

## Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

Supplement to: Armanios MY, Chen JJ-L, Cogan JD, et al. Telomerase mutations in families with idiopathic pulmonary fibrosis. *N Engl J Med* 2007;356:1317-26.

**Supplementary Table 1.** Clinical Features of Relatives of Probands with Telomerase Mutations

<b>Pedigree ID</b>	<b>Gender</b>	<b>Age at diagnosis (death)</b>	<b>Method of Diagnosis</b>	<b>Clinical Impression</b>
All.4	M	61 (d.63)	Family history, Autopsy	UIP/IPF
BIII.1	F	52 (d.63)	Records, CXR, CT, Biopsy	IIP not classifiable
BIII.2	M	64 (d.67)	Records, CXR, CT, Biopsy	UIP/IPF
CII.1	M	67 (d. 68)	Family history	Probable IPF
CII.5	F	58 (d.61)	Records, CXR, CT	IPF
DII.1	M	50 (d.56)	Family history, Death certificate	IPF
EI.2	F	61 (d.64)	Family history, Death certificate	IPF
FI.2	F	(d.69)	Family history	Possible IPF
FII.3	F	(d.70)	Family history	Possible IPF
FII.7	F	62 (d.63)	Records, CXR, Transbronchial biopsy	IPF
FII.9	F	54 (d.57)	Family history	Possible IPF
FII.11	M	(d.60)	Records, CXR, Death certificate	IIP not classifiable
FIII.2	M	(d.72)	Family history	Possible IPF

Abbreviations UIP: usual interstitial pneumonia, IIP: idiopathic interstitial pneumonia

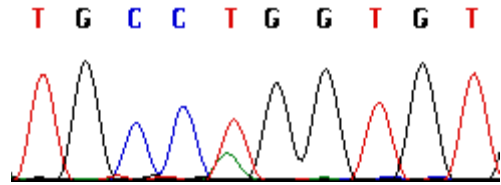
**Supplementary Table 2**  
**hTERT Amplifying and Sequencing Primers**

<b>Exon</b>	<b>Forward Primer</b>	<b>Sequence</b>	<b>Reverse Primer</b>	<b>Sequence</b>
1	TERT1F	gagtttcagggcagcgctgcgctc	TERT1sR	caggtgaaccagcagctcgtcgc
2	TERTsF	caacacggtgaccgacgcactg	TERT1R	ctgtgcgctgaggagtagag
2	TERT2F	caggacgctggaccgagtgacc	TERT2R	gtgaacctcgtaagttatgc
3	TERT3F	cttggtgagctggatgtgcggtg	TERT3R	gagcctgcacagaatccacttg
4-5	TERT4F	gcctcctgaggggctctctattg	TERT5R	ctccaaggtccagcagggctgc
6	TERT6F	gccggatccacttctgactgt	TERT6R	cacagacacgactgcattctagac
7	TERT7F	gtctgatgtgtggtagctgcag	TERT7R	caacagtctgtccggatcatgag
8	TERT8F	gtggtcctgcctgtctcagcacc	TERT8R	gcttgccattccaggcctcgtg
9	TERT9F	ggctgaatggtagacgtgtcg	TERT9R	gagcagtcattggtctccagagc
10	TERT10F	gcacagaattgcacaagctgatg	TERT10R	ctgctctgaggatccagcacc
11	TERT11F	gcatcctggggctgacattgcc	TERT11R	cagccggggcacaggctccact
12	TERT12F	gtccatggagtgagcaccagc	TERT12R	cagtcaccatcagccttgag
13	TERT13F	gatgacacagagtctgactcgc	TERT13R	cggaacagaactgtgcacag
14	TERT14F	cacaccacagagcaccgtctg	TERT14R	acagggcgtcaaggatgacc
15	TERT15F	tgtgactcctcagcctctgtt	TERT15R	cagcagcatctgaggctgctcg
16	TERT16F	gccgctccagcgtcactg	TERT16R	agtgcacattaggattca

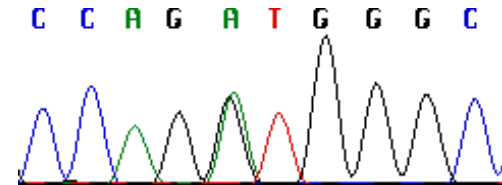
## Supplementary Figure 1

Chromatograms of Telomerase Mutations in Probands from Families A-F

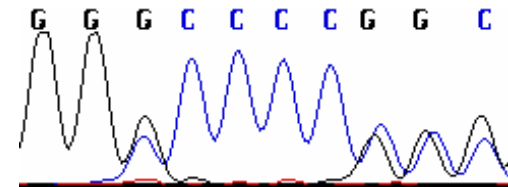
**All.1 *hTERT* Exon 1 CTG→CAG Leu55Gln**



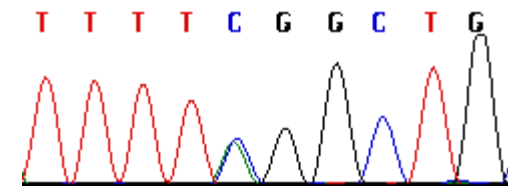
**BIII.5 *hTERT* IVS 1+1 G→A**



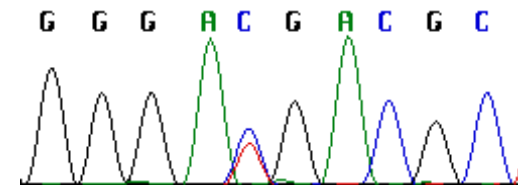
**CII.7 *hTERT* Exon 2 del C codon 112**



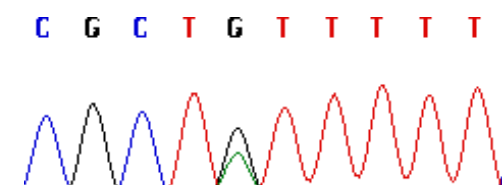
**DIII.2 *hTERT* IVS 9-2 A→C**



**EII.2 *hTERT* Exon 16 ACG→ATG Thr1110Met**



**FIII.5 *hTR* 98 G→A**



**Supplementary Table 3**  
**Sequence Variants in *hTERT* Identified in IPF Probands**

Location	Variant	3' flanking sequence	Minor Allele Frequency (per n=73)	Previous Report*
Exon 2	c.835 G→A (Ala279Thr)	CCGAAGAAGC	0.03	0.02**
	c.915 G→A (Ala305Ala)	GGCCCCCAT	0.47	rs2736098
	c.1269 C→T (Ala423Ala)	GGTGTCTGTG	0.01	
Intron 2	IVS2+39 G→C	CTGAATGCAG	0.07	
Intron 3	IVS 3+130 C→A	GTCACAGGCC	0.50	rs7725218
	IVS3+137 G→A	GCCTGGTCCA	0.01	
Exon 4	c.1812 A→G (Ala604Ala)	GAGGTCAGGC	0.03	
Intron 4	IVS4+10C→T	TTTGGTTTAA	0.01	
	IVS4+145 A→G	GTGAGGTGGC	0.42	rs7734992
	IVS4+245 C→T	GGGCCRGGGC	0.26	rs2242652
	IVS4+309 C→G	CTCCGTGCGC	0.38	rs10054203
	IVS4+483 G→A	TGGCATGAGG	0.29	rs10069690
	IVS4+572 G→A	GGTCTGGGTG	0.01	
Exon 5	c.2031 C→T (Gly677Gly)	GCCTCTGTGC	0.01	
	Ala699Ala C→T	GCCGCTGTAC	0.03	
	c.2106 G→A (Pro702Pro)	CCGCCTGAGC	0.01	
Intron 5	IVS5+182 A→C	TGGGGCCGAC	0.10	
Intron 6	IVS6-160 G→A	CCCCCGTTTC	0.03	
	IVS6-156-155 ins GGCCCCC2→GGCCCCC3	GTTTCCCAA	0.01	
Intron 9	IVS9-121 C>T	GCTTTGGAGA	0.01	
Intron 12	IVS12+25-27 +AG→AG	GTTCAGAGTT	0.01	
	IVS12+59 TG8→TG9	CRCGCGTGCC	0.01	
	IVS12+75 G→A	CGCGTGCCTG	0.04	
Intron13	IVS13+46 C→T	GCGCTCTGCT	0.01	
	IVS13+137 C→A	CTGTGCACAG	0.12	
Exon 14	c.3039 C→T (His1013His)	GCATGTGTGC	0.14	
Intron14	IVS14-94 C→T	CCCGCAGACC	0.01	
Exon 15	c.3184 G→A (Ala1062Thr)	CCGGCCCTST	0.07	0.01**
	c.3193 C→G (Leu1065Leu)	TGCCCTCCGA	0.01	
Intron15	IVS15+101 C→T	GCCCCCGGGC	0.01	
Exon 16	c.3324 G→A (Pro1108Pro)	GGAAGCTCCC	0.05	
3'UTR	C*99 C→T	GCACCGCTGGG	0.49	rs2853690

\* rs identifiers refer to base pair changes cataloged in dbSNP v.126, released 2006.

\*\* Allele frequency in 528 controls reported in Yamaguchi et al *NEJM* 2005.

## **Author Contributions**

Dr. Armanios conceived of the idea, designed the study, performed some of the sequencing, analyzed the data and wrote the paper. Mr. Alder performed the RT-PCR. Ms. Ingersoll analyzed and interpreted the bulk of the sequencing data. Dr. Greider participated in the data interpretation and the writing of the paper. Dr. Chen designed and analyzed the telomerase biochemical studies performed by Mr. Xie. Dr. Lansdorp designed and analyzed the flow-fish studies performed by Ms. Vulto. Drs. Phillips and Loyd established the registry. Drs. Cogan and Phillips oversaw the patient sample selection and processing. Dr. Loyd assessed the families, obtained and analyzed the clinical data. Dr. Lawson reviewed the clinical histories in detail. Ms. Markin was the study coordinator. Drs. Armanios, Greider and Loyd decided to publish the paper. All the authors reviewed the paper and vouch for the data.