The Power of the Front Page Of *The New York Times*

U.S. cancer clinics were swamped with phone calls last week from desperate patients seeking access to two new "drugs" they had heard about through the news media. The compounds—natural proteins called angiostatin and endostatin that block the development of blood vessels—have shown promise in treating cancer in mice. Neither has been tested in humans, however, and they are not likely to be in clinical trials for at least a year. But last week, reports that they might "cure" cancer within 2 years raced through the media.

The trigger for all this excitement was a feature story on the two compounds that appeared high on the front page of *The New York Times* on Sunday, 3 May. Although the story contained several caveats—noting in particular that findings in mice often don't hold up in humans—the message was given an optimistic spin by enthusiastic quotes from Nobel Prize–winner James Watson and National Cancer Institute (NCI) director Richard Klausner. That evening, TV news broadcasts featured the story, and the next day hundreds of newspapers carried hopeful news about angiostatin and endostatin. Within days, however, the media frenzy had shifted. Articles debunking the notion of an imminent cancer cure appeared in the *Los Angeles Times*, *The Boston Globe*, and *The Washington Post*. Watson and Klausner backed away from their quotes. Even the *Times* dashed some cold water on the quick-cure idea. By midweek, many people concluded that the science had been "hyped" in the first wave of stories.

These events provide a troubling vignette of the binge-and-purge dynamic of some science reporting, in which overenthusiastic initial coverage provokes a surge of negative reports. And many questions remain about the episode, among them why the *Times* chose to give such prominence to the story when the basis for it had already been widely reported—including two articles in the *Times* itself last year. *Times* spokesperson Nancy Nielsen said that the newspaper "stands behind" the original report, the quotes about a cancer cure, and the decision to place the story high on Sunday's front page.

Setting the spark. The episode began at a dinner last March. Included among the guests at a conference on gene therapy in Los Angeles were veteran *Times* reporter Gina Kolata and James Watson, president of the Cold Spring Harbor Laboratory on Long Island and the molecular biologist who received a Nobel Prize with Francis Crick for identifying the structure of DNA. By her own account, Kolata turned to Watson during dinner and asked something like: "What's new and important in cancer research?"

Watson—whose unguarded comments have gotten him in hot water before—responded by talking about the buzz among cancer researchers over experiments by Judah Folkman. For 30 years, Folkman and his colleagues at Harvard University's Children's Hospital in Boston have been looking into the cancer-fighting power of compounds that block the signals leading to the formation of new blood vessels. These so-called antiangiogenesis compounds have shown promise in animal studies for treating diseases ranging from some potentially blinding eye conditions to cancer, which nourishes itself by spurring the growth of new blood vessels (*Science*, 24 January 1997, p. 482). Folkman's latest results indicate not only that angiostatin and endostatin stop the spread of cancer in mice but that they can eliminate existing tumors as well (see sidebar).

As quoted in Kolata's story on 3 May, Watson said "Judah is going to cure cancer in 2 years." The *Times* story continued: "Dr. Watson said that Dr. Folkman would be remembered along with scientists like Darwin as someone who permanently altered civilization." Watson says he was unaware that his dinnertime comments were going to be quoted and was "horrified" when they were.

Klausner was quoted in the story as saying angiostatin and endostatin are "the single most exciting thing on the horizon" for the treatment of cancer, and that they were the top priority of NCI. These heady phrases were offset by a careful headline, however: "A Cautious Awe Greets Drugs That Eradicate Tumors in Mice." The story also included warnings that the promised cure might not materialize, such as a sentence in the second paragraph stating that "the history of cancer treatments is full of high expectations followed by dashed hopes when drugs with remarkable effects in animals are tested in people."

But the caveats didn't blunt the impact. When TV broadcasts carried the news, says Eric Rosenthal, spokesperson for the Fox Chase Cancer Center in Philadelphia, they often used "less sophisticated teasers" to promote the story, along the lines of: "New cancer cure—more at 11." Even though some of the stories made it clear that the new results were from mice, the effect was explosive. The Memorial Sloan-Kettering Cancer Center in New York City, for example, was "flooded with calls," says its president, Paul Marks. "We even had patients calling us to say they didn't want to start their chemotherapy—that they wanted to wait for the new drugs."

The frenzy began to cool almost immediately, however, as other journalists began investigating. According to a staffer at Memorial Sloan-Kettering, another *Times* reporter who had been working on a cancer-related story at Sloan-Kettering, Ian Fisher, inquired on behalf of a colleague with cancer about getting treated with angiostatin and endostatin. He learned firsthand that these compounds were still unavailable. And on 5 May the *Times* published Fisher's front-page story on the lack of clinical data on these compounds and the potential drawbacks of antiangiogenesis therapy. The headline: "In Excitement Over Cancer Drugs, A Caution Over Premature Hopes." Other newspapers pounced. *The Washington Post*, for example, reported on the same day that "more than a dozen similar drugs have been in clinical trials" but that "none has yet lived up to the hopes generated by animal experiments."

The *Times* also began to hear complaints from sources cited in the 3 May report. Watson challenged the accuracy of the quote. The *Times* declined to publish a correction, but ran a carefully negotiated letter from Watson on 7 May, in which the Nobelist wrote that "my recollection of the con-

A Cautious Awe Greets Drugs That Eradicate Tumors in Mice

By GINA KOLATA

Within a year, if all goes well, the first cancer patient will be injected with two new drugs that

HOPE IN THE LAB

A special report.

In Excitement Over Cancer Drugs, A Caution Over Premature Hopes

By IAN FISHER

Dr. Larry Norton, a prominent oncologist in New York City, received a telephone call at his home at 7:30

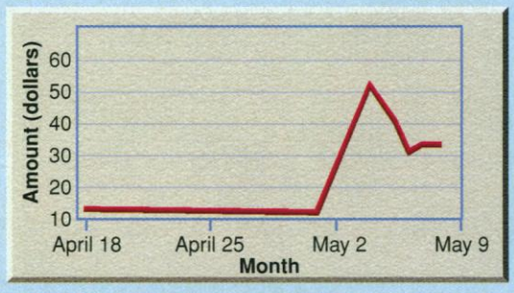
ble edged. On one hand, he said, it is good that cancer patients and the public learn about the research,

Two views. The *Times*' first story *(top)* focused on the promise of antiangiogenesis factors, its second emphasized the problems.

The Roadblocks to Angiogenesis Blockers

Like many experts on cancer drugs, Edward Sausville, the National Cancer Institute's (NCI's) associate director for developmental therapeutics, was surprised by the heated speculation last week over angiostatin and endostatin. It's been 11 months since NCI signed an agreement with a small company to explore the clinical uses of these two natural proteins, which block the development of new blood vessels, such as those that nourish cancers. But as Sausville notes, "from a pharmacological perspective, this research is just beginning."

These antiangiogenesis compounds, as they are called, were identified as antitumor agents several years ago by researchers in the lab of Judah Folkman at Harvard University's Children's Hospital in Boston. EntreMed Inc. of Rockville, Maryland, has rights from Children's Hospital (which has filed for patents) to turn them into commercial drugs, and NCI has begun working with the company to collect animal data before testing the drugs in humans. But the early stage of the research didn't stop EntreMed's stock from going through the roof last week, following publication of an upbeat story on the compounds in *The New York Times* on 3 May. After closing at $12 a share on Friday, 1 May, it opened at $83 on Monday. After reality set in, however, it was down to nearly $30 a share by week's end.



Therapeutic effect. A news report on angiostatin and endostatin's promise did wonders for EntreMed's stock.

SOURCE: STANDARD & POOR'S COMSTOCK, INC. / 1996–1998 MICROSOFT CORP.

All the optimism about antiangiogenesis drugs, as Sausville and others point out, is based on studies of mouse tumors. In a paper published on 27 November 1997 in *Nature*, Folkman, Michael O'Reilly, and their colleagues at Children's Hospital reported that when they administered endostatin to mice with a virulent cancer, they saw the cancers shrink and stop proliferating. They noticed no harmful effects. The Folkman group is reportedly waiting for the mice to die before claiming that endostatin permanently "cured" the cancer. (Folkman declined press interviews last week and had to cancel a talk at a scientific meeting because of the fuss following the *Times* article.) Nephrologist Vikas Sukhatme of Harvard Medical School and Beth Israel Deaconess Medical Center in Boston says he and his colleagues have run an independent study on endostatin that replicates Folkman's findings. Sukhatme says the paper is under prepublication review.

If the mouse study holds up, EntreMed's next steps will be to test endostatin on human tumors implanted in animals, perhaps try it in primates, and, finally, run a trial with real cancer patients. However, human clinical trials aren't likely to begin "for 1 or 2 years," according to a note published last week on the Internet by Folkman's lab. One reason it will take so long, Folkman's note says, is that "at this time, it is not possible to produce the large quantities of endostatin or angiostatin necessary for human trials." His lab has cloned the genes for the two proteins, but Sausville says NCI is still evaluating several biological vectors—yeast or other organisms that would be equipped with the human genes to mass-produce these proteins.

Other researchers in the field of antiangiogenesis, meanwhile, sought to draw attention last week to their own products—some of which are more fully developed than angiostatin or endostatin. At least 300 of these substances are being explored by more than 100 labs in this field, says William Li, medical director of the Angiogenesis Foundation in Cambridge, Massachusetts, a clinical data clearinghouse. Li says that more than 20 of these products have begun clinical testing, and at least three have entered phase III (the final stage) of clinical trials. As Sausville says, "there's more than one bird in the air in this field." **–E.M.**

versation [with Kolata] ... is quite different" from the printed version. Nevertheless, his letter added that "this is the most exciting cancer research of my lifetime." Klausner also claimed in a phone interview that he never singled out research on angiostatin and endostatin as NCI's "top priority," saying he would not highlight specific compounds in that way. On 8 May, the *Times* ran a correction of "an imprecise paraphrase," noting that Klausner "did not say that the drugs were his highest priority," but rather—as quoted in another part of the original article—that he was "putting nothing on a higher priority" than clinical trials of the drugs.

Leaving the accuracy of the quotes aside, many journalists were still puzzled by the *Times*' decision to give Folkman's research so much play last week. The paper itself had already covered Folkman's latest results from treating cancerous mice, which formed the basis of Kolata's article. On 27 November 1997, a story by *Times* reporter Nicholas Wade summed up data in a *Nature* paper by Folkman on those treatments and described other encouraging results with endostatin. The article quoted an expert in the field saying that the results were "unprecedented" and "could herald a new era of cancer treatment." A second, longer profile by Wade on 9 December described Folkman's 30-year search for drugs that stop the growth of blood vessels, noting that his pioneering work had encouraged more than 100 laboratories to follow this path.

The *Times* decided to give Kolata's story front-page play, says spokesperson Nielsen, because Kolata "uncovered a markedly new level of optimism among researchers in the field. That met our journalistic test of a trend"—a subject that was "much broader" than previous stories. Kolata herself says she was "shocked" and "stunned" by the explosive reaction the story triggered.

Besides forcing journalists to take a hard look at their approach to high-profile science stories, the episode is leading to questions about another practice. Shortly after Kolata's story ran, other journalists discovered that Kolata's literary agent, John Brockman, was floating a proposal for a book about the research, reportedly asking for an advance of $2 million. Brockman subsequently explained in a statement that he had asked Kolata to draw up the book proposal only after he read the story in the *Times*, circulating the idea to publishers on 4 May. After the furor broke, however, Brockman said he withdrew the proposal at Kolata's request because she did not want to be drawn into a "media circus." Reporter Robert Cooke of *Newsday* has since been negotiating a deal with Random House, reportedly for $1 million, for a book on the same subject.

The *Times* promptly issued a ruling that its reporters should not solicit book advances on events they are covering regularly. It is, however, common practice for journalists to turn their reporting into books, and a total ban on such deals would probably be unenforceable, says George Gibson, publisher of Walker and Co. in New York: "The bottom line is, the writers are the stars."

–Eliot Marshall