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Researchers identify stem cells in pancreatic cancer

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University of Michigan Comprehensive Cancer Center researchers have discovered the small number of cells in pancreatic cancer that are capable of fueling the tumor's growth. The finding is the first identification of cancer stem cells in pancreatic tumors.

Cancer stem cells are the small number of cancer cells that replicate to drive tumor growth. Researchers believe current cancer treatments sometimes fail because they are not attacking the cancer stem cells. By identifying the stem cells, researchers can then develop drugs to target and kill these cells.

This is particularly crucial for pancreatic cancer, which has the worst survival rate of any major cancer type. Nearly everyone who develops pancreatic cancer dies from the disease.

"Over the last one to two decades we have not had a significant improvement in the long-term survival rates with pancreatic cancer. I believe that if we can target cancer stem cells within pancreatic cancer we may have an avenue to really make a breakthrough in therapy for this awful disease," says lead study author Diane Simeone, M.D., director of the Gastrointestinal Oncology Program at the U-M Comprehensive Cancer Center.

Researchers looked at cell markers on the surface of tumor cells and identified a small number of cells that quickly produced new tumors. The researchers suggest these cells are the pancreatic cancer stem cells.

Results of the study appear in the Feb. 1 issue of Cancer Research.

Tissue samples were taken from 10 patients with pancreatic cancer. The samples were divided and implanted into mice to grow new tumors, allowing a larger sample to be studied. The researchers sorted the tumor cells based on whether they expressed certain antibody markers on the cell surface, specifically CD44, CD24 and epithelial-specific antigen, or ESA. These three markers were chosen as a starting point based on previous work in breast cancer stem cells. The researchers found that only 0.2 percent to 0.8 percent of the pancreatic cells expressed all three markers.

Researchers then took the sorted cells and injected them into mice to see if new tumors formed. When 100 cells that expressed CD44, CD24 and ESA were injected, six of the 12 mice developed tumors. No tumors developed from the cells negative for all three markers until 10,000 cells were injected, at which point one mouse developed a tumor. Further, tumors that developed from these negative cells were smaller and grew more slowly than tumors from the CD44, CD24 and ESA positive cells. The tumors that developed from these sorted cells appeared similar to the original tumor.
In addition, the positive cells were able to reproduce cells that expressed the three markers as well as cells negative for those markers. This ability to self-renew and produce different cells is a hallmark of stem cells.

"The fact that we saw very consistent results in 10 different patients supports that these cells are important," says Simeone, associate professor of surgery and of molecular and integrative physiology at the U-M Medical School.

Stem cells have been identified in several other cancer types, including breast, brain, central nervous system and colon cancers, as well as leukemia. U-M researchers in 2003 were the first to report the existence

of stem cells in a solid tumor, finding them in breast cancer. CD44, CD24 and ESA were also found to play a role in breast cancer stem cells. A study published in January 2007 by U-M and Stanford University researchers narrowed the field for head and neck cancer stem cells, again finding that cells expressing CD44 were involved.

Researchers suggest that a small subpopulation of cancer cells are the critical cells in cancer growth and progression, and the key to treating cancer is to kill these stem cells. It's a radically different model than current treatment approaches, which are designed to shrink the tumor by killing as many cells as possible. Researchers suspect cancer recurs because the treatments are not killing the stem cells.

"The current model may lead to treatments limited in their effectiveness, because we have not been targeting the most important cells in the tumor – the cancer stem cells. If we hope to cure more cancers we will need to target and eliminate this critical type of cancer cell," says study author Max S. Wicha, M.D., Distinguished Professor of Oncology and director of the U-M Comprehensive Cancer Center.

"With this finding in pancreatic cancer, we can now define what we believe are the important cells – the cells that determine whether the cancer will come back or be cured – and target treatment directly to those cells," says Wicha, who was part of the team that discovered stem cells in breast cancer.

About 33,700 people will be diagnosed with pancreatic cancer this year, and about 32,300 will die from it. Five year survival rates are a dismal 3 percent. The disease is difficult to detect early and is often diagnosed at advanced stages. Only 10 percent to 15 percent of patients can benefit from surgery.

"Stem cells are going to radically change how we treat cancer," Simeone

says.

Source: University of Michigan Health System