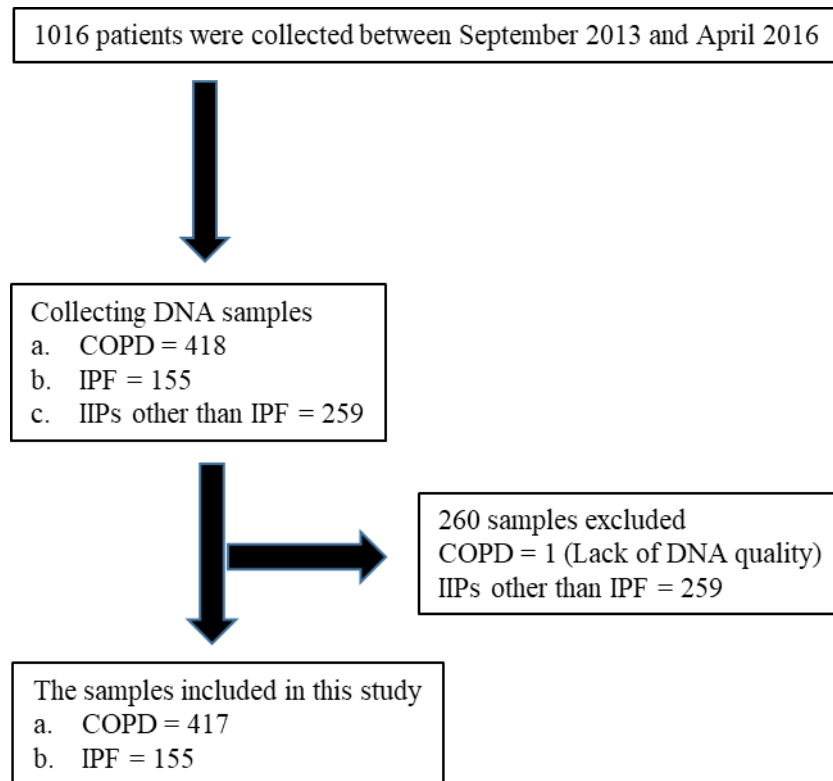


Supplement and Supporting Data (SSD)

SSD 1. Flow diagram of study samples



SSD 2. The distributions of selected characteristics among study subjects

	IPF (n = 155)	COPD (n = 417)	Controls (n= 379)
Age (year), median (IQR)	74 (69–78) ***	73 (67–78) ***	58 (48–65)
Male, n (%)	113 (72.9) †††	365 (87.5) ***	283 (74.7)
Ever smoker ^b , n (%)	98 (63.2) ***, †††	403 (96.6) ***	170 (44.8)
Dust exposure, n (%)	24 (15.5)	58 (13.9)	–
Familial history, n (%)			
IIPs	7 (4.5) ††	2 (0.5)	–
COPD	5 (3.2)	16 (3.8)	–
Cancer history, n (%)	22 (14.2)	66 (15.8)	–
Lung cancer, n (%)	5 (3.2)	8 (1.9)	–
Other, n (%)	17 (11.0)	58 (13.9)	–
GERD, n (%)	9 (5.8)	31 (7.4)	–
COPD, n (%)			
Emphysema	–	363 (87.1)	–
Non emphysema	–	54 (12.9)	–
Surgical lung biopsy, n (%)	13 (8.4)	–	–
BMI (kg/m ²), median (IQR)	22.9 (20.9–25.5) ††	21.8 (19.4–24.1)	–
FVC (L), median (IQR)	2.37 (1.8–2.8) †††	2.73 (2.04–3.31) ^a	–
% FVC predicted, median (IQR)	75.6 (64.5–88.9) ††	84.5 (67.5–99.7) ^a	–
FEV _{1.0} (L), median (IQR)	2.06 (1.49–2.32) †††	1.40 (0.91–1.95) ^a	–
% FEV _{1.0} predicted, median (IQR)	82.3 (73.4–91.8) †††	53.9 (39.3–69.1) ^a	–
Tiffeneau Index (FEV ₁ /FVC (L)), median (IQR)	0.85 (0.80–0.90) †††	0.54 (0.41–0.65) ^a	–

COPD, chronic obstructive pulmonary disease; IIPs, idiopathic interstitial pneumonias; IPF, idiopathic pulmonary fibrosis; IQR, interquartile range; GERD, gastro esophageal reflux disease; BMI, body mass index; FEV_{1.0} forced expiratory volume in one second; FVC, forced vital capacity.

^a 3 missing values.

^b Current and former smokers were combined.

As compared with controls (*p < 0.01, **p<0.005, ***p<0.0001).

As compared with COPD patients (†p < 0.01, ††p<0.005, †††p<0.0001).

SSD 3. The allelic frequencies of telomere-related genetic polymorphisms in study subjects

Polymorphism	IPF n (%)	COPD n (%)	Controls n (%)
<i>TERT</i> rs2736100 (T>G)			
TT	82 (52.9)	154 (36.9)	137 (36.2)
TG	57 (36.8)	204 (48.9)	171 (45.1)
GG	16 (10.3)	59 (14.2)	71 (18.7)
MAF	0.287	0.386	0.413
P-value ^a	0.001	0.202	–
HWE ^b	–	–	0.177
<i>TERC</i> rs1881984 (T>C)			
TT	79 (51.0)	188 (45.1)	160 (42.2)
TC	60 (38.7)	190 (45.6)	165 (43.5)
CC	16 (10.3)	39 (9.3)	54 (14.3)
MAF	0.297	0.321	0.360
P-value ^a	0.151	0.099	–
HWE ^b	–	–	0.281
<i>OBFC1</i> rs11191865 (G>A)			
GG	84 (54.2)	170 (40.8)	173 (45.7)
AG	56 (36.1)	189 (45.3)	160 (42.2)
AA	15 (9.7)	58 (13.9)	46 (12.1)
MAF	0.277	0.366	0.332
P-value ^a	0.196	0.366	–
HWE ^b	–	–	0.341

HWE, Hardy-Weinberg equilibrium; MAF, minor allele frequency

^a P for χ^2 test (compared with control subjects)

^b P for Hardy-Weinberg equilibrium test among controls

SSD 4. The association between the combination of telomere-related genetic polymorphisms and the risk of COPD

Presence of "at-risk" genotype			Case/controls	Adjusted OR ^a (95% CI)	P-value	Adjusted OR ^a (95% CI)	P-value	
<i>TERC</i> rs1881984	<i>OBFC1</i> rs11191865	<i>TERT</i> rs2736100						
0	0	0	84/73	1.00 (Reference)		1.00 (Reference)		
1	0	0	75/56	0.82 (0.38–1.74)	0.597	0.78 (0.42–1.45)	0.431	
0	1	0	62/69	0.64 (0.30–1.36)	0.242			
0	0	1	49/43	0.97 (0.42–2.24)	0.937			
1	1	0	42/44	1.01 (0.40–2.56)	0.984	0.81 (0.41–1.62)	0.557	
1	0	1	39/34	0.71 (0.29–1.71)	0.443			
0	1	1	34/34	0.76 (0.30–1.96)	0.573			
1	1	1	32/26	1.34 (0.51–3.55)	0.553	1.34 (0.51–3.54)	0.553	
P _{trend} = 0.771								

95% CI, 95% confidence interval; OR, odds ratio

Based on recessive model.

^a Adjusted for age, sex and smoking status

SSD 5. All of the investigators participating in the Fukuoka Tobacco-Related Lung Disease (FOLD) registry group

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