

Simplicity is knowing your health  
and wellbeing are being cared for

**PHILIPS**  
sense and simplicity

 [Back to Article](#)

 [Click to Print](#)



Monday, Apr. 17, 2006

## Stem Cells That Kill

By Alice Park

Imagine a cell nestled happily in the human body and enjoying the best of all possible worlds. It is endowed with immortality, the remarkable ability to divide indefinitely. Each time it cleaves, it makes two daughter cells with different fates. One divides again and again and again, spawning hundreds of copies of itself before exhausting its powers of duplication and dying out. The other progeny is a bit more cunning, inheriting from its parent the gift of never-ending life. That cell resists the temptation to multiply and march to an inevitable death, choosing instead to divide only occasionally and, by doing so, live forever.

It is that cell that is suddenly sparking the interest of cancer researchers and molecular biologists around the world. Known as a cancer stem cell, it could be the culprit behind a malignant tumor's nasty habit of recurring year after year and popping up in distant parts of the body long after the primary growth is gone. Studies of that cell are helping scientists unravel some of cancer's deepest secrets and leading doctors closer to the ultimate goal of any cancer therapy--a cure. Think of the stem cell as a tumor's master print; as long as the original exists, copies can be made, and the disease can persist. But destroy the tumor at its source, and the abnormal cells can't survive. "This represents a conceptual revolution in cancer biology," says Dr. Robert Weinberg, a cancer-research pioneer at the Whitehead Institute in Cambridge, Mass. "This is going to explain the way a wide variety of human cancers originate and the way they grow." Says Dr. Jean-Pierre Issa, a leukemia researcher at MD Anderson Cancer Center in Houston, Texas: "If we are able to eradicate the cancer stem cell, we will be able to cure patients."

Those ideas are already changing the way doctors think about cancer. They are starting to set aside their decades-old obsession with reducing the bulk of a cancerous growth and appreciate instead that the vast majority of its mass is cellular noise, a distraction from the tiny percentage of cells--perhaps as few as 3% to 5%--that are the real culprits. At the latest meeting of the American Association for Cancer Research, researchers at City of Hope Cancer Center in Duarte, Calif., announced that they had isolated a group of stem cell--like cells in lungs that seed the abnormal growth of small-cell lung cancers. Scientists at Stanford University took the concept even further. They were able to isolate stem cells from breast-cancer tumors and identify a genetic signature that allowed them to predict the progression of the disease. "Everybody wants to talk about cancer stem cells now," says John Dick, a University of Toronto professor and one of the leading researchers in the field. "From funding agencies to institutions to scientists, people are recognizing that this is probably the game to be in."

It's easy to see why. More than 30 years after the War on Cancer was declared, malignancies in all parts of the body are still managing to evade the best therapies thrown at them. For some leukemias, survival rates have not budged since the 1970s.

To be sure, there are gentler and more sophisticated forms of chemotherapy and radiation, as well as clever new drugs like Gleevec and Herceptin that take better aim at cancerous cells. But those therapies treat all cancer cells as equals. The next generation of treatments, doctors say, needs to recognize and target the root cause of tumors. "It requires a reorientation in people's thinking," says Weinberg. "We need to focus on wiping out the stem cells rather than eradicating the bulk of the tumor."

Such a shift in thinking is already under way, thanks to the special nature of cancer stem cells. Unlike embryonic stem cells, which stir up moral and political passions because they can, in theory, be used to create an entire human being, cancer stem cells are mutated forms of adult stem cells that can only make copies of their own cell type, be it blood or skin or lung tissue. What gives those adult cells their "stemness" is the ability to generate more stem cells like themselves (and thus continue to regenerate blood or skin tissue) and to churn out new generations of progeny to replace the cells that mature and die off.


The idea that the same process could be at work in cancer originated with leukemia researchers. In a series of studies in the 1990s, scientists began taking leukemia cells from human patients, separating out fractions of those cells and putting them into mice specially bred to tolerate human implants. Some of the cell fractions developed into tumors in the animals, while others did not. That was the first proof that the cells in a cancer were not homogeneous. Some cells were more dangerous than others.

The challenge is to find a way to identify and isolate those cells. Scientists are starting with what they know, analyzing the proteins that stud the surface of normal stem cells and looking for proteins unique to the cancerous cells. So far, leukemia experts have the edge, working from the knowledge of blood stem cells they have been building since the 1940s. Dick's group in Toronto was the first to identify a protein, CD34, as a potential screen for leukemia stem cells. He showed that tumor cells with plenty of CD34, when injected into mice, flowered into cancerous growths. Leukemia cells without the protein, by contrast, did nothing.

The hope is that once those "stem-defining" proteins are identified, they might be used as targets for drug therapies that could lead to better cancer treatments. Irv Weissman, the developmental biologist at Stanford University who first isolated the blood-forming stem cell, is working on pinpointing just such a suite of proteins for leukemia.

Weissman and others are finding no shortage of targets. For one thing, cancer stem cells seem to be extremely mobile, able to migrate easily from their birthplace to other parts of the body, where they can churn out more stem cells and launch new tumors. Eradicating those cells at their source might help control the spread of cancers like leukemia that flare from the blood to the bone marrow and other tissues. Blocking a stem cell's source of nutrients might be another effective strategy for drug development. Unlike normal stem cells, which tap into many different blood supplies for the oxygen and growth factors they need to survive, cancerous stem cells seem to have more addictive personalities, zeroing in on one source and siphoning off everything they need. Exploiting that dependency by finding and cutting off the source would provide another way to tackle malignancies.

It could be years before any of those approaches yields an approved treatment. But interest in the field is growing rapidly, thanks in part, paradoxically, to President George W. Bush's restrictions on embryonic-stem-cell research. Some of the federal funds that might otherwise have gone to embryonic stem cells could be finding their way into cancer-stem-cell studies. "Don't expect anything before five years," says Weissman, "but be angry if you don't see anything in 15 years." Cancer patients, mark your calendars.

 Click to Print

**Find this article at:**

<http://www.time.com/time/magazine/article/0,9171,1184084,00.html>