Research identifies links between high levels of blood clotting proteins and poorer breast cancer outcomes

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New research from RCSI University of Medicine and Health Sciences has found that high levels in the bloodstream of a key protein involved in blood clotting called von Willebrand Factor, can lead to poorer outcomes for breast cancer patients. The findings will help researchers and doctors to better understand and treat breast cancer to reduce the risk of life-threatening blood clots and cancer spread in patients.

Published in the *Journal of Thrombosis and Haemostasis*, the research found that patients with breast cancer had very high levels of von Willebrand Factor in their blood and that patients with the highest levels had the poorest outcomes. This work suggests that analysis of von Willebrand Factor levels may be useful to help predict clinical outcomes in patients with breast cancer.

The study also examined how breast cancer triggers high levels of von Willebrand Factor and found that breast tumor cells cause release of the clotting protein which helps the breast tumor cells to circulate in the blood stream and may aid breast tumor spreading to other organs in the body. Anticoagulant medication or blood-thinners which are already used to treat blood clots, could inhibit this effect by reducing levels of von Willebrand Factor and also preventing the spread of cancer cells in the blood stream.

The findings of the research will help doctors to better understand why patients with breast cancer have increased risk of blood clots and also why this may contribute to worse disease, cancer progression and spread throughout the body.

Dr. Jamie O'Sullivan, Irish Center for Vascular Biology, School of Pharmacy and Biomolecular Sciences, RCSI, said: "There are over 2 million people worldwide diagnosed with breast cancer every year, making it the world's most prevalent cancer. Importantly, it is not the primary breast tumor, but its spread to distant sites in the body such as

bone, brain and lungs that are the main cause of death. In addition, as they spread via the bloodstream, these breast cancer cells cause blood clotting in approximately 1 in 5 patients, which increases their risk of life-threatening complications.

"Our findings now show, for the first time, that this blood clotting may be caused by increased levels of a key pro-clotting protein, von Willebrand Factor, and that the breast tumor cells directly interact with the blood vessel wall to promote release of this protein. Interestingly, this not only increases risk of blood clotting for these patients but may also promote breast cancer cells spreading throughout the body via the circulation. Our work helps to better understand why patients with breast cancer have increased risk of blood clots and also why this may contribute to worse disease, cancer progression and spread throughout the body which will have a huge impact on the treatment of breast cancer and the outcomes for patients worldwide."

More information: Sukhraj Pal Singh Dhami et al, Breast cancer cells mediate endothelial cell activation, promoting von Willebrand Factor release, tumour adhesion and transendothelial migration, *Journal of Thrombosis and Haemostasis* (2022). DOI: 10.1111/jth.15794

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