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# Migration alert -- How tumor cells home in on the lymphatic system

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A Swiss-based research team has published a new mechanistic description of how tumor cells migrate to the lymphatic system in the early stages of tumor metastasis. This new understanding holds significant potential for developing anti-metastasis therapies.

Scientists know that tumor cells spread via the lymphatic system, but they don't understand the details of how this deadly migration takes place. In the June 2007 issue of the journal Cancer Cell, EPFL Professor Melody Swartz and postdoctoral researcher Jacqueline Shields provide an explanation along with data to support it.

Tumors produce excess fluid that continually percolates from the tumor towards nearby lymphatic vessels. The EPFL research shows how tumor cells use a clever chemical strategy to exploit this slow, one-way flow in order to migrate to functional lymphatic vessels.

As part of their intercellular drainage job, lymphatic tissues secrete small quantities of a signaling molecule. Cells migrate towards high concentrations of this molecule, so if they are close enough to the lymphatic to sense the molecule, they will migrate towards the vessel. Swartz's group showed that tumor cells secrete this same molecule. Since lymphatics drain fluid, there will always be slow fluid flow going away from the tumor into the lymphatic vessel. This slow flow biases the concentration distribution of this molecule towards the lymphatic, and the tumor cell follows it, like the proverbial carrot on a stick. Near the vessel, concentrations of the signaling molecule are reinforced by the

lymphatic's own secretions, fine tuning the tumor cells' migration and guaranteeing that they will home in on the lymphatic.

To demonstrate this new concept, the researchers engineered a tissue culture model of the tumor-lymphatic microenvironment and developed computational models to calculate the gradients of the signaling molecule.

The study provides the first evidence that tumor cells can both produce and use the same signaling molecule, and it highlights the significance of the biophysical environment in the vicinity of a tumor, particularly the existence of continuous slow flow in the direction of functional lymphatics.

This research could open new avenues for combating metastasis, says Swartz. "It implies that if a lymphatic was blocked, tumor cells would be less attracted to it. This means that tumor cells "know" which lymphatic vessels will be more effective routes for dissemination," she explains. "Therapeutically, it indicates that a drug target for lymph node metastases could be blocking the signaling molecule or its receptor on the tumor cell."

Source: Ecole Polytechnique Fédérale de Lausanne