New discovery may help explain smoking-pancreatic cancer link

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If lung cancer and heart disease aren't bad enough, cigarette smokers are also at higher risk for developing, among other things, pancreatic cancer. Now, researchers at the Kimmel Cancer Center at Jefferson in Philadelphia have preliminary evidence indicating one possible reason why. Data being presented April 13, 2008 during the Annual Meeting of the American Association for Cancer Research shows that they have found that nicotine in cigarettes increases the production of a protein that is known to promote cancer cell survival, invasion and spread.

According to Hwyda Arafat, M.D., Ph.D., associate professor of Surgery at Jefferson Medical College of Thomas Jefferson University, the protein, osteopontin, is found in a variety of fluids in the body, such as plasma, cerebrospinal fluid, synovial fluid and breast milk. Osteopontin is also present in different organs and plays an important role during embryonic development. Recent studies have demonstrated that osteopontin levels are significantly higher in the blood and pancreas tissue of pancreatic cancer patients. The protein, when over-produced, can make cancer cells more likely to become metastatic.

Dr. Arafat wanted to see if osteopontin might play a role in the cigarette smoking-pancreatic cancer connection. In collaboration with groups at the University of Nebraska and Rutgers University, Dr. Arafat and her co-workers looked at rats exposed to cigarette smoke and measured the amount of osteopontin in the rat pancreas and blood. They found that the more cigarette smoke to which the rats were exposed, the greater the amount of nicotine in the blood and osteopontin in the pancreas.

The researchers also looked at osteopontin expression in pancreatic cancer cell lines exposed to nicotine, finding that osteopontin expression went up when the cells were exposed to more nicotine. “We found that dose-dependently, nicotine increased osteopontin expression not only through transcriptional but also translational (protein secretion) levels in pancreatic cancer cells,” Dr. Arafat explains. Pancreas tissue samples from pancreatic cancer patients also showed higher than normal levels of the protein.

Dr. Arafat believes that osteopontin could be a drug target. “We are now proposing that perhaps blocking osteopontin can interfere with the progression of pancreatic cancer and other cancers,” she says, adding that her team would like to understand more about osteopontin’s effects on pancreatic cancer cell behavior. Dr. Arafat’s group now is comparing differences in osteopontin expression between smokers and non-smokers.

“For example, if you put the cells with nicotine and block osteopontin, will the cells still be migratory? Is it osteopontin or something else in combination that is at work here?”

Pancreatic cancer, the fourth-leading cause of cancer death in this country, takes some 34,000 lives a year. The disease is difficult to treat; it frequently is detected after it has spread. Only 4 percent of individuals with pancreatic cancer live for five years after diagnosis, and about 25 percent of those who undergo successful surgical removal of their disease live at least that long.

Source: Thomas Jefferson University