proinflammatory cytokine (TNF-α, IFN-γ, IL-2, GM-CSF, IL-17A, IL-22, IL-4) production was markedly different between ACPA neg and ACPA pos RA patients with hierarchical clustering and PCA analysis revealing endotype specific cytokine profiles with ACPA neg RA patient synovial T cells showing increased TNF-α (P<0.01) expression. RNAseq analysis of RA patient synovial tissue revealed significant disease endotype specific gene signatures with specific enrichment for B cell receptor signalling and T cell specific pathways in ACPA pos compared to ACPA neg RA patients. Additionally, significantly different chemokine receptor expression based on RA patient ACPA status was observed with increased CXCR3 (P<0.001), CCR7 (P=0.002), and CCR2 (P=0.004) but decreased CXCR7 (P=0.007) expression in ACPA pos compared to ACPA neg RA patient synovial biopsies.

Conclusion: ACPA status associates with unique synovial tissue immune cell and gene profile signatures highlighting differences in the underlying immunological mechanisms involved, therefore reinforcing the need for a treat to target approach for both endotypes of RA.

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