Glycosylated protein targets open access to multiple tumor indications for different therapeutic modalities

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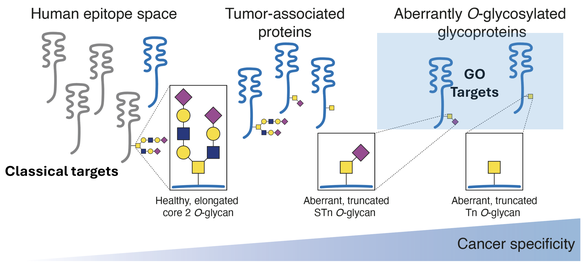
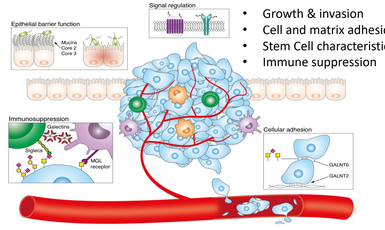
GOTx glyco-platform

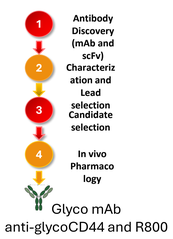
Revitalizing classical cancer targets with novel GO glyco-targets



Truncated O-glycans drive tumor formation

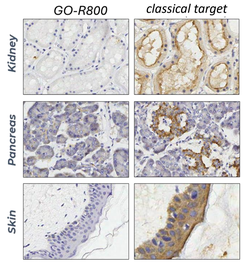


- Growth & invasion
- Cell and matrix adhesion
- Stem Cell characteristics
- Immune suppression

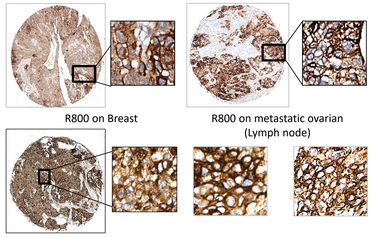


GO-R800 selectively targets multiple cancer tissue

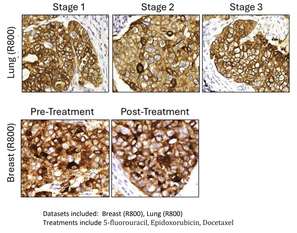
Normal Tissue



Cancer Tissue



Cancer stages and post-treatment



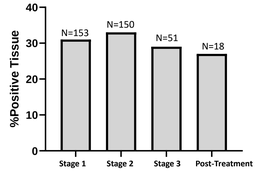
Datasets included: Breast (R800), Lung (R800)
Treatments include 5-fluorouracil, Epidoxorubicin, Docetaxel

R800 selectively binds to multiple cancer tissue

Tissue	3+/2+	1+	Total
Ovarian Cancer *Metastatic*	19% (24/130) *37% (14/38)*	30% (40/130) *5% (2/38)*	49% (64/130) *42% (16/38)*
Lung Cancer (NSCLC) *Metastatic*	19% (26/140) *25% (10/40)*	11% (15/140) *3% (1/40)*	30% (41/140) *28%(11/40)*
Breast Cancer (including TNB) *Metastatic*	22% (16/72) *33% (33/104)*	0% (31/72) *1% (1/104)*	22% (16/72) *33% (34/104)*
Normal Tissue	0% (0/96)	0% (0/96)	0% (0/96)

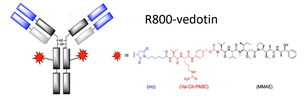
3+/2+ = >25% of cancers cells with positive stan; 25% cut off defined by efficacy in PDx
1+ = 0-25% of cancer cells with positive stain

Prevalence in cancer stages and after chemotherapy



In vitro activity of R800-vedotin

ADC Platform



- Site-specific, DAR2 ADC (mc-vc-PAB-MMAE)
- Potent killing across multiple in-vivo models

R800 :
- Binds to tumor-specific glyco-proteins with low nanomolar affinity
- Tumor selectivity arises from targeting of cancer-specific glycan together with the backbone peptide
- R800 glyco-epitope is expressed in a broad range of tumors including NSCLC, BC, OVC, PDAC
- Overlaps with 80% of ROS1 expression 50% of PDL1 expression and consistent targeting across all cancer stages and pre- and post-chemotherapy treatments

In vitro plasma stability

Day	DAR (% of starting material)		
	Cyno	Human	Mouse
0	100	98.6	100
1	100	100	97.4
3	100	99	100
7	96.7	98	94.9
14	87.4	93.1	87.8

GO-R800-vedotin is stable in human, cyno and mouse plasma

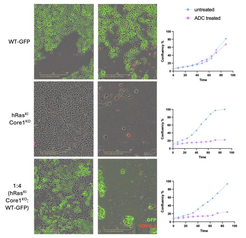
In vitro cytotoxicity

ADC	EC50	
	MCF7M	PANC1M
R800 vedotin	0.48 nM	1.18 nM

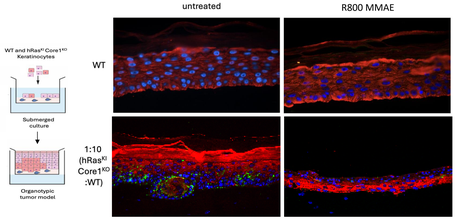
Potent activity against breast and pancreatic cancer cells.

Bystander effect in N/TERT cells analysed by Incucyte live-cell imaging. ADC kills WT-GFP target negative cells when co-cultured with target positive cells.

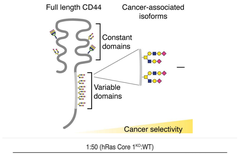
Bystander killing

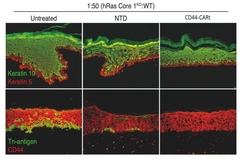


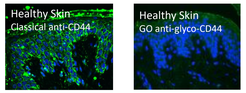
Human organotypic skin tumor model

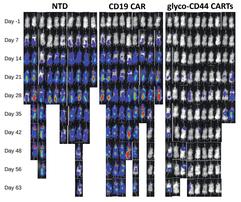


Efficacy of glyco-CD44 GO-CARTs





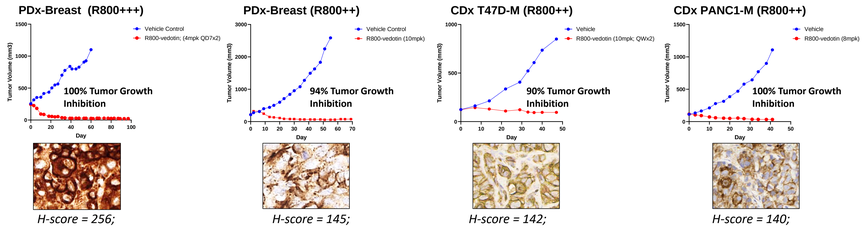




CARTs derived from GO-glyco-CD44 targeting Tn-CD44 show high cancer specificity in human 3D skin models and murine CDX models[1]. A, Illustration of CD44. **B,** immunofluorescence of healthy human skin. **C**, Human Cancer Tissue models treated with GO-glyco-CARTs. **D,** Luminescence images of mice inoculated with Jurkat cells and treated with NTD, CD19, or GO-glyco-CARTs.

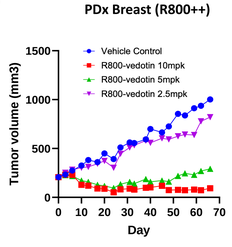
Efficacy in PDx/CDx models R800-vedotin

PDx/CDx models with variable R800 expression levels



Model	Target Expression	H-Score	Receptor Count	TGI
PDx-Breast	High (+++)	256	857K	100%
PDx-Breast	Medium (++)	145	150K	94%
CDx-Breast (T47D-M)	Medium (++)	142	140K	90%
CDx-Pancreas (PANC1-M)	Medium (++)	140	191K	100%

Minimum effective dose



Determination of minimum effective dose (MED): R800-vedotin shows a minimum effective dose (MED) in PDx-Breast (R800++).

Summary

- **GO-R800 is a Tn-glycopeptide specific antibodies with sub-nM binding affinities and exquisite cancer specificities.**
- **GO-R800 is selective for multiple cancer types, including triple-negative breast, lung and metastatic cancers.**
- **ADCs were produced using site-specific DAR2.**
- **MMAE was conjugated via mc-vc-PAB cleavable linker.**
- **R800-vedotin shows potent activity in vivo (MED ~3-4mg/kg).**
- **Tn-CD44 mAb is selective for multiple cancer, including head and neck cancer and shows efficacy in vivo and safety in human 3D cancer tissue models**

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