



SEPTIN9

(Epi *pro*Colon 2.0)

A Non-Invasive Screening for the Detection of Colon Cancer

Medical background

Colorectal cancer is one of the most common cancers in industrialised countries and the second most common cause of cancer-related deaths. More than 230.000 people die of this disease annually in the European region. The incidence increases with age - the average age at diagnosis is around 70 years. Men are more often affected than women. If diagnosed early colorectal cancer (CRC) can be treated successfully in more than 90% of the cases (Fig. 1).

How does colorectal cancer arise?

Approximately 90% of the CRCs evolve from initially benign polyps. The degeneration from a benign polyp (adenoma) into a malignant carcinoma, also called **adenoma-carcinoma-sequence**, occurs slowly within a timeframe of around 5-10 years. The reason for this are mutations in the intestinal mucosa cells. The risk for these mutations increases with age.

But further factors do also influence the risk for colorectal cancer:

- A familial predisposition
- Chronic inflammatory bowel disease
- Diabetes mellitus type 2
- An unbalanced diet rich in fat and red meat
- Overweight
- Lack of exercise and smoking
- Excessive alcohol consumption

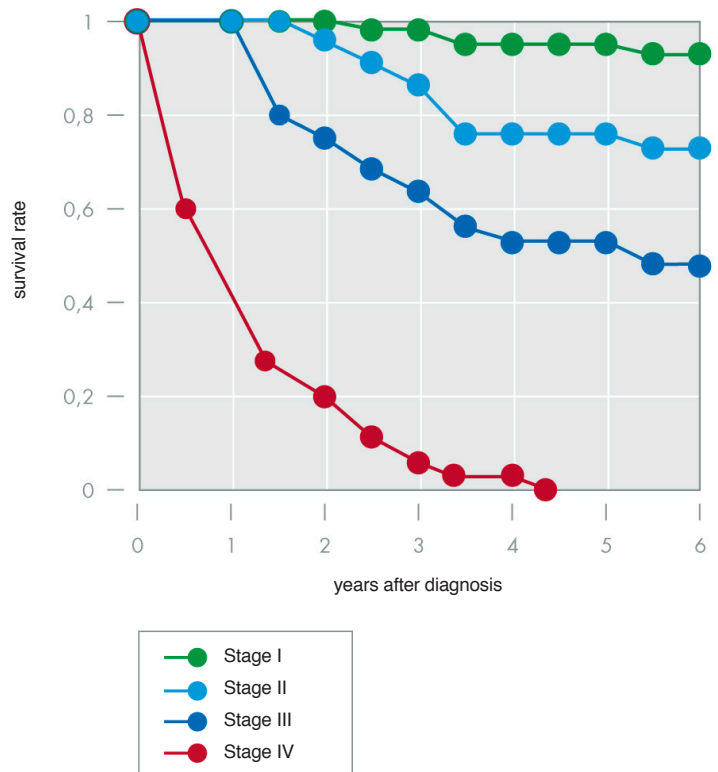
Which methods are available for a preventive screening of CRC?

In most cases CRC is curable if diagnosed early. A regular preventive screening is therefore essential. Healthy people 50 years and older and free of symptoms should undergo a preventive screening for CRC periodically. For this several tests are available. The 2 most established methods are:

The occult blood-test: with the occult blood-test the stool is investigated for hidden blood, that is liberated from intestinal polyps or tumors. Available are the chemical occult blood-test and immunological tests. The latter are much more sensitive than the chemical Guajak test.

Colonoscopy: the colonoscopy is the goldstandard for the detection of colorectal cancer. Early stages, like polyps, as well as malignant tumors in the intestine can be captured.

Fig. 1: Survival rate – Colorectal cancer



Why Septin9?

Even though both screening methods have been proven to be very effective the acceptance within the population is still low. Reasons for the low acceptance are a dismissive attitude towards self-retrieved stool samples and towards colonoscopy.

A survey, carried out in the US by the *Colorectal Cancer Alliance*, has shown that 75% of the respondents would undergo a preventive screening for colorectal cancer on a regular basis if a blood-test would be available. Especially for those patients the **Septin9 blood-test** provides an alternative as a simple, secure and non-invasive screening method.

How does the test work?

In many diseases associated with tumors the methylation pattern of several genes can change. In colorectal cancer the Septin9 gene is methylated within a certain promotor region while it is not methylated in cells of the healthy intestinal mucosa^{1,2}. This methylated DNA can be detected by the Septin9 blood test. Due to the strong correlation between the existence of methylated DNA in the blood and the existence of cancer in the large intestine, the Septin9 biomarker provides an efficient non-invasive screening method for the detection of CRCs. Only 1 blood draw is necessary.

Results and interpretation

A negative test result means that methylated Septin9-DNA could not be detected. So with this method, a CRC can then be excluded. The negative predictive value of this test is 99,9 %. That means that 999 of 1000 patients tested negative are correctly classified as being CRC negative (with an assumed CRC prevalence of 0,7 %). A positive test result means that there is an increased likelihood for the presence of colorectal cancer. Since 45,7 % of the patients tested positive are truly positive (positive predictive value) individuals with a positive test result are requested to undergo a colonoscopy for a definitive diagnosis (Fig. 2)³.

Additional information

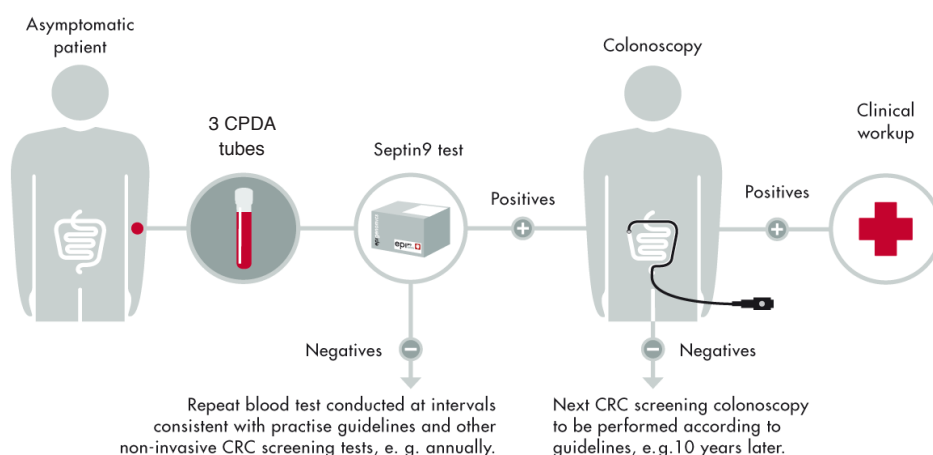
The Septin9 blood test can be conducted at any time and without any discomfort. No dietary restrictions are required before performing the test.

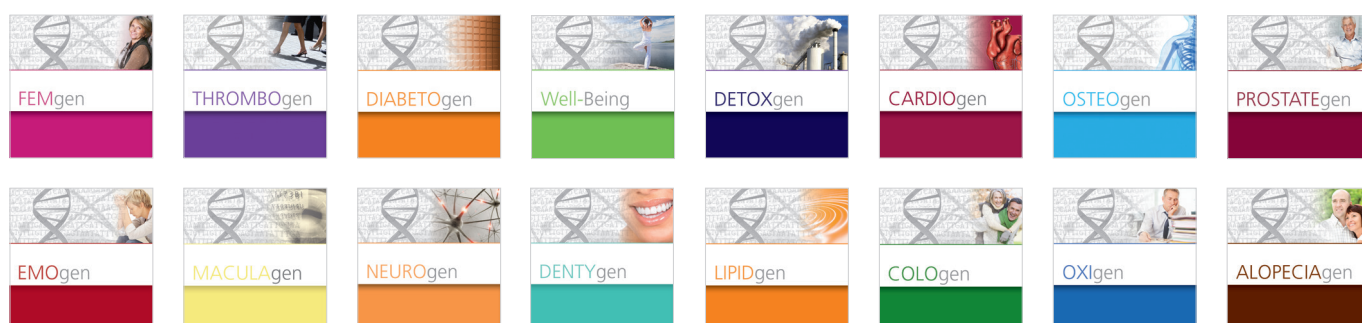
To perform the test 3 CPDA tubes per patient have to be completely filled with blood. The filled uncentrifuged vials are stable for a maximum of **48h** at room temperature, and have to be sent to Laboratoires Réunis within this timeframe. Please contact us for more detailed information.

References

1. Grutzmann, R. et al. Sensitive detection of colorectal cancer in peripheral blood by septin 9 DNA methylation assay. PLoS One 3, e3759 (2008).
2. Toth, K. et al. Detection of methylated SEPT9 in plasma is a reliable screening method for both left- and right-sided colon cancers. PLoS One 2012; 7 (9): e46000.
3. Tetzner, R. UEGW Stockholm 2011, poster presentation.

Fig. 2: Clinical principle





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Examples of our Genetic Profiles:

FEMgen:	Sporadic breast cancer	LIPIDgen:	Lipid metabolism disorders
OSTEOgen:	Osteoporosis	DIABETOgen:	Diabetes type II
THROMBOgen:	Thrombosis	COLOgen:	Sporadic colon carcinoma
PROSTATEgen:	Prostate cancer	ALOPECIAgen:	Androgenetic alopecia
DETOXgen:	Detoxification capacities	EMOgen:	Emotional instability
OXIgen:	Oxidative stress	SKINgen:	Skin health
DENTYgen:	Periodontitis	WEIGHTgen:	Weight control
NEUROgen:	Neurodegenerative diseases	WELL-BEING:	Anti-aging
CARDIOgen:	Cardiovascular diseases	NICOTINEgen:	Nicotine addiction
MACULAgen:	Age-Related Macular Degeneration		