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Study shows long-term safety of genetically modified immune effector cells

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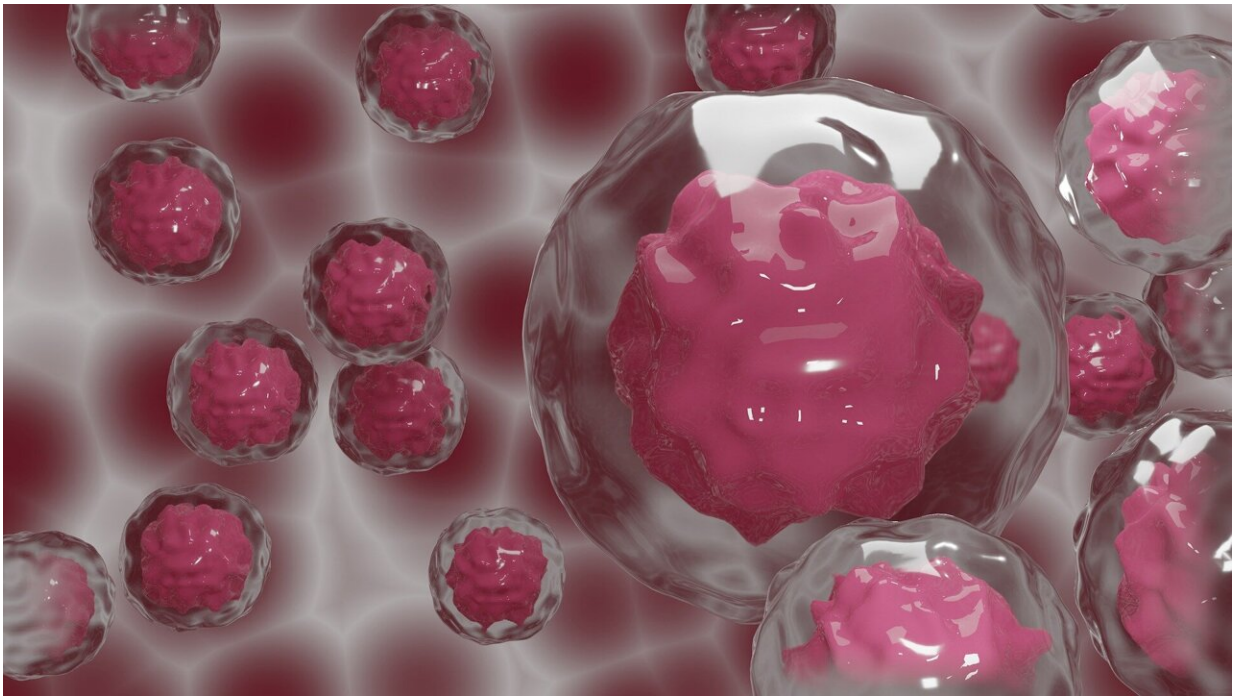

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A new study from researchers at the Center for Cell and Gene Therapy at Baylor College of Medicine, Texas Children's Hospital and Houston Methodist Hospital shows that cancer patients who receive treatment with genetically modified immune cells (IECs) are not at increased risk for subsequent malignancy when compared to patients who receive standard chemotherapy. The results are published in the journal *Blood*.

Researchers examined data from 340 cancer patients who received genetically modified IECs to treat hematological malignancies and solid tumors that had relapsed or not responded to treatment. The patients all were part of phase 1 or phase 2 clinical trials at Baylor dating back to 1998, and were a part of two studies started at St Jude Children's Research Hospital in 1993 and continued at Baylor.

"While the short-term complications of IECs are well described, there have not been large-scale studies summarizing long-term follow-up, including subsequent malignancies," said Dr. David Steffin, co-first author of the study, assistant professor of pediatrics—hematology and oncology at the Center for Cell and Gene Therapy at Baylor and pediatric hematologist at Texas Children's. "This is one of the largest studies of its kind, and our findings reinforce the long-term safety profile of genetically modified IECs."

Thirteen patients in the cohort developed 16 secondary cancers in the months or years following treatment, a rate comparable to patients who receive standard-of-care therapies including chemotherapy and hematopoietic stem cell transplant. Researchers reviewed biopsy results for 11 of the secondary tumors and found no transferred genetic material from the therapy. All 13 patients tested negative for replication competent retrovirus at time of diagnosis.

"With the increased use of cell and gene therapy, some literature has discussed a potential risk for the genetically modified component of cells to integrate into genetic material of patients, leading to future risk of genetic mutations that could increase the risk for secondary malignancies. We found that did not happen in this patient cohort," said Dr. Ibrahim Muhsen, co-first author of the study, chief medical resident at Houston Methodist and an incoming hematology and oncology fellow at Baylor.

The authors stress that patients treated with genetically modified IECs still should be considered a high-risk population and monitored closely with routine cancer screenings. The researchers say future studies will be necessary to determine the risk for other long-term complications like cardiotoxicity.

"This study shows the importance of long term follow up and we are grateful to all the patients who agreed to be followed long-term and all the clinical research staff who ensured that we had comprehensive follow up," said Dr. Helen Heslop, senior author of the study, director of the Center for Cell and Gene Therapy and interim director of the Dan L Duncan Comprehensive Cancer Center at Baylor.

More information: David Steffin et al, Long Term Follow-up for the Development of Subsequent Malignancies in Patients Treated with Genetically Modified IEs, *Blood* (2022). DOI: 10.1182/blood.2022015728

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