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

# Anti-Globo H ADC against Cancer

Institute of Pharmaceutics
Development Center for Biotechnology

**Presenter : Shih-Hsien Chuang Ph.D.**
**Adam Deyao Wang**

OOOO/OO/OO Updated

# Development Center for Biotechnology, DCB

400+

**RD/BD professionals** serving as the innovation hub for early drug development.

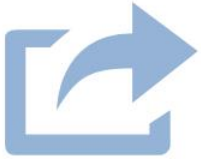
36

**Founded in 1984**, non-profit RD institution subsidized by the Ministry of Economic Affairs of Taiwan.

1200+

The premium drug development entity and connected with **1200+ biotech** of TW.

25



20+ out licensed assets and 5 Spin offs under **out-licensing** and **co-development** model.

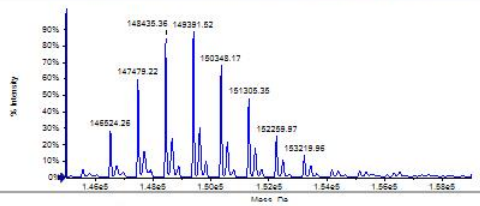
# Project Team

T
E
A
M

**Project leader**
Simon Shih-Hsien Chuang, Ph.D
Yi-Jen Chen, Ph.D.
Synthetic Chemistry & Conjugation

**Biology**
Shih-Chong Tsai, Ph.D.
Monoclonal Antibody
Ying-Shuan E. Lee, Ph.D.
Cytotoxicity
Chuan Lung Hsu, Ph.D.
Binding & Internalization

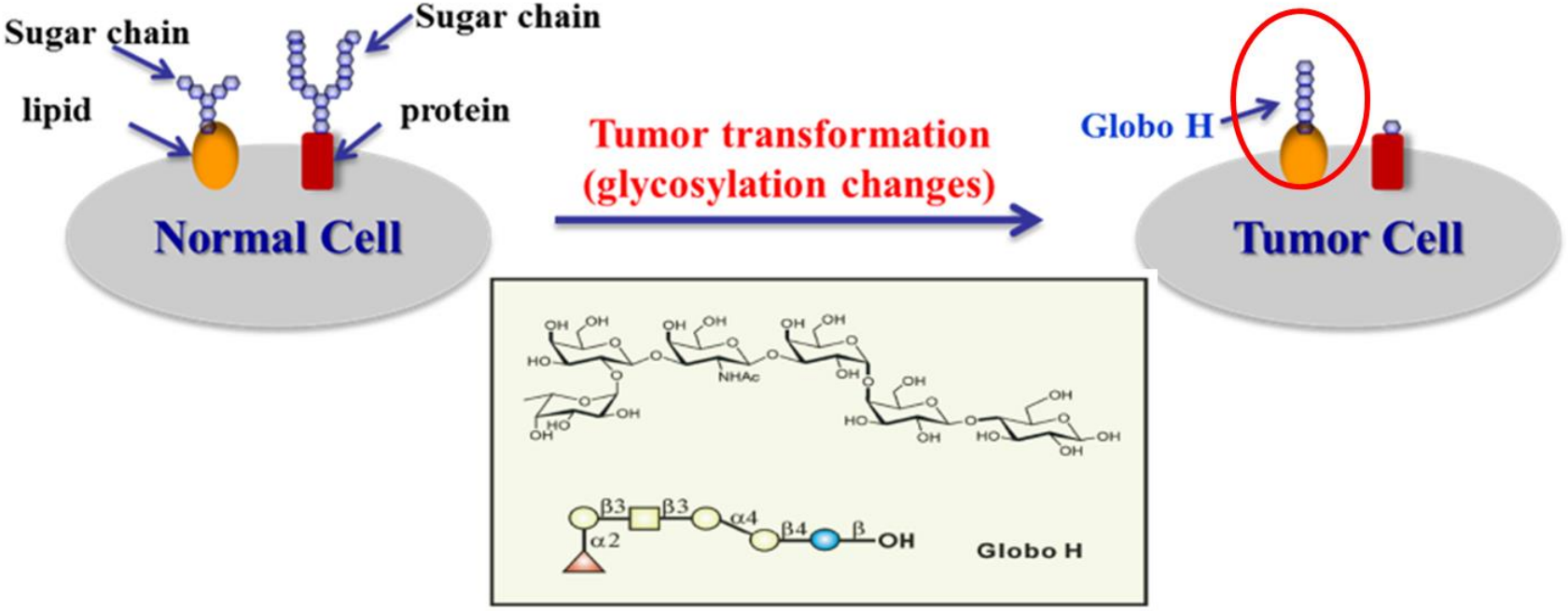
**DMPK**
Tzungjie Yang, Ph.D.
LC/MS Characterization




***In vivo* Pharmacology**
Mei-Ling Hou, Ph.D
Animal Models

# Globo H : A Potential Target against Cancer

Globo H is a glycolipid antigen highly expressed in many cancer cell surface.




Fuc$\alpha$1 → 2Gal$\beta$1 → 3GalNAc$\beta$1 → 3Gal$\alpha$1 → 4Gal$\beta$1 → 4Glc-

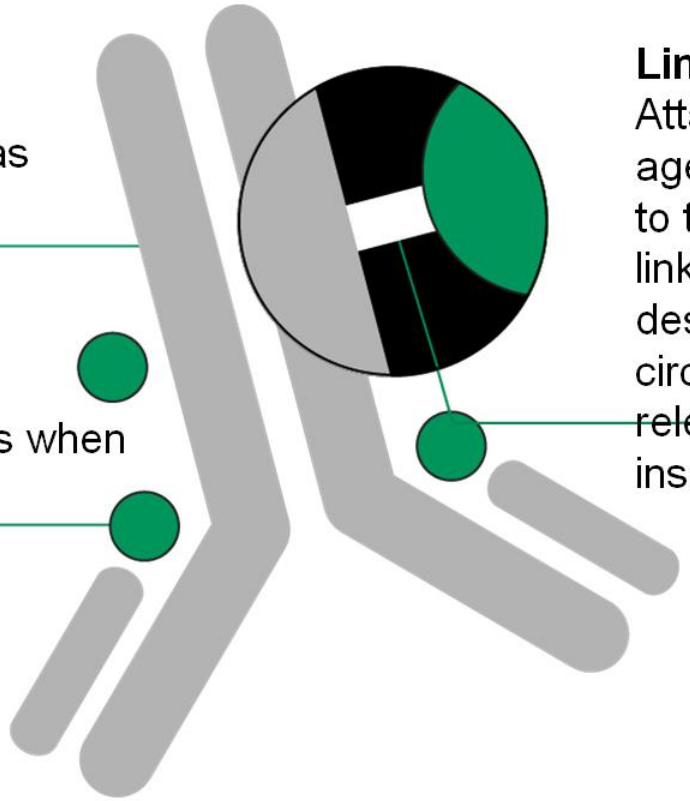
| Tumor | Brain | Lung | Breast | Mouth | Esophagus | Stomach | Liver |
|---|---|---|---|---|---|---|---|
| Cell-lines | 6/17 | 13/20 | 14/23 | 11/13 | 2/2 | 6/6 | 9/10 |
| **Tumor** | **Bile duct** | **Pancreas** | **Colon** | **Kidney** | **Cervix** | **Ovary** | **Prostate** |
| Cell-lines | 3/5 | 6/8 | 6/7 | 5/6 | 1/4 | 2/9 | 1/4 |


Proc Natl Acad Sci U S A. 2008 August 19; 105(33): 11661–11666.
Proc Natl Acad Sci U S A. 2014 February 18, 111(7): 2482–2487.

# Antibody-Drug Conjugate (ADC)

**Antibody**
Specific for a tumor-associated antigen that has restricted expression on normal cells.

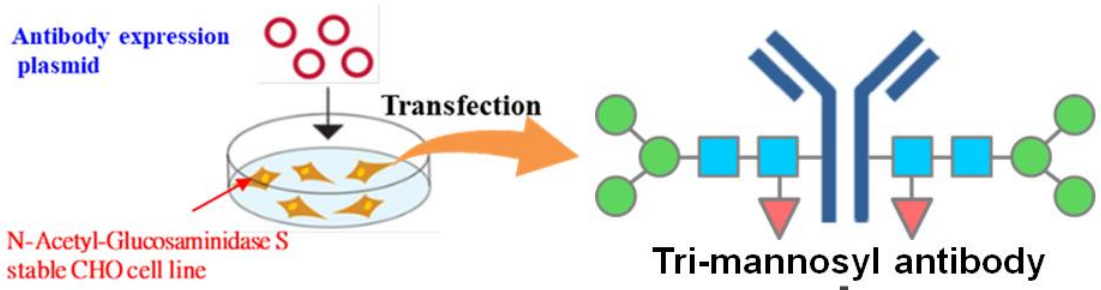
**Cytotoxic agent**
Designed to kill target cells when internalized and released.



**Linker**
Attaches the cytotoxic agent to the antibody. Newer linker systems are designed to be stable in circulation and release the cytotoxic agent inside targeted cells.

**References: 1.** Carter PJ et al. *Cancer J.* 2008;14(3):154-169. **2.** Senter PD. *Curr Opin Chem Biol.* 2009;13(3):235-244. **3.** Polson AG et al. *Cancer Res.* 2009;69(6):2358-2364.

# Tri-mannosyl ADC Platform




GnT-I : N-Acetyl glucosamin transferase I
GnT-II : N-Acetyl glucosamin transferase II
UDP-GlcNAz : Azido-N-acetylglucosamine

One-step : DAR4 with homogenous payload

Sequential : DAR4 with Dual payloads

GnT-I and GnT-II

UDP-GlcNAz

GnT-I

Payloads A

UDP-GlcNAz

GnT-II

Payloads B

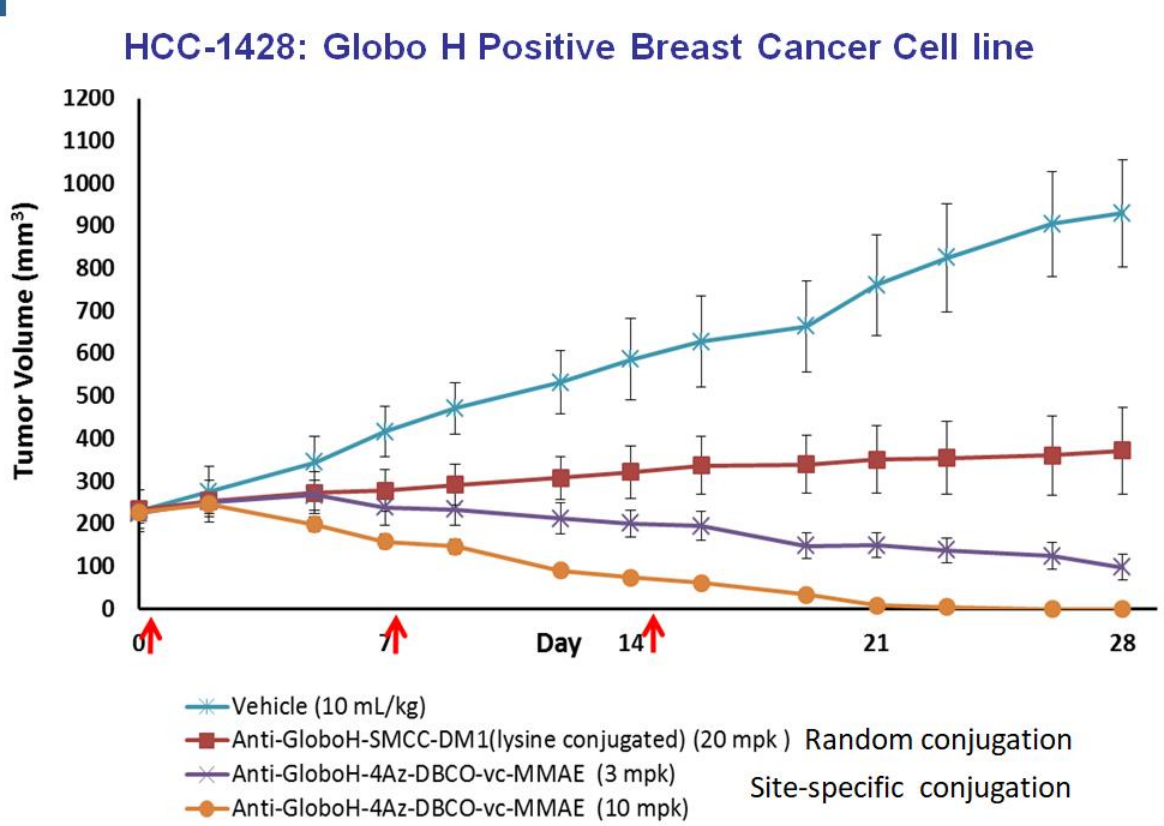
DAR= 4

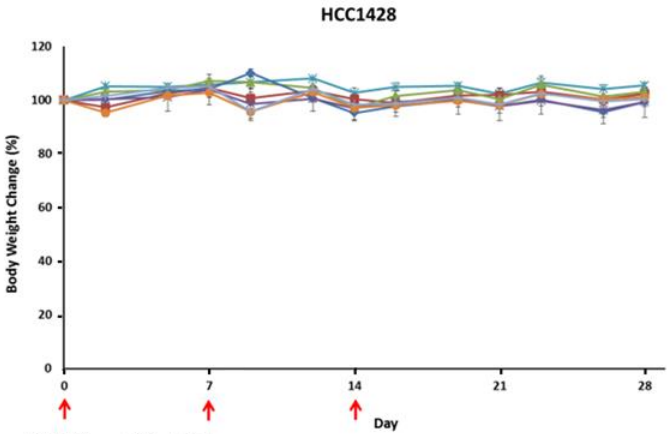
DAR= 2 + 2

# Summary of Trimannosyl ADC Platform

| | |
|---|---|
| **IP position** | **WO2018126092A** and<br>TW patent number: **106146600** |
| **UDP-GlcNAz transfer percentage** | Over **95%** |
| **Payload conversion rate** | Over **95%** for homogeneous and **90%** for dual payloads |
| **Yield** | about **60%** **for homogeneous payload** |
| **Optimal temperature** | Not determined but the **room temperature** is satisfied |
| **Conversion enzyme activity** | GnT-1 (limited step)=**39mg antibody /hr/mg**<br>(UDP-GlcNAZ as substrate) |
| **Scale** | **10 g** level (2020) |
| **Tri-mannosyl antibody production CHO cell line** | Over 95% purity of Tri-mannosyl antibody . |
| **GnT-1 and GnT-2 production** | CHO cells over-expressed both enzymes are under way. |

# Trimannosyl anti-Globo H ADC showed Great Antitumor Activity in 3 mpk

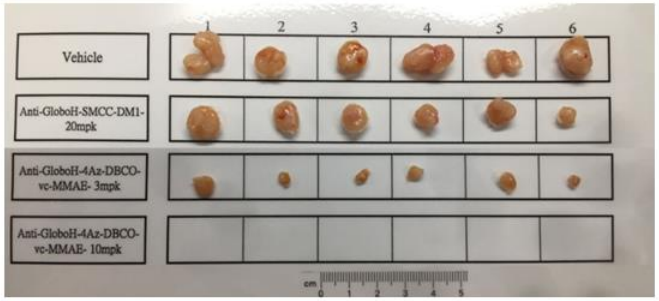



TGI : 68.7%

TGI : 91.4%

TGI : 100%




- Trimannosyl anti-Globo H ADCs showed great antitumor activity in 3 mpk and 10 mpk without any death or body weight loss.
- The six mice in trimannosyl anti-Globo H ADC 10 mpk group showed complete tumor remission and no any tumor regression after 60 days.

# Early Toxicity Study of Anti-Globo H ADC

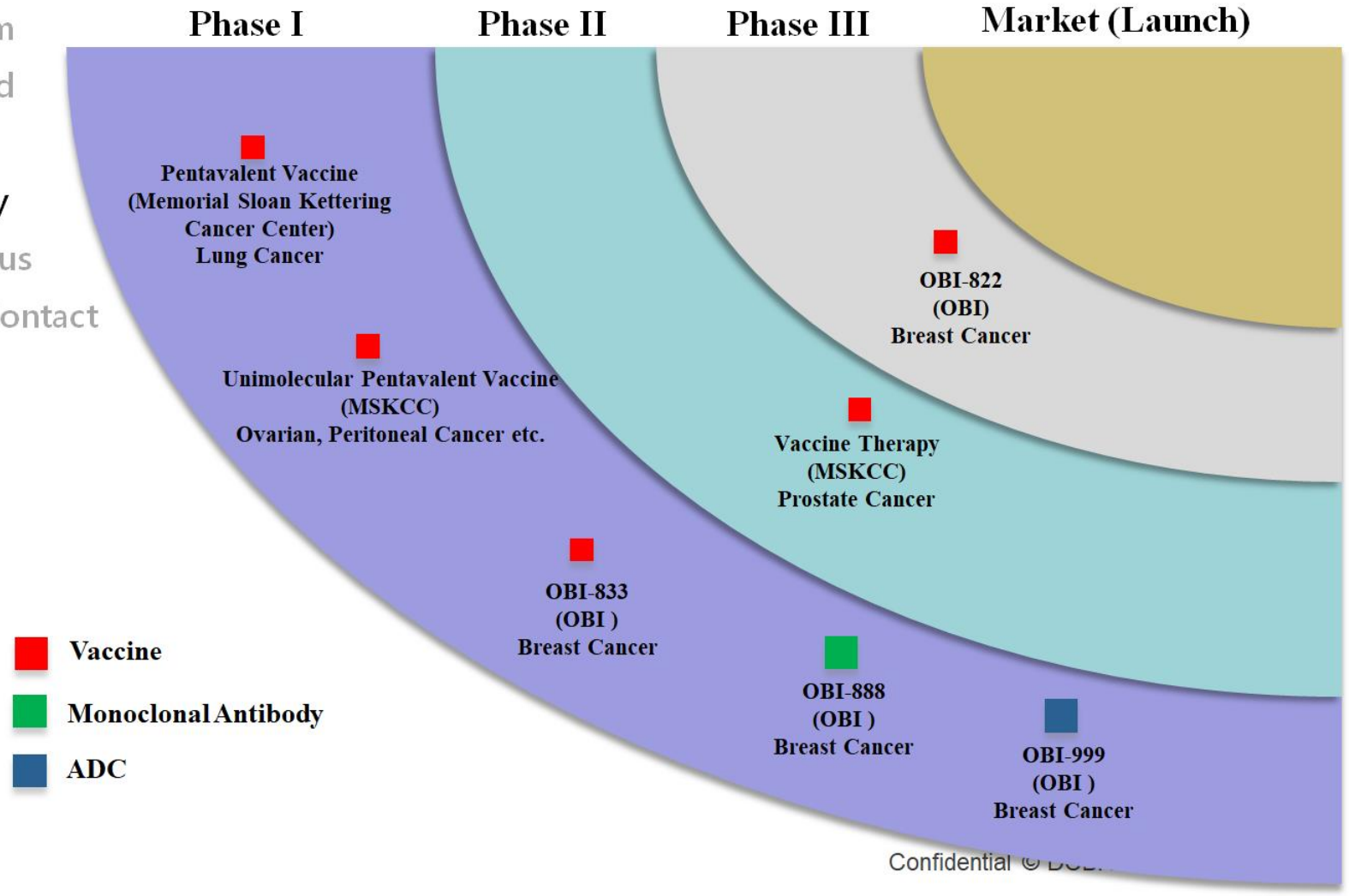
| Group | Treated | No. of Animals (Female/BALB/c) |
|---|---|---|
| Blank Control | Day 0 | 3 |
| Trimannosyl anti-Globo H-4MMAE | 30 mg/kg IV Day 5 | 3 |
| Trimannosyl anti-Globo H-4MMAE | 30 mg/kg IV Day 12 | 3 |

- Body Weight:
  The results showed no body weight loss on ADC Groups
- Organ Weight (Heart, Lung, Liver, Spleen, Kidney):
  The results showed no organ weight loss on ADC Groups
- Hematology:
  The results showed WBC slightly decreased caused by cytotoxic drug.
  The results showed no effect on RBC, HGB, HCT, MCV and MCH.
- Liver function:
  The results showed ALT slightly increased at Day 5 and recovered at Day 12.
  The results showed AST, LDH slightly increased.

# Competitive Landscape of Globo H Products

Globo H related products in clinical trials mainly on vaccines. However, anti-Globo H ADC expected more effective and clear MOA on cancer treatment than vaccines.





# IP Protection over Anti-Globo H mAb/ADC

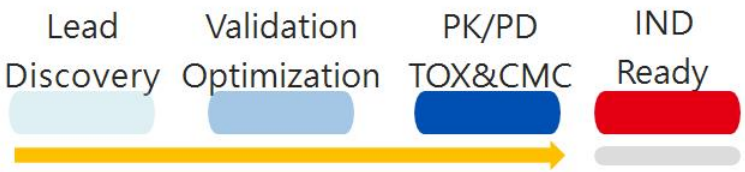
## IP

| Title | App No. and Filing (Priority) Date |
|---|---|
| HUMANIZED ANTIBODIES AGAINST GLOBO H AND USES THEREOF IN CANCER TREATMENTS | PCT/US2018/034469<br>TW Pat. App. No. 107117759<br>(Priority Date: 2017.05.24) |
| ANTIBODY-DRUG CONJUGATES CONTAINING ANTI-GLOBO H ANTIBODIES AND USES THEREOF | PCT/US2018/037912<br>TW Pat. App. No. 107120867<br>(Priority Date: 2017.06.15) |

## Partnership

- Exclusive License
- Co-development
- Other Ways of Partnership

## Development status



# Summary and Contact

## DCB's anti-Globo H ADC

- DCB's anti-Globo H ADC showed high affinity, fast internalization, good in vitro cytotoxicity.
- DCB's anti-Globo H ADC showed great tumor growth inhibition (>90%, 3 mg/kg) in HCC-1428 animal models without any body weight loss.
- DCB's anti-Globo H ADC can be prepared reproducibly at gram scale.

## BD Contact

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# Thank you for your attention