Vivo-seq: A New Era of Single-Cell Biology Beyond Transcriptomics

Over the past decade, single-cell RNA sequencing (scRNA-seq) has revolutionized biology by allowing us to peer into individual cells and map which genes are active. Yet even with its transformative power, scRNA-seq misses a critical layer of biology:

"It reveals gene expression, but not the signaling events that actually drive cellular decisions."

A new solution is now closing this gap. Vivo-seq simultaneously captures gene expression and intracellular signaling dynamics, giving us a more complete and mechanistic view of cell states and their underlying drivers.

What Exactly Is Vivo-seq?

Vivo-seq is an innovative single-cell platform that measures:

- Gene expression (RNA)
- Intracellular protein signaling activity, specially phosphorylation states

This matters because cellular signaling, such as activation of kinases, stress pathways, or immune cascades happens within seconds to minutes, long before changes in gene expression appear. Traditional scRNA-seq misses this layer entirely.

Vivo-seq fills that gap by preserving signaling proteins during cell processing and integrating them directly into the sequencing readout.

Why Vivo-seq Is a Big Deal

1. It reveals what drives cell states, not just what reflects them
    - Gene expression shows downstream responses. Signaling pathways show upstream triggers.
    - With Vivo-seq, we get both and thereby, enable causal inference.
2. It gives unprecedented insight into immune cell behavior

Immune cells - T cells, macrophages, dendritic cells - make fate decisions based on fast signaling events (e.g., JAK/STAT, MAPK, NF-κB).
Vivo-seq can detect:

- Early activation signals
- Cytokine-driven transcriptional changes
- Pathway rewiring in disease contexts

This has direct implications for immuno-oncology and autoimmune research.

3. It improves the ability to map disease mechanisms

Diseases such as cancer, neurodegeneration, and infection involve signaling dysregulation. By measuring phospho-signaling and transcription in parallel, Vivo-seq can identify:

- Hyperactive vs suppressed pathways
- Drug-responsive cell states
- Mechanisms of resistance
- Biomarker candidates

This can accelerate both target discovery and drug development.

Conclusion

Vivo-seq represents a major milestone in single-cell technology. It allows to see both *what a cell is saying* (RNA) and *what a cell is sensing* (signaling pathways) at the same moment. As multimodal and spatiotemporal technologies continue to evolve, tools like Vivo-seq will be essential for building a deeper, more actionable understanding of biology-one that moves us from snapshots to dynamic, mechanistic insight.

Reference:

Integration of phospho-signaling and transcriptomics in single cells reveals distinct Th17 cell fates