



Umoja
BIOPHARMA

Your Body. Your Hope. Your Cure.

**In vivo engineering of CAR-T cells:
A promising new approach to cancer
immunotherapy**

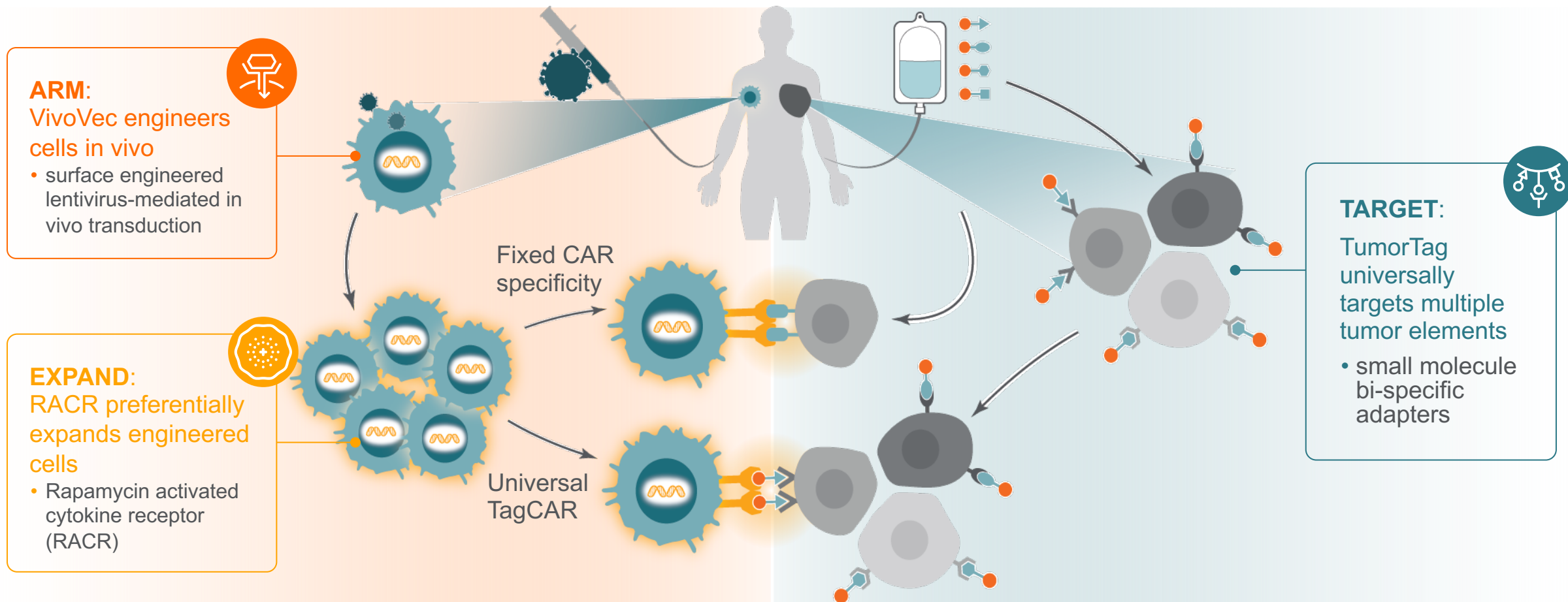
Next Generation CAR and T Cell Therapies, June 2021



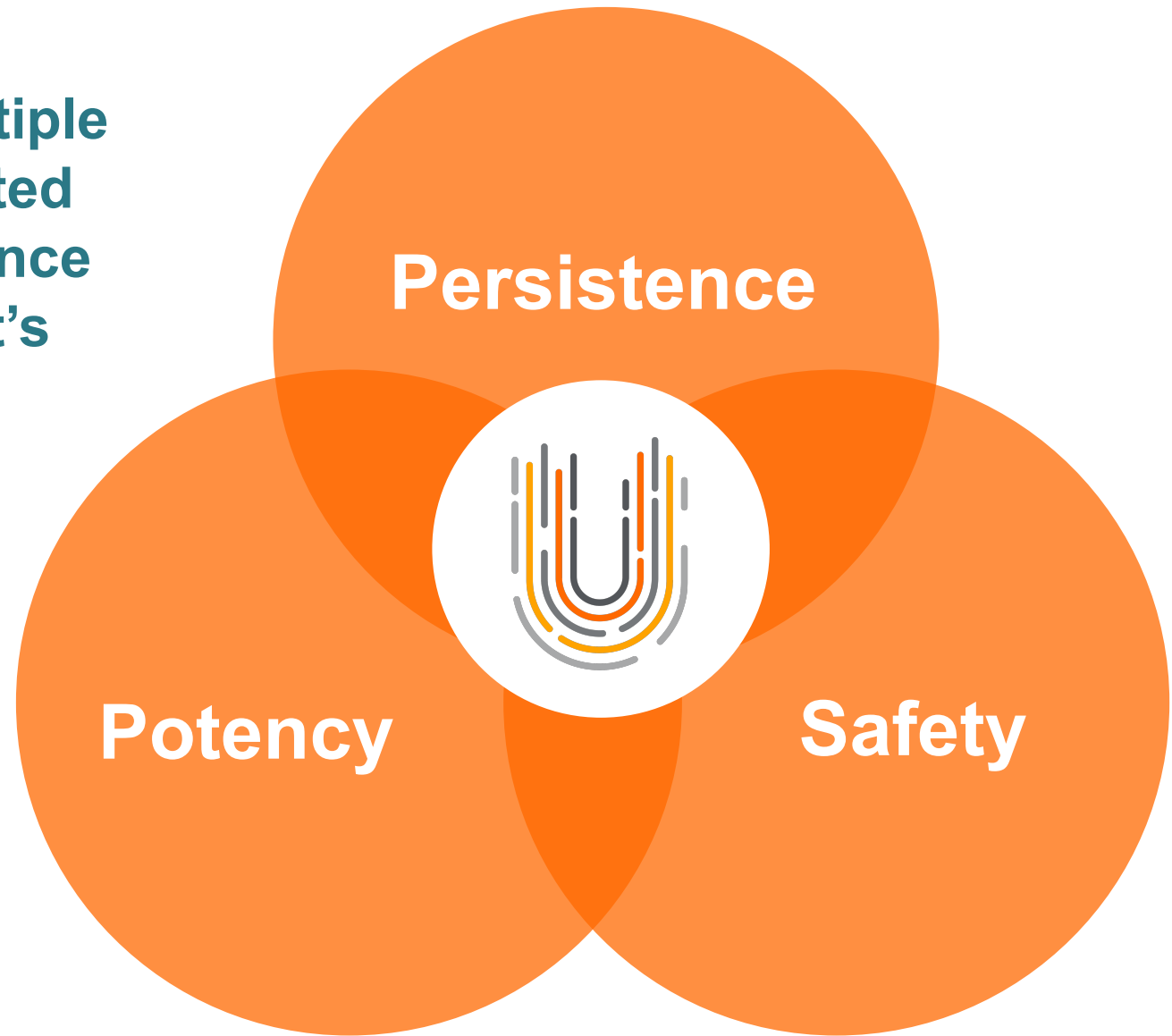
Our mission is to advance and improve access to immunotherapy by retooling the patient's immune system in vivo, freeing them from the burden of cancer in their daily lives



Umoja's integrated immunotherapy platform provides solutions to the challenges in both blood and solid tumor CAR T therapies

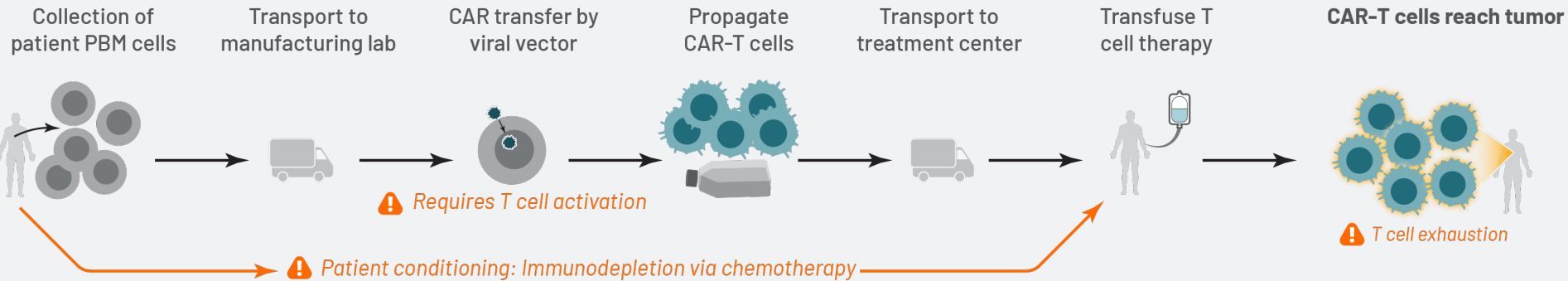


Umoja's platform captures multiple key potency attributes associated with autologous CAR-T cells since it is compatible with the patient's own immune system...



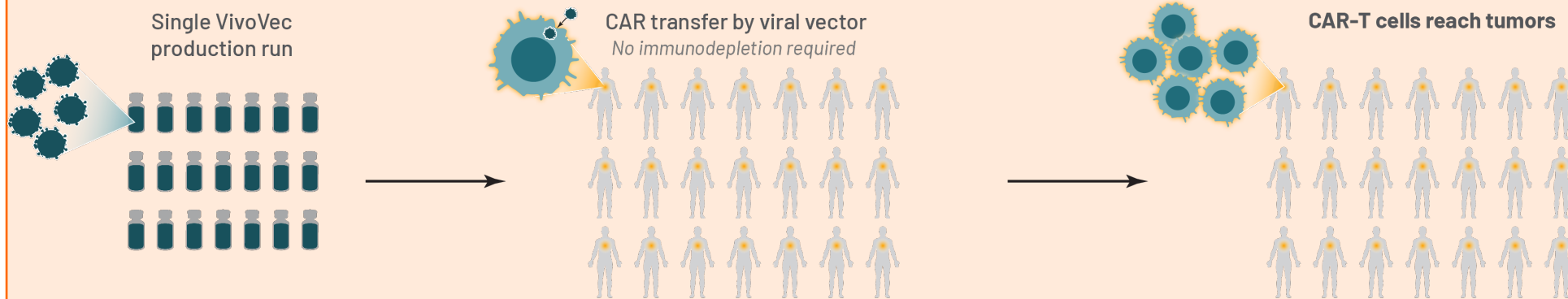
... while expanding convenience and scalability beyond allogeneic products

Autologous or Allogeneic approaches require extensive ex vivo manipulations



Logistically complex, expensive, introduces less-than ideal activation and expansion conditions that may lead to unfavorable T cell health

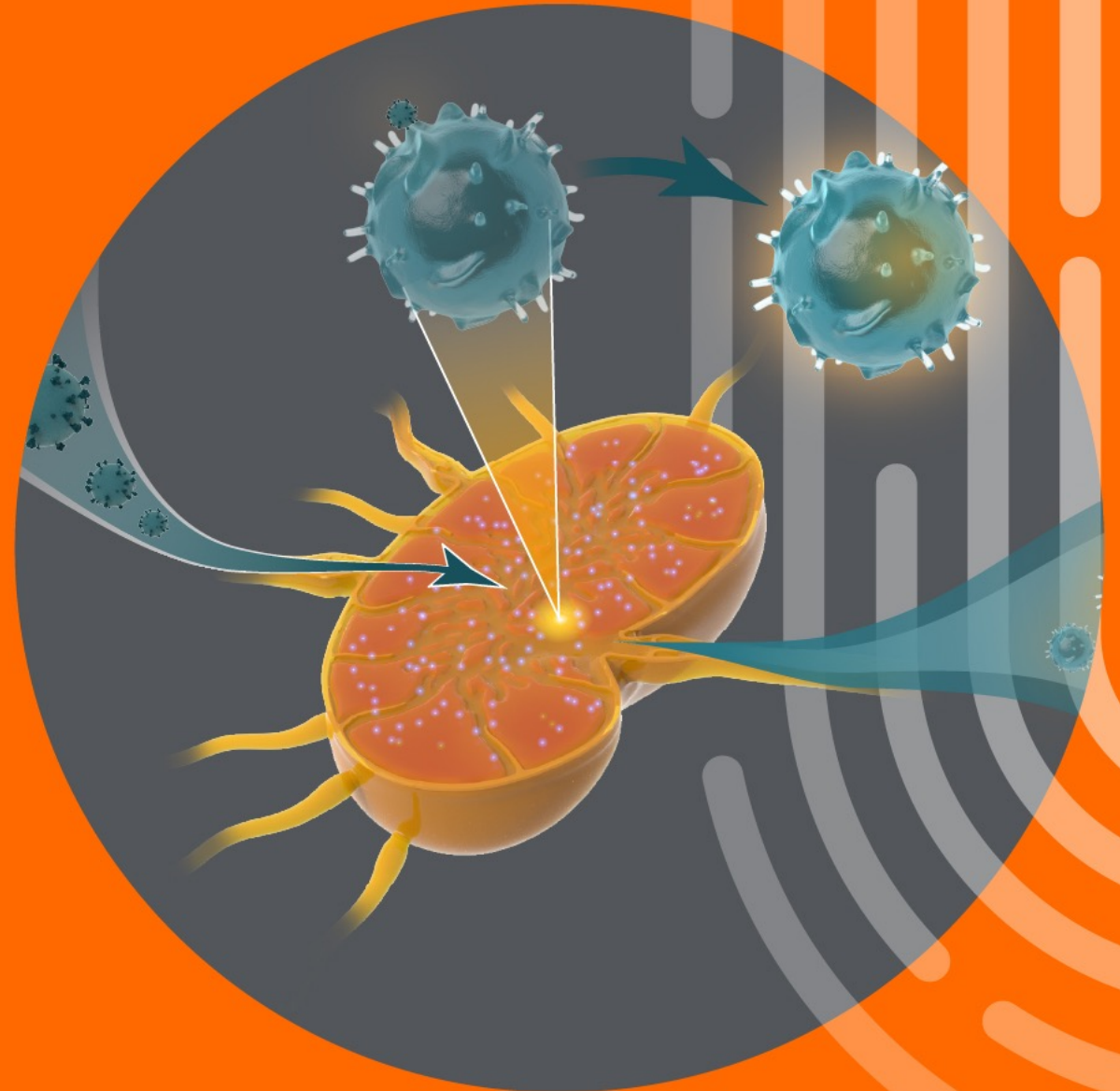
VivoVec — one manufacturing process treats thousands of patients in vivo



One lot treats many patients who “manufacture” their own CAR-T cells with minimal manipulation and with potentially enhanced potency

VivoVec

In vivo CAR T
cell generation



VivoVec platform solves the technical barriers to *in vivo* genetic engineering of T cells

Technical hurdles for *in vivo* genetic engineering

"Condition"/activate T cells for efficient transduction

In vivo expansion of engineered T cells

Avoid exhaustion during expansion

VSV-G enveloped lenti particles are highly immunogenic and rapidly rejected

VivoVec Solutions



Lentivirus surface engineering for efficient T cell activation and transduction *in vivo*



Drug-regulated cytokine receptor in the payload enables *in vivo* stimulation and expansion of transduced cells



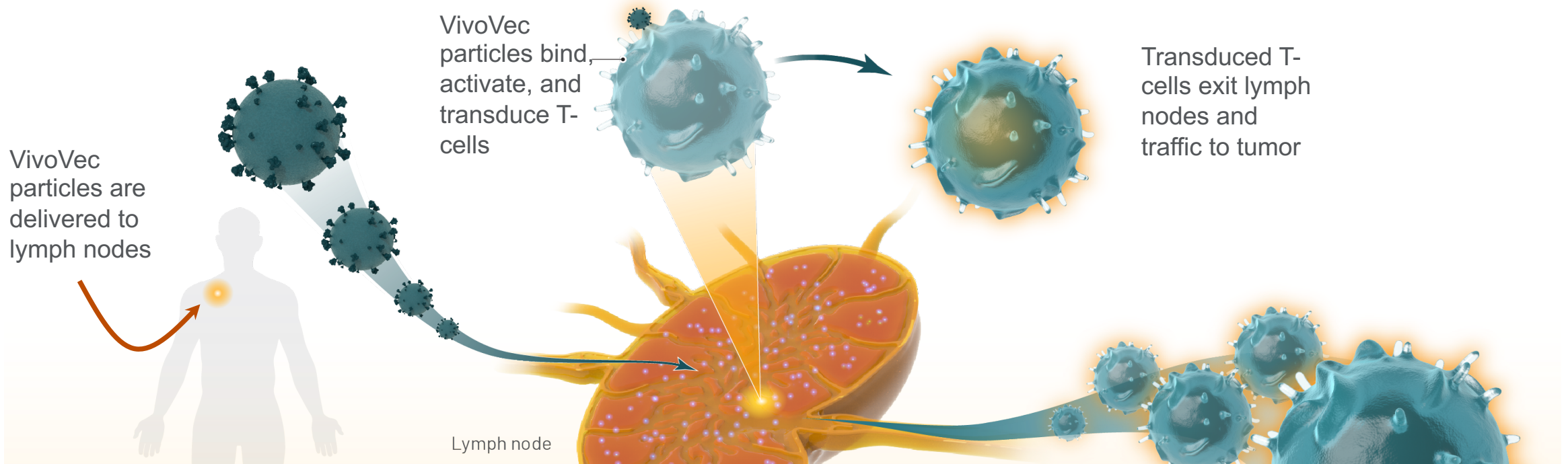
"Natural" expansion process in the body maintains high potency



Cocal glycoprotein reduces potential for immunogenicity (relative to VSV-G)

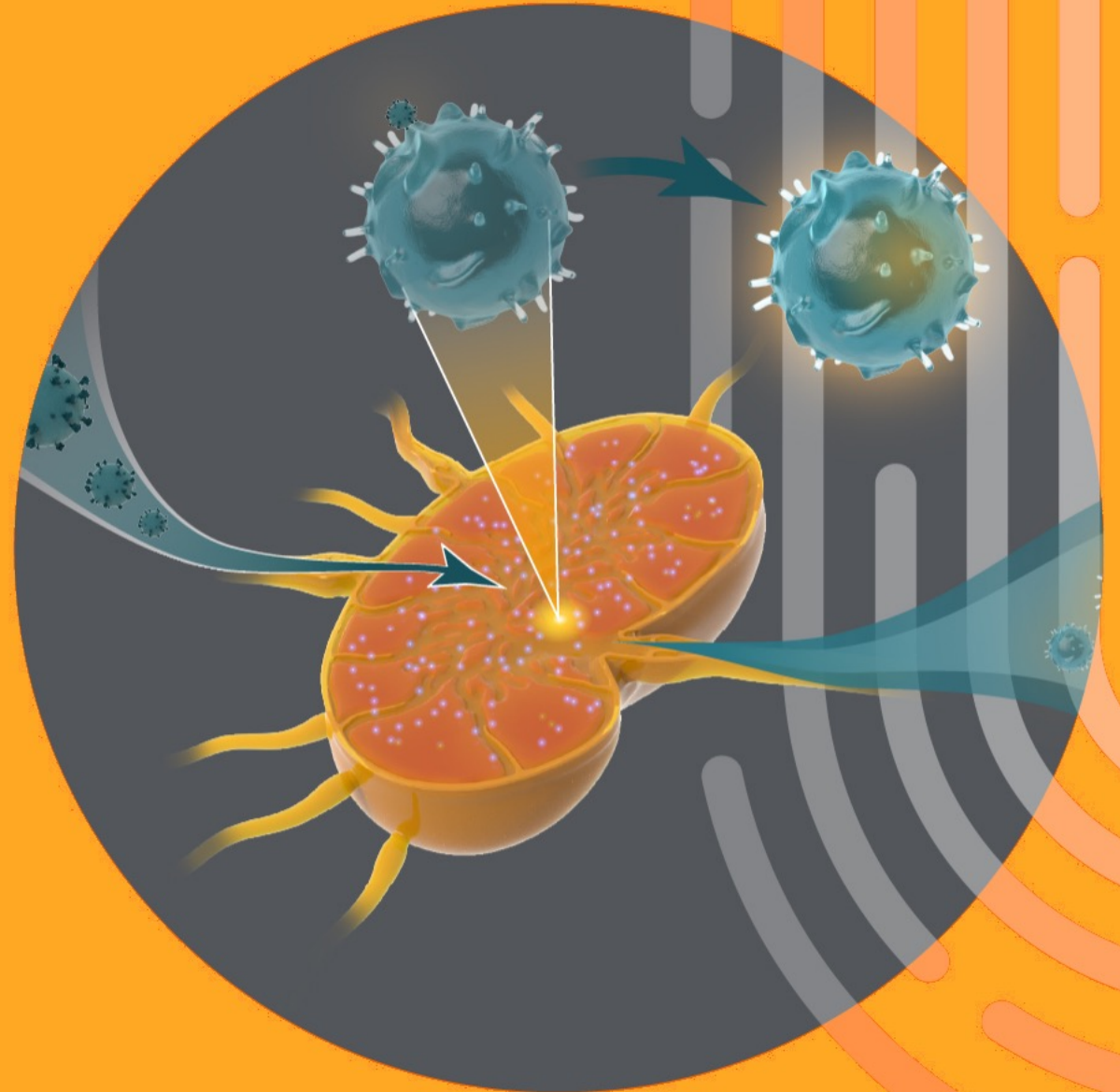
Foundational concept: lymph nodes are nature's optimized T cell "manufactory"

Umoja leverages a deep understanding of the human immune system's physiology for its proprietary approach to *in vivo* T cell engineering



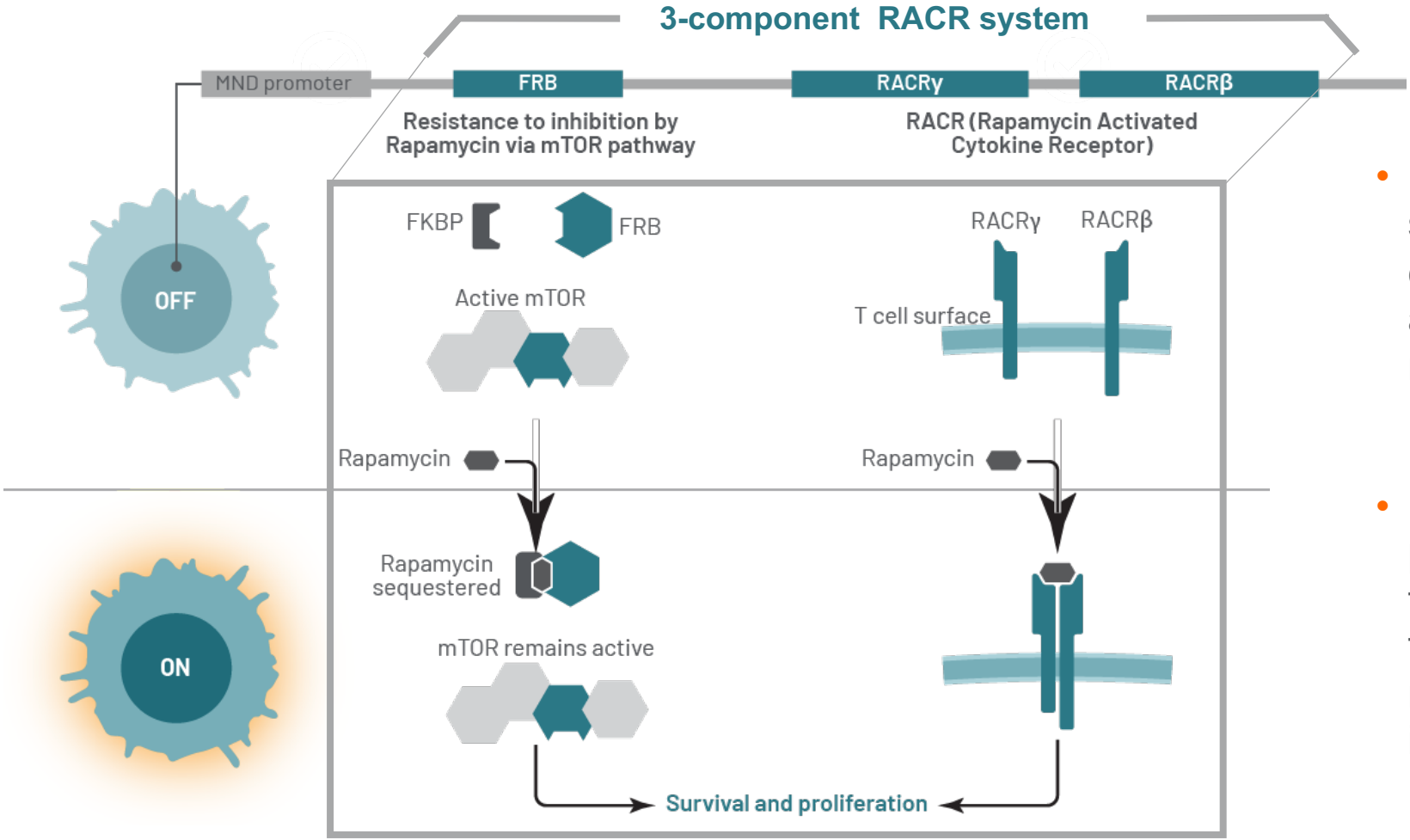
RACR

In vivo CAR T
cell expansion



RACR: Rapamycin Activated Cytokine Receptor provides control over expansion

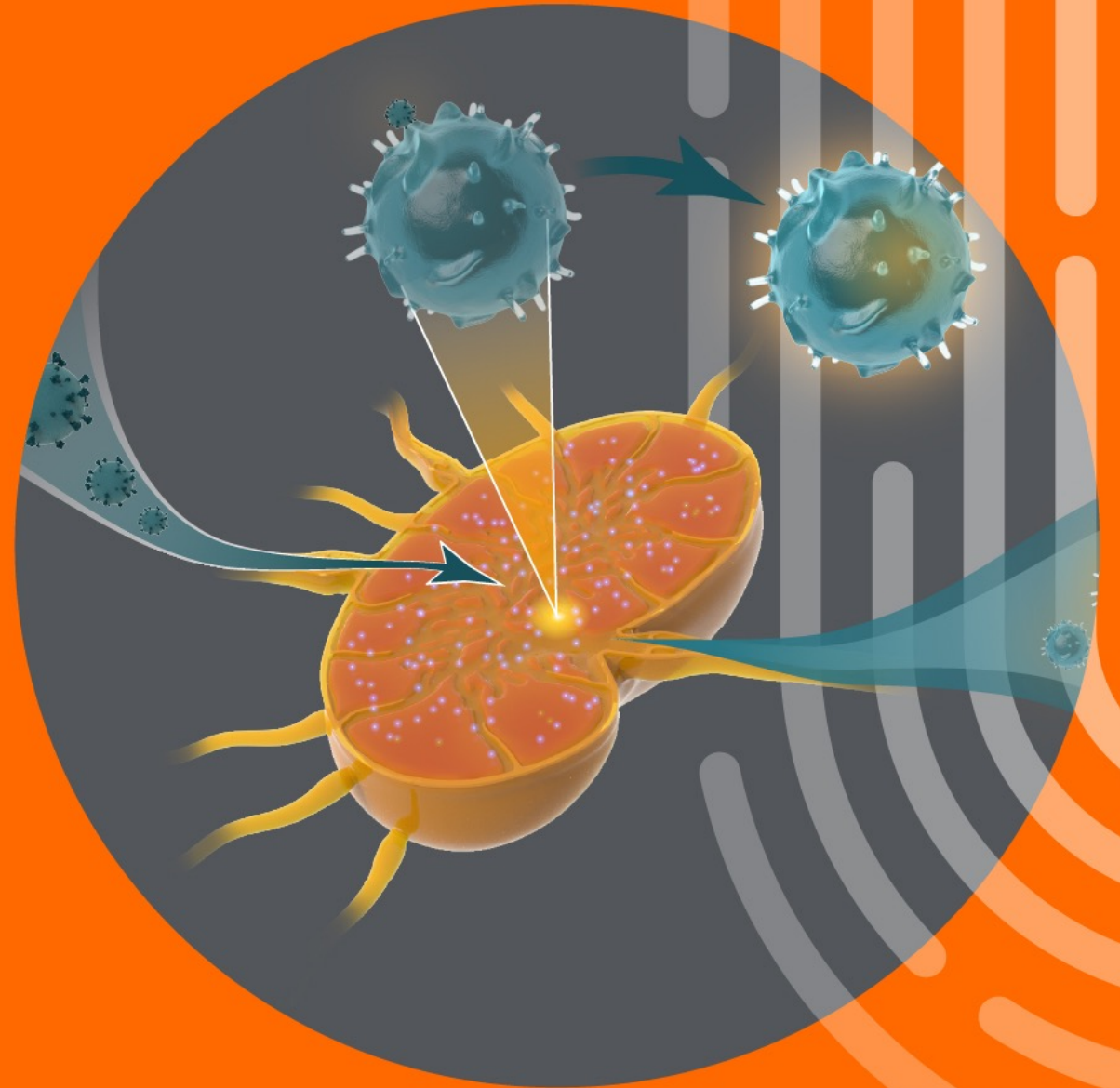
RACR: In vivo CAR T cell expansion



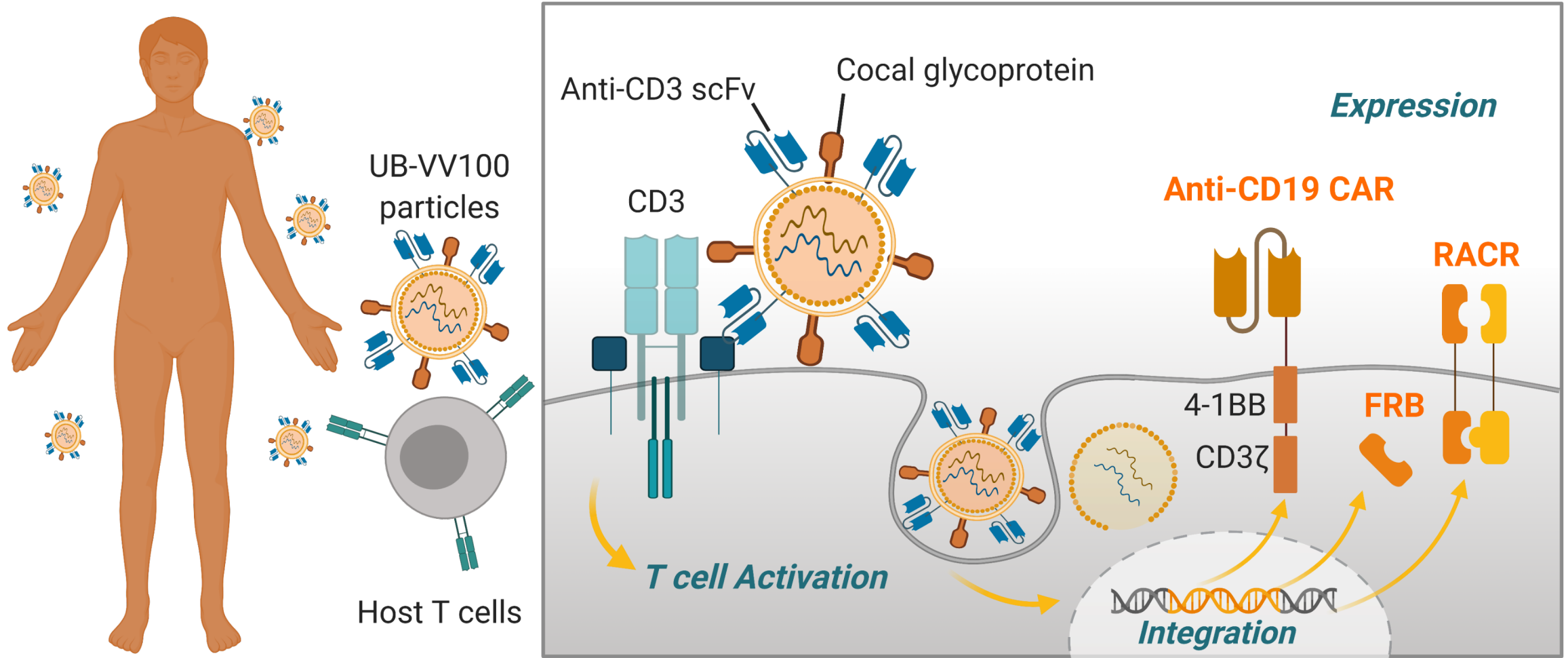
- Rapamycin activates the RACR system which replicates common γ chain cytokine activating STAT5 signaling for robust proliferation and survival
- Naked intracellular FRB domain provides rapamycin resistance to transduced cells while non transduced T and B cells are repressed through mTOR inhibition

UB-VV100

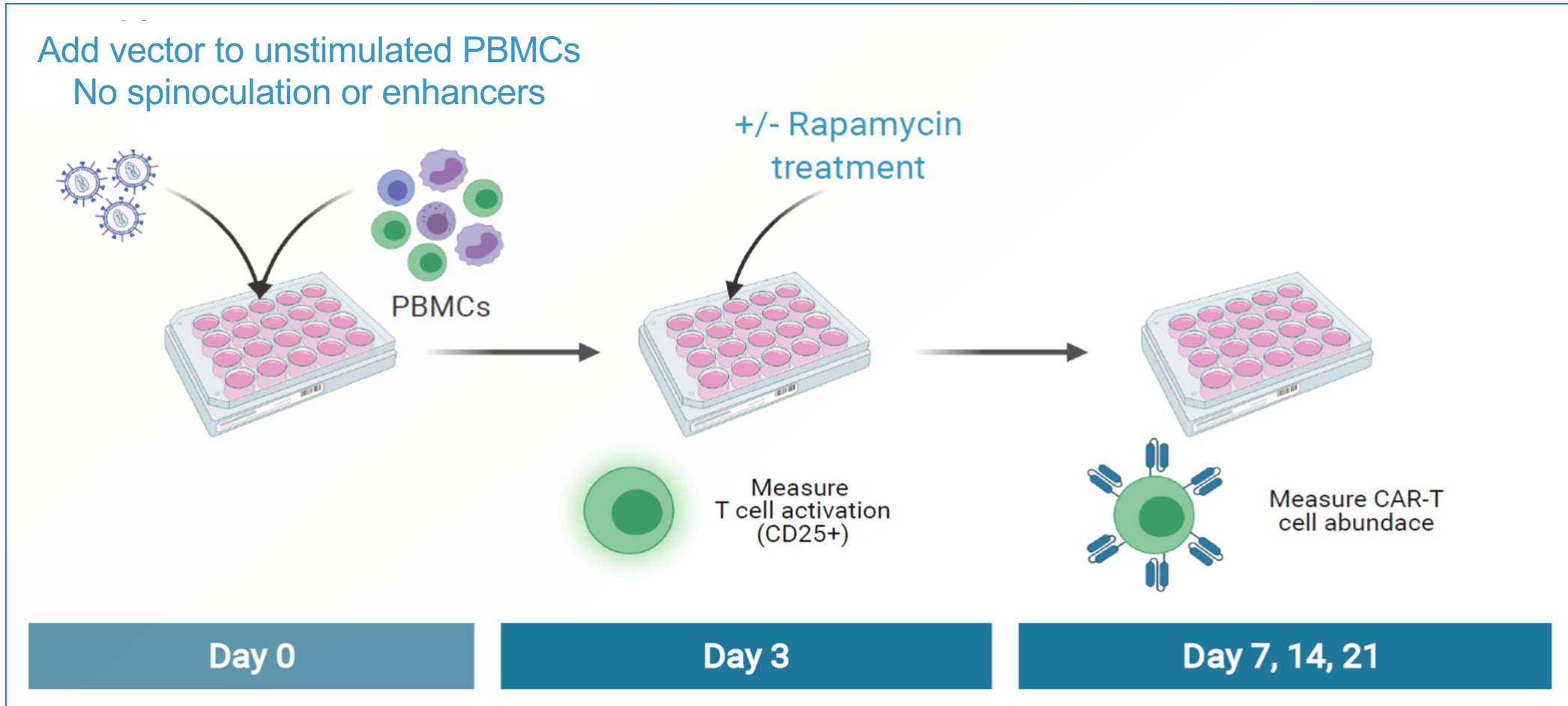
In vivo CD19 CAR T
generation
for the treatment of B
cell malignancies



UB-VV100 is designed to harnesses the body's own immune system to manufacture CD19 CAR T cells in vivo



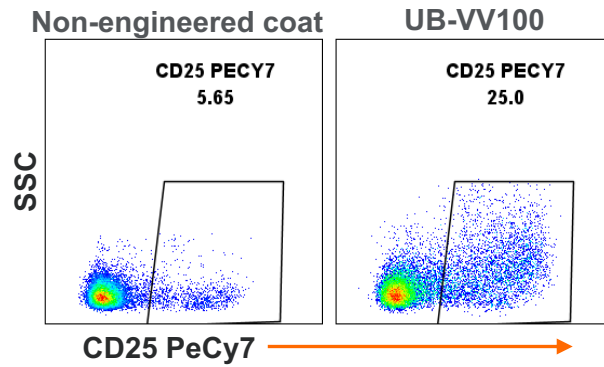
Methodology for testing UB-VV100 transduction efficiency in vitro



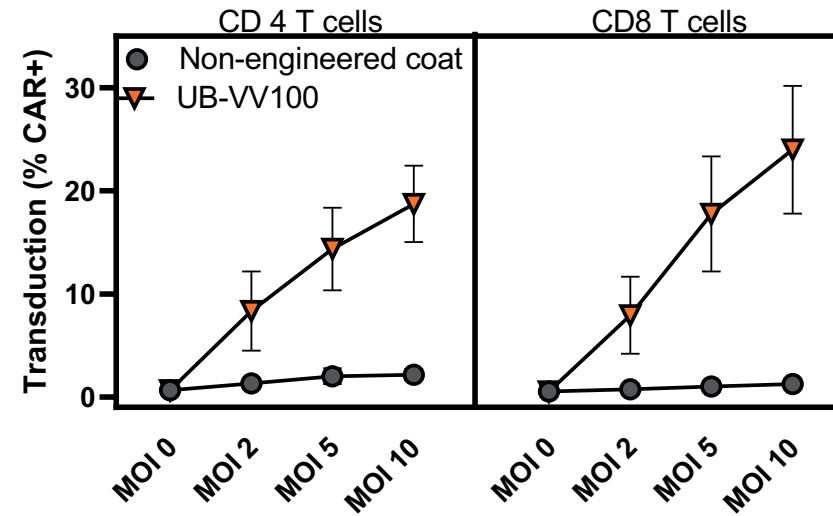
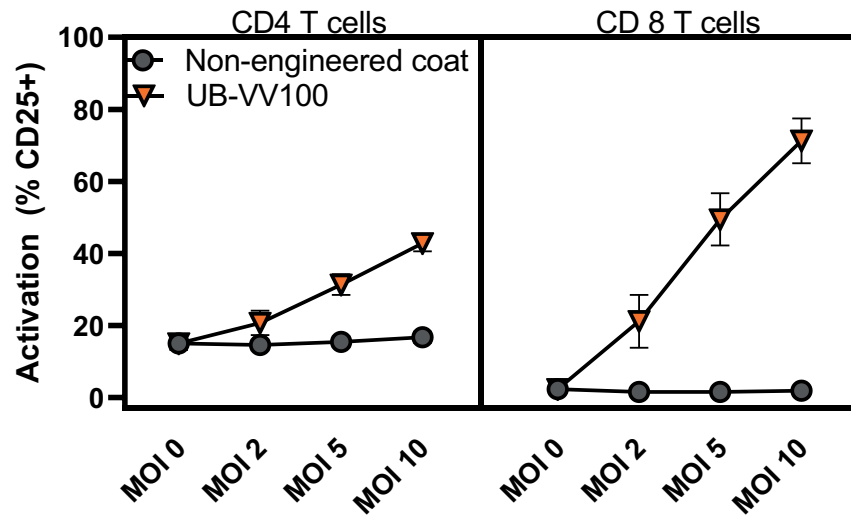
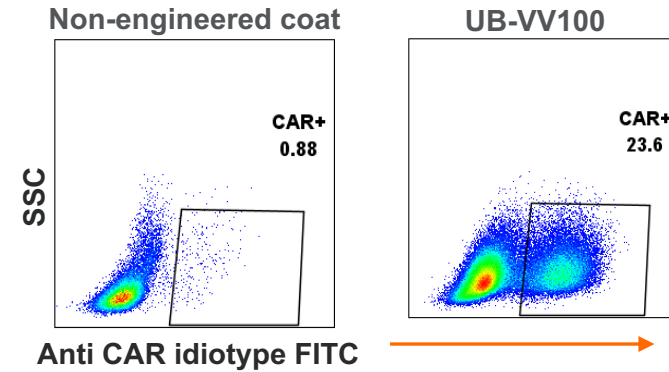
Anti-CD3 + Cocal surface engineering facilitates activation and transduction of T cells

Day 3 Activation

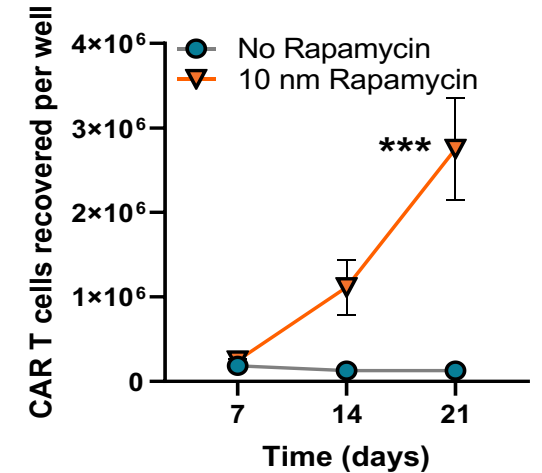
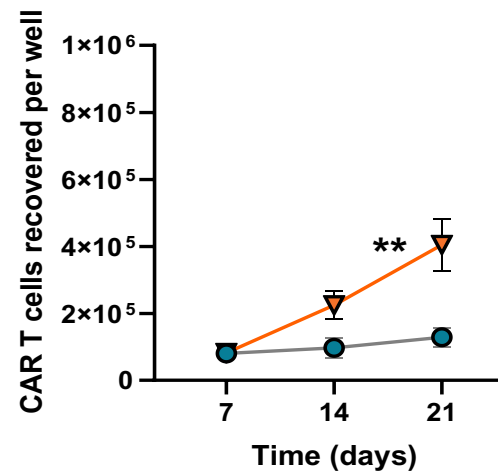
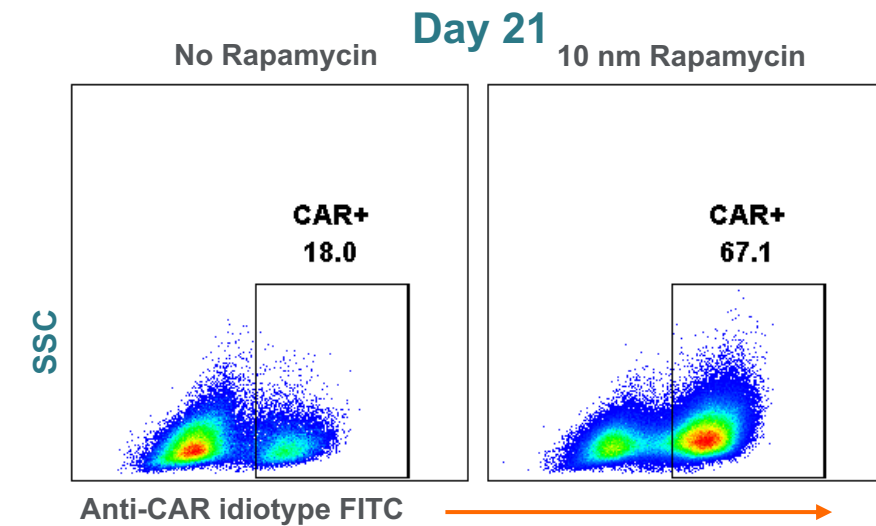
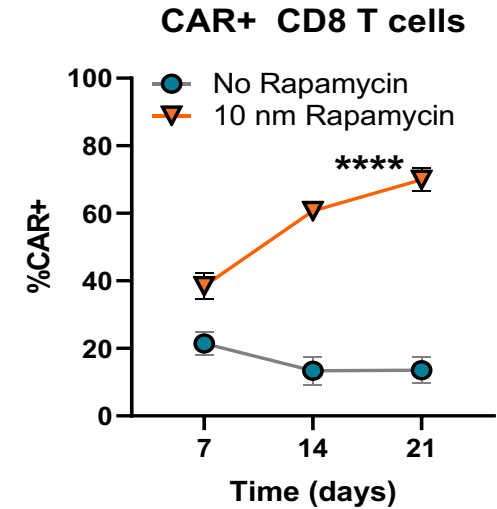
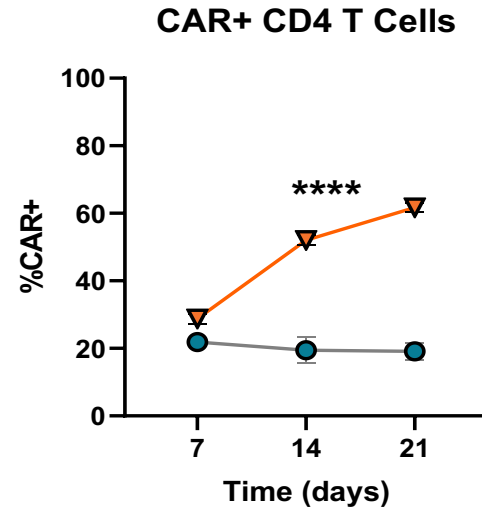
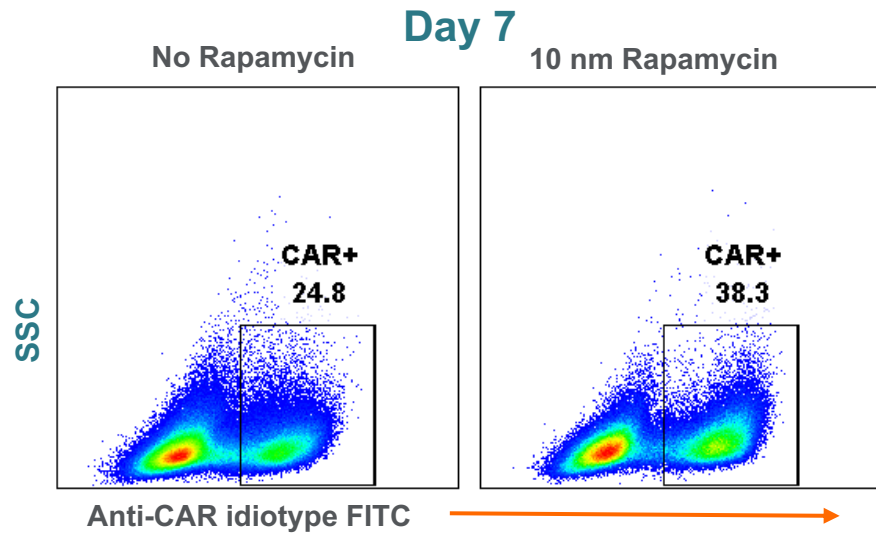
N= 3 PBMC donors



Day 7 Transduction

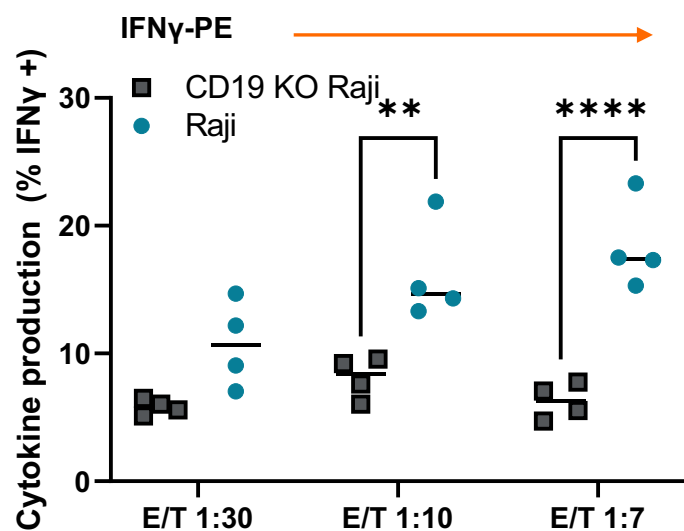
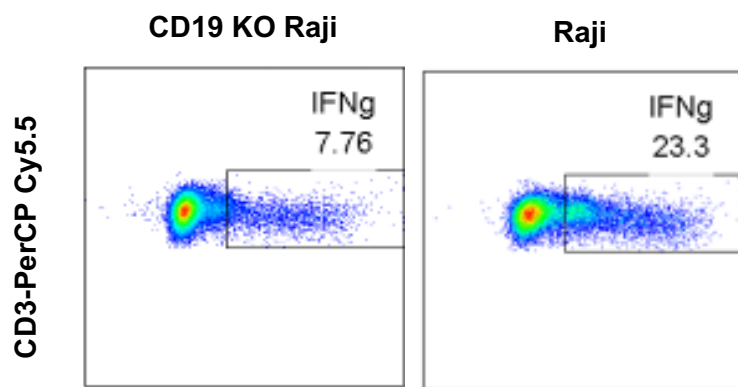


RACR engine drives enrichment and proliferation of CAR T cells in vitro

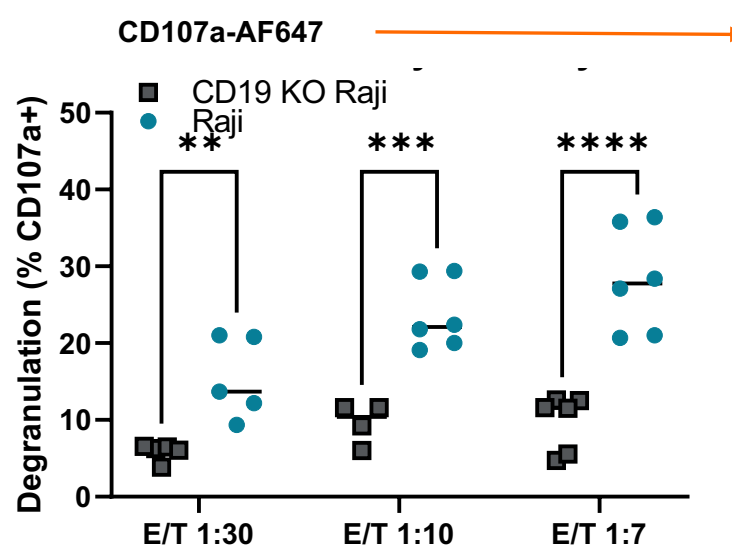
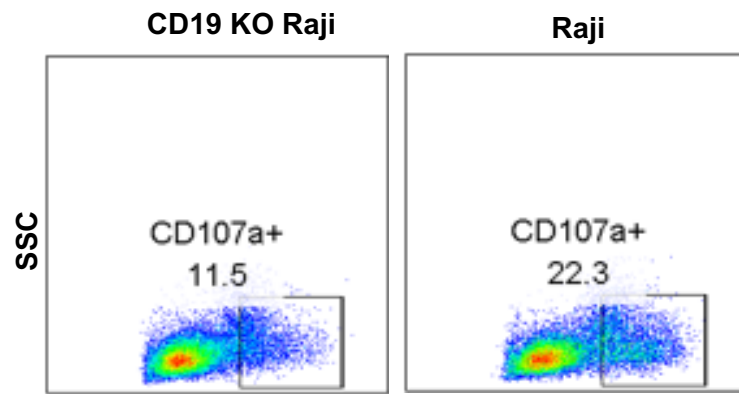


UB-VV100-transduced CAR T cells display CD19-dependent cytotoxicity against Raji cells in vitro

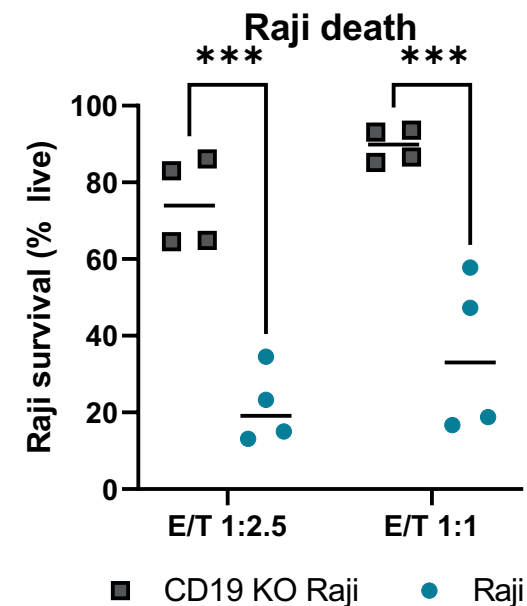
CD8 CAR T cell intracellular IFN γ



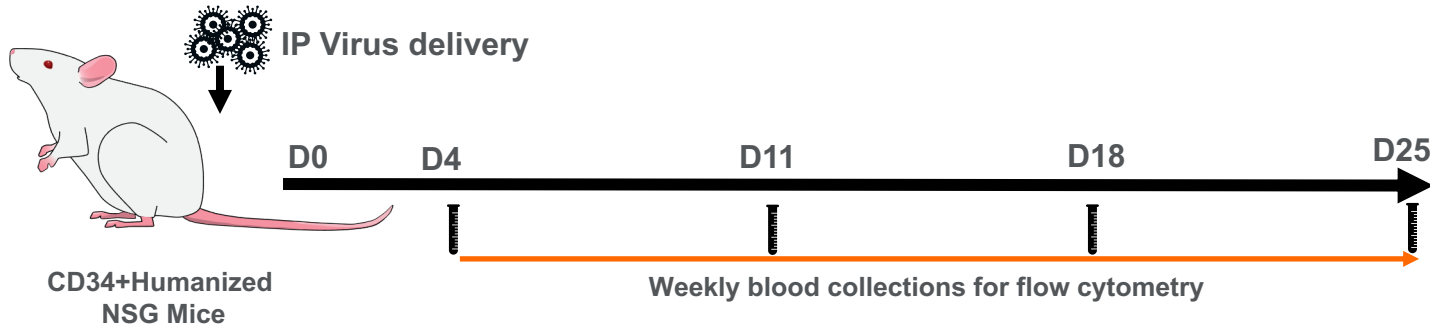
CD8 CAR T cell degranulation



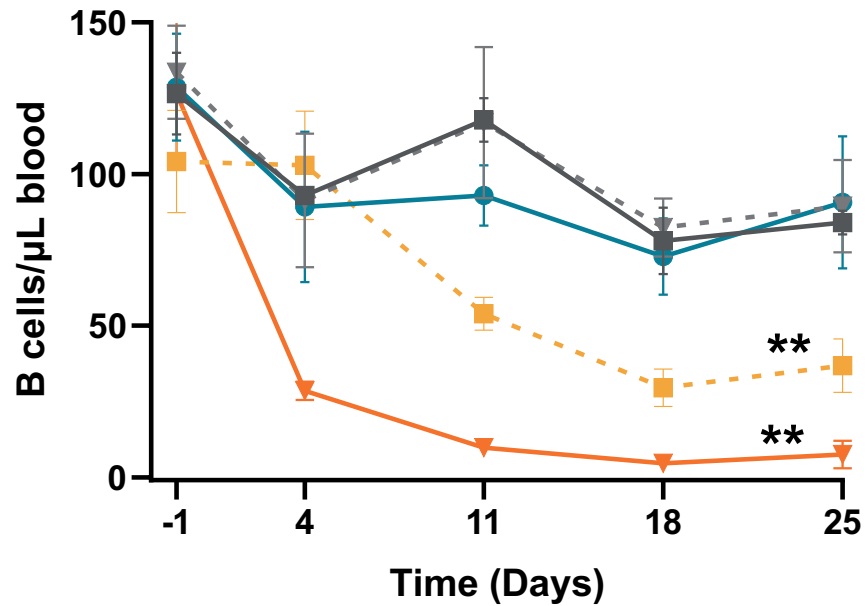
Target Killing



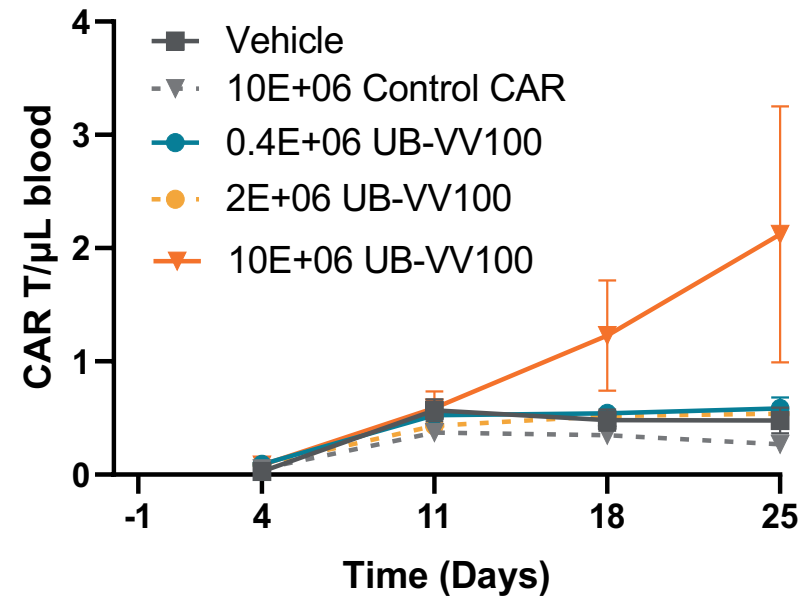
UB-VV100 injection into CD34-humanized mice results in dose-dependent B cell depletion



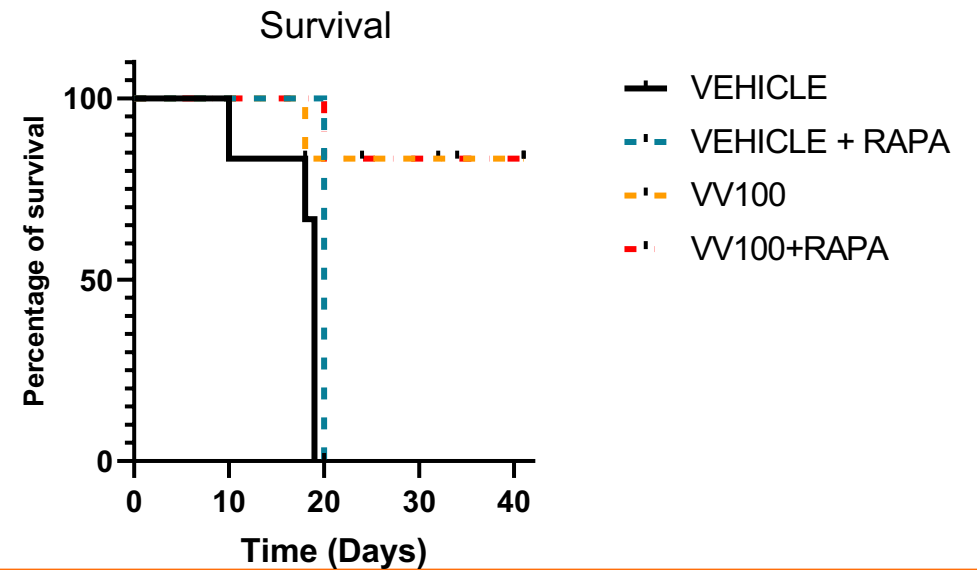
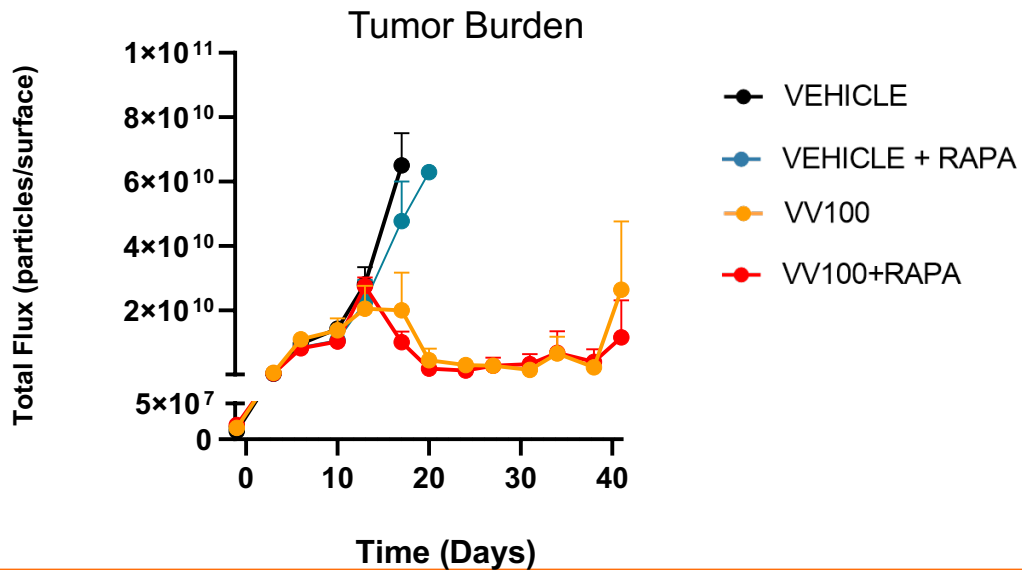
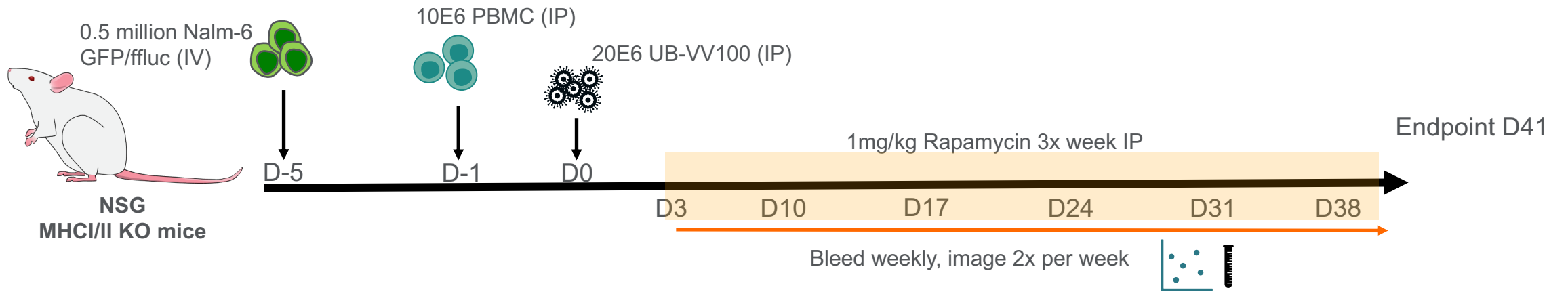
Circulating B cells



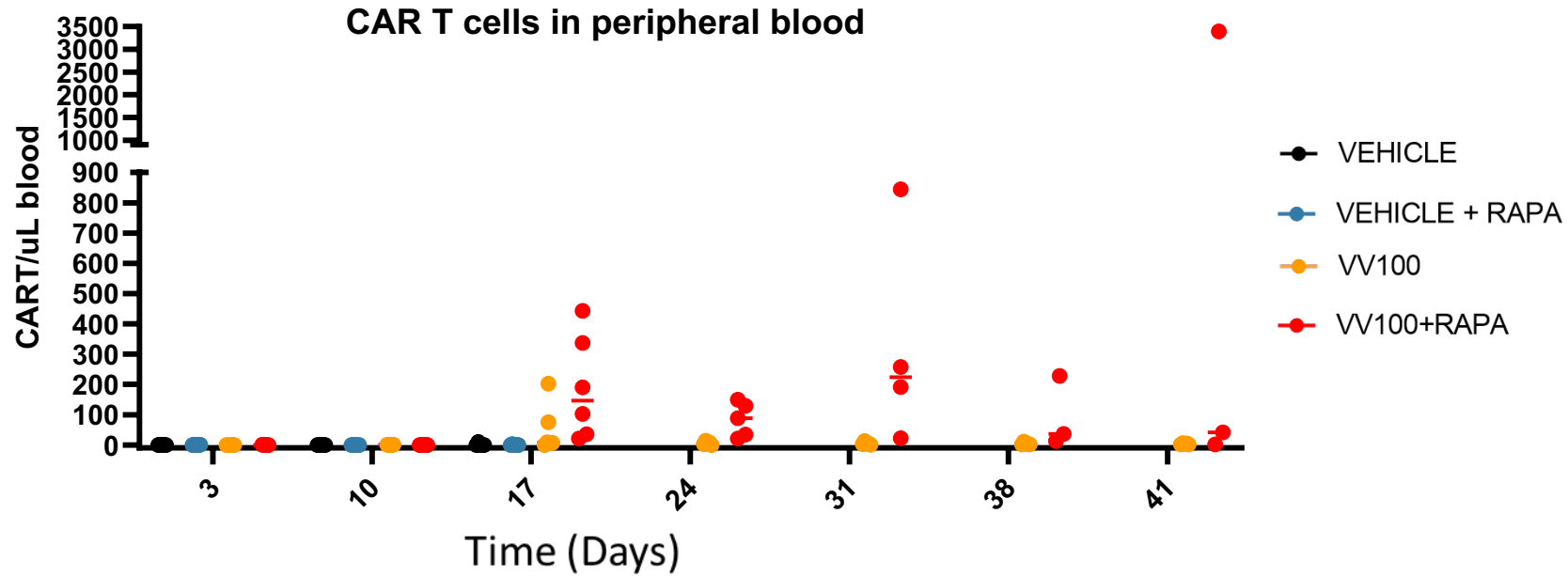
Circulating CAR T cells



UB-VV100 prolongs survival and slows tumor progression in a NALM6 systemic tumor model



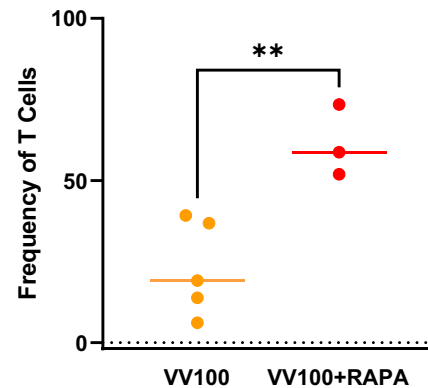
Rapamycin treatment enhances CAR T cell expansion in blood, bone marrow, and spleen



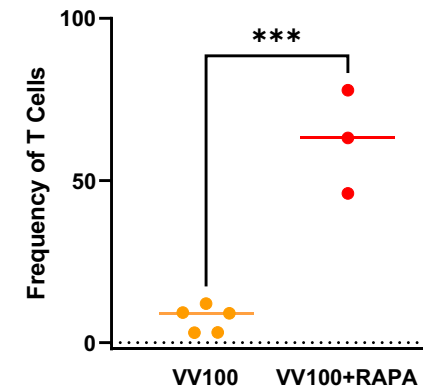
CAR T cells peak at day 17 in mice not treated with rapamycin, while they continue to expand in mice treated with rapamycin

At Day 41 bone marrow and spleen show enrichment for CAR T cells in the rapamycin treatment group

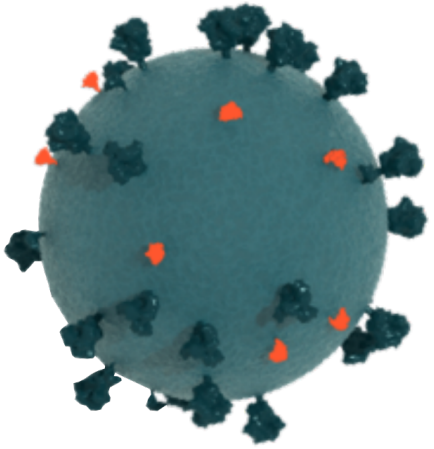
CAR T cells in bone marrow



CAR T cells in spleen



Our preliminary data demonstrates that UB-VV100 can:



ARM T cells in vitro and in vivo using only its surface engineering and no other additives or stimulants



EXPAND transduced cells in vitro and in vivo using rapamycin to engage the RACR system



TARGET and destroy normal and malignant B cells in vitro and in vivo



Thank you

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