

Low levels of key protein may indicate pancreatic cancer risk

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A protein that dwindles in response to obesity and a sedentary lifestyle may one day help doctors predict which people are at increased risk for pancreatic cancer, new research by Dana-Farber Cancer Institute and collaborating scientists indicates.

In a report in the Aug. 15 issue of *Cancer Research*, the investigators found that, in a large study group, people with the lowest blood levels of a protein called IGFBP-1 were twice as likely to develop pancreatic cancer as those with higher levels. Though much work remains to determine if the protein -- whose acronym stands for insulin-like growth factor binding protein-1 -- is a reliable indicator of pancreatic cancer risk, the finding adds to the scientific understanding of how the disease develops.

"The levels of insulin and another circulating hormone, insulin-like growth factor or IGF, are modified by obesity and sedentary lifestyle, and there is evidence that these hormones may stimulate the growth of pancreatic cancer cells," said the study's lead author, Brian Wolpin, MD, of Dana-Farber. "When IGF binds to proteins like IGFBP-1, there may be less IGF available to bind to pancreatic cancer cells and promote their growth. We wanted to determine whether IGFBP-1 levels in the blood were associated with pancreatic cancer risk."

The investigators measured circulating IGFBP-1 levels in a select group of participants in four large, ongoing health studies: the Health Professionals Follow-up Study, the Nurses' Health Study, the Physicians' Health Study, and the Women's Health Initiative. They collected blood samples from 573 participants and, four or more years later, checked IGFBP-1 levels in the samples of 144 people who developed pancreatic cancer and 429 who did not.

They found that the quarter of the group whose IGFBP-1 levels were lowest had twice the risk of

developing pancreatic cancer of those in the top three quarters. The connection became even stronger over time: Among cases diagnosed at least eight years after blood collection, those in the bottom quarter of IGFBP-1 levels had nearly three-and-a-half times the pancreatic cancer risk of those in the upper quarters.

The risk may be elevated because higher amounts of IGFBP-1 are able to "soak up" more IGF, leaving less available to spur pancreatic cancer cell growth, or because IGFBP-1 has some cancer-blocking properties of its own, said Wolpin, who is also an instructor in medicine at Harvard Medical School. Another possibility is that other molecules may be involved, for which IGFBP-1 acts as an intermediary.

"It's known that a variety of proteins are affected by obesity and sedentary lifestyle," he added. "Studies are exploring whether a subset of these may play a role in the risk of developing pancreatic cancer. More research is also needed on how alterations in insulin and proteins in the IGF family alter the risk of this difficult disease."

Source: Dana-Farber Cancer Institute

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