Massively parallel sequencing technology for single-cell gene expression published

February 5 2015

A publication released today in the journal *Science* demonstrates a new, massively parallel technology to interrogate gene expression at the single-cell level using next-generation sequencing (NGS). Authors Christina Fan, Ph.D., Glenn Fu, Ph.D., and Stephen Fodor, Ph.D., from Cellular Research, Inc., describe the technology and report results from several gene expression studies of cells from the human hematopoietic system.

Fan et al. note in the publication that single-cell analysis is increasingly necessary for understanding heterogeneous systems. Without this level of resolution, for example, large expression changes from a few cells appear the same as small expression changes from many cells.

In the manuscript, the scientists describe "a technically simple approach for gene expression cytometry" that uses cell- and molecule-specific barcodes to allow for the study of large numbers of genes in tens of thousands or even hundreds of thousands of cells at a time. Individual cells and primer-bearing beads are placed into microwells; when the cells are lysed, mRNAs hybridize to the barcoded primers on the beads. The beads are magnetically retrieved and moved to a tube for reverse transcription and amplification, followed by NGS analysis. "Sequencing of amplification products reveals the cell label, the molecular index, and the gene identity," the authors write. "Computational analysis groups the reads based on the cell label and collapses the reads with the same molecular index and gene sequence into a single entry to correct for amplification bias, allowing the determination of absolute transcript numbers for each gene in each cell."

"This unique labeling strategy and massively parallel approach make single-cell analysis of gene activity feasible and straightforward for any researcher with access to an NGS platform," said Christina Fan, Ph.D., lead author on the paper and Staff Scientist at Cellular Research.

The publication also reports data from various types of hematopoietic cells using this technology. The scientists analyzed some 15,000 cells, estimating a consumable cost of pennies per cell when performed at high throughput. In a number of experiments, Fan et al. recapitulated decades of research results characterizing the individual cellular subtypes constituting an active hematopoietic system. They used other challenging biological problems to show the power of this new technology, demonstrating for example the detection of rare malignant cell types at very low numbers in a large background of normal cells.

"The Resolve technology will open vast new opportunities, and reveal new insights, in developmental biology and disease," said Stephen Fodor, senior author on the paper and Chief Executive Officer of Cellular Research. "Examining the genetic profile of large populations of individual cells should enable the discovery of therapeutics with higher patient response rates and the development of more informative and earlier-stage diagnostics."

The paper, entitled "Combinatorial labeling of single cells for gene expression cytometry," appears in the February 6, 2015 issue of *Science*.

More information: www.sciencemag.org/lookup/doi/ … 1126/science.1258367

Provided by Bioscribe