Epi proColon®

Septin 9 Gene Methylation Detection

Available nationally for the first time through LabCorp

An FDA-approved blood-based test for **Colorectal Cancer Screening**

Colorectal Cancer Background

Colorectal cancer is the third most commonly diagnosed cancer among women and men in the United States, with 90% of cases occurring after age 50.[1] A majority of colorectal cancer cases are due to somatic genetic mutations and occur later in life; however, a subset of approximately 5% to 10% of patients have inherited mutations that predispose them to the development of colorectal cancer.[2]

Colorectal cancers are characterized by both their clinical presentation and the cascade of genetic mutations associated with the disorders. Genetic mutations or changes in genes can be detected in a tumor, and even at the earliest stages colorectal tumors shed genetic material into blood, which can be detected in a blood specimen.

Sometimes patients will refuse a colonoscopy or may be non-compliant with orders that involve stool collections or fecal manipulations. Most patients are familiar with and reasonably compliant with phlebotomy requests. Greater colorectal screening compliance may lead to earlier detection of colorectal cancer and a reduction in mortality rates.

Quick Facts About Colorectal Cancer

- An individual's lifetime risk of developing colorectal cancer in the US is approximately 4.5% to 4.8%.[3]
- It is estimated that more than 134,000 adults will be diagnosed with colorectal cancer in 2016, while more than 49,000 will die from the disease in 2016.[4]
- If diagnosed and treated at the localized stage, the five-year survival rate is 90%. Unfortunately, only 39% of all cases are found at the localized stage.[4]
- Most colorectal cancers are detected at the regional or distant stages, which carry five-year survival rates of 70% and 13%, respectively.[1]

Introduction of Epi proColon®

Now available through LabCorp, **Epi proColon®, Septin 9 Gene Methylation Detection (481160)** is an innovative blood-based test for colorectal cancer screening that has been approved for clinical use by the US Food and Drug Administration (FDA). Epi proColon is the latest in a broad spectrum of DNA-based diagnostics offered by LabCorp to aid in the detection, diagnosis, prognosis, therapy selection, and surveillance of cancer.

The convenient Epi proColon test is designed to screen patients for colorectal cancer who are defined as average risk for colorectal cancer (CRC) by current CRC screening guidelines, and who decline screening by colonoscopy or fecal occult blood testing. The Epi proColon test results, together with the physician's assessment of history, other risk factors, and professional guidelines, may be used to guide patient management, which can include diagnostic colonoscopy for patients with positive Epi proColon test results.

How Epi proColon Works

Hypermethylated Septin 9 tumor DNA is shed into the bloodstream. The Epi proColon test detects the *SEPT9* DNA methylation marker for colorectal cancer in cell-free DNA circulating in blood. The kit provides reagents for efficient nucleic acid isolation from plasma, bisulfite conversion, and analysis of *SEPT9* methylation by real-time polymerase chain reaction (PCR). Methylation of the target DNA sequence in the promoter region of the *SEPT9_v2* transcript has been associated with the occurrence of colorectal cancer (CRC).

In three separate studies, the clinical performance of Epi proColon was reported with sensitivity of 68.2%, 73.3%, and 72.25%, respectively, and specificity of 78.8%, 81.5%, and 80.8%, respectively, when compared to colonoscopy.[5]

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Collection Instructions

It is recommended that patients be referred to a LabCorp patient service center for collection. Otherwise, take care to follow the procedure of specimen collection and preparation outlined below:

- Collect six 4-mL BD® K_2EDTA blood collection tubes.
- Immediately following specimen collection, label all tubes with appropriate patient identification information.
- Centrifuge the six BD K_2EDTA blood collection tubes for 10 minutes at 1600 ± 90 rcf.
- Remove blood collection tubes from the centrifuge. Plasma sample will be rejected if it is hemolyzed.
- Using a fresh 6-inch disposable transfer pipette, transfer plasma from three 4-mL blood collection tubes to one 8.5-mL Sarstedt centrifuge tube (55.598.006). Repeat this process with the second set of three 4-mL blood collection tubes. Two 8.5-mL transfer tubes will result from six 4 mL blood collection tubes.
- Centrifuge plasma in the two 8.5-mL centrifuge tubes for 10 minutes at 1600 ± 90 rcf.
- Using a fresh 6-inch disposable transfer pipette or serological pipette, transfer 3.5 mL of plasma from one 8.5 mL centrifuge tube into a labeled 7-mL Sarstedt screw cap, flat bottom, purple transport tube, **frozen** (62.550.019). Repeat this process with the second 8.5-mL centrifuge tube. Two 7.0-mL tubes will be collected.
- Ship and store **frozen** plasma at -15°C to -25°C. Stable for 14 days.

Note: Take care not to disturb or transfer the buffy coat (white blood cells) layered above the red blood cells in the blood collection tube after the first centrifugation, or sedimented at the bottom of the centrifuge tube after the second centrifugation.

Test Name	Epi proColon®, Septin 9 Gene Methylation Detection
Test N°	481160

For more information, visit the online test menu at **www.labcorp.com/testmenu.**

References

1. American Cancer Society. *Colorectal Cancer Facts & Figures 2014-2016.* Atlanta,Ga: American Cancer Society; 2014.
2. American Cancer Society. What are the risk factors for colorectal cancer? Atlanta,Ga: American Cancer Society. Available at: http://www.cancer.org/cancer/colonandrectumcancer/detailedguide/colorectal-cancer-risk-factors. Accessed April 13, 2016.
3. American Cancer Society. Lifetime Risk of Developing or Dying From Cancer. Atlanta,Ga: American Cancer Society. Available at: http://www.cancer.org/cancer/cancerbasics/lifetime-probability-of-developing-or-dying-from-cancer. Accessed April 13, 2016.
4. American Cancer Society. *Colorectal Cancer Facts & Figures 2016.* Atlanta,Ga: American Cancer Society; 2016.
5. Epi proColon Instructions for Use [package insert]. Berlin, Germany: Epigenomics AG; 2014.

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Intended Use Statement[5]

The Epi proColon test is a qualitative in vitro diagnostic test for the detection of methylated Septin 9 DNA in EDTA plasma derived from patient whole blood specimens. Methylation of the target DNA sequence in the promoter region of the *SEPT9_v2* transcript has been associated with the occurrence of colorectal cancer (CRC). The test uses a real-time polymerase chain reaction (PCR) with a fluorescent hydrolysis probe for the methylation-specific detection of the Septin 9 DNA target.

The Epi proColon test is indicated to screen adults of either sex, 50 years or older, defined as average risk for CRC, who have been offered and have a history of not completing CRC screening. Tests that are available and recommended in the USPSTF 2008 CRC screening guidelines should be offered and declined prior to offering the Epi proColon test. Patients with a positive Epi proColon test result should be referred for diagnostic colonoscopy. The Epi proColon test results should be used in combination with physician's assessment and individual risk factors in guiding patient management.

Contraindications

The Epi proColon test is not intended to replace colorectal cancer screening tests that are recommended by appropriate guidelines (e.g., 2008 USPSTF guidelines) such as colonoscopy, sigmoidoscopy and high sensitivity fecal occult blood testing.

The Epi proColon test is not intended for patients who are willing and able to undergo routine colorectal cancer screening tests that are recommended by appropriate guidelines.

The Epi proColon test is not intended for patients defined as having elevated risk for developing CRC or based on previous history of colorectal polyps, CRC or related cancers, inflammatory bowel disease (IBD), chronic ulcerative colitis (CUC), Crohn's disease, familial adenomatous polyposis (FAP). People at higher risk also include those with a family history of CRC, particularly with two or more first degree relatives with CRC, or one or more first degree relative(s) less than 50 years of age with CRC.

The Epi proColon test has not been evaluated in patients who have been diagnosed with a relevant familial (hereditary) cancer syndrome such as non-polyposis colorectal cancer (HNPCC or Lynch Syndrome), Peutz-Jeghers Syndrome, MYH-Associated Polyposis (MAP), Gardner's syndrome, Turcot's (or Crail's) syndrome, Cowden's syndrome, Juvenile Polyposis, Cronkhite-Canada syndrome, Neurofibromatosis, or Familial Hyperplastic Polyposis, or in patients with anorectal bleeding, hematochezia, or with known iron deficiency anemia.

Warnings, Precautions and Limitations

The Epi proColon test demonstrated inferiority to a fecal test (OC FIT-CHEK® Polymedco, Inc.) for specificity, indicating that the Epi proColon test exhibited a higher rate of false positive results compared to the FIT test. The Epi proColon demonstrated noninferiority to a fecal test for sensitivity.

A positive Epi proColon test result is not confirmatory evidence for CRC. Patients with a positive Epi proColon test result should be referred for diagnostic colonoscopy.

A negative Epi proColon test result does not guarantee absence of cancer. Patients with a negative Epi proColon test result should be advised to continue participating in a recommended CRC screening program according to screening guidelines.

Screening with Epi proColon in subsequent years following a negative test result should be offered only to patients who after counseling by their healthcare provider, again decline CRC screening methods according to appropriate guidelines. The screening interval for this follow-up has not been established.

The performance of Epi proColon has been established in cross-sectional (i.e., single point in time) studies. Programmatic performance of Epi proColon (i.e., benefits and risks with repeated testing over an established period of time) has not been studied. Performance has not been evaluated for patients who have been previously tested with Epi proColon. Noninferiority of Epi proColon programmatic sensitivity as compared to other recommended screening methods for CRC has not been established.

The rate of false positive Epi proColon results increases with age. Test results should be interpreted with caution in elderly patients.

CRC screening guideline recommendations vary for people over the age of 75. The decision to screen people over the age of 75 should be made on an individualized basis in consultation with a healthcare provider.

Positive test results have been observed in healthy subjects and in patients diagnosed with chronic gastritis, lung cancer and in pregnant women.

Test results should be interpreted by a health care professional. Patients should be advised of the cautions listed in the Epi proColon Patient Guide.