Nothing to sneeze at—battling mucus to beat cancer

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Inside their laboratory at the University of Oklahoma Sciences Center, Altaf Mohammed, Ph.D. (left) and C.V. Rao, Ph.D. focus on the role of mucins, a principal component of mucus, in pancreatic cancer tumor growth. Mucins appear to shield cancer cells, making them resistant to chemotherapy. Now, this Stephenson Cancer Center team has identified a new gene target common to many of those mucins. The discovery may be a chink in pancreatic cancer's defensive armor, and may point to new targeted therapies as well as a way to help make current treatments for this deadly cancer more effective. Credit: Jim Green, EPI

What do cancer cells and a runny nose have in common? The answer is mucus; and researchers at the Stephenson Cancer Center at the University of Oklahoma have shown it may hold the key to making cancer treatment better.

Most of us know about the thick, gooey stuff we blow from our noses when we have a cold. In that instance, mucus protects the normal tissue in the nose from drying out and helps the body recognize and fight off invaders like bacteria and viruses.

Mucus also has been shown to play a role in cancer's resistance to chemotherapy drugs, shielding cancer cells from the very drugs intended to kill them, thereby allowing the cancer cells to grow and multiply rapidly. Now, researchers at the Stephenson Cancer Center have identified a way to potentially break through that defense when it comes to pancreatic cancer.

"Pancreatic cancer is a lethal disease, and its management is an ongoing challenge," said Principal Investigator Altaf Mohammed, Ph.D., assistant professor of Internal Medicine with the OU College of Medicine. "Pancreatic cancer is the fourth leading cause of deaths due to cancer in the United States. It is a highly aggressive cancer that is usually diagnosed at an advanced stage and has the worst prognosis of any malignancy."

Almost 49,000 people in the United States will be diagnosed with it this year alone, according to estimates from the American Cancer Society. For those patients diagnosed with pancreatic cancer, the prognosis generally is not good. The five-year survival for patients is less than 7 percent, largely due to the cancer's resistance to chemotherapy.

The Stephenson Cancer Center team has identified a gene target called GCNT3 that may offer promise in improving the treatment of pancreatic

cancer. GCNT3 plays an important role in the biosynthesis of mucins, a principal component of mucus.

"The mucins appear to somehow shield the cancer cells, making them resistant to chemotherapy," said C.V. Rao, Ph.D., Professor of Internal Medicine and Director of Center for Cancer Prevention and Drug Development at the Stephenson Cancer Center.

"GCNT3 is minimally expressed in the normal pancreas, but our research showed that it is significantly overexpressed during the development of pancreatic cancer," said Mohammed. "This overexpression correlates to excessive mucin production, rapid tumor growth and reduced patient survival."

Rao explained the mucins effectively form a mesh that functions as shield keeping chemotherapy drugs and the body's own immune system from killing the cancer cells. There are many mucins involved in this process, but they found GCNT3 was involved in the function of many of them. Thus, by targeting that single gene, they theorized they might effectively shut down multiple mucins at once, breaking down cancer's protective barrier.

The team utilized talniflumate, a molecule that has been used to regulate mucus production in cystic fibrosis, asthma and other diseases. Researchers evaluated the molecule's impact on their gene target.

"We determined that talniflumate effectively binds to GCNT3. Use of talniflumate was shown to reduce mucin synthesis during the development of pancreatic cancer in laboratory models," Mohammed said.

In addition, he added the molecule appears to boost the body's own tumor-fighting abilities.

The findings may point to a potential new therapy - one that might be used in combination with chemotherapy to help current cancer-fighting drugs be more effective against pancreatic cancer. Mohammed said the work also is critically important to understanding the mechanisms involved in pancreatic cancer tumor growth and to developing new targeted therapies.

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