Genotypes of patients with factor XI deficiency

Mutation	Location	Domain	Type	Genotype	Origin	Activity U/dL	Antigen U/dL	Expression	comments	Reference
nt-1296G>A nt 823 del C	Promoter Exon 8	Promoter Apple 3	Regulatory Frameshift	Comp het	Nigeria	3				1
Met-18Ile* Cys128stop*	Exon 2 Exon 5	Signal Apple 2	Missense	Comp het		<1	<3			2 3
Met-18Ile*	Exon 2	Signal	Missense	Het		43,50		Yes		2 3
Ser-4Leu	Exon 2	Signal	Missense	Hom	Morocco	3	3			4
Gly-1Arg Gln263stop	Exon 2 Exon 8	Signal Apple3	Missense Nonsense	Comp het	China	3	3			5
IVS2+6 T>G + 10 ins AG	Intron 2		Splicing	Hom	Czechoslovakia	1.4	3			6
Glu1stop	Exon 2	Apple 1	Nonsense	Het		43				2
nt 73 del 14 bp Glu117stop	Exon 3 Exon 5	Apple 1 Apple 2	Frameshift Nonsense	Comp het	Non-Ashkenazi Jew	<1	<1			7
nt 78 del GGA	Exon 3	Apple 1	Frameshift	Het	Italy	20	32			8
Thr10Ala Cys527Arg*	Exon 3 Exon 14	Apple 1 Catalytic	Missense Missense	Comp het		22				9
Asp16His*	Exon 3	Apple 1	Missense	Het				Yes		10,11
Val20Ala	Exon 3	Apple 1	Missense	Het	France	32		Yes		7
Pro23Leu	Exon 3	Apple 1	Missense	Het	Africa	30	39			12
Pro23Gln	Exon 3	Apple 1	Missense	Het		56				2
Ser24Arg	Exon 3	Apple 1	Missense	Het		29				13
Ala25Thr Glu602Gln	Exon 3 Exon 15	Apple 1 Catalytic	Missense Missense	Comp het		28	27			9
Cys28Phe	Exon 3	Apple 1	Missense	Het		31	41			14
Gln29His	Exon 3	Apple 1	Missense	Het						2
Thr33Pro*	Exon 3	Apple 1	Missense	Het	Iran	23				15
Thr33Pro*	Exon 3	Apple 1	Missense	Het	Turkey	42	46	Yes		16
Thr33Ile	Exon 3	Apple 1	Missense	Het	Iran	27				15
Cys38Arg*	Exon 3	Apple 1	Missense	Hom	French Basque	<1		Yes	Founder mutation	17

Cys38Arg*	Exon 3	Apple 1	Missense	Het		33	29			9
Cys38Arg* Arg308His	Exon 3 Exon 9	Apple 1 Apple 4	Missense Missense	Comp het		4	5			9
Cys38Arg* Pro382Leu*	Exon 3 Exon 11	Apple 1 Catalytic	Missense Missense	Comp het	Portugal	<1				12
Cys38Arg* Tyr493His	Exon 3 Exon 13	Apple 1 Catalytic	Missense Missense	Comp het	French Basque	1-2		Yes Yes		17
Cys38stop	Exon 3	Apple 1	Nonsense	Het	Ireland	56				18
Cys38Trp	Exon 3	Apple 1	Missense	Het		20	46	Yes		8
nt 192 ins G Gln88stop*	Exon 3 Exon 4	Apple 1 Apple 1	Frameshift Nonsense	Comp het	West France	<1	<1			19
Arg54Pro	Exon 3	Apple 1	Missense	Het	Czechoslovakia	63	77	Yes		8
IVS3+2 T>A Lys252Ile*	Intron 3 Exon 8	- Apple 3	Splicing Missense	Comp het	Czechoslovakia	2	4			6
nt 226 del T	Exon 4	Apple 1	Frameshift	Hom	France	1				20
Cys58Arg	Exon 4	Apple 1	Missense	Het		42				2
Cys58Tyr	Exon 4	Apple 1	Missense	Het	Yemenite Jew	25		Yes		7
Cys58Phe	Exon 4	Apple 1	Missense	Hom		<1				2
Ser78Phe*	Exon 4	Apple 1	Missense	Het		43	30			9
Gly79Ala Glu117stop*	Exon 4 Exon 5	Apple 1 Apple 2	Missense Nonsense	Comp het	Czechoslovakia	1.3	3			6
Ser81Tyr	Exon 4	Apple 1	Missense	Het		57				13
Lys83Arg	Exon 4	Apple 1	Missense	Het		38				14
nt 308 ins 7bp	Exon 4	Apple 1	Frameshift	Het	Portugal	40	48			21
Gln88stop*	Exon 4	Apple 1	Nonsense	Hom	West France	<1	<1			19
Gln88stop* Thr575Met*	Exon 4 Exon 15	Apple 1 Catalytic	Nonsense Missense	Comp het	West France	1	42			19
nt 325 G>A*	Exon 4	Apple 1	Splicing	Het	Italy	52		Yes		22
nt 325 G>A* Reported as Ala91Thr	Exon 4	Apple 1	Splicing	Het	Australia	57				23
nt 325 G>A* Gly104Asp*	Exon 4 Exon 5	Apple 1 Apple 2	Splicing Missense	Comp het	Australia	2				23
nt 325 G>A* Phe283Leu*	Exon 4 Exon 9	Apple 1 Apple 4	Splicing Missense	Comp het	Italy	1.6	6			24

nt 325 G>A* Reported as Ala91Thr Glu323Lys*	Exon 4 Exon 9	Apple 1 Apple 4	Splicing Missense	Comp het		9				2
IVS4+1 G>A*	Intron 4		Splicing	Het		45				2
IVS4+1 G>A* Cys128stop*	Intron 4 Exon 5	- Apple 2	Splicing Nonsense	Comp het		2				2
Cys92Gly	Exon 5	Apple 2	Missense	Het	Vietnam	47	40			12
Met102Thr	Exon 5	Apple 2	Missense	Het		40,45		Yes		2,3
Gly104Asp*	Exon 5	Apple 2	Missense	Het		33				2,11
Gln116stop*	Exon 5	Apple 2	Nonsense	Het	Austria	43	52			25
Gln116stop* Thr123Met	Exon 5 Exon 5	Apple 2 Apple 2	Nonsense Missense	Comp het	Italy	<1	4			24
Glu117stop (type II)*	Exon 5	Apple 2	Nonsense	Hom	Ashkenazi and non Ashkenazi Jews, Arabs	<1	1	Yes	Common in Ashkenazi and Iraqi Jews, Arabs. Founder mutation	26,27,28,29, 30,31
Glu117stop*	Exon 5	Apple 2	Nonsense	Hom	Portugal (non Jewish)	1			2 unrelated families with Jewish haplotype	21
Glu117stop*	Exon 5	Apple 2	Nonsense	Hom	Italy (non Jewish)	1			Several unrelated patients with the Jewish haplotype	32,33
Glu117stop* Cys118Arg	Exon 5 Exon 5	Apple 2 Apple 2	Nonsense Missense	Comp het	Italy	<1				34
Glu117stop* Cys122Tyr*	Exon 5 Exon 5	Apple 2 Apple 2	Nonsense Missense	Comp het	Italy	<1	10			24
Glu117stop* Cys212Ser	Exon 5 Exon 7	Apple 2 Apple 3	Nonsense Missense	Comp het	France	<1				20
Glu117stop*	Exon 5	Apple 2	Nonsense	Comp het		<1	<3			2

Gln233stop*	Exon 7	Apple 3	Nonsense							
Glu117stop* Cys237Tyr and Cys321Phe	Exon 6 Exon 8 Exon 9	Apple 1 Apple 3 Apple 4	Nonsense Missense Polymorphism	Comp het	Mixed Basque/ Jewish	<1		Yes Yes Yes		17
Glu117stop* (type II) Phe283Leu* (type III)	Exon 5 Exon 9	Apple 2	Nonsense Missense	Comp het	Ashkenazi Jewish	2-8			Common in Ashkenazi Jews	26,27,28
Glu117stop* Cys309stop*	Exon 5 Exon 9	Apple 2 Apple 4	Nonsense Nonsense	Comp het	Italy	<1	4			24
Glu117stop* Gly350Arg	Exon 5 Exon 10	Apple 2 Apple 4	Nonsense Missense	Comp het	France	<1	<1			20
Glu117stop* Tyr427Cys	Exon 5 Exon 12	Apple 2 Catalytic	Nonsense Missense	Comp het	Ashkenazi Jew	<1	<1	- Yes		7
Cys118stop*	Exon 5	Apple 2	Nonsense	Hom	Italy	<1				32
Cys118stop* Pro382Leu*	Exon 5 Exon 11	Apple 2 Catalytic	Nonsense Missense	Comp het		<1				2
Cys122Tyr*	Exon 5	Apple 2	Missense	Hom	Italy	4	3	Yes		8
Cys122Tyr*	Exon 5	Apple 2	Missense	Het		25				4
Cys128stop*	Exon 5	Apple 2	Nonsense	Het	UK	49	41			35
Cys128stop*	Exon 5	Apple 2	Nonsense	Hom	UK	<1				36,37
Cys128stop* Undefined	Exon 5	Apple 2	Nonsense	Comp het	UK	<1	<1			36
Cys128stop* nt? ins 1 bp	Exon 5 Exon 4	Apple 2 Apple 1	Nonsense Frameshift	Comp het		<2				36
Cys128stop* Gene deletion*	Exon 5	Apple 2	Nonsense Deletion	Comp het	Australia	<2				23
Thr132Met	Exon 5	Apple 2	Missense	Het		23				2
Tyr133Cys*	Exon 5	Apple 2	Missense	Het						2,14
Tyr133Cys* Cys128stop*	Exon 5 Exon 5	Apple 2 Apple 2	Missense Nonsense	Comp het		<1				2
Tyr133Ser*	Exon 5	Apple 2	Missense	Het		50		Yes		2,3
Ala134Pro	Exon 5	Apple 2	Missense	Hom		<1				2
IVS5+5 G>C	Intron 5		Splicing							10

IVS5-2 A>G*	Intron 5		Splicing	Hom		3				11
IVS5-2 A>G*	Intron 5		Splicing	Het	Italy	36	25			2,4
Gly155Glu	Exon 6	Apple 2	Missense	Het		41				11
IVS6+3 A>G*	Intron 6		Splicing	Het	Basque France	40				2,17,20,25
IVS6+3 A>G*	Intron 6		Splicing	Hom	Mexico	<1				7
IVS6+3 A>G* Arg184Gly	Intron 6 Exon 7	- Apple 3	Splicing Missense	Comp het	Italy	10	46	 Yes		22
Ala181Val Ala412Thr*	Exon 7 Exon 11	Apple 3 Catalytic	Missense Missense	Comp het	France	7	7			38
Cys182Tyr*	Exon 7	Apple 3	Missense	Het		34				2
Cys182Tyr*	Exon 7	Apple 3	Missense	Het	Australia	47				23
Pro188Ser*	Exon 7	Apple 3	Missense	Het	France	30				4
Pro188Ser* Cys527Arg*	Exon 7 Exon 14	Apple 3 Catalytic	Missense Missense	Comp het		3				9
nt 644 del 6 bp*	Exon 7	Apple 3	In frame del	Het	Austria	39	34			25
nt 644 del 6 bp*	Exon 7	Apple 3	In frame del	Het	Iran	23				15
nt 644 del 6 bp* Glu117stop*	Exon 7 Exon 5	Apple 3 Apple 2	In frame del Nonsense	Comp het	Italy	<1	5	Yes		32
Arg210stop Gly336Arg	Exon 7 Exon 10	Apple 3 Apple 4	Nonsense Missense	Comp het	Lebanon	<1	<3			19
Cys212Arg	Exon 7	Apple 3	Missense	Hom		<1				2
Gly217Ser Trp501stop*	Exon 7 Exon 13	Apple 3 catalytic	Missense Nonsense	Comp het	Turkey	22	26	Yes		16
Phe221Ser	Exon 7	Apple 3	Missense	Hom	Japan	<3		Yes		39
nt 717 ins T Arg250His	Exon 7 Exon 8	Apple 3 Apple 3	Frameshift Missense	Comp het	Australia	24				23
Ser225Phe	Exon 7	Apple 3	Missense	Het		20-30		Yes		40
Gln226stop*	Exon 7	Apple 3	Nonsense	Hom	Japan	<3				39
Gln226stop* Gly400Val*	Exon 7 Exon 11	Apple 3 Catalytic	Nonsense Missense	Comp het	Japan	<3				39
Gln226Arg* Ser248Asn	Exon 7 Exon 8	Apple 3 Apple 3	Polymorphism Missense	Het	African American	42-55	70	Yes Yes	Polymorphism	41,42,43

Trp228stop Trp383stop	Exon 7 Exon 11	Apple 3 Catalytic	Nonsense Nonsense	Comp het	China					44
Trp228Cys	Exon 7	Apple 3	Missense	Hom	Italy	1.6	<5			45
Arg234Ile	Exon 7	Apple 3	Missense	Het		38				2
Arg234Lys	Exon 7	Apple 3	Missense	Het	Australia	41				23
Arg234Ser*	Exon 8	Apple 3	Missense	Het		42				2
Arg234Ser* Undefined	Exon 8	Apple 3	Missense	Comp het		9	5			9
Glu243Asp Pro520Leu*	Exon 8 Exon 14	Apple 3 Catalytic	Missense Missense	Comp het	France	30-40	28			12
Gly245Glu	Exon 8	Apple 3	Missense	Het		31	26			14
Arg250Cys*	Exon 8	Apple 3	Missense	Hom		8				2
Arg250Cys*	Exon 8	Apple 3	Missense	Het		53				2
Lys252Ile* Cys128stop*	Exon 8 Exon 5	Apple 3 Apple 2	Missense Nonsense	Comp het	Caucasian	4		Yes		2,46
Lys252Ile* Arg308Cys*	Exon 8 Exon 9	Apple 3 Apple 4	Missense Missense	Comp het	Australia	52				23
Gln263stop*	Exon 8	Apple 3	Nonsense	Hom	Japan	<1	<1			47
Gln263stop* Undefined	Exon 8	Apple 3	Nonsense	Comp het	Japan	<1	<1			48
Gln263stop* Tyr351stop	Exon 8 Exon 10	Apple 3 Catalytic	Nonsense Nonsense	Comp het	China	1				49
Val271Leu Gly460Arg*	Exon 8 Exon 12	Apple 3 Catalytic	Splicing? Missense	Comp het	India	1.6				50
Phe283Leu* (type III)	Exon 9	Apple 4	Missense	Hom	Ashkenazi Jewish	3-14		Yes	Common in Ashkenazi Jews, founder mutation	26,27,28,29, 30,51
Phe283Leu* (type III)	Exon 9	Apple 4	Missense	Het	Italy				4 subjects with the Jewish haplotype	33
Phe283Leu* Glu323Lys*	Exon 9 Exon 9	Apple 4 Apple 4	Missense Missense	Comp het	Ashkenazi Jew	9	9			7
Phe283Leu* Ala412Thr*	Exon 9 Exon 11	Apple 4 catalytic	Missense Missense	Comp het	Czechoslovakia	2	2			6
Phe283Leu*	Exon 9	Apple 4	Missense	Comp het	France	1	<1			20

Arg479stop*	Exon 13	catalytic	Nonsense							
nt 908 del G	Exon 9	Apple 4	Frameshift	Het		48				17
nt 919 del G	Exon 9	Apple 4	Frameshift	Het						14
Glu297Lys*	Exon 9	Apple 4	Missense	Het	France	40, 58	52			4,12
Glu297Lys*	Exon 9	Apple 4	Missense	Het	Israeli Arab	29	23			7
Glu297Lys*	Exon 9	Apple 4	Missense	Het		40	32			9
Glu297Lys* Cys527Tyr	Exon 9 Exon 14	Apple 4 Catalytic	Missense Missense	Comp het	Belgium	<2	<5	Yes		7
nt 951 ins 19 bp	Exon 9	Apple 4	Frameshift	Het		66				13
Leu302Pro	Exon 9	Apple 4	Missense					Yes		10
nt961 del TG*	Exon 9	Apple 4	Frameshift	Hom	France	<1	<1			4,7
nt961 del TG*	Exon 9	Apple 4	Frameshift	Het		57				2
Thr304Ile*	Exon 9	Apple 4	Missense	Het		51		Yes		2,10
Thr304Ile*	Exon 9	Apple 4	Missense	Hom	France	11	26			12
Val307Phe*	Exon 9	Apple 4	Missense	Het		55				13
Val307Phe*	Exon 9	Apple 4	Missense	Het		38	50			9
Arg308Cys*	Exon 9	Apple 4	Missense	Het	Caucasian	41, 45	33			2,52
Cys309stop* Gly578Cys	Exon 9 Exon 15	Apple 4 Catalytic	Nonsense Missense	Comp het	Italy	<1	<2			24
Thr313Ile	Exon 9	Apple 4	Missense	Hom		<1				15
Glu323Lys*	Exon 9	Apple 4	Missense					Yes		10
nt1026 G>T* Cys398Tyr*	Exon 9 Exon 11	Apple 4 Catalytic	Splicing Missense	Comp het	Portugal	2				7
nt1026 G>T* Lys518Asn	Exon 9 Exon 14	Apple 4 Catalytic	Splicing Missense	Comp het	Portugal	1	5			21
nt 1027 ins G Phe283Leu*	Exon 9	Apple 4	Frameshift Missense	Comp het	Caucasian	4			Unknown Jewish ancestry	53
IVS9+5 G>T	Intron 9		Splicing	Het		45				13
IVS9-2 A>G	Intron 9		Splicing							10
nt1075 del A*	Exon 10	Apple 4	Frameshift	Hom	Portugal	1				21
nt1075 del A*	Exon 10	Apple 4	Frameshift	Hom	Morocco	2	<5			7
nt1075 del A*	Exon 10	Apple 4	Frameshift	Comp het	Portugal	2				7

Cys398Tyr*	Exon 11	Catalytic	Missense							
Ile341Met	Exon 10	Apple 4	Missense	Het						2
Leu342Pro	Exon 10	Apple 4	Missense	Hom	Iran	<1				15
Gly344Arg	Exon 10	Apple 4	Missense	Het		38				2
Gly350Ala Cys581stop*	Exon 10 Exon 15	Apple 4 Catalytic	Missense Nonsense	Comp het	West France	1	44			19
Gly350Glu	Exon 10	Apple 4	Missense		Japan			Yes		54
Tyr351Ser	Exon 10	Apple 4	Missense	Hom	India	<1				50
Leu355Ser	Exon 10	Apple 4	Missense	Het		67				2
Cys356Arg	Exon 10	Apple 4	Missense	Het		40				2
IVS10+1 G>A	Intron 10		Splicing	Het	Japan	50				39
IVS10+5 G>A*	Intron 10		Splicing	Het		73				2
IVS10+5 G>A*	Intron 10		Splicing	Het		39				23
IVS10-4 del gttg	Intron 10		Splicing	Hom	China	<10	<10			55
Val371Ile	Exon 11	Catalytic	Missense	Het	Italy	34	102	Yes		56
Gly372Ala Glu547Lys*	Exon 11 Exon 14	Catalytic Catalytic	Missense Missense	Comp het	Iran	4				57
Ala375Val	Exon 11	Catalytic	Missense	Het		35	65			13
Arg378Cys	Exon 11	Catalytic	Missense	Het		61	83	Yes		2,3
Trp381Leu	Exon 11	Catalytic	Missense	Het	France	35	40			20
Thr386Asn	Exon 11	Catalytic	Missense	Hom	Arab	2				58
Leu387Gln	Exon 11	Catalytic	Missense	Het		23	37			9
His388Pro	Exon 11	Catalytic	Missense	Het		36	37			38
Thr389Pro	Exon 11	Catalytic	Missense	Het		35				2
Cys398Tyr*	Exon 11	Catalytic	Missense	Hom		<1		Yes		2,40
Cys398Tyr*	Exon 11	Catalytic	Missense	Het		25,39				2,40
Gly400Val*	Exon 11	Catalytic	Missense	Het	Italy/ Czechoslovakia	15	<20	Yes		31
Gly400Val* (Nagoya II)	Exon 11	Catalytic	Missense		Japan	<1				31,59
Gly400Val*	Exon 11	Catalytic	Missense	Hom	China	2				2,31
Gln406stop	Exon 11	Catalytic	Nonsense	Het		51				2
Trp407Cys	Exon 11	Catalytic	Missense	Het	Africa	22	27			38
Thr410Ile	Exon 11	Catalytic	Missense	Het		38				13

Ala412Ser	Exon 11	Catalytic	Missense	Het		35	35			13
Ala412Thr*	Exon 11	Catalytic	Missense	Hom	Australia	2				23
Ala412Val*	Exon 11	Catalytic	Missense	Het		46	38			52
Ala412Val* Gene deletion*	Exon 11	Catalytic	Missense	Comp het		<1				14
IVS11+12 G>A	Intron 11		Splicing	Het		50				13
IVS11-10 T>A	Intron 11		Splicing	Hom	Portugal	1				21
Arg425Cys	Exon 12	Catalytic	Missense	Het		46				2
Gln433Glu nt 1560 ins G*	Exon 12 Exon 13	Catalytic Catalytic	Missense Frameshift	Comp het	Japan	<1				60
Phe442Val	Exon 12	Catalytic	Missense	Het		47	50			35
Glu447stop nt1560 ins G*	Exon 12 Exon 13	Catalytic	Nonsense Frameshift	Comp het	Japan	<1				61
Gly460Arg*	Exon 12	Catalytic	Missense	Hom		<1				2
Gly460Arg*	Exon 12	Catalytic	Missense	Het		42				11
Gly460Arg*	Exon 12	Catalytic	Missense	Hom	India	<1			Another patient from Sri Lanka	12,50
Thr475Ile*	Exon 12	Catalytic	Missense	Het		39	27	Yes		2,23,62
Thr475Ile*	Exon 12	Catalytic	Missense	Het	France	40	50			20
Arg479stop*	Exon 13	Catalytic	Nonsense	Het		55				2
Cys482Arg Undefined	Exon 13	Catalytic	Missense	Comp het		9				13
Cys482Trp	Exon 13	Catalytic	Missense	Het		37				2
Ser485Pro	Exon 13	Catalytic	Missense	Hom	Iran	<1				15
Trp497Gly	Exon 13	Catalytic	Missense	Het	Italy	36				34
Trp497Cys	Exon 13	Catalytic	Missense	Het	Sri Lanka	22	25			12
Val498Met nt 1560 ins G*	Exon 13 Exon 13	Catalytic Catalytic	Missense Frameshift	Comp het	Korea	1				63
Trp501stop	Exon 13	Catalytic	Nonsense	Hom	Japan	<5	<5			64
Trp501Cys*	Exon 13	Catalytic	Missense	Hom	Lebanon	1.6	<1			65,66
IVS13+2 T>G	Exon 13		Splicing	Het	Ashkenazi Jew	38	20			7
Pro520Leu*	Exon 14	Catalytic	Missense	Het		43	90	Yes		2,14,67
Pro520Leu*	Exon 14	Catalytic	Missense	Het	France	50	74			20
Pro520Leu*	Exon 14	Catalytic	Missense	Het		45	91		Combined with heterozygote	68

									FVII deficiency	
Gly544Ser	Exon 14	catalytic	Missense	Het		62				13
Glu547Lys*	Exon 14	Catalytic	Missense	Het		49	37			12,14
Glu547Lys*	Exon 14	Catalytic	Missense	Hom		23				20
nt1714 del 3+ IVS14 del 11* (type IV) Glu117stop*	Exon14 Exon 5	Catalytic Apple 2	Splicing Nonsense	Comp het	Ashkenazi Jewish	<1				69
IVS14+1 G>A* (type I) Glu117stop*	Intron 14 Exon 5	Catalytic Apple 2	Splicing Nonsense	Comp het	Ashkenazi Jewish	<1				26
IVS14+1 G>A* (type I)	Intron 14	Catalytic	Splicing	Hom	Ashkenazi Jewish	<1			Prevalent in Ashkenazi Jews. Founder mutation	70
IVS14+1 G>A*	Intron 14	Catalytic	Splicing	Het		71				2
IVS14-2 A>G	Intron 14	Catalytic	Splicing	Het	Iran	40				15
Gly555Glu*	Exon 15	Catalytic	Missense	Hom	Bucharan Jew	<1	100	Yes		71
Gly555Glu*	Exon 15	Catalytic	Missense	Het		51				2
Cys563Phe	Exon 15	Catalytic	Missense	Het		45				2
Trp569Ser	Exon 15	Catalytic	Missense	Het	Germany	10-20	<20	Yes		31
Thr575Met*	Exon 15	Catalytic	Missense	Hom	Lebanon	2	105			66
Thr575Met*	Exon 15	Catalytic	Missense	Het		51	85	Yes		2,3
Ser576Arg	Exon 15	Catalytic	Missense	Het	Caucasian	27	22			2,52
Glu579Lys	Exon 15	Catalytic	Missense	Het		15				4
Cys581stop*	Exon 15	Catalytic	Nonsense	Hom	West France	1	20			19
Tyr590His	Exon 15	Catalytic	Missense	Hom	Iran	<1				15
Tyr590stop*	Exon 15	Catalytic	Nonsense	Het		30				2,14
Trp599Arg	Exon 15	Catalytic	Missense	Hom	Japan	<1	<1			72
Ile600Ser*	Exon 15	Catalytic	Missense	Hom		<2				2
Ile600Ser*	Exon 15	Catalytic	Missense	Het		42	35			2,14
Leu601Pro	Exon 15	Catalytic	Missense	Hom	Italy	<1	<1	Yes		8
Exons 11-15 deletion		Catalytic	Big deletion	Hom	Tunis	<1				7
Gene deletion*			Whole gene	Het		32				2,14,73

			deletion I							
Gene deletion*			whole gene deletion II	Het						2

Nucleotide numbers are based on the Genebank file M13142 using the A (nucleotide 44) of the ATG initiator methionine as +1.
*A mutation that was identified in more than 1 family.

Mutations causing Factor XI deficiency according to their types

Promoter	Missense						Nonsense	Splice	Deletion/Insertion
nt -1296 G>A	M-18I*	S81Y	A184G	T304I*	P382L*	W497G	G1X	IVS2+6 T>G + 10 ins AG	nt 73 del 14 bp
nt -54 G>A	S-4L	K83R	P188S*	V307F*	T386N	W497C	C38X	nt 325 G>A*	nt 78 del GGA
	G-1R	C92G	C212R	R308C*	L387Q	V498M	Q88X*	IVS3+2 T>A	nt 192 ins G
	T10A	M102T	C212S	R308H	H388P	W501C*	Q116X*	IVS4+1 G>A*	nt 226 del T
	D16H*	G104D*	G217S	T313I	T389P	K518N	E117X*	IVS5+5 G>C	nt 308 ins 7 bp
	V20A	C118R	F221S	C321F	C398Y*	P520L*	C118x*	IVS5-2 A>G*	nt 643 del 6 bp*
	P23L	C122Y*	S225F	E323K*	G400V*	C527Y	C128X*	IVS6+3 A>G*	nt 717 ins T
	P23Q	T123M	W228C	G336R	W407S	C527R*	R210X	IVS9 +5 G>T	nt 823 del C
	S24R	T132M	R234I	I341M	T410I	G544S	Q226X	IVS9-2A>G	nt 908 del G
	A25T	Y133S*	R234K	L342P	A412T*	E547K*	W228X	IVS10+1 G>A	nt 919 del G
	C28F	Y133C*	R234S*	G344R	A412V*	G555E*	Q233X	IVS10+5 G>A*	nt 933-951 dup ins 19 bp
	Q29H	A134P	C237Y	G350R	A412S	C563F	Q263X*	IVS10-4 del GTTG	nt 961 del TG*
	T33P*	G155E	E243D	G350A	R425C	W569S	C309X*	IVS11+12 G>A (nt1304)t	nt 1026 G>T*
	T33I	L172P	G245E	G350E	Y427C	T575M*	Y351X	IVS11-10 T>A	nt 1027 ins G
	C38R*	A181V	S248N	Y351S	Q433E	S576R	W383X	IVS13+2 T>G	nt 1075 del A*
	C38W	C182Y*	R250C	L355S	F442V	G578C	Q406X	nt 1714 del 3+ IVS14 del 14	nt 1560 ins G
	R54P	A184G	R250H	C356R	G460R*	E579K	E447X	IVS14+1G>A*	
	C58R	P188S*	K252I*	V371I	T475I*	Y590H	R479X*	IVS14-2 A>G	
	C58Y	G155E	V271Lsplice?	G372A	C482W	W599R	W501X*		
	C58F	L172P	F283L*	A375V	C482R	I600S*	C581X*		
	S78F*	A181V	E297K*	R378C	S485P	L601P	Y590X*		
	G79A	C182Y*	L302P	W381L	Y493H	E602Q	L601P		

* Mutation was identified in more than 1one family

References

1. Vasileiadis I, El-Ali M, Nanas S, et al: First diagnosis of factor XI deficiency in a patient with subarachnoid haemorrhage. *Blood Coagul Fibrinolysis* 20:309, 2009.

2. Mitchell M, Mountford r, Butler R, et al: Spectrum of factor XI (F11) mutations in the UK population – 116 index cases and 140 mutations. *Hum Mutat* 27:829, 2006.

3. Mitchell MJ, Dai L, Clarke JB, et al: Characterisation of five factor XI mutations. *Thromb Haemost* 97:884, 2007.

4. Quelin F, Mathonnet F, Potentini-Esnault C, et al: Identification of five novel mutations in the factor XI gene (F11) of patients with factor XI deficiency. *Blood Coagul Fibrinolysis* 17:69, 2006.

5. Wang J, Wang X, Dai J, et al: A case of factor XI deficiency caused by compound heterozygous F11 gene mutation. *Haemophilia* 15:603, 2009.

6. Castaman G, Giacomelli SH, Habart D, et al: Factor XI gene mutations in factor XI deficient patients of the Czech Republic. *Am J Hematol* 83:916, 2008.

7. Zucker M, Zivelin A, Landau M, et al: Characterization of seven novel mutations causing factor XI deficiency. *Haematologica* 92:1375, 2007.

8. Spena S, Asselta R, Caccia S, et al: Analysis of the structural effects of four novel and a previously known mutations causing factor XI deficiency. *Thromb Haemost* 102:603, 2009.

9. Rugeri L, Quelin F, Chatard B, et al: Thrombin generation in patients with factor XI deficiency and clinical bleeding risk. *Haemophilia* 16:771, 2010.

10. Pugh RE, McVey JH, Tuddenham EGD, Hancock JF: Six point mutations that cause factor XI deficiency. *Blood* 85:1509, 1995.

11. Mitchell M, Harrington P, Cutler J, et al: Eighteen unrelated patients with factor XI deficiency, four novel mutations and a 100% detection rate by denaturing high-performance liquid chromatography. *Br J Haematol* 121:500, 2003.

12. Quelin F, Francois D, d'Oiron R: Factor XI deficiency: Identification of six novel missense mutations (P23L, P69T, C92G, E243D, W497C and E547K). *Haematologica* 90:1149, 2005.

13. Saunders RE, Shiltagh N, Gomez K, et al: Structural analysis of eight novel and 112 previously reported missense mutations in the interactive FXI mutation database reveals new insight on FXI deficiency. *Thromb Haemost* 102:287, 2009.

14. Hill M, McLeod F, Franks H, et al: Genetic analysis in FXI deficiency: six novel mutations and the use of a polymerase chain reaction-based test to define a whole gene deletion. *Br J Haematol* 129:825, 2005.

15. Fard-Esfahani P, Lari GR, Ravanbod S, et al: Seven novel point mutations in the F11 gene in Iranian FXI-deficient patients. *Haemophilia* 14:91, 2008.

16. Berber E, Rimoldi V, Usluer S, et al: Characterization of the genetic basis of FXI deficiency in two Turkish patients. *Haemophilia* 16:564, 2010.

17. Zivelin A, Bauduer F, Ducout L, et al: Factor XI deficiency in French Basques is caused predominantly by an ancestral Cys38Arg mutation in the factor XI gene. *Blood* 99:2448, 2002.

18. Ramadan KM, McNulty O, Anderson JA, Jones FG, Winter PC: A novel factor XI gene mutation associated with mild factor XI deficiency in a symptomatic patient. *Blood Coagul Fibrinolysis* 17:499, 2006.

19. Quelin F, Trossaert M, Sigaud M et al: Molecular basis of severe factor XI deficiency in seven families from the west of France. Seven novel mutations, including an ancient Q88X mutation. *J Thromb Haemost* 2:71, 2004.

20. Quelin F, Frere C, Pouymayou C, et al: Prospective analysis of factor XI deficiencies in the Marseilles area identified four novel mutations among 12 consecutive unrelated families. *Blood Coagul fibrinolysis* 20:84, 2009.

21. Ventura C, Santos AIM, Tavares A, et al: Molecular genetic analysis of factor XI deficiency: Identification of five novel gene alterations and the origin of type II mutation in Portuguese families. *Thromb Haemost* 84:833, 2000.

22. Guella I, Solda G, Spena S, et al: Molecular characterization of two novel mutations causing factor XI deficiency: A splicing defect and a missense mutation responsible for a CRM+ defect. *Thromb Haemost* 99:523, 2008.

23. Duncan EM, Casey GJ, Fenech MP, et al: Partial and severe factor XI deficiency in South Australia and the usefulness of factor XI mutation analysis for diagnosis. *Pathology* 40:401, 2008.

24. Castaman G, Giacomelli SH, Dragani A, et al: Severe factor XI deficiency in the Abruzzo region of Italy is associated to different FXI gene mutations. *Haematologica* 93:957, 2008.

25. Dossenbach-Glaninger A, Hopmeir P: Coagulation factor XI gene analysis in three factor XI deficient Austrian patients. *Eur J Haematol* 76:317, 2006.

26. Asakai R, Chung DW, Batnoff OD, Davie EW: Factor XI (plasma thromboplastin antecedent) deficiency in Ashkenazi Jews is a bleeding disorder that can result from three types of point mutations. *Proc Natl Acad Sci* USA 86:7667, 1989.

27. Asakai R, Chung DW, Davie EW, Seligsohn U: Factor XI deficiency in Ashkenazi Jews in Israel. *New Engl J Med* 325:153, 1991.

28. Hancock JF, Wieland K, Pugh RE, et al: A molecular genetic study of factor XI deficiency. *Blood* 77:1942, 1991.

29. Shpilberg O, Peretz H, Zivelin A, et al: One of the two common mutations causing factor XI deficiency in Ashkenazi Jews (type II) is also prevalent in Iraqi Jews, who represent the ancient gene pool of Jews. *Blood* 85:429, 1995.

30. Peretz H, Mulai A, Usher S, et al: The two common mutations causing factor XI deficiency in Jews stem from distinct founders: One of ancient Middle Eastern origin and another of more recent European origin. *Blood* 90:2654, 1997.

31. Kravtsov DV, Wu W, Meijers JC, et al: Dominant factor XI deficiency caused by mutations in the factor XI catalytic domain. *Blood* 104:128, 2004.

32. Zadra G, Asselta R, Malcovati M, et al: Molecular genetic analysis of severe coagulation factor XI deficiency in six Italian patients. *Haematologica* 89:1332, 2004.

33. Zadra G, Asselta R, Tenchini ML et al: Simultaneous genotyping of coagulation factor XI type II and type III mutations by multiplex real-time polymerase chain reaction to determine their prevalence in healthy and factor XI-deficient Italians. *Haematologica* 93:715, 2008

34. Tomaiuolo M, Favuzzi G, Cappucci F, et al: Factor XI deficiency: Two novel mutations in asymptomatic Italian patients. *Haemophilia* 16:767, 2010.

35. Imanaka Y, Lal K, Nishimura T, et al: Identification of two novel mutations in non-Jewish factor XI deficiency. *Br J Haematol* 90:916, 1995.

36. Bolton-Maggs PHB, Peretz H, Butler R, et al: A common ancestral mutation (C128X) occurring in 11 non-Jewish families from the UK with factor XI deficiency. *J Thromb Haemost* 2:918, 2004.

37. Zacharski LR, French EE: Factor XI (PTA) deficiency in an English-American kindred. *Thromb Haemost* 39:215, 1978.

38. De Raucourt E, De Mazancourt P, Quelin F: Four novel FXI gene mutations in three factor XI-deficient patients. *Blood Coagul Fibrionolysis* 19:240, 2008.

39. Okumura K, Kyotani M, Kawai R, et al: Recurrent mutations of factor XI gene in Japanese. *Int J Hematol* 83:462, 2006.

40. Kravtsov DV, Monahan PE, Gailani D: A classification system for cross-reactive material negative factor XI deficiency. *Blood* 105:4671, 2005.

41. Martincic D, Zimmerman SA, Ware RE, et al: Identification of mutations and polymorphisms in the factor XI genes of an African American family by Dideoxyfingerprinting. *Blood* 92:3309, 1998.

42. Cargill M, Altshuler D, Ireland J, et al: Characterization of single-nucleotide polymorphisms in coding regions of human genes. *Nat Genet* 22:231, 1999.

43. Sun MF, Baglia FA, Ho D, et al: Defective binding of factor XI-N248 to activated human platelets. *Blood* 98:125, 2001.

44. Wu WM, Want HL, Wang XF, et al: Identification of two novel factor XI non-sense mutation Trp228stop and Trp383stop in a Chinese pedigree of congenital factor XI deficiency. *Zhonghua Xue Ye Xue Za Zhi* 24:126, 2003.

45. Alhaq A, Mitchell M, Sethi M, et al: Identification of a novel mutation in a non-Jewish factor XI deficient kindred. *Br J Haematol* 104:44, 1999.

46. Dai L, Mitchell M, Carson P, et al: Severe factor XI deficiency caused by compound heterozygosity. *Br J Haematol* 125:817, 2004.

47. Sato E, Kawamata N, Kato A, Oshimi K: A novel mutation that leads to a congenital factor XI deficiency in a Japanese family. *Am J Hematol* 63:165, 2000.

48. Kawaguchi T, Koga S, Hongo H, et al: A novel type of factor XI deficiency showing compound genetic abnormalities: a nonsense mutation and an impaired transcription. *Int J Hematol* 71:84, 2000.

49. Au WY, Cheung JW, Lam CCK, Kwong YL: Two factor XI mutations in a Chinese family with factor XI deficiency. *Am J Hematol* 74:136, 2003.

50. Jayandharan G, Shaji RV, Nair SC, et al: Novel missense mutations in two patients with factor XI deficiency (Val271Leu and Tyr351Ser) and one patient with combined factor XI and factor IX deficiency (Phe349Val). *J Thromb Haemost* 3:808, 2005.

51. Meijers JC, Davie EW, Chung DW: Expression of human blood coagulation factor XI: Characterization of the defect in factor XI type III deficiency. *Blood* 79:1435, 1992.

52. Mitchell M, Cutler J, Thompson S, et al: Heterozygous factor XI deficiency association with three novel mutations. *Br J Haematol* 107:763, 1999.

53. Dossenbach-Glaninger A, Krugluger W, Schrattbauer K, et al: Severe factor XI deficiency caused by compound heterozygosity for the type III mutation and a novel insertion in exon 9 (codons 324/325+G). *Br J Haematol* 114:875, 2001.

54. Meijers JC, Mulvihill ER, Davie EW, Chung DW: Apple four in human blood coagulation factor XI mediates dimmer formation. *Biochemistry* 31:4680, 1992.

55. Xie S, Wang HL, Wang XF, et al: The inherited coagulation factor XI deficiency caused by intronic mutation IVS J-4delgttg. *Zhonghua Xue Ye Xue Za Zhi* 26:144, 2005.

56. Bozzao C, Rimoldi V, Asselta R, et al: A novel factor XI missense mutation (Val371Ile) in the activation loop is responsible for a case of mild type II factor XI deficiency. *FEBS J* 274:6128, 2007.

57. Karimi M, Jafari H, Lahsaeizadeh S, et al: Factor XI deficiency in Southern Iran: Identification of a novel missense mutation. *Ann Hemato* 88:359, 2009

58. Wistinghausen B, Reischer A, Oddoux C, et al: Severe factor XI deficiency in an Arab family associated with a novel mutation in exon 11. *Br J Haematol* 99:575, 1997.

59. Sato T, Iyama S, Araki N, et al: Factor XI deficiency caused by a mutation of Gly400Val. *Rinsho Ketsueki* 48:148, 2007.

60. Ishikawa N, Okada S, Sato T, et al: A novel mutation (Gln433Glu) in exon 12 combined with the G insertion in exon 13 causes severe factor XI deficiency in Japanese patients. *Blood Coagul Fibrinolysis* 18:519, 2007.

61. Tsukahara A, Yamada T, Takagi A, et al: Compound heterozygosity for two novel mutations in a severe factor XI deficiency. *Am J Hematol* 73:279, 2003.

62. McVey JH, Lal K, Imanaka Y, et al: Characterisation of blood coagulation factor XI T475I. *Thromb Haemost* 93:1082, 2005.

63. Kwon MJ, Kim HJ, Bang SH, Kim SH: Severe factor XI deficiency in a Korean woman with a novel missense mutation (Val498Met) and duplication G mutation in exon 13 of the F11 gene. *Blood Coagul Fibrinolysis* 19:679, 2008.

64. Iijima K, Udagawa A, Kawasaki H, et al: A factor XI deficiency associated with a nonsense mutation (Trp501stop) in the catalytic domain. *Br J Haematol* 111:556, 2000.

65. de Moerloose P, Germanos-Haddad M, Boehlen F, Neerman-Arbez M: Severe factor XI deficiency in a Lebanese family: Identification of a novel missense mutation (Trp501Cys) in the catalytic domain. *Blood Coagul Fibrinolysis* 15:269,2004.

66. Germanos-Haddad M, de Moerloose P, Boehlen F, et al: Homozygosity for a Thr575Met missense mutation in the catalytic domain associated with factor XI deficiency. *Haematologica* 90:418, 2005.

67. Gailani D, Schmidt A, Sun MF, Bolton-Maggs PH, Bajaj SP: A cross-reactive material positive variant of coagulation factor XI (FXI) with a catalytic defect. *J Thromb Haemost*, 5:781, 2007.

68. Quelin F, De Raucourt E, Mathonnet F, et al: Characterization of combined factor VII and factor XI deficiencies. *Haemophilia* 14:639, 2008.

69. Peretz H, Zivelin A, Usher S, Seligsohn U: A 14-bp deletion (Codon 554 del AAGgtaacagagtg) at exon 14/Intron N junction of the coagulation factor XI gene disrupts splicing and causes severe factor XI deficiency. *Hum Mutat* 8:77, 1996.

70. Peretz H, Salomon O, Seligsohn U et al: Unpublished

71. Zivelin A, Ogawa T, Bulvik S, et al: Severe factor XI deficiency caused by a Gly^{555} to Glu mutation (factor XI-Glu^{555}): A cross-reactiv emaqterial positive variant defective in factor IX activation. *J Thromb Haemost* 2:1782, 2004.

72. Takamiya O, Machida S, Yamamoto M: Factor XI deficiency with a novel homozygous mutation Trp599Arg near the C-terminal region. *Haematologica* 90:999, 2005.

73. Mitchell M, Dai L, Savidge G, Alhaq A: An Alu-mediated 31.5-kb deletion as the cause of factor XI deficiency in 2 unrelated patients. *Blood* 104:2394, 2004.