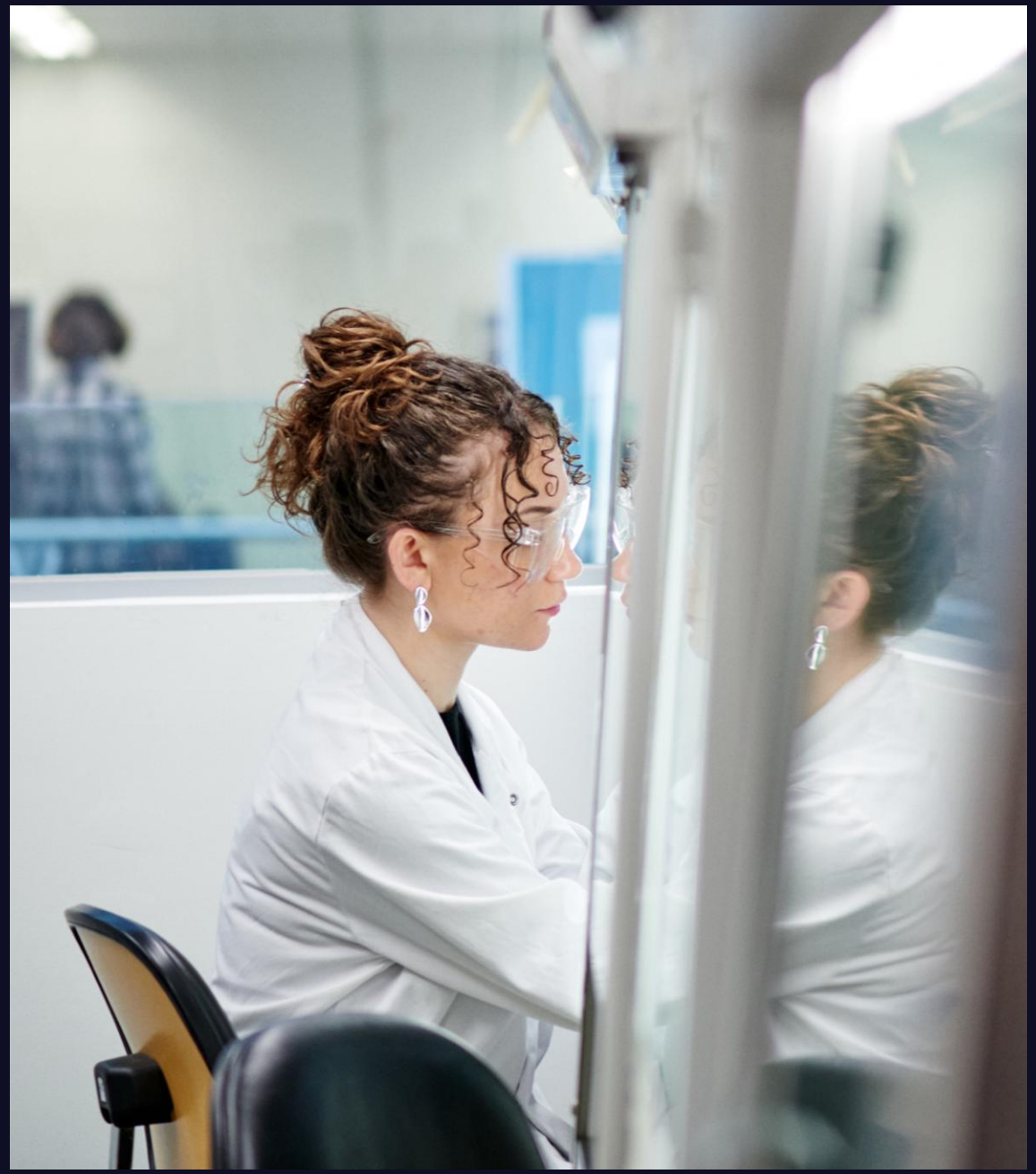


CANCER RESEARCH HORIZONS

Enhanced cell therapy cytotoxicity

Platform technology

Available for licensing and collaboration

FURTHER FASTER TOGETHER
We are beating cancer

Opportunity overview

Novel platform technology
- L-type voltage gated calcium channel (Ca_V) GOF/agonism to enhance immune cells cytotoxicity
- Platform potential for augmenting efficacy of adoptive cell therapies

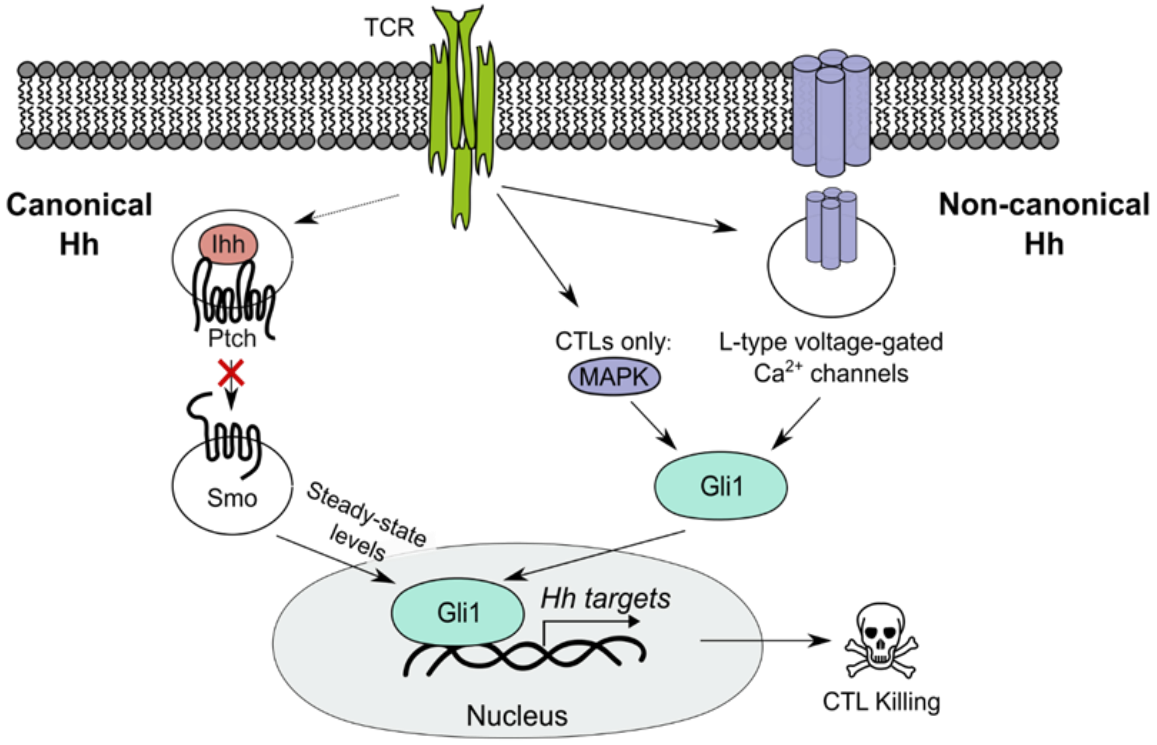
Broad applicability to existing technology
- Directly addresses the cytotoxic potency limitations of cell immunotherapies in development
- Compatible add-in solution for CAR-T, TIL, CAR-NK, and NK cell-based approaches

Ready to partner
- Priority GB patent application filed in March 2022 with broad claim coverage
- Available either for licensing or collaboration with the lead investigator

Background

Increasing T lymphocyte non-canonical hedgehog signalling via heightened CaV channel activity enhances the cytotoxic performance of cell therapies

- Cytotoxic T lymphocytes (CTLs) and Natural Killer (NK) cells are critical to the anti-tumour immune response. Engineering CTLs and NK cells to express chimeric antigen receptors (CARs) recognising the tumour directly has revolutionised cellular therapy.
- Tumour antigen recognition by T cell receptors (TCRs) triggers intracellular cascades, including both canonical and non-canonical hedgehog (Hh) signalling, which is critical for effective killing of tumour cells.
- The non-canonical Hh pathway is Ca^{2+}-dependent and stimulated by activation of L-type voltage gated calcium channels (Ca_V).
- Enhancing Ca_V activity should increase the cytotoxic performance in allogenic and autologous cell therapies.



Technical summary

A proprietary method to enhance tumour cell killing through gain-of-function mutation of Cav1.4 within cytotoxic T-lymphocytes.

- Compatible with CTL populations used in existing adoptive therapies, including CD8+ T-cells, NK, CAR-T and CAR-NK (including “off-the-shelf” CAR-NKs)
- Has a controlled impact on T cell behaviour as it modulates only one specific aspect of T-cell phenotype

Further data available under CDA (publication pending)

- Treatment of T cells, NK cells, gamma delta T cells with Cav1 agonist increases killing capacity *in vitro*
- Cav gain-of-function mutation increases target cell killing by NK cells and CD8 T cells *in vitro*

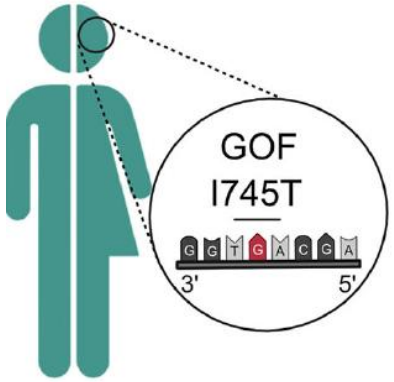
Next developments

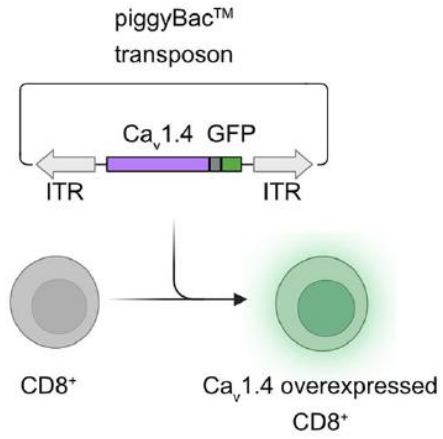
- Team currently developing and scaling up viral vectors for first CAR-T production
- First *in vivo* CAR-T data anticipated Q1 2027

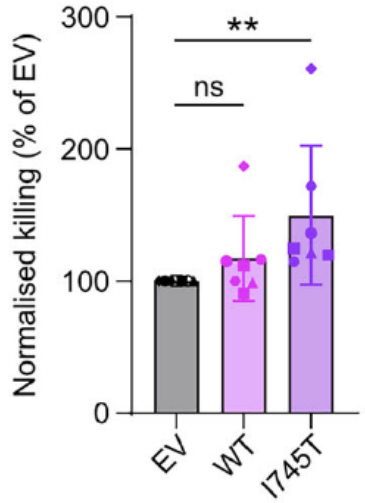
Data supporting hypothesis

Cav gain of function increases killing

Overexpression of a gain-of-function Cav1.4 construct leads to increased killing ability of human CD8+ T cells without affecting their expansion, activation and differentiation characteristics (see publication)







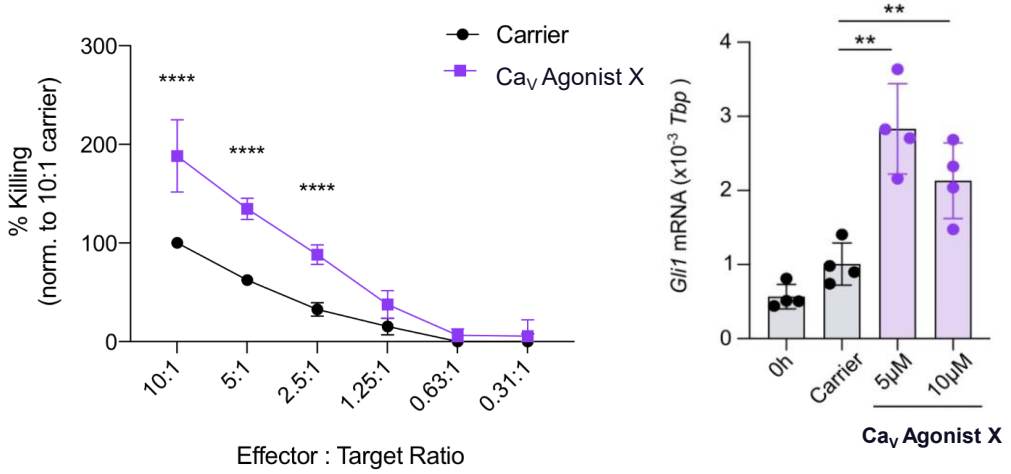
CaV1.4 constructs were introduced into human CTLs via electroporation using PiggyBac transposon system, and on day 26-34 co-incubated with P815 target cells (mouse mastocytoma) for 3h.

Source: Beke et al 2026

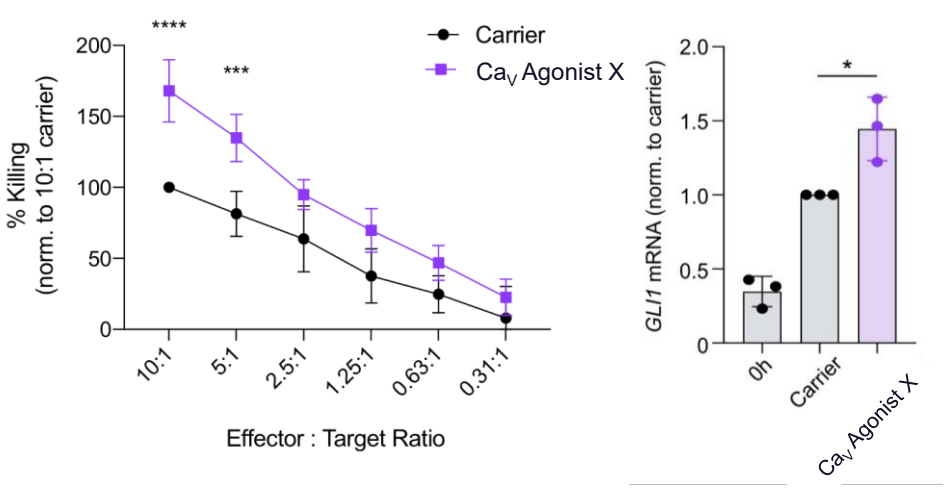
Cav agonism increases tumour cell killing

In vitro experiments in CD8+ T cells treated with a specific agonist (CaV Agonist X) enhances cytotoxicity against tumour cells through activation of the non-canonical Hh pathway

Mouse CD8⁺ T cells



Human CD8⁺ T cells



In murine and human CD8+ T Cells : L-type Ca_V channel enhances specific tumour cell killing by murine CD8⁺ CTLs (left); this effect has been shown through activation of the non-canonical Hh pathway, as measured by Gli1 expression (right)

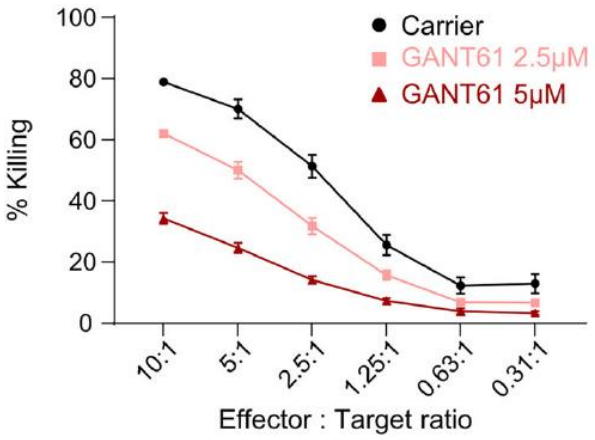
Source: Beke et al 2026

Cav agonism enhances T-cell killing via the non-canonical Hh pathway

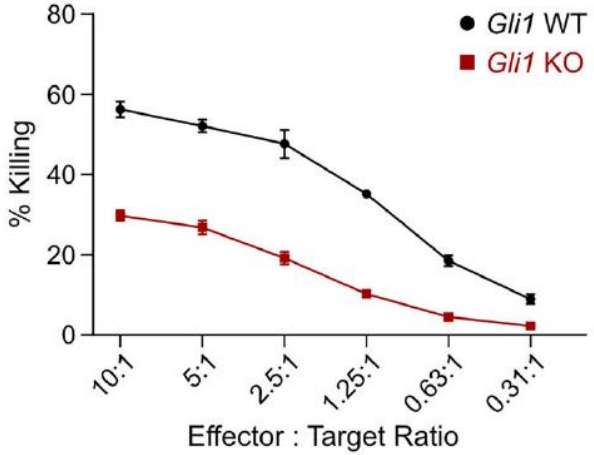
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Non-canonical Hh signalling is dependent on Ca2+ influx and mediated via the non-canonical effector Gli1

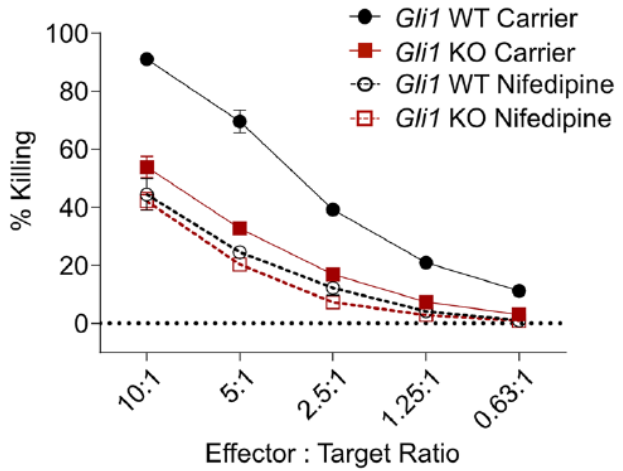
Human CD8⁺ T cells treated with Gli inhibitor GANT61 have reduced killing capacity



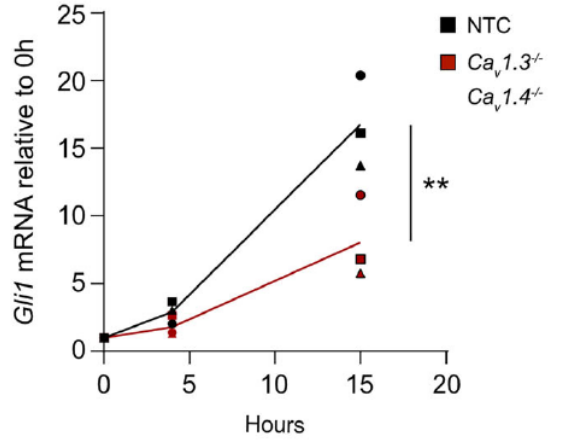
Gli1 KO murine CD8⁺ T cells have reduced killing potential



Ca_V antagonist Nifedipine reduces T cell killing efficiency in a Gli1-dependent manner



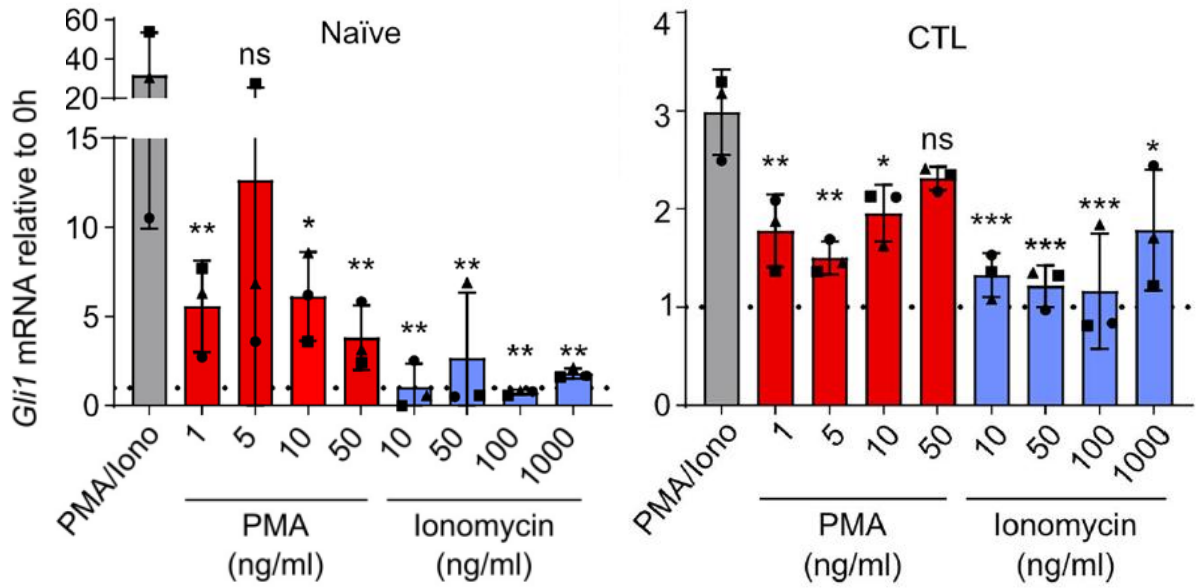
Cav1.3/1.4 channel double CRISPR knockout reduces Gli1 expression in CD8⁺ T cells



Source: Beke et al 2026

Generalised Ca^{2+} increase does not drive Gli1 expression

Generalised calcium increase by Ca2+ or induction of the canonical Hh pathway in CD8+ T cells did not replicate the increased Gli1 mRNA observed from CaV agonism



General increase of Ca^{2+} in T cells does not enhance cell killing/Gli1 expression. Naïve or cytotoxic $CD8^{+}$ T lymphocytes (CTLs) were treated with indicated doses of Ionomycin (calcium ionophore) or PMA (induces canonical Hh pathway - used as control) does not induce the non-canonical Hh pathway, measured by Gli1 expression.

Source: Beke et al 2026

Commercial summary

Commercial summary

Intellectual property

- Patent application with priority March 2022 now in national phase with broad regional filing
- Broad claims covering multiple cell types and therapeutic applications

Competitive differentiation

- No others in the field modulating Cav channels for adoptive cell therapy
- Platform potential for multiple cell types, moving with an evolving landscape
- As well as enhanced tumour cell killing, platform will improve cell therapy persistence

Commercial position

- Potential to infiltrate the established CAR-T market as well as fast growing CAR-NK/gammadelta markets

Partnerships

- Collaboration and licensing opportunities - interested in partners looking to improve the performance of their portfolio of cell therapies

Thank you

For further information, please contact:

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