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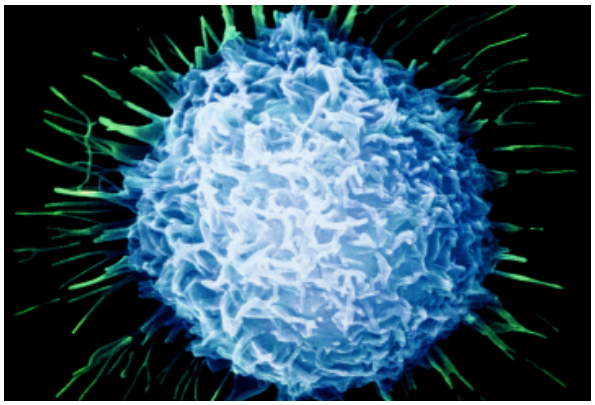
CANCER

Mapping Cancer: Largest Set of Tumor Genomes Could Lead to Better Anticancer Drugs

By Alice Park @aliceparkny | July 16, 2013 | 1 Comment



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The latest map of all the genes involved in a set of tumor cells exposes which mutations drive cancer and how to possibly treat them.

The Human Genome Project provided the first glimpse of the power of genetic maps, and ever since, sequencing the DNA code of not just people but also tissues like tumors has become an invaluable tool in medicine. Laying out the biological code that instructs a fertilized egg to mature into the cells, tissues, organs and body systems that define a human being has led to important discoveries about how we get sick when those directions go awry.

And applying that same technique to cancer cells, experts are exposing some of the critical factors that drive cells to divide out of control to form tumors. In the latest advance, researchers at the National Cancer Institute have sequenced all of the genes in a cancer-cell database that was designed to test promising new drug compounds. With the most complete map of tumor aberrations now

available, they can determine whether some of the failed drug candidates discarded over the years — there are thousands of them — may actually be useful in treating certain cancers.

(**MORE:** Decoding Cancer: Scientists Release 520 Tumor Genomes From Pediatric Patients)

“There is an unlimited amount of matching anyone could do,” says Dr. Yves Pommier, chief of the Laboratory of Molecular Pharmacology at the National Cancer Institute and lead investigator of the study, which was published in the journal *Cancer Research*. “As we integrate this data into the current process of molecular medicine, I think more links [to new drugs] will be made.”

Sequencing the DNA of tumors, and exposing their mutations, is a potent technique for understanding what fuels tumors to develop in the first place, as well as what keeps them going. But until recently, the cost and technology required to sequence all 20,000 or so genes in each of these cancer cells weren’t feasible. The process, says Pommier, “is easy to say, much harder to do,” and it took his team more than two and a half years to complete the maps for the 60 tumor-cell lines, representing nine different cancers, from breast, prostate, brain, lung, colon and kidney tumors. Mapping each of the genes from these cell lines tallied up 6 billion data points that Pommier’s team sequenced, aligned, curated and compared with normal cell genomes in order to come up with the most exhaustive dossier of all the mutations in a specific cancer-cell type to date.

(**MORE:** Cracking Cancer’s Code — Health Special: Cancer)

Previous sequencing projects have focused on mapping specific genes or sets of genes known to be involved in cancer — the BRCA genes in breast cancer, for example. But the latest data set provides a complete look at the entirety of genes in a cancer cell, as well as how active those genes are in pumping out their respective proteins, which can include enzymes, signaling molecules and other agents that cancer cells rely upon to survive. Having information on all of the genes that may be involved in contributing to a breast cancer, for example, could lead researchers to identify new genes and new pathways that they hadn’t discovered before. The more complete set of genetic mutations could also yield clues as to which cancer cells might respond better to certain drug treatments.

“I think this is a wonderful addition to a very powerful data set,” says Dr. Gordon Mills, co-director of the Institute for Personalized Cancer Therapy at MD Anderson Cancer Center, who was not involved in the research. “This is a necessary and important step forward, but it needs to be looked at as a step forward in a process that we need to have complemented by many other

emerging technologies."

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The main issue is that Pommier's team sequenced a relatively small set of cancer-cell lines, which may not represent the breadth of ways that specific cancers like those in the breast, prostate and lung can develop. Matching genetic mutations to the right drugs that might combat them, says Dr. Todd Golub, chief scientific officer at the Broad Institute of the Massachusetts Institute of Technology and Harvard University and investigator at the Dana-Farber Cancer Institute, "is kind of like a cube. There are three dimensions — one dimension is the cell line, with the number of cell lines reflecting the diversity of the disease. Another dimension involves the genetic features of the tumor such as what the mutations are, which genes are turned on and which proteins are turned on. The third dimension includes what drugs are these cell lines sensitive to."

The set of cell lines that Pommier and his colleagues used, known as the NCI-60, is an iconic panel of tumor cells that has led to the discovery of more than 300 Food and Drug Administration–approved anticancer drugs. The cells were created as a screen for promising drug candidates, to see whether new agents could effectively curb the growth of the cancer cells in the dish, and 16,000 compounds have been tested since the cells were generated in the late 1980s. "The NCI-60 concept was really ahead of its time," says Golub. "It represented a pretty advanced concept that the field is now embracing, and that is the challenge of how to read off a cancer genome and use that information to predict what drugs will benefit that particular patient."

(**MORE:** Genetic Study Identifies Four Main Types of Breast Cancer)

In order to do that, sequencing more cell lines will be a priority in coming years, says Mills. "Characterizing just a few patients in depth is a wonderful first step, but the breadth of abnormalities behind cancer will only come out only as we start to characterize larger numbers of patient samples in a breadth and depth that we have never done before," he says.

Combining the growing number of such data sets will also speed along the matching of new potential drugs to cancer-causing mutations. Golub and his group, for example, published a detailed atlas of 1,600 genes (out of the human genome's more than 20,000) from a group of 1,000 different cancer-cell lines, and the National Institutes of Health are currently mapping with painstaking detail the sequence of 25 different tumor types from more than 6,000 samples. International efforts to map tumor genomes, including the International Cancer

Genome Consortium and the U.K.-based Catalogue of Somatic Mutations in Cancer, or COSMIC, also contribute to the global move toward making cancer diagnosis and treatment more precise and personalized.

Pommier says that the latest addition of genetic-mapping data is available on a user-friendly website to any scientist — or even doctor — around the world without charge. The more people access the information and start to make connections between mutations and drug candidates, the sooner new therapies might emerge, he says. There's no guarantee that cancer cells in a lab dish will act in exactly the same way as they do in a patient's body, but teasing out these matchups in the lab first is necessary in order to isolate reliable weapons against cancer in the clinic. "This process will help us learn what is the core problem in cancer, and how that core relates to a tumor's response to drugs," he says. And that knowledge may ultimately produce more accurately targeted, potent anticancer medications that can stop tumors in their tracks.

Read more: http://healthland.time.com/2013/07/16/mapping-cancer-largest-set-of-tumor-genomes-could-lead-to-better-anti-cancer-drugs/#ixzz2ZUj46t00