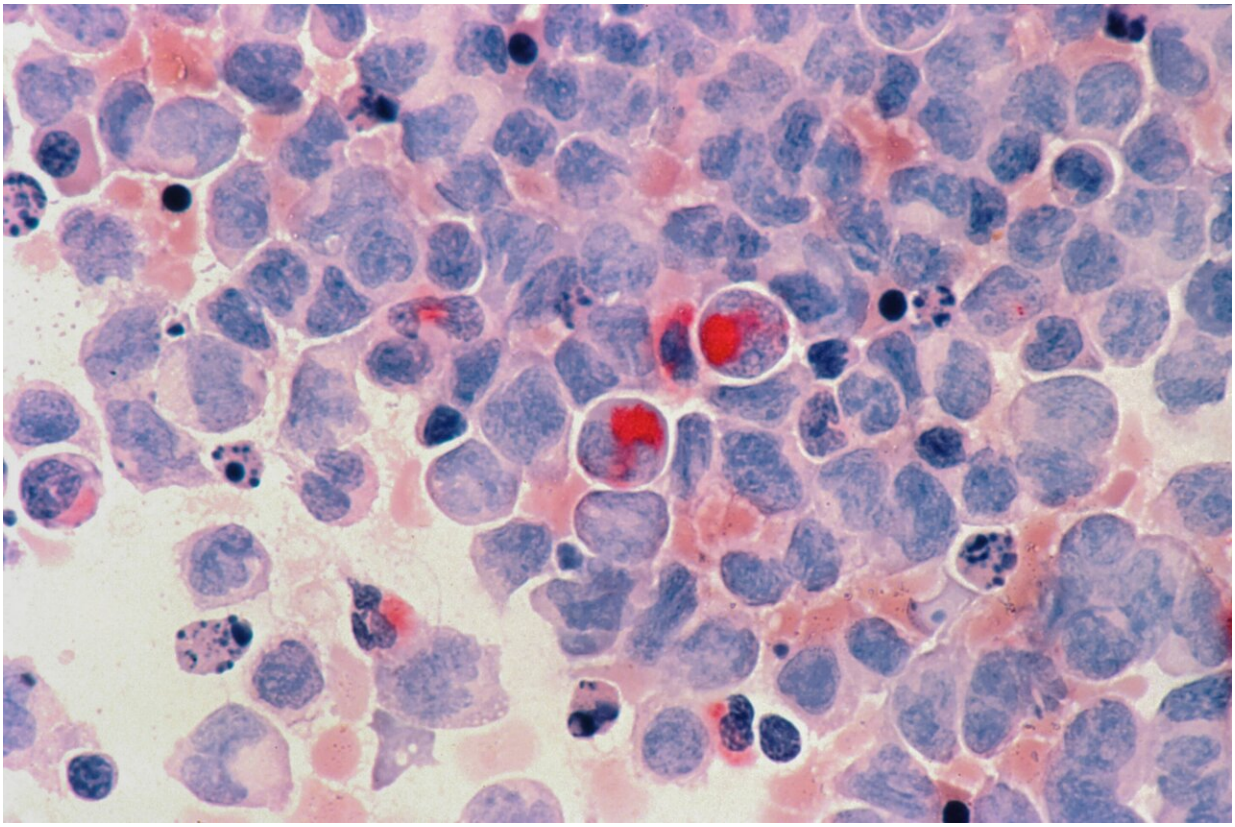
MedicalXpress

New immunotherapy for leukemia discovered

December 6 2021



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Researchers at Karolinska Institutet, University of Oslo and Oslo University Hospital have developed a new kind of immunotherapy for leukemia. The results of a study published in *Nature Biotechnology* show that the therapy kills cancer cells from patients with acute lymphoblastic leukemia. The researchers now want to conduct a clinical study and also

test the method on other types of cancer.

Acute lymphoblastic leukemia is the most common form of childhood leukemia, affecting approximately 70 children a year in Sweden. The disease is characterized by the unregulated growth of immature white blood cells, an essential component of the immune system, in the bone marrow and suppression of other healthy blood cells.

The condition is normally treated with chemotherapy or, in severe cases, bone marrow transplantation or immunotherapy, involving the genetic modification of the patient's own T cells to make them attack another type of white blood cell called B cells. However, the therapy, known as CAR-T after the name of the genetically modified receptor, only works on patients with B-cell leukemia and not those with T-cell leukemia, which affects an estimated 15 to 20 percent of patients with acute lymphoblastic leukemia. Side effects can also occur, as healthy B cells can also be affected.

Spares healthy immune cells

Scientists at Karolinska Institutet, University of Oslo and Oslo University Hospital have now discovered another way to reprogramme the T cells so that they bind to a target expressed inside the cancer cells instead of on the cell surface. The new immunotherapy is focused on the enzyme terminal deoxynucleotidyl transferase (TdT), which is expressed in both T and B-cell leukemia, but only momentarily during the early development of healthy T and B cells. This means that the therapy has the potential to spare healthy T and B cells while eliminating leukemia cells of both the B and T cell type.

To date, the method, which has been developed by Professor Johanna Olweus at the University of Oslo, has been tested on mice with B-cell leukemia and on cell samples from patients with acute lymphoblastic

leukemia of both cell types.

"Our results show that genetically modified T cells equipped with TdT-specific receptors are able to find and eliminate leukemia cells distributed in different organs in mice with B-cell leukemia and in cell samples from patients with both B and T-cell leukemia," says Petter S. Woll, researcher at the Department of Medicine, Huddinge, Karolinska Institutet, who along with Professor Sten Eirik Jacobsen, doctoral students Madeleine Lehander and Stina Virding Culleton, postdoc researcher Stefania Mazzi and research assistant Amy Hillen, has tested the efficacy and safety of the method in mice transplanted with leukemia cells from patients.

"We also saw no negative effect on healthy B and T cells or on the development of new blood cells, which suggests that the treatment can be safe," Petter S. Woll adds.

Planning clinical trial

The Oslo team is now planning for a clinical trial to test the therapy on patients with acute lymphoblastic leukemia who lack therapeutic alternatives. The researchers in Oslo and at Karolinska Institutet are also planning to conduct laboratory and animal studies to test the method on more cancer types.

The study was financed by grants from several bodies, including the Knut and Alice Wallenberg Foundation, the Tobias Foundation, the Swedish Research Council and numerous research foundations in Norway. Some of the Norwegian authors of the study have reported conflicts of interest, which are described in detail in the scientific paper.

More information: Johanna Olweus, T cells targeted to TdT kill leukemic lymphoblasts while sparing normal lymphocytes, *Nature*

Biotechnology (2021). DOI: 10.1038/s41587-021-01089-x.
www.nature.com/articles/s41587-021-01089-x

Provided by Karolinska Institutet