CAR T cells more powerful when built with CRISPR, researchers find

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Researchers from Memorial Sloan Kettering Cancer Center (MSK) have harnessed the power of CRISPR/Cas9 to create more-potent chimeric antigen receptor (CAR) T cells that enhance tumor rejection in mice. The unexpected findings, published in *Nature* on February 22, uncover facets of CAR immunobiology and underscore the potential of CRISPR/Cas9 genome editing to advance immunotherapies for cancer.

CRISPR is a genome-editing tool that enables scientists to cut and manipulate a cell's DNA with high precision. In the *Nature* paper, MSK investigators show that CRISPR technology can deliver the CAR gene to a very specific location in the genome of the T cell. This precise approach creates CAR T cells with more stamina—they can kill tumor cells for longer because they are less prone to becoming exhausted. This could eventually lead to safer, more effective use of this powerful form of immunotherapy in patients.

"Cancer cells are relentless in their attempt to evade treatment, so we need CAR T cells that can match and outlast them," explained Michel Sadelain, MD, PhD, senior author on the *Nature* paper and Director of the Center for Cell Engineering and the Gene Transfer and Gene Expression Laboratory at MSK. "This new discovery shows that we may be able to harness the power of genome editing to give these 'living therapies' a built-in boost. We are eager to continue exploring how genome-editing technology could give us the next generation of CAR T cell therapy."

Some of the first clinical trials using CRISPR technology are currently in the planning stages. Dr. Sadelain and his team aim to eventually explore the safety and efficacy of these CRISPR-built CAR T cells in a trial. Currently, CAR T cells are usually made using a retroviral or lentiviral technology to deliver the CAR gene into the T cells. This delivery method results in the CAR gene being inserted at random into the genome of the recipient cells, which can result in unwanted genetic side effects.

More information: Justin Eyquem et al, Targeting a CAR to the TRAC locus with CRISPR/Cas9 enhances tumour rejection, *Nature* (2017). DOI: 10.1038/nature21405

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