Biomarker set forms the basis for new blood test to detect colorectal cancer

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Colorectal cancer is the third most common form of cancer globally and the second most common cause of cancer deaths. The chance of a cure is high if the cancer is detected early enough, but early detection is not a given. Researchers from VIB and KU Leuven - together with various European oncology centers, including UZ Leuven - have identified biomarkers that can be incorporated in a new diagnostic test. This should make it possible to detect colorectal cancer in an early stage using a simple blood test.

Max Mazzone (VIB/KU Leuven): "This research demonstrates how important it is to gain a thorough understanding of the role of our immune system in cancer. In this case, this knowledge will hopefully result in a new, more sensitive test to detect colorectal cancer at an early stage, so that more patients can be cured. I hope that we can soon find an industrial partner to help us achieve the following step, which is the development of the test."

Colorectal cancer: a growing medical problem

In 2012, a total of 1.4 million people worldwide were diagnosed with colorectal cancer, this figure is expected to increase to 2.4 million by 2035. This is a condition that affects a growing number of people each year. Colorectal cancer is very treatable if it is detected at an early stage, with approximately 95 % chance of a cure. If detected at a late stage, the chance of surviving 5 years after diagnosis is less than 10 %. Therefore,

it is very important to be able to detect the disease in an early stage. And therein lies the rub.

Population screening

There are no global screening guidelines, but because early detection is so important, there are a number of national initiatives to screen the population. For example, in Flanders, the population group between the ages of 56 and 74 years is invited to undergo testing via the "immunological Fecal Occult Blood test" (iFOB), which detects blood in the stools. If this test is positive, a colonoscopy needs to be performed to confirm the presence of premalignant polyps or cancer.

Even though the iFOB test is the best test available, sensitivity is suboptimal. In other words the available test doesn't detect all colon cancers. There is a need for a test that offers greater certainty and that can detect bowel cancer at an early stage and at the same time reaches the whole population. If this can be achieved with a blood test, this might lower the reluctance seen in patients towards the stool test.

Our immune system responds to cancer

If we are affected by cancer, our immune system responds to this and tries to remove the cancer cells from our body. A specific role in this process is assigned to a specific type of white blood cell: the peripheral blood monocyte. From the moment that colorectal cancer cells are present in the body, the peripheral blood monocytes respond to the substances secreted by the cancer cells.

Alexander Hamm (VIB/KU Leuven): "The substances secreted by the cancer cells activate specific genes in the monocytes. Now we have identified these genes, and they can be used to diagnose colorectal

cancer through blood collection by using standard techniques."

Hans Prenen (UZ Leuven): "This new test will probably be more sensitive, because it detects tumor-induced changes directly and not merely blood in the stools. An additional benefit is that this process takes place at a point when the tumor is forming, the earliest stage of tumor development. Since this test is based on how our body reacts to the presence of colorectal cancer cells, it can also be used to detect distant metastasis even after the primary tumor has been removed. This unique potential makes it a valid tool for patient follow-up after the primary tumor has been removed through surgery."

Set of biomarkers identified

For the identification of the genes involved in this process, Hans Prenen (UZ Leuven) and his colleagues from oncology centers in Brussels, Heidelberg and Rome collected samples from patients. This allowed the researchers led by Max Mazzone (VIB/KU Leuven) to identify 43 relevant genes.

Wouter Van Delm (VIB Nucleomics Core Facility): "As 43 different genes are too many genes to incorporate in a diagnostic test, it was important to find a more limited gene set with the same predictive value. We eventually succeeded in creating a set of 23 genes, but we are still trying to further reduce this number."

The challenge facing the investigators now is to develop a test using a minimal set of bio-markers. They are looking for an industrial partner for the development of the test.

More information: "Tumour-educated circulating monocytes are powerful candidate biomarkers for diagnosis and disease follow-up of colorectal cancer." *Gut* gutjnl-2014-308988 Published Online First: 26

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