



LINEBERGER
COMPREHENSIVE
CANCER CENTER

CAR-T Immunotherapy at UNC Lineberger

Personalized, precision medicine

UNC Lineberger Comprehensive Cancer Center is one of only a select few academic centers in the United States with the scientific, technical and clinical capabilities to design, develop and deliver a novel form of immunotherapy that uses the patient's immune cells to attack their cancer.

Chimeric antigen receptor T-cell, or CAR-T, immunotherapy is truly personalized cancer treatment. It involves extracting T-cells – disease-fighting immune cells – from the patient's blood and genetically engineering them to recognize and destroy the patient's own cancer cells. The engineered T-cells are then multiplied by the tens of millions and infused back into the patient. For many patients, immunotherapy is a last resort, as their cancer has not responded to other treatments.

Building the CAR-T program

An expert team

The vision for an immunotherapy program was initiated by Jonathan Serody, MD, the Elizabeth Thomas Professor of Medicine, and Jenny Ting, PhD, the William R. Kenan Distinguished Professor of Genetics in 2008. This vision became actualized by Ned Sharpless, MD, then-Director of UNC Lineberger Comprehensive Cancer Center in 2015 with the recruitment of cellular immunotherapy pioneers Gianpietro Dotti, MD, and Barbara Savoldo, MD, PhD, from the Center for Cell and Gene Therapy at the Baylor College of Medicine.

Prior to their arrival, UNC had invested in building a clinical Good Manufacturing Practices (GMP) facility off campus where cells for immunotherapy could be generated. Led by Dotti and Savoldo, the facility has generated more than 175 products used to treat patients with cancer.

In 2024, UNC Lineberger finished expansion of the GMP facility that allows a greater number of cellular products and viral vectors to be produced for UNC studies. UNC Lineberger has quickly created one of the preeminent and most productive CAR-T and cellular therapy programs in the country.



"The only major thing I've had was a fever. I never had any of the hallucinations or the other major neurological symptoms. For that to be the biggest side effect that I had, I was certainly blessed."

- Sabrina Shelton, CAR-T patient

"We had a very heartwarming moment recently where a patient filmed his phone call with his oncologist as he was getting the news that he was in remission – the first time he was in remission in many years – and we were given permission to share this video with our lab team. It was very rewarding for them to see how the work they are doing directly affects patients!"

- Natalie Grover, MD Clinical Director UNC Medical Center Cellular Therapy Program

Advanced Cellular Therapeutics Facility

Expanding our reach

UNC Lineberger made a strategic investment into the immunotherapy program a decade ago, and is a testament to the dedication of the cancer center's leadership and the success of its immunotherapy team.

The facility was recently renovated and expanded to meet increased patient demand for CAR-T, making this the largest facility in the Southeast, and the only facility in the region that offers patients this personalized treatment all in one place. There are fewer than 15 centers like this in the nation, making UNC Lineberger uniquely placed to advance the field. Over 150 patients have been treated since opening in 2016, and the expansion will allow that number to grow.

- Previously the program was limited to the production of 40 to 50 products per year, limiting the number of patients who could be treated
- The substantial increase in GMP space will now allow the production of 120 products per year
- This increase allows the GMP facility to produce vectors and cellular products that can be shipped to affiliated cancer programs outside of UNC.

"What we envisioned has come to fruition better than we initially anticipated. We are the only academic medical institution in the past 10 years to develop a program of our size and are treating patients. Philanthropic investment has brought innovation to the therapy of North Carolinians with far advanced cancer."

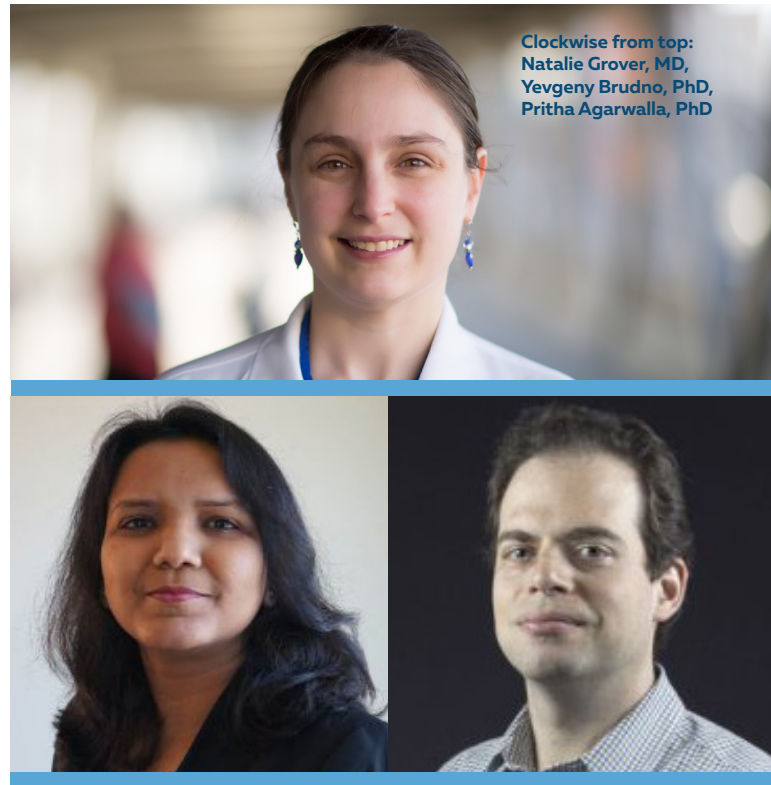
- Jonathan Serody, MD, director,
UNC Medical Center Cellular Therapy Program



Our progress

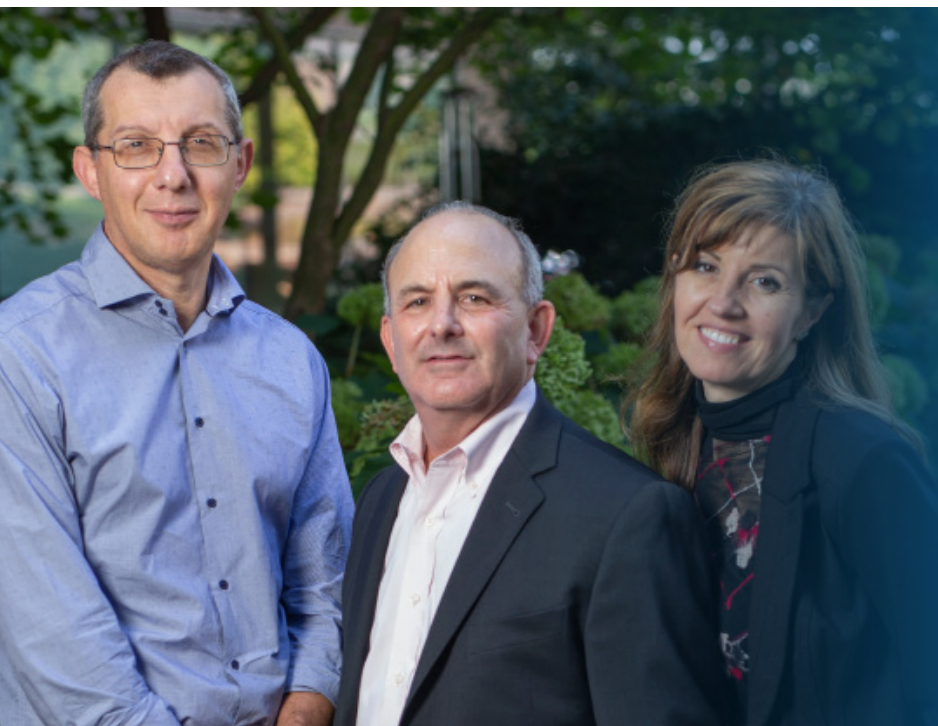
Results from CAR-T clinical trials are generating insights that are advancing the field.

- In relapsed or refractory B-cell acute lymphoblastic leukemia, a difficult-to-treat cancer that occurs in children, adolescents and young adults, researchers successfully used an experimental safety switch designed by investigators at Bellicum and first utilized by Dotti and his colleagues to decrease the severity of bone marrow transplant complications. The safety switch successfully reduced the severity of the neurological complications with CD19 CAR-T therapy. These findings show there is the potential to use CAR-T designed with the built-in safety switch to treat other cancers as published in Blood (Foster et al. Blood 137(23) : 2021).
- In another clinical trial, Savoldo and Natalie Grover, MD, showed that CAR-T immunotherapy was both safe and highly effective for patients with relapsed/refractory Hodgkin lymphoma. The treatment led to the complete disappearance of tumor in 77% of patients treated at the highest dose level of therapy at UNC-CH, with almost all patients having clinical benefit after treatment (Ramos et al. Journal of Clinical Oncology, 38(32) : 2020). Additionally, use of this product, after stem cell transplantation performed as well as brentuximab vedotin as adjuvant therapy (Grover et al. Lancet Haematology in the press).



Clockwise from top:
Natalie Grover, MD,
Yevgeny Brudno, PhD,
Pritha Agarwalla, PhD

CD30.CAR Therapy Received Fast Track Breakthrough Designation from the FDA



"We are actively working to create relationships with other institutions to offer the possibility to manufacture the CAR-T at UNC but to ship the cells to other hospitals.

This would be particularly important for pediatric patients considering all the challenges with traveling that they have."

– Gianpietro Dotti, MD, director, UNC Lineberger Immunotherapy Program



The Advanced Cellular Therapeutics facility was recently renovated and expanded to meet increased patient demand for CAR-T, making this the largest facility in the Southeast, and the only facility in the region that offers this personalized treatment all in one place.

- New Phase I Trials for patients with neuroblastoma / osteosarcoma, glioblastoma multiforme, and ovarian cancer are currently being conducted with a primary focus on treatment safety. If these trials determine that patients are safely tolerating CAR-T therapy, expansion trials will be performed for additional patients with pancreatic and triple negative breast cancer by targeting B7-H3 as previously published by Dr. Dotti (Du et al. Cancer Cell 35(2) : 2019).
- Working in partnership with North Carolina State University, UNC Lineberger's researchers have developed an implantable biotechnology that produces and releases CAR-T to attack cancerous tumors. In a proof-of-concept study involving lymphoma in mice, the researchers found that treatment with the implants was faster and more cost effective than conventional CAR-T treatment (Agarwalla et al. Nature Biotechnology, 40(8) : 2022).
- Further research found that pairing a newly developed gel with immunotherapy improved the treatment's effectiveness in mouse brains with glioblastoma, a highly malignant and deadly brain cancer. The researchers were able to fill in the surgical site with a scaffold-like web, and stop tumors from recurring. If this can be replicated in humans, it may lead to better treatment outcomes in patients with glioblastoma multiforme and improve on the current poor survival rate.
- Working with investigators at the National Cancer Institute, Serody and his colleagues have developed a novel method for improving the function of CAR-T therapy in breast cancer by activating innate sensors in the CAR-T cells (Xu et al. Journal of Experimental Medicine, 218(2) : 2021). Further work is evaluating this approach for other solid tumors.

☆ What's next

UNC Lineberger has been a driver of innovation in immunotherapy, and it is strategically positioned to make even greater therapeutic advances in this field. With success in blood cancers, the immunotherapy team is now looking to find similar success, conducting clinical trials into solid tumors, such as breast, lung, head and neck, and ovarian cancers, the first of their kind in the immunotherapy field.

Other cancer centers, like Emory University and Massachusetts General Hospital, have taken notice of UNC Lineberger's success, and these major institutions are looking to partner with us on clinical trials in order to reach a wider group of patients who could benefit from this treatment.

