Researchers attack stem cells that cause colon cancer

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Many of the colon cancer cells that form tumors can be killed by genetically short-circuiting the cells' ability to absorb a key nutrient, a new study has found. While the findings are encouraging, the test tube study using human colon cancer cells also illustrates the difficulty of defeating these cells, known as cancer stem cells (CSCs).

"It is becoming more evident that only a small number of cells in the tumor are capable of forming the tumor, namely the cancer stem cells," said one of the study's authors Adhip P.N. Majumdar of the VA Medical Center and Karmanos Cancer Institute, Wayne State University in Detroit. "So the new strategy is to eliminate the cancer stem cells and thus lower the recurrence of cancer."

Colorectal cancer remains the third deadliest cancer in the U.S. There are 147,000 new cases of colorectal cancer each year, and 49,920 deaths, according to the American Cancer Society. About half of all cancers, including colon cancer, reoccur within five years of treatment, Majumdar said.

Majumdar will present the study, "IFG-1R regulation of colon cancer stem cells," on Wednesday, April 28 at the Experimental Biology 2010 conference. The presentation is part of the cancer stem cell track sponsored by the American Society for Investigative Pathology. The conference takes place April 24-28 at the Anaheim Convention Center. Majumdar carried out the study with Yingie Yu and Bhaumik B. Patel, who are also with Wayne State University.

Tumor factories

Unlike most cells in the body, which are programmed to die after dividing a number of times, normal adult stem cells have a remarkable ability to renew themselves by dividing almost without limit. In addition to this ability to replicate, they can also develop into many different types of cells, such as new heart muscle cells or intestinal cells. In the mature organism, stem cells play a critical role of renewal, replacing dead cells and repairing tissue.

CSCs are a type of stem cell discovered less than 15 years ago and are believed to be the result of mutations of normal stem cells. When CSCs divide, they can develop into new CSCs or into any type of cancer cell. While CSCs make up only 1% of a tumor's cells, they are believed to play a pivotal role in the recurrence of tumors following chemotherapy.

Traditional chemotherapy is good at killing most tumor cells, but not CSCs. Cell studies have found that chemotherapy kills only some of the tumor's CSCs. As a result, tumors may shrink or even disappear with chemotherapy, but the CSCs survive, replicating themselves and eventually producing new tumor cells.

Given the crucial role they play in cancer, it is no surprise that research has focused on destroying the CSCs. But there is a problem: these cells are so similar to normal stem cells that eradicating CSCs may also eradicate normal stem cells, an unacceptable outcome.

Starving them out

"Because CSCs have properties similar to normal stem cells, we have to find a way to attack them while keeping the adult stem cells alive," Majumdar said. To do that, the research team inactivated a receptor that

is found in increased amounts in colon cancer cells: the insulin-like growth factor receptor (IGF-1R). The colon cancer CSCs seem to need a fair amount of IGF to live, more than other cells, and they can't function without the IGF receptor.

"We found that cells that survive chemotherapy show high activation of the IGF receptor and other receptors," Majumdar said. "We thought if we could inhibit or lower the receptor, we may have a treatment strategy."

Working with human colon cancer cells, the researchers manipulated the cellular genetics using small interfering RNA (siRNA) to prevent the synthesis of IGF-1R. In this way, they reduced the number of IGF receptors by half, and reduced the number of CSCs by 35%.

Questions about toxicity remain

Interestingly, Majumdar's laboratory has also had success disabling CSCs with curcumin, a principal constituent of turmeric, a spice commonly used in Indian cuisine. His studies have found that curcumin also can lower the number of IGF-1R and can reduce CSCs further when paired with the siRNA method he outlined in the current study.

The problem with combining the above mentioned anti-CSC strategies is that they can adversely affect normal adult stem cells which, if damaged, would only cause greater harm to the organism.

In addition, it is not yet clear whether reducing the number of CSCs can reduce the recurrence rate of colon cancer. However, Majumdar's laboratory has tried out the curcumin treatment with animals, with some encouraging results.

"Whether we can do this on humans without harming normal stem cells,

that's the biggest challenge," Majumdar concluded.

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