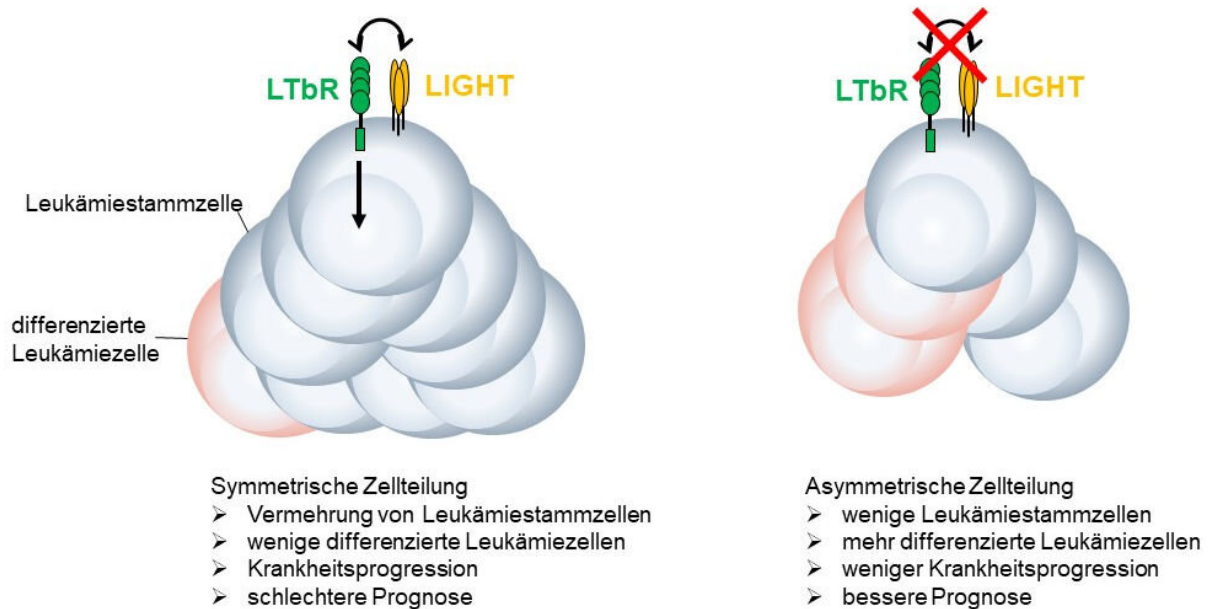


Targeted elimination of leukemic stem cells

February 16 2021



Activated LIGHT/LTbR signaling pathway (left) leads to symmetric cleavage and a propagation of leukemic stem cells. Credit: A. Ochsenbein, University Hospital Bern

Leukemia is caused by leukemic stem cells which are resistant to most known therapies. Relapses are also due to this resistance. Leukemic stem cells arise from normal blood-forming (hematopoietic) stem cells.

Because they are closely related, leukemic and hematopoietic stem cells share many of the same signaling pathways. If the proliferation of leukemic stem cells is to be stopped, it is crucial to find signaling pathways that are active only in the leukemic stem cell, but not the normal one. With this goal in mind, Prof. Adrian Ochsenbein and his team are conducting research at the Department of Medical Oncology at Inselspital, Bern University Hospital. The latest discovery, the so-called LIGHT/LTbR pathway, is presented in Sabine Höpner's article published today in *Nature Communications*.

A new approach to controlling leukemic stem cells

In normal blood formation, the LIGHT/LTbR signaling pathway plays no role in [hematopoietic stem cells](#). It is important in maintaining stem cell function only in situations of increased demand, such as after chemotherapy. In contrast, [leukemic stem cells](#) always rely on this signaling pathway. The LIGHT/LTbR signaling pathway leads to increased symmetric cell division and thus proliferation of leukemic stem cells. If the pathway is blocked with [monoclonal antibodies](#), for example, the stem cells lose their stem cell function and die.

Furthermore, the LIGHT binding site is significantly more abundant in leukemic stem cells than in normal stem cells. In laboratory experiments, animals with leukemia survived significantly longer when the newly discovered signaling pathway had been blocked.

The latest contribution is a beacon of hope for future leukemia treatment

The results published show that multiple receptor/ligand pairs are involved in the maintenance of leukemic [stem cells](#). The researchers believe that the new approach (blocking LIGHT) may lead to an improved therapy of various types of leukemia in the future.

Therapy with medications that aim to block various immune receptors and ligands has revolutionized the treatment of cancer diseases. However, important drugs used to treat solid tumors are not effective in treating leukemia. Therefore, the CD70/CD27 and LIGHT/LT β R signaling pathways that we have defined represent an important advance in improving immunotherapy in myeloid leukemia. Research groups at Stanford have developed antibodies against CD47 that activate another immune [signaling pathway](#) (phagocytosis). These new drugs are already in phase II development for the treatment of acute myeloid leukemia.

More information: Radpour, R. et al. LIGHT/LT β R signaling regulates self-renewal and differentiation of hematopoietic and leukemia stem cells. *Nat Commun*, 1065 (2021).
doi.org/10.1038/s41467-021-21317-x

Provided by Inselspital, Bern University Hospital

Citation: Targeted elimination of leukemic stem cells (2021, February 16) retrieved 25 February 2023 from <https://medicalxpress.com/news/2021-02-leukemic-stem-cells.html>

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