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NOVEL LONG NON-CODING RNA FOR THE TREATMENT OF COLORECTAL CANCER

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Non-coding RNA as a novel biomarker and therapeutic target for treating colon cancer.

Researchers at Washington University in St. Louis have developed a novel non-coding RNA, named RAMS11, as a diagnostic marker and clinical target for treating colorectal cancer (CRC). Presently, colorectal cancer is a disease with a 5-year survival rate (i.e., 14%) largely due to the development of metastasis in ~70% of patients. Currently, there are numerous therapeutic treatments for patients with metastasis colorectal cancer (mCRC) including surgery, cytotoxic chemotherapy, targeted therapy, immunotherapy, radiation, and combination strategies. However, there is little pre-treatment data that can predict response to treatment and development of resistance. While there are promising developments in second-line treatment options for mCRC patients using cytotoxic agents or targeted agents, the mechanisms driving metastatic progression remain poorly characterized thus prohibiting effective drug development.

This invention prioritizes the use of a novel non-coding RNA, RAMS11, due to its association with poor disease-free survival across independent patient cohorts that also do not respond to traditional chemotherapy,to promote resistance to topoisomerase inhibitors and improve the survival rate of patients with colorectal cancer.

Performed a high-throughput viability assay using FDA-approved drugs, which revealed that elevated RAMS11 expression increased resistance to topoisomerase inhibitors. Subsequent experiments demonstrated RAMS11-dependent recruitment of Chromobox protein 4 (CBX4) to transcriptionally activate Topoisomerase II alpha (TOP2α). A meta-analysis of ~7,000 patients across 22 cancer types revealed RAMS11 is overexpressed and promotes oncogenic phenotypes in multiple cancer types.

Jessica M. Silva-Fisher,… Christopher A Maher. Long non-coding RNA RAMS11 promotes metastatic colorectal cancer progression. Nat Commun. 2020 May 1;11(1):2156. Https:// doi: 10.1038/s41467-020-15547-8. PMID: 32358485; PMCID: PMC7195452.

- Treatment of colorectal cancer
- Cancer diagnosis

- Improves the survival rate of patients with CRC
- Promotes resistance to topoisomerase inhibitors

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