

**Supplementary Table 1.** Levels of pentraxin 3 (PTX3) and fibroblast growth factor-2 (FGF2) in systemic sclerosis (SSc) patients grouped by the presence or absence of each organ involvement

		PTX3			FGF2		
		Mean ± SD (ng/mL)	High <sup>1</sup>	Low <sup>1</sup>	Mean ± SD (pg/mL)	High <sup>1</sup>	Low <sup>1</sup>
DU	Presence	9.4 ± 4.3	16	1	14.6 ± 9.4	10	7
	Absence	4.3 ± 2.8	70	84	11.7 ± 9.4	76	78
<i>P</i>		<0.001	<0.001		0.13	0.6	
ILD	Presence	5.0 ± 3.2	44	39	12.1 ± 9.6	42	41
	Absence	4.6 ± 3.4	42	46	11.9 ± 9.3	44	44
<i>P</i>		0.3	0.5		0.9	1.0	
ILD extensive stage	Presence	4.7 ± 2.6	15	14	11.7 ± 8.2	15	14
	Absence	4.8 ± 3.5	71	71	12.1 ± 9.6	71	71
<i>P</i>		0.4	1.0		0.9	1.0	
PAH	Presence	6.8 ± 4.6	15	6	8.1 ± 12.3	3	18
	Absence	4.5 ± 3.0	71	79	12.5 ± 8.9	83	67
<i>P</i>		0.006	0.06		<0.001	<0.001	
Heart involvement	Presence	6.3 ± 4.1	8	3	13.2 ± 10.9	6	5
	Absence	4.7 ± 3.2	78	82	11.9 ± 9.3	80	80
<i>P</i>		0.08	0.2		0.9	1.0	
Upper GI involvement	Presence	5.2 ± 3.5	52	40	13.2 ± 9.9	54	38
	Absence	4.3 ± 3.0	34	45	10.6 ± 8.6	32	47
<i>P</i>		0.07	0.09		0.09	0.02	
Lower GI involvement	Presence	4.4 ± 2.0	5	3	15.1 ± 5.6	7	1
	Absence	4.8 ± 3.4	81	82	11.9 ± 9.5	79	84
<i>P</i>		0.8	0.7		0.09	0.06	
Renal involvement	Presence	4.6 ± 1.5	1	1	6.4 ± 4.8	1	1
	Absence	4.8 ± 3.3	85	84	12.1 ± 9.4	85	84
<i>P</i>		0.6	1.0		0.4	1.0	

<sup>1</sup>Cut-off levels for PTX3 and FGF2 were 3.88 ng/mL and 9.82 pg/mL, respectively.

DU: digital ulcer, ILD: interstitial lung disease, PAH: pulmonary arterial hypertension, GI: gastrointestinal

**Supplementary Table 2.** Multivariate analysis for identifying independent factors affecting the presence of DU

Variables	Univariate		Multivariate (Model #1)		Multivariate (Model #2)	
	P	OR (95% CI)	P	OR (95% CI)	P	OR (95% CI)
Female	0.7	1.60 (0.20-13.0)				
Age at SSc onset	0.3	0.98 (0.95-1.02)				
Age at entry	0.9	1.00 (0.96-1.04)				
Disease duration from the first non-RP symptoms	0.07	1.06 (0.99-1.13)	0.8	0.99 (0.90-1.09)	0.7	0.98 (0.90-1.07)
Disease duration from the first RP	0.10	1.04 (0.99-1.09)				
dcSSc	0.04	2.90 (1.05-8.10)	0.3	0.33 (0.04-2.45)	0.3	0.37 (0.06-2.28)
RP	1.0	ND <sup>1</sup>				
Previous history of DU	<0.001	35.2 (9.95-124)	<0.001	61.7 (7.09-537)	<0.001	45.6 (8.16-254)
Organ involvement:						
ILD	0.7	1.22 (0.45-3.32)				
ILD, extensive stage	0.6	0.63 (0.14-2.90)				
PAH	0.9	0.95 (0.20-4.47)				
Heart involvement	0.4	2.15 (0.42-10.9)				
Upper GI	0.02	4.55 (1.26-16.5)	0.4	2.46 (0.38-16.0)	0.15	3.30 (0.64-17.0)
Lower GI	0.8	1.31 (0.15-11.4)				
Renal involvement	1.0	ND <sup>1</sup>				
Autoantibodies						
Anticentromere	0.3	1.76 (0.65-4.82)				
Anti-topo I	0.06	2.71 (0.98-7.52)	0.04	8.01 (1.13-57.1)	0.09	4.29 (0.82-22.6)
Anti-U1RNP	1.0	ND <sup>1</sup>				
Anti-Th/To	1.0	ND <sup>1</sup>				
Anti-RNAP III	0.7	1.54 (0.17-13.7)				
Anti-U3 RNP	1.0	ND <sup>1</sup>				
Anti-Ku	1.0	ND <sup>1</sup>				

Corticosteroids	0.6	1.44 (0.38-5.44)				
PTX3		<0.001	1.50 (1.22-1.85)	-	-	-
FGF2		0.3	0.96 (0.90-1.03)	-	-	-
PTX3/FGF2 ratio		-	-	0.04	1.001 (1.000-1.002)	

Model #1 adopted PTX3 and FGF2 as variables, whereas model #2 adopted PTX3/FGF2 ratio instead.

<sup>1</sup>OR was unable to calculate because one of 4 columns in the 2 x 2 table was “0”.

OR: odds ratio, CI: confidence interval, ND: not determined, RP: Raynaud's phenomenon, dcSSc: diffuse cutaneous SSc, DU: digital ulcer, ILD: interstitial lung disease, PAH: pulmonary arterial hypertension, GI: gastrointestinal, topo I: topoisomerase I, RNAP: RNA polymerase

**Supplementary Table 3.** Multivariate analysis for identifying independent factors affecting the presence of PAH

Variables	Univariate		Multivariate (Model #1)		Multivariate (Model #2)	
	P	OR (95% CI)	P	OR (95% CI)	P	OR (95% CI)
Female	1.0	ND <sup>1</sup>				
Age at SSc onset	0.3	1.02 (0.98-1.06)				
Age at entry	0.10	1.03 (0.99-1.08)				
Disease duration from the first non-RP symptoms	0.3	1.03 (0.97-1.10)				
Disease duration from the first RP	0.11	1.04 (0.99-1.08)	0.4	1.02 (0.98-1.08)	0.6	1.01 (0.96-1.07)
lcSSc	0.2	2.26 (0.63-8.07)	0.7	1.44 (0.27-7.76)	0.6	1.59 (0.26-9.67)
RP	0.7	0.69 (0.08-6.21)				
Previous history of DU	1.0	ND <sup>1</sup>				
Organ involvement:						
DU	0.9	0.95 (0.20-4.47)				
ILD	0.7	1.19 (0.48-2.97)				
ILD, extensive stage	0.8	1.18 (0.37-3.79)				
Heart involvement	1.0	ND <sup>1</sup>				
Upper GI	1.0	ND <sup>1</sup>				
Lower GI	1.0	ND <sup>1</sup>				
Renal involvement	1.0	ND <sup>1</sup>				
Autoantibodies						
Anticentromere	0.2	1.75 (0.70-4.37)				
Anti-topo I	0.07	0.25 (0.06-1.14)	0.3	0.37 (0.06-2.24)	0.3	0.37 (0.06-2.37)
Anti-U1RNP	0.14	2.21 (0.78-6.29)				
Anti-Th/To	1.0	ND <sup>1</sup>				
Anti-RNAP III	1.0	ND <sup>1</sup>				
Anti-U3 RNP	1.0	ND <sup>1</sup>				
Anti-Ku	1.0	ND <sup>1</sup>				

Corticosteroids	0.2	2.29 (0.75-7.01)				
PTX3		0.002	1.23 (1.08-1.40)	—	—	—
FGF2		0.02	0.92 (0.85-0.99)	—	—	—
PTX3/FGF2 ratio		—	—	<0.001	1.001 (1.001-1.002)	

Model #1 adopted PTX3 and FGF2 as variables, whereas model #2 adopted PTX3/FGF2 ratio instead.

<sup>1</sup>OR was unable to calculate because one of 4 columns in the 2 x 2 table was “0”.

OR: odds ratio, CI: confidence interval, ND: not determined, RP: Raynaud's phenomenon, dcSSc: diffuse cutaneous SSc, DU: digital ulcer, ILD: interstitial lung disease, PAH: pulmonary arterial hypertension, GI: gastrointestinal, topo I: topoisomerase I, RNAP: RNA polymerase

**Supplementary Table 4.** Multivariate analysis for identifying factors predicting future development of DU

Variables	Univariate		Multivariate (Model #1)		Multivariate (Model #2)	
	P	HR (95% CI)	P	HR (95% CI)	P	HR (95% CI)
Female	0.2	0.47 (0.14-1.64)				
Age at SSc onset	0.3	0.98 (0.95-1.01)				
Age at entry	0.7	0.99 (0.96-1.03)				
Disease duration from the first non-RP symptoms	0.16	0.94 (0.87-1.02)	0.3	0.96 (0.88-1.05)	0.4	0.96 (0.89-1.05)
Disease duration from the first RP	0.4	0.97 (0.92-1.03)				
dcSSc	0.02	3.09 (1.22-7.82)	0.2	2.10 (0.62-7.13)	0.16	2.45 (0.71-8.76)
RP	0.6	ND <sup>1</sup>				
Organ involvement:						
ILD	0.7	1.21 (0.48-3.04)				
ILD, extensive stage	0.6	1.35 (0.45-4.11)				
Heart involvement	0.7	1.61 (0.21-12.2)				
Upper GI	0.15	2.15 (0.77-6.05)				
Lower GI	0.4	1.94 (0.44-8.48)				
Renal involvement	0.8	ND <sup>1</sup>				
Autoantibodies						
Anticentromere	0.2	1.82 (0.72-4.58)				
Anti-topo I	0.08	2.32 (0.91-9.89)	0.3	1.84 (0.53-6.32)	0.6	1.41 (0.41-4.80)
Anti-U1RNP	0.13	0.21 (0.03-1.61)				
Anti-Th/To	0.4	ND <sup>1</sup>				
Anti-RNAP III	0.6	1.64 (0.22-12.4)				
Anti-U3 RNP	0.7	ND <sup>1</sup>				
Corticosteroids	0.2	1.99 (0.65-6.07)				
PTX3			0.001	1.25 (1.09-1.42)	—	—
FGF2			0.08	0.95 (0.90-1.01)	—	—

PTX3/FGF2 ratio	—	—	0.003	1.001 (1.000-1.001)
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Model #1 adopted PTX3 and FGF2 as variables, whereas model #2 adopted PTX3/FGF2 ratio instead.

<sup>1</sup>HR was unable to calculate because one of 4 columns in the 2 x 2 table was “0”.

HR: hazard ratio, CI: confidence interval, ND: not determined, RP: Raynaud's phenomenon, dcSSc: diffuse cutaneous SSc, DU: digital ulcer, ILD: interstitial lung disease, PAH: pulmonary arterial hypertension, GI: gastrointestinal, topo I: topoisomerase I, RNAP: RNA polymerase