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Popular Article

Single Cell Genomics

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Abstract

Single-cell genomics is the study of cellular uniqueness utilizing omics methodologies. While being young, the field has now reached adolescence and is starting to demonstrate definite maturity. Its roots can be found in early studies that made it possible for microarrays to measure gene expression in individual cells. But, single-cell genomics really took off with the development of "next-generation" DNA sequencing. Even though the first studies were small in scale and produced noisy and unreliable data, they were able to demonstrate the enormous potential for biological discoveries. It quickly became apparent that in order to allow for meaningful data mining and interpretation of the data, the significant technical and biological diversity required data from many single cells. Hence, the following years were devoted to working on a few lines of development: enhancing the precision and applicability of single-cell technologies, raising throughput, and lowering cost.
Keywords: DNA, phenotypic, RNA, tumor

Introduction

Currently, we are capable of consistently quantifying gene expression in tens of thousands of single cells with good accuracy (although the sensitivity for detecting mRNAs varies greatly depending on the procedure and sequencing depth). At least the costs are controllable and are going down. The focus of technical advancement has turned to other modalities, including DNA, protein, chromatin changes, and more, even though single-cell RNA-sequence is already developed and almost regular. Single-cell whole-genome DNA sequencing is problematic because sequencing

errors are difficult to identify from actual mutations and material loss results in dropouts in the sequence. Notwithstanding these difficulties, lineages based on somatic mutations that accumulated during development have been reconstructed using single human cortex neurons. Similarly, by identifying somatic copy number differences in individual cells, clonal evolution inside solid tumors can be identified.

The use of single-cell analysis to detect epigenetic states such as DNA accessibility, methylation, and chromosomal conformation is another emerging trend. These techniques typically present difficulties comparable to those of DNA sequencing, but they provide access to pure cellular epigenetic states that are unattainable by bulk techniques. In single-cell protein analysis, which traditionally used fluorescence-activated cell sorting (FACS) for up to eight targets but more recently with mass cytometry targeting up to hundreds of proteins, fewer proteins can be studied but in very large numbers of cells. The need for top-notch affinity reagents, such antibodies, continues to be a constraint for protein analysis.

The combination of techniques to measure two or more modalities simultaneously in a single cell is a new discovery. For instance, RNA and protein, transcriptome and methylome, and genome and transcriptome. These studies will soon be able to connect the genotypes of individual cells developing in tumors to their behaviors. Computational analysis techniques are striving to keep up with the rapid advancement of single-cell genomics technologies. The core of single-cell genomics is statistical and computational approaches, which are essential for deriving biology and useful information from the data. The definition of significant variations in the cell-to-cell variance in gene expression (as opposed to mean expression levels) is presented for individual genes. There is unquestionably a huge need for new developments in computational methods in the field of tumour heterogeneity in terms of cell-to-cell variation at the DNA level (Linnarsson and Teichmann, 2016).

Recent applications

Understanding of immune system, brain, and hematopoietic cell types, as well as single-cell RNA sequencing, has had a significant influence. New regulators and subpopulations of CD4+ T cells, as well as a window into the mouse immune system's unexpected abundance of dendritic cells, are a few examples of recent insights in immunity. Several single-cell transcriptomics studies in hematopoiesis have concentrated on hematopoietic stem cells, and the single-cell approach has

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helped to clarify proliferation characteristics, a more comprehensive perspective on the early specification of hematopoietic cell types.

It may not come as a surprise that single-cell transcriptomics can be used to nonadherent cells, such as those involved in immunology and hematopoiesis, because they are stable after being isolated as single cells using FACS or microfluidic devices. The success of single-cell RNA sequencing in neurobiology and neuronal cell populations is particularly remarkable because these cells are connected by networks of adherent junctions. A full catalogue of molecularly defined cell types in the entire nervous system will one day be available. Lately, detailed maps of cell types and subtypes have been created for a number of important brain regions, including the developing and adult cerebral cortex. The validation of novel cell states, cell populations, and variables in this field is encouraging for expanding the use of single-cell transcriptomics to solid organs and tissues. In both somatic cell types like neurons and cancer, the DNA dimension—that is, tracking mutations, copy number variations, and chromosomal abnormalities at the single-cell level—has proved crucial. In a xenograft model, single-cell dissection of tumor heterogeneity can result in new combinatorial medicines.

Future prospects

Looking into our crystal ball, it is simple to forecast that single-cell genomics will play an increasingly important role in discovery science, translational applications, and even ecology. The breakthrough in DNA, epigenetic, and RNA sequencing resolution to the level of a single cell is the main force behind the single-cell genomics revolution. Since the cell is the fundamental unit of an organism, sequencing individual cells separately yields information that is fundamentally distinct from genomic data that pertains to cell ensembles. The RNA present in a cell provides extensive information on its phenotypic and function in terms of single-cell transcriptomics. It is conceivable that the community will eventually map all mammalian organs, tissues, and cell types at single-cell resolution because this method is so effective and instructive. A comprehensive collection like this, which is essentially a "human cell atlas," would be a very valuable and special set of reference data for biology and medicine.

Single-cell genomics began in academia and fundamental research, much like many prior waves of biotechnology, but is now poised to enter the pharmaceutical industry and the clinical

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setting. Every sick tissue can be compared to the atlas of human cell types once it is available. A single-cell analytic makeover will be particularly appropriate for cancer, the archetypal single-cell disease. Diagnostic assays will be significantly more effective once they are brought down to the level of the specific transformed cell, in the context of its surrounding tissue, with cell-type specificity, and with a thorough understanding of somatic mutations. Currently, diagnostic assays are based on crude bulk methods (Linnarsson and Teichmann, 2016).

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