Cancer debate: Are tumors fueled by stem cells?

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How can a cancer come back after it's apparently been eradicated? Three new studies from American, Belgian, British and Dutch researchers are bolstering a long-debated idea: that tumors contain their own pool of stem cells that can multiply and keep fueling the cancer, seeding regrowth.

If that's true, scientists will need to find a way to kill those cells, apart from how they attack the rest of the tumor.

Stem cells in healthy tissues are known for their ability to produce any kind of cell. The new research deals with a different kind, cancer stem cells. Some researchers, but not all, believe they lurk as a persisting feature in tumors.

Over the past decade, studies have found evidence for them in tumors like breast and colon cancers. But this research has largely depended on transplanting human cancer cells into mice that don't have immune systems, an artificial environment that raises questions about the relevance of the results.

Now, three studies reported online Wednesday in the journals *Nature* and *Science* present evidence for cancer stem cells within the original tumors. Again, the research relies on mice. That and other factors mean the new findings still won't convince everyone that cancer stem cells are key to finding more powerful treatments.

But researcher Luis Parada, of the University of Texas Southwestern Medical Center in Dallas, believes his team is onto something. He says that for the type of brain tumor his team studied, "we've identified the true enemy."

If his finding applies to other cancers, he said, then even if chemotherapy drastically shrinks a tumor but doesn't affect its supply of cancer stem cells, "very little progress has actually been made."

The three studies used labeling techniques to trace the ancestry of cells within mouse tumors.

Collectively, they give "very strong support" to the cancer stem cell theory, said Jeffrey M. Rosen, a professor of molecular and cellular biology at Baylor College of Medicine in Houston. He did not participate in the work but supports the theory, which he said is widely accepted.

Parada's team worked with mice genetically primed to develop a certain type of brain tumor. The scientists genetically labeled particular cells in the tumor and then attacked the cancer with the same drug given to human patients. It kills growing tumor cells and temporarily stops the cancer's growth.

After treatment, when the tumor started growing again in the mice, the researchers showed that the vast majority, if not all, of its new cells had descended from the labeled cells. Apparently these were the tumor's cancer stem cells, they concluded.

Parada said his team is now trying to isolate cancer stem cells from mouse brain cancers to study them and perhaps get some leads for developing therapies to eradicate them.

He also said that preliminary study of human brain tumors is producing

results consistent with what his team found in the mice.

Parada's study appears in Nature. In a second Nature report, British and Belgian researchers found evidence for cancer stem cells in early stage skin tumors in mice. And in the journal Science, a Dutch group found such evidence in mouse intestinal polyps, which are precursors to colon cancer.

Scott Kern of the Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins University in Baltimore is skeptical about whether tumors contain cancer stem cells. He said that since the new studies didn't involve human tumors, it's not clear how relevant they are to people.

The two European studies focused largely on lesions that can lead to tumors, he said. And as for Parada's brain cancer study, he said he believed the results could be explained without relying on the cancer stem cell theory.

More information: *Nature* papers are: DOI: 10.1038/nature11287 , DOI: 10.1038/nature11344. Science paper is: DOI: 10.1126/science.1224676