Transforming Drug Discovery Through Precision Research | 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

Target Identification → Target Validation → Preclinical Studies → Clinical Research Studies

Drug Development Phase	Featured Publication	Experiment Snapshot	Research Highlights
Target Identification	**Massively Parallel Single-Cell B-Cell Receptor Sequencing Enables Rapid Discovery of Diverse Antigen-Reactive Antibodies** L Goldstein et al., *Commun. Biol.* (2019). **Genentech**, SciGenom Labs.	**Sample type:** B cells from blood and lymph nodes **10x Genomics product:** Chromium Single Cell Immune Profiling Solution	• 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** F do Valle Duraes et al., *JCI Insight.* (2020). **Novartis Institutes for Biomedical Research**, Cantonal Hospital Baselland.	**Sample type:** 2 mouse models, $CD45^+$ kidney immune cells, and $CD4^+$ kidney T cells **10x Genomics product:** Chromium Single Cell Gene Expression Solution	• Identified a T regulatory cell population capable of preventing kidney injury and fibrosis • Redefined the immunologic mechanism underlying kidney fibrosis

10x GENOMICS

Drug Development Phase	Featured Publication	Experiment Snapshot	Research Highlights
Target Identification	**CD3 Bispecific Antibody-Induced Cytokine Release Is Dispensable for Cytotoxic T Cell Activity** J Li et al., *Sci. Transl. Med.* (2019). **Genentech**.	**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** Q Zhao et al., *Cancer Res.* (2018). **Regeneron Pharmaceuticals**.	**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 Dll4 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** HM Ægidius et al., *Sci. Rep.* (2020). **Novo Nordisk Foundation Center**, University of Copenhagen, University of Southern Denmark.	**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** C Wohnhaas et al., *Sci. Rep.* (2019). **Boehringer Ingelheim Pharma**, University of Konstanz.	**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

Drug Development Phase	Featured Publication	Experiment Snapshot	Research Highlights
Clinical Research Studies	**An Optimized Workflow for Single-Cell Transcriptomics and Repertoire Profiling of Purified Lymphocytes from Clinical Samples** R Hanamsager et al., *Sci. Rep.* (2020). **Sanofi**, New York University College of Arts and Sciences.	**Sample type:** Human PBMCs **10x Genomics product:** Chromium Single Cell Immune Profiling Solution	• Provided guidelines for obtaining high-quality scRNA-seq and immune profiling data from clinical samples • 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
Clinical Research Studies	**Peripheral T Cell Expansion Predicts Tumour Infiltration and Clinical Response** T Wu et al., *Nature.* (2020). **Genentech**.	**Sample type:** T cells from 14 treatment-naive patients with solid tumors **10x Genomics product:** Chromium Single Cell Immune Profiling Solution	• Single cell immune repertoire profiling to understand origin and fate of T cells implicated in tumor immunity • 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

1. TL Tang-Huau et al., Human In Vivo-Generated Monocyte-Derived Dendritic Cells and Macrophages Cross-Present Antigens Through a Vacuolar Pathway. *Nat. Commun.* 9, 2570 (2018).
2. S Sun et al., Hair Cell Mechanotransduction Regulates Spontaneous Activity and Spiral Ganglion Subtype Specification in the Auditory System. *Cell.* 174, 1247–1263.e15 (2018).
3. A Arazi et al., The Immune Cell Landscape in Kidneys of Patients with Lupus Nephritis. *Nat. Immunol.* 20, 902–914 (2019).
4. R Peyser et al., Defining the Activated Fibroblast Population in Lung Fibrosis Using Single-Cell Sequencing. *Am. J. Respir. Cell Mol. Biol.* 61, 74–85 (2019).
5. FA Vieira Braga et al., A Cellular Census of Human Lungs Identifies Novel Cell States in Health and in Asthma. *Nat. Med.* 25, 1153–1163 (2019).
6. U Eskiocak et al., Differentiated Agonistic Antibody Targeting CD137 Eradicates Large Rumors Without Hepatotoxicity. *JCI Insight.* 5, pii: 133647 (2020).
7. Z Li et al., Angiopoietin-2 Blockade Ameliorates Autoimmune Neuroinflammation by Inhibiting Leukocyte Recruitment Into the CNS. *J. Clin. Invest.* 130, 1977–1990 (2020).
8. LD Orozco et al., Integration of eQTL and a Single-Cell Atlas in the Human Eye Identifies Causal Genes for Age-Related Macular Degeneration. *Cell Rep.* 30, 1246–1259.e6 (2020).

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LIT000073 Rev A *Drug Discovery Research Highlights*