Immunology research highlights: Redefining the understanding of immunology

Introduction

Immunologists around the world are leveraging 10x Genomics products to advance our knowledge of the heterogeneity and developmental progression of immune cells. With a more comprehensive atlas of the immune system, researchers are elucidating the cellular and molecular mechanisms underlying the adaptive and innate immune response, enabling diverse and revolutionary applications. Today, 10x customers can identify and secure the paired B-cell receptor heavy- and light-chain sequences for an increasing number of new antibodies to known and novel targets, and they are working to understand the complex biology underlying immunotherapy failure and success. Explore the applications of single cell and spatial technologies for immunology research in the publications highlighted below, and consider what discoveries you will add to help unravel the complexity of the immune system.

Featured Publication	Experiment Snapshot	Research Highlights
High-Throughput Mapping of B Cell Receptor Sequences to Antigen Specificity I Setliff et al., *Cell*. (2019).	Research area: Vaccines & Immunotherapies - Antibody Discovery 10x Genomics product: Chromium Single Cell Immune Profiling Solution Sample type: Human B cells from HIV-infection samples	• Used single cell immune profiling solutions to develop an unbiased, high-throughput method to screen the antibody repertoire of single B cells, enabling simultaneous capture of oligo-barcoded antigens and B-cell receptor (BCR) sequences • Screened B cells from human HIV-infection samples, and identified a diverse panel of new antibodies, including broadly neutralizing antibodies
Anti-idiotypic Antibodies Elicit Anti-HIV-1–Specific B Cell Responses P Dosenovic et al., *J Exp Med*. (2019).	Research area: Vaccines & Immunotherapies - Antibody Discovery 10x Genomics product: Chromium Single Cell Immune Profiling Solution Sample type: Naive B cells from wild-type and 3BNC60^{SI} knock-in mice (carrying germline IgH of human bNAb)	• Explored the utility of a monoclonal anti-idiotypic antibody, iv8, to activate and expand B cells expressing broadly neutralizing VRC01-class antibodies against HIV-1 in a murine adoptive transfer system • Obtained BCR sequences using single cell immune profiling solutions, discovering that iv8 induced B cells to expand and mature in the context of a polyclonal immune system and produced an antibody response targeting conserved epitopes on the HIV-1 envelope

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Spatiotemporal Immune Zonation of the Human Kidney B Stewart et al., *Science*. (2019).	Research area: Infectious Disease, Cellular & Molecular Immunology 10x Genomics product: Chromium Single Cell Gene Expression Solution Sample type: Human fetal and mature kidney cells	• Used single cell RNA sequencing to identify postnatal acquisition of transcriptional programs in tissue-resident myeloid and lymphoid immune cells that promote proinflammatory and infection defense capabilities • Discovered anatomically defined expression patterns of immune genes within the epithelial compartment, suggesting epithelial–immune cross-talk that localizes macrophages and neutrophils to regions susceptible to infection
Single-Cell Survey of Human Lymphatics Unveils Marked Endothelial Cell Heterogeneity and Mechanisms of Homing for Neutrophils A Takeda et al., *Immunity*. (2019).	Research area: Infectious Disease, Cellular & Molecular Immunology 10x Genomics product: Chromium Single Cell Gene Expression Solution Sample type: Human lymphatic endothelial cells (LECs)	• Profiled 33,000 lymphatic endothelial cells (LECs) in human lymph nodes (LNs) by single cell RNA sequencing, revealing six transcriptionally distinct subpopulations of human LECs • Found that LECs lining the medullary sinus express a C-type lectin, CD209, that binds with a carbohydrate, CD15, to mediate neutrophil-selective homing and clearance of lymph-borne pathogens before they spread through the LNs
The Transcription Factor TCF-1 Enforces Commitment to the Innate Lymphoid Cell Lineage C Harly et al., *Nat Immunol*. (2019).	Research area: Cellular & Molecular Immunology - Cell Lineage Determination 10x Genomics product: Chromium Single Cell Gene Expression Solution Sample type: Mouse early innate lymphoid progenitors and ILC precursors	• Examined the transcriptional and functional heterogeneity of innate lymphoid cell (ILC) progenitors, and studied the precursor–product relationships that link the subsets identified • Observed two successive stages of ILC development within T-cell factor 1-positive (TCF-1+) early innate lymphoid progenitors, and found that activity of TCF-1 enforces commitment to ILC fate while TCF-1 is dispensable for the generation of dendritic cells

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Massively Parallel Single-Cell B-Cell Receptor Sequencing Enables Rapid Discovery of Diverse Antigen-Reactive Antibodies L Goldstein et al., *Commun Biol*. (2019).	Research area: Vaccines & Immunotherapies - Antibody Discovery 10x Genomics product: Chromium Single Cell Immune Profiling Solution Sample type: Naive and anti-ovalbumin B cells from rat, mouse, and human	• Performed high-throughput single cell B-cell receptor sequencing (scBCR-seq) on 250,000 cells to obtain accurately paired full-length variable regions in a massively parallel fashion • Tested predicted antigen-reactive antibody sequences against ovalbumin-specific hybridomas, observing a high degree of overlap between B-cell lineages and an additional 710 candidate lineages from scBCR-seq data • Demonstrated the utility of scBCR-seq for rapid discovery of large, diverse panels of high-affinity, antigen-specific antibodies
Massively Parallel Single-Cell Chromatin Landscapes of Human Immune Cell Development and Intratumoral T Cell Exhaustion A Satpathy et al., *Nat Biotechnol*. (2019).	Research area: Immuno-oncology 10x Genomics product: Chromium Single Cell ATAC Solution Sample type: Human blood and basal cell carcinoma	• Obtained chromatin profiles of more than 200,000 single cells in human blood and basal cell carcinoma • Analyzed serial tumor biopsies before and after PD-1 blockade, revealing chromatin regulators of therapy-responsive T cell subsets • Identified a shared regulatory program that governs intratumoral CD8+ T cell exhaustion and CD4+ T follicular helper cell development
Clonal Replacement of Tumor-Specific T Cells Following PD-1 Blockade K Yost et al., *Nat Med*. (2019).	Research area: Immuno-oncology 10x Genomics product: Chromium Single Cell Immune Profiling Solution Sample type: Primary tumors from patients with advanced basal cell carcinoma	• Performed paired single cell RNA and T-cell receptor sequencing on 79,046 cells from site-matched tumors from patients with basal or squamous cell carcinoma, before and after anti-PD-1 therapy • Observed preferential clonal replacement in exhausted CD8+ T cells after checkpoint blockade, but found that expanded T cell clones did not derive from reinvigorating pre-existing exhausted tumor-infiltrating T lymphocytes and may have been recruited from outside the tumor microenvironment

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Acquired Cancer Resistance to Combination Immunotherapy from Transcriptional Loss of Class I HLA K Paulson et al., *Nat Commun*. (2018).	Research area: Immuno-oncology 10x Genomics product: Chromium Single Cell Gene Expression Solution and Chromium Single Cell Immune Profiling Solution Sample type: Serial PBMCs and tumor biopsies from patients with metastatic Merkel cell carcinoma	• Treated two patients with metastatic Merkel cell carcinoma with autologous Merkel cell polyomavirus-specific CD8+ T cells and immune-checkpoint inhibitors, observing dramatic remissions initially but late relapse • Used scRNA-seq to identify dynamic transcriptional suppression of the specific HLA genes presenting the targeted viral epitope in the resistant tumor as a consequence of intense CD8-mediated immunologic pressure

Additional Publications

1. J Granja et al., Single-Cell Multiomic Analysis Identifies Regulatory Programs in Mixed-Phenotype Acute Leukemia. *Nat Biotechnol*. 37, 1458–1465 (2019).
2. B Huang et al., Mucosal Profiling of Pediatric-Onset Colitis and IBD Reveals Common Pathogenics and Therapeutic Pathways. *Cell*. 179, 1160–1176 (2019).
3. B Miller et al., Subsets of Exhausted CD8+ T cells Differentially Mediate Tumor Control and Respond to Checkpoint Blockade. *Nat Immunol*. 20, 326–336 (2019).
4. J Oh et al., Migrant Memory B Cells Secrete Luminal Antibody in the Vagina. *Nature*. 571, 122–126 (2019).
5. B Dulken et al., Single-Cell Analysis Reveals T Cell Infiltration in Old Neurogenic Niches. *Nature*. 571, 205–210 (2019).
6. A Chapuis et al., T Cell Receptor Gene Therapy Targeting WT1 Prevents Acute Myeloid Leukemia Relapse Post-Transplant. *Nat Med*. 25, 1064–1072 (2019).
7. G Ledergor et al., Single Cell Dissection of Plasma Cell Heterogeneity in Symptomatic and Asymptomatic Myeloma. *Nat Med*. 24, 1867–1876 (2018).
8. J Neal et al., Organoid Modeling of the Tumor Immune Microenvironment. *Cell*. 175, 1972–1988 (2018).
9. A Lundmark et al., Gene Expression Profiling of Periodontitis-Affected Gingival Tissue by Spatial Transcriptomics. *Sci Rep*. 8, 9370 (2018).
10. G Zheng et al., Massively Parallel Digital Transcriptional Profiling of Single Cells. *Nat Commun*. 8, 14049 (2017).

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