

High-fat, high-calorie diet may cause pancreas cancer in mice

08 October 2013 | News | By Bureau Report



A study published in *Cancer Prevention Research* shows that mice made obese by being given high-calorie, high-fat diets (HFCD) developed abnormally high numbers of lesions known as pancreatic intraepithelial neoplasias (PanINs), which are known to be precursors to pancreas cancer. This is the first study to show a direct causative link in an animal model between obesity and risk of this cancer.

The availability of genetically engineered model mice that have the same genetic mutation found in human pancreas cancer patients (the KR as mutation) has made study of the possible causes of pancreatic cancer more feasible, because changes in the mouse metabolism caused by obesity are similar to those in humans. The researchers set out to develop diet-induced obesity and development of pancreas cancer in a set of mice and then compare them to another set of mice that are genetically identical but not given a high-fat, high-calorie diet. Obesity in these mice resembles several important clinical features of human obesity such as weight gain and disturbance of metabolism, and this mouse model was ideal for unraveling any underlying biological mechanisms of pancreas cancer that are put in motion by obesity.

The researchers also set parameters to assess the impact of the effects of the high-fat, high-calorie diet on mouse pancreas tissue, such as increased inflammation and other biological signs that indicate pancreas problems. These indicators were measured and used to create an overall score (pancreatitis score) to indicate negative effects on the pancreas. They then conducted pathology tests on mouse pancreas tissue to determine how many PanIN precursor lesions had developed.

Mice that ate the normal diet gained an average of approximately 7.2 g, plus or minus approximately 2.8 g over 14 months. Mice that ate the high-fat, high-calorie diet gained an average of 15.9 g, plus or minus 3.2 g. Mice fed the normal diet had mostly normal pancreases with very few scattered PanIN lesions. Mice fed the high-fat, high-calorie diet had significantly more PanIN lesions and fewer overall healthy pancreases.

The study showed that the mice fed a diet high in fats and calories gained significantly more weight, had abnormalities of their metabolism and increased insulin levels, and had marked pancreatic tissue inflammation and development of PanIN lesions. These observations suggest that such a diet leads to weight gain, metabolism disturbances, can cause pancreas

inflammation and promotes pancreas lesions that are precursors to cancer.

“The development of these lesions in mice is very similar to what happens in humans,” said lead author Guido Eibl, member of UCLA’s Jonsson Comprehensive Cancer Center and Professor-in-residence in the Dept. of Surgery at David Geffen School of Medicine. “These lesions take a long time to develop into cancer, so there is enough time for cancer preventive strategies, such as changing to a lower fat, lower calorie diet, to have a positive effect.”