

Differences between tumors of younger and older colorectal cancer patients

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Colorectal cancer (CRC) is on the rise among younger patients. Although some of the younger-onset cases can be explained by hereditary factors, the majority arise spontaneously. Researchers have now found that tumours in younger colorectal cancer patients may be molecularly distinct from those of older patients, and that these differences are related to the way genes are switched on and off (epigenetics) in the tumours of the younger patients. Such a discovery may lead to better treatment options tailored specifically to a younger age group, they say.

Presenting their results to the 2015 European Cancer Congress, Dr Andrea Cercek, an Assistant Attending Physician at the Memorial Sloan Kettering Cancer Center, and Assistant Professor of Medicine at Weill Cornell Medical Center, New York, USA, will describe her team's analysis of genetic mutations in tumours from 126 patients aged under 50 and 368 aged 50 and over. "Interestingly, we found a different frequency of mutation of genes known to be [cancer](#)-causing in the different age groups," she says.

Tumours from two groups of CRC patients were analysed; the first included patients treated at Memorial Sloan Kettering, and the second patients from The Cancer Genome Atlas, a project aiming to catalogue cancer-causing genetic mutations, run by the US National Cancer Institute. Genomic sequencing techniques were used to look for gene mutations and other changes to DNA that affect the ways genes behave (processes known as gene expression and methylation). Patients with very large numbers of mutations or where the proteins controlling errors of DNA replication were not functioning correctly (microsatellite instability) were excluded.

"In the early onset group we found that 154 genes were under-methylated. Both under (hypo) and over (hyper) methylation of genes are found in cancer," Dr Cercek explains. "We also found that

an increase in methylation went hand in hand with an increase in age among the younger patients, and that this intensification was beyond that which would occur naturally in normal tissue. Finding such a distinctive molecular make-up in this group encourages us to believe that we may, in the future, be able to tailor treatments to them and attempt to prevent or slow down these processes in order to improve outcomes for them."

Younger-onset CRC has increased at a continuous rate of 1.5% per year in men and 1.6% per year in women during the period 1992-2011, according to data from the Surveillance, Epidemiology, and End Result Registries (SEER), the agency that collects and collates cancer statistics on behalf of the US National Cancer Institute. Although CRC is the third most common cancer in the world, with nearly 1.4 million new cases diagnosed in 2012, younger patients tend to present and be diagnosed later, when their disease is more advanced and hence more difficult to treat. This is most likely to be due to a lack of awareness of symptoms in patients as well as doctors, in addition to the tendency to attribute those symptoms to other causes.

"Changes in bowel habits may be attributed to Crohn's disease, food allergies, or simply stress, for example, and doctors send younger patients for early CRC screening much less frequently than they do older ones," says Dr Cercek. "I believe that raising awareness of the increasing frequency of younger-onset CRC among clinicians is very important."

Younger CRC patients tend to be treated more aggressively, though currently there is no other difference in the therapies used. "That is why our findings are important," Dr Cercek will say. "We hope to be able to continue research on the molecular and epigenetic characterisation of tumours from younger-onset CRC patients in order to be able to develop better therapies for them, and improve their overall survival as well as their quality

of life."

Professor Peter Naredi, the ECCO scientific co-chair of the Congress, who was not involved in the research, commented: "While we have indications that screening for CRC in an older age group is important, this is not the case in a younger general population. Therefore, it is important to identify younger persons with a higher risk of CRC, and Dr Cercek's epigenetic analyses are an important step towards this. As Dr Cercek also says, identifying specific genetic patterns in CRC tumours in younger patients may lead to better treatment options."

More information: Abstract no 2189. "Early onset colorectal cancer - does the difference lie in epigenetics?"

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