

Our Colorectal Cancer Program



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Since the early days of our Company, we have focused on developing a test for the early detection of colorectal cancer. Today, colorectal cancer screening is still our leading development program. For very good reasons: The improved early detection of this cancer can potentially save many lives and provides an unprecedented market opportunity in the diagnostic space. However, to address this market, screening tests are needed that solve the fundamental dilemma in colorectal cancer screening: the lack of patient acceptance of screening, despite the obvious medical benefit.

With our recently launched Epi *pro*Colon blood test and similar tests that are all based on our proprietary ^mSEPT9 biomarker and are to be marketed by our partners in the diagnostics industry, we believe we can help to overcome this fundamental hurdle to effective colorectal cancer screening.

The Colorectal Cancer Screening Dilemma: Great Benefit, Little Acceptance

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Colorectal cancer is very often curable. More than 90% of all patients survive if the cancer is diagnosed at an early stage while it is still localized. This may be a surprising fact since this dreaded disease is amongst the most frequent causes of cancer-related death in the industrialized world. In the U.S., approximately 150,000 people will be diagnosed with the disease in 2009 and about 50,000 people will die of this cancer in the same period¹. In Europe, 413,000 people were diagnosed with colorectal cancer and 207,000 died of the disease in 2006². This makes colorectal cancer one of the most frequent and the second-most deadly cancer after lung cancer. The dilemma: the majority of colorectal cancers are diagnosed in advanced stages when they already show symptoms lowering the chances of survival to less than 10% once the cancer has spread to distant organs. These figures clearly demonstrate that early diagnosis can potentially save many lives.

But catching colorectal cancer in its earliest stages requires systematic screening of the asymptomatic average risk population with suitable diagnostic procedures. Screening guidelines in many countries recommend regular fecal occult blood tests (FOBTs) – laboratory tests that are performed on stool samples – or invasive endoscopic procedures such as colonoscopy performed on average every ten years and which requires extensive bowel preparation. Despite these

recommendations and their life-saving effect, only a minority of the target population participates in regular colorectal cancer screening. Thus, annual FOBTs are only performed by 12% of the individuals aged 50 years and older and less than half attend a colonoscopy within ten years³. The most widely reported reason for this low acceptance is the lack of convenience. The American Cancer Society identified screening compliance as the major issue in colorectal cancer and is committed to drive compliance up to 75% by 2015, a goal that is essentially shared by many patient advocacy groups and government initiatives throughout Europe. Reaching this goal may be facilitated by novel screening tests that are competitive with the best available non-invasive test in differentiating between cancer patients and healthy individuals but convenient enough to ensure broad acceptance in the guideline eligible population. Such tests could address about 300 million people aged 50 years and older in the major markets that should be screened regularly for colorectal cancer, a unique opportunity in the in vitro diagnostics space that has a market potential in the billions of Euros.

A Simple Innovative Blood Test to Revolutionize Colorectal Cancer Screening

At Epigenomics, we set ourselves the goal to develop innovative molecular diagnostic tests that address unmet needs in cancer screening and diagnostics. We believe the solution for the colorectal cancer dilemma is surprisingly simple: A blood test that reliably detects the cancer in its earliest stages and can easily be integrated into an annual physical check-up at the family doctor's office. With our unique DNA methylation technology, we have made this vision a reality: Our Septin9 colorectal cancer blood test Epi *pro*Colon is available to patients and doctors in Europe as a CE-marked in-vitro-diagnostic kit as of October 2009. Further we expect the first of our partners in the diagnostics industry, Abbott Molecular and Quest Diagnostics to start offering their Septin9 tests in Europe and the United States, respectively, towards the end of 2009. (for test availability, click [here](#))

Our cancer screening tests rely on a rather simple biological phenomenon: Even at the earliest stages, tumors shed DNA into body fluids they are exposed to. Thus, tumor DNA in blood or urine is a formidable indicator – or “biomarker” – for the presence of a tumor. But how to detect this tumor DNA? With a great amount of DNA derived from healthy cells in the same body fluids, it is like looking for a needle in a haystack. At Epigenomics, we have solved this problem by analyzing differences in DNA methylation. DNA methylation is a fundamental biological mechanism that regulates genes. Cells chemically add methyl groups to the regulatory regions of genes that are not required, shutting them off permanently. As different cell types require different genes to be activated, the pattern of methyl groups on the DNA provides a unique “fingerprint” that differs between various healthy tissues but also changes specifically in diseases such as cancer. At Epigenomics, we have developed the technologies to read this DNA methylation “fingerprint” and use it for the sensitive detection of tumor DNA in a blood or urine sample. With this technology, we can reliably detect minute amounts of DNA in a routine blood sample.

Most importantly, by looking at the DNA methylation of the right genes, the exact origin of the tumor DNA can be determined, an important prerequisite for the development of diagnostic tests that are specific for different cancer indications. Thus, we have shown in numerous clinical studies with more than 3,000 clinical

blood samples from colorectal cancer patients of all stages and healthy controls, that the presence of methylated DNA of the gene SEPT9 in a blood sample reliably indicates the presence of colorectal cancer in all stages and all locations in the colon. The Septin9 test for colorectal cancer not only outperforms the currently most widely used laboratory test (Fecal Occult Blood Test or FOBT), but, more importantly, it has the potential to vastly drive acceptance of colorectal cancer screening as it is noninvasive and does not require a stool sample. When tests and test services based on Septin9 are available, any patient willing to have an additional tube of blood drawn in their primary care physician's office can receive colorectal cancer screening. The blood sample will be picked up by established courier services and shipped to a regional diagnostic laboratory where it is analyzed for Septin9 DNA methylation. The test result is then reported to the family doctor who can discuss it with the patient within a few days after the blood sample was taken. If the test comes back positive, a colonoscopy should be performed to confirm the test result and localize the tumor as a first step towards cancer therapy.

While Septin9 testing is initially only available to self-payors and privately insured patients, we and our partners firmly believe that broad access to this screening option for all guideline eligible patients with coverage by public health care schemes is key to improve effectiveness of colorectal cancer screening. To this end, we are conducting the PRESEPT Study. PRESEPT is one of the largest privately sponsored studies ever in colorectal cancer screening and has the objective of demonstrating the clinical and health economic benefit of Septin9 testing in a guideline-eligible colorectal cancer screening population. Positive data from this study are expected to be key in obtaining guideline inclusion and coverage under public health care schemes in Europe and the United States.

Beyond our current activities to ensure broad availability of Septin9 blood testing for colorectal cancer early detection, the R&D work in our Colorectal Cancer Program focuses on further applications of our validated disease biomarkers in disease recurrence and drug response monitoring and prognosis assessment. Further we are working on future product generations with additional benefits in clinical performance, ease-of-handling, through-put, and level of automation.

References:

1. American Cancer Society. Cancer Facts & Figures 2009. Atlanta: American Cancer Society; 2009.
2. Ferlay J, Autier P, Boniol M, Heanue M, Colombet M, Boyle P. Estimates of the cancer incidence and mortality in Europe in 2006. *Ann Oncol.* 2007 Mar;18(3):581-92.
3. Shapiro JA, Seeff LC, Thompson TD, Nadel MR, Klabunde CN, Vernon SW. Colorectal cancer test use from the 2005 National Health Interview Survey. *Cancer Epidemiol Biomarkers Prev.* 2008 Jul;17(7):1623-30.

The products by Epigenomics or its partners mentioned on this page are not available for sale in the United States. The analytical and performance characteristics of any product to be eventually sold in the U.S. based on this technology have not been established.

