

Single-Cell Immune Profiling in Autoimmune Disease Progression

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DESCRIPTION

Autoimmune diseases, characterized by the immune system mistakenly attacking the body's own tissues, pose a significant challenge in both diagnosis and treatment. Conditions such as rheumatoid arthritis, systemic lupus erythematosus, and multiple sclerosis exhibit complex, dynamic immune responses that are difficult to fully capture with traditional bulk tissue analyses. Recent advances in single-cell immune profiling have provided unprecedented resolution in understanding the cellular and molecular underpinnings of these diseases. By analyzing individual immune cells rather than averaged populations, researchers can uncover heterogeneity, identify rare pathogenic cell types, and monitor disease progression with far greater precision. This commentary explores the promise of single-cell immune profiling in autoimmune disease research and its implications for personalized medicine.

Unveiling immune heterogeneity single-cell technologies in autoimmunity

A major limitation in conventional immunological studies is the reliance on bulk analyses, which average signals across thousands or millions of cells. While bulk RNA sequencing or flow cytometry can provide valuable information about overall immune activity, they often obscure the contributions of rare but pathogenic cell populations. Single-cell technologies, including Single-Cell RNA Sequencing (scRNA-seq), mass cytometry, have revolutionized our ability to dissect complex immune landscapes at cellular resolution. These approaches enable scientists to profile individual T cells, B cells, dendritic cells, and other immune populations, revealing previously hidden heterogeneity that drives disease pathology.

In autoimmune diseases, immune cell heterogeneity is not just an academic curiosity it has direct clinical relevance. For instance, studies of rheumatoid arthritis synovial tissue using scRNA-seq have uncovered distinct subsets of fibroblasts and macrophages that contribute to inflammation and joint destruction. Similarly, in systemic lupus erythematosus, single-cell profiling of peripheral blood mononuclear cells has identified hyperactive B cell populations that correlate with

disease flares. By linking specific cell subsets to disease activity, researchers can better understand the mechanisms driving autoimmunity and identify novel therapeutic targets.

Another key advantage of single-cell profiling is the ability to study immune cell dynamics over time. Autoimmune diseases often follow a relapsing-remitting course, with periods of quiescence punctuated by flares of inflammation. Longitudinal single-cell analyses allow researchers to track changes in immune cell composition and gene expression as the disease progresses or responds to therapy. This temporal dimension is particularly valuable for identifying early biomarkers of disease flares, understanding treatment resistance, and monitoring patient responses to immunomodulatory therapies.

Moreover, single-cell immune profiling facilitates the discovery of rare pathogenic cells that might otherwise go undetected. These rare cells, such as autoreactive T or B cells, can have outsized effects on disease progression despite their low abundance. By characterizing their transcriptional and epigenetic states, researchers can gain insights into the molecular pathways that drive autoimmunity and potentially develop strategies to selectively target these cells without broadly suppressing the immune system.

Translational implications and personalized therapeutics

The insights gained from single-cell immune profiling have profound implications for precision medicine in autoimmune diseases. By identifying specific immune cell subsets and their molecular signatures, clinicians can tailor therapies to the individual patient, moving beyond the one-size-fits-all approach of conventional immunosuppressive treatments. For example, patients with multiple sclerosis may have distinct T cell or B cell profiles that predict responsiveness to certain monoclonal antibodies or small-molecule inhibitors. Profiling these cells at a single-cell level could help stratify patients for optimal therapeutic interventions, minimizing side effects and improving outcomes.

Single-cell technologies also enable the identification of novel biomarkers for disease progression and prognosis. In autoimmune

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diseases, early detection of pathogenic immune signatures could allow preemptive interventions before irreversible tissue damage occurs. For example, in type 1 diabetes, single-cell profiling of pancreatic islet-infiltrating immune cells has revealed early changes in autoreactive T cells, offering potential biomarkers for predicting disease onset in high-risk individuals. Such predictive capabilities could revolutionize disease management and shift the paradigm from reactive to proactive treatment.

Furthermore, the integration of single-cell immune profiling with other omics approaches, such as proteomics, metabolomics, and spatial transcriptomics, provides a holistic view of autoimmune disease pathology. Spatially resolved single-cell analyses, for instance, can map the physical organization of immune cells within affected tissues, shedding light on cell-cell interactions that drive inflammation. Combining these datasets allows researchers to construct comprehensive models of autoimmune progression, identify key regulatory nodes, and design multi-targeted therapeutic strategies.

CONCLUSION

Single-cell immune profiling has emerged as a transformative tool in the study of autoimmune diseases. By dissecting immune heterogeneity, uncovering rare pathogenic cells, and enabling longitudinal tracking of disease progression, these technologies provide insights that were previously unattainable with conventional approaches. The translational potential is equally significant: single-cell analyses can guide personalized therapeutic strategies, identify early biomarkers of disease activity, and facilitate the development of targeted interventions. While challenges remain in terms of cost, accessibility, and data integration, the continued advancement of single-cell methodologies promises to redefine our understanding and management of autoimmune diseases. Ultimately, these innovations herald a future in which treatment is tailored not only to the disease but to the individual patient's unique immune landscape.