

FIG. 1A

FIG. 1B

FIG. 1C



FIG. 2

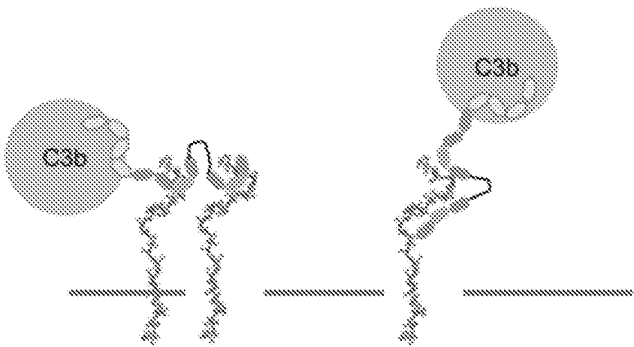


FIG. 3

FHL-1 CFH	P08603-2 P08603	CFH_HUMAN CFH_HUMAN	1	MRLLATLICIAMVAVAEADQMLPPRRNTLITGSNSDQTYPESTDAIYKCRPVSISLG	SCR1	60
			1	MRLLATLICIAMVAVAEADQMLPPRRNTLITGSNSDQTYPESTDAIYKCRPVSISLG		60
P08603-2 P08603	CFH_HUMAN CFH_HUMAN		61	NVIMCKGKGEWALNPLRKCKRCKGHPGDPFGFTIFGKNVFESGVKAVYTCSEGYQL	SCR2	120
			61	NVIMCKGKGEWALNPLRKCKRCKGHPGDPFGFTIFGKNVFESGVKAVYTCSEGYQL		120
P08603-2 P08603	CFH_HUMAN CFH_HUMAN		121	LGEINRECDTGGTNDIPICQVWVCLPVPAPENGKIVSSAMEPDRFVHFGQAVRFVNS	SCR3	180
			121	LGEINRECDTGGTNDIPICQVWVCLPVPAPENGKIVSSAMEPDRFVHFGQAVRFVNS		180
P08603-2 P08603	CFH_HUMAN CFH_HUMAN		181	GYNIDGDEEMHCDDGFWNSKSKPKQVEIICKSPDVINGSPISOKIITYKENERFOYKCNMG	SCR4	240
			181	GYNIDGDEEMHCDDGFWNSKSKPKQVEIICKSPDVINGSPISOKIITYKENERFOYKCNMG		240
P08603-2 P08603	CFH_HUMAN CFH_HUMAN		241	YEYSRCDAVCTSGMRPLPSDEKQCDNPYLENGDYSPLIKIKHRGDEIITYQCRNGFYR	SCR5	300
			241	YEYSRCDAVCTSGMRPLPSDEKQCDNPYLENGDYSPLIKIKHRGDEIITYQCRNGFYR		300
P08603-2 P08603	CFH_HUMAN CFH_HUMAN		301	ATRGNTAKCTSTGWIAPAFCKLKHCDYFDIKHGGLYHENWRRPYFPVAVGKYYSYICDEH	SCR6	360
			301	ATRGNTAKCTSTGWIAPAFCKLKHCDYFDIKHGGLYHENWRRPYFPVAVGKYYSYICDEH		360
P08603-2 P08603	CFH_HUMAN CFH_HUMAN		361	FETPSGYSWQHICTQDQNSPAVCLRRCYFTPYLENGYQNYGRKFTVQKSIDVACHPGY	SCR7	420
			361	FETPSGYSWQHICTQDQNSPAVCLRRCYFTPYLENGYQNYGRKFTVQKSIDVACHPGY		420
P08603-2 P08603	CFH_HUMAN CFH_HUMAN		421	ALPKAGTTVTCNKNQWSPTPRQIKVSFLL	SCR8	449
			421	ALPKAGTTVTCNKNQWSPTPRQIKVSFLL		480
P08603-2 P08603	CFH_HUMAN CFH_HUMAN		430	YVTADGETSGSITGCKDQNSAQPTQIKGCDIPVFNNAKTNDFTNFLNDTLDIYCHDGY	SCR9	449
			481	YVTADGETSGSITGCKDQNSAQPTQIKGCDIPVFNNAKTNDFTNFLNDTLDIYCHDGY		540
P08603-2 P08603	CFH_HUMAN CFH_HUMAN		430	ESWTGCTGSIYCGTNGWSDLFCYERKCLPKIDVHDVFDKKKQKQKGVLEKPSCKPG		449
			541	ESWTGCTGSIYCGTNGWSDLFCYERKCLPKIDVHDVFDKKKQKQKGVLEKPSCKPG		600

FIG. 4

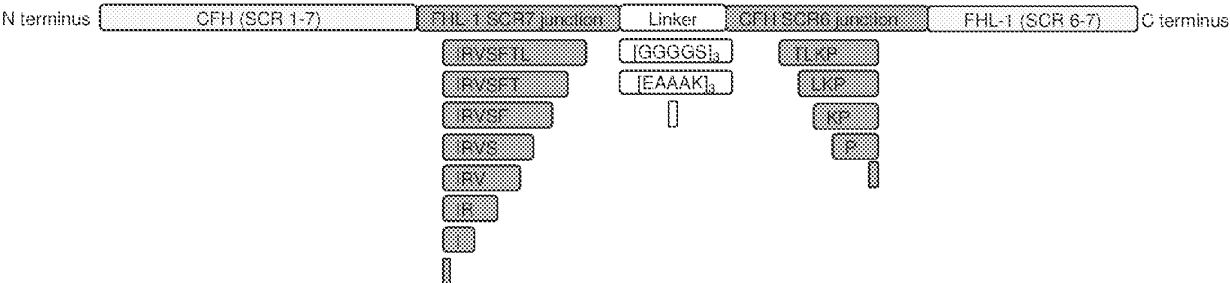


FIG. 5

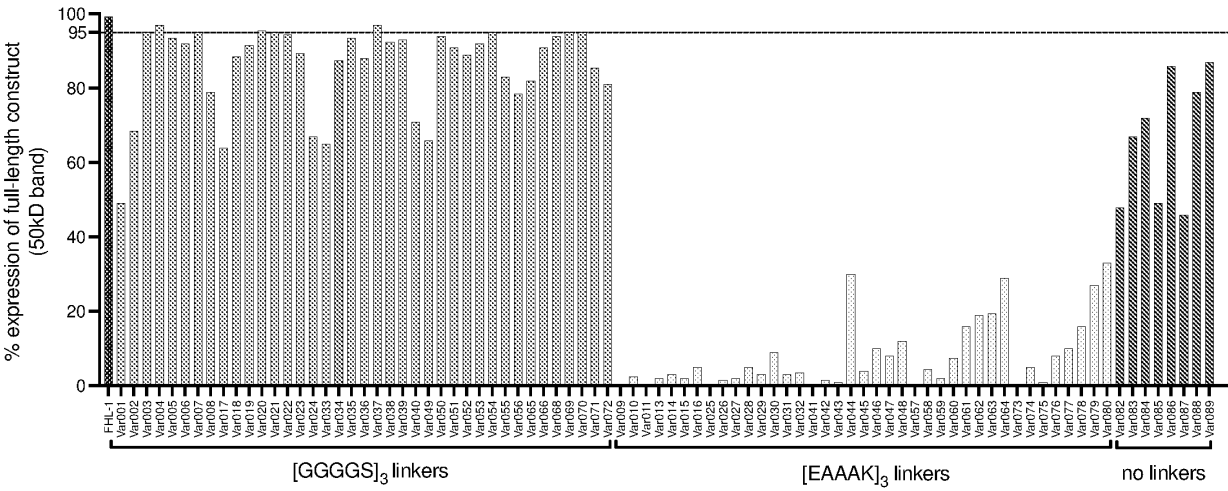


FIG. 6

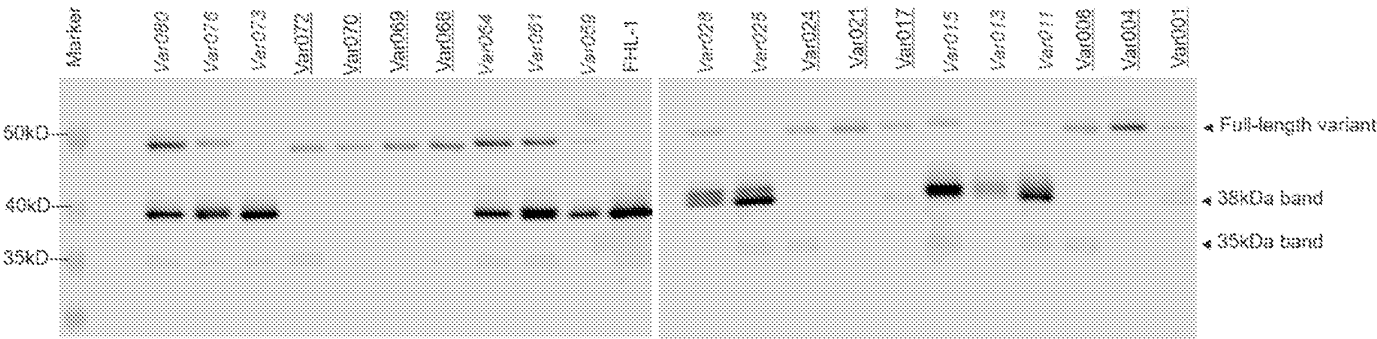


FIG. 7A

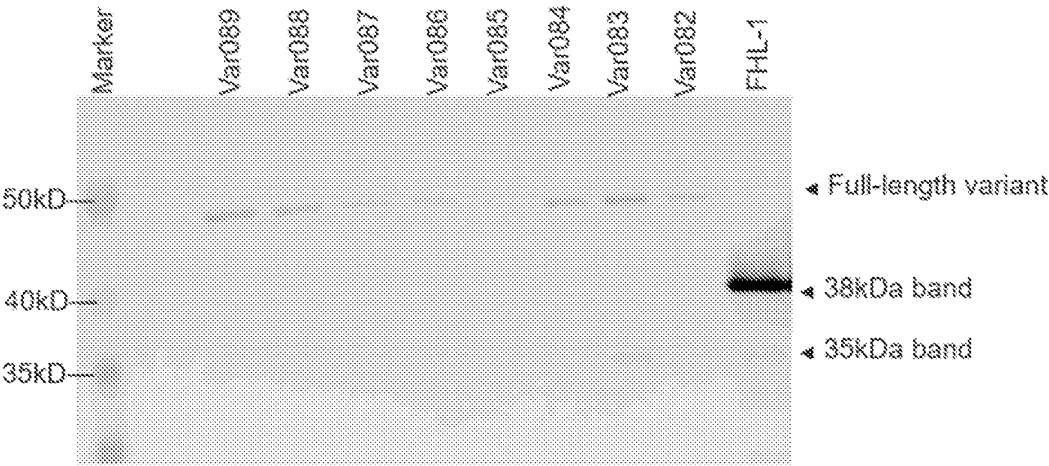


FIG. 7B

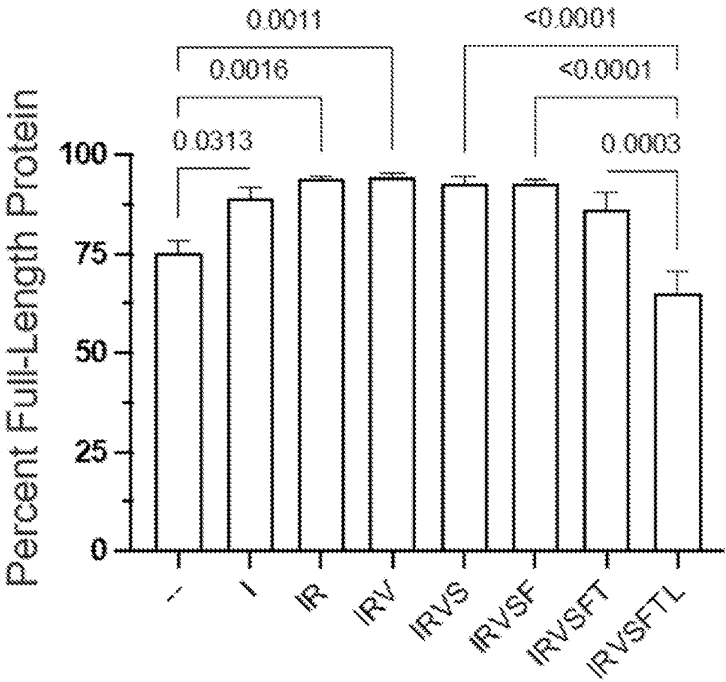


FIG. 8A

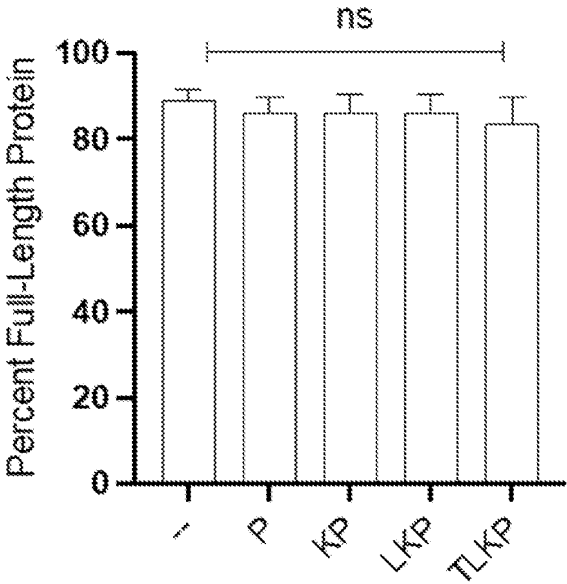


FIG. 8B

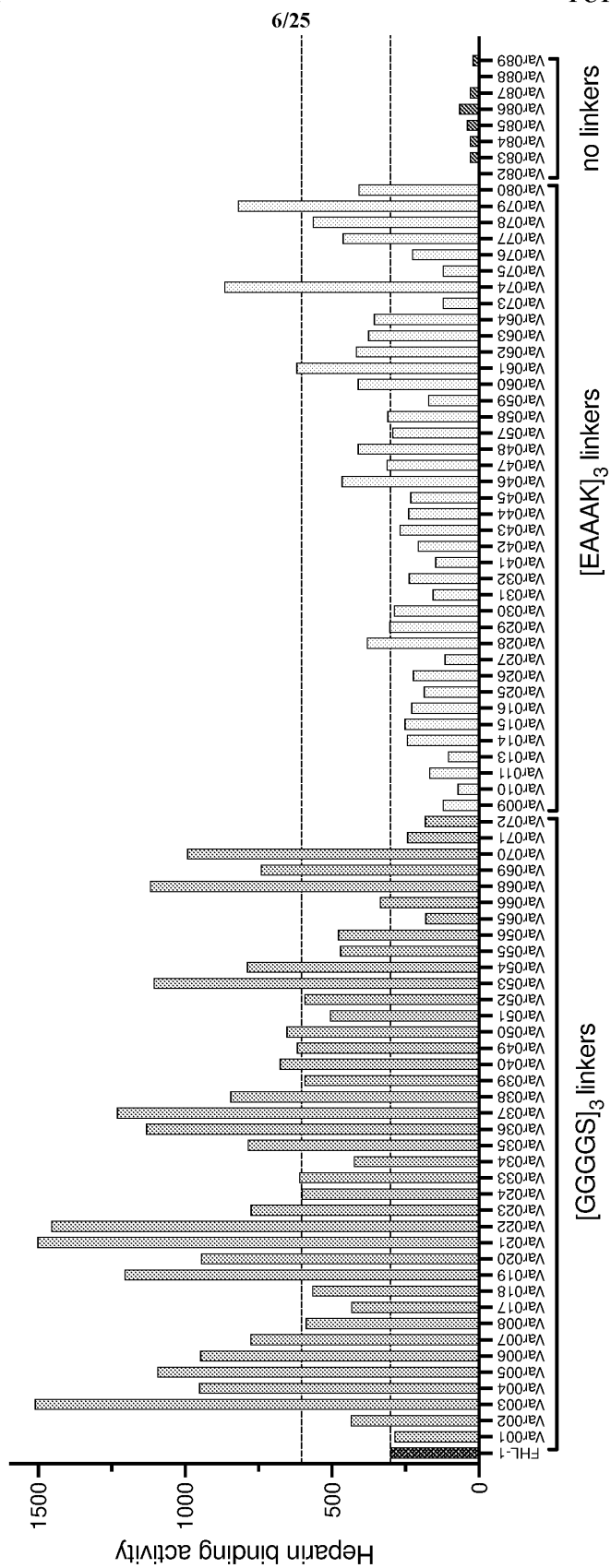


FIG. 10A

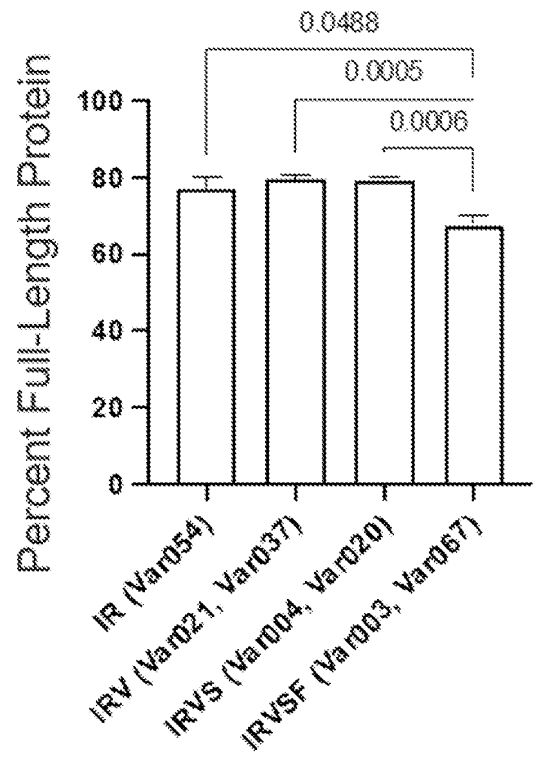


FIG. 10B

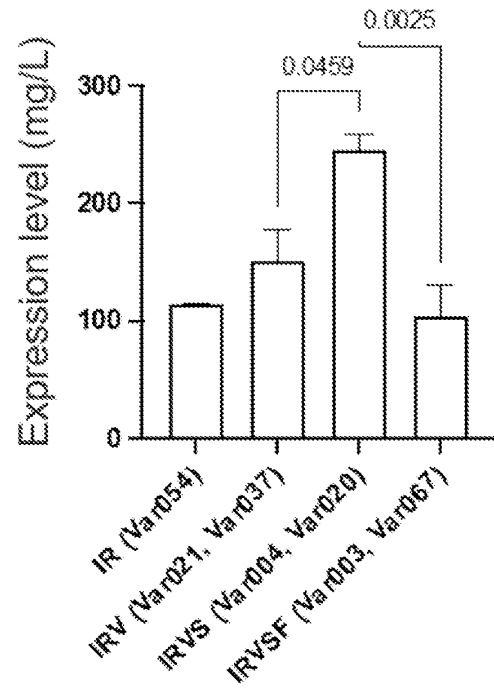


FIG. 11A

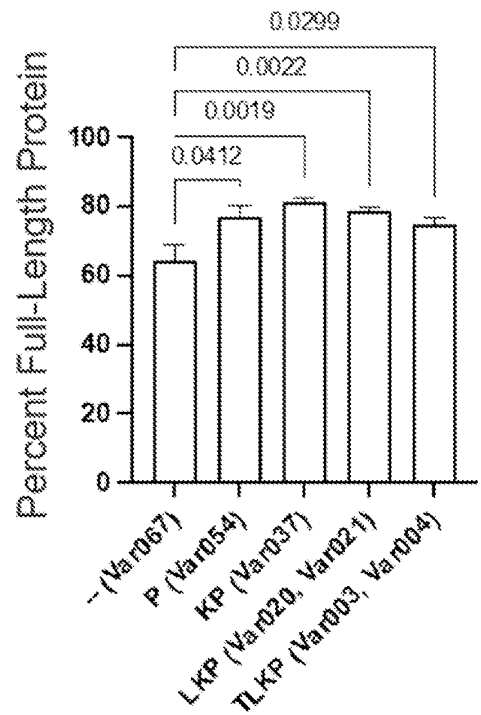
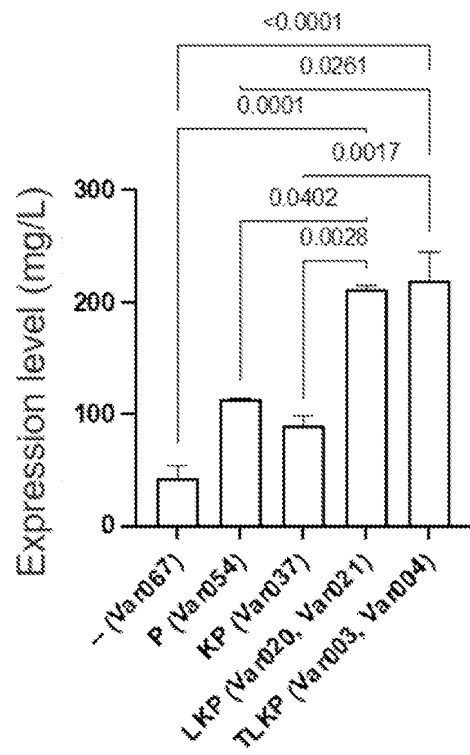


FIG. 11B



Attribute	Source data	Optimal FHL-1 SCR7 junction	Optimal CFH SCR6 junction
Protein integrity	FIG. 8	IR, IRV, IRVS, IRVSF	--, P, KP, LKP, TLKP
Protein integrity	FIG. 10A, FIG. 11A	IR, IRV, IRVS	P, KP, LKP, TLKP
Expression level	FIG. 10B, FIG. 11B	IRVS	LKP, TLKP
Consensus		IRVS	LKP, TLKP

FIG. 12

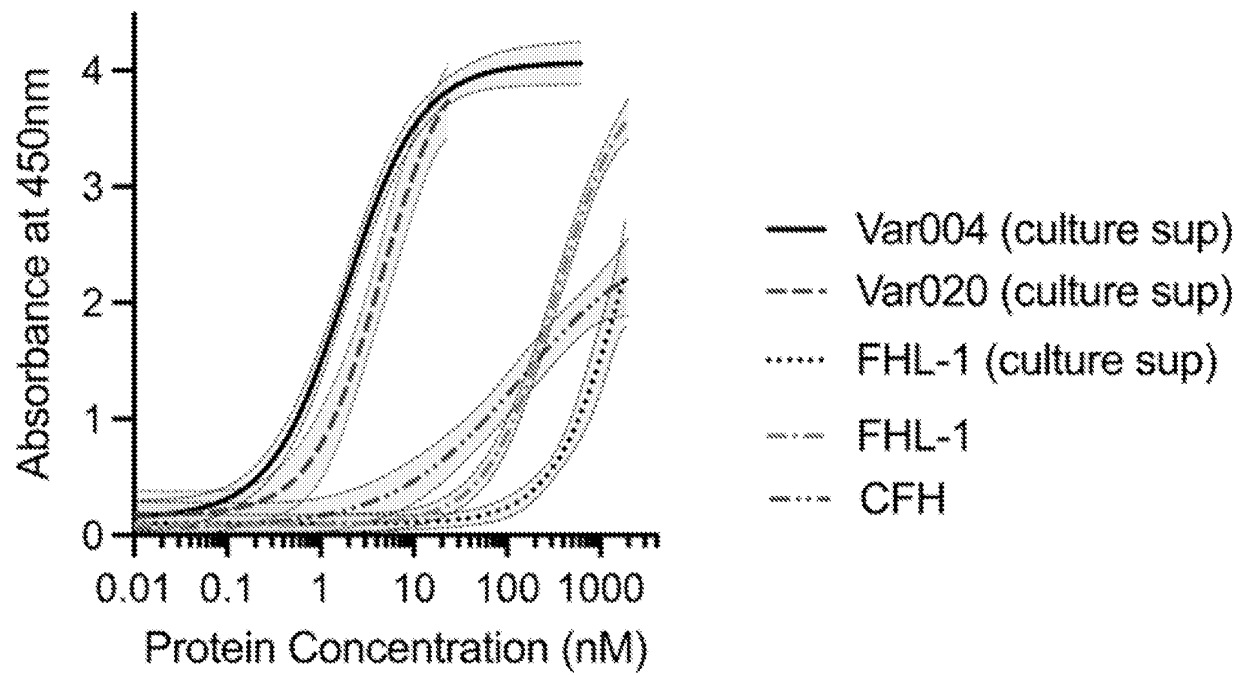


FIG. 13A

Compound	EC ₅₀ nM ± SD
CFH	595.6 ± 737.4
FHL-1	414.6 ± 271.5
FHL-1 culture sup	703.0 ± 399.6
Var004 culture sup	2.2 ± 0.8
Var020 culture sup	4.3 ± 1.6

FIG. 13B

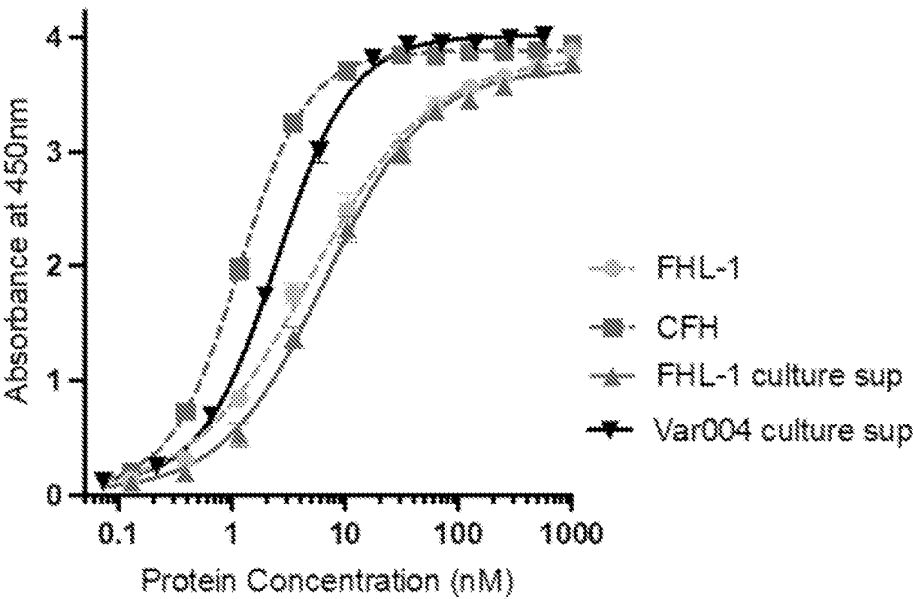


FIG. 14A

Protein	EC ₅₀ nM ± SD
CFH	1.2 ± 0.2
FHL-1	7.1 ± 3.7
FHL-1 culture sup	6.9 ± 1.9
Var004 culture sup	2.5 ± 0.2

FIG. 14B

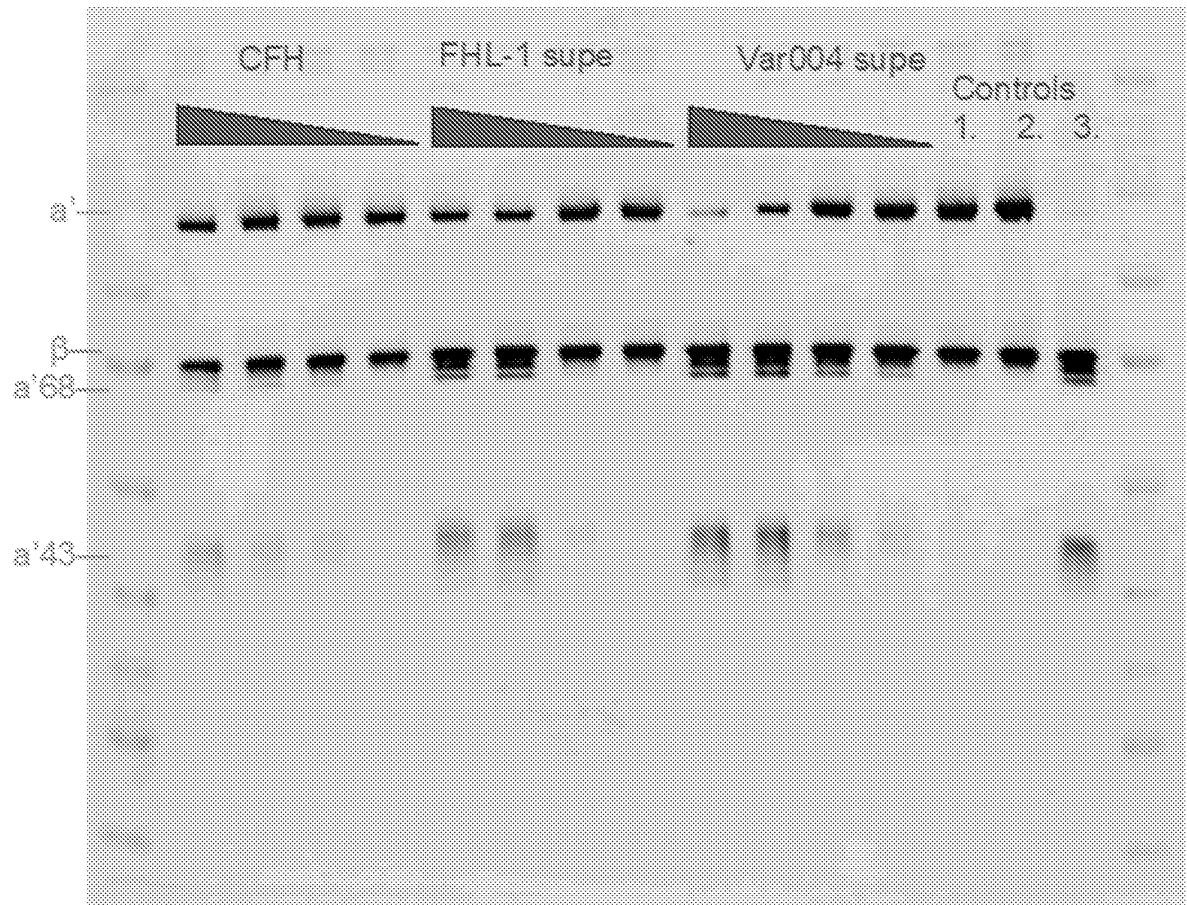


FIG. 15

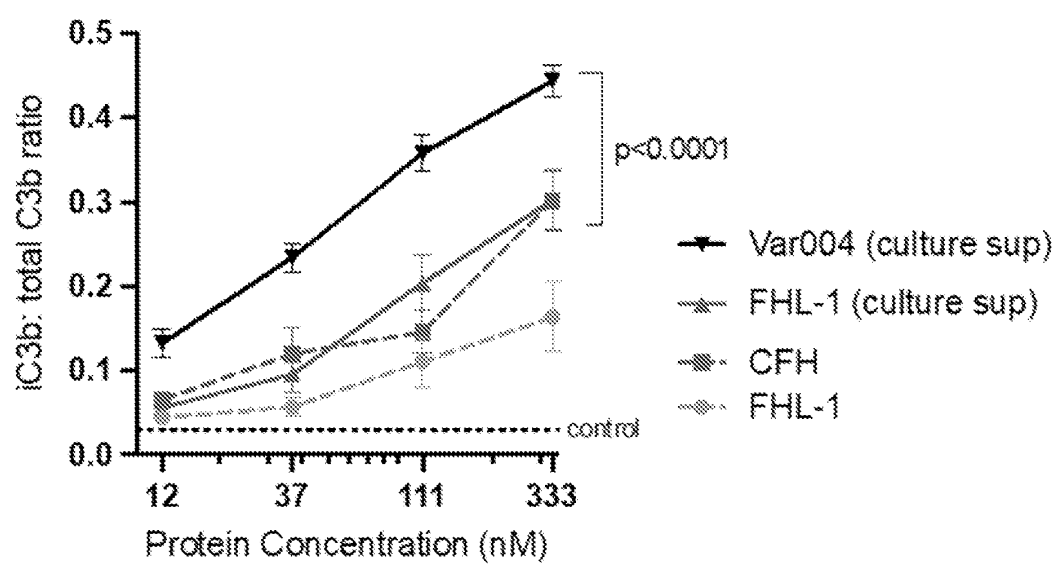


FIG. 16

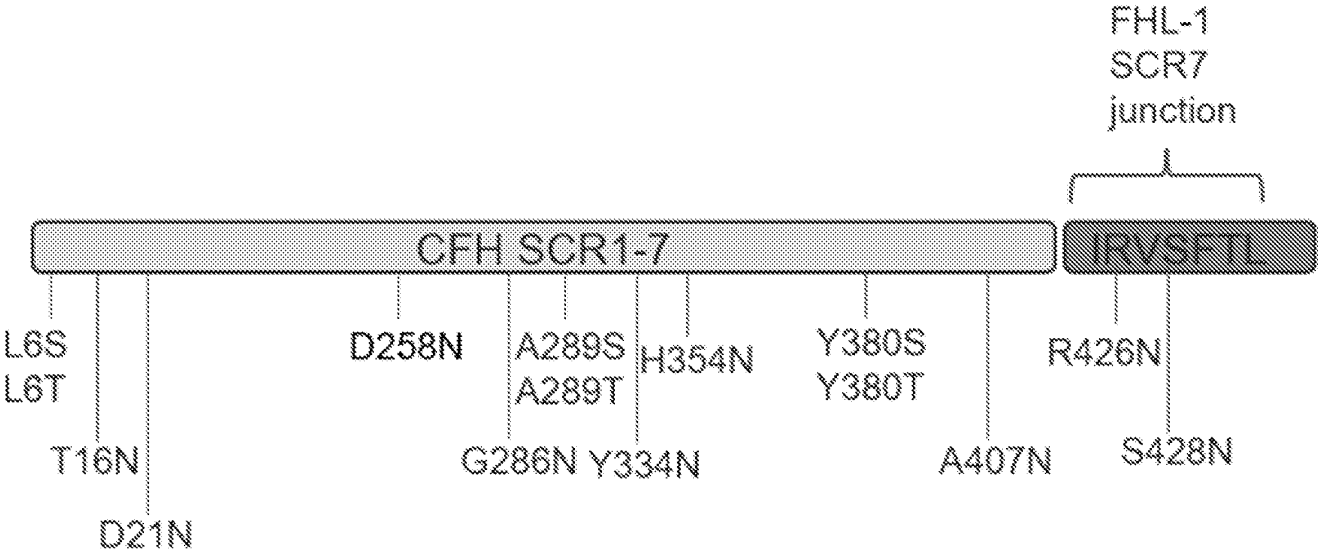


FIG. 17A

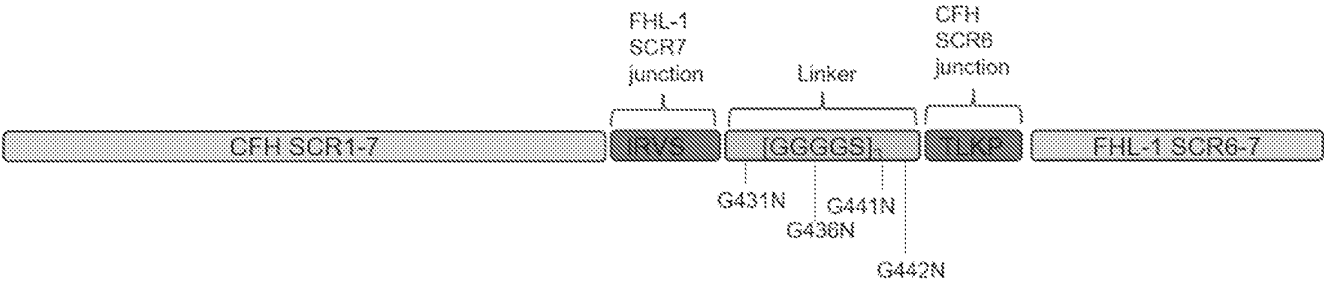


FIG. 17B

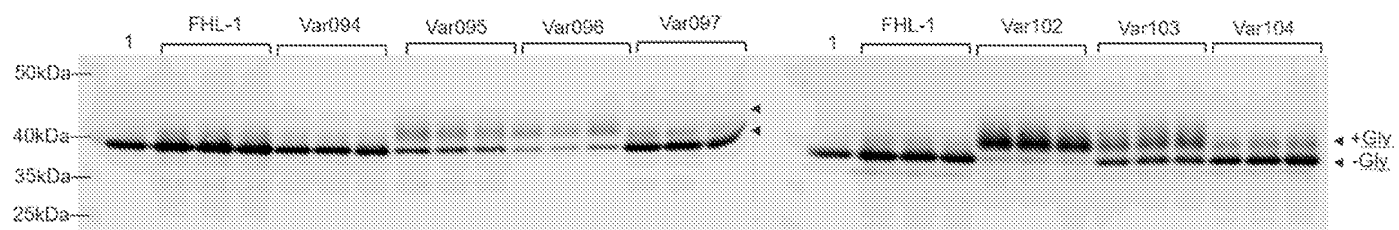


FIG. 18A

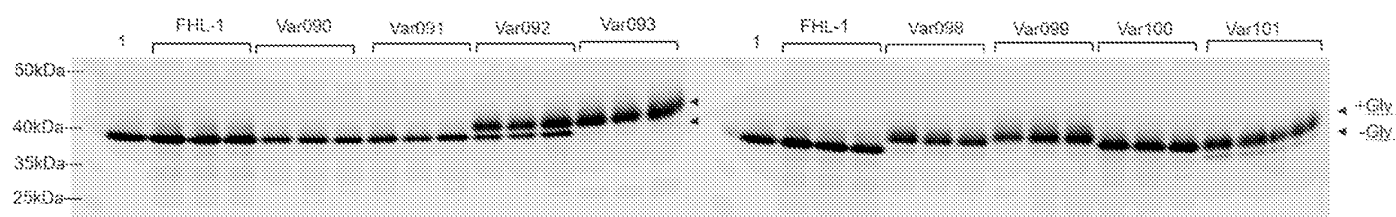


FIG. 18B

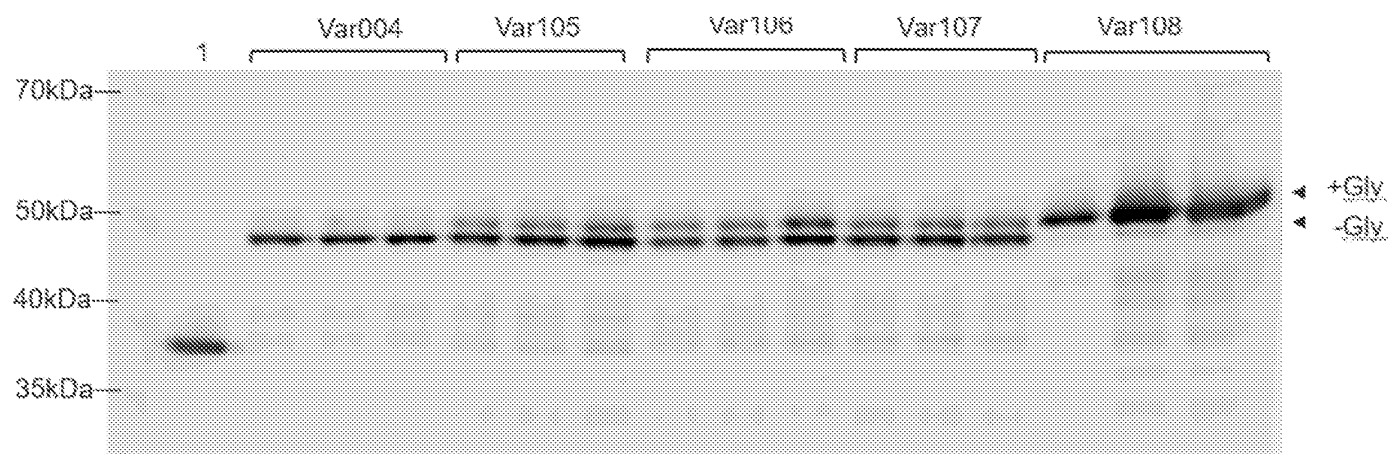


FIG. 19

Variant ID	AA Substitution	% Glycosylation	SD
FHL-1	none	14%	2%
Var090	L6S	16%	3%
Var091	L6T	13%	3%
Var092	A289S	59%	6%
Var093*	A289T	96%	0%
Var094	Y380S	14%	0%
Var095	Y380T	37%	7%
Var096	T16N	55%	1%
Var097	D258N	15%	3%
Var098	Y334N	89%	1%
Var099*	D21N	94%	1%
Var100*	G286N	91%	2%
Var101	H355N	86%	6%
Var102*	A407N	94%	0%
Var103	R426N	56%	5%
Var104	S428N	29%	2%
Var004	None	11%	2%
Var105	G431N	33%	2%
Var106	G436N	39%	3%
Var107	G441N	36%	3%
Var108*	G442N	95%	2%

FIG. 20

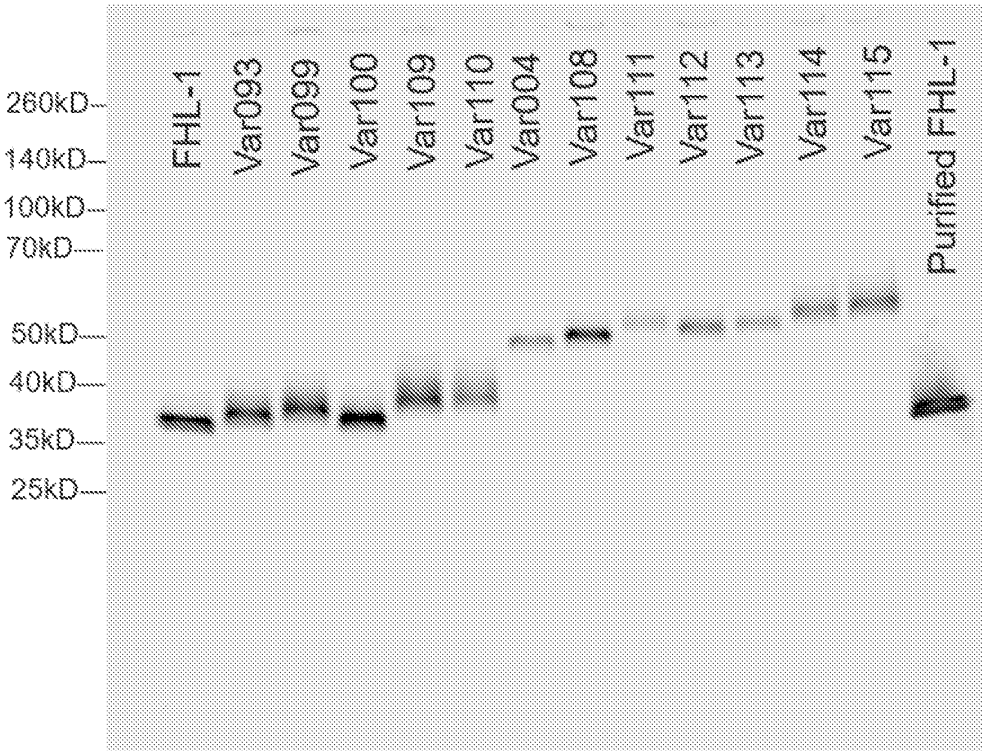


FIG. 21A

	Variant	AA Substitutions
FHL-1 framework	FHL-1	None
	Var093	A289T
	Var099	D21N
	Var100	G286N
	Var109	D21N, G286N
	Var110	D21N, A289T
Var004 framework	Var004	None
	Var108	G442N
	Var111	G442N, D21N
	Var112	G442N, G286N
	Var113	G442N, A289T
	Var114	G442N, D21N, G286N
	Var115	G442N, D21N, A289T

FIG. 21B

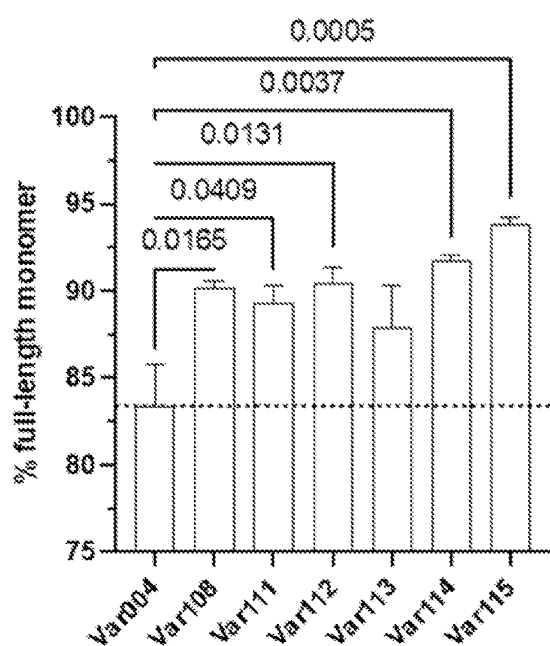


FIG. 22A

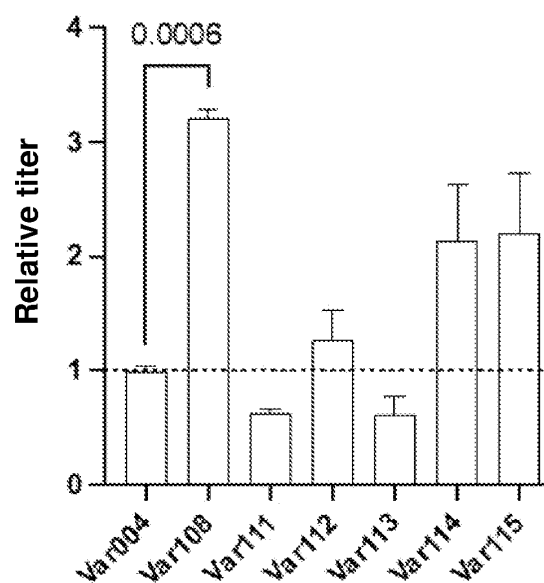


FIG. 22B

VarID	AA Substitutions	Titer (Relative vs Var004)	% FL monomer
Var004	Reference		83.4
Var108	G442N	3.21	90.2
Var111	G442N; D21N	0.64	89.3
Var112	G442N; G286N	1.27	90.5
Var113	G442N; A289T	0.62	87.9
Var114	G442N; D21N; G286N	2.14	91.8
Var115	G442N; D21N; A289T	2.20	93.9

FIG. 23

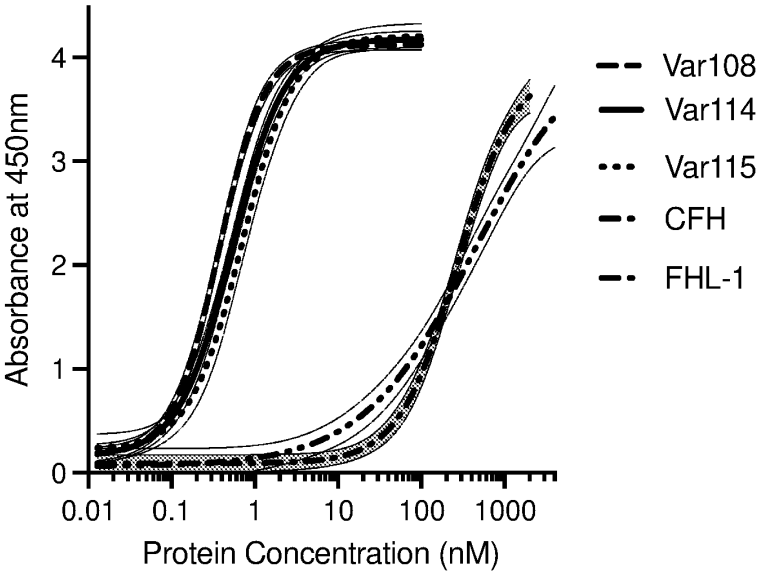


FIG. 24A

Protein	EC ₅₀ nM (+/- SD)		Relative fold CFH	Relative fold FHL-1
CFH	442.7 (558.3)			
FHL-1	394.6 (270.5)			
Var108	0.4	(0.1)	1128	986
Var114	0.6	(0.3)	739	658
Var115	0.8	(0.4)	546	493

FIG. 24B

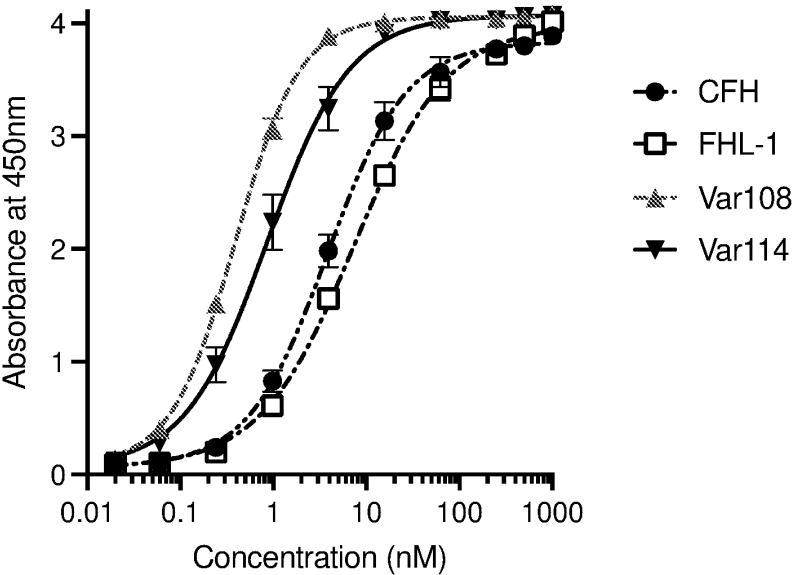


FIG. 25A

Protein	EC ₅₀ nM (+/- SD)
CFH	4.5 (2.8)
FHL-1	7.4 (0.8)
Var108	0.4 (0.1)
Var114	1.1 (1.0)

FIG. 25B

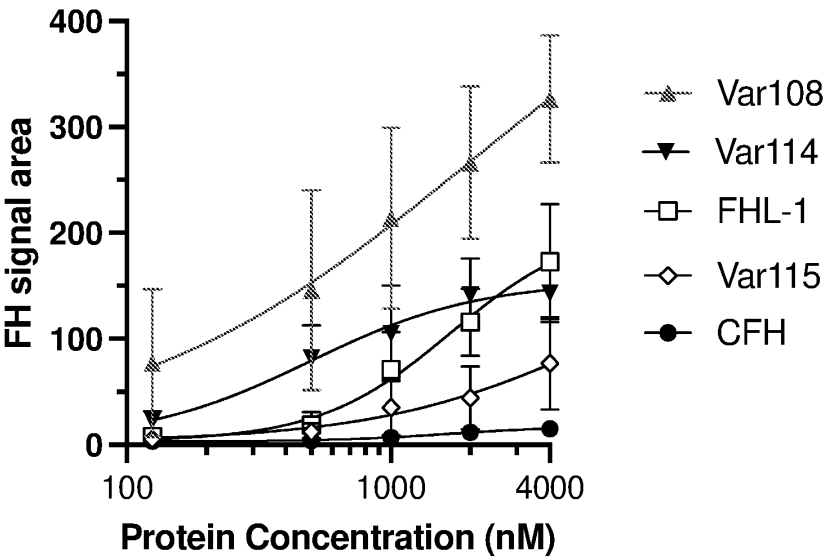


FIG. 26A

Condition	Binding EC ₅₀ (nM ± SD)	Binding at 4000nM (signal ± SD)
CFH	2681.2 ± 2002.5	15.2 ± 12.4
FHL-1	1983.0 ± 648.7	172.7 ± 94.3
Var108	790.5 ± 681.1	326.6 ± 104.0
Var114	701.2 ± 525.6	143.4 ± 62.2
Var115	4153.5 ± 2899.8	76.8 ± 76.0

FIG. 26B

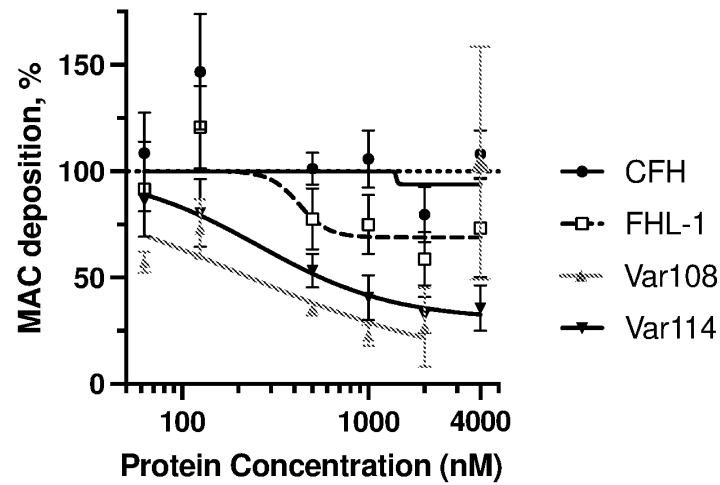


FIG. 27A

Condition	MAC IC ₅₀ (nM ± SD)	Max MAC inhibition (100%-I _{max} ± SD)
CFH	729.4 ± 416.7	8.4 ± 9.1
FHL-1	609.1 ± 275.6	39.5 ± 52.4
Var108 **	249.1 ± 150.7	--
Var114	260.3 ± 139.1	71.4 ± 24.5

FIG. 27B

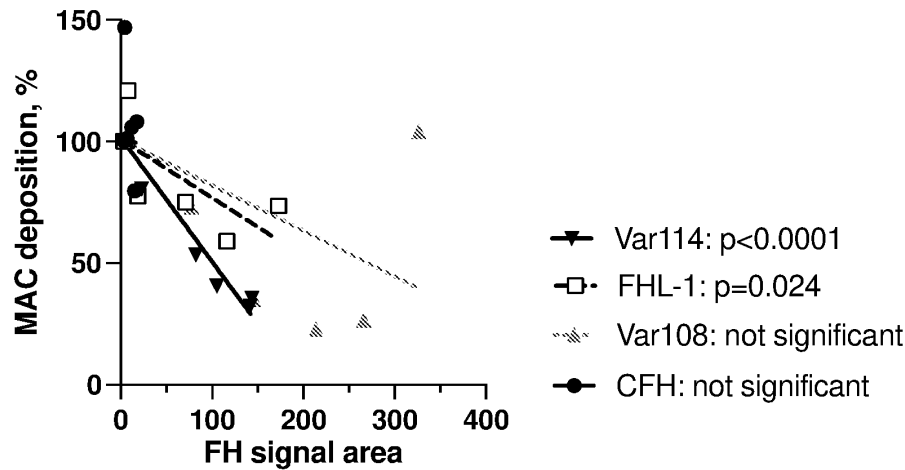


FIG. 28

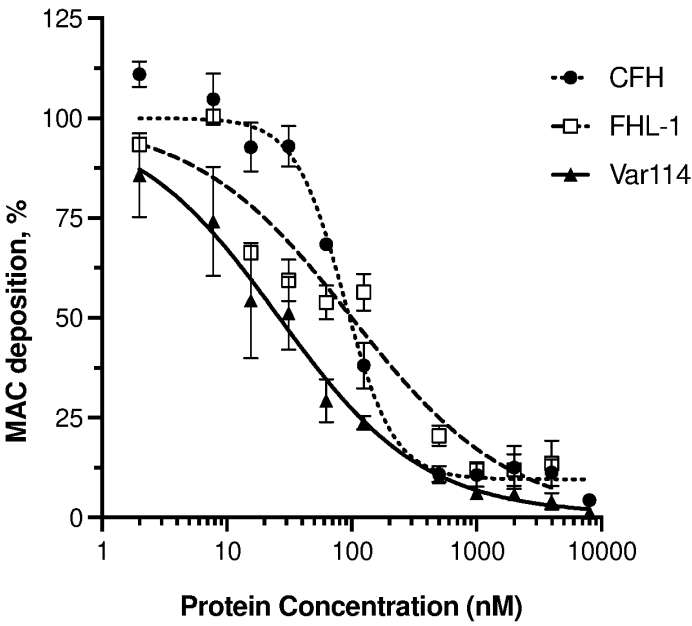


FIG. 29A

Compound	IC ₅₀ (nM) ± SD
CFH	115.7±44.8
FHL-1	116.5±51.1
Var114	32.0±25.7

FIG. 29B

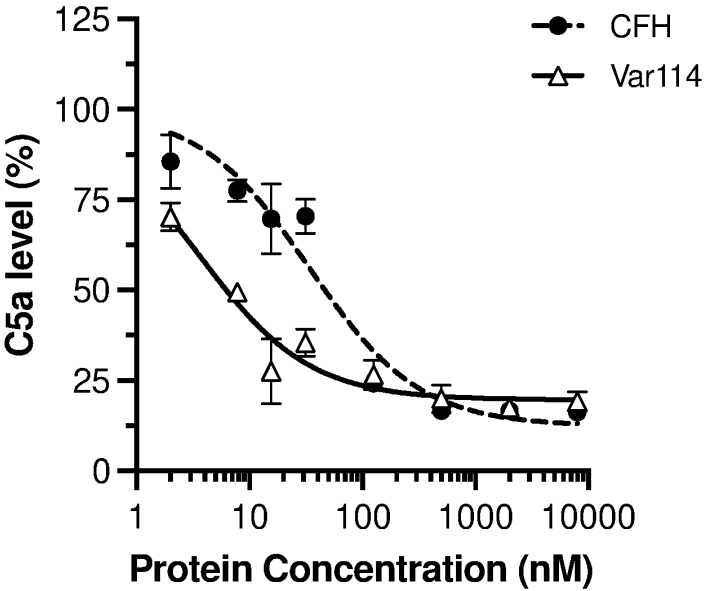


FIG. 30A

Compound	IC ₅₀ (nM) ± SD
Var114	4.3±1.5
CFH	34.2±14.5

FIG. 30B

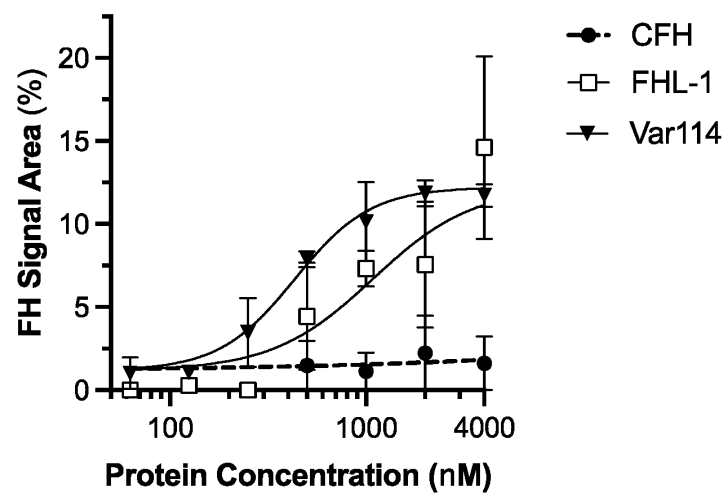


FIG. 31A

Condition	Binding EC ₅₀ (nM ± SD)
CFH	--
FHL-1	1591.8 ± 589.3
Var114	537.8 ± 80.4

FIG. 31B

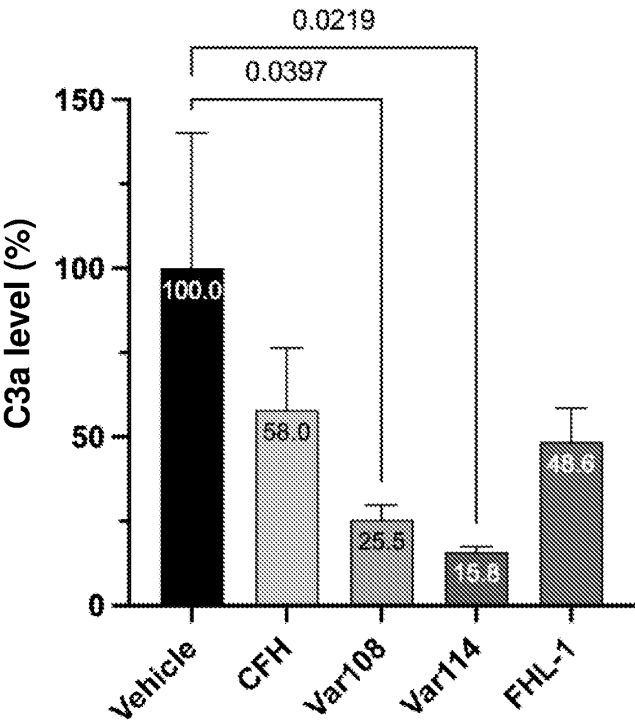


FIG. 32

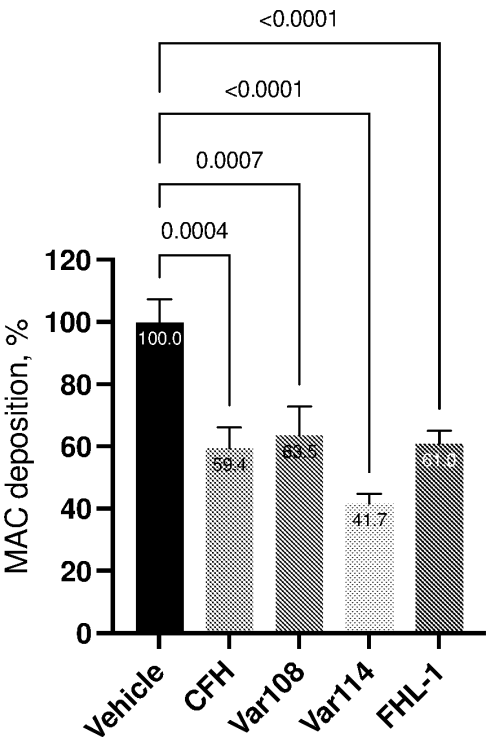


FIG. 33

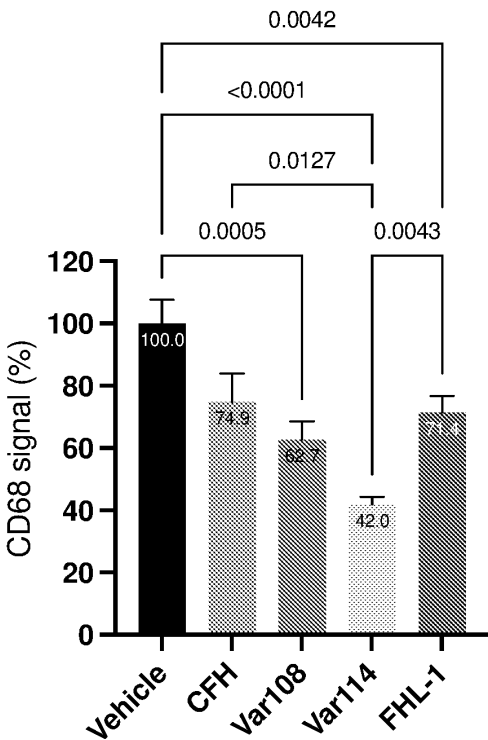


FIG. 34