



SCIENCE & MEDICINE

Cancer Drugs Face Long Road From Mice to Men

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TIMES STAFF WRITERS

WASHINGTON — The scientific process has given birth to many medical miracles over the years. But sometimes it can be a cruel parent.

As a result of a New York Times story Sunday trumpeting news that two chemicals discovered by a Boston researcher can cure cancer in mice, oncologists across the country have been overwhelmed by patients seeking this remarkable new therapy.

But the doctors have told them that it won't be available for years, if ever.

"They are desperate to find something that is an easy way out of a difficult situation," said Dr. Philip DiScaia, deputy director of UC Irvine's Chao Family Comprehensive Cancer Center. "I get very concerned for the patients who have a false sense of hope that something can come of this immediately, when that is just not the case."



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Researchers note that as many as nine other drugs acting on the same basic principle--and that also cure cancer in mice--are in clinical trials in humans. So far, the results haven't overly impressed physicians. "This is not penicillin," said Dr. Lee Rosen of UCLA's Jonsson Comprehensive Cancer Center.

The widespread reactions from patients have raised questions about how the media report word of preliminary medical advances. Those questions were deepened in the current case by confirmation from several publishing houses that the New York Times reporter whose story kicked off the current fever had circulated a book proposal about the alleged cancer cure--only to withdraw it Tuesday.

Nearly every week, researchers report that they have found new compounds that kill HIV in the test tube or that eradicate tumors in mice. Most often, these stories are downplayed by the media, which recognize that the path from test tubes or mice to humans is both long and strewn with potholes and land mines.

"The history of cancer research has been a history of curing cancer in the mouse," said Dr. Richard Klausner, director of the National Cancer Institute. "We have cured mice of

cancer for decades--and it simply didn't work in humans."

Recent medical history is rife with stories of cancer "cures," such as interferon, interleukin and taxol, that produced exciting results in animals and later proved disappointing in humans.

Dr. LaMar McGinnis, an oncologist and medical consultant to the American Cancer Society, agreed. "We thought interferon was 'chicken soup' in the early '80s," he said. "I remember how excited everyone was; it seemed to work miracles in animals, but it didn't work in humans."



The new miracle cure involves a phenomenon called angiogenesis. More than 30 years ago, a young physician named F. Judah Folkman at Children's Hospital in Boston discovered that tumors secrete chemicals that stimulate the growth of blood vessels into the mass of tumor cells, or angiogenesis. Without nourishment from these blood vessels, the tumors are unable to grow beyond microscopic clumps of cells.

Some Drugs Are Tested in People

Folkman reasoned that drugs that blocked the production of these angiogenesis factors might prevent tumors from growing larger. But it took him more than 25 years to persuade the cancer community that his concept would work.

Recently, however, the idea has gained popularity among cancer researchers. Current counts suggest that more than 100 academic laboratories and 40 biotechnology companies are developing such drugs.

Some of these are being tested in humans. One is the tranquilizer thalidomide, notorious for causing severe limb defects in children whose mothers used it during pregnancy. The breast cancer drug Tamoxifen also is thought to act, in part, by restricting blood vessel growth.

UCLA's Rosen and Dr. Timothy Cloughesy are testing two different anti-angiogenesis drugs developed by the Northern California firm Sugen. Cloughesy is testing them in brain tumors, and Rosen in a broad spectrum of cancers.

Dr. David Cheresch of the Scripps Research Institute has been testing another drug, Vitaxin, in patients with terminal cancer. Cheresch was the first to show that the anti-angiogenesis drugs could actually make tumors shrink both in mice and people. But the results in humans thus far have been in Phase I safety trials and require confirmation in larger studies.

All are hopeful that the drugs someday will represent a major advance in cancer therapy. "We're beginning to see results that are clinically meaningful," Rosen said. Cloughesy noted that the brain tumors had stabilized or even shrunk in some patients. Brain tumors are notoriously difficult to treat, he said, and "finding responses in any treatment setting is remarkable."

Researchers are particularly enthusiastic because most of these new agents, unlike traditional cancer drugs, have no side effects. And because they exert their effects on blood vessels rather than the tumors themselves, cancer cells do not seem to develop resistance to them.

Folkman's newest agents, called angiostatin and endostatin, seem to be more potent than previously identified agents. Folkman reported last November in *Nature* that the naturally occurring proteins could cause a broad variety of tumors to simply shrink away to nothingness in mice.

But he has been working with proteins obtained from mice. The Maryland company that he is collaborating with, Entremed, has been trying to produce the human form of the proteins, but is still short of that goal.

"People do not understand how very far off this [clinical trials] is; these proteins are very difficult to make . . . and we are working very hard to make the human versions," Klausner said. "The mouse versions don't work in humans."

Patients Ask About Treatment

Nevertheless, said Dr. Allen Lichter of the University of Michigan, president-elect of the American Society of Clinical Oncology, "I haven't had a single patient who hasn't asked me about this," he said. "It's certainly on everyone's mind. But I have to tell them, honestly, that I don't know if it will work in humans."

The New York Times ran its front page story on the research Sunday, although the paper had run a similar piece--a profile of Folkman--reporting the results in January.

In New York, several publishing houses confirmed Tuesday that they had received copies of a book proposal about the alleged cancer cure from John Brockman, an agent representing Gina Kolata, who wrote Sunday's story. The proposal was sent via e-mail and it arrived Monday, outlining a book that Kolata hopefully would deliver for publication in late 1999.

The brief proposal "reflected what she wrote [in the New York Times]," said Stephen Morrow, an editor with the Free Press. "And since it would be delivered next year, there

would be more developments about the research in the book.”

Meanwhile, Kolata is under contract to another publisher, Farrar, Straus & Giroux Inc., to write a book about a flu epidemic--also based on a New York Times story she wrote.

“It could be that [Kolata] knew she was breaking the story on Sunday and she prepared the proposal in advance of that, and Brockman circulated it yesterday,” said one publishing official, who spoke on condition of anonymity.

“I don’t have a problem with it,” said the publishing official. “But [some people might] in this day of public wailing over media ethics.”

Late Tuesday, however, after the New York Times had been questioned about the story, Brockman abruptly withdrew the cancer book proposal and offered no explanation to publishers, Morrow added.

Neither Brockman nor Kolata could be reached for comment.

New York Times spokeswoman Lisa Carparelli, however, said, “This was Ms. Kolata’s own decision, to withdraw the book proposal. She made the decision after a discussion with her editors . . . after the difficulties became clear, of staying with the story after she acquired a financial stake in it.”

News organizations generally try to avoid such situations to avoid the appearance of a conflict of interest. Critics charge that reporters cannot function as honest brokers of information on a story when they have simultaneously contracted to write a book about their sources.

Scientists themselves question the process.

“It’s really too bad that we make these sorts of announcements,” McGinnis said. “It’s great for the public in general, great for the stock market--but for the cancer patient with only six months to live, it’s unbelievably cruel.”

Cimons reported from Washington, Getlin from New York and Maugh from Los Angeles.

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