



Young Onset Colorectal Cancer: Transforming the Future of Research and Care September 2020

In the United States this year, nearly 150,000 new cases of colorectal cancer will be diagnosed; globally, this figure is nearly 2 million. Despite steady gains in early detection through colonoscopies, colorectal cancer remains a dangerous, even lethal disease—one that’s particularly virulent when it reaches an advanced, metastatic stage.

In recent years, oncologists have discovered an alarming trend: More people under age 50 are being diagnosed with colorectal cancer than ever before. To counter this pressing issue, in March 2018 Memorial Sloan Kettering Cancer Center (MSK) opened the **Center for Young Onset Colorectal Cancer**, the country’s first program singularly focused on patients facing colorectal cancer at an early age. Oncologist **Andrea Cercek, MD**, and gastroenterologist **Robin Mendelsohn, MD**, are Co-Directors of this groundbreaking initiative. We are delighted to describe the group’s latest progress and plans below.

Impact to Date

A world-recognized pioneer in colorectal cancer treatment and research, MSK cares for more than 2,500 patients with this disease each year. Among them, more than 400 are 50 years old or younger. So far, over 800 patients have come to the center, which is attracting people from as far away as China and Saudi Arabia. The endeavor has been so successful that it is expanding to MSK’s regional sites across New Jersey and New York, and is establishing a collaboration with our national MSK Cancer Alliance network of hospitals.

A major focus of research for the center is uncovering what has led to the increase in colorectal cancer among younger people. In a patient record investigation led by Dr. Mendelsohn, she found that in the past decade, MSK has treated more than 4,000 people with colorectal cancer who were under 50 years old. While the years of data from these patients provides an opportunity to study risk factors, including obesity, smoking, and alcohol consumption, Dr. Mendelsohn found that these young people had lower rates of risk factors compared to their peers who did not develop cancer. Knowing this, a priority for the group will be to shift research efforts to studying the community of bacteria that live in our gut, known as the microbiome, which help digest food and regulate our immune system, and compare what may be affecting the microbiome now that is different from 40 years ago.

Complementing research that could reveal the roots of this worrisome trend, Dr. Cercek and her team are focused on new screening, diagnosis, and treatment approaches. Their multidisciplinary research is underway, translating discoveries made in the laboratory into innovative clinical strategies, always with an eye on quality of life. In addition to developing novel tools for screening and diagnosis, the center is actively engaged with experts from [genetics](#), [pathology](#), [immunology](#), and [epidemiology—determined](#) to set the pace on how to manage these complex diseases.

Integrating Clinical Data With Genomics to Guide Treatment

MSK is a global leader in precision oncology, which involves identifying the genetic mutations that cause an individual's cancer and targeting them with drugs that hone in on those mutations. In fact, investigators at MSK invented a sophisticated technology called MSK-IMPACT™, which searches tumors for 468 cancer-causing genes, from the most common to the rarest forms of the disease.

While many mutations do not yet have associated medications to counter them, drugs called targeted therapies have shown promising results in some cancers. This means that patients receive the best drugs to combat their disease while avoiding unnecessary treatment and related side effects.

To translate more findings from precision oncology to colorectal cancer, the center is drawing on the expertise of Nicholls-Biondi Chair **Sohrab Shah, PhD**, Chief of Computational Oncology. Dr. Shah and his team are integrating biological and clinical data with advanced computer modeling to develop predictive tools that will serve as the gateway to precision cancer medicine.

Because changes in the microbiome have been suggested as a possible cause of early-onset colon cancer, the center collected stool samples from patients to look for any viral and bacterial changes. Working alongside Dr. Shah's group, the center will refine the process through which colorectal tumors are characterized molecularly while integrating data on patients' tissue, stool, blood, and other samples taken throughout treatment. This will help physicians diagnose early-stage disease, guide therapeutic decisions, predict outcomes, and evaluate how patients respond to treatment.

Through this collaboration, the center has completed the largest, most comprehensive molecular analysis of young onset tumors and associated clinical characteristics, including risk factors for developing the disease early. Today, Dr. Cercek, in addition to preparing a manuscript, is expanding the analysis to include an even deeper test called whole-exome sequencing and working with researchers in other countries that are also seeing a rise in young onset diagnoses.

All of these initiatives lay the groundwork for an exciting window of opportunity. By improving the methods used to accurately determine the severity of a tumor and its likelihood of spreading, the center will be poised to design more-targeted clinical trials. Eventually, the goal is to design and implement clinical trials at MSK specifically for young people with colorectal cancer—to prevent or slow down the processes by which these early-onset diseases form and dramatically improve outcomes.

Investigating Changes in the Colon in Young People With Colorectal Cancer

The center is undertaking a project that focuses on identifying potential mutational changes in healthy colon tissue that may be caused by diet. The theory is that something in the environment is leading to premature cellular aging and the development of cancer in younger patients. Together with a team in pathology and computational biology, the group will compare healthy colon tissue from both young and older patients with colon cancer to see if the degree of genetic mutations is the same in both groups. This represents a completely new avenue of research that

could lead to a potential clue about environmental triggers for younger patients and how they can be avoided.

Treating the Whole Patient

Since the center's inception, the group has recognized the unique needs of young people diagnosed with colorectal cancer. Working with experts from social work, sexual health, integrative medicine, and nutrition, they have implemented a coordinated clinical care program that systematically addresses the myriad issues that cancer might introduce. They are developing and promoting educational programs, psychosocial tools, and resources to meet the needs of these patients throughout their care and into survivorship.

The rapid expansion of telemedicine has granted patients wider access to these services. The team is developing an app that will serve as a virtual hub where young patients can reduce the social isolation they are particularly vulnerable to experiencing. Patients will be able to share photos, ask experts questions, and stay up to date on any programming related to their treatment.

Addressing the Impact of Fertility

The center recognizes the unique needs of young people diagnosed with colorectal cancer, including their sexual health. Research into the impact of treatment on a patient's reproductive and sexual function is limited. In 2013, Dr. Cercek was lead author on an important paper describing preliminary work on this topic. As she described in *Clinical Colorectal Cancer*, about 24% of women who underwent the standard FOLFOX chemotherapy regimen to treat colorectal cancer experienced a persistently altered menstrual cycle after therapy.

To drive this project forward, Dr. Cercek has established a longitudinal study to measure the effect of chemotherapy on the fertility of young patients with colorectal cancer. The study, to open sometime this year, will monitor the effects of chemotherapy and radiation on fertility and sexual function in men and women with early-onset colorectal cancer. This work will go a long way toward building MSK's program, and it will provide the necessary preliminary data for a larger government grant.

The group has also partnered with MSK's **Jeanne Carter, PhD**, a clinical psychologist and certified sexual health therapist, to focus on the emotional impact of colorectal cancer on people diagnosed at young ages. Using a robust clinical database and tissue biobank, patients will be followed over time to monitor the course of the disease, as well as the long-term side effects of therapy, including its impact on fertility.

Looking Ahead

At Memorial Sloan Kettering, we are on the cusp of many critical advances in the care and treatment of early-onset colorectal cancers—especially as physician-scientists start incorporating novel, leading-edge approaches to make therapy even more precise, targeted, and effective.

Today we have an unprecedented opportunity to change the lives of countless people impacted by cancer. Philanthropy is crucial to driving this momentum. Thank you for your support.