

# Telomere attrition is common in patients with germline *RUNX1* pathogenic variants

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**Supplemental Table 1. Individual patient age, sex, MTL and RUNX1 variant (P, LP)**

Age/Sex	Family ID	PATHOGENICITY	RUNX1 Variant	MTL (kb) Lymphocytes	MTL (kb) Granulocytes
2*F	1.1	LP	Arg346Profs*249	9.5	9.4
3M	2.1	P	Ala134Glnfs*2	8.3	8.9
5F	3.1	P	Arg201*	7.4	7
6F	4.1	P	Arg201*	7.2	6.8
8*F	1.1	LP	Arg346Profs*249	8.1	8.4
8M	5.1	P	Deletion Exons 3-5	7.4	7.1
9M	6.1	P	Arg320*	7.5	7.4
9F	7.1	P	Asp93GlyfsTer45	6.2	7
11*F	1.1	LP	Arg346Profs*249	6.8	6.5
11F	8.1	P	Arg201*	7	7.4
12^F	1.2	LP	Arg346Profs*249	6.8	7.3
12F	9.1	P	SS/NA	7.6	6.7
13M	10.1	LP	Gln274fs	7.2	7.3
15M	6.2	P	Arg320*	6.5	6.6
19M	12.1	P	21q22.12del	6	6.7
19^F	1.2	LP	Arg346Profs*249	6	6.5
20M	13.1	P	Pro277HisfsTer35	6.7	7.1
21M	13.2	P	Pro277HisfsTer34	6.5	6.6
21^F	1.2	LP	Arg346Profs*249	5.7	6.1
22M	14.1	LP	Glu316Aspfs*12	4.2	6.4
28F	15.1	P	Arg201*	6.8	7.6
30M	16.1	P	Deletion Exons 5-6	4.8	5.1
32F	15.2	P	Arg201*	6.3	6.3
35M	16.2	P	Deletion Exons 5-6	4.6	4.8
36M	3.2	P	Arg201*	4.8	6

37F	17.1	LP	Gly168Arg	5.4	5.2
38F	18.1	P	21q22.11q22.12del	4.4	5.8
39M	5.2	P	Deletion Exons 3-5	4.9	5.2
41F	19.1	P	Arg201*	5.1	5.4
41F	20.1	LP	Deletion Exon 2	5.3	5.5
41F	17.2	LP	Gly168Arg	5.2	5.3
42M	6.3	P	Arg320*	5.3	6.2
42M	16.3	P	Deletion Exons 5-6	5.8	5.6
44M	7.2	P	Asp93GlyfsTer45	4.4	4.9
44F	21.1	P	Leu56Profs*6	6.3	7.3
46M	22.1	P	508+3delA	3.7	4.6
46F	1.3	LP	Arg346Profs*249	4.9	5.4
47F	12.2	P	21q22.12del	4.6	4
55M	10.2	LP	Gln274fs	4.4	5.4
59F	23.1	P	806-1G>A	4.6	5.5
63F	24.1	LP	Deletion Exon 2	4.4	5.4
63M	25.1	P	Arg201*	4.5	5.9
64F	26.1	P	Leu472fs	3.7	4.4
66F	17.3	LP	Gly168Arg	4.8	4.6

2\*F, 8\*F, 11\*F - serial TL measurements for patient P1 (Figure 2A-D).

12^F, 19^F, 21^F - serial TL measurements for patient P2 (Figure 2A-D).

MTL – median telomere length.

**Supplemental Table 2.** Telomere shortenings in FPDMM patients by age groups and in two pediatric patients.

**2A.** Numbers of patients and percentages of total patients in each indicated percentiles of TLs in lymphocytes and granulocytes for the indicated age groups.

	Age					Percentile
	0-20	21-40	41-60	61-80		
<b>Lymphocytes</b>						
5/40 (12.5%)	0/13 (0%)	2/11 (18%)	2/12 (17%)	1/4 (25)	10 <sup>th</sup> -50 <sup>th</sup> (Normal)	
23/40(57.5%)	10/13 (77%)	3/11(27%)	8/12 (66%)	2/4 (50%)	1 <sup>st</sup> -10 <sup>th</sup> (Short)	
12/40(30%)	3/13 (23%)	6/11(55%)	2/12(17%)	1/4 (25%)	<1 <sup>st</sup> ( Very Short )	
<b>Granulocytes</b>						
2/40 (5%)	0/13 (0%)	1/11 (9%)	1/12 (8%)	0/4 (0)	10 <sup>th</sup> -50 <sup>th</sup> (Normal)	
15/40 (37.5%)	6/13 (46%)	5/11(45.5%)	2/12 (17%)	2/4 (50%)	1 <sup>st</sup> -10 <sup>th</sup> (Short)	
23/40 (57.5%)	7/13 (54%)	5/11(45.5%)	9/12 (75%)	2/4 (50%)	<1 <sup>st</sup> ( Very Short )	

**2B.** Telomere base pair loss per year for 2 related pediatric patients in lymphocytes (upper table) and granulocytes (lower table).

<b>Lymphocytes</b>					
	Age (yr)	MTLN (kb)	MTLP (kb)	MTLN Rate (bp/yr)	MTLP Rate (bp/yr)
FPD P1	2	10.1	9.5		
	8	9.2	8.1	<b>-900/6y= -150</b>	<b>-1400/6y= -233</b>
	11	8.9	6.8	<b>-300/3y= -100</b>	<b>-1300/3y= -433</b>
FPD P2	12	8.8	6.8		
	19	8.1	6.0	<b>-700/7y= -100</b>	<b>-800/7y= -114</b>
	21	7.9	5.7	<b>-200/2y= -100</b>	<b>-300/2y= -150</b>

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**Granulocytes**

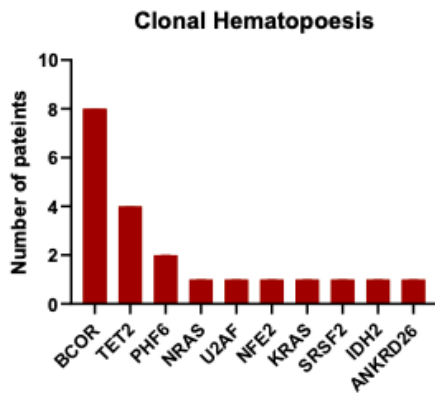
	Age (yr)	MTLN (kb)	MTLP (kb)	MTLN Rate (bp/yr)	MTLP Rate (bp/yr)
FPD P1	2	10.4	9.4		
	8	9.8	8.4	<b>-600/6y= -100</b>	<b>-1000/6y= -166</b>
	11	9.5	6.5	<b>-300/3y= -100</b>	<b>-1900/3y= -633</b>
FPD P2	12	9.5	7.3		
	19	9.0	6.5	<b>-500/7y= -71</b>	<b>-800/7y= -114</b>
	21	8.9	6.1	<b>-100/2y= -50</b>	<b>-400/2y= -200</b>

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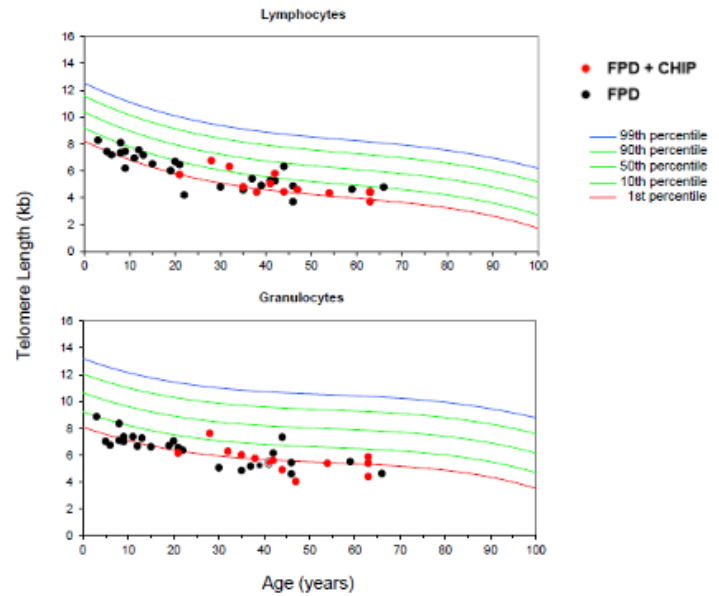
Kb- kilobase; bp- base pairs; L- lymphocyte; G- granulocyte; MTLN<sup>1</sup>- normal median telomere length for age; MTLP- patient median telomere length for age; yr- year; FPD – familial platelet disorder; P1- patient1; P2- patient 2.

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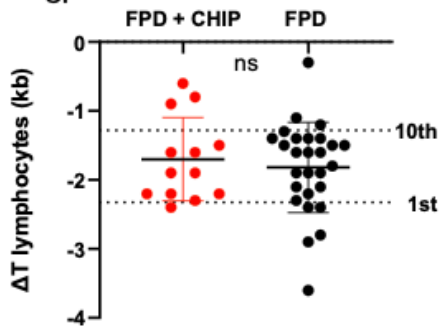
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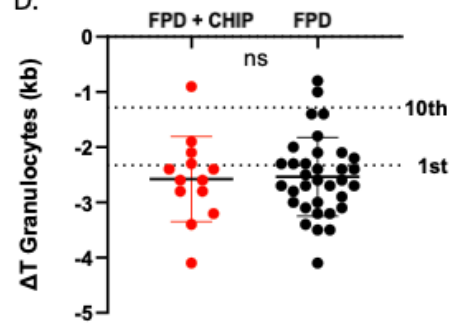
B.



C.



D.



**Supplemental Figure 1. Telomere lengths according to CHIP status in patients with germline *RUNX1* FPDMM.** (A) Bar graph showing the number of patients with somatic mutations (VAF > 2%) in the indicated CHIP or leukemia genes. (B) Nomograms of lymphocyte and granulocyte TLs from FPDMM patients with (red circles) or without (black circles) CHIP. Distribution of age-adjusted deviation in telomere length according to CHIP status (with CHIP: red circles; without CHIP: black circles) in lymphocytes (C) and granulocytes (D). FPD- familial platelet disorder; CHIP- clonal hematopoiesis of indeterminate potential,  $\Delta T$ - deviation of TL from the age-adjusted median; kb- kilobase. CHIP is defined as somatic mutations in genes related to clonal hematopoiesis or leukemia with variant allele frequency (VAF) > 2%.