

Study of human tissue reveals potential colon cancer biomarker

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Cincinnati scientists have identified a new biomarker that could help predict a person's risk of developing colon cancer and how aggressive it may become.

The University of Cincinnati (UC) team has identified "hotspots"—areas of deleted genetic data—that play a critical role in regulating gene expression and influence colon cancer progression. Researchers speculate that these hotspots could be used as a biomarker for colon cancer.

They report their findings in the Jan. 16, 2009, issue of *PLoS Genetics*. This study is the first to explain how a gene—AMACR—is regulated in relation to cancer development and to identify specific genetic events (a polymorphism and somatic cell mutations) related to colon cancer.

For this study, UC researchers looked at the actions of the AMACR gene in human tissue. AMACR breaks down branched-chain fatty acids, a type of molecule only found in animals that eat plants. Previous research showed that plant-derived fatty acids, such as those found in red meat and dairy products, can accelerate cancer growth.

"From the colon tissues, we've identified two types of genetic deletions that may allow us to predict whether people will have a good or bad cancer outcome," says Xiang Zhang, PhD, first author of the study and UC environmental health research associate. "If a person carries one of the deletions, it may predispose him or her to a more aggressive type of

colon cancer."

UC researchers analyzed the AMACR gene's abnormal expression patterns using a sophisticated laser-capture microdissection technique to identify the key biological events that lead to colon cancer progression. They also compared gene sequencing data from the general population—obtained from whole blood samples—to that of the human colon cancer tissue samples.

In addition to discovering the hotspots that trigger abnormal AMACR expression, they also identified specific proteins (transcription factors) that would normally bind to the deleted sequences to maintain normal gene expression.

"Our hope is that this new knowledge will help us develop better diagnostic tools for colon cancer," says Zhang.

Researchers say this discovery could also help people make strategic lifestyle choices to reduce their risk for developing colon and other cancers from a gene-environmental interaction.

"For years, scientists have believed that a diet including a large amount of red meat and low in fiber may lead to increased risk for colon cancer, but it's not that linear," says Shuk-mei Ho, PhD, senior author of the study and chair of UC's environmental health department. "We need to start paying closer attention to how the environment we live in and the things we put in our bodies interact with our genetic makeup to influence our cancer risk."

The UC research team expects to expand this research into a multi-center study in the near future. The project is currently funded by the National Institutes of Health and U.S. Army Prostate Cancer Program.

Source: University of Cincinnati

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