

Wnt stem cell signaling pathway implicated in colorectal cancer in patients under 50

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Christopher Lieu, MD, and colleagues show Wnt cancer stem cell signaling pathway is more upregulated in colorectal cancer patients under age 50. Credit: University of Colorado Cancer Center

While increased screening continues to drive down overall colorectal cancer rates, the rate of colorectal cancer in patients under age 50 is increasing, and the disease is commonly more aggressive in these young patients. A University of Colorado Cancer Center study presented at the American Society for Clinical Oncology (ASCO) Annual Meeting 2016 shows one possible reason for the increased danger of colorectal cancers (CRCs) found in younger patients: while many genetic changes are shared between younger and older CRC patients, younger patients are more likely to have alterations in genes involved in what is known as the Wnt signaling pathway, a system of communication that drives the growth, survival and proliferation of cancer stem cells.

"This pathway has had a lot of interest in CRC and other cancers as well. We found that [genes](#) associated with the WNT pathway appear to be more frequently altered in younger patients," says Christopher Lieu, MD, investigator at the CU

Cancer Center and assistant professor of medical oncology at the University of Colorado School of Medicine.

Lieu and his team worked with Foundation Medicine to analyze the genetics of 4,699 samples of CRC tissue. Then the group explored the genetic differences between samples that had been taken from patients older and younger than age 50. Though cancers from younger and older patients shared many of the same [genetic changes](#), younger cancers were more likely to have alterations in the genes CTNNB1 and FAM123B. These genes are important players in the larger system known as the Wnt signaling pathway.

Like many signaling pathways, the Wnt pathway controls gene transcription - how often the information contained in particular genes is manufactured into proteins. These proteins then go on to define almost everything in the ecosystem of the body, from tissue growth to brain function. The Wnt signaling pathway, in particular, is especially active during embryonic development, helping to shape the differentiation of [stem cells](#) into more specialized cells. Many cancers restart and coopt this developmental stem cell pathway to promote the ability of their own [cancer stem cells](#) to grow tumor tissue.

While it is impossible to simply mute the genes CTNNB1 or FAM123B implicated in the development of aggressive CRC in young patients, it may be possible to intercede elsewhere in the Wnt pathway that is improperly upregulated by these genes. For example the CU Cancer Center has been involved in clinical trials testing the Wnt inhibitor OMP-54F28 and a handful of additional Wnt inhibitors are currently in human clinical trials.

"This is an important finding because it can help us discover who is most likely to benefit from this new class of drugs. It may be that Wnt inhibition is even more important in younger [colorectal cancer](#)

patients," Lieu says.

Provided by CU Anschutz Medical Campus

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