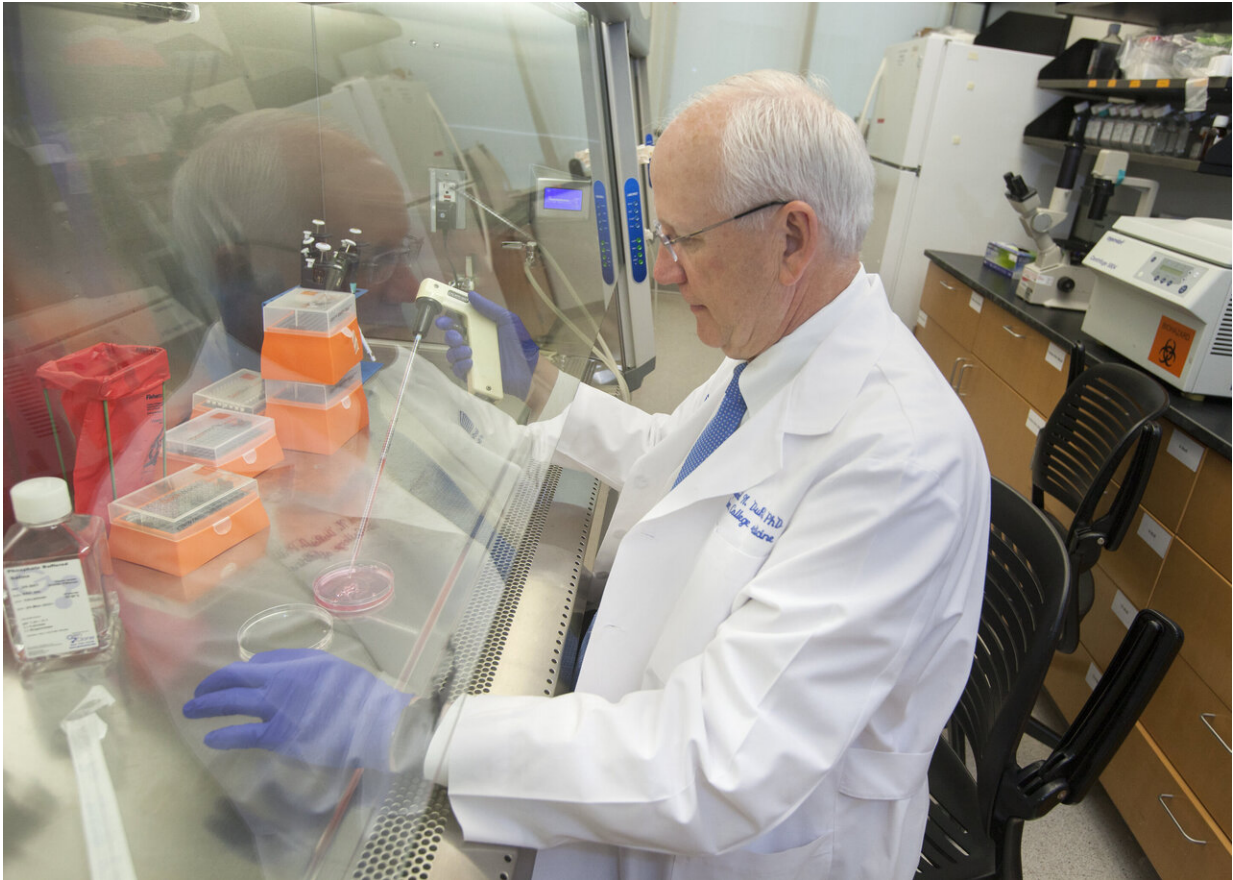


A novel pathway to target colorectal cancer

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Dr. Raymond N. Dubois, noted cancer researcher and dean of the College of Medicine at the Medical University of South Carolina, is senior author on the Gastroenterology article. Credit: Sarah Pack, Medical University of South Carolina

While the emergence of precision medicine and immunotherapy has

greatly improved outcomes for patients with colorectal cancer, new approaches are still needed for patients with late-stage disease who do not respond to these therapies. According to the American Cancer Society, patients who present with stage 4 colorectal cancer have a five-year survival rate of only 14%. Therefore, researchers are interested in finding new ways to try to inhibit colorectal tumor growth.

Prostaglandin E₂, or PGE₂, promotes metastasis of [colorectal cancer](#) through a microRNA, MIR675, report researchers at the Medical University of South Carolina (MUSC) in an article published online in November by *Gastroenterology*.

In the study funded by the National Institutes of Health, the MUSC researchers showed that mice treated with PGE₂ in a preclinical model of colorectal cancer had vastly more metastatic lesions in the liver and lung than untreated mice. This preclinical evidence suggests that targeting the microRNA could have some therapeutic potential.

"We're still learning more about some of the pathways involved in the development and progression of colorectal cancer," said Raymond N. DuBois, M.D., Ph.D., a noted cancer researcher, dean of the College of Medicine at MUSC and senior author on the article. "I think this is one example where a microRNA could be targeted in a therapeutic way in a subset of patients."

PGE₂ is thought to promote tumor cell proliferation, survival and migration. To investigate how PGE₂ does this in colorectal cancer, DuBois and the other MUSC investigators, who included first author Bo Cen, Ph.D., a research assistant professor in the DuBois laboratory, performed a screen on colorectal cancer cells treated with PGE₂ to detect if there were any changes following treatment. Voucher funding from the South Carolina Clinical & Translational Research Institute paid for a portion of this project.

"We found that many microRNAs changed in response to treatment," explained Cen. "We focused on MIR675-5p because its levels increased more than any other in response to PGE₂ treatment."

A microRNA is a small RNA molecule that can silence the expression of certain genes. In this case, MIR675-5p can suppress the expression of p53. P53 is one of the most well-known genes in cancer because it enables production of a protein that can put the brakes on cell division. However, cancer can be clever and find ways to suppress p53 so that cells can continue to divide uncontrollably.

The researchers next identified a potential site on p53 to which MIR675-5p could bind. Then, investigators confirmed that MIR675-5p suppresses p53 to promote metastasis. In a preclinical colorectal cancer model, mice were treated with PGE₂ or a vehicle control. Mice treated with PGE₂ were found to have more metastases compared to the control.

Further, tumor cells in the group of mice treated with PGE₂ had increased expression of MIR675-5p and decreased expression of p53, confirming that PGE₂ promotes tumor progression through MIR675-5p and p53.

"We found that PGE₂ was able to decrease the expression of p53, which is a very well-known tumor suppressor, and we found it was able to do this by increasing the expression of MIR675-5p," said Cen.

Next, the researchers plan to analyze samples from patients with different stages of colorectal [cancer](#) and investigate how levels of PGE₂ and MIR675-5p correlate with prognosis or response to therapy.

"Ultimately, we discovered a key mechanism by which PGE₂ promotes tumor development and progression," said DuBois. "These findings provide important preclinical evidence that microRNA could possibly be

targeted in a therapeutic way to treat a subset of patients."

More information: Bo Cen et al, Prostaglandin E2 Induces MIR675-5p to Promote Colorectal Tumor Metastasis via Modulation of p53 Expression, *Gastroenterology* (2019). [DOI: 10.1053/j.gastro.2019.11.013](https://doi.org/10.1053/j.gastro.2019.11.013)

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