Profiling chromatin accessibility at single cell resolution

Chromium Single Cell ATAC

Chromatin organization compacts meters of DNA into the nucleus, making just a small fraction of DNA accessible for transcription within each cell. The Chromium Single Cell ATAC (Assay for Transposase Accessible Chromatin) solution provides a robust and scalable approach to map the epigenetic landscape at single cell resolution. Using a transposase enzyme to preferentially tag accessible DNA regions with sequencing adaptors, researchers can now generate sequencing-ready libraries and identify open chromatin regions. Our simple workflow, combined with intuitive software, enables understanding of epigenetic and regulatory variation across tens of thousands of cells.

Figure 1. Characteristic open chromatin profiles at single cell resolution. Top: Representative tracks of open chromatin regions from GM12878 cell line. The upper track (orange) represents data gathered from 50,000 nuclei using bulk ATAC-seq, while the lower track (green) is aggregated from 390 individual nuclei run on Chromium Single Cell ATAC. Even with data from 100-fold fewer nuclei, Chromium Single Cell ATAC demonstrates a similar sensitivity to that of bulk ATAC-seq. Bottom: Transposition events detected in single cells using Chromium Single Cell ATAC from the same sample and genomic locus of GM12878 cell line.

Highlights

- Resolve cell types and states using genome-wide, epigenetic profiles with single cell resolution
- Discover cis-regulatory elements that drive gene expression differences between cell types and states
- Characterize cell-specific gene regulatory networks to understand the epigenetic underpinnings of disease, developmental plasticity, and cell identity
- Identify transcription factors (TFs) that determine cell identity, and perform lineage and developmental tracing
Product features

- Analyze open chromatin regions at single cell resolution, enabling deeper understanding of cellular epigenetic heterogeneity
- Perform epigenetic profiling for hundreds to tens of thousands of nuclei, enabling detection of rare cells
- Examine non-coding sequences to discover cis-regulatory elements and drivers of gene expression differences between cell types and states
- Follow a ready-to-use, robust workflow with demonstrated protocols for diverse sample types, including cell lines, primary cells, and fresh and frozen tissue
- Apply easy-to-use software and visualization tools for straightforward analysis of single cell ATAC data

Figure 2. The Chromium Next GEM Single Cell ATAC workflow. Nuclei are transposed in bulk, followed by partitioning on a microfluidic chip into nanoliter-scale GEMs in the Chromium instrument. The transposed DNA of individual nuclei are identified with a unique 10x Barcode. Libraries are generated and sequenced, and 10x Barcodes are used to associate individual reads back to individual partitions and, thereby, each individual cell.
Figure 3. High-quality single cell ATAC-seq libraries. Left: Insert size distribution of Single Cell ATAC fragments from GM12878 cells reveals protection of DNA by individual nucleosomes and nucleosome multimers, along with a nucleosome periodicity of 184 base pairs. Right: Cumulative footprinting signal at predicted transcription factor (CTCF)-binding sites in GM12878 cell line generated by aggregating Chromium Single Cell ATAC data. The dotted lines indicate the location of the known CTCF motif (pictogram above the plot; JASPAR CTCF motif MA01391).

Figure 4. Single nuclei epigenetic profiling of peripheral blood mononuclear cells (PBMCs). Left: t-SNE projection of ~10,000 PBMCs from a healthy donor. Each cell is plotted in t-SNE coordinates, colored by their annotated cell types. Major subpopulations were identified based on enrichment scores of well characterized TF motifs and cell type–specific peaks. Clustering patterns suggest that there is extensive substructure within each major classification. Middle, Right: Single nuclei epigenetic profiles overlaid on t-SNE projections for CEBPA (marker of monocytes) and ELF1 (marker of T cells and natural killer (NK) cells). The PBMC population comprises 20% of monocytes and 66% of T and NK cells—consistent with FACS analysis of the cells.
## Product Specifications

- Efficiently partition 500–10,000 nuclei per channel, for up to 80,000 nuclei per run
- Scalable; run up to 8 samples in parallel
- High nuclei capture rates of up to 65%
- Low doublet rates of 0.8% per 1,000 cells

### Chromatin Accessibility Profiling Products

| Product Name | Product Code |
|--------------|--------------|
| Chromium Next GEM Single Cell ATAC Kit v2, 16 rxns | 1000390 |
| Chromium Next GEM Single Cell ATAC Kit v2, 4 rxns | 1000406 |
| Chromium Next GEM Single Cell ATAC Library and Gel Bead Kit v1.1, 16 rxns | 1000175 |
| Chromium Next GEM Single Cell ATAC Library and Gel Bead Kit v1.1, 4 rxns | 1000176 |
| Chromium Next GEM Chip H Single Cell Kit, 48 rxns | 1000161 |
| Chromium Next GEM Chip H Single Cell Kit, 16 rxns | 1000162 |
| Single Index Kit N Set A, 96 rxns | 1000212 |

### Sample Preparation Products

- Chromium Nuclei Isolation Kit
  - Expected mid-2022

### Instrument Compatibility

| Product Name | Product Code |
|--------------|--------------|
| Chromium iX & Accessory Kit, 12 Mo. Warranty | 1000328 |
| Chromium iX & Accessory Kit, 24 Mo. Warranty | 1000329 |
| Chromium X & Accessory Kit, 12 Mo. Warranty | 1000331 |
| Chromium X & Accessory Kit, 24 Mo. Warranty | 1000332 |
| Chromium X Upgrade Package | 1000330 |
| Chromium Controller & Next GEM Accessory Kit, 12 Mo. Warranty | 1000202 |
| Chromium Controller & Next GEM Accessory Kit, 24 Mo. Warranty | 1000204 |

### Software

- Cell Ranger ATAC Pipeline
  - [Download](go.10xgenomics.com/scATAC/)
- Loupe Browser
  - [Download](go.10xgenomics.com/scATAC/loupe-cell/)