SLE, Sjögren's and APS - aetiology, pathogenesis and animal models

Figure 1.

Keywords: Systemic lupus erythematosus, -omics, Sjögren syndrome

Methods: preclinical patients and established SLE and pSS.

Results: Consensus networks were constructed for Preclinical-SLE and Preclinical/pSS to identify fatigue-associated modular signatures which are retained in established CTDs. Gene ontology enrichment was evaluated using g:profiler.

Results: Within the preclinical transcriptomic network 5 module eigengenes showed significant and specific association with patient fatigue VAS. A type-I IFN signature, centred upon canonical ISGs, MX1, IRF7 and IFIT5, was positively correlated with fatigue score (R=0.48, p=0.003) and conserved across preclinical, SLE and pSS networks, with subtly different modular organisation. One further module, enriched for RNA modification was significantly correlated with fatigue in preclinical subjects (R=0.41, p<0.01) but with no counterpart preserved in either SLE or pSS networks.

Association with fatigue (R² = 0.35, p=0.004) in preclinical subjects was enriched for mitogen-activated protein kinase (MAPK) cascades, heat shock and protein folding chaperone activity, and included transcription factors JUN and ATF3. This signature was retained in pSS patients, but did not persist in the SLE consensus network.

Conclusion: We describe novel modular transcriptomic signatures associated with fatigue in the preclinical phase of autoimmunity which demonstrate differential persistence and activity in SLE and pSS. These pathways may help identify individuals with immune-mediated fatigue most amenable to therapy, and could provide insights into new therapeutic targets for fatigue across a range of auto-immune diseases.

REFERENCE:

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