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Title: The functional MUC5B rs35705950 promoter polymorphism is associated with IPF but not with systemic sclerosis related interstitial lung disease

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Body: A MUC5B promoter polymorphism has been associated with IPF in the North American population (frequency of T risk allele 35% in IPF patients compared to 10% in controls. The polymorphism of MUC5B has not been investigated in the European population or in non-IPF pulmonary fibrosis. MUC5B was genotyped in the first 168 patients of the French national prospective IPF cohort (COFI), in 870 French patients with systemic sclerosis (SSc) (346 with interstitial lung disease, ILD), in 598 Italian SSc patients (207 with ILD), 1383 French controls and 494 Italian controls. The diagnosis of IPF was based on the 2000 ATS/ERS criteria and centrally reviewed. The T risk allele frequency was strongly increased in the IPF patients compared to the control population: 38.6% vs 10.8%, P = 2x10-44, OR 19 [9-36] for homozygotous patients. No statistical difference of frequency was observed in both SSc and SSc-ILD in the French population: 10% and 11.1%, respectively.

Polymorphism of MUC5B in the French populations

	TT (%)	GT (%)	GG (%)
IPF n=168	11.9	53.5	34.5
SSc n= 981	1.2	17.5	81.2
SSc-ILD+ n= 346	1.4	19.5	79.1
Controls n = 1383	1.4	18.7	79.8

Similar results were observed in the Italian population regarding the T allele frequency in SSc and SSc-ILD when compared to controls: 12% and 13.5%, respectively vs 11.7%. Our study provide for the first time i) an independent replication of an association between MUC5B rs35705950 T risk allele and IPF in the French population ii) a lack of association of MUC5B rs35705950 with SSc-related ILD suggesting a distinct pathogenesis. Supported by chancellerie des Universites de Paris and PHRC Ile de France.