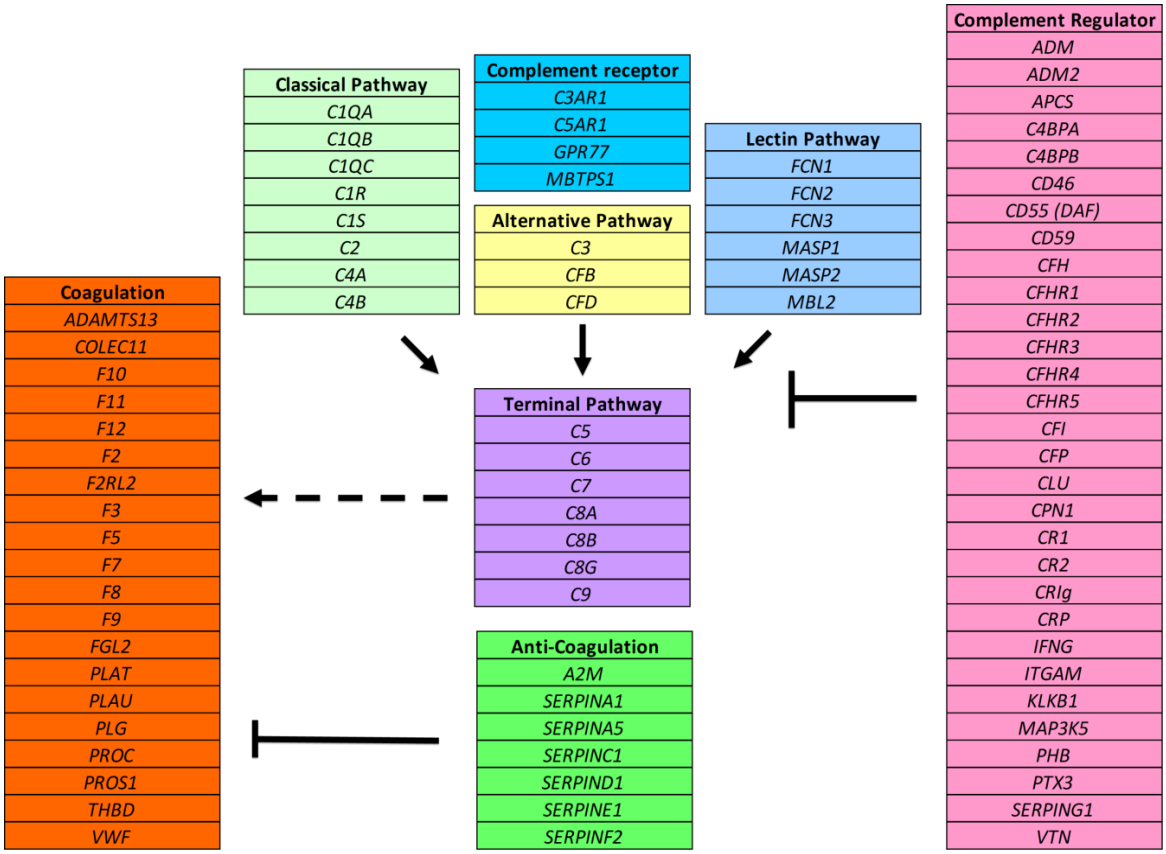
SUPPLEMENTAL RESULTS

Supplemental Figure 1. CasCADE platform (Capture and Sequencing of Complement-Associated Disease Exons) includes 1,071 exons in 85 complement/coagulation genes, with a length of 198,457 base pairs. Targeted sequence is captured using a modified Agilent SureSelect protocol.



Supplemental Figure 1.

Supplemental table 1: Identification of novel nonsynonymous rare variants

Gene	Nucleotide	AA Change	Pathology
FCN1	c.685 G>A	p.A229T	1
F5	[1]c.3221 A>G	p.N1074S	3
MBTPS1	c.2658 G>T	p.Q886H	2
CR1	c.997 A>G	p.R333G	-
C3	c.188 C>T	p.P63L	3
C3	c.3085 G>A	p.D1029N	6
VWF	c.4165 G>C	p.E1389Q	4
KLKB1	c.514 C>A	p.P172T	0
ADAMTS13	c.3056 T>C	p.M1019T	0
MASP2	c.1633 A>G	p.N545D	4
CR1	c.4750 C>T	p.R1584W	4
C2	c.443_453 del	p.148_151del	-
CFH	c.272 C>G	p.T91S	2
F12	c.193 G>A	p.G65S	3
CFH	c.1160-2 A>G		-
MASP1	c.1770 del G	p.G590fs	-
CFH	c.595 A>G	p.S199G	4

[1] Mutation carried by two patients.

Supplemental table 2: Patients carrying multiple deleterious variants

Patients	Gene	Nucleotide	AA change	[1]Pathology Score	[2]MAF (EVS_EA)	dbSNP 137	Reference
1	*CD46*	c.692 C>G	p.P231R	6	-	-	aHUS [1]
	VWF	c.2561 G>A	p.R854Q	4	0.0056	rs41276738	Von Willebrand disease [2]
2	*C8A*	c.1331 G>A	p.R444H	6	0.0050	rs143908758	-
	CFHR5	c.832 G>A	p.G278S	4	0.0088	rs139017763	-
	PLG	c.505 C>T	p.P169S	4	0.0005	rs143256245	-
3	*CFI*	c.355 G>A	p.G119R	3	0.0013	rs141853578	aHUS [1]
	CFI	c.859 G>A	p.G287R	5	0.0001	rs182078921	aHUS [1]
	THBD	c.1502 C>T	p.P501L	3	0.0029	rs1800579	aHUS [3]
4	*CFH*	c.1825 G>A	p.V609I	1	0.0006	rs148165372	aHUS [1]
	CFHR5	c.832 G>A	p.G278S	4	0.0088	rs139017763	-
5	*C9*	c.460 C>T	p.R154X	-	0.0002	rs144138616	C9 deficiency [4]
	PLG	c.2134 G>A	p.G712R	3	0.0007	-	Plasminogen deficiency [5]
6	*CFH*	c.3644 G>A	p.R1215Q	2	-	-	aHUS [6]
	PHB	c.128 G>T	p.R43L	4	0.0088	rs2233665	-
7	*C1S*	c.943 G>A	p.D315N	6	0.0053	rs117907409	-
	C3	c.3085 G>A	p.D1029N	6	-	-	-
	PLG	c.758 G>A	p.R253H	5	0.0006	rs143034754	Plasminogen deficiency [7]
8	*CD46*	c.565 T>G	p.Y189D	5	-	-	aHUS [8]
	F12	c.1681-1 G>A		-	0.0006	-	Factor XII deficiency [9]
	VWF	c.4165 G>C	p.E1389Q	4	-	-	-
9	*CFH*	c.3644 G>A	p.R1215Q	2	-	-	aHUS [6]
	CR1	c. 4750 C>T	p.R1584W	4	-	-	-
10	*CFH*	c.1160-2 A>G	-	-	-	-	-
	CR2	c.524 C>T	p.P175L	4	0.0074	rs75282758	-
11	*C3*	c.4855 A>C	p.S1619R	4	0.0028	rs2230210	-
	CFH	c.3583 G>T	p.E1195X	-	-	-	aHUS [1]
	MASP1	c.1770delG	p.G590fs	-	-	-	-
12	*CFH*	c.3514 G>T	p.E1172X	-	-	rs121913060	aHUS [10]
	CFH	c.595 A>G	p.S199G	4	-	-	-

All variants are heterozygous.

[1] PS calculated using PhyloP, SIFT, PolyPhen2, LRT, MutationTaster and GERP++. The mean PS of predicted deleterious missense nsSNVs is 4.57.

[2] Minor allele frequency values in the Euro pean-American population are from Exome Variant Server (EVS). N.D., no data. Novel variants are those not reported in the EVS, 1000 Genomes and dbSNP databases.

Supplemental table 3: Deleterious variants in 23 genes identified in 25 patients

Genes	Reported disease related variants	Predicted deleterious novel variants	Predicted deleterious rare variants	Total
CFH	9	2	0	11
PLG	3	0	1	4
CD46	3	0	0	3
C3	0	1	1	2
CFI	2	0	0	2
MASP2	0	1	1	2
VWF	1	1	0	2
C1S	0	0	2	2
C2	0	1	0	1
C3AR1	0	0	1	1
C8A	0	0	1	1
C9	1	0	0	1
CFB	1	0	0	1
CFHR5	0	0	2	2
CR1	0	1	0	1
CR2	0	0	1	1
F12	1	0	0	1
FCN1	0	0	1	1
MASP1	0	1	0	1
PHB	0	0	1	1
THBD	1	0	0	1

Deleterious variants include reported DRVs, predicted deleterious novel mutations (PS > 4) and predicted deleterious rare variants (PS > 4)

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