Supporting Information

Alder *et al.* 10.1073/pnas.0804280105

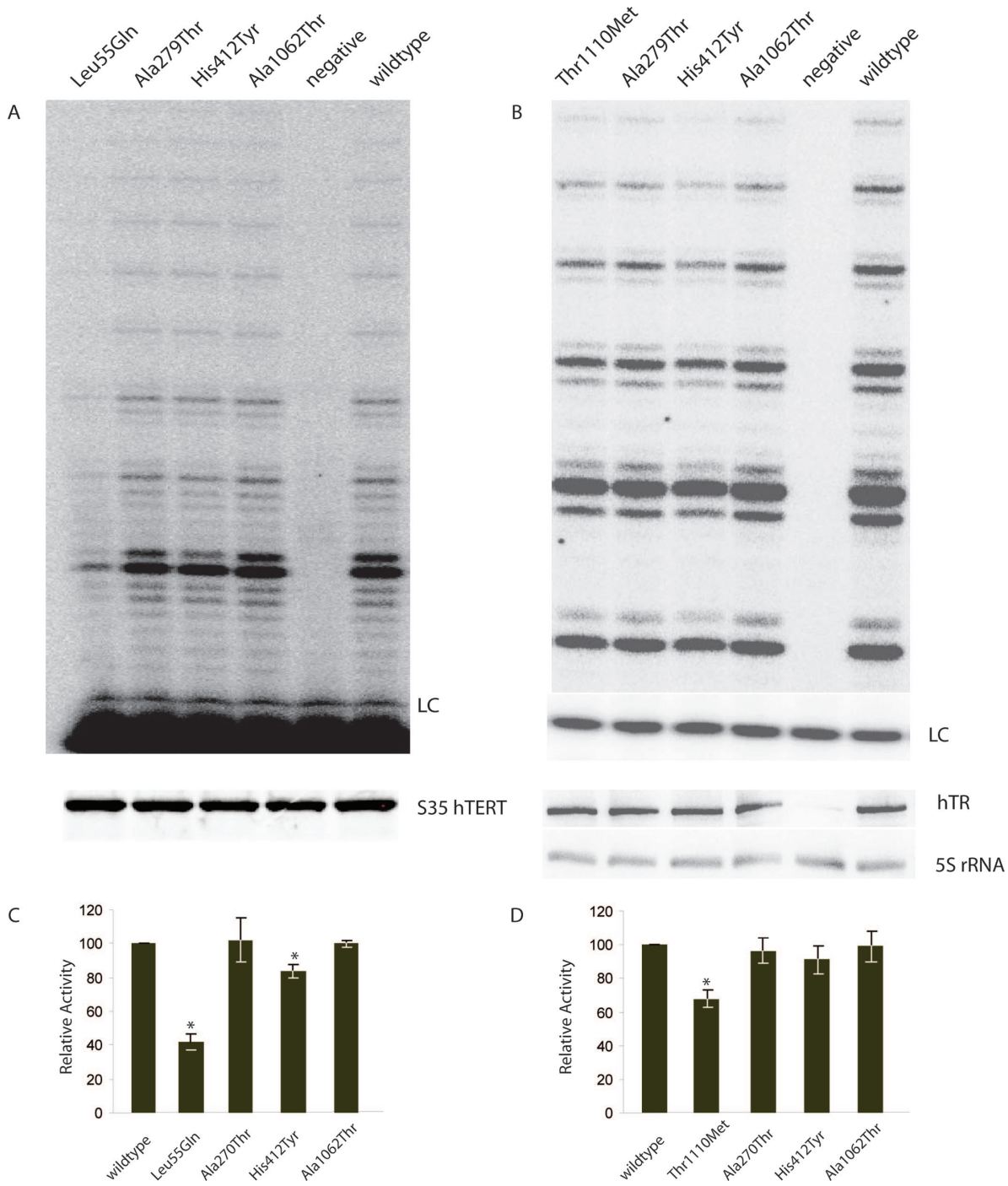

Fig. S1. Telomerase activity of non-synonymous hTERT variants identified in sporadic IIP patients and healthy controls. Telomerase activity of hTERT Ala279Thr and Ala1062Thr was intact showing no compromise as quantitated by the direct assay both *in vitro* (*A*) and after reconstitution in 293FT cells (*B*) ($P = 0.892$ and 0.990 respectively, *in vitro*). In contrast, hTERT Leu55Gln and Thr1110Met identified in IPF families show decreased activity as previously described (5). The His412Tyr allele showed a modest decrease in catalytic activity *in vitro* (mean 84% of wild type, $P = 0.002$, two-sample *t*-test) but not *in vivo* (mean 91% of wildtype, $P = 0.359$). Quantitation of the *in vitro* assays is shown in *C* and of assays performed in cells in *D*. The His412Tyr allele did not have a 3 processivity defect. LC identifies the loading controls and * refers to statistically significant *P*-values (all <0.01).

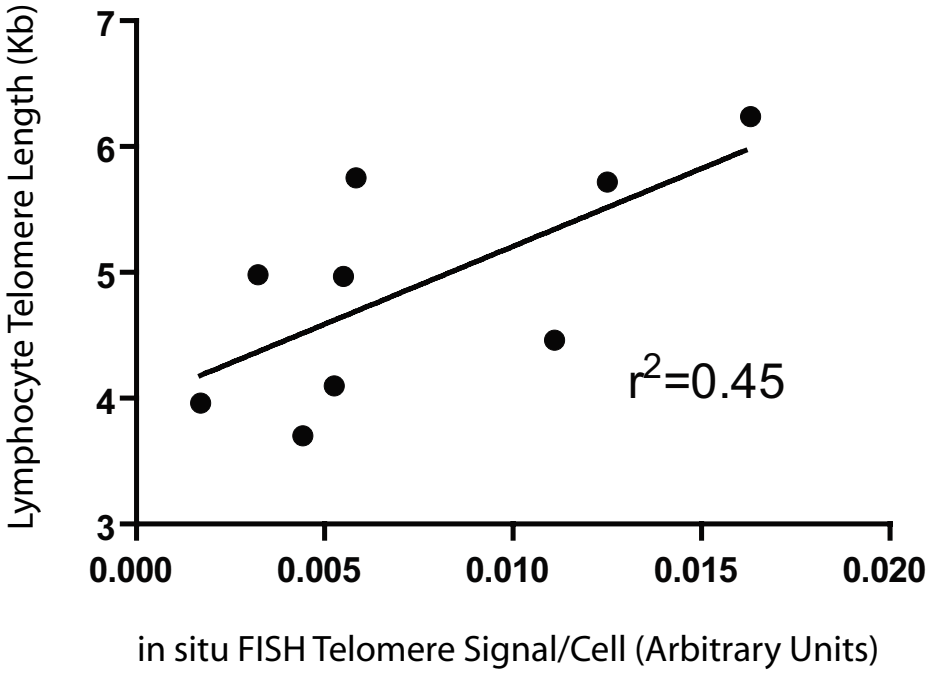

Fig. S2. Correlation between alveolar telomere length quantitated from archived tissues in surfactant protein C positive cells and lymphocyte telomere length as measured by flow-FISH. A positive correlation can be seen in this dataset of nine IPF patients (Pearson's correlation coefficient = 0.67, $r^2 = 0.45$: $P = 0.047$).

Table S1. Patient characteristics

	Number
Total IIP	100
Telomere length studies	62
Age (years)	
Median	64
Range	35–80
Sex	
Male	68
Female	32
IPF	84
IIP other than IPF	16
Lung biopsy	60
Smoking history	
Never	28
Less than 15 pack-years	18
15–50 pack years	29
≥50 pack-years	13
Unknown	12
Race	
Caucasian	97
Platelet count available ($n = 85$)	
Mean platelet count/mm^3	248
Platelet count < 150/mm^3	10%

Table S2. *hTERT* variants identified in sporadic IIP patients

Location	Variation	3′ flanking sequence	Minor allele frequency (n = 200)	Previous report*
Exon 2	c.835 G→A (Ala279Thr)†	CCGAAGAAGC	0.04	0.02**
	c.915 G→A (Ala305Ala)	GGCCCCCCAT	0.24	rs2736098
	c.1234 C→T (His412Tyr)†	ACTGCCCGCT	0.01	rs34094720
Intron 2	IVS2 + 39 G→C	CTGAATGCAG	0.03	
	IVS2–166 G→A	CCAGGCCCTT	0.01	
Intron 3	IVS 3 + 130 C→T	GTCACAGGCC	0.29	rs7725218
	IVS3 + 137 G→A	GCCTGGTCCA	0.01	rs34301490
Intron 4	IVS4 + 10C→T	TTTGGTTTAA	0.01	rs33948291
	IVS4 + 15 G→A	TTTAACTTCC	0.01	rs35695689
	IVS4 + 78 G→A	GGCCCGGAGG	0.01	
	IVS4 + 140 C→T	GCACRGTGAG	0.01	
	IVS4 + 145 A→G	GTGAGGTGGC	0.34	rs7734992
	IVS4 + 245 C→T	GGGCCRGGGC	0.19	rs2242652
	IVS4 + 309 C→G	CTCCGTGCGC	0.31	rs10054203
	IVS4 + 483 G→A	TGGCATGAGG	0.23	rs10069690
	IVS4 + 572 G→A	GGTCTGGGTG	0.01	rs35247701
	IVS4 + 646 C→T	GGATCCACTT	0.01	rs28428579
Exon 5	c.2031 C→T (Gly677Gly)	GCCTCTGTGC	0.01	rs33956095
	c.2097 C→T (Ala699Ala)	CAGGACCCGC	0.02	rs33963617
Intron 5	IVS5 + 182 A→C	TGGGGCCGAC	0.04	rs35241335
	IVS5 + 414 G→A	CCAGGCCAGG	0.01	
Intron 6	IVS6–162 C→T	GRCCCCCGTT	0.01	
Exon 7	c.2328 C→T (Phe776Phe)	GTGGCTCACC	0.01	
Intron 11	IVS11 + 65 T→C	GCGTCCACCT	0.01	
Intron 12	IVS12 + 50 C→T	GCAAGTATGT	0.01	
	IVS12 + 59 TG8→TG9	CRCGCGTGCC	0.04	
	IVS12 + 75 G→A	CGCGTGCCTG	0.04	
Intron13	IVS13 + 137 C→A	CTGTGCACAG	0.02	
	IVS13–96 G→A	TGCACGCACA	0.01	rs35083412
Exon 14	c.3039 C→T (His1013His)	GCATGTGTGC	0.11	rs33954691
	c.3105 C→T (Val1035Val)	ATCTCTGACA	0.01	
Intron14	IVS14 + 3 A→G	TGTGCAGGTG	0.01	
Exon 15	c.3184 G→A (Ala1062Thr)†	CCGGCCCTST	0.03	rs35719940,0.01**
Intron15	IVS15 + 111 C→T	CTGACCCTGG	0.01	
Exon 16	c.3324 G→A (Pro1108Pro)	GGGACGACGC	0.04	rs35033501
3′UTR	C*99 C→T	GCACCGCTGGG	0.22	rs2853690
	C*154 G→C	GCTGAAGGCT	0.01	

* rs identifiers refer to dbSNP cluster ID; v.129.

**Allele frequency in 528 controls as reported in Yamaguchi H, *et al.* (2005) Mutations in TERT, the gene for telomerase reverse transcriptase, in aplastic anemia. *N Engl J Med* 352:1413–1424.

†The functional significance of these nonsynonymous variants was examined in the telomerase activity assays shown in Fig. S1.