



Conditionally Activated Anti-MUC16 x CD3 Bispecific Antibodies Targeting the Non-Shed MUC16 Region

Leveraging iBio's Epitope Steering, ShieldTx, and EngageTx Technologies

MUC16 Potentially for Ovarian and Other Cancers

Target Mechanism

Bind a membrane-proximal MUC16 epitope

Membrane-proximal binding avoids epitope elimination by tumors

Bind a non-glycosylated epitope to avoid altered glycosylation on tumors

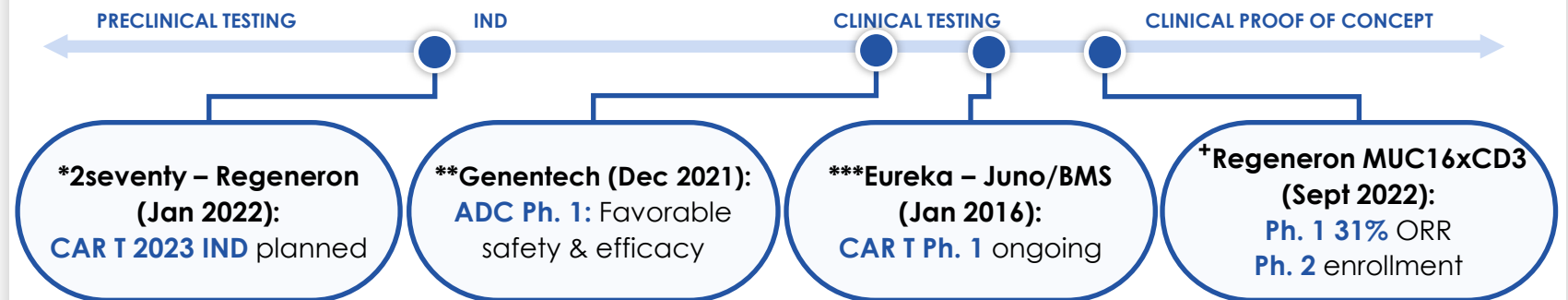
Potential Indications

- Ovarian
- Uterine
- Pancreatic

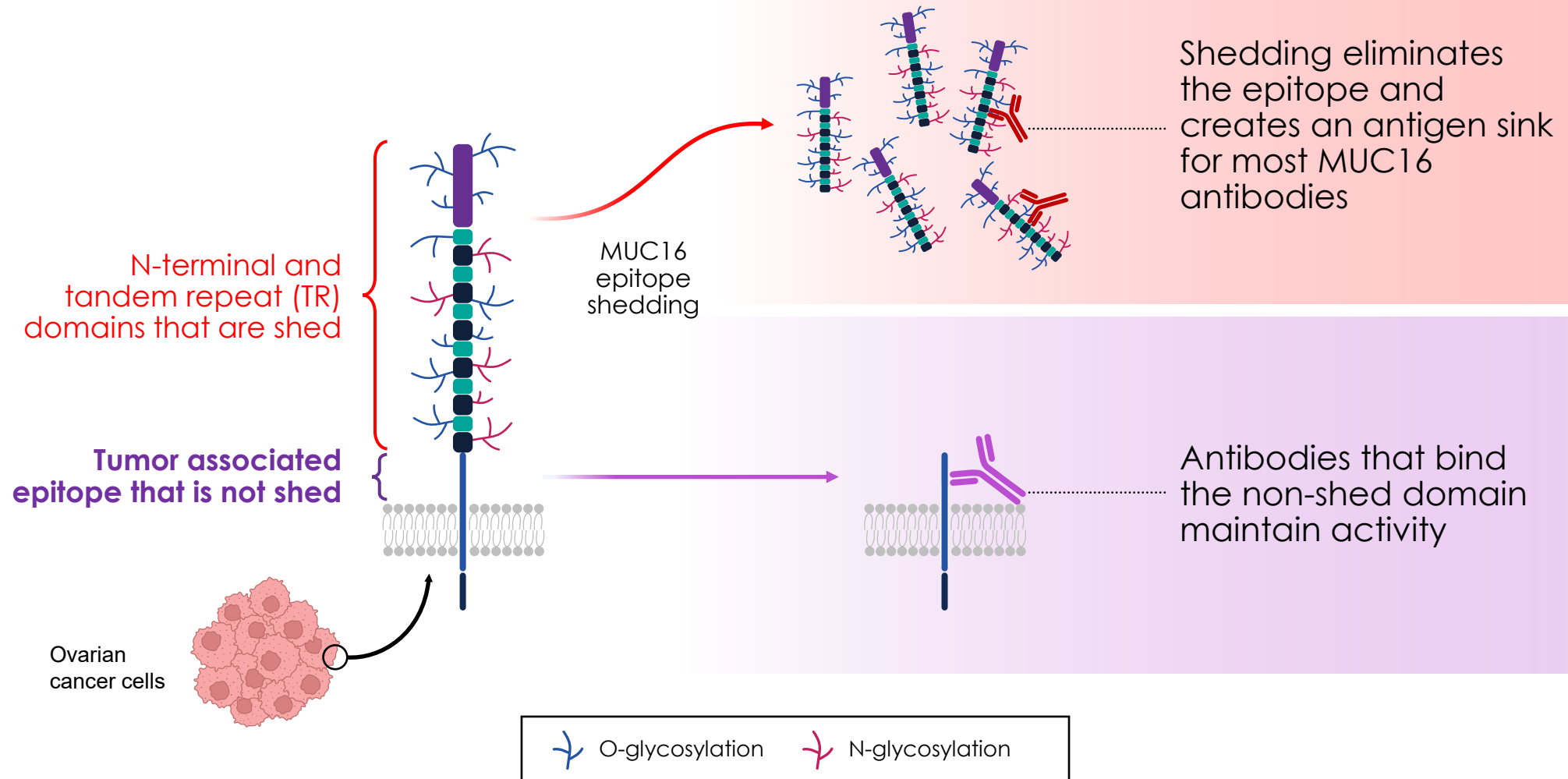
Differentiation / Opportunity

- MUC16 epitope avoids primary modes of tumor evasion
- Enabling modalities: T Cell engager, ADC, CAR-T

Recent Transactions & Milestones

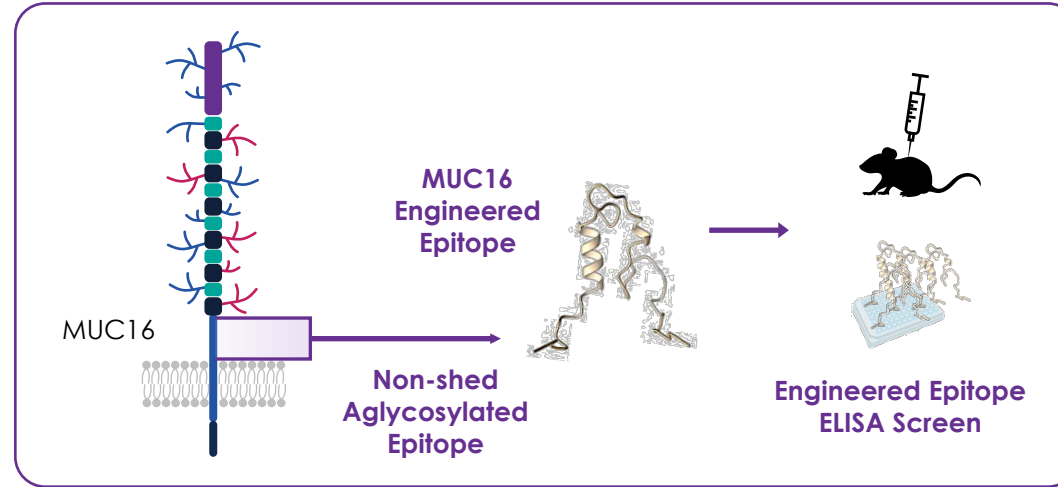


MUC16 Is Overexpressed and Shed by Tumor Cells

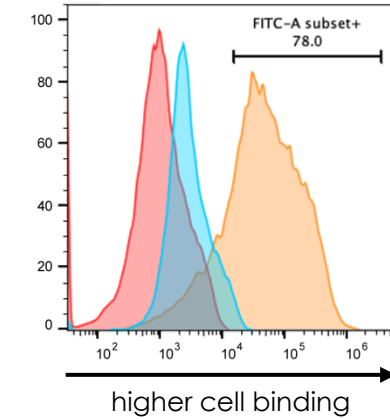


Immunizations Were Steered to a MUC16 Epitope that Avoids Epitope Shedding

Structural-epitope Immunization & Screening

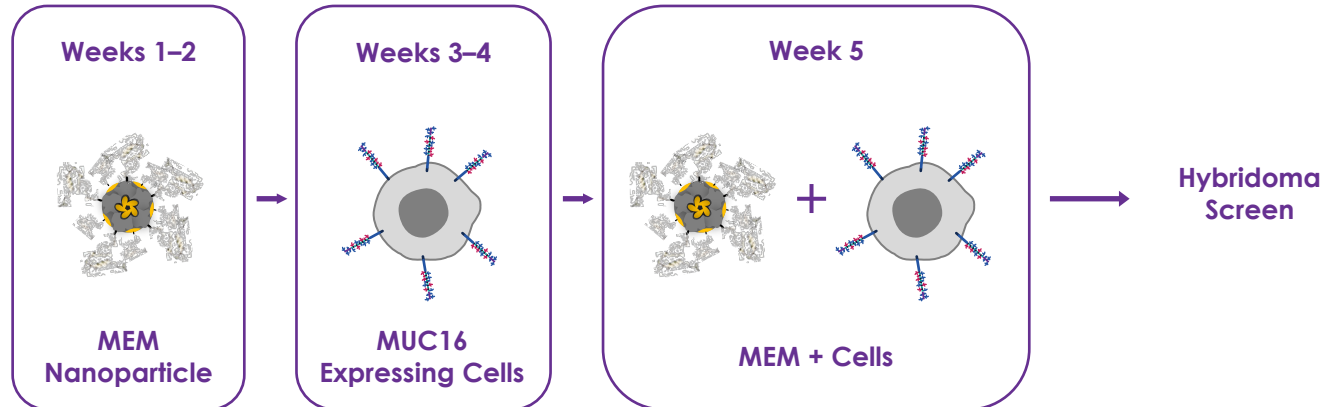


OVCAR-3 MUC16^{high} Cell Binding Screen



AI Discovery Engine

Engineered Epitope Prime + MUC16 Cell Boost



Top Three Hit Clones Bind the Non-Glycosylated MUC16 Epitope Closest to the Membrane

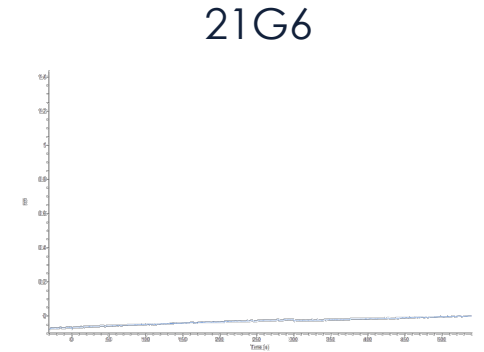
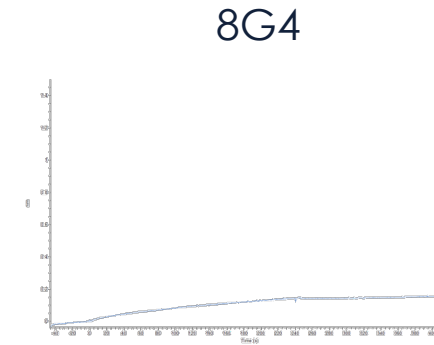
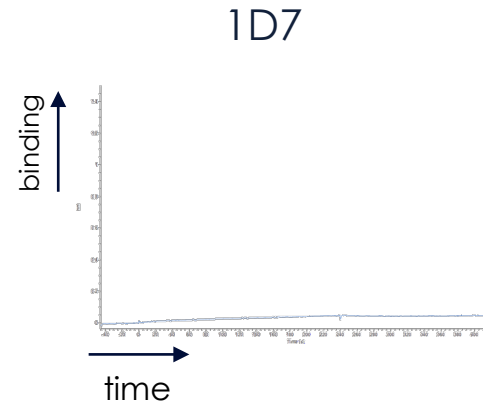
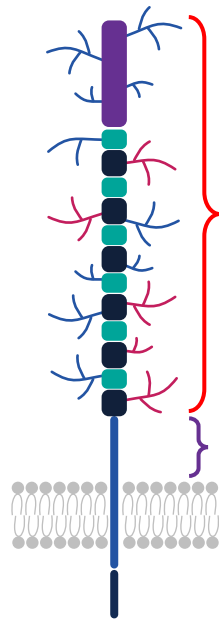
Hits do not bind shed 230-mer

N-terminal and tandem repeat (TR) domains that are shed

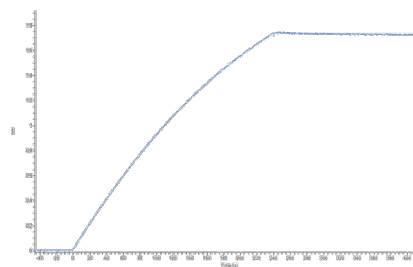
Epitope

Shed 230-mer

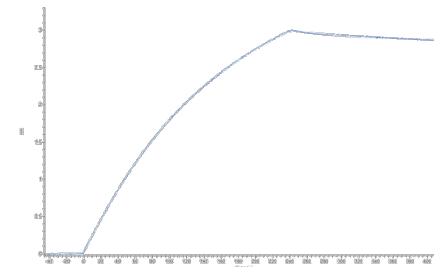
Aglycosylated non-shed 29-mer



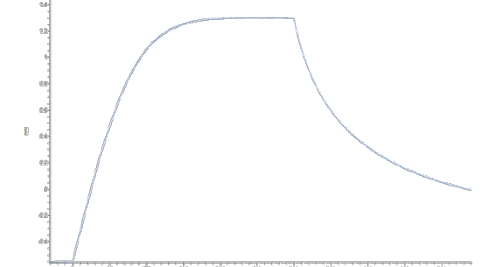
Hits bind non-glycosylated non-shed 29-mer



KD = 8.0 nM



KD = 5.4 nM



KD = 14 nM

O-glycosylation N-glycosylation

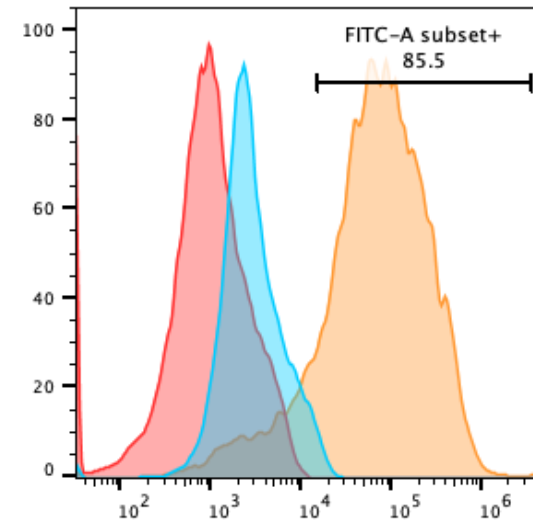
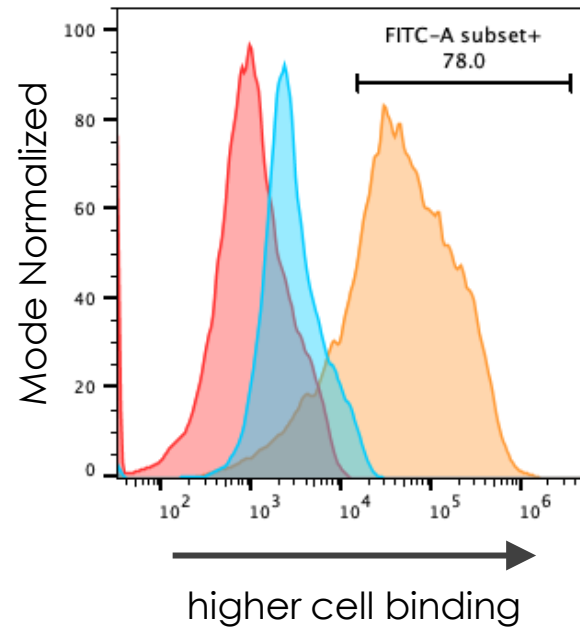


Top MUC16 Clone 8G4 Binds OVCAR-3 Cells Comparable to Regeneron Benchmark

Clone ID: 8G4
top clone

Regeneron
benchmark

- Unstained
- Secondary Only
- OVCAR-3 Cells



8G4 Clone Maintains OVCAR-3 Cell and MUC16 Epitope Binding in a Fully Human Framework

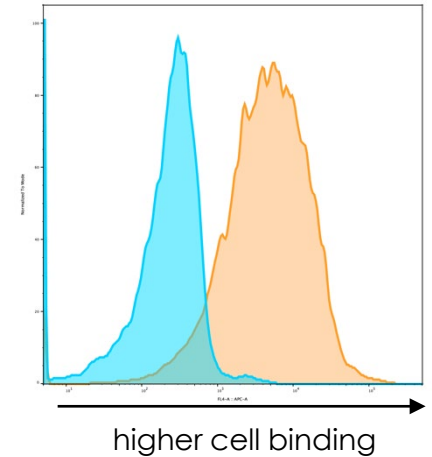
8G4 with fully human framework reduces immunogenicity risk

Glycosylated MUC16 membrane-proximal epitope SPR:

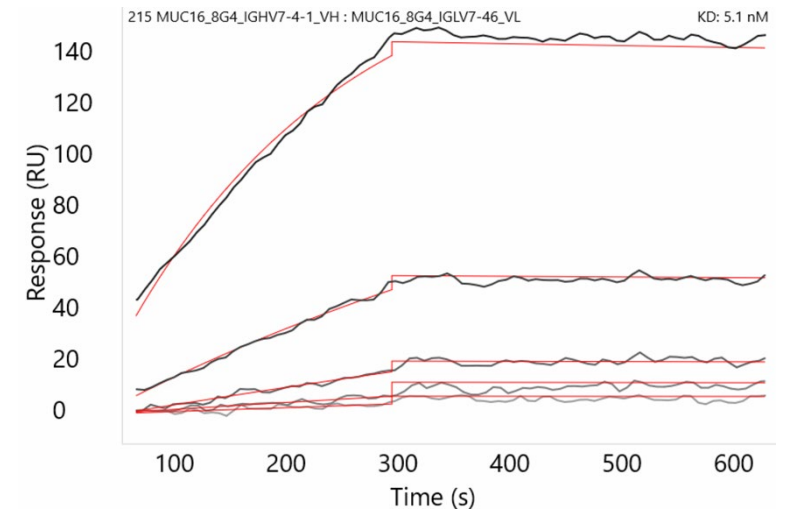
$KD = 5.1 \text{ nM}$

Cell binding

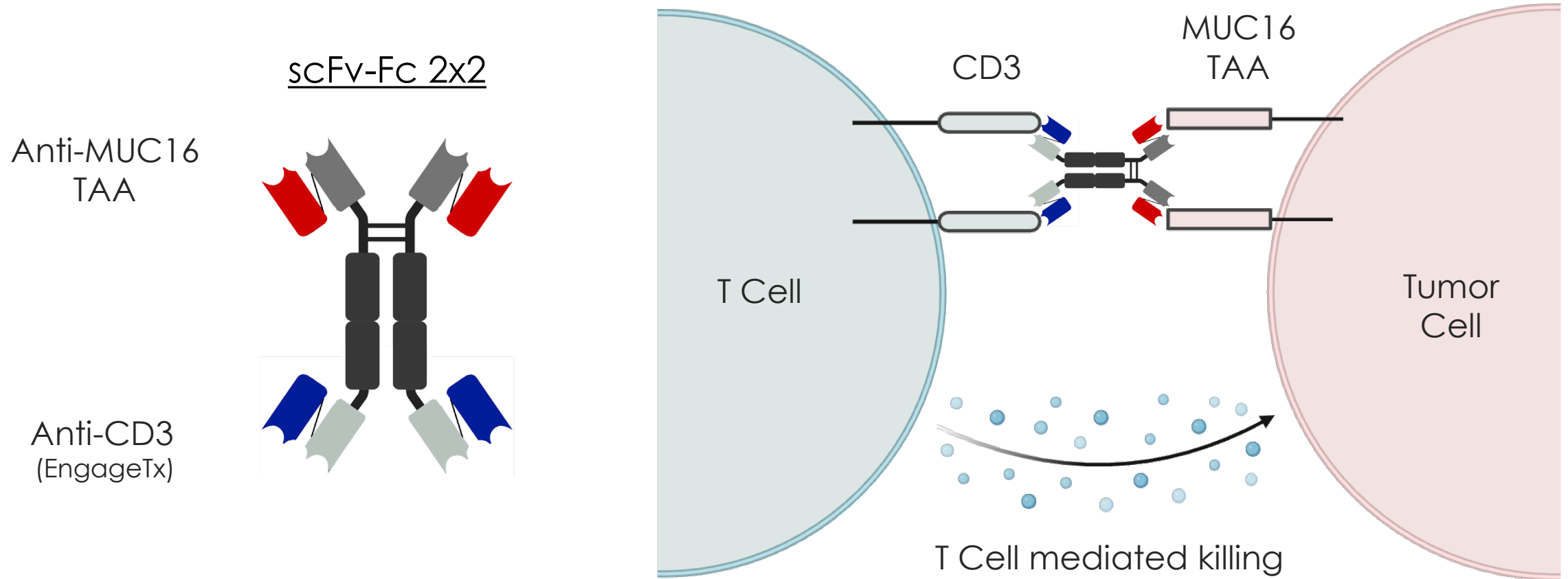
○ OVCAR-3 Cells
○ Iso. Ctl



Epitope binding



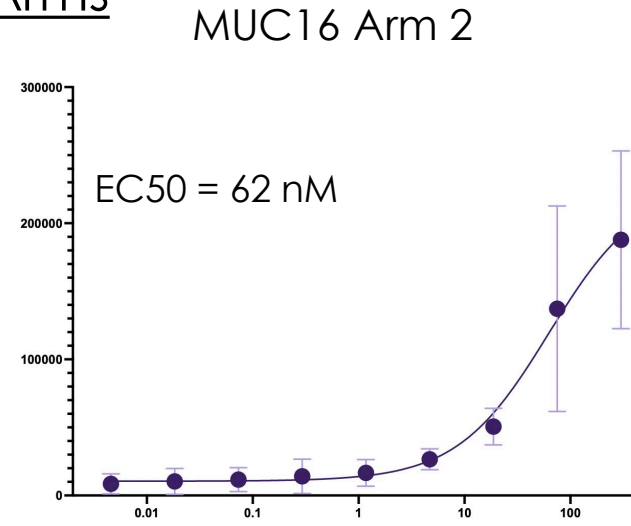
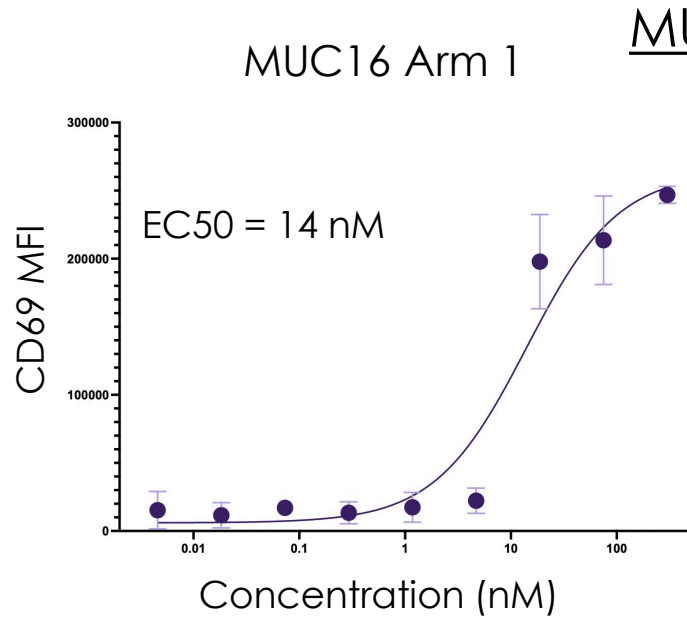
Efficient Expression with 2x2 Format: Anti-CD3 x MUC16 Bispecific T-Cell Engagers



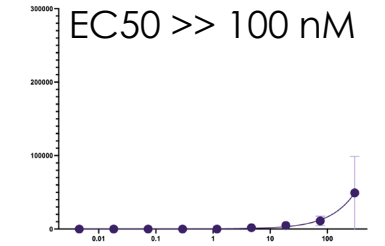
2X2 Anti-CD3 X MUC16 T Cell Engagers Stimulate T Cells in Donor PBMCs

CD3 Arms

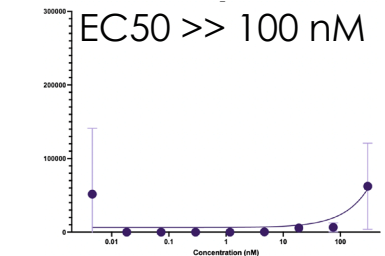
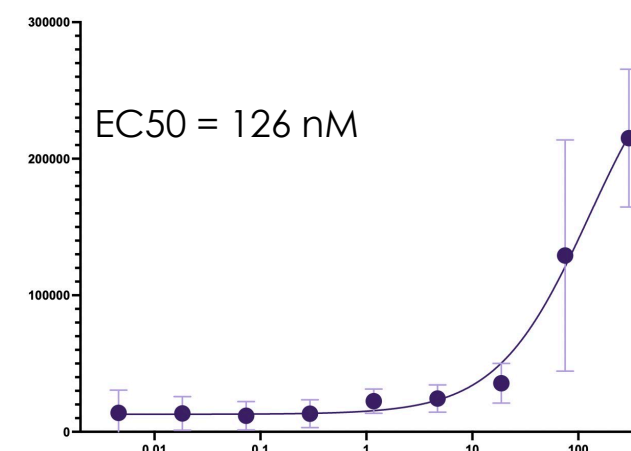
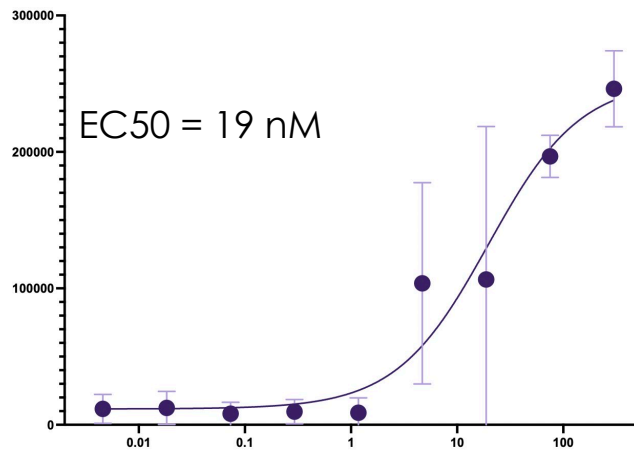
Epitope-Steered
Immunized Hit



(-)CD3 Arm only



StableHu
Hit



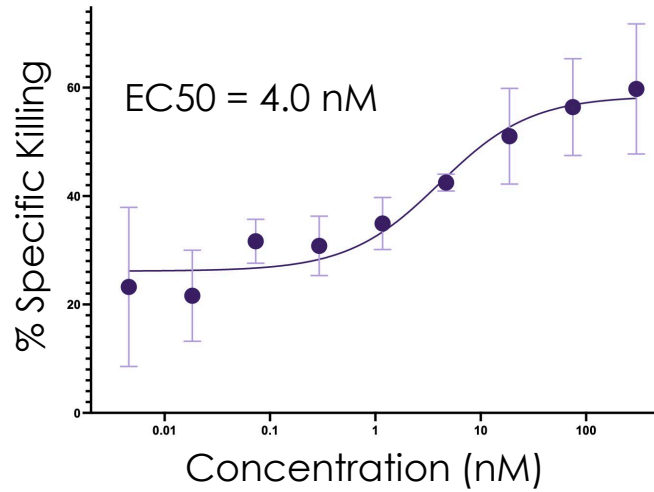
2X2 Anti-CD3 X MUC16 T Cell Engagers Kill OVCAR-3 Ovarian Cancer Cells

CD3 Arms

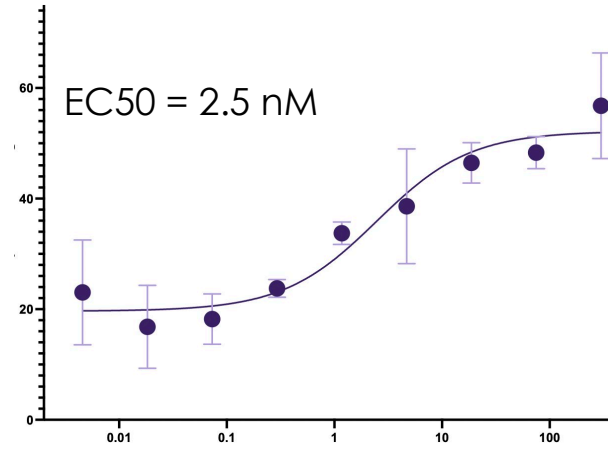
MUC16 Arms

Epitope-Steered
Immunized Hit

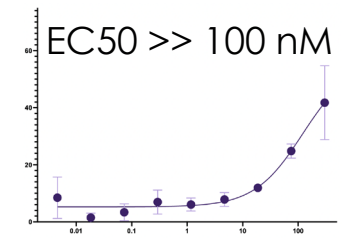
MUC16 Arm 1



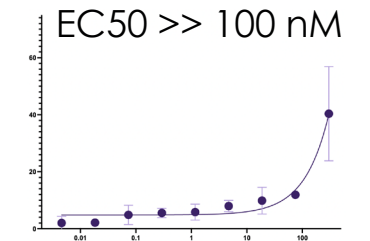
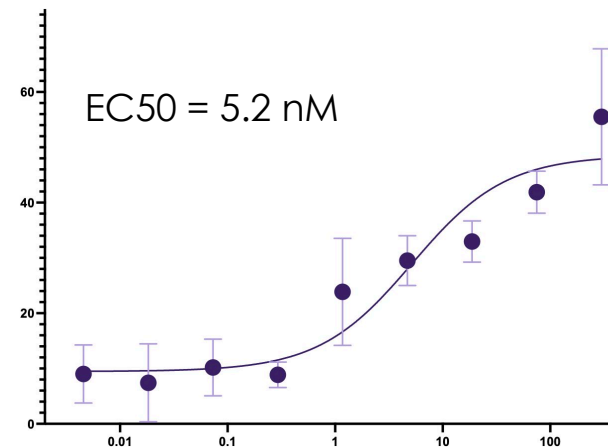
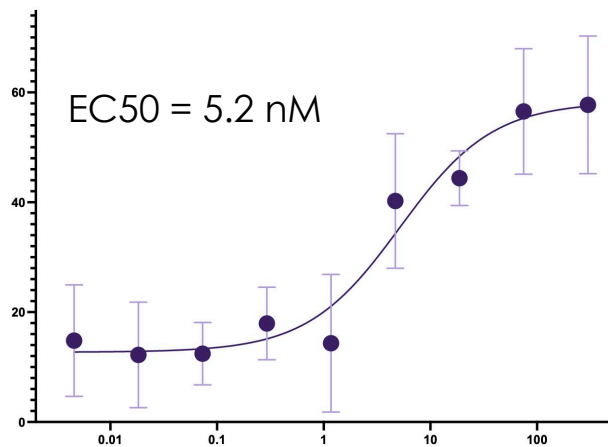
MUC16 Arm 2



(-)CD3 Arm only

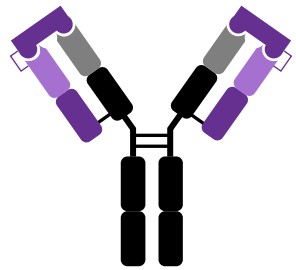


StableHu
Hit




ShieldTx Engineered Epitope Mask Conditionally Activates MUC16 and CD3 Hits

Engineered Epitope
Mask Intact



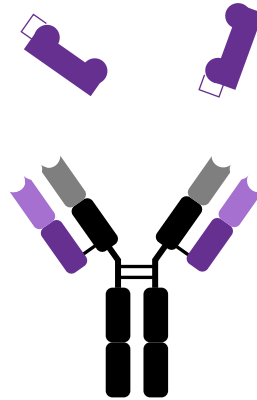
Inactive
Antibody

MMP
protease



An arrow points from the inactive antibody to the active antibody, with the text 'MMP protease' and a blue circular icon representing the enzyme.

Mask Cleavage



Active
Antibody

