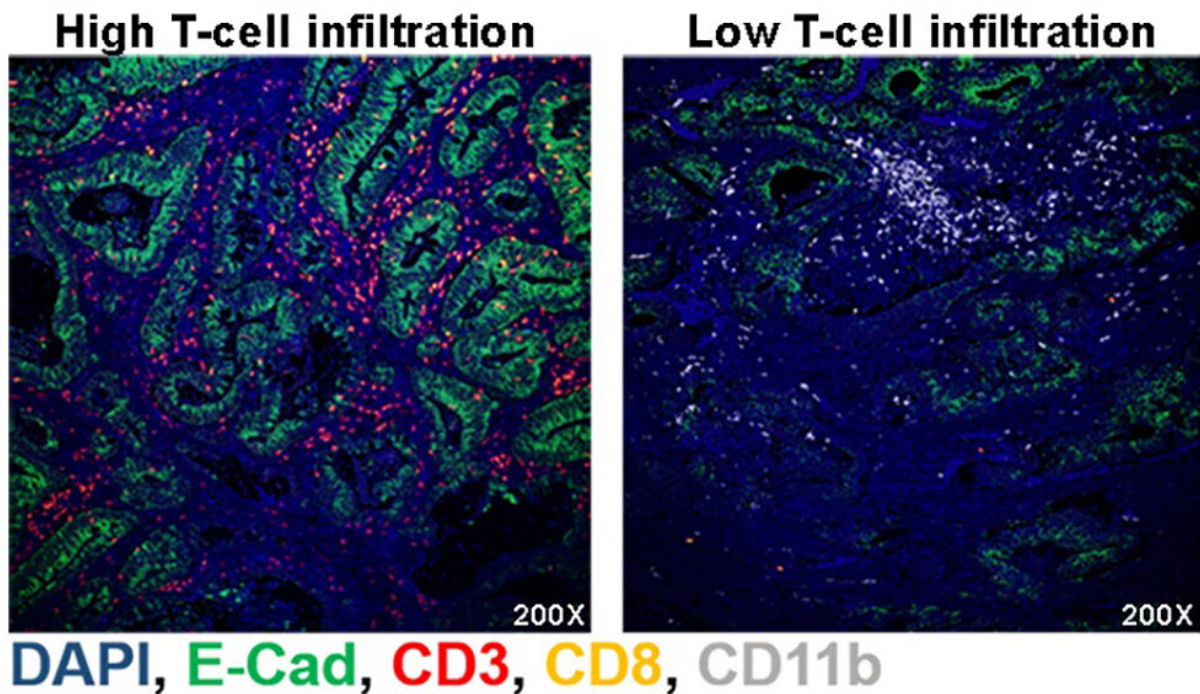


Novel late-stage colorectal cancer treatment proves effective in preclinical models

April 28 2021, by Angel Mendez



The low T cells are due to exosomal, immunosuppressive miRNAs that disrupt T cell function and loss of T cells in the tumor environment. Credit: University of Minnesota Medical School

In a recent discovery by University of Minnesota Medical School, researchers uncovered a new way to potentially target and treat late-stage colorectal cancer—a disease that kills more than 50,000 people each year in the United States. The team identified a novel mechanism by

which colorectal cancer cells evade an anti-tumor immune response, which helped them develop an exosome-based therapeutic strategy to potentially treat the disease.

"Late-stage [colorectal cancer](#) patients face enormous challenges with current treatment options. Most of the time, the patient's immune system cannot efficiently fight against tumors, even with the help of the FDA-approved cancer immunotherapies," said Subree Subramanian, Ph.D., an associate professor in the U of M Medical School's Department of Surgery, and a senior author of the study.

In partnership with Xianda Zhao, MD, Ph.D., a postdoctoral fellow in Subramanian's laboratory, the duo set out to investigate how colorectal cancer becomes resistant to available immunotherapies. What they found was recently published in *Gastroenterology*, including:

- Colorectal cancer cells secrete exosomes that carry immunosuppressive microRNAs (miR-424) that actually prevent T cell and dendritic cell function because they block key proteins (CD28 and CD80) on these immune cell types, respectively. In the absence of these proteins, the T cells, which would normally kill the cancer cells, become ineffective and are eliminated from tumors, allowing tumors to grow.
- By blocking these immunosuppressive microRNAs in [cancer cells](#), the team observed an enhanced anti-tumor [immune response](#) and discovered that cancer cell-secreted exosomes also contain tumor-specific antigens that can stimulate the tumor-specific T cell response.
- The researchers tested tumor-secreted exosomes without immunosuppressive microRNAs, in combination with immune checkpoint inhibitors, as a novel combination therapy in preclinical models with advanced-stage colorectal cancer, which proved effective.

"Our studies indicate that disrupting specific immunosuppressive factors in tumor cells helps unleash the [immune system](#) to effectively control tumor growth and metastasis in preclinical models with late-stage colorectal cancer," said Subramanian, who is also a member of the Masonic Cancer Center. "Eliminating the immune suppressive effects of those exosomes is now the focus of a new treatment option for patients with this deadly disease."

The [intellectual property](#) behind the modified exosome technology has been protected with assistance from the U of M Technology Commercialization. The team is currently developing clinical-grade exosomes that can be tested in clinical trials for patients with colorectal cancer.

More information: Xianda Zhao et al, Tumor secreted extracellular vesicles regulate T-cell costimulation and can be manipulated to induce tumor specific T-cell responses, *Gastroenterology* (2021). [DOI: 10.1053/j.gastro.2021.04.036](#)

Provided by University of Minnesota Medical School

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