**Simultaneous profiling of RNA and chromatin accessibility by multiomic Assay for Transposase-Accessible Chromatin with sequencing (ATAC-Seq) using microwell-based single-cell partitioning technology**

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Recent advances in genomics have enabled single-cell transcriptome profiling from various cell types and tissues. However, the upstream regulation of gene expression via epigenetic changes remains unknown. Dynamic variations in chromatin accessibility frequently regulate epigenetic modification, cell development stages and ultimately its functions. Therefore, profiling of accessible chromatins at single-cell resolution is of great importance to impart insights into gene regulation as well as cell functions.

Using the gentle and robust microwell-based single-cell partitioning technology, we have developed an assay for single-cell profiling of RNA and chromatin accessibility simultaneously. Briefly, in our assay, nuclei are transposed by Tn5 transposase to mark open chromatin regions in bulk and then loaded onto a cartridge with microwell partitions for single nucleus separation. In each microwell, there is a magnetic bead with unique cell label and two distinct capture oligos that are used to capture mRNAs and ATAC fragments of given nuclei simultaneously. Accordingly, mRNA and ATAC libraries on beads are amplified separately, and cell label and unique molecular index (UMI) information are gained from bead oligos. As a proof of concept, we profiled more than 20,000 nuclei from human peripheral blood mononuclear cells. Single-cell ATAC-Seq data showed over 90% mapped reads and high transcription start site (TSS) enrichment. Cell clustering analysis was performed based on transcriptome profiles as well as chromatin accessibility profiles. Additionally, we determined a strong correlation between mRNA expression and ATAC signals at promoter regions. Taken together, our findings demonstrated that the newly developed assay utilizing a microwell-based single-cell partitioning technology can analyze mRNA in conjunction with open chromatin regions in the genome at the single-cell level, providing an opportunity for users to characterize cell states and functions more deeply.