

What T-Cell Cancers Can Teach Us About T-Cell Therapy

Exploiting naturally occurring mutations may offer a promising approach to treatment.

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Adoptive T cell therapies, in which a patient's own immune cells are genetically engineered to target their cancer cells, have been remarkably effective in treating certain blood cancers. Unfortunately, this success has not translated to solid tumors, where T cells face unique challenges in the tumor environment that limit their persistence and function.

Recently, researchers have been turning to an unlikely source for answers, one infamously good at making genetic changes to overcome environmental obstacles. At Northwestern University, former Damon Runyon Clinical Investigator Jaehyuk Choi, MD, PhD, and his colleagues are modeling new T cell therapies after T cell cancers. The results, published in [Nature](#), are promising.

In T cell lymphomas, tumor cells overcome many of the same challenges that therapeutic T cells face through acquired mutations. Fueled by natural selection, these tumor mutations produce novel and elegant solutions to address T cell deficits. Understanding that these natural modifications may outperform current bioengineering capabilities, Dr. Choi and his team introduced 71 of these mutations into therapeutic T cells, hoping to grant them the ability to survive, proliferate, and function in the tumor environment.

Excitingly, they were able to identify a gene fusion present in certain T cell lymphomas that enhanced therapeutic T cell signaling and function. To demonstrate that this technique could be deployed safely, the team evaluated the genetically engineered T cells more than a year later and found they showed no signs of malignancy.

"Collectively, our results indicate that exploiting naturally occurring mutations represents a promising approach," Dr. Choi wrote, "to discover how solutions derived from evolution of malignant T cells can improve a broad range of T cell therapies."

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