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Epigenetics predicts the efficacy of T-lymphocyte treatments in hematological malignancies

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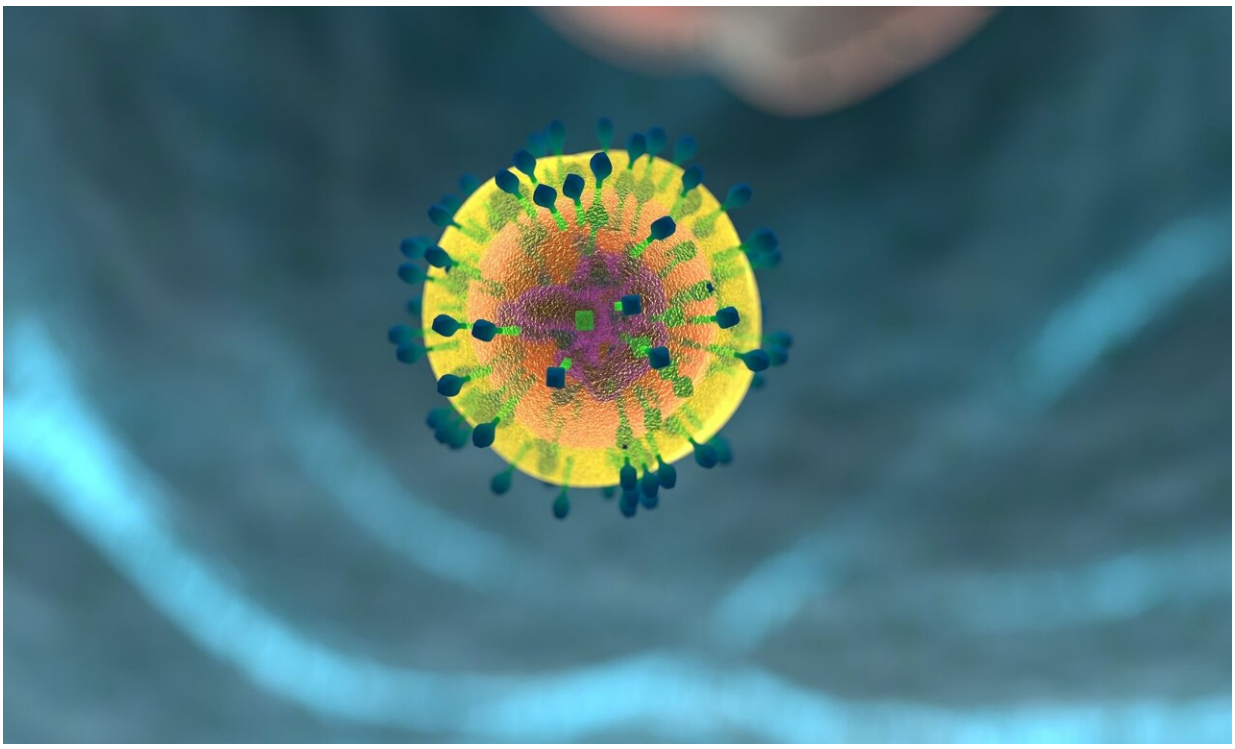

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In the last few years, an alternative for these cases has emerged: a cell therapy known as CAR-T that collects the T-lymphocytes of these patients, modifies them through genetic engineering in the laboratory

and administer them again to the patient so that they attack the cancer more effectively. This strategy has meant a revolution in the treatment of hematological malignancies. This innovative new cellular medicine, also called chimeric antigen receptor T-lymphocyte therapy (CAR-T), is not without problems that can be summarized in the appearance of side effects, cases that are insensitive to the therapy and its high economic cost. Therefore, it would be very important to be able to select which patients are most likely to benefit from the use of CAR-T cells and understand how to improve the healing abilities of these cells.

In an article published in September 28th in *The Journal of The National Cancer Institute*, the official magazine of the National Cancer Center (NCI) of the United States, the group of Dr. Manel Esteller, Director of the Josep Carreras Leukemia Research Institute (IJC), ICREA Research Professor and Professor of Genetics at the University of Barcelona, shows that the profile of chemical modifications of the DNA of CAR-T cells administered to the patient determines their clinical efficacy. The study was made possible thanks to the collaboration with researchers from the Barcelona Clinic Hospital, the Bambino Gesù Pediatric Hospital in Rome and the Sheba Medical Center in Israel, all of them pioneers in this novel therapy.

"CAR-T cell treatment has restored hope to patients with leukemia and lymphoma where all previous therapies had failed. However, we know very little about the factors that influence the success or not of this treatment," Dr. Esteller comments, and adds "we decided to look in detail at the molecular characteristics of more than 100 samples of CAR-T cells provided to patients with leukemias and lymphomas. We discovered that there was a genetic regulation profile (epigenome) that was associated with the absence of disease relapse and an improved overall survival of these people. In addition, we observed that this epigenetic pattern is typical of young T lymphocytes that, as they have a long life ahead and a greater capacity to remain in the patient's

bloodstream, perhaps for this reason they are more efficient CAR-T cells. It is worth investigating now whether these cell subpopulations would be ideal to be selected and administered, or if we can also enrich them using epigenetic drugs that are already used in the context of other leukemias and lymphomas," concludes the researcher.

More information: Carlos A Garcia-Prieto et al, Epigenetic Profiling and Response to CD19 Chimeric Antigen Receptor T-Cell Therapy in B-Cell Malignancies, *JNCI: Journal of the National Cancer Institute* (2021). DOI: 10.1093/jnci/djab194

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