

## Supplementary tables

**Supp. Table 1. Overall statistical power of the study for each analyzed *TYK2* genetic variant accordingly with global disease.**

Significance level	OR=1.2		OR=1.3		OR=1.4		OR=1.5	
	0.05	5x10 <sup>-8</sup>	0.05	5x10 <sup>-8</sup>	0.05	5x10 <sup>-8</sup>	0.05	5x10 <sup>-8</sup>
<b>rs2304256</b>	<b>1.00</b>	<b>0.98</b>	1.00	1.00	1.00	1.00	1.00	1.00
<b>rs34536443</b>	<b>0.76</b>	<b>0.01</b>	<b>0.97</b>	<b>0.08</b>	1.00	0.42	1.00	0.84
<b>rs35018800</b>	0.34	0.01	0.62	0.01	0.83	0.01	<b>0.94</b>	<b>0.03</b>
<b>rs12720356</b>	<b>0.99</b>	<b>0.24</b>	1.00	0.93	1.00	1.00	1.00	1.00

OR, odds ratio.

**Supp. Table 2. Inverse variance meta-analysis of four *TYK2* SNPs in the validation cohort (4,985 SSc patients and 7,478 controls).**

Chr	SNP	Minor/ Major	Comment	MAF Cases	MAF Controls	Inverse variance test		
						<i>P</i> -value	OR [CI 95%]*	Q
19	rs34536443 (P1104A)	C/G	missense Pro > Ala	0.026	0.029	0.019	0.82 [0.70-0.97]	0.06
19	rs35018800 (A928V)	A/G	missense Ala > Val	0.004	0.008	6.00E-03	0.57 [0.38-0.85]	0.19
19	rs12720356 (I684S)	C/A	missense Ile > Ser	0.068	0.078	9.54E-05	0.81 [0.73-0.90]	0.59
19	rs2304256 (V362F)	A/C	missense Val > Phe	0.250	0.283	2.26E-10	0.82 [0.77-0.87]	0.58

\*Odds ratio for the minor allele.

Chr, chromosome; CI, confidence interval; MAF, minor allele frequency; OR, odds ratio; Q heterogeneity value; SNP, single nucleotide polymorphism; SSc, systemic sclerosis.

**Supp. Table 3. Allelic combination analysis of 4 *TYK2* SNPs in the overall combined cohort.**

<b>Chr</b>	<b>From bp</b>	<b>To bp</b>	<b>Allelic Combination</b>	<b>Frequency</b>	<b>P-value</b>	<b>OR</b>
19	10463118	10475652	GGCA	0.074	1.24E-06	0.81
19	10463118	10475652	GAAA	0.006	1.45E-04	0.54
19	10463118	10475652	CGAA	0.024	6.35E-06	0.70
19	10463118	10475652	GGAA	0.162	0.014	0.93
19	10463118	10475652	GGAC	0.730	5.95E-12	1.19

\*SNP order of the allelic combination: rs34536443, rs35018800, rs12720356 and rs2304256. Minor allele is highlighted in red.

Bp: base-pair ; Chr, chromosome; OR, odds ratio.