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Identifying early pulmonary arterial hypertension biomarkers in systemic sclerosis: machine learning on proteomics from the DETECT cohort

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Early screening for pulmonary arterial hypertension in patients with systemic sclerosis improves patient outcome. This study identified a novel eight-protein biomarker panel that has the potential to assist early detection of PAH in this patient group. https://bit.ly/373BNkL

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ABSTRACT Pulmonary arterial hypertension (PAH) is a devastating complication of systemic sclerosis (SSc). Screening for PAH in SSc has increased detection, allowed early treatment for PAH and improved patient outcomes. Blood-based biomarkers that reliably identify SSc patients at risk of PAH, or with early disease, would significantly improve screening, potentially leading to improved survival, and provide novel mechanistic insights into early disease. The main objective of this study was to identify a proteomic biomarker signature that could discriminate SSc patients with and without PAH using a machine learning approach and to validate the findings in an external cohort.

Serum samples from patients with SSc and PAH (n=77) and SSc without pulmonary hypertension (non-PH) (n=80) were randomly selected from the clinical DETECT study and underwent proteomic screening using the Myriad RBM Discovery platform consisting of 313 proteins. Samples from an independent validation SSc cohort (PAH n=22 and non-PH n=22) were obtained from the University of Sheffield (Sheffield, UK).

Random forest analysis identified a novel panel of eight proteins, comprising collagen IV, endostatin, insulin-like growth factor binding protein (IGFBP)-2, IGFBP-7, matrix metallopeptidase-2, neuropilin-1, N-terminal pro-brain natriuretic peptide and RAGE (receptor for advanced glycation end products), that discriminated PAH from non-PH in SSc patients in the DETECT Discovery Cohort (average area under the receiver operating characteristic curve 0.741, 65.1% sensitivity/69.0% specificity), which was reproduced in the Sheffield Confirmatory Cohort (81.1% accuracy, 77.3% sensitivity/86.5% specificity).

This novel eight-protein biomarker panel has the potential to improve early detection of PAH in SSc patients and may provide novel insights into the pathogenesis of PAH in the context of SSc.