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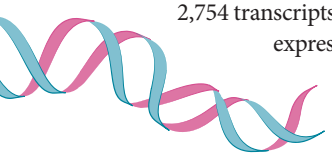
CONNECTIVE TISSUE DISEASES

Skin gene expression profiles in SSc

The pathogenesis of systemic sclerosis (SSc) is poorly understood, which has hampered the development of effective therapeutics for this multisystem autoimmune disease. Skin is one of the organs predominantly affected in SSc. The easy accessibility of skin for biopsies has been taken advantage of in two papers now published in *Arthritis & Rheumatology* investigating skin gene expression profiles in this disease.

Assassi *et al.* examined global transcriptome patterns in a large sample of patients with SSc from the GENISOS cohort ($n = 61$) and healthy controls ($n = 36$). The team used Illumina HT-12 arrays (30.5 K) to identify differentially expressed transcripts. The transcriptomes of most patients with SSc differed from those of controls and were heterogeneous. 2,754 transcripts were differentially expressed in patients with SSc versus controls. Cluster analysis of these transcripts showed the presence of two predominant signatures: a keratin and a fibroinflammatory transcriptome. Increased keratin scores, which were prominent in patients with SSc, were asssociated with shorter duration of disease and interstitial lung disease; higher fibroinflammatory scores were associated with diffuse cutaneous involvement. A subgroup of patients with SSc had transcript patterns resembling those of controls, which were associated with a longer disease duration.



Cell-type-specific signatures were again highly heterogeneous between patients, but genes specifically expressed by fibroblasts, macrophages and dendritic cells predominated. Assassi *et al.* hope in the future that the heterogeneity of SSc skin gene profiles might be useful clinically for patient stratification and for selection of targeted treatments.

Rice *et al.* focused on skin gene expression profiles of patients with diffuse cutaneous SSc. They assessed only the transcripts whose expression correlated with changes in modified Rodnan skin score (MRSS) over time on a nanostring platform and defined two pharmacodynamic biomarkers, one defined mathematically and the other based on weighted selection of genes. Their two skin biomarkers correlated nearly as well as MRSSs with skin fibrosis and inflammation over time. The authors hope, after further validation, that these biomarkers can be used in addition to the MRSS in clinical trials and in patients to assess the extent of skin disease in diffuse cutaneous SSc.

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Original articles Assassi, S. *et al.* Dissecting the heterogeneity of skin gene expression patterns in systemic sclerosis. *Arthritis Rheumatol.* doi:10.1002/art.39289 | Rice, L. M. *et al.* A longitudinal biomarker for the extent of skin disease in patients with diffuse cutaneous systemic sclerosis. *Arthritis Rheumatol.* doi:10.1002/art.39287