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Title: LSC 2013 abstract - Hypoxia-inducible factor 1 alpha polymorphisms in relation to pulmonary involvement in systemic sclerosis

Harpreet Lota harpreet.lota@hotmail.co.uk [1], Carmel Stock [1], Hiroe Sato [1], Carmen Fonseca [2], Athol Wells [1], Christopher Denton [2], David Abraham [2], Gisela Lindahl [1] and Elisabetta Renzoni [1]. [1] Interstitial Lung Disease Unit, Royal Brompton Hospital, London, United Kingdom and [2] Centre for Rheumatology, Royal Free Hospital, London, United Kingdom .

Body: Introduction: Transcription factor hypoxia-inducible factor 1 (HIF1) upregulates the expression of angiogenic genes including vascular endothelial growth factor. Systemic sclerosis (SSc) is a multisystem disease characterised by organ fibrosis and widespread vasculopathy. We assessed the association of two transcriptionally active, single nucleotide polymorphisms (SNPs) of the hypoxia-inducible factor 1 alpha gene (HIF1A) in SSc. Methods: Using a case-control study design, HIF1A SNPs (rs11549465 C/T, rs12434438 A/G) were genotyped in SSc patients (n=426) and UK controls from the Wellcome Trust Case-Control Consortium (n=5564 and 5659). The SSc cohort was subdivided according to the presence or absence of pulmonary fibrosis (PF) (n=227 v. 199), pulmonary hypertension (PH) on echocardiography (n=17 v. 129) and autoantibody subsets; anti-topoisomerase I antibodies (n=108) and anti-centromere antibodies (n=105). Results: Genotype distribution in all groups conformed to Hardy-Weinberg equilibrium. There were no significant differences in genotype or allele frequencies between SSc and controls (SSc: CC:82.1%, CT:16.7%, TT:1.2% v. controls: CC:81.3%, CT:17.8%, TT:0.9% and SSc: AA:63.9%, AG:32.6%, GG:3.5% v. controls: AA:63.4%, AG:32.5%, GG:4.1%). On subgroup analysis, no significant differences were observed according to PF, autoantibodies, or in the group with available echocardiography (n=146), according to PH. Conclusion: An association was not detected between HIF1A SNPs and SSc. Due to limited power in the PH subgroup, an association with pulmonary vascular involvement cannot be excluded and requires further evaluation and longitudinal analysis.