Single–Cell Genome Sequencing:

Sharp-Shooting the Cancer-Cells' Genome.

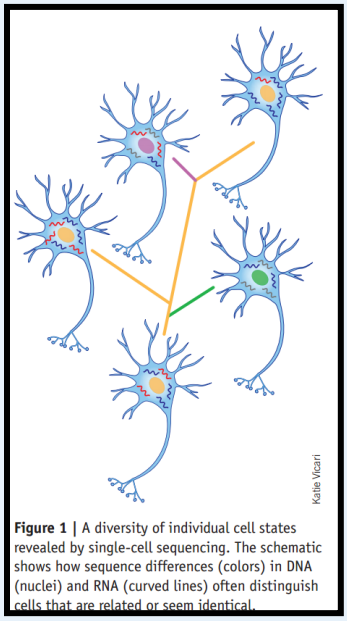


Figure 1 | A diversity of individual cell states revealed by single-cell sequencing. The schematic shows how sequence differences (colors) in DNA (nuclei) and RNA (curved lines) often distinguish cells that are related or seem identical.

Background:

Cells that are phenotypically the same are generally seen as identical functional units. Recent developments based on the sequencing capabilities that have been created over the last two decades suggest that there is "a more complex ecology of heterogeneous cell states that together produce emergent system-level function"(1). The figure on the right shows an illustration of how cells of the same type may have genome that is more variable than we previously understood.

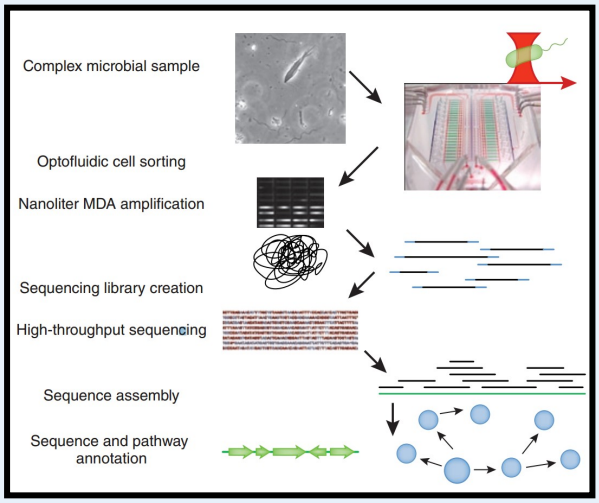
Concept and applications

In order to better understand this variation within a cell's own microenvironment, there are studies with the goal of obtaining accurate and real-time measurements of genomic data from single cells in the same microenvironment. Some examples of application are:

- Studies of intra-tumor heterogeneity of cancer cells and treatment response.
- Identify genomes of "unculturable" microorganisms.
- Evaluate roles of "genetic mosaicism" in normal and diseased physiology. (2)

How It works:

The figure on the right demonstrates an example how single-cell genome analysis works. You must first use microfluidics to sort single cells from a complex tissue sample. Next you must amplify and create a library of the DNA. Lastly, you must perform high throughput sequencing so that you can assemble and annotate the sequence.



Challenges:

(3)

Currently, in 2016, the challenge of cell isolation has been achieved with enough throughput to keep up with the sequencing technology. According to the paper by Gawad et al., the challenges also lie in

- whole genome amplification
- interrogation of amplified products
- single cell sequenced errors
- single cell variant calling (because of errors)
- determining genetic relationships between cells (variation vs relative distance)(1).

1. Eberwine, J.-Y. Sul, T. Bartfai, J. Kim, The promise of single-cell sequencing. *Nat Meth* **11**, 25-27 (2014).
2. C. Gawad, W. Koh, S. R. Quake, Single-cell genome sequencing: current state of the science. *Nat Rev Genet* **17**, 175-188 (2016).
3. T. Kalisky, S. R. Quake, Single-cell genomics. *Nat Meth* **8**, 311-314 (2011).