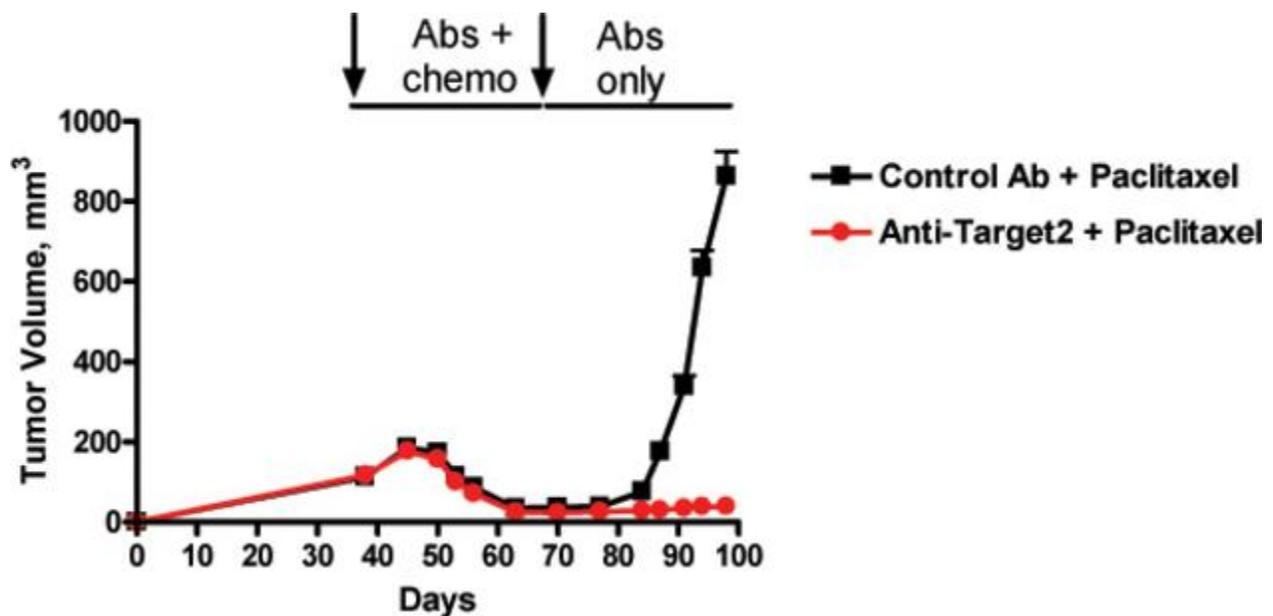


Cancer Stem Cells Could Cause Tumors, Be Key to Cure

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A radical new cancer treatment is about to emerge from a scientific breakthrough in the understanding of how tumors grow.

The theory is that a fraction of tumor cells, dubbed cancer stem cells, is responsible for the malignancy of tumors. While controversial, the theory is gaining adherents among once-skeptical oncologists and investors. It posits that a small fraction of cancerous cells are responsible for stimulating the growth of tumors. In the way other stem cells create organs, these cells create tumors.

In two signs of the theory's perceived potential, the [Journal of Clinical Oncology](#) published a [special 18-article supplement](#) last week on research in the field, just as the leading cancer stem cell treatment startup, Oncomed, finishes readying its first drug candidate for human trials.

Company officials told Wired.com that it will file an investigational new drug application within two months, which should put the drug in human bodies for the first time by the end of the year.

"We think it's going to be very possible to develop safe and effective agents targeting cancer stem cells, based on the work we've already achieved to date," said John Lewicke, Oncomed's vice president of research and development.

If Oncomed can bring this technique to the public, it would be a landmark advance in cancer treatment, and among the most promising of the [more than 750](#) cancer therapies currently in development.

Through public health and treatment efforts, cancer rates have [declined substantially](#) over the last 15 years, but some forms of cancer remain resistant to treatment. Traditional cancer treatments like chemotherapy and radiation have proven effective at sending many types of cancer into remission. Unfortunately, some of them come back, and other forms remain difficult to treat with chemo.

Cancer stem cell researchers say that's because the small percentage of tumor cells capable of driving tumor growth are resistant to chemotherapy. As a result, even if you kill most of the other tumor cells and some of the cancer stem cells, if a small number of stem cells survive they can cause new tumor growth.

If this theory is correct, and stem cells really are the engines of malignancy, then targeting and killing them could end cancer as we know it.

"I think cancer stem cells are a new burgeoning field," Nora Disis, a professor of oncology at the University of Washington and deputy editor of the Journal of Clinical Oncology. "People are studying them in multiple ways, not only pluripotent stem cells as the cause of cancer, but looking at them as the cause chemo resistance."

The diversity of research approaches to cancer stem cells was on full display in the supplement with articles on stem cells' importance in a variety of cancers, mathematical models of their behavior, and techniques for imaging them. Looking at the supplement, it would seem to indicate that cancer stem cells are the key to finding a cure for cancer.

That massive potential was apparent early on in the research. Groundbreaking cancer stem cell researchers Max Wicha and Michael Clarke, then both of the University of Michigan, filed patent protection on their work while they were submitting it for scientific publication.

It was a good decision. Their intellectual property forms the basis of Oncomed's cancer drug pipeline.

And at least a year before any human was slated to undergo a cancer stem cell treatment, GlaxoSmithKline [signed an incentive-laced \\$1.4 billion deal](#) with Oncomed for the commercialization of its technology. It is thought to be the largest deal ever for a preclinical stage biotech company.

One piece of particularly persuasive evidence is a picture of a mouse that has been injected on one breast with cells marked to be stem cells and on the other with standard cancer cells. The cancer stem cells generated a visible tumor while the standard cancer cells did not.

A separate set of studies seem to show that Oncomed's lead drug candidate, known as M2118, has the potential to combine with standard treatment to flatline tumor volumes and prevent, at least over the medium term, tumor recurrence. Other antibodies, like the one labeled Anti-Target2 in the chart above, have shown similar promise.

Paul Hastings, Oncomed's CEO, was careful to note that animal studies like the ones that Oncomed has thus far completed cannot assure success in humans, but he said the company was looking forward to reaching the clinical trials phase.

"At the end of the day, what most people care about is: when we put these drugs into humans, will it have an impact?" said Hastings.

Oncomed's particular therapeutic is what's known as a monoclonal antibody, a cloned antibody that the company designed to bind to cancer stem cells and disrupt their signaling pathways. A similar, if more general, strategy scored a major hit with [the cancer drug Avastin](#), and hundreds of monoclonal antibody treatments are in clinical trials or awaiting approval.

But the cancer stem cell theory does have its detractors.

Scott Kern, a Johns Hopkins professor of oncology and cancer geneticist, published a paper last year in the journal *Cancer Research*, "[The Fuzzy Math of Solid Tumor Stem Cells](#)," in which he attacked what he called the "weak" mathematical support for the existence of cancer stem cells.

The basis of Kern's criticism is a series of animal studies that cancer stem cell researchers have done in which they injected tumor cells into mice. It appears that some types of cells are far more likely to generate tumors than others. Cancer stem cell researchers say this proves that a small, rare subset of cells drive what is known as tumorigenesis, or cancer growth.

But Kern argues that Oncomed researchers' math doesn't add up and that a variety of other factors could be at play in determining which cells thrive in the animal environment, like the availability of blood supply.

"There are many explanations for why small fractions of cells could behave differently but most of the explanations are kind of boring," said Kern. "By attaching the word 'stem cell' to them, it becomes pretty exciting.

Kern himself believes that all tumor cells are malignant, but to varying degrees. In his view, some cells would be extremely tumorigenic while others are only mildly so.

Increasingly, however, Kern finds himself among a dwindling minority of cancer stem cell critics. And Oncomed CEO Hastings brushed off criticism of his company's core technology.

"Most of the folks who are saying this is not a real theory are writing editorials and most of the people who are saying this is real theory are writing papers," he said.

Luckily for cancer sufferers, this academic battle won't remain in journals and papers for very long. By next year, Oncomed's first clinical trial results could be available, and we'll begin to see if these evil cousins of standard stem cells can live up to their billing as, [in Max Wicha's words](#), "a step toward the cure."

Image: In this chart obtained from Oncomed, Anti-Target2 clearly outperforms a control antibody treatment in delaying tumor regrowth in breast cancer.

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