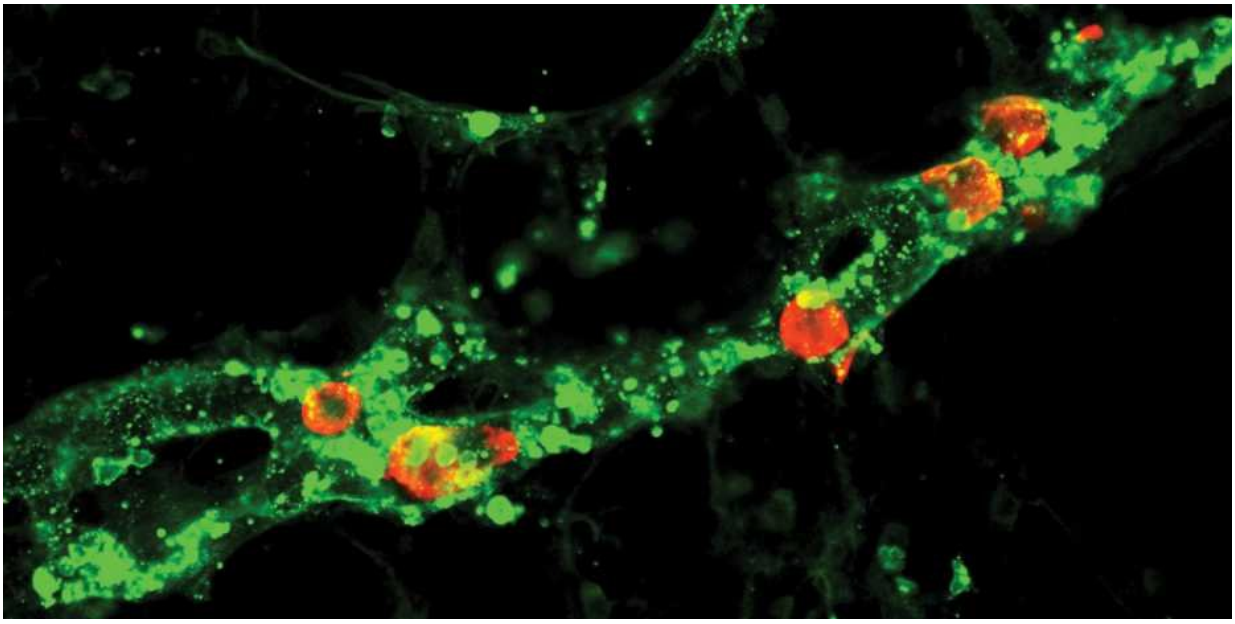
MedicalXpress

Lymphatic vessels unexpectedly promote the spread of cancer metastases

August 14 2018, by Florian Meyer



Lymph vessels in the lungs (green) increase the spread of metastatic melanoma cells (red). Credit: Science Advances / Michael Detmar Group

Lymphatic vessels actively contribute to the spread of cancer metastases from various organs. This unexpected realisation is the result of a joint study by researchers from ETH Zurich and the University Hospital Zurich as part of the research initiative Skintegrity.

Together with medical experts from the University Hospital Zurich,

researchers from ETH Zurich have discovered a new mechanism by which cancer cells in mice and humans can spread from organ to organ.

The lymphatic vessels play an unexpectedly active role in this process. These vessels transport tissue fluids and also play an important role in the body's immune system, according to recent research results.

"For the first time, we were able to show that the lymphatic vessels can promote the spread of cancer not only in primary tumours, but also when the cancer has already spread to distant organs of the body," says Qiaoli Ma, a doctoral student at the ETH Institute of Pharmaceutical Sciences and primary author of the study published in the online research magazine *Science Advances*.

Primary tumours are malignant tumours from which cancer cells spread, resulting in the growth of further tumours in more distant parts of the body. These tumours, which may affect tissues or organs, are called metastases.

Lymphatic vessels promote the spread of tumours

The research team headed by Michael Detmar, Professor of Pharmacogenomics, of which Ma is a member, had already discovered in an earlier study on primary tumours that cancer can spread not only through the bloodstream, but also through newly formed lymphatic vessels.

"The surprise in the current study was that the lymphatic vessels also play an amplifying role if the metastases are not propagating from the primary tumour, but from distant organs," says Detmar.

The ETH researchers obtained preliminary results based on anonymous data from skin cancer patients at the University Hospital Zurich that they

analysed together with research groups headed by Reinhard Dummer, UZH Professor of Dermatology and Mitchell Paul Levesque, UZH Professor of Experimental Skin Cancer Research. Both professors are from the Department of Dermatology of the University Hospital Zurich.

Based on data from melanoma patients, they determined that the probability that metastatic tumours spread from organ to organ correlated with the density and growth of lymphatic vessels in the metastasised lung.

The more lymphatic vessels that were in the lung, the more tumours grew in distant organs as well and the likelihood of patient survival also decreased. The tumour cells therefore appeared to use the lymphatic vessels to spread throughout the body.

Confirmed for skin and breast cancer

The researchers succeeded in testing and confirming this relationship in mouse models. These mouse models were developed by cancer researchers from the University of California, San Francisco. The Cantonal Ethics Committee of Zurich had approved all of the experiments in this study.

"With the help of mouse models with increased density of lymphatic vessels in the lung, we found that in both skin and breast cancer, more metastatic tumours were found in the lung and its draining lymph nodes, and that there was a correlation between the growth of lymphatic vessels in lung metastases and a greater spread to other organs," says Qiaoli Ma.

The density of the lymphatic vessels can therefore be used to predict the course of advanced cancer. Detmar is thinking of a yet-to-be-developed imaging technique that shows the density of the lymphatic vessels.

Even further in the future is a possible therapy approach: "Recent research results suggest that a higher density of lymphatic vessels makes it more difficult for the immune system to eliminate tumours. The suppression of this function of the lymphatic vessels could possibly contribute to the treatment of cancer," says Detmar.

Success of the research initiative Skintegrity

The present study was conducted in the context of the research initiative Skintegrity. In this multi-institutional flagship project, a total of 26 research groups from ETH Zurich, the University of Zurich and the University Hospitals Zurich combine their specialist knowledge, their expertise and the infrastructure to approach important medical issues related to skin.

"Our study is a model of success for the close collaboration of researchers conducting fundamental scientific research from ETH Zurich with clinicians from the University and the University Hospital of Zurich," says Detmar.

For this study, Ma and Detmar also used the biobank with biopsy samples and isolated skin cells that was established as part of Skintegrity and which is run by Levesque and Dummer.

The expertise of both the pharmaceutical researchers and the clinicians was necessary to prepare and analyse the data. "Skintegrity has created the framework for this research collaboration, and thus made this study possible," says Detmar.

More information: Qiaoli Ma et al. Unexpected contribution of lymphatic vessels to promotion of distant metastatic tumor spread, *Science Advances* (2018). DOI: 10.1126/sciadv.aat4758

Provided by ETH Zurich