



SENTI BIO

Logic-gated gene circuits expand the range of tumor-associated antigens addressable by CAR-NK and -T cell therapies

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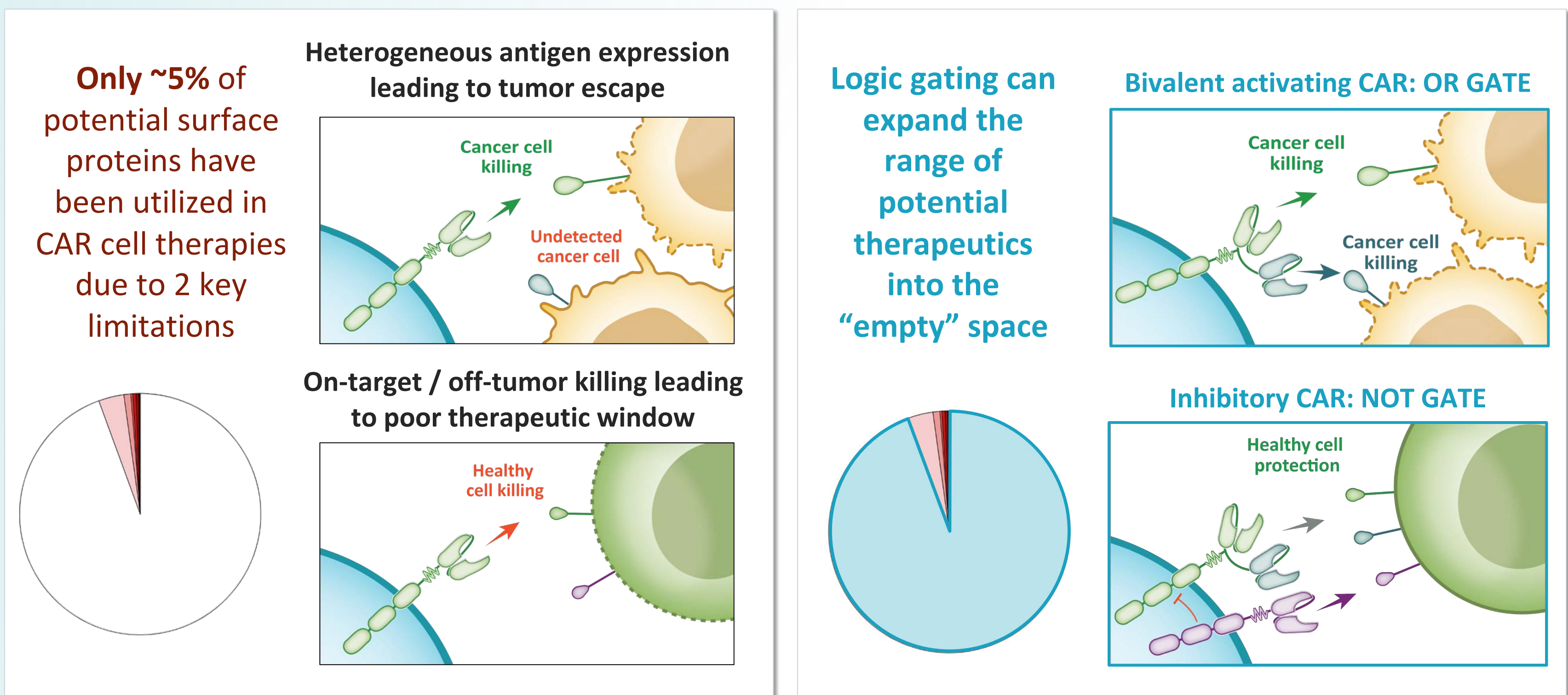
²GeneFab Alameda, CA



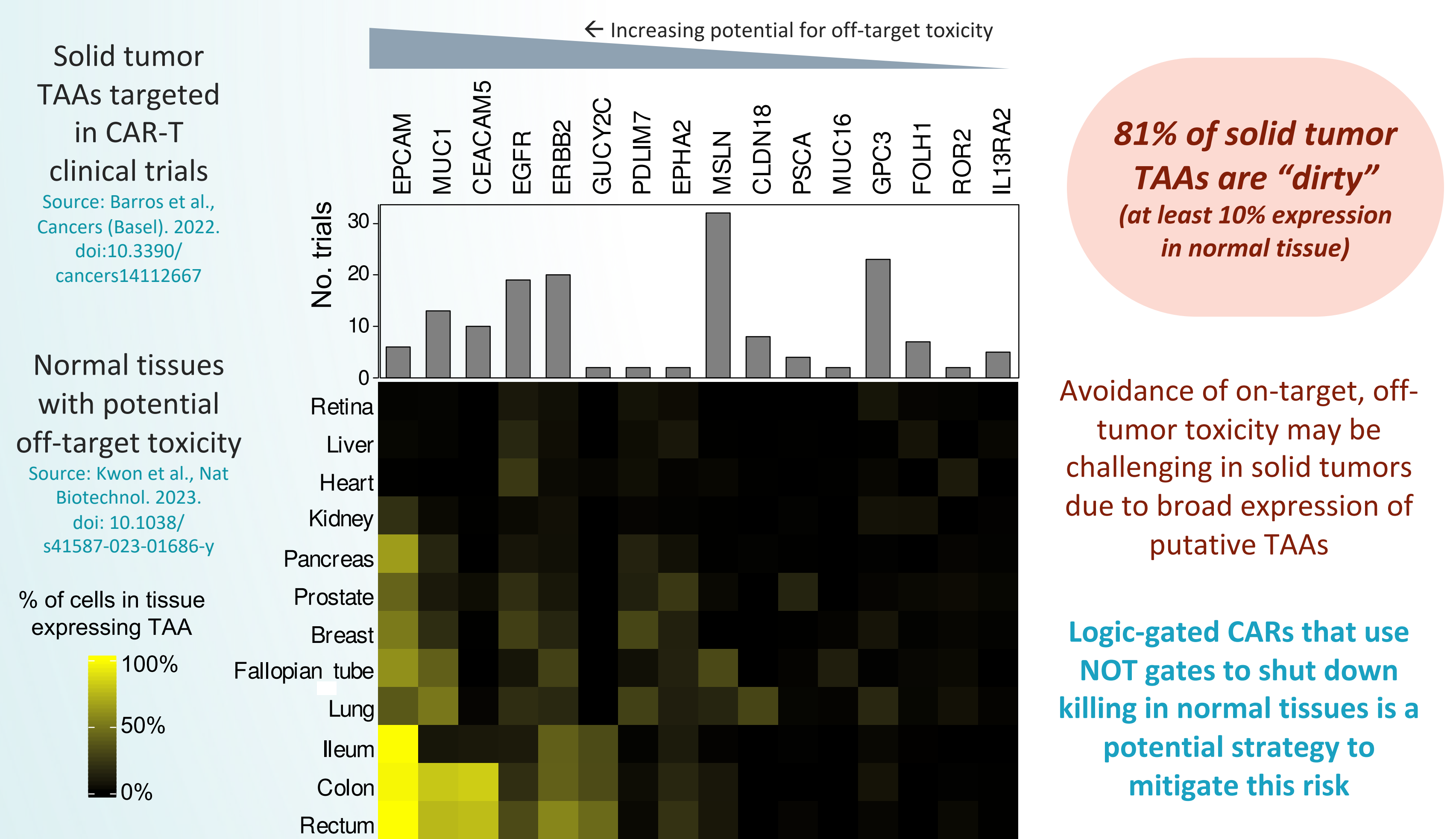
GENEFAB

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Abstract
#257

Logic gating broadens tumors addressable by CAR cell therapies

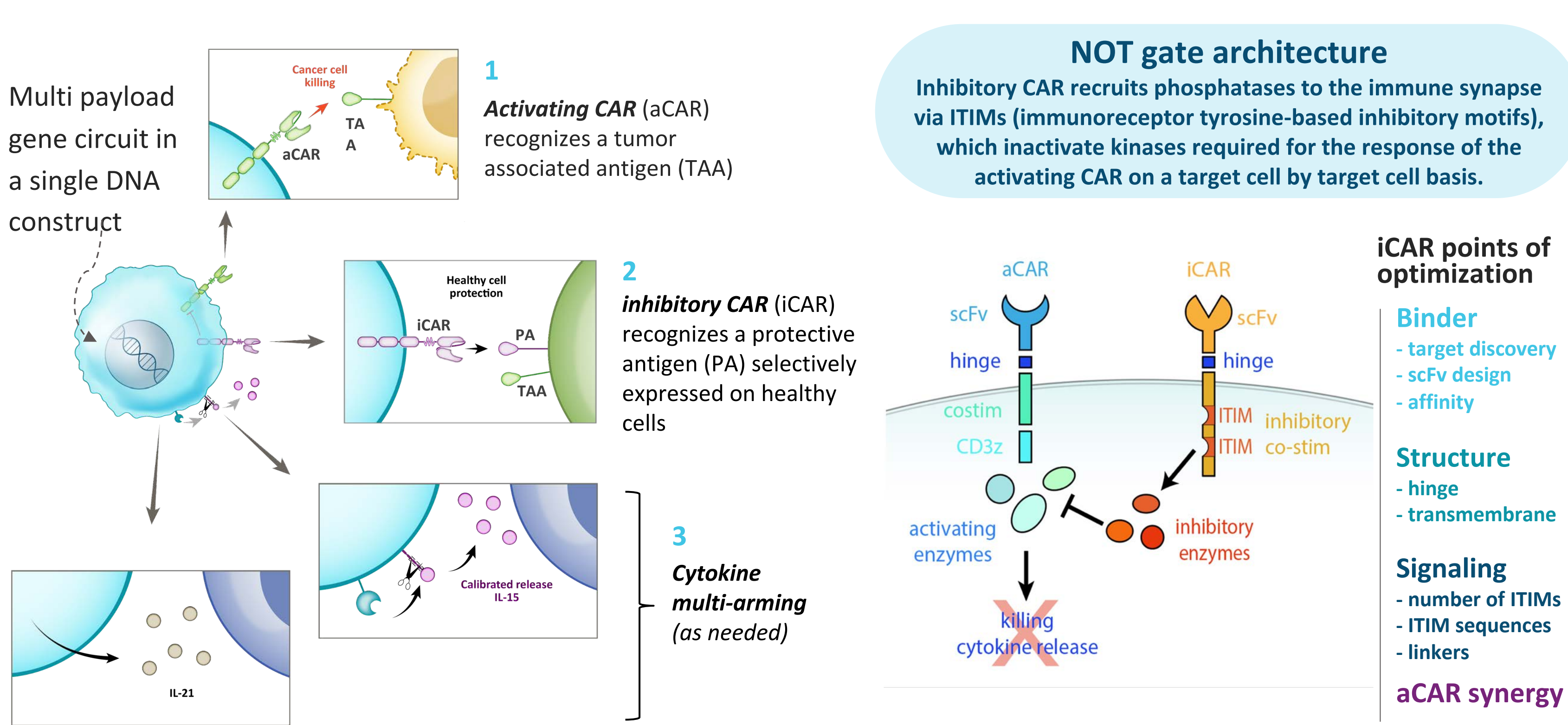


Many tumor-associated antigens are expressed on normal tissues

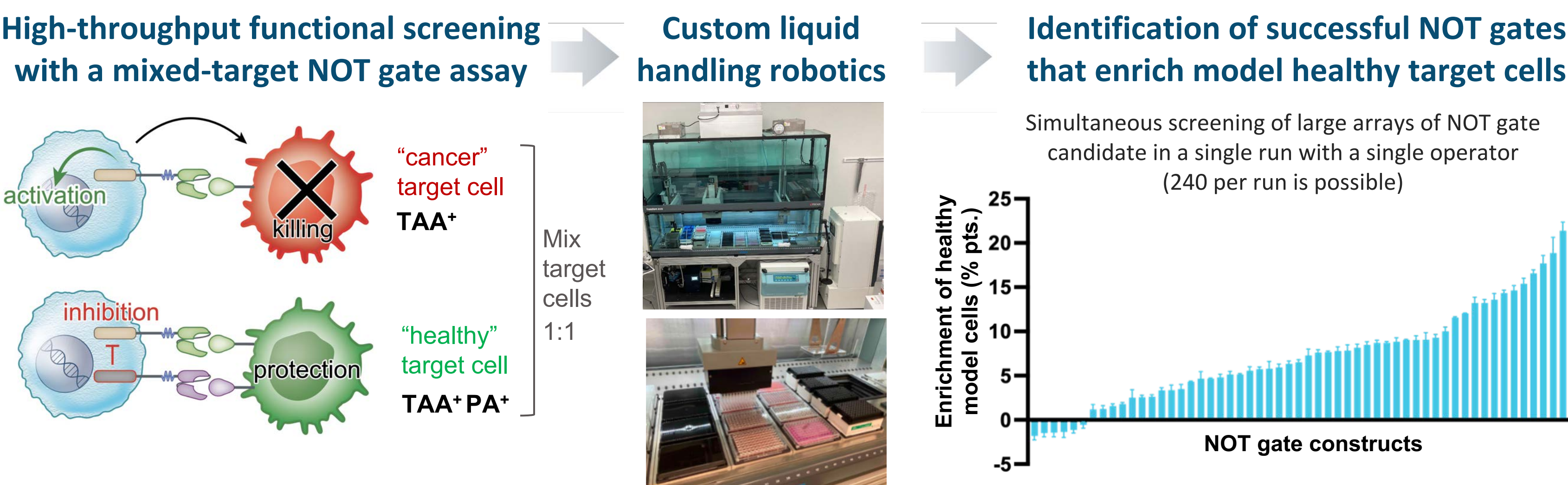


Program	Target	Indications	Discovery	IND enabling	Phase 1	Gene Circuits
SENTI-202	CD33 and/or FLT3	AML, MDS and other blood cancers	2H 2023 IND			- Multi-Arming: designed for enhanced efficacy - crIL-15: activate neighboring immune cells and boost NK activity/function - OR GATE: bivalent activation - NOT GATE selectivity: healthy cell protection
SENTI-401	CEA	CRC and other solid tumors				- Multi-Arming: designed for enhanced efficacy - crIL-15: activate neighboring immune cells and boost NK activity/function - NOT GATE selectivity: healthy cell protection - IL-21: sustained anti-tumor function

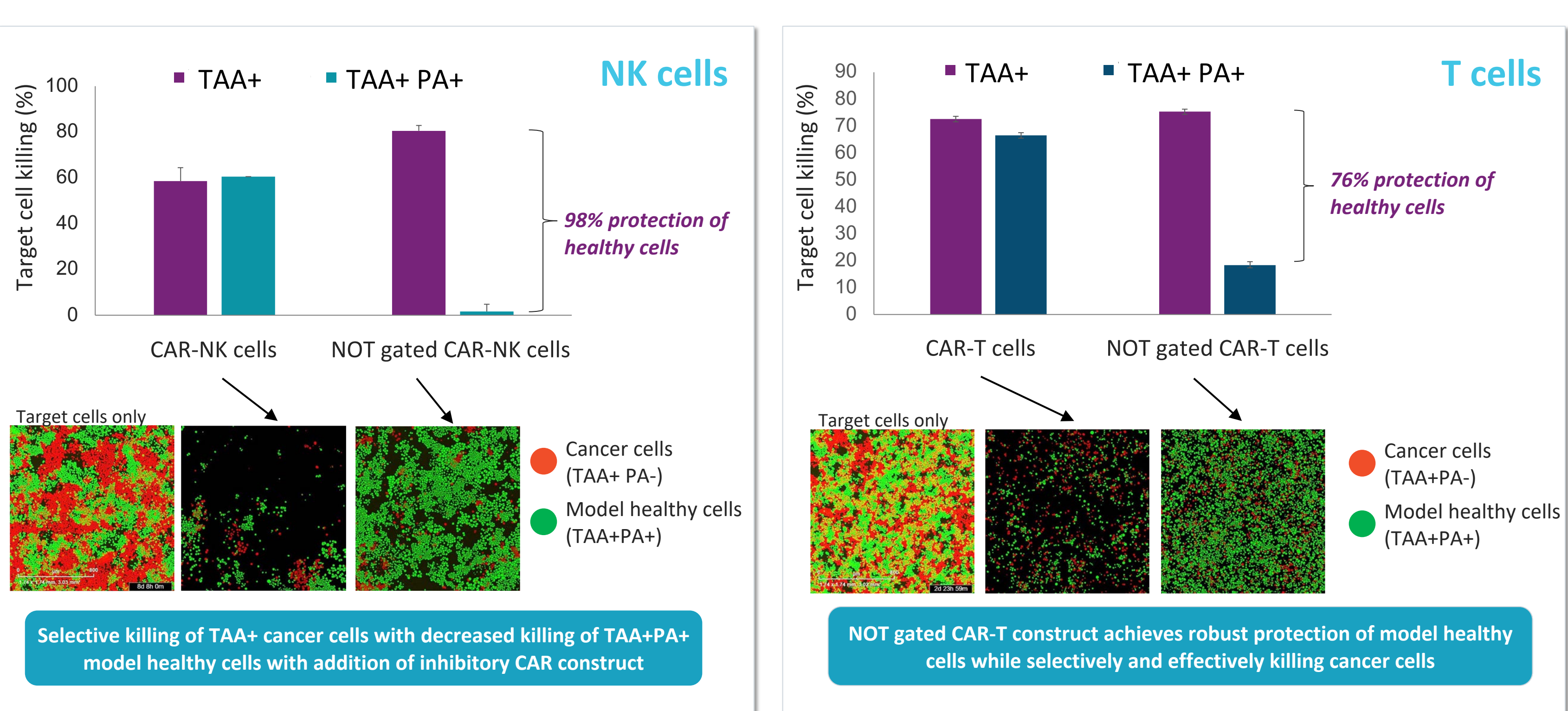
NOT gate design leverages a two-receptor system with armoring



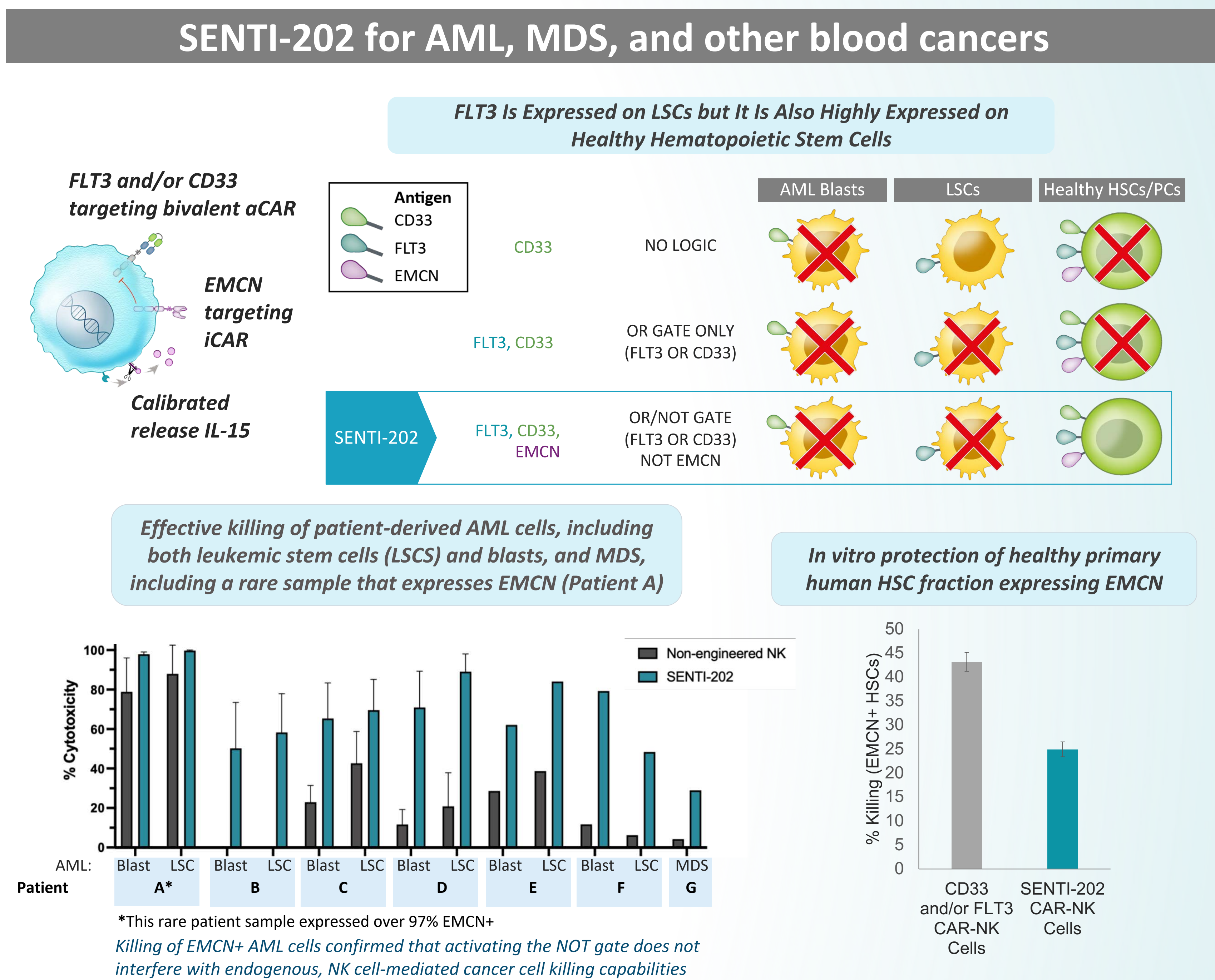
Optimization of NOT gates using an automated HTS system



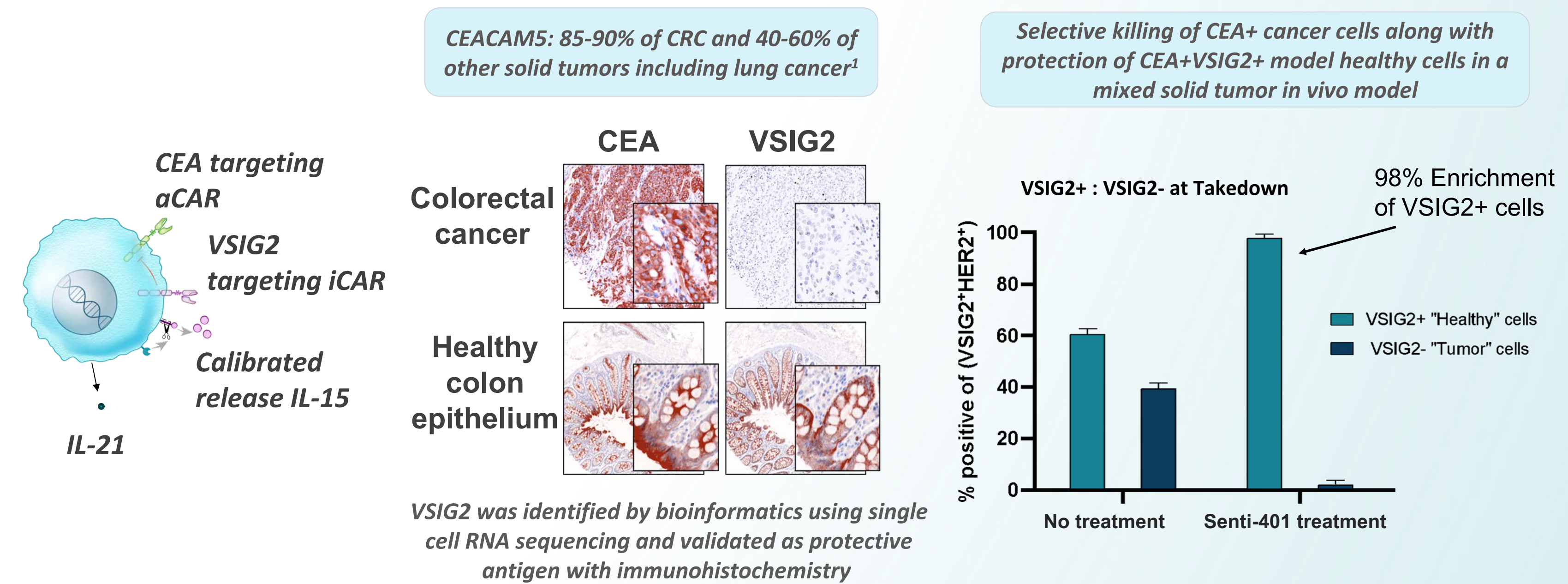
Robust NOT gated CAR circuits are validated in both NK and T cells



Senti products deploy NOT gates for selective tumor killing



SENTI-401 for CRC and other solid tumors



Take aways

Many tumor-associated antigens are also expressed on healthy cells, risking on-target/off-tumor toxicity.

Logic gating will help design cell therapies that address more tumor types by increasing the therapeutic window.

Senti's NOT gate (used in SENTI-202 and -401) protects healthy cells in vitro and in vivo without interfering with cancer killing and works in T or NK cells.