Table S1: Complement gene abnormalities identified in index cases as well as in affected and healthy carriers with their frequency, pathogenicity and classification.

Gene	Index Cases (n)	Healthy Carriers (n)	Affected Carriers (n)	Nucleotide Change	Aminoacid Change	Variant Effect	Allele Frequncy (ExAC)	aHUS DB	Varsome	Franklin	REFERENCES (Doi, PMID)	Final Classification
	1	1	1	c.193A>C	p.(Lys65Gln)	Missense	4.77*10 ⁻⁵	Ρ	VUS	VUS	#, 30046676, 22669319, 29500241 25608561	Ρ
	1	1	0	c.199C>G	p.(Leu67Val)	Missense	ND	А	LB	VUS	-	VUS
	1	0	4	c.485C>G	p.(Thr162Arg)	Missense	ND	VUS	LB	VUS	§, 27064621, 24161037, 29500241 25608561	Ρ
	1 ^A	2	0	c.831T>G	p.(Asp277Glu) ^A	Missense	1.19*10 ⁻⁵	А	LB	VUS	-	VUS
	0	2	0	c.1228A>G	p.(Ser410Gly)	Missense	ND	А	VUS	VUS	-	VUS
	0	2	0	c.1518G>T	p.(Ala540Ser) ^C	Missense	ND	А	VUS	VUS	-	VUS
C3 ⁽¹⁾	1	2	1	c.1774C>T	p.(Arg592Trp)	Missense	3.98*10 ⁻⁶	VUS	LP	VUS	25879158, 18796626, 31118930, 29500241 25608561	Ρ
	1	2	0	c.2203C>T	p.(Arg735Trp)	Missense	2.18*10 ⁻³	В	LB	VUS	18796626, 30890598, 29500241	VUS
	1	1	0	c.3133G>A	p.(Ala1045Thr)	Missense	3.19*10 ⁻⁵	А	VUS	VUS	-	VUS
	1	1+1 ^M	0	c.3343G>A	p.(Asp1115Asn) ^{L,M}	Missense	ND	Ρ	LP	VUS	#, 30890598, 29500241, 18796626 25608561	Ρ
	1	2	0	c.4383C>A	p.(Phe1461Leu)	Missense	ND	А	VUS	VUS	-	VUS
	1	2	0	c.4484C>T	p.(Pro1495Leu)	Missense	2.39*10 ⁻⁵	А	LB	VUS	-	VUS
	1	1	0	c.4811T>C	p.(Met1604Thr)	Missense	2.78*10 ⁻⁵	А	LB	VUS	-	VUS
CFB ⁽¹⁾	1	3	0	c.1407C>G	p.(Ile469Met)	Missense	9.72*10 ⁻⁵	VUS	LB	VUS	29500241	VUS
	1	1	0	c.7C>G	p.(Leu3Val)	Missense	2.43*10 ⁻⁴	А	LB	VUS	25814826	VUS
	1 ^B	1	0	c.29T>G	p.(Leu10Arg) ^B	Missense	ND	А	VUS	VUS	-	VUS
	1 ^c	6	2	c.157C>T	p.(Arg53Cys) ^C	Missense	1.99*10 ⁻⁵	Ρ	VUS	VUS	#, 25188723, 26826462, 29500241	Р
	1	3	0	c.239G>C	p.(Cys80Ser)	Missense	ND	LP	VUS	VUS	29500241	LP
	1	1	3	c.388G>A	p.(Asp130Asn)	Missense	1.4*10 ⁻⁴	ND	LB	VUS	22456601	VUS
СЕН ⁽¹⁾	2	2	0	c.1832G>A	p.(Cys611Tyr)	Missense	ND	А	VUS	VUS	#	LP
	1	4	1	c.1873G>A	p.(Glu625Lys)	Missense	3.99*10 ⁻⁶	А	LB	VUS	-	VUS
0111	1	4	0	c.2383G>A	p.(Gly795Arg)	Missense	ND	LP	VUS	VUS	29500241	LP
	1	1	0	c.2650T>C	p.(Ser884Pro)	Missense	2.79*10 ⁻⁵	VUS	LB	VUS	29500241	VUS
	1	1	0	c.2776T>C	p.(Cys926Arg)	Missense	ND	A	VUS	VUS	31118930	LP
	4	9	0	c.2850G>T	p.(Gln950His)	Missense	3.94*10 ⁻³	LB	В	В	#, 16621965, 24799305, 25188723, 31118930, 29500241 25733390	VUS

$ \begin{array}{ c c c c c c c c c c c c c c c c c c c$			2	0	c.3489C>G	p.(Cys1163Trp)	Missense	ND	LP	VUS	vus	#, 14583443, 18796626,	LP
$ \begin{array}{ c c c c c c c c c c c c c c c c c c c$												29500241 #, 12697737,	
2 3 0 c.3572>T p.(Ser1191Leu) Missense ND P LB VUS 138860 138860 250000 1 3 0 c.35907>C p.(Val1197Ala) Missense 3.98'10 ⁴ P LB VUS 1398'10' 1 ⁰ 1 ⁰ 1 ^N 0 c.361G>A p.(Val1197Ala) Missense ND A VUS 1378'1 1 ⁰ 1 ^N 0 c.361G>A p.(Ag(120Cys) ^{C/D,RLO}) Missense ND A VUS 12180' 1 6+1 ⁰ 3 c.3628C>T p.(Ag(1210Cys) ^{C/D,RLO}) Missense 1.43'10' P LB P 25600' 1 6+1 ⁰ 3 c.3624G>A p.(Ag(1215G)n) Missense ND LP LP LP P 25600' 1 3 0 CFHCFHR1 p.(Ag(1215G)n) Missense ND LP LP LP 1.9''''''''''''''''''''''''''''''''''''		1	2	0	c.3514G>T	p.(Glu1172*)	Nonsense	1.2*10 ⁻⁵	LP	Р	LP	29215813, 29500241	LP
$ \frac{1}{1} + 1 + 1 + 1 + 1 + 1 + 1 + 1 + 1 + 1 +$		2	3	0	c.3572C>T	p.(Ser1191Leu)	Missense	ND	Р	LB	VUS	#, 10577907, 19856002,	Р
$ \begin{array}{ c c c c c c c c c c c c c c c c c c c$		1	3	0	c.3590T>C	p.(Val1197Ala)	Missense	3.98*10 ⁻⁶	Р	LB	VUS	29500241 #, 16470555, 31791575,	Р
$ \frac{1}{1} + 1^{6} + 1^{4} + 1$		1 ^D	1 ^N	0	c.3611G>A	p.(Gly1204Glu) ^{D,N}	Missense	ND	А	VUS	VUS	24799305, 25188723, 17089378	Ρ
Image: book of the section o		1 ^E +1 ^F +1 ^G +1 ^H	6+1 ⁰	3	c.3628C>T	p.(Arg1210Cys) ^{E,F,G,H,O}	Missense	1.43*10 ⁻⁴	Р	LB	LP	#, 11170895, 25188723, 29500241	Ρ
Image: CFH and Related LGR A 0 CFH:CFHR1 p.(*1232llefs*38) Frameshift ND LP VUS VUS VUS 271774 CFH and Related LGR 1 3 0 CFH:CFHR1 p.CFH/CFH1/CFH18) p.2 LGR ND LGR ND ND ND 2000 1 1 0 DupCFH(CFH1/CFH18) p.2 LGR ND LGR ND LGR ND ND -0 -0 1 1 0 DupCFHex23- CFHR1x25 p.2 LGR ND LGR ND ND -0 -0 238807 1 4 0 CFHR1:CFH p.CFHR1/CFH hybrid LGR ND LGR ND ND 238807 1 4 0 CFH3:CFHR4 hybrid* LGR ND LGR ND ND 238807 1 2 1 c.96_110del p.(Cys32_Lys37del) Deletion ND LP VUS 220108		1	6	5	c.3644G>A	p.(Arg1215Gln)	Missense	ND	LP	LP	LP	#, 24799305, 31791575, 29500241	LP
1 3 0 CFH:CFHR1 p.CFH/CFHR1hybrid LGR ND LGR ND ND 209746 1 3 2 DupCFH0CFH1/CFH18 p.? LGR ND LGR ND ND ND ND 1 1 0 DupCFH023- CFHR1ex3 p.? LGR ND LGR ND ND 3 4 3 CFHR1ex3 p.CFHR1/CFH hybrid LGR ND LGR ND ND 24904 1 4 0 CFHR3:CFHR4 p.CFHR3/CFHR4 hybrid* LGR ND LGR ND ND 24904 1 4 0 CFHR3:CFHR4 p.CFHR3/CFHR4 hybrid* LGR ND LGR ND ND 28907 1 2 1 c.96_110del p.(Cys33_Lys37del) Deletion ND LP VUS 205131 277996 1 2 0 c.355G>A p.(Gly119Arg) ¹		1	3	0	c.3693_3696delATAG	p.(*1232llefs*38)	Frameshift	ND	LP	VUS	VUS	#, 24799305, 17599974, 27177491, 29500241	LP
CFH and Related LGR 1 3 2 DupCFH(CFH1/CFH18) p.? LGR ND LGR ND LGR ND		1	3	0	CFH::CFHR1	p.CFH/CFHR1 hybrid	LGR	ND	LGR	ND	ND	20974643	Р
$ \frac{\mbox{CFH and Related LGR}}{\mbox{Related LGR}} = \frac{1}{1} + \frac$		1	3	2	DupCFH(CFH1/CFH18)	p.?	LGR	ND	LGR	ND	ND	-	Р
$ \frac{1}{1} + \frac{1}{2} + 1$	CFH and	1			DunCEHex23-								
1 4 0 CFHR3::CFHR4 p.CFHR3/CFHR4 hybrid ^E LGR ND LGR ND ND 238807 1 2 1 c.96_110del p.(Cys33_Lys37del) Deletion ND LP LP VUS 295002 1 2 0 c.355G>A p.(Gly119Arg) ¹ Missense 4.22*10 ⁻⁴ VUS LP VUS 205031 1 2 0 c.482+8C>T p.? Splice site? 3.94*10 ⁻⁴ A VUS LB - 1 2 0 c.4805G>A p.(Gly269Ser) Missense 1.43*10 ⁻⁴ A VUS VUS 266138 1 1 0 c.949C>T p.(Arg317Trp) Missense 8.76*10 ⁻⁵ P VUS VUS 295002 CFI ⁽¹⁾ 1 4 0 c.1045G>A p.(Gly349Arg) Missense 8.76*10 ⁻⁵ P VUS VUS 295002 295002 1 4 0 c.1045G>A<	CFH and Related I GR	1	1	0	CFHR1ex3	p.?	LGR	ND	LGR	ND	ND	-	Р
1 2 1 c.96_110del p.(Cys33_Lys37del) Deletion ND LP LP VUS 29502 1 2 0 c.355G>A p.(Gly119Arg) ⁱ Missense 4.22*10 ⁴ VUS LP VUS 205131 277996 295002 1 2 0 c.482+8C>T p.? Splice site? 3.94*10 ⁴ A VUS LB - 1 2 0 c.805G>A p.(Gly269Ser) Missense 1.43*10 ⁴ A VUS VUS #,24656 266138 1 1 0 c.949C>T p.(Arg317Trp) Missense 8.76*10 ⁻⁵ P VUS VUS 295002 1 4 0 c.1045G>A p.(Gly349Arg) Missense ND LP VUS 295002 1 4 0 c.1045G>A p.(Gly349Arg) Missense ND LP VUS 295002 201068 1 4 0 c.1045G>A p.(Gly349Arg) Missense	CFH and Related LGR	3	1	0	CFHR1::CFH	p.? p.CFHR1/CFH hybrid	LGR	ND ND	LGR LGR	ND ND	ND ND	- 23880784, 24904082	P
Image: CFI ⁽¹⁾ Image: Lp line Image:	CFH and Related LGR	3	1 4 4	0 3 0	CFHR1ex3 CFHR1::CFH CFHR3::CFHR4	p.? p.CFHR1/CFH hybrid p.CFHR3/CFHR4 hybrid ^E	LGR LGR LGR	ND ND ND	LGR LGR LGR	ND ND ND	ND ND ND	- 23880784, 24904082 23880784	P P P
1 2 0 c.482+8C>T p.? Splice site? 3.94*10 ⁻⁴ A VUS LB - 1 2 0 c.805G>A p.(Gly269Ser) Missense 1.43*10 ⁻⁴ A VUS VUS 266138 1 1 0 c.949C>T p.(Arg317Trp) Missense 8.76*10 ⁻⁵ P VUS VUS 295002 1 4 0 c.1045G>A p.(Gly349Arg) Missense ND LP LP VUS 295002 CFI ⁽¹⁾ 1 4 0 c.1045G>A p.(Gly349Arg) Missense ND LP LP VUS 295002	CFH and Related LGR	3 1 1	1 4 4 2	0 3 0 1	CFHR1ex3 CFHR1::CFH CFHR3::CFHR4 c.96_110del	p.? p.CFHR1/CFH hybrid p.CFHR3/CFHR4 hybrid ^E p.(Cys33_Lys37del)	LGR LGR LGR Deletion	ND ND ND ND	LGR LGR LGR LP	ND ND ND LP	ND ND ND VUS	- 23880784, 24904082 23880784 29500241	P P P LP
1 2 0 c.805G>A p.(Gly269Ser) Missense 1.43*10 ⁻⁴ A VUS VUS #, 24656 266138 1 1 0 c.949C>T p.(Arg317Trp) Missense 8.76*10 ⁻⁵ P VUS VUS 166219 295002 1 4 0 c.1045G>A p.(Gly349Arg) Missense ND LP LP VUS 295002 CFI ⁽¹⁾ 1 4 0 c.1045G>A p.(Gly349Arg) Missense ND LP LP VUS 295002	CFH and Related LGR	3 1 1 1'	1 4 2 2	0 3 0 1 0	CFHR1ex3 CFHR1::CFH CFHR3::CFHR4 c.96_110del c.355G>A	p.? p.CFHR1/CFH hybrid p.CFHR3/CFHR4 hybrid ^E p.(Cys33_Lys37del) p.(Gly119Arg) ⁱ	LGR LGR LGR Deletion Missense	ND ND ND 4.22*10 ⁻⁴	LGR LGR LGR LP VUS	ND ND LP LP	ND ND VUS VUS	- 23880784, 24904082 23880784 29500241 #, 20016463, 20513133, 27799617, 29500241	P P LP VUS
Image: 1 1 0 c.949C>T p.(Arg317Trp) Missense 8.76*10 ⁻⁵ P VUS VUS 166219 295002 CFI ⁽¹⁾ 1 4 0 c.1045G>A p.(Gly349Arg) Missense ND LP LP VUS 295002 CFI Image: 1 Image: 2 Image: 1 Image: 2	CFH and Related LGR	3 1 1 1 ¹	1 4 2 2 2 2	0 3 0 1 0	CFHR1ex3 CFHR1::CFH CFHR3::CFHR4 c.96_110del c.355G>A c.482+8C>T	p.? p.CFHR1/CFH hybrid p.CFHR3/CFHR4 hybrid ^E p.(Cys33_Lys37del) p.(Gly119Arg) ⁱ p.?	LGR LGR Deletion Missense Splice site?	ND ND ND 4.22*10 ⁻⁴	LGR LGR LGR LP VUS	ND ND LP LP VUS	ND ND VUS VUS LB	- 23880784, 24904082 23880784 29500241 #, 20016463, 20513133, 27799617, 29500241	P P LP VUS VUS
CFI ⁽¹⁾ 1 4 0 c.1045G>A p.(Gly349Arg) Missense ND LP LP VUS 295002 201068	CFH and Related LGR	1 3 1 1 1 ¹ 1 1	1 4 2 2 2 2 2 2	0 3 0 1 0 0 0	CFHR1ex3 CFHR1::CFH CFHR3::CFHR4 c.96_110del c.355G>A c.482+8C>T c.805G>A	p.? p.CFHR1/CFH hybrid p.CFHR3/CFHR4 hybrid ^E p.(Cys33_Lys37del) p.(Gly119Arg) ⁱ p.? p.(Gly269Ser)	LGR LGR Deletion Missense Splice site? Missense	ND ND ND 4.22*10 ⁻⁴ 3.94*10 ⁻⁴ 1.43*10 ⁻⁴	LGR LGR LP VUS A A	ND ND LP LP VUS VUS	ND ND VUS VUS LB VUS	- 23880784, 24904082 23880784 29500241 #, 20016463, 20513133, 27799617, 29500241 - - #, 24656451, 26613809	P P LP VUS VUS VUS
201068	CFH and Related LGR	3 1 1 1 ¹ 1 1 1 1	1 4 2 2 2 2 2 1	0 3 0 1 0 0 0 0	CFHR1ex3 CFHR1::CFH CFHR3::CFHR4 c.96_110del c.355G>A c.482+8C>T c.805G>A c.949C>T	p.? p.CFHR1/CFH hybrid p.CFHR3/CFHR4 hybrid ^E p.(Cys33_Lys37del) p.(Gly119Arg) ⁱ p.(Gly269Ser) p.(Arg317Trp)	LGR LGR Deletion Missense Splice site? Missense Missense	ND ND ND 4.22*10 ⁻⁴ 3.94*10 ⁻⁴ 1.43*10 ⁻⁴ 8.76*10 ⁻⁵	LGR LGR LP VUS A A P	ND ND LP LP VUS VUS VUS	ND ND VUS VUS LB VUS VUS	- 23880784, 24904082 23880784 29500241 #, 20016463, 20513133, 27799617, 29500241 - - #, 24656451, 26613809 16621965, 29500241	P P LP VUS VUS VUS P
0 1 0 c.1071T>G p.(Ile357Met)' Missense 3.58*10 ⁻⁵ VUS P VUS 295002	CFH and Related LGR	3 1 1 1 ¹ 1 1 1 1 1	1 4 2 2 2 2 1 4	0 3 0 1 0 0 0 0 0 0	CFHR1ex3 CFHR1::CFH CFHR3::CFHR4 c.96_110del c.355G>A c.482+8C>T c.805G>A c.949C>T c.1045G>A	p.? p.CFHR1/CFH hybrid p.CFHR3/CFHR4 hybrid ^E p.(Cys33_Lys37del) p.(Gly119Arg) ⁱ p.(Gly269Ser) p.(Arg317Trp) p.(Gly349Arg)	LGR LGR Deletion Missense Splice site? Missense Missense Missense	ND ND ND 4.22*10 ⁻⁴ 3.94*10 ⁻⁴ 1.43*10 ⁻⁴ 8.76*10 ⁻⁵ ND	LGR LGR LGR VUS A A P LP	ND ND LP LP VUS VUS VUS LP	ND ND VUS VUS LB VUS VUS VUS	- 23880784, 24904082 23880784 29500241 #, 20016463, 20513133, 27799617, 29500241 - - #, 24656451, 26613809 16621965, 29500241 29500241	P P LP VUS VUS VUS P LP
0 4 0 c.1217G>A p.(Arg406His) ^A Missense 1.68*10 ⁻² A B B 313127 151732	CFH and Related LGR	1 3 1 1 1' 1 1 1 1 0	1 4 2 2 2 2 1 4 1	0 3 0 1 0 0 0 0 0 0 0 0	CFHR1ex3 CFHR1::CFH CFHR3::CFHR4 c.96_110del c.355G>A c.482+8C>T c.805G>A c.949C>T c.1045G>A c.1071T>G	p.? p.CFHR1/CFH hybrid p.CFHR3/CFHR4 hybrid ^E p.(Cys33_Lys37del) p.(Gly119Arg) ⁱ p.(Gly269Ser) p.(Gly269Ser) p.(Gly349Arg) p.(Ile357Met) ^F	LGR LGR Deletion Missense Splice site? Missense Missense Missense Missense	ND ND ND 4.22*10 ⁻⁴ 3.94*10 ⁻⁴ 1.43*10 ⁻⁴ 8.76*10 ⁻⁵ ND 3.58*10 ⁻⁵	LGR LGR LGR VUS A A A P LP VUS	ND ND LP LP VUS VUS VUS LP P	ND ND VUS VUS LB VUS VUS VUS VUS	- 23880784, 24904082 23880784 29500241 #, 20016463, 20513133, 27799617, 29500241 - - #, 24656451, 26613809 16621965, 29500241 29500241 20106822, 29500241	P P LP VUS VUS VUS P LP VUS
1^{L} 1 0 c.1246A>C p.(Ile416Leu) ^{L,M} Missense 1.68*10 ⁻² VUS B B B 23078 295002	CFH and Related LGR	3 1 1 1 1 1 1 1 1 0 0	1 4 2 2 2 2 1 4 1 4	0 3 0 1 0 0 0 0 0 0 0 0 0 0 0	CFHR1ex3 CFHR1::CFH CFHR3::CFHR4 c.96_110del c.355G>A c.355G>A c.482+8C>T c.805G>A c.949C>T c.1045G>A c.1071T>G c.1217G>A	p.? p.CFHR1/CFH hybrid p.CFHR3/CFHR4 hybrid ^E p.(Cys33_Lys37del) p.(Gly119Arg) ⁱ p.(Gly269Ser) p.(Gly269Ser) p.(Arg317Trp) p.(Gly349Arg) p.(Ile357Met) ^F p.(Arg406His) ^A	LGR LGR Deletion Missense Splice site? Missense Missense Missense Missense Missense Missense	ND ND ND 4.22*10 ⁻⁴ 3.94*10 ⁻⁴ 1.43*10 ⁻⁴ 8.76*10 ⁻⁵ ND 3.58*10 ⁻⁵ 1.68*10 ⁻²	LGR LGR LP VUS A A P LP VUS A	ND ND LP LP VUS VUS VUS LP P B	ND ND VUS VUS LB VUS VUS VUS VUS B	- 23880784, 24904082 23880784 29500241 #, 20016463, 20513133, 27799617, 29500241 - #, 24656451, 26613809 16621965, 29500241 20106822, 29500241 20106822, 29500241 31312772, 15173250	P P LP VUS VUS VUS P LP VUS VUS
1 1 0 c.1343G>T p.(Arg448Leu) Missense ND A VUS VUS -	CFH and Related LGR	3 1 1 1 1 1 1 1 0 0 1 ^L	1 4 2 2 2 2 1 4 1 4 1 4	0 3 0 1 0 0 0 0 0 0 0 0 0 0 0	CFHR1ex3 CFHR1::CFH CFHR3::CFHR4 c.96_110del c.355G>A c.355G>A c.482+8C>T c.805G>A c.949C>T c.1045G>A c.1071T>G c.1217G>A c.1246A>C	p.? p.CFHR1/CFH hybrid p.CFHR3/CFHR4 hybrid ^E p.(Cys33_Lys37del) p.(Gly119Arg) ⁱ p.(Gly269Ser) p.(Gly269Ser) p.(Arg317Trp) p.(Gly349Arg) p.(Ile357Met) ^F p.(Arg406His) ^A p.(Ile416Leu) ^{LM}	LGR LGR LGR Deletion Missense Splice site? Missense	ND ND ND A.22*10 ⁻⁴ A.22*10 ⁻⁵ A.22*10 ⁻⁵ A.25*10 ⁻⁵ A.25*10 ⁻⁵ A.25*10 ⁻² A.25*10 ⁻² A.25*1	LGR LGR LP VUS A A LP VUS A VUS	ND ND LP LP VUS VUS VUS LP P B B	ND ND VUS VUS LB VUS VUS VUS VUS B B B	- 23880784, 24904082 23880784 29500241 #, 20016463, 20513133, 27799617, 29500241 - - #, 24656451, 26613809 16621965, 29500241 20106822, 29500241 31312772, 15173250 20016463 23307876 29500241	P P LP VUS VUS VUS P LP VUS VUS VUS
1 10 0 c.1555G>A p.(Asp519Asn) ^G Missense 7.96*10 ⁻⁶ P LP VUS 198770 175972	CFH and Related LGR	3 1 1 1 1 1 1 1 0 0 1 ^L 1	1 4 2 2 2 2 1 4 1 4 1 4 1 1	0 3 0 1 0 0 0 0 0 0 0 0 0 0 0 0 0	CFHR1ex3 CFHR1::CFH CFHR3::CFHR4 c.96_110del c.355G>A c.482+8C>T c.805G>A c.949C>T c.1045G>A c.1071T>G c.1217G>A c.1246A>C c.1343G>T	p.? p.CFHR1/CFH hybrid p.CFHR3/CFHR4 hybrid ^E p.(Cys33_Lys37del) p.(Gly119Arg) ⁱ p.(Gly269Ser) p.(Gly269Ser) p.(Arg317Trp) p.(Gly349Arg) p.(Ile357Met) ^F p.(Arg406His) ^A p.(Ile416Leu) ^{LM} p.(Arg448Leu)	LGR LGR LGR Deletion Missense Splice site? Missense Missense Missense Missense Missense Missense Missense	ND ND ND 4.22*10 ⁻⁴ 3.94*10 ⁻⁴ 1.43*10 ⁻⁴ 8.76*10 ⁻⁵ ND 3.58*10 ⁻⁵ 1.68*10 ⁻² 1.68*10 ⁻² ND	LGR LGR LP VUS A A LP VUS A VUS A VUS	ND ND LP LP VUS VUS LP P B B VUS	ND ND VUS VUS LB VUS VUS VUS B B B VUS	23880784, 24904082 23880784 29500241 #, 20016463, 20513133, 27799617, 29500241 #, 24656451, 26613809 16621965, 29500241 20106822, 29500241 31312772, 15173250 20016463 23307876 29500241	P P LP VUS VUS VUS P LP VUS VUS VUS VUS

											29500241	
CD46 ⁽¹⁾	1	0	1	c.98-1G>C	p.?	Splice site	ND	А	Р	LP	16621965, 1984685	LP
	0	0	0	c.104G>A	p.(Cys35Tyr) ^{H,O}	Missense	1.19*10 ⁻⁵	LP	VUS	VUS	#, 16621965, 25188723, 29500241	LP
	1	5	0	c.175C>T	p.(Arg59*) ^{H,O}	Nonsense	1.19*10 ⁻⁵	Р	LP	LP	#, 26054645, 29500241, 16621965	Р
	4	7	1	c.286+2T>G	p.? ^{D,F,N}	Splice site	5.21*10 ⁻⁵	LP	Р	LP	#, 16762990, 25899302, 29500241	LP
	1	1	0	c.404G>A	p.(Gly135Asp)	Missense	4.02*10 ⁻⁶	ND	VUS	VUS	#, 21706448, 25188723	VUS
	1	1	0	c.523T>G	p.(Phe175Val)	Missense	7.96*10 ⁻⁶	A	LB	VUS	-	VUS
	2	4	0	c.565T>G	p.(Tyr189Asp) ^B	Missense	1.59*10 ⁻⁵	LP	VUS	VUS	16762990, 25188723, 29644059, 29500241	LP
	1	2	0	c.664G>T	p.(Glu222*)	Nonsense	ND	Α	Р	LP	-	LP
	2	4	0	c.685C>T	p.(Arg229*)	Nonsense	ND	LP	Р	Р	#, 25443527, 29500241	LP
	3	6	0	c.1148C>T	p.(Thr383lle)	Missense	7.12*10 ⁻⁴	VUS	LB	VUS	#, 29500241, 21706448	VUS

DB= database; A= absent; B= benign; LB= likely benign; VUS= variant of unknown significance; LP=likely pathogenic; P=pathogenic; ND= not defined; LGR= large genomic rearrangement;

⁽¹⁾ C3: NM_000064, NP_000055; CFB: NM_001710, NP_001701; CFH: NM_000186, NP_000177; CFHR1: NM_002113, NP_002104; CFHR3: NM_021023, NP_066303; CFHR4: NM_001201550, NP_001188479, CFI: NM_000204, NP_000195; CD46: NM_002389, NP_002380;

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Letters identify members of families with multiple gene variants (from A to L identify the ten index cases; from M to O identify the three healthy carriers).

Modified STROBE Statement—checklist of items that should be included in reports of observational studies (Cohort/Cross-sectional and case-control studies)

	Item No	Recommendation	Page No
Title and abstract	1	(<i>a</i>) Indicate the study's design with a commonly used term in the title or the abstract	2
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	2
Objectives	3	State specific objectives, including any prespecified hypotheses	3
Methods			
Study design	4	Present key elements of study design early in the paper	3
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	3
Participants	6	 (a) Cohort study—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up Case-control study—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls 	3-4
		Cross-sectional study—Give the eligibility criteria, and the sources and methods of selection of participants	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	4
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	4
Bias	9	Describe any efforts to address potential sources of bias	-
Study size	10	Explain how the study size was arrived at	3
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	5
Statistical methods	12	(<i>a</i>) Describe all statistical methods, including those used to control for confounding	5

		(b) Describe any methods used to examine subgroups and interactions	5
		(c) Explain how missing data were addressed	-
		(d) Cohort study—If applicable, explain how loss to follow-up was addressed	-
		Case-control study—If applicable, explain how matching of cases and controls was addressed	
		Cross-sectional study—If applicable, describe analytical methods taking account of sampling strategy	
		(<u>e</u>) Describe any sensitivity analyses	-
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	5
		(c) Consider use of a flow diagram	Fig.1
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	5
		(b) Indicate number of participants with missing data for each variable of interest	5
		(c) Cohort study—Summarise follow-up time (eg, average and total amount)	5
Outcome data	15*	Cohort study—Report numbers of outcome events or summary	5-6
		measures over time	tab. 2
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	
		Cross-sectional study—Report numbers of outcome events or summary measure	
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-	Tab.2
		adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	6

Discussion			
Key results	18	Summarise key results with reference to study objectives	7
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	7-8
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	8
Generalisability	21	Discuss the generalisability (external validity) of the study results	8

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.