Genome analysis of pancreas tumors reveals new pathway

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The latest genomic analysis of pancreatic tumors identified two new pathways involved in the disease, information that could be capitalized on to develop new and earlier diagnostic tests for the disease

"We now know every gene involved in pancreatic cancer," said Dr. William Fisher, professor of surgery and director of the Elkins Pancreas Center at BCM. "This study ushers in a whole new era of taking care of patients with pancreatic cancer. We will look back on this as a turning point in understanding and treating this disease."

The study follows a five-year collaboration between the Michael E. DeBakey Department of Surgery and the Baylor College of Medicine Human Genome Sequencing Center, said Fisher.

The Baylor College of Medicine Human Genome Sequencing Center was one of three sequencing centers worldwide that analyzed the genomes of pancreatic tumors and normal tissues taken from 142 patients with the disease. The BCM center, along with the Australian Pancreatic Center Genome Initiative and the Ontario Institute for Cancer Research Pancreatic Cancer Genome Study carried out detailed studies on 99 of the tumors, identifying 1982 mutations that resulted in a change to a protein and 1,628 significant copy number variations events in which the structure of the chromosomes themselves are changed, either deleting or duplicating genetic information.

The multi-institution, international consortium of researchers discovered mutations in genes involved in chromatin modification (changes that affect the way DNA is packaged inside the cell) and axon guidance (the process by which the axon – a long threadlike project that carries impulses away from the neuron – is guided to grow to its proper target).

"This is a category of genes not previously linked to pancreatic cancer," said Fisher. "We are poised to jump on this gene list and do some exciting things."

New information is much welcome in the field of pancreatic cancer, which is the fourth leading cause of cancer death with an overall five-year survival rate of less than 5 percent. The figures have not changed substantially in the past 50 years.

The study is the first to report findings from primary tumors in the disease. Previously only cell lines or tumors transplanted into mice had been used because the tumors are so small. "Therefore it required new techniques to sensitively identify mutations that were important to the development of cancer," said Dr. David Wheeler, associate professor in the BCM Human Genome Sequencing Center who oversees the center's cancer projects. Wheeler and Fisher are also members of the NCI-designated Dan L. Duncan Cancer Center at BCM.

A report appears online in the journal *Nature*.

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