Study Identifies Hundreds of Potential Targets for Cancer Drugs

Analysis of proteogenomic data opens up entirely new avenues for attacking cancer.

October 2, 2024 By National Cancer Institute

Most targeted cancer drugs work by blocking proteins in or on cancer cells that help tumors grow. But the process of identifying promising proteins to target can be painstaking and often leads to false starts and dead ends.

Now, a team of researchers from the United States and China has identified hundreds of proteins that appear to be either promising targets for existing drugs or leads for the development of new cancer treatments.

Their findings were based in part on a comprehensive analysis of proteogenomic data—that is, detailed information on genes and proteins—collected from more than 1,000 tumors representing 10 types of cancer. These data were compiled and made available by NCI's Clinical Proteomic Tumor Analysis Consortium (CPTAC).

Published June 24 in Cell, the study's findings open up entirely new avenues for attacking cancer, said the study's co-leader, Bing Zhang, Ph.D., of Baylor College of Medicine.

"The potentially targetable space is much, much bigger than what we are currently pursuing," Dr. Zhang noted.

In the study, the researchers put several of their predicted targets to the test. For example, in laboratory studies, they showed that they could stunt the growth of cancer cells by blocking the production of several proteins that their predictions suggested would be good drug targets.

Ana I. Robles, Ph.D., of NCI's Office of Cancer Clinical Proteomics Research and a program director for CPTAC, said that this proteogenomic approach to identifying new targets has the potential to substantially streamline the development of new cancer treatments.

Focusing on targets identified in this way could help drug developers prioritize those that are most likely to be important in different cancers, potentially improving the currently low success rate in developing new cancer drugs, said Dr. Robles, who was not involved in the study.

Shifting the search to proteins

Targeted drugs currently approved to treat cancer disrupt the activity of fewer than 200 proteins, which, according to some estimates, is only about 5% of the proteins that are potentially targetable.

Past efforts to better understand the molecular underpinnings of cancer have focused on finding genetic alterations associated with the disease. But because of the complexity of how genes behave under different circumstances, such as in cancer cells residing in the hectic environment that surrounds tumors, researchers have begun looking more closely at proteins—the end products of gene activity.

But proteins have been more difficult to study than genes, largely because the technology to analyze proteins has lagged behind the technology to analyze DNA and RNA, Dr. Zhang explained.

That's changed in recent years, with new technologies that are allowing researchers to more precisely analyze proteins themselves rather than the genes that encode them—that is, provide the blueprints for their creation.

For more than a decade, Dr. Robles explained, CPTAC has been a leader in generating proteogenomic data, which meshes together information on tumors' genetic and protein makeup.

Last year, for example, CPTAC-supported researchers released comprehensive proteogenomic data on 10 different cancer types, including breast, lung, colon, and ovarian cancer, and made the data publicly available to researchers around the world. This huge repository of data has made investigating proteins and genes across different cancers much more practical, Dr. Zhang explained.

"Our goal is to translate the data generated by our collaborators in the consortium into actionable insights," he said.

The study by Dr. Zhang and his colleagues is an example of why it's important to make these data publicly available, Dr. Robles said. Their analysis "is a beautiful use of the CPTAC data set," she said.

Uncovering a trove of potential targets

For their study, Dr. Zhang and his colleagues integrated CPTAC data on genetic mutations and protein variations across the 10 different cancer types with data from other large data sources used to identify potential drug targets.

Based on this information, the team identified more than 2,800 proteins as potential targets for the two most common types of cancer drugs, called small molecule drugs or antibodies, then classified the target proteins into five groups, or tiers.

Five Tiers of Cancer Drug Targets

Tier 1: Proteins that can be targeted by drugs that have already been approved for cancer treatment.

Tier 2: Proteins that can be targeted by drugs already approved to treat other diseases.

Tier 3: Proteins that can be targeted by investigational drugs that have not yet been approved.

Tier 4: Proteins that can potentially be targeted with the development of new small molecule drugs.

Tier 5: Cell surface proteins that can potentially be targeted with the development of new antibody or immunotherapy drugs.

Next, they whittled the potential targets down to several hundred that their analysis indicated were critical to the survival of cancer cells. These included proteins that were overproduced or overactive in tumor tissue compared with normal tissue, as well as proteins involved in helping the immune system attack cancer cells.

Some of the targets the team identified represent opportunities for "repurposing" already-approved drugs. For example, one experiment showed that naftifine, an antifungal drug, could kill cells of several different cancer types.

Their analysis also indicated that alvespimycin, an investigational cancer drug that blocks the activity of a protein called HSP90, showed activity against cell lines from several cancer types. In mice with colorectal tumors grown from human cancer cells, the drug shrank tumors after only 7 days.

They also identified specific protein fragments, or peptides, on cancer cells that can engage the immune system to attack tumors, making them potential targets for immunotherapy.

Among these were peptides from mutated forms of the KRAS protein, which are thought to be fundamental drivers of many different cancers. Their analysis specifically identified KRAS peptides in four cancer types: pancreatic, lung, uterine, and colon.

Creating a public resource for future cancer studies

To help accelerate drug discovery efforts, the team has compiled the targets into a free database that can be used by researchers around the world to learn more about the specific proteins they are investigating.

The public resource could also serve as a springboard for early-career researchers who are exploring new ideas for research projects, Dr. Robles said.

And as CPTAC generates data on additional cancer types, the team will continue expanding their

database to include more potential drug targets.

“I hope eventually we will have data for all cancer types,” Dr. Zhang said.

This blog was published by the National Cancer Institute on September 11, 2024. It is republished with permission.

© 2026 Smart + Strong All Rights Reserved.
http://beta.docker.cancerhealth.com/blog/study-identifies-hundreds-potential-targets-cancer-drugs