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# Genomic signature of colon cancer may individualize treatment

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Researchers in the Duke Institute for Genome Sciences & Policy have developed a model for predicting risk of recurrence in early stage colon cancer patients, and have used the model to also predict sensitivity to chemotherapy and targeted therapy regimens.

"These findings have important implications for individualizing therapy," said Katherine Garman, M.D., a gastroenterology fellow at Duke and lead investigator on the study. "By examining gene expression in early-stage colon cancer tumors, we have found certain patterns that seem to put some patients at higher risk for recurrence. By identifying these patients up front, we may be able to treat them in a targeted and proactive manner to prevent this recurrence and help them live longer and healthier lives."

The findings are due to appear in the online edition of the *Proceedings of the National Academy of Sciences*, between November 24 and November 26, 2008. The study was funded by the Emilene Brown Cancer Research Fund and the National Institutes of Health.

The researchers studied gene expression data from 52 samples of early stage colon cancer tumors, looking for patterns. Then they correlated the gene expression patterns with patient progress reports to track the recurrence of cancer. The predictive power of the correlations was subsequently tested in two independent data sets from 55 and 73 tumors, respectively.

"In our small dataset, we were able to predict which tumors were at risk for recurring, with 90 percent accuracy," Garman said.

In collaboration with colon cancer specialist David Hsu, M.D., the researchers then took their study one very significant step further, using the data garnered about gene expression and prognosis to examine response to several different types of therapy.

"Importantly, we found that the traditional chemotherapy given to patients with colon cancer varies considerably in its ability to treat tumors with a high likelihood of cancer recurrence," Garman said. "Using the gene-expression data to guide us, we then identified several other drugs and tested those drugs in our samples. The drugs chosen were novel targeted therapies and anti-inflammatory agents that go after certain cancer cell pathways and had been previously shown to alter colon cancer biology."

"Two of the drugs we tested seemed to cause significant changes in tumor biology in a laboratory dish, effectively making a high-recurrence-risk tumor into a low-recurrence-risk tumor by altering the genetic makeup," Garman said. "These therapies would need to be tested further in a clinical trial."

Conventional methods of characterizing tumors currently rely on pathological information such as tumor size, lymph node involvement and degree of metastasis, Garman said. Doctors use these kinds of clinical data to determine whether an early stage colon cancer patient receives chemotherapy after surgery, and if so, what type.

"Integration of genomic and genetic markers will revolutionize the way we care for patients," Garman said.

"This is a perfect example of how science can change the way cancer

care is practiced," said Anil Potti, M.D., a researcher in the Duke Institute for Genome Sciences & Policy and senior investigator on this study. "We hope that advances such as this will individualize the treatment plans for patients with colon cancer and improve survival."

About 150,000 people are diagnosed with colorectal cancer each year in the United States and almost 50,000 are expected to die of the disease in 2008. Up to 30 percent of patients diagnosed with early stage colon cancer can go on to experience recurrences despite initial cure with surgery and chemotherapy when indicated.

Source: Duke University