

CHROMIUM FLEX ENABLES SCFFPE-SEQ AND SINGLE CELL-SPATIAL DATA INTEGRATION FROM HUMAN TUMOR BLOCKS

Tingsheng Y Drennon*, Jawad Abousoud, Ryan Stott, Juan Pablo Romero, Paul Lund, Sarah Taylor, Peter Smibert, Andrew Kohlway. *x Genomics, Pleasanton, CA, USA*

Background FFPE tissues are the most commonly generated sample type in clinical settings. They provide valuable diagnostic information about disease etiology. However, many existing technologies for profiling gene expression at the RNA level are either incompatible with FFPE tissues due to formaldehyde crosslinking and RNA degradation or lack the ability to resolve expression patterns at single cell resolution.

Methods The new and highly sensitive Chromium Single Cell Gene Expression Flex assay (Flex) from 10x Genomics uses a probe-based approach to profile the whole transcriptome in fixed samples, including FFPE tissues. The Flex assay enables single cell sequencing of FFPE tissues (scFFPE-Seq) with highly sensitive detection of whole transcriptome gene expression.

Results To demonstrate the robustness of the Flex assay, we separately dissociated FFPE sections from 38 human tissue blocks containing both healthy and diseased/cancer samples derived from a variety of tissues including Alzheimer's brain, glioblastoma, breast, colon, heart, liver, lung, ovary, prostate, and skin. Data derived from these samples provided important biological insights including distinct cell clustering along with identification of representative cell types. Additionally, consistent data quality observed across different sections from the same FFPE block highlights the reproducibility and reliability of the assay.

The ability to integrate Flex single cell data with Visium CytAssist spatial data from the same FFPE block through spot deconvolution allows for a more comprehensive understanding of biology. Each spot in Visium CytAssist data may include multiple cells. Using spot deconvolution methods that annotate scFFPE data as reference, the proportion of different cell types in each Visium spot can be determined to further refine cell heterogeneity for spatial visualization. After data integration for a colon cancer sample, we identified distinct tumor stroma with plasma cells expressing MZB1 surrounding tumor regions with high expression of BRCA1, nicely overlapping the H&E images. The integration of both platforms opens opportunities to leverage single cell resolution while preserving spatial context.

Conclusions In summary, Chromium Single Cell Gene Expression Flex enables characterization of the biology preserved in human FFPE tumor samples at a single cell level. The assay expands the capabilities of 10x Genomics' Chromium platform, enabling cross-assay compatibility with Visium CytAssist Spatial Gene Expression for FFPE samples and serves as a powerful tool to facilitate discoveries in disease progression and therapeutic target development.

<http://dx.doi.org/10.1136/jitc-2023-SITC2023.0960>