

Boosting stem cell activity can enhance immunotherapy benefits

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Scanning electron micrograph of a human T lymphocyte (also called a T cell) from the immune system of a healthy donor. Credit: NIAID

Immune-system T cells have been reprogrammed into regenerative stem cell-like memory (TSCM) cells that are long-lived, highly active "super immune cells" with strong antitumor activity, according to new research from Georgetown Lombardi Comprehensive Cancer Center.

The reprogramming involves a novel approach the researchers developed that inhibits the activity of proteins known as MEK1/2. Currently, several MEK inhibitors are used to effectively treat melanoma, but this study demonstrates that MEK inhibitors don't just target certain types of cancer cells, but rather, more broadly, reprogram T cells to fight many types of cancer.

The finding appears November 23, 2020, in *Nature Immunology*.

"Although immunotherapies have improved survival for cancer patients over recent years, survival rates remain sub-optimal. Therefore, there is an urgent need to develop novel, more effective anti-cancer immunotherapies," says Samir N. Khleif, MD, director of The Loop Immunology and Immunotherapy Center at Lombardi Comprehensive Cancer Center and head of the team that conducted this research. "Our research shows that using drugs that have already been approved for [human use](#) may significantly enhance currently available immune therapeutic approaches, thereby leading to better and more durable anti-cancer responses."

The researchers performed experiments with [human cells](#) in the lab and then confirmed the effects of such an approach in mice. The investigators were able to not only identify a novel strategy to reprogram

T cells into TSCM cells by using MEK1/2 inhibition, they were able to identify a novel molecular mechanism by which the TSCMs were induced.

The scientists found that reprogramming T cells into TSCM can significantly improve T cell therapies for cancer patients. T cell therapy is a process that is widely used in specific cancers and in clinical trials, where immune-system T cells are separated out from a patient's blood, engineered and expanded with special tumor-targeting capabilities and infused back into the patient to fight cancer. In their experiments, human T cells were reprogrammed with MEK inhibitors into TSCM; additionally, when treating mice with MEK inhibitors, the reprogramming of T [cells](#) was also found to induce effective TSCMs.

"Stem cell research has played a vital role this century in enhancing the progress against many diseases. Recent public and private support for stem cell therapy is very gratifying," says Khleif. "Having stem cell research-specific funding from both governmental and private funders will greatly help accelerate the development of this under-utilized area of research."

Now that MEK inhibitors have been shown to enhance an anti-tumor immune response, the researchers are starting to look into designing [clinical trials](#) to test their research approach in [cancer patients](#). "Our approach is quite novel and we're anxious to see it put to use in the clinical arena as soon as possible," concludes Khleif.

More information: MEK inhibition reprograms CD8+ T lymphocytes into memory stem cells with potent antitumor effects, *Nature Immunology* (2020). [DOI: 10.1038/s41590-020-00818-9](https://doi.org/10.1038/s41590-020-00818-9) , www.nature.com/articles/s41590-020-00818-9

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