



財團法人生物技術開發中心  
Development Center for Biotechnology

# Tri-mannosyl Antibody: A Versatile Payload ADC Platform

## Development Center for Biotechnology

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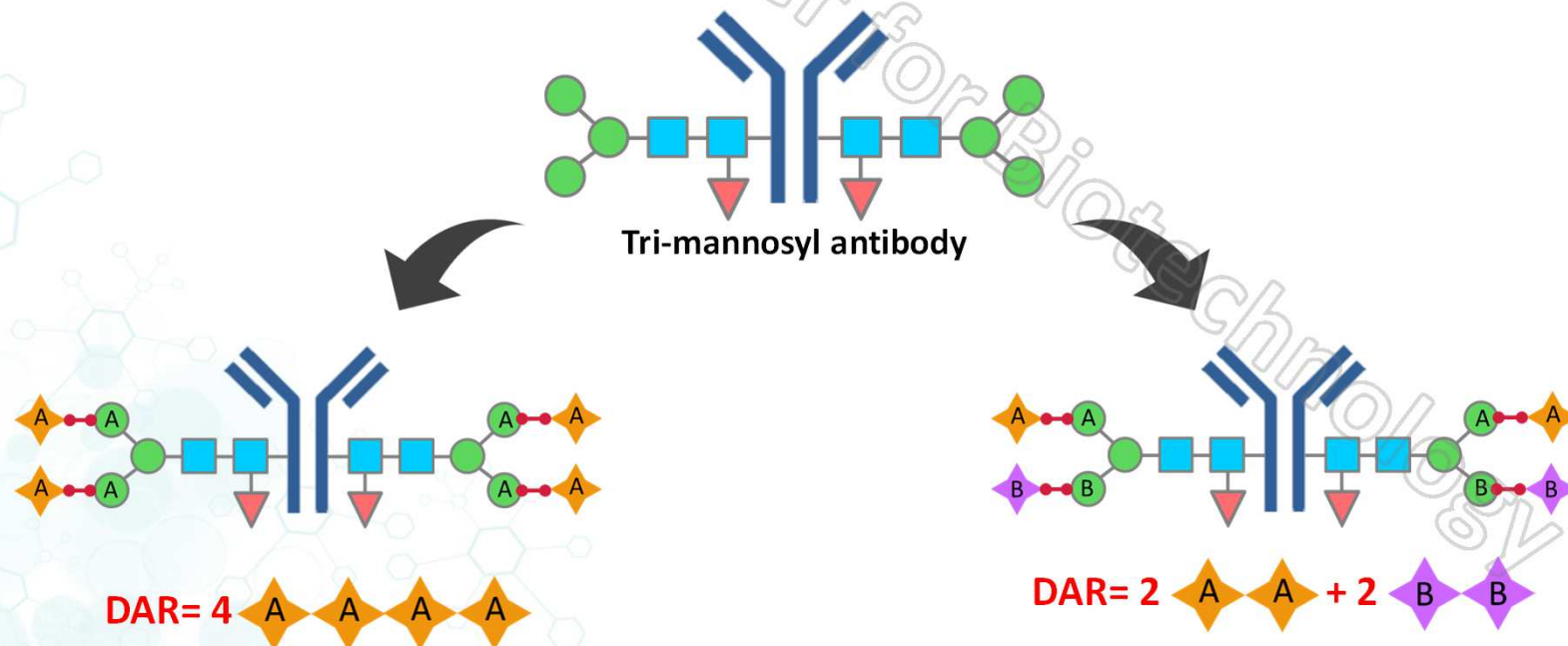
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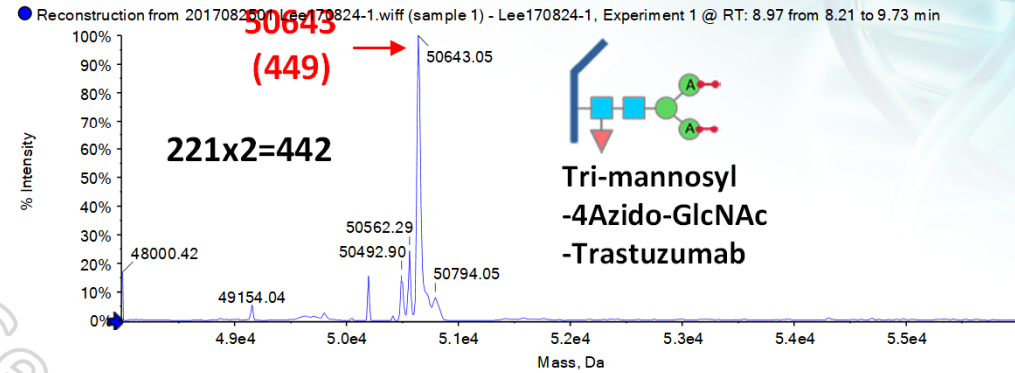
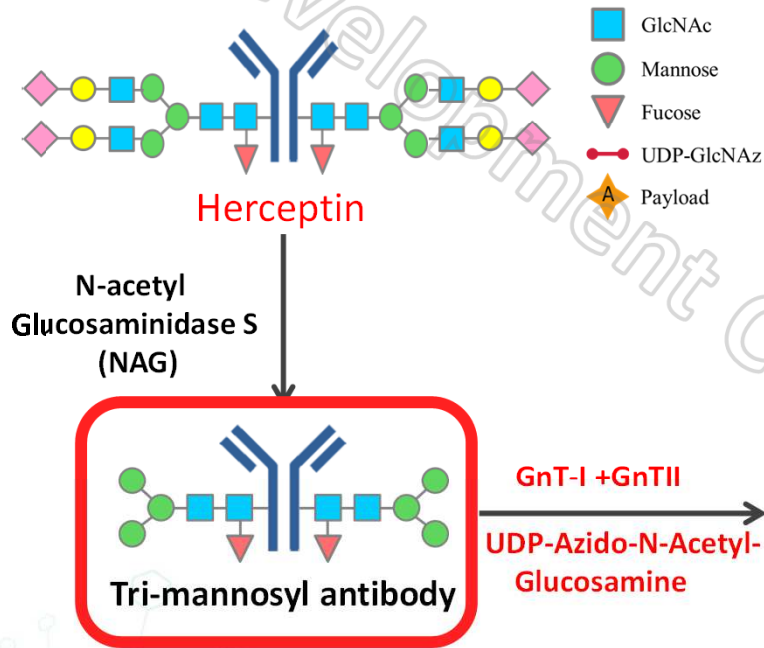


# Tri-mannosyl Antibody Drug Conjugation Platform

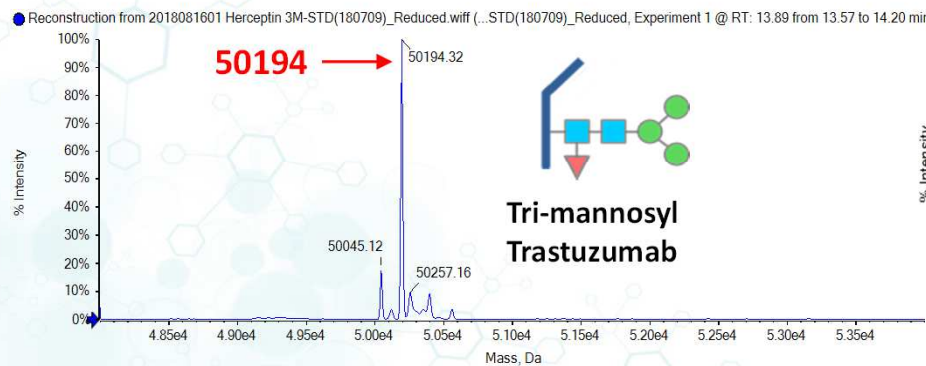
1. **Site specific** ADC at the N297 of an antibody.
2. Homogeneous **DAR** (drug antibody ratio) with **2 or 4**.
3. Homogeneous payload or dual payload: **High diversity** in cancer applications.
4. **Manufacturing condition**: liquid phase, room temperature, user friendly and within overnight.
5. Materials including tri-mannosyl antibody, GnT-1 and GnT-2 are **mass-produced** by cell line process developments.



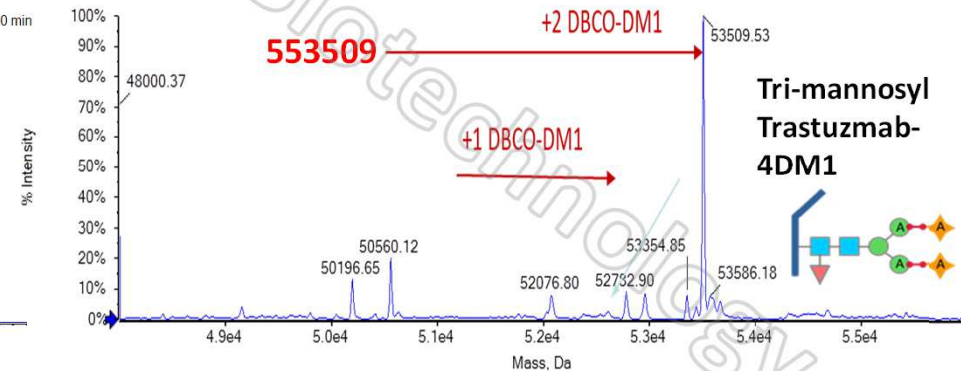
# Tri-mannosyl Trastuzumab-4DM1 Is Generated by Single Step Enzyme Process and SPAAC Reaction



Reduced Mass



Reduced Mass



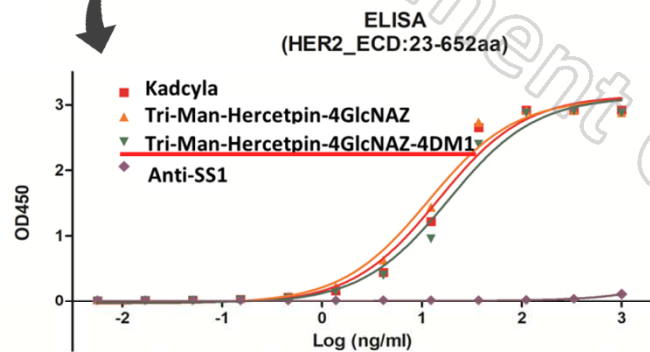
Reduced Mass



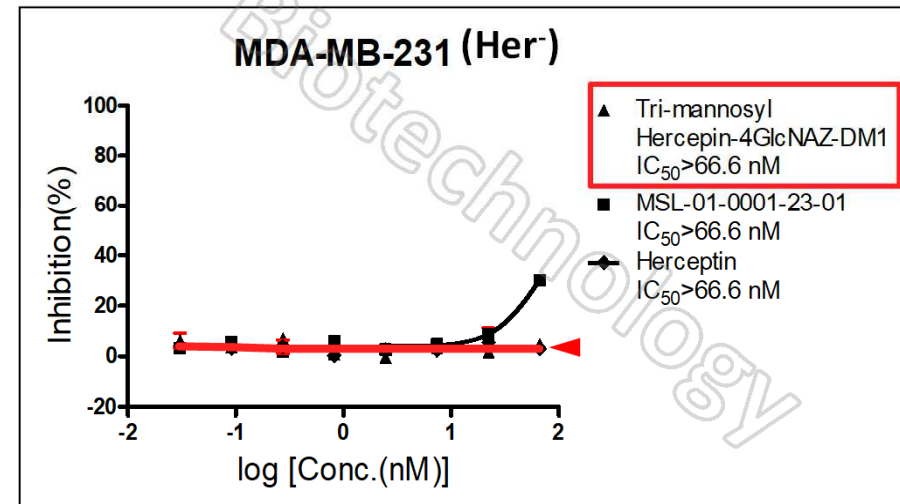
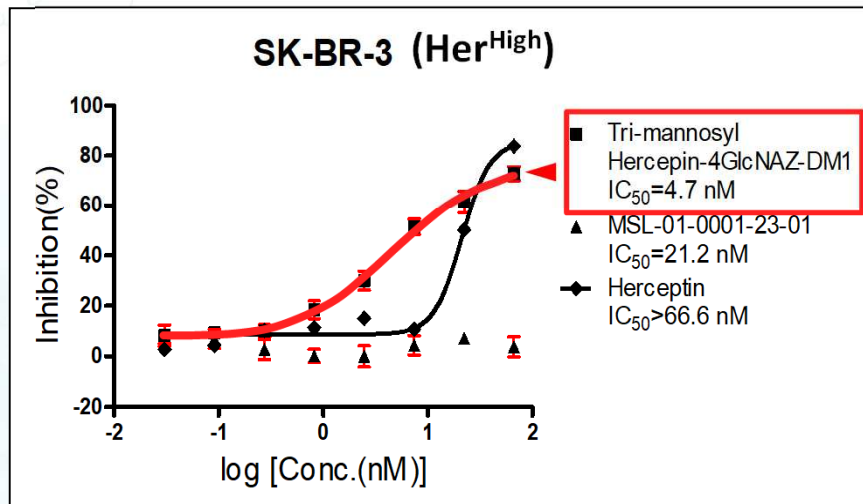
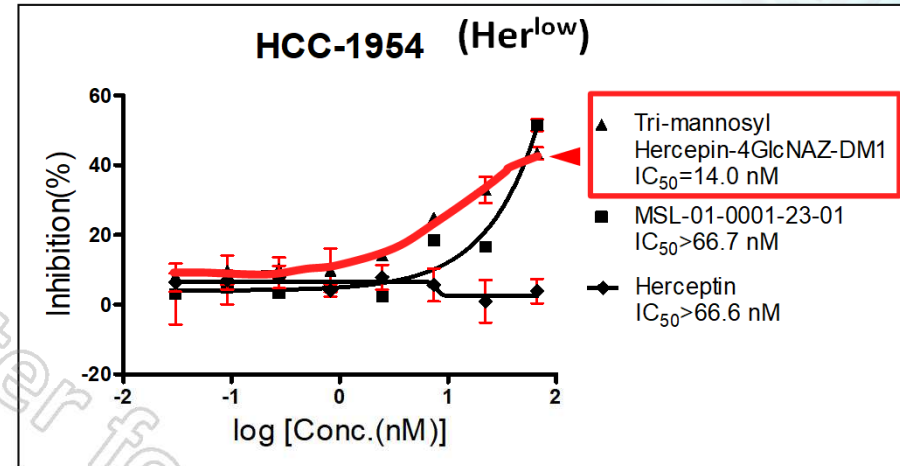
# Effective Tumor Cell Growth Inhibition by Tri-mannosyl Trastuzumab-4DM1



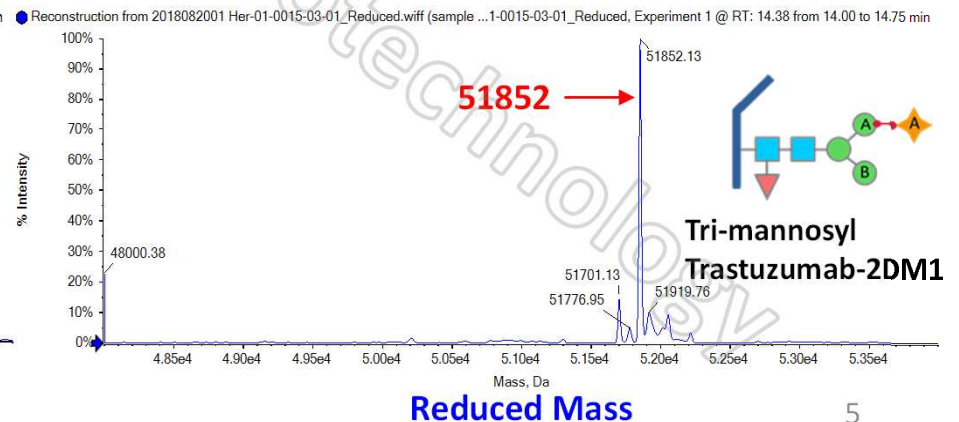
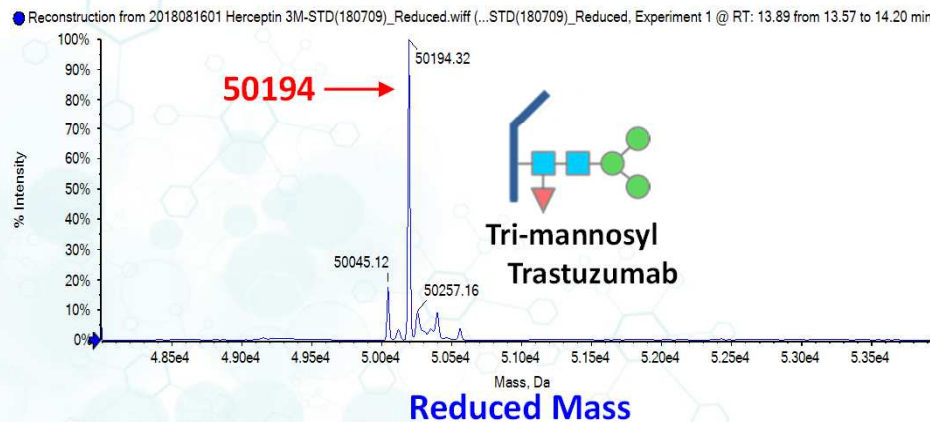
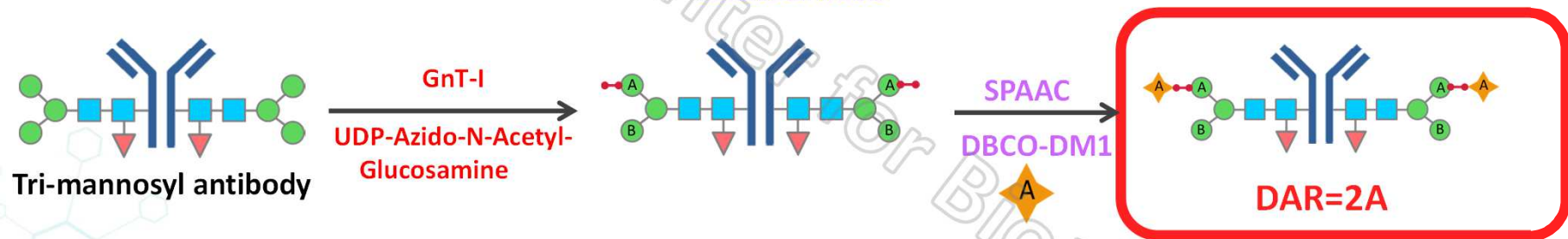
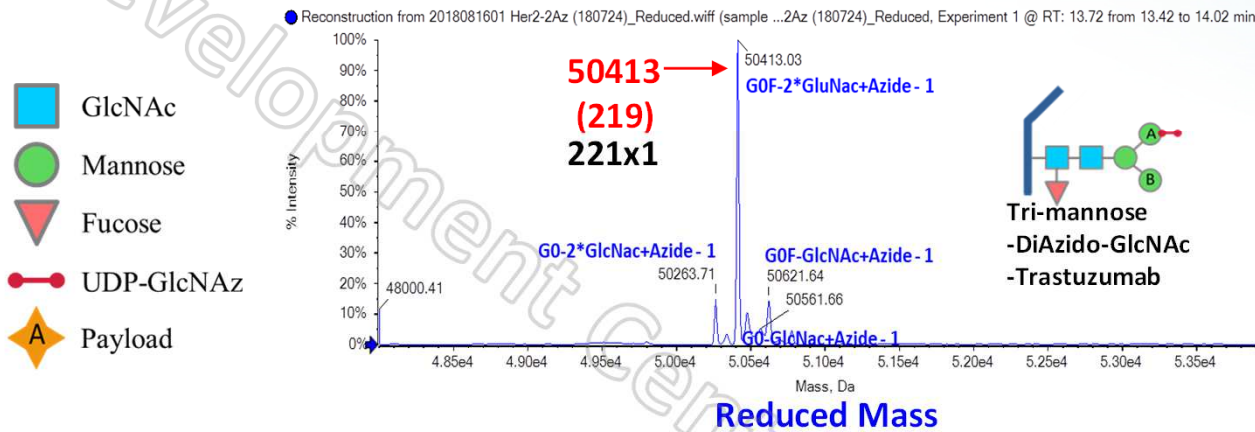
**Tri-Mannosyl-Trastuzumab-4GlcNAz-4DM1**



Name	Kadcyla	4az-HER2	4D-HER2-DM1	antiSS1
Kd (M)	9.43e-011	7.48e-011	11.87e-011	NA

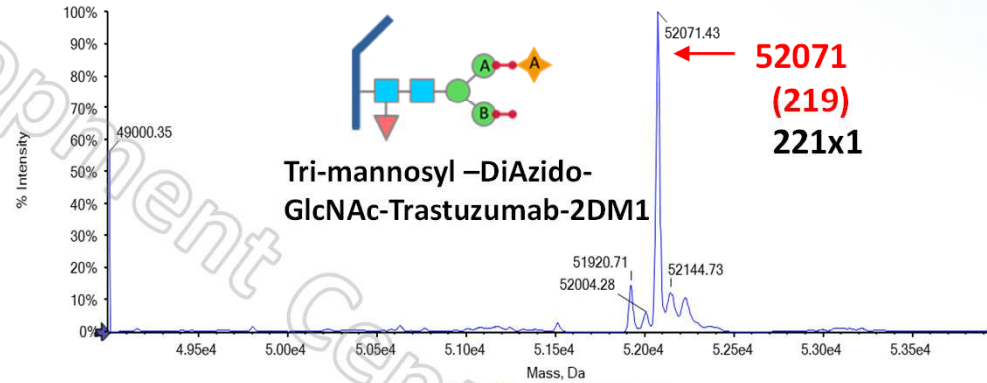


# Coupling of First Payload DM-1 by GnT-I and SPAAC Reaction

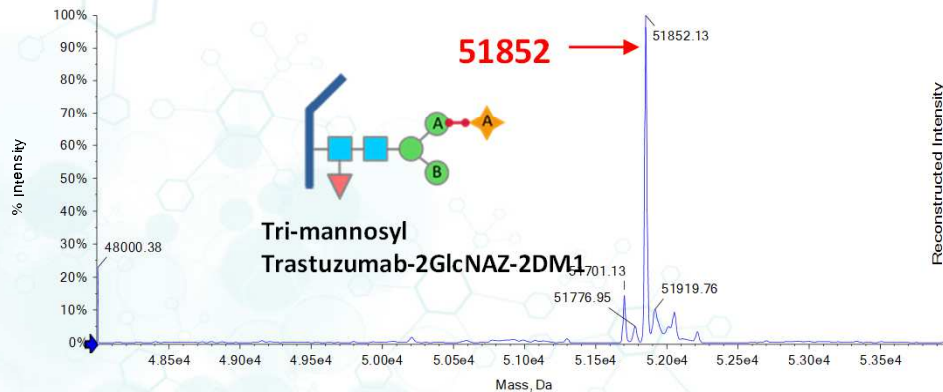
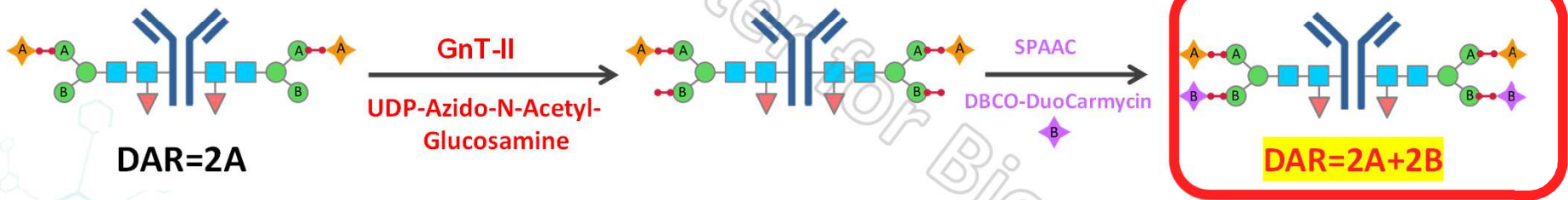


# Coupling of The Second Payload Duocarmycin by GnT-II and SPAAC Reaction

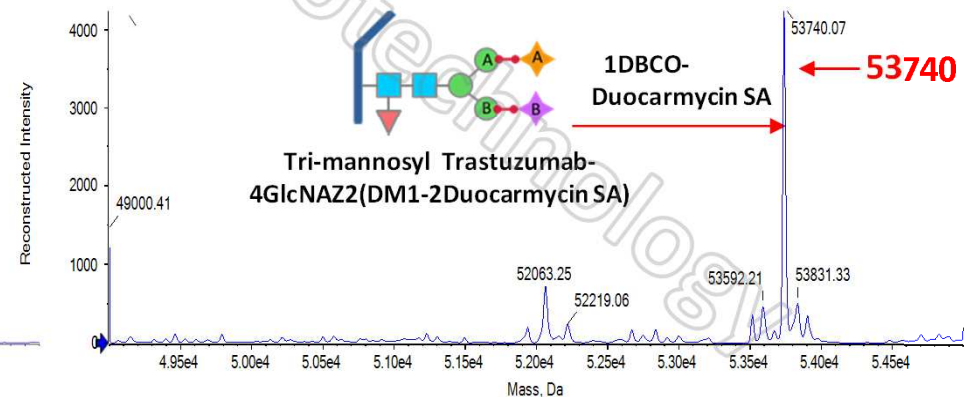
- GlcNAc
- Mannose
- ▼ Fucose
- UDP-GlcNAz
- ★ Payload



Reduced Mass



Reduced Mass

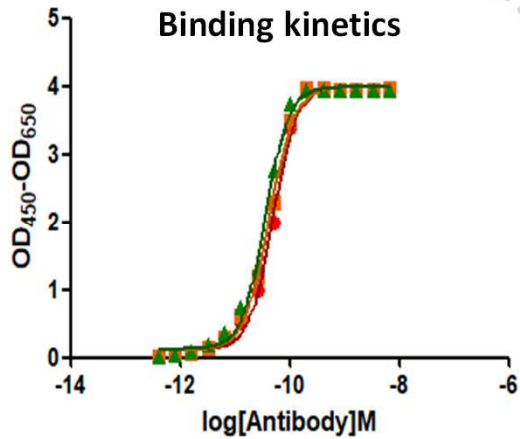
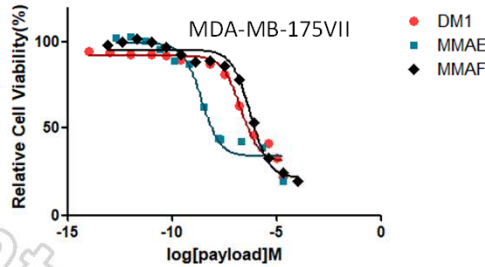
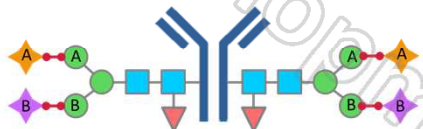


Reduced Mass

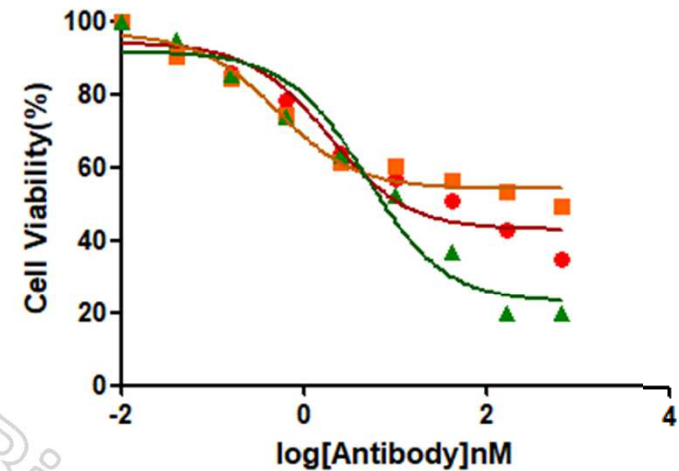


# The Dual Payload of Tri-mannosyl Trastuzumab ADC Shows Superior Potency to Kadcylla-Resistant Breast Cancer Cell Line MDA-MB-175VII

Dual payload of tri-mannosyl ADC



MDA-MB-175VII

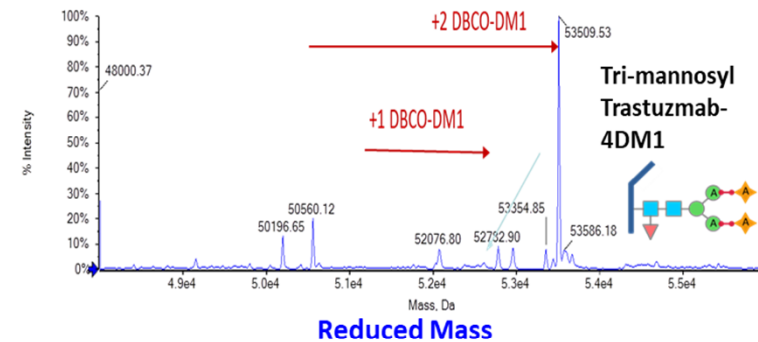


	Herceptin	Kadcylla	Tri-mannosyl-Trastuzumab-4GlcNAZ-2(DM1-2Duocarmycin SA)
LD50 (nM)	193.42	45.72	10.03
ID50 (nM)	0.52	1.92	4.91
Net killing(%)	50.9	65.37	80.13
Kd (M)	4.23e-011	4.93e-011	3.54e-011

# The Profile of Tri-mannosyl Antibody Platform

IP position	<b>WO2018126092A</b> and TW application number: <b>106146600</b>
UDP-GlcNAz transfer percentage	Over <b>95%</b>
Payload conversion rate	Over <b>95%</b> for homogeneous and <b>90%</b> for dual payloads
Yield	about <b>60%</b> for homogeneous payload
Optimal temperature	Not determined but the <b>room temperature</b> is satisfied
Conversion enzyme activity	GnT-1 (limited step)= <b>1.5 g antibody /hr/mg</b> (UDP-GlcNAz as substrate)
Scale	<b>200 mg level</b> , <b>1 g level</b> (2019)
Tri-mannosyl antibody production	CHO cell over-expressed N-acetylglucosaminidase is in the final evaluation
GnT-1 and GnT-2 production	CHO cell over-expressed both enzymes are under way

## Homogeneous Payload with DAR4



## Dual Payloads with DAR4

