Researchers chart a course for understanding, preventing and treating young-onset colorectal cancer

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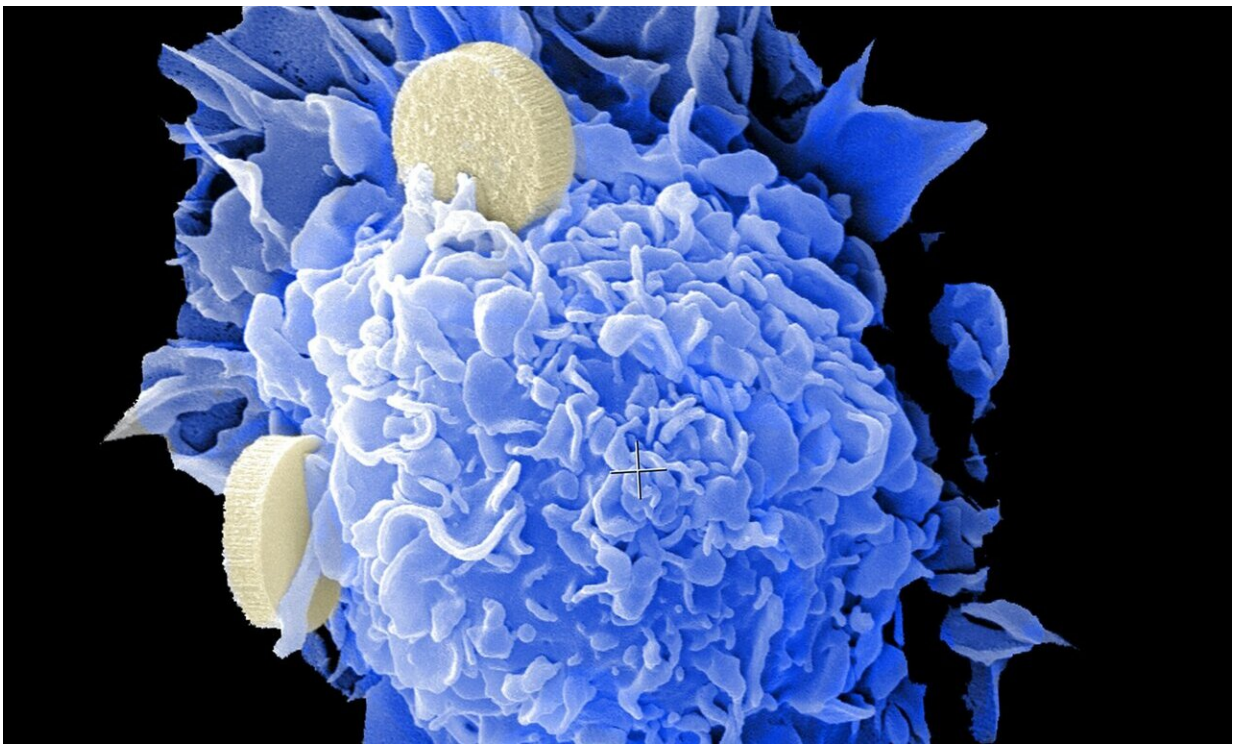

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Colorectal cancer among young people is increasing globally and rapidly. Experts expect it to become the leading cause of cancer death in individuals aged 20-49 in the U.S. by the year 2030.

Yet no one is certain why this disease is suddenly affecting so many young people. In a new paper published in *Science*, Dana-Farber Cancer Institute researchers outline the complexities of the disease and the research needed to map out a path toward understanding it.

"The rising incidence of young-onset colorectal cancer is extremely concerning, and it is urgent that the scientific community comes together to better understand the underlying causes and biology," said co-author Kimmie Ng, MD, MPH, associate chief of gastrointestinal oncology and director of the Young-Onset Colorectal Cancer Center at Dana-Farber. The Center provides expert care for patients and conducts the multidisciplinary research required to understand colorectal cancer in young adults and develop new ways to prevent, detect and treat it.

Young-onset colorectal cancer: A unique challenge

Young-onset colorectal cancer (CRC), also called early-onset CRC, differs from later-onset CRC in several ways, according to the authors. Young-onset disease is often more aggressive, presents on the left side of the colon rather than the right, and often presents with rectal bleeding and abdominal pain.

At a molecular level, however, studies have shown conflicting results that suggest both similarities and differences in the genetic mutations that drive the diseases. This is likely due to the complexity of the disease, according to the authors, and future research should account for this variability.

More study is also needed to determine if CRC risk factors for young people are similar to those for older adults. Obesity and environmental exposures, for instance, have been associated with young-onset disease, but other factors could also play a role, such as increased antibiotic use or the frequency of Cesarean sections, both of which could influence the

microbiome.

To begin to understand the risk factors, the authors suggest that investigations should include a combination of genetics, environmental exposures, diet and lifestyle measures, as well as immune system interactions and the microbiome composition.

One clear difference is that young-onset CRC is typically discovered after the disease has advanced. This is due in part to the fact that screening for colorectal cancer starts at age 45 in the U.S., so the disease often goes undetected in younger people.

"It's important not to dismiss the idea that a young person could have colorectal cancer even though the disease is still more common in older adults," said co-author Marios Giannakis, MD, Ph.D., a gastrointestinal oncologist at Dana-Farber.

Responding with multidisciplinary research involving diverse populations

To account for the complexity of young-onset CRC, Ng and Giannakis said that research should be multidisciplinary and include many areas of investigation simultaneously. For instance, genome-wide association studies, which aim to find risk genes for the disease, should also include data about environmental exposures that could also increase risk.

These types of studies could point to new ways to identify young people who are at high risk of young-onset disease and should be screened for CRC. "Risk stratification is going to be very important as we think about screening for young-onset disease," said Giannakis.

Clinical studies should also include the collection of blood, tissue, and

stool samples from patients over time to shed light on the role of immune cells, environmental exposures and the microbiome in disease onset, progression, and treatment response. Ng and Giannakis encourage global collaborations aimed at facilitating the collection of these specimens, such as the Count Me In Colorectal Cancer Project, which directly partners with patients in the U.S. and Canada and makes all data available for research.

Ng and Giannakis also call for more effort in ensuring diverse populations are included in studies of young-onset CRC. Studies show underrepresented minorities are disproportionally burdened by young-onset CRC and non-Hispanic Black patients have a higher mortality rate when compared to non-Hispanic whites.

"Although each of these steps require commitment and perseverance," said the authors, "it is the growing numbers of young patients bravely battling this disease that will be the compass that keeps us on the path towards better understanding, preventing, and treating young-onset colorectal cancer."

More information: Marios Giannakis et al, A common cancer at an uncommon age, *Science* (2023). DOI: 10.1126/science.ade7114. www.science.org/doi/10.1126/science.ade7114

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