Researchers perform complete genomic sequencing of brain cancer cell line

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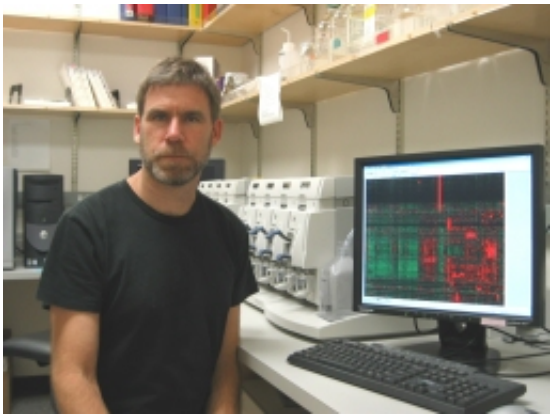

Dr. Stan Nelson

(PhysOrg.com) -- Researchers at UCLA's Jonsson Comprehensive Cancer Center have performed the first complete genomic sequencing of a brain cancer cell line, a discovery that may lead to personalized treatments based on the unique biological signature of an individual's cancer and a finding that may unveil new molecular targets for which more effective and less toxic drugs can be developed.

The study also may lead to new and better ways to monitor for brain cancer recurrence, allowing for much earlier diagnosis and treatment when the cancer returns. Clinicians also could use the finding to develop a test to determine when the brain cancer has been killed, preventing overtreatment with harmful drugs that can later cause debilitating health

problems.

Using the latest technology, the sequencing was done in less than a month and cost about $35,000. By comparison, the sequencing of the human genome took years, required huge teams of scientists and cost more than $1 billion, said Dr. Stan Nelson, a professor of human genetics, a researcher at UCLA's Jonsson Comprehensive Cancer Center and senior author of the study.

"This is very exciting because we, as scientists, can now move forward with revealing complete cancer genomes," said Nelson, who directs the cancer center's Gene Expression Shared Resource. "Cancer is at its heart a genetic disease. Cancer cells have acquired mutations that allow them to invade tissues and to not live by the normal rules. The changes from normal (mutations) that have given the cancer these special properties are encoded in DNA, and the entire DNA sequence has just been to complex and costly to decode until now."

The study appears in the Jan. 29, 2009 issue of PLoS Genetics, a peer-reviewed journal of the Public Library of Science.

The sequencing was done on a much studied glioblastoma cell line called U87, which is being used in more than a dozen UCLA cancer laboratories and studied in more than 1,000 laboratories worldwide, Nelson said. They picked the cell line, he said, because it has been so thoroughly examined. The sequencing will allow scientists who have studied the cell line to reinterpret their findings and may prompt researchers to move in new directions going forward.

The sequencing revealed virtually all potentially cancer-causing chromosomal translocations and genetic deletions and mutations that may have resulted in this cancer's development. The study involved taking the very long strands of genetic material from the cancer cells and

sheering them, or cutting them up randomly. Billions of different DNA fragments from this cancer were simultaneously read with next generation sequencing technology. The genetic material was analyzed more than a billion times to ensure the results would be both highly sensitive and accurate, Nelson said.

"This was the most thorough sequencing analysis of an individual cancer cell line that has been performed to date," Nelson said. "We developed specific informatics tools to help with the analysis and used the most powerful technology available. As scientists, we previously didn't know most of the mutations that occur within a given cancer - we're blind to them. Now this new technology allows us to look at every single cancer and decode that cancer genome completely so there's no chance we're missing a mutation that may be causing the disease."

Knowing the genes that are mutated and driving the cancer's growth could allow clinicians to choose therapies most suited to attack the specific molecular signature of that patient's disease to provide more effective treatment. The sequencing also could reveal a molecular abnormality that is driving the cancer, unveiling a target that could lead to the development of new therapies that home in on cancer cells and leave the healthy cells alone.

Patient-specific diagnostics also could be developed to monitor for cancer recurrence, Nelson said.

"Sometimes it's difficult to tell if a cancer is coming back or if what you're seeing is scar tissue," Nelson said. "Scientists could develop a sensitive molecular assay that looks for a unique mutation found only in the cancer cells and not in the healthy cells. If that mutation is found by the assay, the cancer has returned and patients could be promptly treated when the recurrence is at its earliest stage and easiest to treat. Conversely, such an assay could be used to determine when the cancer

has been effectively eliminated and it's safe to discontinue what are harmful treatments."

Just that one simple assay, Nelson said, would have an amazing impact on how cancers are treated.

"Oncologists would be able to know, definitively, when they can stop giving chemotherapy because it's no longer needed or when they have to resume chemotherapy because the cancer has returned," he said.

Nelson and his team created a web site where researchers can access and retrieve the sequencing data for use in their own experiments, a sort of mini human genome project. Nelson believes sequencing all cancer genomes will result in a significant paradigm shift in the way cancers are treated.

The team of scientists within Nelson's lab has set up a process at UCLA to sequence other cancer cell lines in a highly accurate and cost effective way. His goal is to be able to sequence a patient's individual cancer and turn the data around quickly enough to provide oncologists with the information they need to make immediate treatment decisions.

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