# Supporting Information

## Alder et al. 10.1073/pnas.1720427115

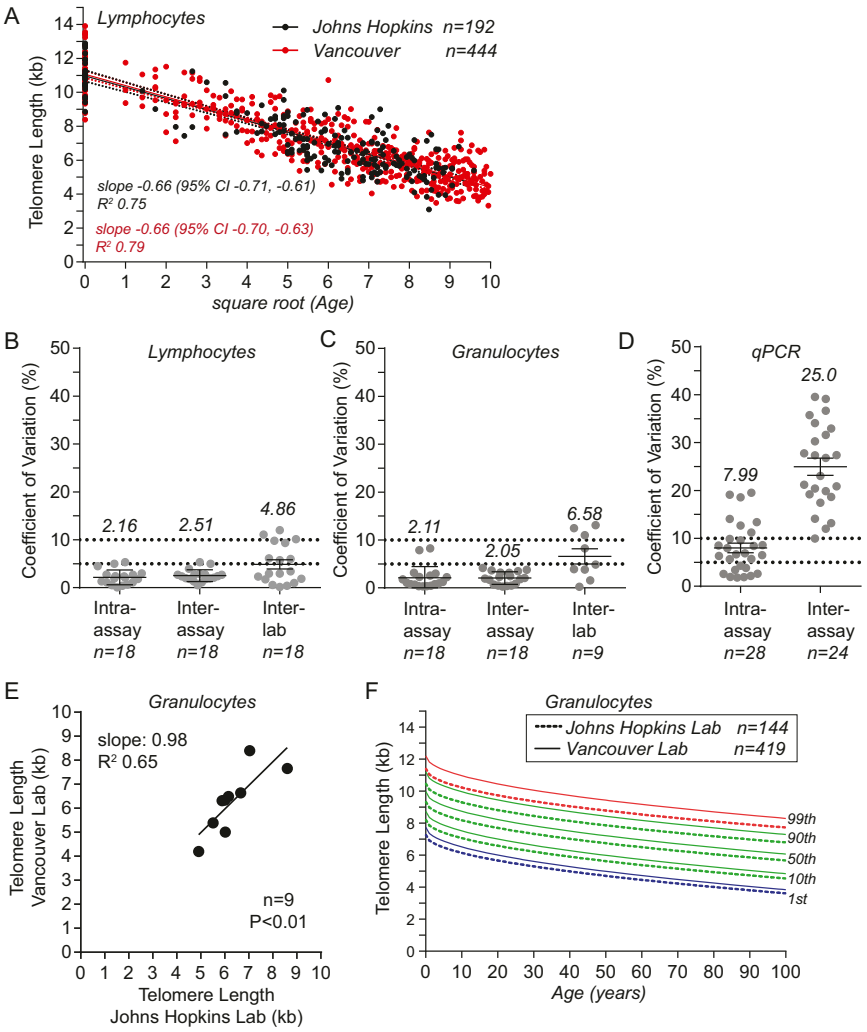


**Fig. S1.** Performance characteristics of TL measurement by flowFISH. (*A*) Best fit curves for raw lymphocyte TL data from Johns Hopkins controls relative to age, showing a linear relationship with the square root of the age. A comparison with the Vancouver-derived controls is also included. The dashed lines indicate the 95% confidence lines for each of the linear regression lines and the $R^2$ and slope values are annotated for each dataset, respectively. (*B* and *C*) Intraassay (single run) and interassay (different days) CV at the Johns Hopkins laboratory for TL for each of lymphocyte and granulocytes, respectively. The interlaboratory values for each of lymphocytes and granulocytes refer to comparison for identical samples measured at the Johns Hopkins and a Vancouver laboratory. The numbers refer to each sample used to derive these means. (*D*) Intra- and interassay CV for TL, as measured by quantitative PCR (T/S). (*E*) Interlaboratory concordance in granulocyte TL values measured at Johns Hopkins and Vancouver laboratories. (*F*) Overlay of granulocyte TL nomograms derived at Johns Hopkins and Vancouver with the percentile lines labeled. Where means are shown, error bars represent ±SEM.

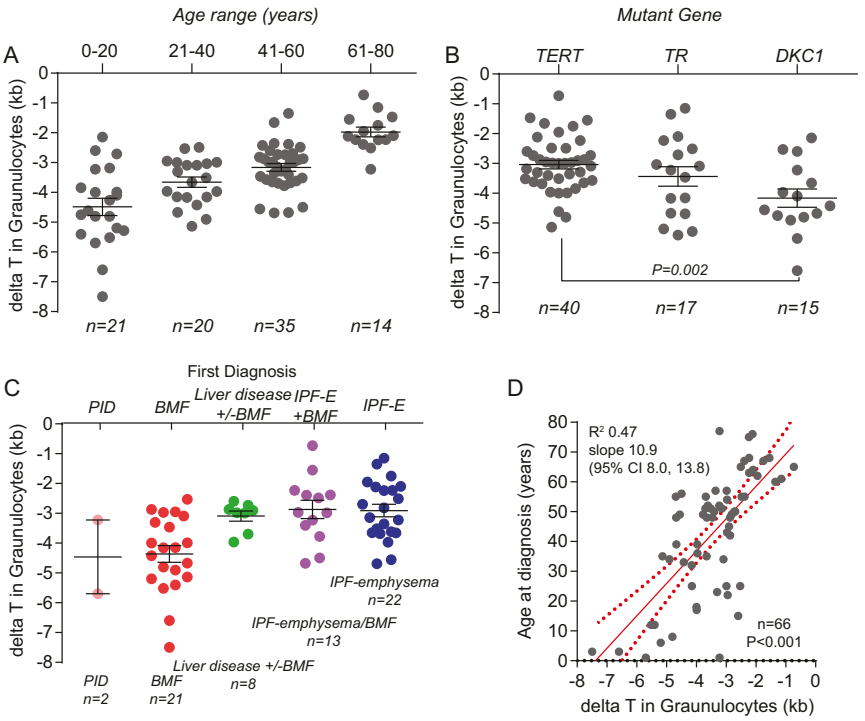


**Fig. S2.** Granulocyte TL data in patients with mutations in telomerase and telomere maintenance genes. (*A*) Deviation from age-adjusted median values (ΔT) of granulocyte TL in 90 of the 100 individuals plotted in Fig. 2*A* in four age groups, as delineated. (*B*) ΔT of granulocyte TL in *TERT*, *TR*, and *DKC1* mutation carriers corresponding to lymphocyte TL data shown in Fig. 2*E*. (*C*) The severity of TL deviation correlates with four core degenerative short-telomere syndrome complications, as is shown for this granulocyte TL dataset, which corresponds with the data in Fig. 3*C*. PID refers to primary immunodeficiency, BMF refers to bone marrow failure, and IPF-E to idiopathic pulmonary fibrosis with or without emphysema. Mean values are shown ±SEM. (*D*) Correlation between granulocyte TL and age at onset of the four studied telomere phenotypes with the linear regression line and 95% confidence intervals are shown. These data correspond to the lymphocyte data shown in Fig. 3*B*.

**Table S1. Characteristics of donors recruited to generate telomere nomogram**

| Characteristic | Total (*n* = *192*) |
|---|---|
| Gender | |
| Male | 89 |
| Female | 103 |
| Racial background (self-reported) | |
| European | 73 |
| African | 70 |
| Asian | 49 |
| Age range, y | |
| 0 (cord blood) | 25 |
| 1–10 | 7 |
| 11–20 | 12 |
| 21–30 | 36 |
| 31–40 | 26 |
| 41–50 | 23 |
| 51–60 | 26 |
| 61–70 | 17 |
| 71–80 | 16 |
| 81–90 | 4 |

**Table S2. TL data used to generate lymphocyte and granulocyte nomograms**

| Age, y | Lymphocyte TL *n* = *192* | Granulocyte TL *n* = *140* |
|---|---|---|
| 0 | 10.79 | |
| 0 | 10.81 | 8.76 |
| 0 | 10.19 | |
| 0 | 12.63 | 10.52 |
| 0 | 12.81 | 10.93 |
| 0 | 11.71 | 9.38 |
| 0 | 11.15 | 9.37 |
| 0 | 9.73 | 7.83 |
| 0 | 12.75 | |
| 0 | 9.42 | 7.94 |
| 0 | 12.89 | 10.81 |
| 0 | 11.91 | 9.81 |
| 0 | 10.98 | 9.17 |
| 0 | 8.86 | |
| 0 | 10.96 | 8.99 |
| 0 | 10.46 | 8.90 |
| 0 | 12.29 | |
| 0 | 10.35 | 8.79 |
| 0 | 11.28 | 9.19 |
| 0 | 10.38 | 8.75 |
| 0 | 10.98 | |
| 0 | 10.93 | |
| 0 | 11.04 | |
| 0 | 10.52 | 8.97 |
| 0 | 11.95 | 10.50 |
| 9 | 10.60 | 10.00 |
| 7 | 11.25 | 10.28 |
| 6 | 7.44 | 6.89 |
| 3 | 9.01 | 8.45 |
| 2 | 10.09 | 8.68 |
| 5 | 7.96 | 7.60 |
| 7 | 7.95 | 7.94 |
| 12 | 9.78 | 9.14 |
| 16 | 8.78 | 8.53 |
| 14 | 8.89 | 8.40 |
| 18 | 7.60 | |
| 19 | 7.69 | 6.74 |
| 19 | 9.24 | 9.23 |
| 12 | 7.52 | 7.34 |
| 14 | 7.67 | 7.55 |
| 14 | 8.78 | 7.67 |
| 12 | 10.56 | 9.70 |
| 19 | 8.17 | 8.70 |
| 26 | 6.63 | 6.57 |
| 25 | 6.91 | 7.09 |
| 28 | 7.32 | 7.06 |
| 28 | 6.58 | 6.00 |
| 25 | 8.60 | 7.73 |
| 27 | 7.25 | |
| 29 | 6.61 | 6.60 |
| 25 | 6.50 | 6.35 |
| 24 | 8.07 | 6.52 |
| 26 | 6.45 | |
| 25 | 8.83 | 7.90 |
| 29 | 6.83 | 6.77 |
| 26 | 7.58 | 7.44 |
| 21 | 8.42 | 8.30 |
| 24 | 8.60 | 7.75 |
| 23 | 7.66 | 7.69 |
| 22 | 7.53 | 7.61 |
| 20 | 8.01 | 7.07 |
| 29 | 7.23 | |

**Table S2. Cont.**

| Age, y | Lymphocyte TL *n* = *192* | Granulocyte TL *n* = *140* |
|---|---|---|
| 29 | 8.69 | 8.11 |
| 28 | 7.36 | 7.93 |
| 22 | 8.59 | 8.28 |
| 22 | 8.44 | 8.07 |
| 25 | 6.41 | 7.06 |
| 27 | 8.25 | 7.51 |
| 24 | 9.56 | |
| 24 | 7.72 | 7.70 |
| 24 | 8.47 | |
| 24 | 8.13 | 7.47 |
| 38 | 7.46 | 8.42 |
| 30 | 6.41 | 6.88 |
| 35 | 8.70 | 8.34 |
| 35 | 5.79 | |
| 32 | 7.04 | 7.05 |
| 30 | 6.00 | |
| 30 | 5.43 | 6.03 |
| 30 | 6.76 | |
| 39 | 6.86 | 7.11 |
| 36 | 6.96 | 8.31 |
| 38 | 8.44 | |
| 35 | 7.82 | |
| 35 | 7.74 | 7.95 |
| 30 | 6.84 | 7.17 |
| 32 | 6.23 | 5.98 |
| 39 | 6.47 | 7.92 |
| 38 | 6.86 | |
| 30 | 8.97 | 8.40 |
| 38 | 6.50 | 6.37 |
| 30 | 6.28 | 6.72 |
| 34 | 5.40 | 6.57 |
| 32 | 6.23 | 6.90 |
| 33 | 8.29 | 8.75 |
| 39 | 7.04 | 7.09 |
| 35 | 6.15 | 6.49 |
| 31 | 6.09 | 7.23 |
| 30 | 7.25 | |
| 36 | 5.98 | 5.74 |
| 34 | 7.65 | |
| 37 | 5.70 | 7.28 |
| 39 | 9.09 | |
| 47 | 4.80 | 5.01 |
| 43 | 6.48 | 6.48 |
| 42 | 5.28 | |
| 42 | 5.39 | 6.54 |
| 48 | 5.78 | 7.44 |
| 47 | 6.38 | 7.37 |
| 40 | 7.32 | 7.34 |
| 45 | 6.58 | 6.80 |
| 48 | 6.51 | 7.28 |
| 47 | 6.37 | |
| 49 | 5.77 | |
| 40 | 4.91 | 6.40 |
| 47 | 6.04 | 6.31 |
| 46 | 5.82 | 5.78 |
| 47 | 7.01 | |
| 42 | 7.33 | 7.98 |
| 42 | 5.95 | |
| 40 | 5.21 | 6.08 |
| 41 | 7.75 | 7.65 |
| 47 | 5.02 | 5.66 |
| 44 | 6.17 | 8.93 |

**Table S2. Cont.**

| Age, y | Lymphocyte TL *n* = *192* | Granulocyte TL *n* = *140* |
|---|---|---|
| 53 | 5.30 | 6.07 |
| 55 | 5.64 | 5.85 |
| 58 | 6.55 | 6.58 |
| 51 | 5.74 | 6.04 |
| 52 | 5.59 | 6.86 |
| 50 | 6.06 | 6.18 |
| 52 | 7.77 | 8.08 |
| 54 | 6.32 | |
| 59 | 6.22 | 6.25 |
| 50 | 8.54 | |
| 52 | 6.97 | 6.88 |
| 51 | 6.06 | 6.23 |
| 53 | 6.57 | 7.10 |
| 51 | 6.00 | |
| 54 | 6.78 | 7.52 |
| 55 | 5.55 | |
| 54 | 7.59 | 7.25 |
| 50 | 7.05 | 8.14 |
| 59 | 5.71 | 7.05 |
| 55 | 7.19 | 7.26 |
| 58 | 5.81 | |
| 52 | 5.18 | |
| 54 | 5.75 | 5.60 |
| 52 | 4.73 | |
| 51 | 5.29 | |
| 50 | 7.10 | 7.44 |
| 53 | 9.00 | 8.68 |
| 50 | 4.98 | |
| 56 | 8.02 | |
| 61 | 5.81 | 6.62 |
| 63 | 5.01 | |
| 65 | 6.14 | 7.32 |
| 69 | 5.00 | 5.42 |
| 68 | 5.08 | 5.97 |
| 60 | 6.01 | 6.51 |
| 63 | 6.19 | 7.16 |
| 66 | 5.39 | 5.29 |
| 65 | 4.76 | 4.35 |
| 66 | 7.19 | 6.29 |
| 63 | 5.50 | |
| 66 | 5.99 | |
| 66 | 4.10 | |
| 66 | 5.96 | 6.92 |
| 64 | 6.35 | 6.55 |
| 60 | 5.67 | 6.44 |
| 63 | 5.49 | 6.64 |
| 70 | 4.86 | |
| 71 | 7.14 | |
| 78 | 5.27 | 6.13 |
| 79 | 5.56 | 7.25 |
| 79 | 3.94 | 5.53 |
| 76 | 6.63 | |
| 73 | 7.50 | |
| 76 | 3.96 | |
| 76 | 5.54 | 6.65 |
| 75 | 6.65 | |
| 74 | 4.96 | 6.12 |
| 70 | 5.08 | |
| 73 | 4.25 | 5.52 |
| 71 | 3.84 | |
| 71 | 4.70 | 5.24 |
| 72 | 3.09 | 5.63 |

**Table S2. Cont.**

| Age, y | Lymphocyte TL *n* = *192* | Granulocyte TL *n* = *140* |
|---|---|---|
| 75 | 5.80 | 7.25 |
| 78 | 5.51 | |
| 85 | 6.80 | 6.95 |
| 82 | 4.51 | 5.62 |
| 82 | 5.53 | 5.59 |
| 82 | 5.49 | |

**Table S3. Clinical features and mutant gene of 100 mutation carriers**

| Age, y | Gender | Mutant gene | First symptom | Age, y | Gender | Mutant gene | First symptom |
|---|---|---|---|---|---|---|---|
| 1 | M | *DKC1* | PID | 46 | M | *TERT* | IPF |
| 1 | F | *TERT* | Asymptomatic | 48 | F | *TR* | BMF |
| 1 | F | *RTEL1* | PID | 48 | M | *TERT* | IPF |
| 1 | M | *TERT* | Asymptomatic | 48 | M | *DKC1* | IPF/BMF |
| 1 | M | *TERT* | Asymptomatic | 48 | M | *TERT* | Liver disease |
| 3 | F | *TINF2* | BMF | 49 | F | *TERT* | Asymptomatic |
| 3 | M | *DKC1* | BMF | 49 | M | *DKC1* | IPF |
| 6 | M | *TR* | BMF | 49 | M | *RTEL1* | IPF |
| 8 | F | *TERT* | BMF | 49 | M | *RTEL1* | IPF/BMF |
| 10 | M | *DKC1* | Asymptomatic | 50 | F | *TINF2* | IPF |
| 12 | M | *DKC1* | BMF | 50 | F | *TERT* | IPF/BMF |
| 12 | M | *TR* | BMF | 50 | M | *TERT* | Asymptomatic |
| 13 | F | *TR* | Asymptomatic | 50 | M | *TERT* | Liver disease |
| 14 | M | *DKC1* | Asymptomatic | 51 | F | *TERT* | IPF |
| 15 | M | *DKC1* | Liver disease | 51 | M | *PARN* | IPF |
| 16 | M | *DKC1* | Asymptomatic | 51 | M | *RTEL1* | IPF |
| 17 | F | *TERT* | BMF | 52 | F | *TR* | IPF/BMF |
| 17 | M | *DKC1* | Asymptomatic | 52 | M | *TR* | BMF |
| 18 | M | *TERT* | BMF | 52 | M | *TERT* | IPF |
| 20 | F | *TR* | Asymptomatic | 52 | M | *RTEL1* | IPF/BMF |
| 20 | M | *TERT* | Asymptomatic | 53 | F | *TERT* | Asymptomatic |
| 22 | F | *TERT* | Asymptomatic | 53 | F | *TERT* | IPF |
| 22 | M | *TERT* | BMF | 54 | F | *NAF1* | PF-emphysema/BMF |
| 23 | F | *TERT* | Asymptomatic | 55 | F | *TERT* | IPF |
| 23 | M | *TERT* | BMF | 55 | F | *RTEL1* | PF-emphysema |
| 25 | F | *RTEL1* | BMF | 55 | F | *TERT* | IPF/BMF |
| 25 | M | *DKC1* | BMF | 55 | F | *TR* | Emphysema |
| 25 | M | *TERT* | BMF | 56 | F | *NAF1* | Asymptomatic |
| 30 | F | *TR* | Asymptomatic | 56 | F | *NAF1* | IPF/BMF |
| 32 | F | *TR* | BMF | 57 | F | *RTEL1* | Asymptomatic |
| 33 | F | *TR* | Asymptomatic | 57 | M | *TERT* | IPF |
| 33 | M | *DKC1* | BMF | 57 | M | *RTEL1* | IPF/BMF |
| 34 | F | *TR* | BMF | 60 | F | *TR* | IPF |
| 34 | M | *TERT* | Asymptomatic | 61 | F | *TERT* | Asymptomatic |
| 34 | M | *DKC1* | BMF | 61 | F | *TR* | IPF |
| 35 | M | *TERT* | BMF | 62 | F | *TERT* | IPF |
| 35 | M | *DKC1* | IPF | 63 | F | *TR* | IPF/BMF |
| 36 | F | *TERT* | Asymptomatic | 64 | F | *TR* | IPF |
| 36 | M | *TERT* | Asymptomatic | 65 | F | *TR* | IPF |
| 36 | M | *TERT* | BMF | 65 | M | *TERT* | IPF/BMF |
| 39 | M | *TR* | BMF | 67 | M | *TERT* | IPF |
| 39 | M | *DKC1* | IPF | 67 | M | *RTEL1* | IPF |
| 42 | F | *TERT* | BMF | 68 | M | *TERT* | IPF |
| 43 | F | *TERT* | Asymptomatic | 68 | M | *TERT* | IPF/BMF |
| 43 | F | *TERT* | Asymptomatic | 70 | M | *TERT* | IPF |
| 43 | F | *TERT* | BMF | 72 | F | *TERT* | Asymptomatic |
| 43 | M | *TERT* | BMF | 75 | M | *PARN* | IPF |
| 44 | F | *TERT* | Asymptomatic | 76 | F | *TERT* | IPF |
| 45 | M | *TERT* | Liver disease | 77 | M | *TERT* | IPF |
| 46 | F | *TERT* | IPF | 77 | M | *TR* | IPF |

BMF, bone marrow failure; F, female; IPF, idiopathic pulmonary fibrosis; M, male.

**Table S4. Catalog of mutations for subjects included in Figs. 2–4**

| Gene | Substitution* | Prior report |
|---|---|---|
| *TERT* | p.Leu55Gln | (1) |
| | p.Phe71Leu | Not previously reported |
| | IVS1+1G > A | (1) |
| | p.Gly135Glu | (2) |
| | p.Val170Met | (3) |
| | p.Val170Leu | Not Previously reported |
| | p.Phe487Leu | Not previously reported |
| | p.Asn571Ser | Not previously reported |
| | p.Val664Leu | Not previously reported |
| | p.Ala716Thr | (3) |
| | p.Gln722Ter | Not previously reported |
| | p.Val747Alafs*20 | (4) |
| | p.Leu841Phe | (3) |
| | p.Arg858Trp | (5) |
| | IVS9-2A > C | (1) |
| | p.Val867Met | (6) |
| | p.Lys902Asn | (7) |
| | p.His983Tyr | (2) |
| | p.Val1025Phe | (3) |
| | p.Thr1039Ala | Not previously reported |
| | p.Lys1050Asn | (2) |
| | p.Thr1110Met | (1) |
| *TR* | r.35C > A | (8) |
| | r.80U > A | (9) |
| | r.98G > A | (1) |
| | r.110-113delGACU | (10) |
| | r.143G > A | (3, 11) |
| | r.182G > C | (8) |
| | r.204C > G | (3, 12) |
| | r.257G > U | Not previously reported |
| | r.325G > U | (13) |
| | r.375-377delGGA | (14) |
| *DKC1* | IVS1+592C > G | (2, 15) |
| | p.Gln31Glu | (16, 17) |
| | p.Thr49Ser | (18) |
| | IVS2-5C > T | Not previously reported |
| | IVS2-5C > G | (19) |
| | p.Arg158Trp | (15, 20) |
| | p.Leu317Phe | (20, 21) |
| | p.Ala308Gly | Not previously reported |
| | p.Pro409Arg | (18) |
| *RTEL1** | p.Arg574Cys | Not previously reported |
| | p.Arg974Ter | (22, 23) |
| | p.Arg986Ter | (22) |
| | p.Arg1264His | (23) |
| *TINF2* | p.Gln269Ter | (24, 25) |
| | p.Thr284Arg | (24, 26) |
| *PARN* | p.Phe8Leufs* | Not previously reported |
| | pPhe90Val | Not previously reported |
| *NAF1* | p.Lys319Argfs*21 | (27) |
| | p.Ser329Ilefs*12 | (27) |
| *GATA2* | p.Phe265Glufs*58 | Not previously reported |
| | p.Thr354Met | (28) |
| *RUNX1* | p.Pro401Leufs*200 | Not previously reported |

Literature search for prior reports was updated on October 1, 2017.
*All of the mutations included were heterozygous except for *RTEL1* p.Arg1264His which was homozygous in one case, and one patient had compound heterozygous *RTEL1* p.Arg1010Ter/p.Arg574Cys. We used the 1,300 amino acid isoform to annotate the *RTEL1* mutations (NP_001269938.1).


1. Armanios MY, et al. (2007) Telomerase mutations in families with idiopathic pulmonary fibrosis. *N Engl J Med* 356:1317–1326.
2. Gorgy AI, et al. (2015) Hepatopulmonary syndrome is a frequent cause of dyspnea in the short telomere disorders. *Chest* 148:1019–1026.
3. Parry EM, Alder JK, Qi X, Chen JJ, Armanios M (2011) Syndrome complex of bone marrow failure and pulmonary fibrosis predicts germline defects in telomerase. *Blood* 117:5607–5611.
4. Tsakiri KD, et al. (2007) Adult-onset pulmonary fibrosis caused by mutations in telomerase. *Proc Natl Acad Sci USA* 104:7552–7557.
5. Newton CA, et al. (2016) Telomere-related lung fibrosis is diagnostically heterogeneous but uniformly progressive. *Eur Respir J* 48:1710–1720.
6. Alder JK, et al. (2011) Ancestral mutation in telomerase causes defects in repeat addition processivity and manifests as familial pulmonary fibrosis. *PLoS Genet* 7:e1001352.
7. Armanios M, et al. (2005) Haploinsufficiency of telomerase reverse transcriptase leads to anticipation in autosomal dominant dyskeratosis congenita. *Proc Natl Acad Sci USA* 102: 15960–15964.
8. Silhan LL, et al. (2014) Lung transplantation in telomerase mutation carriers with pulmonary fibrosis. *Eur Respir J* 44:178–187.
9. Stanley SE, Rao AD, Gable DL, McGrath-Morrow S, Armanios M (2015) Radiation sensitivity and radiation necrosis in the short telomere syndromes. *Int J Radiat Oncol Biol Phys* 93: 1115–1117.
10. Vulliamy T, Marrone A, Dokal I, Mason PJ (2002) Association between aplastic anaemia and mutations in telomerase RNA. *Lancet* 359:2168–2170.
11. Vulliamy T, et al. (2004) Disease anticipation is associated with progressive telomere shortening in families with dyskeratosis congenita due to mutations in TERC. *Nat Genet* 36:447–449.
12. Fogarty PF, et al. (2003) Late presentation of dyskeratosis congenita as apparently acquired aplastic anaemia due to mutations in telomerase RNA. *Lancet* 362:1628–1630.
13. Alder JK, et al. (2008) Short telomeres are a risk factor for idiopathic pulmonary fibrosis. *Proc Natl Acad Sci USA* 105:13051–13056.
14. Alder JK, et al. (2011) Telomere length is a determinant of emphysema susceptibility. *Am J Respir Crit Care Med* 184:904–912.
15. Knight SW, et al. (2001) Identification of novel DKC1 mutations in patients with dyskeratosis congenita: Implications for pathophysiology and diagnosis. *Hum Genet* 108:299–303.
16. Wong JM, Kyasa MJ, Hutchins L, Collins K (2004) Telomerase RNA deficiency in peripheral blood mononuclear cells in X-linked dyskeratosis congenita. *Hum Genet* 115:448–455.
17. Parry EM, et al. (2011) Decreased dyskerin levels as a mechanism of telomere shortening in X-linked dyskeratosis congenita. *J Med Genet* 48:327–333.
18. Alder JK, et al. (2013) Telomere phenotypes in females with heterozygous mutations in the dyskeratosis congenita 1 (DKC1) gene. *Hum Mutat* 34:1481–1485.
19. Knight SW, et al. (1999) X-linked dyskeratosis congenita is predominantly caused by missense mutations in the DKC1 gene. *Am J Hum Genet* 65:50–58.
20. Jonassaint NL, Guo N, Califano JA, Montgomery EA, Armanios M (2013) The gastrointestinal manifestations of telomere-mediated disease. *Aging Cell* 12:319–323.
21. Rostamiani K, et al. (2010) Novel mutations of the DKC1 gene in individuals affected with dyskeratosis congenita. *Blood Cells Mol Dis* 44:88.
22. Ballew BJ, et al. (2013) Germline mutations of regulator of telomere elongation helicase 1, RTEL1, in dyskeratosis congenita. *Hum Genet* 132:473–480.
23. Walne AJ, Vulliamy T, Kirwan M, Plagnol V, Dokal I (2013) Constitutional mutations in RTEL1 cause severe dyskeratosis congenita. *Am J Hum Genet* 92:448–453.
24. Vulliamy T, et al. (2012) Telomere length measurement can distinguish pathogenic from non-pathogenic variants in the shelterin component, TIN2. *Clin Genet* 81:76–81.
25. Sasa GS, Ribes-Zamora A, Nelson ND, Bertuch AA (2012) Three novel truncating TINF2 mutations causing severe dyskeratosis congenita in early childhood. *Clin Genet* 81:470–478.
26. Alder JK, et al. (2015) Exome sequencing identifies mutant TINF2 in a family with pulmonary fibrosis. *Chest* 147:1361–1368.
27. Stanley SE, et al. (2016) Loss-of-function mutations in the RNA biogenesis factor NAF1 predispose to pulmonary fibrosis-emphysema. *Sci Transl Med* 8:351ra107.
28. Hsu AP, et al. (2011) Mutations in GATA2 are associated with the autosomal dominant and sporadic monocytopenia and mycobacterial infection (MonoMAC) syndrome. *Blood* 118: 2653–2655.

**Table S5. Clinical characteristics of subjects recruited to study**

| Characteristic | Total (*n* = *38*) |
|---|---|
| Median age | |
| Range 0–31 y | 14 |
| Gender | |
| Male | 23 |
| Female | 15 |
| Recruiting sites | |
| Johns Hopkins Pediatric Clinics | 19 |
| Johns Hopkins Adult Clinics | 8 |
| Self-referral | 3 |
| Outside institutions | 8 |
| Genetic evaluation | |
| Targeted next-generation panel | 28 |
| Clinical testing | 6 |
| Not tested* | 4 |
| Disease severity | |
| Nonsevere aplastic anemia | 25 |
| Severe or very severe aplastic anemia | 13 |
| Endpoints reached | |
| Genetic diagnosis identified | 12 |
| Response to immunosuppression (partial or complete) | 10 |
| Constitutional aplastic anemia, no genetic diagnosis found | 8 |
| Not treated, no genetic diagnosis identified | 8 |

*These patients were positive for a paroxysmal nocturnal hemoglobinuria clone by flow cytometry, ruling out the possibility of an inherited disorder as the cause of the bone marrow failure (1).

1. DeZern AE, et al. (2014) Detection of paroxysmal nocturnal hemoglobinuria clones to exclude inherited bone marrow failure syndromes. *Eur J Haematol* 92:467–470.

**Table S6. Characteristics of severe aplastic anemia patients studied after response to immunosuppression**

| Characteristic | Total (*n* = *8*) |
|---|---|
| Median age at diagnosis of severe aplastic anemia | |
| Range 19–65 y | 39 |
| Gender | |
| Male | 6 |
| Female | 2 |
| Recruiting sites | |
| Johns Hopkins Adult Clinics | 8 |
| Age at assessment | |
| Range 23–69 y | 46 |
| Immunosuppression treatment | |
| High-dose Cyclophosphamide | 7 |
| ATG/Cyclosporin | 1 |
| Mean duration of response* | |
| Range 14–180 mo | 67 |

*Remission criteria were assessed according to the Camitta criteria (1).

1. Camitta BM, et al. (1976) Severe aplastic anemia: A prospective study of the effect of early marrow transplantation on acute mortality. *Blood* 48:63–70.