Single-Cell Combinatorial Indexing RNA-seq for Computational Phenotyping of Complex Biological Samples

Challenge

Upon perturbations, biological systems often show **highly cell-type-specific responses**. This is central to research on developmental robustness, where environmental conditions such as temperature can alter developmental timing, proteostasis, and cell-type composition in fish embryos. The same challenge is relevant more broadly to human tissue studies, disease models, drug-response experiments, and other complex biological samples.

A key method in this context is **cell-resolved transcriptomic profiling** across large numbers of samples. Here, conventional single-cell RNA-seq workflows can become cost- and instrument-limited when projects need very large cell numbers, broad sample multiplexing, or repeated comparative phenotyping.

Therefore, there is a **need for scalable single-cell genomics** approaches that can turn complex samples into quantitative phenotypes, linking cell types, cell states, gene expression programs, and biological trajectories to genetic, environmental, or experimental conditions.

Technology

The Dorrity Group has unique expertise in **single-cell combinatorial indexing RNA-seq**, a scalable technology enabling **transcriptomic profiling of millions of cells with extensive sample multiplexing at low cost**. In this workflow, cells or nuclei are labelled through **combinatorial barcoding across multiple indexing steps**, allowing individual transcriptomes and sample identities to be recovered computationally. There is no dependence on dominant commercial droplet-based single-cell platforms making the approach particularly attractive for projects involving large numbers of samples, conditions, perturbations, or biological replicates.

The group combines this molecular technology with **computational phenotyping**: single-cell genomics is used as a platform to quantify cell types, cell states, gene-expression programs, developmental or biological trajectories, and variation across individuals or conditions. This is applied to **zebrafish and medaka embryo systems for whole-animal and complex-sample single-cell analysis** to study developmental robustness, temperature sensitivity, proteostasis, and cell-type-specific stress responses.

Internal EMBLEM Reference

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Applications

This technology is relevant to organizations seeking scalable, cost-efficient single-cell phenotyping across large sample sets.

- **Human tissue and biomedical sample profiling** - large-scale transcriptomic phenotyping of complex tissue collections, cohorts, disease models, or perturbation studies.
- **Drug discovery and translational R&D** - cell state and gene expression readouts for treatment response, mechanism-of-action studies, disease modelling, and screening workflows.
- **Computational phenotyping** - quantitative analysis of cell types, cell states, gene expression programs, trajectories, and condition-specific responses across many samples.
- **Developmental robustness and stress response biology** - use of fish embryo model systems to study how environmental conditions, proteostasis, and developmental timing shape cell-type-specific outcomes.

Benefits

- **Scalable single-cell profiling** - enables analysis of very large numbers of cells in many samples through combinatorial indexing.
- **Flexible sample multiplexing** - supports large experimental designs, cohorts, perturbation series, and comparative studies.
- **Computational phenotyping** - converts single-cell genomics data into quantitative biological readouts of cell type, cell state, trajectory, variability, and response.

Keywords

Single-Cell Combinatorial Indexing RNA-Seq
Single-Cell Genomics
Computational Phenotyping
Sample Multiplexing
Human Tissue Profiling
Developmental Robustness
Environmental Stress
Zebrafish
Whole-Animal Phenotyping

Intellectual Property

☒ Know-how based
☒ Copyright

Commercial Opportunity

This platform offers commercial partners access to scalable single-cell transcriptomic phenotyping for projects that require profiling of many cells, samples, donors, tissues, perturbations, or experimental conditions.

By combining single-cell combinatorial indexing RNA-seq with computational phenotyping, the approach can support collaborative R&D programs and service-oriented partnerships that need broader scale, lower per-sample cost, and more flexible multiplexing than conventional single-cell workflows.

Further Reading

[1] 10.1016/j.cell.2023.10.013

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