Medical Xpress

Project to capture and interrogate single cancer cells wins innovator award

January 11 2013

From a single cell gone bad, cancer evolves into an increasingly complex tumor built of a variety of normal cells and diverse malignant cells, some of which escape to create dangerous colonies in other organs, further jumbling the treatment picture.

Nicholas Navin, Ph.D., an assistant professor in The University of Texas MD Anderson Cancer Center Department of Genetics, believes the key to sorting out this cellular chaos is by identifying important mutations in single tumor cells at various stages of the cancer's development.

Successfully analyzing differences in active mutations among cells would help researchers understand, map and eventually block the lethal path to metastasis – spread of the primary cancer to other organs.

"The genetic diversity of tumor cells inhibits our understanding of metastasis. Single-cell sequencing will allow us to detail the genetic heterogeneity and trace the cell's lineage as mutations allow the cell to escape the primary tumor site, form a circulating cell and then seeds metastasis," Navin said. "Using genetic markers, we can reconstruct this evolutionary process."

The Damon Runyon Cancer Research Foundation wants Navin to test his idea, naming him the Nadia's Gift Foundation Innovator, one of its 2013 Damon Runyon-Rachleff Innovation Awards, providing $150,000 a year for three years.

Potential to predict metastasis, treatment response

Navin is one of seven early career scientists chosen for innovation awards because their projects have the potential to significantly improve prevention, diagnosis and treatment of cancer. The foundation announcement notes the innovation awards are for "cancer research by exceptionally creative thinkers with "high-risk/high-reward" ideas who lack sufficient preliminary data to obtain traditional funding."

The foundation noted that Navin's method "will have myriad clinical applications, which have prognostic value in predicting invasion, metastasis, survival and response to chemotherapy."

Navin is grateful to the foundation for support of the project, which he agrees is high-risk, high-reward because it aims to break new ground in the genomic analysis of cancer.

First, he must develop tools to reliably isolate individual cancer cells and identify mutations in all of the genes that encode proteins. Then he will apply single-cell gene sequencing to triple-negative breast cancer, the most lethal form of the disease.

Develop tools, apply them to triple-negative breast cancer

"Most of the tools we have now operate on bulk tumor tissue samples, which include normal supportive cells, or stroma, and immune system cells as well as cancer cells, which have different genetic mutations," Navin said. "So when we analyze tissue in bulk, we find the average genetic signal of the tumor. What you miss are the rare cells that may be most malignant."

Identifying these cells is particularly important for those with triple-negative breast cancer, which does not have the three protein targets that make other breast cancers much more treatable.

"Triple-negative breast cancer is the most aggressive type, with lowest survival rates, the most intratumor genetic heterogeneity, and it metastasizes the most," Navin said. "So there's really a dire need to help these patients by developing new therapies to inhibit metastasis."

To sequence the full coding regions of each single cell, Navin's lab will isolate single cells that have naturally doubled their chromosome content. The cell will be dissolved and the DNA will be expanded from picogram (trillionth of a gram) to nanogram (billionth) quantities using whole-genome amplification. This will provide sufficient material to generate libraries for 'next-generation' sequencing on the Illumina platform.

From this data, the full set of coding mutations can be detected in each cancer cell and compared to trace the lineage of their evolution during metastasis.

The project also will examine fundamental issues in cancer metastasis. "In cancer biology there's a big question about whether cells metastasize early in the growth of the primary tumor or if that occurs after the tumor has grown to a large size," Navin said. "Another model proposes that tumor cells can travel back and forth between primary and metastatic tumor sites. We're interested in looking at and understanding those models in triple- negative breast cancer."

Provided by University of Texas M. D. Anderson Cancer Center

interrogate-cancer-cells-award.html