Biomarkers for identifying tumor aggressiveness

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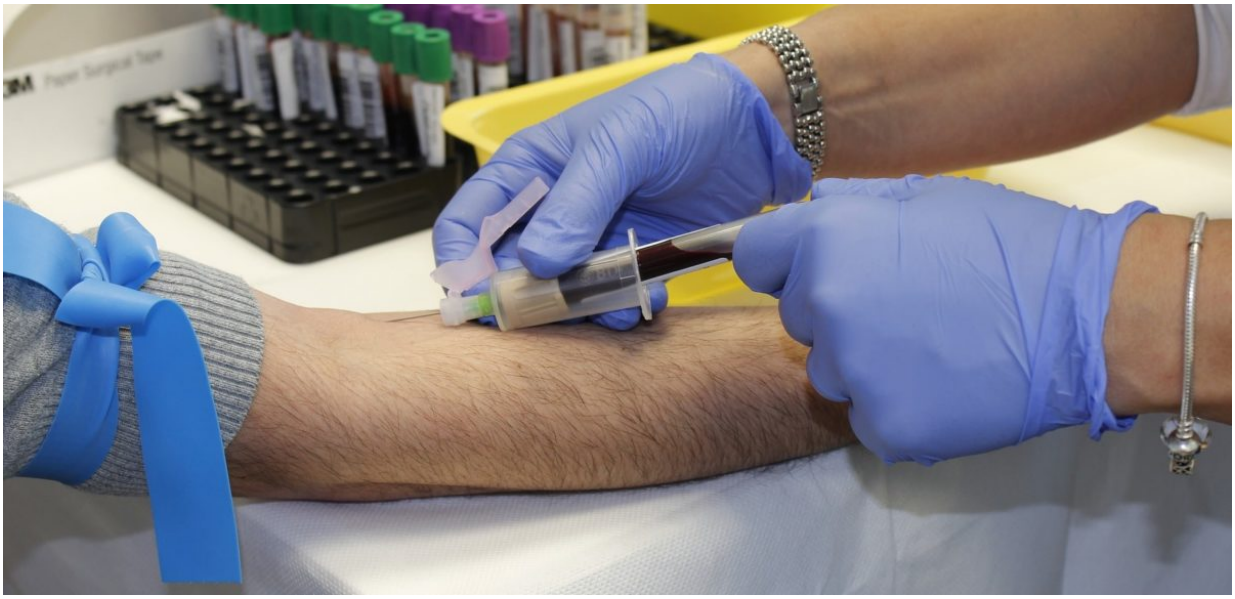

Credit: Max Delbrück Center for Molecular Medicine

Early-stage colon cancer patients could benefit in the future from specific genetic tests that forecast their prognosis and help them make the right decision regarding chemotherapy. Two of the biomarkers involved are the MACC1 gene, high levels of which promote aggressive tumor growth and the development of metastasis, and a defective DNA mismatch repair (dMMR) system, which plays a role in tumor formation. Life expectancy is longer for patients with dMMR tumors and with low MACC1 gene activity.

In a study of around 600 stage II colon cancer patients (locally aggressive tumors without metastases), scientists at the Max Delbrück Center for Molecular Medicine (MDC) and the Charité - Universitätsmedizin Berlin have shown for the first time that the MACC1 genetic test can help further differentiate between patients with defective repair mechanisms. The prognosis is as positive for those with low MACC1 gene expression as it is for patients with defective repair mechanisms: a 100 percent five-year survival rate. The genetic test may also have implications for the recommended course of treatment, as these patients would not benefit from chemotherapy.

The results of the Berlin study led by Prof. Ulrike Stein of MDC/Charité - Universitätsmedizin Berlin were published in the journal *Annals of Oncology*. The study was done in cooperation with Hoffmann La-Roche (Switzerland and Germany) and Ventana Medical Systems (Tucson, United States), as well as the Walter and Eliza Hall Institute (Melbourne, Australia) and the University of Freiburg (Germany).

Blood tests can help predict chemotherapy success

Colon cancer is the second most common type of cancer in Germany, affecting around 60,000 male and female patients every year. The five-year survival rate averages 70 percent. Treatment success is largely dependent on whether the tumor is detected early on, whether it can be completely surgically removed, and whether it responds to chemotherapy.

In recent years, scientists have successfully identified genetic subtypes of malignant colon tumors, all of which carry a different prognosis for how the disease will develop. Up to 15 percent of these malignant tumors, for example, exhibit defective DNA repair mechanisms - known as DNA mismatch repair deficiency or dMMR. Another important biomarker is the gene MACC1 (metastasis-associated in colon cancer 1),

which was identified by Ulrike Stein and her colleagues at MDC in 2009. There is now a patented blood test for MACC1 detection.

The five-year survival rate for patients with stage I-III colon cancer who exhibit low levels of MACC1 lies at 80 percent - in comparison to just 15 percent for patients with high MACC1 levels. "The blood test can indicate whether there is a higher risk of the tumor returning or metastasizing," says Stein. "It helps with the difficult decision of whether early-stage patients should receive chemotherapy." This now also includes patients in stage II of the disease with impaired DNA repair mechanisms.

In an editorial, also published in *Annals of Oncology*, scientists at Houston's MD Anderson Cancer Center quote this study as further proof of how important it is to identify genetic subtypes and subtype combinations even in the early stages of the cancer, not least to help with prognosis and decisions regarding chemotherapy. They recommend that, in the future, genetic test results should be combined with further genetic and epigenetic data from patients, "in order to understand the prognostic value of the complex molecular scenarios of early-stage colon cancer."

More information: U.-P. Rohr et al, Prognostic value of MACC1 and proficient mismatch repair status for recurrence risk prediction in stage II colon cancer patients: the BIOGRID studies, *Annals of Oncology* (2017). DOI: 10.1093/annonc/mdx207

Provided by Max Delbrück Center for Molecular Medicine