Conclusion: Our study reveals potential causal genes for SSC-associated loci, some of them acting in a cell type specific manner, suggesting novel drug targets and biological mechanisms that may mediate SSC pathogenesis.

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IDENTIFICATION AND FUNCTIONAL PREDICTION OF LONG NONCODING RNA RELATED TO CONNECTIVE TISSUE DISEASE-ASSOCIATED INTERSTITIAL LUNG DISEASES

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Background: Recently, the role of long noncoding RNA (IncRNA) in rheumatic immune diseases has attracted widespread attention1. However, knowledge of IncRNA in connective tissue disease-associated interstitial lung disease (CTD-ILD) is limited.

Objectives: To explore the expression profile of IncRNA in peripheral blood mononuclear cells (PBMCs) of CTD-ILD patients and the possible mechanisms of significantly differentially expressed IncRNA involved in CTD-ILD, especially systemic sclerosis (SSc)-ILD and rheumatoid arthritis (RA)-ILD.

Methods: LncRNA microarray analysis was used to identify the pattern of IncRNA dysregulation between CTD-ILD and connective tissue disease without associated interstitial lung disease (CTD-NILD). Differential genes were identified by bioinformatic analysis. Relative expression levels of five differentially expressed IncRNAs in 120 SSc and RA patients with or without ILD were detected by quantitative reverse-transcription PCR (qRT-PCR).

Results: The differential gene expression analysis revealed 46 IncRNAs were upregulated while 194 IncRNAs were downregulated in the CTD-ILD group compared to the CTD-NILD group (Figure 1). Gene Ontology and Kyoto Encyclopedia of Genes and Genomes pathway analyses identified several significant biological processes and signaling pathways, including NF-kappa B signaling pathway, IL-17 signaling pathway, Toll-like receptor signaling pathway, B cell receptor signaling pathway. qRT-PCR confirmed that the selected target genes were differentially expressed in different groups. In particular, the ENST00000604692 expression level was significantly higher in the ILD than the NILD group (p<0.05, Figure 1); T311354 and arginase-1 were significantly higher in the ILD than the NILD group. qRT-PCR showed that ENST00000604692 can effectively distinguish ILD group from NILD group compared to the CTD-NILD group (Figure 1). Gene Ontology and Kyoto Encyclopedia of Genes and Genomes pathway analyses classified the patients based on the following criteria:

• Rapid progressors (N Discovery=288, N Replication=107), subjects with baseline KL grade 0-1 and increase up to KL≥3 during 48-month follow-up; or baseline KL grade 2 and increase up to KL grade 4 during the follow-up.
• Non-rapid progressors (N Discovery=827, N Replication=992), subjects with the same baseline characteristics as rapid progressors, but with a slower or no evolution over time.

mtDNA variants were screened in the OAI by in-depth sequencing. Resulting variant was analyzed in the replication cohort by mini-sequencing techniques. Appropriate statistical approaches adjusting for confounding variables followed by a meta-analysis were applied.

Disclosure of Interests: None declared