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New study provides insight into the mechanisms of blood clots in cancer patients

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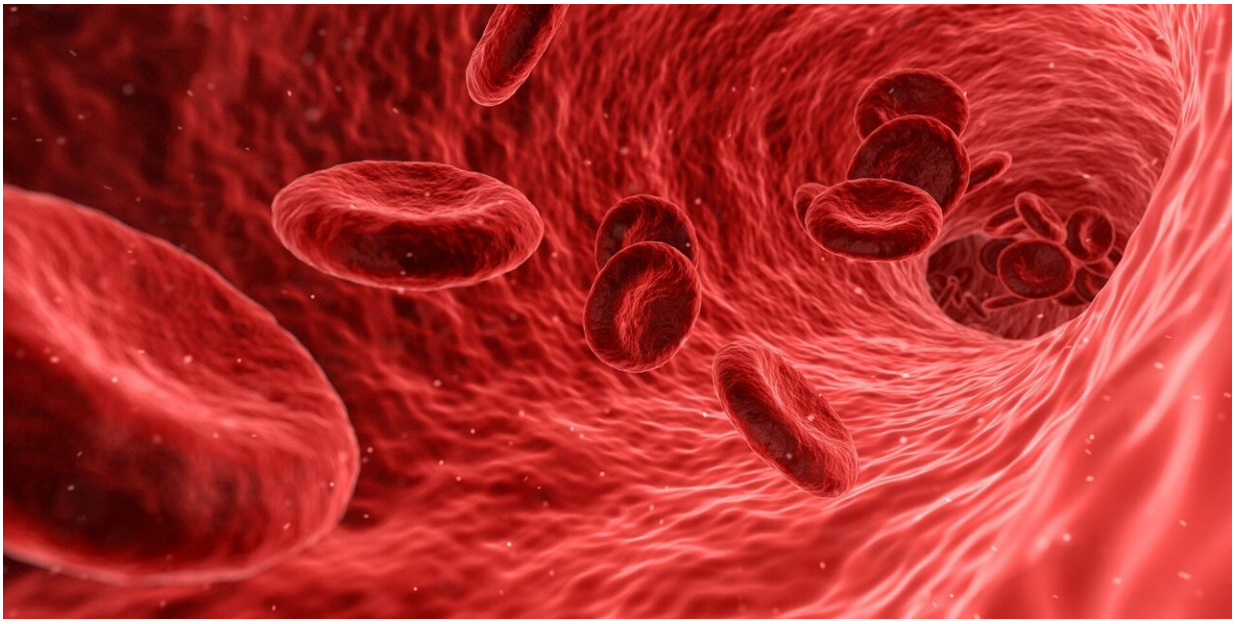

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Researchers have identified a potential new signaling pathway that may help further the understanding of blood clot formation in cancer patients and ultimately help prevent this complication from occurring.

A pulmonary embolism generally occurs when a clot from the deep veins of the extremities also known as deep vein thrombosis (DVT) becomes dislodged and travels to the lungs. This event combined with the DVT is

the second most common cause of non-cancer related death in patients with malignancy. Patients with cancer are at an increased risk of developing blood clots for reasons that had previously been unclear until now.

Researchers from Boston University School of Medicine (BUSM) performed a detailed analysis examining the levels of different molecules and break down products—known as metabolites in the blood as well as within blood clots from experimental tumor models. They discovered increased blood levels of two molecules called kynurenine and indoxyl sulfate, both of which are metabolites of the amino acid, tryptophan, often a dietary component. These high levels of kynurenine and indoxyl sulfate were also associated with increased blood clot size in an experimental model.

The study shows that by pharmacologically inhibiting the aryl hydrocarbon receptor (AHR) pathway, a known target of indoxyl sulfate and kynurenine, they could reduce blood clot size, suggesting that this may be a target for future drug development.

According to researchers, this study suggests that Kynurenine and indoxyl sulfate might be key culprits in generating clot formation in patients with cancer via AHR signaling. Moreover, they may provide exciting new opportunities for treating and preventing these known complications in the future. "The importance for the patient is two-fold," explained corresponding author Vipul Chitalia, MD, Ph.D., associate professor of medicine at BUSM. "First, these metabolites can be measured in the blood of patients with cancer and can potentially guide us in predicting risk of deep vein thrombosis. Also, the signaling pathway triggered by these metabolites can be potentially inhibited by compounds that can be developed in the future as a drug for this complication."

"In addition, dietary modifications could also be considered in such cases," adds coauthor Katya Ravid, DSc, professor of medicine and biochemistry at BUSM.

More information: Mostafa Belghasem et al, Metabolites in a Mouse Cancer Model Enhance Venous Thrombogenicity Through Aryl Hydrocarbon Receptor-Tissue Factor Axis, *Blood* (2019). DOI: 10.1182/blood.2019001675

Provided by Boston University School of Medicine