

## **EARLY DETECTION RESEARCH NETWORK STUDIES IN COLORECTAL CANCER**

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Though colonoscopy is a valuable tool for the early detection of colon cancer, there is a need to develop alternative tests for people unwilling or unable to get a colonoscopy-based screening test. The DNA changes which happen in colon cancer can be detected in stools of patients who are diagnosed with colon cancer or who have pre-cancerous colon polyps. A colon cancer screen test using stool samples would complement colonoscopy to identify colon cancer when it should be easier to treat, to screen people who are not able to have a colonoscopy, and to screen people between colonoscopy tests to improve detection of fast growing lesions in the right colon.

Researchers are developing a detection method to find an abnormal change in DNA present in stool. This change in vimentin DNA methylation is present in 80% of colon cancers. During this research it was determined that sensitivity (the probability of correctly diagnosing a condition) of this stool test was high: 77% for stage 1 colon cancer, 84% for stage 2 and 86% for adenomas greater than 1cm. Specificity (the probability of correctly identifying a nondiseased person) is between 83-90%. By comparison, Fecal Immunochemical Tests (FIT) have shown 41% sensitivity for detection of adenomas greater than 1 cm. and 98% specificity.

A commercial test, ColoSure, for screening for colon cancer has been developed based on this approach of detecting a methylated DNA in stools of individuals. Development of successor tests, based on a panel of methylated and mutated DNA markers is underway.

In addition, further studies of this change in DNA in other gastrointestinal tract cancers determined that methylated vimentin is found in a pre-cancerous condition called Barrett's Esophagus with a 91% sensitivity, suggesting that some individuals who have methylated DNA detected in their stools and in whom a colonoscopy is normal, may harbor lesions in the esophagus or upper gastrointestinal tract.

Another EDRN project is to research the role of the protein 15-PGDH (15-hydroxyprostaglandin dehydrogenase) in colon cancer. The presence of low levels of 15-PGDH has been shown to suppress the development of colon tumors. These discoveries are made using cutting-edge gene technologies that allow researchers to check every gene in a tumor to see if it is being turned on or off and to see if it is being chemically altered in the DNA. For example, 15-PGDH was discovered as a gene in that a normal colon turns on but that colon cancers turn off, a pattern now also recognized in lung cancers and breast cancers as well.

A test for 15-PGDH can be used to predict whether an individual will have a cancer prevention benefit from taking the drug celecoxib. Using specimens from the Adenomas Prevention with Celecoxib (APC) trial, investigators found that individuals who developed new adenomas while receiving celecoxib treatment had low levels of colonic 15-PGDH. This suggests that it may be possible to determine which individuals might benefit from celecoxib by measuring the level of 15-PGDH in their colon.