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Measuring Chromatin Accessibility and Gene Expression in Single Nucleus Using Particle-templated Instant Partition

Researchers at Stanford have developed particle-templated instant partition sequencing (PIP-seq) methods for single-nucleus chromatin-accessibility profiling and paired chromatin-accessibility and gene-expression profiling. The technology includes PIP-ATAC-seq for profiling accessible chromatin and PIP-Multiome-seq for measuring chromatin accessibility and RNA expression from the same nucleus.

Single-cell and single-nucleus epigenomic assays are valuable for identifying cell types, regulatory states, and gene-regulatory mechanisms in heterogeneous samples. However, existing approaches can require specialized microfluidic equipment, have limited throughput in plate-based formats, or involve complex split-pool workflows. These limitations can increase cost and experimental complexity, while contributing to nuclei clumping and nucleic-acid leakage.

The PIP-seq workflow uses uniformly sized beads to generate monodispersed water-in-oil droplets through vortexing, eliminating the need for specialized microfluidic hardware. Individual nuclei and barcoded beads are co-encapsulated for library preparation, enabling chromatin fragments—and, in the multiomic workflow, RNA-derived cDNA—to be associated with the same bead barcode. Compared with existing approaches, the technology is designed to provide a lower-cost, higher-throughput, and more accessible alternative for single-nucleus chromatin and multiomic analysis, while reducing compromised data quality.

Stage of Development
Research - in vitro

Applications

- Single-nucleus chromatin-accessibility profiling
- Paired single-nucleus ATAC and RNA profiling
- Analysis of complex, heterogeneous, or difficult-to-process samples
- Research-use kits for academic, pharmaceutical, biotechnology, and genomics laboratories

Advantages

- Microfluidics-free workflow that avoids reliance on conventional microfluidic partitioning
- High throughput and cost-effective
- Reduced handling issues
- Enables chromatin and RNA measurements from the same barcoded bead and nucleus

Publications

- Zhifei Luo, William J Greenleaf (**2026**). A Simple, Cost-Effective, High-Throughput Method for Measuring Chromatin Accessibility and Gene Expression in Single Nuclei. *bioRxiv* 2026.06.29.735326.

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