

Scientists develop new gene delivery and immune cell engineering technology for future cancer cell therapies

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Scientists at Yale have developed a new gene delivery and immune cell engineering technology with the potential to advance cell therapies for

cancer and other diseases.

Adoptive cell therapy (ACT), also known as cellular immunotherapy, harnesses a patient's own immune system to treat diseases such as cancer.

By genetically altering immune T cells in a lab, the transfer of these "living drugs" through CAR T-cell therapy has had significant clinical success in targeting and destroying [tumor cells](#) more effectively.

Immune cell engineering is critical for the production, research, and development of cell therapy, with most of the current CAR-T cells produced for [clinical trials](#) being generated from lentiviral or retroviral systems. But these sources have limitations due to their relative safety to make, shortness of lifespan, and in some cases their heightened risk of cellular toxicity.

Led by Sidi Chen, Associate Professor of Genetics, a research team at the Yale Systems Biology Institute has developed a new gene delivery system to produce a superior cell engineering system called MAJESTIC (mRNA AAV-Sleeping-Beauty Joint Engineering of Stable Therapeutic Immune Cells). The MAJESTIC system is an organic combination of gene delivery approaches like mRNA, transposon and adeno-associated virus (AAV), and is superior to current gene delivery platforms for cell therapy.

Published in *Nature Biomedical Engineering*, the scientists show how the new system delivers transgenes into human immune cells and other [cell types](#) with higher efficiency, lower cellular toxicity, and stable transgene expression to safely produce CAR-T cells and other therapeutic immune cells.

The versatility of the MAJESTIC system offers advantages that could

lead to an increase in the number and variety of immune cell-based therapeutics being approved to treat cancer and other diseases.

Authors of the article include Lupeng Ye, a former Yale postdoc who is now assistant professor at Nanjing University, and Yale College student Stanley Lam. The research was supported by the NIH, DoD and foundations such as the Advanced Center for Genome Technology and the Pershing Square Sohn Cancer Research Alliance.

More information: Lupeng Ye et al, AAV-mediated delivery of a Sleeping Beauty transposon and an mRNA-encoded transposase for the engineering of therapeutic immune cells, *Nature Biomedical Engineering* (2023). [DOI: 10.1038/s41551-023-01058-6](https://doi.org/10.1038/s41551-023-01058-6)

Provided by Yale University

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