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Mini Review

# Single-Cell Multiomics: Tools and Techniques for Data Analysis

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#### Abstract

Unprecedented chances to characterise DNA, mRNA, and proteins at a single-cell resolution are now possible thanks to advancements in single-cell isolation and barcoding technology. For gaining a thorough understanding of biological events, bulk multiomics analyses, such as multidimensional genomic and proteogenomic investigations, have recently proven helpful. This advantage has aided in the development of single-cell multiomics analysis, allowing for the investigation of cell type-specific gene regulation (Yusuf SR et al., 2017). The fundamental components of single-cell multiomics analysis are (1) technologies for single-cell isolation, barcoding, and sequencing to measure various types of molecules from individual cells, and (2) integrative analysis of molecules to characterise different cell types and their functions in relation to pathophysiological processes based on molecular signatures. The technologies for single-cell multiomics analyses (mRNA-genome, mRNA-DNA methylation, mRNA-chromatin accessibility, and mRNA-protein) are outlined here, along with the procedures for integrative analysis of single-cell multiomics data (Edem VF et al., 2012).

## INTRODUCTION

The essential and inherent properties of stem cell populations are cell-to-cell variation and heterogeneity, but when bulk cells are employed for omic research, these distinctions are obscured. Even within a population of 'homogeneous' stem cells, single-cell sequencing methods are effective tools for fully analysing cellular heterogeneity and recognising different phenotypic cell types. These technologies, such as those for sequencing the single-cell genome, epigenome, and transcriptome, have advanced quickly in recent years. Exciting new discoveries in the stem cell field have resulted from the application of these techniques to many types of stem cells, including pluripotent stem cells and tissue-specific stem cells (Kingsley CK et al., 2016). In this review, we cover recent developments as well as potential directions for single-cell omic sequencing technologies' techniques and applications. The number of proteins that can be detected using current single-cell multiomics technology is limited due to low sensitivity. This could result in biassed proteome interpretation. This is a problem because the activities of the measured proteins in individual cells should be determined by their interactions with other proteins. New single-cell experimental techniques must be created in order to increase the sensitivity (mutations, CNVs, and proteomes), accuracy (DNA methylation and phosphoproteome), and coverage (mutations, CNVs, and proteomes) of single-cell multiomics measurements. To infer previously unknown regulatory linkages, such as the mutation and phosphorylation of signalling molecules, novel omics combinations for various multichannels of molecules are also necessary (Ozer J et al., 2008).

Cellular heterogeneity, which is a widespread occurrence, is crucial to biological processes like embryonic development, cell differentiation, and disease progression. For identifying various cell populations, finding new cell types, exposing instructive cell properties, and revealing major intercellular interactions, single-cell omics-based heterogeneity investigations are very important. Due to its advantages in terms of throughput, sensitivity, and accuracy, microfluidics has recently developed into a potent technique for singlecell omics investigation (Haratym-Maj A 2002). This article reviews the most current developments in microfluidic single-cell omics analysis, including various microfluidic platform designs, lysis techniques, and omics analysis methods. The results of a selection of sophisticated biological research using microfluidic single-cell omics analysis are then compiled. Finally, a few viewpoints on potential issues and future directions for single-cell omics analysis using microfluidics are explored (Tela IA et al., 2016).

### DISCUSSION

In contrast to single omics data based on multichannel molecular readouts, single-cell multiomics techniques enable a more thorough delineation of the state of single cells, opening up previously unexplored opportunities to systematically examine cellular variety and heterogeneity. Based on the relationships between causal factors and target genes in cell populations, the integration of several molecular readouts can offer insights into the causal factors that regulate cellular states (Chaudhry D et al., 2014). The relationship between genomic changes and the transcriptional repercussions for target genes engaged in disease-related processes, for instance, can be discovered using genotype-phenotype correlations assessed through the integrative analysis of single-cell genome and transcriptome data. Additionally, regulatory connections between epigenetic modifications and the expression of target genes can be revealed by an integrative investigation of the transcriptome and epigenome. Additionally, combining data from other omics layers, such as DNA, RNA, and protein data, can improve the precision of identifying cell populations, cellular trajectories, or lineage tracing, as well as novel or uncommon cell types (Mohamed SA 2017).

Single-cell multiomics analysis has only recently begun to be applied. There are still a lot of options for growth and various pathways that need to be explored. In addition, there are still a number of technical and computational obstacles that need to be removed in order to enhance the informational value and content of single-cell multiomics analysis. For instance, bisulfite treatment might cause DNA damage, which may compromise the precision of the DNA methylome measurement. Cell fixation is also likely to lower information yield, which introduces bias into the data. Because the functions of the measured proteins in single cells should be determined by their interactions with other proteins, the number of proteins that can be detected using current single-cell multiomics technologies is constrained due to insufficient sensitivity, which may introduce bias in the interpretation of the proteome (Friday U et al., 2015). To increase the sensitivity (mutations, CNVs, and proteomes), accuracy (DNA methylation and phosphoproteome), and coverage (mutations, CNVs, and proteomes) of single-cell multiomics measurements, existing single-cell experimental protocols must be optimised, or new protocols must be developed. In addition, novel omics combinations for various multichannels of molecules are required in order to infer hitherto unrecognised regulatory linkages, such as the mutation and phosphorylation of signalling molecules.

### CONCLUSION

The number of proteins that can be detected using current single-cell multiomics technologies is limited due to insufficient sensitivity, which may introduce bias in the interpretation of the proteome. This is problematic because the functions of the measured proteins in single cells should be determined by their interactions with other proteins. Existing single-cell experimental procedures must be improved, or new protocols must be created, in order to increase the sensitivity (mutations, CNVs, and proteomes), accuracy (DNA methylation and phosphoproteome), and coverage (mutations, CNVs, and proteomes) of single-cell multiomics measurements. In order to infer previously unknown regulatory linkages, such as the mutation and phosphorylation of signalling molecules, novel omics combinations for various multichannels of molecules are also necessary. Due to poor sensitivity, the number of proteins that can be detected with current single-cell multiomics technologies is constrained (Yunusa H et al., 2018). This may lead to bias in the interpretation of the proteome. The activities of the measured proteins in individual cells should be dictated by their interactions with other proteins, therefore this is a concern. To improve the sensitivity (mutations, CNVs, and proteomes), accuracy (DNA methylation and phosphoproteome), and coverage (mutations, CNVs, and proteomes) of single-cell multiomics measurements, new single-cell experimental protocols must be developed. Novel omics combinations for diverse multichannels of molecules are also required to infer hitherto unidentified regulatory linkages, such as the mutation and phosphorylation of signalling molecules.

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