

Newly identified gene powerful predictor of colon cancer metastasis

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Cancer Researchers at the Max Delbrück Center for Molecular Medicine (MDC) Berlin-Buch and the Charité – Universitäts Medizin Berlin (Germany) have identified a gene which enables them to predict for the first time with high probability if colon cancer is going to metastasize.

Assistant Professor Dr. Ulrike Stein, Professor Peter M. Schlag, and Professor Walter Birchmeier were able to demonstrate that the gene MACC1 (Metastasis-Associated in Colon Cancer 1) not only promotes tumor growth but also the development of metastasis. When MACC1 gene activity is low, the life expectancy of patients with colon cancer is longer in comparison to patients with high MACC1 levels.

According to the National Institutes of Health in Bethesda, Maryland, USA, more than 108,000 people developed colon cancer in the US in 2008. Despite surgery, chemo- and radiotherapy, only 50 percent of patients can be cured because 20 percent of the patients have already developed metastasis by the time their colon cancer is diagnosed. In addition, one-third of patients whose treatment of the original colon cancer was successful will, nevertheless, go on to develop metastasis.

The MDC and Charité researchers are convinced that the identification of the MACC1 gene will aid medical doctors in identifying those patients as early as possible who are at high risk of developing life-threatening metastasis in the liver and the lungs. As a result, more intensive treatment and follow-up care could be offered to high risk patients.

MACC1 turns on a signaling pathway which is important for tumor growth and the formation of metastasis. Researchers call this pathway HGF/Met signaling pathway. Once MACC1 has activated this HGF/Met signaling pathway, tumor cells proliferate much faster, get rid of their ties within the cellular tissue, and eventually settle down as metastasis at various sights throughout the body far from the original tumor.

High MACC1 Levels – Higher Risk for Metastasis

The researchers discovered the MACC1 gene by comparing tissue from healthy persons with tissue from 103 patients with colon cancer between 20 to 88 years of age. Sixty (60) cancer patients had no metastasis at the time they underwent surgery.

Of these 60 patients, 37 had no metastasis five years after surgery and treatment. These patients were shown to have had low levels of MACC1 when first diagnosed with colon cancer. In contrast, 23 patients had developed metastasis in the course of five years after surgery.

Researchers detected high levels of MACC1 in their colon cancer tissue. Thus, patients with high MACC1 levels have a much higher risk for developing metastasis than patients with a MACC1 gene that is not very active.

The researchers are convinced that MACC1 will enable physicians to decide if a patient needs a more intense therapy or if a less aggressive treatment is sufficient. "The expression analysis of MACC1 in the original tumor tissue will probably contribute to individualize and optimize colon cancer therapy", they assume.

Now the MDC and Charite researchers and their colleagues want to find out if the MACC1 gene also allows for a more precise prediction about the outcome of lung cancer, breast cancer, and stomach cancer.

Further information: www.cancer.gov/cancertopics/types/colon-and-rectal .

Paper: MACC1, a newly identified key regulator of HGF-Met signaling, predicts colon cancer metastasis, *Nature Medicine*, doi: 10.1038/nm.1889

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