Pancreatic cancer loses viral defenses when talking with supporting cells

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Dr. John Bell. Credit: Ottawa Hospital Research Institute

Ottawa researchers have unlocked a way to make pancreatic cancer cells more vulnerable to cancer-killing viruses, known as oncolytic viruses. Outlined in a paper published today by *Nature Medicine*, the scientists have discovered how they can exploit the communication, or cross-talk, between pancreatic cancer and a specific cell type that supports the tumour. They found that this cross-talk weakens the ability of both cell types to fight off cancer-fighting viruses.

The cross-talking cells in question are called cancer-associated fibroblasts (or CAFs), which are genetically normal cells that the cancer has conditioned to support the tumour. This conditioning by the tumour makes the CAFs susceptible to virus infection, compared to their normal counterparts. In turn, the CAFs secrete a protein called FGF2 that makes the tumours more susceptible to virus infection.

Pancreatic cancer is among the deadliest of cancers, killing approximately 4,400 Canadians every year. Only 6 per cent of people diagnosed with pancreatic cancer live longer than five years—a survival rate that has not improved in the last 40 years.

CAFs make tumours more resistant to standard therapies and pancreatic cancers are known to have a lot of CAFs. This study shows that the opposite is true when it comes to cancer fighting viruses. More CAFs and higher levels of FGF2 make them more susceptible to oncolytic virus therapy.

"Our findings could be important for patients in a couple of ways," said Dr. John Bell, the study's author and a senior scientist at the Ottawa Hospital Research Institute and professor of medicine at the University of Ottawa. "First, they could help us predict which cancer patients will be more likely to respond to oncolytic virus treatment."

"More importantly, we saw improved outcomes in tumours treated with an oncolytic virus that expressed FGF2," added Dr. Bell, who is also scientific director of BioCanRx, a new network devoted to accelerating the journey of promising cancer biotherapeutic discoveries from the lab to clinical trials. "Combined with the fact that the five-year survival rate for pancreatic cancer has been stuck in the single digits, we are motivated to move this knowledge into clinical testing."

The experiments for this paper, whose lead author is postdoctoral fellow Dr. Carolina Ilkow, were conducted with mouse models and cells from human patients with pancreatic cancer. The findings require further study before they can be translated into a clinical trial.

Still, the paper is positive news for at least one woman living with pancreatic cancer.

"This discovery is so encouraging to me, even though I fully realize it's still at an early stage," said Sindy Hooper, an Ottawa mother of two and triathlete who was diagnosed with pancreatic

cancer in January 2013. "For me, research progress like this means hope, and that hope helps me live with the stark reality of my diagnosis."

Hooper recently passed her latest six-month cancer screening, but she says that if her cancer comes back, she will think long and hard about whether or not to undergo chemotherapy again, because the side effects were so bad.

One of the potential benefits of oncolytic virus therapy is that it is far less toxic than standard chemotherapy. Oncolytic viruses attack and kill cancer cells while leaving healthy cells unharmed. The expected side effects of oncolytic virus treatments being tested in clinical trials are usually a mild fever or flu-like symptoms that last a day or two.

Hooper is now training to run the marathon at the 2015 Tamarack Ottawa Race Weekend. She is leading a team called Marathoners Gone Viral, made up of more than 120 marathon runners raising money for pancreatic cancer research at The Ottawa Hospital through the Foundation's Run for a Reason charity program.

More information: "Reciprocal cellular cross-talk within the tumor microenvironment promotes oncolytic virus activity" was published online on April 20, 2015, by *Nature Medicine*: DOI: 10.1038/nm.3848

Provided by Ottawa Hospital Research Institute