

Chitinase1 Regulates Pulmonary Fibrosis by Modulating TGF- β /SMAD7 Pathway via TGFBRAP1 and FOXO3

Chang-Min Lee¹, Jin Wook Park¹, Jae Hyun Lee², Emily Chen¹, Suchita Kamle¹, Bing Ma¹, Bedia Akosman¹, Roberto Cotez¹, Chuan-Hua He¹, Yang Zhou¹, Erica L. Herzog³, Changwan Ryu², Xueyan Peng², Ivan O. Rosas⁴, Sergio Poli⁴, Carol Feghali Bostwick⁵, Augustine M. Choi⁶, Jack A. Elias^{1,7,*}, and Chun Geun Lee^{1,*}

List of Supplementary Materials

Table S1. CHIT1 interacting proteins detected by Yeast-2 Hybrid analysis

Table S2. Demographic feature of IPF patients and controls used in this study

Table S3. Baseline demographics of a patient cohort and controls used to isolate AEC type 1 and type 2 cells

Table S4. Demographic feature of SSc patients and controls used in this study

Fig. S1. FOXO3 siRNA silencing efficacy on NHLF cells.

Fig. S2. Generation of deletion mutant of FOXO consensus sequence.

Fig. S3. Expression levels of CHIT1 and Smad7 in the lung epithelial cells from the patients with IPF and controls.

Fig. S4. Intracellular localization of Chit1 expression in the bleomycin-stimulated lung.

Supplementary Tables

Table S1: Chit1 interacting proteins detected by Yeast Two Hybrid analysis.

Bait	Potential interacting proteins
CHIT1	SNAP-associated protein (SNAPIN)
	Ferritin Light Polypeptide (FTL)
	Forkhead Box O3 (FOXO3)
	Transforming Growth Factor beta Receptor Associated Protein 1 (TGFBRAP1)
	Zyxin (ZYG)
	Mitogen-Activated Protein Kinase Kinase 2 (MAP2K2)

Table S2. Baseline demographics IPF and controls used in this study.

	IPF	Control
<i>N</i>	17	19
<i>Sex:</i>		
Male	9	14
Female	8	4
<i>Age:</i>		
Mean±SD	65.54±5.5	43.05±14
<i>Race</i>		
<i>Ethnicity:</i>		
Caucasian	17	19
<i>Smoking:</i>		
Never	9	14
Ever	8	4
<i>Spirometry (Mean±SD):</i>		N/A
FEV1(%)	52.94±11.5	
FVC(%)	47.47±12.4	
FEV1/FVC	87.8±6	
TLC (%)	50.53±12.4	
IC(%)	41±10.5	
FRC(%)	59.2±18	
RV (%)	54±27	
<i>DLCO(%)</i>	29±7.5	N/A
<i>Cardiac Catheterization</i>		N/A
<i>(Mean±SD):</i>		
PAP	25.4±8.3	
PCWP	9.76±3.01	
Mean RA	5.5±2.52	
CO(l/m)	5.97±0.8	

N/A, not available

Table S3. Baseline demographics of patient cohort that was used to isolate AEC type 1 and type 2 isolated cells.

	IPF	Control
<i>N</i>	10	10
<i>Sex:</i>		
Male	8	9
Female	2	1
<i>Age:</i>		
Mean	64.5	44.5
<i>Ethnicity:</i>		
Caucasian	10	10
<i>Smoking:</i>		
Never	4	8
Ever	6	2
<i>Spirometry (Mean):</i>		
FVC	47	N/A
FEV1/FVC	109	
TLC	45.3	
FRC	50.1	
<i>DLCO adjusted:</i>		
Mean	26.8	N/A
<i>Cardiac Catheterization (Means):</i>		
PAP	25.6	N/A
PCWP	10.7	

N/A, not available

Table S4: Demographic feature of scleroderma (SSc) patients used in this study.

	Chit1 activity (above median)	p-value
<i>N</i>	28	
Sex: n(%)		0.7516
Male	7(17.65)	
Female	21(82.35)	
<i>Age_at_Blood_Draw:</i>		0.002519
Mean \pm SD	58.99 \pm 10.09	
<i>Ethnicity: n(%)</i>		0.4257
Caucasian	21(75.00)	
African American	5(17.86)	
Asian	0(0)	
Latino	2(7.14)	
<i>Smoking: n(%)</i>		0.0002253
Never	14(14.28)	
Ever	14(50.00)	
Missing	10(35.72)	
<i>FVC predicted:</i>		0.3865
Mean \pm SD	69.07692 \pm 16.23311	
<i>DLCO adjusted:</i>		0.4155
Mean \pm SD	54.26316 \pm 16.82869	
<i>SSc type: n(%)</i>		0.8363
Diffuse	14(50.00)	
Limited	12(42.86)	
Sine	2(7.14)	
<i>MRSS at entry:</i>		0.68
Mean \pm SD	10.11 \pm 6.06	
<i>GERD (0= no, 1=yes): n(%)</i>		0.7366
Absent	5(17.86)	
Present	23(82.14)	
<i>ScI70</i>		0.64
Negative	12 (42.8)	
Positive	16 (57.2)	