MedicalXpress

Scientists find protein helps pancreatic cancer cells evade immune system and spread

January 11 2008

A protein that helps prevent a woman's body from rejecting a fetus may also play an important role in enabling pancreatic cancer cells to evade detection by the immune system, allowing them to spread in the body.

Researchers at Jefferson's Kimmel Cancer Center in Philadelphia found that the metastatic cancer cells in the lymph nodes of patients with pancreatic cancer produce enough of the protein, IDO, to essentially wall-off the immune system's T-cells and recruit cells that suppress the immune system's response to the tumor. The findings might mean not only a better way to detect pancreatic cancer spreading to lymph nodes, but also could enhance tumor immune therapy strategies against the fast-moving, deadly disease.

According to Jonathan Brody, Ph.D., assistant professor of Surgery at Jefferson Medical College of Thomas Jefferson University, one way that metastatic cancer cells can survive in nearby lymph nodes is by avoiding the immune system. Evidence from studies by scientists looking at other cancers has indicated that IDO (indolamine 2'3 dioxygenase) is critical to regulating the "immune environment." The Jefferson scientists wanted to know if metastatic pancreatic cancer cells residing in the lymph nodes expressed IDO to avoid being found, and if so, could they target this enzyme with available drugs to prevent the cancer cells from hiding from the immune system.

Dr. Brody, Charles Yeo, M.D., Samuel D. Gross Professor and chair of Surgery at Jefferson Medical College and their co-workers analyzed IDO

expression in 14 lymph nodes to which pancreatic cancer cells had spread and compared them to the primary tumors that had not spread in the same patients. In every case, they found greater expression of the IDO protein in the cancerous lymph nodes. They also looked at three cases of lymph node-negative pancreatic cancers, finding little IDO present.

Scientists know that IDO shuts off tryptophan production in T-cells, putting them in a resting state, and recruits a different type of immune cell called T-regulatory cells, which can inhibit the immune system. “If cells are escaping the primary tumor and going into another environment such as the lymph nodes, what are they doing to evade detection by the immune system?” says Dr. Brody. “These data point to the fact that IDO may play a role in helping cancer cells avoid the immune system.” His team reported its findings at the recent meeting of the Southern Surgical Association in Hot Springs, VA. The results have been accepted for publication in the Journal of the American College of Surgeons.

The group also examined pancreatic cancer cell lines in the laboratory for IDO expression. Using antibodies to IDO, they didn’t find any IDO expression until they treated the cells with interferon to mimic the conditions in the lymph nodes. The tumor cells were then able to make the enzyme.

Whether or not the cancer has spread to the lymph nodes can affect a patient’s prognosis, particularly after surgery. While scientists know a great deal about how a pancreatic cancer develops from a pre-cancerous growth into a cancer, they still don’t have a clear understanding of how it progresses from a primary cancer to metastatic disease. IDO, Dr. Brody says, may play an important part in the process.

“The immune system appears to have a balance that can allow cancer cells to grow but also can detect and destroy them, Brody explains.

“While IDO is crucial to regulating this balance, too much IDO tips the balance toward an immune suppression, supporting cancer growth.”

Dr. Brody notes that IDO inhibitors are available clinically, and these could in theory be used with chemotherapy or perhaps other forms of immune therapy against pancreatic cancer. An inhibitor might be able to activate T-cells to kill cancer cells, for example. “Presumably we could give IDO inhibitors up front to patients who we know are lymph node-positive to try to reduce the cancer and possibly convert them to surgical candidates,” he explains.

Pancreatic cancer, the fourth-leading cause of cancer death in this country, takes some 33,000 lives a year. The disease is difficult to treat, particularly because it is frequently detected after it has spread to other areas on the body. Only 5 percent of all individuals with pancreatic cancer live for five years after diagnosis, and approximately 25 percent of those diagnosed with pancreatic cancer who undergo successful surgical removal of their disease live at least that long. But recent figures give new hope: of those who live for five years after surgical resection, some 55 percent will be alive at least another five years.

Source: Thomas Jefferson University