

A Novel In Vivo Genome-Wide CRISPR Screening Platform for Enhancing T Cell Immunotherapies in Solid Tumors

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TECHNOLOGY DESCRIPTION

This cutting-edge platform enables genome-scale, in vivo CRISPR screening in primary human T cells, transplanted into tumor-bearing mice. By engineering solid tumor cells to express anti-CD3 scFv, this system dramatically enhances tumor-infiltrating T cell recovery, overcoming previous limitations of low T cell yields in vivo. The platform replicates key challenges of the tumor microenvironment, including nutrient deprivation, suppressive metabolic and cytokine conditions, and physical barriers to infiltration. Using this model, scientists performed the first genome-wide CRISPR knockout screens in human T cells within solid tumors, identifying key genetic regulators of T cell trafficking and effector function.

Key discoveries include the identification of the **P2RY8-Gα13 signaling pathway**, which suppresses T cell infiltration, and **GNAS (Gas)**, which mediates resistance to multiple suppressive ligands in the tumor microenvironment. Genetic disruption of these pathways enhances both T cell accumulation in tumors and their ability to maintain effector functions, leading to improved therapeutic performance across diverse preclinical solid tumor models. Furthermore, dual knockout of **P2RY8** and **GNAS** synergistically improves tumor control, paving the way for multiplexed T cell engineering strategies to combat solid tumors.

STAGE OF DEVELOPMENT

Disruption of **P2RY8** and **GNAS** has been shown to dramatically enhance T cell efficacy across multiple solid tumor models, with favorable safety profiles observed in vivo.

RELATED MATERIALS

- ▶ [In vivo genome-wide CRISPR screens in human T cells to enhance T cell therapy for solid tumors - 09/24/2025](#)

PATENT STATUS

Patent Pending

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OTHER INFORMATION

KEYWORDS

Solid tumor, T Cell, Platform, CRISPR, Cell Therapy

CATEGORIZED AS

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