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Resources for Genetics Professionals — Genetic Disorders Associated with Founder Variants Common in the La Réunion Island Population

Stephanie E Wallace, MD[1,2] and Madelyn A Gillentine, PhD[3,4]

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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 >50% of the pathogenic variants identified in a single gene in individuals of a specific ancestry** – in individuals of La Réunion 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.

Author Affiliations: 1 Senior Editor, GeneReviews; Email: editor2@uw.edu. 2 Clinical Professor, Pediatrics, University of Washington, Seattle, Washington; Email: editor2@uw.edu. 3 Consulting Editor, GeneReviews. 4 Variant Scientist, Department of Laboratories, Seattle Children's Hospital, Seattle, Washington.

Table. Genetic Disorders Associated with Founder Variants Common in the La Réunion Island Population

Gene	Disorder	MOI	DNA Nucleotide Change (Alias [1])	Predicted Protein Change	% of Pathogenic Variants in Gene [2]	Carrier Frequency	Ethnicity (Specific Region)	Reference Sequences	References
ARL6	Bardet-Biedl syndrome	AR	c.535G>A [3] (IVS9-1G>A)	--	~100% [4]	Unknown	La Réunion Islanders	NM_177976.3	Gouronc et al [2020]
B4GALT7	Ehlers-Danlos syndrome, spondylodysplastic type (OMIM 130070)	AR	c.808C>T	p.Arg270Cys	~100% [4]	1/26	La Réunion Islanders	NM_007255.3 NP_009186.1	Cartault et al [2015]
CAPN3	Calpainopathy	AR	c.946-1G>A (IVS6-1G>A)	--	~75%	Unknown	La Réunion Islanders (Southern)	NM_000070.3	Fardeau et al [1996]
CFTR	Cystic fibrosis	AR	c.1521_1523delCTT	p.Phe508del	44%	Unknown	La Réunion Islanders	NM_000492.4 NP_000483.3	Chevalier-Porst et al [1992]
			c.366T>A	p.Tyr122Ter	27%				
COL4A3	Alport syndrome	AR	c.4929-388G>T [5] (IVS51-388G>T)	--	~100% [4]	Unknown	La Réunion Islanders (Southern)	NM_000091.5	Knebelmann et al [1995], Finielz et al [1998]
LEPR	Leptin receptor deficiency (OMIM 614963)	AR	(del exons 6-8)	p.Pro166CysfsTer7	~92%	Unknown	La Réunion Islanders	NG_015831.2	Huvenne et al [2015]
LHFPL5	Nonsyndromic deafness	AR	c.185delT	p.Phe62SerfsTer23	~89%	1/53	La Réunion Islanders	NM_182548.4 NP_872354.1	Lerat et al [2019]
LMNA	Familial partial lipodystrophy type 2 (OMIM 151660)	AD/AR	c.1961dupG	p.Thr655AsnfsTer49	~93%	NA	La Réunion Islanders	NM_170707.4 NP_733821.1	Le Dour et al [2011], Treiber et al [2021]
MARS1	Interstitial lung & liver disease (OMIM 615486)	AR	c.1700C>T & c.1177G>A [6]	p.Ser567Leu & p.Ala393Thr [6]	~100% [4]	1/100	La Réunion Islanders	NM_004990.4 NP_004981.2	Hadchouel et al [2015]
PIGN	Fryns syndrome	AR	c.329_549+1907del5064 (5064-bp del incl part of ex 5, ex 6, & ex 7)	p.Ser110ArgfsTer15	~100% [4]	Unknown	La Réunion Islanders	NM_176787.5 NP_789744.1	Alessandri et al [2018]

Table. continued from previous page.

Gene	Disorder	MOI	DNA Nucleotide Change (Alias [1])	Predicted Protein Change	% of Pathogenic Variants in Gene [2]	Carrier Frequency	Ethnicity (Specific Region)	Reference Sequences	References
SLC7A2	Infantile encephalopathy w/ anorexia	AR	c.-23+3307A>G (IVS1-1713A>G)	--	~100% [4]	1/50	La Réunion Islanders	NM_001008539.4	Cartault et al [2012]
ST3GAL5	GM3 synthase deficiency	AR	c.740G>A	p.Gly247Asp	~100% [4]	Unknown	La Réunion Islanders	NM_003896.4 NP_003887.3	Heide et al [2022]

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

AD = autosomal dominant; AR = autosomal recessive; ex = exon; LGMD = limb-girdle muscular dystrophy; MOI = mode of inheritance

1. Does not conform to standard HGVS nomenclature

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

3. Nucleotide change affects donor splice site resulting in deletion of exon 8.

4. To date, no additional pathogenic variants in this gene have been reported in individuals from La Réunion Island.

5. G-to-T transversion activates a cryptic acceptor splice site located in an Alu element within intron 5, resulting in a 74-bp insertion into the mature transcript at the junction of exons 4 or 5 and exon 6.

6. Affected individuals have been found to be homozygous for both variants listed.

Revision History

- 19 October 2023 (sw) Revision: *LEPR* and *SLC7A2* added; DNA nucleotide change aliases added
- 20 July 2023 (sw) Revision: *ST3GAL5* added
- 8 December 2022 (sw) Initial posting

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