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Resources for Genetics Professionals — Genetic Disorders Associated with Founder Variants Common in the Finnish Population

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A founder variant is a pathogenic variant observed in high frequency in a specific population due to the presence of the variant in a single ancestor or small number of ancestors. The presence of a founder variant can affect the approach to molecular genetic testing. When one or more founder variants account for a large percentage of all pathogenic variants found in a population, testing for the founder variant(s) may be performed first.

The table below includes common founder variants – here defined as **three or fewer variants that account for >50% of the pathogenic variants identified in a single gene in individuals of a specific ancestry** – in individuals of Finnish ancestry. Note: Pathogenic variants that are common worldwide due to a DNA sequence hot spot are not considered founder variants and thus are not included.

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Table. Genetic Disorders Associated with Founder Variants Common in the Finnish Population

Gene	Disorder	MOI	DNA Nucleotide Change	Predicted Protein Change	% of Pathogenic Variants in Gene	Carrier Frequency	Ethnicity (Specific Region)	Reference Sequences	References [1]
ABCC8	Familial hyperinsulinism	AR/AD	c.560T>A	p.Val187Asp	~60%	NA	Finnish	NM_000352.6 NP_000343.2	Otonkoski et al [1999], Huopio et al [2000], Männistö et al [2020]
		AD	c.4516G>A	p.Glu1506Lys	~30%				
AGA	Aspartylglucosaminuria	AR	c.488G>C	p.Cys163Ser	98%	1/30	Finnish (E Finland)	NM_000027.4 NP_000018.2	Arvio & Mononen [2016]
AICDA	Immunodeficiency with hyper-IgM type 2 (AID deficiency) (OMIM 605258)	AR	c.416T>C	p.Met139Thr	100%	1/274	Finnish (E & NE Finland)	NM_020661.4 NP_065712.1	Trotta et al [2016]
AIP	*AIP* familial isolated pituitary adenomas	AD	c.40C>T	p.Gln14Ter	~85%	NA	Finnish	NM_003977.4 NP_003968.3	Vierimaa et al [2006]
AIRE	APECED (OMIM 240300)	AR	c.769C>T	p.Arg257Ter	83%	1/80 [2]	Finnish	NM_000383.4 NP_000374.1	Nagamine et al [1997], Peterson et al [2004]
ANO5	LGMD2	AR	c.2272C>T	p.Arg758Cys	95%	Unknown	Finnish	NM_213599.3 NP_998764.1	Ylikallio et al [2016]
ASL	Argininosuccinate lyase deficiency	AR	c.1153C>T	p.Arg385Cys	60%	1/190 [2]	Finnish	NM_000048.4 NP_000039.2	Keskinen et al [2008], Keskinen et al [2008]
BCS1L	GRACILE syndrome (OMIM 603358)	AR	c.232A>G	p.Ser78Gly	100% [3]	1/494	Finnish	NM_004328.5 NP_004319.1	Visapää et al [2002], Fellman et al [2008]
CC2D2A	Meckel syndrome, type 6 (OMIM 612284)	AR	c.1762C>T [4]	--	100% [3]	1/190	Finnish	NM_001080522.2	Tallila et al [2008]

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Gene	Disorder	MOI	DNA Nucleotide Change	Predicted Protein Change	% of Pathogenic Variants in Gene	Carrier Frequency	Ethnicity (Specific Region)	Reference Sequences	References [1]
CERKL	Retinal dystrophy	AR	c.193G>T	p.Glu65Ter	22%	1/242	Finnish	NM_001030311.3 NP_001025482.1	Avela et al [2018]
		AR	c.375C>G	p.Cys125Trp	72%	1/66			
CHCHD10	Late-onset spinal motor neuronopathy (See *CHCHD10*-Related Disorders.)	AD	c.197G>T	p.Gly66Val	<100% [5]	NA	Finnish	NM_213720.3 NP_998885.1	Penttilä et al [2015]
CHM	Choroidemia	XL	c.1609+2dupT	--	~90%	NA	Finnish (Salla, Finland)	NM_000390.4 NP_000381.1	Sankila et al [1992]
CLCN1	Myotonia congenita	AR	c.1238T>G	p.Phe413Cys	41%	1/60 [2]	Finnish (N Finland)	NM_000083.3 NP_0000743	Papponen et al [1999]
			c.1592C>T	p.Ala531Val	18%		Finnish (W Lapland, Finland)		
			c.2680C>T	p.Arg894Ter	41%		Finnish (N Finland)		
CLN3	CLN3 disease (OMIM 204200)	AR	c.461-280_677+382del	p.Gly154AlafsTer29	90%	1/70	Finnish	NM_001042432.2 NP_001035897.1	International Batten Disease Consortium [1995]
CLN5	CLN5 disease (OMIM 256731)	AR	c.1028_1029delAT	p.Tyr343Ter	94%	1/24	Finnish (S Ostrobothnia, Finland)	NM_006493.4 NP_006484.2	Varilo et al [1996], Savukoski et al [1998]
						1/100	W Finland		

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Gene	Disorder	MOI	DNA Nucleotide Change	Predicted Protein Change	% of Pathogenic Variants in Gene	Carrier Frequency	Ethnicity (Specific Region)	Reference Sequences	References [1]
CLN8	CLN8 disease (OMIM 600143)	AR	c.70C>G	p.Arg24Gly	~98%	1/46	Finnish (Kainuu, Finland)	NM_018941.4 NP_061764.2	Ranta et al [1999], Ranta & Lehesjoki [2000], Siintola et al [2006]
						1/135	Finland		
CLRN1	Usher syndrome, type IIIA (OMIM 276902)	AR	c.528T>G	p.Tyr176Ter	~98%	1/145	Finland	NM_174878.3 NP_777367.1	Joensuu et al [2001]
CRADD	Frontotemporal predominant pachygyria (OMIM 614499)	AR	c.509G>A	p.Arg170His	100	1/41	Finnish (NE Finland)	NM_003805.5 NP_003796.1	Polla et al [2019]
CSTB	Unverricht-Lundborg disease (OMIM 254800)	AR	g.513685_513696(30_125) (dodecamer repeat in promoter region)	--	99%	1/115 [2]	Finnish	NT_011515.11	Virtaneva et al [1997], Sipilä et al [2020]
CUBN	Megaloblastic anemia 1 (OMIM 261100)	AR	c.3890C>T	p.Pro1297Leu	91%	1/158	Finnish	NM_001081.4 NP_001072.2	Aminoff et al [1999]
DARS2	Leukoencephalopathy with brain stem and spinal cord involvement and lactate elevation	AR	c.228-21_228-20delTTinsC	--	~50%	1/95	Finnish	NM_108122.5	Isohanni et al [2010]
			c.492+2T>C	--	44%	1/380	Finnish		
FAH	Tyrosinemia type 1	AR	c.786G>A	p.Trp262Ter	~93%	1/50 [2]	Finnish (S Ostrobothnia)	NM_000137.4 NP_000128.1	St-Louis et al [1996], Äärelä et al [2020]
FSHR	Ovarian dysgenesis (OMIM 233300)	AR	c.566C>T	p.Ala189Val	98%	1/85	Finnish (N Finland)	NM_000145.4 NP_000136.2	Aittomäki et al [1996], Doherty et al [2002]

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Gene	Disorder	MOI	DNA Nucleotide Change	Predicted Protein Change	% of Pathogenic Variants in Gene	Carrier Frequency	Ethnicity (Specific Region)	Reference Sequences	References [1]
GLDC	Glycine encephalopathy (See Nonketotic Hyperglycinemia.)	AR	c.1691G>T	p.Ser564Ile	70%	1/55 [2]	Finnish (N Finland)	NM_000170.3 NP_000161.2	Kure et al [1992], Kure et al [1999], Coughlin et al [2017]
					53%	Unknown	Finnish		
			c.2281G>A	p.Gly761Arg	26%	Unknown	Finnish		
			Deletion of exons 1-8 [6]	--	12%	Unknown	Finnish	NG_016397.1	
GLE1	Lethal arthrogryposis with anterior horn cell disease (OMIM 611890)	AR	c.433-10A>G	--	50%	1/50	Finnish (NE Finland)	NM_001003722.2	Nousiainen et al [2008]
						1/100	Finnish		
	Lethal congenital contracture syndrome (OMIM 253310)	AR	c.433-10A>G	--	~99%	1/50	Finnish (NE Finland)		
						1/100	Finnish		
GSN	Amyloidosis, Finnish type (OMIM 105120)	AD	c.640G>A	p.Asp214Asn	<100% [5]	NA	Finnish	NM_000177.5 NP_000168.1	Paunio et al [1992]
HYLS1	Hydrolethalus syndrome type 1 (OMIM 236680)	AR	c.632A>G	p.Asp211Gly	100% [3]	1/40	Finnish (C & E Finland)	NM_145014.3 NP_659451.1	Mee et al [2005]
						1/91	Finnish (W Finland)		
IDUA	Mucopolysaccharidosis type 1	AR	c.208C>T	p.Gln70Ter	62%	Unknown	Finnish	NM_000203.5 NP_000194.2	Bunge et al [1994]
			c.1205G>A	p.Trp402Ter	19%	Unknown			
KERA	Cornea plana 2 (OMIM 217300)	AR	c.740A>G	p.Asn247Ser	100% [3]	1/63	Finnish (NE Finland)	NM_007035.4 NP_008966.1	Pellegata et al [2000]
LCT	Congenital lactase deficiency (OMIM 223000)	AR	c.4170T>A	p.Tyr1390Ter	90%	1/35	Finnish (Nilsiä, Finland)	NM_002299.4 NP_002290.2	Kuokkanen et al [2006]
LDLR	Familial hypercholesterolemia	AD	g.39215_47749del8535	--	80%	NA	Finnish	NG_009060.1	Lahtinen et al [2015]
			c.925_931delCCCATCA	p.Pro309LysfsTer59				NM_000527.5 NP_000518.1	
			c.1784G>A	p.Arg595Gln					

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Gene	Disorder	MOI	DNA Nucleotide Change	Predicted Protein Change	% of Pathogenic Variants in Gene	Carrier Frequency	Ethnicity (Specific Region)	Reference Sequences	References [1]
LMNA	*LMNA*-related dilated cardiomyopathy	AD	c.427T>C	p.Ser143Pro	~56%	NA	Finnish	NM_170707.4 NP_733821.1	Ollila et al [2017]
MKS1	Meckel syndrome, type 1 (OMIM 249000)	AR	c.1408-34_1408-6del29	--	>95%	~1/60 [2]	Finnish	NM_017777.4	Kyttälä et al [2006]
MLH1	Lynch syndrome	AD	c.1731+2247_1897-402del (deletion of exon 16)	p.Pro579_Glu633del	~50%-60%	AD	Finnish	NM_000249.3	Nyström-Lahti et al [1995], Nyström-Lahti et al [1996]
			c.454-1G>A	--	~15%-20%	AD		NM_000249.4	
NOTCH3	CADASIL	AD	c.397C>T	p.Arg133Cys	86%	1/80-1/112 [2]	Finnish	NM_0004353 NP_000426.2	Mykkänen et al [2004], Narayan et al 2012
NPHS1	Nephrosis, congenital, Finnish type (OMIM 256300)	AR	c.121_122delCT	p.Leu41AspfsTer50	78%	1/50 [2]	Finnish	NM_004646.4 NP_004637.1	Kestilä et al [1998], Lenkkeri et al [1999]
			c.3325C>T	p.Arg1109Ter	16%				
OAT	Gyrate atrophy of the choroid and retina (OMIM 258870)	AR	c.1205T>C	p.Leu402Pro	~90%	1/112 [2]	Finnish	NM_000274.4 NP_000265.1	Heinänen et al [1998], Bangal et al [2012]
PALB2	Hereditary breast cancer (OMIM 610355)	AD	c.1592delT	p.Leu531CysfsTer30	<100% [5]	NA	Finnish	NM_024675.4 NP_078951.2	Erkko et al [2007]
POLG	Ataxia neuropathy spectrum (See *POLG*-related disorders.)	AR	c.2243G>C	p.Trp748Ser	100% [3]	1/125	Finnish	NM_002693.3 NP_002684.1	Hakonen et al [2005]
POMGNT1	Muscular dystrophy-dystroglycanopathy, type A3 (OMIM 253280)	AR	c.1539+1G>A	--	97%	1/60	Finnish	NM_017739.4	Diesen et al [2004], Arvio et al [2019]

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Gene	Disorder	MOI	DNA Nucleotide Change	Predicted Protein Change	% of Pathogenic Variants in Gene	Carrier Frequency	Ethnicity (Specific Region)	Reference Sequences	References [1]
PPT1	CLN1 disease (OMIM 256730)	AR	c.364A>T	p.Arg122Trp	98%	1/70	Finnish	NM_000310.4 NP_000301.1	Vesa et al [1995]
RECQL4	RAPADILINO (OMIM 266280)	AR	c.1390+2delT	--	82%	1/137	Finnish	NM_004260.4	Siitonen et al [2003]
RMRP	Cartilage-hair hypoplasia	AR	g.71A>G	--	92%	1/86	Finnish	NG_017041.1	Thiel et al [2007]
RS1	Retinoschisis, X-linked juvenile	XL	c.214G>A	p.Glu72Lys	70%	NA	Finnish	NM_000330.4 NP_000321.1	Huopaniemi et al [1999]
			c.221G>T	p.Gly74Val	6%				
			c.325G>C	p.Gly109Arg	19%				
SERPINB7	Palmoplantar keratoderma, Nagashima type (OMIM 615598)	AR	c.1136G>A	p.Cys379Tyr	~70%	1/156	Finnish	NM_003784.4 NP_003775.1	Hannula-Jouppi et al [2020]
SIL1	Marinesco-Sjögren syndrome	AR	c.506_509dupAAGA	p.Asp170GlufsTer4	100% [3]	1/96	Finnish	NM_022464.5 NP_071909.1	Anttonen et al [2005]
SLC17A5	Salla disease (See Free Sialic Acid Storage Disorders.)	AR	c.115C>T	p.Arg39Cys	95%	1/100	Finnish (NE Finland)	NM_012434.5 NP_036566.1	Aula et al [2000]
SLC26A2	Diastrophic dysplasia	AR	c.-26+2T>C	--	~80%	Unknown	Finnish	NM_000112.4	Härkönen et al [2021]
SLC26A3	Congenital secretory diarrhea, chloride type (OMIM 214700)	AR	c.951_953delGGT	p.Val318del	99%	1/145	Finnish	NM_000111.3 NP_000102.1	Wedenoja et al [2011]
SLC7A7	Lysinuric protein intolerance	AR	c.895-2A>T	--	100% [3]	1/138 [2]	Finnish	NM_001126106.4	Torrents et al [1999], Sperandeo et al [2008]
SPINK5	Netherton syndrome	AR	c.652C>T	p.Arg218Ter	~75%	1/224 [2]	Finnish (W Finland)	NM_006846.4 NP_006837.2	Hannula-Jouppi et al [2016]

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Gene	Disorder	MOI	DNA Nucleotide Change	Predicted Protein Change	% of Pathogenic Variants in Gene	Carrier Frequency	Ethnicity (Specific Region)	Reference Sequences	References [1]
TIA1	Welander distal myopathy (OMIM 604454)	AD	c.1150G>A	p.Glu384Lys	100% [5]	NA	Finnish	NM_022173.4 NP_071505.2	Hackman et al [2013]
TK2	*TK2*-related mitochondrial DNA depletion syndrome, myopathic form	AR	c.388C>T	p.Arg130Trp	~71%	Unknown	Finnish (NE Finland)	NM_004614.5 NP_004605.4	Götz et al [2008]
			c.547C>T	p.Arg183Trp	~29%	Unknown	Finnish (SW Finland)		
TRIM37	Mulibrey nanism (OMIM 253250)	AR	c.493-2A>G	--	98%	Unknown	Finnish	NM_015294.6	Avela et al [2000], Karlberg et al [2004]
TTN	Udd distal myopathy – tibial muscular dystrophy	AD	c.100076_100086delAAGTA ACATGGinsTGAAAGAAAAA	p.Glu33359_Trp33362 delinsValLysGluLys	<100% [5]	NA	Finnish	NM_133378.4 NP_596869.4	Hackman et al [2002]
TWNK	Infantile-onset spinocerebellar ataxia	AR	c.1523A>G	p.Tyr508Cys	~97%	1/42	Finnish (Pirkanmaa Co, Finland)	NM_021830.5 NP_068602.2	Nikali et al [2005]
						1/50	(E Finland)		
						1/227	(Finland)		
TYROBP	PLOSL	AR	c.-2897_277-1227del5265 (deletion of exons 1-4)	--	100% [3]	Unknown	Finnish	NM_003332.4	Paloneva et al [2000]
VPS13B	Cohen syndrome	AR	c.3348_3349delCT	p.Cys1117PhefsTer8	75%	Unknown	Finnish	NM_017890.5 NP_060360.3	Kolehmainen et al [2003]

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Gene	Disorder	MOI	DNA Nucleotide Change	Predicted Protein Change	% of Pathogenic Variants in Gene	Carrier Frequency	Ethnicity (Specific Region)	Reference Sequences	References [1]
ZNHIT3	PEHO syndrome (OMIM 260565)	AR	c.92C>T	p.Ser31Leu	100% [3]	1/108	Finnish	NM_004773.4 NP_004764.1	Anttonen et al [2017]

Included if ≤3 pathogenic variants account for ≥50% of variants identified in a specific ethnic group

AD = autosomal dominant; APECED = autoimmune polyendocrinopathy-candidiasis-ectodermal dystrophy; AR = autosomal recessive; C = Central; Co = County; E = Eastern; MOI = mode of inheritance; N = Northern; NE = Northeastern; PEHO = progressive encephalopathy with edema, hypsarrhythmia, and optic atrophy; PLOSL = polycystic lipomembranous osteodysplasia with sclerosing leukoencephalopathy; S = Southern; W = Western; XL = X-linked

1. See also www.findis.org.

2. Calculated carrier frequency based on the incidence of the disorder in individuals of Finnish ancestry; estimated carrier frequency is not based on molecular testing of the population.

3. To date, no additional pathogenic variants in this gene have been reported in individuals of Finnish descent.

4. Nucelotide substitution results in a new donor splice site at the end of *CC2D2A* exon 16 [Tallila et al 2008].

5. This percentage does not account for the possibility of rare *de novo* pathogenic variants occurring in this population.

6. Does not conform to standard HGVS nomenclature

Revision History

- 4 May 2023 (sw) Revision: *RMRP* variant nomenclature updated from g.70A>G to g.71A>G
- 30 June 2022 (sw) Revision: added *AICDA*, *ANO5*, *CERKL*, *CHM*, *CRADD*, *SERPINB7*, *SPINK5*; extensive additional edits
- 14 June 2018 (sw) Initial posting

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