Myelodysplasia and liver disease extend the spectrum of RTEL1 related telomeropathies

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Table S1. Characteristics of families with biallelic *RTEL1* variants

Family	Individuals	Age at study (years)	Gender	Clinical status	Nucleotide	Amino acid	Variant status	Clinical features/diagnosis
1	I-1	NA	F	asymptomatic	NA	NA	NA	None
	I-2	NA	M	asymptomatic	NA	NA	NA	None
	II-1	NA	M	asymptomatic	NA	NA	NA	None
	II-2	36	F	affected	c.2942G>A	p.R981Q	Homozygous	AA; short stature
2	I-1	70	F	affected	NA	NA	NA	Pulmonary fibrosis
	I-2	NA	M	NA	NA	NA	NA	NA
	II-1	40	F	asymptomatic	c.3286G>T	p.G1096W	Heterozygous	None
	II-2	43	M	asymptomatic	c.3286G>T	p.G1096W	Heterozygous	None
	III-1	16	F	asymptomatic	NA	NA	NA	None
	III-2	15	F	asymptomatic	NA	NA	NA	None
	III-3	12	F	affected	c.3286G>T	p.G1096W	Homozygous	AA, pulmonary fibrosis, corrugated tongue
	III-4	3	M	affected	c.3286G>T	p.G1096W	Homozygous	AA
3	I-1	40	F	asymptomatic	c.2300G>A	p.R767Q	Heterozygous	None
	I-2	37	M	asymptomatic	c.2300G>A	p.R767Q	Heterozygous	None
	II-1	15	M	asymptomatic	NA	NA	NA	None
	II-2	14	M	affected	c.2300G>A	p.R767Q	Homozygous	DC, blepharitis, conjunctivitis, pancytopenia, atrial septal defect, low birth weight, growth restriction
	II-3	13	M	asymptomatic	NA	NA	NA	None
	II-4	12	F	asymptomatic	NA	NA	NA	None
	II-5	10	M	asymptomatic	NA	NA	NA	None
	II-6	8	M	asymptomatic	c.2300G>A	p.R767Q	Heterozygous	None
	II-7	5	M	asymptomatic	NA	NA	NA	None
4	I-1	46	F	asymptomatic	c.2785_2787delCAG	p.Q929del	Heterozygous	None
	I-2	50	M	asymptomatic	c.2992C>T	p.R998*	Heterozygous	None
	II-1	24	F	asymptomatic	c.2992C>T	p.R998*	Heterozygous	None
	II-2	15	F	affected	c.2785_2787delCAG c.2992C>T	p.Q929del p.R998*	Compound heterozygous	DC
5	I-1	25	F	asymptomatic	c.1716C>T	p.I572M	Homozygous	None
	I-2	31	M	asymptomatic	c.1716C>T	p.I572M	Heterozygous	None
	II-1	still birth	M	NA	NA	NA	NA	NA
	II-2	Still birth	M	NA	NA	NA	NA	NA
	II-3	6 weeks	NA	affected	NA	NA	NA	Turner syndrome
	II-4	2	F	affected	c.1716C>T	p.I572M	Homozygous	HH
	II-5	NA	F	NA	NA	NA	NA	NA

AA: aplastic anemia; DC: dyskeratosis congenita; HH: Hoyeraal Hreidarsson syndrome; NA: not available; F: female; M: male.

Table S2. Characteristics of index cases with heterozygous VUS and bystander *RTEL1* variants

	Index	Age at study (years)	Gender	Diagnosis	Additional relevant clinical features
Unknown significance	10	23	F	AML	Short stature
	11	20	F	MDS	Skin pigmentation abnormality and squamous cell carcinoma of oesophagus. This patient harbours variants in *TERT* (heterozygous c.3197C>T; p.P1066L and c.322C>T; p.R108C)
	12	10	M	DC	Developmental delay, short stature, dysmorphic facial features, microcephaly, BMF and pulmonary disease
	13	24	M	DC	Skin pigmentation abnormality, leukoplakia, thin hair and BMF
	14	24	F	AA	
	15	6	F	AA	Short stature and oral ulceration with dysphagia. This patient harbours variant in *DNAJC21* (homozygous c.793G>T; p.Q265*)
	16	28	F	AA	
	17	8	F	DC	Nail dystrophy and leukoplakia
	18	18	M	DC	Skin pigmentation abnormality, thin hair, extensive dental caries and BMF
	19	28	M	AA	
	20	10	F	AA	
	21	16	F	DC	Skin pigmentation abnormality, nail dystrophy, leukoplakia, small teeth, sparse scalp hair, epiphora, microcephaly and BMF
Bystander	22	18	M	DC	Skin pigmentation abnormality, nail dystrophy, hair loss, extensive dental caries, developmental delay and short stature
	23	37	M	DC	Skin pigmentation abnormality, nail dystrophy, hair loss, frequent otitis, mild hearing loss and extensive caries/ dental loss
	24	4	F	AA	
	25	50	F	DC	Nail dystrophy, cirrhosis, duodenal ulcers, deafness and developmental delay
	26	NA	M	DC	Skin pigmentation abnormality, nail dystrophy, leucoplakia and leukemia
	27	61	F	MDS/AML	
	28	4	M	DC	Skin pigmentation abnormality, nail dystrophy, microcephaly, low birthweight, developmental delay and cerebellar atrophy. This patient harbours variants in *TERT* (heterozygous c.1336_1337insC; p.R446Pfs93* and c.329G>C; p.G110A)
	29	3	M	DC	Skin pigmentation abnormality, nail dystrophy, abnormal facies, microcephaly, ear abnormality and difficulty in swallowing
	30	0	M	HH	Congenital cytomegalovirus infection, microcephaly, generalized seizures, intracranial calcifications, growth restriction, low birth weight and BMF
	31	54	M	DC	Skin pigmentation abnormality, nail dystrophy, hair loss, tooth loss, renal failure and BMF. This patient harbours variants in *TERT* (homozygous c.3150G>C; p.K1050N) and *TERC* (heterozygous c.205C>T)
	32	7	M	AA	
	33	31	M	DC	Skin pigmentation abnormality, leukoplakia, epiphora, duodenal ulcers, cirrhosis, hepato-pulmonary syndrome and BMF. This patient harbours variant in *TINF2* (heterozygous c.838A>G; p.K280Q)
	34	34	M	AA	
	35	3	M	DC	Skin pigmentation abnormality, nail dystrophy, leucoplakia, hair loss, microcephaly, premature birth with intrauterine growth restriction, glaucoma, premature aging, malabsorption, developmental delay and BMF. This patient harbours variant in *DKC1* (hemizygous c.941A>C; p.K314T)

AML: acute myeloid leukemia; MDS: myelodysplasia; DC: dyskeratosis congenita; AA: aplastic anemia; HH: Hoyeraal Hreidarsson syndrome; BMF: bone marrow failure; NA: not available; F: female; M: male.