Treatment of solid tumors with antibody drug conjugates targeting aberrant O-glycoproteins

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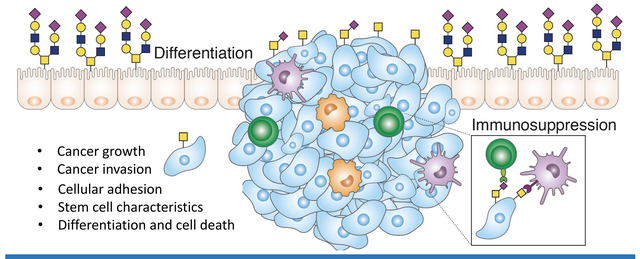
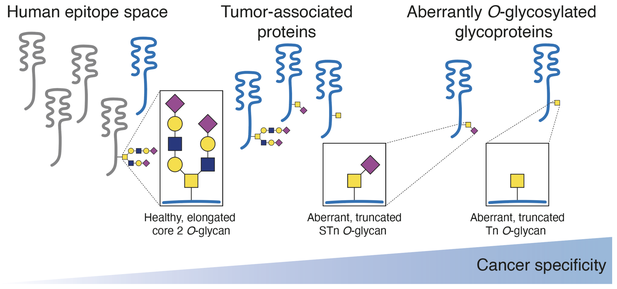
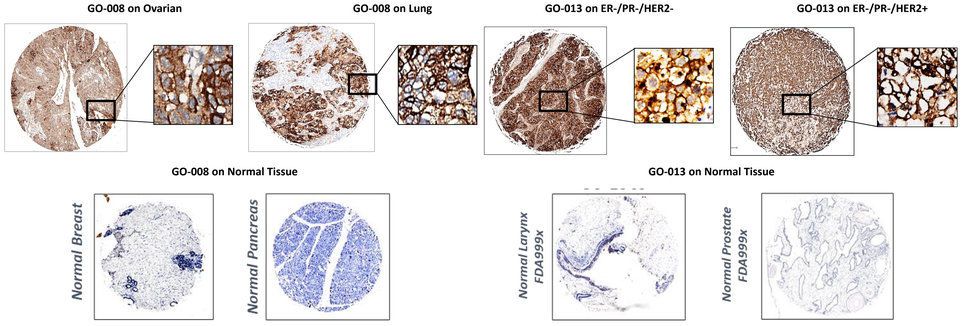
O-glycans affect cancer hallmarks



Cancer specific aberrant *O*-glycans



GO-008 & GO-013 selectively target cancer tissues



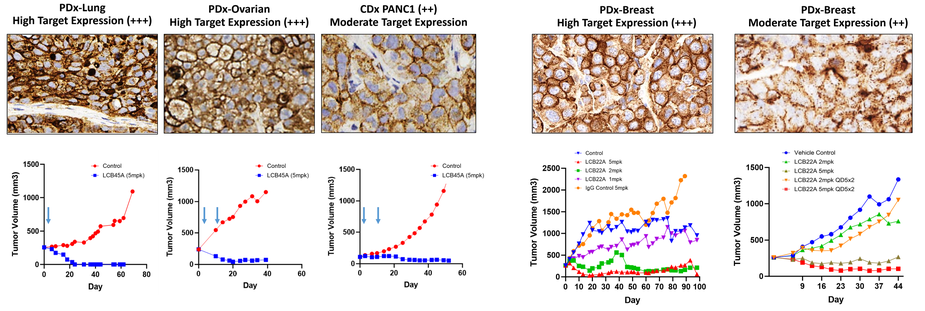
GO-008 IHC of cancer and normal tissue. GO-008 selectively stains the surface of cancer cells."Positive" tissue includes moderate (++) and HIGH (+++) target expression.

Tissue	Positive Surface Stain
Ovarian Cancer	**33%** (43/130)
Colon Cancer	**19%** (14/72)
Pancreatic Cancer	**15%** (15/101)
Lung Cancer	**17%** (20/120)
Cholangiocarcinoma	**14%** (11/80)
Normal Tissue	**0%** (0/96)

GO-013 IHC of cancer and normal tissue. GO-013 selectively stains the surface of cancer cells. "Positive" tissue includes moderate (++) and HIGH (+++) target expression.

Tissue	Positive Surface Stain
Breast Cancer (non-metastatic; IDC, including TNB)	**28%** (24/85)
Lung	**13%** (15/120)
Normal	**0%** (0/96)

Potent efficacy in PDX models

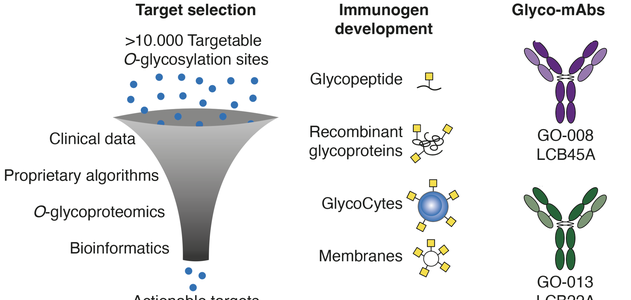


Model	Target Expression	Receptors (per cell)	TGI	Complete Response
PDx Lung	High (+++)	800K	100%	5/5 mice
PDx Ovarian	High (+++)	600K	>95%	2/5 mice
PANC1 CDx	Moderate (++)	130K	100%	6/6 mice

Model	Target Expression	Receptors (per cell)	TGI	Complete Response
PDx Breast	High (+++)	270K	98%	5/6 mice
PDx Breast	Moderate (++)	90K	93%	3/6 mice

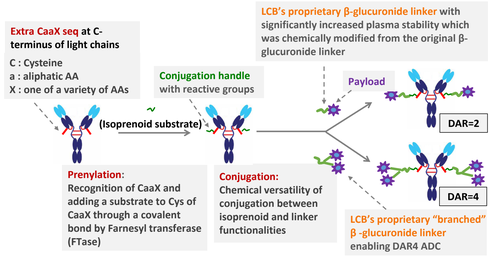
Potent ADC efficacy in multiple tumor models with moderate and high target expression. The properties of PDx and CDx models used for xenograft studies were analyzed. GO-008 and GO-013 expression (receptor counts) was assessed by IHC calibrated by flow cytometry (FACS) in cultured cells; representative images are shown at 40X magnification. The efficacy of LCB45A (GO-008) was tested in in Lung and Ovarian PDx and Pancreatic CDx models. The efficacy of LCB22A (GO-013) was tested in Breast PDx xenograft models. All mice were given either a single dose or double dose (arrow heads) of ADC at 5mg/kg (DAR 4).

Strategy



ADC platform - *ConjuAll*™

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



In vitro cytotoxicity

ADC	In vitro cytotoxicity in cancer cells (EC50)				
	MCF7M	T3M4M	OVCARM	T47DM	PANC1M
LCB45A	0.92 nM	8 nM	4.9 nM	1.3 nM	2.8 nM
LCB22A	63 nM	N/A	N/A	4.3 nM	N/A

ADC	In vitro cytotoxicity in normal cells (EC50)		
	Fa2N4 (Liver)	HK2 (Kidney)	hPBMC (blood)
LCB45A	>1000 nM	>1000 nM	741 nM
LCB22A	>1000 nM	501 nM	574 nM

In vitro cytotoxicity of LCB45A (GO-008) and LCB22A (GO-013). LCB45A shows potent activity over multiple cancer cell lines and LCB22A shows potent activity against breast cancer cell. LCB45A and LCB22A shows low toxicity to normal cell lines

Summary

- GO-008 and GO-013 are Tn-glycopeptide specific antibodies with sub-nM binding affinities and exquisite cancer specificities.
- GO-008 targets multiple solid tumor carcinomas, including ovarian, CRC, pancreatic, lung, and cholangiocarcinoma.
- GO-013 is selective for ~25% of all breast cancer types, including triple-negative and metastatic cancers.
- ADCs were produced using LigaChem Biosciences' *ConjuAll*™ technology
- The microtubule disrupting payload MMAE was conjugated via a site-specific beta-glucuronidase cleavable linker
- LCB45A (GO-008 MMAE) and LCB22A (GO-013 MMAE) show potent activity in vivo (MED ~2mg/kg).
- LCB22A (GO-013) is well tolerated at 7.5 mpk in cynomolgus toxicity studies.

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