


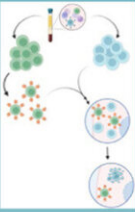
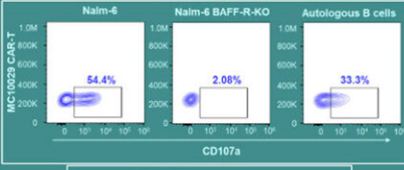
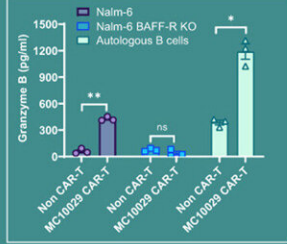


Could CAR-T cell therapy improve kidney transplants?

April 9 2024, by Susan Buckles, Mayo Clinic News Network

CAR T-cell therapy - Paving the way for sensitized kidney transplant patients.

Cohort	Methods	Outcomes	
<p>The primary objective of this study is to investigate the cytotoxicity of patient-derived MC10029 (anti-BAFF-R) CAR T-cells against their own autologous B cells.</p>  <p>A total of 10 eligible patients, who exhibited a high sensitization level with a calculated panel reactive antibody (cPRA) of 98% or higher, were recruited for this study. These Patients include 9 kidney transplant recipients and one patient received lung transplant.</p>	<ul style="list-style-type: none"> Collect blood. Isolate T cells to generate patient-derived MC10029 CAR T-cells. Autologous B cells are freshly isolated serving as target cells. The antigen- specific cytotoxicity of patient-derived MC10029 CAR T-cells is determined against autologous B cells. 	<p>Outcomes</p>  	<ul style="list-style-type: none"> Patient-derived MC10029 CAR T-cells were successfully generated for all 10 enrolled patients. The CAR T-cells were confirmed for their antigen specificity. Sufficient autologous B cells were obtained from 7 out of ten patients. Patient-derived MC10029 CAR T-cells elicited cytotoxicity against autologous B cells as evidenced by T cell degranulation and release of cytotoxic granule proteins. For the remaining three patients with insufficient autologous B cell availability, we demonstrated the cytotoxicity of their CAR T-cells using cell lines as the target.

Jarmi and Luo, et al. 2024

CONCLUSION: MC10029 CAR T-cells derived from sensitized patients exhibited cytotoxic effects against autologous B cells, which substantiates the viability of employing CAR T-cell therapy as a desensitization strategy in kidney transplant.

Credit: *Kidney International* (2024). DOI: 10.1016/j.kint.2024.02.008

Chimeric antigen receptor-T cell therapy (CAR-T cell therapy) could provide a revolutionary approach to organ transplantation for patients who are hard to match and susceptible to rejection, Mayo Clinic researchers discovered.

Their pioneering [research](#) focuses on using CAR-T cells derived from

the patient's own immune system to prevent rejection of donated organs. Sensitized [patients](#) are those who have high levels of antibodies that cause their immune systems to react negatively to potential donor organs. These patients often face extended waiting periods for a transplant.

Research from this proof-of-concept [study](#) is published in *Kidney International*.

"This study was designed to evaluate the feasibility of using an immunotherapy that would remove B cells that cause sensitization in patients waiting for a kidney transplant," says Tambi Jarmi, M.D., first author on the study and a transplant nephrologist at Mayo Clinic in Florida.

"This research is one of the first steps toward applying CAR-T cells in the field of transplantation to try to make more donor organs available for transplant and reduce the wait for patients who need a new kidney."

Research on CAR-T cell therapy and transplantation

Researchers in the lab of Hong Qin, M.D., Ph.D., developed a new type of CAR-T cell therapy that targets a protein known as B cell activating factor receptor (BAFF-R), which is present on B cells. B cells play a key role in regulating the immune system and generating antibodies. They investigated whether the BAFF-R CAR-T cells could target and remove B cells that cause sensitization.

For this study, researchers generated BAFF-R CAR-T cells from 10 patients considered sensitized to [organ transplantation](#). Nine of them had undergone kidney transplants and one had received a lung transplant.

"We isolated T cells from a small quantity of the patient's blood. These CAR-T cells were then engineered to identify and neutralize B cells

carrying a specific antigen, effectively targeting and eliminating the sensitizing cells," says Dr. Qin, lead author on the study, who is an immunologist and CAR-T cell researcher.

Then, the research team compared the activity of BAFF-R CAR-T cells to T cells after they were treated with B cells from healthy donors. Researchers saw a reduction in B cells from the sensitized patient group that had been treated with patient-derived CAR-T cells when compared to the non-CAR-T control group.

"Our study demonstrated that BAFF-R CAR-T cells derived from sensitized patients exhibited killing effects against B cells, which substantiates the viability of using BAFF-R CAR-T cell therapy as a desensitization strategy in kidney transplant," says Dr. Jarmi.

Mayo Clinic now is preparing to biomanufacture the BAFF CAR-T cells at its commercial-grade facilities in Florida for testing in early-stage clinical trials.

The use of BAFF-R CAR-T cell therapy to desensitize [kidney transplant](#) patients is considered experimental. It is among the first investigations into the use of this immunotherapy for diseases beyond cancer. This research is a collaboration between the Mayo Clinic Regenerative Immunotherapy and CAR-T Translational Research Program, Mayo Clinic Department of Transplant Florida and Mayo Clinic Division of Hematology and Medical Oncology.

Additional research is needed to validate the findings of this study.

More information: Tambi Jarmi et al, CAR T-cell therapy—paving the way for sensitized kidney transplant patients, *Kidney International*

(2024). [DOI: 10.1016/j.kint.2024.02.008](https://doi.org/10.1016/j.kint.2024.02.008)

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