**Docket #:** S23-162

# Composition and Method for Autonomous RNA Switches for Translational Control

Stanford scientists have engineered the untranslated region (UTR) of RNA into autonomous switches that sense cell type and cell state, then respond by turning on translation of a therapeutic payload such as a chimeric antigen receptor (CAR). These switches can provide dynamic regulation in cellular immunotherapies and offer broad utility in next-generation mRNA therapeutics, including in vivo CAR T cell engineering.

Ex vivo CAR T therapy successfully combats malignant tumors, but is expensive, takes weeks to manufacture, and typically delivers a single dose, leaving room for relapse. Engineering T cells directly inside the patient with mRNA would be faster and more customizable, but it requires a way to sense the right biological conditions and tightly restrict where the payload is expressed.

These engineered UTRs act as ON/OFF and tunable switches that activate payloads in target immune or cancer cell populations while staying quiescent in healthy cells. In engineered T cells, the switch drove CAR expression and killing of antigen-positive tumor cells.

**Stage of Development**
Preclinical, in vitro proof of concept: ongoing work covers in vivo efficacy, additional cell-type and cell-state classifiers, and delivery.

## Applications

- mRNA switches that sense and respond to native biological conditions such as T cell activation
- Synthetic regulation of therapeutic payloads in situ

- In vivo engineering of cellular immunotherapies

## Advantages

- Precise control over translation of genetic payloads
- Rapid, customizable mRNA switch production
- Flexible temporal dosing control from the transient nature of mRNA

## Patents

- Published Application: WO2025160191

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