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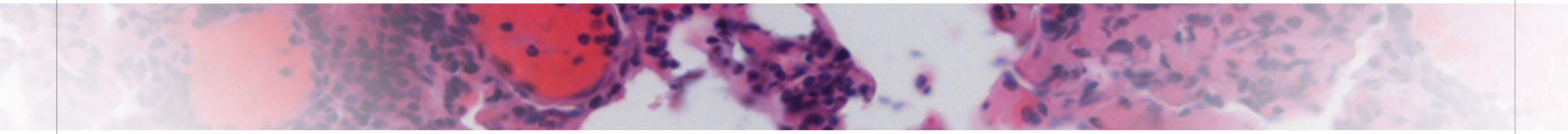
Abstract #1436



Preclinical Development of EDIT-201, a Multigene Edited Healthy Donor NK Cell with Enhanced Anti-Tumor Function and Superior Serial Killing Activity in an Immunosuppressive Environment

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Disclosures

Employees and shareholders of Editas Medicine:
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EDIT-201 has been engineered to enhance the anti-tumor function of NK cells

Objective:

To evaluate the *in vitro* anti-tumor activity of EDIT-201, an NK cell therapy derived from healthy human donor NK cells with enhanced effector function through Cas12a knockout of *CISH* and *TGFBR2*

Advantages of NK cells

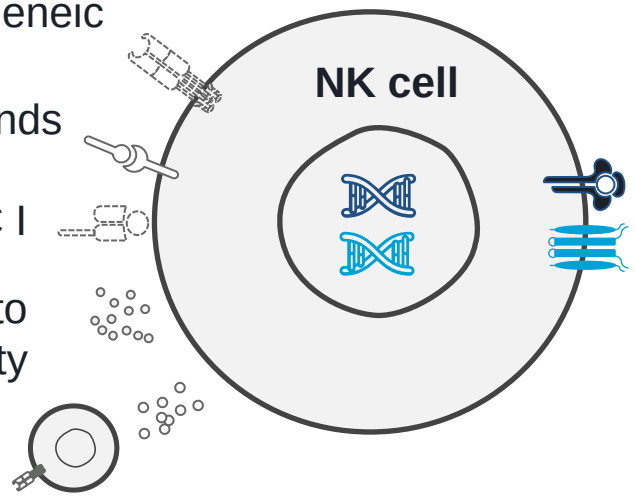
Allogeneic

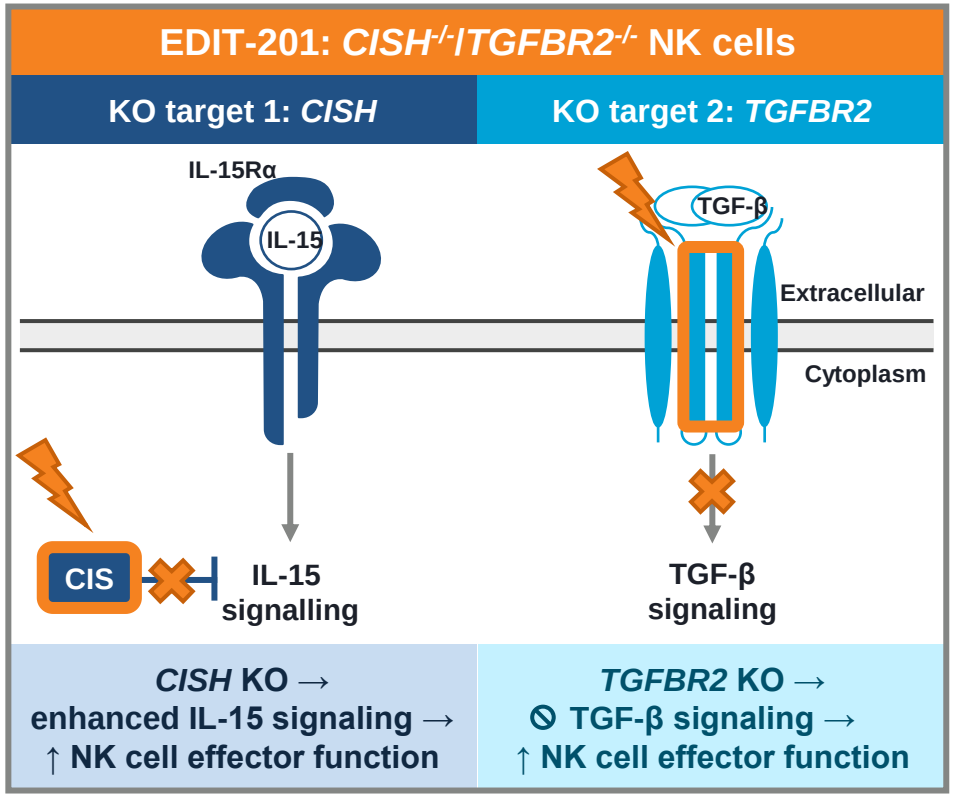
Recognize broad array of tumor ligands

Recognize malignant cells that lack MHC I

Rapid degranulation leads to robust tumor cytotoxicity

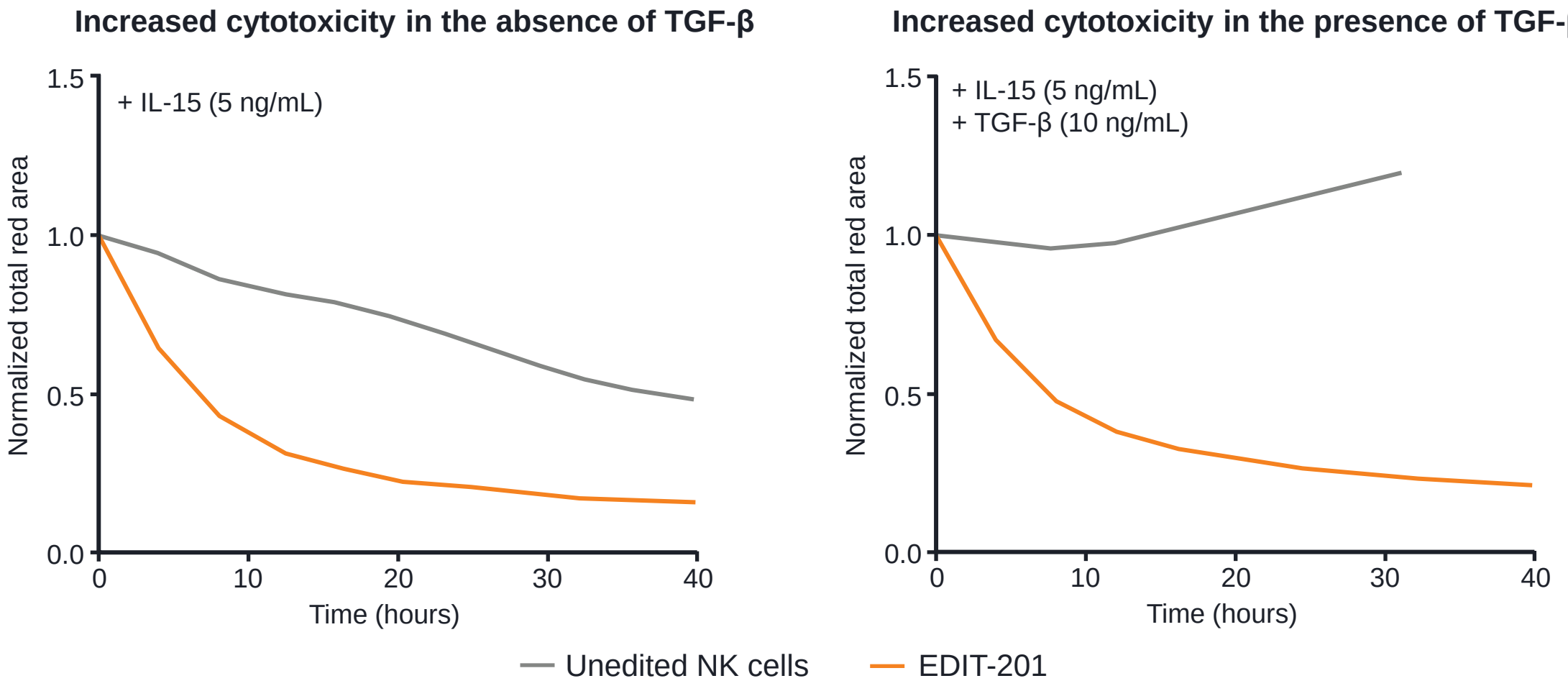
Recruit and engage cells of the adaptive immune system to enhance tumor cytotoxicity





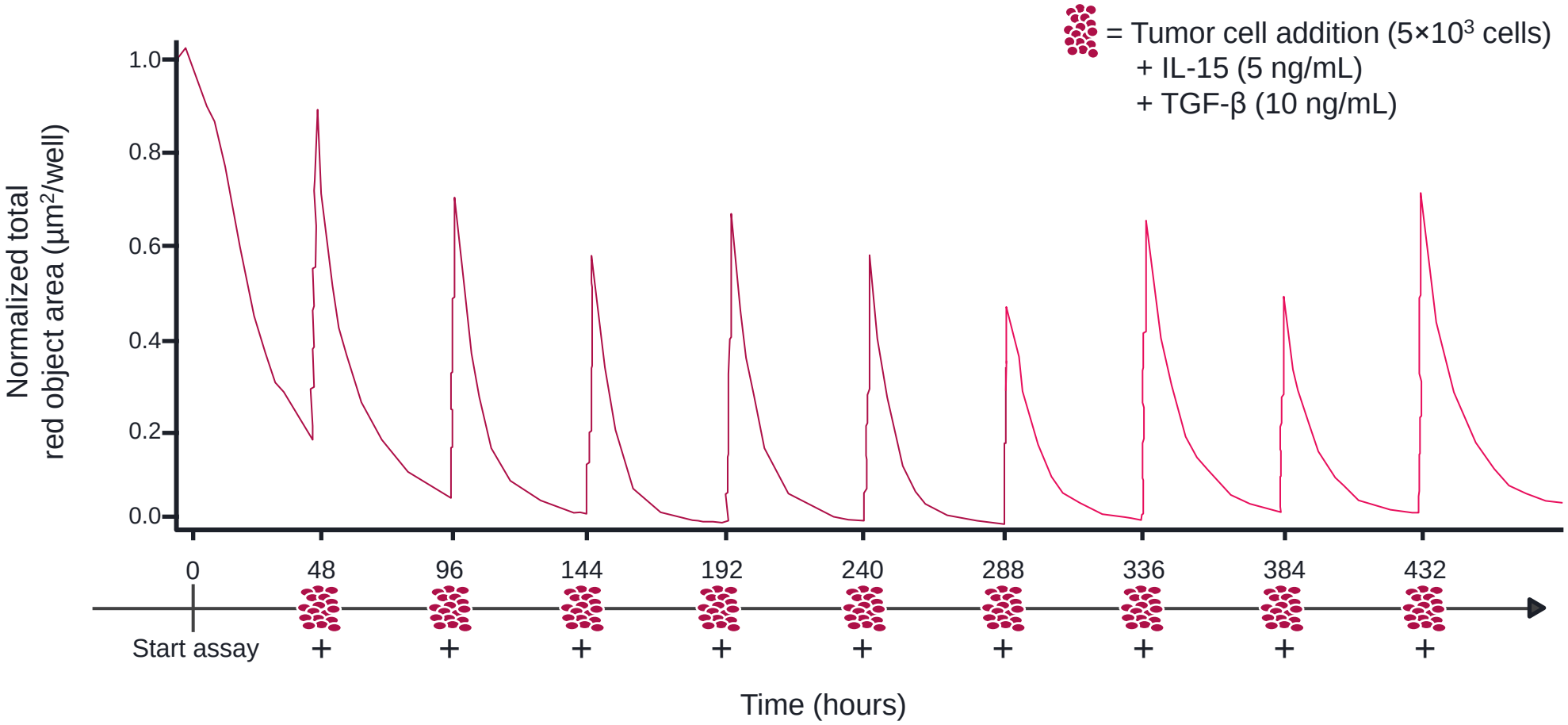
CISH: cytokine-inducible SH2-containing protein gene; IL: interleukin; KO: knockout;
MHC: major histocompatibility complex; NK: natural killer; TGF-β: tumor growth factor beta; TGFBR2: TGF-β receptor II gene

EDIT-201 demonstrated enhanced anti-tumor activity against Nalm6 cells (B cell leukemia cell line) in the presence of TGF-β

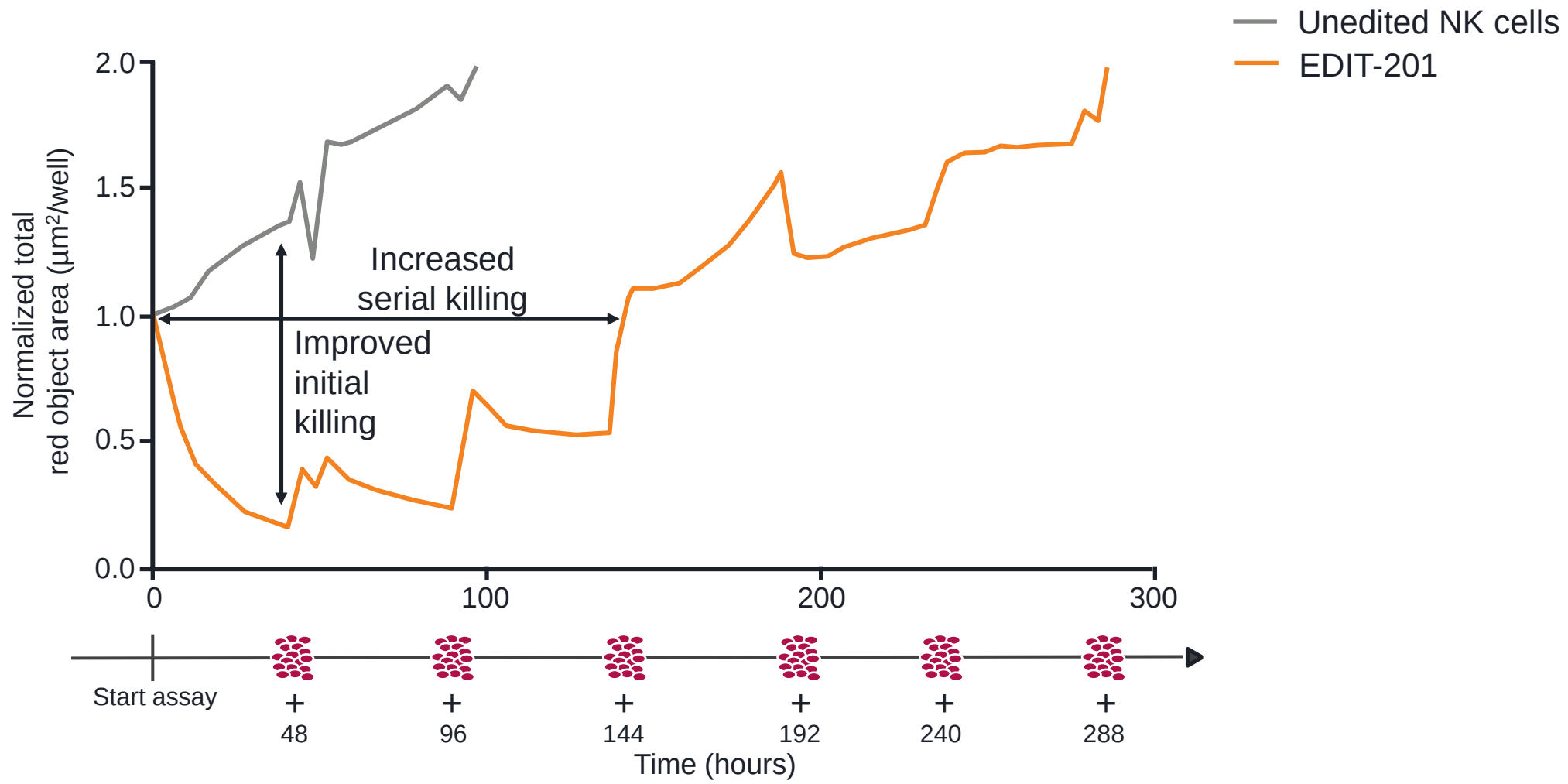


Representative data of 5 unique donors and 2 independent experiments

Serial-killing activity of NK cells can be measured by challenging NK cells with a bolus of Nalm6 cells every 48 hours for up to 20 days

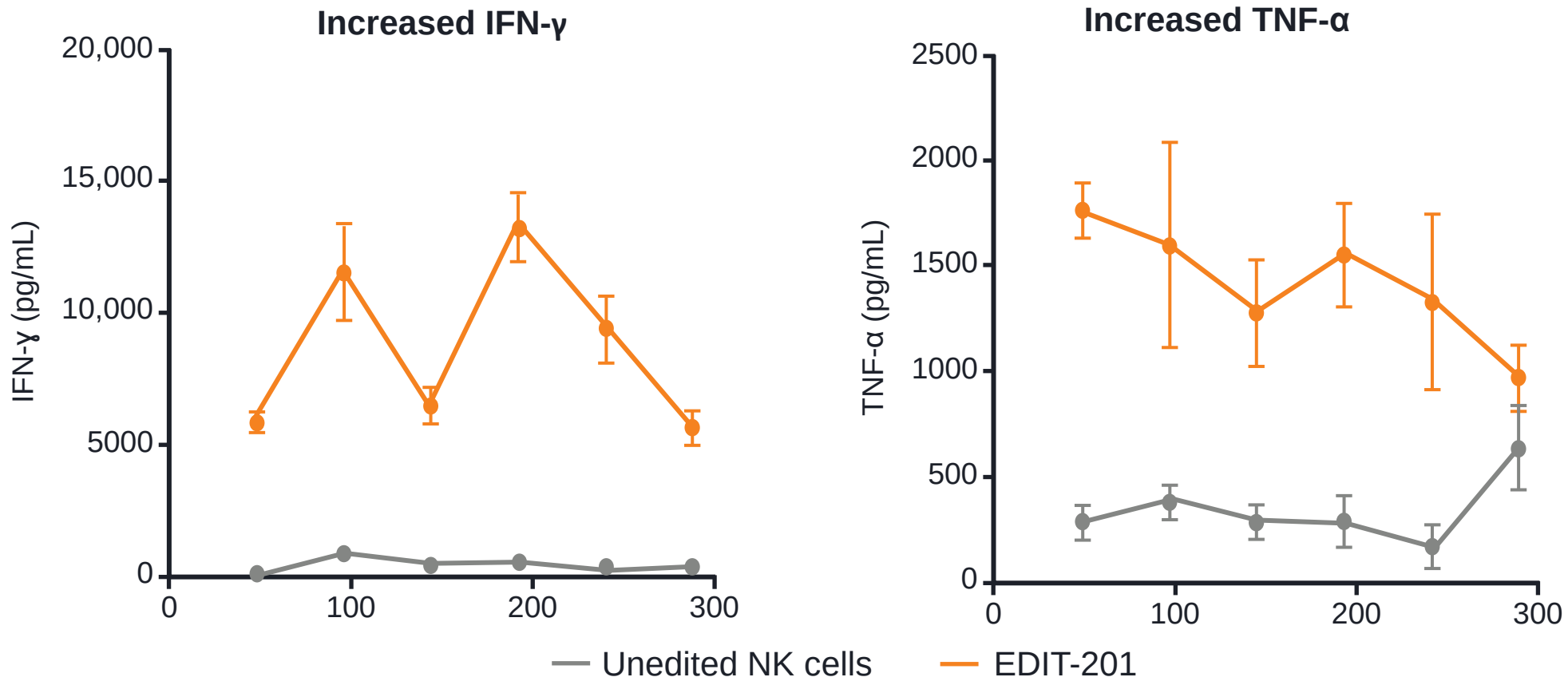


EDIT-201 demonstrated sustained serial killing of Nalm6 cells for >8 days in the presence of TGF-β



Representative data of 6 unique donors and 2 independent experiments

EDIT-201 produced increased levels of inflammatory cytokines throughout the serial-killing assay in the presence of TGF-β

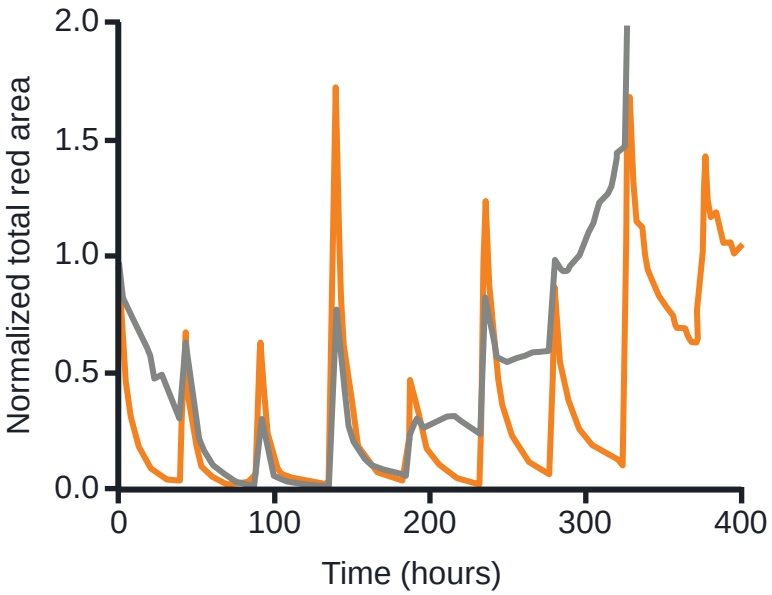


Supernatants from Nalm6 serial-killing assay (representative data of 3 unique PBMC donors)

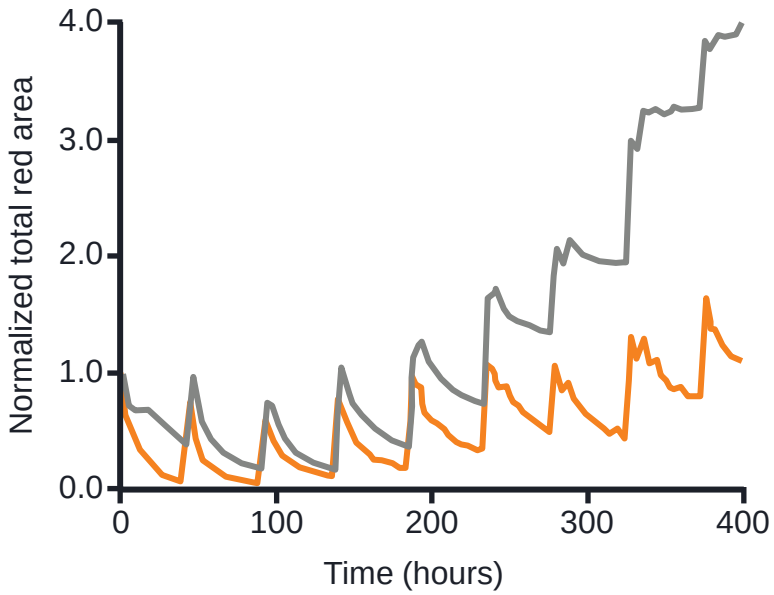
IFN: interferon; PBMC: peripheral blood mononuclear cell

EDIT-201 demonstrated sustained serial-killing activity against numerous hematologic tumor cell lines in the presence of TGF-β

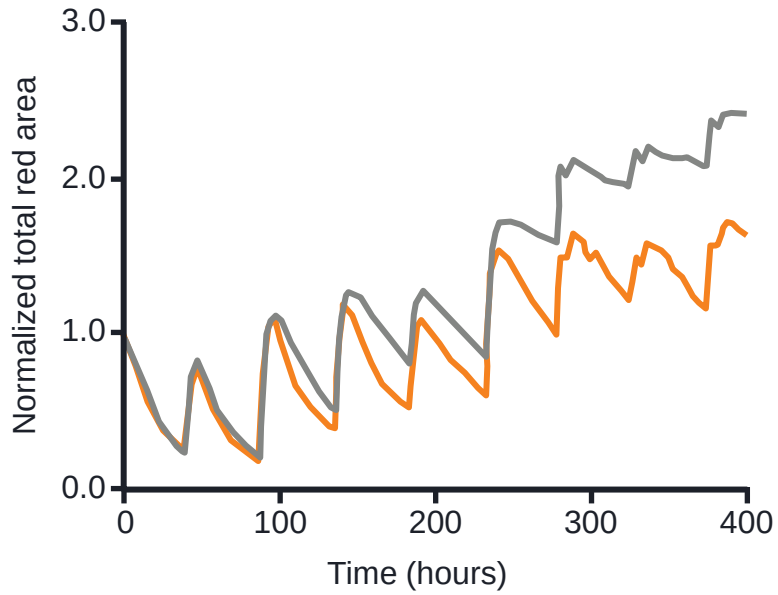
Sustained cytotoxicity against Raji cells (Burkitt's lymphoma)



Sustained cytotoxicity against RPMI8226 cells (multiple myeloma)



Sustained cytotoxicity against THP-1 cells (acute monocytic leukemia)



Unedited NK cells — EDIT-201

Representative data of minimum 5 unique donors and 5 independent experiments

Conclusions

EDIT-201 is being developed as a **healthy donor-derived NK cell therapy** with CRISPR-Cas12a-mediated editing at ***CISH*** **and** ***TGFBR2*** **loci**

EDIT-201 demonstrated **sustained anti-tumor serial-killing activity** in the presence of the potent immunosuppressive cytokine TGF-β across various hematologic cell lines *in vitro*, suggesting that EDIT-201 is a potent and versatile cell-based medicine

EDIT-201 is being advanced to **clinical development** as an allogeneic cell-based medicine for solid tumors

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