Transforming Drug Discovery Through Precision Research I Single Cell Solutions

Introduction

The high resolution and scale that single cell analysis provides is revolutionizing drug discovery and development by introducing comparative, longitudinal, and causal information that transforms our ability to understand biology and disease. Pharmaceutical and biotech companies are harnessing the power of 10x Genomics’ suite of solutions to identify and sustain a pipeline of novel targets, and accelerate key promising assets through development. These cutting edge technologies play an integral role in biomarker discovery, resolve complex therapeutic mechanism(s) of action, and further our understanding of how therapies can be deployed to minimize resistance and separate responders versus non-responders.

Gain insight into how top pharmaceutical companies are leveraging 10x Genomics platforms throughout the drug discovery and development process with these publication highlights.

Drug Discovery & Development Phase

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| Target Identification  | Massively Parallel Single-Cell B-Cell Receptor Sequencing Enables Rapid Discovery of Diverse Antigen-Reactive Antibodies | Sample type: B cells from blood and lymph nodes | • Identified 710 novel antibody lineages not captured in hybridoma format. 99% of these novel antibodies (n=93) are antigen-reactive.  
• Developed bioinformatics framework to predict antigen-reactive antibody sequences from full-length B-cell receptor genes  
• Characterized immune repertoires for over 250,000 single B cells from human, mouse, and rat |
| Target Identification  | Immune Cell Landscaping Reveals a Protective Role for Regulatory T Cells During Kidney Injury and Fibrosis | Sample type: 2 mouse models, CD45+ kidney immune cells, and CD4+ kidney T cells | • Identified a T regulatory cell population capable of preventing kidney injury and fibrosis  
• Redefined the immunologic mechanism underlying kidney fibrosis |
<p>|                        | F do Valle Duraes et al., JCI Insight. (2020), Novartis Institutes for Biomedical Research, Cantonal Hospital Baselland. | 10x Genomics product: Chromium Single Cell Gene Expression Solution |                                                                                     |</p>
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| Target Identification  | CD3 Bispecific Antibody-Induced Cytokine Release Is Dispensable for Cytotoxic T Cell Activity | Sample type: Human PBMCs 10x Genomics product: Chromium Single Cell Gene Expression Solution | • Found that T cell-generated tumor necrosis factor drives systemic cytokine release by monocytes after T cell-activating therapies  
• Identified a mechanistic pathway for cytokine release syndrome and druggable targets to prevent its clinical onset |
| Preclinical Studies    | Single-Cell Transcriptome Analyses Reveal Endothelial Cell Heterogeneity in Tumors and Changes Following Antiangiogenic Treatment | Sample type: Human colon cancer cell line xenografts 10x Genomics product: Chromium Single Cell Gene Expression Solution | • Profiled heterogeneity of endothelial cells from tumor xenografts in mice treated with inhibitors of VEGF or D114 signaling  
• Defined subpopulations based on rapid changes in gene expression following antiangiogenic treatment |
| Preclinical Studies    | Multi-Omics Characterization of a Diet-Induced Obese Model of Nonalcoholic Steatohepatitis | Sample type: Mouse liver biopsies 10x Genomics product: Chromium Single Cell Gene Expression Solution | • Profiled the liver transcriptome of a murine model of nonalcoholic steatohepatitis (NASH)  
• scRNA-seq data resolved cellular heterogeneity to identify key cell types involved in the development and pathogenesis of NASH |
| Preclinical Studies    | DMSO Cryopreservation is the Method of Choice to Preserve Cells for Droplet-Based Single-Cell RNA Sequencing | Sample type: Primary immune cells 10x Genomics product: Chromium Single Cell Gene Expression Solution | • Compared and identified optimal methods to store and preserve cells for comparative and longitudinal scRNA-seq analysis  
• Cryopreservation best maintained cell integrity, with data highly similar to fresh cells |
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• Compared sample preparation techniques for single cell sequencing of lymphocytes |
| Clinical Research Studies | Single-Cell RNA-Sequencing From Clinically Relevant Core Needle Biopsies for Evaluation of Tumor-Immune Cell Interactions in the Tumor Microenvironment N Kumar et al., Poster presented at: SITC 2019. Bristol Myers Squibb. | **Sample type:** Small biopsies from multiple tumor types 10x Genomics product: Chromium Single Cell Gene Expression Solution | • Single cell transcriptome analysis comparing cells in the tumor microenvironment with healthy PBMCs  
• Demonstrated use of scRNA-seq to identify biomarkers in clinically relevant specimens |
• In patients responsive to anti-PDL1 therapy, intratumoral T cells are replenished with non-exhausted cells from outside the tumor  
• Clonotypic expansion of T cells (detectable in peripheral blood) emerged as a potential biomarker for response to anti-PDL1 therapy |
Additional Pharma Publications


