Supplementary information

Telomere Integrity, Epigenetic Aging, and Genetic Burden Shape Biological Aging Trajectories in Idiopathic Pulmonary Fibrosis

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Supplementary table 1. Literature-based panel of 44 SNPs associated with IPF susceptibility.

SNP	Gene [b]	Locus	Annotation	Reference
rs2736100	*TERT*	5p15		1
rs7725218	*TERT*	5		2
rs4727443		7q22	Intergenic	1
rs7934606	*MUC2*	11p15		2
rs2034650	*IVD*	15q14-15		1
rs1981997	*MAPT*	17q21		1
rs12610495	*DPP9*	19p13		1
rs6793295	*LRRC34*	3q26		1
rs12696304	*LRRC34 /TERC*	3		3
rs9860874	*TERC*	3		2
rs2609255	*FAM13A*	4q22		1
rs2609259	*FAM13A*	4		2
rs11191865	*OBFC1*	10q24		1
rs4387287	*OBFC1*	10		4
rs1278769	*ATP11A*	13q34		1
rs9577395	*ATP11A*	13		2
rs78238620	*KIF15*	3		5
rs2292181	*KIF15*	3		2
rs12699415	*MAD1L1*	7		6
rs12537430	*MAD1L1*	7		2
rs28513081	*DEPTOR*	8		5
rs10808505	*DEPTOR*	8		2
rs537322302	*HECTD2*	10		5
rs41308092	*RTEL1*	20		2
rs2076295	*DSP*	6		2
rs2897075	*ZKSCAN1*	7		2
rs79684490		10q25.1	Intergenic	2
rs35705950	*MUC5B*	11p15.5		7
rs2304645	*IVD*	15		2
rs12912339	*KNL1*	15		2
rs11073517	*AKAP13*	15		2
rs62025270	*AKAP13/KLHL25*	15		8
rs74614704	*NPRL3*	16		2
rs2077551	*MAPT*	17		2
rs112087793	*STMN3*	20		2
rs111521887	*TOLLIP*	11p15.5		9
rs5743894	*TOLLIP*	11p15.5		2
rs5743890	*TOLLIP*	11p15.5		2
rs7144383	*MDGA2*	14q21.3		9
rs17690703	*SPPL2C*	17q21.31		9

rs184498750	*SUCLG1*	2		10
rs60514164	*UBE2Q2*	15		10
rs35647788	*PCSK6*	15		10
rs3893252	*DAZAP1*	19		10

[b] Name of gene if SNP falls in body of gene

Supplementary Table 2. Multiple regression analysis: the influence of independent variables at T0 as BMI (Kg/m^2), gender, pack-years ((cigarettes/20)xyears), age, FVC, FVC percent of the predicted value (FVC%pred), leucocytes (x10^3/ml), neutrophils (x10^3/ml), lymphocytes (x10^3/ml) and monocytes (x10^3/ml), on the dependent variable LTL.

Variables	B	R	t	p
BMI	b1=-0.001	r=-0.016	t=-0.140	P=0.889
Gender	b2=-0.063	r=-0.040	t=-0.355	P=0.723
Pack Years	b3=0.001	r=0.067	t=0.597	P=0.552
Age	b4=-0.005	r=-0.106	t=-0.945	P=0.347
FVC	b5=0.066	r=0.063	t=0.559	P=0.577
FVC%pred	b6=0.001	r=0.021	t=0.185	P=0.854
Leucocytes (x10^3/ml)	b7=0.0003	r=0.099	t=0.881	P=0.381
Neutrophils (x10^3/ml)	b8=0.034	r=0.132	t=1.181	P=0.241
Lymphocytes (x10^3/ml)	b9=-0.040	r=-0.081	t=-0.721	P=0.473
Monocytes (x10^3/ml)	b10=-0.077	r=-0.040	t=-0.357	P=0.722

Acronyms: BMI=body mass index; **FVC**= forced vital capacity**; FVC(%pred)**= forced vital capacity (percentage of the predicted normal value).

Supplementary Table 3. Identification and selection by literature analysis of n=17 genetic variants included in the GSA associated with IPF disease. The following were identified in the GSA and were further selected. The table shows the rs ID of the n=17 rs identified, the risk allele according to the analyzed literature, as well as the non-effect allele, and the literature reference.

rsID	Risk allele	Non-effect allele	Reference
rs11191865	A	G	1
rs12610495	G	A	1
rs1278769	G	A	1
rs1981997	G	A	1
rs2034650	A	G	1
rs2076295	G	T	1
rs2609255	G	T	1
rs2736100	A	C	1
rs35705950	T	G	7
rs4387287	A	C	4
rs4727443	C	A	1
rs5743890	T	C	1
rs5743894	C	T	1
rs6793295	C	T	1
rs7725218	G	A	2
rs7934606	C	T	1
rs3893252	T	C	10

Supplementary Table 4. Baseline characteristics of IPF patients and healthy controls.

	IPF Patients	**Controls**
Number of subjects	101	23
Chronological age, years *Mean ± SD*	69.0 ± 9.00	70.0 ± 11.5
Sex (Male), n (%)	84 (83%)	12 (52%)
LTL (T/S ratio, 2018) *Mean ± SD*	1.27 ± 0.34*	1.61 ± 0.61*

* Mann Whitney Test p=0.0177

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