Editorial

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T Cell Receptor (TCR) Repertoire Signatures in Autoimmune Diseases: Insights into Pathogenesis and Precision Medicine

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Introduction

T cells are central to adaptive immunity, and their antigen specificity is determined by the T cell receptor (TCR) repertoire. Recent advances in high-throughput sequencing have enabled comprehensive profiling of TCR diversity, providing TCR repertoire signatures that reflect immune status, disease activity, and pathogenic mechanisms in autoimmune diseases such as rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), and multiple sclerosis (MS).

TCR Repertoire and Autoimmune Pathogenesis

The TCR repertoire consists of unique sequences generated through V(D)J recombination, allowing recognition of diverse antigens. In autoimmune diseases, clonal expansion of autoreactive T cells can be detected, indicating antigen-driven immune responses. Reduced TCR diversity and skewed clonotype distributions are associated with chronic inflammation, tissue damage, and disease progression, highlighting their potential as biomarkers for disease activity.

Clinical Applications

TCR repertoire signatures can inform diagnosis, prognosis, and therapeutic decisions. Specific clonotypes or patterns correlate with disease severity, organ involvement, and treatment responsiveness. For example, in RA, expanded TCR clones targeting synovial antigens predict aggressive disease, while in SLE, distinct TCR patterns associate with nephritis risk. Monitoring repertoire changes during therapy provides insights into treatment efficacy and immune reconstitution.

Technological Advances

High-throughput sequencing, single-cell RNA sequencing, and computational bioinformatics enable detailed TCR repertoire analysis. Integration with transcriptomic and proteomic data allows simultaneous assessment of T cell function, phenotype, and antigen specificity. These tools facilitate patient stratification and identification of novel therapeutic targets in autoimmune disorders.

Future Directions

Emerging strategies aim to leverage TCR repertoire signatures for precision medicine. Predictive models combining TCR diversity, clonality, and clinical features may guide early intervention, optimize immunomodulatory therapy, and minimize adverse effects. Additionally, engineering T cells based on TCR specificity could offer novel therapeutic approaches in autoimmune disease.

Conclusion

T cell receptor repertoire signatures provide a window into the adaptive immune landscape in autoimmune diseases. By capturing clonal diversity, specificity, and dynamics, TCR profiling offers critical insights into pathogenesis, disease monitoring, and therapeutic response. Integration of TCR data into clinical practice holds promise for advancing personalized, mechanism-based management of autoimmune disorders.