Status-agnostic therapy of breast cancer using antibodies targeting O-glycosylated proteins

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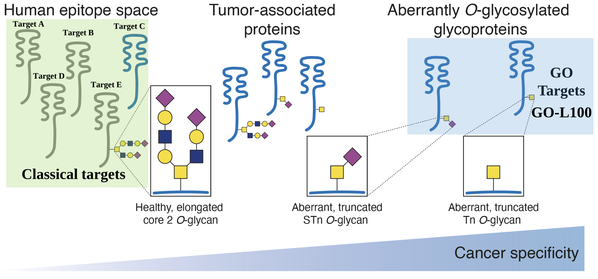
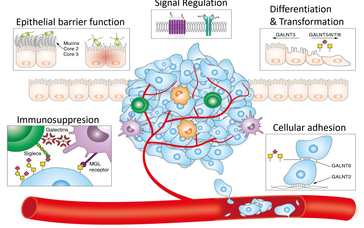
GOTx glyco-platform

Revitalizing classical cancer targets with novel GO glyco-targets



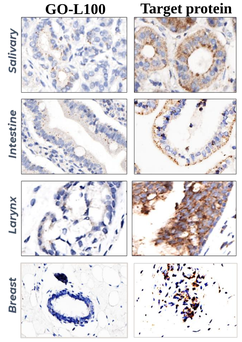
Truncated O-glycans drive tumor formation

- Cancer growth
- Cancer invasion
- Cellular adhesion
- Stem cell characteristics
- Differentiation and cell death

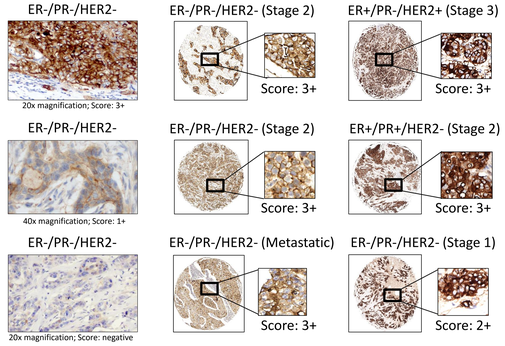


GO-L100 selectively targets breast cancer tissue

Normal Tissue



Cancer Tissue



GO-L100 Prevalence in Breast Cancer

Tissue	3+/2+	1+	Total
Breast Cancer (all subtypes, all stages)	20% (17/85)	39% (33/85)	59% (50/85)
Normal	0% (0/96)	0% (0/96)	0% (0/96)

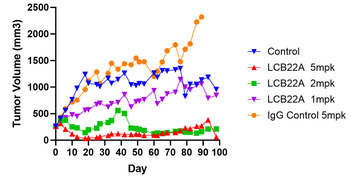
3+/2+ = >25% of cancers cells with positive stain.
1+ = 0-25% of cancer cells with positive stain

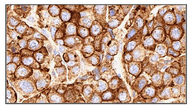
Positive tissue defined by efficacy in PDx

L100 selectively binds to breast cancer tissue. L100 binds to ~59% of all breast cancer tissue (all stages) independent of Her2/ER/PR/Trop2 status. L100 does not bind to normal tissue.

Efficacy in PDX models

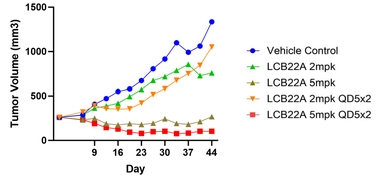
PDx-Breast High Target Expression (+++)

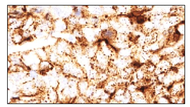




H-score = 229; 224K receptors

PDx-Breast Moderate Target Expression (++)





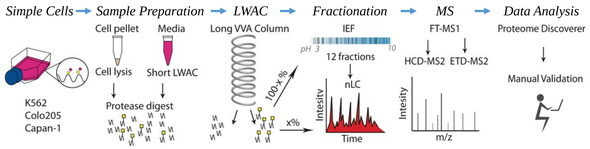
H-score = 145; 90K receptors

Model	Target Expression	Receptors (per cell)	TGI	Complete Response
PDx Breast	High (+++)	224K	98%	5/6 mice
PDx Breast	Moderate (++)	90K	93%	3/6 mice

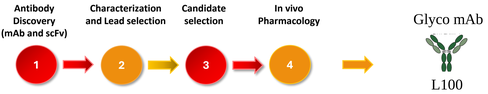
Potent ADC efficacy in multiple tumor models with moderate and high target expression. The properties of PDx models used for xenograft studies were analyzed. GO-L100 expression (receptor counts) was assessed by IHC calibrated by flow cytometry (FACS) in cultured cells; representative images are shown at 40X magnification. The efficacy of LCB22A (GO-L100 MMAE) was tested in Breast PDx xenograft models. All mice were given either a single dose or double dose of ADC at 5mg/kg (DAR 4).

Strategy

Antigen Discovery

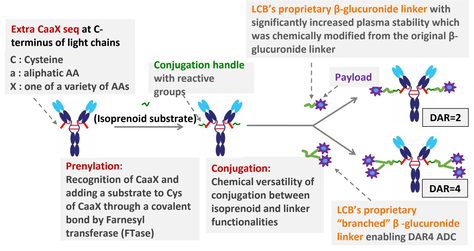


Antibody Discovery



ADC platform – *ConjuAll™*

ConjuAll™: site-specific, homogeneous, and non-reversible conjugation



In vitro activity

In vitro Cytotoxicity (cancer cells)

ADC	In vitro cytotoxicity in cancer cells (EC50)	
	*MCF7M	**T47DM
LCB22A	63 nM	4.3 nM

*MCF7M: Gene modified Tn-positive MCF7, **T47DM: Gene modified Tn-positive T47D

In vitro Cytotoxicity (normal cells)

ADC	In vitro cytotoxicity in normal cells (EC50)		
	Fa2N4 (Liver)	HK2 (Kidney)	hPBMC (blood)
LCB22A	>1000 nM	501 nM	574 nM

In vitro cytotoxicity of LCB22A (GO-L100 MMAE). LCB22A shows potent activity against breast cancer cell. LCB22A shows low toxicity to normal cell lines

Summary

- GO-L100 is a Tn-glycopeptide-specific antibody with sub-nM affinity and high cancer specificity
- Selective for ~59% of breast cancers, including triple-negative and metastatic types
- ADCs were generated using LigaChem Biosciences' ConjuAll™ technology
- MMAE was conjugation via site-specific, beta-glucuronidase-cleavable linker
- LCB22A (GO-L100 MMAE) demonstrated potent in vivo activity (MED ~2 mg/kg)
- LCB22A (GO-L100 MMAE) was well-tolerated in cynomolgus toxicity studies.

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