Medical Xpress

Blood clotting and bowel cancer risk

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Back in the mid 19th century, a French doctor, Armand Trousseau, discovered a connection between cancer and thrombosis – the formation of often dangerous blood clots that can lead to venous occlusion. Today it is known that cancer and its treatment change blood flow properties and thus promote the formation of clots. However, clots do not only occur as a side effect and consequence of cancer, but, vice versa, an increased blood clotting tendency may also be associated with an elevated cancer risk.

About twelve different blood proteins called clotting factors interact in a coordinated manner in the blood clotting (coagulation) process. In the same way as hemophilia (decreased blood clotting) is inherited, genes also play a role in an increased clotting tendency (thrombophilia): There are well studied gene variants (polymorphisms) of a number of clotting factors which are associated with an increased or decreased clotting tendency. Between two and five percent of the population carry such genetic variants.

At the German Cancer Research Center (Deutsches Krebsforschungszentrum, DKFZ) in Heidelberg, scientists headed by Professor Dr. Hermann Brenner have been studying six gene variants of different clotting factors for a possible connection with colorectal cancer risk. In a large study, they analyzed the occurrence of these six variants in approximately 1.800 colorectal cancer patients and in the same number of healthy control persons.

The team found the most obvious connection for a variant that

substantially increases the risk of thrombosis and which is known as factor V Leiden (FVL). Study participants who carry this genetic variant on both copies of their chromosome 1 were found to have a six fold increase in colorectal cancer risk compared to participants who carry two copies of the "standard variant" of factor V. If only one copy of chromosome 1 had the FVL variant, bowel cancer risk was not elevated.

Another connection with bowel cancer prevalence was found by the research team for a particular gene variant of clotting factor XIII: People with this mutation are slightly more rarely affected by venous thrombosis than those who carry the factor XIII standard version. Now the DKFZ team has shown that their colorectal cancer risk is also 15 percent lower. For the other four gene variants studied the team found no connection with bowel cancer risk.

It is known today that coagulation and carcinogenesis are associated. Thus, the interplay of all coagulation (clotting) factors leads to the formation of active thrombin, which, in turn, activates hemostatic fibrin. However, thrombin also contributes to the formation of new blood vessels and is able to dissolve the extracellular matrix, which is the adhesive that keeps cells together. Thrombin may thus make it easier for cancer cells to invade surrounding tissue.

"It is interesting that not every gene variant that increases the tendency to clot automatically also increases the risk of developing colorectal cancer. It also makes a difference whether the gene variant is present on both chromosomes or just on one of them. We therefore have to analyze in detail which clotting factors affect cancer risk and in what manner," explained study head Hermann Brenner. The knowledge of these connections is the first prerequisite for finding out whether and for whom drugs that affect blood clotting may prevent bowel cancer.

More information: Carla Y. Vossen, Michael Hoffmeister, Jenny C.

Chang-Claude, Frits R. Rosendaal, and Hermann Brenner: Clotting Factor Gene Polymorphisms and Colorectal Cancer Risk. *Journal of Clinical Oncology* 2011, DOI: 10.1200/JCO.2010.31.8873