

# Therapy using immune system cells preserves vision in mice implanted with rare eye cancer

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Barbara Savoldo, MD, PhD, and colleagues at the University of North Carolina Lineberger Comprehensive Cancer Center report that a treatment that uses immune system T cells, combined with an immune-boosting drug packaged in an injectable gel, preserved the vision of mice implanted with retinoblastoma tissue. The cancer, which is most commonly diagnosed in infants and young children, is treatable in early stages but can still lead to the loss of vision in about 5% of cases. Credit: UNC Lineberger

A treatment that uses immune system T cells, combined with an immune-boosting drug packaged in an injectable gel, was found to preserve the vision of mice implanted with tissue from a human eye cancer known as retinoblastoma. The cancer is treatable in early stages but can still lead to the loss of vision in about 5% of cases.

The research findings from scientists at the University of North Carolina Lineberger Comprehensive Cancer Center were published in *Nature Cancer* on Oct. 12, 2020.

Retinoblastoma is primarily diagnosed in infants and young children. It is considered rare, with approximately 200-300 children diagnosed with the [cancer](#) each year in the U.S. Current treatments for retinoblastoma use cold, heat, chemotherapy, lasers or radiation but vision loss still occurs, so the UNC researchers wanted to search for methods that could preserve vision.

"Based on our mouse study and the existence of an active cell immunotherapy program at UNC Lineberger, along with infrastructure for generation of CAR-Ts for clinical use, we feel confident that our efforts could be translated into a phase I [clinical study](#) in people," said Zongchao Han, MD, Ph.D., an associate professor in the UNC School of Medicine and UNC Eshelman School of Pharmacy and a UNC Lineberger member.

The researchers used an incremental process to determine the best method for treatment of retinoblastoma. First, the researchers turned to chimeric antigen receptor-T (CAR-T) cell therapy, a type of immunotherapy where T cells that comprise the [immune system](#) are modified in the laboratory to express chimeric antigen receptors, CARs, that target surface proteins on cancer cells. In a lab test, they found that a molecule, GD2, is expressed in retinoblastoma but the possibility to target this molecule to safely eliminate the [tumor](#) in the eye was

unknown.

Next, to test the safety and benefit of targeting GD2, the investigators injected the CAR-T that recognizes this molecule into the retina of mice implanted with retinoblastoma cancer cells and found the therapy delayed tumor development but did not eradicate the tumor. Then they combined the CAR-Ts with interleukin (IL)-15, a protein that can boost immune response, and found that 60% of mice were tumor-free for up to 70 days.

Finally, they injected a water-based gel containing the CAR-Ts and IL-15 into the retinas of the mice. The CAR-Ts and IL-15 retained an extended ability to attack the cancer [cells](#), control tumor growth and prevent tumor recurrence. They corroborated the lack of tumor growth with several imaging exams of the retina.

This gel-encapsulated therapy is currently being tested in clinical trials in children with neuroblastoma, an embryonal tumor that can progress rapidly and has some of the same genetic characteristics of retinoblastoma.

"We are always looking to improve the lives of children at Lineberger," said Barbara Savoldo, MD, PHD, professor of pediatric Hematology/Oncology at UNC School of Medicine and UNC Lineberger member. "Therefore, we hope to look at the safety of gel injection in a clinical trial of [retinoblastoma](#) in children, and if that proves safe, we could move on to see if our methodology can reduce or eliminate these tumors."

**More information:** GD2-specific CAR T cells encapsulated in an injectable hydrogel control retinoblastoma and preserve vision, *Nature Cancer* (2020). [DOI: 10.1038/s43018-020-00119-y](https://doi.org/10.1038/s43018-020-00119-y)

Provided by UNC Lineberger Comprehensive Cancer Center

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