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

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A founder variant is a pathogenic variant observed at 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 more than 50% of the pathogenic variants identified in a single gene in individuals of a specific ancestry** – in individuals of Costa Rican 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.

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

Gene	Disorder	MOI	DNA Nucleotide Change	Predicted Protein Change	% of Pathogenic Variants in Gene [1]	Carrier Frequency	Ethnicity	Reference Sequences	References
ATM	Ataxia-telangiectasia	AR	c.5908C>T	p.Gln1970Ter	61%	Unknown	Costa Rican	NM_000051.4 NP_000042.3	Telatar et al [1998]
			c.7449G>A	p.Trp2483Ter	12%				
			c.4507C>T	p.Gln1503Ter	10%				
ATP7B	Wilson disease	AR	c.3809A>G	p.Asn1270Ser	61%	1/72 [2]	Costa Rican	NM_000053.4 NP_000044.2	Shah et al [1997]
CLN6	Ceroid lipofuscinosis (OMIM 601780)	AR	c.214G>T	p.Glu72Ter	~85%	Unknown	Costa Rican	NM_017882.3 NP_060352.1	Gao et al [2002], Wheeler et al [2002], Sharp et al [2003]

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Gene	Disorder	MOI	DNA Nucleotide Change	Predicted Protein Change	% of Pathogenic Variants in Gene [1]	Carrier Frequency	Ethnicity	Reference Sequences	References
GALK1	Galactokinase deficiency (OMIM 230200)	AR	c.1144C>T	p.Gln382Ter	~92%	1/190 [2]	Costa Rican	NM_000154.2 NP_000145.1	Kolosha et al [2000]
PNKP	Axonal Charcot-Marie-Tooth disease type 2B2 (OMIM 605589)	AR	c.1221_1223delCAC	p.Thr408del	~100% [3]	Unknown	Costa Rican	NM_007254.4 NP_009185.2	Leal et al [2018]
			c.1549C>T	p.Gln517Ter					
RPE65	Leber congenital amaurosis	AR	c.292_311del20	p.Ile98HisfsTer26	30%	Unknown	Costa Rican	NM_000329.3 NP_000320.1	Glen et al [2019]
			c.1338G>T	p.Arg446Ser	30%				
			c.242G>T	p.Arg81Ile	25%				
			c.419G>A	p.Gly140Glu	12.5%				
SLC12A1	Bartter syndrome, type 1 (OMIM 601678)	AR	c.1875G>A	p.Trp625Ter	57%	~1/145 [2]	Costa Rican	NM_000338.3 NP_000329.2	Kurtz et al [1997]
TCIRG1	Osteopetrosis (OMIM 259700)	AR	c.1213G>A	p.Gly405Arg	~66%	~1/86 [2]	Costa Rican	NM_006019.4 NP_006010.2	Sobacchi et al [2001]
			c.1331G>T	p.Arg444Leu	~33%				
UBR1	Johanson-Blizzard syndrome (OMIM 243800)	AR	c.1537C>T	p.Glu513Ter	~100% [3]	Unknown	Costa Rican	NM_174916.3 NP_777576.1	Sukalo et al [2014]

Included if ≤3 pathogenic variants account for ≥50% of variants identified in a specific ethnic group
AR = autosomal recessive; MOI = mode of inheritance
1. This percentage does not account for the possibility of rare *de novo* pathogenic variants occurring in this population.
2. Calculated carrier frequency based on the incidence of the disorder in individuals of Costa Rican 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 Costa Rican descent.

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