

Single cell transcriptomics view of cell lineage, cell fate and cellular differentiation

Wenfa Ng

Unaffiliated researcher, 33-B Newton Road, Singapore 307985, Singapore

Email: ngwenfa771@hotmail.com

Abstract

Single cell studies increasing reveal myriad cellular subtypes beyond those postulated or observed through optical and fluorescence microscopy as well as DNA sequencing studies. While gene sequencing at the single cell level offer a path towards illuminating, in totality, the different subtypes of cells present, the technique nevertheless does not offer answers concerning the functional repertoire of the cell, which is defined by the collection of RNA transcribed from the genome. Known as the transcriptome, transcribed RNA defines the function of the cell as proteins or effector RNA molecules, while the genome is the collection of all information endowed in the cell type, expressed or not. Thus, a particular cell state, lineage, cell fate or cellular differentiation is more fully depicted by transcriptomic analysis compared to delineating the genomic context at the single cell level. While conceptually sound and could be analysed by contemporary single cell RNA sequencing technology and data analysis pipelines, the relative instability of RNA in view of RNase in the environment would make sample preparation particularly challenging, where degradation of cellular RNA by extraneous factors could provide a misinterpretation of specific functions available to a cell type. Hence, RNA as the *de facto* functional molecule of the cell defining the proteomics landscape as well as effector RNA repertoire, meant that RNA transcriptomics at the single cell level is the way forward if the goal is to understand all available cell types, lineage, cell fate and cellular differentiation. Given that a cell state is defined by the functions encoded by functional molecules such as proteins and RNA, single cell RNA sequencing offers a larger contextual basis for understanding cellular decision making and functions, for example, proteins are increasingly known to work in concert with RNA effector molecules in enabling a function. Hence, providing a view of the diverse cell types and lineages present in a body, single cell RNA sequencing is only hampered by the high sensitivity required to analyse the small amount of RNA available in single cells, as well as the perennial problem of RNA studies: how to prevent or reduce RNA degradation by environmental RNase enzymes. Ability to reduce RNA degradation would provide the cell biologist a unique view of the functional landscape of different cells in the body through the language of RNA.

Keywords: single cell RNA sequencing, RNA repertoire, protein landscape, cell lineage, cell differentiation, cellular decision making, RNA degradation, RNase, cell fate, cellular subtypes,

Subject areas: microbiology, biotechnology, molecular biology, biochemistry, cell biology,

Genomics is commonly thought to be the method for understanding the functional repertoire of cells, which, by extension, would reveal the different cell types, fates, lineages and cellular differentiation available to a consortium of cells within a locale such as the human body.

However, most of the genes encoded within the genome of a cell are not expressed; thus, the functional repertoire of a cell as defined by the proteome and effector RNA molecules would be better represented by the transcriptome, which is the collection of all RNA transcribed by the genome. From the perspective of understanding cellular function and physiology, the transcriptomics approach bears closer resemblance to the true depiction of cellular activities and functions than a genomics strategy.

Given that different cell types, fates, lineages and cellular differentiation are each defined by the collection of proteins and effector RNA molecules present, a transcriptomic view of cellular activities would be better able to highlight the differentiator molecules that help potentiate a cell into one fate rather than another. The same is true for cell lineage and cellular differentiation.

Thus, a transcriptomics view of the functional landscape of a cell at the single cell level, through a relatively new technique known as single cell RNA sequencing, is the preferred approach for defining the differentiators that help classify different cell subtypes into distinct lineages, fates, and cellular differentiation. While difficulty of extracting meaningful results from the small amount of RNA present in each cell remains a significant challenge, future improvement in sensitivity and reliability of the technique would help classify different cellular differentiation and lineages based on averages of a small consortium of cells from single cell RNA sequencing. Currently, there needs to be alignment of the different packages important to analysis of the wealth of single cell RNA sequencing data into software amenable for use by the average researcher. Another challenge lies in the relative instability of RNA with respect to RNase enzymes. Thus, sample preparation is a key area for refining the approach of single cell RNA sequencing for understanding the different cellular subtypes, lineages, fates and differentiation present in a consortium of cells in a locale, where absence of key RNA due to sample degradation could lead to erroneous results.

Conflicts of interest

The author declares no conflicts of interest.

Author's contribution

The author thought about the possibility of using a genomic context to define the differing cell lineage, cell fate and cellular differentiation exhibited by diverse cell subtypes in the human body, and come to the conclusion that given that not all genes are expressed, a cell type differentiator based on genomics may not capture the full functional repertoire of a cell, which

is abstracted by the cell's RNA transcriptome. Hence, he wrote to highlight to the biology community on the possibility of using RNA transcriptomics at the single cell level to classify various cell lineage, cell fate and cellular differentiation.

Funding

No funding was used in this work.