Major cancer genotyping study logs 5,000th tumor profile

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More than 5,000 genetic profiles of tumor DNA have been completed in a large research study by scientists at Dana-Farber Cancer Institute, Brigham and Women's Hospital, and Boston Children's Hospital designed to speed the development of personalized cancer care with precision treatments. Scientists have also moved to the next generation of tumor DNA sequencing technology, which will significantly expand the range of genes and possible mutations to be analyzed, and the speed at which they are catalogued. They have also expanded the program to include pediatric cancer patients.

The project, known as Profile, is creating one of the world's largest databases of genetic abnormalities in cancer, a resource that will make possible a wealth of studies on the genetic roots of the disease. Every patient at Dana-Farber/Brigham and Women's Cancer Center in Boston, and now pediatric cancer patients treated at Dana-Farber and Boston Children's Hospital, is offered the opportunity to participate in the study; to date, nearly 20,000 have consented.

"Profile represents the future of cancer treatment – tailoring highly specific drugs to the particular genetic mutations and other abnormalities that drive a patient's cancer," said Barrett Rollins, MD, PhD, Dana-Farber's chief scientific officer.

A tumor profile, or genotype, is the set of DNA changes that drives a tumor and causes it to spread. The DNA from surgical or biopsy specimens is genotyped by pathologists in an advanced molecular

diagnostic laboratory in the Brigham and Women's Hospital Department of Pathology. Results are entered into data banks, which are accessible to cancer investigators for a variety of research projects to increase their understanding of the disease. Results that can guide treatment are transmitted to physicians taking care of the Profile participants. In the near future, what's learned about the genetic culprits in a patient's cancer may be used to guide his or her treatment or to develop clinical trials of drugs targeted against those genetic anomalies.

The first Profile analysis platform enabled scientists to scan tumor DNA for 471 known cancer-related mutations – small errors in the genetic code that have been implicated in causing cancer – in 41 genes thought to have a relationship to cancer. The new technology platform, OncoPanel, uses massively parallel or "next-generation" sequencing to decode the DNA blueprint of 305 genes and find mutations – potentially millions of them, both previously known and those being discovered for the first time. It can also detect other important genetic alterations, such as deleted or amplified pieces of DNA, or chromosomes that have been broken and incorrectly repaired.

"Previously, we tended to find none or one or two mutations in a tumor sample," said Neal Lindeman, MD, director of the Center for Advanced Molecular Diagnostics laboratory in the Brigham and Women's Department of Pathology. "Now we're finding about 20 mutations per sample."

"Next-generation sequencing reveals a lot more of what could be potentially driving a patient's cancer; it reveals a lot more about what might be treatable by personalized medicine in the future," said Rollins.

Now that Profile has accumulated a critical mass of data, researchers are starting to mine it for leads to new cancer discoveries. For example, one investigator is looking for mutations in melanoma tumors that may affect

how the immune system responds to cancer. Another scientist is seeking a link between mutations in aggressive testicular cancers and patients' responses to treatment.

All patients at the Dana-Farber/Brigham and Women's Cancer Center in Boston are eligible to enroll in the Profile research project, and they may choose to have their physician notified if their test reveals genetic mutations for which treatments exist. In addition, Dana-Farber/Brigham and Women's Cancer Center clinics offer a wide variety of genetic tests, for lung, breast, colon cancer and melanoma, for example, as part of their clinical care.

Select pediatric patients at Dana-Farber and Boston Children's Hospital will be eligible to enroll.

"When it comes to cancer, children are not just small adults," said Katherine A. Janeway, MD, MMSc, a pediatric oncologist at Dana-Farber/Boston Children's Cancer and Blood Disorders Center. "They get different types of cancers and, in many cases, the genetic roots of the disease are different."

The inclusion of pediatric patients in Profile, Janeway explained, will enable researchers to better understand the range of genetic abnormalities present in childhood cancers, conduct of smarter clinical trials, and ultimately help more children with cancer.

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