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Advancing the Arizona State University Knowledge Enterprise

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Single-cell In Situ DNA and/or RNA Sequencing

-Sequencing platforms have come a long way and are now capable of delivering enormous amounts of high-quality data, allowing for the possibility of sequencing the genomes of thousands of individual cells. Single-cell sequencing enables the examination of heterogeneity within populations and identifying rare or low frequency mutations that contribute to biological behaviors. However, current methods to isolate and tag single-cell genomes for sequencing require specialized equipment, making them expensive, low throughput and arduous.

Researchers at the Biodesign Institute of Arizona State University have developed novel methods for in situ, high throughput, single-cell, whole genome sequencing. Not only can these methods be used to sequence the genomic DNA of individual cells in large heterogeneous cell populations, they can also be used to sequence the RNA in those same individual cells at the same time. This allows for instantaneous mapping of genotype to phenotype in the same cell. Further these methods are more user-friendly and highly scalable, permitting multiplexing of single cells from up to 96 different growth conditions or genetic backgrounds at one time. With the use of barcodes, the reads, once sequenced, can be mapped back to their original cell and the genome can be assembled.

By dramatically improving the throughput, cost and accessibility of single cell genomic sequencing, many more research goals and studies become attainable.

Potential Applications

- Single cell DNA and/or RNA sequencing
  - Cancer evolution – tumor pathogenicity, drug resistance, transcriptional profiling of tumor diversity, etc.
  - Microbiome diversity
  - Transcriptome diversity – particularly in mutant strains/libraries
  - Developmental genetics – gametocyte characterization
  - Plant genetics – understanding genes that contribute to drought or temperature tolerance

Benefits and Advantages

- Highly scalable - allows simultaneous multiplexing of single cells from up to 96 different growth conditions or genetic backgrounds
  - Can identify rare or low frequency mutations in a population
  - Provides a more detailed picture of microbes in specific environments
  - Can characterize cells that all have unique DNA assortment, such as gametocytes
  - Can determine the distribution of heterogeneous genomes in a population of cells, such as a tumor
  - Captures genetic diversity broadly or at a region of interest while simultaneously sampling the transcriptome
- User-friendly - does not require cell sorting or isolation
- Each whole genome is amplified and tagged with barcodes inside the original cell
- Conflicting reagents can be washed without interfering with the genetic material within the cell – multiple chemical and/or enzymatic reactions can be applied

For more information about the inventor(s) and their research, please see

Dr. Geiler-Samerotte's Biodesign webpage

Dr. Geiler-Samerotte's laboratory webpage