The secret of lymph: How lymph nodes help cancer cells spread
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For decades, physicians have known that many kinds of cancer cells often spread first to lymph nodes before traveling to distant organs through the bloodstream. New research from Children’s Medical Center Research Institute at UT Southwestern (CRI) provides insight into why this occurs, opening up new targets for treatments that could inhibit the spread of cancer.

The study, published today in Nature, found melanoma cells that pass through the lymph nodes pick up a protective coating, allowing them to survive high levels of oxidative stress and go on to form distant tumors. Credit: UT Southwestern Medical Center

Researchers hypothesized this difference could be explained by the high levels of oxidative stress cancer cells experience when they migrate through the blood. Exposure to oxidative stress in the blood is one reason why metastasis is a very inefficient process in which most cancer cells die before they have an opportunity to grow at a distant site.

"After further analysis, we discovered that the oxidative stress in the blood causes the cancer cells to undergo a specific form of cell death called ferroptosis," says Jessalyn Ubellacker, Ph.D., lead author of the study and a postdoctoral researcher in the Morrison lab. "In contrast, cancer cells in lymph experience lower levels of oxidative stress and are protected from ferroptosis."

To better understand why melanoma cells undergo ferroptosis in the blood but not the lymph, researchers looked for metabolic differences between cancer cells in the blood versus the lymph. They discovered cancer cells from the lymph had higher levels of a monounsaturated fatty acid known as oleic acid, which is the main component of olive oil. They also found this monounsaturated fatty acid was incorporated into the membranes of cancer cells in the lymph. This diluted polyunsaturated fatty acids in the membranes of
these cells, inhibiting the chemical reactions that lead to ferroptosis and protecting the cells.

This protective coating of oleic acid from the lymph thus allowed the cancer cells to safely enter the blood, travel to other locations, and form metastatic tumors. This explains why cancer cells often form tumors first in lymph nodes before metastasizing to distant sites through the blood: They are able to load up on antioxidants in the lymph that protect the cells when they subsequently enter the blood.

"Now that we understand more about why cancer cells are most likely to metastasize initially through lymph, it raises the possibility of treating patients with drugs that target those protective mechanisms in the lymph to inhibit the early stages of metastasis," says Morrison.


Provided by UT Southwestern Medical Center


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