

High-fat/calorie diet accelerates development of pancreatic cancer

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Study results presented at the American Association for Cancer Research's Pancreatic Cancer: Progress and Challenges conference, held here June 18-21, strongly suggest that a diet high in fat and calories can hasten the development of pancreatic cancer in humans.

"Our results showed that in mice, a diet high in fat and calories led to obesity and metabolic disturbances such as [insulin resistance](#) that are seen in obese humans. It also greatly enhanced pancreatic inflammation and pancreatic [cancer development](#)," said Guido Eibl, M.D., an associate professor in the department of surgery at the David Geffen School of Medicine at the University of California, Los Angeles and a researcher at UCLA's Jonsson Comprehensive Cancer Center.

Human [epidemiological studies](#) have linked high fat intake and obesity to an increased risk of pancreatic cancer, but the mechanism driving this association has not been understood.

To understand the link, Eibl and his colleagues first tested the hypothesis that diet is linked to cancer. They fed a corn oil-based diet that had a high content of fat and calories to mice with a genetic mutation that caused them to develop pancreatic precancer. The same gene, KRAS, is mutated in the majority of human pancreatic cancers.

The results showed that 90 percent of the mice fed the special diet became obese, and all of these mice developed insulin resistance and inflammation in the pancreas. Both of these conditions can stimulate the

growth of [precancerous cells](#) and cancer. These mice also developed significantly more advanced [precancerous lesions](#) than did mice fed a normal diet.

"This suggests that the high-fat, high-calorie diet accelerated pancreatic cancer development," said Eibl. "A KRAS mutation in the pancreas might not be sufficient to cause an individual to develop pancreatic cancer. It likely needs something in addition [?] a secondary hit. Our study showed that a high-fat, high-calorie diet could provide an environmental secondary hit and trigger cancer development."

The researchers are now defining the role that inflammation produced by obesity plays in development of the cancer, and if agents such as antidiabetic drugs or fish oil can halt this disease process.

More information:

Abstract

A diet high in fats and calories leads to obesity and metabolic disturbances and accelerates pancreatic cancer development in the conditional KrasG12D mouse model. Aune Moro, Aurelia Lugea, David Dawson, Steven Pandol, Anna Gukovskaya, Enrique Rozengurt, Vay-Liang Go, Guido Eibl. David Geffen School of Medicine at UCLA, Los Angeles, CA.

Introduction: There is strong epidemiologic evidence that obesity increases the risk of several human cancers, including pancreatic cancer. Several mechanisms, including inflammation and insulin resistance with hyperinsulinemia, are proposed, by which obesity may promote tumor development. However, the driving mechanisms in pancreatic cancer are still poorly understood.

Aim: Our aim was to investigate whether a diet high in fats and calories leads to obesity with metabolic disturbances similar to humans and promotes pancreatic cancer development in the conditional KrasG12D mouse model of pancreatic cancer.

Methods and Results: Offspring of Pdx-1-Cre and LSL-KrasG12D mice were randomly allocated to either a diet high in fats and calories (HFCD; ~4,535 kcal/kg; 40% of calories from fats) or control diet (CD; ~3,725 kcal/kg; 12% of calories from fats) for 3 months. Compared to control animals, mice fed the HFCD significantly gained more weight (16.9 ± 2.1 g vs. 7.1 ± 3.1 g; p

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