NEW YORK GENOME CENTER® | Collaboration Research Discovery

Single Cell/Nuclei Sequencing and Spatial Transcriptomics

NYGC's Technology Development lab provides comprehensive single cell, spatial, and multi-omics expertise to support complex research projects. As an early adopter of the 10x Genomics portfolio, NYGC has deep expertise across a broad range of single cell and spatially resolved multi-omics applications, including single cell RNA sequencing, single nucleus RNA sequencing, single cell Multiome (ATAC + gene expression), CITE-seq, ECCITE-seq, ASAP-seq, DOGMA-seq, DLP+ amplification-free single cell whole genome sequencing, and long-read single-cell sequencing.

NYGC offers expertise in spatial genomics technologies, including 10x Genomics Visium and Xenium platforms. Through close collaboration between Technology Development, Computational Biology, and research investigators, NYGC develops integrated analytical strategies and multimodal approaches to extract meaningful biological insights from complex genomic datasets.

We have experience working with a wide variety of cell and tissue types and can collaborate with researchers to optimize workflows for challenging or less-characterized samples. For new sample types, we are also open to piloting approaches to improve nuclei isolation, cell viability, sample collection, and other key steps in the workflow.

Customized Project Planning

Single cell and spatial genomics projects are highly dependent on the research question, sample type, sample quality, and storage conditions. We therefore begin with an initial consultation with our Technology Development and Project Management teams to understand your goals, assess project requirements, and determine the most appropriate approach.

Project pricing and turnaround times are customized to the scope and scale of each engagement and are provided following consultation with our team.

10x Single-Cell Sequencing

NYGC offers comprehensive **single cell RNA sequencing (scRNA-seq)** services using the 10x Genomics Chromium X platform. Available workflows include 3′ and 5′ gene expression assays, as well as FLEX probe-based whole-transcriptome profiling.

On-Chip Multiplexing (OCM) enables multiple samples to be processed concurrently in a single 10x reaction, providing flexibility for studies with multiple samples while helping streamline experimental workflows.

CITE-seq and ECCITE-seq

NYGC offers advanced single cell approaches that extend RNA profiling to additional molecular features, enabling more comprehensive characterization of individual cells.

CITE-seq combines 3′ scRNA-seq with cell surface protein detection, allowing researchers to measure both gene expression and protein markers from the same cells. This approach can provide complementary information for identifying and characterizing cell populations, particularly in heterogeneous tissues and immune systems.

ECCITE-seq expands on CITE-seq by incorporating a 5′ scRNA-seq workflow with cell surface protein detection and CRISPR-compatible features. The approach can integrate RNA expression, protein markers, and clonotype information to provide detailed phenotypic and functional characterization of individual immune cells.

FLEX Whole-Transcriptome Profiling

10x Genomics' FLEX workflow uses probe-based whole transcriptome profiling and supports DNA-barcoded antibody-based feature barcoding for simultaneous detection of selected cell-surface proteins. FLEX provides flexibility in experimental design, with the number of samples, number of cells, and transcriptome sampling per cell balanced according to study requirements. These parameters are determined in consultation with our team during project planning.

10x Single Nucleus Sequencing

For tissues and cell types that are difficult to dissociate into intact cells, **single nucleus RNA sequencing (snRNA-seq)** provides an alternative approach for transcriptomic profiling.

NYGC offers single nucleus sequencing using 10x Genomics Chromium 3′ and FLEX workflows, with extensive experience developing nuclei isolation protocols for challenging sample types, including FFPE-preserved tissues. Our workflows can accommodate parallel processing of multiple samples and can be adapted to the specific characteristics of each tissue or sample type.

Multiome Sequencing and DOGMA-seq

For studies requiring simultaneous analysis of gene expression and chromatin accessibility, NYGC offers 10x Genomics Chromium Epi Multiome ATAC workflows. This assay is typically performed on isolated nuclei and enables paired measurement of transcriptional activity and chromatin accessibility from the same individual nuclei.

For studies requiring additional cellular phenotyping, NYGC developed **DOGMA-seq**, an integrated single cell approach that combines gene expression, chromatin accessibility, and cell surface protein profiling from the same cells. DOGMA-seq can also incorporate mitochondrial DNA detection, providing an expanded view of cellular state and identity.

NYGC also offers **single cell ATAC sequencing (scATAC-seq)** for studies focused on chromatin accessibility. **ASAP-seq** extends scATAC-seq with cell surface protein detection, enabling simultaneous characterization of chromatin state and cellular phenotype.

Submission Requirements

To support high-quality single cell data generation, samples should meet the following minimum requirements:

- **Sample type:** Depending on the assay, tissue, frozen or live cell suspension
- **Viability:** Greater than 90% viability as measured by Trypan Blue staining (for live cell suspensions)
- **Cell input:**
    - Minimum of 100,000 cells per sample for multiplexed experiments (up to 4 samples)
    - Up to 1 million cells for single-sample experiments
- **Sequencing depth:** Target 25,000 read pairs per cell

Standard Analysis

- Alignment of raw reads to human or mouse genome, if applicable
- Quality control summary metrics
- Gene quantification
- Additional assay-specific analyses

Standard Deliverables

- FASTQ files
- Aligned data
- Count matrix (gene-cell UMI count matrix)
- Additional assay-specific deliverables

Direct Library Preparation Plus (DLP+)

NYGC offers **Direct Library Preparation Plus (DLP+)**, a single cell, amplification-free whole genome sequencing approach developed in the laboratory of Dr. Sam Aparicio. DLP+ enables genome-wide characterization of individual cells, providing insights into copy number variation (CNV), loss of heterozygosity (LOH), somatic variants, and clonal relationships within heterogeneous cell populations.

DLP+ uses a high-throughput, automated cell-isolation workflow on a CellenOne F1.4 piezo droplet dispensing platform, enabling interrogation of thousands of individual cell genomes. Integrated imaging allows accurate identification of individual live cells and, when fluorescent markers are used, selection of specific cell populations or cells of interest.

Cells are typically sequenced at shallow whole genome coverage (~0.1x per cell), which is sufficient for robust detection of copy number states at the single cell and clonal cell level. Higher sequencing depth can be used when additional variant detection is required. Both intact cells and nuclei can be used as input.

Submission Requirements

- **Sample types:** Live or frozen cell suspensions, tissue, and other sample types upon consultation
- **Cell input:** ~1 million cells per sample
- **Typical loading:** ~1,200 cells per sample, with two samples per chip
- **Typical sequencing depth:** ~0.1x genome coverage per cell

Sample requirements and loading parameters may vary depending on sample type and study objectives and are confirmed during project planning.

Standard Analysis

- Quality control and summary metrics
- Somatic copy number variation calling
- Pseudo-bulk SNV calling, where supported by the data
- Pseudo-bulk indel calling, where supported by the data

Standard Deliverables

- FASTQ files
- Quality control metrics
- Raw SNV and indel variant calls in VCF format
- Consolidated SNV and indel files in VCF, MAF, and tab-delimited formats
- Raw CNV caller output

10x Spatial Transcriptomics

NYGC offers end-to-end **10x Genomics Visium and Xenium spatial transcriptomics** services, enabling researchers to characterize gene expression within intact tissue while preserving spatial context. Our team supports projects across fresh frozen, fixed-then-frozen, and formalin-fixed, paraffin-embedded (FFPE) tissues, with workflows selected based on the tissue type, research goals, and desired spatial resolution.

Sample Preparation and Submission

High-quality tissue preparation is essential for successful spatial profiling. NYGC works with researchers during project planning to review sample characteristics and recommend the most appropriate workflow.

Depending on project requirements, tissue sectioning may be performed by the NYGC Technology Development team.

10x Visium

Visium is well suited for studies focused on tissue architecture and broad spatial characterization of gene expression. It enables researchers to identify spatially variable expression patterns and characterize molecular differences across tissue regions while maintaining the spatial organization of the sample.

Visium V2 Spatial Gene Expression

The Visium Spatial Gene Expression V2 assay uses probe-based chemistry to measure mRNA abundance across intact tissue sections. The assay provides unbiased spatial profiling and is compatible with a range of tissue types and preservation methods.

Visium HD Spatial Gene Expression

Visium HD provides high-resolution spatial gene expression profiling at **2 µm resolution**, enabling gene expression patterns to be mapped at near-single-cell scale. The assay uses probe-based chemistry targeting approximately 25,000 protein-coding mRNAs, providing robust transcript detection while reducing the impact of factors such as RNA degradation and fixation-associated crosslinking.

Visium HD is particularly well suited for studies requiring both broad transcriptome coverage and high spatial resolution, including tissue architecture, cellular heterogeneity, and spatially organized biological programs.

Visium Tissue Requirements

- Tissue sectioning may be performed by the NYGC Technology Development team, depending on project requirements
- Tissue quality should support preservation of RNA integrity and tissue morphology
- Section thickness and preparation requirements depend on the specific Visium workflow and tissue type

Standard Analysis

- Sequencing and spatial quality control metrics
- Space Ranger processing

- Spatial clustering and visualization
- Batch-effect correction, when appropriate
- Integration with reference cell-type annotations, when appropriate

Standard Deliverables

- Tissue histology images
- Raw sequencing data in FASTQ format
- Space Ranger output
- Processed Seurat object

10x Xenium

Xenium is an imaging-based spatial transcriptomics platform that provides single cell and subcellular localization of RNA molecules within intact tissue. It is particularly well suited for studies requiring precise localization of defined gene sets, including cellular phenotyping, tissue microenvironment characterization, cell–cell interactions, and spatial organization of specific biological programs.

10x Genomics offers a range of pre-designed, tissue-specific Xenium panels, as well as options for custom panel design. Available panels span applications including oncology, spatial cell typing, tumor microenvironment, developmental biology, and other areas of biological research.

Depending on the Xenium workflow and specific needs, projects can use pre-designed panels and can incorporate additional custom targets. Panel selection and experimental design can be determined in consultation with the NYGC team based on the biological objectives of the study.

Xenium Tissue Requirements

- Tissue sections should be prepared on compatible Xenium slides
- Recommended section thickness is approximately **10 µm for fresh frozen tissue** and **5 µm for FFPE tissue**
- Tissue quality should support preservation of RNA integrity and spatial morphology
- For FFPE samples, pre-submission tissue quality assessment is recommended

Samples with lower RNA quality or challenging tissue characteristics may require additional evaluation to determine suitability for Xenium analysis.

Standard Analysis

- Spatial and molecular quality control metrics
- Dimensionality reduction and clustering
- Identification and visualization of spatially distinct tissue regions
- Integration with reference cell-type annotations, when appropriate

Standard Deliverables

- Tissue histology images
- Processed Xenium data
- Standard analysis and quality control outputs

Experimental Guidance

Visium and Xenium offer complementary approaches to spatial genomics. Visium is well suited for broad, transcriptome-scale spatial discovery, while Xenium provides targeted single-cell and subcellular resolution. Our Technology Development and Project Management teams can help evaluate tissue characteristics, biological objectives, and desired resolution to determine the most appropriate workflow for each project.

Frequently Asked Questions – Single Cell/Nuclei Sequencing and Spatial Transcriptomics

What information is needed to start a project?

To begin planning a library sequencing project, we typically request:

- Species and tissue type or cell source
- Assay requirements, including whether additional modalities such as CITE-seq, ECCITE-seq, or DOGMA-seq are of interest
- Target number of cells and desired final cell recovery
- Required timeline
- Data delivery requirements
- Any planned downstream analyses

How are projects initiated?

Once project scope and service requirements have been finalized with your NYGC Project Manager, NYGC will provide a formal service quote outlining the agreed-upon deliverables, pricing, and project details. To begin project execution and submit samples, NYGC requires a signed copy of the quote and an approved purchase order (PO). For large-scale projects, additional discussions regarding customized terms and conditions may be accommodated.

What is the expected turnaround time?

All turnaround times can be found on our 'main research services page'.

How should samples be submitted?

Materials submitted for single cell, single nuclei, and spatial transcriptomics projects, including FFPE and fresh frozen tissue, and cell suspensions, can be shipped directly to NYGC. Your Project Manager will provide the appropriate shipping address and an electronic sample manifest to complete prior to shipment. Please provide at least 24

hours' advance notice before shipping samples to ensure proper receipt and processing. To maintain sample integrity and ensure successful delivery, samples should arrive during NYGC business hours, as the laboratory is closed on weekends and holidays. For those in the NYC area, dropping off samples directly may also be advisable.

Do you offer downstream alignment and analysis services?

Depending on the library type and species, yes, for an additional cost. See more about Bioinformatics and Data Analysis Services on 'main research services page'.

How is data returned?

We support data delivery to a variety of client-managed endpoints and storage environments. Before delivery, we can perform a test transfer to confirm connectivity and ensure efficient transfer of large sequencing datasets.