Single-cell analysis: Advances and future perspectives

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ABSTRACT

The last several years have seen rapid development of technologies and methods that permit a detailed analysis of the genome and transcriptome of a single cell. Recent evidence from studies of single cells reveals that each cell type has a distinct lineage and function. The lineage and stage of development of each cell determine how they respond to each other and the environment. Experimental approaches that utilize single-cell analysis are effective means to understand how cell networks work in concert to coordinate a response at the population level; recent progress in single-cell analysis is offering a glimpse at the future.

Introduction: In living tissues, there are a large number of cell types with the assumption that each cell type has a distinct lineage and function. However, recent evidence from studies of single cells reveals that this assumption is incorrect. Cells may be morphologically and genetically identical but are actually heterogeneous, made up of individual cells that differ dramatically. These differences can have important consequences for the health and function of the entire population. Single-cell analysis allows the study of cell-to-cell variation within a cell population (organ, tissue, and cell culture). In order to study diseases and drug development, in-depth analysis of stem cell differentiation, cancer, physiological functions in embryos and adults can only be accomplished with single-cell analysis [1-4].

Sample Preparation: To isolate a single cell from a heterogeneous population of cells in a manner that preserves biological integrity, there are several approaches available [5]. Besides several well-established methods, such as micromanipulation, laser-capture microdissection and fluorescence-activated cell sorting, there is an increasing number of novel techniques to isolate single cells with even greater accuracy and specificity [6,7].

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In recent years, innovative technologies for single-cell genomics, transcriptomics, and proteomics, with a particular emphasis on quantification and multiplicity that can perform measurements on many single cells in a given experimental run, include microfluidics, optical tweezers, transcriptome *in vivo* analysis, and mass cytometry [4,8-10].

Applications: Advances in whole-genome and whole-transcriptome amplification have permitted the gene expression profiling and sequencing of the minute amounts of DNA and RNA present in a single cell, offering a window into the extent and nature of genomic and transcriptomic heterogeneity which occurs in both normal development and disease. Each cell in the body has a unique genomic structure, which allows the reconstruction of cell lineage trees with very high precision that can predict the existence of small population of steam cells. This information is important for cancer research for detection of rare tumor cells, preimplantation, and genetic diagnosis [11-13]. Single-cell approaches have been utilized for understanding the intricate cellular interplay involved in immune response that requires single-cell resolution, especially with rare antigen-specific T- or B-cells [14,15]. In addition, protein expression analysis is vital to understand the true metabolic or functional state of cells and the single-cell approach enables simultaneous analysis of more than 35 proteins of individual cells [16,17]. Currently, researchers are starting to combine single-cell genomics with single-cell proteomics to tackle important questions in fields including cancer, stem cell biology, neuroscience, developmental biology, and infectious disease. As more investigators explore heterogeneity in cell populations, knowledge of intricate biological

cellular networks will empower researchers to discover new ways to diagnose and treat disease.

Challenges: The advances of single-cell analysis over the past 5 years have happened at a lightning pace, and the potential for their use in various fields is high. However, the novelty of these single-cell techniques also implies various limitations. There is a lack of cross-disciplinary collaboration to more effectively utilize advantage of single-cell analysis. Another caveat is that algorithms for the analysis of single-cell data are even less mature than the experimental platforms, and effective interpretations of what are increasingly large datasets remain challenging, with techniques that vary across research groups [4,11,17].

DECLARATION OF INTERESTS

The author declares no conflict of interests.

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