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Survival niche for cancer cells

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Cancer cells do not grow equally well everywhere in the body. Often, they first create the conditions in which they can grow. Many years ago researchers discovered that solid tumors attract blood vessels to ensure their supply of nutrients by secreting specific factors. Now the immunologist Dr. Uta Höpken (Tumor and Immunogenetics Research Group at the Max Delbrück Center for Molecular Medicine, MDC, Berlin-Buch in the Helmholtz Association) and the hematologist Dr. Armin Rehm (Charité – Virchow-Klinikum, Department of Hematology, Oncology and Tumor Immunology, MDC) have shown for the first time that specific forms of lymphoma also create their own survival niche.

Lymphoma is the term used to describe a group of cancers of the lymphatic system. Lymphoma cells are abnormal immune cells (B cells or T cells), a specific group of white blood cells (lymphocytes). Using a mouse model, Dr. Rehm and Dr. Höpken demonstrated for the first time that the dissemination of lymphoma cells and their accumulation in the lymph nodes or spleen is dependent on specific signaling or growth substances, the chemokines CCL19 or CCL21.

Chemokines normally attract immune cells to a site of infection or inflammation. As former immune cells, lymphoma cells have special antennas (receptors) on their cell surface to which these signaling substances bind. If the lymphoma cells receive the signal via their CCR7 receptor, they migrate into the lymph nodes and into specific areas within the spleen.

Paradox

CCR7 not only mediates the migration of the lymphoma cells, it is also apparently crucial for their development and survival. As the two researchers showed in a next step, the lymphoma cells proliferate in the lymph nodes or in the spleen very slowly if this receptor is absent.

However, with the aid of CCR7 the cancer cells find their survival niche in the T-cell zones of the lymph nodes and the spleen. In these zones T cells are usually made fit for defense. "It is paradoxical that lymphoma cells as former B cells find an absolutely optimal microenvironment for their growth in these T-cell zones," Dr. Höpken said.

There the lymphoma cells crosstalk with stromal cells (connective tissue cells), which subsequently secrete increased quantities of the chemokines CCL19/CCL21. The CCR7 receptor not only mediates the homing of additional lymphoma cells to the lymph nodes or spleen, but also stimulates their proliferation.

On the other hand, the lymphoma cells themselves secrete a signaling substance (lymphotoxin) which induces the stromal cells to secrete more and more chemokines. In this way the lymphoma cells ensure their survival. This may also explain why some lymphomas are so aggressive.

In mice the researchers succeeded in breaking this vicious cycle. Using an active substance that blocks the binding of the lymphotoxins to the stromal cells, they were able to stop tumor growth. "In the future," Dr. Rehm said, "it may be that therapeutic strategies will not target the lymphoma cells directly, but rather the connective tissue so vital for their survival."

More information: Cooperative function of CCR7 and lymphotoxin in the formation of a lymphoma-permissive niche within murine secondary lymphoid organs, *Blood*, doi:10.1182/blood-2010-11-321265

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