Editorial

A focus on single-cell omics

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Cellular heterogeneity lies at the heart of biological complexity and plays a critical role in development, homeostasis and disease. Single-cell omics technologies are paving the way to mapping this diversity.

Until recently, our understanding of cellular dynamics was limited to 'bulk' omics analyses, which yield average measurements for a cell population. The advent of single-cell omics technologies, accompanied by the rapid development of novel computational methods and tools[1], has revolutionized the field by enabling the high-resolution characterization of individual cells. In this Focus issue and its accompanying online collection, we delve into the exciting developments in single-cell omics, highlighting its transformative potential.

Single-cell omics approaches offer a unique perspective on the genome, transcriptome, epigenome, proteome and other omics modalities at the level of individual cells. By capturing the full spectrum of cellular states, these techniques have the power to identify and characterize rare cell types, transitional cell states and cell-to-cell variability previously hidden in bulk analyses.

Single-cell RNA sequencing (scRNA-seq) was a transformative breakthrough, enabling researchers to profile gene expression patterns in thousands of individual cells simultaneously. By illuminating transcriptomic landscapes, scRNA-seq has revealed new cellular subpopulations, cell states and dynamics, shedding light on lineage trajectories, cell fate decisions and cellular responses to external stimuli. The subsequent integration of scRNA-seq with sequencing- or imaging-based spatial omics techniques has rapidly advanced our ability to construct comprehensive cellular atlases and delineate tissue architectures.

Beyond gene expression, single-cell omics has expanded to encompass other layers of cellular information, such as chromatin accessibility, DNA methylation and histone modifications, offering insights into the regulatory landscape of individual cells[2]. By deciphering the epigenetic regulation underlying cellular heterogeneity, these single-cell epigenomics approaches deepen our understanding of gene regulation and cellular plasticity. Additionally, single-cell proteomics techniques have revealed new insights into cellular signalling, protein function and protein–protein interactions at the single-cell level.

Integrating these diverse omics layers offers a holistic view of cellular diversity and will enhance our understanding of cellular function and dysfunction in health and disease. To this end, single-cell and spatial multi-omics techniques (also known as multimodal omics) will be essential, as they allow researchers to explore the complex interplay between genetic variation at the genome level,

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gene regulation at the epigenome level and gene expression at the transcriptome and/or proteome levels in the same cells throughout development, ageing and disease[3].

Single-cell omics has immense potential to decipher the complexities of human diseases. For example, single-cell expression quantitative trait locus (eQTL) studies are enabling the investigation of genetic variants that influence gene expression at the level of individual cells[4]. Linking single-cell data and matched genotype data for hundreds or thousands of people will help to delineate how genetic variation affects cellular phenotypes, including causal pathways in disease. In cancer research, single-cell genomics has helped to profile intratumoral heterogeneity, identify and characterize rare cell types and study clonal evolution.

One of the most exciting prospects of single-cell omics lies in its clinical application. By capturing the molecular heterogeneity within a tissue or tumour, single-cell analyses can reveal the cellular states that drive disease progression, identify novel therapeutic targets and guide personalized medicine approaches. However, despite remarkable achievements, there remain challenges in translating single-cell omics from bench to bedside[5]. Technical considerations need to be addressed to ensure scientific accuracy and reproducibility. Furthermore, integrating different omics data modalities remains a complex task, demanding advanced computational methods and standardization[1].

Looking to the future, the refinement of techniques for other omics 'layers', such as single-cell metabolomics and spatial proteomics, promises the capture of additional cellular information. Moreover, the development of new statistical and computational methods to analyse omics data, for example, the inference of cell–cell interactions from gene expression data, will continue to lead to new biological insights that drive the field forward.

Single-cell omics has empowered researchers to explore the intricacies of cellular heterogeneity at unparalleled resolution. As these technologies advance, we embark on a journey that paves the way for a deeper understanding of biological systems.

References

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