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Personalized immunotherapeutics based on single-cell analysis.

Martin Fury*

Department of Cardiovascular Medicine, Tohoku University Graduate School of Medicine, Japan

Correspondence to: Martin Fury, Department of Cardiovascular Medicine, Tohoku University Graduate School of Medicine, Japan, E-mail: martin@som.umaryland.edu

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Introduction

In the age of precision medicine, immunotherapy has revolutionized treatment strategies for cancer, autoimmune diseases, and infectious conditions. However, variable patient outcomes reveal the need for more tailored approaches. Enter single-cell analysis, a transformative technology that enables unprecedented resolution into the cellular and molecular landscape of the immune system—unlocking personalized immunotherapeutics with enhanced accuracy, efficacy, and safety. Traditional bulk RNA sequencing and proteomics provide average profiles across thousands of cells, obscuring cellular heterogeneity. In contrast, single-cell analysis (including single-cell RNA sequencing [scRNA-seq], ATAC-seq, and CyTOF) identifies cell-specific transcriptional, epigenetic, and surface marker profiles, illuminating: Rare immune cell populations, Cellular states and lineage trajectories, Functional diversity in immune response [1, 2].

This granularity allows clinicians and researchers to interrogate individual cellular behavior, offering a roadmap for truly personalized immunotherapies. Single-cell analysis has provided deep insights into the tumor microenvironment (TME), revealing: Exhausted T-cell populations expressing PD-1, TIM-3, and LAG-3 Immunosuppressive regulatory T cells (Tregs), Myeloid-derived suppressor cells (MDSCs) [3, 4].

Tailoring checkpoint inhibitor therapies—such as anti-PD-1 or CTLA-4—based on these profiles can improve patient outcomes. In CAR-T and TCR-T cell therapies, single-cell analysis enables: Tracking persistence and phenotype of engineered cells, Identifying activation or exhaustion markers, Adjusting construct designs for enhanced efficacy. This has guided enhancements in CAR construct engineering and patient selection strategies. Single-cell platforms are redefining vaccine development, particularly in infectious diseases: scRNA-seq helps identify durable B cell and T cell subsets post-vaccination [5, 6].

Epitope-specific profiling allows creation of customized antigens based on HLA type and prior infection history. In COVID-19, single-cell approaches helped dissect immune memory and disease severity correlations. Personalized therapeutics—such as antigen-specific tolerizing agents—can be designed to modulate only pathogenic cells without broad immunosuppression. Diseases with neuroinflammatory components (e.g., Alzheimer's, Parkinson's) are being explored through cerebrospinal fluid and brain tissue single-cell mapping: Identification of pro-inflammatory microglia subsets, Peripheral immune cell infiltration signatures, Potential targets for immune-based neuroprotective therapies [7, 8].

Advanced analytics and AI-driven models are central to translating single-cell data into actionable therapeutics: Clustering algorithms identify cellular states and dynamics. Predictive models forecast immunotherapy responsiveness. Decision trees guide selection of immunomodulators or biologics based on patient-specific cellular landscapes. Large-scale single-cell datasets require sophisticated bioinformatics pipelines [9, 10].

Conclusion

Initiatives like the Human Cell Atlas and standardized benchmarking projects aim to mitigate these barriers. Miniaturized devices may allow bedside immune profiling. Tracking immune

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changes over time in individuals. Matching therapies to cells rather than diseases. Ultimately, personalized immunotherapeutics based on single-cell insights may replace one-size-fits-all approaches with dynamic, responsive care models tailored to each individual's immunobiology.

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