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Newly identified biomarker may help predict colon cancer progression, personalize therapy

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Researchers at Baylor Research Institute have identified a small RNA molecule that appears to enable certain colorectal cancers to become especially aggressive, resistant to treatment and likely to migrate and invade normal tissue.

Findings suggest that detecting high levels of the molecule—SNORA42—in patient tissues could serve as a "biomarker" to help clinicians determine which patients might benefit from more aggressive therapy against the disease that is the second-leading cause of cancer-related deaths in the U.S.

This is the first RNA molecule of its kind to be identified as a biomarker for colorectal cancer. Because this type is more stable than other RNA molecules, the researchers believe noninvasive blood or stool tests eventually may be developed to quickly and easily detect SNORA42 and others that may be discovered in the future.

"We need predictive biomarkers that can identify patients who are at high risk for developing tumor recurrence, especially in those with stage 2 colorectal cancer," said Ajay Goel, PhD, director of the Center for Gastrointestinal Cancer Research and for Epigenetics and Cancer Prevention at Baylor Research Institute.

In stage 2 of the disease, the cancer has grown to some extent but has not spread to lymph nodes or distant organs. At this stage, doctors and patients often face a difficult decision: treat with surgery alone, or

follow surgery with chemotherapy and its potential side effects?

"The majority of patients with stage 2 colorectal cancer will be cured with surgery alone, but some will relapse and eventually die. Molecular biomarkers, such as SNORA42, could help determine which patients might have a better prognosis with more aggressive treatment. They also provide us with targets for the development of very specific, personalized anti-cancer interventions," said Goel, the study's lead investigator and senior author of an article in the Oct. 15, 2015, journal *Gut*.

Goel and his colleagues studied levels of SNORA42 in six established colorectal cancer cell lines and in 250 samples of cancer tissue taken from patients, comparing these with 24 matched specimens from normal tissue.

According to their results:

- SNORA42 was "overexpressed" in colorectal cancer cells, compared with normal tissue, and its expression significantly correlated with disease progression.
- Overexpression resulted in cancer cells' ability to multiply rapidly, form tumors, migrate, invade normal tissue and survive a natural cell death process.
- When SNORA42 was experimentally suppressed, these effects were reversed.
- Elevated expression appeared to be a predictor for recurrence and poor prognosis in patients with colorectal cancer.

Goel said these experimental findings about SNORA42, if confirmed in additional studies, may become useful in clinical settings within several years. He also expects other molecular biomarkers will be discovered, giving researchers and clinicians new potential therapeutic targets,

helping to predict patient prognosis and guiding treatment decisions.

Small RNA molecules, called microRNAs, were discovered about 15 years ago and provided a new area of exploration for cancer researchers. Goel's laboratory has identified several microRNAs that can be used as biomarkers for colorectal cancer. SNORAs—small nucleolar RNAs—are a subset of microRNAs that are only now being recognized for their role in cell fate and the development of various cancers.

SNORA42 is the first SNORA to be identified as a biomarker for colorectal cancer, said Goel, who recently described his group's research at two international scientific conferences. He added that SNORAs are less vulnerable than other microRNAs to biodegradation in a clinical lab setting. Their strength and stability allow them to be studied more extensively, possibly leading to noninvasive blood or stool tests to quickly and easily detect them.

More information: *Gut*: "Clinical significance of SNORA42 as an oncogene and a prognostic biomarker in colorectal cancer." Oct. 15, 2015. DOI: 10.1135/gutjnl-2015-309359

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