Collaborating to Curb Colorectal Cancer

Through recent advances in treatment and effective screening, outcomes for colorectal cancer have vastly improved. However, much remains to be done to eliminate the disease, which continues to be the second most common cause of cancer deaths within the U.S. Colorectal cancer disproportionately impacts marginalized communities, including people of color and those living in poverty. Additionally, rates among people 55 or younger are increasing every year, and more young people are being affected than ever before.

At Fred Hutch Cancer Center, scientists are working to change that. For William M. Grady, MD, a professor at Fred Hutchinson Cancer Center, understanding why colorectal cancer develops is key to improving outcomes for patients, eliminating disparities, and preventing this disease altogether.

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Partners in prevention research

Dr. Grady and his team rely on generous contributions from the community to fuel their research into colorectal cancer prevention. **RACE Charities and the Gensch Family** support Dr. Grady's innovative studies to better understand the genetic and environmental factors at play in colorectal cancer. Here are some recent examples of this work:

- The risk of developing colorectal cancer is influenced by various factors, including age, smoking, obesity, and chronic inflammation. While advanced age is a significant risk factor, the biological age of one's cells can differ from chronological age, with some people aging biologically faster than others. By examining molecular indicators in colon tissue to determine biological age, Dr. Grady and his team discovered that individuals with colon cancer have biologically older colons compared to those without cancer. They also identified senescent cells — damaged cells that accumulate

Colorectal cancer develops when normal epithelial cells lining the colon accumulate molecular changes, progressing from benign polyps to malignant cancers. While almost all colorectal cancers originate from polyps, only 5 percent of all polyps will eventually become cancers. Dr. Grady studies the biology and genetics of colorectal cancer to pinpoint the factors that contribute to both polyp formation and their transformation into cancers — crucial for identifying those who might be vulnerable. By finding out who's at risk, researchers like Dr. Grady can create targeted surveillance and preventive therapies to reduce the likelihood of ever developing the disease.

with age — as potential contributors to colon cancer development. Dr. Grady is currently investigating whether therapies that target and eliminate these senescent cells can prevent colon cancer in mice, and if so, will trial the therapies in people.

- In their previous research, Dr. Grady and his team found that molecular changes in the colon can create premalignant fields — areas of seemingly normal tissue that are predisposed to forming polyps or cancer. The team is currently investigating one such molecular alteration known as abnormal DNA methylation. By developing new methods to identify biomarkers of DNA methylation, researchers can potentially identify individuals at high risk for these premalignant fields. Even better, these biomarkers could help indicate one's precise risk of colorectal cancer and inform personalized therapies tailored to that risk.

Blood work without bowel prep

You may have heard about research validating a new blood test for colorectal cancer called SHIELD, published in the New England Journal of Medicine, as reported by many local and national outlets. Dr. Grady is a trusted advisor to this project, and helped lead this multisite trial, which included nearly 8,000 people between the ages of 45 and 84 years.

The blood test is 84% effective at detecting colorectal cancer, comparable to at-home screening tests with less hassle for the patient. Colonoscopies remain the gold standard, but this test could make screening more accessible. "The results of the study are a promising step toward developing more convenient tools to detect colorectal cancer early while it is more easily treated," Dr. Grady says.

- Dr. Grady's lab is also exploring the potential of phytochemicals, compounds found in certain plants we eat, to reverse premalignant fields and prevent the formation of colorectal cancer.

Together towards a future without colorectal cancer

Dr. Grady's research offers hope as we work to eliminate colorectal cancer. By identifying molecular markers and exploring novel strategies for prevention, his team strives toward a future where colorectal cancer can be more effectively detected and treated — and prevented entirely. Together, with the help of organizations like RACE Charities and the Gensch Family, we can transform outcomes for individuals affected by or at risk of colorectal cancer.

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