An Advancement in Spatial Transcriptomics: Slide-seq

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Normal processes in single cell transcriptomics disassociates the source tissue and the spaciotemporal context of cells (Chen, 2020). The development of Slide-seq in modern transcriptomics has allowed scientists to answer an important question: How much of the gene expression variance in a cell type is a result of the cell's location and environment? This biological technique captures spatial localization of the transcriptome, spatial patterns of gene expression, and identifies cell types via identifying marker genes (Chen, 2020). This approach has uncovered remarkable insight into the heterogeneity of different cells in their biological environment, merging histological and transcriptomics processes into a unified operation.

The development Slide-seq was a collaborative effort between scientists Fei Chen, Sam Rodriques, Evan Macosko, and their colleagues at the Broad Institute of MIT and Harvard (Marx, 2021). This technique was first released in a 2019 publication in *Science,* which highlighted the methods of this ground-breaking technology (Rodriques et al., 2019). This addition to the developing field of spatial transcriptomics has revolutionized the integration of molecular biology with pathology in research.

The methodology of Slide-seq involves common gene profiling techniques yet is inherently unique. Beads are DNA-barcoded and mounted on a slide, then fresh tissue is placed on the beads using histological microtomy techniques. The slide is then placed in a solution with reverse transcriptase, then in a tissue dissolving solution (Rodriques, 2019). This solution acts to remove tissue artifacts from the beads, leaving only the cDNA resulting from reverse transcription (Bachman, 2013). Once the cDNA/bead mixture is isolated, library amplification is performed utilizing PCR techniques (Rodriques, 2019). The cDNA is then sequenced alongside the bead barcodes via NGS to capture the transcriptome data. The gene expression data on each

barcode is associated with the bead's physical location on the slide, allowing for a computational reproduction of the original tissue morphology (Rodriques, 2019). Once mapped, Slide-seq allows scientists to determine the exact location of color-coded genes expressed in the tissues. This approach is an advanced diagnostic tool for tissues, as typical pathological approaches don't capture underlying molecular mechanisms with microscopy (Chen, 2020).

Prior to Slide-seq, molecular studies on varying cell types involved the destruction of the source tissue (Williams, 2023). This significantly limited the cell-in-tissue context for researchers, and the information obtained from these cells was far less capacious. With the development of Slide-seq, researchers have added context regarding environmental gene regulation and its effect on epigenetics (Chen, 2020). During the initial Slide-seq study, researchers discovered cell clusters within the brain cortex that were previously believed to be proportionally dispersed around the cortex (Williams, 2023). Insights like this have begun to shape new thinking and discoveries regarding single-cell research, tissue pathology, and gene up/down regulation.

The Slide-seq biological technique has now been commercialized by Curio Bioscience and is integrated into a kit known as the Curio Seeker. This technology has been used in several publications, including a recent study discovering the specific transcriptomic molecular markers present in mouse ovarian cells during ovulation (Mantri, 2024). Fei Chen, one of the founders of Slide-seq, hopes to see future developments of multidimensional cell atlases of various organisms (Chen, 2020). These models would surely change the future of medical diagnostics and spatial transcriptomics research.

References

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