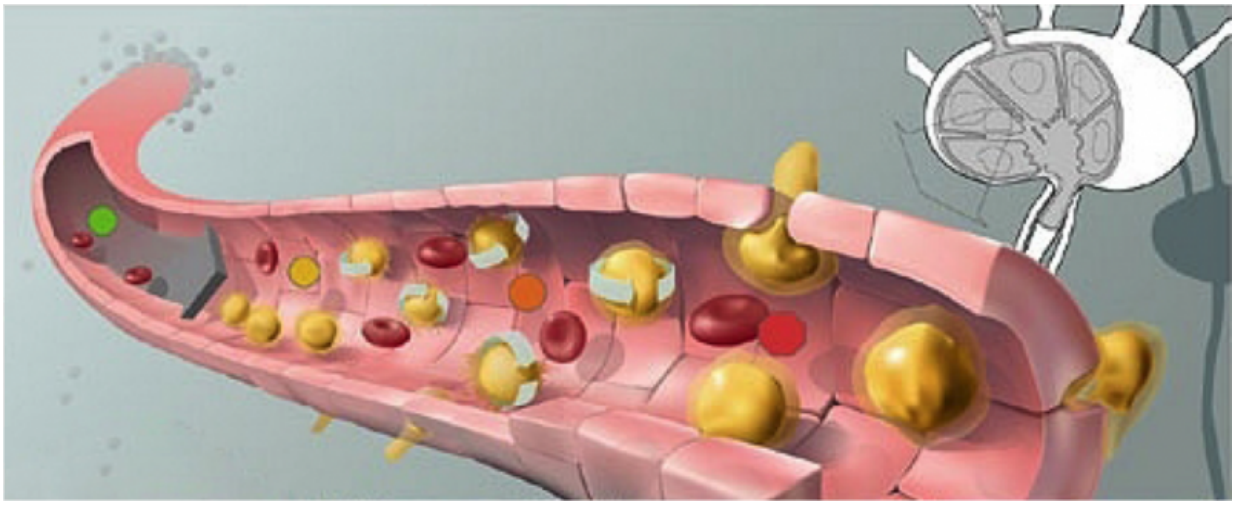
Blocking the migration of cancer cells to destroy them

August 4 2016



Blocking JAM-C on lymphoma cells inhibits their migration through vessel walls. Credit: UNIGE

Lymphoma is a cancer that affects lymphocytes, a type of white blood cell. The disease originates in a lymphoid organ (lymph node, spleen, or bone marrow) before spreading through the blood to infiltrate not only other lymphoid organs but also other tissues. Every year, nearly 2,000 people in Switzerland are diagnosed with lymphoma, a disease that can be very aggressive, resisting standard treatments with chemotherapeutic drugs. Today, researchers at the University of Geneva (UNIGE) and the Geneva University Hospitals (HUG), Switerland, give a new hope to

patients. Their innovative approach consists in using an antibody able to neutralize a specific protein to block the migration of lymphoma cells, thus preventing the disease from developing. This still experimental immunotherapeutic strategy paves the way for new treatments against lymphoma. The results can be read in the *Journal of Leukocyte Biology*.

Lymphocytes, a special type of white blood cell, are essential components of the immune system. But like any other cell, they are not safe from carcinogenic mutations that can cause uncontrolled proliferation. They can then circulate freely in the blood and spread to the lymphatic system, thus causing a tumor called lymphoma.

Lymphoma cells only become truly dangerous when they leave the blood vessels and multiply in the lymphatic system. 'Since they cannot survive in the blood for long, these malignant cells are compelled to find a more accommodating environment – such as the lymphatic system – where they can proliferate. We decided to focus on this Achilles heel by containing them in the blood so as to prevent any resulting harm', explains Thomas Matthes, Professor at UNIGE, Faculty of Medicine, and Doctor at HUG, who supervised the study together with Beat Imhof, Professor at UNIGE, Faculty of Medicine.

A way to prevent malignant cell circulation

The inner wall of blood vessels is formed by a layer of endothelial cells that act as a barrier, which prevents the blood cells from leaving the circulation. Yet, some lymphocytes, having mutated to become cancerous, are equipped with a specific surface marker, the JAM-C protein, also present on the surface of endothelial cells. Like a free pass, its presence on the surface of lymphoma cells facilitates their migration through the vessel walls between adjacent endothelial cells. In order to block the effect of this protein, the scientists drew upon the immune system to develop an antibody targeting JAM-C. Named 'H225' this

molecule was designed to bind solely to JAM-C. What was the effect on the lymphoma cells? By masking JAM-C, H225 was able to prevent the cells from migrating out of the blood vessels.

A two-faceted antibody

The H225 antibody proved itself very efficient, decreasing the transit of cancerous cells into the organs of the lymphatic system by over 50%. 'This is not its only effect, Thomas Matthes adds, H225 also significantly limited cell proliferation, even when tumor cells had already settled in the lymphatic system. In our mice, we observed the nearly-complete disappearance of already-present tumor cells in the organs.'

This discovery is in line with the recent advances in cancer immunotherapy, a field that focuses on the design of treatments based on the human immune system. With their specific interest in the JAM-C marker, the Geneva team has laid the foundation for a new therapeutic strategy against lymphoma. The researchers now focus their ongoing efforts on the quest for an efficient treatment that could, in the near future, be offered to patients.

More information: C. Donate et al. Frontline Science: Anti-JAM-C therapy eliminates tumor engraftment in a xenograft model of mantle cell lymphoma, *Journal of Leukocyte Biology* (2016). DOI: 10.1189/jlb.1HI1114-549RR

Provided by University of Geneva