

Evidence strengthens link between NSAIDs and reduced cancer metastasis

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A new study reveals key factors that promote the spread of cancer to lymph nodes and provides a mechanism that explains how a common over-the-counter anti-inflammatory medication can reduce the spread of tumor cells through the lymphatic system. The research, published by Cell Press in the February 14 issue of the journal *Cancer Cell*, opens new avenues for the design of antimetastatic therapies.

The lymphatic system consists of a network of vessels that carry lymphatic fluid from the body organs back to the general circulation. Along the way, lymphatic fluid percolates through lymph nodes. Unfortunately, cancer cells sometimes spread (via a process called metastasis) through the lymphatic system and can form secondary tumors in the lymph nodes. The spread of cancer cells to the lymph nodes is an important indicator of disease progression.

"Some tumors secrete protein growth factors that can act on the lymphatic vessels to facilitate metastasis. For example, elevated levels of the growth factor VEGF-D in human tumors correlate with lymph node metastasis and poor <u>patient prognosis</u>," explains the senior study author, Steven Stacker, associate professor from the Tumour Angiogenesis Program, Peter MacCallum Cancer Centre in Melbourne, Australia. "However, thus far, mechanisms underlying the transit of cancer cells through the larger lymphatic vessels and into the lymph nodes remain elusive."

In the current study, Stacker and colleagues investigated how collecting <u>lymphatic vessels</u>, conduits that drain lymphatic fluid from tissues into lymph nodes, are altered during VEGF-D-driven metastasis. The researchers discovered that VEGF-D was linked to prostaglandin pathways, which are important regulators of lymphatic vessel dilation. Nonsteroidal anti-inflammatory drugs (NSAIDS), which are known inhibitors of prostaglandin synthesis, reduced lymphatic vessel dilation and,

therefore, inhibited tumor metastasis.

"This key interaction between lymphatic system growth factors and prostaglandins reveals a mechanism for physically preparing collecting vessels for tumor cell dissemination and a mechanism by which NSAIDs can reduce cancer metastases through the lymphatic system," concludes Dr. Stacker. "These insights may assist with the design of additional therapeutics for cancer patients and enhance current approaches that aim to prevent the spread of cancer cells through the lymphatic system and potentially to distant organs."

Provided by Cell Press

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