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Newsweek

Buzz for a Potential New Cancer Drug

Scientists and patients are buzzing about DCA, an existing drug newly recognized as a potentially powerful cancer treatment. But, of course, more research is needed.

WEB EXCLUSIVE

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Newsweek

Updated: 4:46 p.m. MT Jan 23, 2007

Jan. 23, 2007 - There are no magic bullets in the fight against cancer: that's the first thing every responsible scientist mentions when discussing a possible new treatment, no matter how promising. For decades, research has emphasized the differences among the many kinds of cancer, their origins in the complex interplay between genes and environment, and the development of ever more sophisticated and tightly focused therapies. Everyone knows that cancer will not be cured the way antibiotics cure a staph infection.

If there were a magic bullet, though, it might be something like dichloroacetate, or DCA, a drug that kills cancer cells by exploiting a fundamental weakness found in a wide range of solid tumors. So far, though, it kills them just in test tubes and in rats infected with human cancer cells; it has never been tested against cancer in living human beings. There are countless compounds that can do the same thing that never turn into viable treatments. But DCA has one big advantage over most of those: it is an existing drug whose side effects are well-studied and relatively tolerable. Also, it's a small molecule that might be able to cross the blood-brain barrier to reach otherwise intractable brain tumors. Within days after a technical paper on DCA appeared in the journal Cancer Cell last week, the lead author, Dr. Evangelos Michelakis of the University of Alberta, was deluged with calls and e-mails from prospective patients-to whom he can say only, “Hang in there.” There are no magic bullets against cancer.

Still, Michelakis may be onto something important. "The work is very interesting, from a conceptual standpoint," says Dr. Dario Altieri, director of the cancer center at the University of Massachusetts Medical School in Worcester. DCA is a remarkably simple molecule related to acetic acid, better known as vinegar. It acts in the body to promote the activity of the mitochondria, the cellular structures where glucose is oxidized to provide energy; its main pharmaceutical use has been to treat certain rare metabolic disorders. But the mitochondria have another function: they initiate apoptosis, the fail-safe process by which cells with damaged DNA destroy themselves before they can do damage. This goes on continually in the body. But when a cell turns cancerous, it begins processing glucose outside the mitochondria; the mitochondria shut down, and the cell becomes immune to apoptosis—immortal, until it kills its own host. Researchers have assumed that the mitochondria in cancer cells were irreparably damaged. But Michelakis wondered if that was really true. With his colleagues he used DCA to turn back on the mitochondria in cancer cells—which promptly died.

Remarkably, Michelakis isn't even an oncologist; he's a cardiologist who was studying pulmonary hypertension, a deadly condition in which the cells lining the walls of the blood vessels in the lungs inexplicably proliferate. His research suggested that DCA could help that, too, but the possibility that he might be on the track of a treatment for cancer was too tempting to pass up. One of the great things about DCA is that it's a simple compound, in the public domain, and could be produced for pennies a dose. But that's also a problem, because big drug companies are unlikely to spend a billion dollars or so on large-scale clinical trials for a compound they can't patent. So Michelakis and his colleagues Stephen Archer and John Mackey, with the support of the University of Alberta and the Alberta Cancer Board, are embarking on the process themselves, hoping to interest foundations or private philanthropists in underwriting their research. (The Web site for anyone interested in helping is **http://www.depmed.ualberta.ca/dca/**.

They have one advantage: because DCA is already in use, they can combine Phase I trials, meant to establish safety, with Phase II, which look at whether the compound actually works. The first subjects, says Mackey, will probably be patients with breast, lung or colon cancers that have recurred after initial treatment—in other words, people without much hope of a cure. He would like nothing better than to offer them some hope. But again, he warns, in cancer, there are no magic bullets.

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