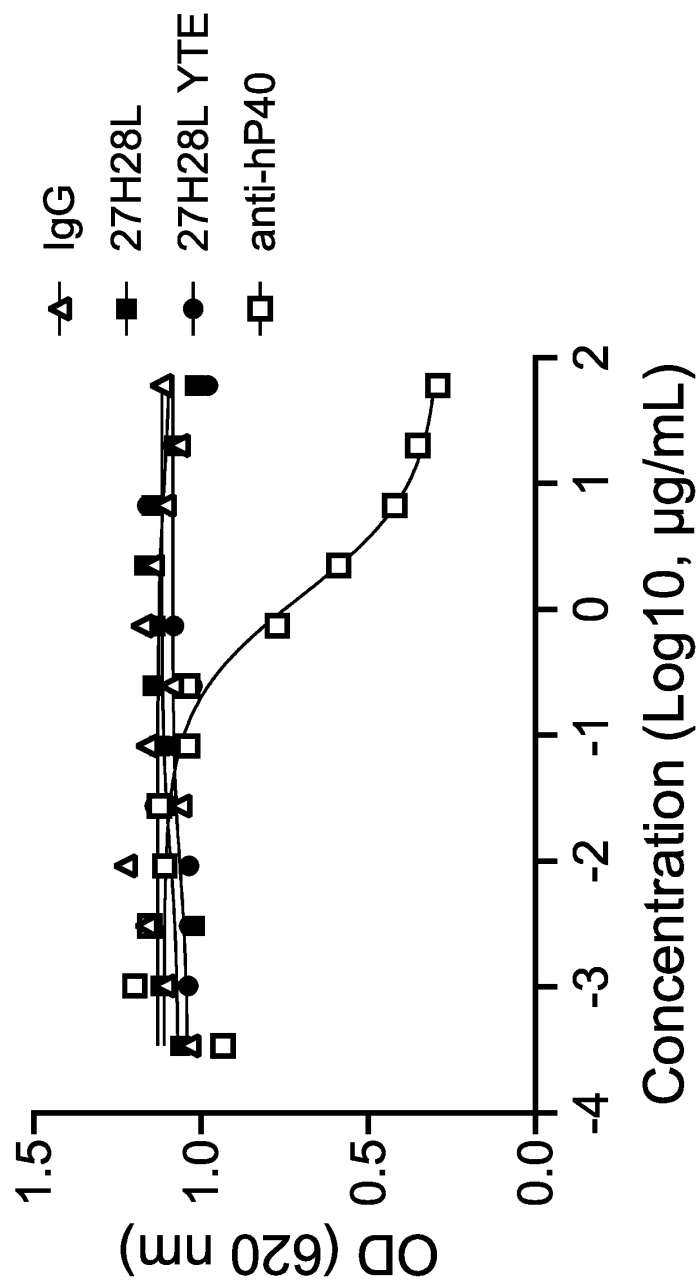


FIG. 9A

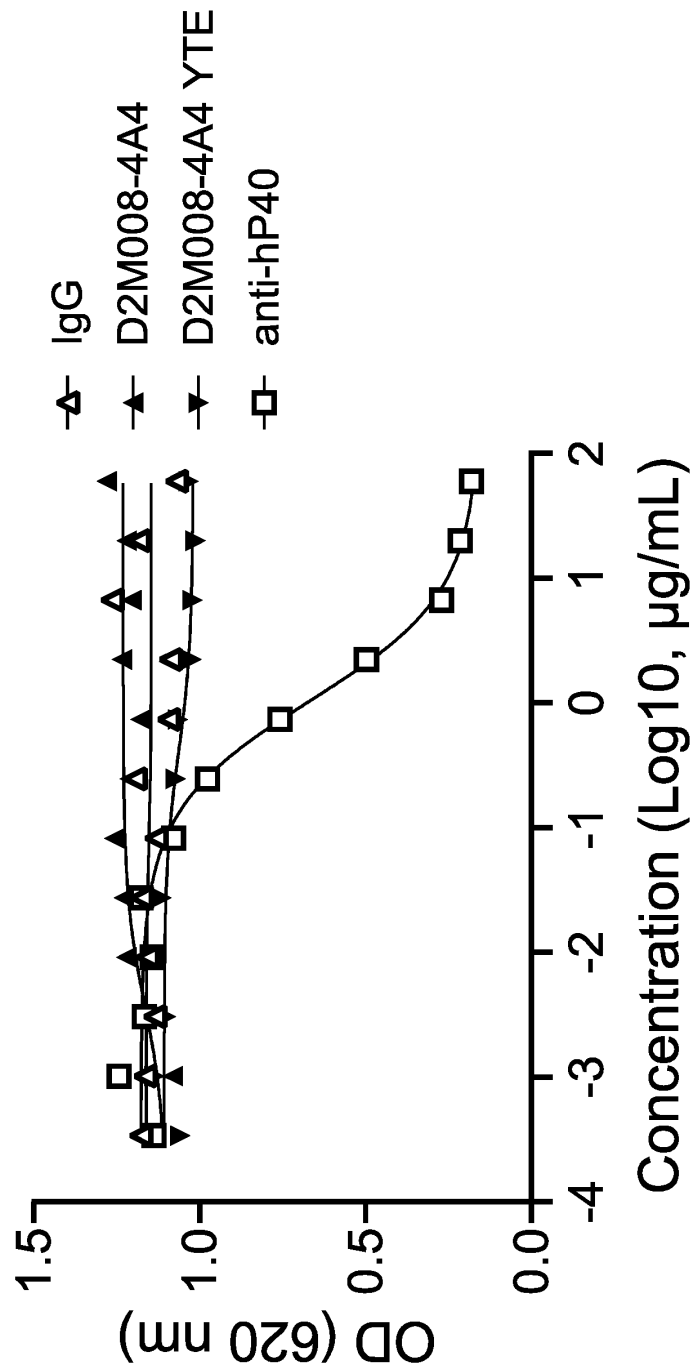


FIG. 9B

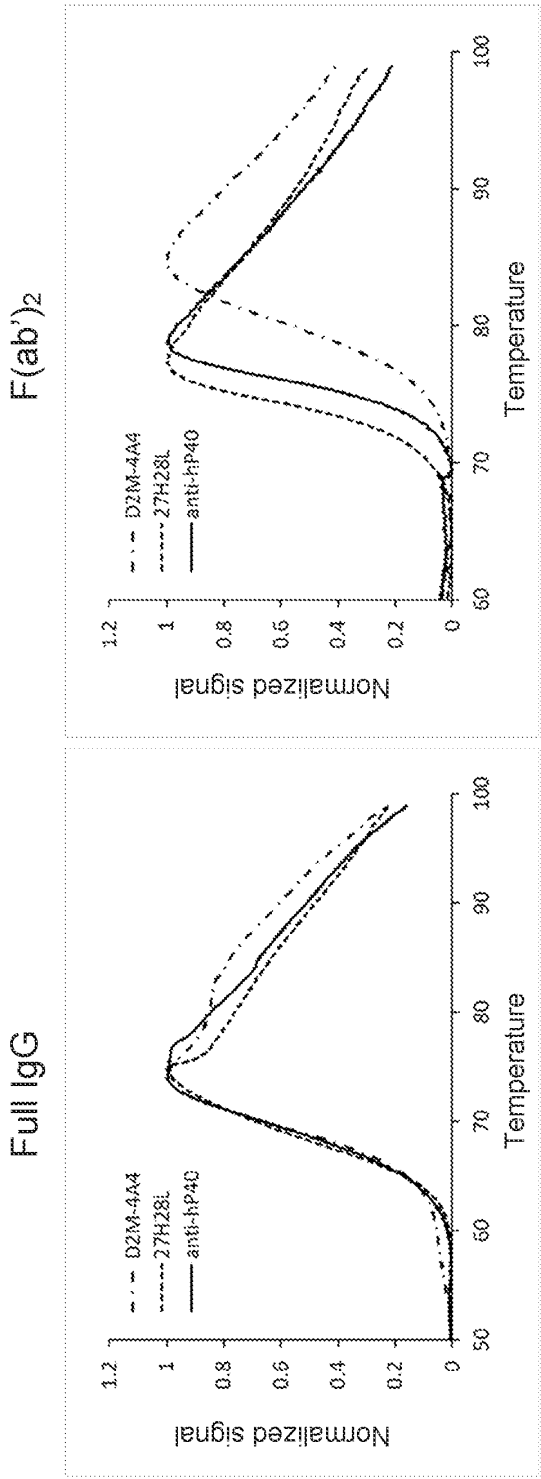


FIG. 10A

	T _m (°C)	
	Full IgG	F(ab') ₂
D2M008-4A4	68.75	79.53
27H28L	68.22	73.99
anti-hp40	68.62	75.79

FIG. 10B

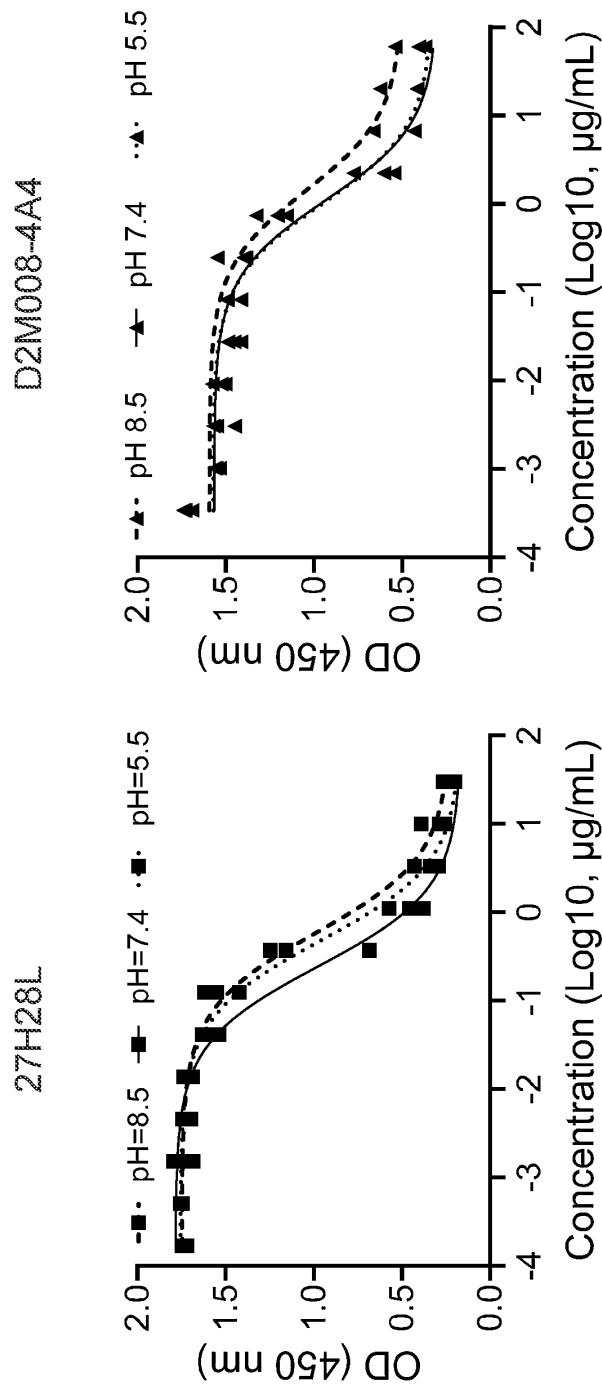


FIG. 11A

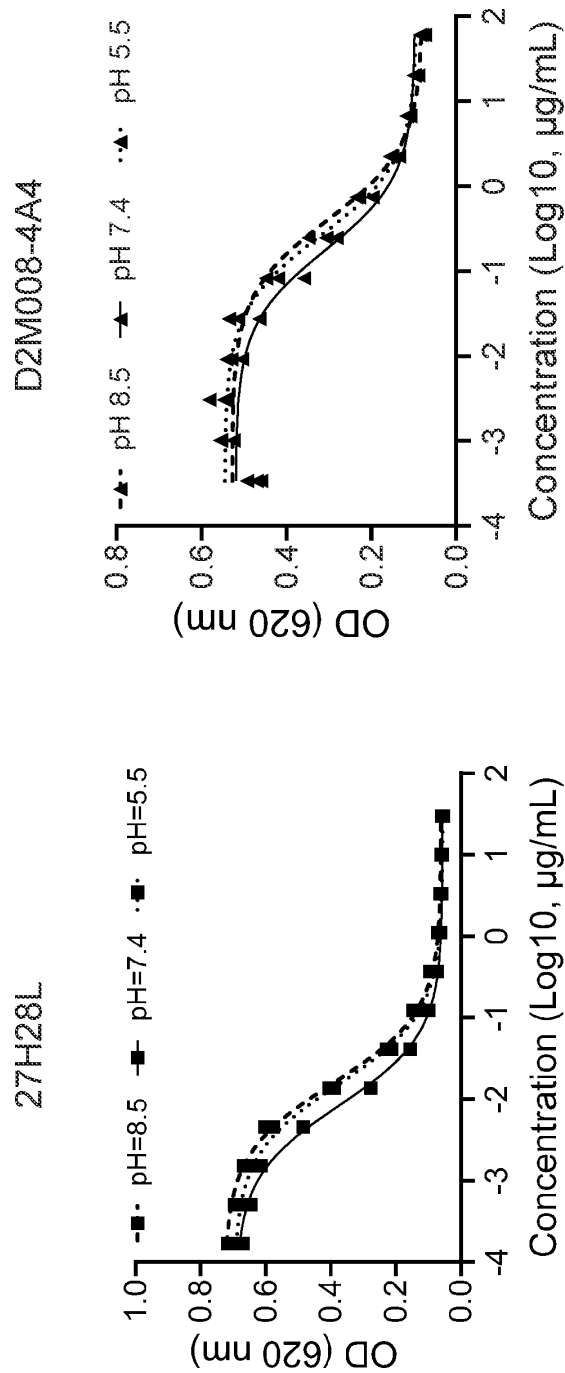


FIG. 11B

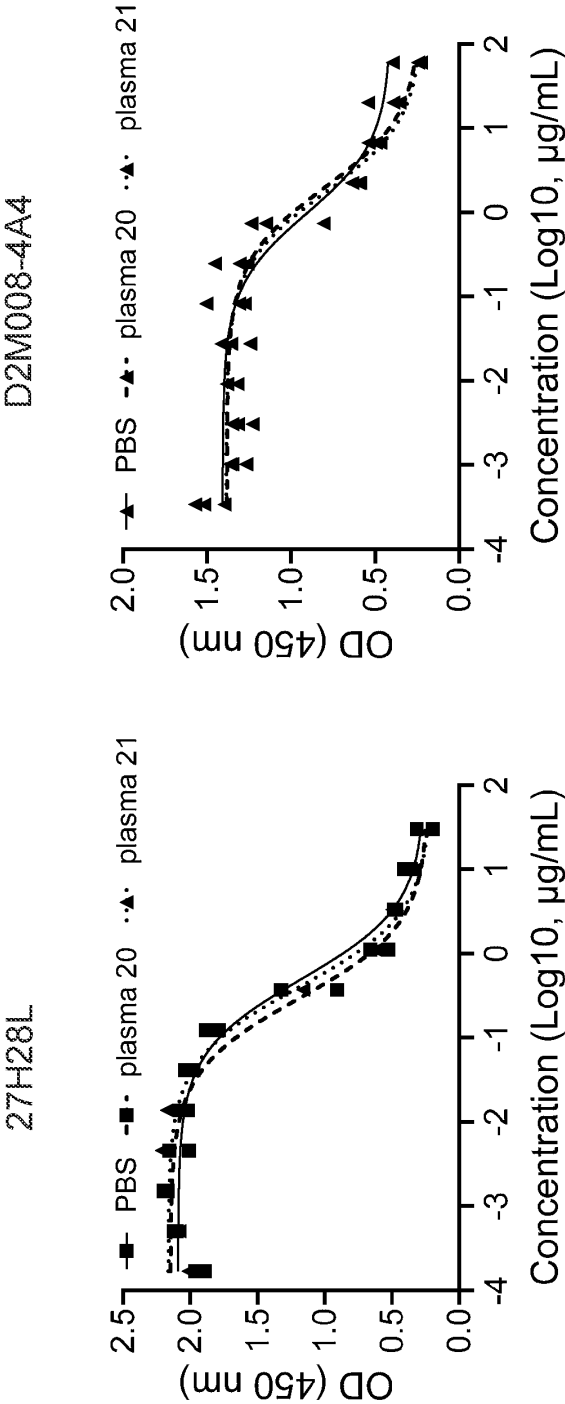


FIG. 12A

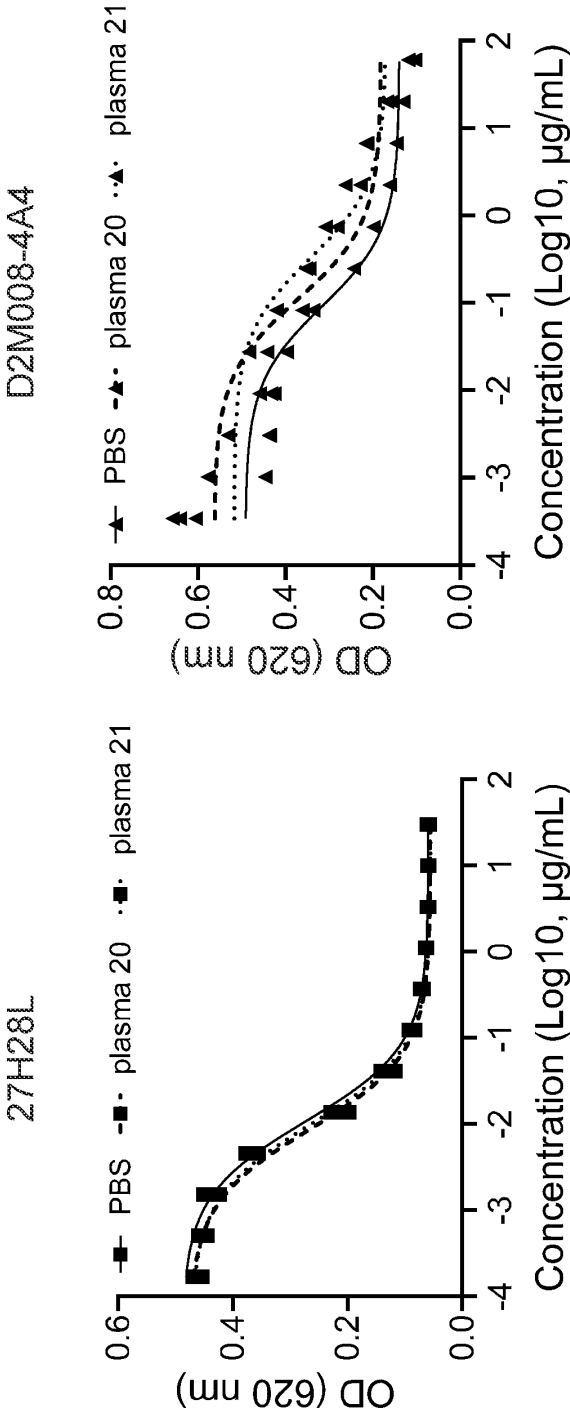


FIG. 12B

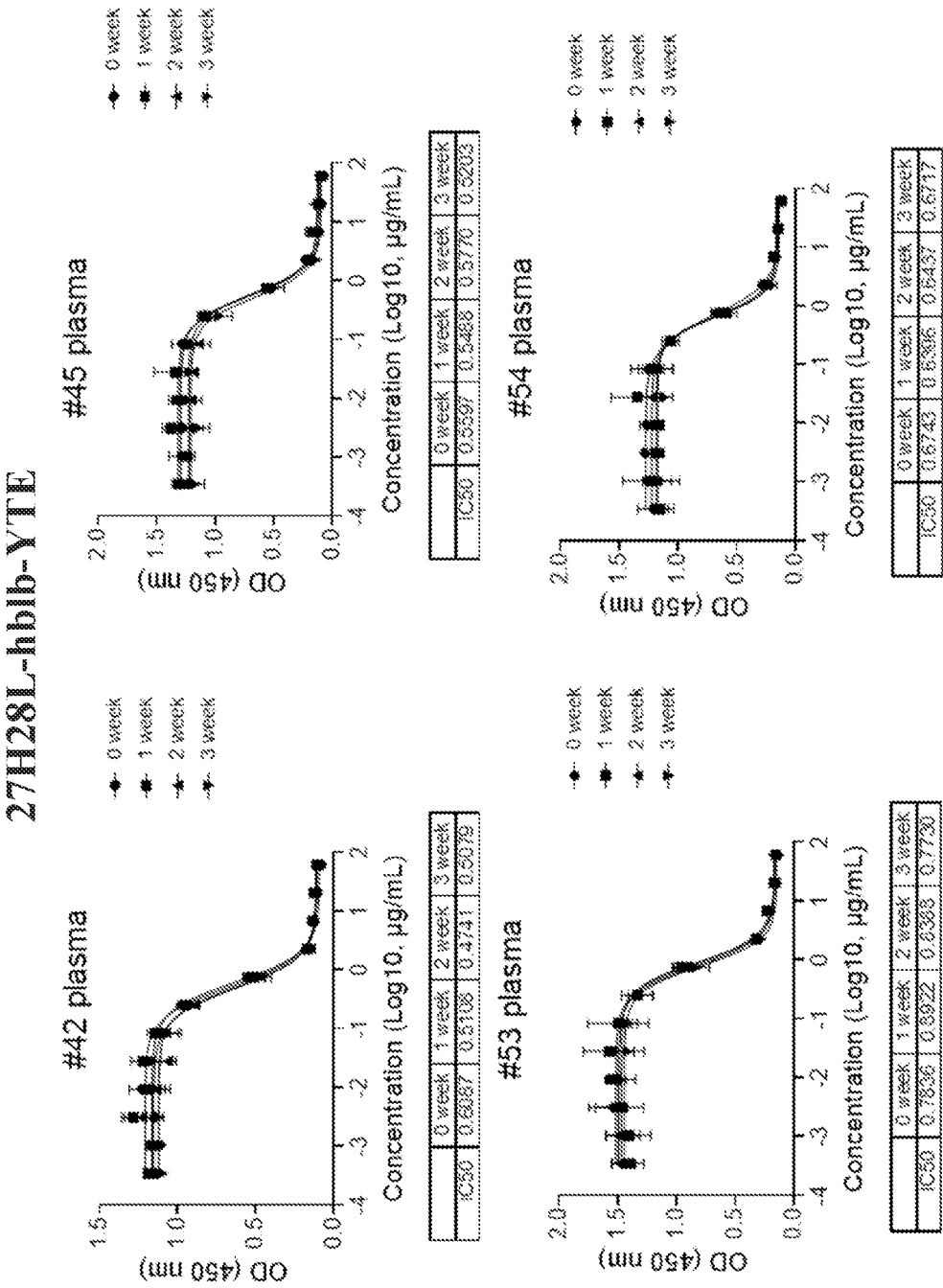


FIG. 12C

4A4-hblb2-YTE

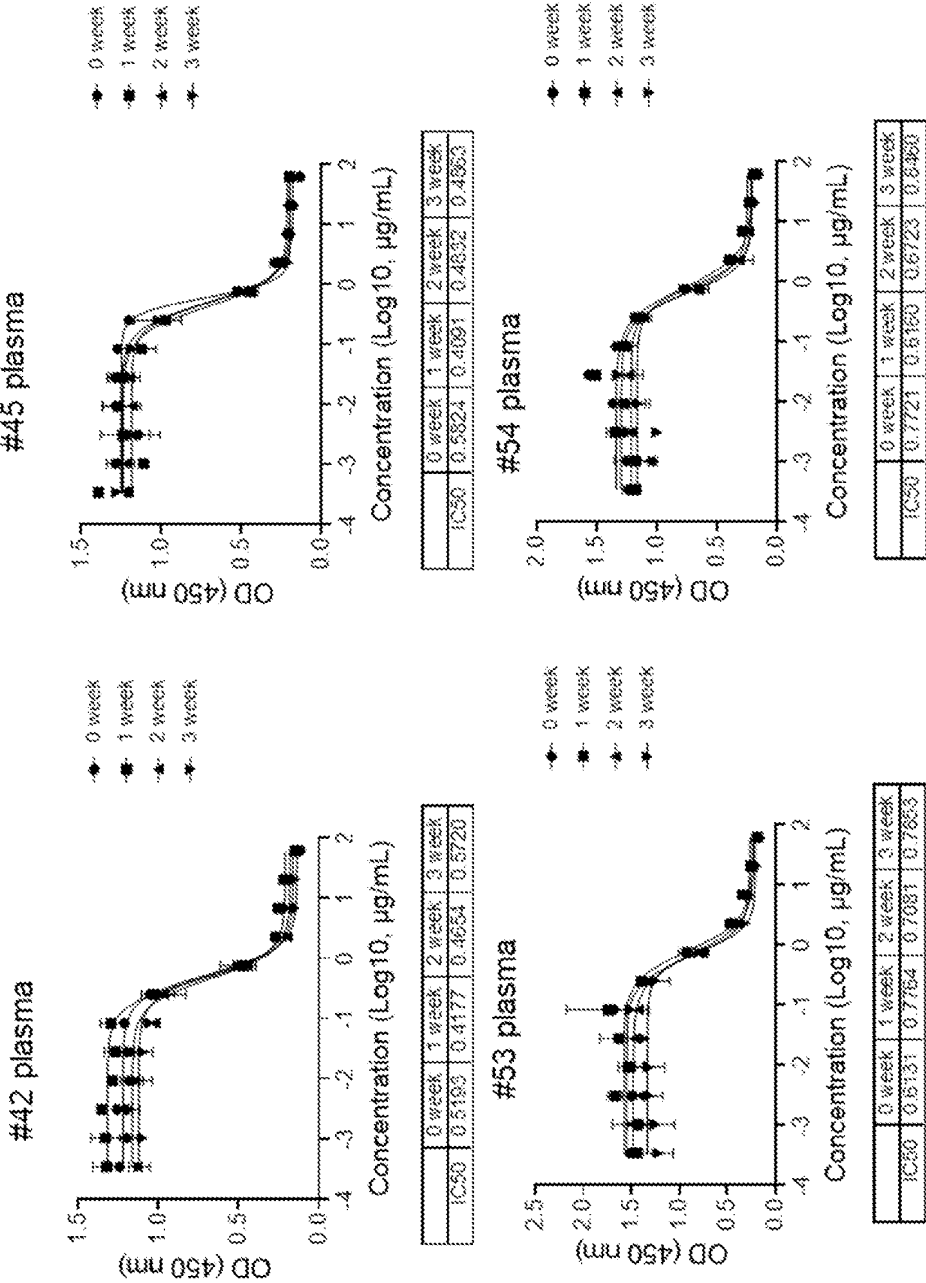
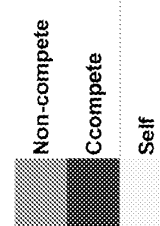


FIG. 12D



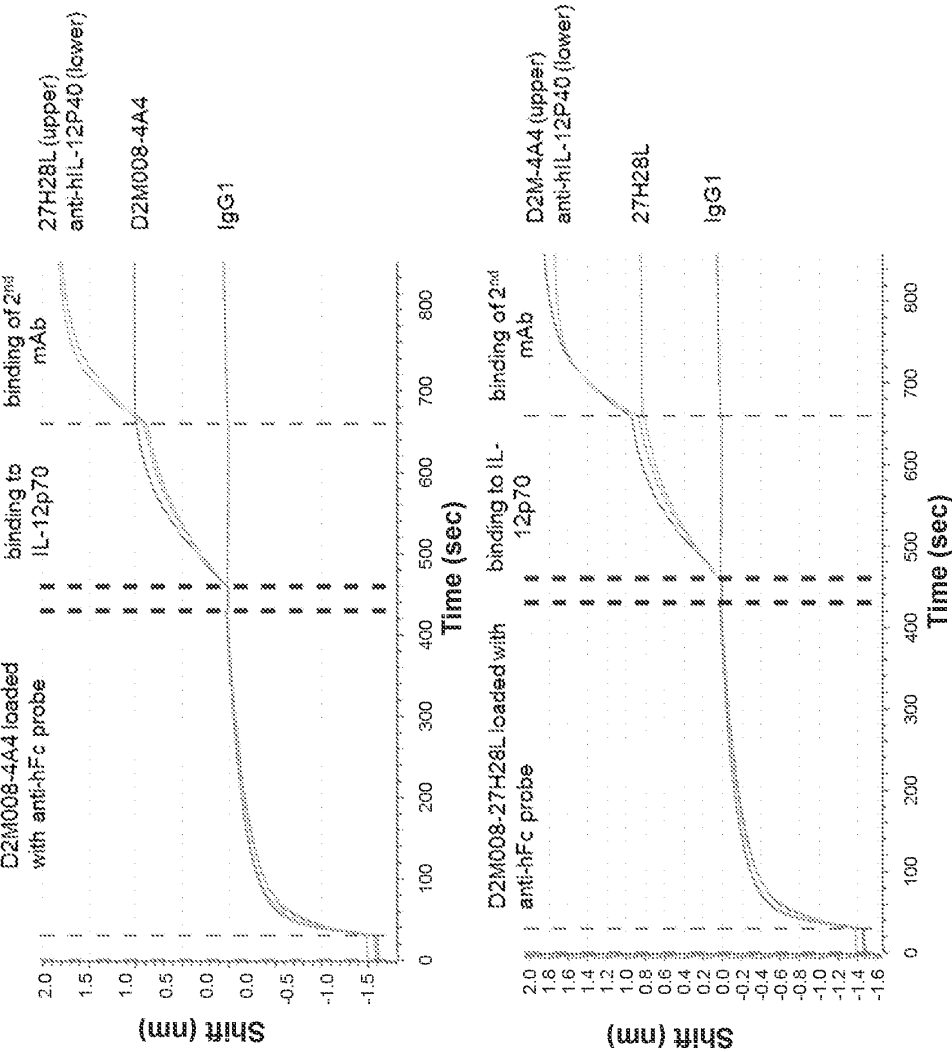


FIG. 13B

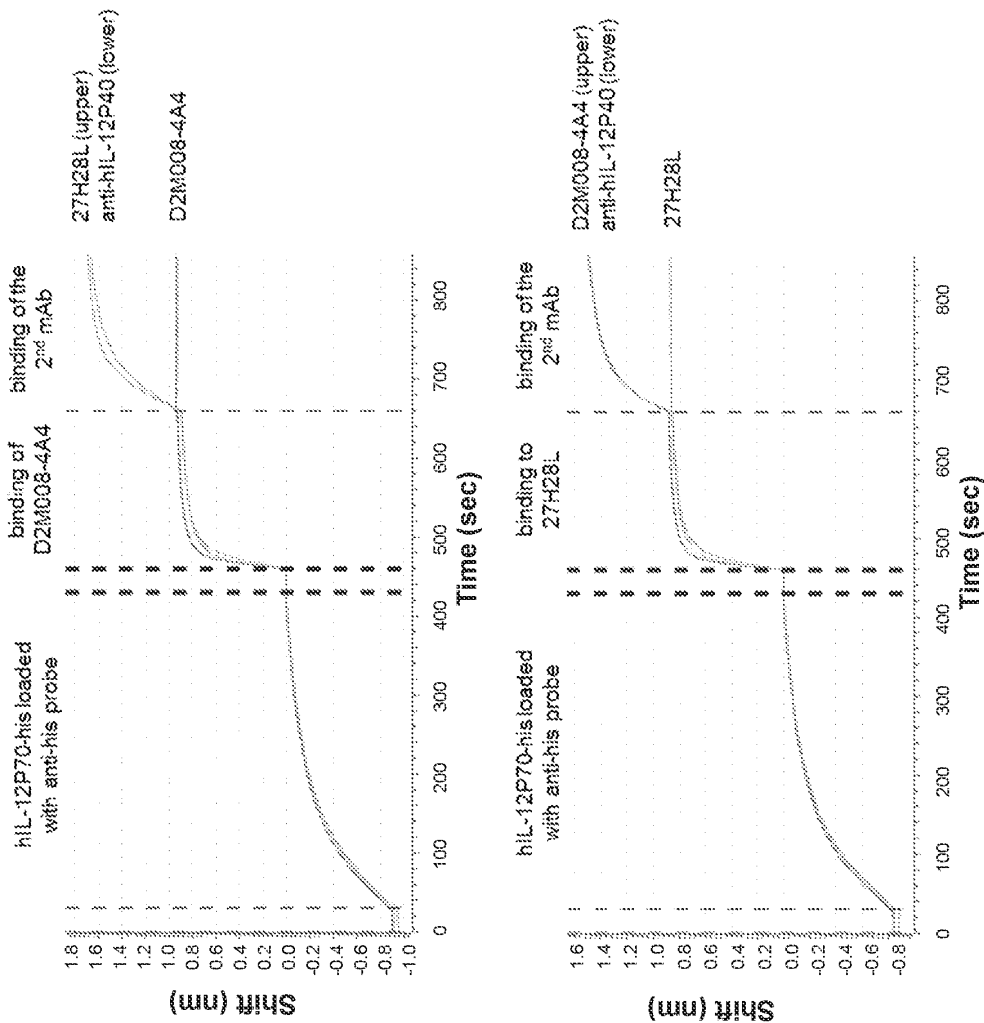
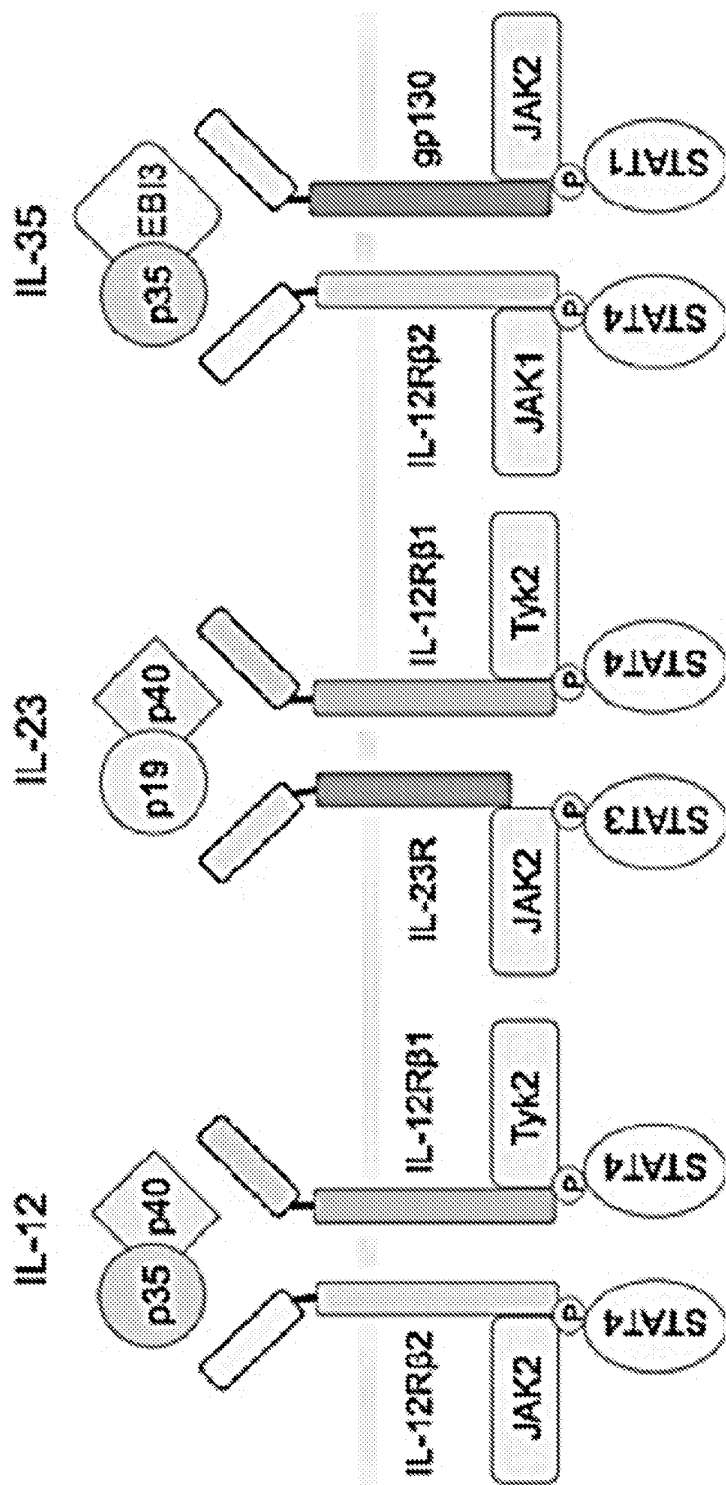


FIG. 13C



IL-12 induces Th1 polarization, production of IFN- γ and TNF α

IL-23 promotes the differentiation of naïve T helper cells into Th17

IL-35 is an inhibitory cytokine produced by T-reg and B-reg cells

FIG. 14

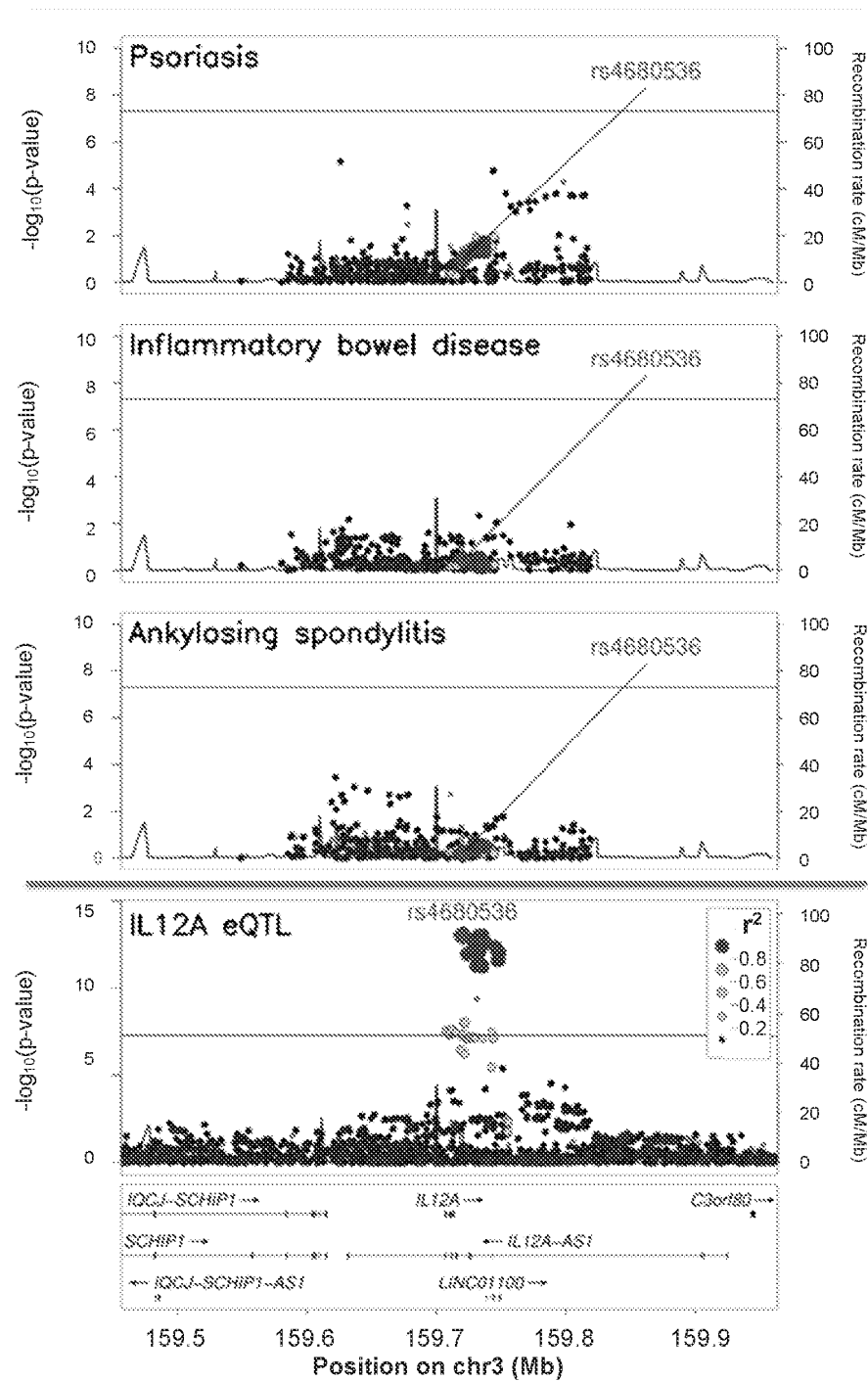


FIG. 15A

38/84

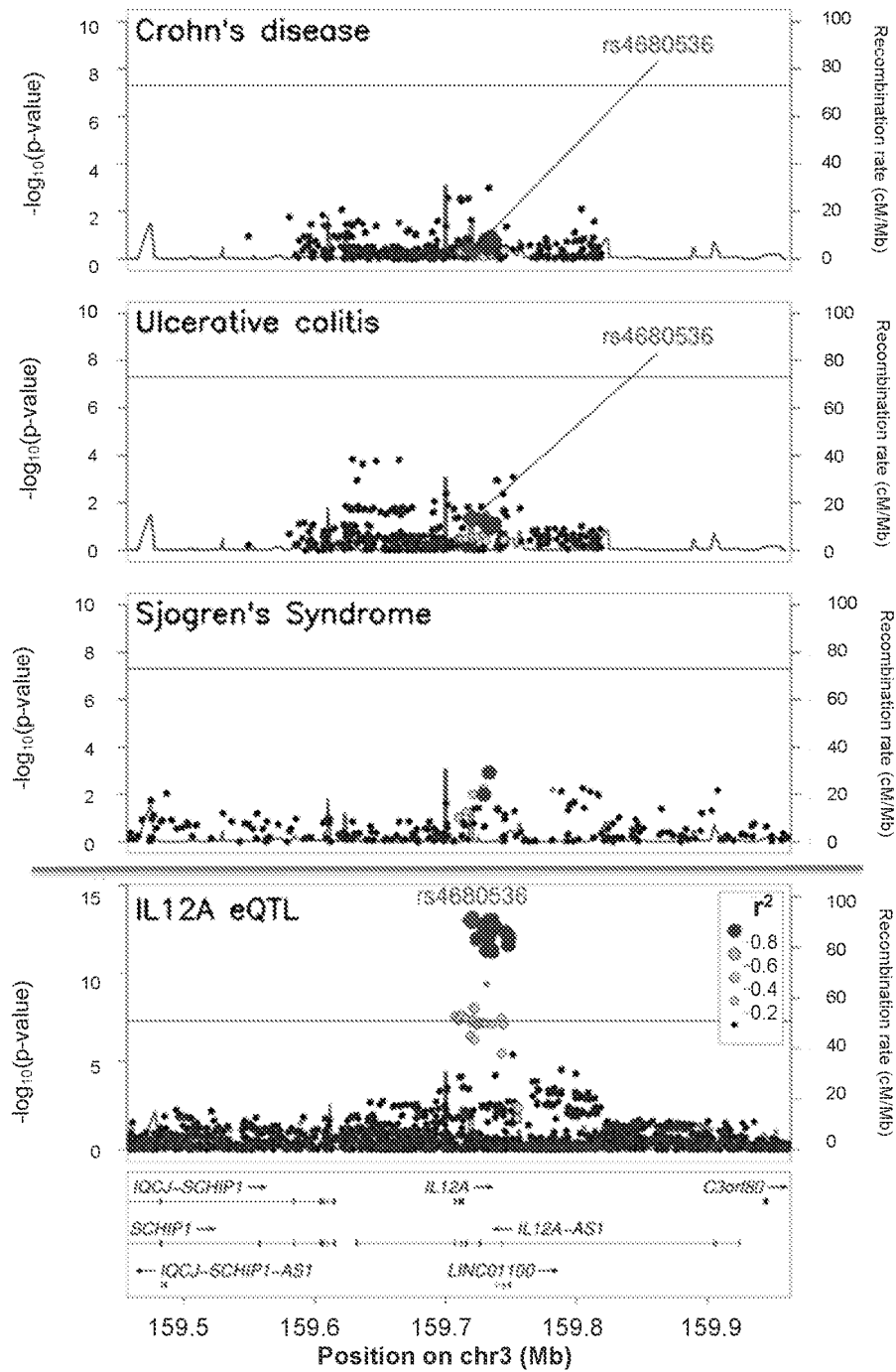


FIG. 15B

39/84

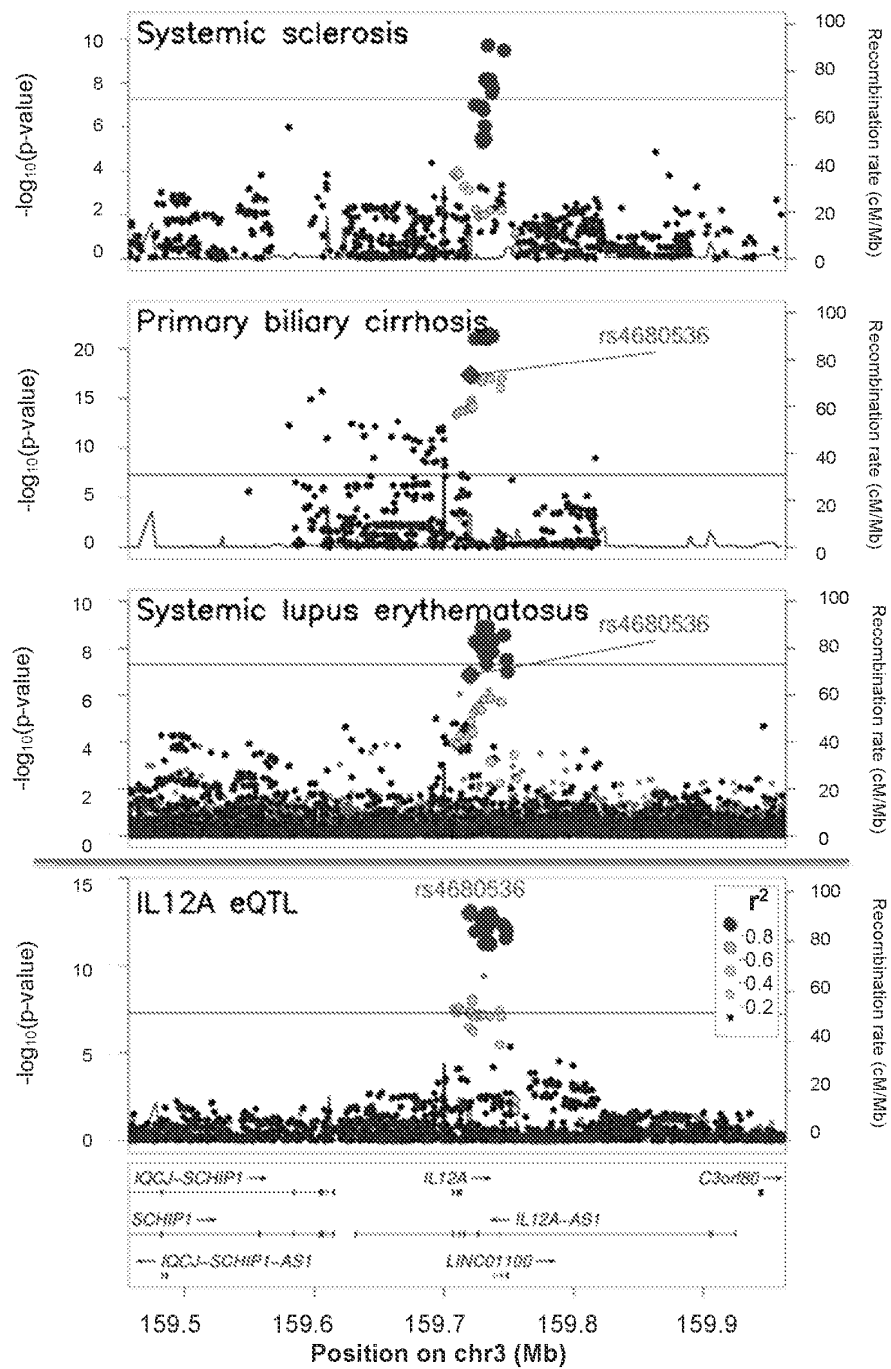


FIG. 15C

SUBSTITUTE SHEET (RULE 26)

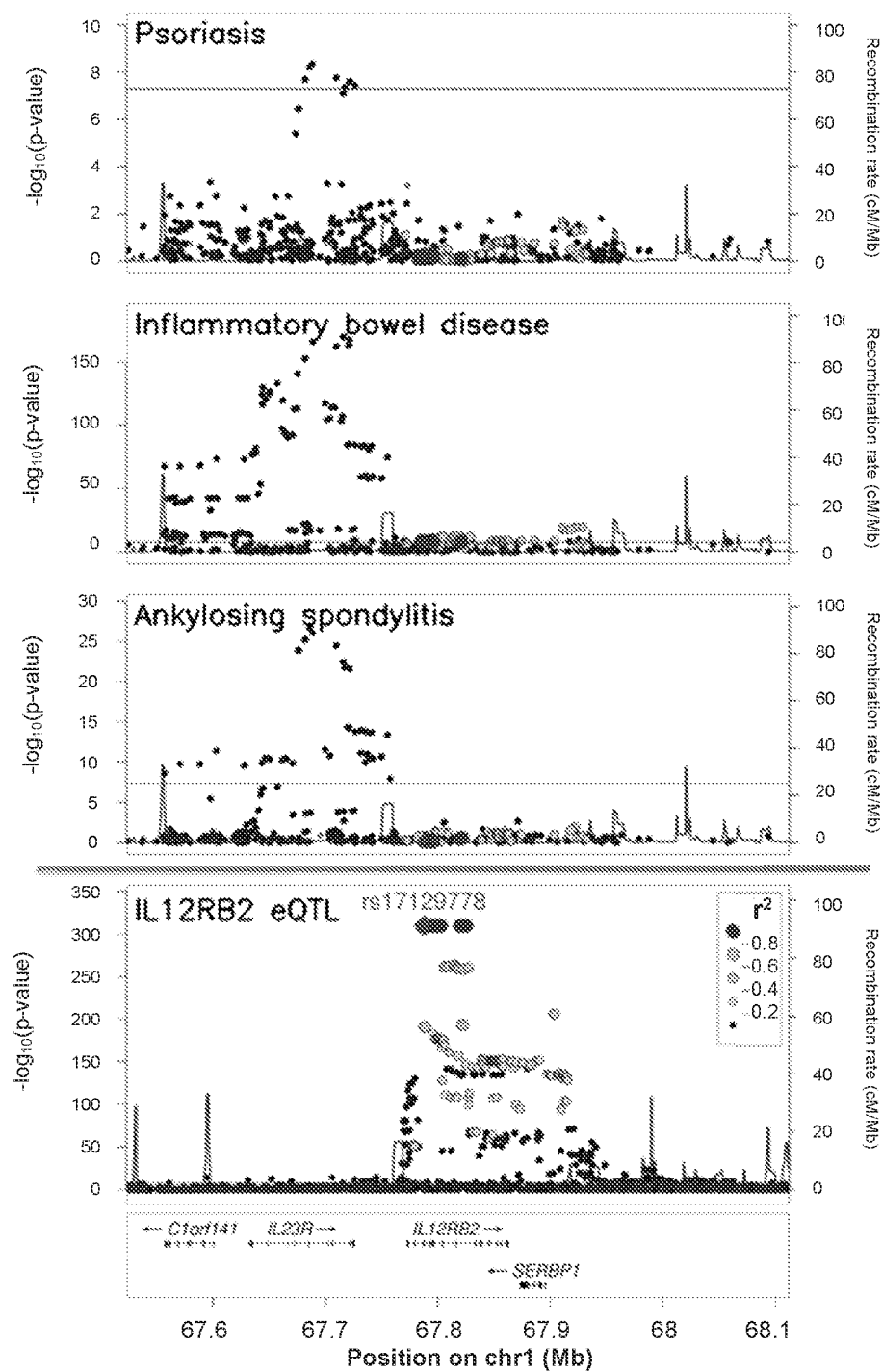


FIG. 16A

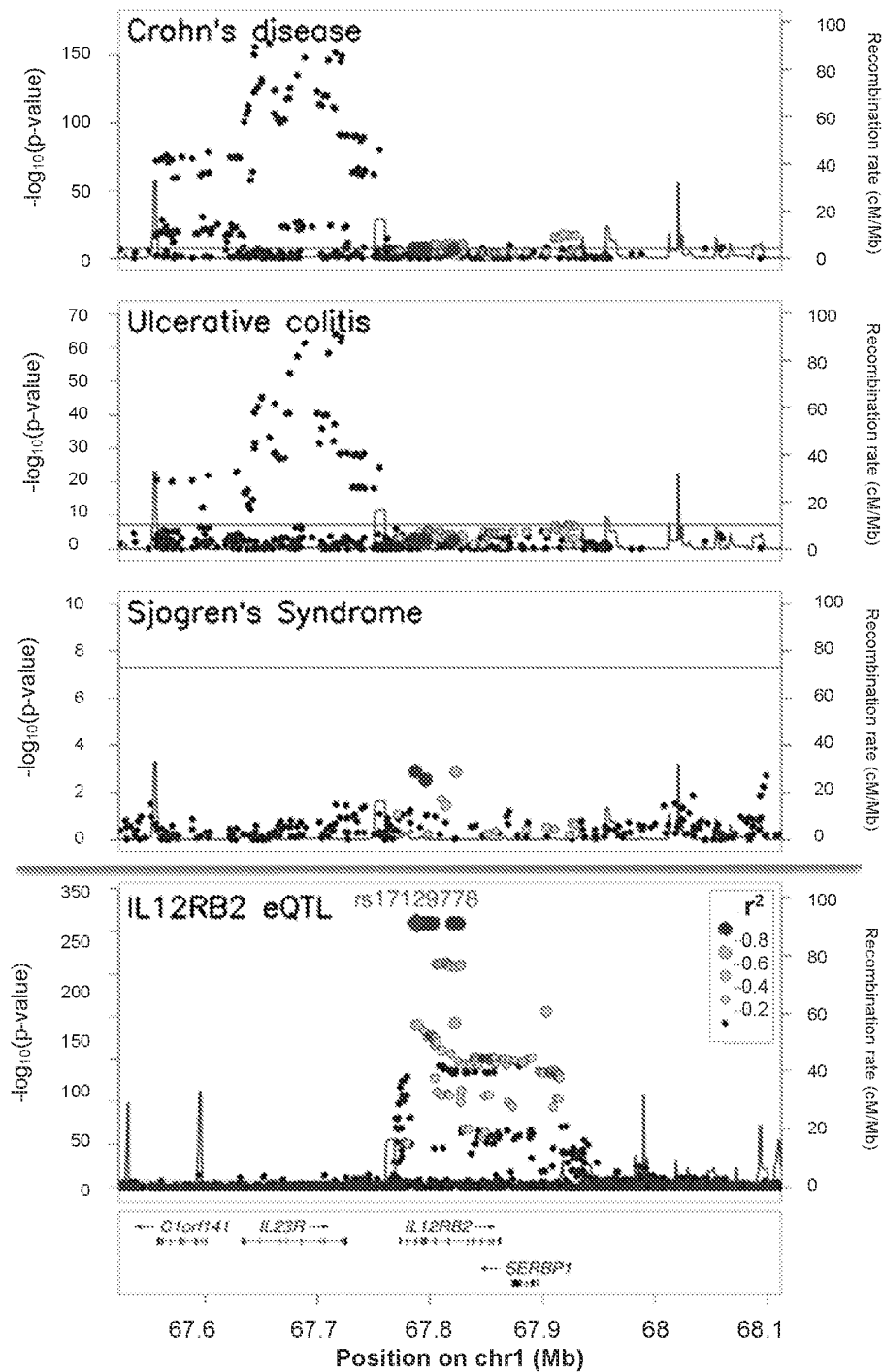


FIG. 16B

42/84

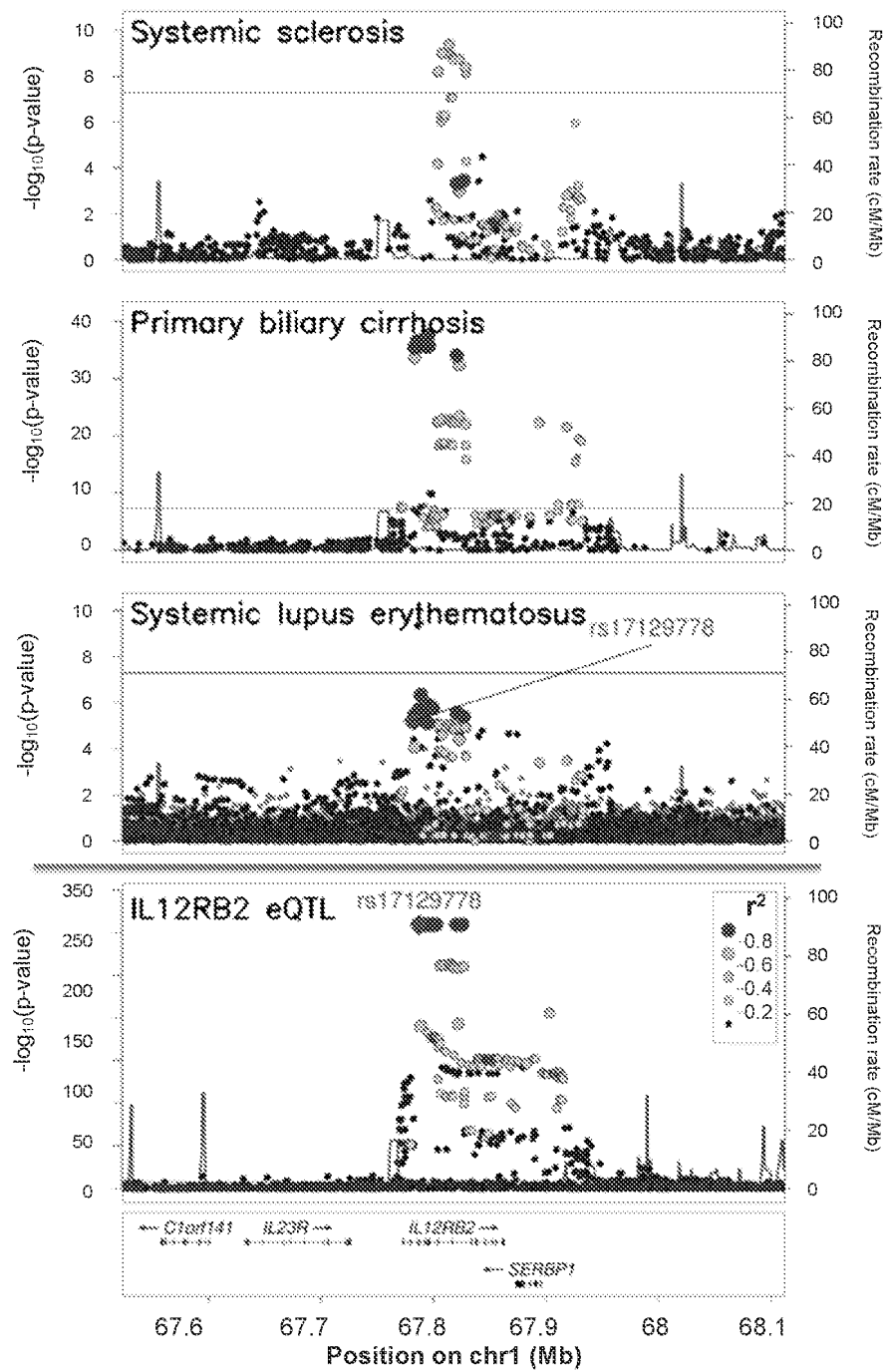


FIG. 16C

SUBSTITUTE SHEET (RULE 26)

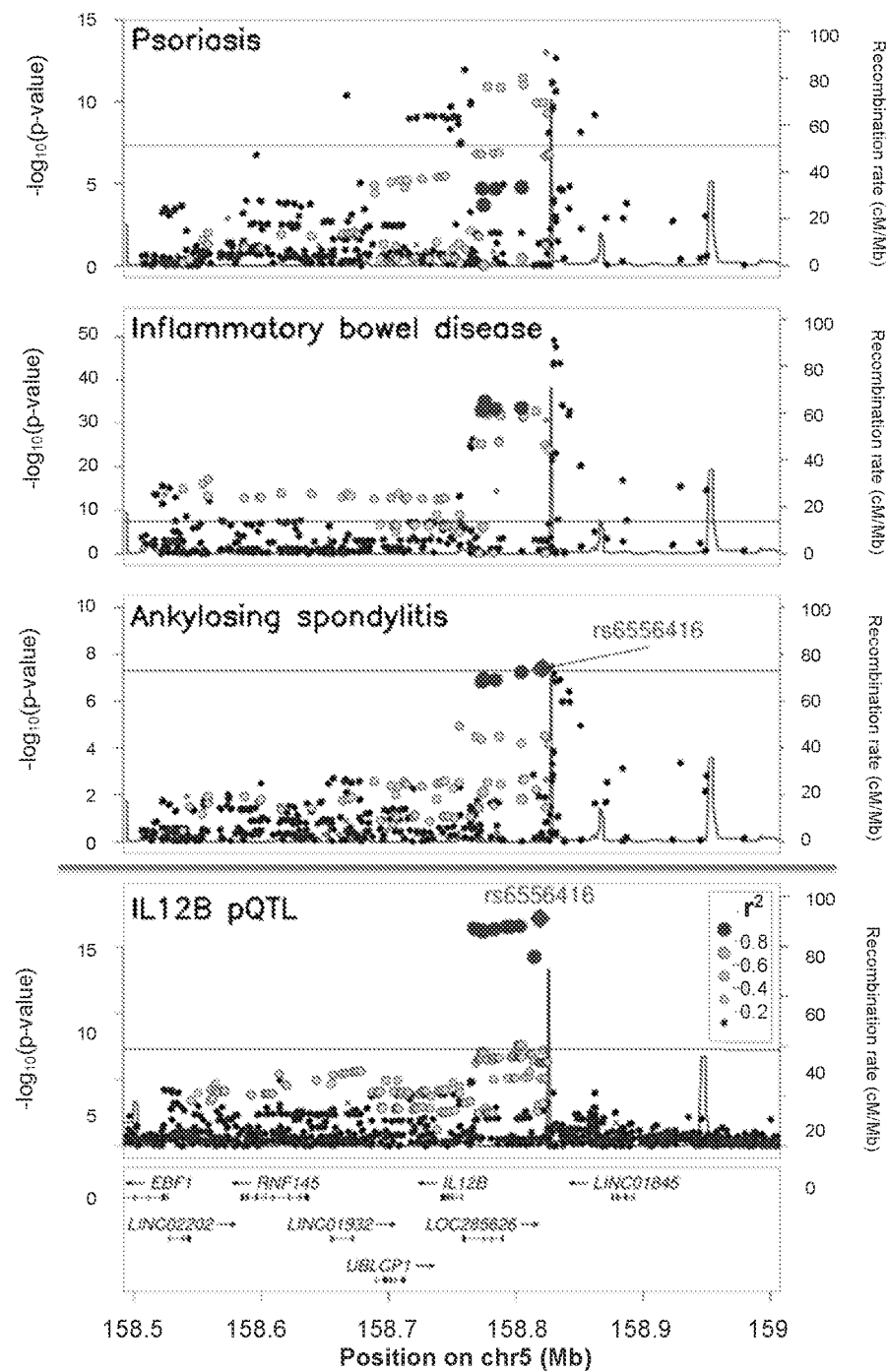


FIG. 17A

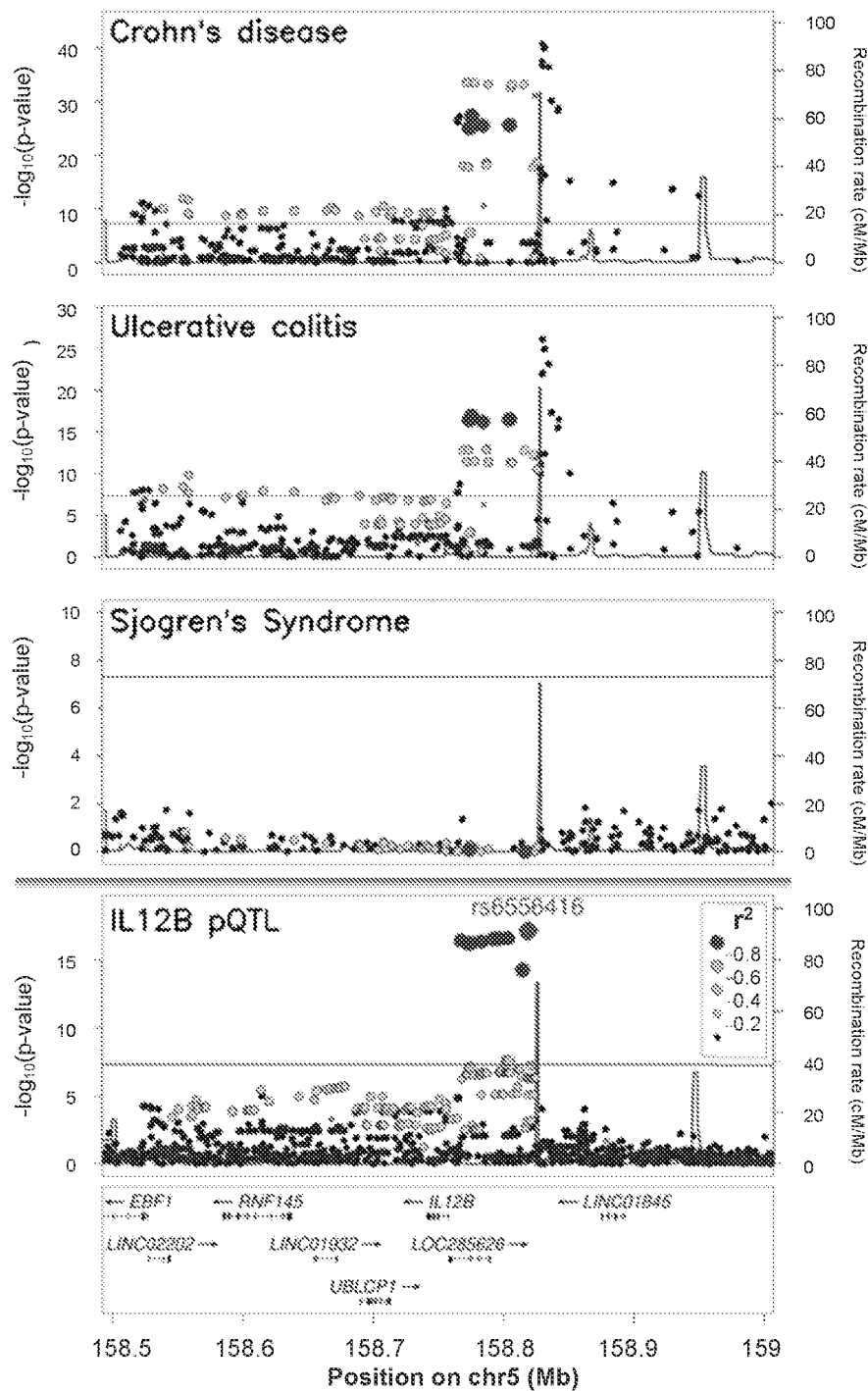


FIG. 17B

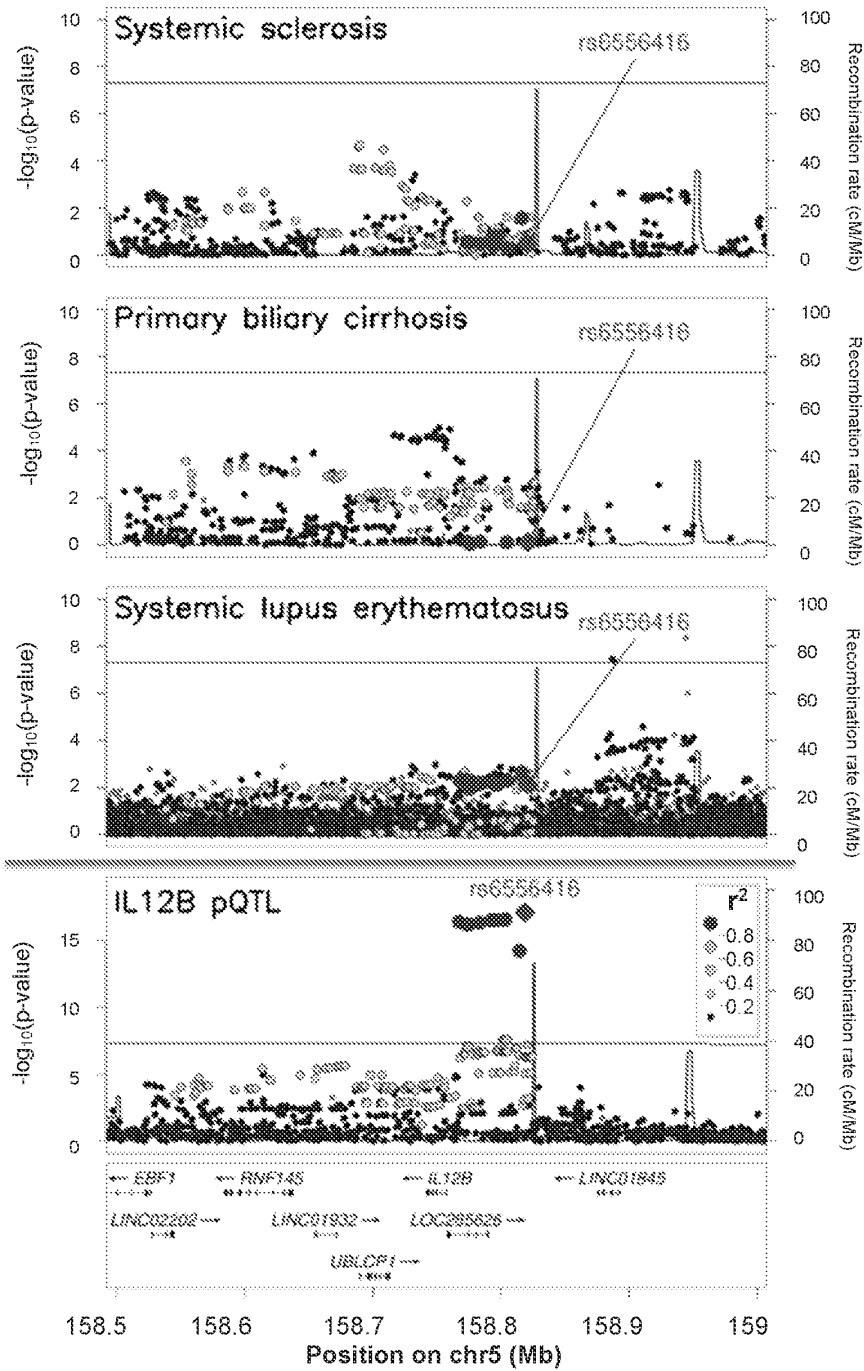


FIG. 17C

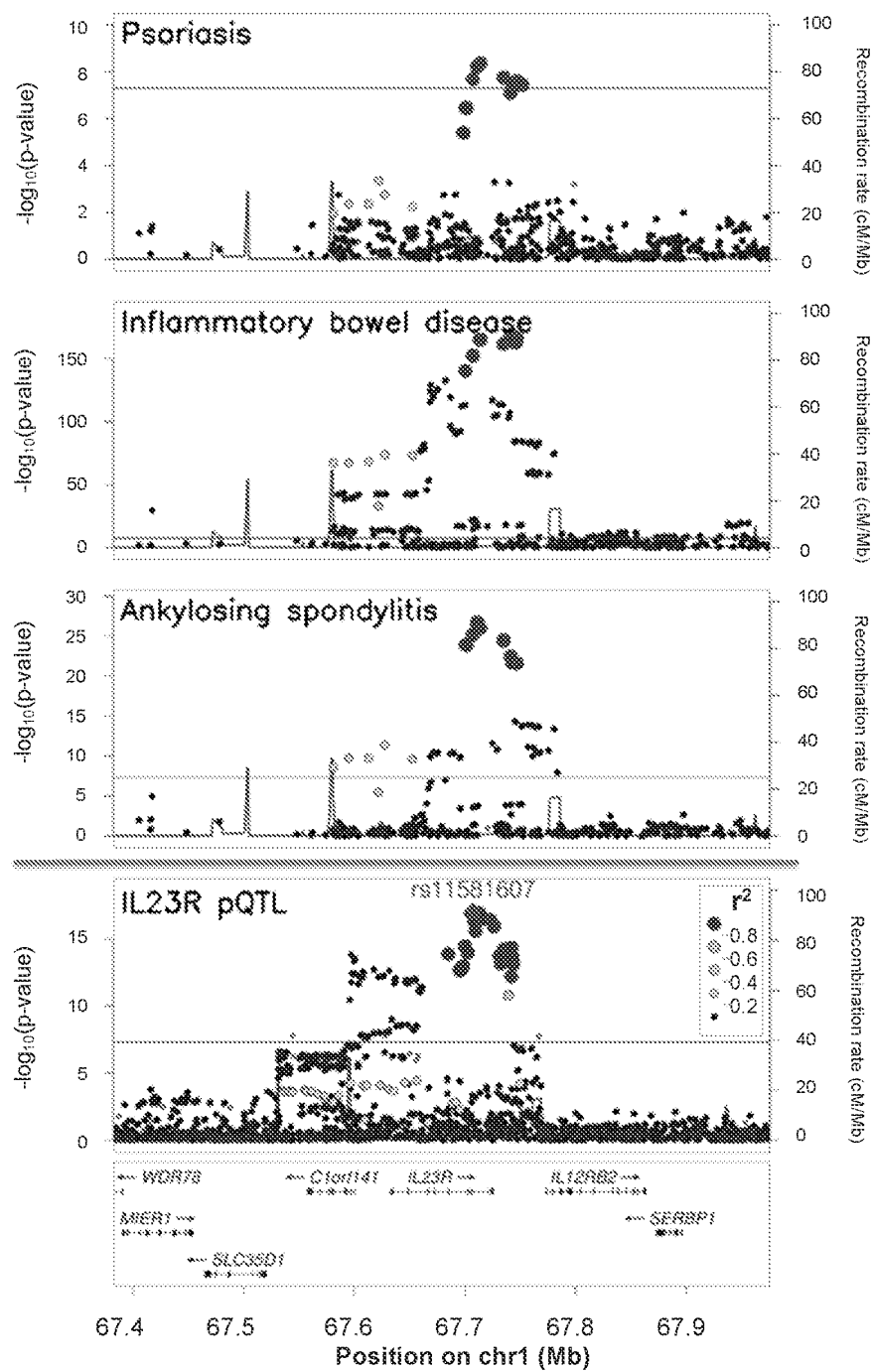


FIG. 18A

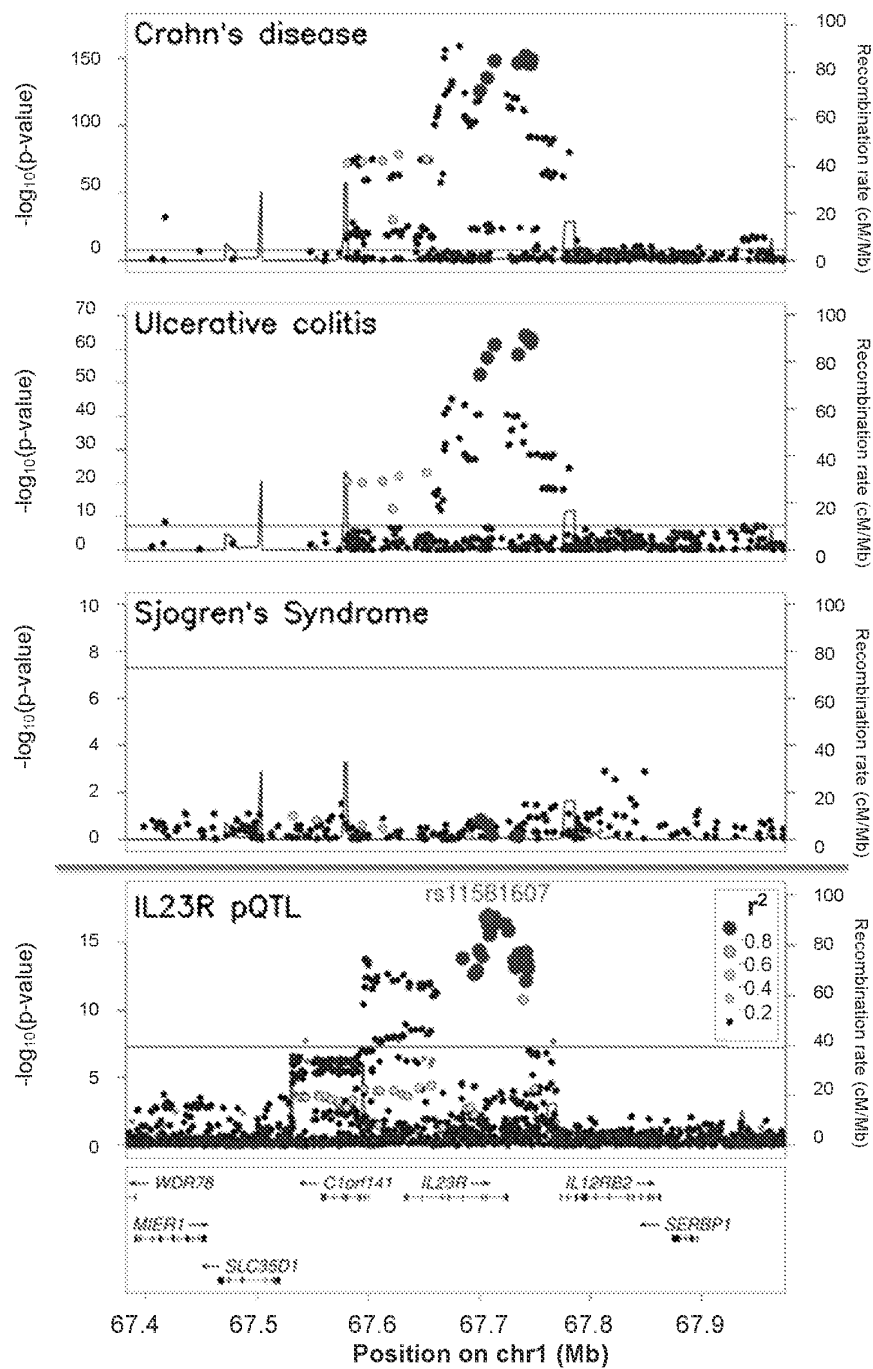


FIG. 18B

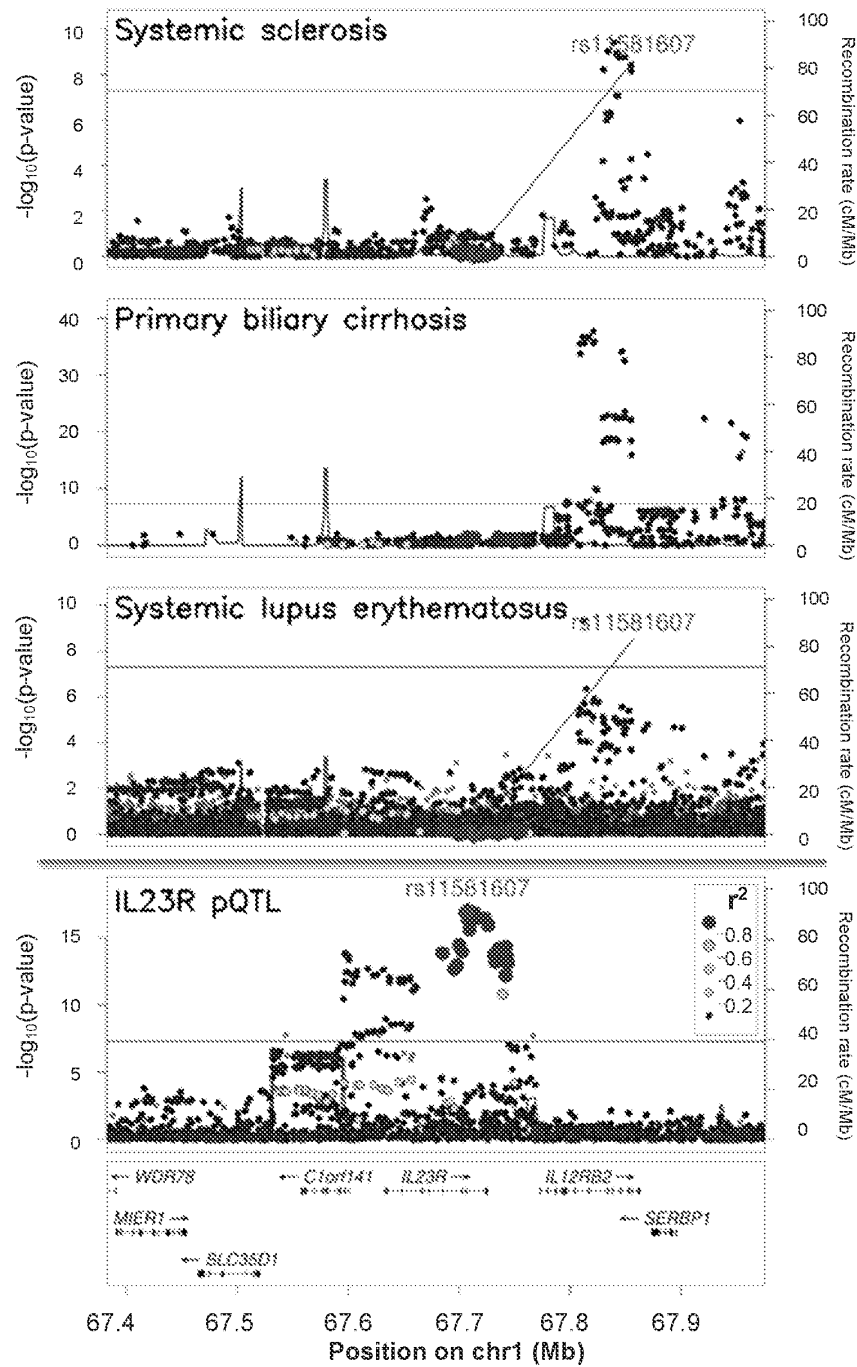


FIG. 18C

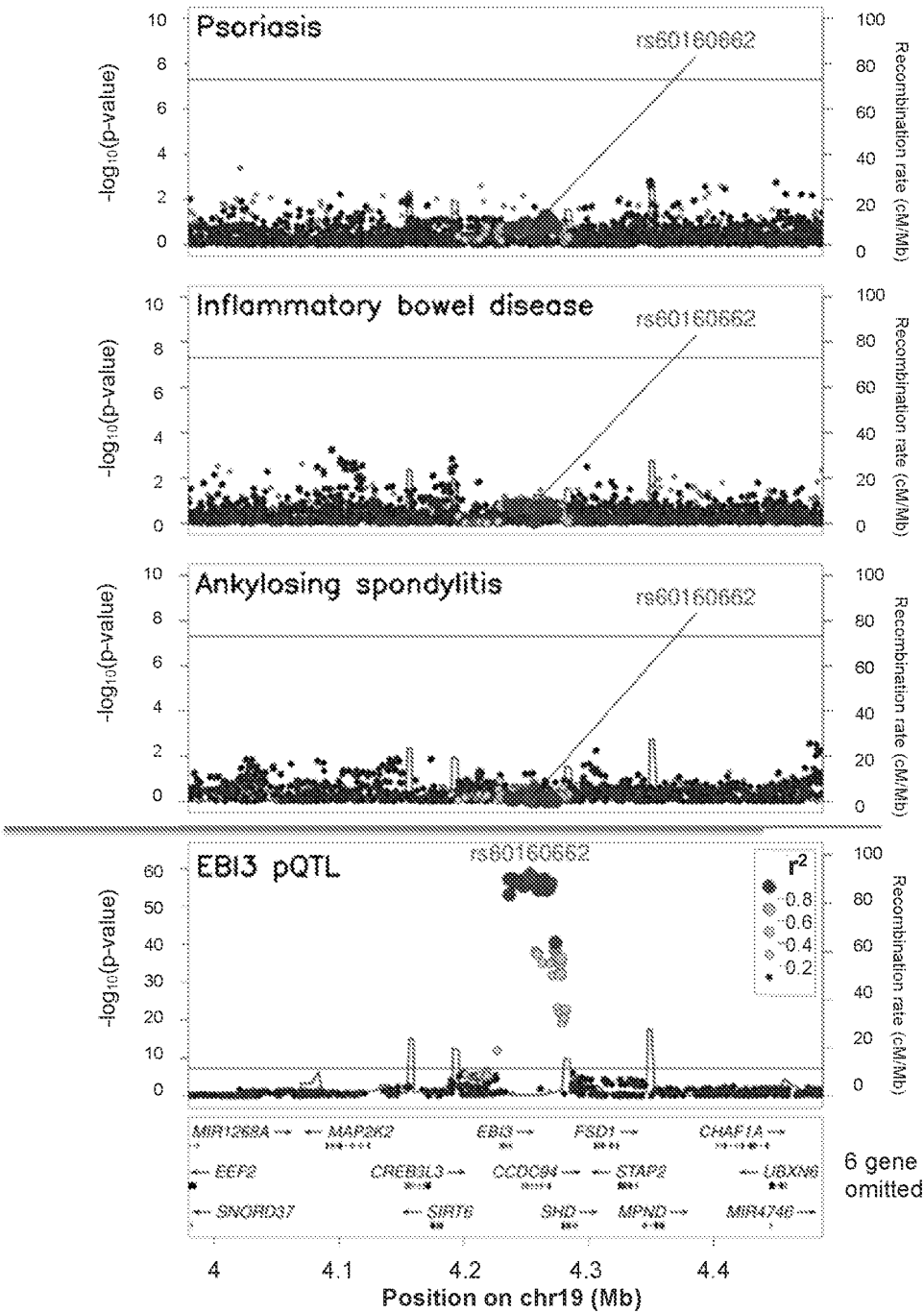


FIG. 19A

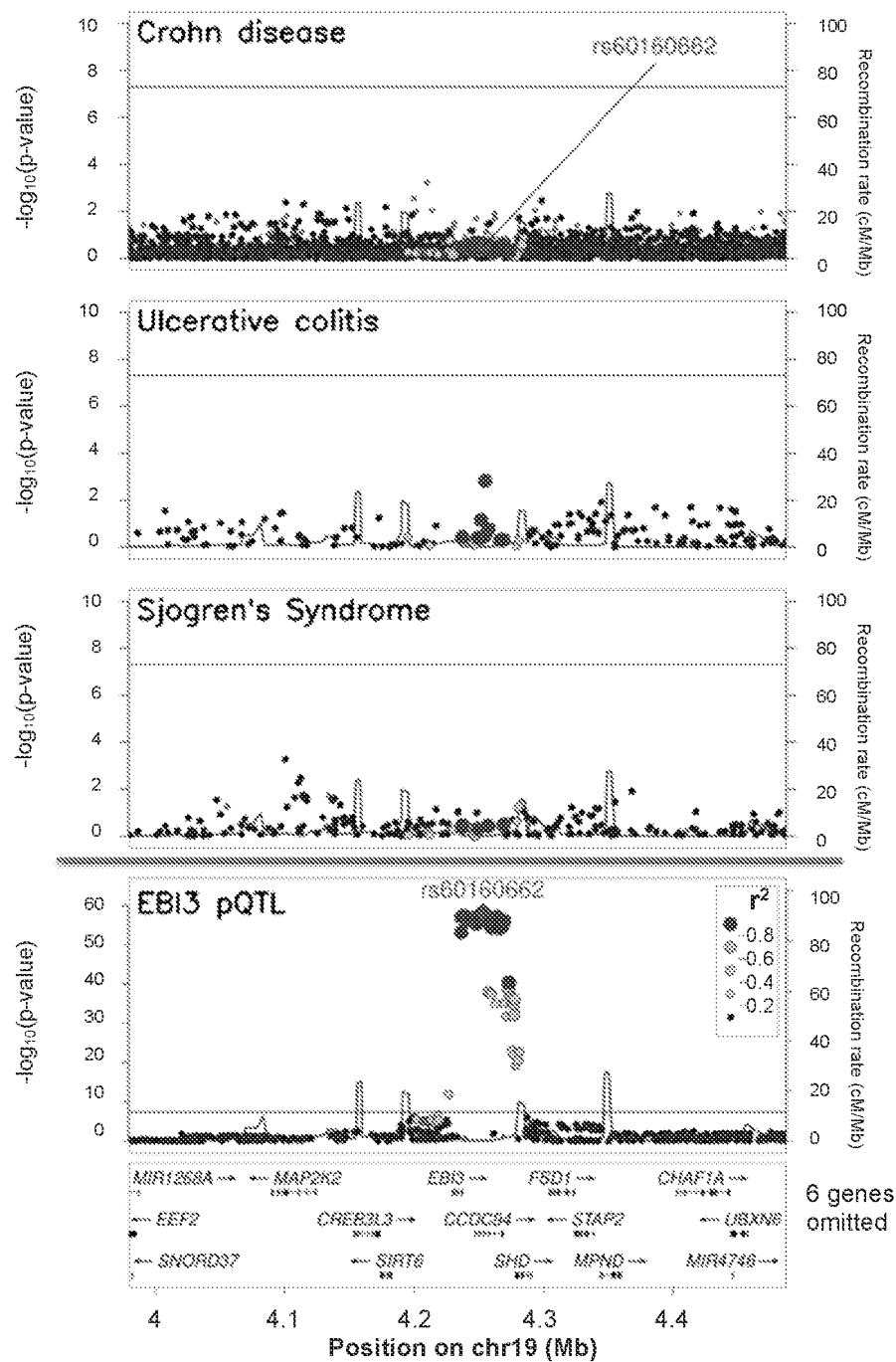


FIG. 19B

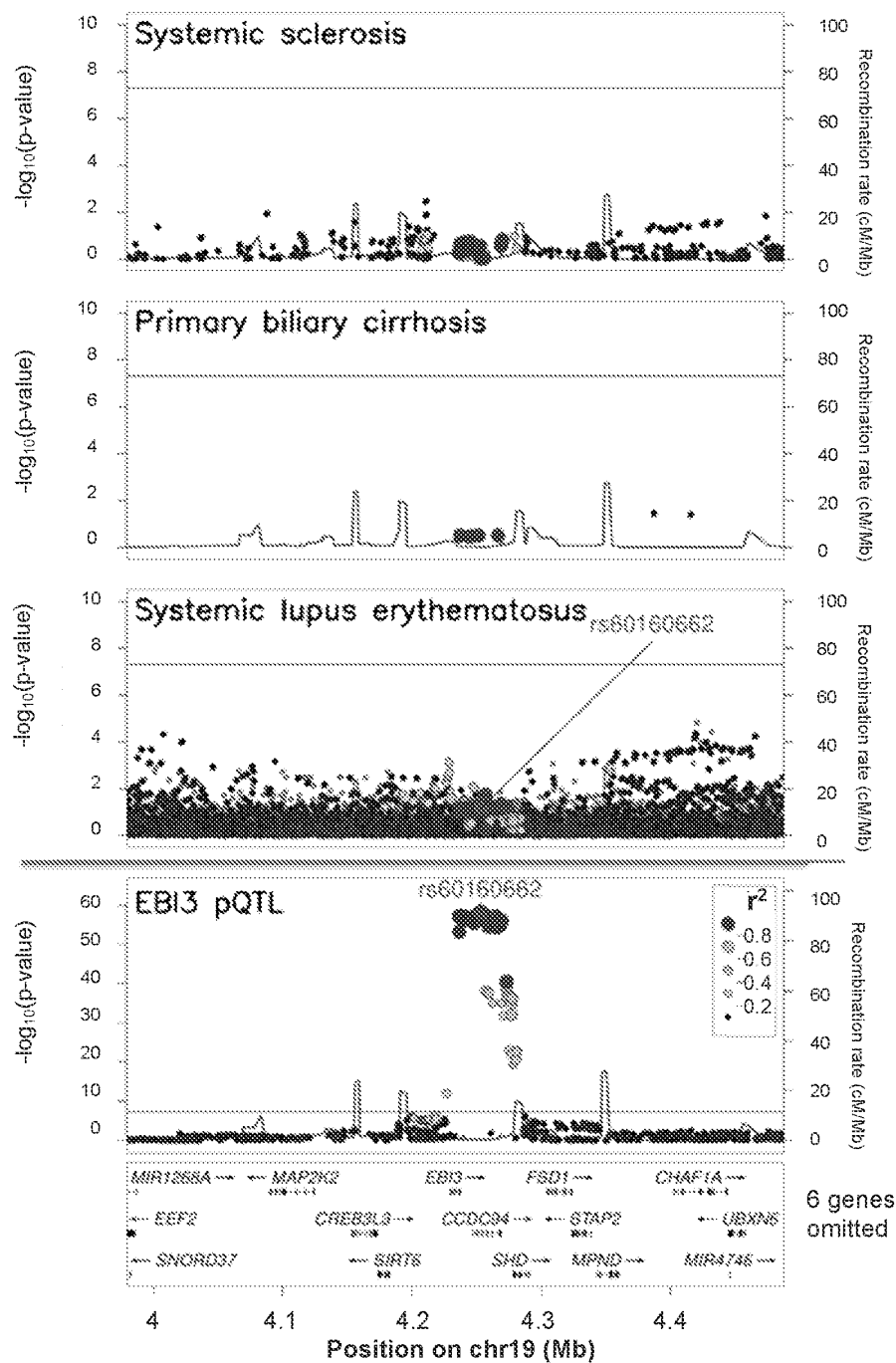


FIG. 19C

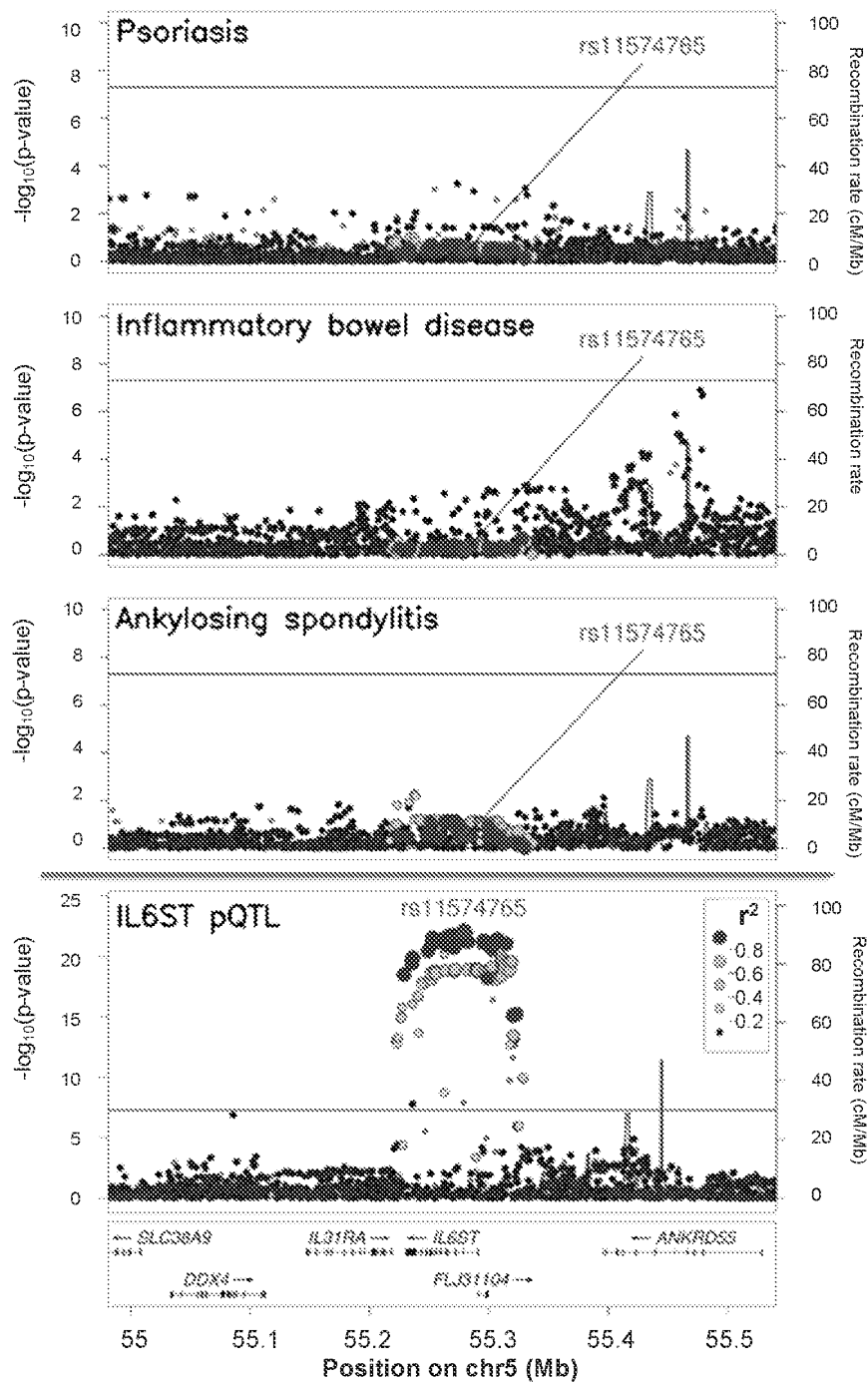


FIG. 20A

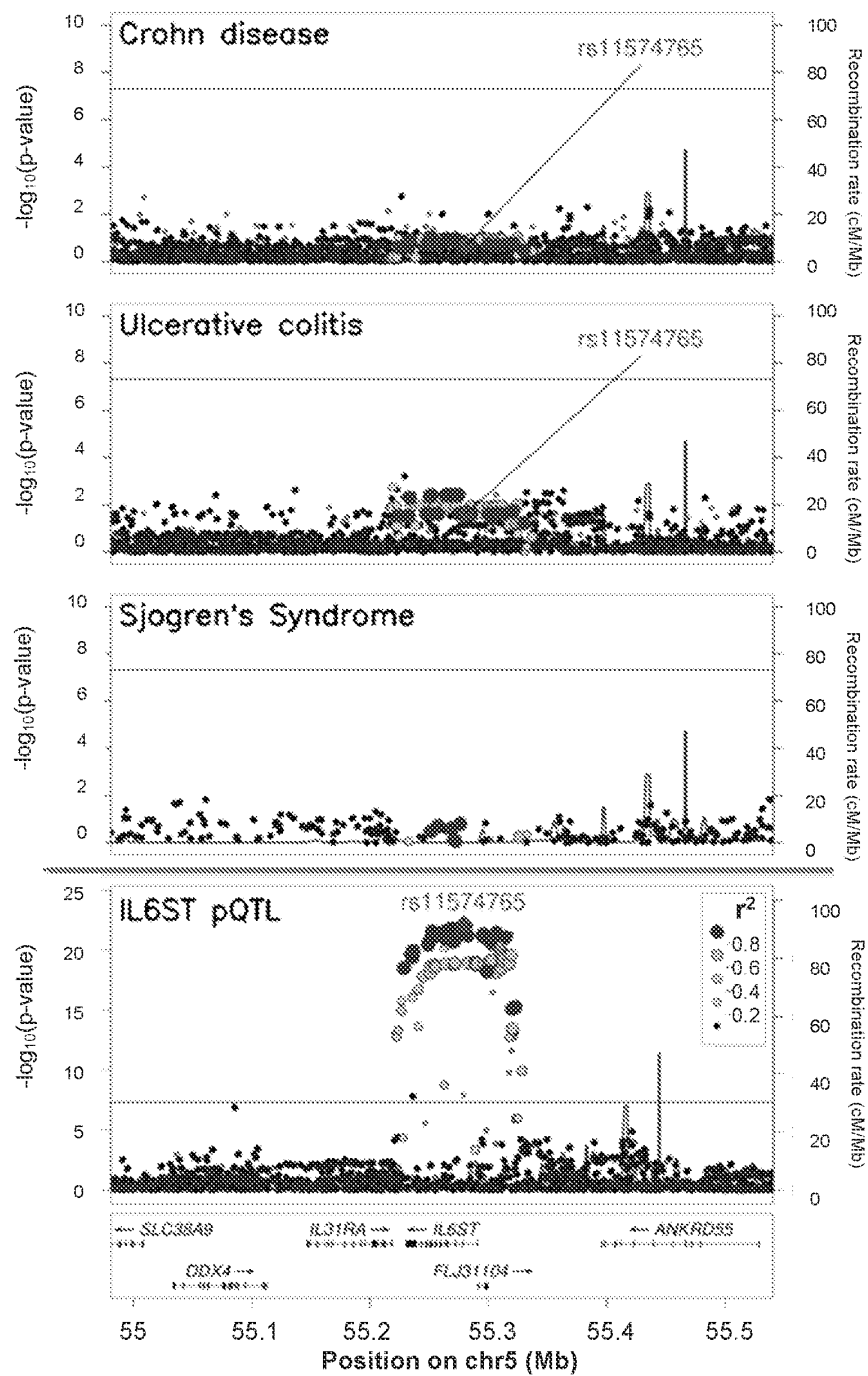


FIG. 20B

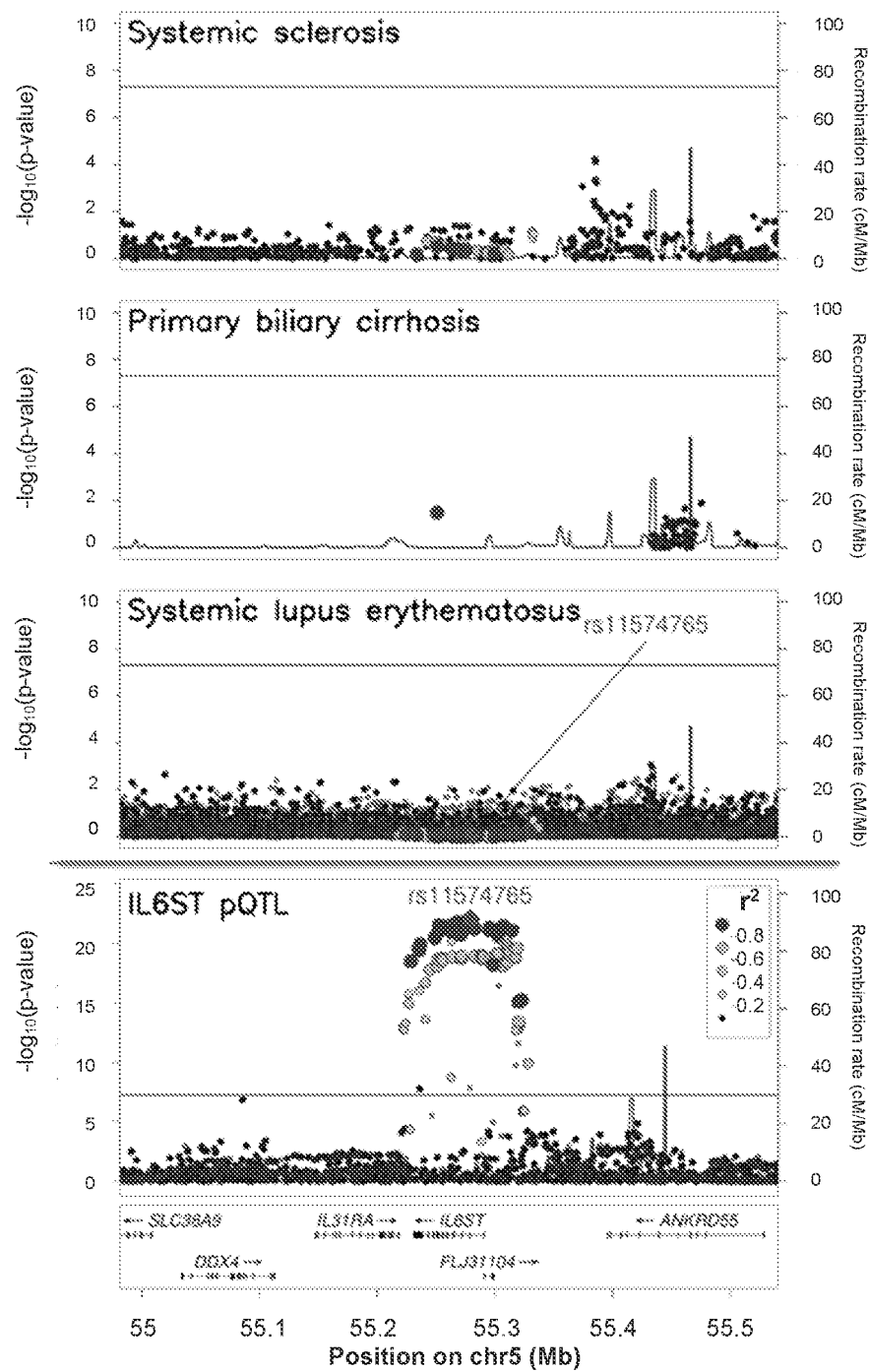


FIG. 20C

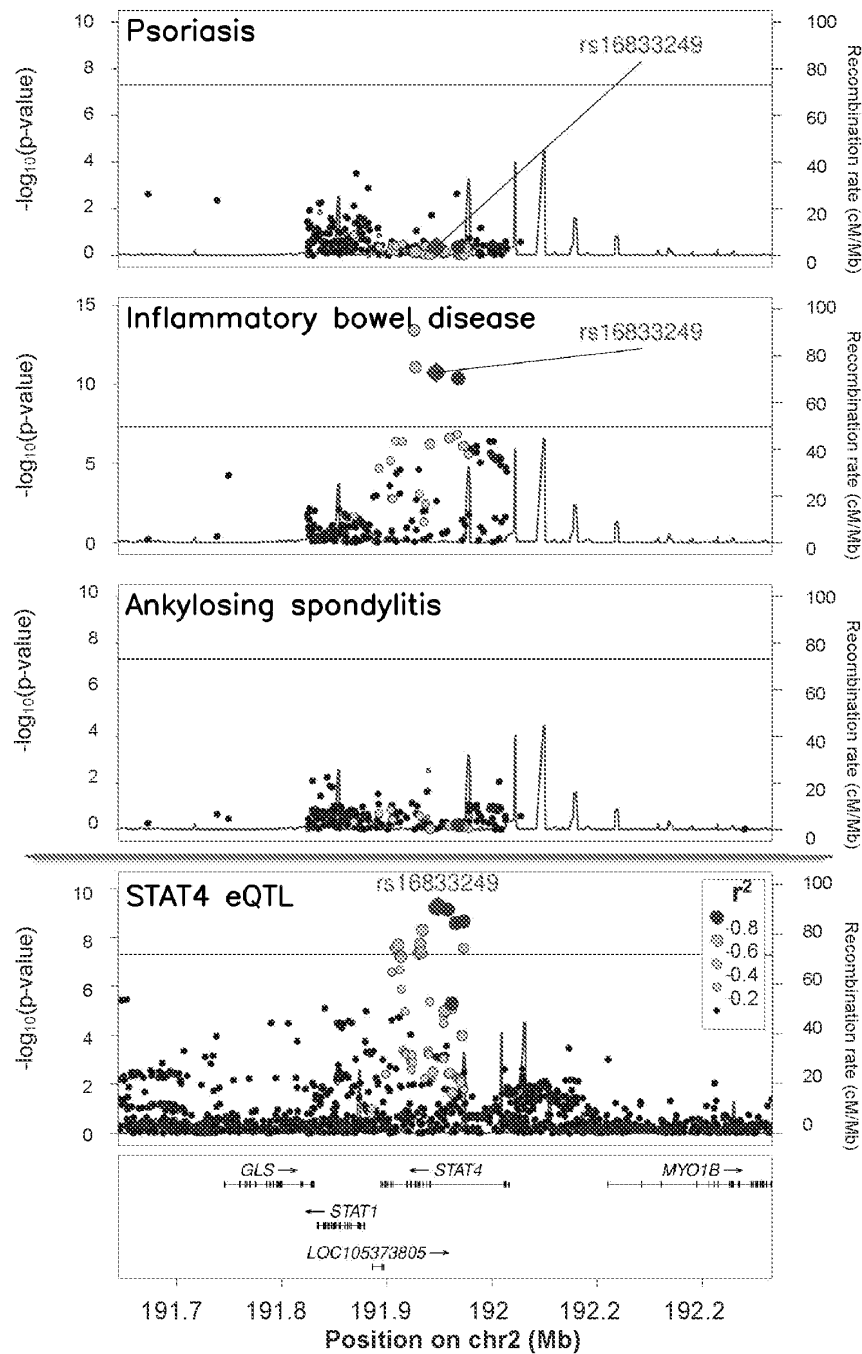


FIG. 21A

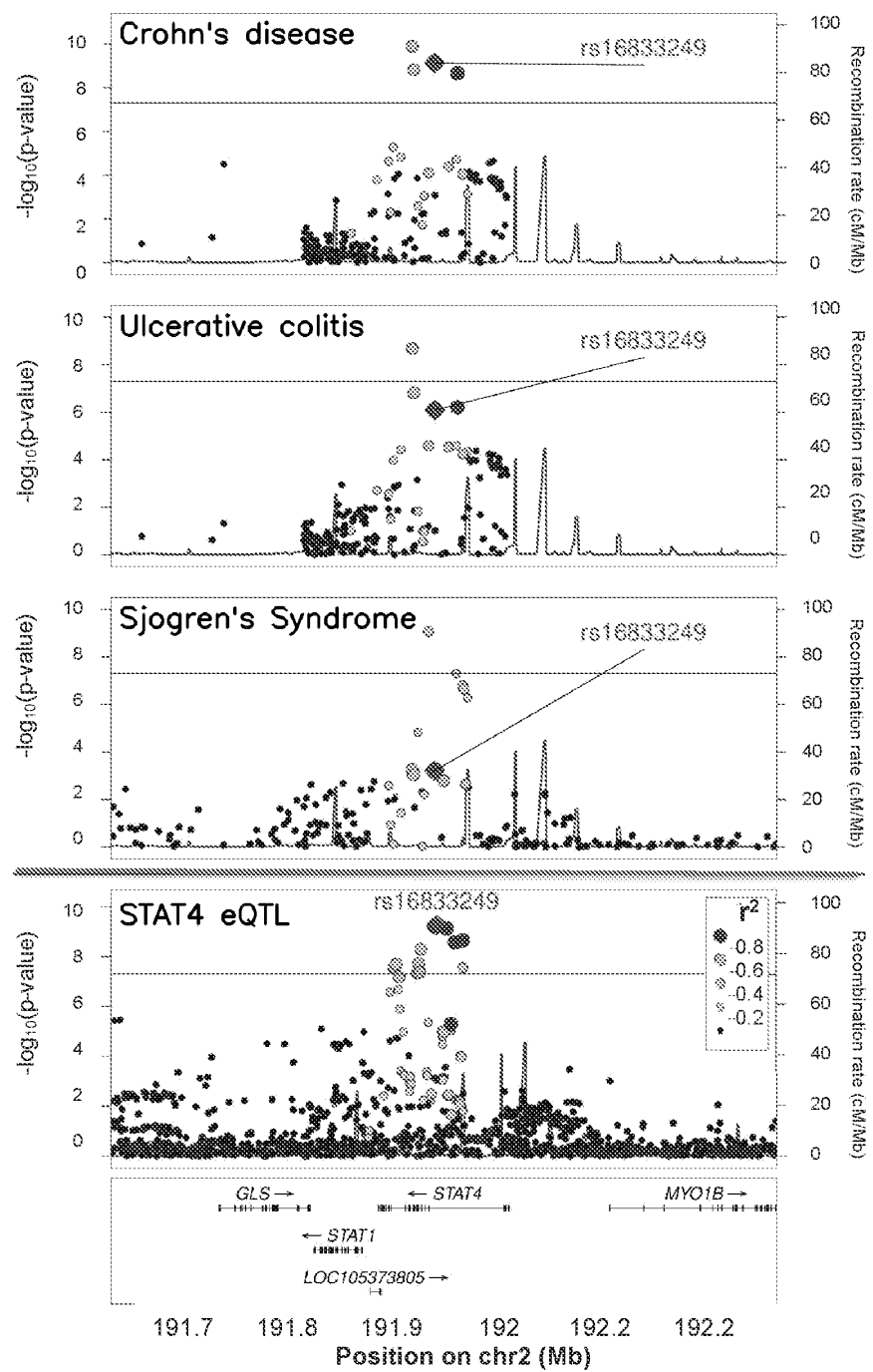


FIG. 21B

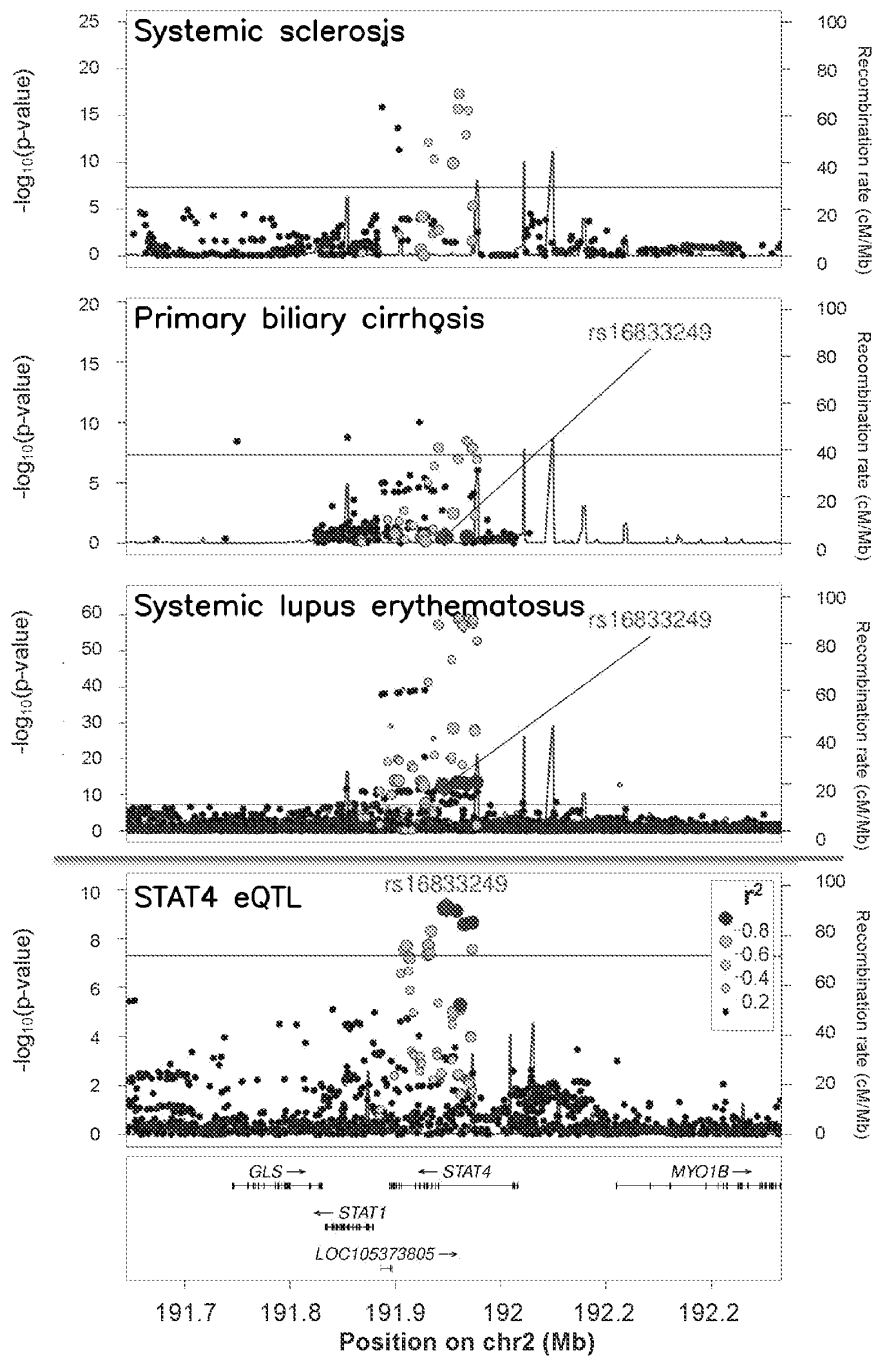


FIG. 21C

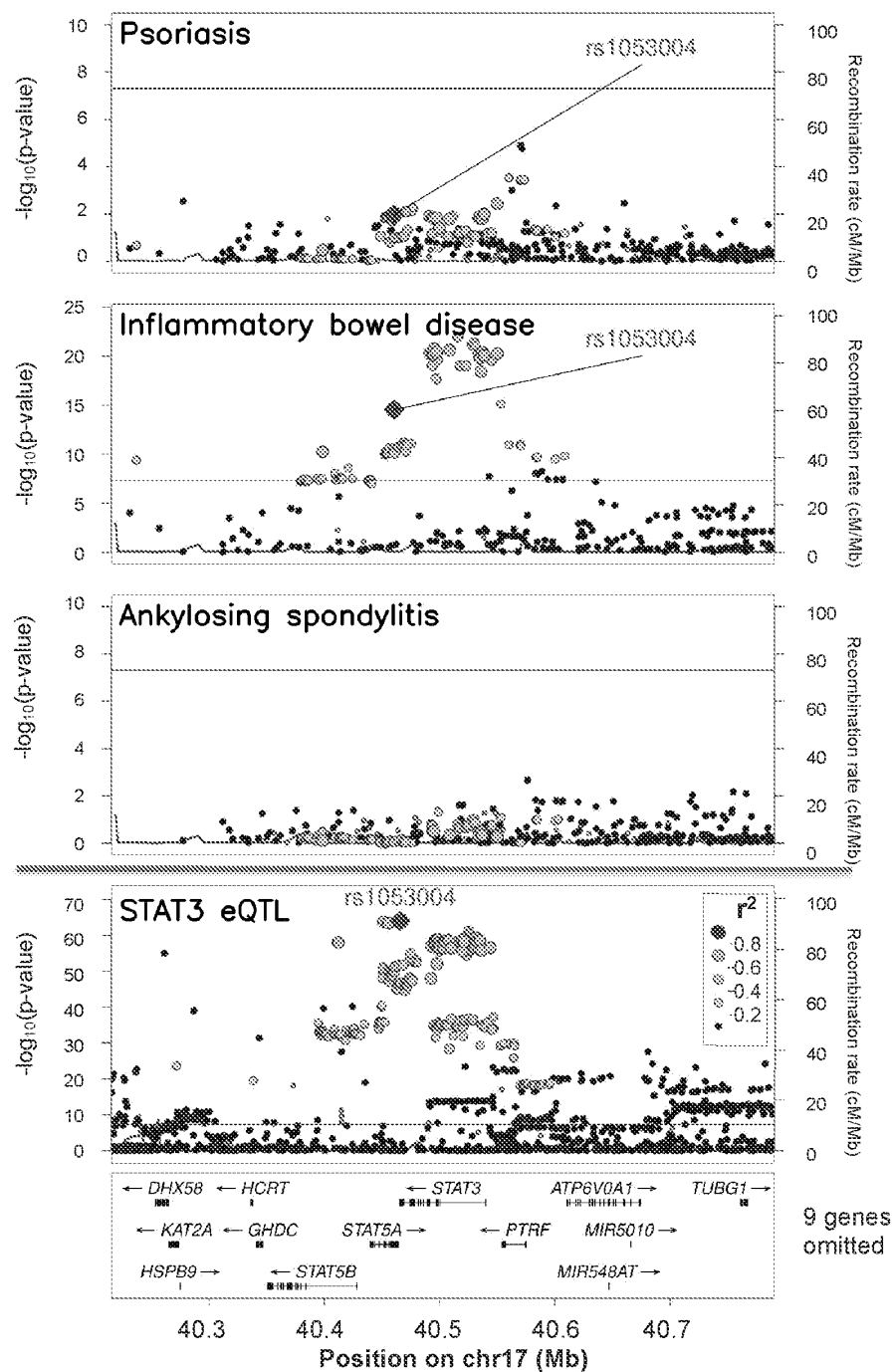


FIG. 22A

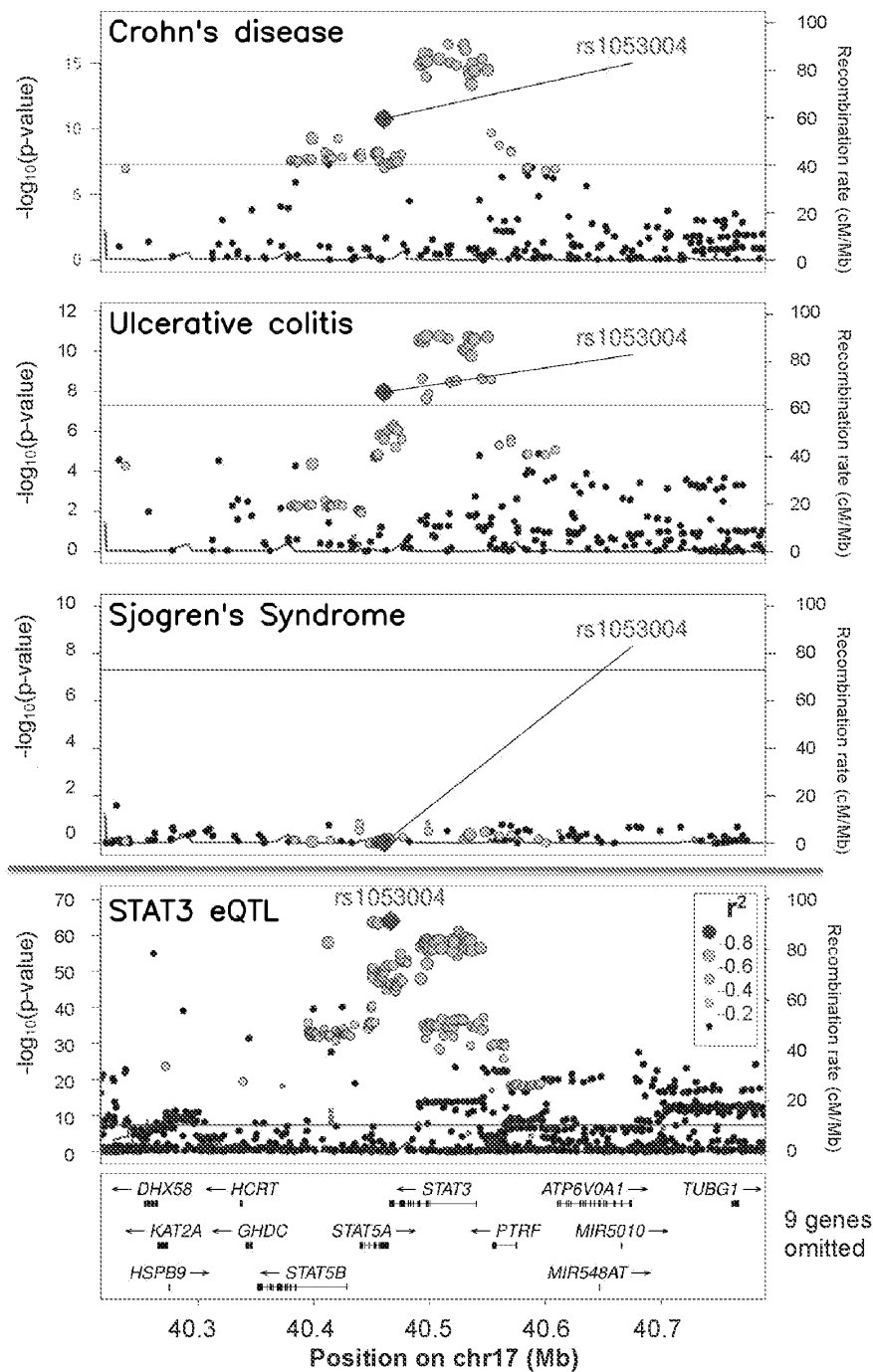


FIG. 22B

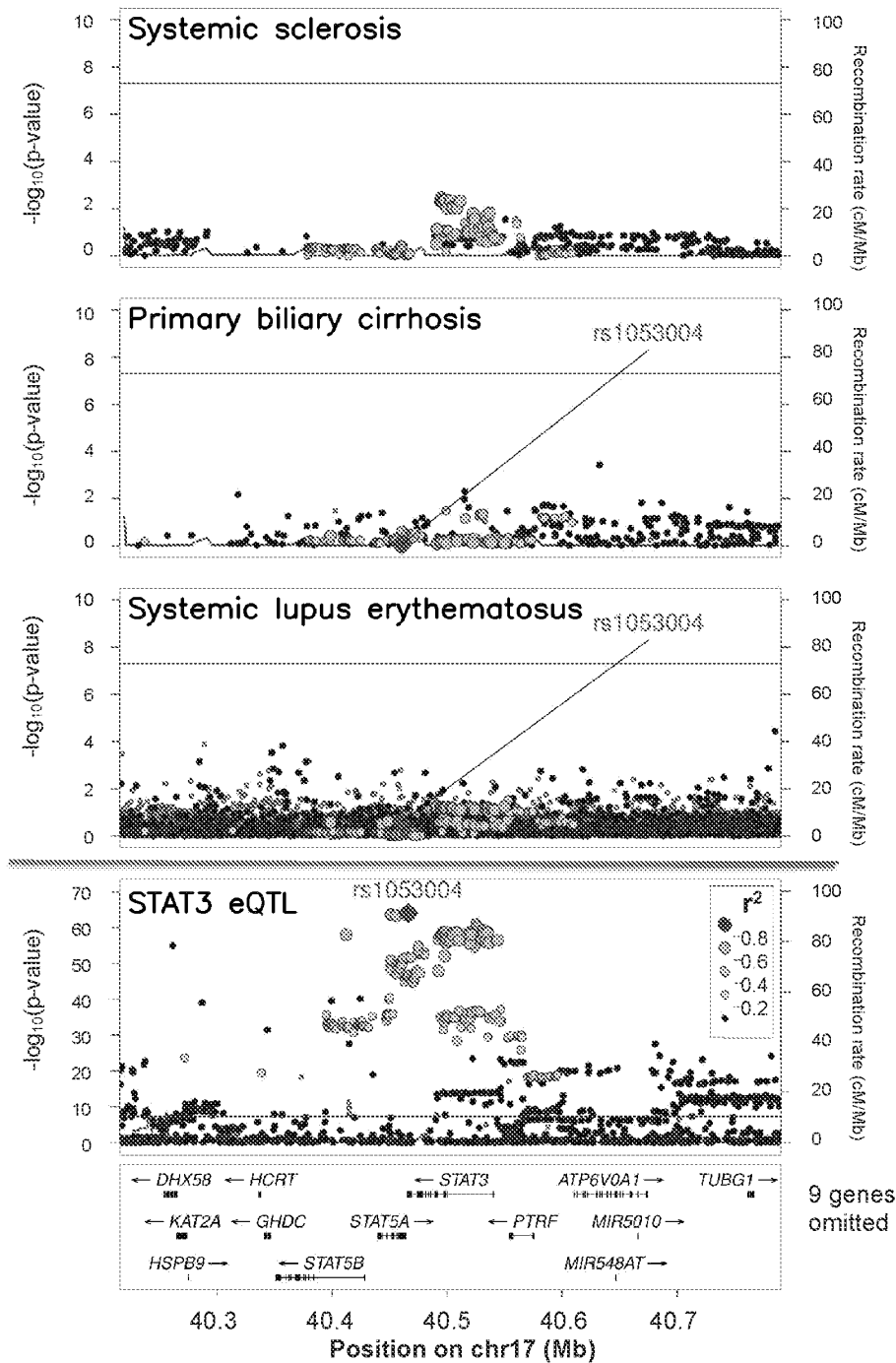


FIG. 22C

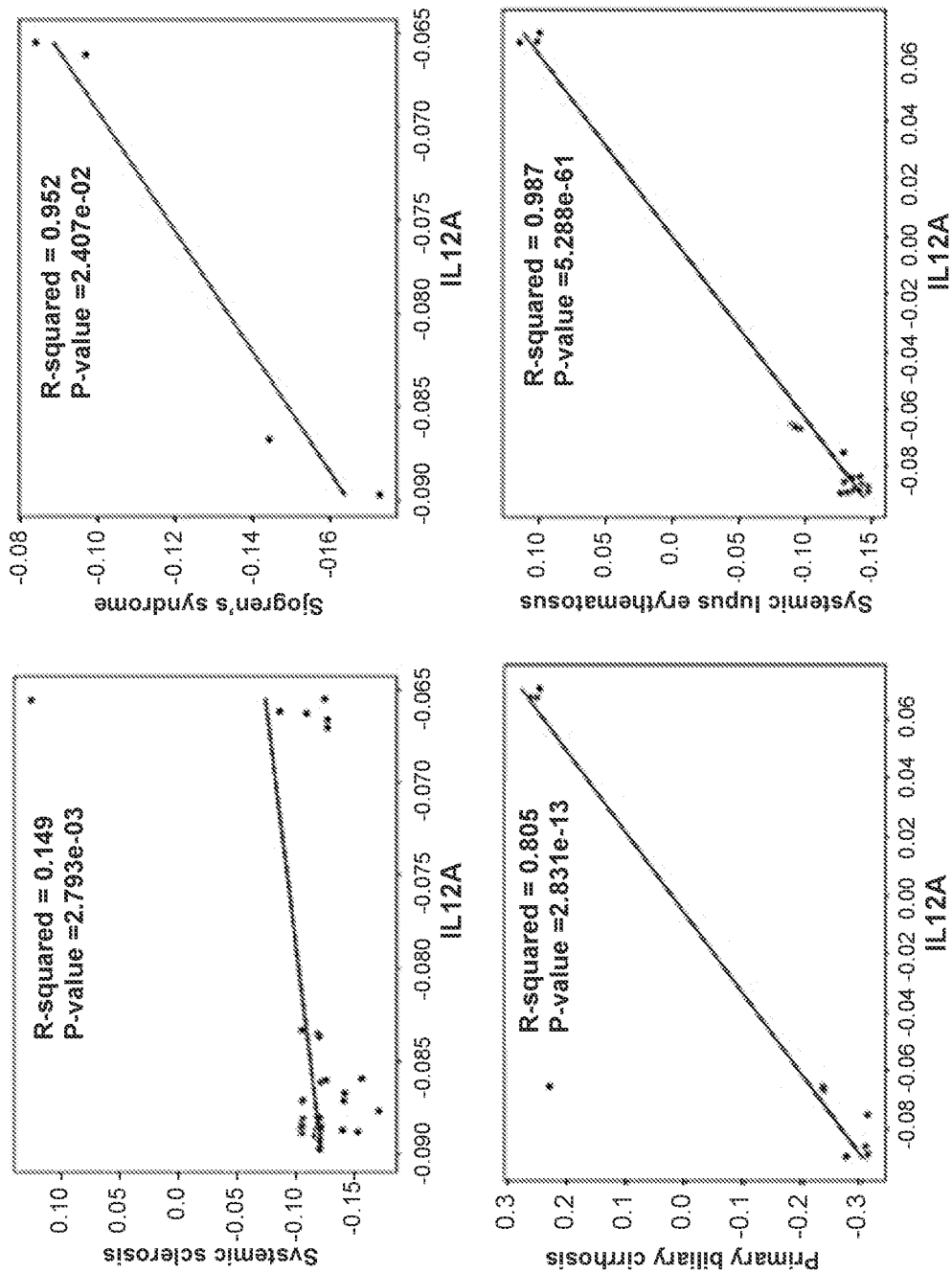


FIG. 23

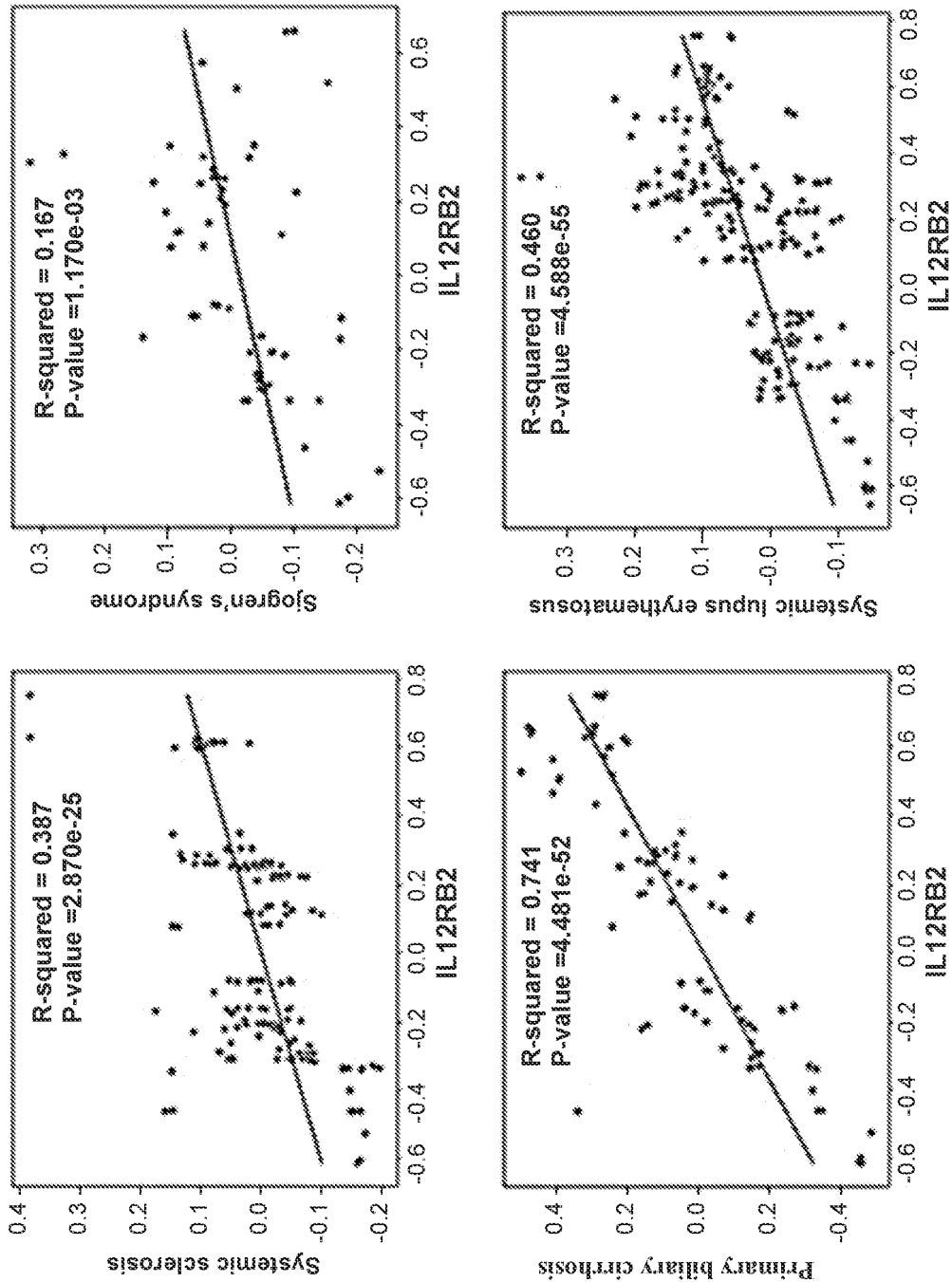


FIG. 24

FIG. 25

D2M-Clone ID	VH	VL
D2M008-A1C6	EVQLVESGGGLVLPKPGASLRLSCAASGFTFRSRYSYMNWVR QAPGKGLEWVSISSDSSIIYYADSVKGRFTISRDNAK NSLYLQMNLSRAEDTAVVYCAREKIALAGSCFDYWGQG TIVTVSS (SEQ ID NO: 1)	DIQMTQSPSSLSASVGDRTVITCRASQGIINDLGWYQQKPG KAPKRLIYAASSLQSGVPSRFSGSGSGTEFTLTISSLQPED FATYYCLQHNNYPYTFGGQTKLEIK (SEQ ID NO: 2)
D2M008-A1A12	EVQLVESGGGLVLPKPGASLRLSCAASGFTFSSYSMNWVR QAPGKGLEWVSISSSSNVIENADSVKGRFTISRDNAK NSLYLQMNLSRAEDTAVVYCARGLMYNNWFEDYWGQGT LIVTVSS (SEQ ID NO: 3)	AIQMTQSPSSLSASVGDRTVITCRASQGIINDLGWYQQKPG KAPKRLIYAASSLQSGVPSRFSGSGSGTEFTLTISSLQPED FATYYCLQDYNYPRTFGQGTKVEIK (SEQ ID NO: 4)
D2M008-A1E5	EVQLVQSGAEVKKPGESLRISCKGSGYFTTIYWISWMR QMPGKGLEWLGITDPGDSYTNSSPSFQGHVTISADTSI STAYLQWSSLKASDTAMVYCARHLGYGEDYWGQGLVLT VSS (SEQ ID NO: 5)	DIVMTQSPSLPLVPFPEPASISCRSSQSLIYSNGYNYLDWY LQKPGQSPQLLIYLGSNRASGVDRFSGSGSGTEFTLTISSLQ VEADVGIYCMQALQTPYTFGGQTKLEIK (SEQ ID NO: 6)
D2M008-A1A2	QLQLQESGPGLVKPSSETLSLTCTVSGGSISSDIYWG IRQPPGKGLEWIGSIYISGRTYYNPSLKSRTVISVDT KNQFSIKLSSVTAADTAVVYCARHWEPDNWFDPWGQGT LIVTVSS (SEQ ID NO: 7)	DIVMTQSPATLSVSEGERDITLCKASQSVSYLAWYQQKPG QTPRLIYGASTRATGIPARFSGSGSGTEFTLTISSLQSED FAVYYCQQYNNWPPYTFGGQTKVEIK (SEQ ID NO: 8)
D2M008-A1E7	QLQLQESGPGLVKPSSETLSLTCTVSGGSISSSNYYWG IRQPPGKGLEWIGSIYISGNTYYNPSLKSRTVISVDT KNQFSIKLSSVTAADTAVVYCARERTVITNAFDIWQGT MIVTVSS (SEQ ID NO: 9)	AIQMTQSPSSLSASVGDRTVITCRASQGIINDLGWYQQKPG KAPNLLIYAASSLQSGVPSRFSGSGSGTEFTLTISSLQPED FATYYCLQDYNYPRTFGQGTKVEIK (SEQ ID NO: 10)
D2M008-A1G9	QLQLQESGPGLVKPSSETLSLTCTVSGGSISSSYXWG IRQPPGKGLEWIGTIYISGNTYYNPSLTSRTVISVDT KNQFSIKLSSVTAADTAVVYCARQWEPDNWFDPWGQGT LIVTVSS (SEQ ID NO: 11)	EMVMTQSPATLSVSEGERASLSCRASQSVNRYLAWYKEKPG QAPRLIYGASTRATGIPARFSGSGSGTEFTLTISSLQSED FAVYYCQQYNSWPPYTFGGQTKVEIK (SEQ ID NO: 12)
D2M008-A1A8	QVQLVESGGGVQVQGRSLRLSCAASGFTFSNYAFHWVR QAPGKGLEWVALISYDGNNEIYADSVKGRFTISRDNK NTLYLQMNLSRVEDMAVYCARPPFTNEGVAILDHWGQ GTIVTVSS (SEQ ID NO: 13)	DIQMTQSPSSLSASVGDRTVITCQASQDIISDYINWYQQKPG KAPKRLIYDASNLETGVPSPRFSGSGSGTEFTLTISSLQPED IATYYCQQYDNLPTTFGGQTKLEIK (SEQ ID NO: 14)
D2M008-A1A9	QVQLVESGGGVQVQGRSLRLSCAASGFTFSNYAFHWVR QAPGKGLEWVAVISYDGSNKYIADSVKGRFTISRDNK NTLYLQMNLSRVEDMAVYCARPPFTNEGVAILDHWGQ GTIVTVSS (SEQ ID NO: 15)	DIQMTQSPSSLSASVGDRTVITCQASQDIISNINWYQQKPG KAPKRLIYDASNLETGVPSPRFSGSGSGTEFTLTISSLQPED LATYYCQKYDYLPTTFGGQTKLEIK (SEQ ID NO: 16)

D2M008-A1B4	QVQLVESGGGVQPGRSRLRLSCAASGFTTFSSYGIHWVR QAPGKGLEWVADIWYDGSINKYADSVKGRFTISRNSK NTLYLQMNSLRAEDTAVYICAREGLITVITNFDYWGQGT LVTVSS (SEQ ID NO: 17)	DIQLTQSPSFLSASVGDRTVITCRASQGISNYLAWYQQKPG KAPKLLIFAASTLQSGVPSRFSGSGTFTLTISLQPED FATYYCQKLNSYPFTFGPGTKVDIK (SEQ ID NO: 18)
D2M008-A1E10	QVQLVESGGGVQPGRSRLRLSCAASGFTTFSSYGIHWVR QAPGKGLEWVAVIWDGSIKYADSVKGRFTISRNSK NTLYLQMNSLRAEDTAVYICVREGRYTLTNFDYWGQGT LVTVSS (SEQ ID NO: 19)	DIQLTQSPSFLSASVGDRTVITCRASQGISNYLAWYQQKPG KAPKLLIYAASLQSGVPSRFSGSGTFTLTISLQPED FATYYCQKLNSYPFTFGPGTKVDIK (SEQ ID NO: 20)
D2M008-B2C5	EVQLVQSGAEVKKPGESLKISCKSGSYFFFTNYIHWVR QMPGKGLEWMGIIPGSDTRYSPSFQGGVTISADKSI STAYLQWSSVKASDTAMYYCVRRGFEGELLDYGMDFWVG QGTVTVSS (SEQ ID NO: 21)	EIVMTQSPATLSVSPGERATISCRASQSVSSNLAWYQQKPG QAPRLLIYGASTRATGIPARFSGSGSGTFTLAISSLQSEH FAYYCCQQYNNWPFTEFGPGTKVDIK (SEQ ID NO: 22)
D2M008-B2B10	EVQLVQSGAEVKKPGESLKISCKSGSYFTTIYIWSVR QMPGKGLEWMGTIDPSGSNNYSPSFQGHVTISADRSI STAYLQWNSLKASDTAMYYCARHLGYGEDYWGQGLVT VSS (SEQ ID NO: 23)	DIIMTQSPLSLPVTPGEPASISCRSSQSLHNSNGYNYLDWY LQKPGQSPQLLIYLGSNRASGVDPDRFSGSGCTDFTLKISR VEAEDIGIYYCMQALQTPYTFGGQTKLEIK (SEQ ID NO: 24)
D2M008-B2B1	QIQLQESGPGGLVKPSETLTCTVSGGSIRSSSYFWVW VPQPPCKGLEWIGSLYYSGNTYNNPSLKSRTISVDTS KNQFSIKLSSVTAADTAVYICARERIVVAGSLDYWGQG TLTVTVSS (SEQ ID NO: 25)	DIQMTQSPSSLSASVGDRTVITCRTNQGIGNDLGWYQQKPG KAPKLLIYAASLQSGVPSRFSGSGTFTLTISLQPED FATYYCLQDYNYPWFTEGGQTKVEIK (SEQ ID NO: 26)
D2M008-B2B12	QVQLQESGPGGLVKPSETLTCTVSGGSISYYWSWIR QPPCKGLEWIGIYYTGSTNNPSLKSRTISADTSKN QFSLKLSVTAADTAVYICARGPRYNNWYEDAFDIWGQ GTMVTVSS (SEQ ID NO: 27)	DIQMTQSPSSVSASVGDRTVITCRASQSFSSWLAWYQQKPG KAPKLLIYAASLQSGVPSRFSGSGSRTGFTLTISLQPED FATYYCQQAANSFPFTFGPGTKLDIK (SEQ ID NO: 28)
D2M008-B2C3	QVQLVESGGGVQPGRSRLRLSCAASGFTFNSYAFHWVR QAPGNGLWVALISYDGSNKYADSVKGRFTISRNSK NTLFLQMNSLRVEDMAVYICARPPFTNFGVALLDHWGQ GTLVTVSS (SEQ ID NO: 29)	DIQMTQSPSSLSASVGDRTVITCQASQDISNYLWYQQKPG KAPKLLIYDASNLETGVPSRFSGSGTFTLTISLQPED IATYCCQQYDNLPTFGQGTKEIK (SEQ ID NO: 30)
D2M008-B2B7	QVQLVESGGGVQPGRSRLRLSCAASGFTFNSYAIHWVR QAPCKGLEWVTVISYDGNKYYTDSVKGRFTISRNSK NTLYLQMNSLRAEDTAVYICARPPFTFGVLILDYWGQ GTLVTVSS (SEQ ID NO: 31)	DIQMTQSPSSLSASVGDRTVITCQASQDINKYLNWYQQKPG KAPKLLIYDASNLETGVPSRFSGSGTFTLTISLQPED FATYYCQQYDNLPTFGQGTKEIK (SEQ ID NO: 32)
D2M008-3A4	EVQLVESGGGLVQPGGSLRLSCAASGLTFSSYEMNWVR QAPCKGLEWVSYYISSSGSTIYADSVKGRFTISRNAK NSLYLQMNSLRAEDTAVYICARDRGALRYEDSYGMDVW GGTGTVTVSS (SEQ ID NO: 33)	DIQMTQSPSSLSASVGDRTVITCQASQDISNYLWYQQKPG RAPKLLIFDASNLETGVPSRFSGSGTFTLTISLQPED IATYYCQQYDNLPTFGGQTKVEIK (SEQ ID NO: 34)

D2M008-3A8	QVQLVQSGAEVKKPGSSVKVSCKASGGTFFSSYAISWVR QAPGQGLEWMGRIIPILGIANSAQKFQVRVITADKST NTAYLELSSLRSEDTAVYYCARWRTRTTEAFDIWGQGT MVTVSS (SEQ ID NO: 35)	DIQMTQSPSTLSASVGDRTVITCRASQISGNWLAWYQQKPG KAPKLLIYKASILETCVPSRFSGSGTEFTLTISSLQSDDD FATYYCQQYNSYTFGQGTLEIN (SEQ ID NO: 36)
D2M008-4A4	QVQLVQSGAEVKKPGSSVKVSCKASGGTFFSSAFSWVR QAPGQGLEWMGRIIPILDTNSAQKFQGRVITADKST DTVSMENVSLRSEDTAVYYCARWKTRATEAYDIWGQGT MVTVSS (SEQ ID NO: 37)	DIQMTQSPSTLSASVGDRTVITCRASQISGNWLAWYQQKPG KVPKLLIYKASSLESGVPSRFSGSGTEFTLTISSLQPD FATYCCQQYNSYTFGQGTKEIK (SEQ ID NO: 38)
D2M008-4A5	QVTLKESGPVLVNPTFTYITCTVSGFSLSNARMGVSW IRQPPGKALEWLAHYNSDEKSYSTSLKNRLTISKDTS RSQVLTMTNMDPVDATFYCARSLGVAGTGWFDWMGQ GTLVTVSS (SEQ ID NO: 39)	DIQMTQSPSTLSASVGDRTVITCRASQISGNWLAWYQQKPG KAPKLLIYKASSLESGVPSRFSGSGTEFTLTISSLQPD FATYYCQQYNNYTFGQGTKEIK (SEQ ID NO: 40)
D2M008-3A11	EVQLVESGGGLVQPGGSLKLSCAASGFTFGSGSAMHWVR QASCKGLEWVGRIIRSKASYATSYDAAVEGRFTISRDD SKNTAYLQMNSLKTEDTAVYYCTRHSSSSGAFDIWGQ TLVTVSP (SEQ ID NO: 41)	DIVMTQSPSLPVTPEGPASISCRSSQSLHNSGYNLHWY LQKPGQSPQLLIYLGSNRASGVDRFSGSGCTDFTLKISR VEAEDVGVYYCLQLEIPITFGQGTLEIK (SEQ ID NO: 42)
D2M008-3A2	QVQLVQSGAEVKKPGSSVKVSCKASGGTFSNFVTSWVR QAPGQGLEWMGRIIPILDIPNYAQNFGQGRVITADKST STAYMELSSLRSEDTAVYYCARWRTRTTEAFDIWGQGT MVTVSS (SEQ ID NO: 43)	DIQMTQSPSTLSASVGDRTVITCRASQISGNWLAWYQQKPG KAPKLLIYKASSLESGVPSRFSGSGTEFTLTISSLQPD FATYYCQQYDSYTFGQGTKEIK (SEQ ID NO: 44)
D2M008- 27H28L	QVQLVESGGGVQPGRRSLRLSCAASGFTFSNYAFHWVR QAPCKGLEWVALISYDGNNEYADSVKGRFTISRNSK NTLYLQMNSLRVEDMAVYYCARPPFTNEGVAILDHWGQ GTLVTVSS (SEQ ID NO: 45)	DIQMTQSPSSLSASVGDRTVITCQASQDISNVLNHWYQQKPG KAPKLLIYDASNLETGVPSRFSGSGTEFTLTISSLQPED LATYYCQKYDYLPTFGQGTKEIK (SEQ ID NO: 46)
4A4-hb1b2	QVQLVQSGAEVKKPGSSVKVSCKASGGTFFSSAFPSWVR QAPGQGLEWMGRIIPILDITNSAQKFQGRVITADKST STAYMELSSLRSEDTAVYYCARWKTRATEAYDIWGQGT MVTVSS (SEQ ID NO: 335)	DIQMTQSPSTLSASVGDRTVITCRASQISGNWLAWYQQKPG KAPKLLIYKASSLESGVPSRFSGSGTEFTLTISSLQPD FATYYCQQYNSYTFGQGTKEIK (SEQ ID NO: 336)
27H28L-hb1b	QVQLVESGGGVQPGRRSLRLSCAASGFTFSNYAFHWVR QAPCKGLEWVALISYDGNNEYADSVKGRFTISRNSK NTLYLQMNSLRAEDTAVYYCARPPFTNEGVAILDHWGQ GTLVTVSS (SEQ ID NO: 337)	DIQMTQSPSSLSASVGDRTVITCQASQDISNVLNHWYQQKPG KAPKLLIYDASNLETGVPSRFSGSGTEFTLTISSLQPED IATYYCQKYDYLPTFGQGTKEIK (SEQ ID NO: 338)

FIG. 26

Kabat CDR

D2M- clone ID	VH CDR1	SEQ ID:	VH CDR2	SEQ ID:	VH CDR3	SEQ ID:	VL CDR1	SEQ ID:	VL CDR2	SEQ ID:	VL CDR3	SEQ ID:
D2M008- A1C6	FRSYT MN	47	FISDSSSYIYY ADSVKG	48	EKIALAGS CFDY	49	QGIRND	50	AASSLQS	51	LQHNNY PYT	52
D2M008- A1A12	FSSYS MN	53	SISSSSNYIFN ADSVKG	54	GLMYNNWF FDY	55	QGIRKD	56	AASSLQN	57	LQDYN PRT	58
D2M008- A1E5	FTIYW IS	59	TIDPGDSYFNS SPSFQG	60	HLGYGEDY	61	QSLLYSNGY NY	62	LGSNRRAS	63	MQALQT PYT	64
D2M008- A1A2	IISSD YWG	65	SIYYSGRTYYN PSLKS	66	HWEPDNWF DP	67	QSVSSY	68	GASTRAT	69	QQYNNW PPT	70
D2M008- A1E7	ISSSN YWG	71	SIYYSGNTYYN PSLKS	72	ERVTTNAF DI	73	QGIIND	74	AASSLQS	75	LQDYN PRT	76
D2M008- A1G9	ISSSS YWG	77	TIYYSGNTYYN PSLTS	78	QWEPDNWF DP	79	QSVNRY	80	GASTRAT	81	QQYNSW PPT	82
D2M008- A1A8	FSNYA FH	83	LISYDGNNEYY ADSVKG	84	PPFTNFGV AILDH	85	QDISDY	86	DASNLET	87	QQYDNL PYT	88
D2M008- A1A9	FSNYA FH	89	VISYDGSNKYY ADSVKG	90	PPFTNFGV AILDH	91	QDISNY	92	DASNLET	93	QKYDYL PYT	94
D2M008- A1B4	FSSYG IH	95	DIWYDGSIKNY ADSVKG	96	EGRLTVTN FDY	97	QGISSY	98	AASTLQS	99	QKINSY PPT	100
D2M008- A1E10	FSSYG IH	101	VIWYDGSIKYY ADSVKG	102	EGRYTLTN FDY	103	QGISNY	104	AASTLQS	105	QKINSY PPT	106
D2M008- B2C5	FTNYW IG	107	IIFYPGDSDFRY SPSFQG	108	RGFGELLD YYGMDV	109	QSVSSN	110	GASTRAT	111	QQYNNW PPT	112
D2M008- B2B10	FTIYW IS	113	TIDPSGSNNY SPSFQG	114	HLGYGEDY	115	QSLHHSNGY NY	116	LGSNRRAS	117	MQALQT PYT	118
D2M008- B2B1	IRSSS YFWV	119	GSLYYSGNTYY NPSLKS	120	ERIVVAGS LDY	121	QGIGND	122	AASSLQS	123	LQDYN PWT	124
D2M008- B2B12	ISSYY WS	125	GYIYYTGSTNY NPSLKS	126	GPRYNNY EDAFDI	127	QSFSSW	128	ASSSLQS	129	QQANSE PPT	130

D2M008- B2C3	FNSYA FH	131	ALISYDGSNKY YADSVKG	132	PPFTNFGV AILDH	133	QDISNY	134	DASNLET	135	QQYDNL PYT	136
D2M008- B2B7	FSNYA IH	137	TVISYDGNKNY YTDsvKG	138	PPFTFFGV LILDY	139	QDINKY	140	DASNLET	141	QQYDNL PYT	142
D2M008- 3A4	FSSYE MN	143	YISSSGSTIYY ADSVKG	144	DRGALRYF DSYGMDV	145	QDISNY	146	DASNLET	147	QQYDNL PLT	148
D2M008- 3A8	FSSYA IS	149	RVIPILGIANS AQKFQV	150	WRTRTTEA FDI	151	QSISTW	152	KASILET	153	QQYNSY ST	154
D2M008- 4A4	FSSSA FS	155	RIIPILDITNS AQKFQG	156	WKTRATEA YDI	157	QSISNW	158	KASSLES	159	QQYNSY ST	160
D2M008- 4A5	LSNAR MGVS	161	HIYSNDERKSYS TSLKN	162	SLGVAGTG WFDP	163	QSIGSW	164	KASSLES	165	QQYNNY WT	166
D2M008- 3A11	FSGSA MH	167	RIRSKAKSYAT SYDAAVEG	168	HSSSSGAF DY	169	QSLHSHNGY NY	170	LGSNRAS	171	LQTLEI PIT	172
D2M008- 3A2	FSNEV IS	173	RIIPILDIPNY AQNFQG	174	WRTRTTEA FDI	175	QSISNW	176	KASSLES	177	QQYDSY ST	178
D2M008- 27H28L	FSNYA FH	179	LISYDGNNEYY ADSVKG	180	PPFTNFGV AILDH	181	QDISNY	182	DASNLET	183	QKYDYL PYT	184

FIG. 27
IMGT CDR

D2M-clone ID	VH CDR1	SEQ ID:	VH CDR2	SEQ ID:	VH CDR3	SEQ ID:	VL CDR1	SEQ ID:	VL CDR2	SEQ ID:	VL CDR3	SEQ ID:
D2M008-A1C6	GFTFR SYT	185	ISSDSSYI	186	AREKIALA GSCFDY	187	QGIRND	188	AAS	189	LQHNNY PYT	190
D2M008-A1A12	GFTFS SYS	191	ISSSSNYI	192	ARGLMYNW NEPDY	193	QGIRKD	194	AAS	195	LQDYNY PRT	196
D2M008-A1E5	GYTFT IYW	197	IDPGDSYT	198	ARHLGYGE DY	199	QSLLYSNGY NY	200	IGS	201	MQALQT PYT	202
D2M008-A1A2	GSII SSDYY	203	IYYSGR	204	ARHWEPDN WFDP	205	QSVSSY	206	GAS	207	QQYNNW PFT	208
D2M008-A1E7	GSIS SSNY	209	IYYSGNT	210	ARERVTN AFDI	211	QGIIND	212	AAS	213	LQDYNY PRT	214
D2M008-A1G9	GSIS SSSYY	215	IYYSGNT	216	ARQWEPDN WFDP	217	QSVNRY	218	GAS	219	QQYNSW PFT	220
D2M008-A1A8	GFTFS NYA	221	ISYDGNNE	222	ARPPFTNF GVAILDH	223	QDISDY	224	DAS	225	QQYDNL PYT	226
D2M008-A1A9	GFTFS NYA	227	ISYDGSNK	228	ARPPFTNF GVAILDH	229	QDISNY	230	DAS	231	QKYDYL PYT	232
D2M008-A1B4	GFTFS SYG	233	IWYDGSIK	234	AREGLTV TNFDY	235	QGISSY	236	AAS	237	QKINSY PFT	238
D2M008-A1E10	GFTFS SYG	239	IWYDGSIK	240	VREGRYTL TNFDY	241	QGISNY	242	AAS	243	QKINSY PFT	244
D2M008-B2C5	GYFT NYW	245	IYPGDSDT	246	VRRFGEL LDYIGMDV	247	QSVSSN	248	GAS	249	QQYNNW PFT	250
D2M008-B2B10	GYTFT IYW	251	IDPSGCSYN	252	ARHLGYGE DY	253	QSLHNSNGY NY	254	IGS	255	MQALQT PYT	256
D2M008-B2B1	GSIR SSSYF	257	IYYSGNT	258	ARERIVVA GSLDY	259	QGIGND	260	AAS	261	LQDYNY PWT	262
D2M008-B2B12	GSIS SY	263	IYTGST	264	ARGPRYNW NYEDAFDI	265	QSFSSW	266	ASS	267	QQANSE PFT	268

D2M008- B2C3	GFTFN SYA	269	ISYDGSNK	270	ARPPFTNF GVAILDH	271	QDISNY	272	DAS	273	QQYDNL PYT	274
D2M008- B2B7	GFTFS NYA	275	ISYDGNK	276	ARPPFTFF GVLIDY	277	QDINKY	278	DAS	279	QQYDNL PYT	280
D2M008- 3A4	GLTFS SYE	281	ISSSGSTI	282	ARDRGALR YFDSYGMD V	283	QDISNY	284	DAS	285	QQYDNL PLT	286
D2M008- 3A8	GGTFS SYA	287	VIPILGIA	288	ARWRTRIT EAFDI	289	QSISTW	290	KAS	291	QQYNSY ST	292
D2M008- 4A4	GGTFS SSA	293	IIPILDIT	294	ARWKTRAT EAYDI	295	QSISNW	296	KAS	297	QQYNSY ST	298
D2M008- 4A5	GFSL NARMG	299	IYSNDEK	300	ARSLGVAG TGWFD	301	QSIGSW	302	KAS	303	QQYNNY WT	304
D2M008- 3A11	GFTFS GSA	305	IRSKAKSYAT	306	TRHSSSG AFDY	307	QSLHNSGY NY	308	LGS	309	LQTEI PIT	310
D2M008- 3A2	GGTFS NFV	311	IIPILDIP	312	ARWRTRIT EAFDI	313	QSISNW	314	KAS	315	QQYDSY ST	316
D2M008- 27H28L	GFTFS NYA	317	ISYDGNNE	318	ARPPFTNF GVAILDH	319	QDISNY	320	DAS	321	QKYDYL PYT	322

FIG. 28

Antibodies	HC	LC
Anti-hP40 (Ustekinumab)	EVQLVQSGAEVKKPGESLKISKCKGSGYFTTYWLGWVRQMPG KGLDWIGIMSPVDSIRYSPFQGGVQVMSVDKSTITAYLQWN SLKASDTAMYYCARRRPGQGYDFWQGTLTVTVSSSTKGPS VFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVMNSGALTSG VHFFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSN TKVDKRVKPKSCDKTHTCPPEPAPELLGGPSVFLFPPKPKDT LMIPTFEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPR EEQYNSTYRVVSVLTVLHQDWLNGKEYCKVSNKALPAPIEK TISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSD IAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQ QGNVFSCSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO: 323)	DIQMTQSPSSLSASVGDRVTITCRASQGISNWLAWYQQK PEKAPKSLIYAASLSQGVPSRFSGSGSGTEFTLTITSSL QPDDFATYCCQQNSYPTFGQGTKLEIKRTVAAPSVEFI FPSDEQLKSGTASVVCILNNFYPREAKVQWKVDNALQSG GNSQESVTEQDSKDSITYSLSTLTLSKADYEKHKVYACE VTHQGLSSPVTKSFNRGEC (SEQ ID NO: 324)
	QVQLVQSGAEVKKPGSSVKVSKCKASGCTFSSSAFSSVRQAPG QGLEWMGRIIPILDITNSAQKFQGRVTITADKSTDTVSMENV SLSEDTAVYYCARWKTRATEAYDIWGQGTMTVSSASTKGP SVFELAPSSKSTSGGTAALGCLVKDYFPEPVTVMNSGALTSG GVHFFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPS NTKVDKRVKPKSCDKTHTCPPEPAPELLGGPSVFLFPPKPKD TLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKP REEQYNSTYRVVSVLTVLHQDWLNGKEYCKVSNKALPAPIE KTIISKAKGQPREPQVYTLPPSRDEMTKNQVSLTCLVKGFYPS DIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRW QGNVFSCSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO: 325)	DIQMTQSPSSLSASVGDRVTITCRASQGISNWLAWYQQK PGKVPKLLIYKASLSGVPSPRFSGSGSGTEFTLTITSSL QPDDFATYCCQQNSYPTFGQGTKLEIKRTVAAPSVEFI FPSDEQLKSGTASVVCILNNFYPREAKVQWKVDNALQSG NSQESVTEQDSKDSITYSLSTLTLSKADYEKHKVYACEV VTHQGLSSPVTKSFNRGEC (SEQ ID NO: 326)
D2M008-4A4	QVQLVQSGAEVKKPGSSVKVSKCKASGCTFSSSAFSSVRQAPG QGLEWMGRIIPILDITNSAQKFQGRVTITADKSTDTVSMENV SLSEDTAVYYCARWKTRATEAYDIWGQGTMTVSSASTKGP SVFELAPSSKSTSGGTAALGCLVKDYFPEPVTVMNSGALTSG GVHFFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPS NTKVDKRVKPKSCDKTHTCPPEPAPELLGGPSVFLFPPKPKD TLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKP REEQYNSTYRVVSVLTVLHQDWLNGKEYCKVSNKALPAPIE KTIISKAKGQPREPQVYTLPPSRDEMTKNQVSLTCLVKGFYPS DIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRW QGNVFSCSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO: 325)	DIQMTQSPSSLSASVGDRVTITCRASQGISNWLAWYQQK PGKVPKLLIYKASLSGVPSPRFSGSGSGTEFTLTITSSL QPDDFATYCCQQNSYPTFGQGTKLEIKRTVAAPSVEFI FPSDEQLKSGTASVVCILNNFYPREAKVQWKVDNALQSG NSQESVTEQDSKDSITYSLSTLTLSKADYEKHKVYACEV VTHQGLSSPVTKSFNRGEC (SEQ ID NO: 326)
D2M008-4A4YTE	QVQLVQSGAEVKKPGSSVKVSKCKASGCTFSSSAFSSVRQAPG QGLEWMGRIIPILDITNSAQKFQGRVTITADKSTDTVSMENV SLSEDTAVYYCARWKTRATEAYDIWGQGTMTVSSASTKGP SVFELAPSSKSTSGGTAALGCLVKDYFPEPVTVMNSGALTSG GVHFFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPS NTKVDKRVKPKSCDKTHTCPPEPAPELLGGPSVFLFPPKPKD TLYITREPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKP REEQYNSTYRVVSVLTVLHQDWLNGKEYCKVSNKALPAPIE KTIISKAKGQPREPQVYTLPPSRDEMTKNQVSLTCLVKGFYPS	DIQMTQSPSSLSASVGDRVTITCRASQGISNWLAWYQQK PGKVPKLLIYKASLSGVPSPRFSGSGSGTEFTLTITSSL QPDDFATYCCQQNSYPTFGQGTKLEIKRTVAAPSVEFI FPSDEQLKSGTASVVCILNNFYPREAKVQWKVDNALQSG NSQESVTEQDSKDSITYSLSTLTLSKADYEKHKVYACEV VTHQGLSSPVTKSFNRGEC (SEQ ID NO: 326)

D2M08- 27H28L	DIAVEWESNGQPENNYKTTPVLDSGSGFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO: 327) QVQLVSGGAVQPGSRSLRSCAASGFTFSNYAFHWVRQAPG KGLWVALISYDGNNEYADSVKGRFTISRDNKNTLYLQMN SLRVEDMAVYICARPFTNFGVAILDHWGGTTLTVSSASTK GPSVFPPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGAL TSGVHTFPFPAVLQSSGLYSLSVTVTPSSSLGTQTYICNVNHK PSNTKVDKKVEPKSCDKTHTCPPCPAPPELLGGPSVFLFPPKPK KDTIMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKT KPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAP IEKTIKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFY PSDIAVEWESNGQPENNYKTTPVLDSGSGFFLYSKLTVDKS RWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO: 328)	DIQMTQSPSSLSASVGRVTITCQASQDISNYLNWYQQK PGKAPKLLIYDASNLEITGVPSRFSGSGSGTFTTITSSL QPEDLATYQCQKYDYLPTFTGQGTKLEIKRTVAAPSVFI FPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQNS GNSQESVTEQDSKDSYSLSSLTITLSKADYEKHKVYACE VTHQGLSSPVTKSFNRGEC (SEQ ID NO: 329)
27H28L-YTE	QVQLVSGGAVQPGSRSLRSCAASGFTFSNYAFHWVRQAPG KGLWVALISYDGNNEYADSVKGRFTISRDNKNTLYLQMN SLRVEDMAVYICARPFTNFGVAILDHWGGTTLTVSSASTK GPSVFPPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGAL TSGVHTFPFPAVLQSSGLYSLSVTVTPSSSLGTQTYICNVNHK PSNTKVDKKVEPKSCDKTHTCPPCPAPPELLGGPSVFLFPPKPK KDTLYITREPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKT KPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAP IEKTIKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFY PSDIAVEWESNGQPENNYKTTPVLDSGSGFFLYSKLTVDKS RWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO: 330)	DIQMTQSPSSLSASVGRVTITCQASQDISNYLNWYQQK PGKAPKLLIYDASNLEITGVPSRFSGSGSGTFTTITSSL QPEDLATYQCQKYDYLPTFTGQGTKLEIKRTVAAPSVFI FPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQNS GNSQESVTEQDSKDSYSLSSLTITLSKADYEKHKVYACE VTHQGLSSPVTKSFNRGEC (SEQ ID NO: 329)
4A4-hb1b2- YTE	QVQLVQSGAEVKKPGSSVKVCKASGGTFSSSAFSAWVRQAPG QGLEWMGRIIPILDITNSAQKFQGRVTITADKSTSTAYMELS SLRSEDTAVYICARWKTATEAYDIWGQGTMTVTSASTKGP SVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTS GVHTFPFPAVLQSSGLYSLSVTVTPSSSLGTQTYICNVNHKPS NTKVDKKVEPKSCDKTHTCPPCPAPPELLGGPSVFLFPPKPKD TLYITREPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTTP REEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIE KTIKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYFS	DIQMTQSPSTLSASVGRVTITCRASQSIENWLAWYQQK PGKAPKLLIYKASSLESQVPSRFSGSGSGTFTTITSSL QPDDEFATYCCQYNSYSTFGQGTKLEIKRTVAAPSVFIF FPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSG NSQESVTEQDSKDSYSLSSLTITLSKADYEKHKVYACEV THQGLSSPVTKSFNRGEC (SEQ ID NO: 332)

	DIQMTQSPSSLSASVGDRTVITCQASQDISNYINWYQQK PGKAPKLLIYDASNLETGVPSRFSGSGDFTFTISSL QPEDIAYYCQKYDYLPTYFGQGTKLEIKRTVAAPSVFI FPPSDEQLKSGTASVVCLLNNFYFPREAKVQWKVDNALQS GNSQESVTEQDSKDYSLSSLTILSKADYKHKVYACE VTHQGLSSPVTKSFNRGEC (SEQ ID NO: 334)
27H281- hb1b-yte	DIAVEWESNGQPENNYKTTPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO: 331) QVQLVESGGGVQPGRSRLRLSCAASGFTFSNYAFHWVRQAPG KGLEWVALISYDGNNEYADSVKGRFTISRDN SKNTLYLQMN SLRAEDTAVYYCARPPFTNFGVAILDHWGQGLTVTVSSASTK GPSVPFLAPSSKSTSGGTAALGCLVKDYFPEPVTISWNVSGAL TSGVHTFPAVLQSSGLYSLSVTVTPSSSLGTQTYICNVNHH PSNTKVDKKVEPKSCDKTHTCPPCPAPPELLGGPSVFLFPPKPK KDTLYITREPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKT KPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAP IEKTIKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFY PSDIAVEWESNGQPENNYKTTPVLDSDGSFFLYSKLTVDKKS RWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO: 333)

Collection Time	Group 1 (D2M-4A4-hblb2-YTE, 1 mg/kg)	Group 2 (D2M008-27H28L-hblb-YTE, 1 mg/kg)
	Mean ± SD (ng/mL)	
2 hr	21,845.750±1,608.723	20,866.833±1,979.669
6 hr	26,829.500±14,756.156	15,936.417±481.381
24 hr	11,998.083±999.447	12,119.833±1,541.920
48 hr	11,183.833±448.752	13,566.583±4,447.213
72 hr	9,614.167±946.984	10,355.833±1,861.537
7 D	10,119.500±456.262	8,872.333±763.569
10 D	8,166.583±3,068.532	6,511.267±1,561.047
14 D	6,774.750±463.837	6,417.000±441.172
17 D	5,604.158±671.069	5,561.750±1,490.161
21 D	4,721.767±293.165	5,377.000±342.913
24 D	3,355.933±1,635.844	4,475.883±759.424
28 D	4,254.133±694.061	4,548.517±132.964

FIG. 29

Pharmacokinetics parameters of 4A4-hblb2-YTE and 27H28L-hblb-YTE after 1 mg/kg single *i.v.* dose

Pharmacokinetics parameters	Group 1 (D2M-4A4-hblb2-YTE, 1 mg/kg)	Group 2 (D2M008-27H28L-hblb-YTE, 1 mg/kg)
$T_{1/2}$ (h)	375	500
T_{max} (h)	6	2
C_{max} (µg/mL)	26.83	20.87
AUC_{last} (h*µg/mL)	4938.31	4807.65
AUC_{all} (h*µg/mL)	4938.31	4807.65

Note: $T_{1/2}$ indicates terminal elimination half-life; T_{max} indicates the time to reach the peak; C_{max} is the peak concentration; AUC_{last} represents the area under the concentration-time curve of the drug (from 0 h to the time of the last quantifiable concentration); AUC_{all} represents the area under the drug concentration-time curve (from 0 h to the last observation time).

FIG. 30

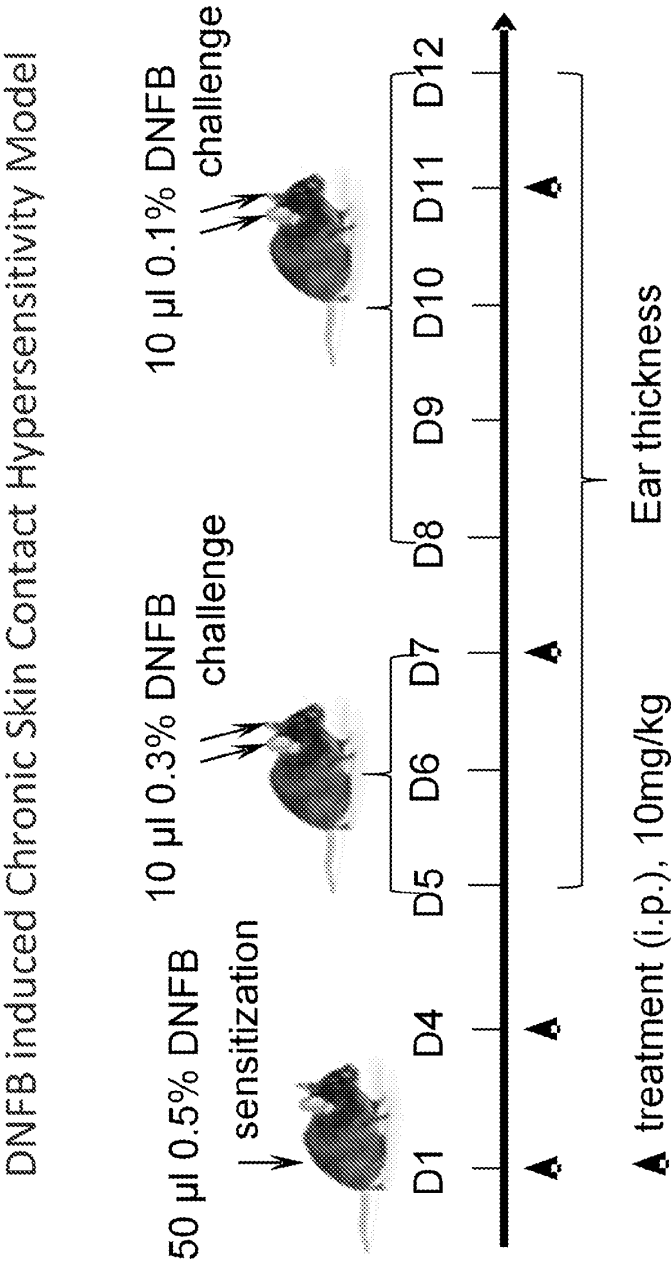


FIG. 31A

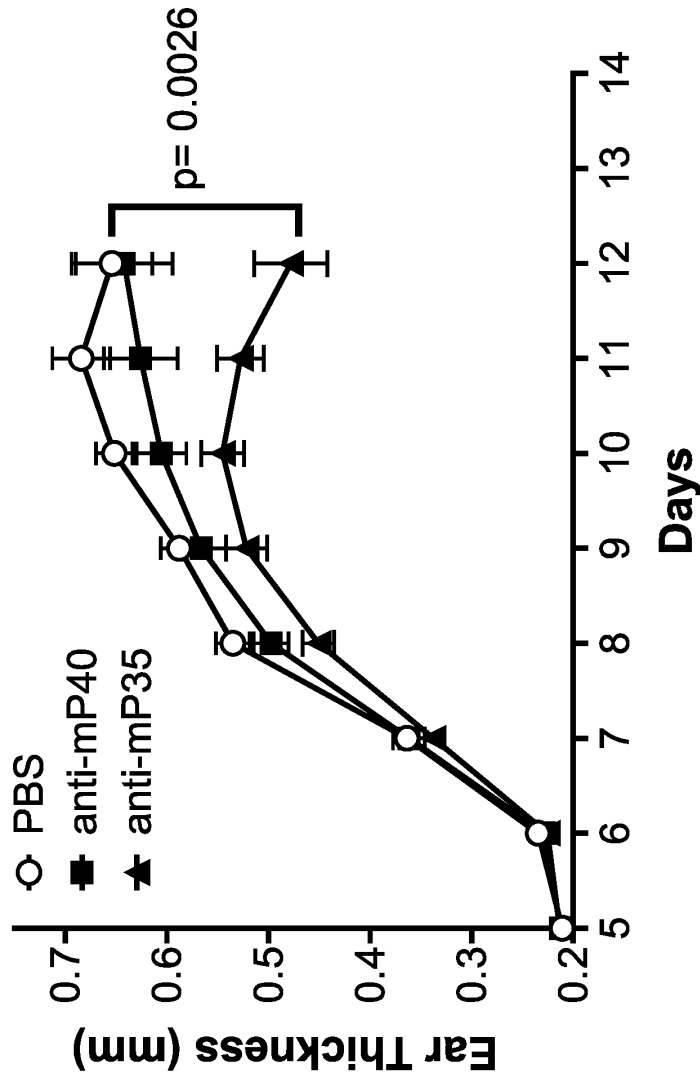


FIG. 31B

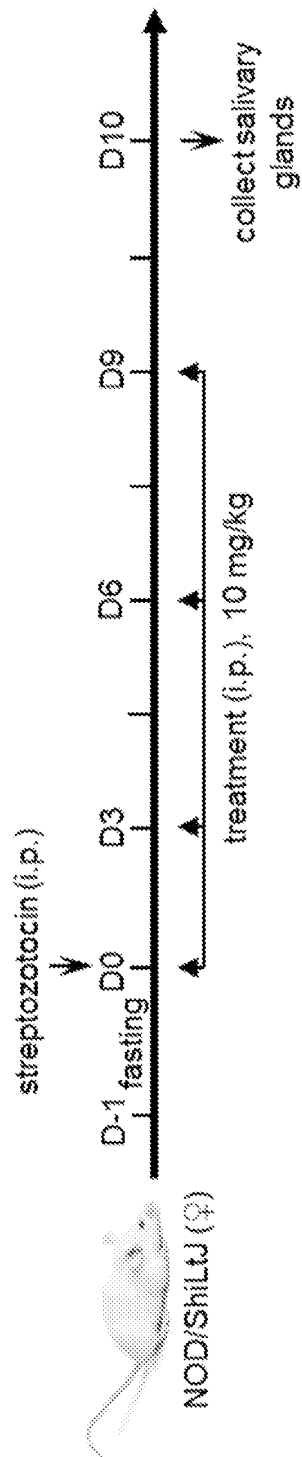


FIG. 32A

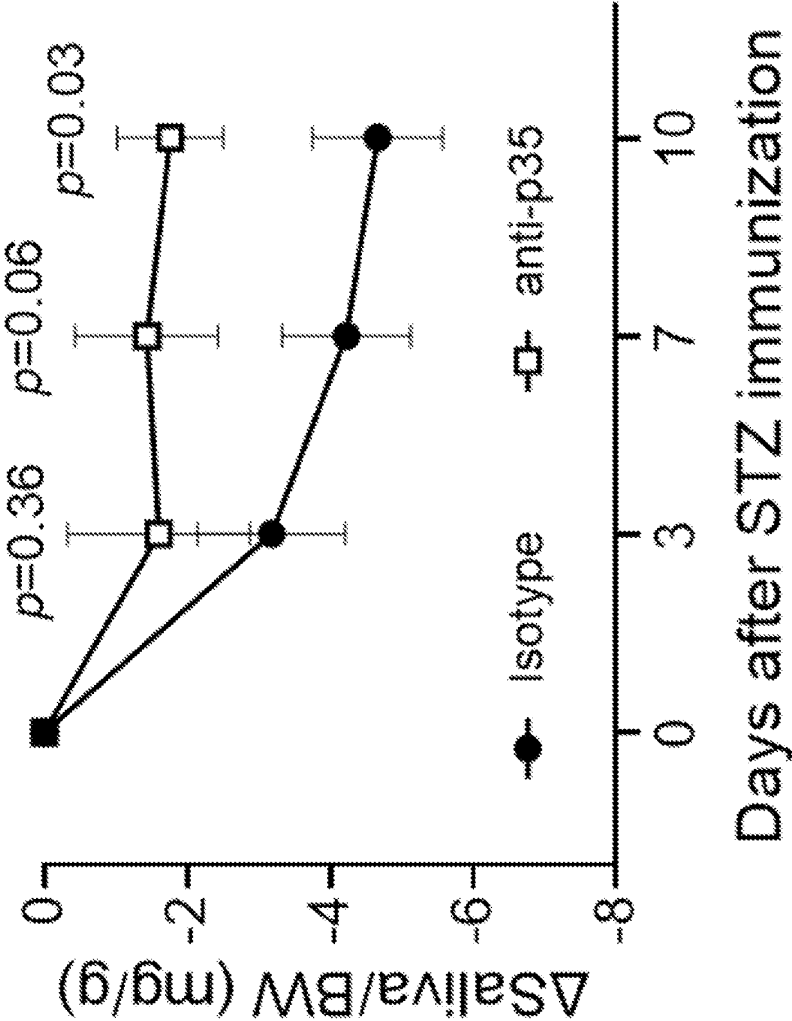


FIG. 32B

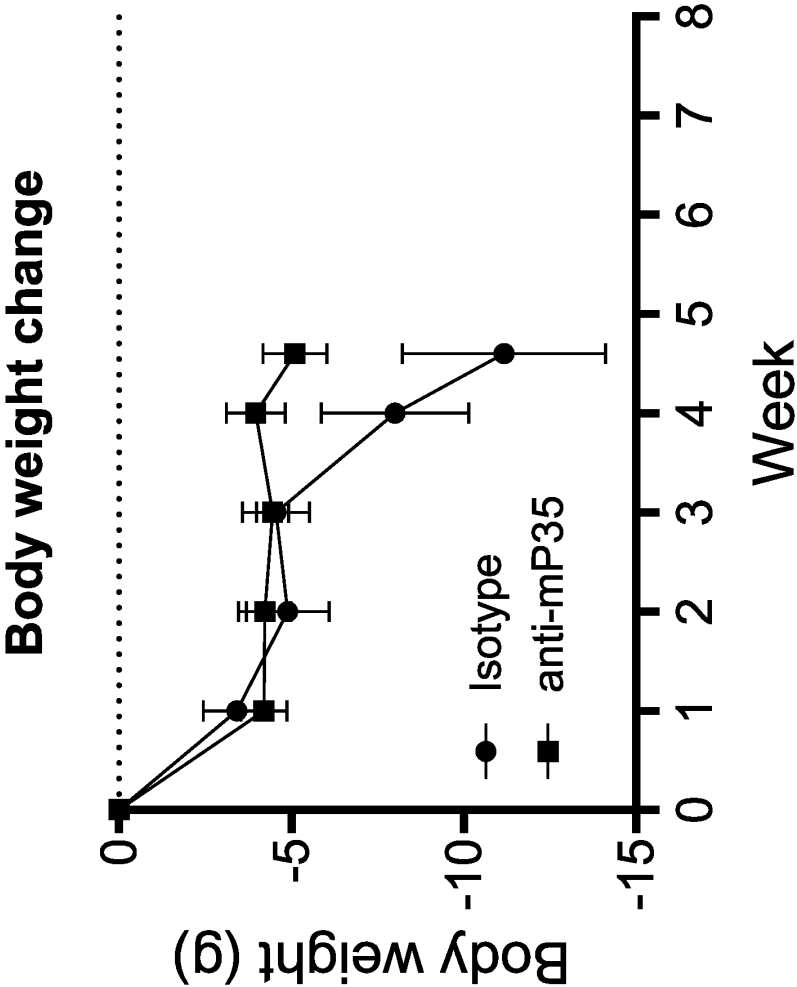


FIG. 33A

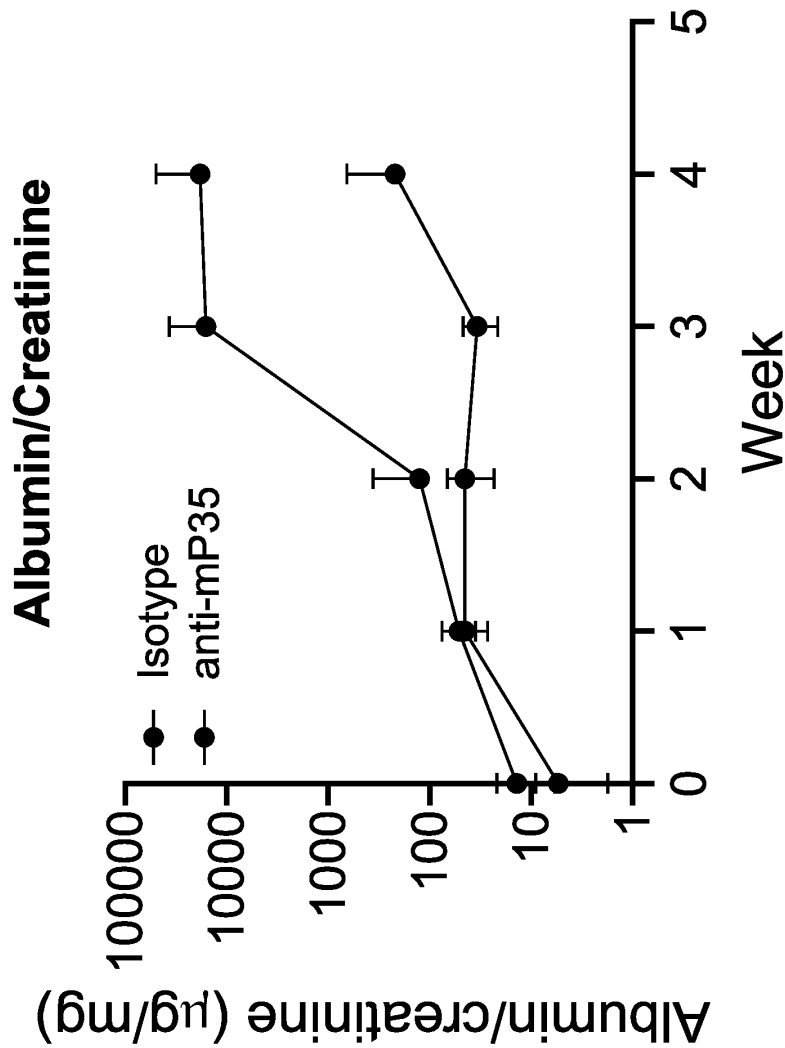


FIG. 33B

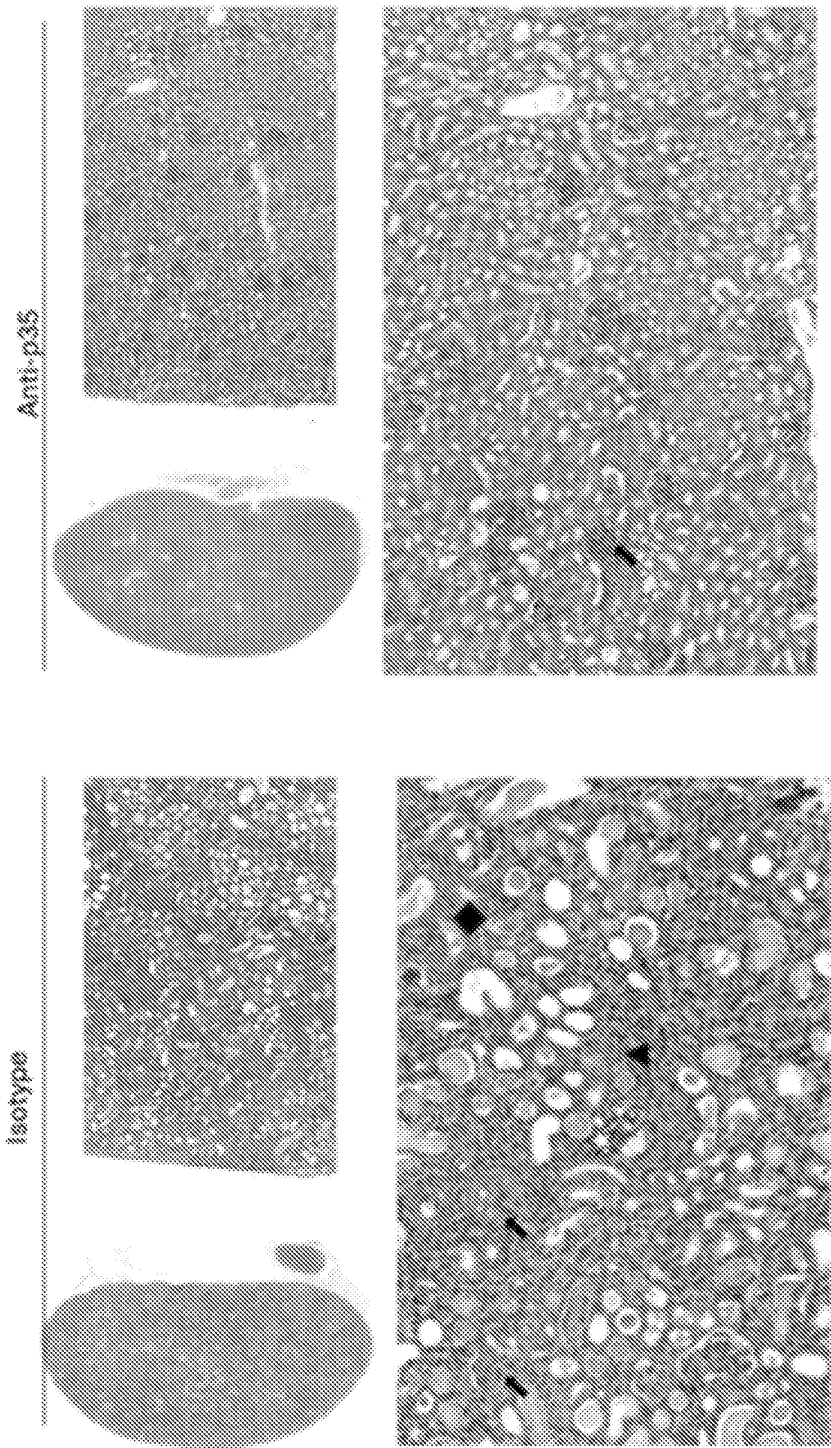


FIG. 33C

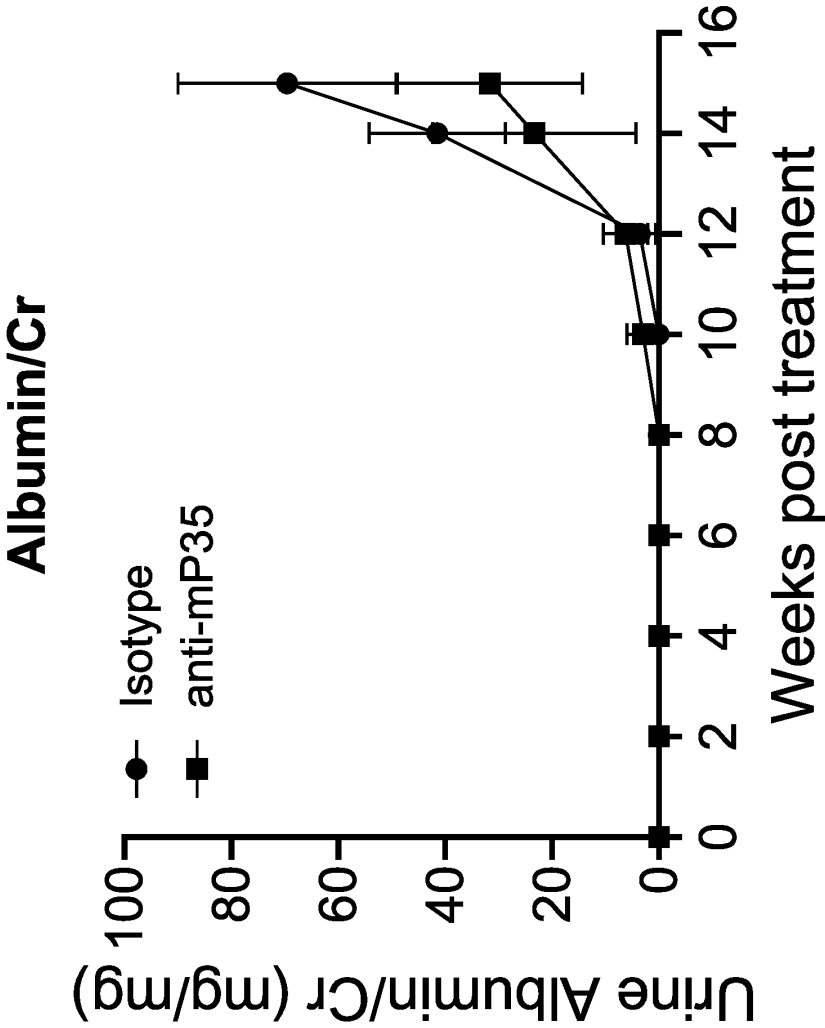


FIG. 34A

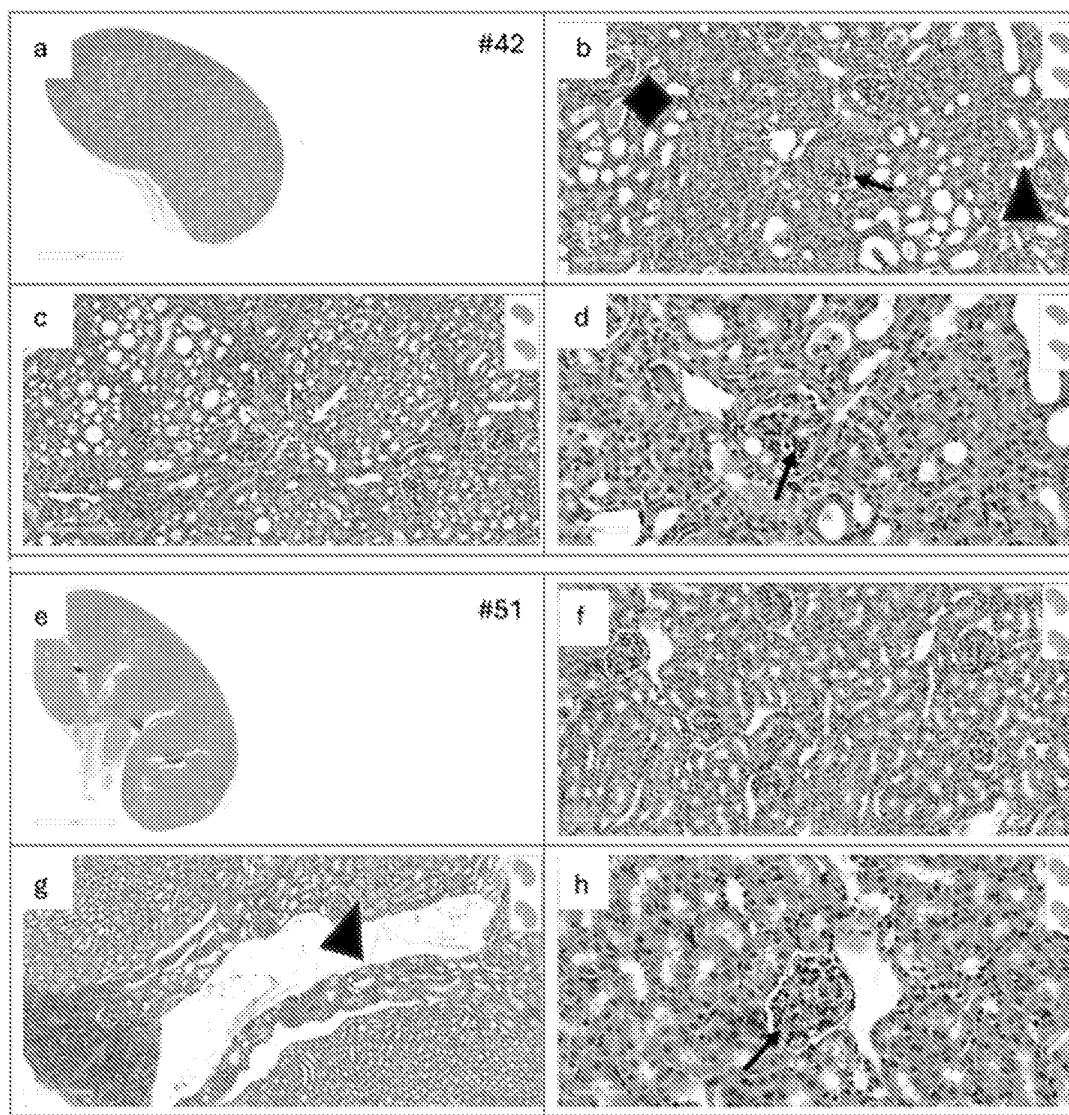
**FIG. 34B**

FIG. 34C

Group	Animal ID	Activity Score (Sum)	Chronicity Score (Sum)	Independent lesion score (Sum)	Weighted Total Score (Sum)
Isotype	#42	0	8	6	18.0
	#44	3	5	5	15.5
	#45	3	0	2	5.0
	#46	6	0	1	7.0
	#47	3	3	5	12.5
	#48	0	9	10	23.5
	#60	0	9	9	22.5
	MEAN	2.1	4.9	5.4	14.9
	SD	2.3	4.0	3.3	7.2
	#51	4	0	3	7.0
Treated	#53	5	0	4	9.0
	#54	6	1	4	11.5
	#55	4	0	1	5.0
	#56	2	3	6	12.5
	#58	2	3	7	13.5
	#59	4	0	1	5.0
	MEAN	3.9	1.0	3.7	9.1
	SD	1.5	1.4	2.3	3.5