# Experimental gene therapy successful in certain lymphomas and leukemia

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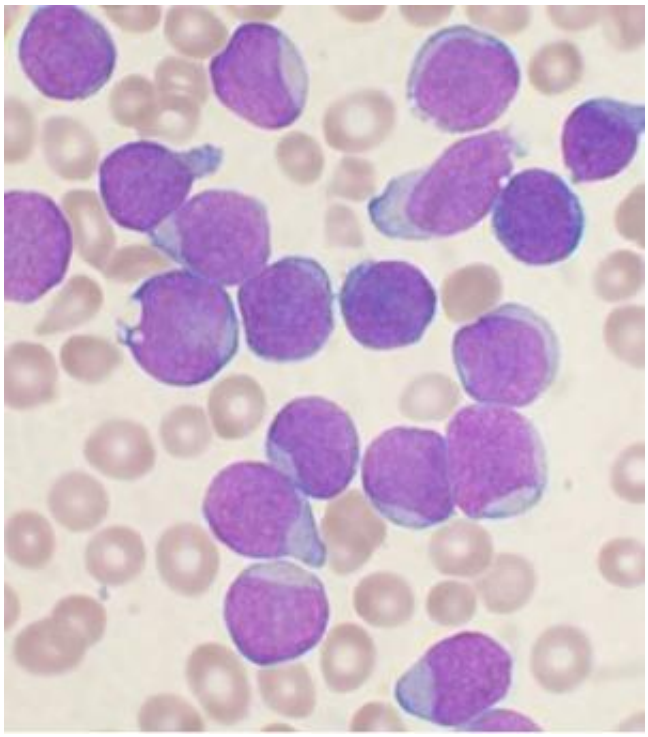

A Wright's stained bone marrow aspirate smear from a patient with precursor B-cell acute lymphoblastic leukemia. Credit: VashiDonsk/Wikipedia

Study results of CD19-directed chimeric antigen receptor (CAR) therapy using the Sleeping Beauty non-viral transduction system to modify T cells has demonstrated further promise in patients with advanced hematologic malignancies.

Patients who had acute lymphocytic leukemia (ALL), non-Hodgkin lymphoma (NHL) or chronic lymphocytic leukemia (CLL) were part of clinical trials at The University of Texas MD Anderson Cancer Center, which used the Sleeping Beauty gene transfer system initially discovered at the University of Minnesota.

Results from the study were presented at the 56th Annual Meeting of the American Society of Hematology (ASH) annual conference in San Francisco and were published in the Dec. 5 issue of the ASH journal *Blood*.

The Sleeping Beauty gene was named for its ability to "awaken" an extinct transposon - DNA that can replicate itself and insert the copy back into the genome. This allows a gene to be transferred into a DNA molecule known as a plasmid. An enzyme called a transposase binds to the plasmid, cuts the transposon and gene out of the plasmid and pastes it into the target DNA sequence. This gene transfer system was the basis for the MD Anderson clinical trials.

Using the Sleeping Beauty gene transfer system, Laurence Cooper, M.D., Ph.D., professor of pediatrics and Partow Kebriaei, M.D., associate professor of stem cell transplantation and cellular therapy, were able to plug a gene into T cells, creating an artificial or chimeric antigen receptor (CAR) on the T cell that recognizes and binds to CD19, a cell surface on B cells. The resultant product known as CAR T cells are produced at MD Anderson and are being employed in the Sleeping Beauty clinical trials.

"We are treating patients with advanced CD19 positive hematologic malignancies using CAR T cells in combination with conventional blood stem cell transplantation," said Kebriaei. "We are also treating patients who had active disease but had not received blood stem cell transplantation."

Patients were recipients of autologous (patient's own cells) or allogeneic (donor cells) stem cell transplantations, which were administered in combination with CAR. Kebriaei reported no acute or long-term toxicity in the 33 patients treated.

"Five patients at high risk for relapse were treated with CAR T cells along with autologous stem cell transplant, and four of those patients remain in complete remission with a median follow-up of 12

months," she said. "Among 13 patients treated with donor CAR T cells after allogeneic stem cell transplantation, six remain in complete remission with a median follow-up of 7.5 months."

Kebriaei also reported that five out of 14 patients treated with CAR T cells for active disease who did not undergo blood stem cell transplantation showed disease regression with a median follow-up of six months.

Provided by University of Texas M. D. Anderson Cancer Center