

Researchers publish review of the 'molecular basis of colorectal cancer'

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Every year in the United States, 160,000 cases of colorectal cancer are diagnosed, and 57,000 patients die of the disease, making it the second leading cause of death from cancer among adults, after lung cancer.

As researchers and clinicians fervently look for causes and cures for colorectal cancer -- simultaneously generating thousands of studies producing more and more promising results - Dr. Sanford Markowitz, professor and researcher of cancer and genetics at Case Western Reserve University School of Medicine and oncologist at the Case Comprehensive Cancer Center at University Hospitals Case Medical Center, today published his forward-looking view of the "[Molecular Basis](#) of Colorectal Cancer" in the Dec. 17, 2009 issue of the [New England Journal of Medicine](#), with co-author, Dr. Monica Bertagnolli, from the Brigham and Women's Hospital, Harvard Medical School.

"Today's challenges are to understand the molecular basis of individual susceptibility to colorectal cancer and to determine factors that initiate the development of the tumor, drive its progression, and determine its responsiveness or resistance to antitumor agents," wrote Dr. Markowitz.

Key advances that the article singled out toward meeting these goals are:

- Discoveries in DNA sequencing technology have made it possible to sequence the entire genome of a human cancer. Colorectal cancer provided the first

example of the power of this technology. Sequencing of 18,000 (nearly all) of the known human genes in 35 colon cancers identified 140 as candidate cancer genes that were mutated in at least two colon cancers and that probably contributed to the cancer phenotype.

- Biological pathways that are deregulated in colon cancer have been identified, and could now form the basis of new therapeutic agents. Although some high-frequency mutations are attractive targets for drug development, common signaling pathways downstream from these mutations may also be tractable as therapeutic targets.
- Studies that aid in the understanding of colorectal cancer on a molecular level have provided important tools for genetic testing for high-risk familial forms of the disease, predictive markers for selecting patients for certain classes of drug therapies and molecular diagnostics for the noninvasive detection of early cancers.
- Recent progress in molecular assays for the early detection of colorectal cancer indicates that understanding the genes and pathways that control the earliest steps of the disease, and individual susceptibility, can contribute to clinical management in the near term. For example, patients whose colon cancers have mutations in either RAS or BRAF genes are known not to benefit from treatment with the anti-colon cancer agent Cetuximab.
- Moreover, patients with inherited mutations in tumor-suppressor genes, such as APC, MLH1, and MSH2 have a very high risk of colorectal cancer and require early and frequent surveillance for colon cancer and often prophylactic surgery.

- Last, the development of molecular diagnostics for the early detection of colorectal cancer is emerging as an important translation of [colon-cancer](#) genetics into clinical practice. One example is the development of stool DNA tests to detect cancer-associated aberrant DNA methylation as a method for early detection of patients with colorectal cancer or advanced adenomas. Stool DNA testing for colorectal cancer has been added to the cancer-screening guidelines of the American Cancer Society.

Dr. Markowitz and Bertagnolli's concluding observations are optimistic ones that the considerable recent and ongoing advances in our knowledge of the molecular basis of colorectal [cancer](#) will continue to result in markedly reducing the burden of this disease.

Dr. Markowitz reports being listed on patents licensed to Exact Sciences and LabCorp and is entitled to receive royalties on sales of products related to methylated vimentin DNA, in accordance with the policies of Case Western Reserve University. No other potential conflict of interest relevant to this article was reported.

Provided by Case Western Reserve University

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