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Medical Research Gets High-Powered 'Search Engine' 'Connectivity Map' quickly links diseases with candidate drugs

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THURSDAY, Sept. 28 (HealthDay News) -- It could someday be like Googling for a cure.

A group of U.S. scientists says it has successfully tested a prototype "Connectivity Map" -- a high-tech computer program that uses unique genetic patterns as "search words" to link up specific illnesses with the drugs that might treat them.

The achievement has already yielded intriguing insights into cancer and Alzheimer's disease, says a team reporting in the Sept. 29 issue of *Science*.

Someday, researchers around the world could use this genetic search engine to speed up drug discovery and gain a broader understanding of disease, the study authors said.

"It's an electronic library -- it helps you understand what genes are present in disease and how those genes can be affected by various 'perturbations' -- medications or other substances," explained Dr. Len Lichtenfeld, deputy chief medical officer at the American Cancer Society.

He was not involved in the research, which was carried out by researchers at the Massachusetts Institute of Technology and Harvard University.

Using the publicly available, online Connectivity Map, scientists worldwide may soon be able to bypass tedious, time-consuming work in the lab and quickly ascertain whether a candidate drug works against a specific illness -- and how.

"As we link together all this computer power, you can begin to imagine how these analyses will become quicker and broader," Lichtenfeld said.

Traditionally, medical research has been anything but quick, however.

"In the old days, for example, we'd send people into the rain forest to bring back a compound, run it through a variety of cell and animal assays to figure out whether or not it might have a potential in cancer research," Lichtenfeld explained. "That was incredibly slow, cumbersome and expensive. It didn't allow for a fast analysis of those products."

Technology has sped up that process somewhat, but scientists still find it tough to link up diseases with molecules that might help fight them. However, the sequencing of the human genome in the 1990s opened up a new era in research as scientists began to understand that healthy and diseased cells carry highly specific gene patterns, or "signatures."

In their work, the MIT-Harvard researchers have compiled an exhaustive database of these signatures, reflecting a wide panorama of disease states. In a similar way, they also cataloged the DNA signatures of more than 160 drugs and other biologically active compounds. The Connectivity Map essentially compares all these signatures to each other, looking for "match-ups" that suggest promising avenues for research.

In this way, the map "works much like a Google search to discover connections among drugs and diseases," study senior author Todd Golub, director of the cancer program at MIT's Broad Institute, said in a statement.

The Connectivity Map remains in a raw, early form, but it is already yielding key findings. For example, when the researchers plugged in the gene signature for a plant-derived medicinal compound, genudin, they found it to be a "match" against prostate cancer. Running the map another time, they discovered that a well-known drug, rapamycin, might help overcome drug resistance in patients battling leukemia.

"So, they were actually able to demonstrate some significant possibilities for cancer treatment already as a result of this database," Lichtenfeld said. "This may, in fact, lead to better investigations into drugs that might be effective."

Running another "query," the map's developers found that gene signatures for cells affected by Alzheimer's disease linked up closely with signatures for a compound called DAPH. DAPH has already been shown to help reverse the build-up of protein "tangles" that characterize Alzheimer's.

The Connectivity Map marks yet another step in an ongoing boom in medical genetics research. Earlier this month, a team led by Dr. Victor Velculescu of Johns Hopkins University in Baltimore sequenced the genetic codes for human breast and colon cancers. Velculescu, assistant professor of oncology at the university's Kimmel Cancer Center, called the new map "extremely exciting and potentially useful," but added that "it's going to take more work to figure out how best to use this."

Lichtenfeld agreed. "This is basically a 'proof-of-concept,' early stage demonstration of the capability of such a system," he said. "It's a beta-test instead of a full-fledged, developed product."

Still, the experts said the potential applications for an easily accessed, online research tool such as the Connectivity Map extend far beyond drug discovery.

"You could get signatures not only for what a drug does, but for normal and diseased states in the body as well as exposure to events in the environment," Velculescu said. "For example, how a certain cell might react to a toxin -- air pollutants or cigarette smoke -- what sort of signature might that provide? Such signatures could be used to determine if different toxins have similar effects and help you begin to understand disease processes."

Perhaps, he added, "connectivity" might even turn science fiction into science fact.

Remember the medical "tricorder" in old *Star Trek* episodes -- a tiny handheld device that Dr. Leonard "Bones" McCoy waved over an individual to quickly diagnose his or her ailment?

"We're not there yet," Velculescu said, "but one can imagine that someday such gene signatures will help pinpoint that a person is sick of a particular disease. You could look at a signature like this and determine both the illness and appropriate therapy. I think in the future that this is where all this technology is heading."

More information

There's more on medical genetics at the [**U.S. National Human Genome Research Institute**](#).

SOURCES: Len Lichtenfeld, M.D., deputy chief medical officer, American Cancer Society, Atlanta; Victor Velculescu, M.D., Ph.D., assistant professor, oncology, Kimmel Cancer Center, Johns Hopkins University, Baltimore; Sept. 28, 2006, news release, Broad Institute, Cambridge, Mass; Sept. 29, 2006, *Science*

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