Scientists find protein may be key in developing deadly form of pancreatic cancer

October 12 2007

A tumor-blocking protein previously implicated in prostate and breast cancer development may also be behind the most aggressive type of pancreatic cancer. Researchers at the Kimmel Cancer Center at Jefferson in Philadelphia have discovered that the protein pp32 – which normally applies the brakes on a cancer-causing gene – is missing in an aggressive form of pancreatic cancer. Though the work is preliminary, the scientists say, the absent protein could eventually become a marker for the disease and a potential drug target.

Scientists led by Jonathan Brody, Ph.D., assistant professor of Surgery, Charles Yeo, M.D., Samuel D. Gross Professor and chair of Surgery and Agnieszka Witkiewicz, M.D., assistant professor of Pathology, Anatomy and Cell Biology, all of Jefferson Medical College of Thomas Jefferson University, have shown in experimental models that without the protein, mutations in the cancer-causing gene K-ras can take over, turning cells cancerous.

Adding pp32 to pancreatic cancer cells that have K-ras mutations and lack the protein can slow the growth of these fast-growing cells, leading the scientists to speculate that losing pp32 might be a critical event in determining how aggressively a pancreatic cancer behaves. They report their initial findings online in the journal *Modern Pathology*.

According to Dr. Brody, previous laboratory and animal studies have shown that pp32 inhibits K-ras-activating gene mutations found in more than 90 percent of all pancreatic cancers and in some early pre-

cancerous lesions as well. But in a subset of fast-moving, “poorly differentiated” pancreatic cancers, the researchers found that “pp32 is either reduced or lost,” Dr. Brody says. “Losing the protein in pre-cancerous lesions could be a marker for an aggressive form of pancreatic cancer.

“It’s rare to find laboratory studies that parallel what we see in actual pancreatic tumors,” Dr. Brody says. “Connecting a protein that can inhibit a critical mutation found in almost every pancreatic cancer to the pathology is powerful information. These types of studies can help us understand more about the early development of pancreatic cancer on a molecular level.

“If we are able to learn more about this molecule, this may be a potential target that we could turn on in aggressive types of pancreatic cancers,” he notes. “In theory, if we could find a way to upregulate this molecule in these pancreatic cancers, we may be able to arrest these fast-growing cancer cells as we did in experiments in this study. As we understand its molecular interactions, we could also somehow find the things that regulate it and extend our molecular understanding of this devastating disease.”

Pancreatic cancer, the fifth-leading cause of cancer death in this country, takes some 30,000 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 4 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