Supplemental Materials

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Supplemental Methods

Guinea pig erythrocyte hemolytic assay

Overall FH functionality was assessed using a modification of the FH-dependent sheep erythrocyte (ShE) hemolytic assay.[1] In our modified assay, we used guinea pig erythrocytes (TCS biosciences, Buckingham, UK) instead of ShE to increase the dynamic range of the assay, and compared the amounts of the FH variants versus wild-type protein required to recover the regulatory capacity of normal human serum that was 75% depleted of FH (NHSΔFH). The negative control was prepared by adding 20 mM ethylenediaminetetraacetic acid (EDTA), and the maximum NHSΔFH-induced lysis was defined as 100%. Each FH variant was analyzed twice in separate experiments. For each experiment, we calculated the relative amount of protein as compared to WT protein required to decrease lysis of guinea pig erythrocytes by 50% (HR_{50}). An HR_{50} value between 0.71 and 1.29 (mean of WT +/- 2SD) was considered normal.

Preparation of C3b-decorated sheep erythrocytes

To assess FH DAA and CA, C3b-decorated ShEs (C3b-ShE) were prepared in isotonic veronal-buffered saline containing 0.1% gelatin (GVB). Briefly, C3b was deposited on washed ShEs (1 mL, 1 × 10^9/mL; Colorado Serum Co.,Denver, CO) by incubation with 45 µL of Factor B (FB)-partially inactivated/FH-depleted human serum at 37°C for 30 minutes in GVB buffer supplemented with 10 mM ethylene glycol-bis(2-aminoethylether)-N N N′N′-tetraacetic acid (EGTA), 5 mM $MgCl_2$ (GVB-Mg2+). Cells were then washed three times and resuspended in 1 mL of GVB-Mg2+ buffer. The amount of FB (Complement Technology Inc., Tyler, TX) needed to generate approximately one C3 convertase per cell was determined by titration (FB 0.4-2 µg) with a constant amount of Factor D (FD) (0.3 µg; Complement Technology Inc., Tyler, TX) in 0.2 mL of C3b-ShE at 30°C for 5 minutes; the reaction was stopped by adding 0.3 mL of ice-cooled GVB-EDTA buffer. Hemolysis was induced by adding rat serum (diluted 1:9

in GVB with 10 mM EDTA; rat serum-EDTA) as a source of C3-9, followed by incubation at 37°C for 60 minutes. After centrifugation, the degree of hemolysis was determined by measuring optical density at 415 nm (OD415). Background (spontaneous lysis) was corrected using GVB-EDTA buffer. The amount of hemolysis was expressed as a percentage of complete lysis by water (100%). Hemolytic sites on ShEs were calculated as Z = -ln(1-hemolysis_percentage).

Decay accelerating activity (DAA)

To assess FH DAA, C3 convertase was assembled with FB (amount previously titrated, Z = 1) and FD (0.3 μg) using 0.2 mL of C3b-ShE (1×10^9/mL) in GVB-Mg2+ buffer at 30°C for 5 minutes. The reaction was stopped by adding 0.3 mL of ice-cooled GVB-EDTA buffer and, immediately thereafter, 50 μL of C3bBb-ShE was transferred into 350 μL of recombinant FH to yield a final concentration of 10 nM. The resulting mixture was allowed to decay for 0, 2.5, 5, 8, and 12 minutes. At each of these time points, a portion of mixture (50 μL) was transferred into rat serum-EDTA (50 μL) to assess residual C3 convertase activity as described earlier. DAA assays for all recombinant FH variants also included WT recombinant FH and were completed on at least three independent runs. The normal threshold for DAA was considered to be hemolysis of <12.5% at 5-minutes (mean of WT from all runs + 2SD).

Factor I cofactor activity (CA)

To assess FH CA, C3b-ShE (50 μL, 1×10^9/mL) were incubated with recombinant FH (final concentration 50 nM) and commercially available FI (final concentration 20 nM; Complement Technology Inc., Tyler, TX) at 37°C for 15 minutes in a total volume of 0.4 mL of GVB-Mg2+ buffer. After three washes, cells were resuspended in 50 μL of GVB-Mg2+ buffer and residual C3bs on ShE were titrated out by using an excess of FB (5× of the amount at Z = 1) and FD (0.3 μg) in GVB-Mg2+ buffer. C3 convertase was formed at 30°C for 5 minutes and the reaction was stopped by adding 300 μL of GVB-EDTA

buffer. A portion of the mixture (50 µL) was then transferred into rat serum-EDTA (50 µL) to assess residual C3 convertase activity, as described earlier. CA assays for all recombinant FH variants also included WT recombinant FH and were completed on at least three independent runs. The normal threshold for CA was considered to be hemolysis < 2.5% after 15-minute incubation (mean of WT from all runs + 2SD).

C3b-binding assay

Binding of FH proteins to immobilized C3b was measured using an in-house plate assay. Briefly, 96-well plates were coated with 50 µL of C3b at 5 µg/mL in phosphate-buffered saline (PBS) overnight. After blocking the plates with Tris-Tween (50 mM Tris pH 7.4, 150 mM NaCl, 0.2% Tween20) containing 1% bovine serum albumin (BSA) for 1 hour at room temperature, 100 µL of the FH proteins was added at different concentrations and the plates were incubated for 1 hour at room temperature. Bound FH was detected using an in-house mouse monoclonal anti-human factor H (mAb 214) followed by a horseradish peroxidase (HRP)-conjugated goat anti-mouse IgG antibody. After incubation with 3,3′,5,5′-tetramethylbenzidine (TMB) substrate, 0.1M sulfuric acid was added to stop the reaction. Absorbance was measured at 450 nm. FH variants were tested in triplicate in at least two different experiments. For each FH variant, we calculated the relative amount of protein as compared to WT protein needed to provide 50% C3b-binding (BD_{50}). A BD_{50} value between 0.33 and 1.67 (mean of WT +/-2SD) was considered normal.

References

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Supplemental Table 1. Clinical and genetic data of patients carrying benign FH variants

Carrier Variant	Gender	Age onset	Outcome	Transplant	Recurrences	Treatment	Other Genetics factors	FH levels	Refs.
p.R2T	M	47	n/a	n/a	n/a	n/a	No	n/a	1
p.M11T	M	42	CKD	0	0	No	No	N	1
p.L74F	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	2
p.K82R	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	2
p.T91S	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	3
p.V111E	M	44	ESRD	1	0	No	No	n/a	1
p.A151T	n/a	n/a	n/a	n/a	n/a	n/a	MCP (p.A353V)	n/a	2
p.V158I	F	30	CKD	0	0	No	MCP (p.D266N)	n/a	1
	F	38	CKD	0	0	No	CFH (p.A1027P)	n/a	1
	F	60	ESRD	1	2	Eculizumab	No	n/a	1
p.S159N	F	44	ESRD	0	1	PE	No	n/a	1
p.A161S	F	31	ESRD	0	n/a	PE	No	N	4
	M	20	CKD	0	n/a	Eculizumab	CFB (p.E566A)	N	5
	M	1	CR	0	0	No	No	n/a	1
p.M162V	n/a	n/a	n/a	n/a	n/a	n/a	n/a	N	6
p.D187V	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	2
p.I216T	M	16	ESRD	0	0	IS/PE/FFP	No	QD	7
p.I221V	M	78	CR	0	n/a	No	No	n/a	1
p.R303Q	F	24	ESRD	2	2	n/a	n/a	N	8
p.R341H	F	23	ESRD	0	n/a	None	C3 (p.R161W)	N	4
p.S411T	M	17	CR	0	1	Eculizumab	FHR-1 (p.L290S;A296V)	N	9
	F	47	ESRD	0	n/a	PE	FHR-1 (p.L290S;A296V)	N	9
p.P503A	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	2
p.N516K	F	26	CR	0	0	Eculizumab (6m)	C3 (p.K65Q)	n/a	10
	M	51	n/a	0	n/a	n/a	No	N	5
	F	3	CKD	0	0	Eculizumab	No	n/a	1
p.D522G	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	2
p.T531A	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	2
p.I551T(*)	M	29	CKD	n/a	n/a	n/a	No	N	5
p.R582H	n/a	n/a	n/a	n/a	n/a	n/a	n/a	N	6
p.V609I	F	20	CKD	0	2	No	C3 (p.T1383N)	n/a	1
	F	21	CKD	0	1	PE/Eculizumab	CFH (p.D1119N)	N	1
	M	< 1	CR	0	0	No	No	n/a	1
p.V641A	F	30	CKD	0	0	No	No	n/a	1
p.G650V	F	46	CKD	0	0	PE	No	QD	5
	M	9	ESRD	0	n/a	PE	CFH (p.S979C); MCP (c.287-2A>G)	n/a	1
p.V686Mº	n/a	n/a	n/a	n/a	n/a	n/a	n/a	QD	11
p.P707L	F	30	CR	0	0	Eculizumab (4m)	n/a	n/a	12
p.H821Y	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	2
p.V835L	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	13
p.S884P	F	10	CKD	0	0	Eculizumab	No	N	1

p.Y951H	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	14
p.T956M	M	1	n/a	n/a	n/a	FFP	No	N	15
	F	23	ESRD	n/a	n/a	n/a	MCP (p.P165S)	N	16
p.F960S	F	34	CKD	n/a	n/a	n/a	C3 (p.R161W)	n/a	17
p.T1017I	M	44	CKD	n/a	n/a	n/a	CFHR1 (p.T205M)	N	5
	M	14	n/a	n/a	n/a	n/a	No	N	1
p.Y1021F	n/a	n/a	n/a	n/a	n/a	n/a	CFH (p.R1210C)	N	18
p.A1027P	M	14	n/a	n/a	n/a	n/a	No	N	1
p.V1054I	M	46	CR	0	0	none	CFH (c.2957-1A>G); MCP (c.286+1G>A)	QD	5
	M	60	ESRD	0	0	Eculizumab	No	N	5
p.Y1058H	M	9	CR	0	2	PE/Eculizumab	C3 (p.I1157T); CFH (p.V1060A)	N	19
	F	11	CKD	0	n/a	Eculizumab	CFH (p.V1060L)	N	1
	M	24	n/a	n/a	n/a	No	CFH (p.V1060L)	N	1
p.I1059T(*)	M	57	n/a	n/a	n/a	n/a	MCP (p.R96G); C3 (p.G1224N)	N	5
p.V1060L	M	9	CR	0	2	PE/Eculizumab	C3 (p.I1157T); CFH (p.Y1058H)	N	19
p.V1060A	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	2
p.S1061P	F	8.5	CKD	0	1	OHCbl	MTHFR (c.677C>T) Hom	N	20
p.Q1076E	n/a	n/a	n/a	n/a	n/a	n/a	*CFH* (Q1187RfsTer84)	n/a	21
	M	53	CR	0	0	None	No	N	5
	M	17	n/a	n/a	n/a	No	No	N	1
p.R1078S	F	25	ESRD	0	1	PE	No	n/a	1
p.E1088D	M	51	R	0	0	Eculizumab (4w)	No	n/a	10
p.P1130L	n/a	n/a	n/a	n/a	n/a	n/a	CFH (p.N516K)	n/a	2
p.E1135D	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	22
p.Q1143E(*)	M	45	CKD	1	2	n/a	C3 (p.V850I)	N	5
p.T1184R	n/a	n/a	n/a	n/a	n/a	n/a	n/a	N	2
p.V1200L	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	2
p.R1203W	M	40	ESRD	0	1	n/a	No	QD	16
	M	22	n/a	na	n/a	n/a	No	QD	1

F (female); M (male); CKD (chronic kidney disease); ESRD (End Stage Renal Disease); CR/PR/R (complete remission/partial remission/remission); N (Normal); QD (Quantitative Deficiency); n/a (data no available); IS (immunosuppression); PE (plasma exchange); FFP (fresh-frozen plasma); OHCbl (hydroxycobalamine); K/L (combined kidney and liver transplant). (*) Variants I551T, I1059T and Q1143E are in complete linkage disequilibrium.

Supplemental Table 2. Clinical and genetic data of patients carrying pathogenic FH variants

Carrier Variant	Gender	Age onset	Outcome	Transplant	Recurrences	Treatment	Other Genetics Factors	FH Levels	Refs.
p.R53C	F	2	CKD	0	0	Eculizumab	No	N	15
	F	27	ESRD	0	0	n/a	No	N	4
	M	0	n/a	0	4	Eculizumab	*C3* (p.R951H)	N	16
p.R78G	n/a	n/a	n/a	n/a	n/a	n/a	No	n/a	14
p.Q81P	F	30	ESRD	0	n/a	PE	No	N	4
p.W134R	F	2	CR	0	2	PE	CFH (p.V1197A;V111E)	QD	23
p.R166L	F	20	CR	0	n/a	Eculizumab	No	N	24
p.R175P	M	30	CKD	0	1	PE	*MCP* (p.S274fs)	n/a	1
p.W198R	M	20	ESRD	0	2	n/a	No	N	16
p.S199G	n/a	n/a	n/a	n/a	n/a	n/a	*CFH* (E1172X)	n/a	2
p.G218E	F	18	ESRD	0	1	PE	No	QD	4
p.P258L	n/a	n/a	n/a	n/a	n/a	n/a	No	QD	5
p.C325Y	F	17	n/a	n/a	n/a	n/a	No	n/a	1
p.Y355S	F	0	CR	0	0	PE	n/a	QD	25
p.G397R	F	25	CR	0	n/a	PE	No	QD	4
p.Q400K	F	21	CKD	0	0	No	No	QD	1
p.C431Y	F	35	CKD	0	n/a	PE	No	QD	4
p.C448Y	F	27	ESRD	3	4	n/a	No	QD	16
p.Y475S	F	25	ESRD	2	3	Eculizumab	No	QD	26
p.Y899D	M	0.5	ESRD	1	1	n/a	*CFH* (p.G1194D)	QD	27
p.C973Y	M	0.4	ESRD	1	Several	FFP	*CFH* (p.V1197A)	QD	28
p.C1077W	F	0	CR	0	4	PE	*CFH* (p.Q1139X)	QD	29
p.D1119N	F	1	n/a	0	n/a	n/a	*THBD (*p.P501L)	N	15
	F	21	CKD	0	1	PE/Eculizumab	*CFH* (p.V609I)	N	1
	F	44	n/a	n/a	n/a	n/a	*CFH* (p.V609I)	n/a	1
p.D1119G	F	2	ESRD	0	1	PE	*MCP* (p.T383I)	n/a	1
p.D1119E	F	<1	Proteinuria	0	1	Eculizumab	No	QD	1
p.Q1137L	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	30
p.Y1142C	F	1	Death	0	3	n/a	No	N	31
	F	22	PR	0	n/a	n/a	No	N	5
p.C1152S	F	33	n/a	n/a	n/a	Eculizumab	No	QD	1
p.W1157R	F	45	n/a	n/a	n/a	PE	No	N	5
	n/a	n/a	n/a	n/a	n/a	n/a	n/a	N	18
p.P1161T	M	43	ESRD	0	1	n/a	No	N	16
p.C1163W	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	14
p.H1165Y	F	31	CR	0	0	PE	MCP (p.A353V)	n/a	32
p.P1166L	F	29	CKD	1	n/a	Eculizumab	No	N	15
	M	45	CKD	1	n/a	n/a	No	N	15

p.V1168A	n/a	n/a	n/a	n/a	n/a	n/a	No	n/a	2
p.I1169L	F	< 1	n/a	n/a	n/a	n/a	Homozygote	n/a	1
p.Y1177C	n/a	n/a	n/a	n/a	n/a	n/a	No	n/a	2
p.W1183R	M	1	ESRD	1 (K/L)	n/a	PE	n/a	N	33
p.W1183C	n/a	n/a	n/a	n/a	n/a	n/a	No	n/a	2
p.T1184A	n/a	n/a	n/a	n/a	n/a	n/a	No	N	2
p.T1184P	n/a	n/a	n/a	n/a	n/a	n/a	No	N	2
p.K1186T	F	30	ESRD	0	1	Eculizumab	No	N	1
p.L1189P	F	< 1	n/a	0	0	n/a	No	n/a	1
	M	< 1	ESRD	2	3	PE	CFHR5 (p.K144N)	N	1
p.L1189H	M	6	ESRD	2	1	PE/FFP/Ecu	n/a	N	34
p.S1191L	M	2	ESRD/Death	4	4	n/a	CFH (p.V1197A)	N	16
	M	19	CR	0	0	Eculizumab	No	N	5
p.S1191W	M	0.5	ESRD	1	3	n/a	No	N	5
	F	6	ESRD	1	2	Eculizumab	No	n/a	1
p.G1194D	F	31	ESRD	1	0	n/a	MCP (p.F242C)	N	35
	M	72	n/a	n/a	n/a	n/a	No	n/a	1
p.E1198V	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	36
p.F1199L	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	2
p.R1206C	F	7	AKF	CR	0	None	No	N	1
p.R1210C	F	29	ESRD	2	2	n/a	No	N	4
	F	0.5	Death	0	5	n/a	CFH (p.T1216del)	N	16
p.R1215Q	M	24	ESRD	0	3	n/a	MCP (p.R103Q)	N	35
	F	22	ESRD	3	3	n/a	No	N	16
	F	15	ESRD	2	3	n/a	CFB (p.I242L)	N	16

F (female); M (male); CKD (chronic kidney disease); ESRD (End Stage Renal Disease); CR/PR/R (complete remission/partial remission/remission); N (Normal); QD (Quantitative Deficiency); n/a (data no available); IS (immunosuppression); PE (plasma exchange); FFP (fresh-frozen plasma); OHCbl (hydroxycobalamine); K/L (combined kidney and liver transplant).

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Supplementary Table 3. FH variants with expression defects.

Transcript	Protein	Abnormality found	Variant previously associated with expression problems
c.400T>C	W134R	W (a)	No
c.974G>A	C325Y	W	No
c.1064A>C	Y355S	W	No
c.1189G>A	G397R	W	Yes [1]
c.1292G>A	C431Y	W	Yes [2]
c.1343G>A	C448Y	W	Yes [3]
c.2695T>G	Y899D	W	Yes [4]
c.2918G>A	C973Y	W	Yes [5]
c.3231T>G	C1077W	W	Yes [6]
c.3454T>A	C1152S	F	Yes [7]
c.3469T>C	W1157R	F	No
c.3481C>A	P1161T	W	No
c.3489C>G	C1163W	F	No
c.3493C>T	H1165Y	F	No
c.3503T>C	V1168A	F	No
c.3581G>A	G1194D	W	No
c.3593A>T	E1198V	W	No
c.3595T>C	F1199L	F	No

(a) **W**, Weak (decreased) intensity of band corresponding to FH in non-reducing SDS-PAGE; **F**, Failed to express *in vitro*.

References

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5. Saland JM, Emre SH, Shneider BL, et al. Favorable Long-Term Outcome after Liver-Kidney Transplant for Recurrent Hemolytic Uremic Syndrome Associated with a Factor H Mutation. *American Journal of Transplantation*. 2006;6(8):1948-1952.
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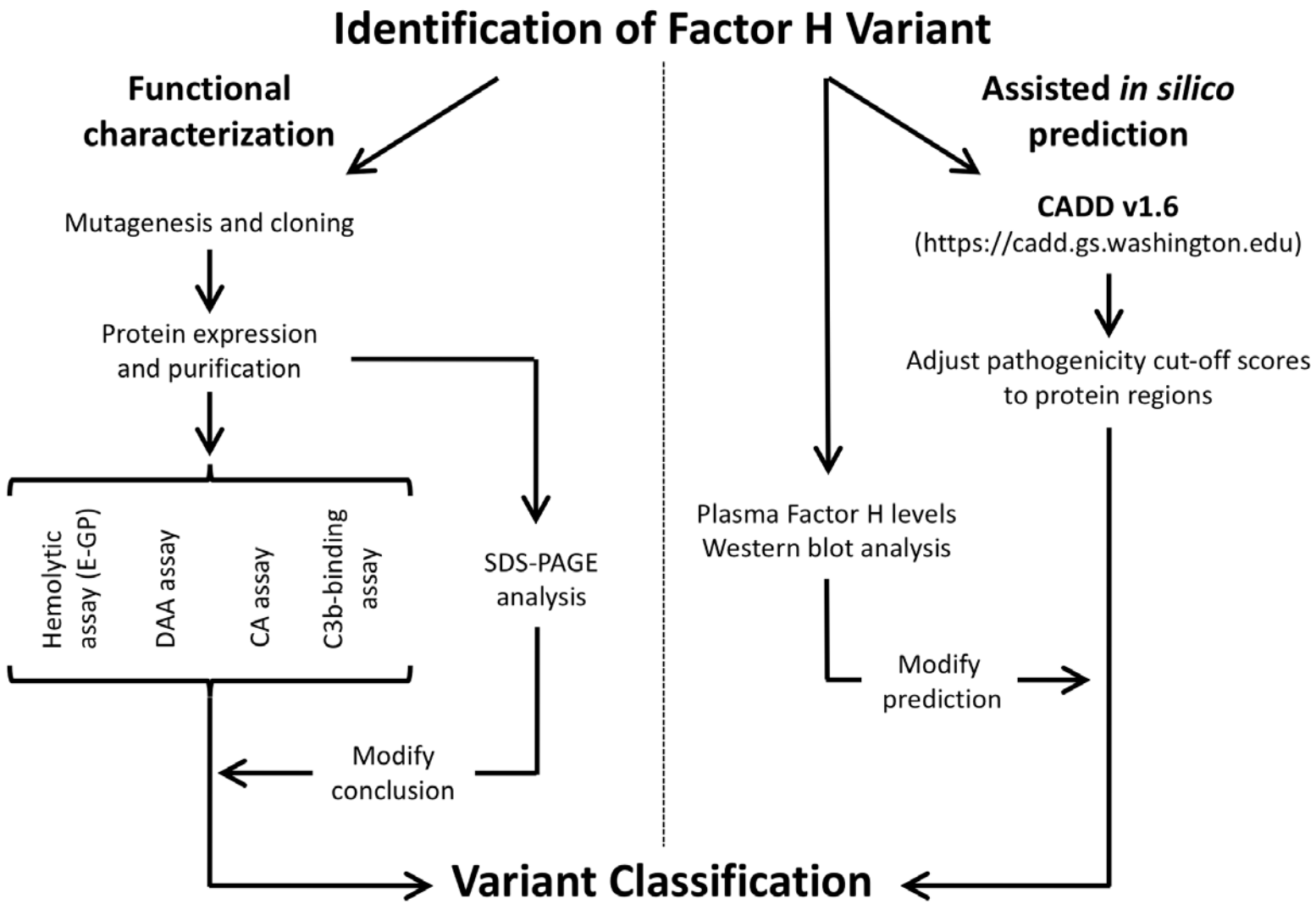
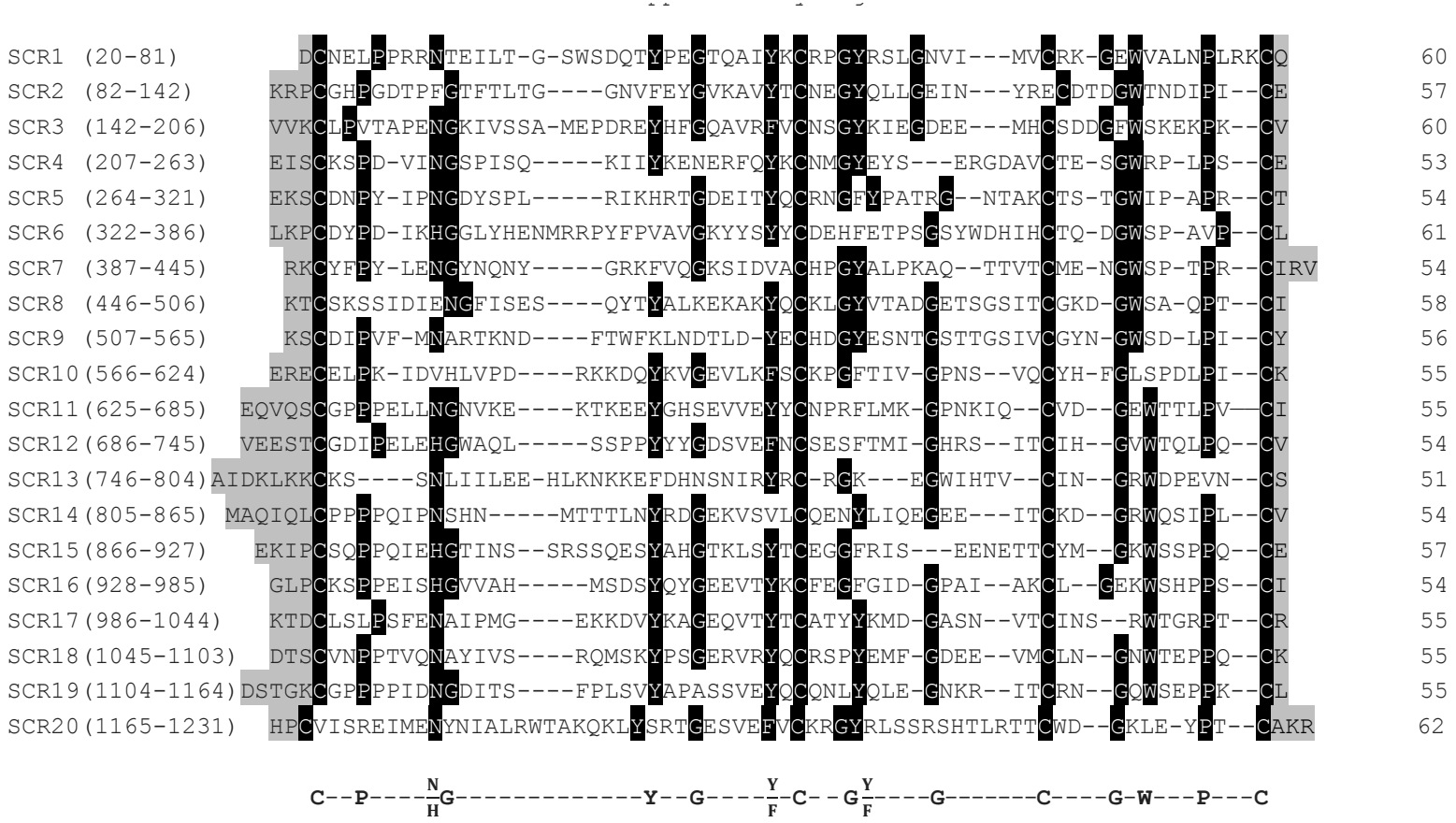
Supplemental Figure 1



Supplemental Figure 2

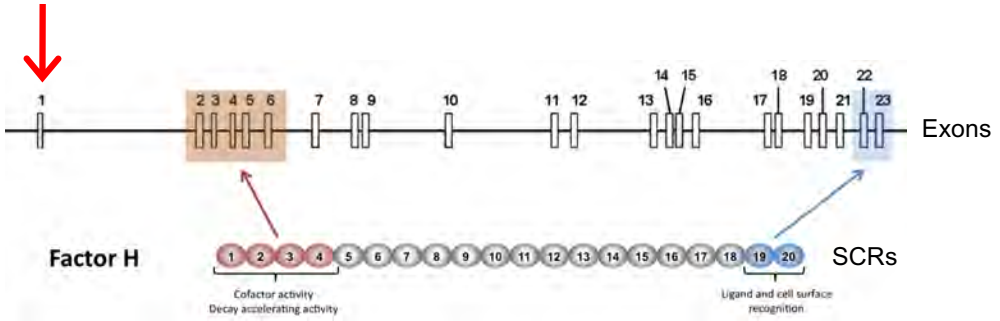


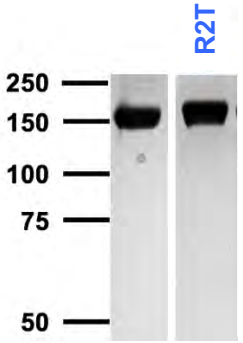
SCR consensus sequence

Individual variant datasheets

c.5G>C (R2T)

CADD: 6.11
gnomAD: $2x10^{-5}$





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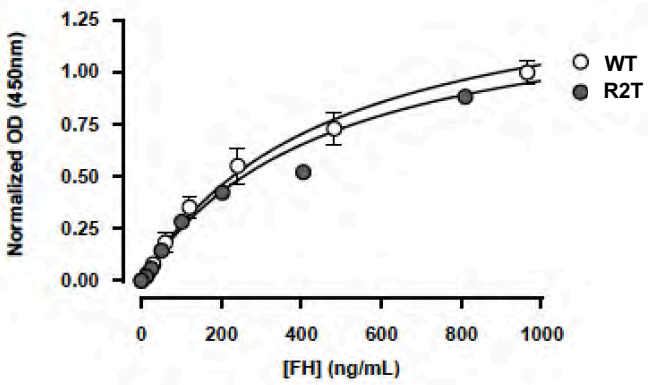
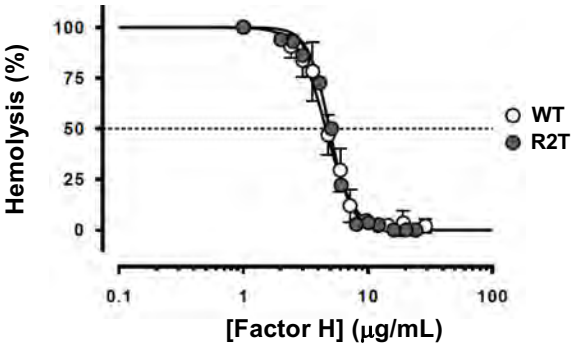


Binding to C3b

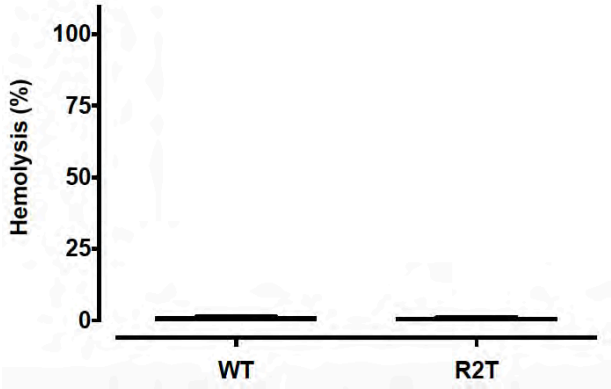


Hemolytic assay

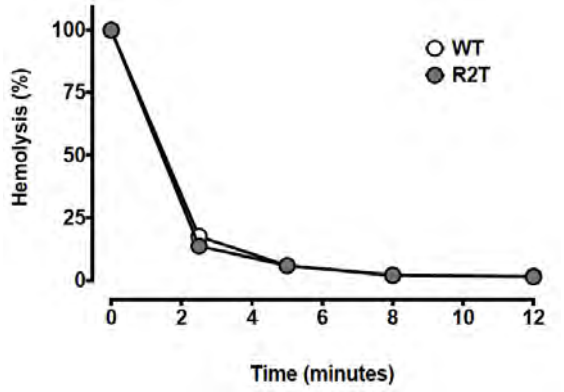
Conclusion: Normal Function
BENIGN

Previous studies: None

Comments:
Variant in the signal peptide. The electrophoretic mobility is similar to the wild type control and therefore this mutation does not appear to have interfered with normal signal peptide processing or secretion.



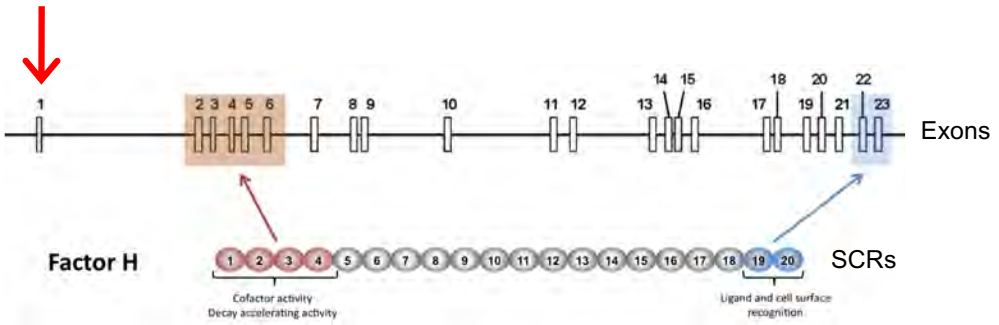
Cofactor activity

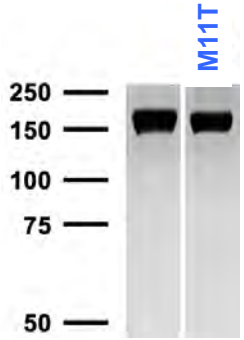


Decay-accelerating activity

c.32T>C (M11T)

CADD: 15.48
gnomAD: Not Present





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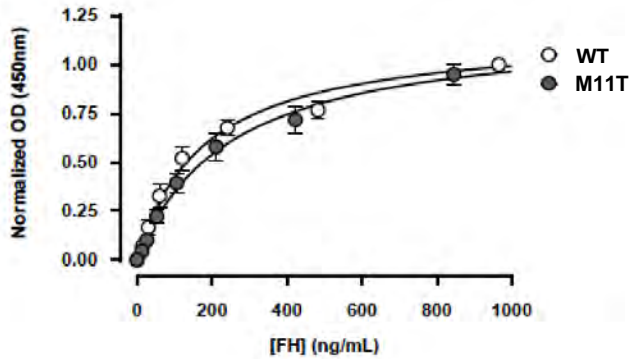
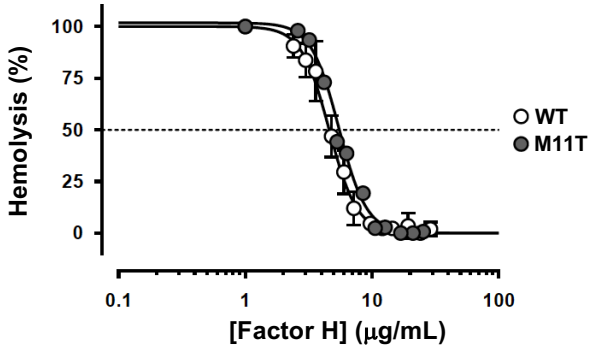


Binding to C3b

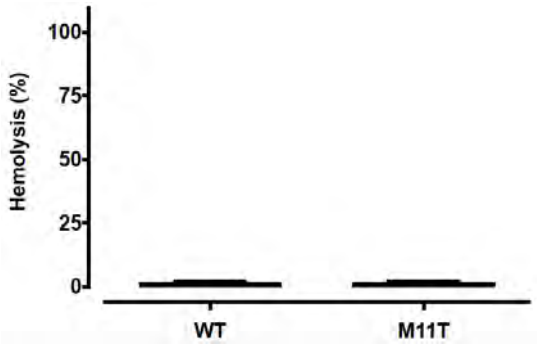


Hemolytic assay

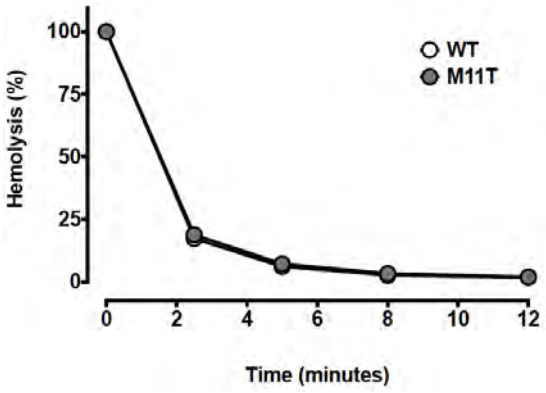
Conclusion: Normal Function
BENIGN

Previous studies: None

Comments:
Variant in the signal peptide. The electrophoretic mobility is similar to the wild type control and therefore this mutation does not appear to have interfered with normal signal peptide processing or secretion.



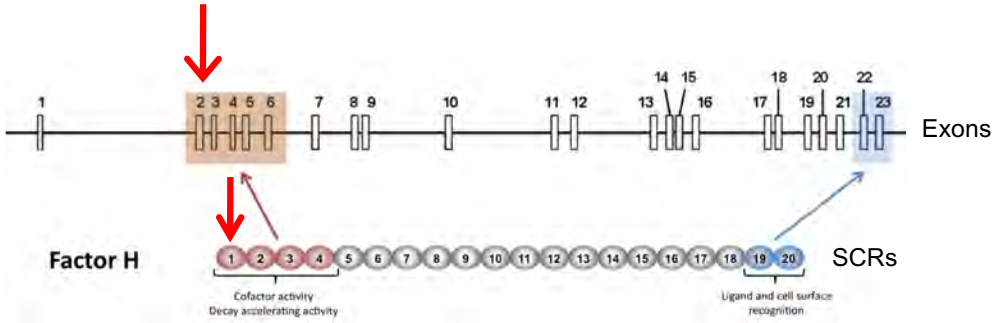
Cofactor activity

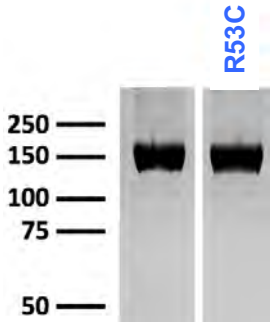


Decay-accelerating activity

c.157C>T (R53C)

CADD: 24.4
gnomAD: $2x10^{-5}$





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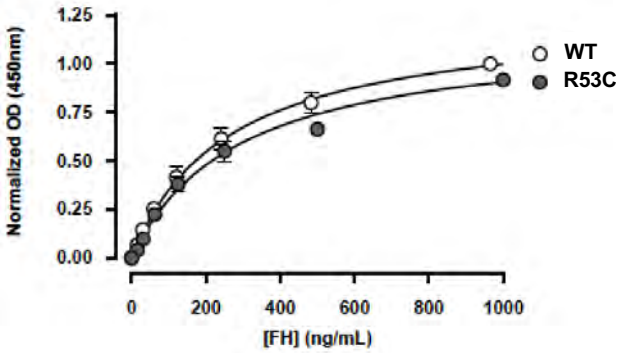
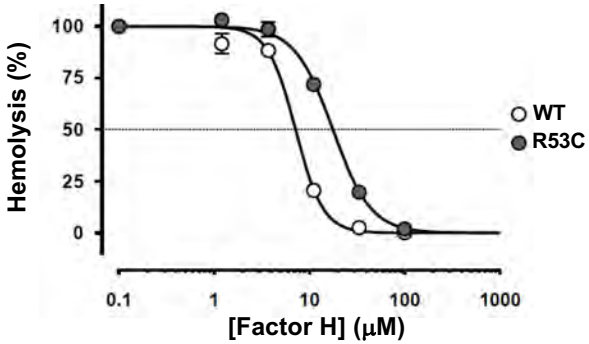
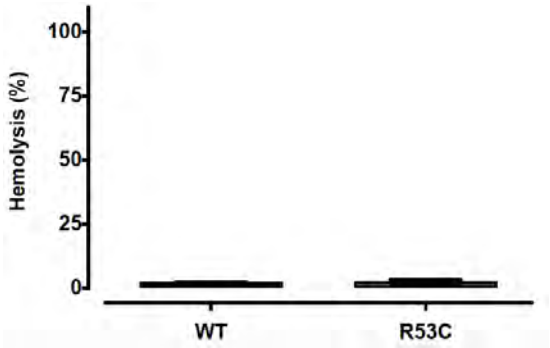


Binding to C3b

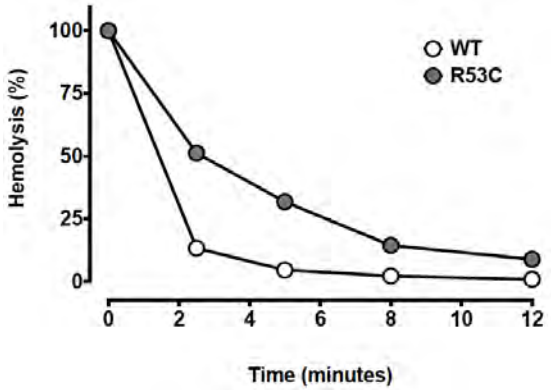


Hemolytic assay

Conclusion: Impaired Function
PATHOGENIC



Cofactor activity



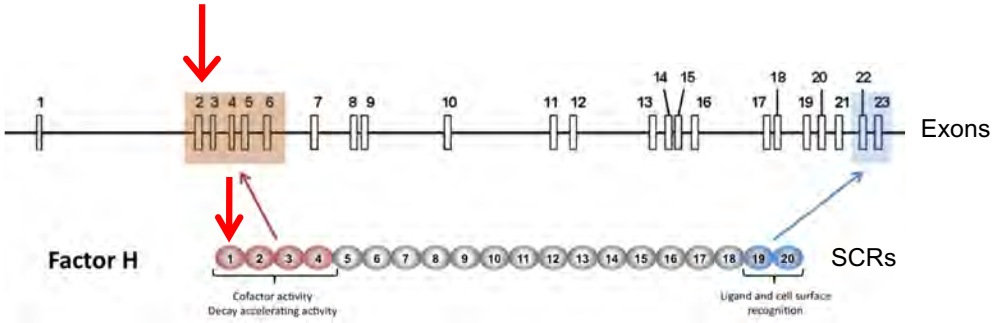
Decay-accelerating activity

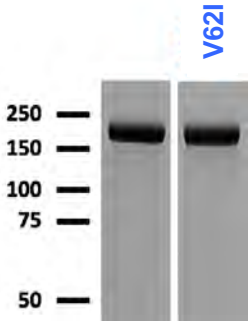
Previous studies: Pathogenic (Merinero HM, García SP, García-Fernández J, Arjona E, Tortajada A, Rodríguez de Córdoba S. Complete functional characterization of disease-associated genetic variants in the complement factor H gene. *Kidney International*. 2018;93(2):470-481).

Comments:

c.184G>A (V62I)

CADD: 7.11
gnomAD: $3x10^{-1}$





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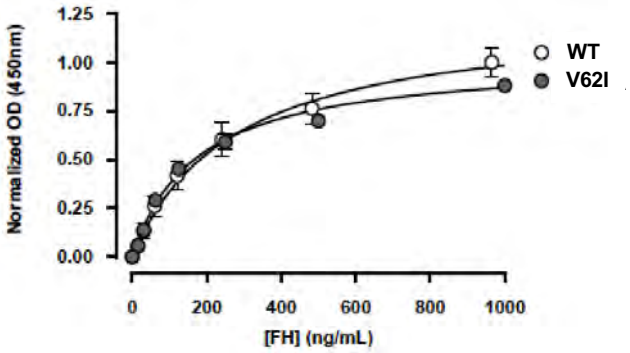
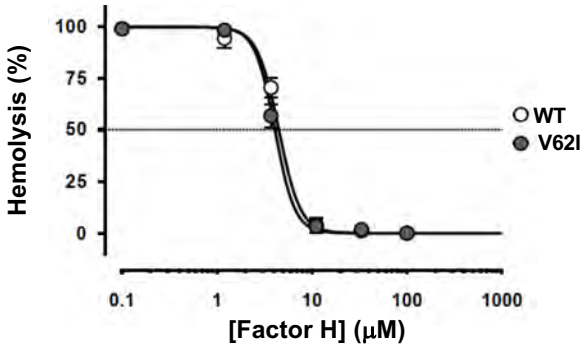
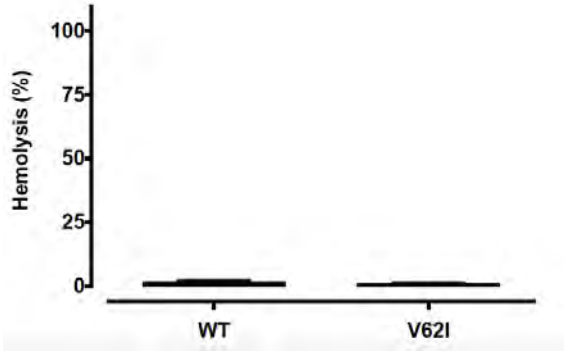


Binding to C3b

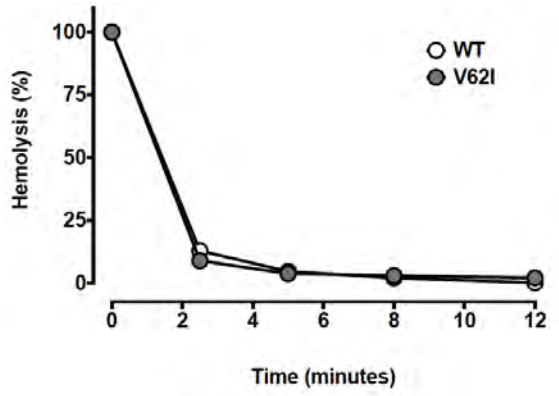


Hemolytic assay

Conclusion: Normal Function
BENIGN



Cofactor activity



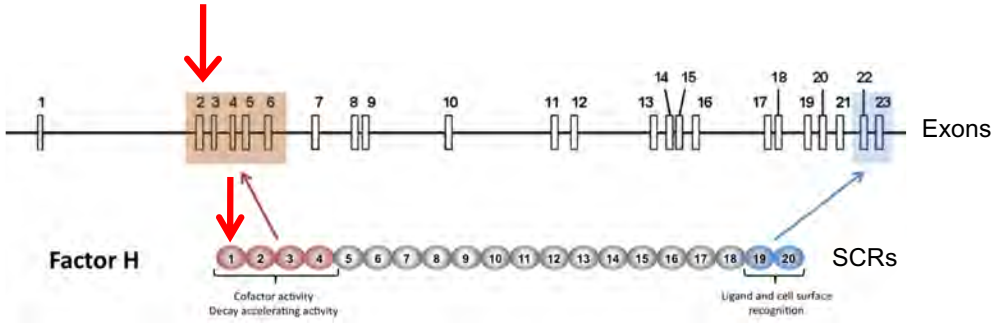
Decay-accelerating activity

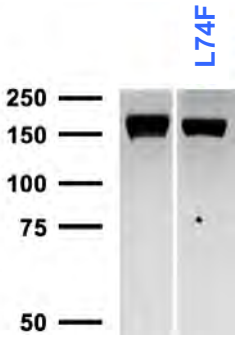
Previous studies: Benign in Tortajada A, Montes T, Martínez-Barricarte R, Morgan BP, Harris CL, de Córdoba SR. The disease-protective complement factor H allotypic variant Ile62 shows increased binding affinity for C3b and enhanced cofactor activity. *Hum Mol Genet*. 2009;18(18):3452-3461.

Comments:

c.220C>T (L74F)

CADD: 13
gnomAD: $4x10^{-6}$





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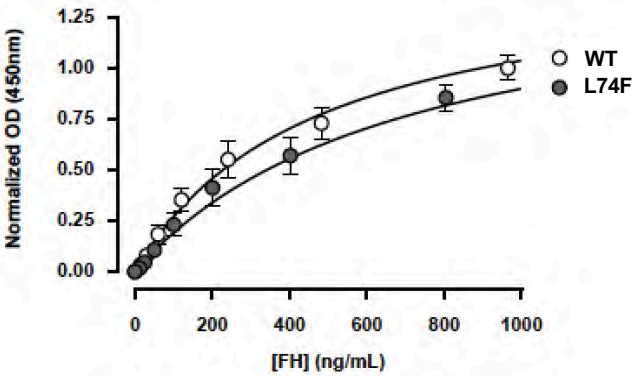
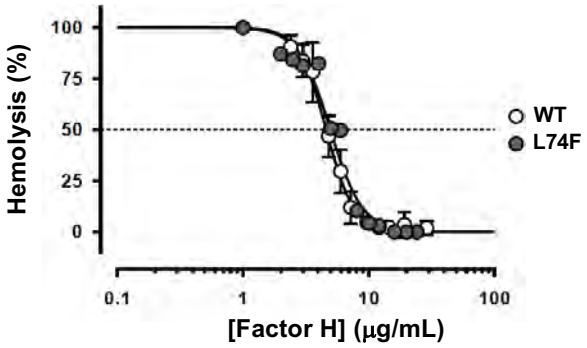


Binding to C3b

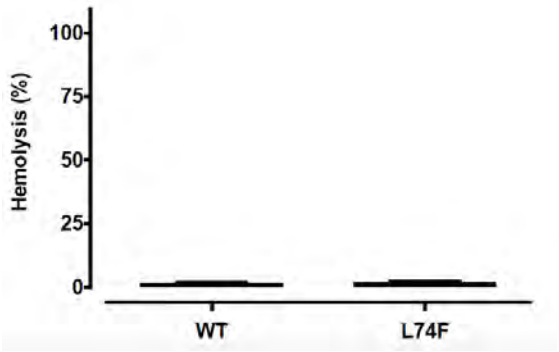


Hemolytic assay

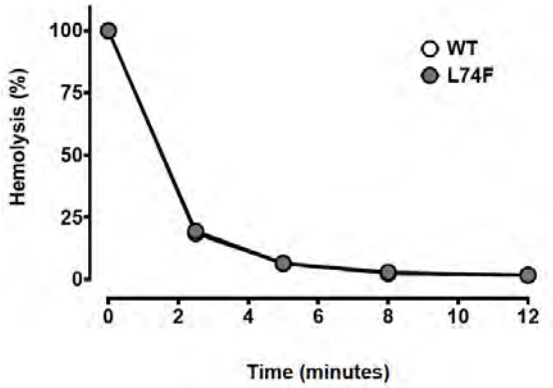
Conclusion: Normal Function
BENIGN

Previous studies: None

Comments:



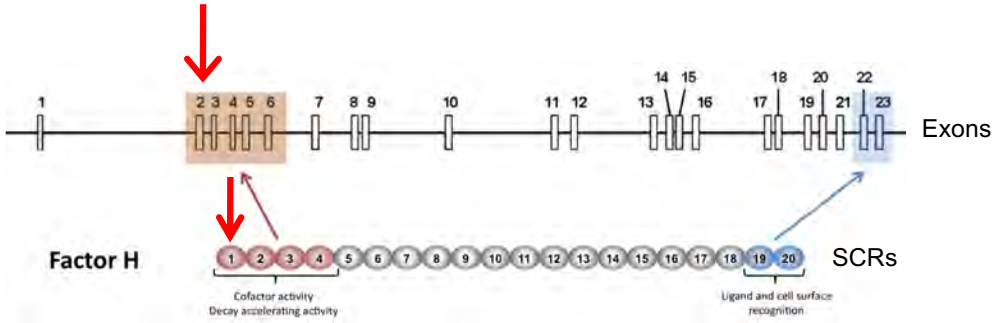
Cofactor activity

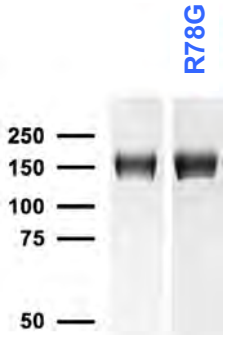


Decay-accelerating activity

c.232A>G (R78G)

CADD: 19.92
gnomAD: Not Present





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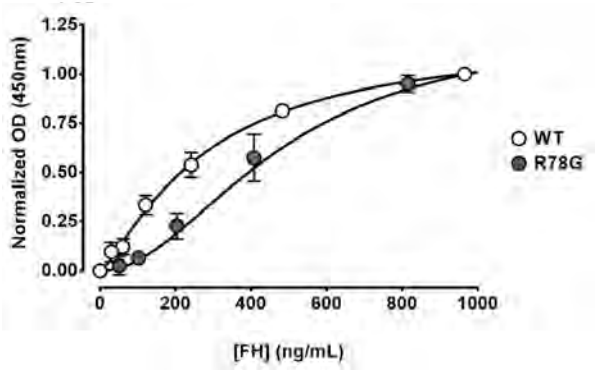
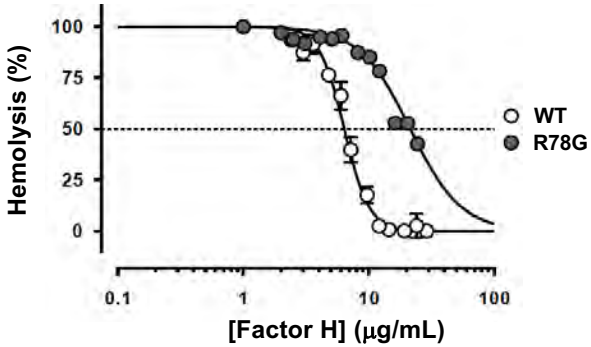
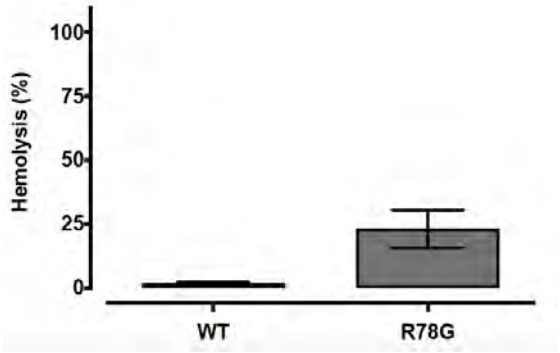


Binding to C3b

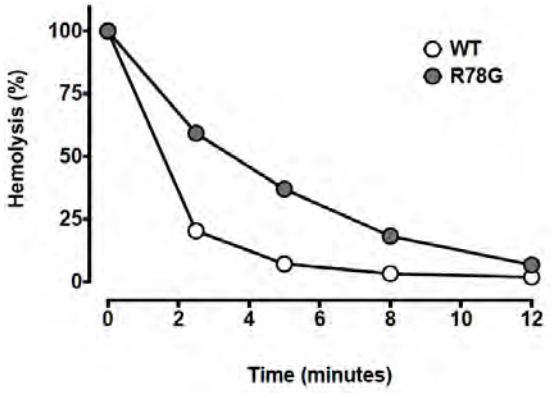


Hemolytic assay

Conclusion: Impaired Function
PATHOGENIC



Cofactor activity



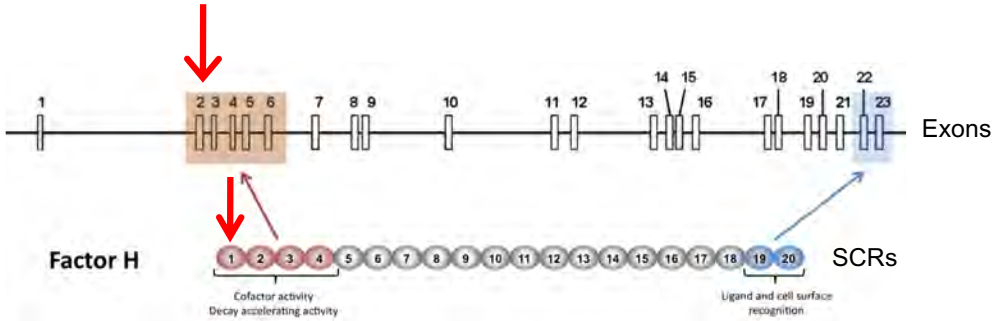
Decay-accelerating activity

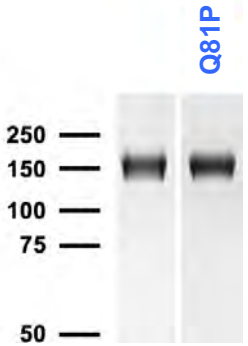
Previous studies: Pathogenic in Pechtl IC, Kavanagh D, McIntosh N, Harris CL, Barlow PN. Disease-associated N-terminal complement factor H mutations perturb cofactor and decay-accelerating activities. *J Biol Chem*. 2011;286(13):11082-11090.

Comments:

c.242A>C (Q81P)

CADD: 22.1
gnomAD: Not present





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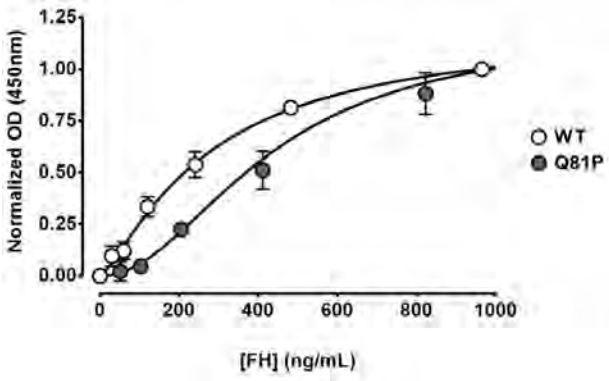
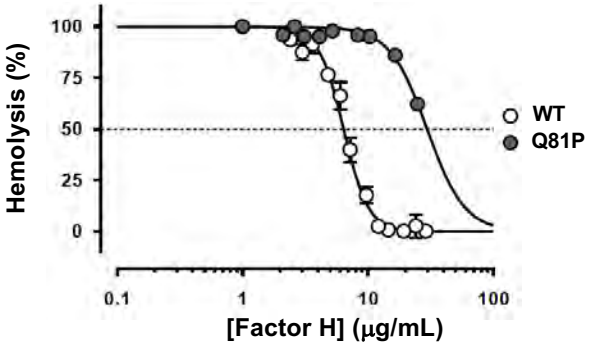


Binding to C3b

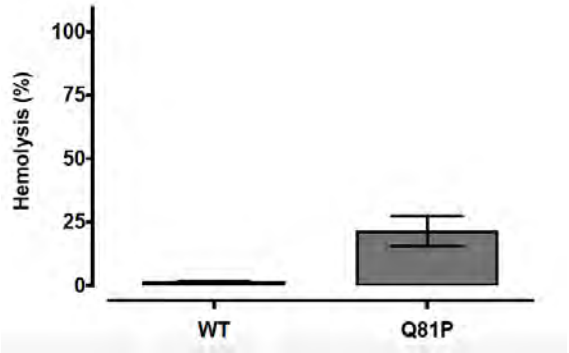


Hemolytic assay

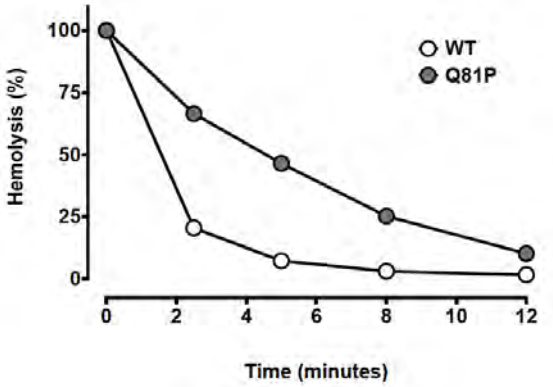
Conclusion: Impaired Function
PATHOGENIC

Previous studies: None

Comments:



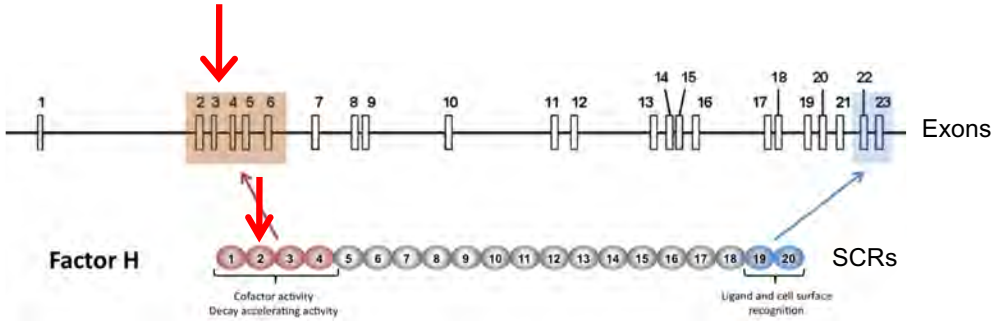
Cofactor activity



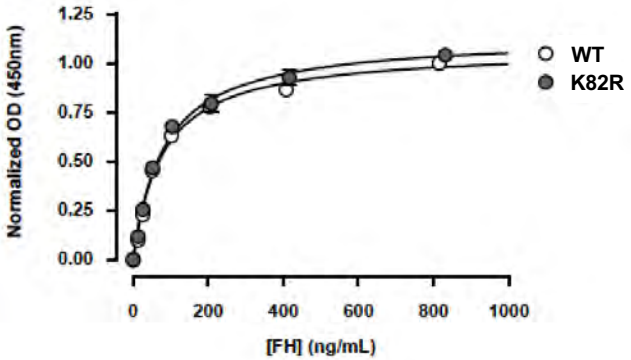
Decay-accelerating activity

c.245A>G (K82R)

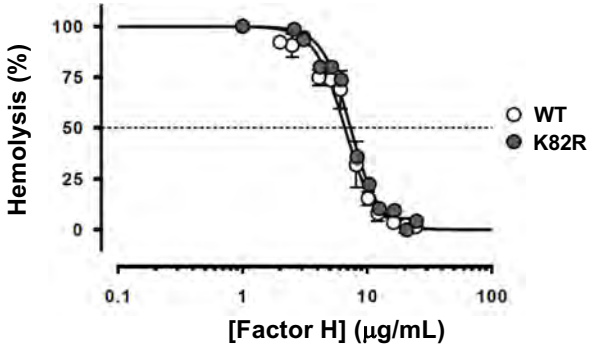
CADD: 22.1
gnomAD: $2x10^{-5}$



SDS-PAGE
(Non-reduced)



Binding to C3b

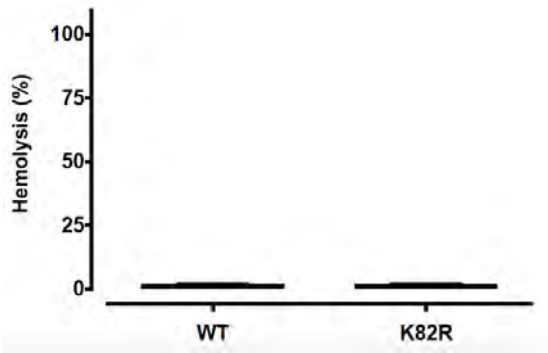


Hemolytic assay

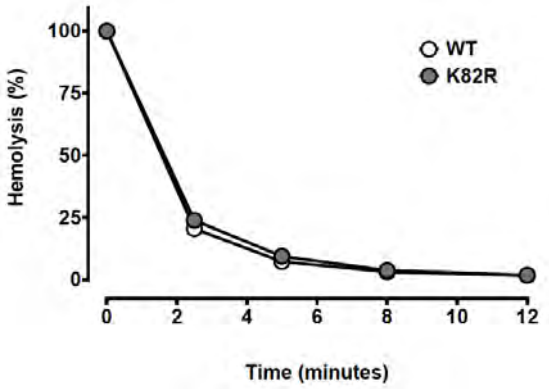
Conclusion: Normal Function
BENIGN

Previous studies: None

Comments:



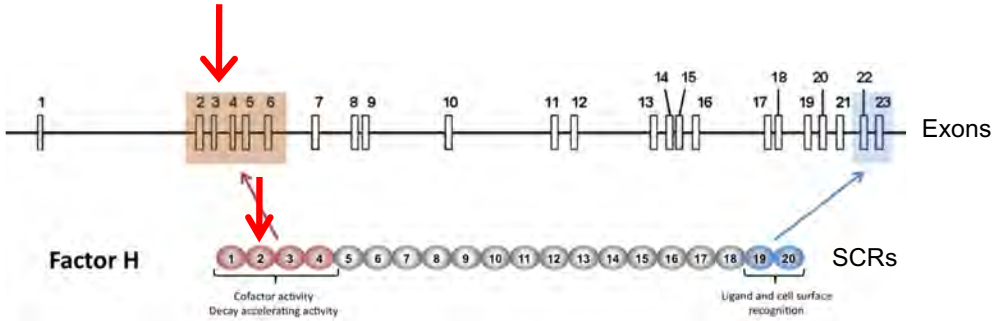
Cofactor activity

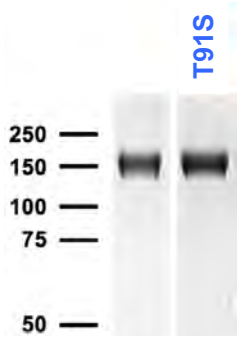


Decay-accelerating activity

c.272C>G (T91S)

CADD: 19.9
gnomAD: $8x10^{-6}$





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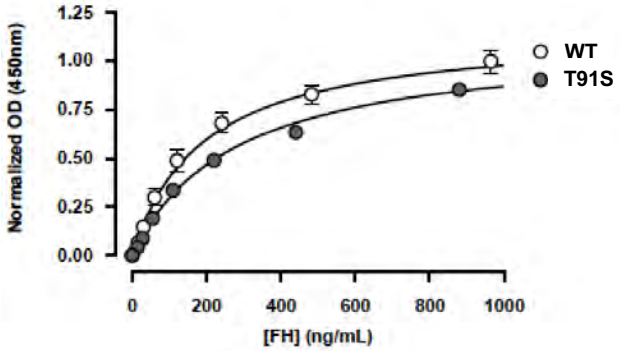
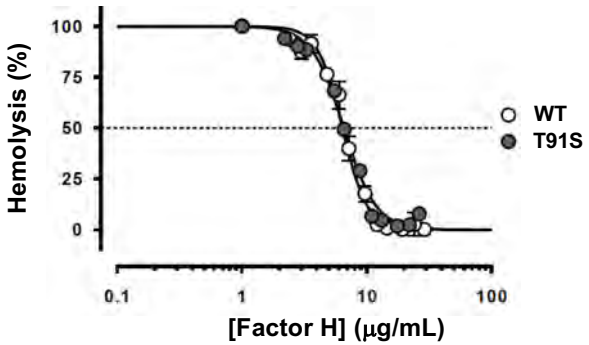
(Non-reduced)



Binding to C3b

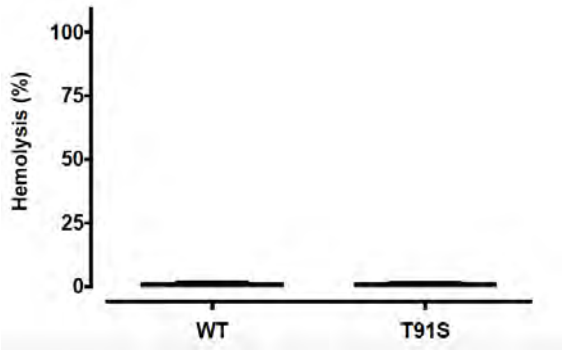


Hemolytic assay

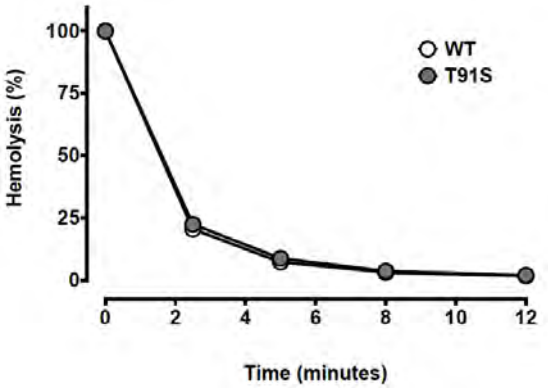
Conclusion: Normal Function
BENIGN

Previous studies: None

Comments:



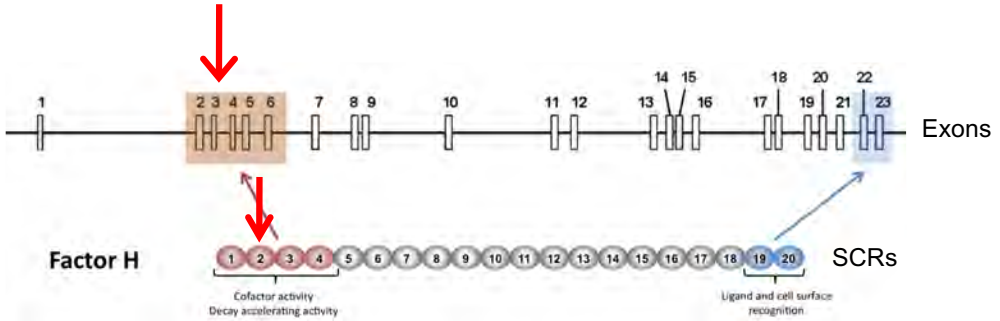
Cofactor activity



Decay-accelerating activity

c.332T>A (V111E)

CADD: 26.3
gnomAD: $1x10^{-4}$



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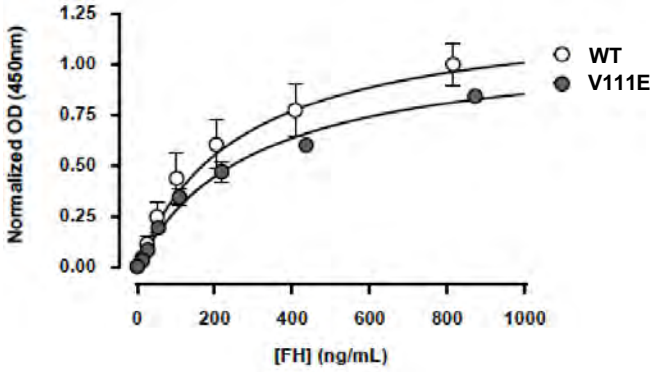
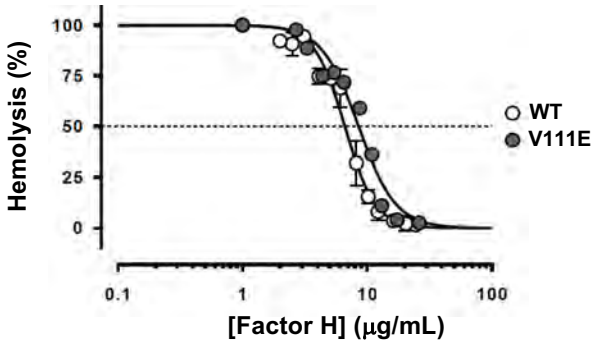
(Non-reduced)



Binding to C3b

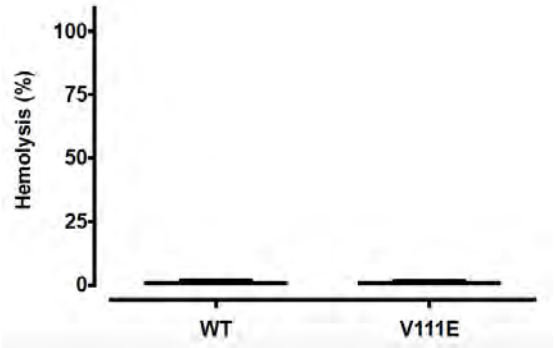


Hemolytic assay

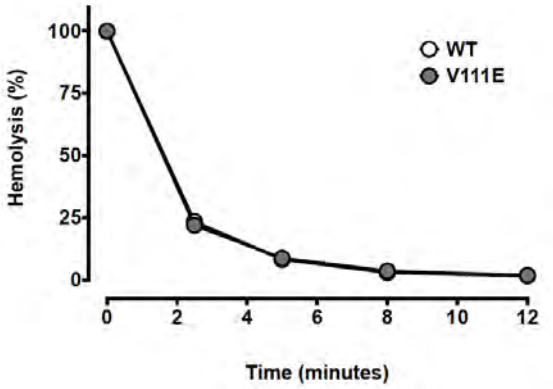
Conclusion: Normal Function
BENIGN

Previous studies: None

Comments:



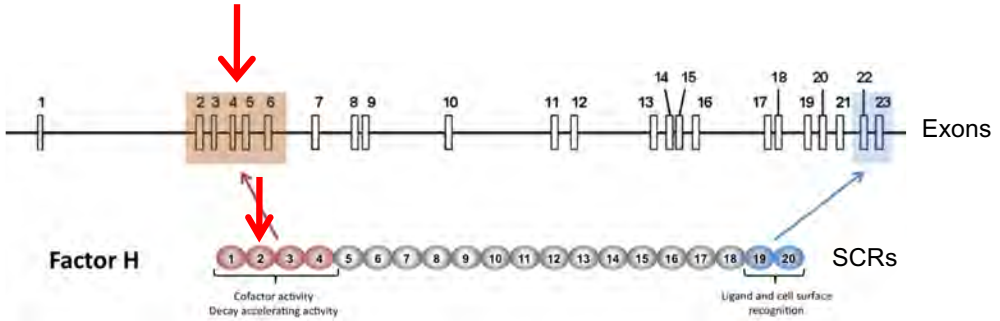
Cofactor activity

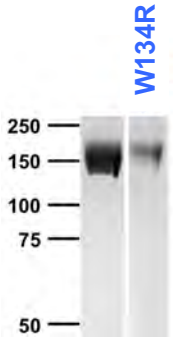


Decay-accelerating activity

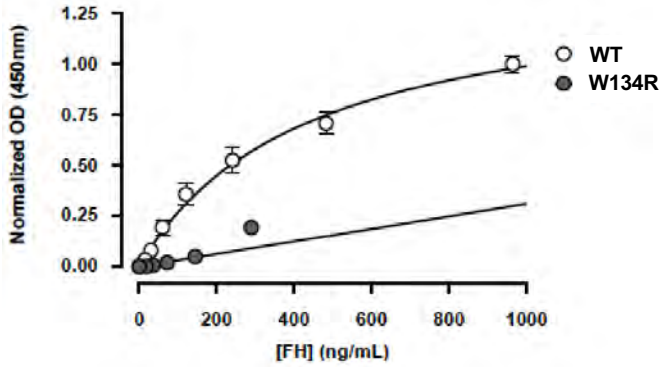
c.400T>C (W134R)

CADD: 27.2
gnomAD: Not present

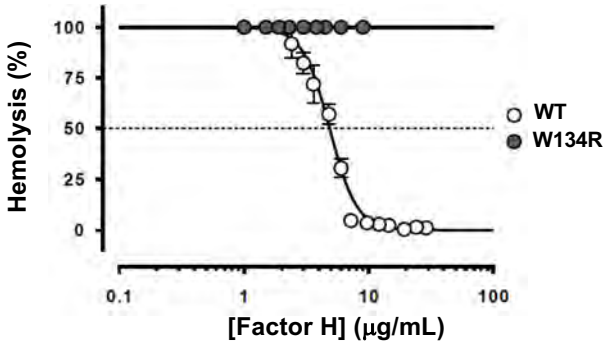




SDS-PAGE
(Non-reduced)



Binding to C3b

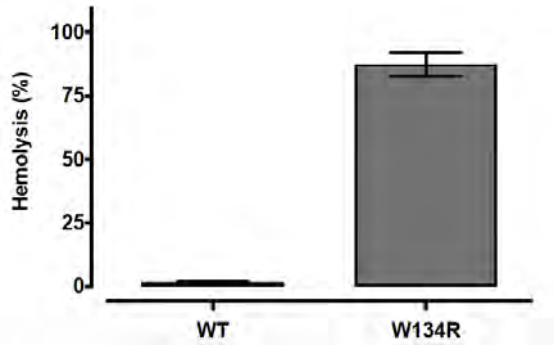


Hemolytic assay

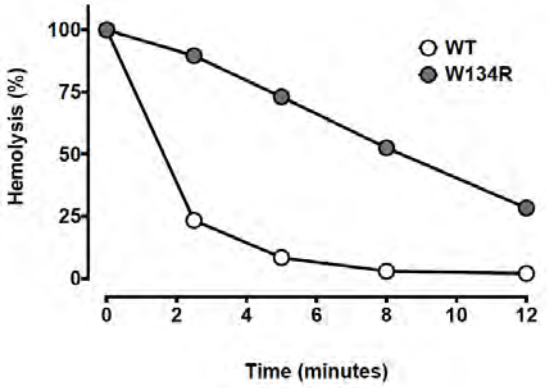
Conclusion: Impaired Expression
PATHOGENIC

Previous studies: None

Comments:
SDS-PAGE shows a weak FH band under non-reducing conditions, suggesting that this variant likely affects expression of the protein and results in a factor H deficiency
.



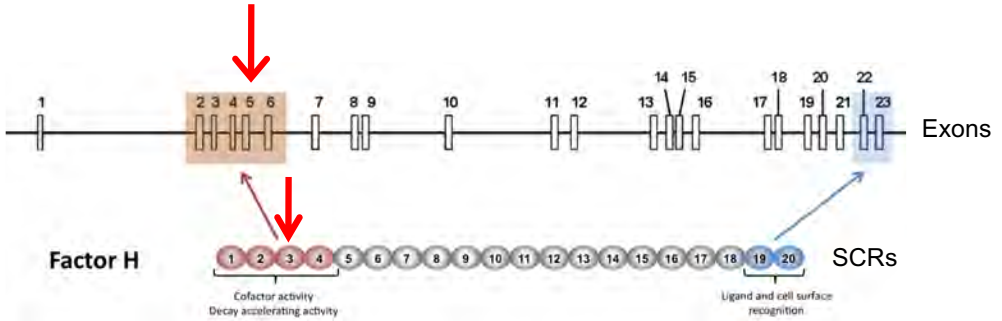
Cofactor activity



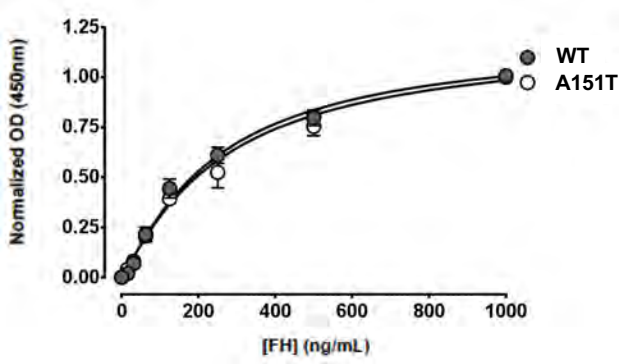
Decay-accelerating activity

c.451G>A (A151T)

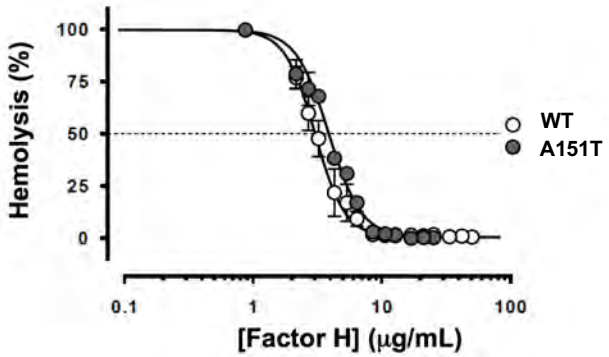
CADD: 3.28
gnomAD: $1x10^{-6}$



SDS-PAGE
(Non-reduced)



Binding to C3b

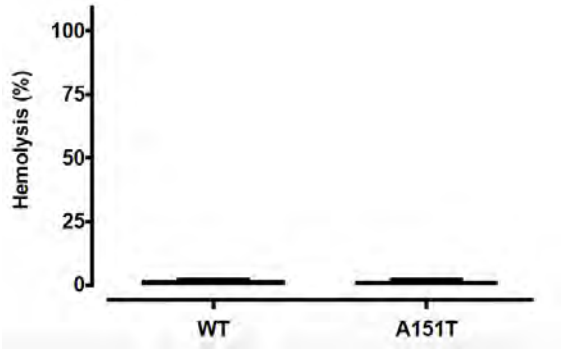


Hemolytic assay

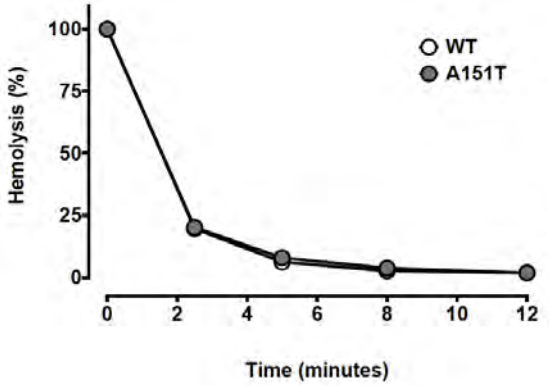
Conclusion: Normal Function
BENIGN

Previous studies: None

Comments:



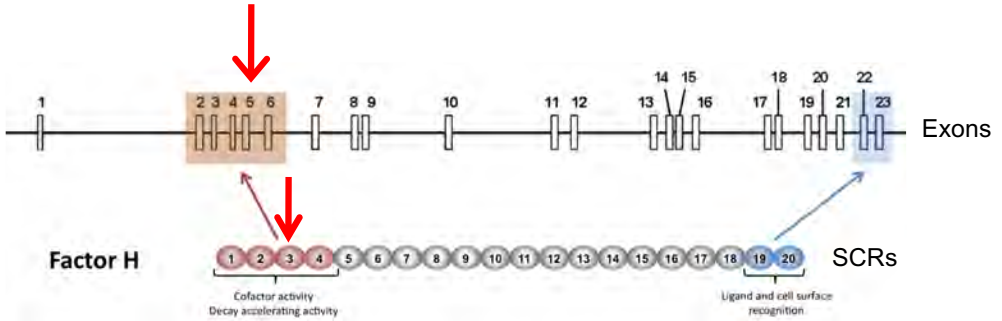
Cofactor activity



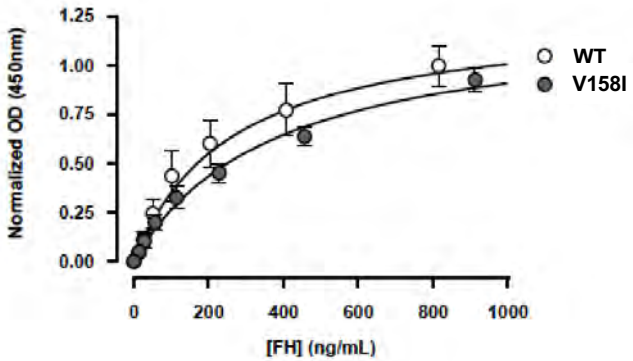
Decay-accelerating activity

c.472G>A (V158I)

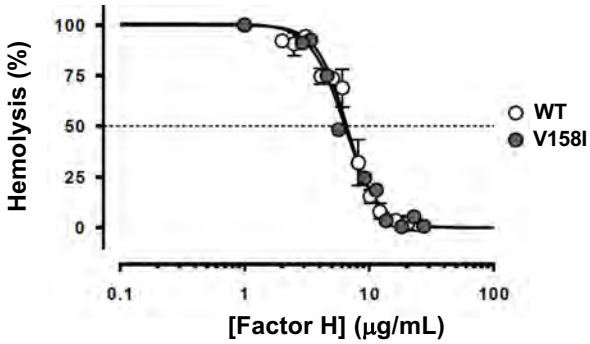
CADD: 0
gnomAD: $1x10^{-4}$



SDS-PAGE
(Non-reduced)



Binding to C3b

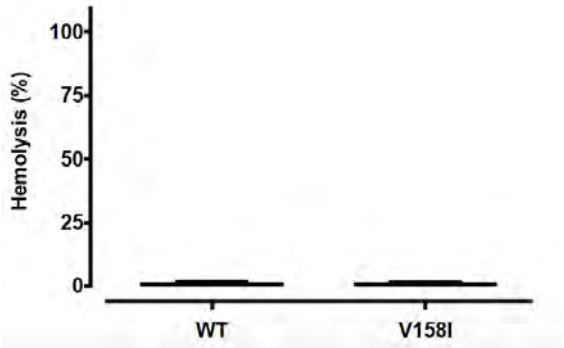


Hemolytic assay

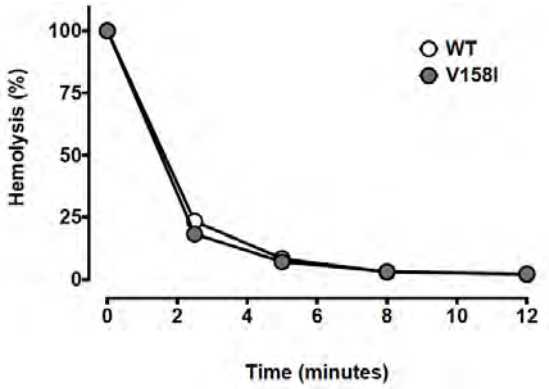
Conclusion: Normal Function
BENIGN

Previous studies: None

Comments:



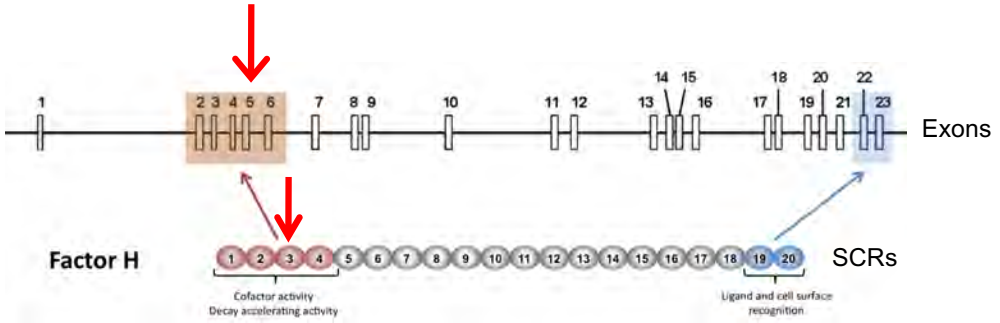
Cofactor activity



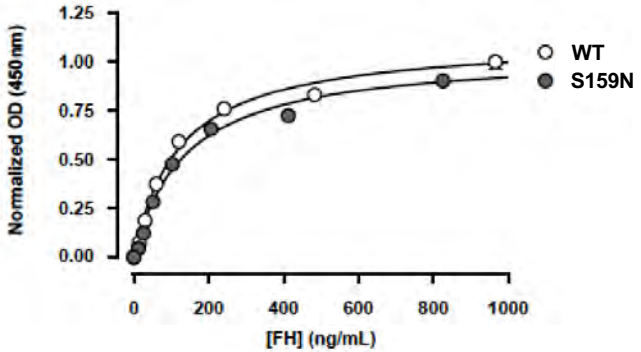
Decay-accelerating activity

c.476G>A (S159N)

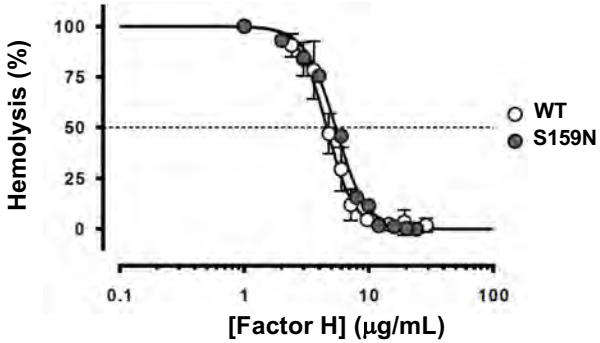
CADD: 16.65
gnomAD: $4x10^{-5}$



SDS-PAGE
(Non-reduced)



Binding to C3b

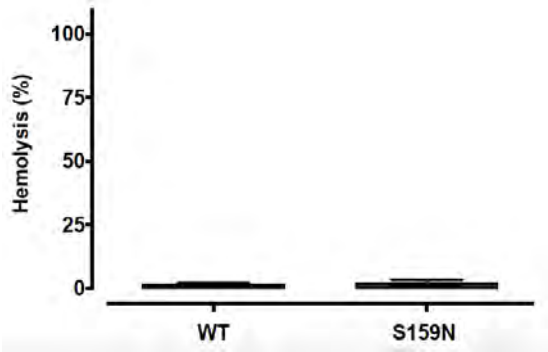


Hemolytic assay

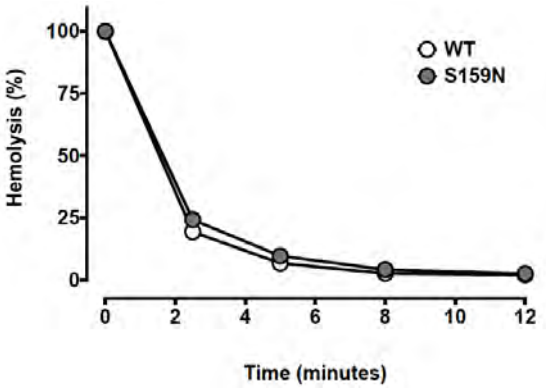
Conclusion: Normal Function
BENIGN

Previous studies: None

Comments:



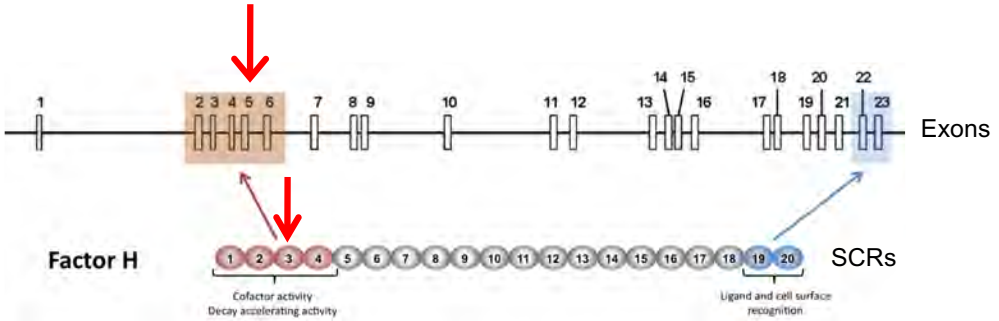
Cofactor activity



Decay-accelerating activity

c.481G>T (A161S)

CADD: 11.9
gnomAD: $9x10^{-5}$



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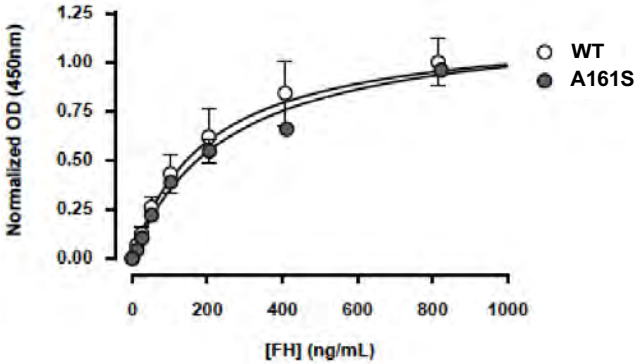
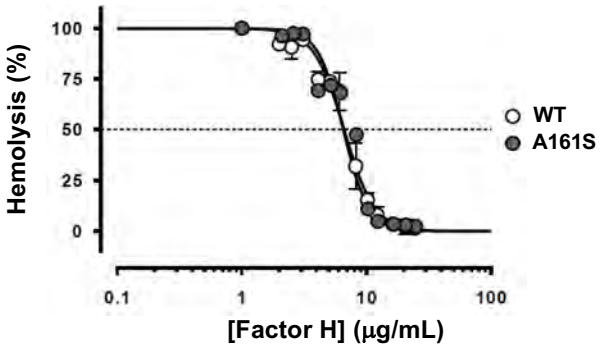


Binding to C3b

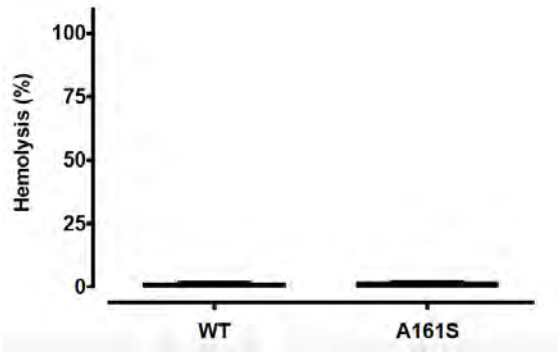


Hemolytic assay

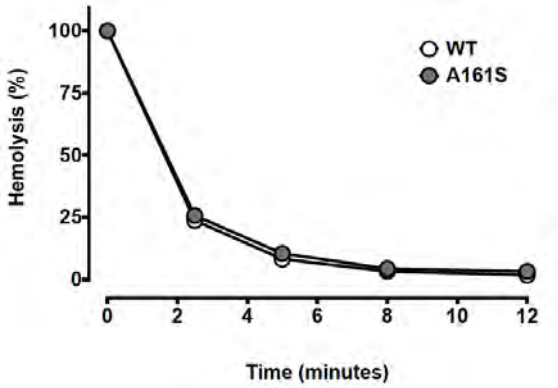
Conclusion: Normal Function
BENIGN

Previous studies: None

Comments:



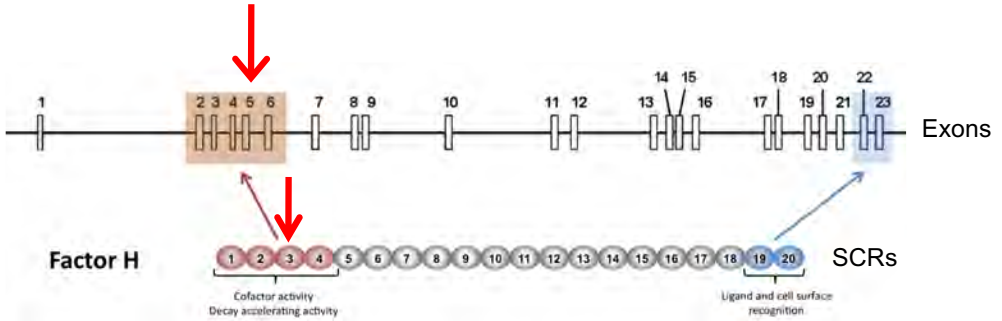
Cofactor activity

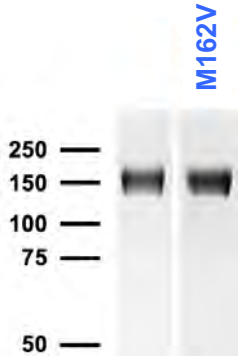


Decay-accelerating activity

c.484A>G (M162V)

CADD: 0
gnomAD: $3x10^{-5}$





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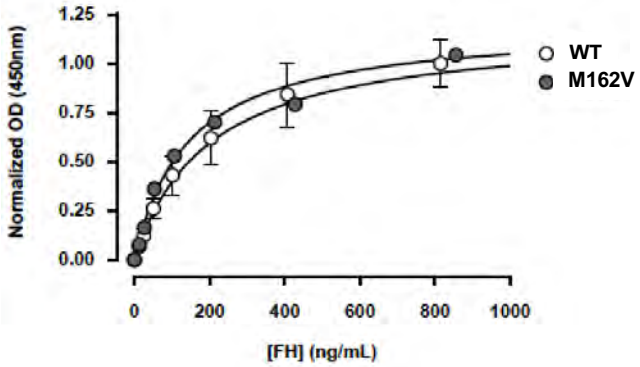
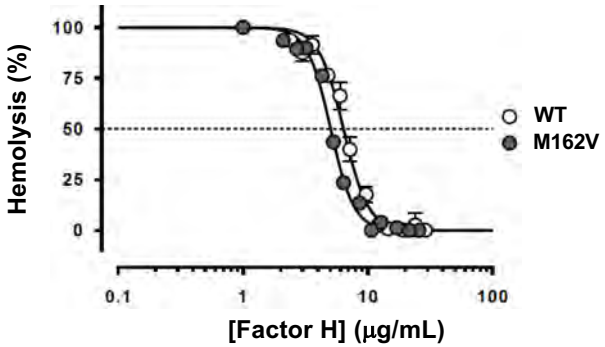
(Non-reduced)



Binding to C3b

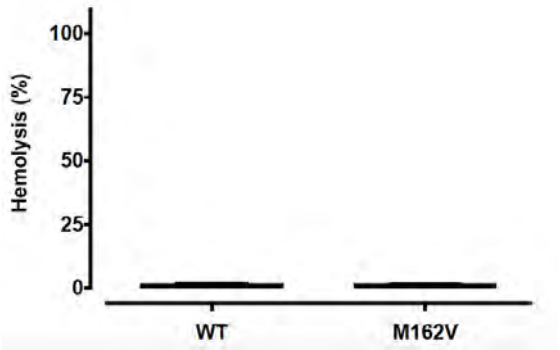


Hemolytic assay

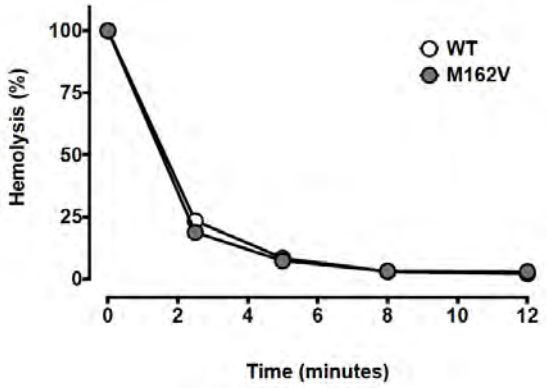
Conclusion: Normal Function
BENIGN

Previous studies: None

Comments:



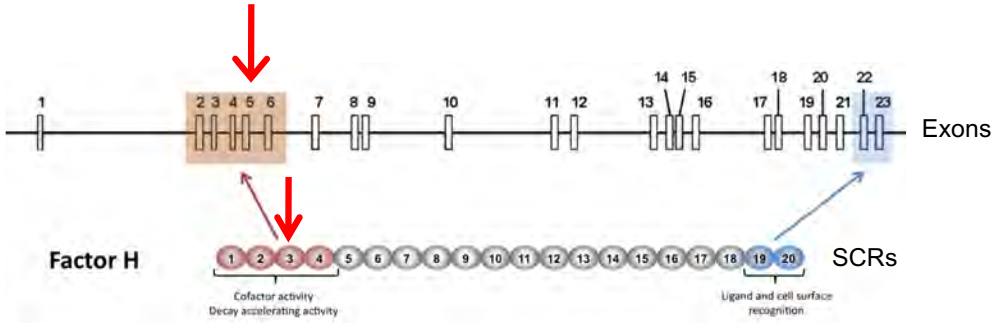
Cofactor activity



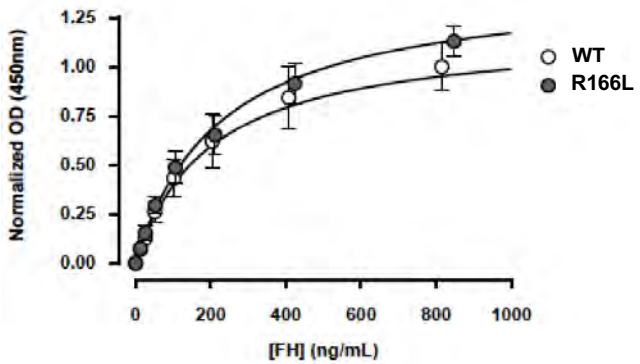
Decay-accelerating activity

c.497G>T (R166L)

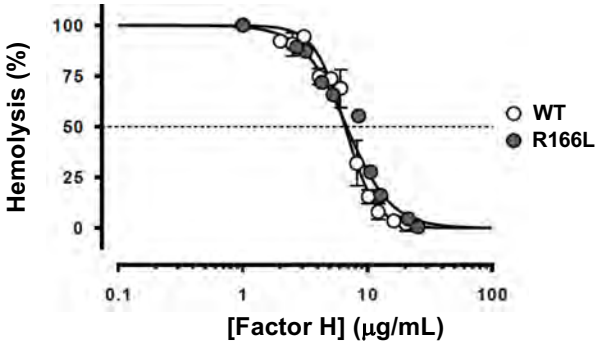
CADD: 17.01
gnomAD: $7x10^{-6}$



SDS-PAGE
(Non-reduced)



Binding to C3b

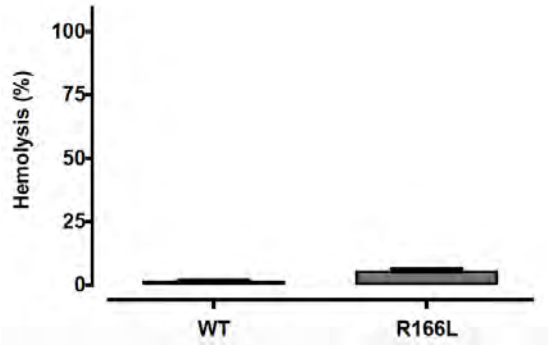


Hemolytic assay

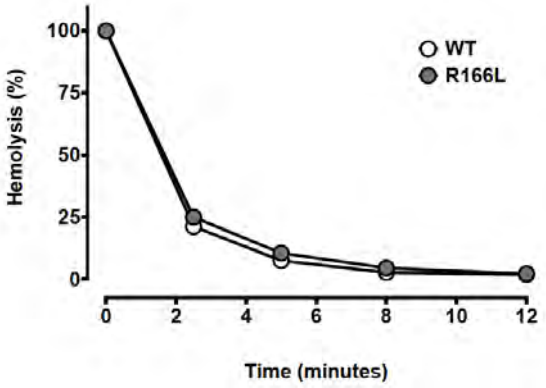
Conclusion: Impaired Expression
PATHOGENIC

Previous studies: None

Comments:



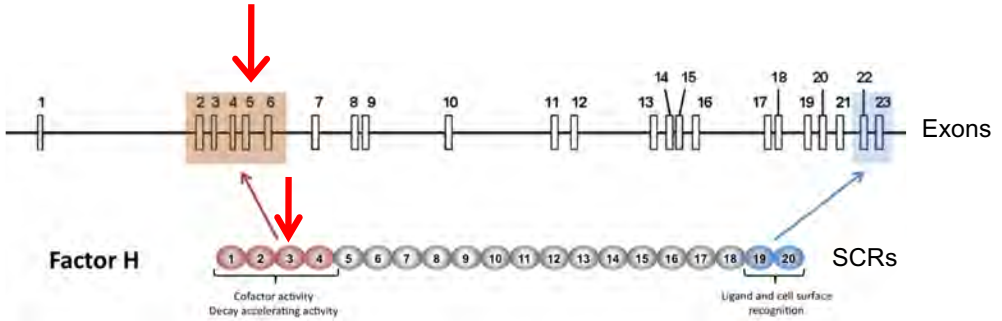
Cofactor activity

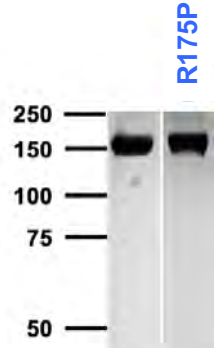


Decay-accelerating activity

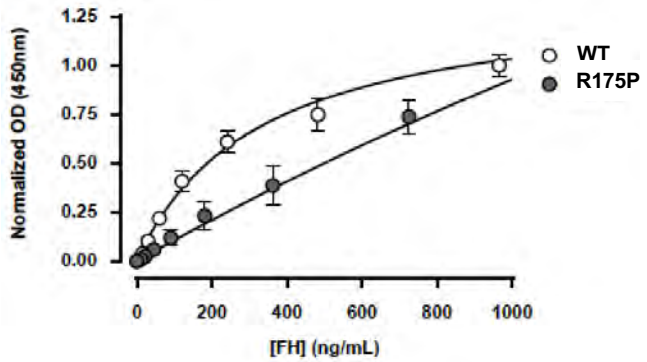
c.524G>C (R175P)

CADD: 7.15
gnomAD: $4x10^{-6}$

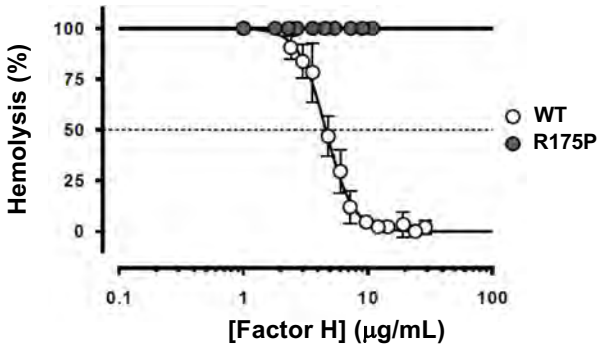




SDS-PAGE
(Non-reduced)



Binding to C3b

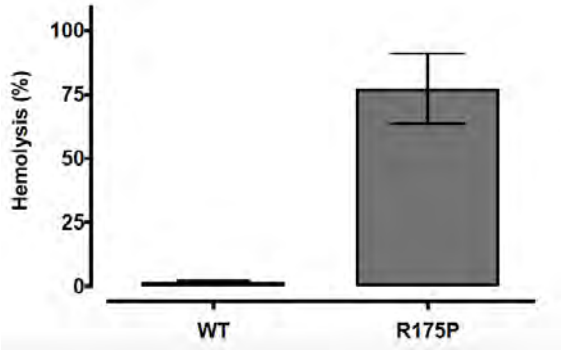


Hemolytic assay

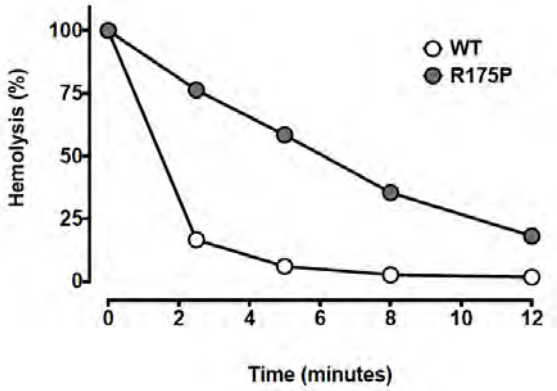
Conclusion: Impaired Function
PATHOGENIC

Previous studies: Pathogenic in Wagner EK, Raychaudhuri S, Villalonga MB, et al. Mapping rare, deleterious mutations in Factor H: Association with early onset, drusen burden and lower antigenic levels in familial AMD. *Scientific Reports*. 2016;6(1):31531.

Comments:



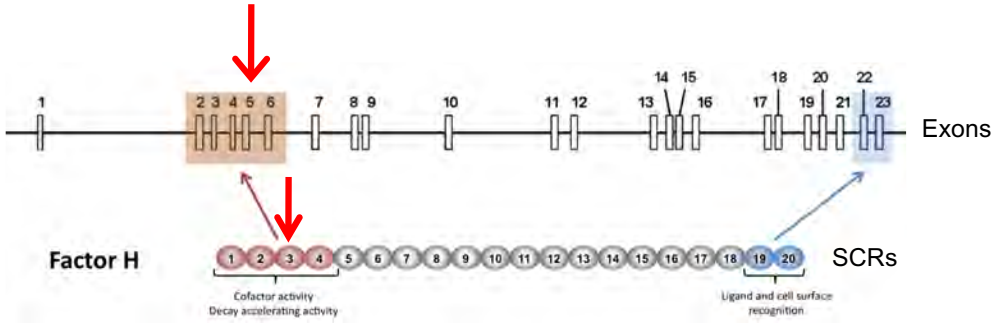
Cofactor activity

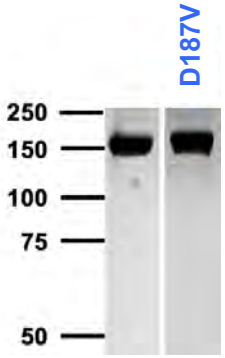


Decay-accelerating activity

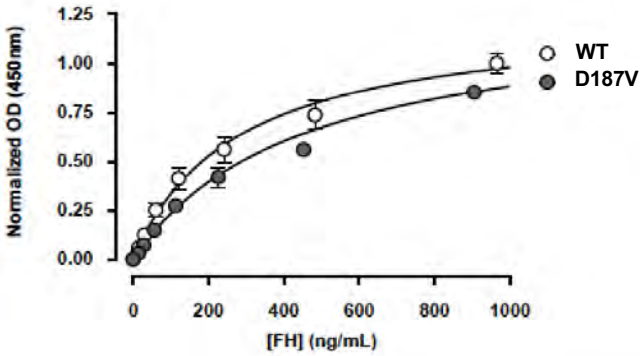
c.560A>T (D187V)

CADD: 17.14
gnomAD: Not present

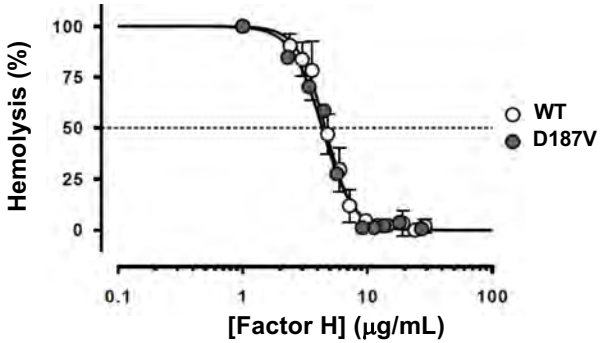




SDS-PAGE
(Non-reduced)



Binding to C3b

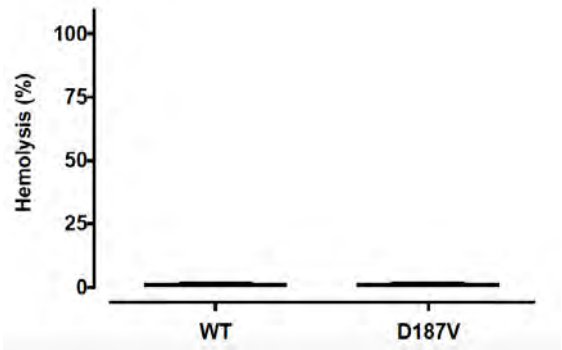


Hemolytic assay

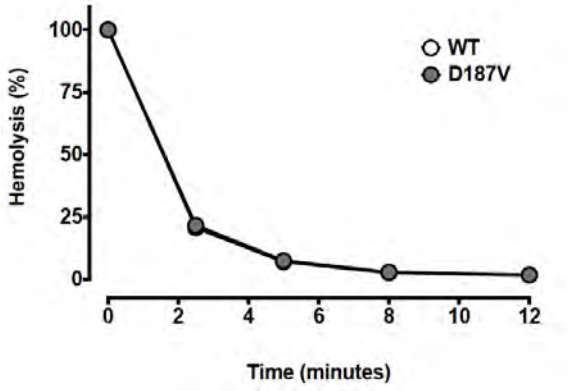
Conclusion: Normal Function
BENIGN

Previous studies: None

Comments:



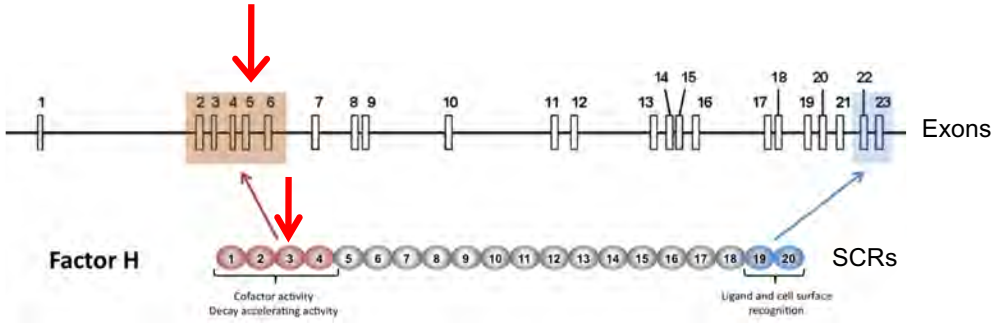
Cofactor activity

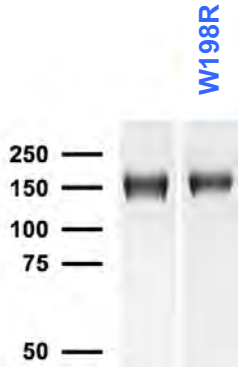


Decay-accelerating activity

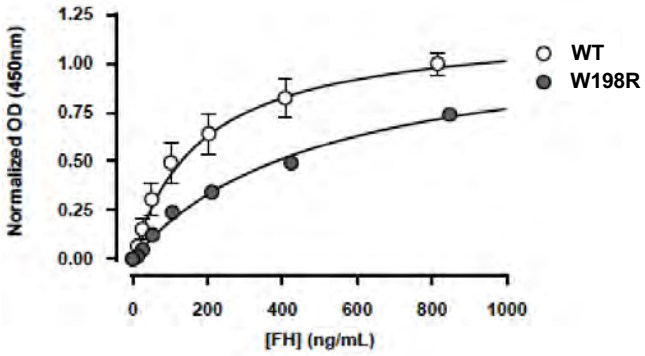
c.592T>C (W198R)

CADD: 24.2
gnomAD: Not present

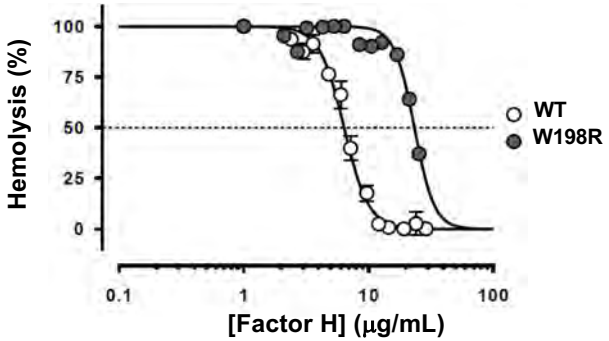




SDS-PAGE
(Non-reduced)

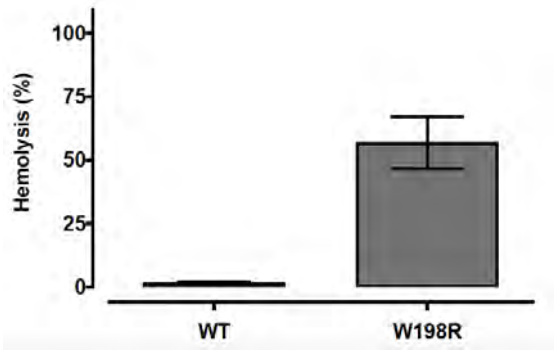


Binding to C3b

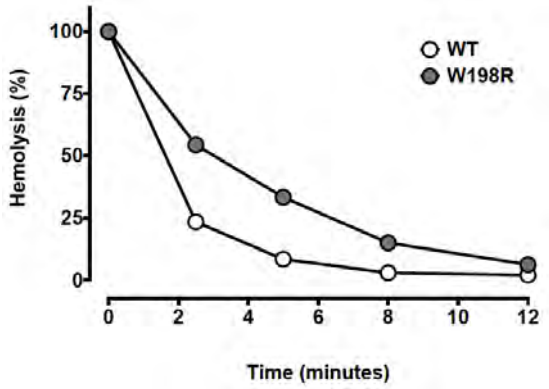


Hemolytic assay

Conclusion: Impaired Expression
PATHOGENIC



Cofactor activity



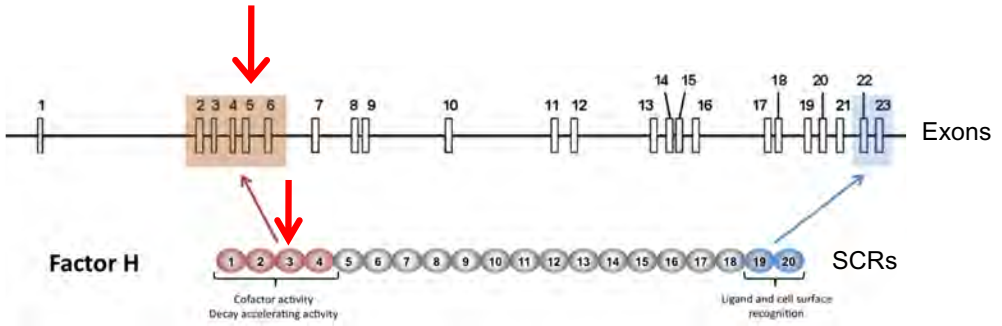
Decay-accelerating activity

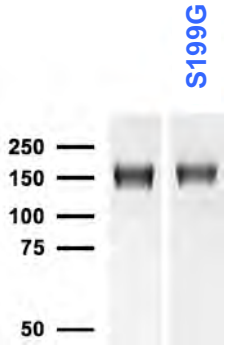
Previous studies: Non expressed in Szarvas N, Szilágyi Á, Csuka D, et al. Genetic analysis and functional characterization of novel mutations in a series of patients with atypical hemolytic uremic syndrome. *Mol Immunol*. 2016;71:10-22.

Comments:
SDS-PAGE shows a FH band with diminished intensity under non-reducing conditions, suggesting that this variant likely affects expression of the protein and results in a factor H deficiency.

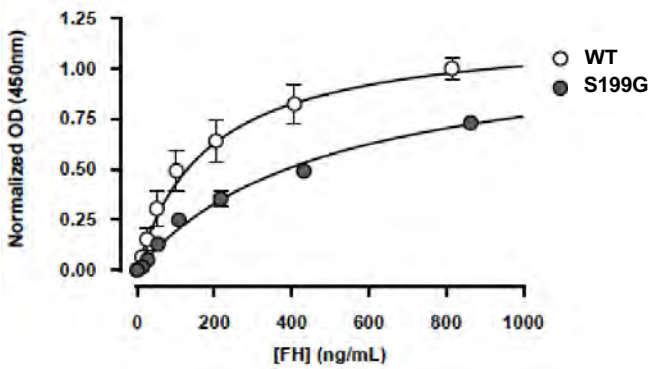
c.595A>G (S199G)

CADD: 24.5
gnomAD: Not present

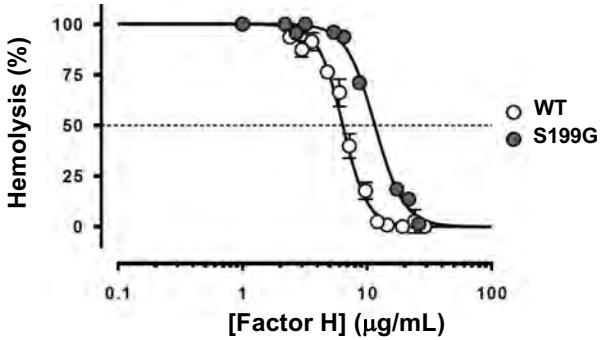




SDS-PAGE
(Non-reduced)



Binding to C3b

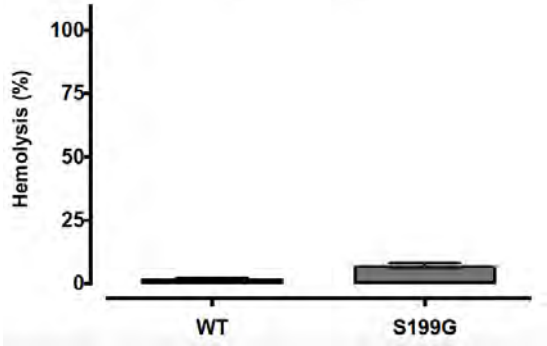


Hemolytic assay

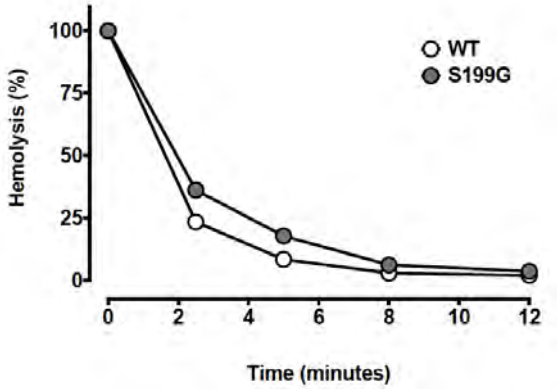
Conclusion: Impaired Expression
PATHOGENIC

Previous studies: None

Comments:
SDS-PAGE shows a FH band with diminished intensity under non-reducing conditions, suggesting that this variant likely affects expression of the protein and results in a factor H deficiency.



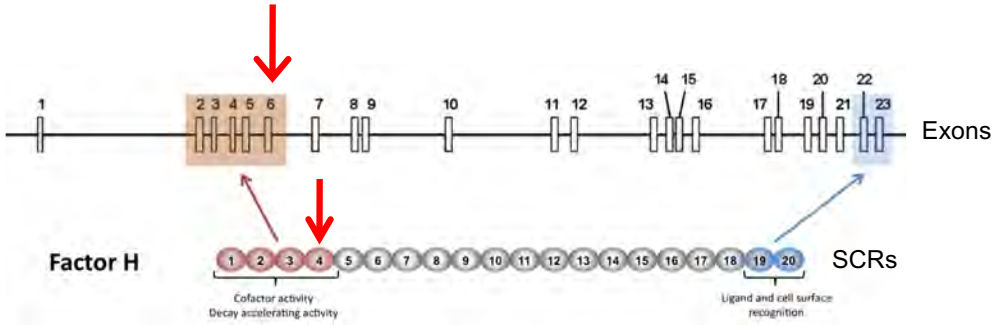
Cofactor activity



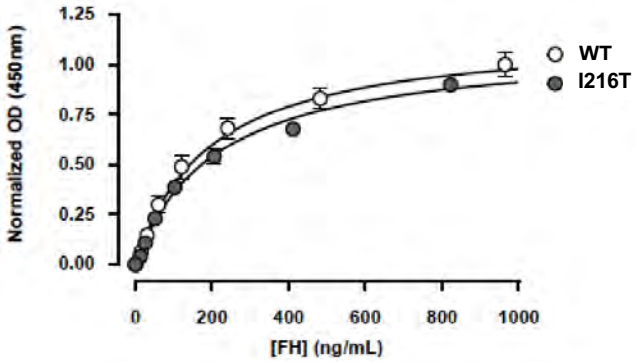
Decay-accelerating activity

c.647T>C (I216T)

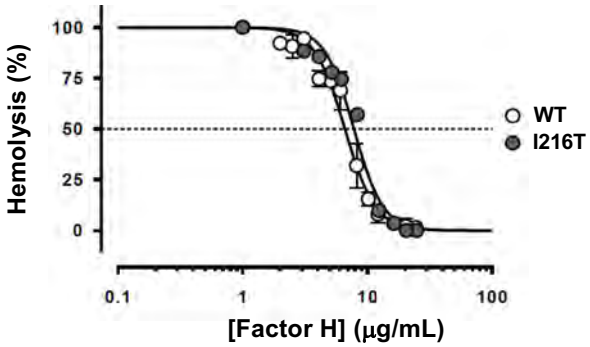
CADD: 0
gnomAD: $1x10^{-4}$



SDS-PAGE
(Non-reduced)



Binding to C3b

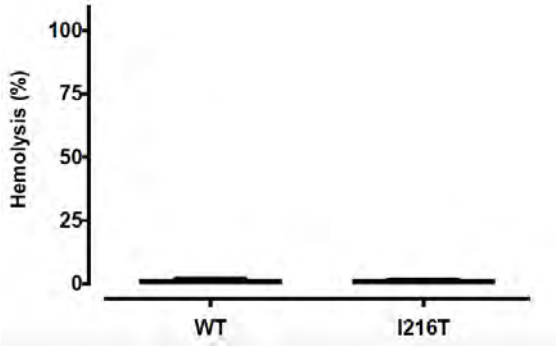


Hemolytic assay

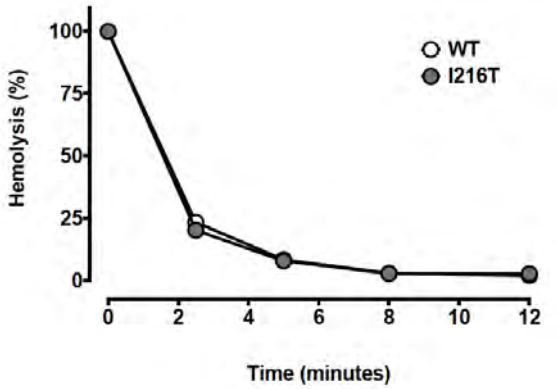
Conclusion: Normal Function
BENIGN

Previous studies: None

Comments:



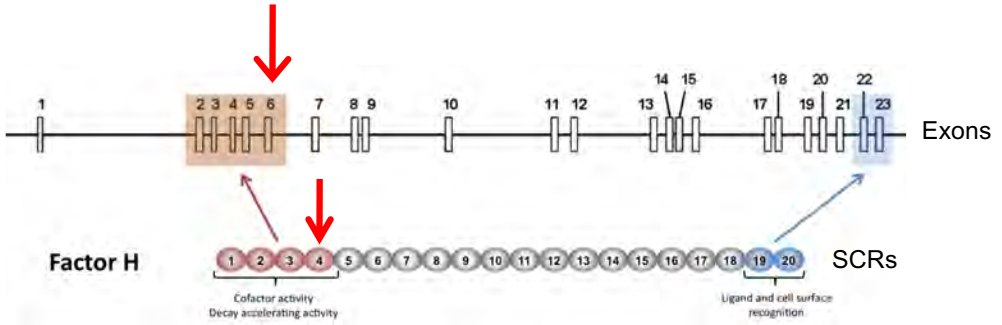
Cofactor activity

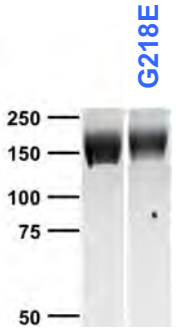


Decay-accelerating activity

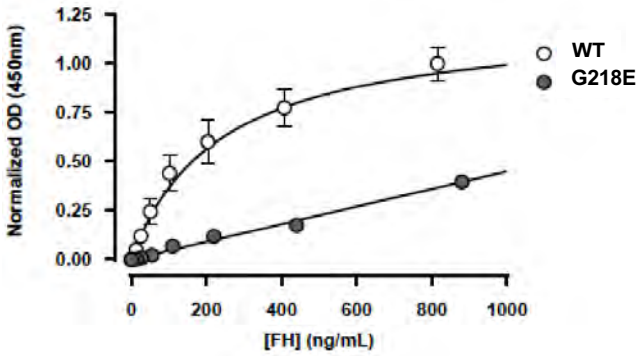
c.653G>A (G218E)

CADD: 24.7
gnomAD: Not present

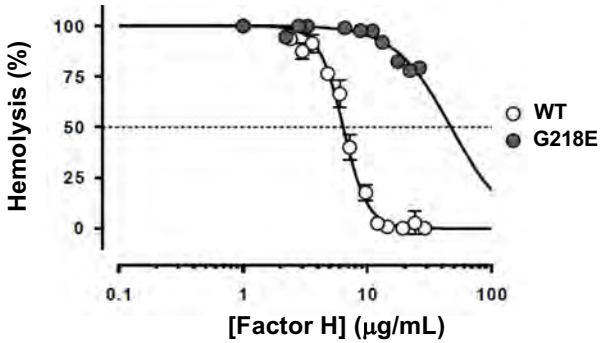




SDS-PAGE
(Non-reduced)

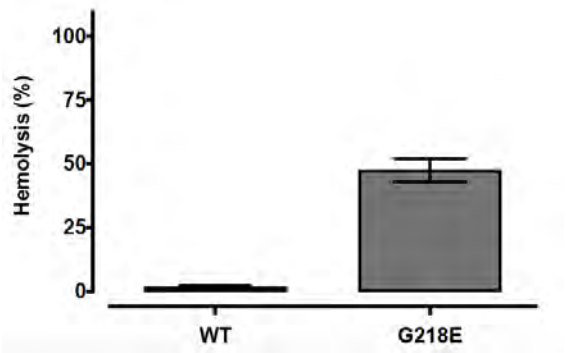


Binding to C3b

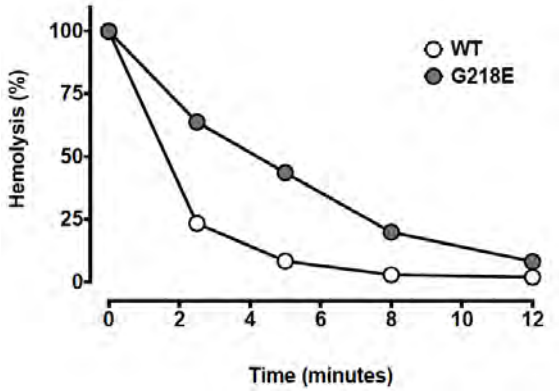


Hemolytic assay

Conclusion: Impaired Expression
PATHOGENIC



Cofactor activity



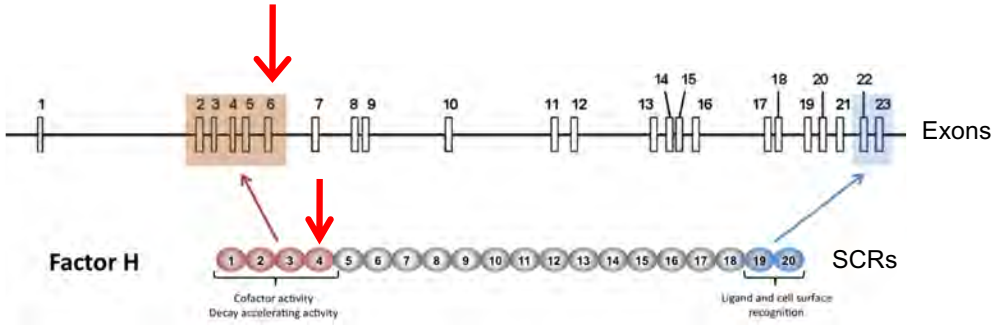
Decay-accelerating activity

Previous studies: Non expressed in Fakhouri F, Roumenina L, Provot F, et al. Pregnancy-Associated Hemolytic Uremic Syndrome Revisited in the Era of Complement Gene Mutations. *Journal of the American Society of Nephrology*. 2010;21(5):859-867.

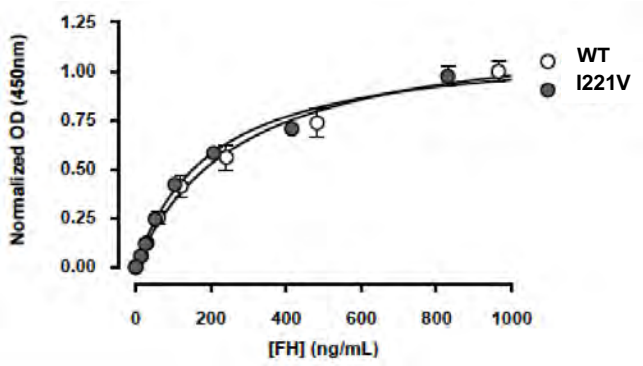
Comments:
SDS-PAGE shows a FH band with diminished intensity under non-reducing conditions, suggesting that this variant likely affects expression of the protein and results in a factor H deficiency.

c.661A>G (I221V)

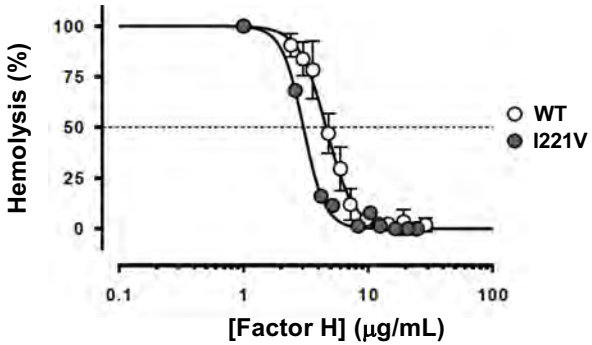
CADD: 0
gnomAD: $2x10^{-5}$



SDS-PAGE
(Non-reduced)



Binding to C3b

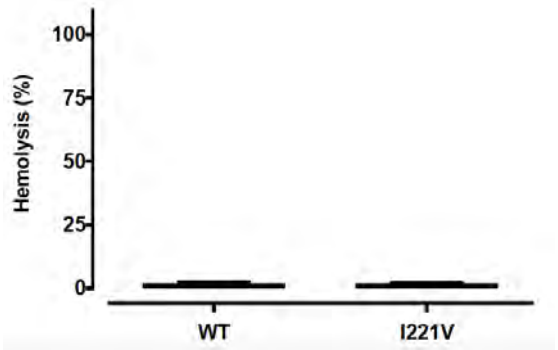


Hemolytic assay

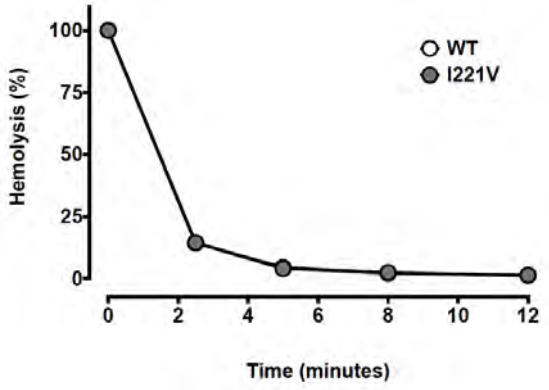
Conclusion: Normal Function
BENIGN

Previous studies: None

Comments:



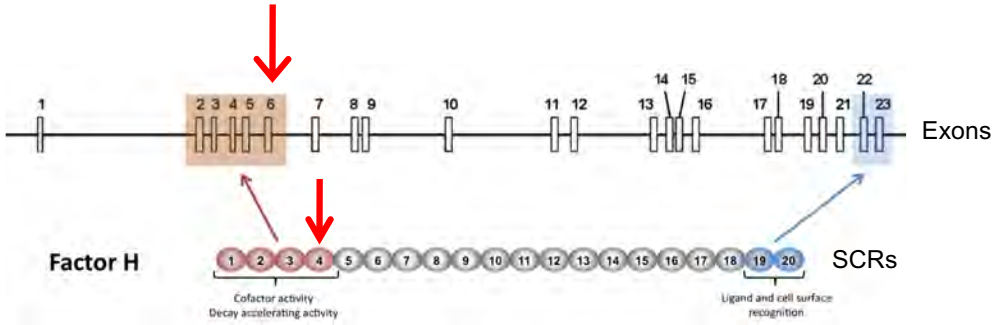
Cofactor activity

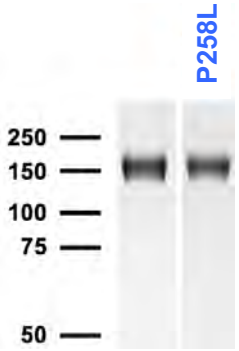


Decay-accelerating activity

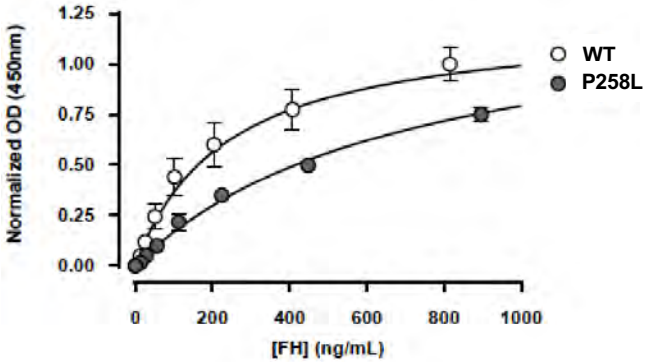
c.773C>T (P258L)

CADD: 21.1
gnomAD: $4x10^{-6}$

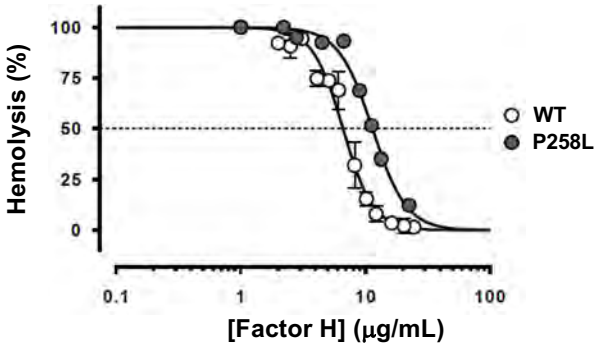




SDS-PAGE
(Non-reduced)

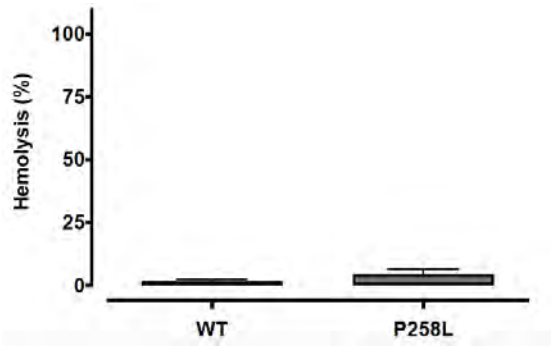


Binding to C3b

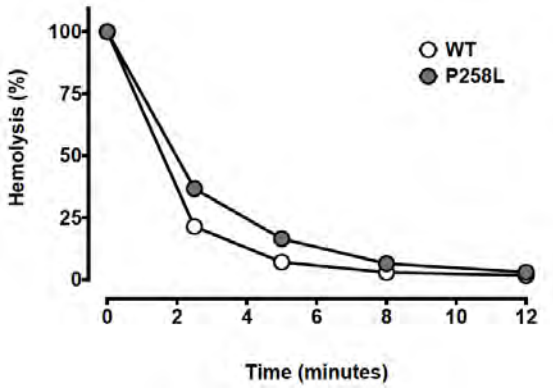


Hemolytic assay

Conclusion: Impaired Function
PATHOGENIC



Cofactor activity



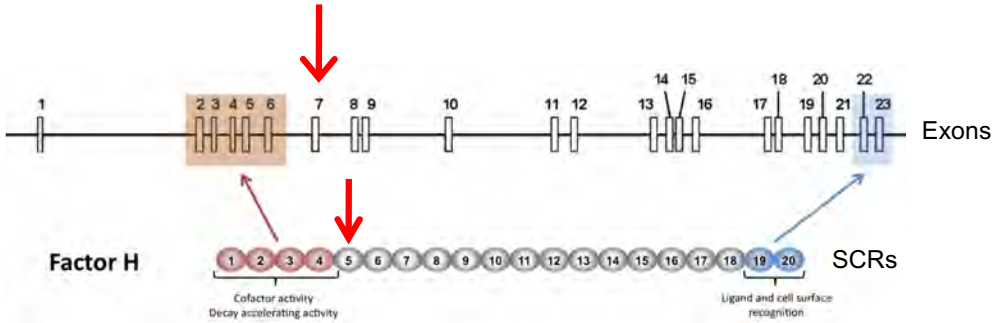
Decay-accelerating activity

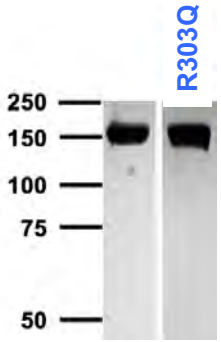
Previous studies: Pathogenic in Osborne AJ, Breno M, Borsa NG, et al. Statistical Validation of Rare Complement Variants Provides Insights into the Molecular Basis of Atypical Hemolytic Uremic Syndrome and C3 Glomerulopathy. *The Journal of Immunology*. 2018:ji1701695.

Comments:

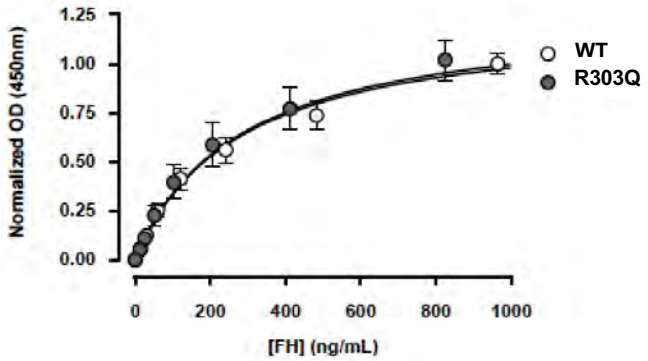
c.908G>A (R303Q)

CADD: 0.17
gnomAD: $2x10^{-5}$

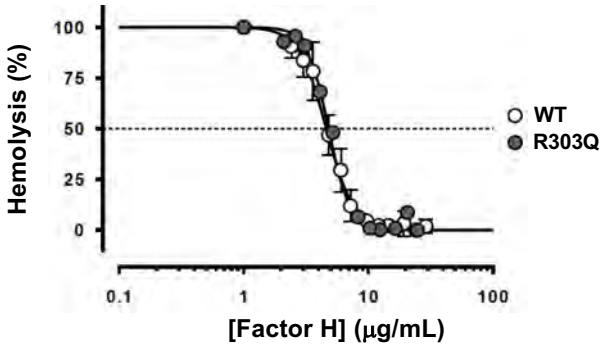




SDS-PAGE
(Non-reduced)



Binding to C3b

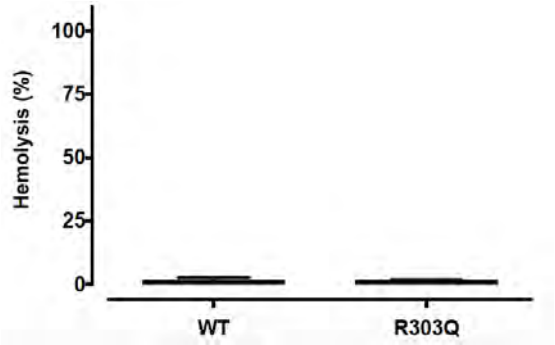


Hemolytic assay

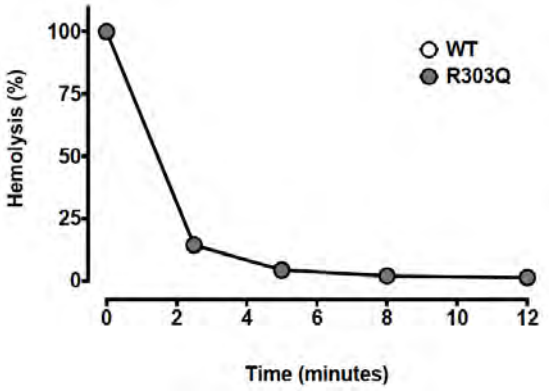
Conclusion: Normal Function
BENIGN

Previous studies: None

Comments:



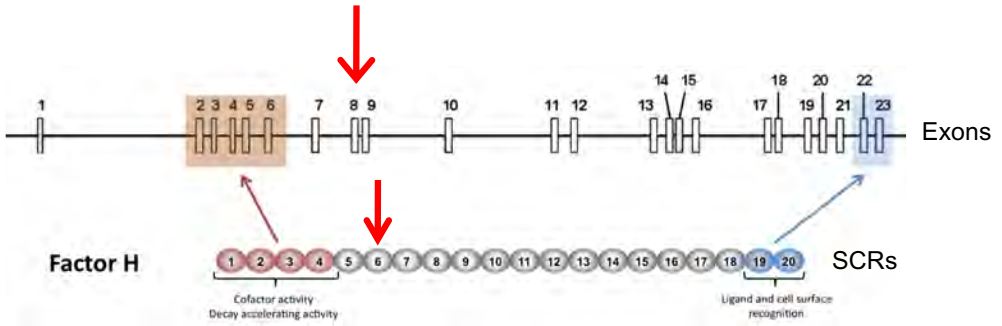
Cofactor activity

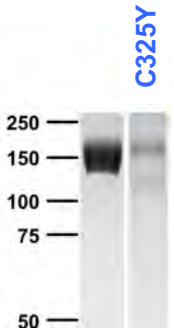


Decay-accelerating activity

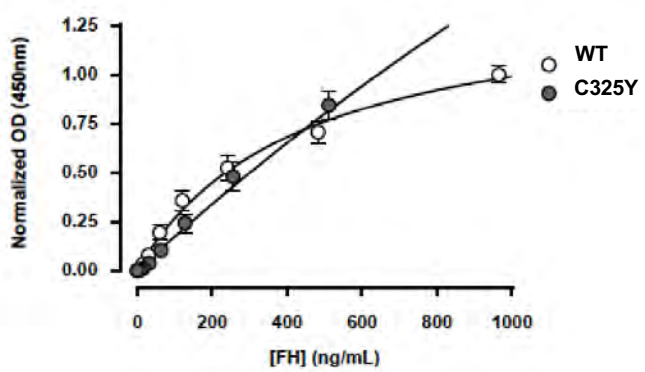
c.974G>A (C325Y)

CADD: 25.7
gnomAD: Not present

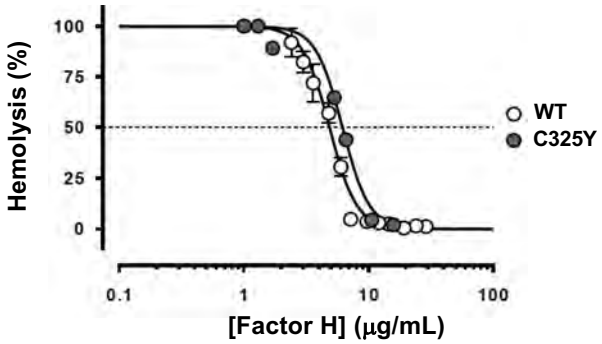




SDS-PAGE
(Non-reduced)



Binding to C3b

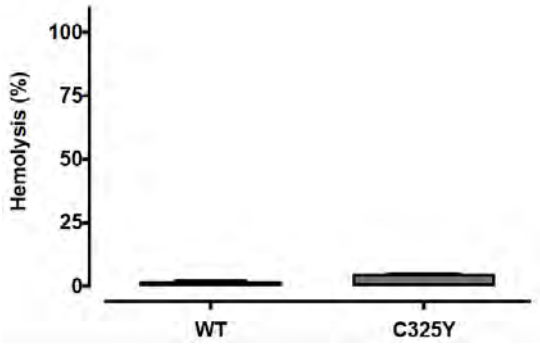


Hemolytic assay

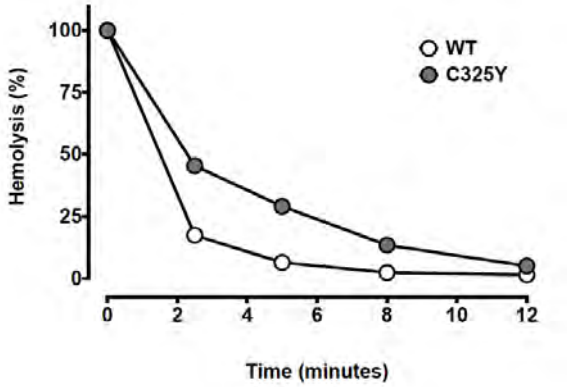
Conclusion: Impaired Expression
PATHOGENIC

Previous studies: None

Comments:
SDS-PAGE shows a weak FH band under non-reducing conditions, suggesting that this variant likely affects expression of the protein and results in a factor H deficiency



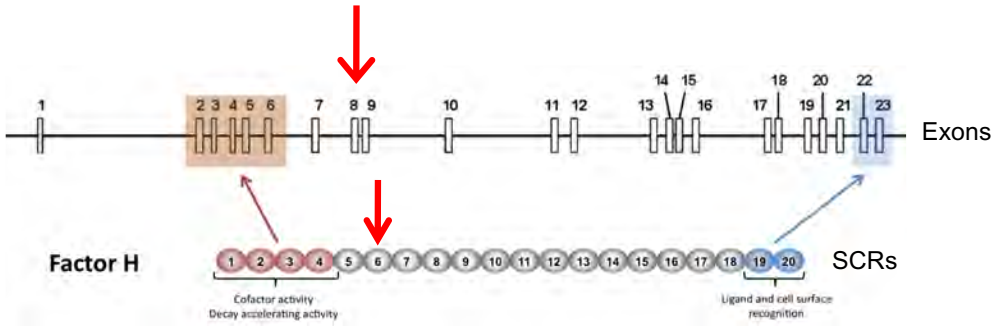
Cofactor activity

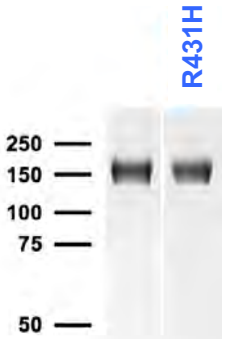


Decay-accelerating activity

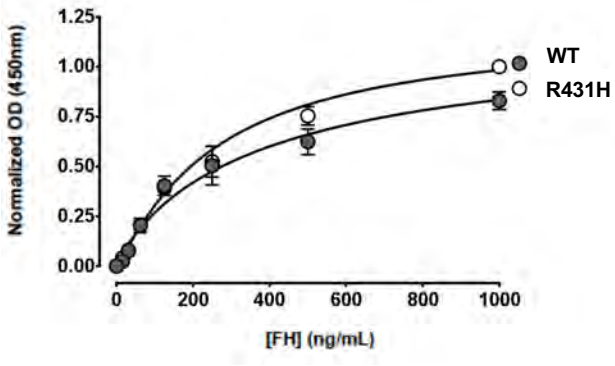
c.1022G>A (R341H)

CADD: 7.70
gnomAD: $4x10^{-5}$

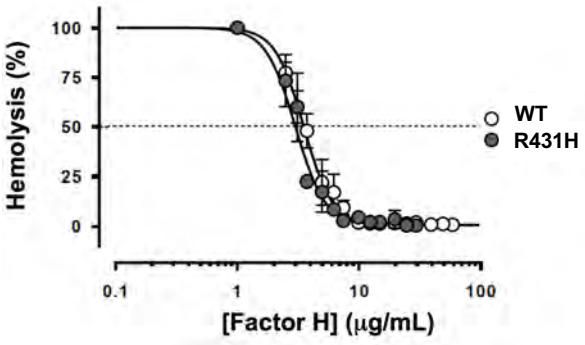




SDS-PAGE
(Non-reduced)



Binding to C3b

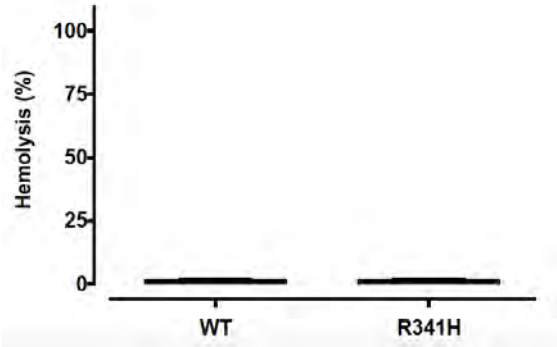


Hemolytic assay

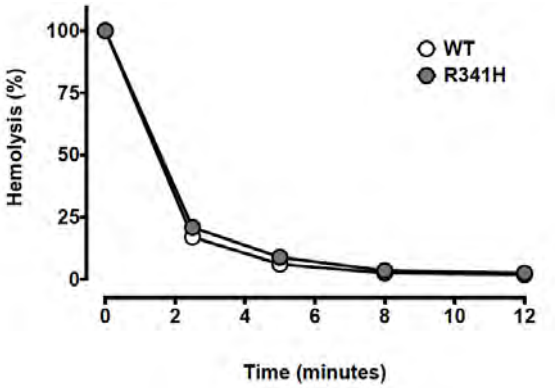
Conclusion: Normal Function
BENIGN

Previous studies: None

Comments:



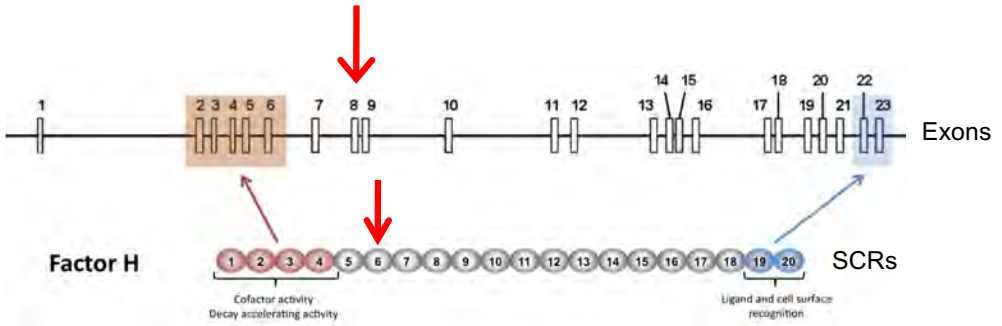
Cofactor activity

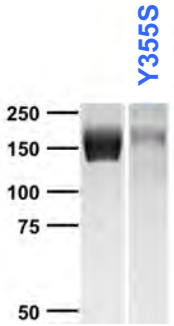


Decay-accelerating activity

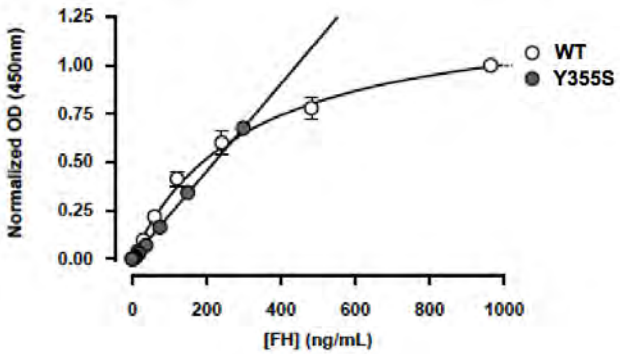
c.1064A>C (Y355S)

CADD: 22.2
gnomAD: Not present

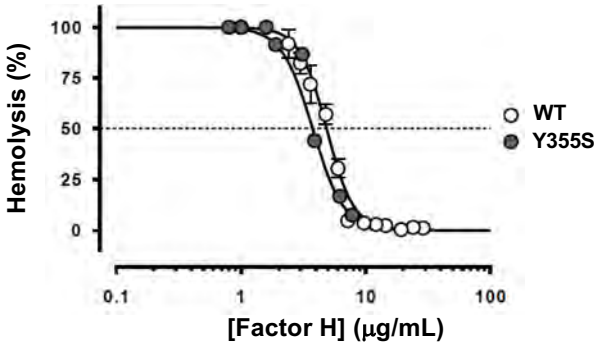




SDS-PAGE
(Non-reduced)

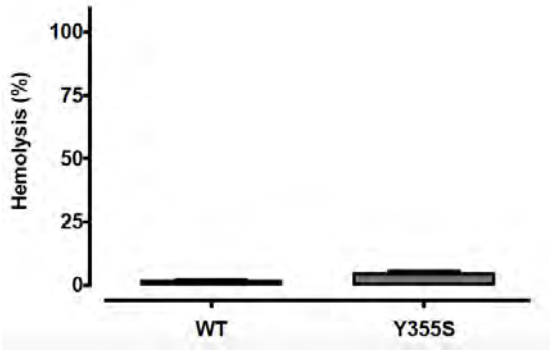


Binding to C3b

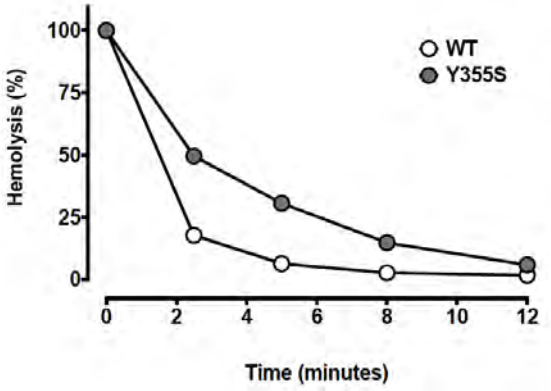


Hemolytic assay

Conclusion: Impaired Expression
PATHOGENIC



Cofactor activity



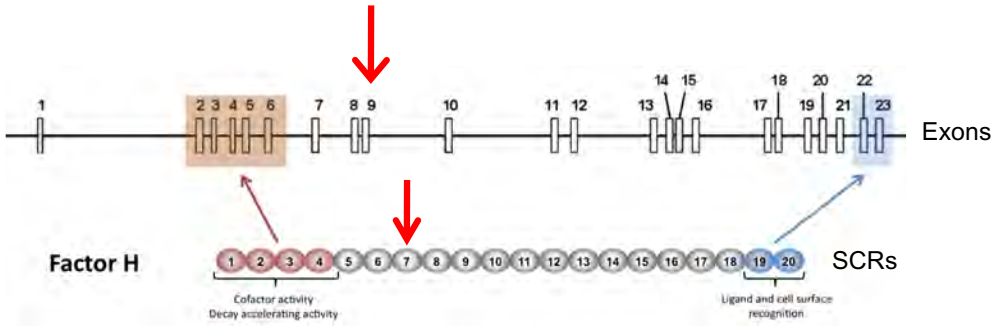
Decay-accelerating activity

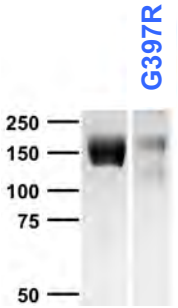
Previous studies: None

Comments:
SDS-PAGE shows a weak FH band under non-reducing conditions, suggesting that this variant likely affects expression of the protein and results in a factor H deficiency

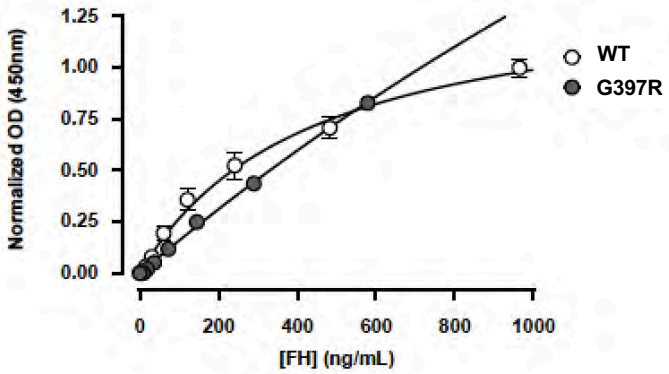
c.1189G>A (G397R)

CADD: 28.8
gnomAD: Not present

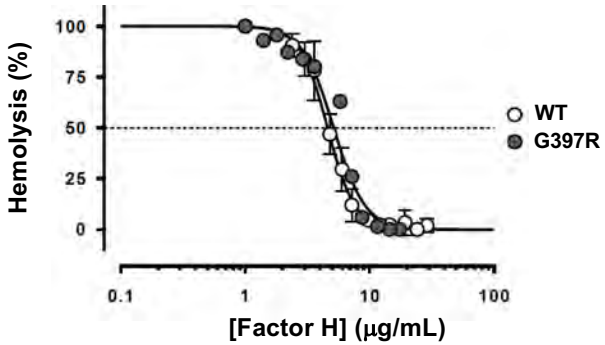




SDS-PAGE
(Non-reduced)



Binding to C3b



Hemolytic assay

Conclusion: Impaired Expression
PATHOGENIC

Previous studies: Non-expressed in Fakhouri F, Roumenina L, Provot F, et al. Pregnancy-Associated Hemolytic Uremic Syndrome Revisited in the Era of Complement Gene Mutations. *Journal of the American Society of Nephrology*. 2010;21(5):859-867.

Comments:
SDS-PAGE shows a weak FH band under non-reducing conditions, suggesting that this variant likely affects expression of the protein and results in a factor H deficiency

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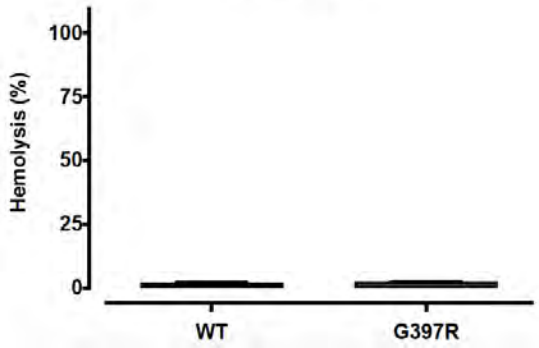
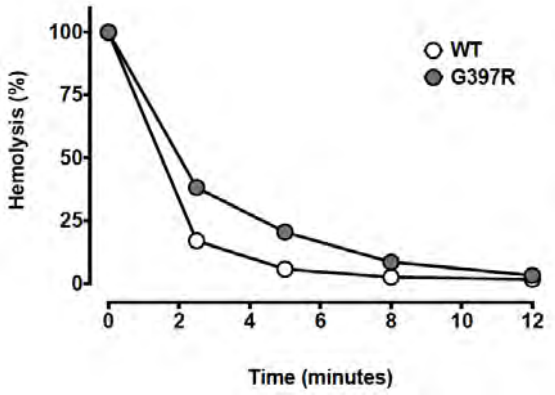


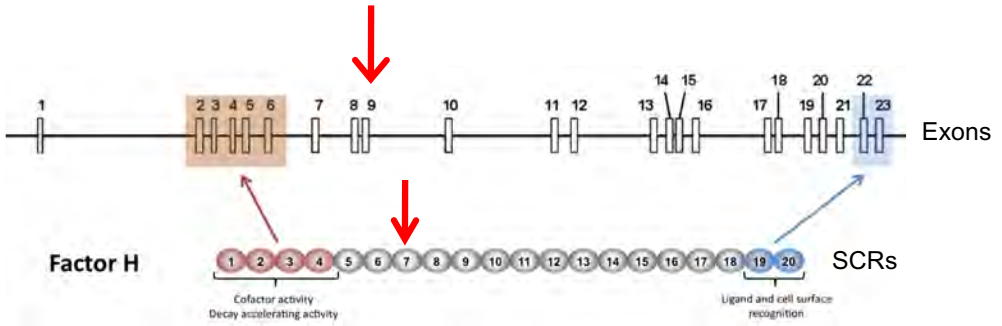
Cofactor activity

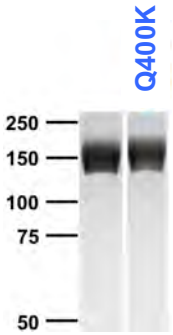


Decay-accelerating activity

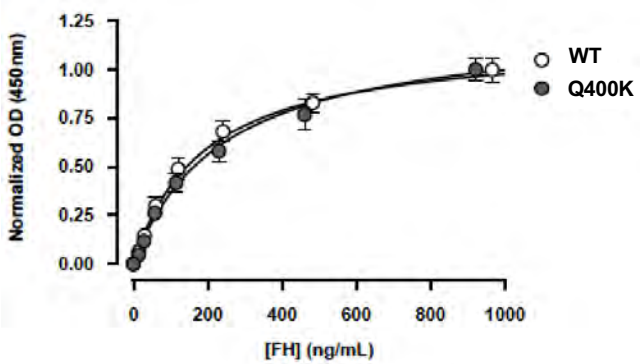
c.1198C>A (Q400K)

CADD: 0
gnomAD: $1x10^{-4}$

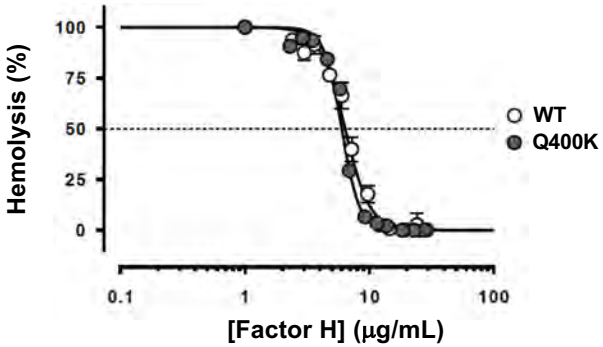




SDS-PAGE
(Non-reduced)



Binding to C3b

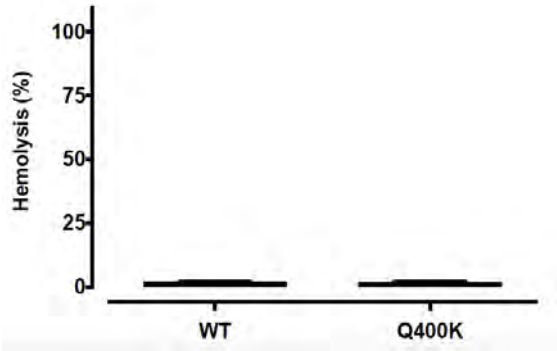


Hemolytic assay

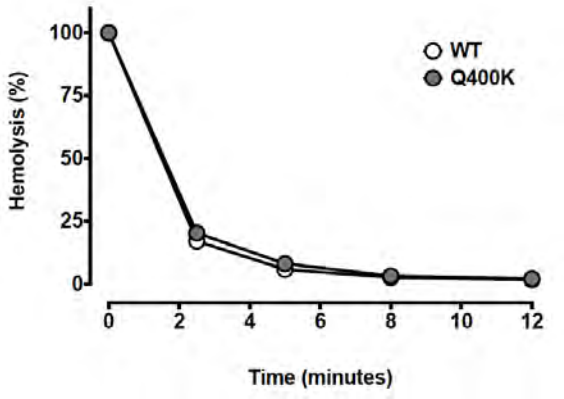
Conclusion: Normal Function
BENIGN

Previous studies: None

Comments:
Reported non-expressed by Dragon-Durey et al. J Am Soc Nephrol. 2004. Discussed in the manuscript.



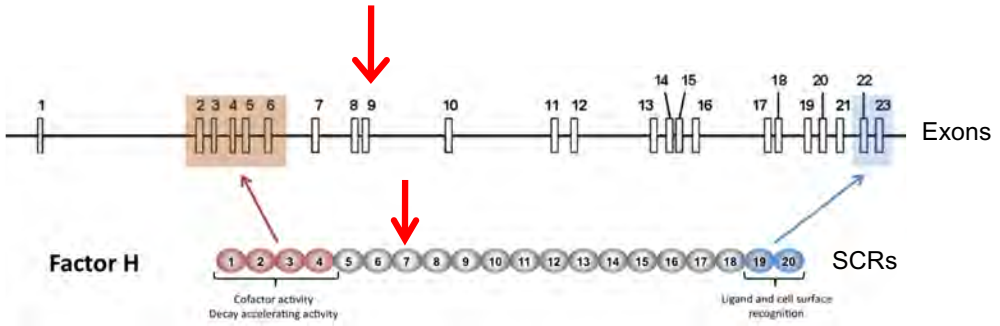
Cofactor activity

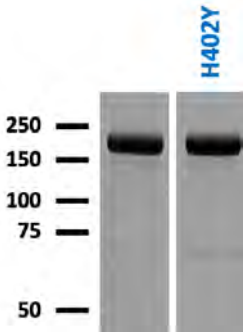


Decay-accelerating activity

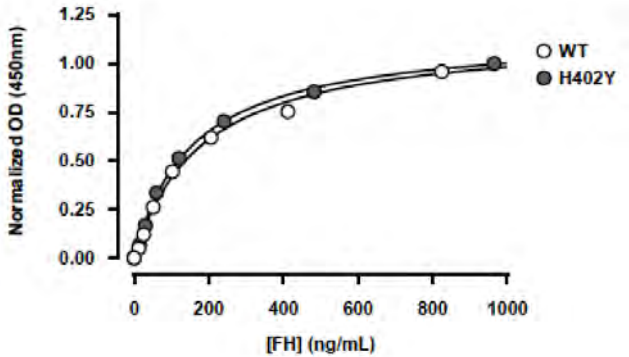
c.1204C>A (H402Y)

CADD: 0
gnomAD: $7x10^{-1}$

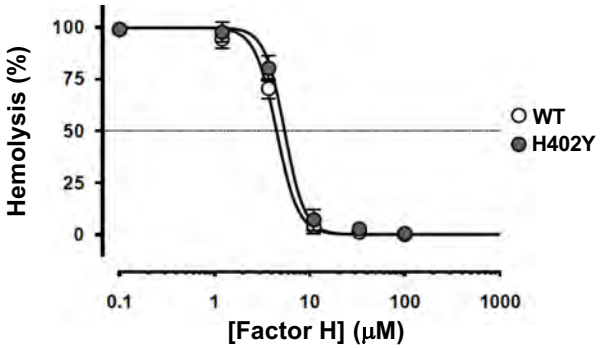




SDS-PAGE
(Non-reduced)



Binding to C3b

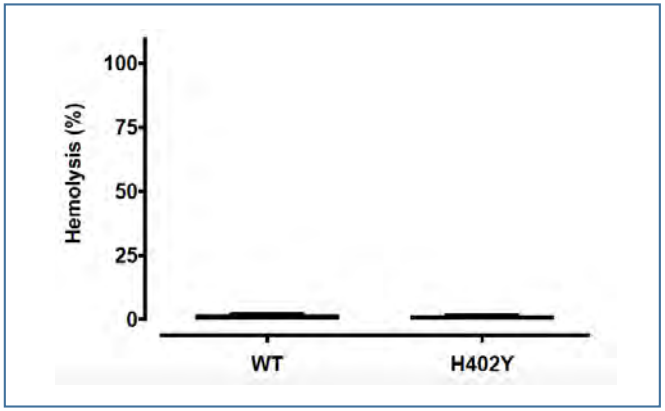


Hemolytic assay

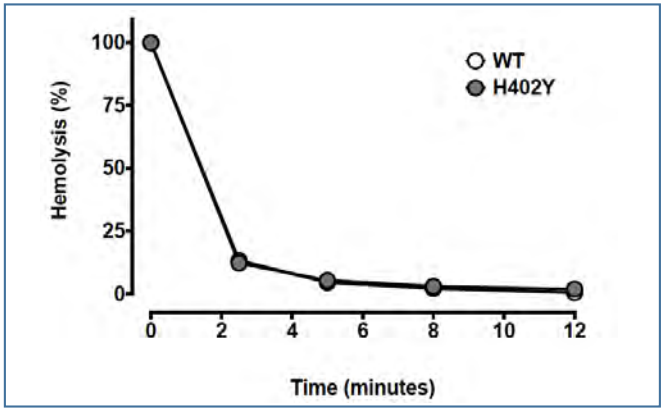
Conclusion: Normal Function
BENIGN

Previous studies:

Comments:
Common polymorphism that does not affect function



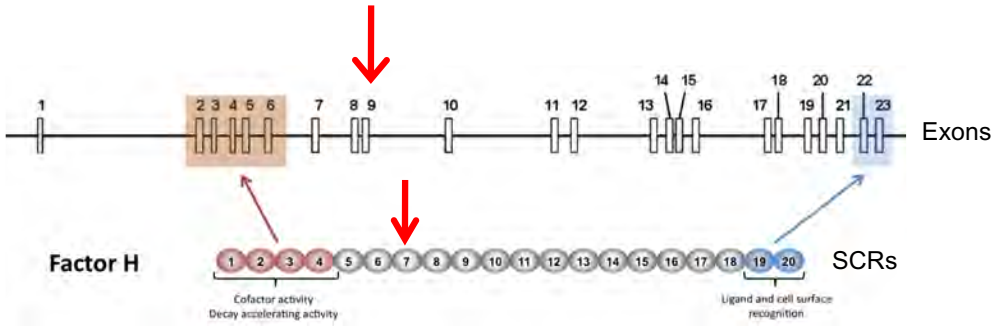
Cofactor activity

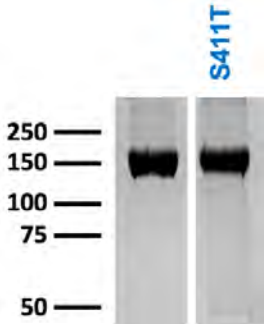


Decay-accelerating activity

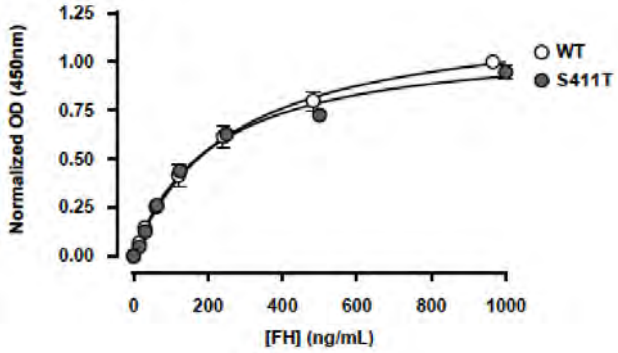
c.1231T>A (S411T)

CADD: 0.15
gnomAD: Not present

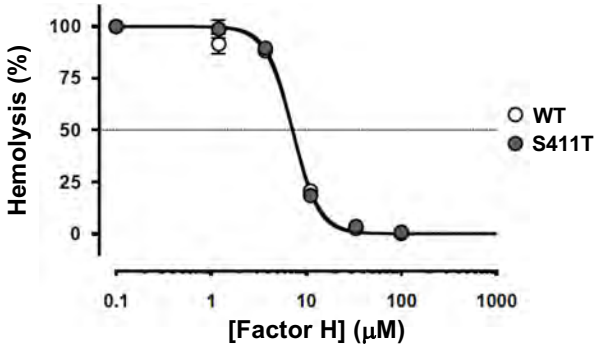




SDS-PAGE
(Non-reduced)

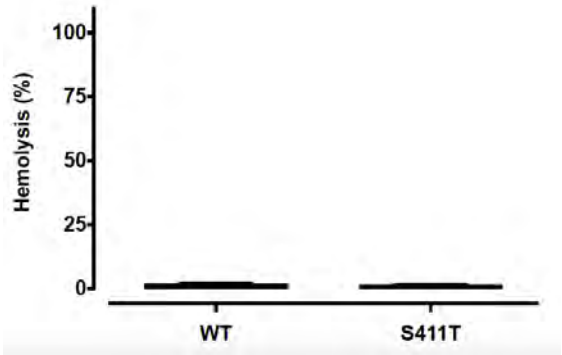


Binding to C3b

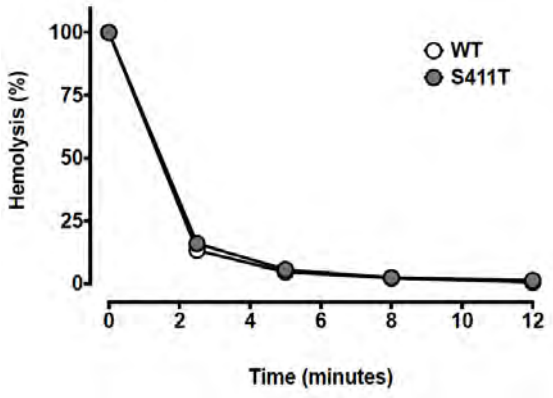


Hemolytic assay

Conclusion: Normal Function
BENIGN



Cofactor activity



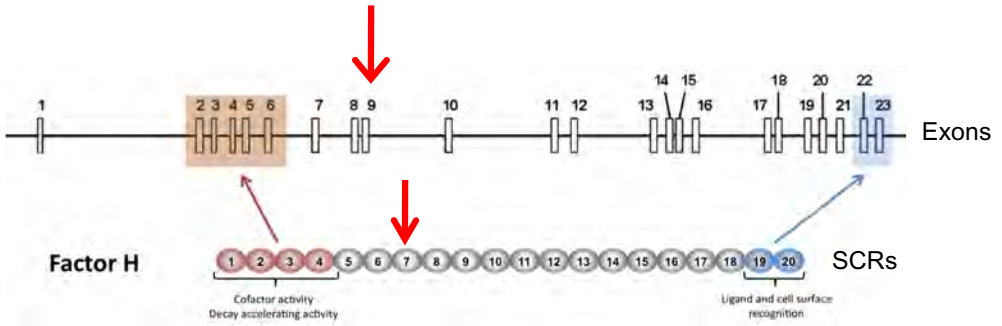
Decay-accelerating activity

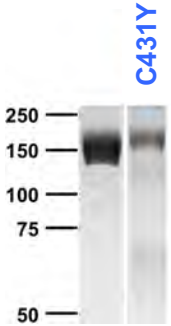
Previous studies: Benign in Goicoechea de Jorge E, Tortajada A, García SP, et al. Factor H Competitor Generated by Gene Conversion Events Associates with Atypical Hemolytic Uremic Syndrome. *Journal of the American Society of Nephrology*. 2018;29(1):240-249.

Comments:

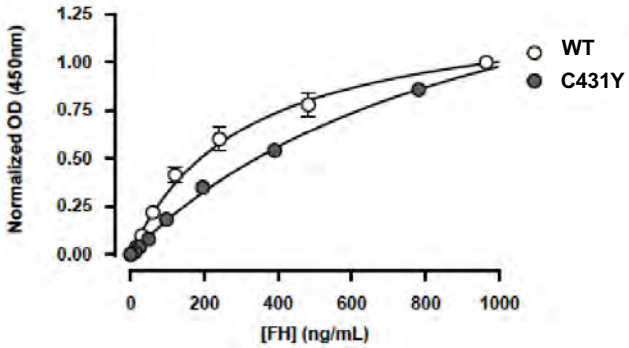
c.1292G>A (C431Y)

CADD: 24.3
gnomAD: Not present

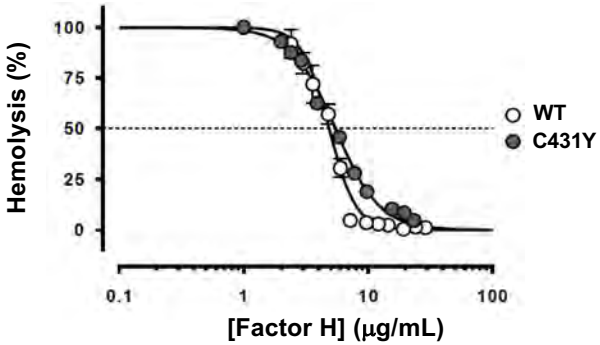




SDS-PAGE
(Non-reduced)



Binding to C3b

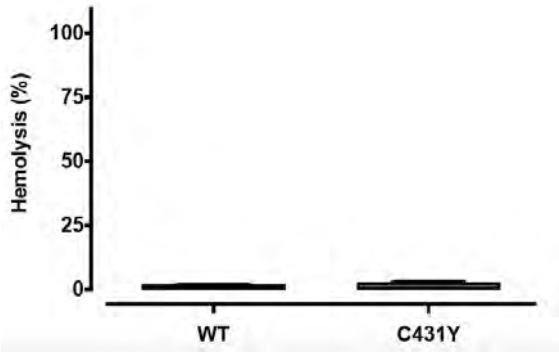


Hemolytic assay

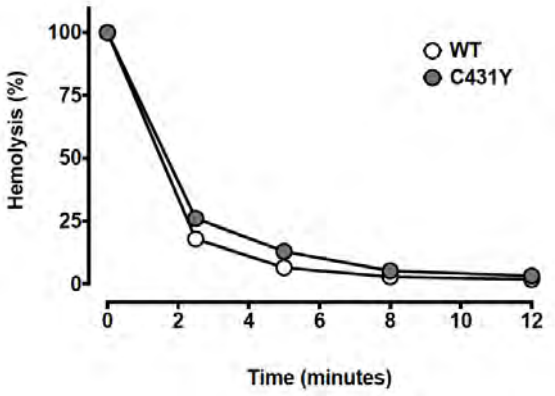
Conclusion: Impaired Expression
PATHOGENIC

Previous studies: Non-expressed in Montes T, Goicoechea de Jorge E, Ramos R, et al. Genetic deficiency of complement factor H in a patient with age-related macular degeneration and membranoproliferative glomerulonephritis. *Molecular Immunology*. 2008;45(10):2897-2904.

Comments:
SDS-PAGE shows a weak FH band under non-reducing conditions, suggesting that this variant likely affects expression of the protein and results in a factor H deficiency.



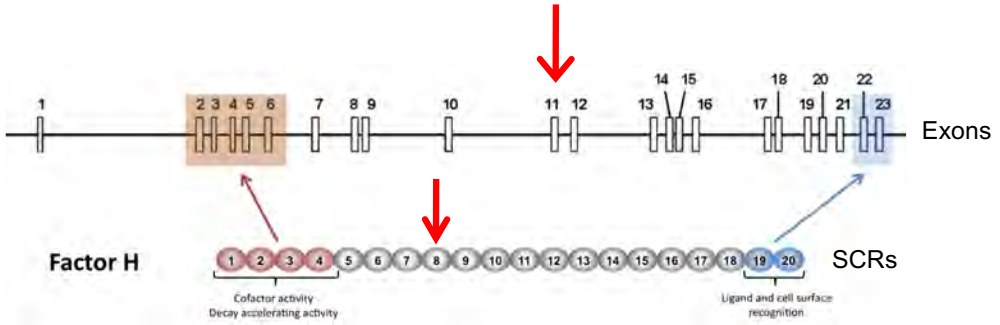
Cofactor activity

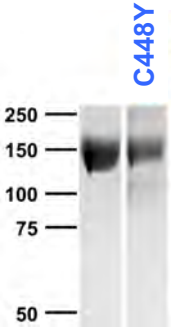


Decay-accelerating activity

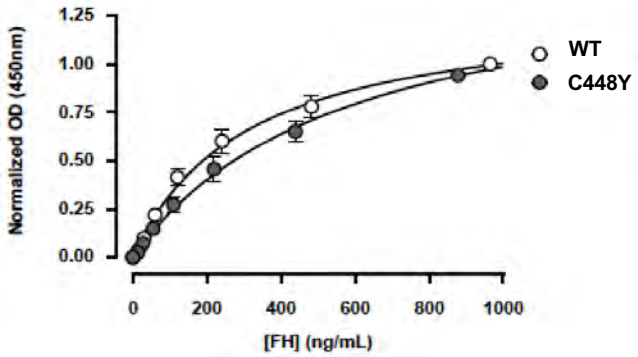
c.1343G>A (C448Y)

CADD: 23
gnomAD: Not present

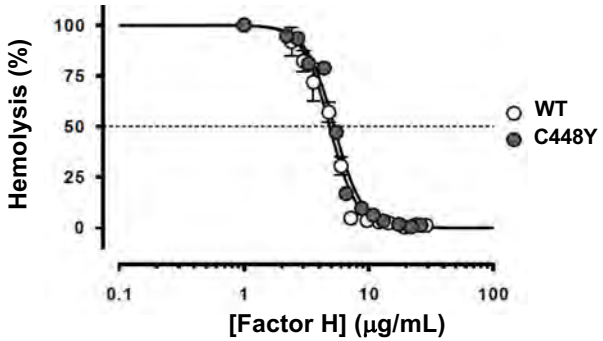




SDS-PAGE
(Non-reduced)

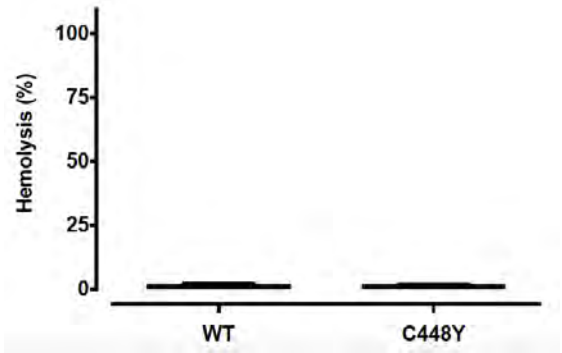


Binding to C3b

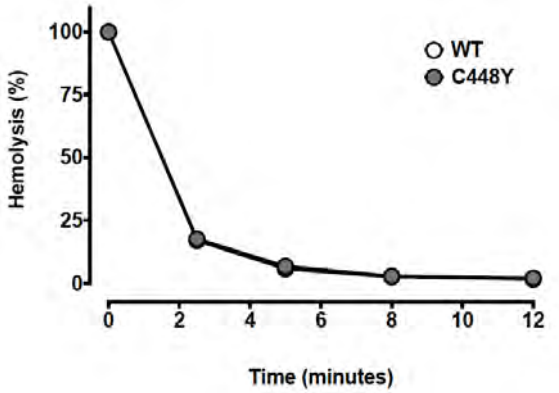


Hemolytic assay

Conclusion: Impaired Expression
PATHOGENIC



Cofactor activity



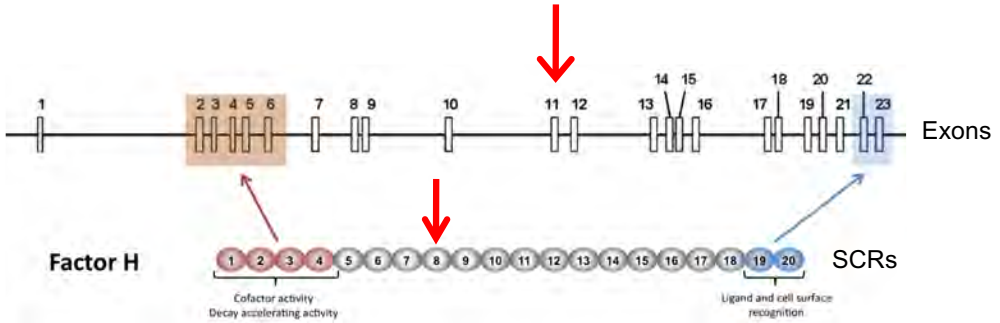
Decay-accelerating activity

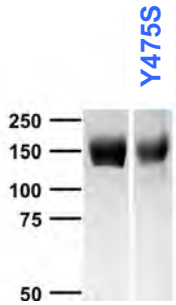
Previous studies: Non-expressed in Szarvas N, Szilágyi Á, Csuka D, et al. Genetic analysis and functional characterization of novel mutations in a series of patients with atypical hemolytic uremic syndrome. *Mol Immunol*. 2016;71:10-22.

Comments:
SDS-PAGE shows a weak FH band under non-reducing conditions, suggesting that this variant likely affects expression of the protein and results in a factor H deficiency.

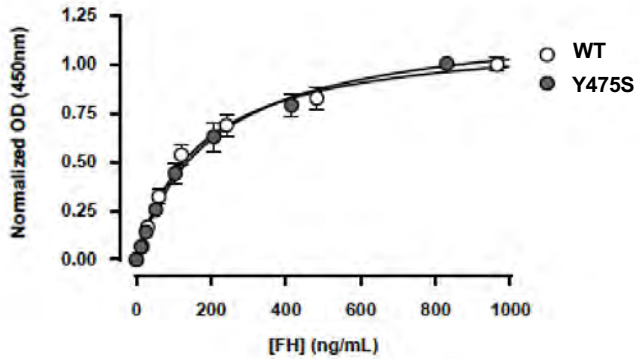
c.1424A>C (Y475S)

CADD: 20.3
gnomAD: Not present

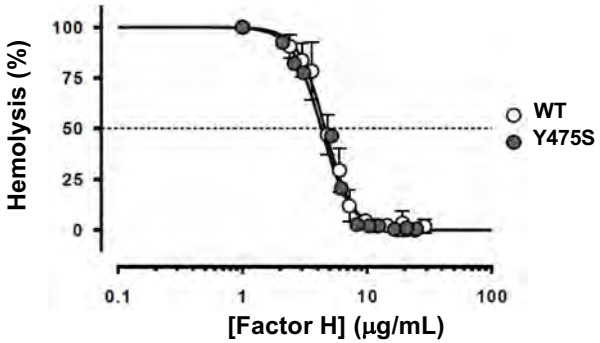




SDS-PAGE
(Non-reduced)

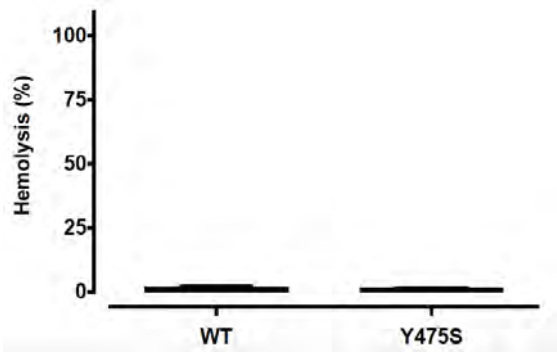


Binding to C3b

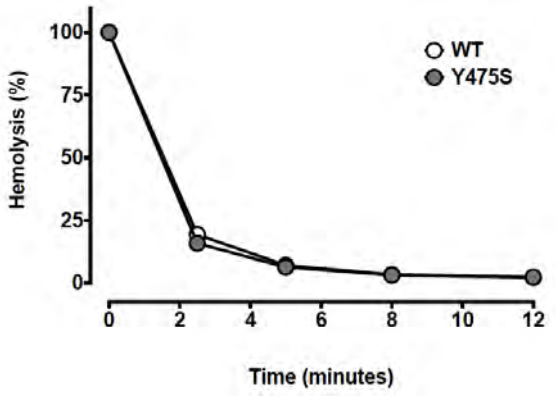


Hemolytic assay

Conclusion: Impaired Expression
PATHOGENIC



Cofactor activity



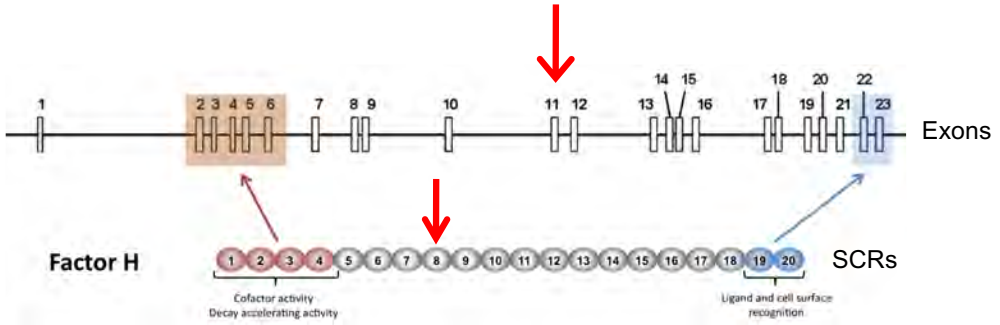
Decay-accelerating activity

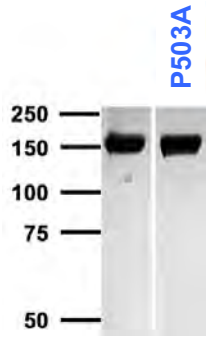
Previous studies: Pathogenic in Nürnberger J, Philipp T, Witzke O, et al. Eculizumab for Atypical Hemolytic–Uremic Syndrome. *New England Journal of Medicine*. 2009;360(5):542-544.

Comments:
SDS-PAGE shows a FH band with diminished intensity under non-reducing conditions, suggesting that this variant likely affects expression of the protein and results in a factor H deficiency.

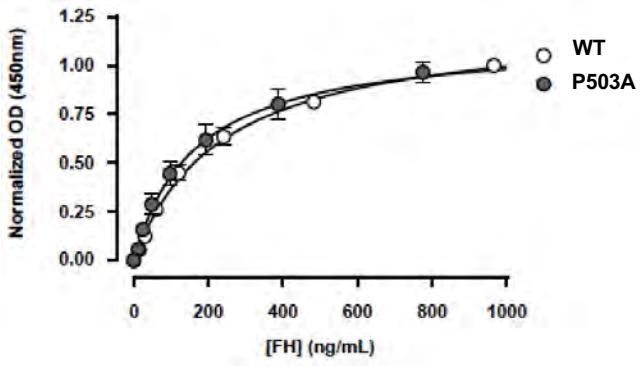
c.1507C>G (P503A)

CADD: 21.9
gnomAD: $2x10^{-5}$

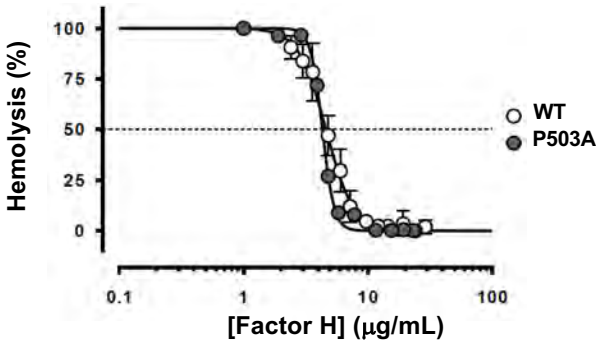




SDS-PAGE
(Non-reduced)



Binding to C3b

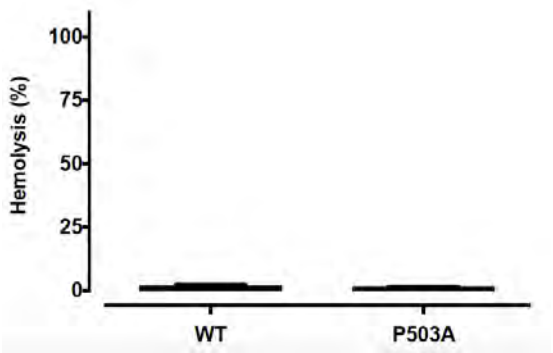


Hemolytic assay

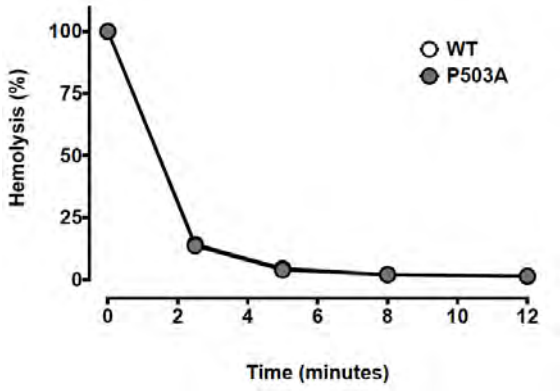
Conclusion: Normal Function
BENIGN

Previous studies: None

Comments:



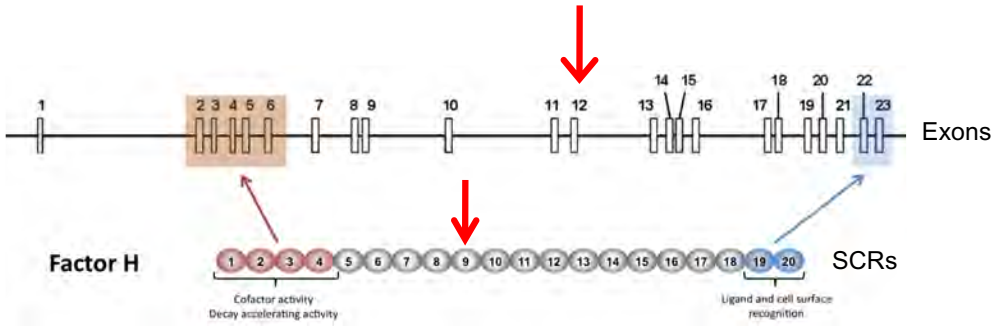
Cofactor activity



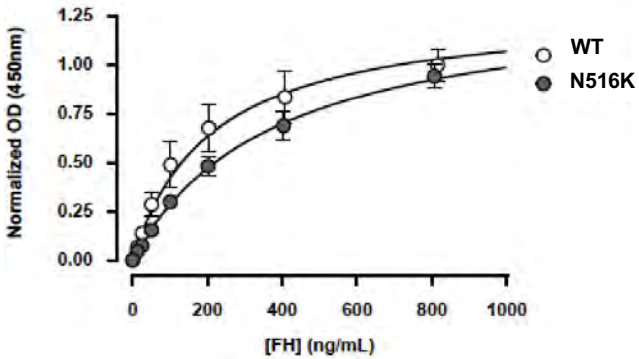
Decay-accelerating activity

c.1548T>A (N516K)

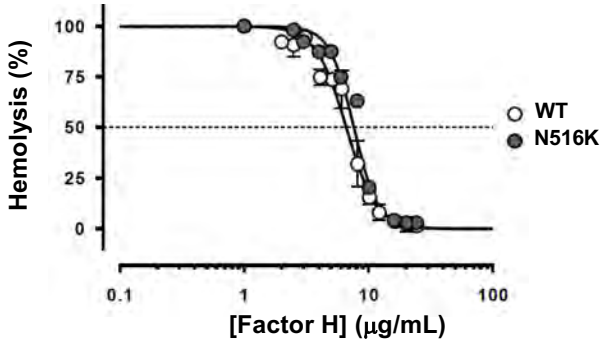
CADD: 21.7
gnomAD: $3x10^{-4}$



SDS-PAGE
(Non-reduced)



Binding to C3b

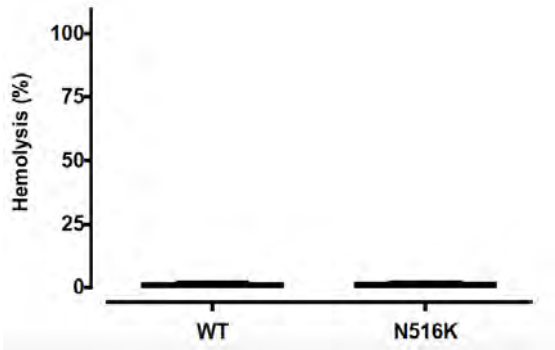


Hemolytic assay

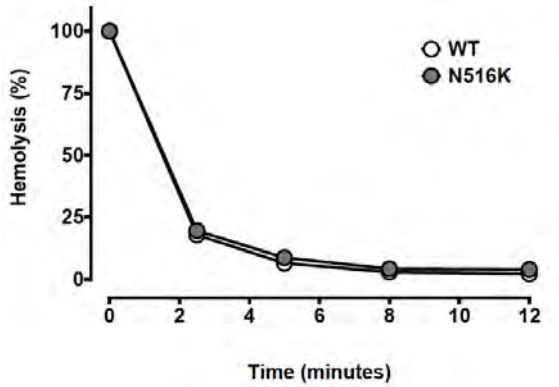
Conclusion: Normal Function
BENIGN

Previous studies: None

Comments:



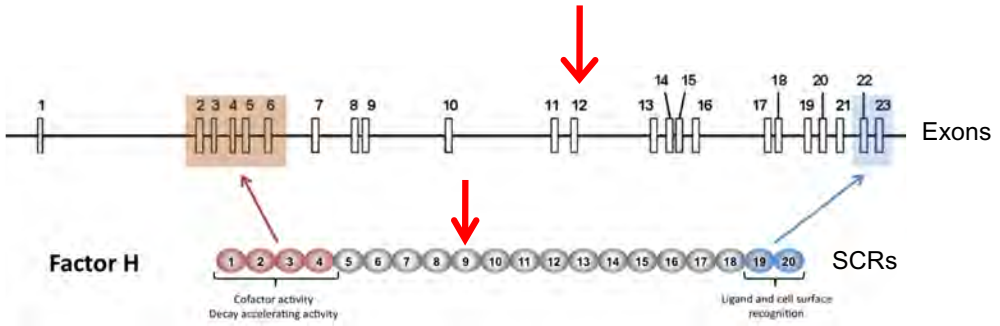
Cofactor activity

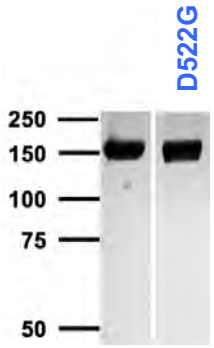


Decay-accelerating activity

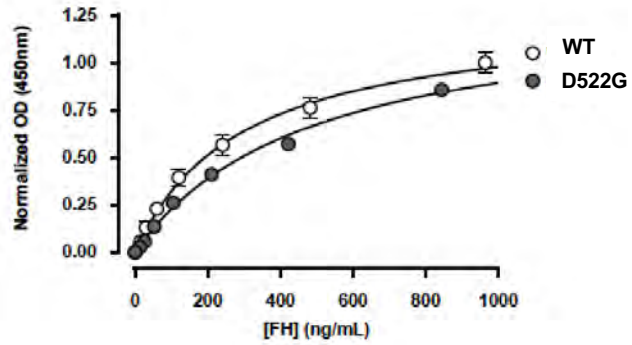
c.1565A>G (D522G)

CADD: 13.1
gnomAD: Not present

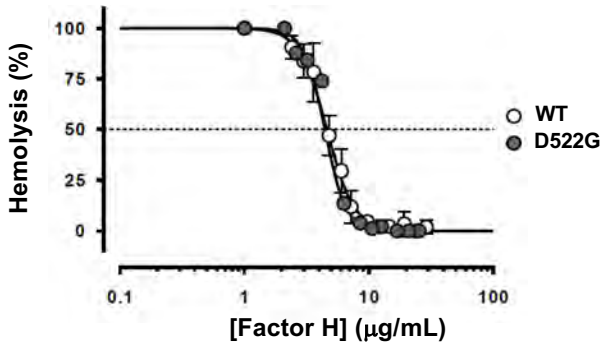




SDS-PAGE
(Non-reduced)



Binding to C3b

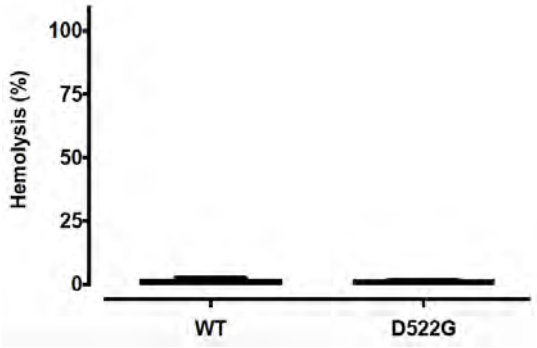


Hemolytic assay

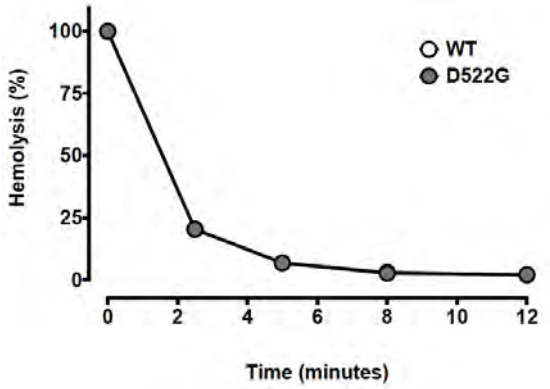
Conclusion: Normal Function
BENIGN

Previous studies: None

Comments:



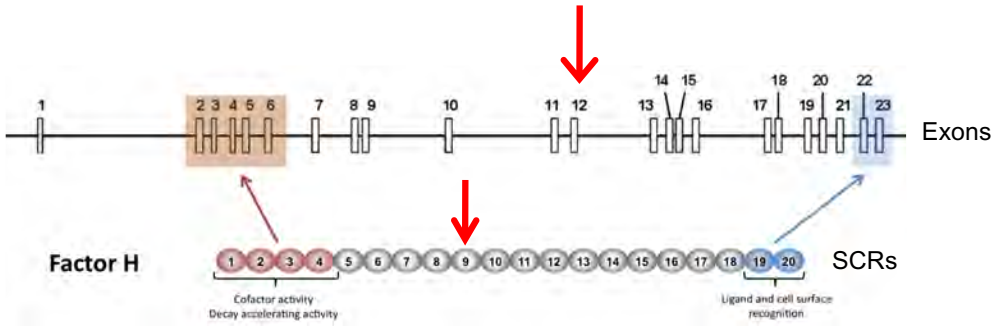
Cofactor activity

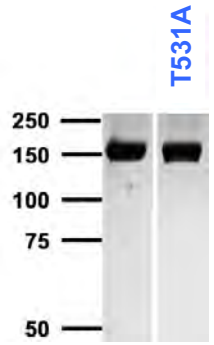


Decay-accelerating activity

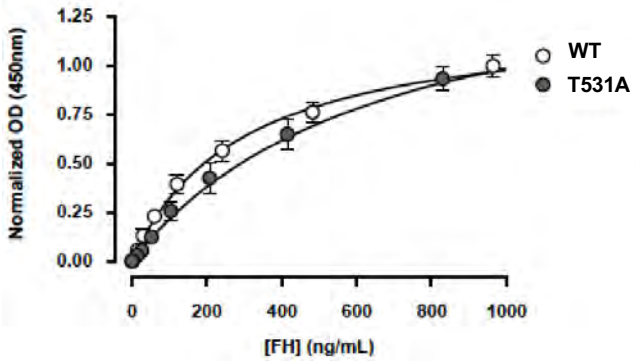
c.1591A>G (T531A)

CADD: 0
gnomAD: $8x10^{-6}$

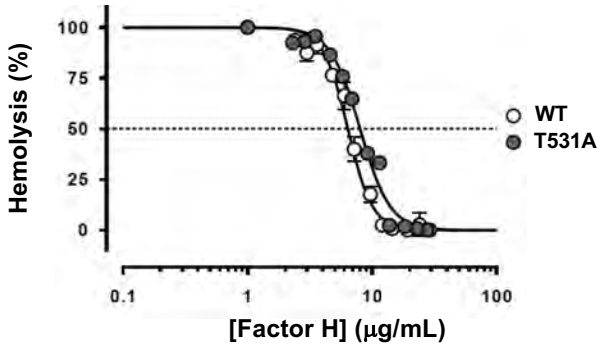




SDS-PAGE
(Non-reduced)



Binding to C3b

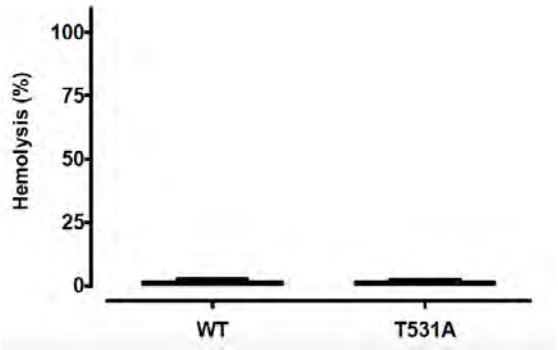


Hemolytic assay

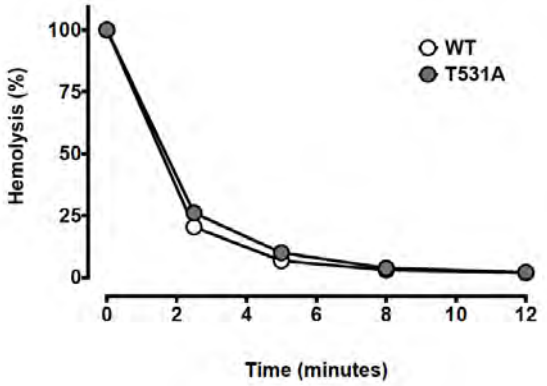
Conclusion: Normal Function
BENIGN

Previous studies: None

Comments:



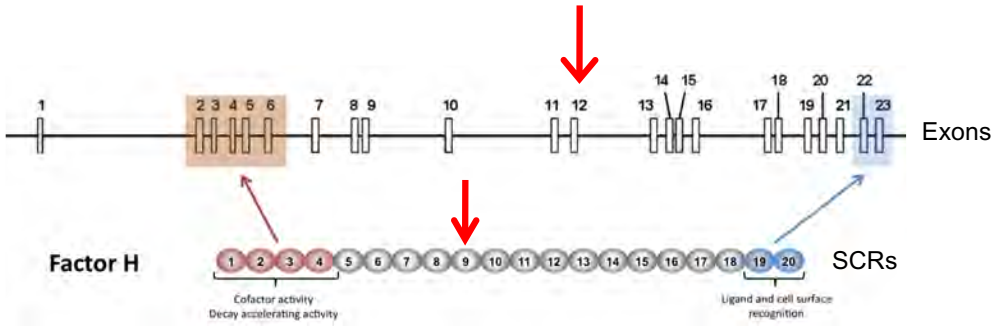
Cofactor activity

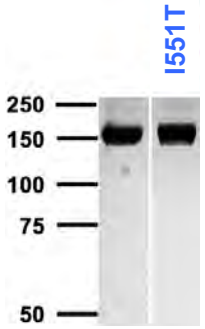


Decay-accelerating activity

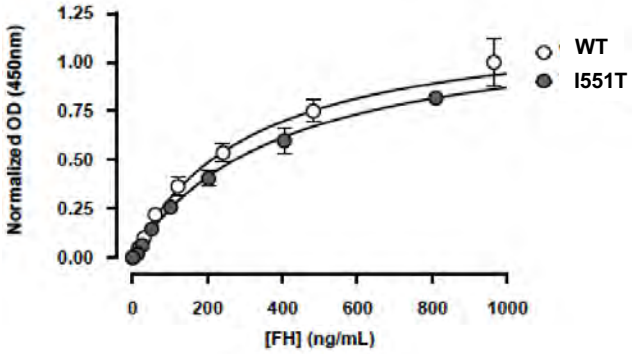
c.1652T>C (I551T)

CADD: 21.4
gnomAD: $5x10^{-3}$

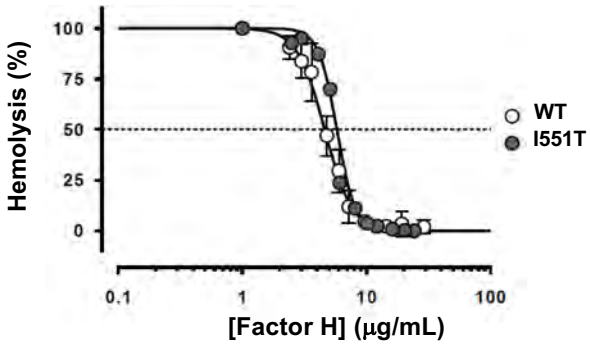




SDS-PAGE
(Non-reduced)



Binding to C3b

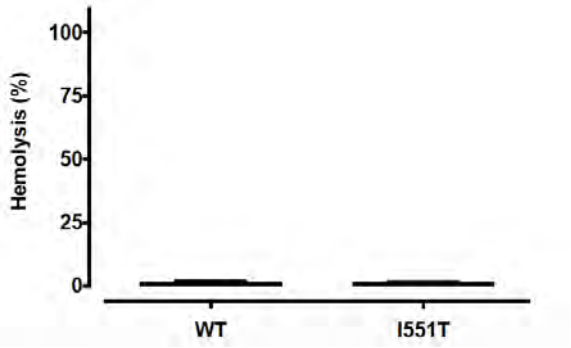


Hemolytic assay

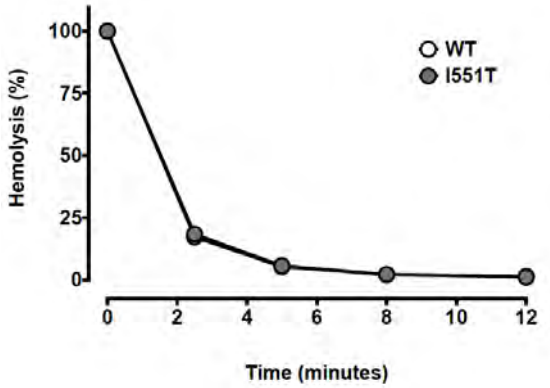
Conclusion: Normal Function
BENIGN

Previous studies: None

Comments:



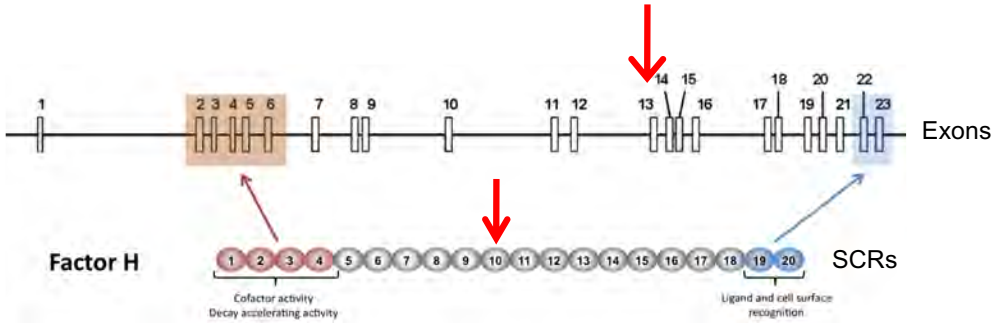
Cofactor activity

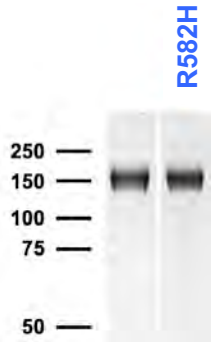


Decay-accelerating activity

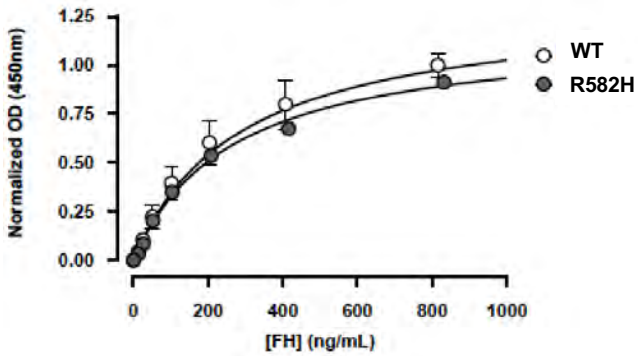
c.1745G>A (R582H)

CADD: 17.7
gnomAD: $2x10^{-5}$

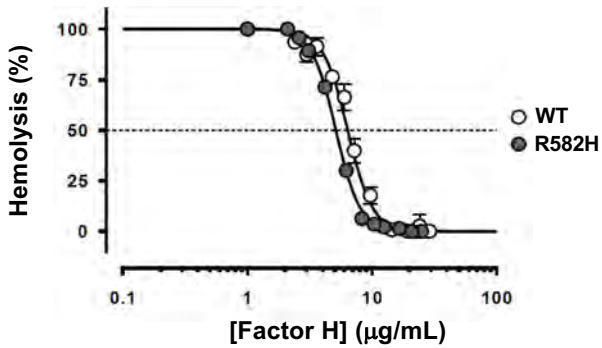




SDS-PAGE
(Non-reduced)



Binding to C3b

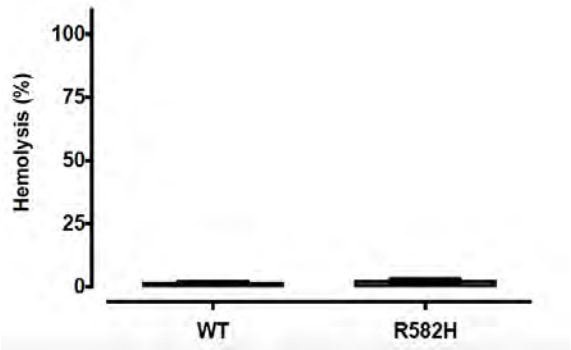


Hemolytic assay

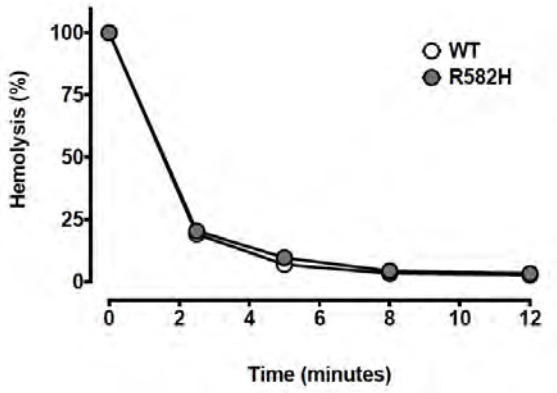
Conclusion: Normal Function
BENIGN

Previous studies: None

Comments:



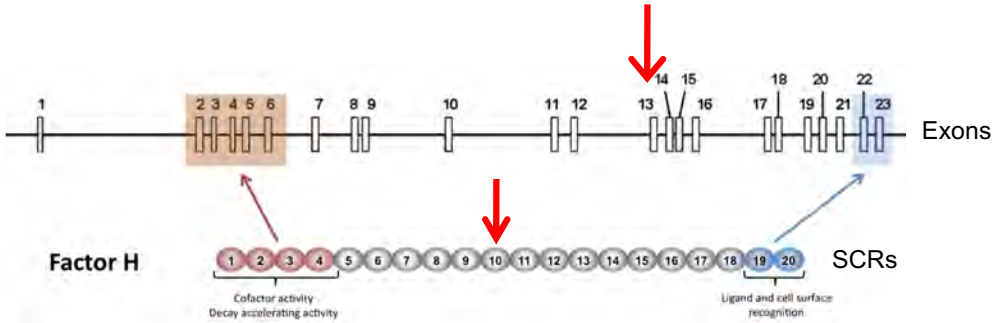
Cofactor activity



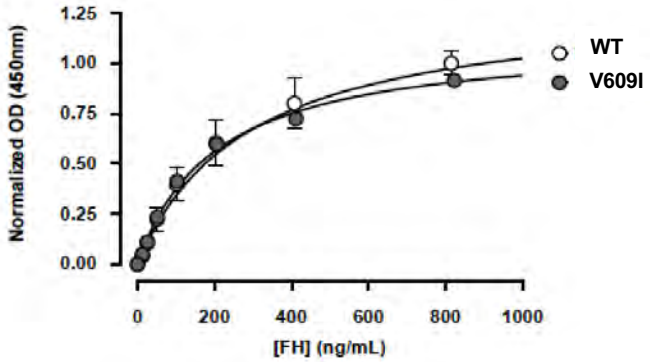
Decay-accelerating activity

c.1825G>A (V609I)

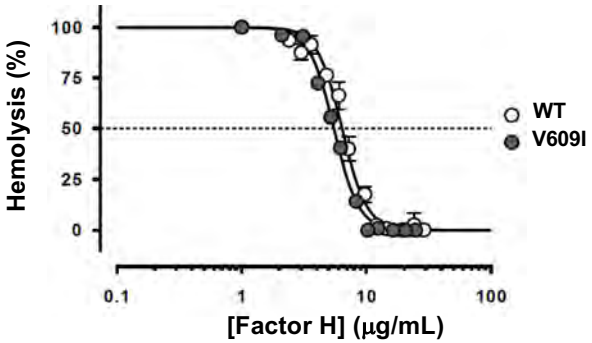
CADD: 0.77
gnomAD: $2x10^{-4}$



SDS-PAGE
(Non-reduced)



Binding to C3b

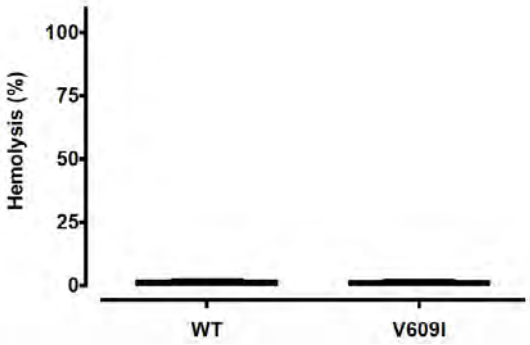


Hemolytic assay

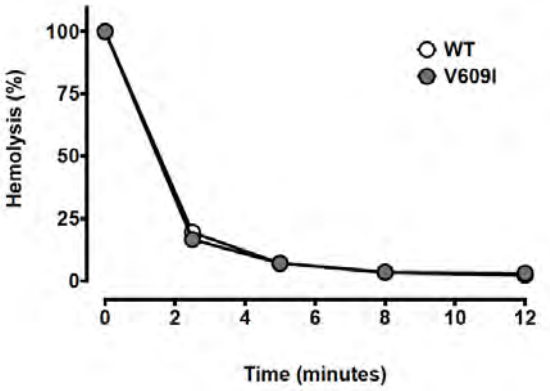
Conclusion: Normal Function
BENIGN

Previous studies: None

Comments:



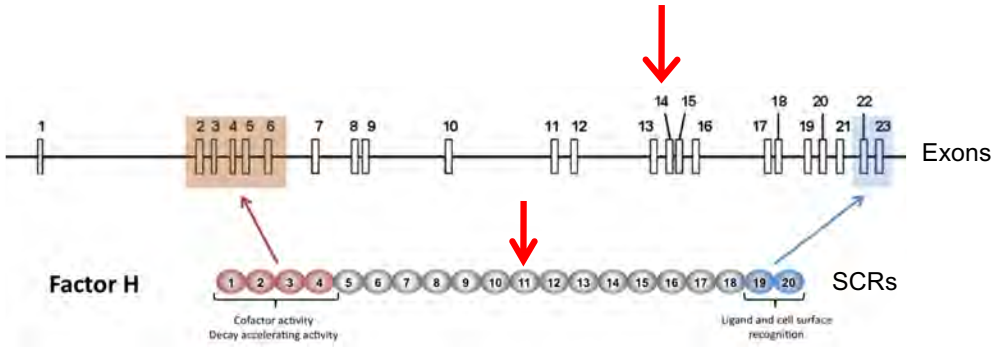
Cofactor activity

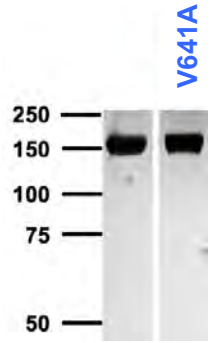


Decay-accelerating activity

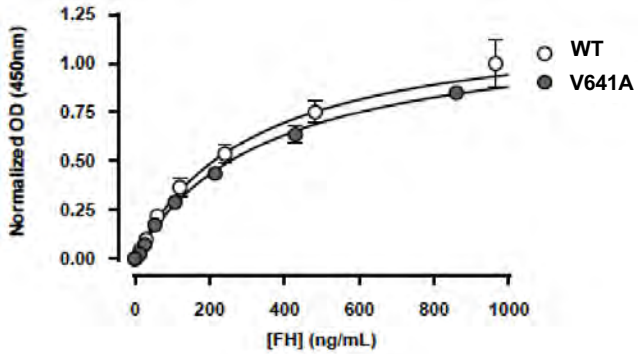
c.1922T>C (V641A)

CADD: 13.51
gnomAD: $5x10^{-5}$

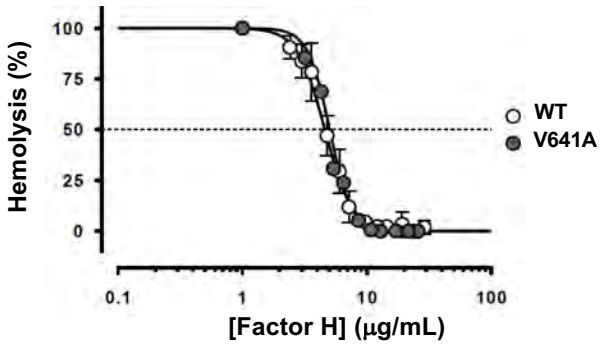




SDS-PAGE
(Non-reduced)



Binding to C3b

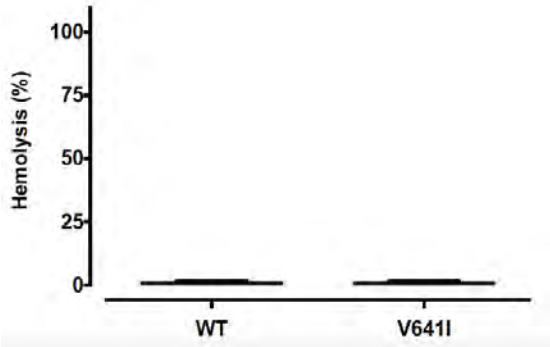


Hemolytic assay

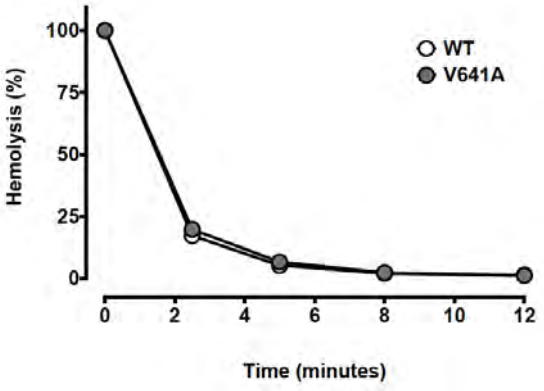
Conclusion: Normal Function
BENIGN

Previous studies: None

Comments:



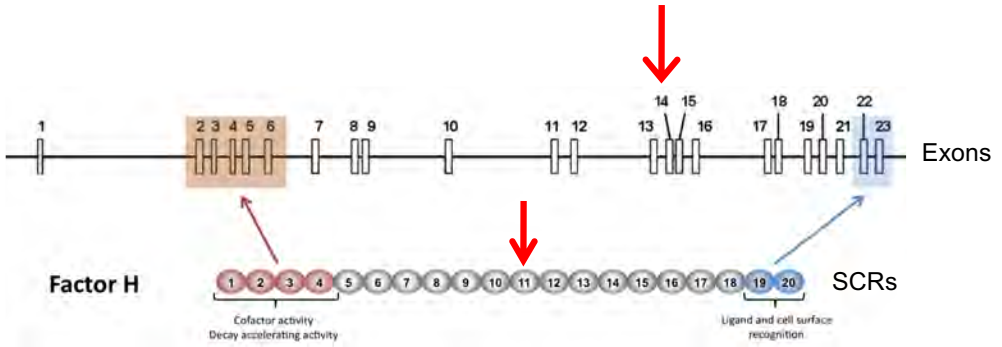
Cofactor activity

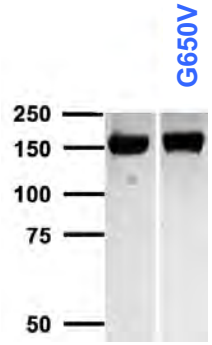


Decay-accelerating activity

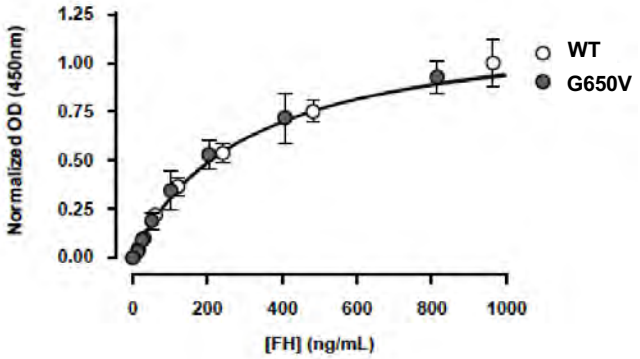
c.1949G>T (G650V)

CADD: 0.18
gnomAD: $2x10^{-4}$

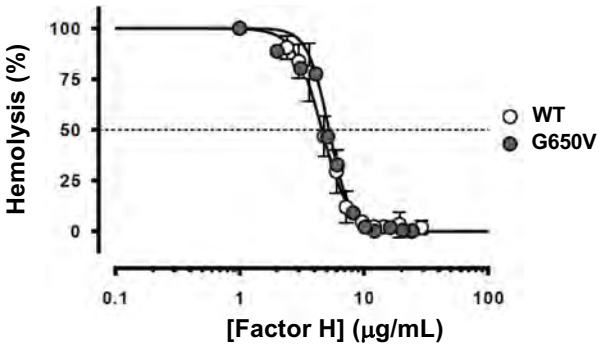




SDS-PAGE
(Non-reduced)



Binding to C3b

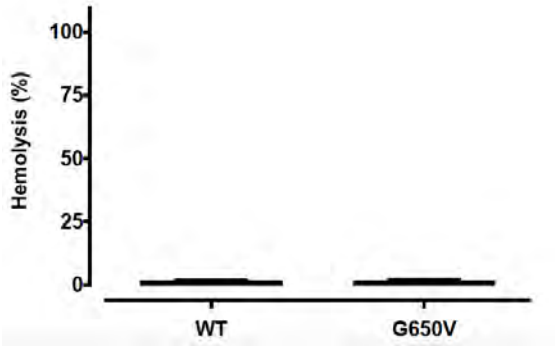


Hemolytic assay

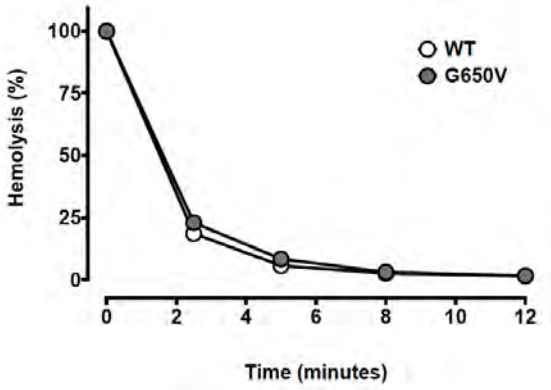
Conclusion: Normal Function
BENIGN

Previous studies: None

Comments:



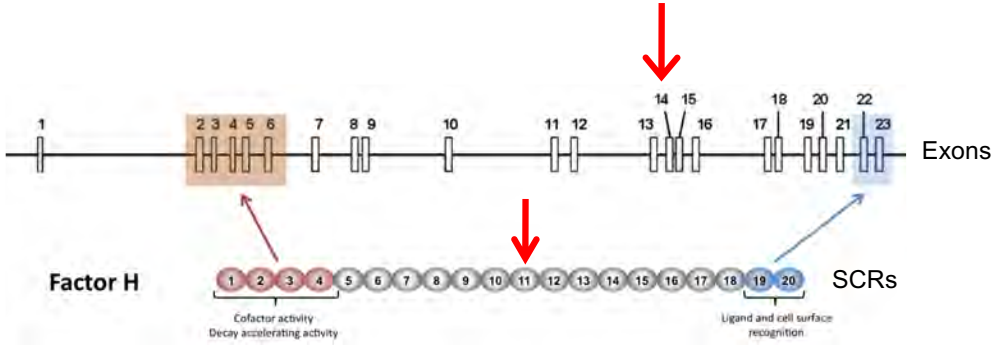
Cofactor activity

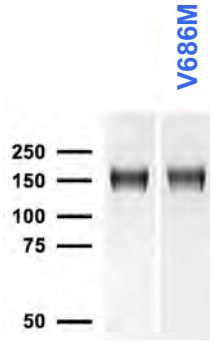


Decay-accelerating activity

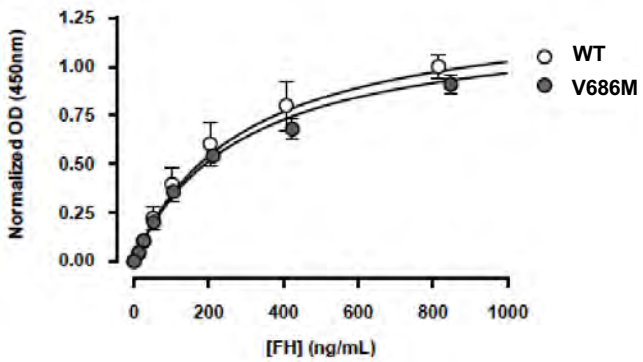
c.2056G>A (V686M)

CADD: 34
gnomAD: Not present

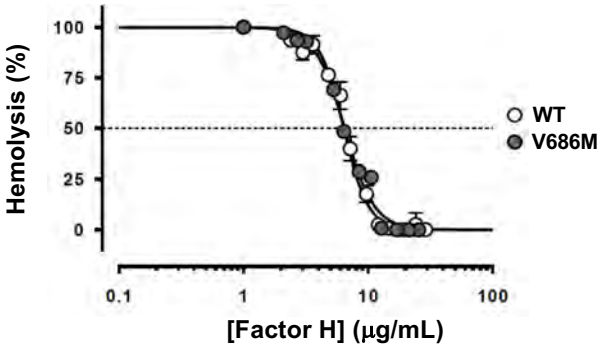




SDS-PAGE
(Non-reduced)



Binding to C3b

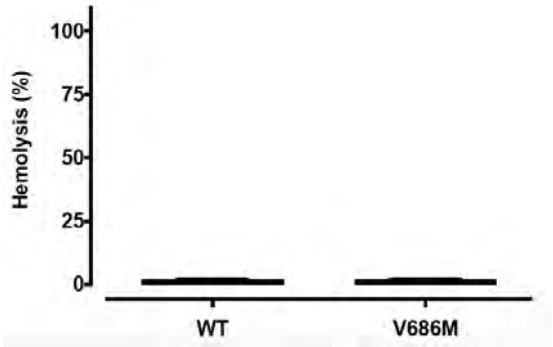


Hemolytic assay

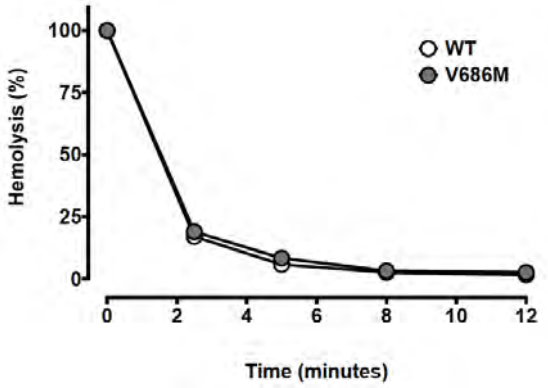
Conclusion: Normal Function
BENIGN

Previous studies: None

Comments:



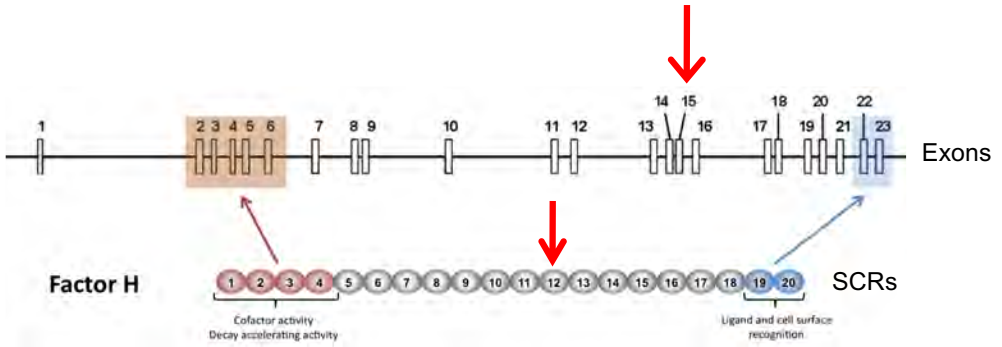
Cofactor activity



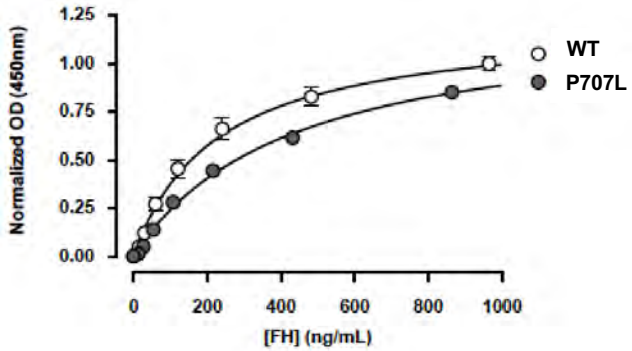
Decay-accelerating activity

c.2120C>T (P707L)

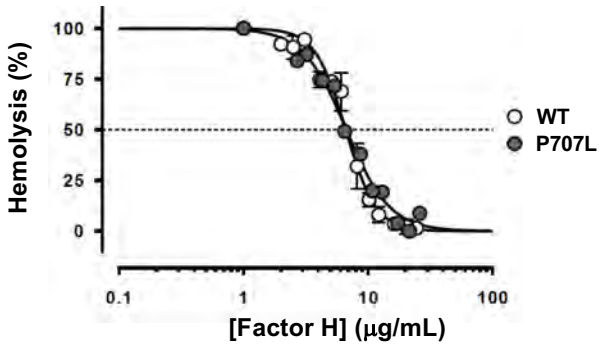
CADD: 25.1
gnomAD: Not present



SDS-PAGE
(Non-reduced)



Binding to C3b

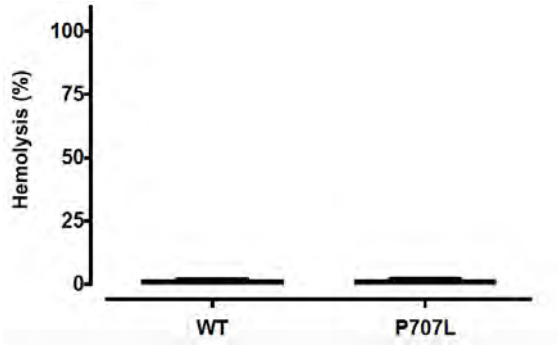


Hemolytic assay

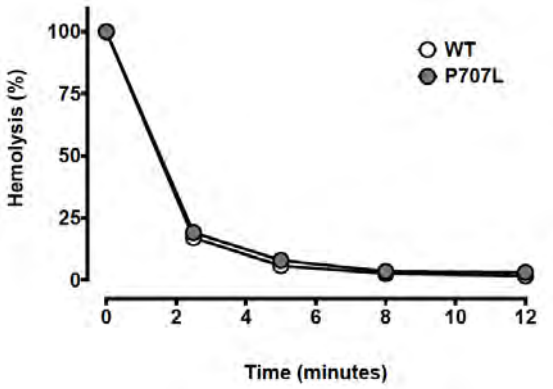
Conclusion: Normal Function
BENIGN

Previous studies: None

Comments:



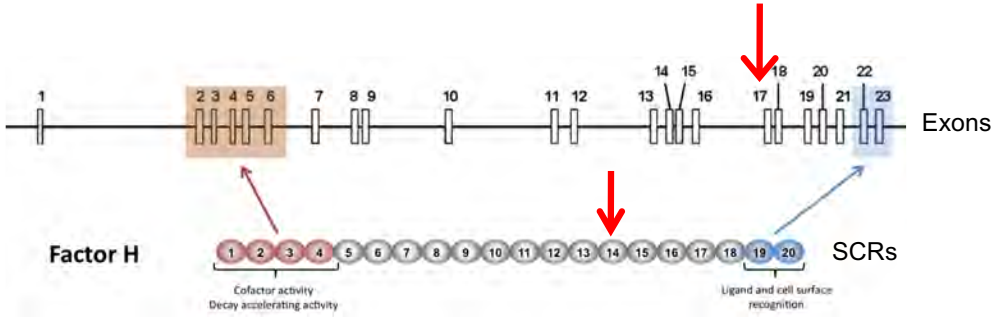
Cofactor activity

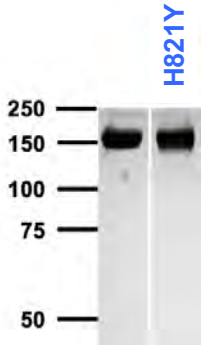


Decay-accelerating activity

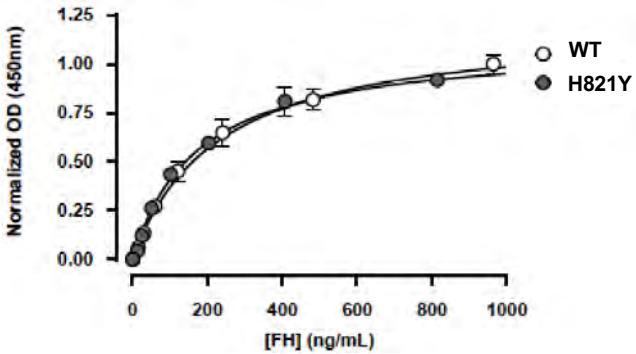
c.2461C>T (H821Y)

CADD: 0.11
gnomAD: $9x10^{-5}$

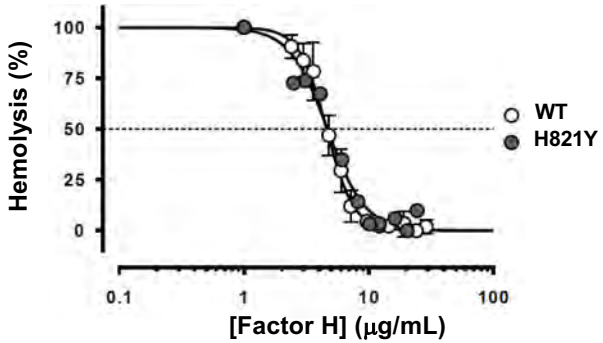




SDS-PAGE
(Non-reduced)



Binding to C3b

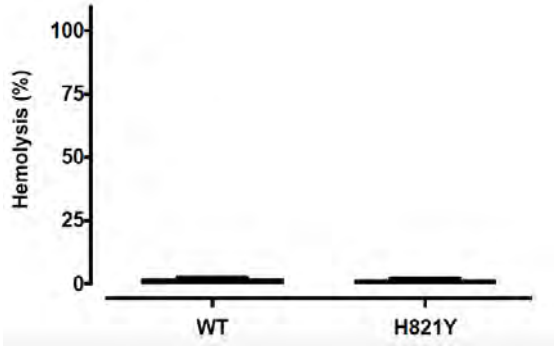


Hemolytic assay

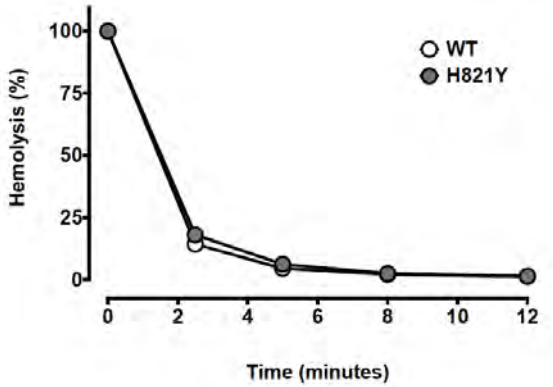
Conclusion: Normal Function
BENIGN

Previous studies: None

Comments:



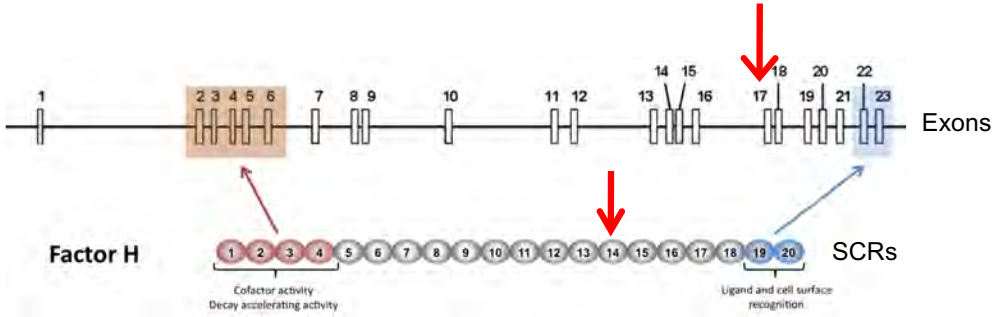
Cofactor activity



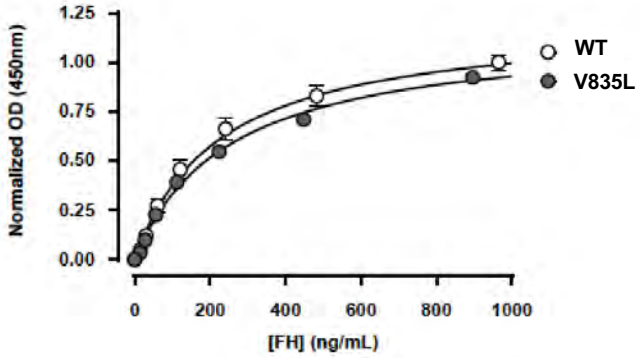
Decay-accelerating activity

c.2503G>T (V835L)

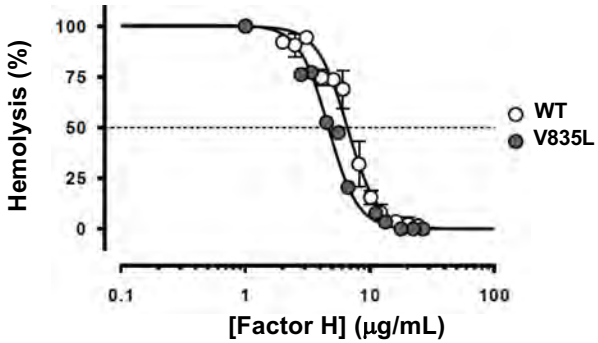
CADD: 0.46
gnomAD: $1x10^{-5}$



SDS-PAGE
(Non-reduced)



Binding to C3b

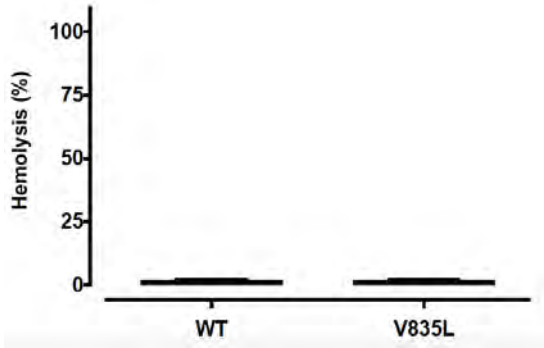


Hemolytic assay

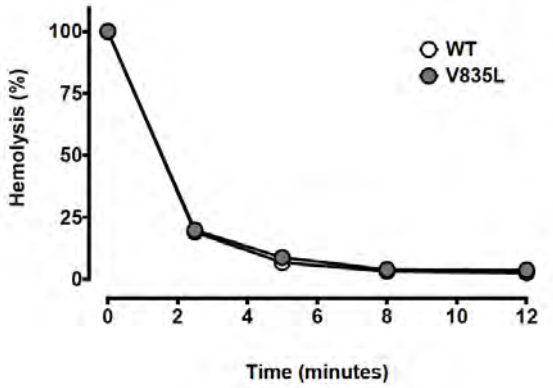
Conclusion: Normal Function
BENIGN

Previous studies: None

Comments:



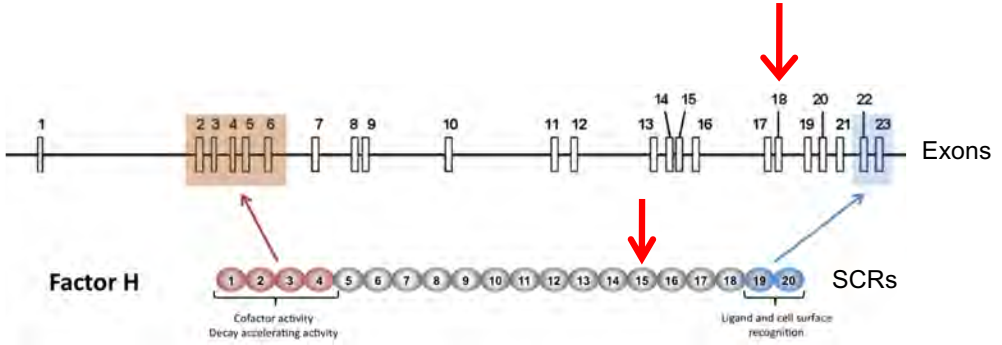
Cofactor activity

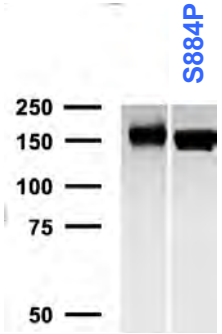


Decay-accelerating activity

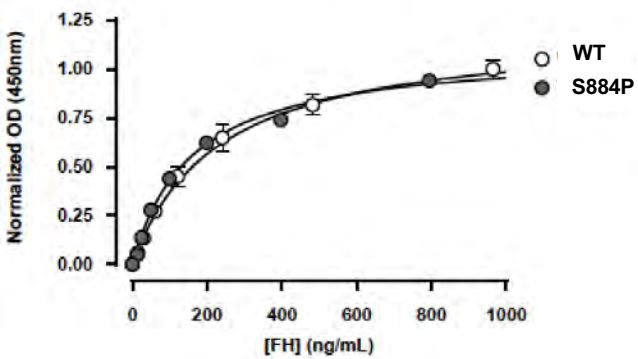
c.2650T>C (S884P)

CADD: 12.28
gnomAD: $3x10^{-5}$

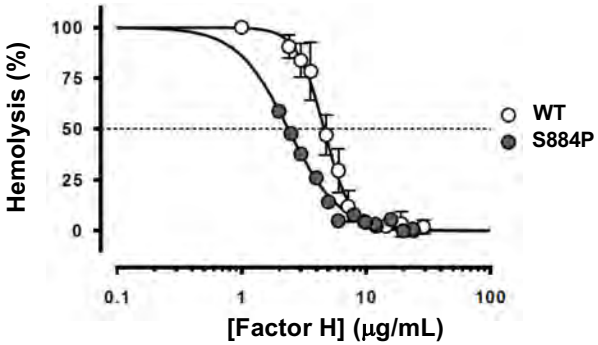




SDS-PAGE
(Non-reduced)



Binding to C3b

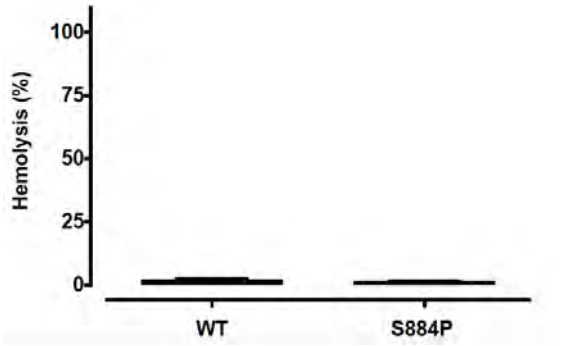


Hemolytic assay

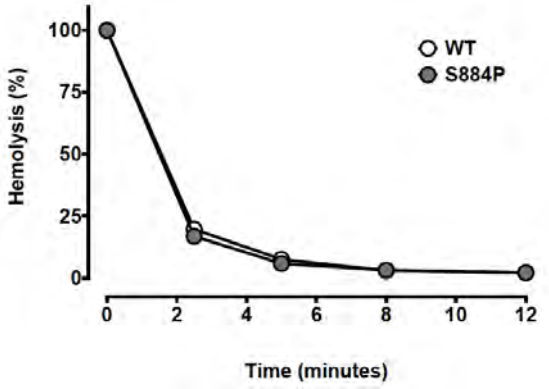
Conclusion: Normal Function
BENIGN

Previous studies: None

Comments:
This variant migrates slightly faster in SDS-PAGE which may indicate a slightly decreased size. Perhaps losing Ser889 eliminates a O-glycosylation site, although no O-glycosylation sites have been described in factor H.



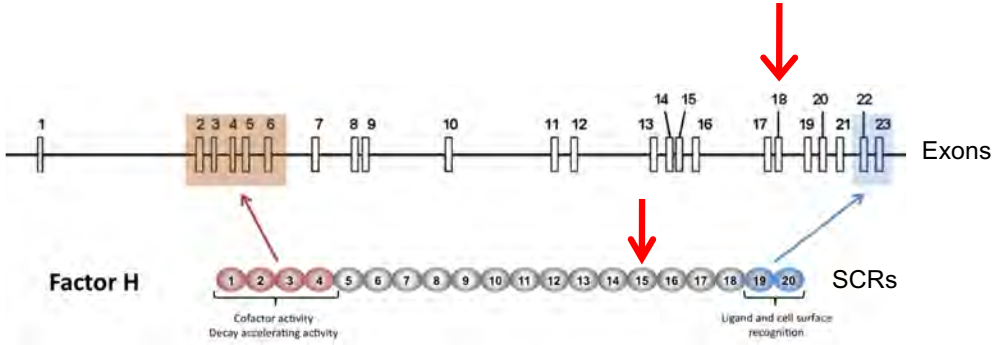
Cofactor activity

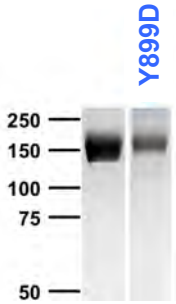


Decay-accelerating activity

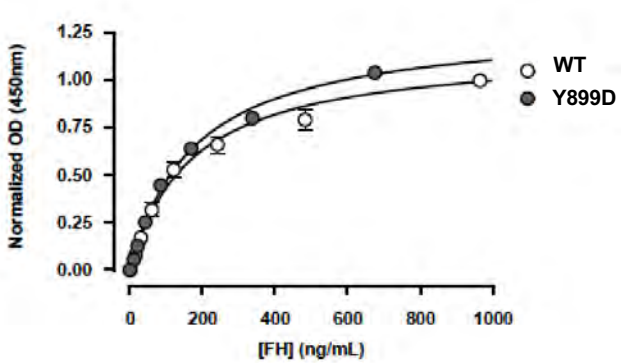
c.2695T>G (Y899D)

CADD: 23
gnomAD: Not present

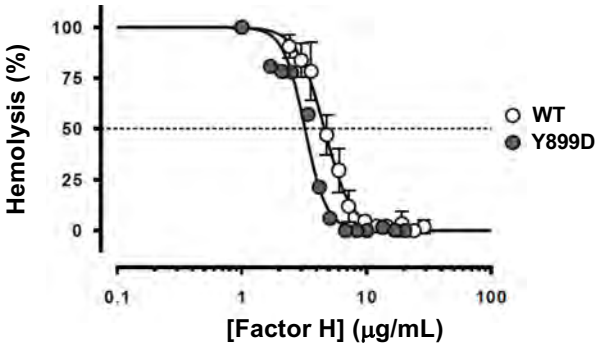




SDS-PAGE
(Non-reduced)

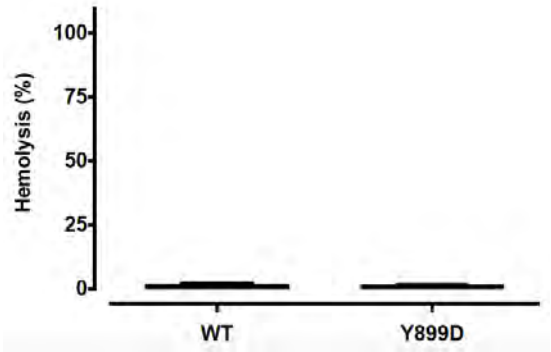


Binding to C3b

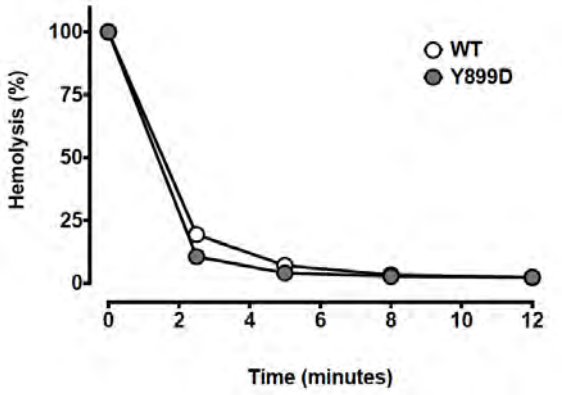


Hemolytic assay

Conclusion: Impaired Expression
PATHOGENIC



Cofactor activity



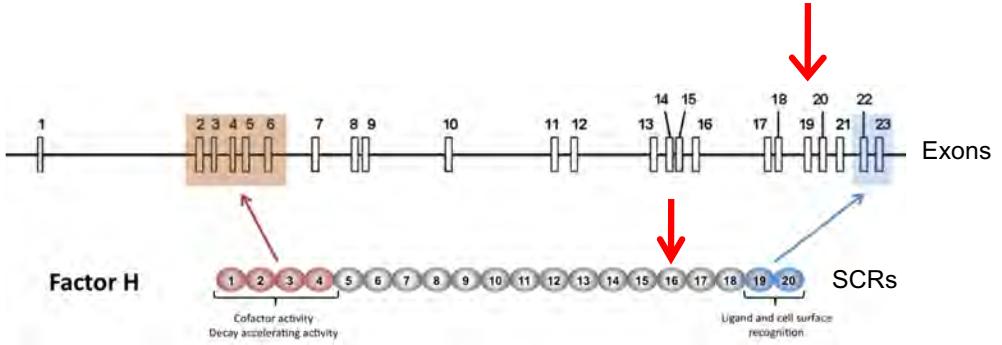
Decay-accelerating activity

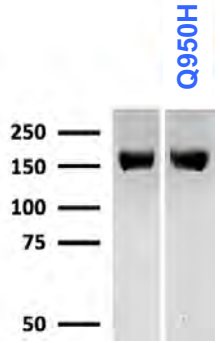
Previous studies: Non expression in Johnson SA, Williams JM, Hakobyan S, et al. Impact of compound heterozygous complement factor H mutations on development of atypical hemolytic uremic syndrome—A pedigree revisited. *Molecular Immunology*. 2010;47(7):1585-1591.

Comments:
SDS-PAGE shows a weak FH band under non-reducing conditions, suggesting that this variant likely affects expression of the protein and results in a factor H deficiency.

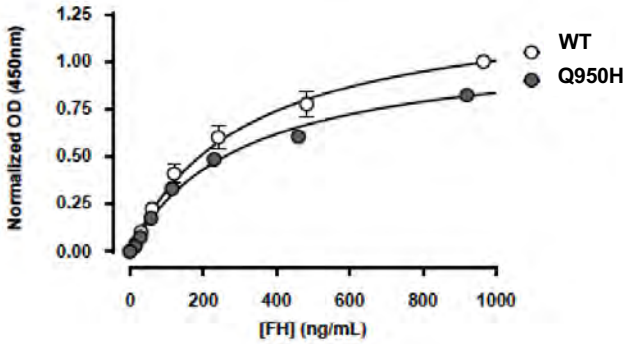
c.2850G>T (Q950H)

CADD: 14.17
gnomAD: $3x10^{-3}$

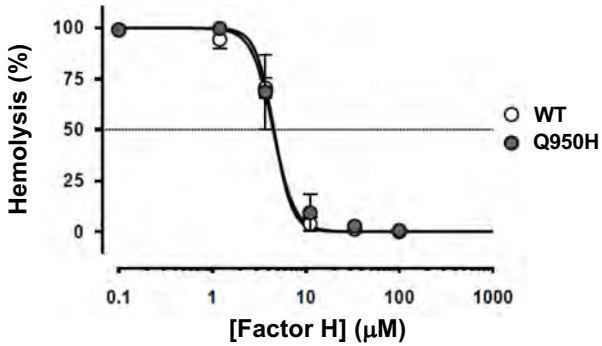




SDS-PAGE
(Non-reduced)



Binding to C3b

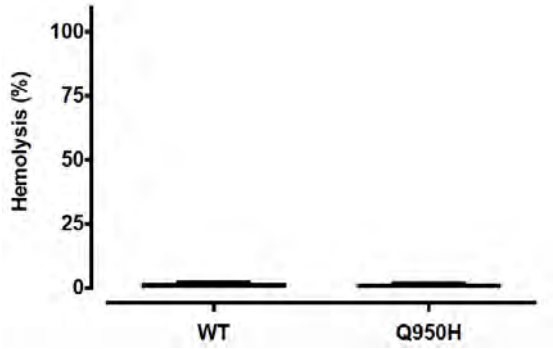


Hemolytic assay

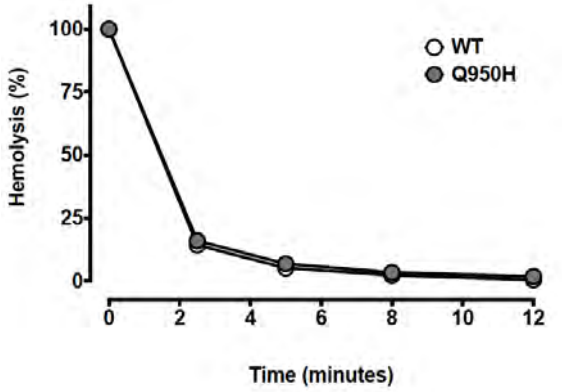
Conclusion: Normal Function
BENIGN

Previous studies: Benign in Mohlin FC, Nilsson SC, Levart TK, et al. Functional characterization of two novel non-synonymous alterations in CD46 and a Q950H change in factor H found in atypical hemolytic uremic syndrome patients. *Molecular Immunology*. 2015;65(2):367-376.

Comments:
Common polymorphism that does not affect function



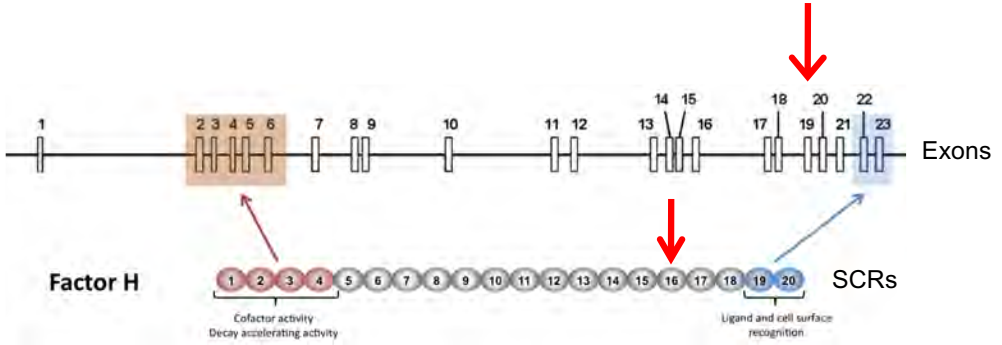
Cofactor activity

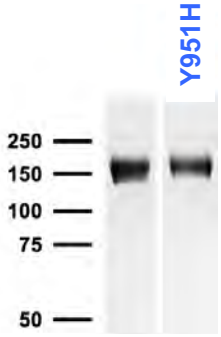


Decay-accelerating activity

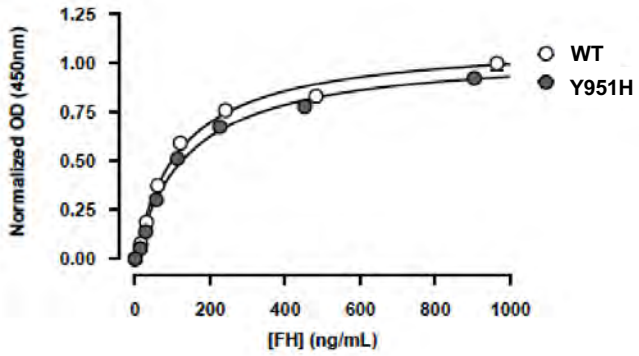
c.2851T>C (Y951H)

CADD: 14.6
gnomAD: $1x10^{-5}$

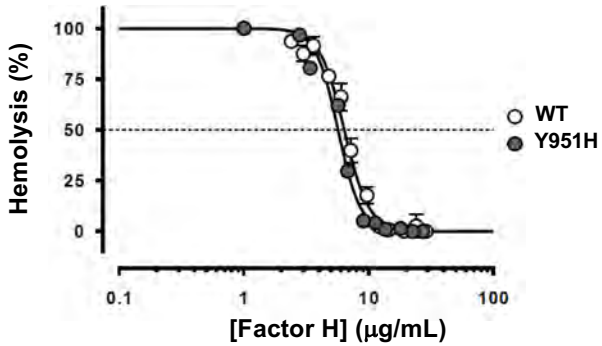




SDS-PAGE
(Non-reduced)



Binding to C3b

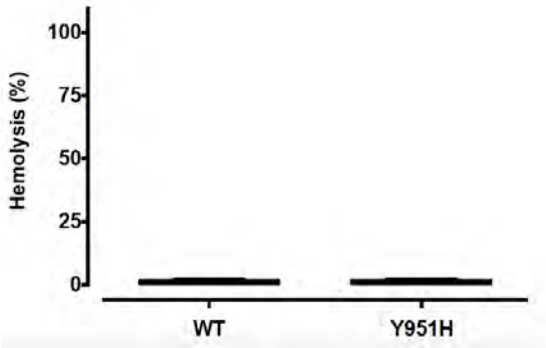


Hemolytic assay

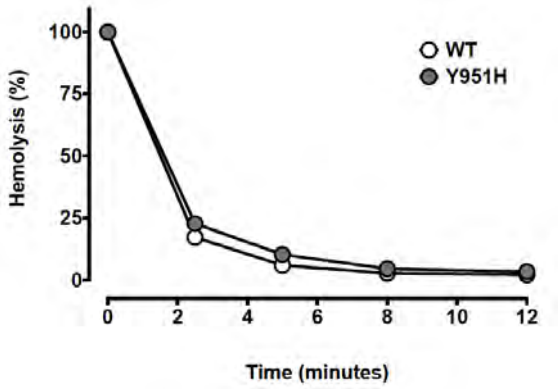
Conclusion: Normal Function
BENIGN

Previous studies: None

Comments:



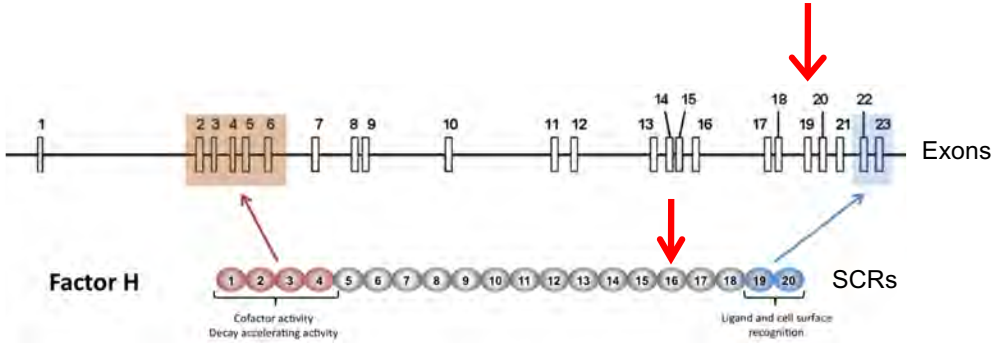
Cofactor activity

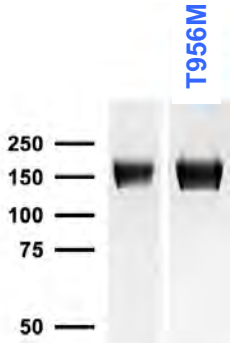


Decay-accelerating activity

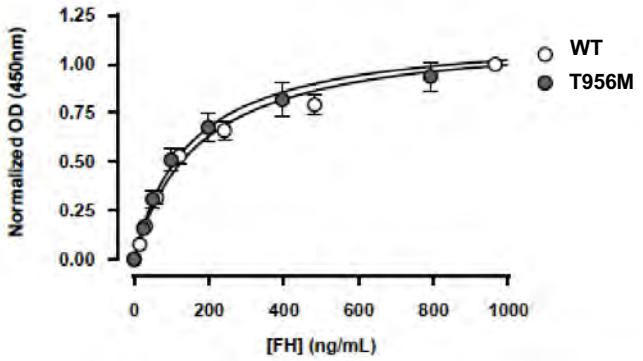
c.2867C>T (T956M)

CADD: 14.99
gnomAD: $1x10^{-3}$

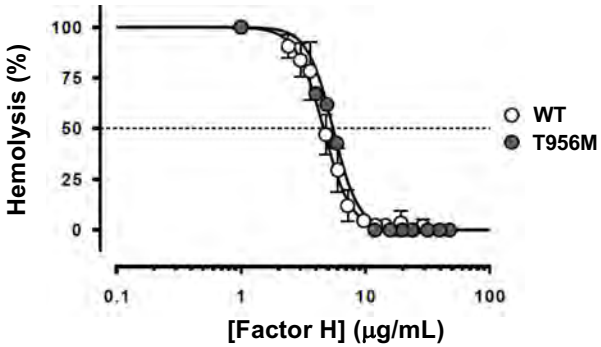




SDS-PAGE
(Non-reduced)

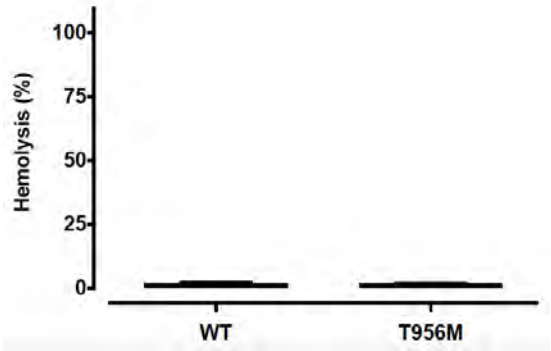


Binding to C3b

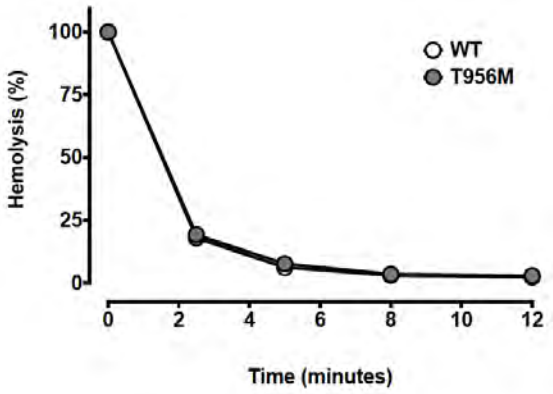


Hemolytic assay

Conclusion: Normal Function
BENIGN



Cofactor activity



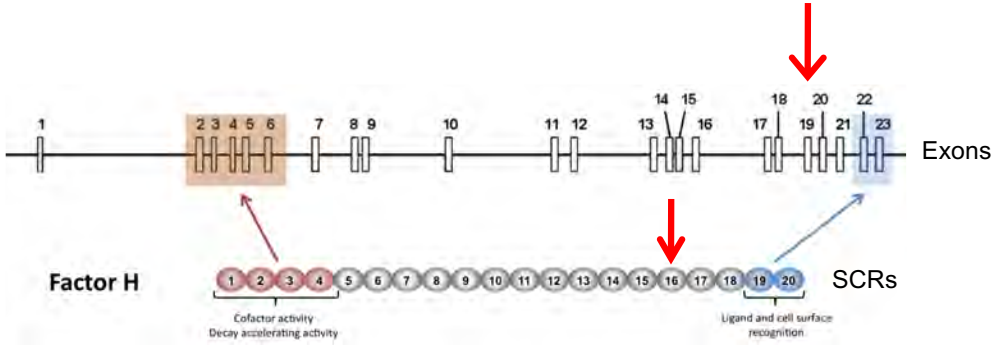
Decay-accelerating activity

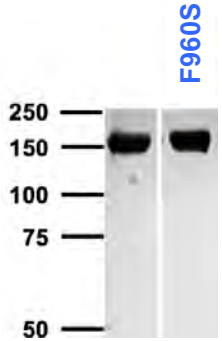
Previous studies: Benign in by Merinero HM, García SP, García-Fernández J, Arjona E, Tortajada A, Rodríguez de Córdoba S. Complete functional characterization of disease-associated genetic variants in the complement factor H gene. *Kidney International*. 2018;93(2):470-481.

Comments:

c.2879T>C (F960S)

CADD: 0
gnomAD: $6x10^{-5}$





SDS-PAGE
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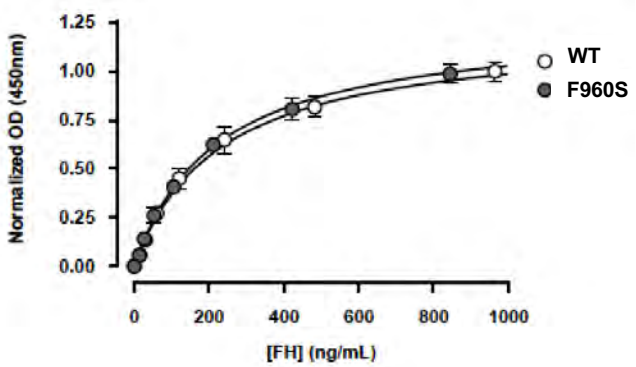
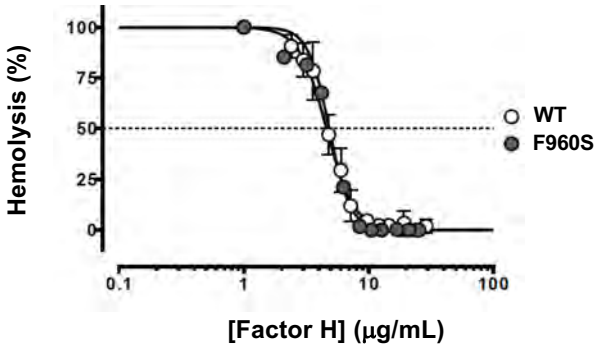


Binding to C3b

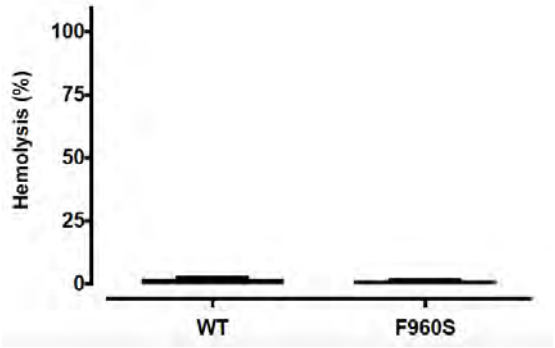


Hemolytic assay

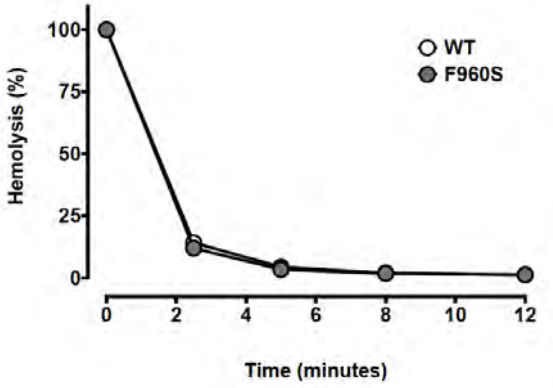
Conclusion: Normal Function
BENIGN

Previous studies: None

Comments:



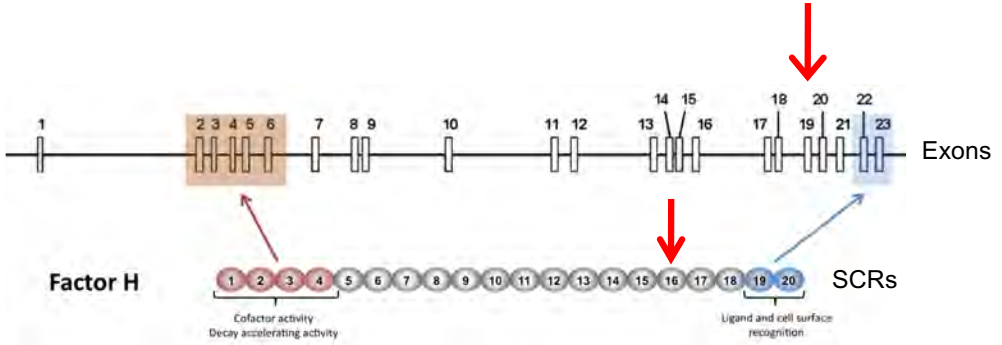
Cofactor activity

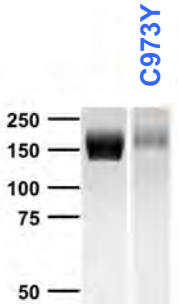


Decay-accelerating activity

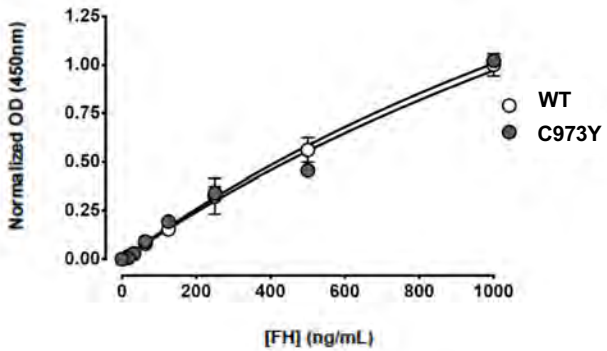
c.2918G>A (C973Y)

CADD: 22.8
gnomAD: Not present

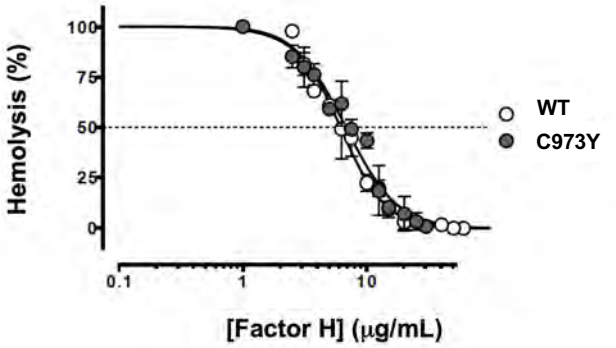




SDS-PAGE
(Non-reduced)

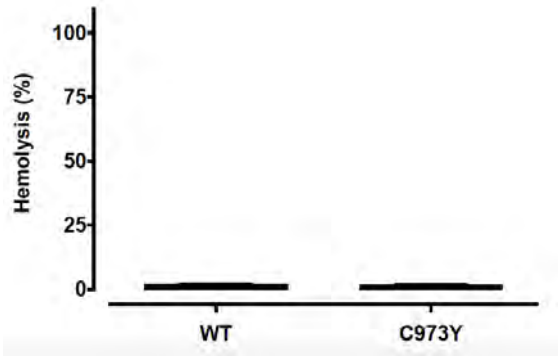


Binding to C3b

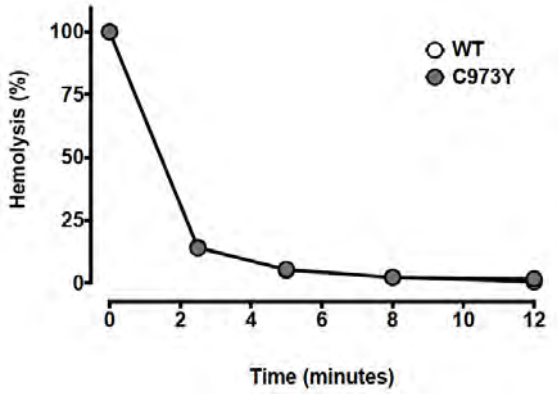


Hemolytic assay

Conclusion: Impaired Expression
PATHOGENIC



Cofactor activity



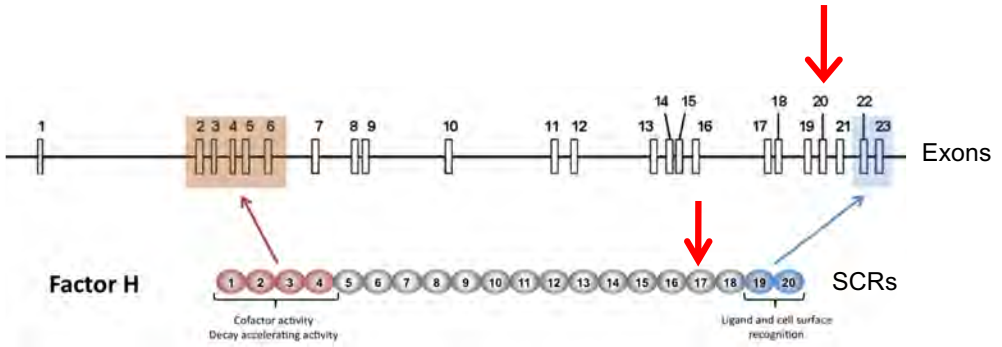
Decay-accelerating activity

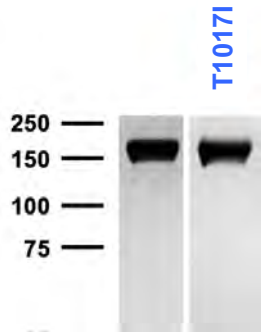
Previous studies: Non expression in Saland JM, Emre SH, Shneider BL, et al. Favorable Long-Term Outcome after Liver-Kidney Transplant for Recurrent Hemolytic Uremic Syndrome Associated with a Factor H Mutation. *American Journal of Transplantation*. 2006;6(8):1948-1952.

Comments:
SDS-PAGE shows a weak FH band under non-reducing conditions, suggesting that this variant likely affects expression of the protein and results in a factor H deficiency.

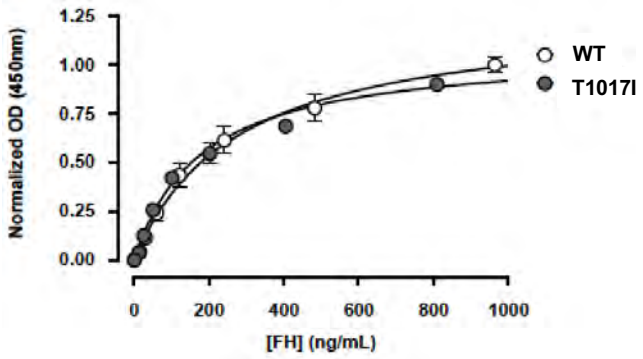
c.3050C>T (T1017I)

CADD: 10.49
gnomAD: $1x10^{-3}$

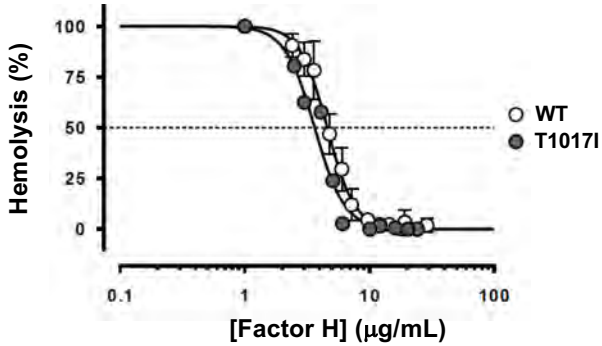




SDS-PAGE
(Non-reduced)



Binding to C3b

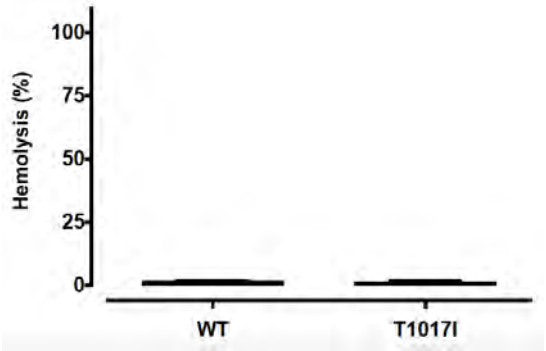


Hemolytic assay

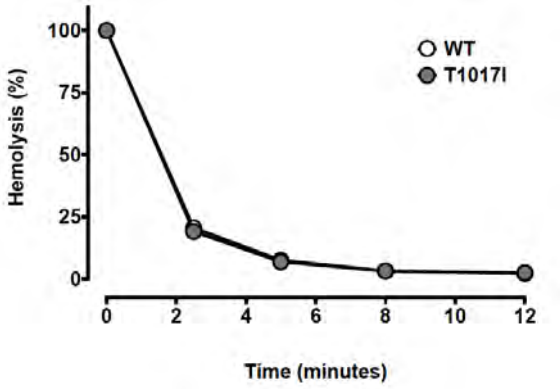
Conclusion: Normal Function
BENIGN

Previous studies: None

Comments:



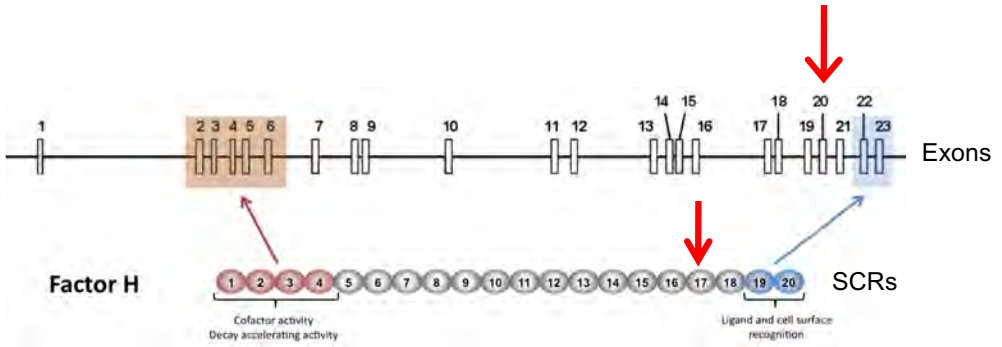
Cofactor activity

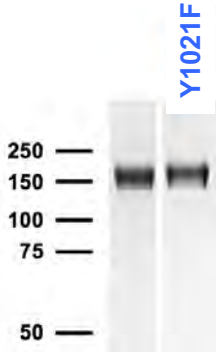


Decay-accelerating activity

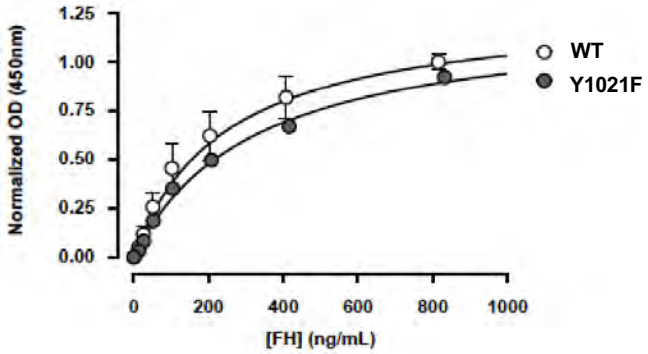
c.3062A>T (Y1021F)

CADD: 0.84
gnomAD: Not present

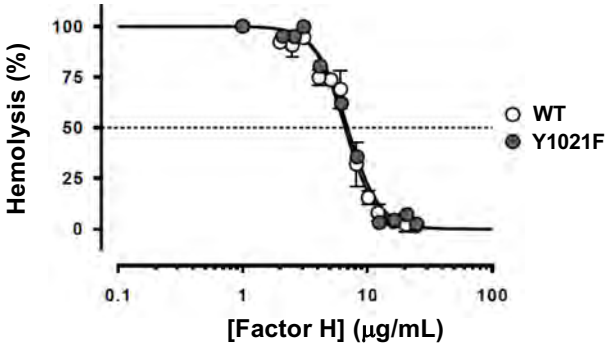




SDS-PAGE
(Non-reduced)



Binding to C3b

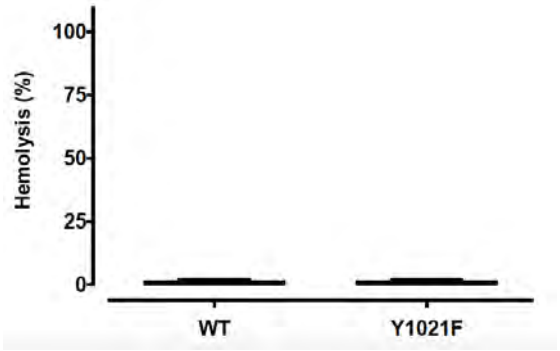


Hemolytic assay

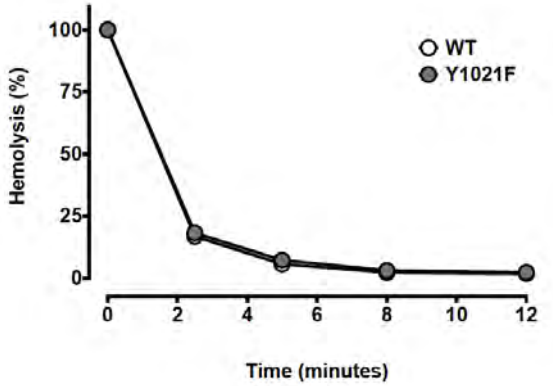
Conclusion: Normal Function
BENIGN

Previous studies: None

Comments:



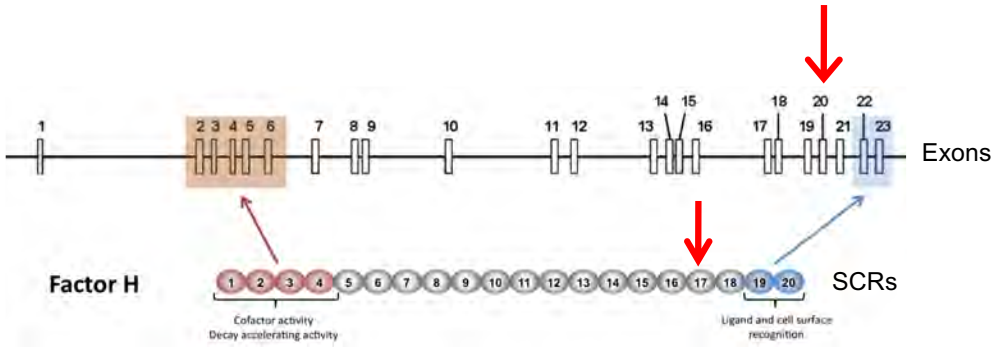
Cofactor activity

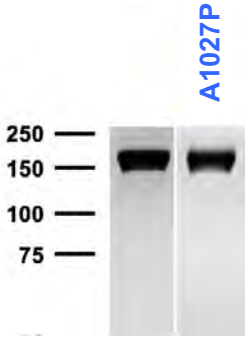


Decay-accelerating activity

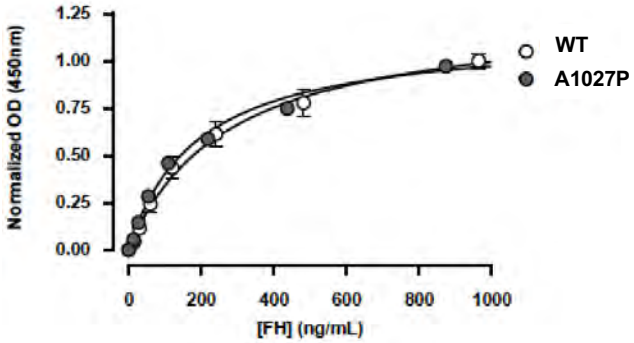
c.3079G>C (A1027P)

CADD: 0
gnomAD: $6x10^{-5}$

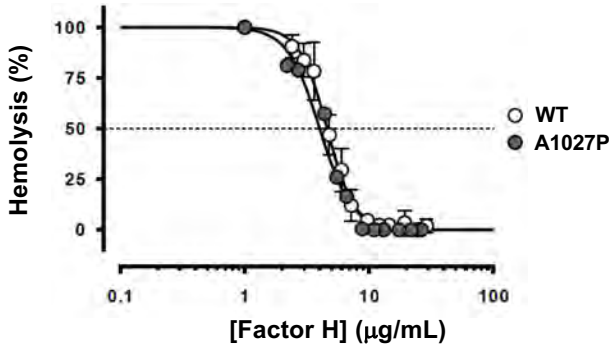




SDS-PAGE
(Non-reduced)



Binding to C3b

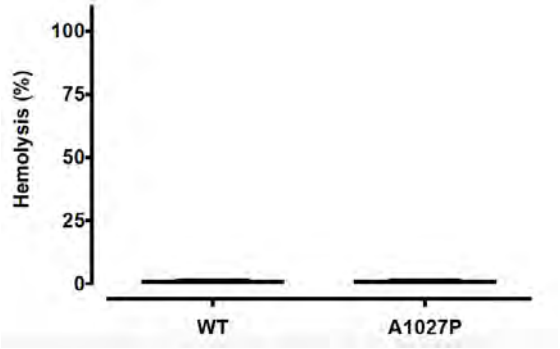


Hemolytic assay

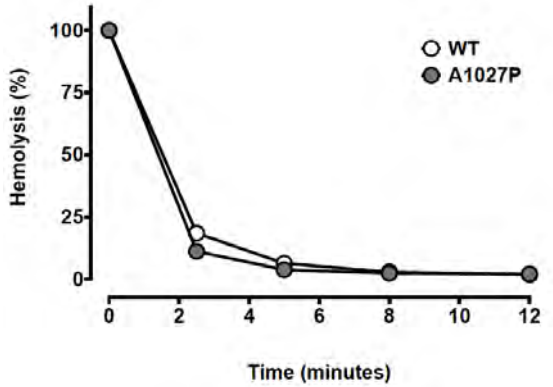
Conclusion: Normal Function
BENIGN

Previous studies: None

Comments:



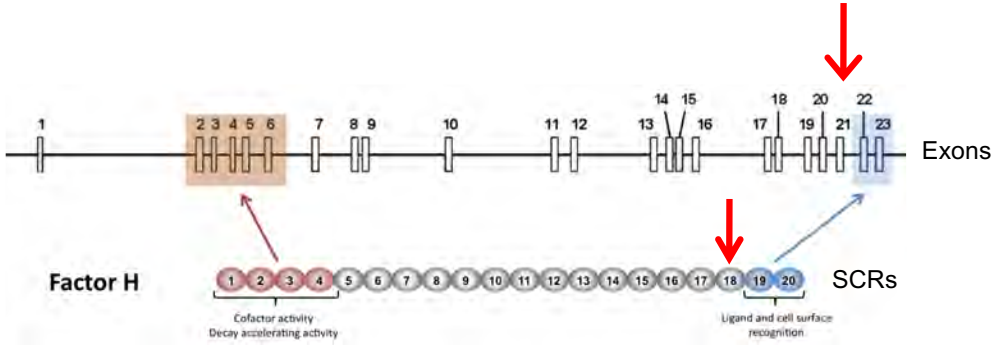
Cofactor activity



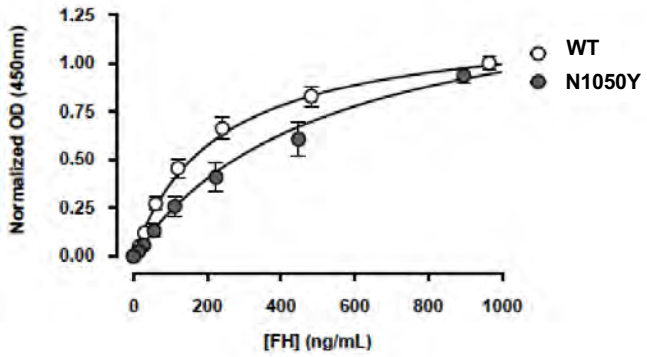
Decay-accelerating activity

c.3148A>T (N1050Y)

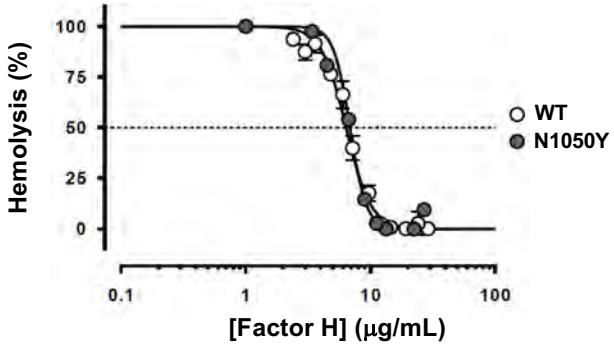
CADD: 14.17
gnomAD: $1x10^{-2}$



SDS-PAGE
(Non-reduced)



Binding to C3b

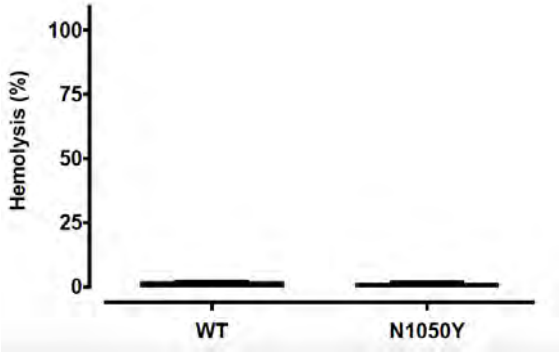


Hemolytic assay

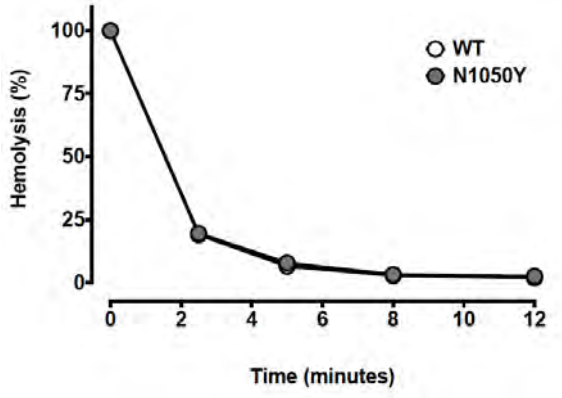
Conclusion: Normal Function
BENIGN

Previous studies: Benign in Richards A, Buddles MR, Donne RL, et al. Factor H Mutations in Hemolytic Uremic Syndrome Cluster in Exons 18–20, a Domain Important for Host Cell Recognition. *The American Journal of Human Genetics*. 2001;68(2):485-490.

Comments:
Common polymorphism that does not affect function



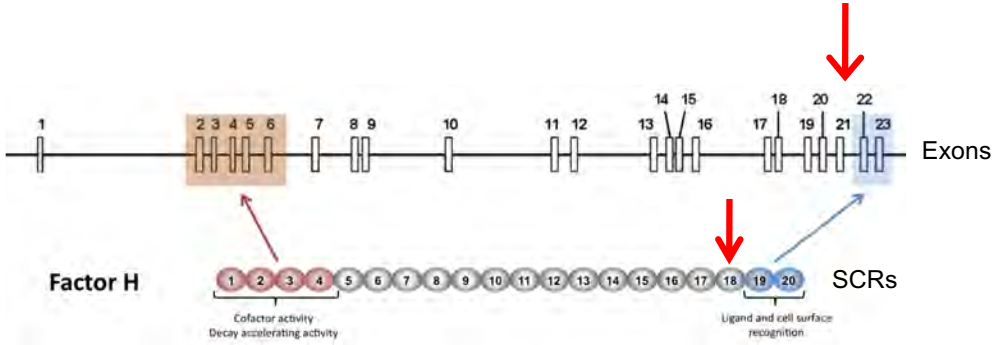
Cofactor activity

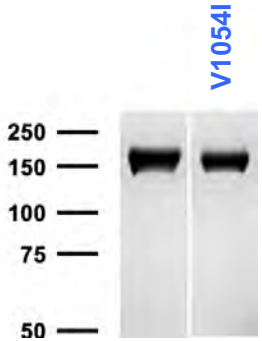


Decay-accelerating activity

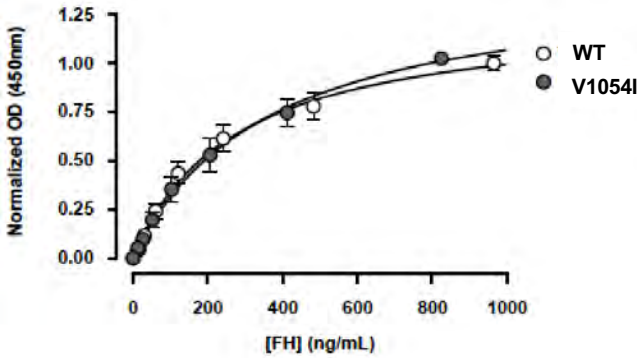
c.3160G>A (V1054I)

CADD: 16.12
gnomAD: $5x10^{-5}$

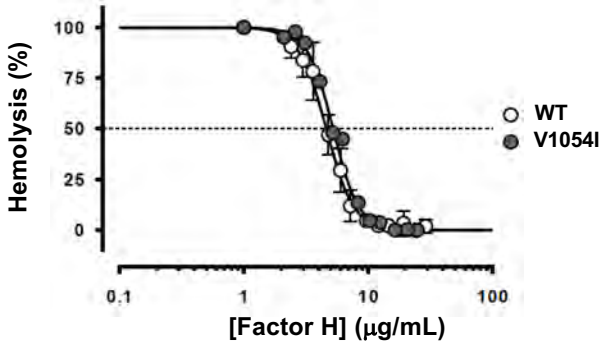




SDS-PAGE
(Non-reduced)



Binding to C3b

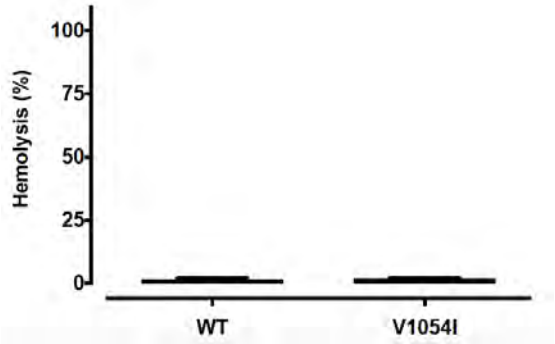


Hemolytic assay

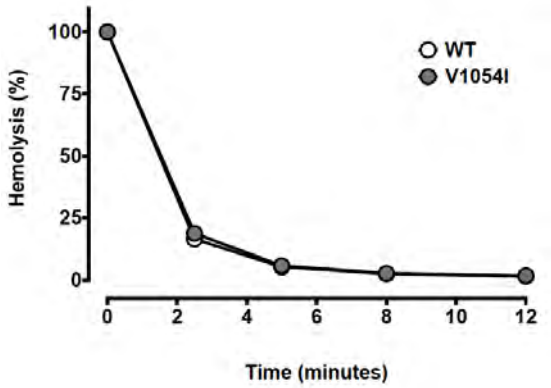
Conclusion: Normal Function
BENIGN

Previous studies: None

Comments:



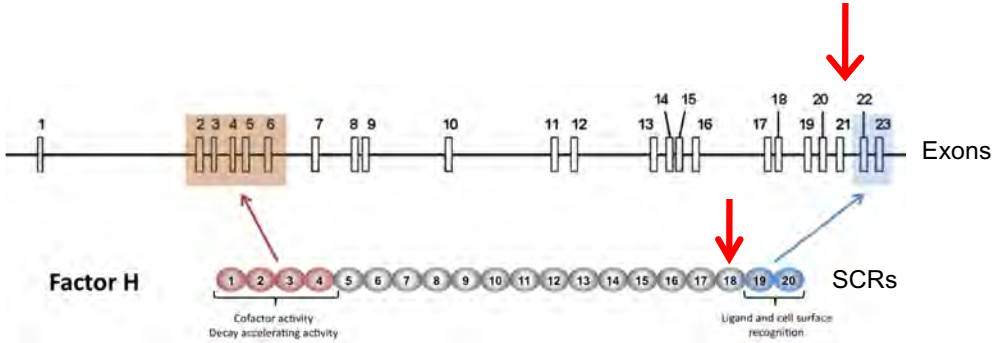
Cofactor activity

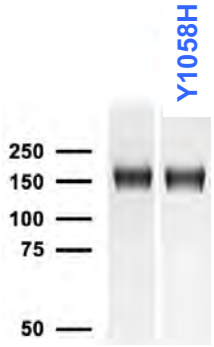


Decay-accelerating activity

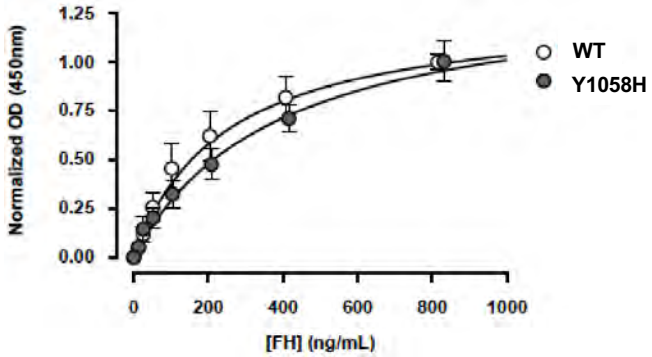
c.3172T>C (Y1058H)

CADD: 0
gnomAD: $6x10^{-4}$

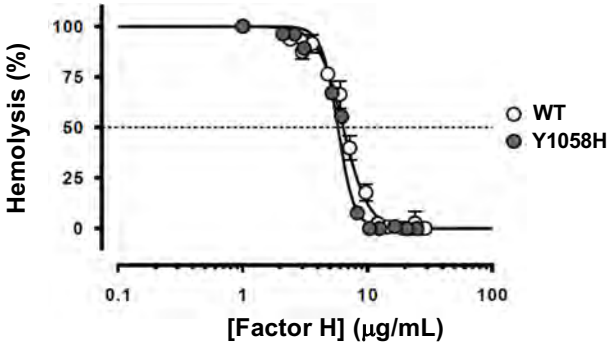




SDS-PAGE
(Non-reduced)



Binding to C3b

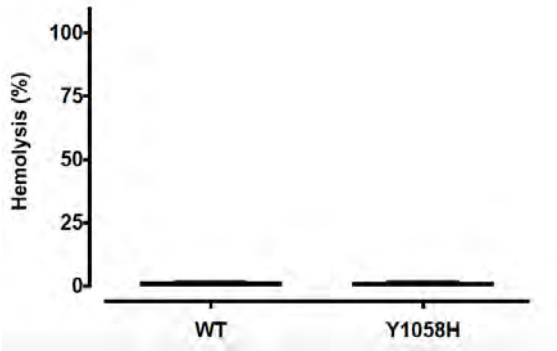


Hemolytic assay

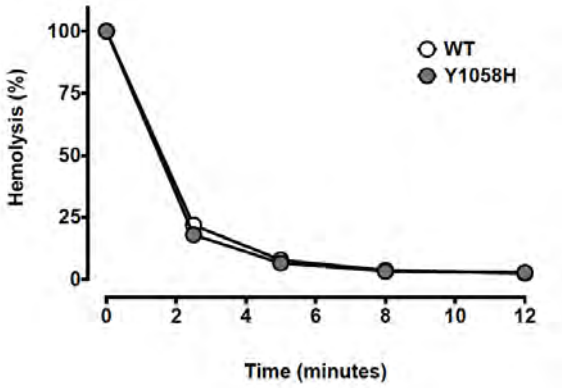
Conclusion: Normal Function
BENIGN

Previous studies: None

Comments:



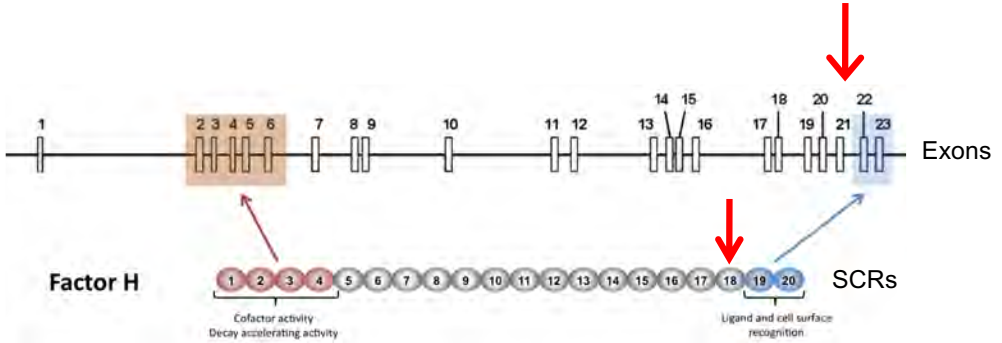
Cofactor activity

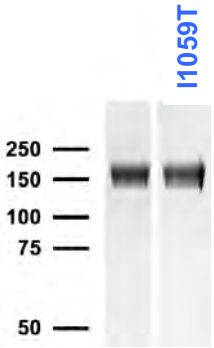


Decay-accelerating activity

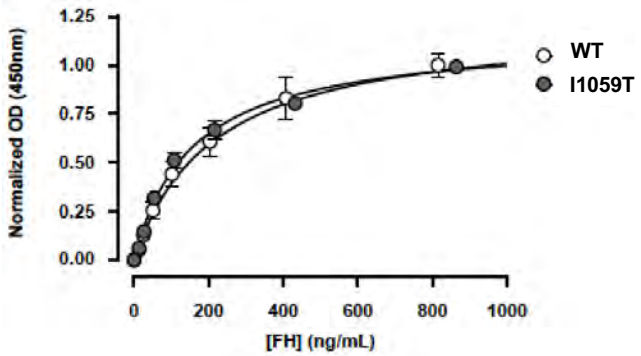
c.3176T>C (I1059T)

CADD: 12.6
gnomAD: $7x10^{-3}$

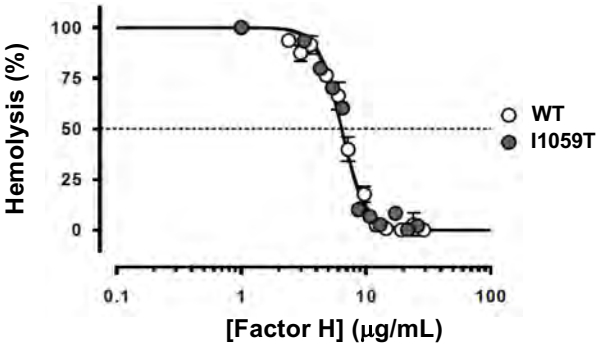




SDS-PAGE
(Non-reduced)



Binding to C3b

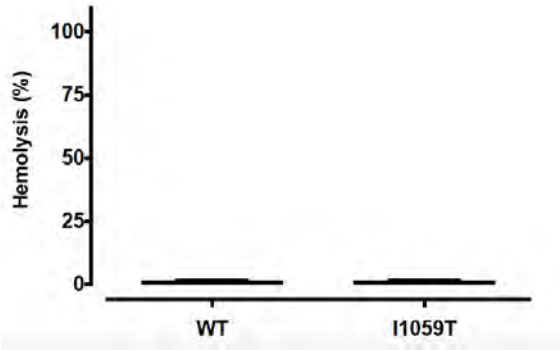


Hemolytic assay

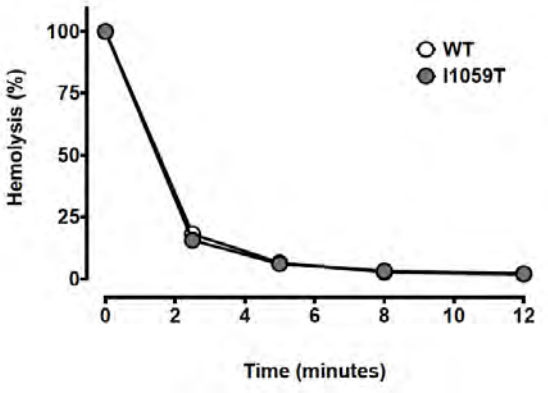
Conclusion: Normal Function
BENIGN

Previous studies: None

Comments:



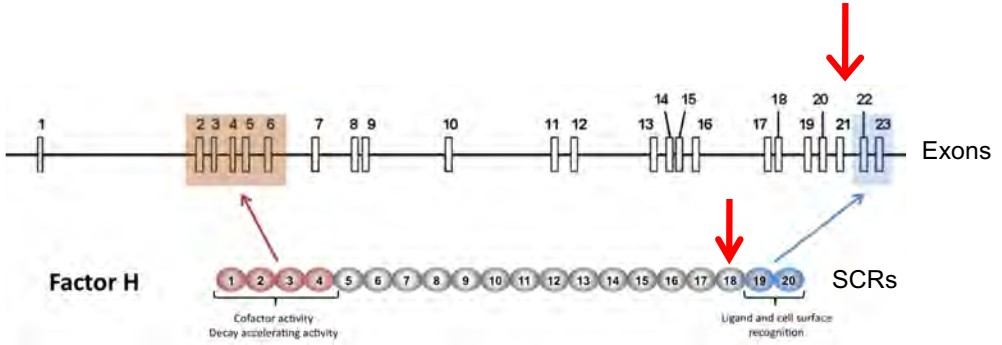
Cofactor activity

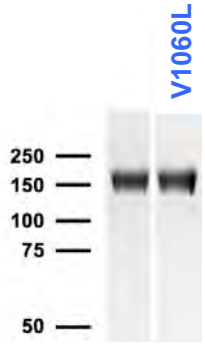


Decay-accelerating activity

c.3178G>C (V1060L)

CADD: 0
gnomAD: $5x10^{-4}$





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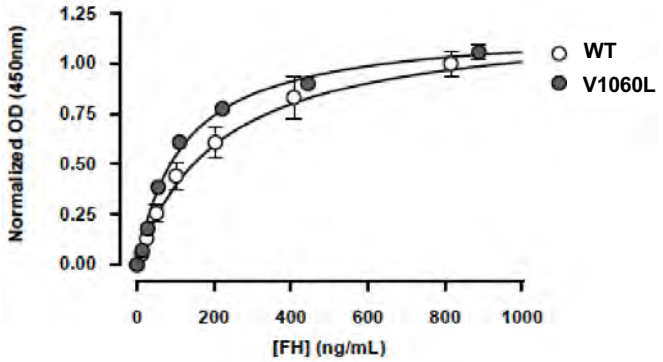
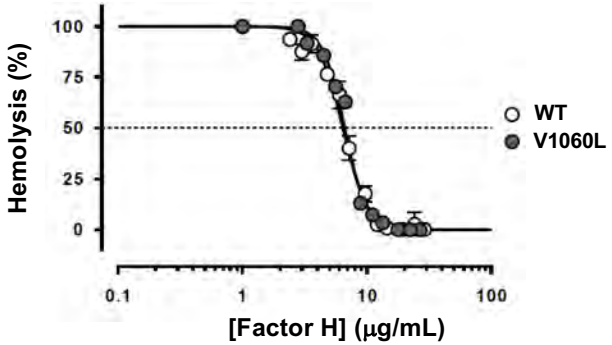


Binding to C3b

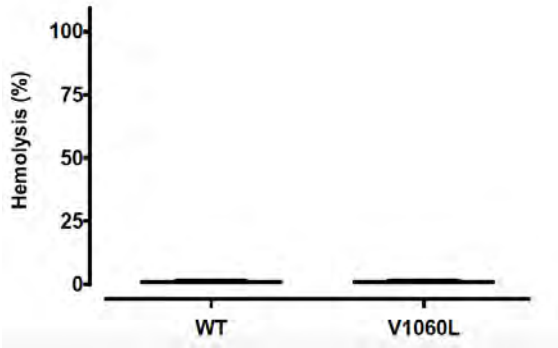


Hemolytic assay

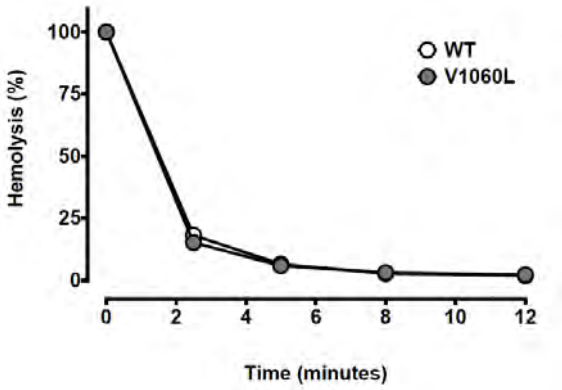
Conclusion: Normal Function
BENIGN

Previous studies: None

Comments:



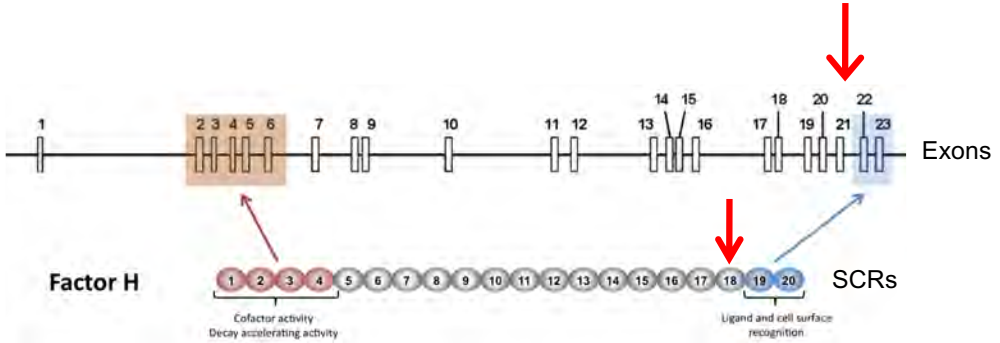
Cofactor activity

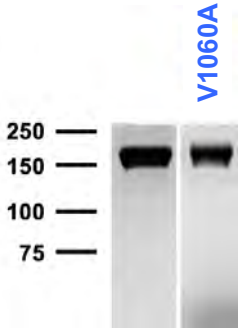


Decay-accelerating activity

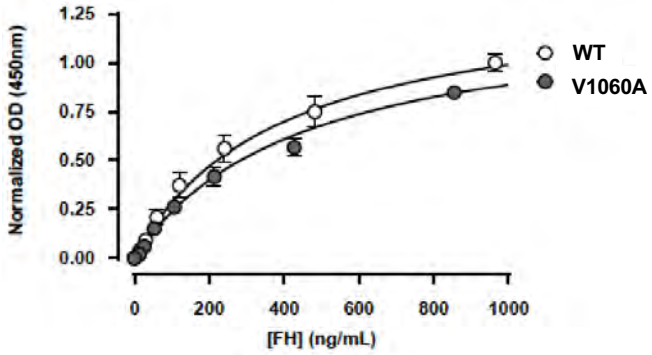
c.3179T>C (V1060A)

CADD: 1.25
gnomAD: Not present

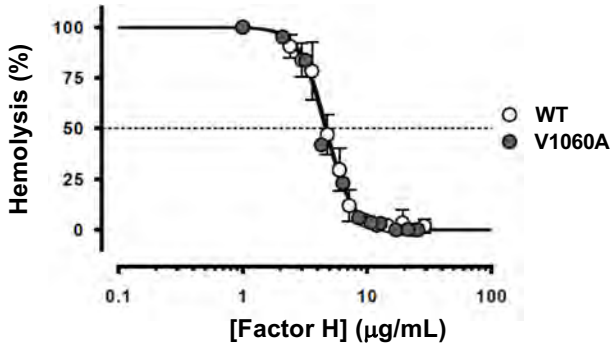




SDS-PAGE
(Non-reduced)



Binding to C3b

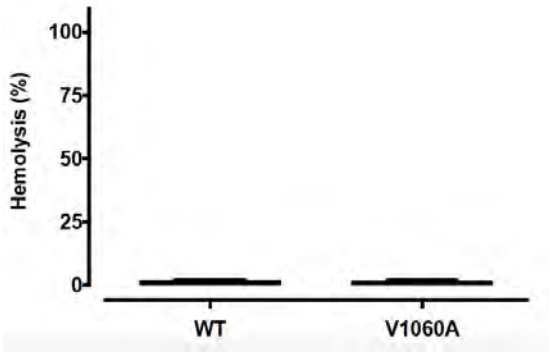


Hemolytic assay

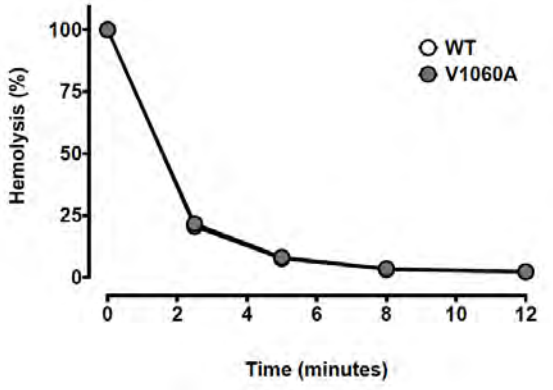
Conclusion: Normal Function
BENIGN

Previous studies: None

Comments:



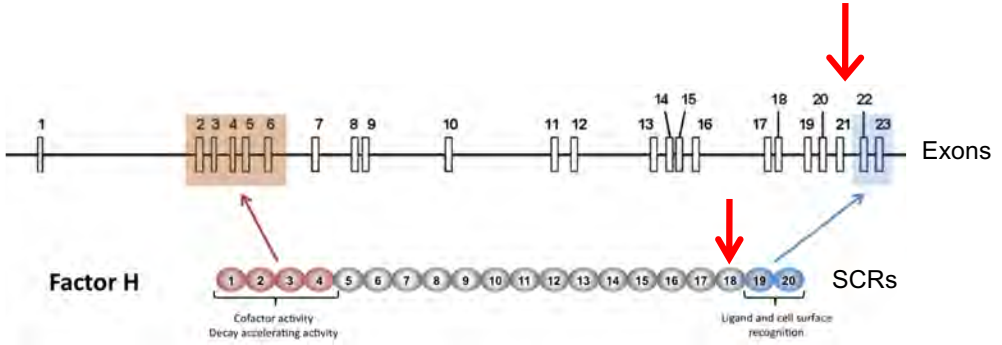
Cofactor activity



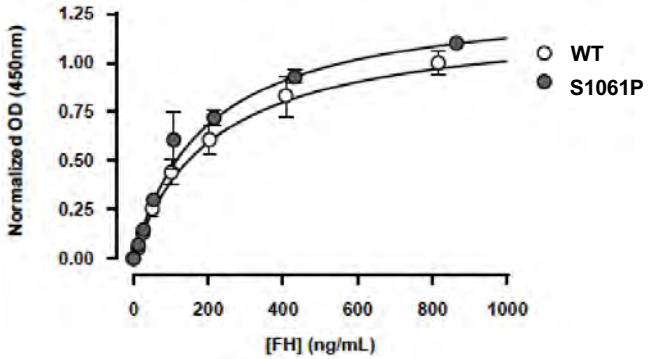
Decay-accelerating activity

c.3181T>C (S1061P)

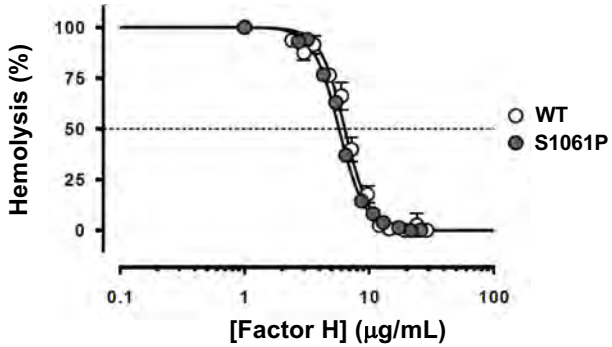
CADD: 4.84
gnomAD: Not present



SDS-PAGE
(Non-reduced)



Binding to C3b

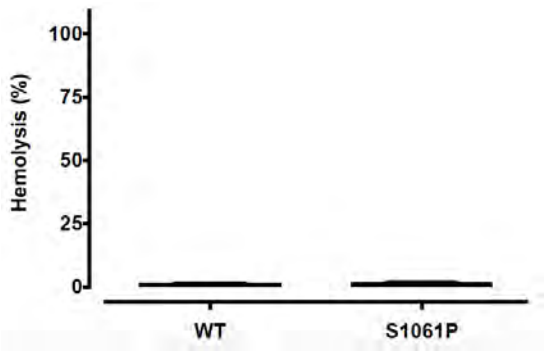


Hemolytic assay

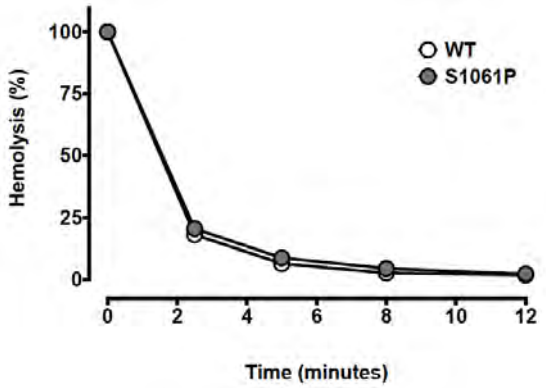
Conclusion: Normal Function
BENIGN

Previous studies: None

Comments:



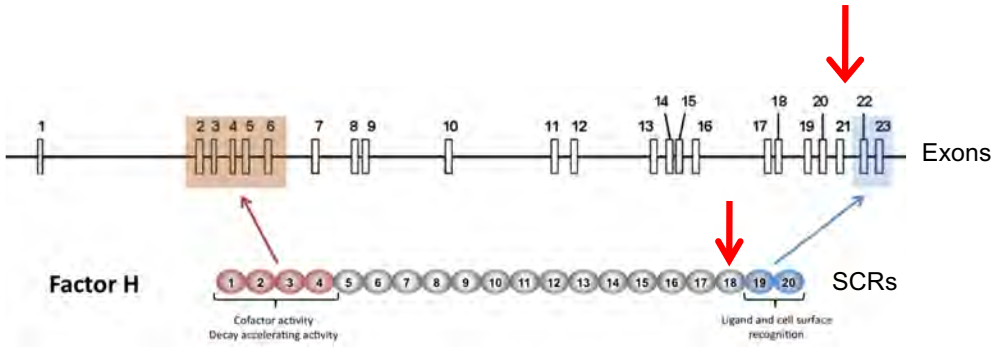
Cofactor activity

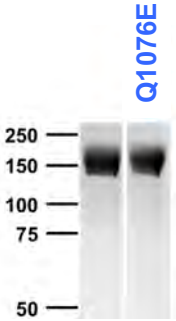


Decay-accelerating activity

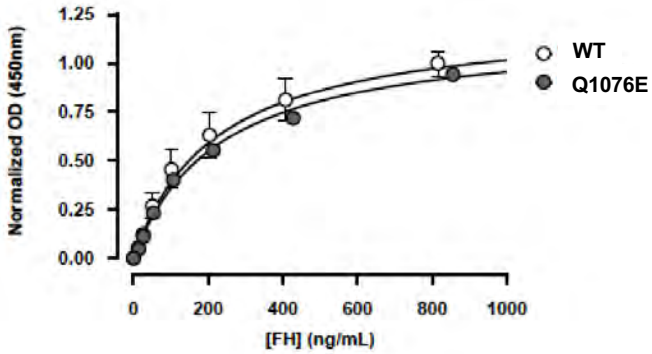
c.3226C>G (Q1076E)

CADD: 3.88
gnomAD: $3x10^{-4}$

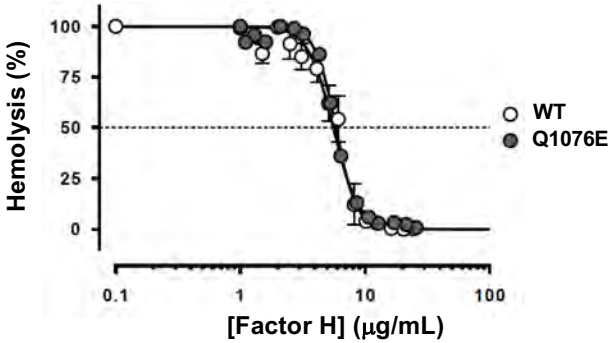




SDS-PAGE
(Non-reduced)



Binding to C3b

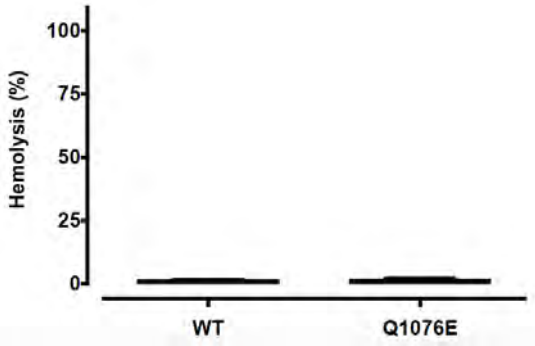


Hemolytic assay

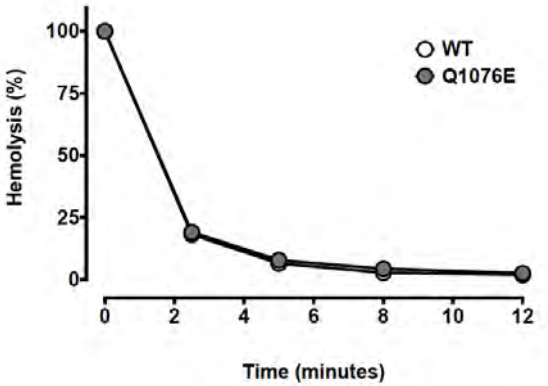
Conclusion: Normal Function
BENIGN

Previous studies: None

Comments:



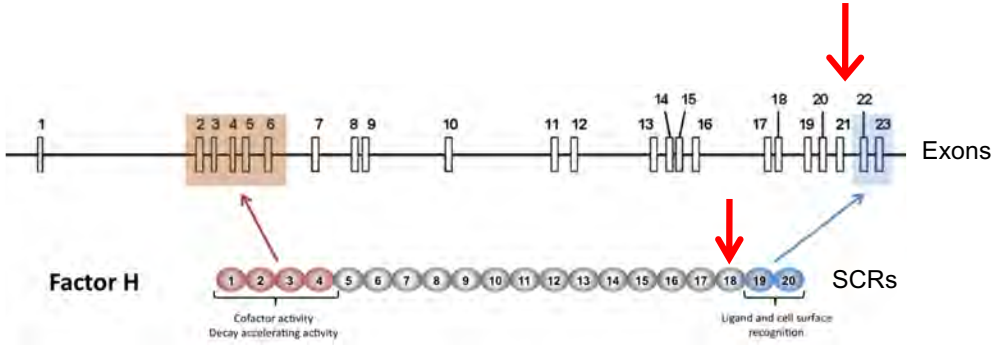
Cofactor activity

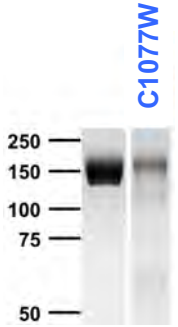


Decay-accelerating activity

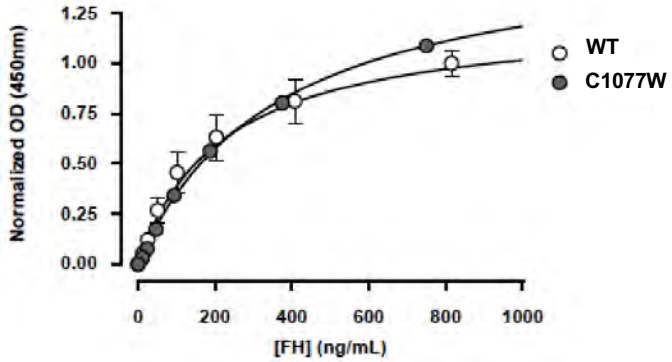
c.3231T>G (C1077W)

CADD: 23.2
gnomAD: Not present

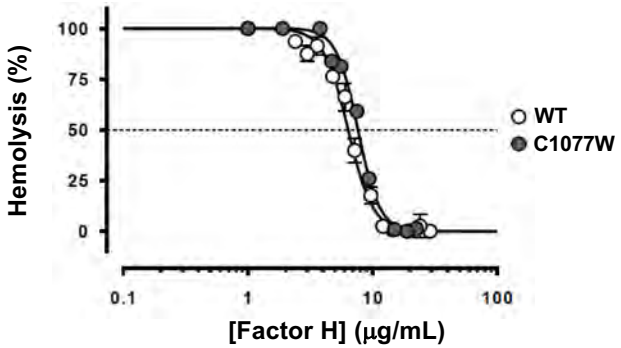




SDS-PAGE
(Non-reduced)



Binding to C3b

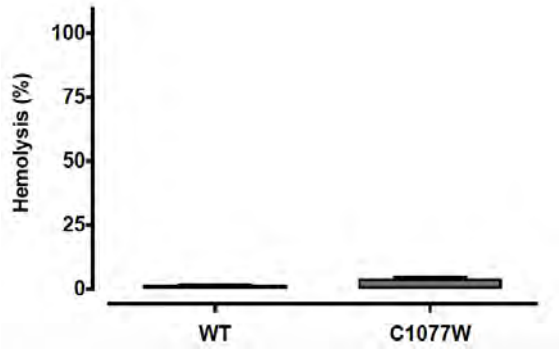


Hemolytic assay

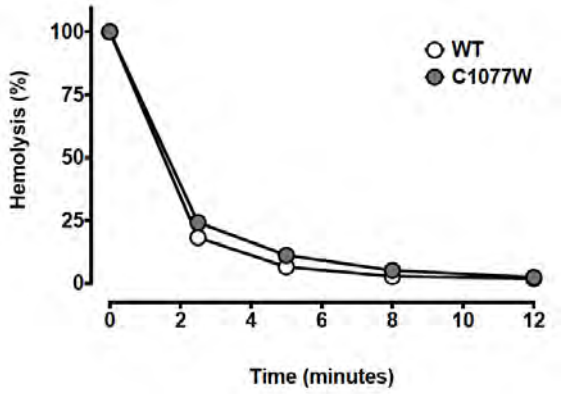
Conclusion: Impaired Expression
PATHOGENIC

Previous studies: None

Comments:
SDS-PAGE shows a weak FH band under non-reducing conditions, suggesting that this variant likely affects expression of the protein and results in a factor H deficiency.



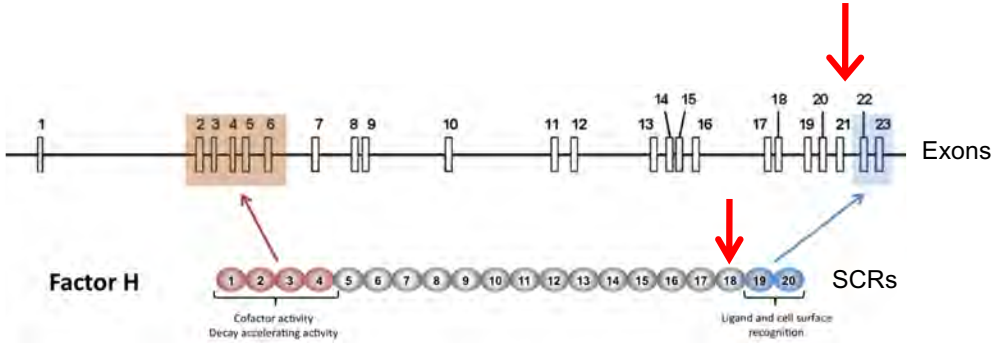
Cofactor activity

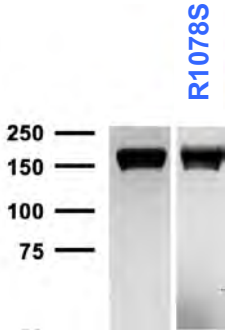


Decay-accelerating activity

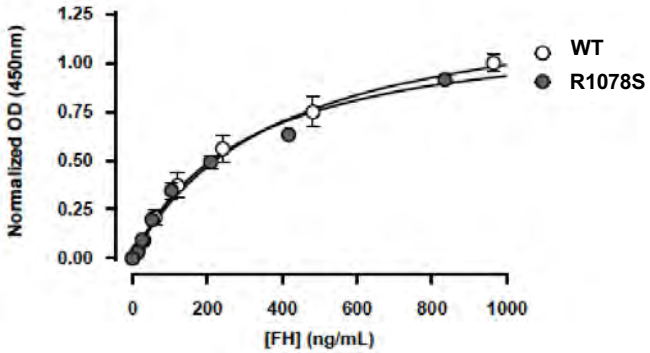
c.3234G>T (R1078S)

CADD: 3.37
gnomAD: $7x10^{-5}$

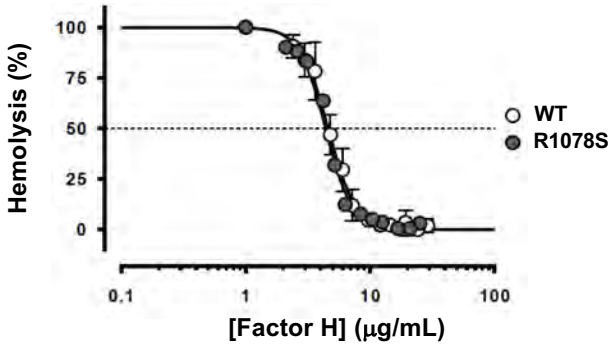




SDS-PAGE
(Non-reduced)



Binding to C3b

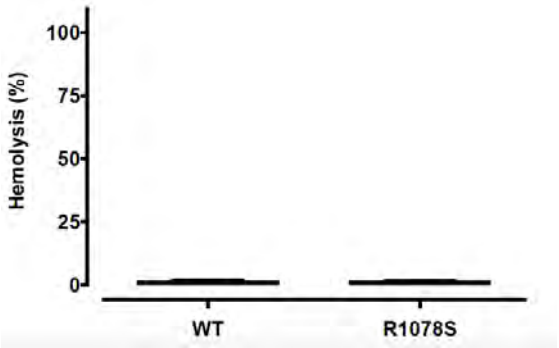


Hemolytic assay

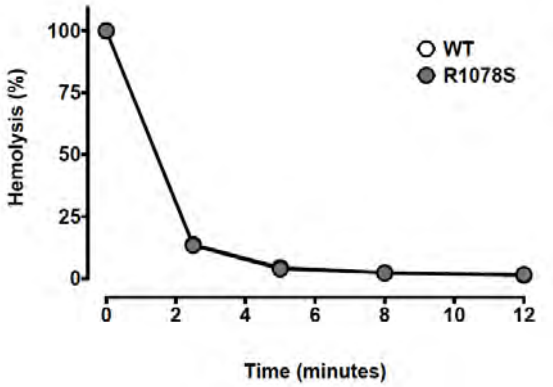
Conclusion: Normal Function
BENIGN

Previous studies: None

Comments:



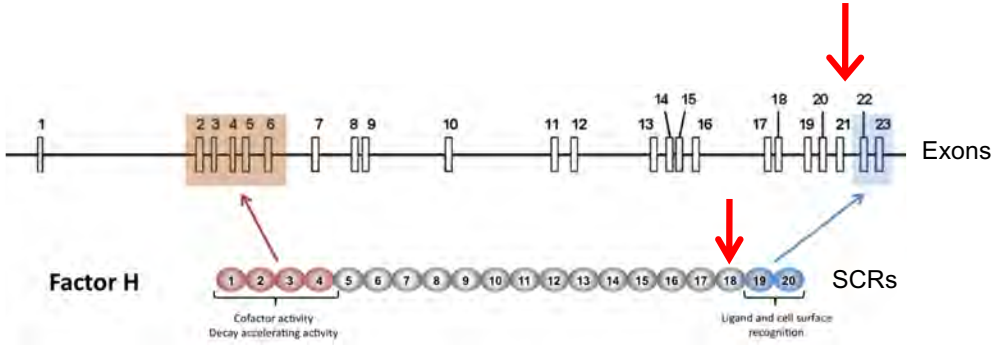
Cofactor activity

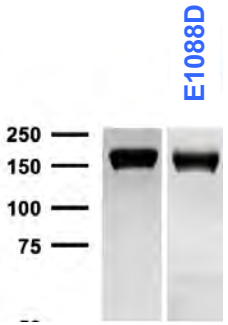


Decay-accelerating activity

c.3264A>C (E1088D)

CADD: 18.53
gnomAD: Not present





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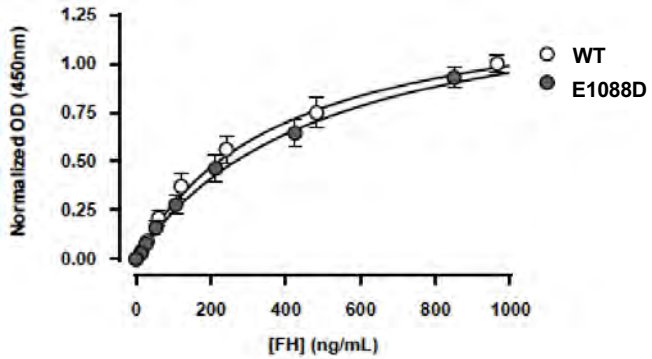
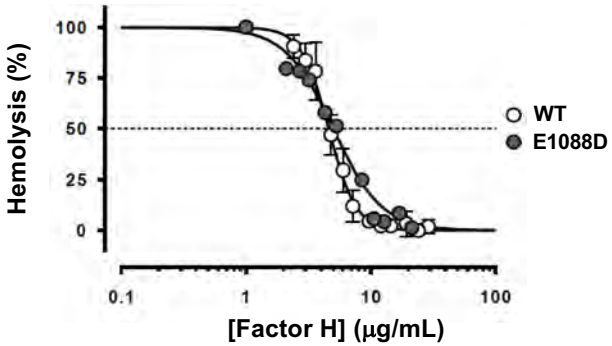
(Non-reduced)



Binding to C3b

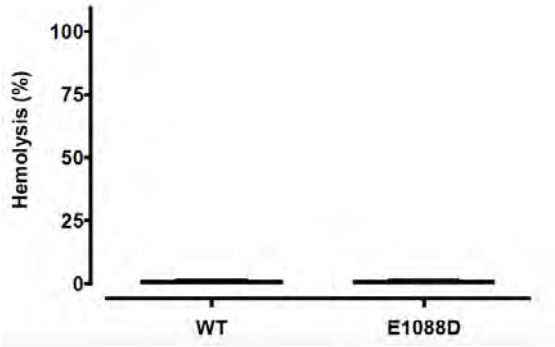


Hemolytic assay

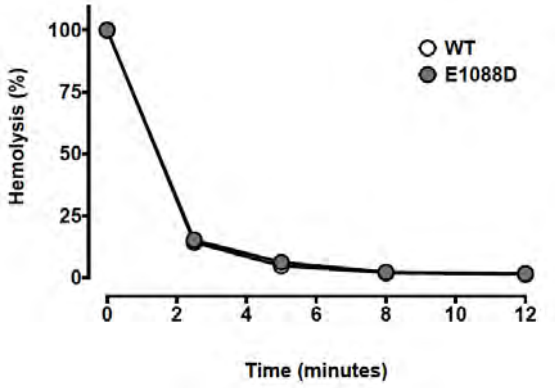
Conclusion: Normal Function
BENIGN

Previous studies: None

Comments:



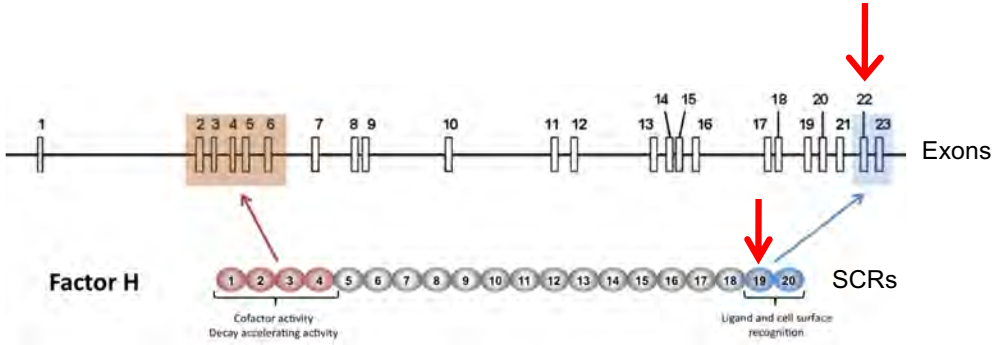
Cofactor activity

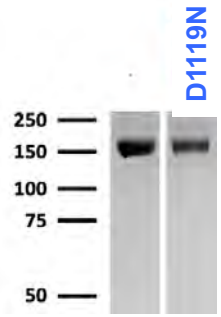


Decay-accelerating activity

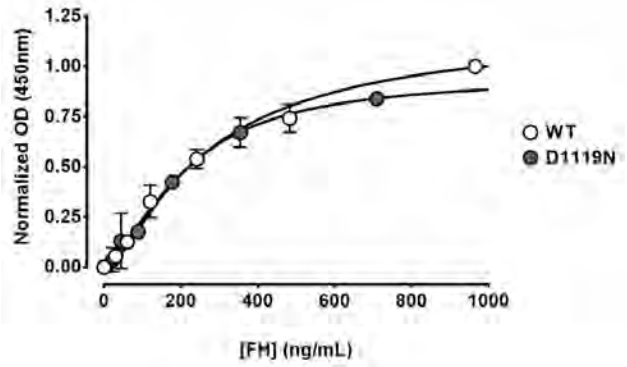
c.3355G>A (D1119N)

CADD: 24.4
gnomAD: Not present

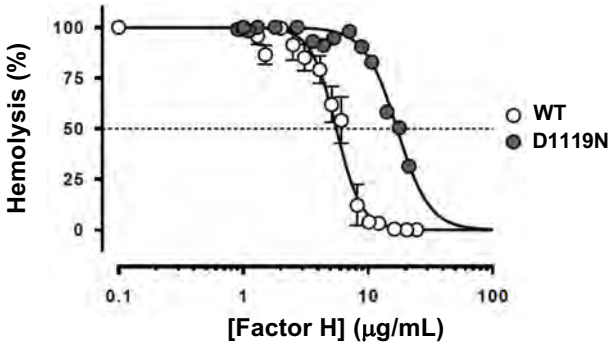




SDS-PAGE
(Non-reduced)

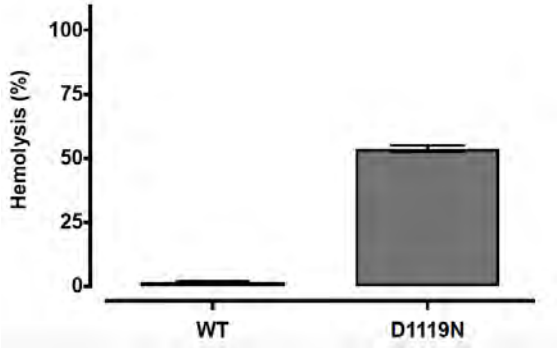


Binding to C3b

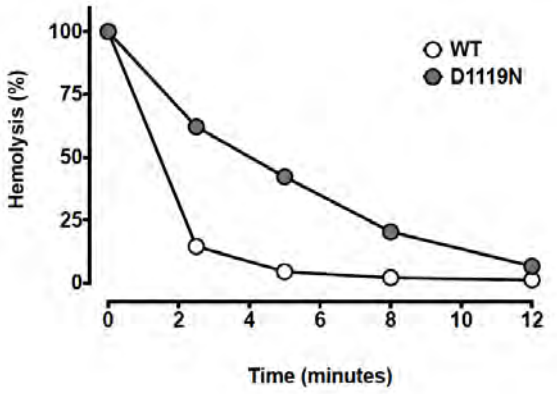


Hemolytic assay

Conclusion: Impaired Function
PATHOGENIC



Cofactor activity



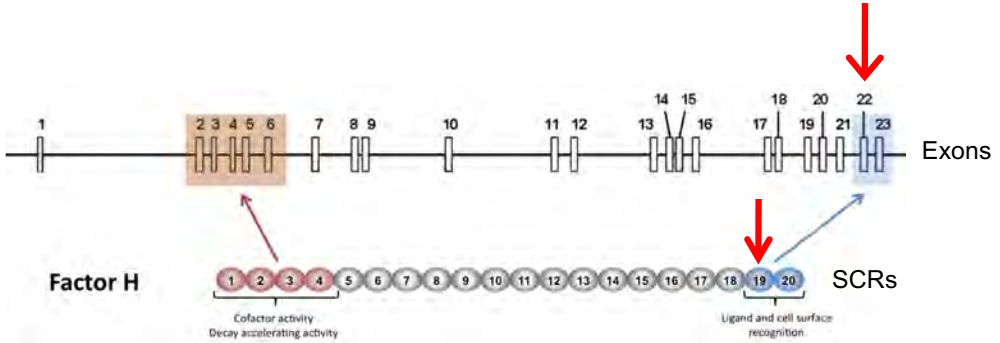
Decay-accelerating activity

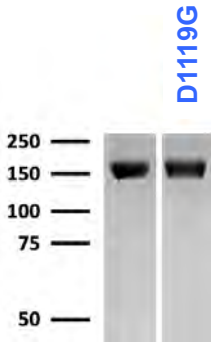
Previous studies: Pathogenic in Merinero HM, García SP, García-Fernández J, Arjona E, Tortajada A, Rodríguez de Córdoba S. Complete functional characterization of disease-associated genetic variants in the complement factor H gene. *Kidney International*. 2018;93(2):470-481.

Comments:

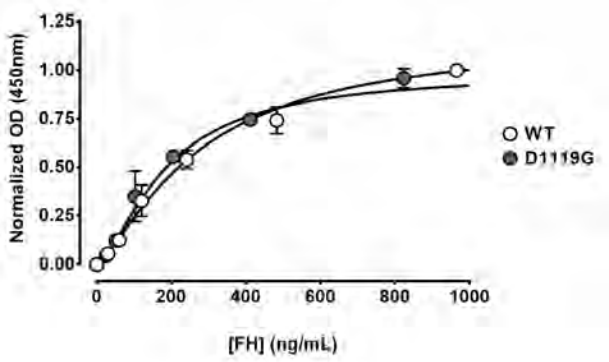
c.3356A>G (D1119G)

CADD: 23
gnomAD: $4x10^{-6}$

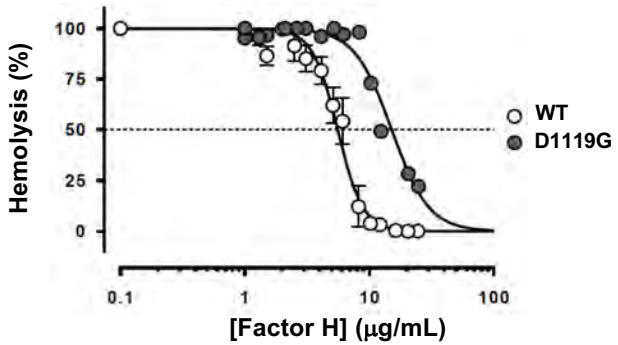




SDS-PAGE
(Non-reduced)



Binding to C3b

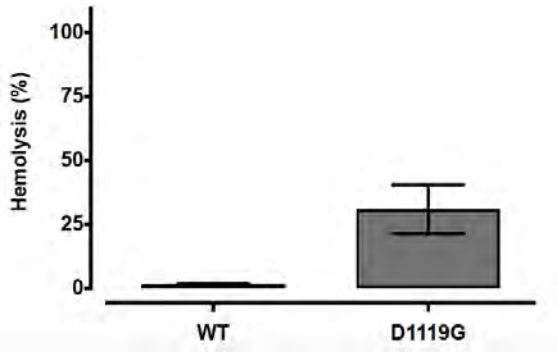


Hemolytic assay

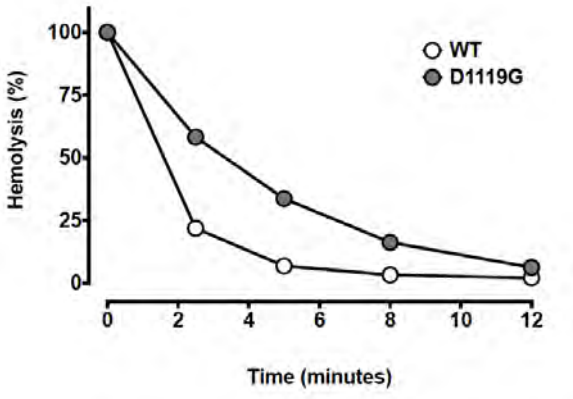
Conclusion: Impaired Function
PATHOGENIC

Previous studies: None

Comments:



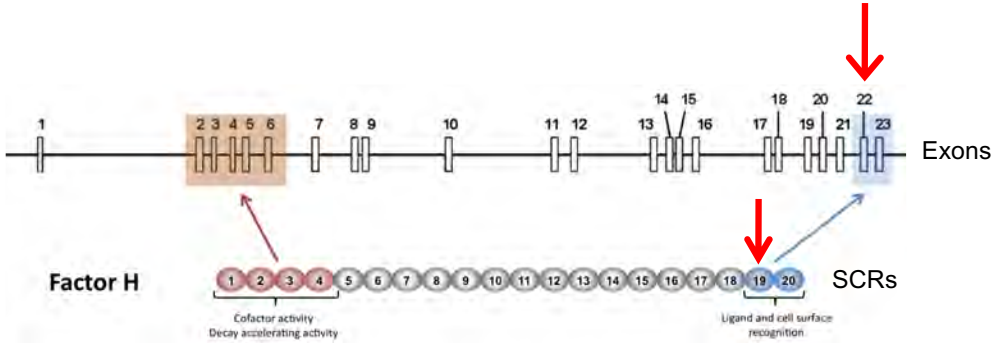
Cofactor activity

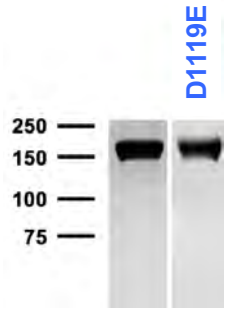


Decay-accelerating activity

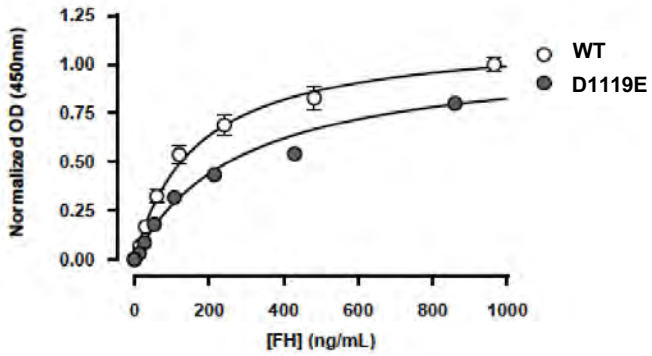
c.3357C>G (D1119E)

CADD: 11.94
gnomAD: $1x10^{-5}$

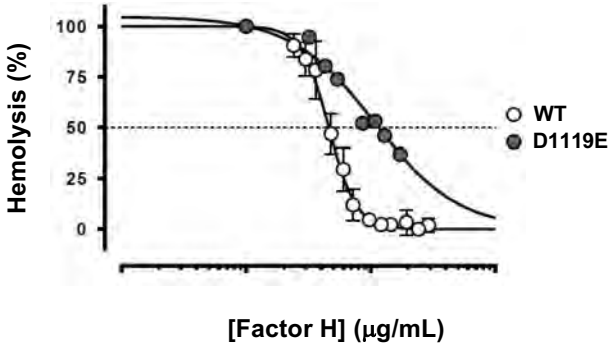




SDS-PAGE
(Non-reduced)



Binding to C3b

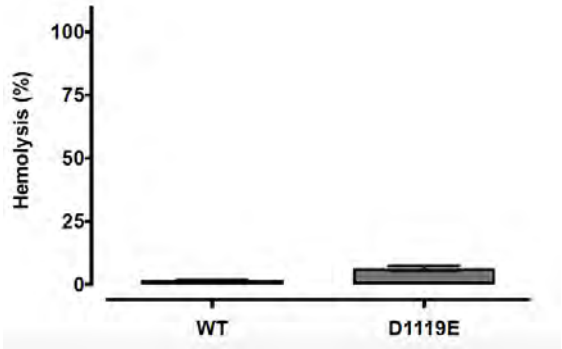


Hemolytic assay

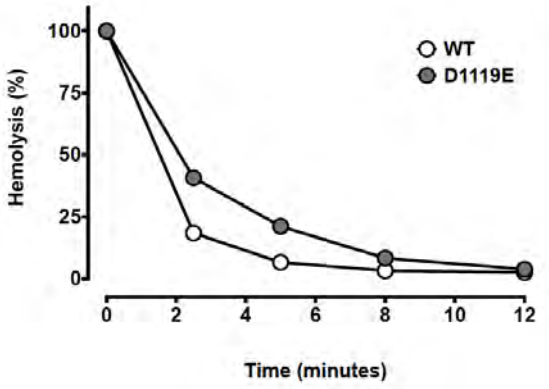
Conclusion: Impaired Function
PATHOGENIC

Previous studies: None

Comments:



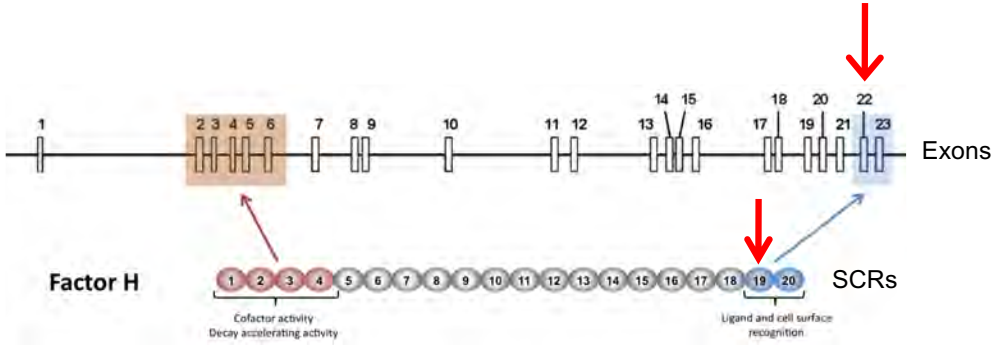
Cofactor activity

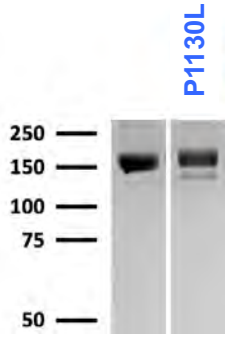


Decay-accelerating activity

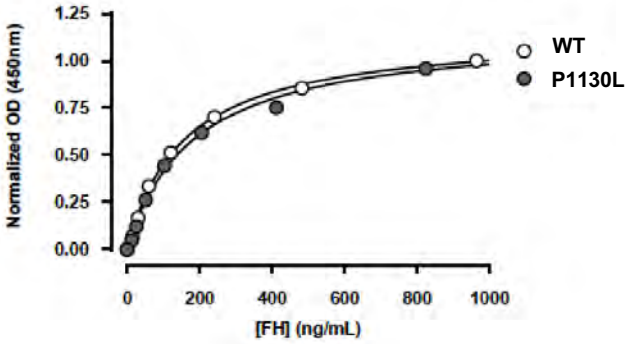
c.3389C>T (P1130L)

CADD: 15.04
gnomAD: Not present

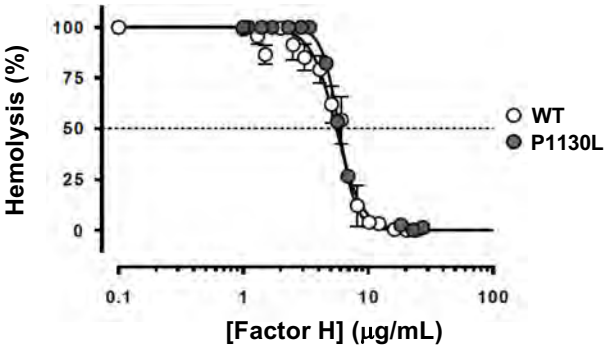




SDS-PAGE
(Non-reduced)



Binding to C3b

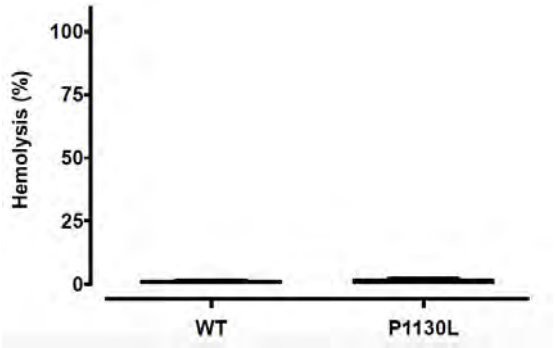


Hemolytic assay

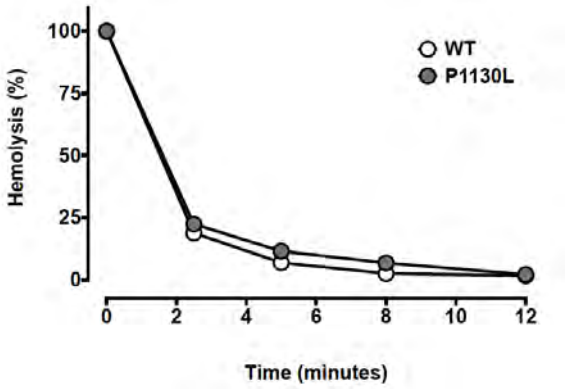
Conclusion: Normal Function
BENIGN

Previous studies: None

Comments:
Potential degradation. Proteolytic fragment seen as lower band.



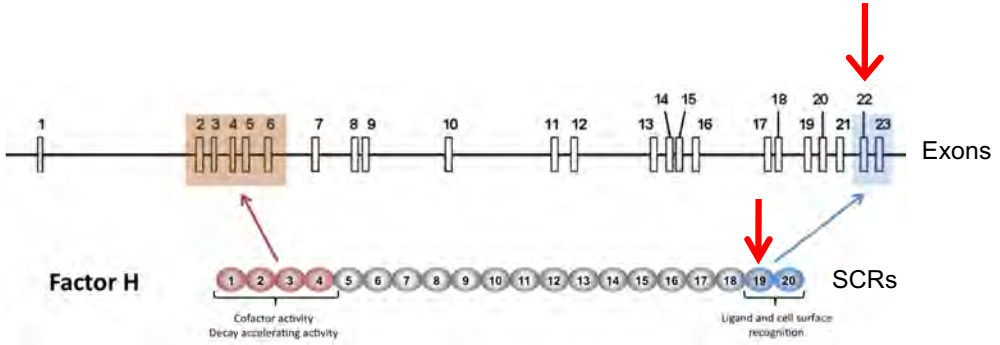
Cofactor activity

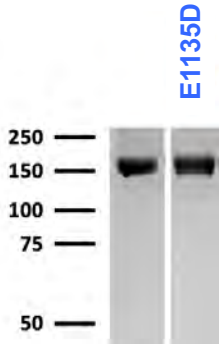


Decay-accelerating activity

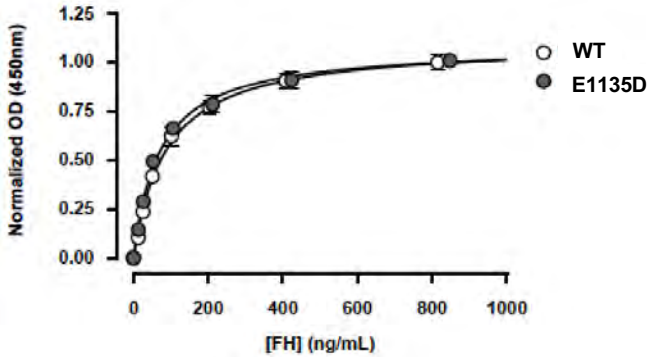
c.3405G>C (E1135D)

CADD: 15.16
gnomAD: $4x10^{-6}$

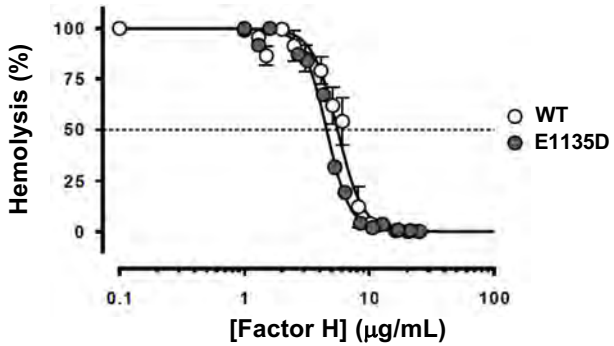




SDS-PAGE
(Non-reduced)



Binding to C3b

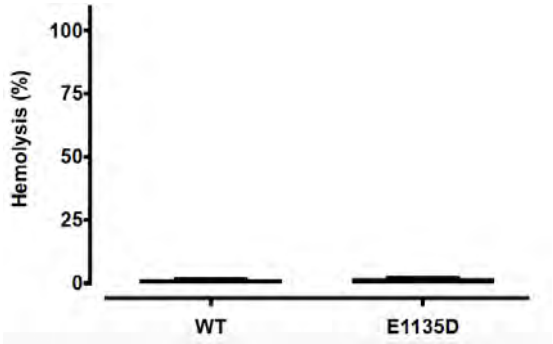


Hemolytic assay

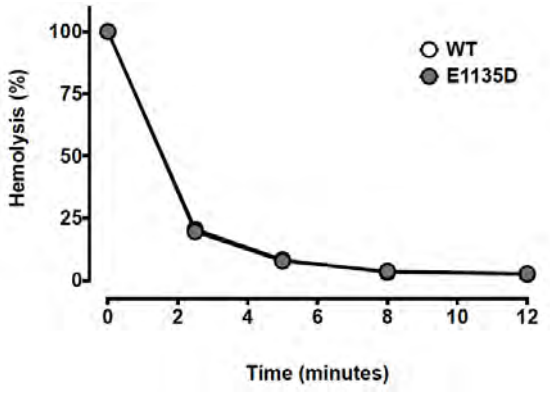
Conclusion: Normal Function
BENIGN

Previous studies: None

Comments:



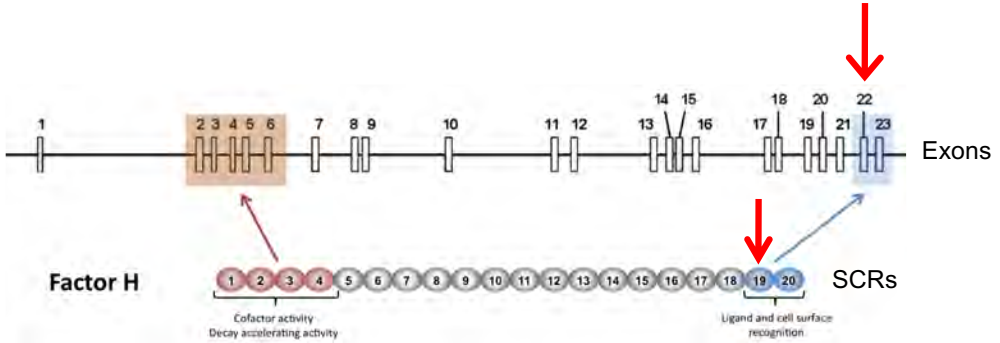
Cofactor activity

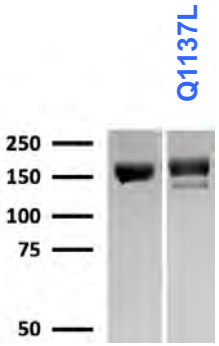


Decay-accelerating activity

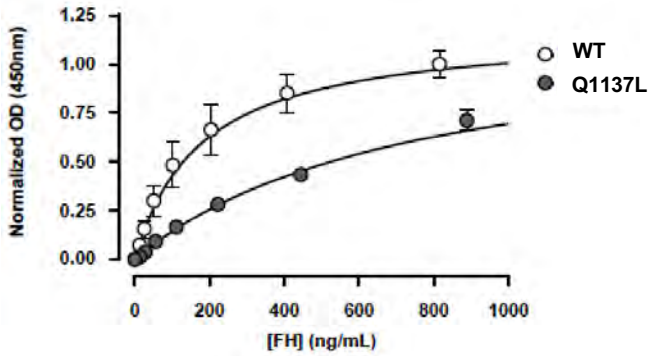
c.3410A>T (Q1137L)

CADD: 16.39
gnomAD: Not present

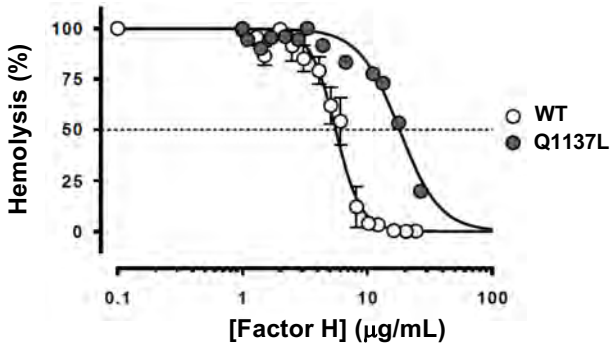




SDS-PAGE
(Non-reduced)



Binding to C3b

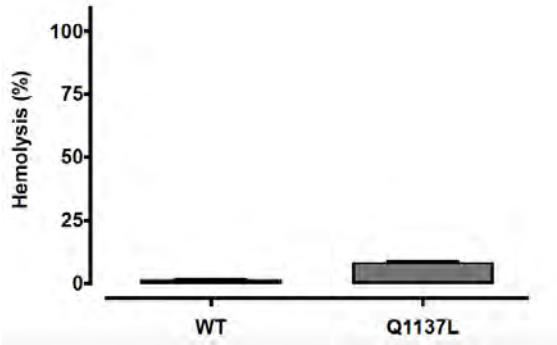


Hemolytic assay

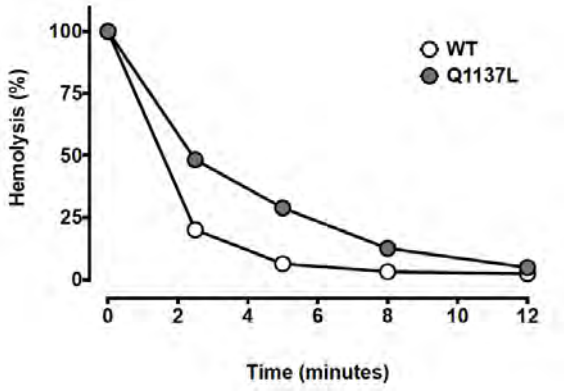
Conclusion: Impaired Function
PATHOGENIC

Previous studies: None

Comments:
Potential degradation. Proteolytic fragment seen as lower band.



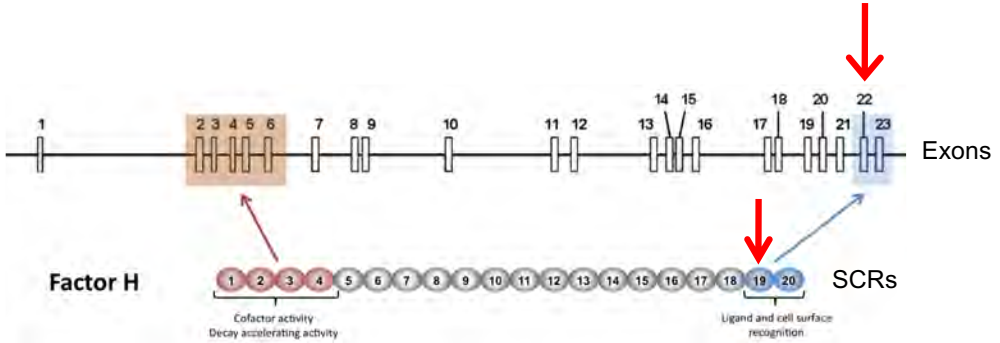
Cofactor activity

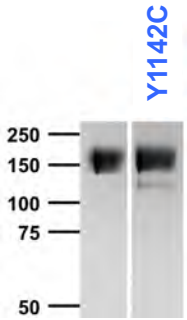


Decay-accelerating activity

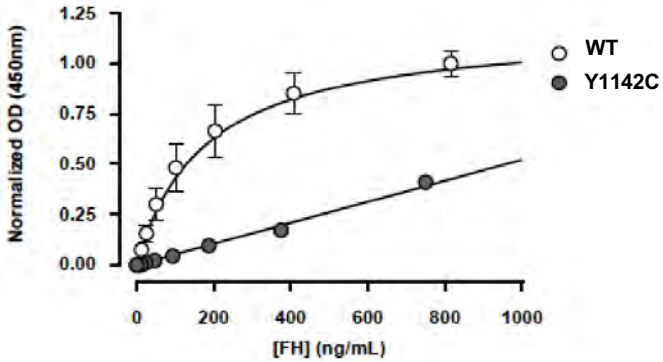
c.3425A>G (Y1142C)

CADD: 22.1
gnomAD: Not present

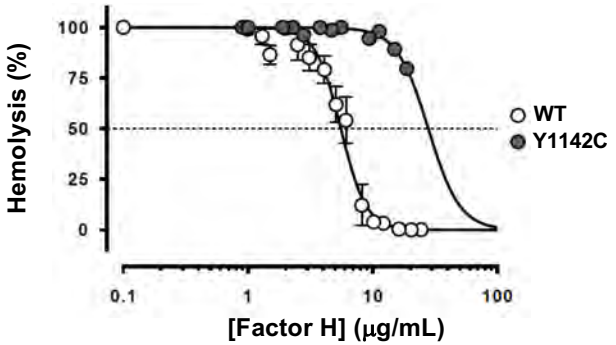




SDS-PAGE
(Non-reduced)



Binding to C3b

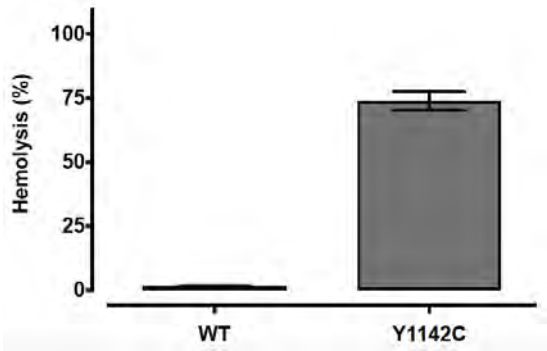


Hemolytic assay

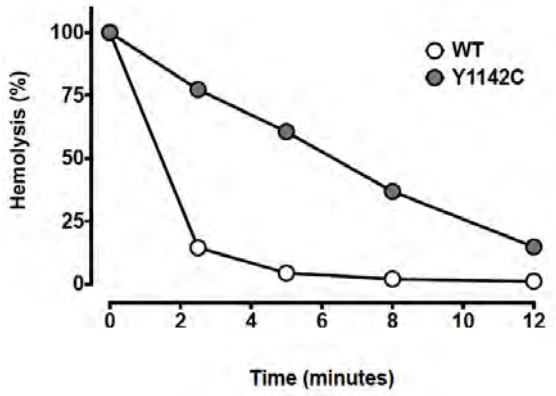
Conclusion: Impaired Function
PATHOGENIC

Previous studies: None

Comments:
Potential degradation. Proteolytic fragment seen as lower band.



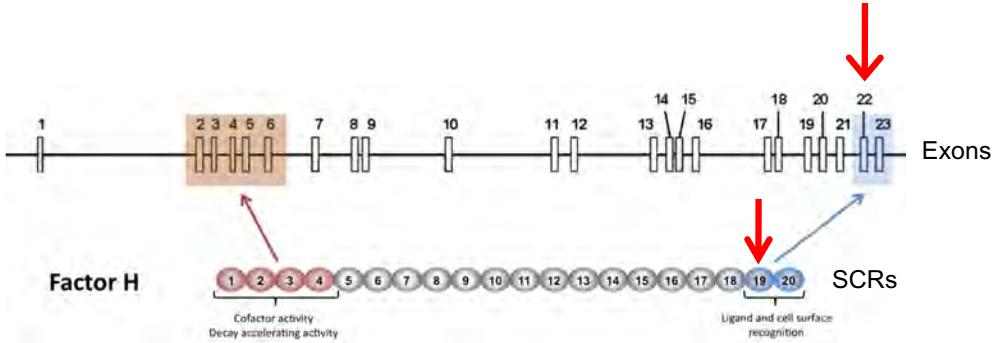
Cofactor activity

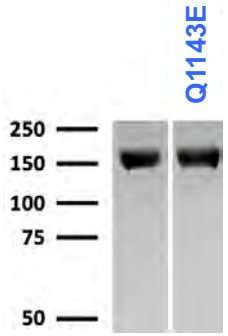


Decay-accelerating activity

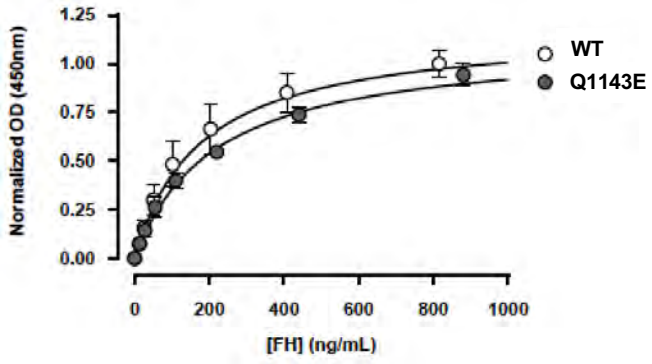
c.3427C>G (Q1143E)

CADD: 0
gnomAD: $9x10^{-3}$

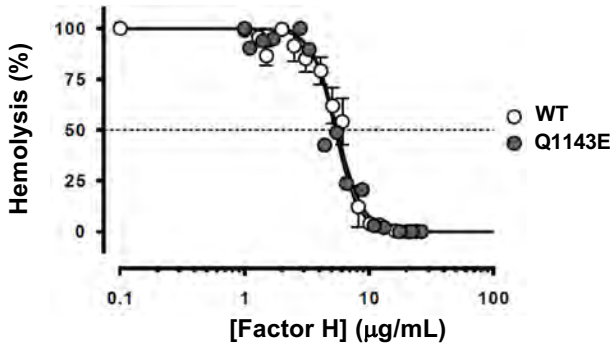




SDS-PAGE
(Non-reduced)



Binding to C3b

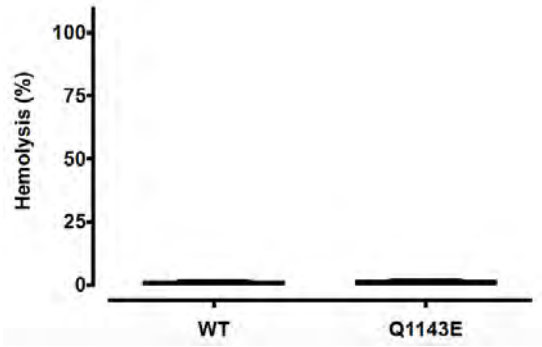


Hemolytic assay

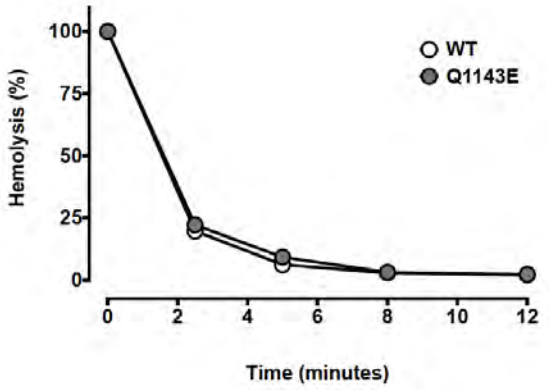
Conclusion: Normal Function
BENIGN

Previous studies: None

Comments:



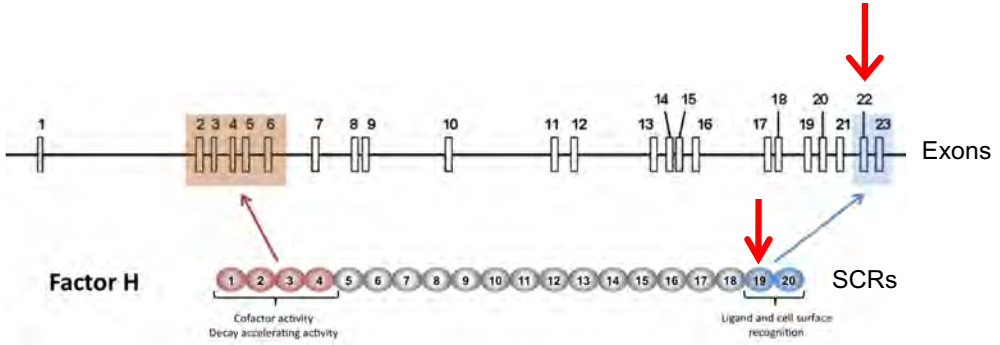
Cofactor activity

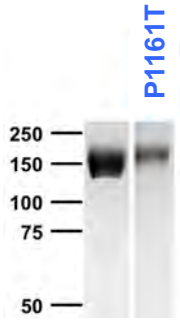


Decay-accelerating activity

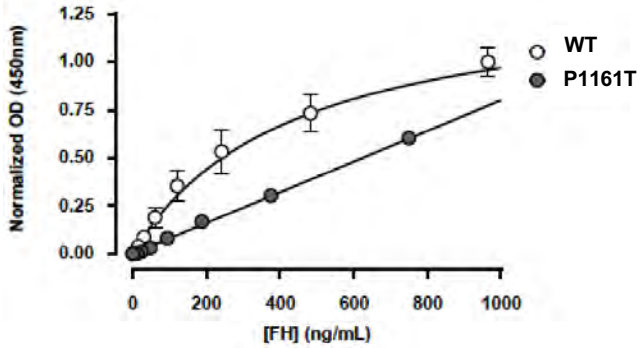
c.3481C>A (P1161T)

CADD: 23.6
gnomAD: Not present

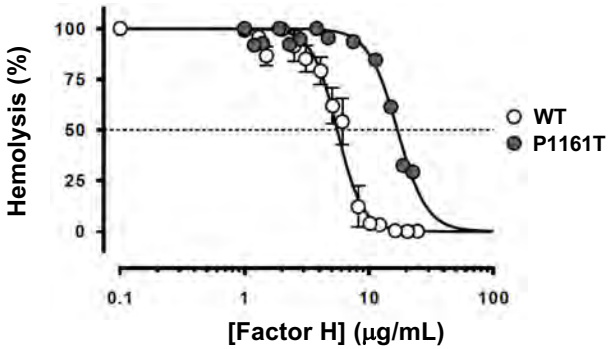




SDS-PAGE
(Non-reduced)

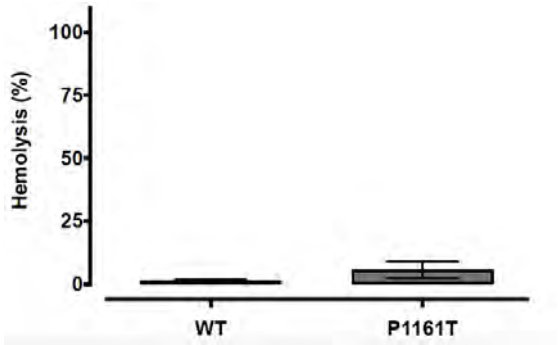


Binding to C3b

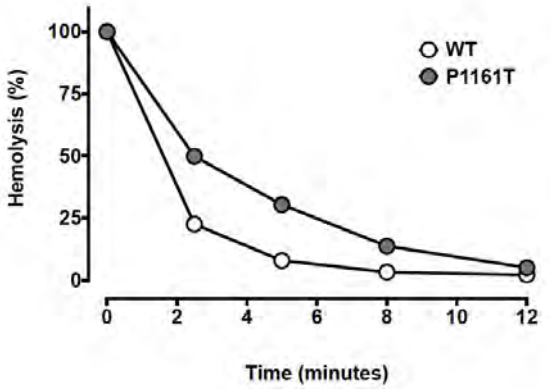


Hemolytic assay

Conclusion: Impaired Expression
PATHOGENIC



Cofactor activity



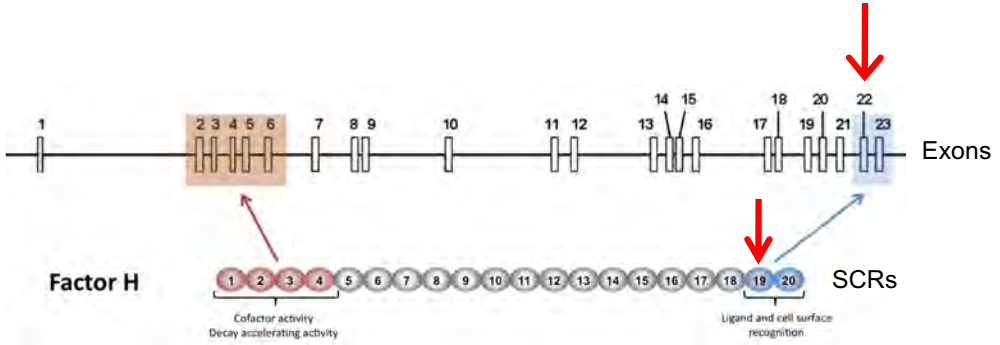
Decay-accelerating activity

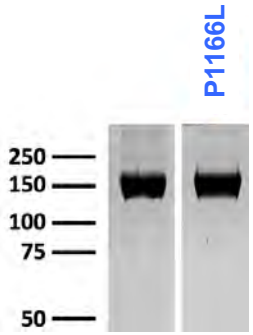
Previous studies: None

Comments:
SDS-PAGE shows a weak FH band under non-reducing conditions, suggesting that this variant likely affects expression of the protein and results in a factor H deficiency.

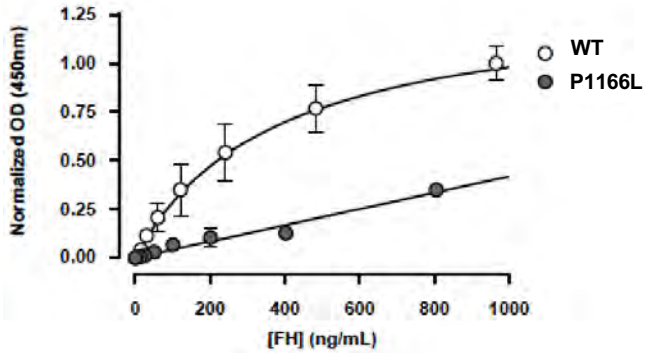
c.3497C>T (P1166L)

CADD: 13.96
gnomAD: Not present

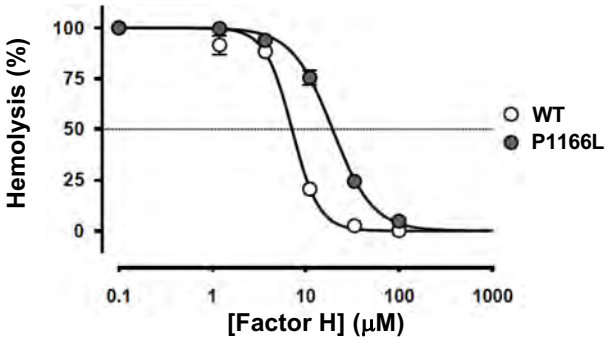




SDS-PAGE
(Non-reduced)

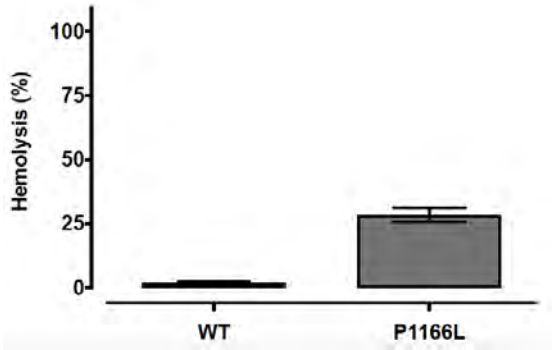


Binding to C3b

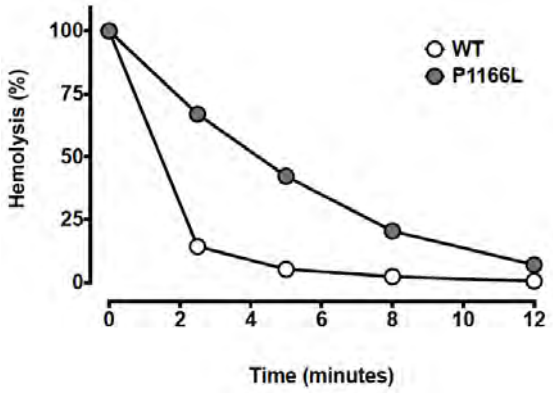


Hemolytic assay

Conclusion: Impaired Function
PATHOGENIC



Cofactor activity



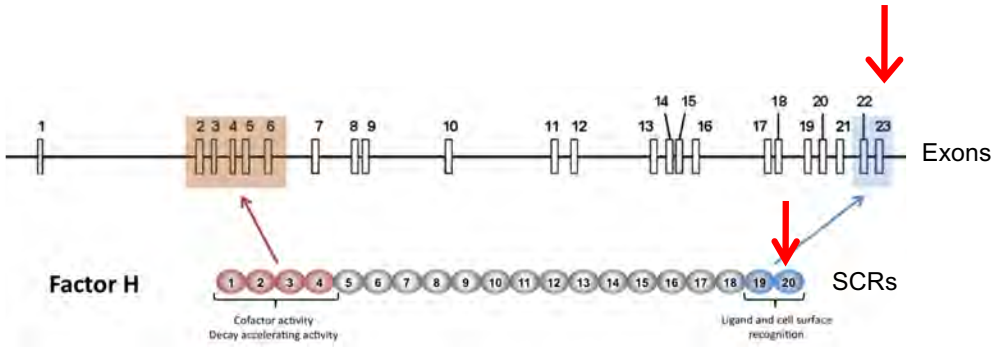
Decay-accelerating activity

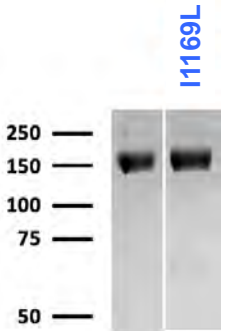
Previous studies: Pathogenic in Merinero HM, García SP, García-Fernández J, Arjona E, Tortajada A, Rodríguez de Córdoba S. Complete functional characterization of disease-associated genetic variants in the complement factor H gene. *Kidney International*. 2018;93(2):470-481.

Comments:

c.3505A>C (I1169L)

CADD: 15.43
gnomAD: Not present





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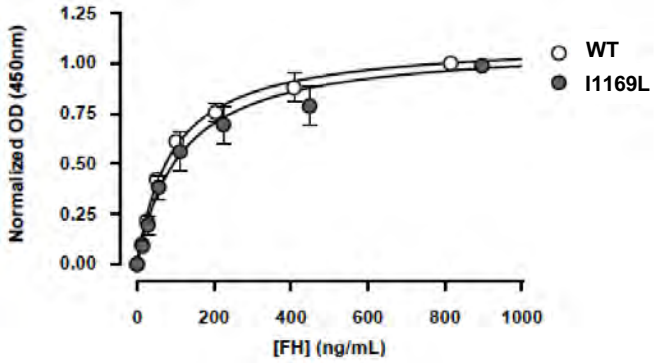
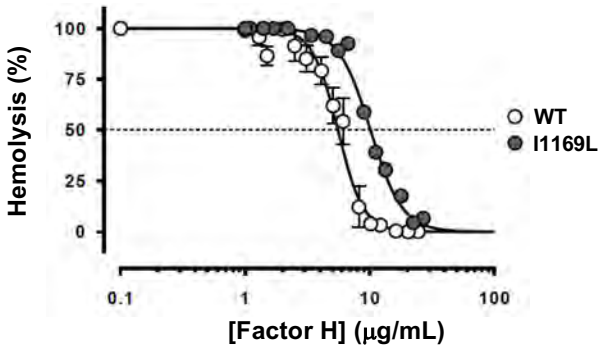
(Non-reduced)



Binding to C3b

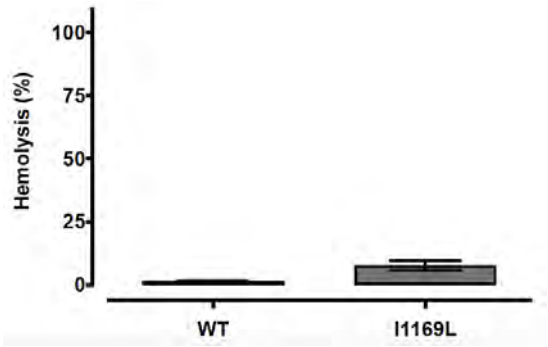


Hemolytic assay

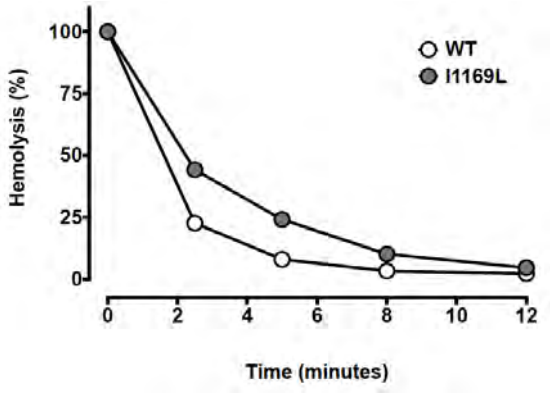
Conclusion: Impaired Function
PATHOGENIC

Previous studies: None

Comments:



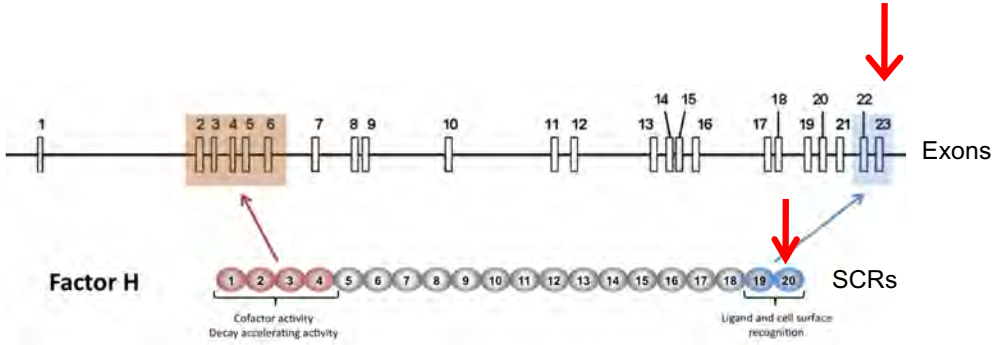
Cofactor activity

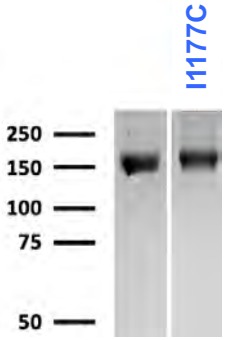


Decay-accelerating activity

c.3530A>G (I1177C)

CADD: 22.8
gnomAD: Not present





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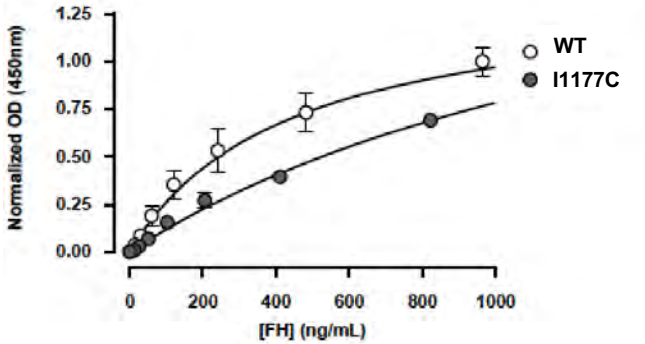
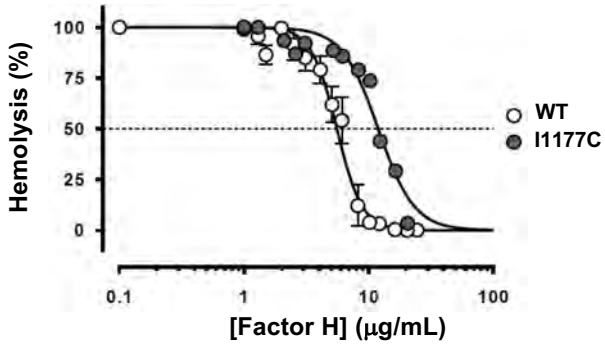


Binding to C3b

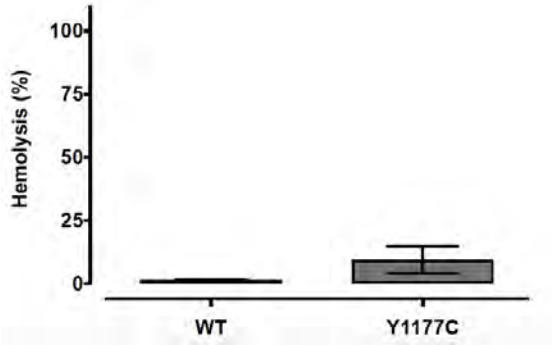


Hemolytic assay

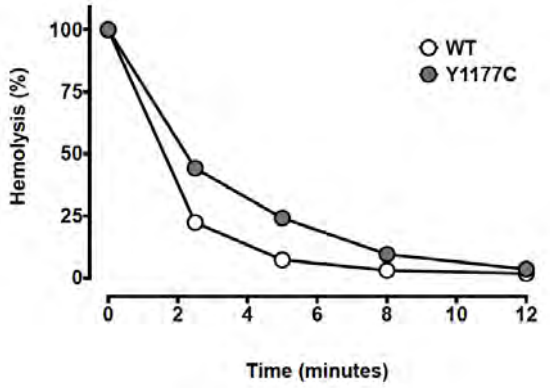
Conclusion: Impaired Function
PATHOGENIC

Previous studies: None

Comments:



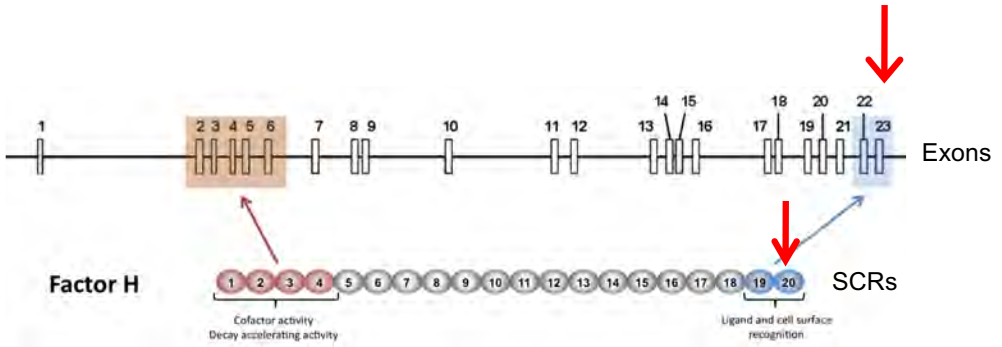
Cofactor activity

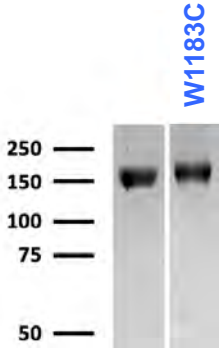


Decay-accelerating activity

c.3549G>T (W1183C)

CADD: 22.5
gnomAD: Not present





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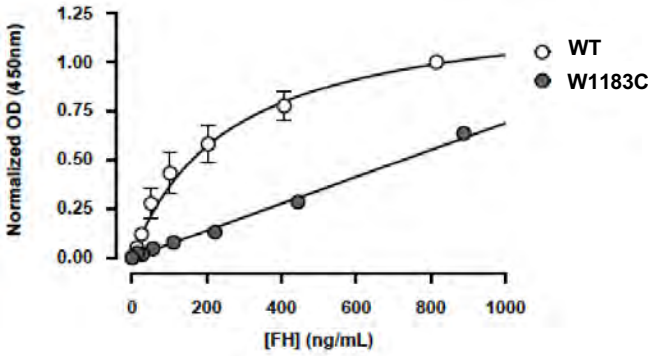
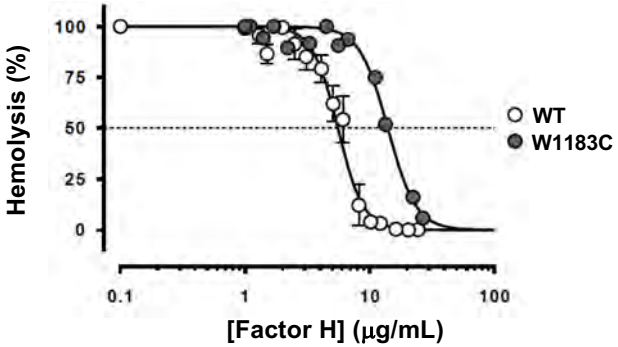


Binding to C3b

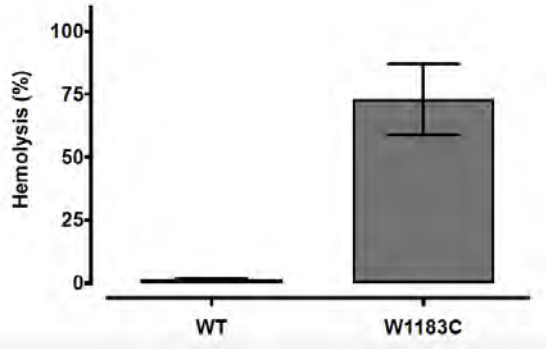


Hemolytic assay

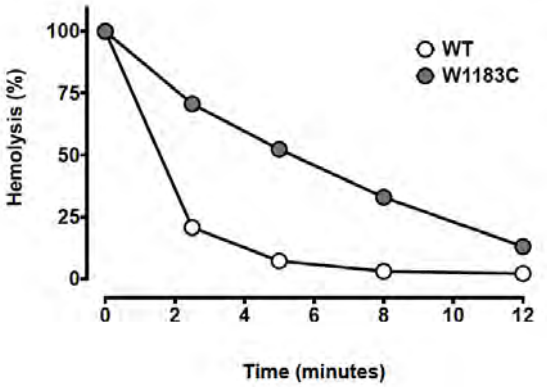
Conclusion: Impaired Function
PATHOGENIC

Previous studies: None

Comments:



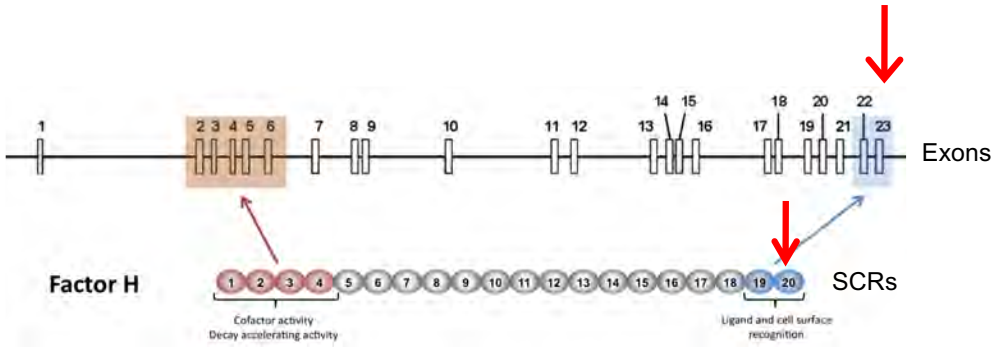
Cofactor activity

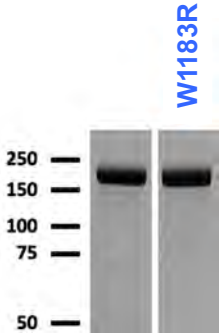


Decay-accelerating activity

c.3547T>A (W1183R)

CADD: 19.26
gnomAD: Not present





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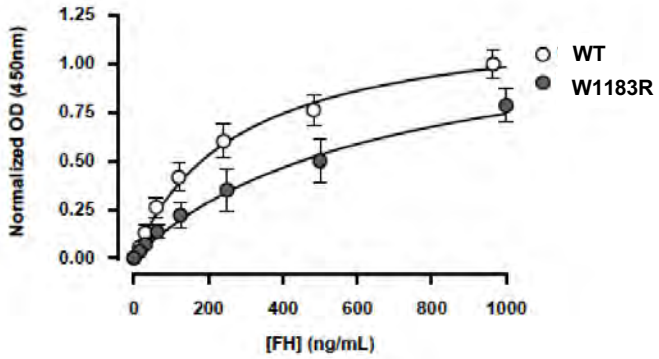
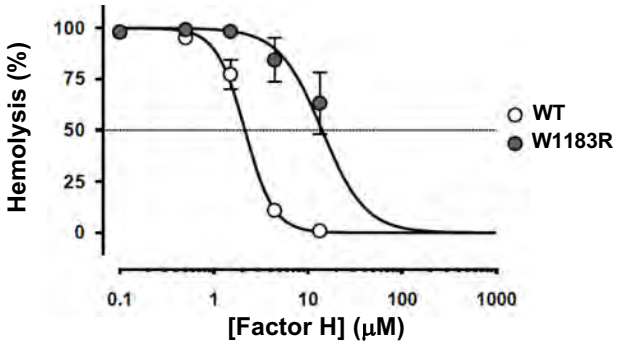


Binding to C3b

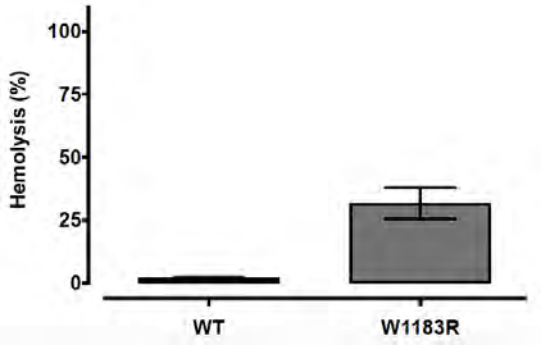


Hemolytic assay

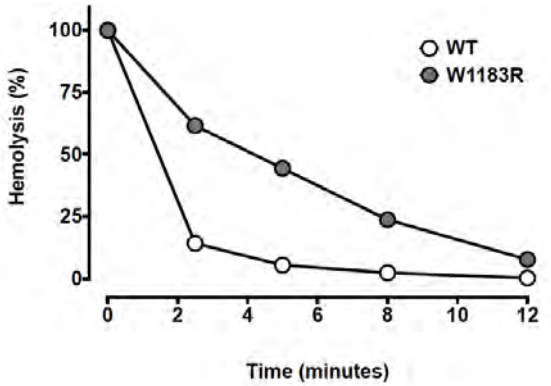
Conclusion: Impaired Function
PATHOGENIC

Previous studies: None

Comments:



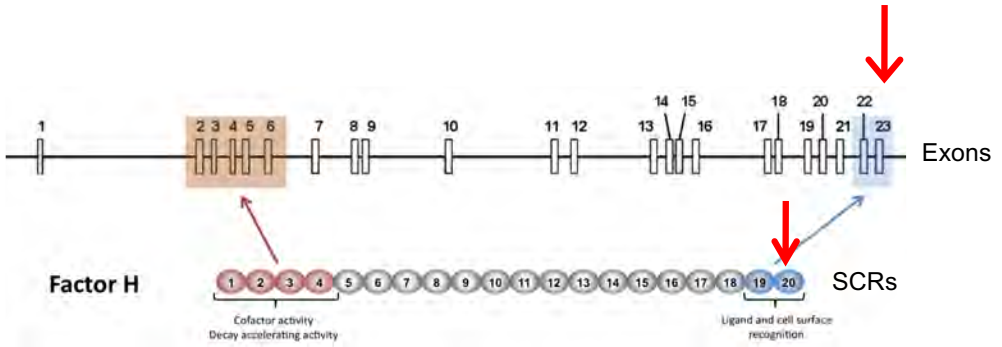
Cofactor activity

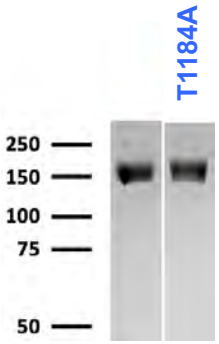


Decay-accelerating activity

c.3550A>G (T1184A)

CADD: 0.5
gnomAD: Not present





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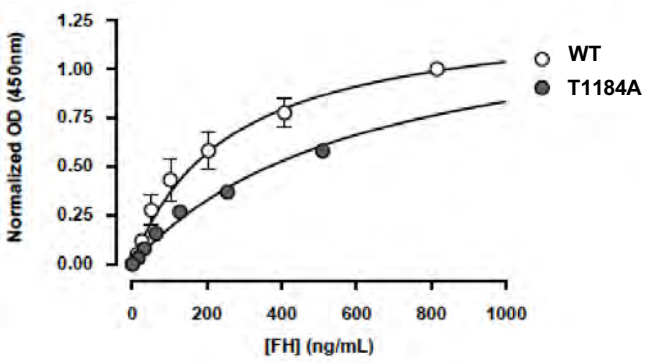
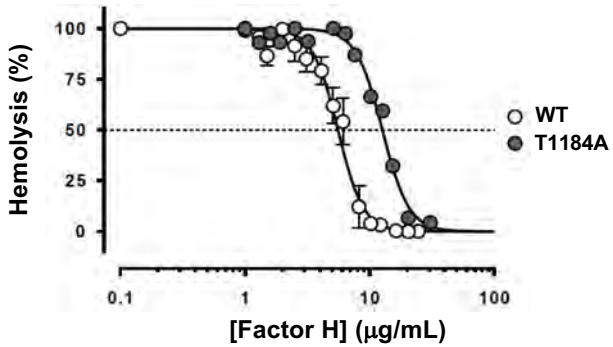
(Non-reduced)



Binding to C3b

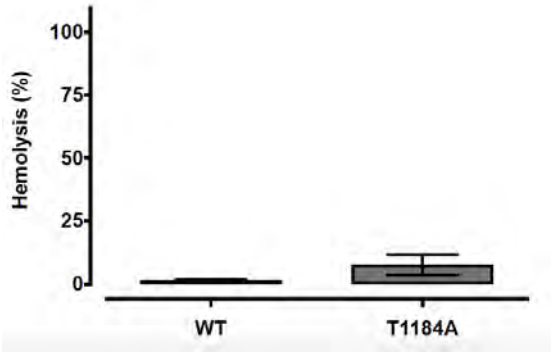


Hemolytic assay

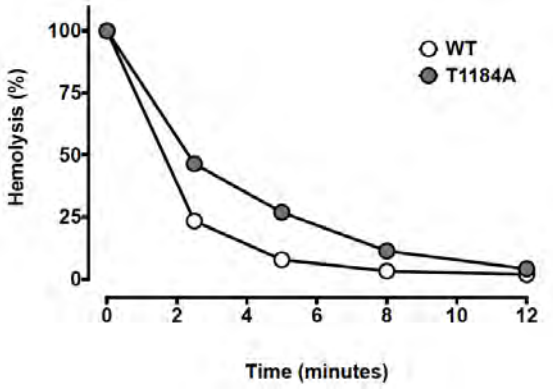
Conclusion: Impaired Function
PATHOGENIC

Previous studies: None

Comments:



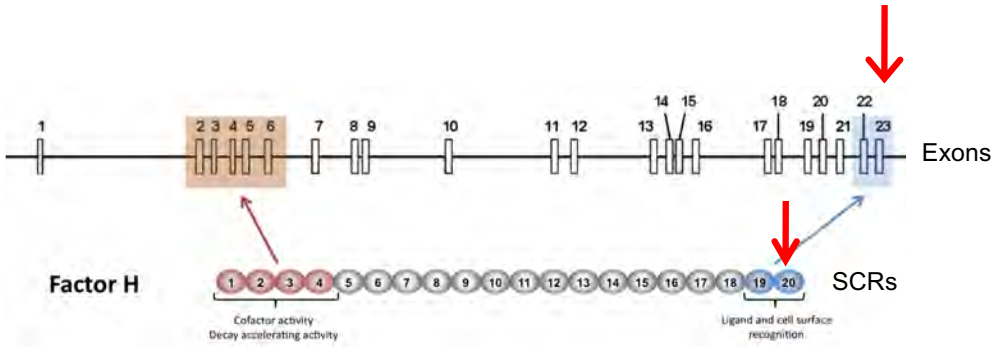
Cofactor activity

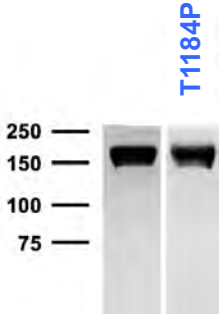


Decay-accelerating activity

c.3550A>C (T1184P)

CADD: 1.49
gnomAD: Not present





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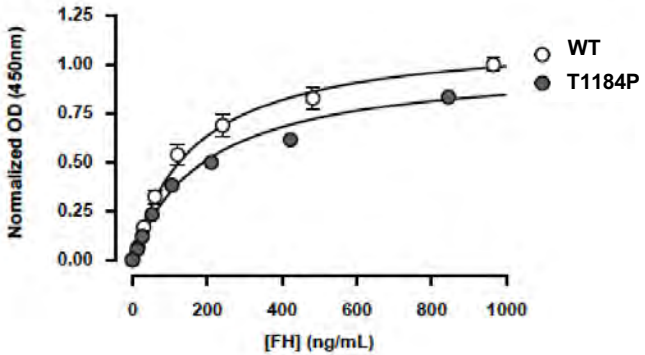
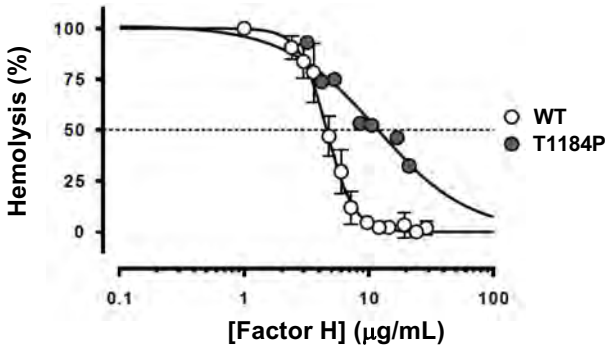


Binding to C3b

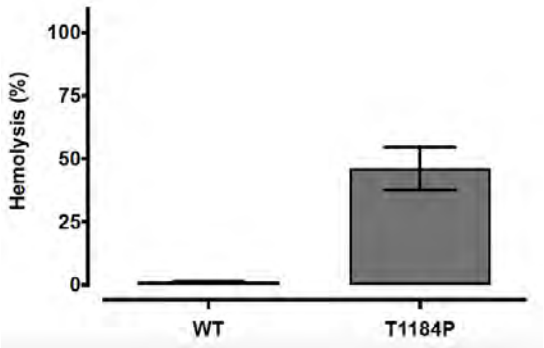


Hemolytic assay

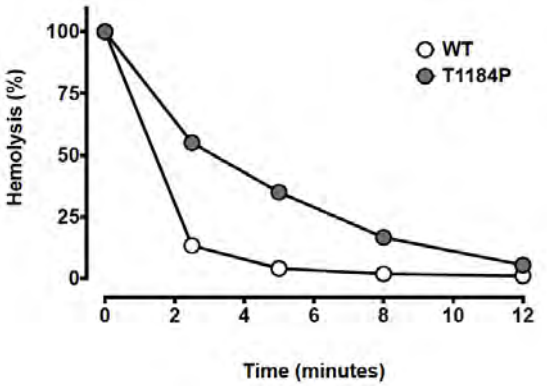
Conclusion: Impaired Function
PATHOGENIC

Previous studies: None

Comments:



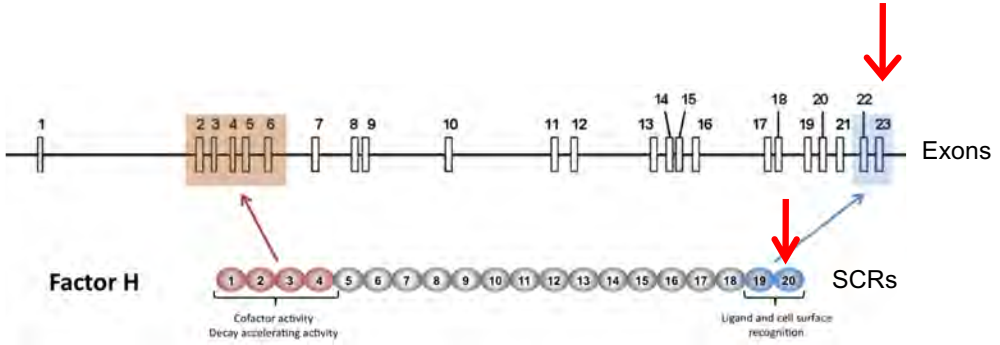
Cofactor activity

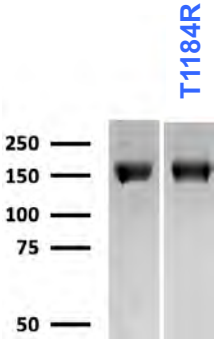


Decay-accelerating activity

c.3551C>G (T1184R)

CADD: 0
gnomAD: Not present





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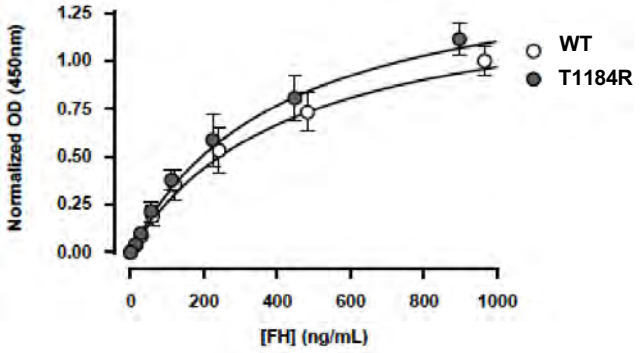
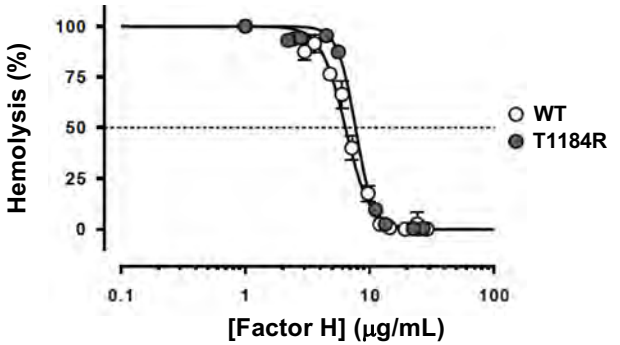


Binding to C3b

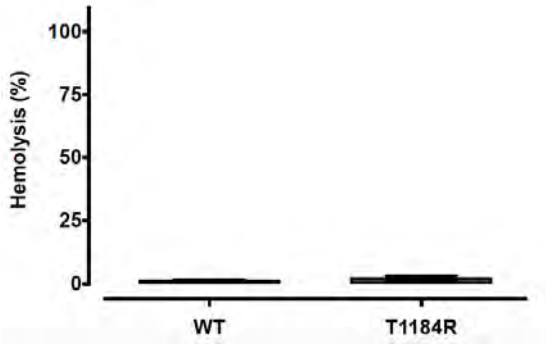


Hemolytic assay

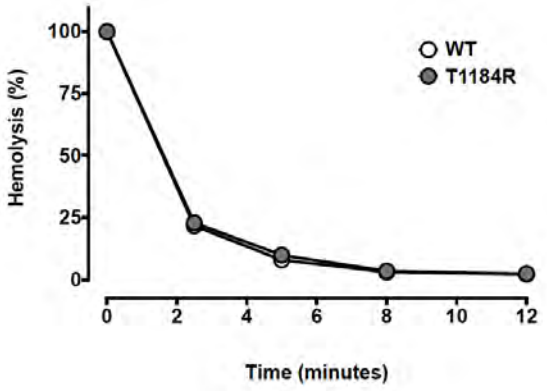
Conclusion: Normal Function
BENIGN

Previous studies: None

Comments:



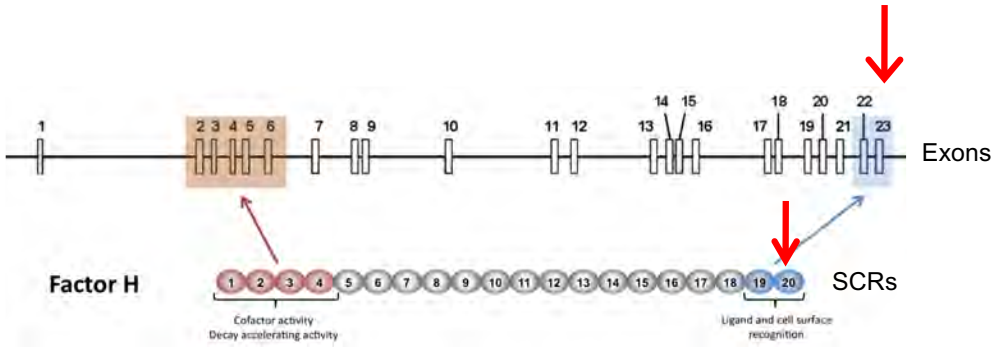
Cofactor activity

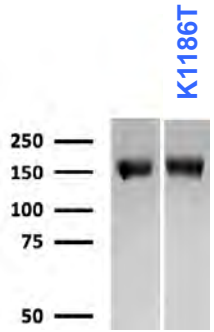


Decay-accelerating activity

c.3557A>C (K1186T)

CADD: 0.26
gnomAD: $4x10^{-6}$





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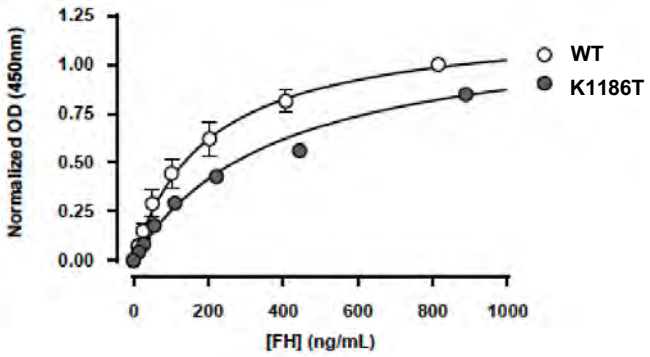
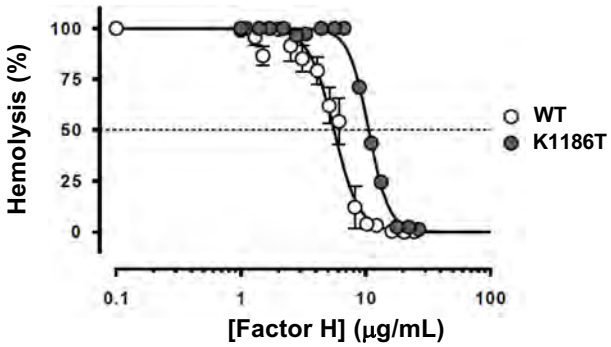


Binding to C3b

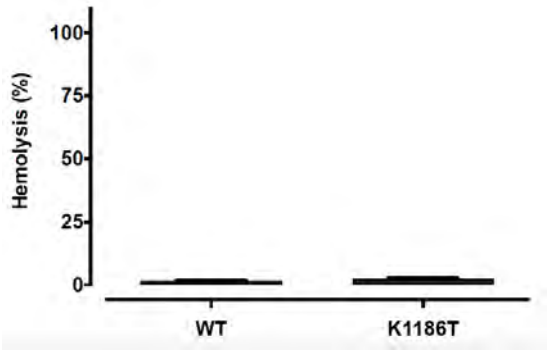


Hemolytic assay

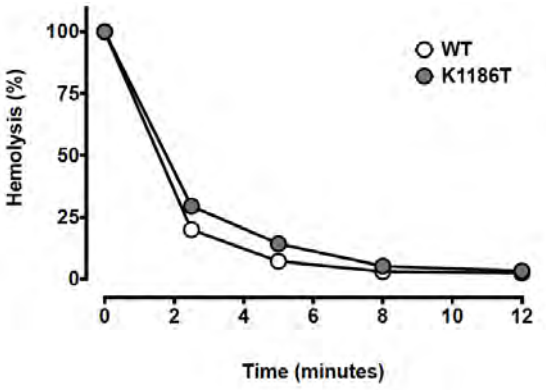
Conclusion: Impaired Function
PATHOGENIC

Previous studies: None

Comments:



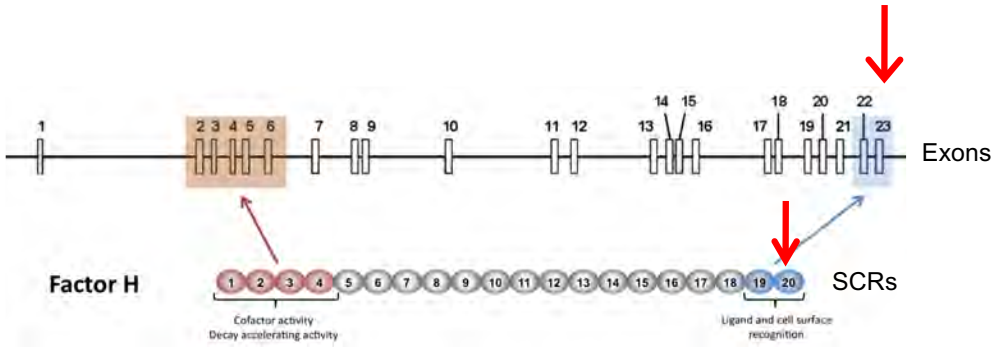
Cofactor activity

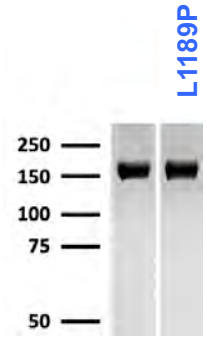


Decay-accelerating activity

c.3566T>C (L1189P)

CADD: 15.81
gnomAD: Not present





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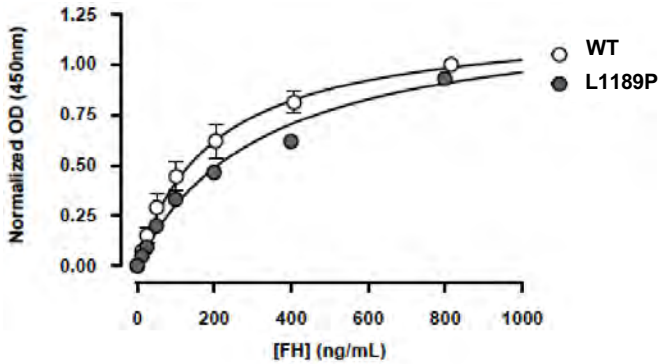
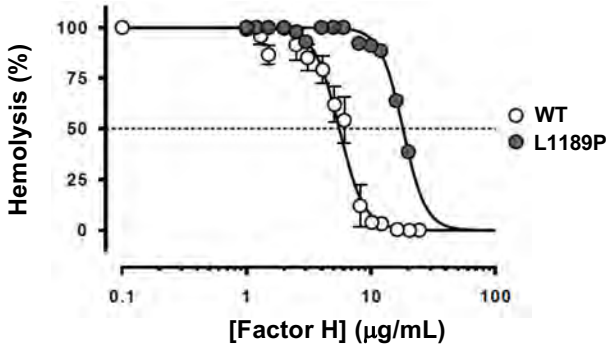


Binding to C3b

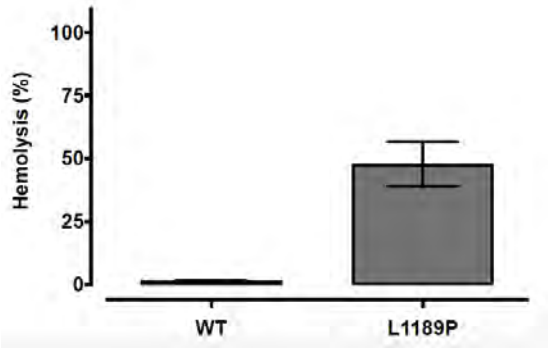


Hemolytic assay

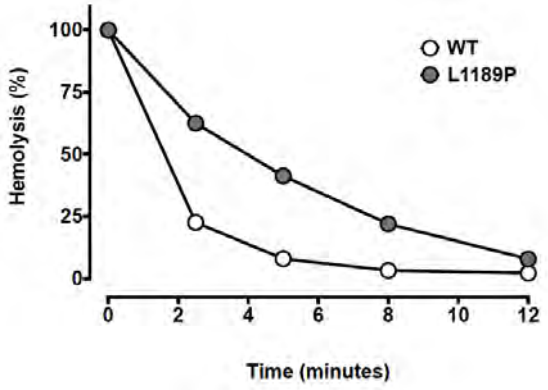
Conclusion: Impaired Function
PATHOGENIC

Previous studies: None

Comments:



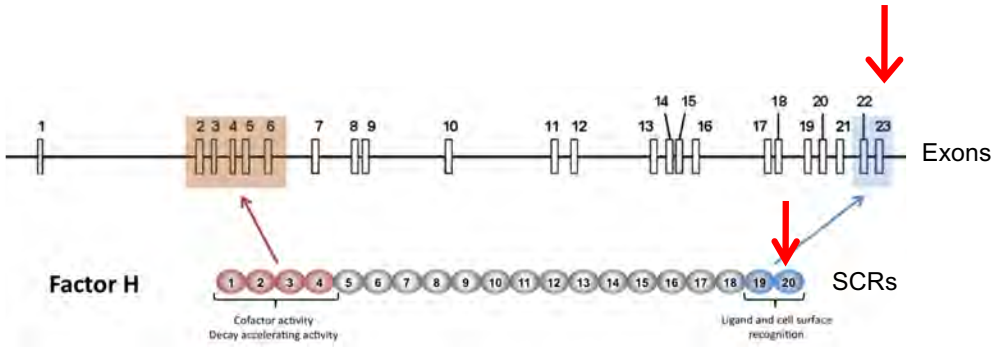
Cofactor activity

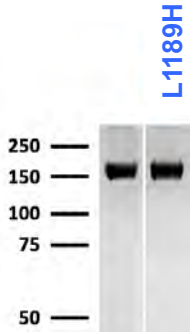


Decay-accelerating activity

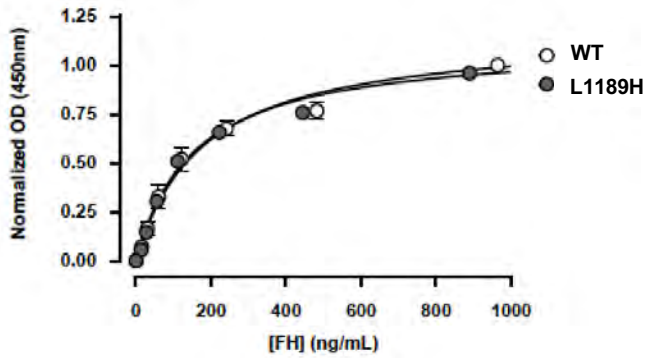
c.3566T>A (L1189H)

CADD: 20.3
gnomAD: Not present

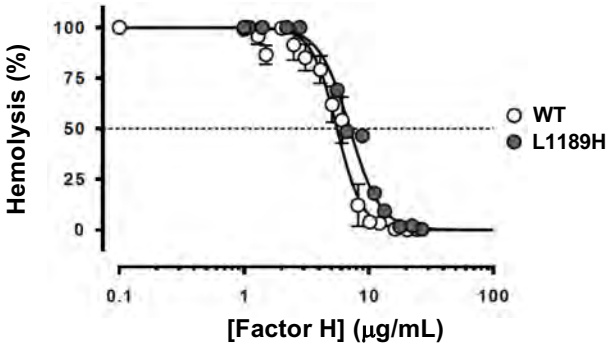




SDS-PAGE
(Non-reduced)



Binding to C3b

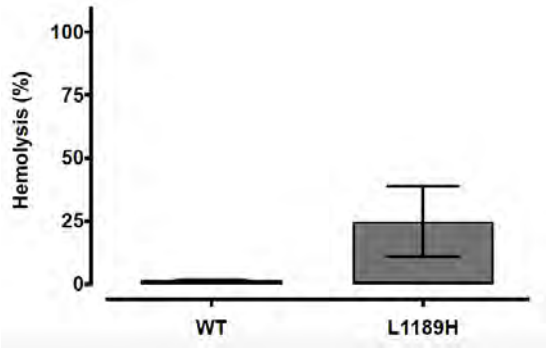


Hemolytic assay

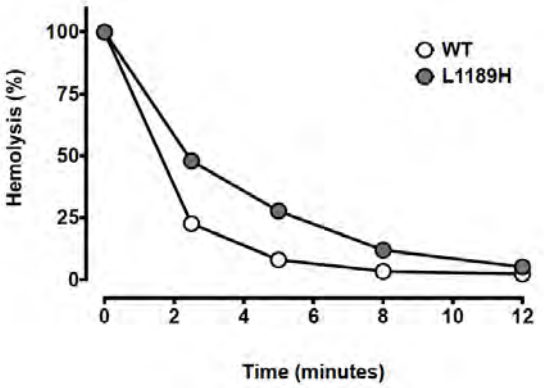
Conclusion: Impaired Function
PATHOGENIC

Previous studies: None

Comments:



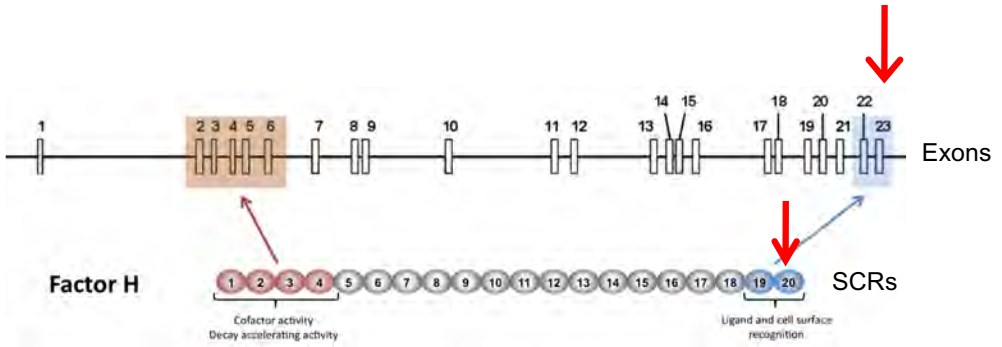
Cofactor activity

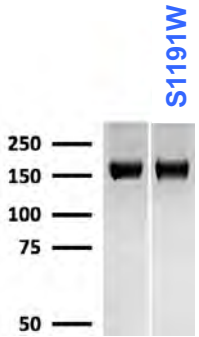


Decay-accelerating activity

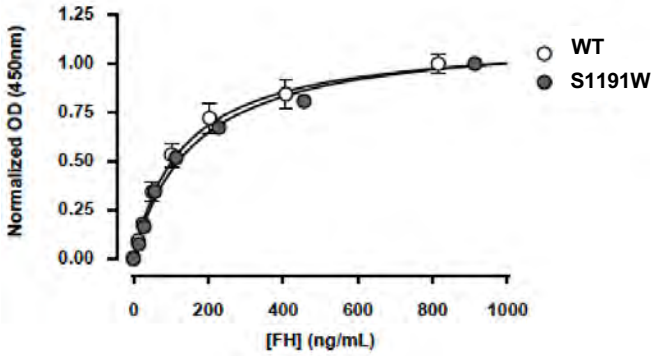
c.3572C>G (S1191W)

CADD: 17.31
gnomAD: Not present

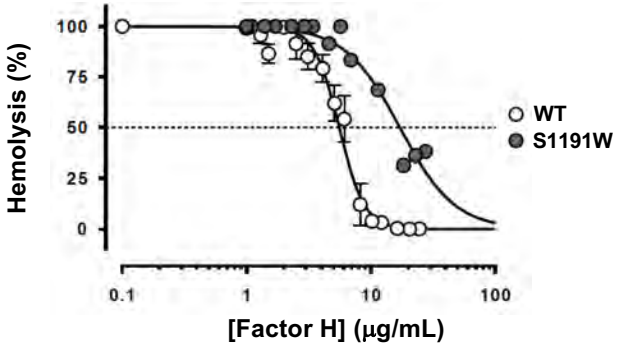




SDS-PAGE
(Non-reduced)



Binding to C3b

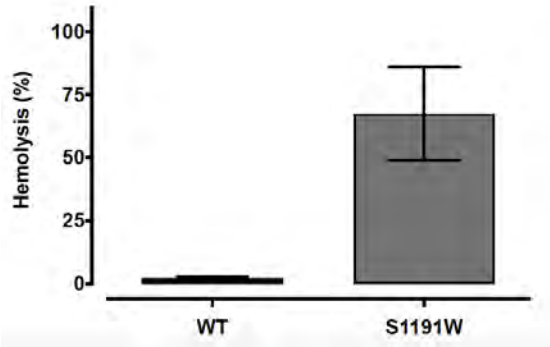


Hemolytic assay

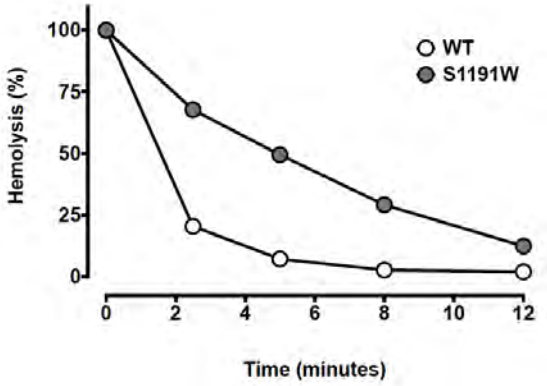
Conclusion: Impaired Function
PATHOGENIC

Previous studies: None

Comments:



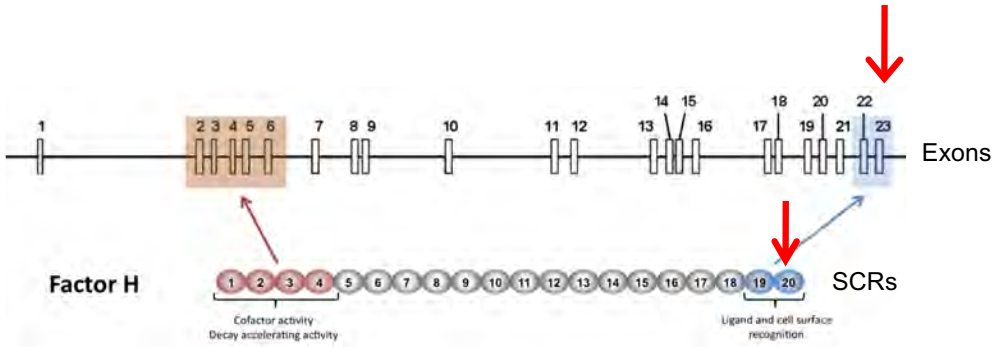
Cofactor activity

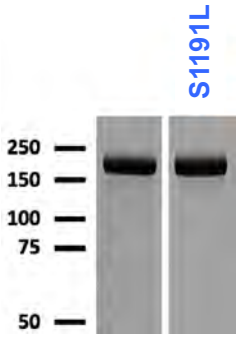


Decay-accelerating activity

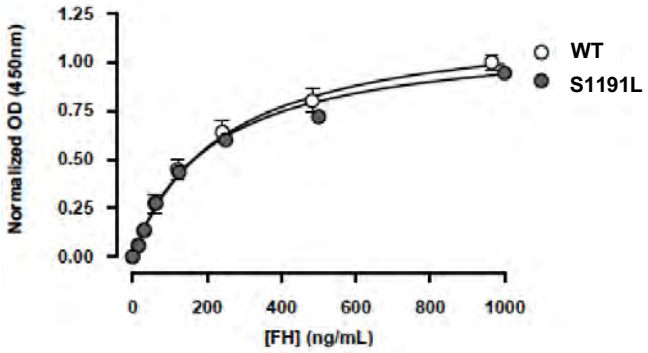
c.3572C>T (S1191L)

CADD: 12.98
gnomAD: Not present

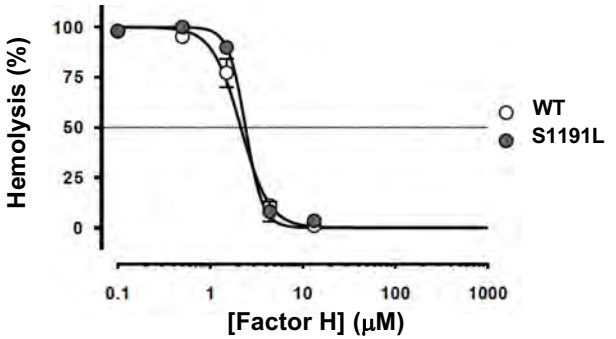




SDS-PAGE
(Non-reduced)



Binding to C3b

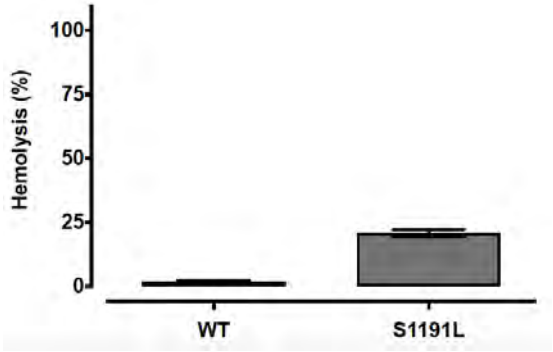


Hemolytic assay

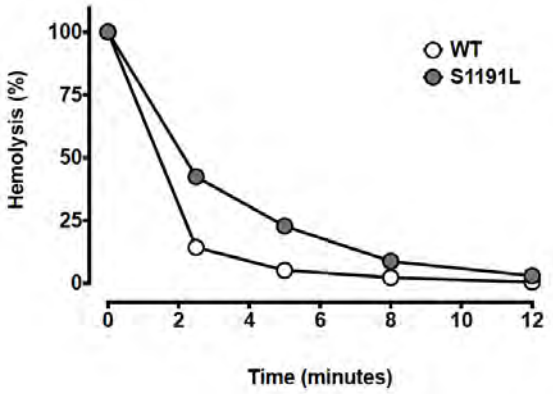
Conclusion: Impaired Function
PATHOGENIC

Previous studies: Pathogenic in Heinen S, Sanchez-Corral P, Jackson MS, et al. De novo gene conversion in the RCA gene cluster (1q32) causes mutations in complement factor H associated with atypical hemolytic uremic syndrome. *Human Mutation*. 2006;27(3):292-293.

Comments:



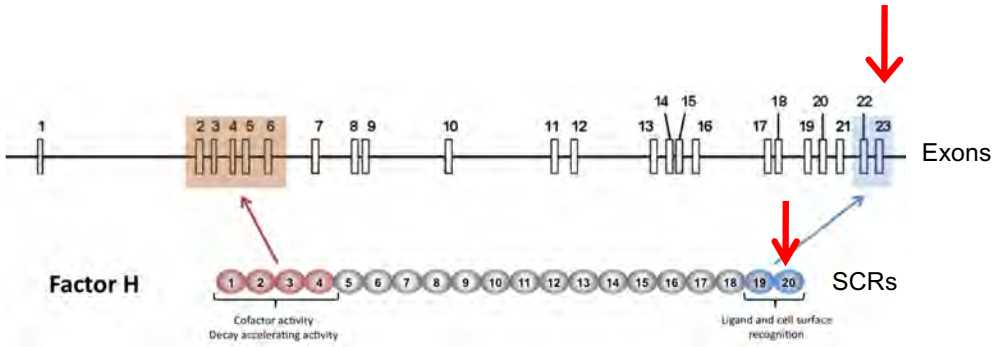
Cofactor activity

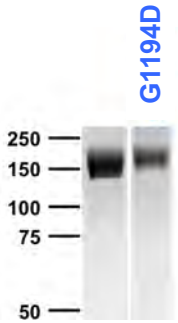


Decay-accelerating activity

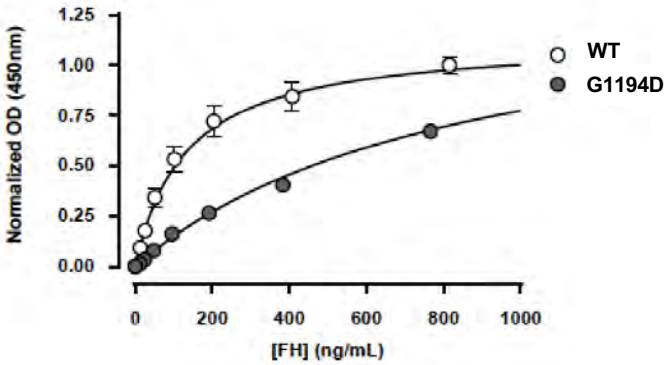
c.3581G>A (G1194D)

CADD: 15.28
gnomAD: $1x10^{-5}$

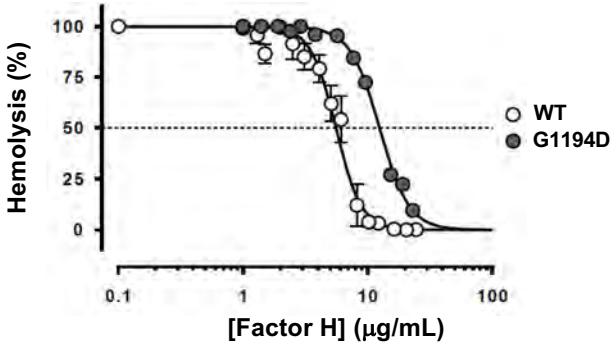




SDS-PAGE
(Non-reduced)



Binding to C3b

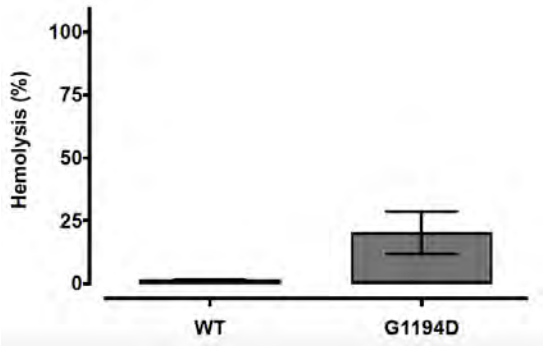


Hemolytic assay

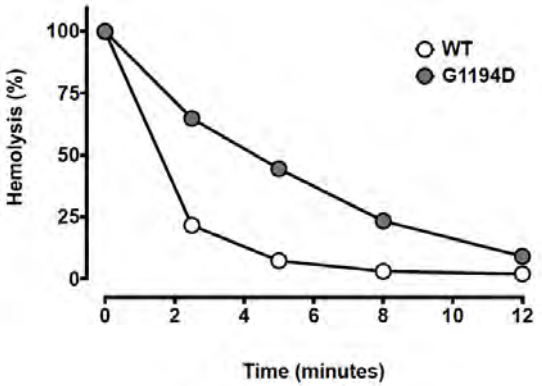
Conclusion: Impaired Expression
PATHOGENIC

Previous studies: None

Comments:
SDS-PAGE shows a FH band with diminished intensity under non-reducing conditions, suggesting that this variant likely affects expression of the protein and results in a factor H deficiency.



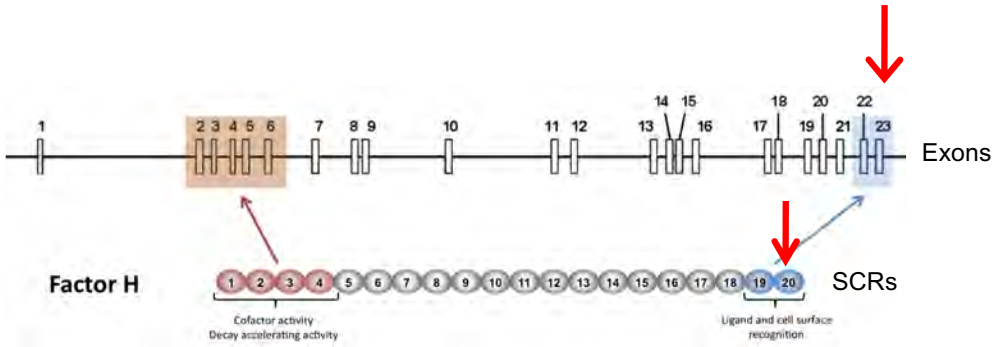
Cofactor activity

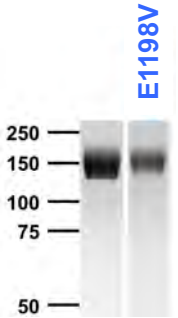


Decay-accelerating activity

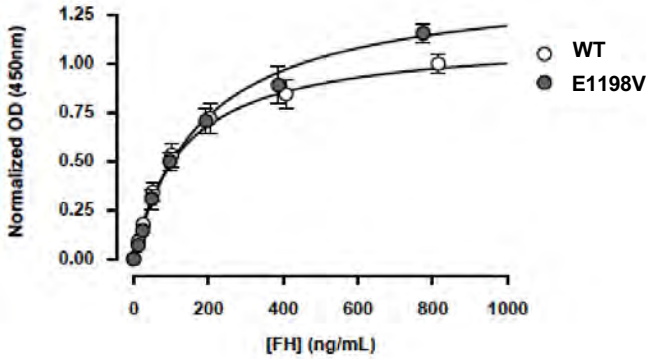
c.3593A>T (E1198V)

CADD: 22.3
gnomAD: Not present

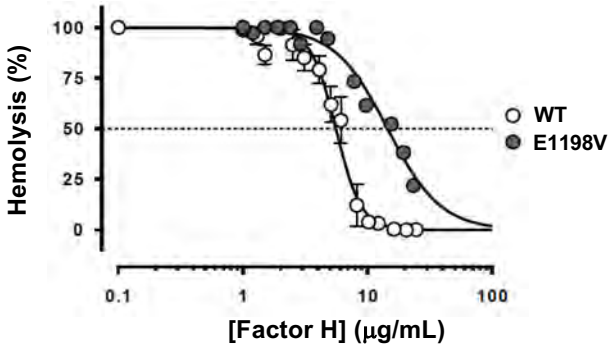




SDS-PAGE
(Non-reduced)



Binding to C3b

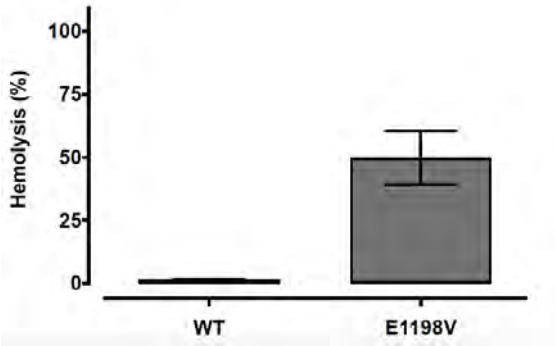


Hemolytic assay

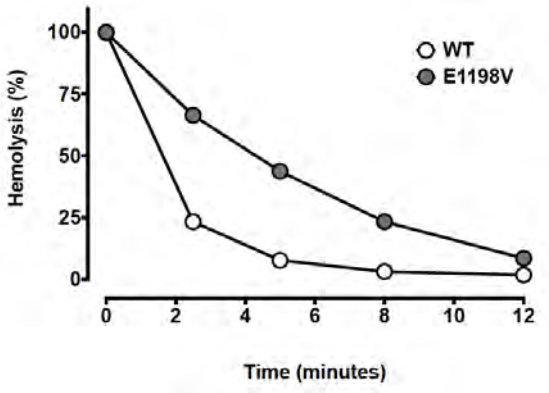
Conclusion: Impaired Expression
PATHOGENIC

Previous studies: None

Comments:
SDS-PAGE shows a FH band with diminished intensity under non-reducing conditions, suggesting that this variant likely affects expression of the protein and results in a factor H deficiency.



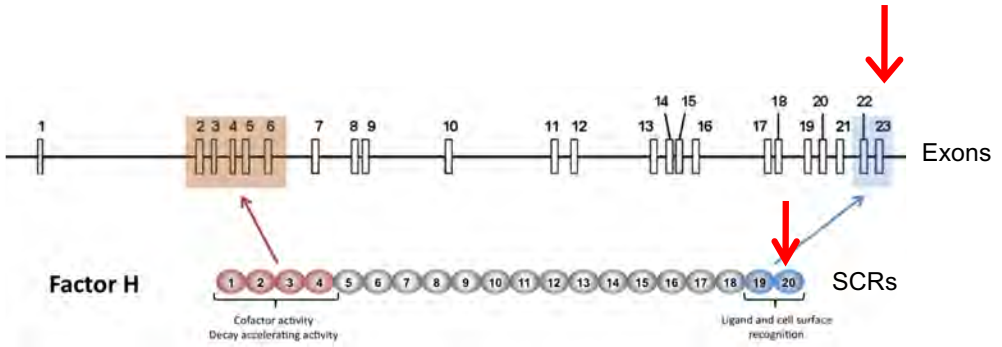
Cofactor activity

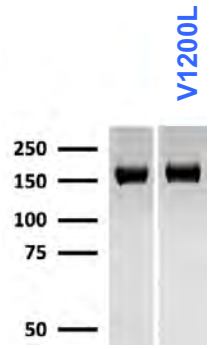


Decay-accelerating activity

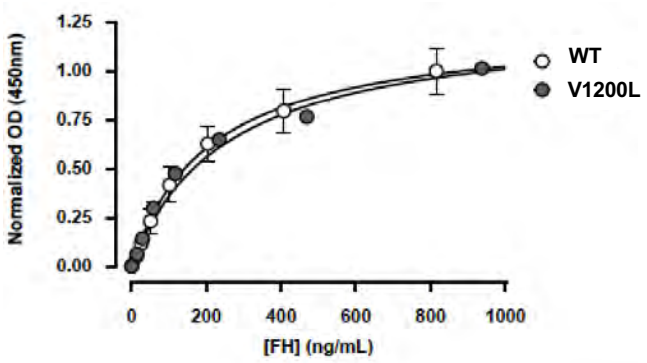
c.3598G>T (V1200L)

CADD: 0
gnomAD: Not present

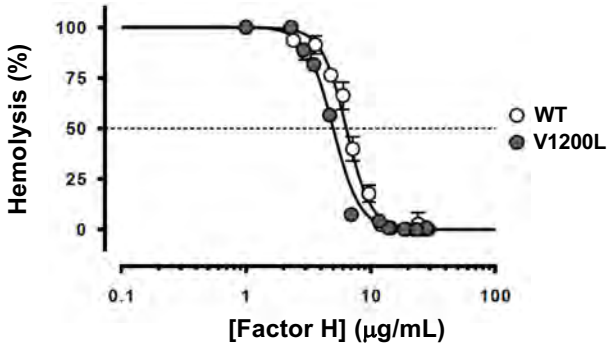




SDS-PAGE
(Non-reduced)



Binding to C3b

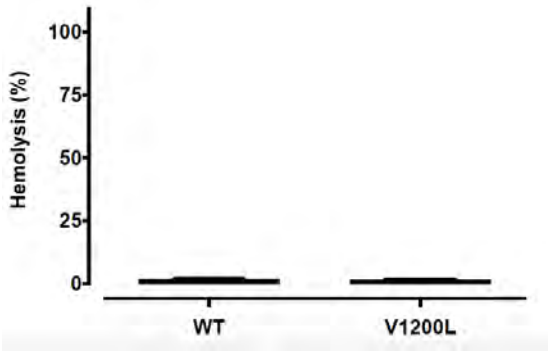


Hemolytic assay

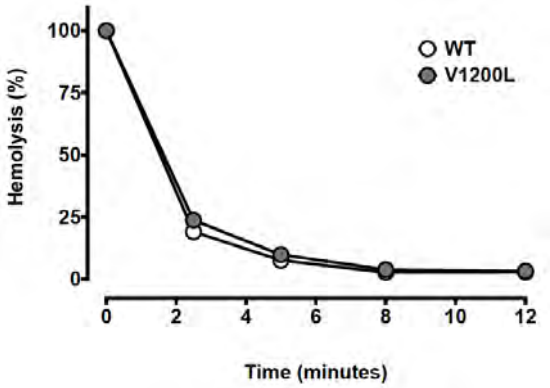
Conclusion: Normal Function
BENIGN

Previous studies: None

Comments:



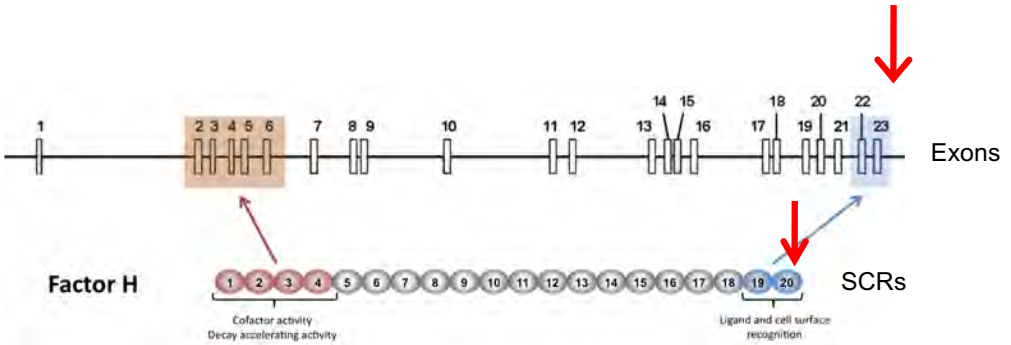
Cofactor activity

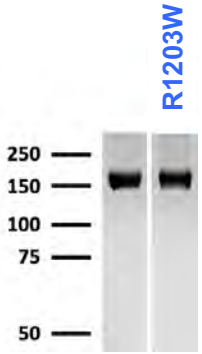


Decay-accelerating activity

c.3607C>T (R1203W)

CADD: 0
gnomAD: $4x10^{-5}$





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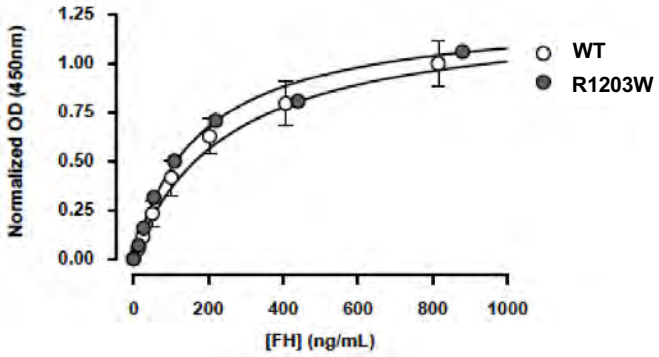
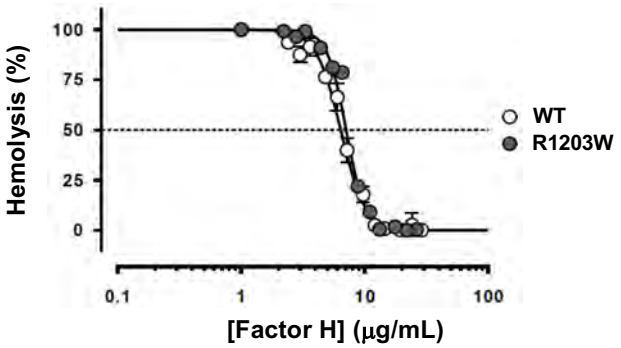
(Non-reduced)



Binding to C3b

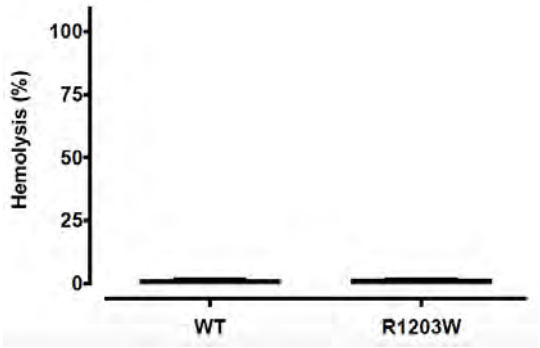


Hemolytic assay

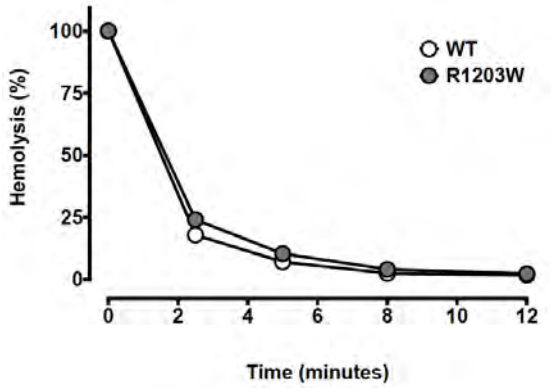
Conclusion: Normal Function
BENIGN

Previous studies: None

Comments:



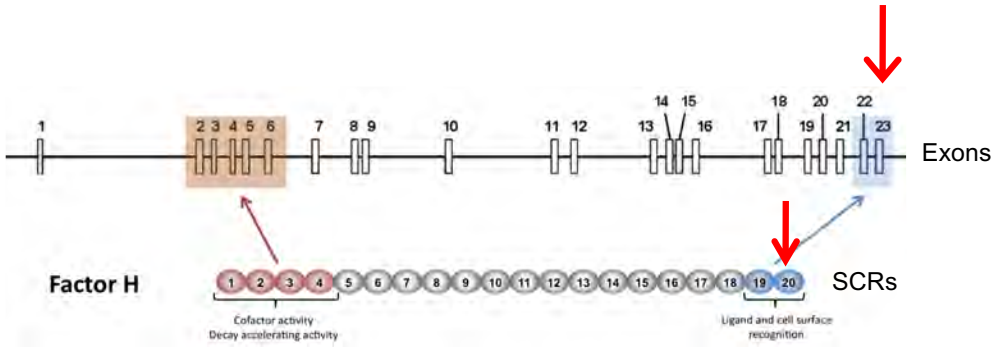
Cofactor activity

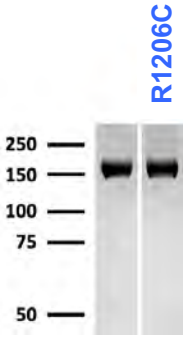


Decay-accelerating activity

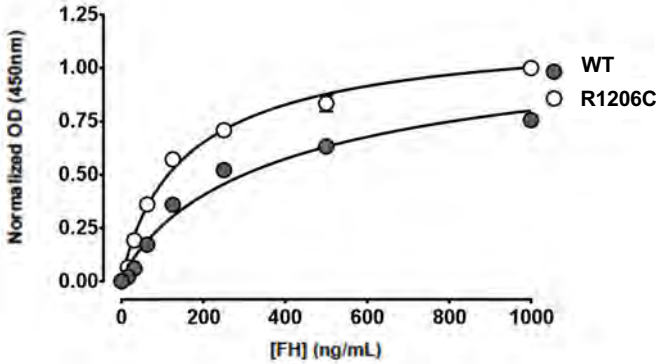
c.3616C>T (R1206C)

CADD: 0.14
gnomAD: Not present

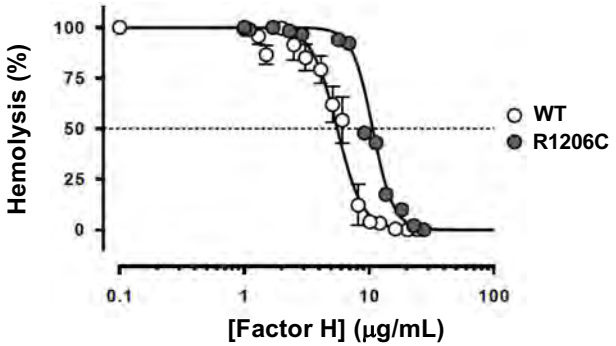




SDS-PAGE
(Non-reduced)



Binding to C3b

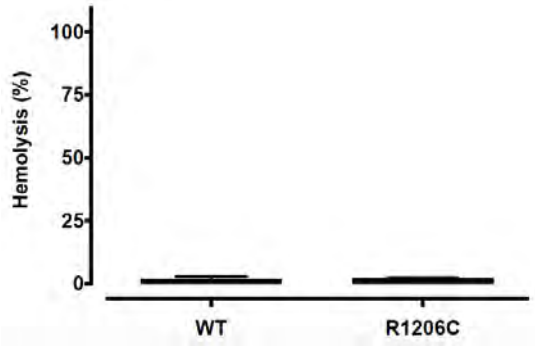


Hemolytic assay

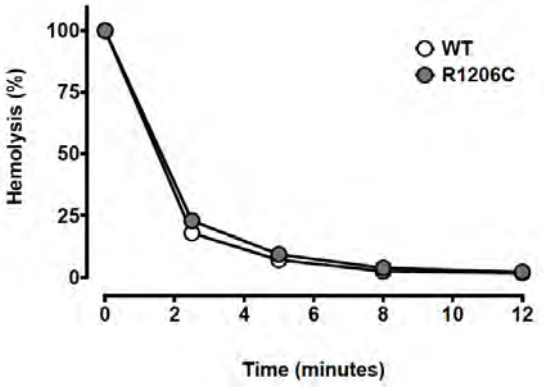
Conclusion: Impaired Function
PATHOGENIC

Previous studies: None

Comments:



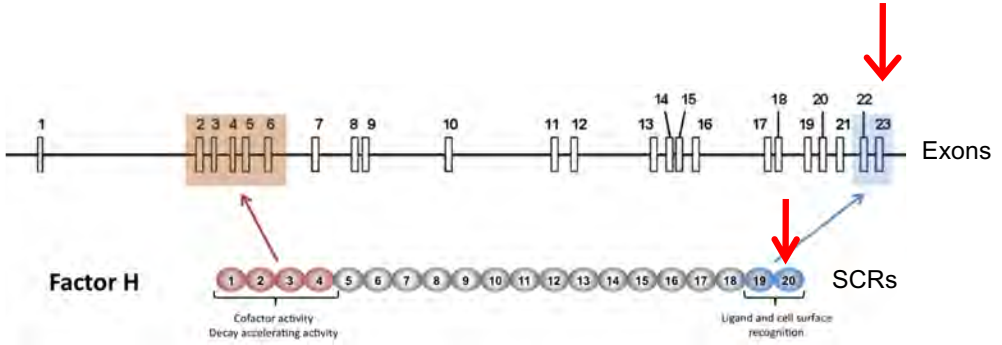
Cofactor activity

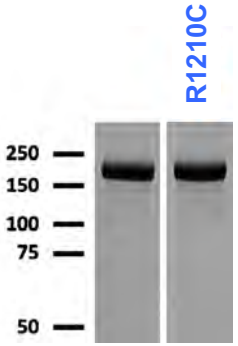


Decay-accelerating activity

c.3628C>T (R1210C)

CADD: 2.95
gnomAD: $1x10^{-4}$





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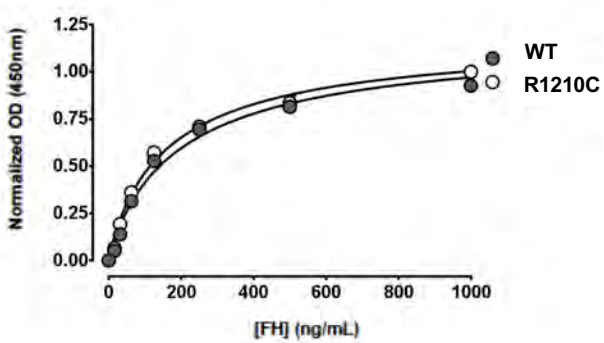
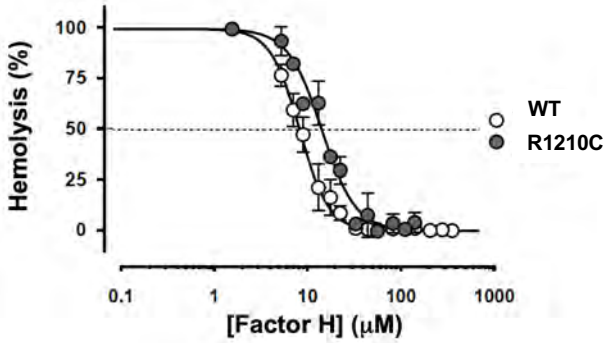
(Non-reduced)

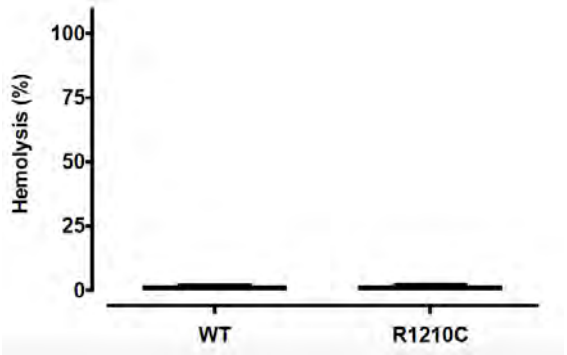


Binding to C3b

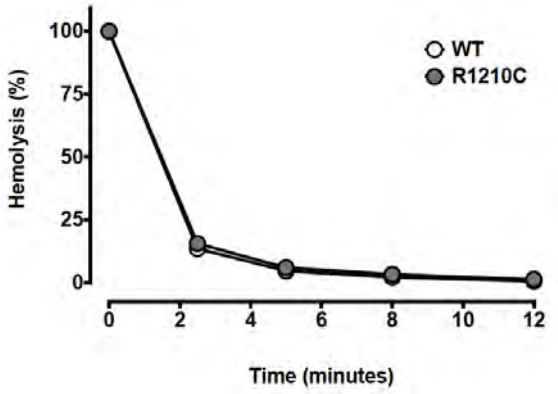


Hemolytic assay

Conclusion: Impaired Function
PATHOGENIC



Cofactor activity



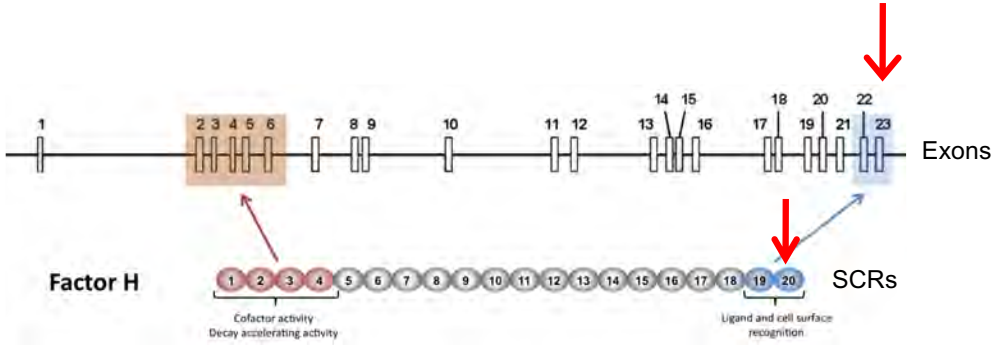
Decay-accelerating activity

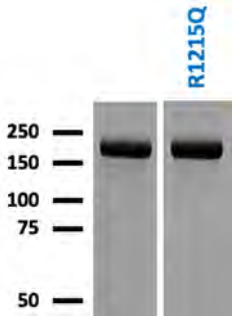
Previous studies: Pathogenic in Sánchez-Corral P, Pérez-Caballero D, Huarte O, et al. Structural and Functional Characterization of Factor H Mutations Associated with Atypical Hemolytic Uremic Syndrome. *The American Journal of Human Genetics*. 2002;71(6):1285-1295.

Comments:
The pathogenicity of this variant is a consequence of the novel cysteine residue organizing a covalent linkage with albumin. The FH-Alb dimers that this mutant forms in vivo are not present in the recombinant protein.

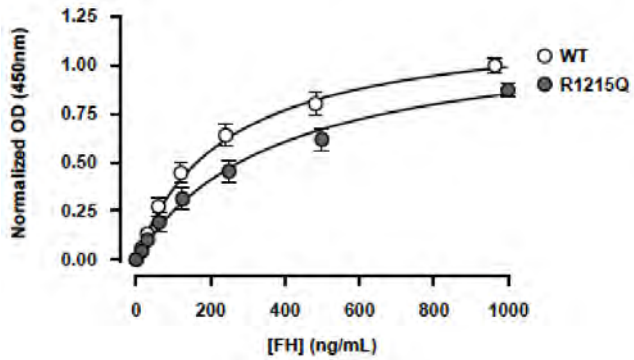
c.3644G>A (R1215Q)

CADD: 15.74
gnomAD: Not present

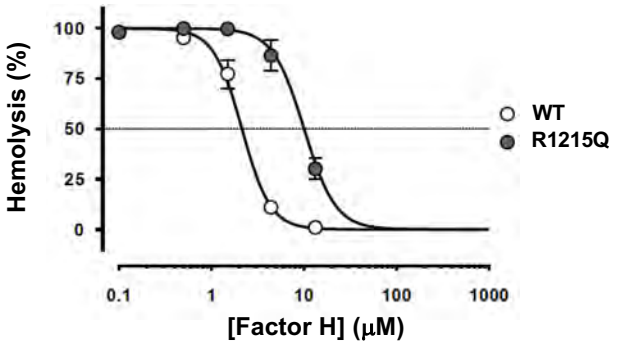




SDS-PAGE
(Non-reduced)

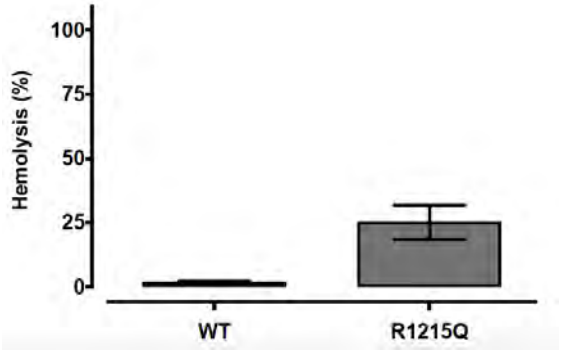


Binding to C3b

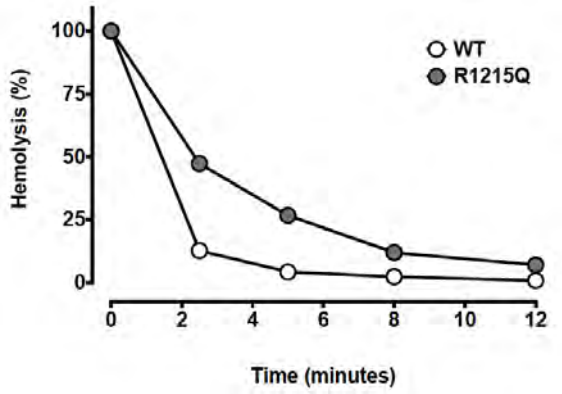


Hemolytic assay

Conclusion: Impaired Function
PATHOGENIC



Cofactor activity



Decay-accelerating activity

Previous studies: Pathogenic in Lehtinen MJ, Rops AL, Isenman DE, van der Vlag J, Jokiranta TS. Mutations of factor H impair regulation of surface-bound C3b by three mechanisms in atypical hemolytic uremic syndrome. *J Biol Chem*. 2009;284(23):15650-15658.

Comments: