Researchers seek to improve success of chimeric antigen receptor-T cell therapy in non-Hodgkin lymphoma

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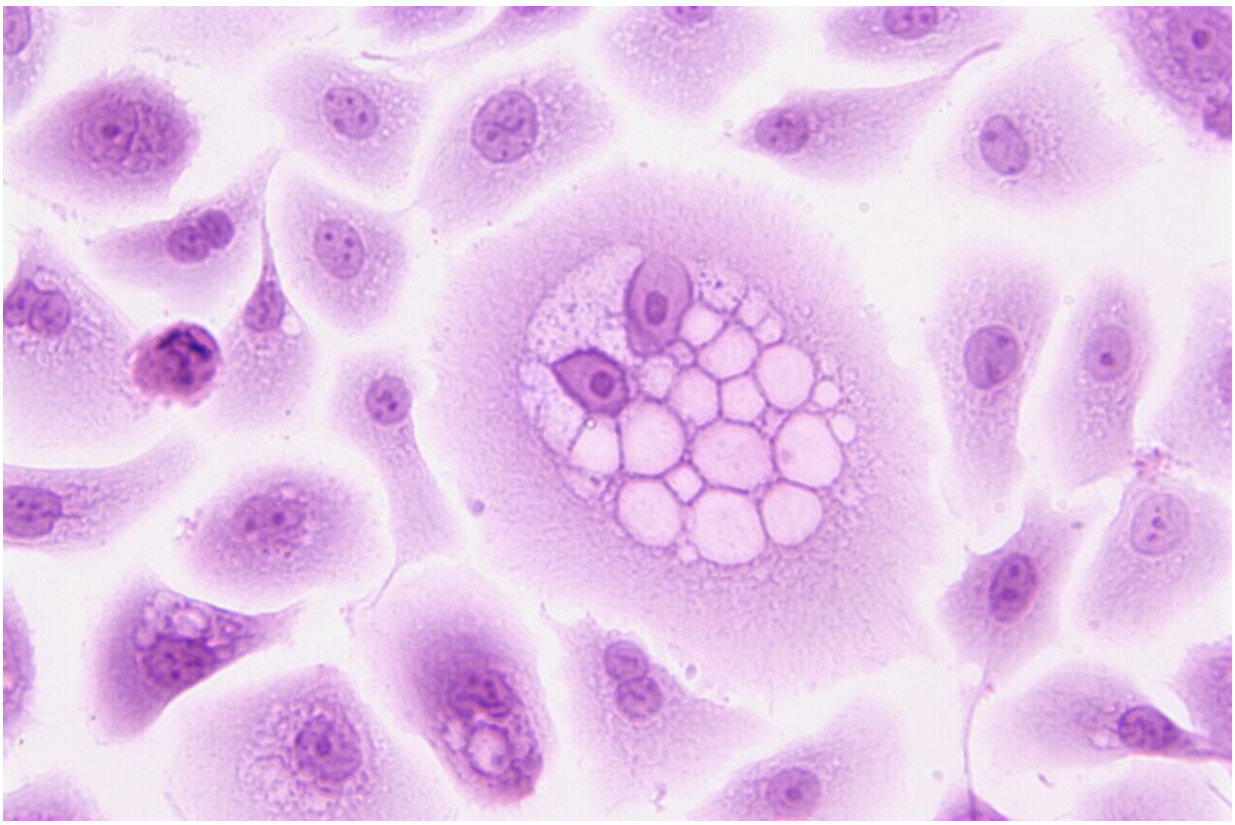

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A study published by researchers from Mayo Clinic Cancer Center at Mayo Clinic in Florida and Case Western, Cleveland Medical Center,

investigates the reasons for decreasing remission rates for patients with non-Hodgkin lymphoma treated with chimeric antigen receptor-T cell therapy (CAR-T cell therapy). The study is published in *Cancer Discovery*.

"CAR-T cell therapy is a promising treatment for non-Hodgkin lymphoma, especially for patients who have relapsed or those who have not responded to prior therapies," says Tae Hyun Hwang, Ph.D., a researcher at Mayo Clinic Cancer Center in Jacksonville, Florida.

However, Dr. Hwang says that recent long-term follow-up data suggest that the success rate of CAR-T cell therapy for patients with non-Hodgkin lymphoma may be decreasing. "Lasting remission in this setting ranges from 30% to 40%, so it is critical to identify a predictive biomarker to measure CAR-T cell resistance so we can better match patients with effective therapy," says Dr. Hwang.

"The overall goal of our research is to support precision oncology care. Novel therapeutic strategies will help us improve the efficacy of CAR-T cell therapy for patients with non-Hodgkin lymphoma," says David Wald, M.D., Ph.D., of Case Western, Cleveland Medical Center, the study's co-author,

"Our team hypothesized there would be distinct molecular patterns in CAR-T cells between patients who responded to treatment and patients who did not respond," says Dr. Hwang. He says the team used innovative computational and experimental approaches to identify these patterns.

Researchers generated single-cell RNA and protein sequencing data for CAR-T cells before they were administered to patients and again at multiple points after being infused in patients. Dr. Hwang says this work generated more than 133,000 single-cell expression profiles that researchers used to develop and apply computational approaches to

dissect single-cell level RNA or protein expression patterns of CAR-T cells associated with treatment response.

Using these computational approaches, the team found that a gene called TIGIT—a T cell—was highly expressed in post-infusion CAR-T cells from patients who did not respond to CAR-T cell therapy. The team also validated that TIGIT drives CAR-T cell exhaustion and dysfunction, and they discovered that blocking TIGIT with CAR-T cell therapy could improve treatment efficacy in an in vivo study.

"If our findings can be validated in prospective clinical trials, our TIGIT blocking strategy with CAR-T cell therapy may improve current CAR-T cell therapy responses in patients with non-Hodgkin lymphoma and may also improve patient survival," says Dr. Hwang.

More information: Zachary Jackson et al, Sequential single cell transcriptional and protein marker profiling reveals TIGIT as a marker of CD19 CAR-T cell dysfunction in patients with non-Hodgkin's lymphoma, *Cancer Discovery* (2022). DOI: 10.1158/2159-8290.CD-21-1586

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