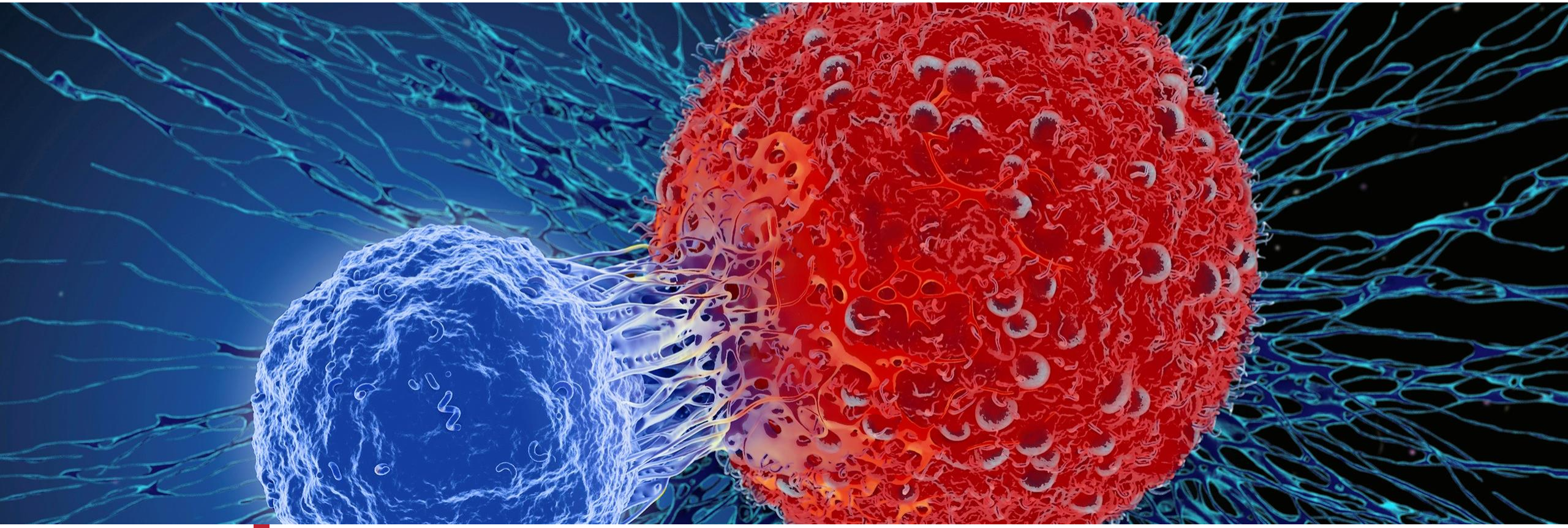
Adaptimmune
TRANSFORMING T CELL THERAPY



In vitro Selection and Engineering of a Human Leukocyte Antigen-Independent T-Cell Receptor (HiT) Recognizing Human Mesothelin

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Adaptimmune, Abingdon, Oxfordshire, UK

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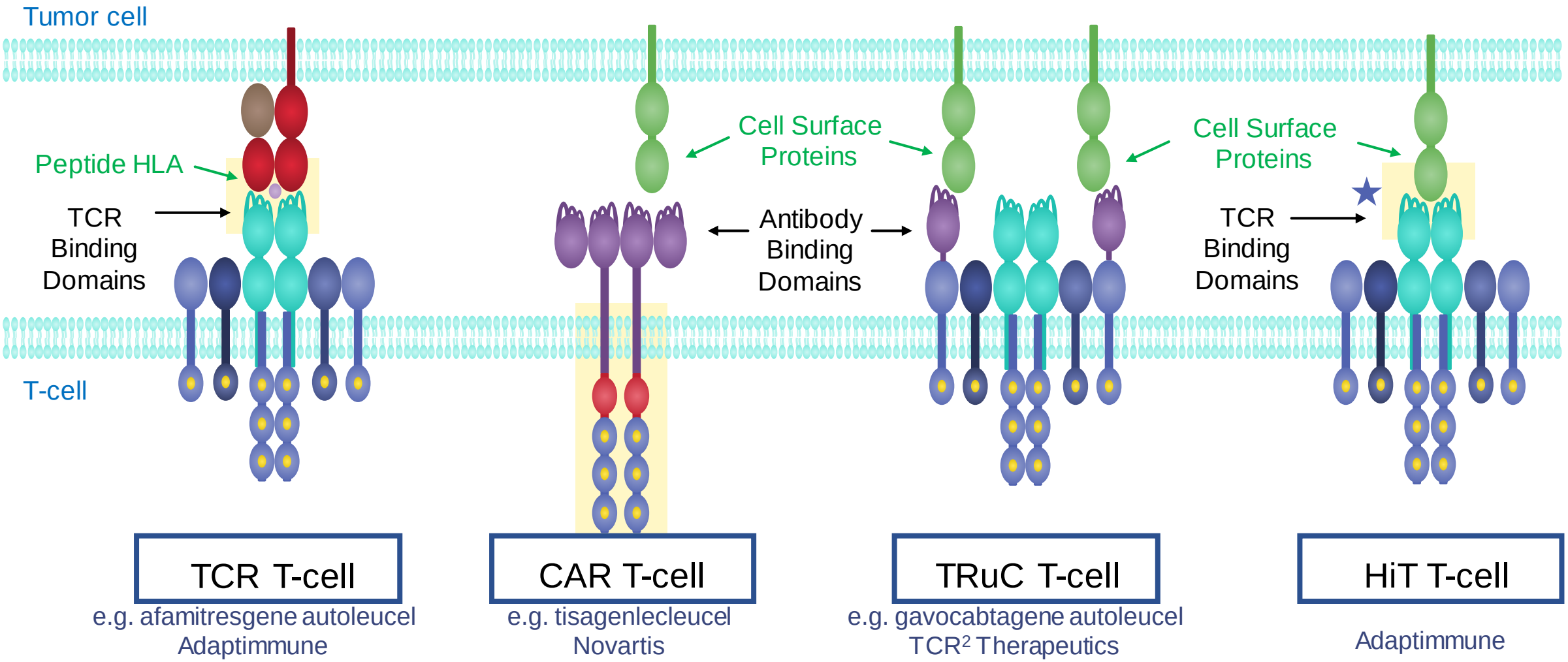
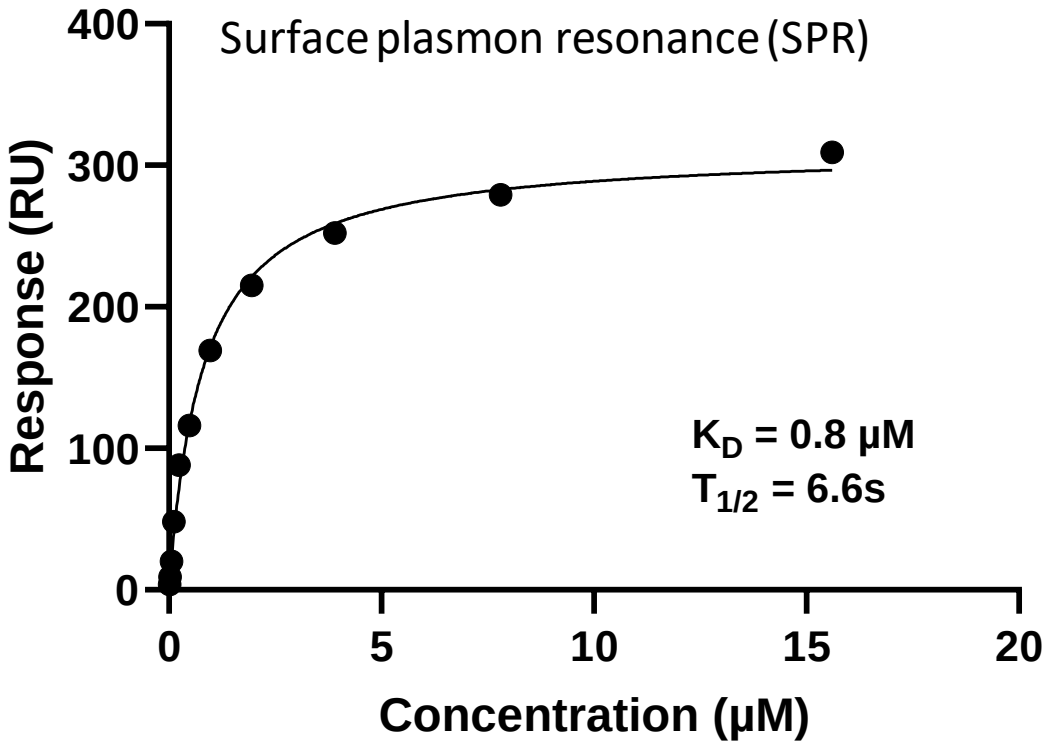
HLA-Independent TCRs (HiTs) bind directly to cell surface target proteins



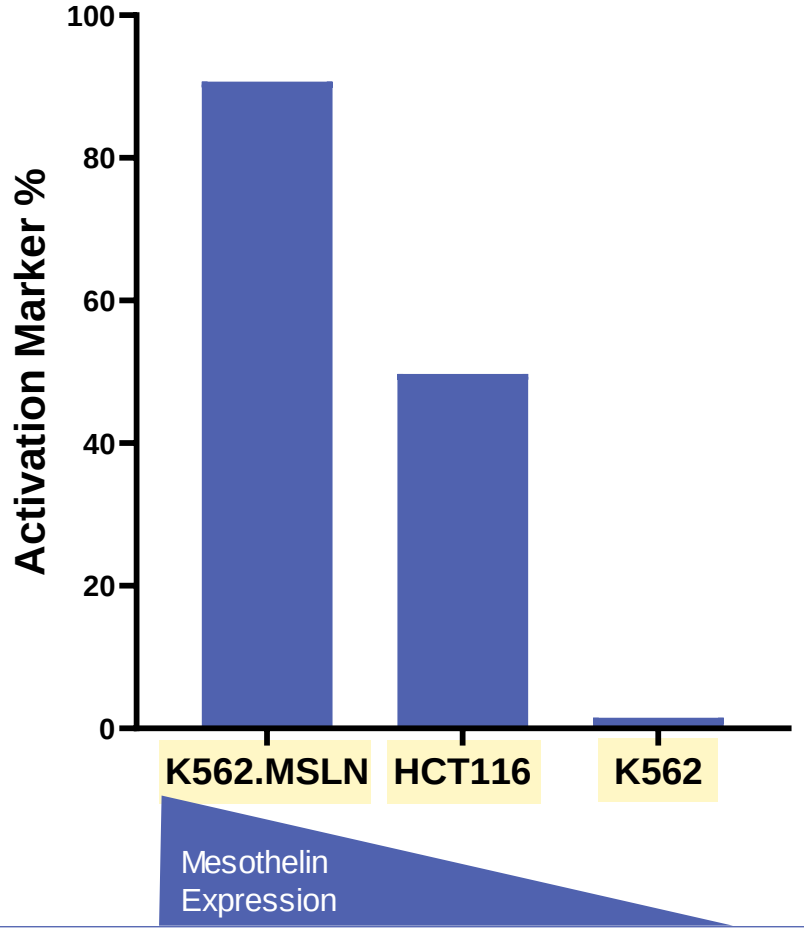
CAR, chimeric antigen receptor; HiT, HLA-independent TCR; HLA, human leukocyte antigen; TRuC, TCR fusion constructs

Isolation of a HiT recognizing mesothelin using phage display

HiT binds directly to mesothelin

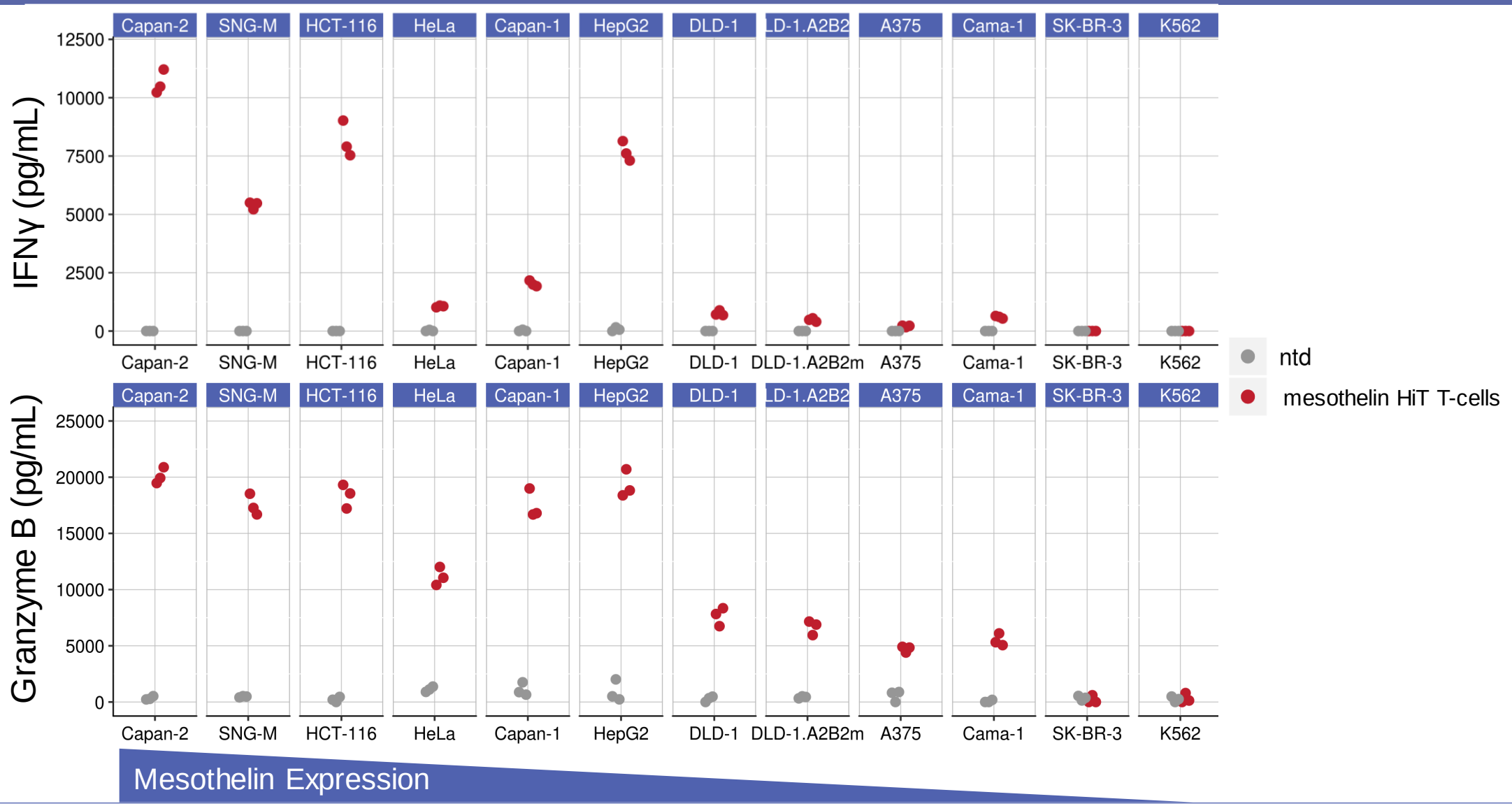


HiT T-cell activated by mesothelin



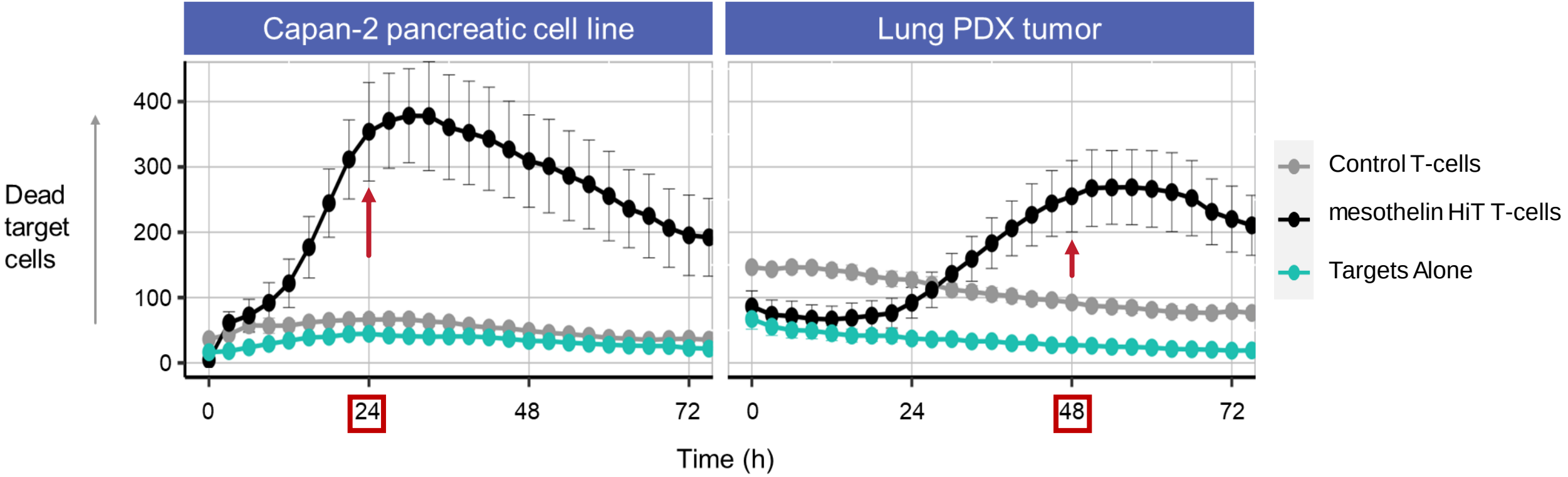
K_D, dissociation constant; HiT, HLA-independent TCR; HLA, human leukocyte antigen; MSLN, mesothelin; T½, half-life

HiT T-cell activation level is mesothelin expression dependent



HiT, HLA-independent TCR; HLA, human leukocyte antigen; IFNγ, interferon gamma; ntd, non-transduced

HiT T-cells kill primary tumor-derived cells *in vitro*

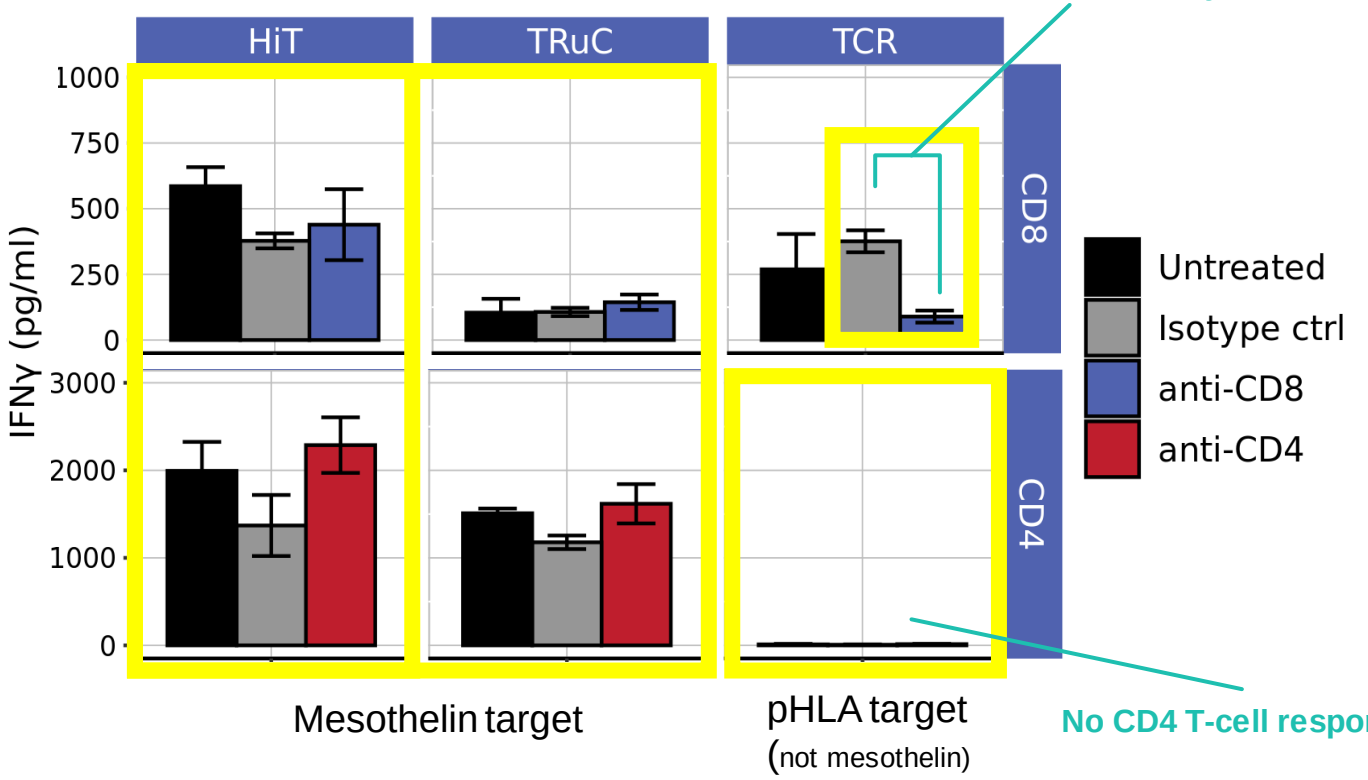


HiT, HLA-independent TCR; HLA, human leukocyte antigen; PDX, patient-derived xenograft

HiTs are active in both CD4 and CD8 T-cells and are not inhibited by soluble protein

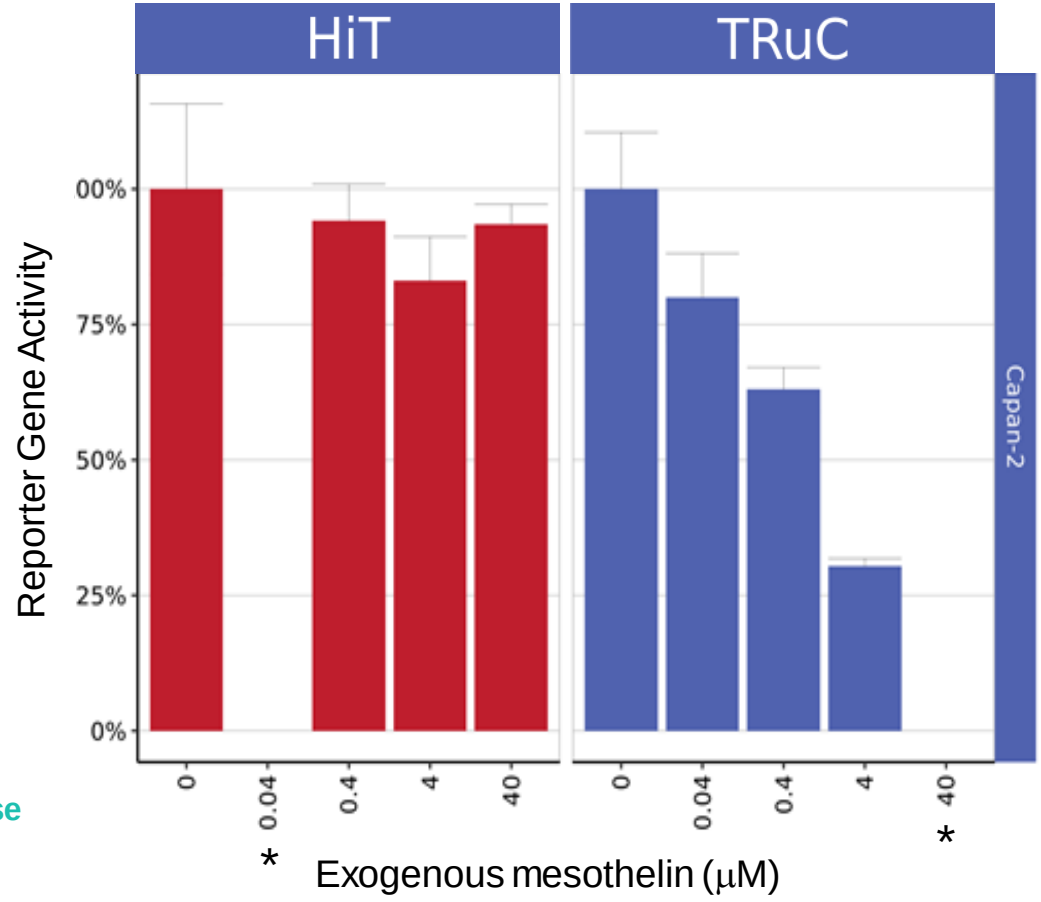
No CD8 or CD4 dependency

Anti-CD8 antibody blocks pHLA TCR activity



No CD4 T-cell response

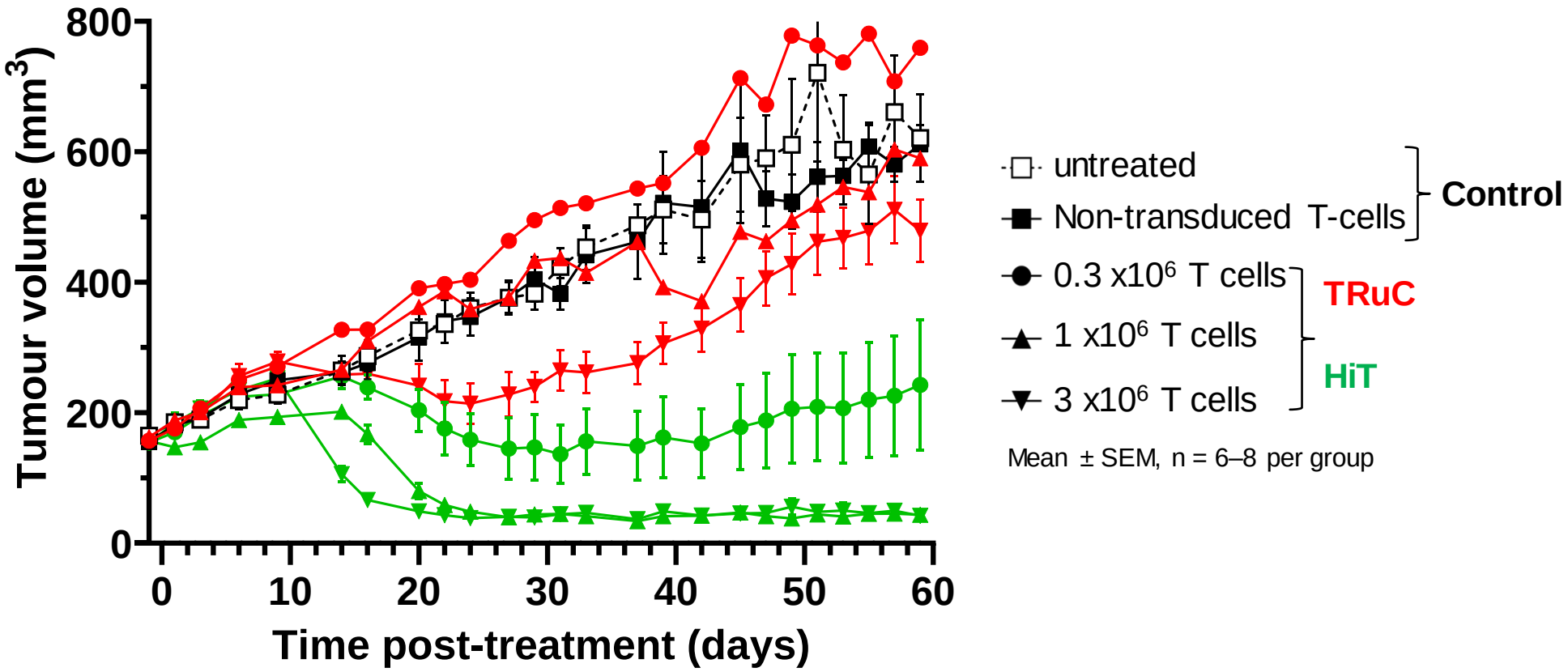
HiT not inhibited by soluble mesothelin



*Value not tested

ctrl, control; HiT, HLA-independent TCR; HLA, human leukocyte antigen; IFNγ, interferon gamma; MSLN, mesothelin; pHLA, peptide–human leukocyte antigen; All T-cells manufactured with Adaptimmune proprietary technology

HiT induces strong, dose-dependent and persistent tumor regression *in vivo*



HiT, HLA-independent TCR; HLA, human leukocyte antigen; MSLN, mesothelin;
All T-cells manufactured with Adaptimmune proprietary technology

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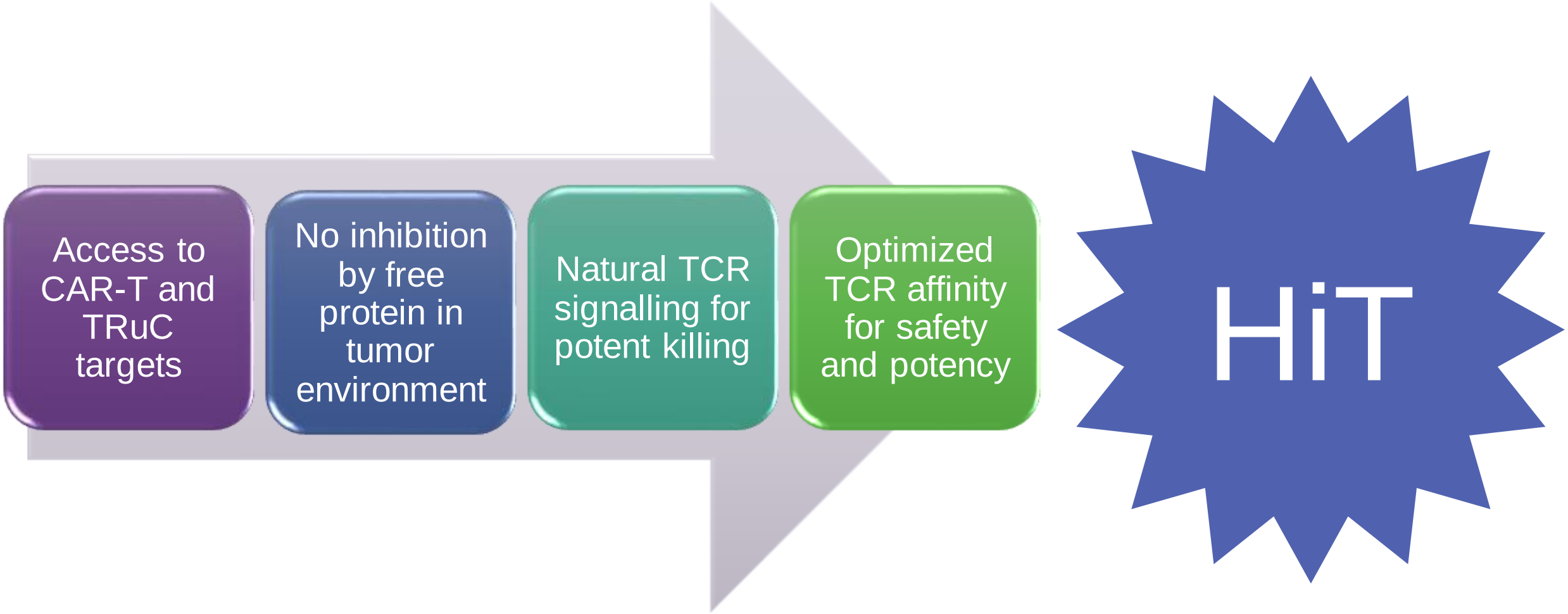
HiTs are an exciting new therapeutic modality for targeting extracellular proteins on tumors



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  - Jaelle Foot
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