New genomic sequencing method enables 'smarter' anaysis of individual cells

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Only by viewing a Seurat painting at close range can you appreciate the hidden complexities of pointillism – small, distinct dots of pure color applied in patterns to form an image from a distance. Similarly, biologists and geneticists have long sought to analyze profiles of genes at the single cell level but technology limitations have only allowed a view from afar until now.

Research published in the July 22 issue of *Nature Biotechnology,* shows for the first time that a novel genomic sequencing method called Smart-Seq can help scientists conduct in-depth analyses of clinically relevant single cells. Smart-Seq has many possible applications, including helping scientists to better understand the complexities of tumor development. This is vitally important as many clinically important cells exist only in small numbers and require single cell analysis. The study was conducted by a team of researchers from the Ludwig Institute for Cancer Research, the Karolinska Institutet in Sweden, the University of California, San Diego and Illumina Inc.

"While our results are preliminary, we showed that it is possible to do studies of individual, clinically relevant cells," says biomedical scientist Rickard Sandberg, researcher at the Ludwig Institute for Cancer Research and principal investigator at the Department of Cell and Molecular Biology, Karolinska Institutet. "Cancer researchers around the world will now be able to analyze these cells more systematically to enable them to produce better methods of diagnosis and therapy in the future."

Previous research showed that it is common for one gene to give rise to several forms of the same protein through different cut-and-paste configurations of its raw copy. The phenomenon, known as splicing, means that cells from the same tissue are not so homogenous as previously thought.

The research team has now taken its study a step further and developed a method for the complete mapping of the gene expression of individual cells. In showing which genes are active, it is now possible to accurately describe and study differences in gene expression between individual cells from the same tissue.

"Scientists have been waiting for a long time for such a method to come along, but technical limitations have made it difficult to produce a sufficiently sensitive and robust method," says Dr. Sandberg. "The method has several areas of applications including cancer research where it can be used to study which cell types form cancer tumors in individual patients."

In the study, scientists studied tumor cells in the blood system of a patient with recurring malignant melanoma. Once they had identified the tumor cells in a regular blood test, the team used Smart-Seq to analyze their gene expression. By using this method, researchers could show that the tumor cells had activated many important membrane proteins that are understood to be responsible for their ability to evade the body's monitoring system and spread in the blood or lymph.

More information: 'Full-Length mRNA-Seq from single cell levels of RNA and individual circulating tumor cells', Daniel Ramsköld, Shujun Luo, Yu-Chieh Wang, Robin Li, Qiaolin Deng, Omid R. Faridani, Gregory A. Daniels, Irina Khrebtukova, Jeanne F. Loring, Louise C. Laurent, Gary P. Schroth and Rickard Sandberg, Nature Biotechnology, online publication 22 July 2012.

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