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Sylvester Investigators Study CAR-T Therapy Issues in B-Cell Lymphoma

New research by Sylvester Comprehensive Cancer Center investigators is helping to uncover why a breakthrough immunotherapy to cure aggressive B-cell lymphomas works in 40% of patients.

Francesco Maura, M.D.

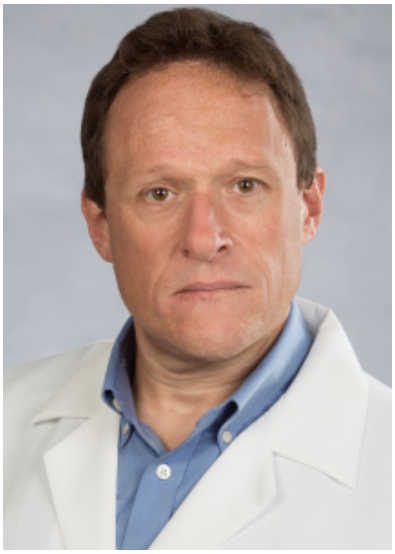
B-cell lymphomas are the most common type of non-Hodgkin's lymphoma in the U.S. and Chimeric antigen receptor T-cell (CART-T) therapy is a type of immunotherapy that aims to kill cancer cells. Specifically, CAR-T therapy that targets a marker on the surface of blood cells called CD19 has given new hope to patients with relapsed or refractory aggressive B-cell lymphomas, who only a few years ago had no treatment options.

Sylvester collaborated with H. Lee Moffitt Cancer Center and University of South Florida investigators to look at what might be driving CAR-T failure in 60% of more of patients, who so badly need a therapy option, according to study author Francesco Maura, M.D., assistant professor of Medicine, Myeloma Program, Division of Hematology at Sylvester.

Study Proving Valuable

“CAR-T therapy is an approach that many hope will become widely available across multiple cancer types,” Dr. Maura said. “Therefore, it is vital to understand why treatment failures occur, which is what motivated our study.”

Study investigators collected and analyzed tumor DNA from 28 patients treated with CAR-T, performing whole genome sequencing to explore which genomic alterations are involved in resistance to the therapy.



Jonathan Schatz, M.D.

"This is the first paper where distinct cancer cell genomic alterations in the tumor DNA have been linked to immune microenvironment dysregulation and CAR-T resistance," Dr. Maura said. "Our study also highlights that CAR-T kill the tumor cell not only by direct interaction through their chimeric receptor, but they are also able to boost the host immune system against the tumor. This last point is critical to achieve a durable response and disease eradication."

The study provides key information for many researchers working on trying to make CAR-T cells work better, according to author Jonathan Schatz, M.D., associate professor of Medicine, Division of Hematology, at Sylvester.

"The specific mechanisms of resistance must be understood before resistance can be overcome in a rational manner," Dr. Schatz said. "Some new CAR-T approaches may be able to benefit from these results rapidly, but other aspects of our findings will require additional research to understand them. My lab, for example, is building new lymphoma disease models directly informed by our data."

Initial Feedback

The paper is published on bioRxiv, an online archive and distribution service for unpublished preprints in the life sciences. By posting preprints on bioRxiv, authors make their findings available to the scientific community and receive feedback before submitting papers to peer-reviewed journals.

University of Miami Miller School of Medicine and Sylvester coauthors on the paper are Bachisio Ziccheddu, senior research analyst in the Division of Hematology; Caroline A. Coughlin,

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