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

Asymmetric Bispecific Antibody Technology for Therapeutics

Institute of Biologics
Development Center for Biotechnology

Presenter：Jei-Hwa Yu, Ph.D.

2020/04/06 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

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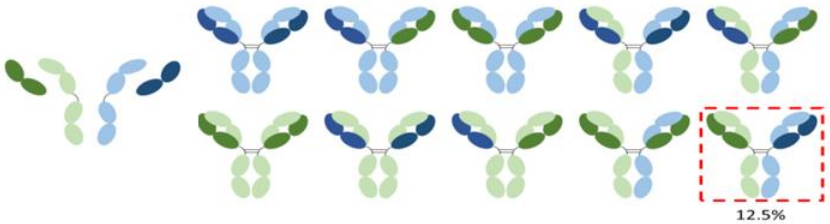
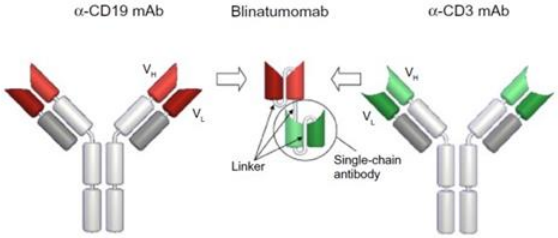
Novel Bispecific Antibody Platform

Bottlenecks of Bispecific Antibody Technologies

- Correct Pairing of the light chain to heavy chain and heavy chain to heavy chain

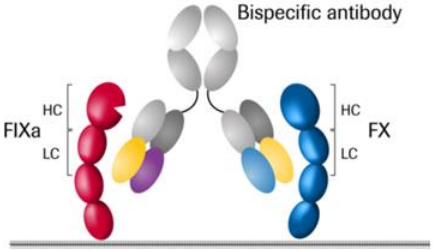


- Plasma Half-life



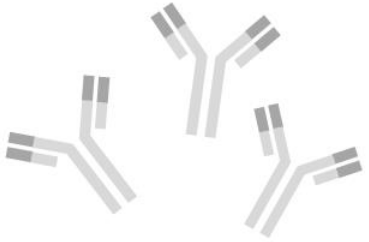
$T_{1/2}$= 1~2 Hours

- Labor-intensive Antibody Screening



Common Light Chain Technology

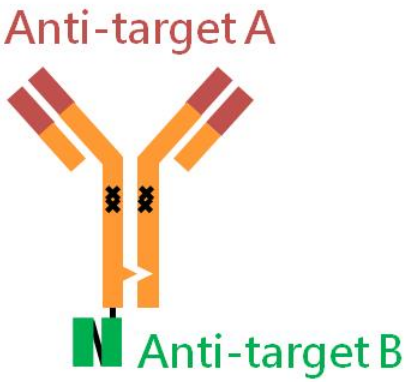
- Production Yield



Science Overview: AIS BsAb

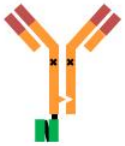
AIS BsAb

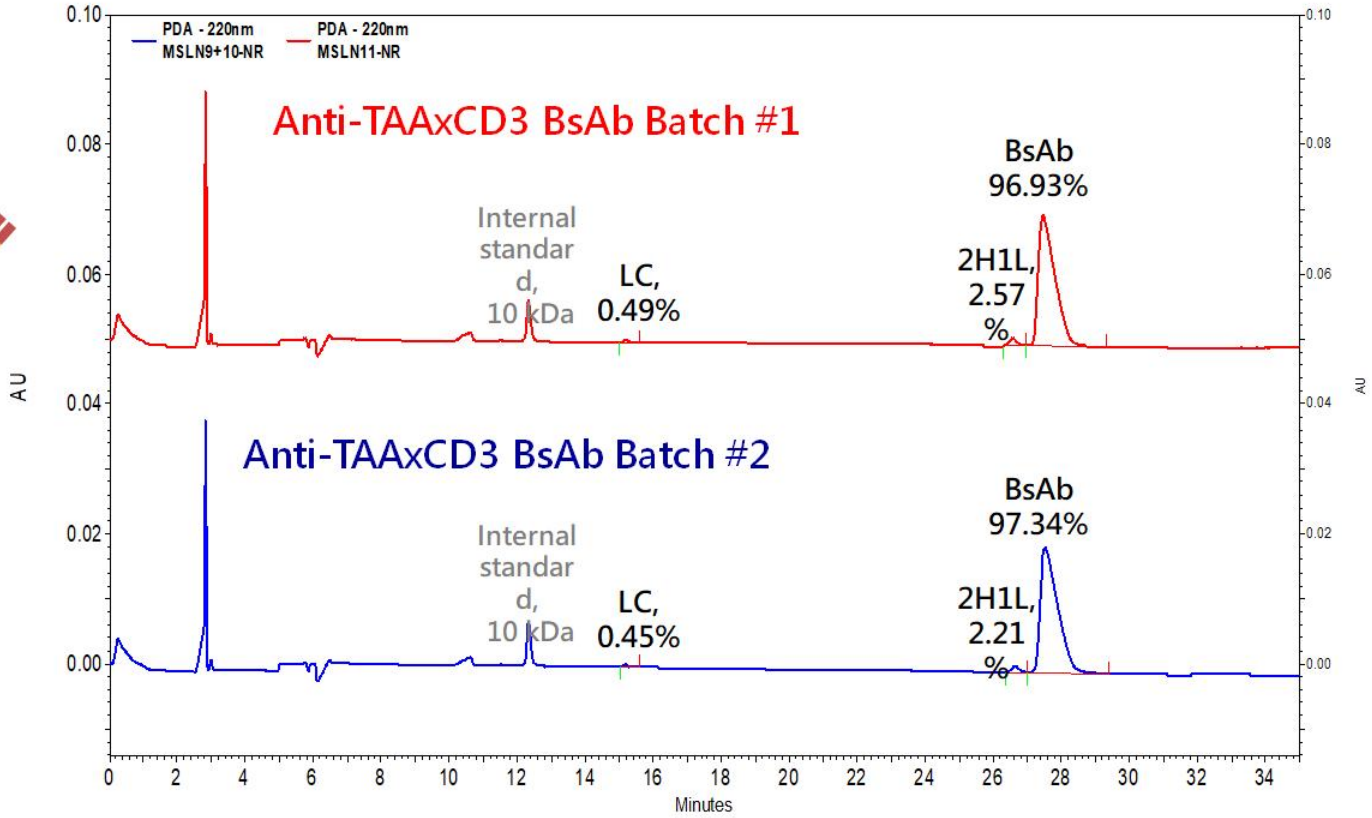
Two anti-TAAxCD3 BsAbs have been tested



1. **Easy to Make**
2. **High Correct Pairing** of the light chain to heavy chain and heavy chain to heavy chain
3. **Target cell-dependent T cell activation** (Better safety profile)
4. **Long plasma half-life** (Comparing to the fragment BsAb format)
5. **Low immunogenicity in rats** (No detectable ADA with multiple dose injections)
6. **High production yield** (Comparable to its parental monoclonal antibody)

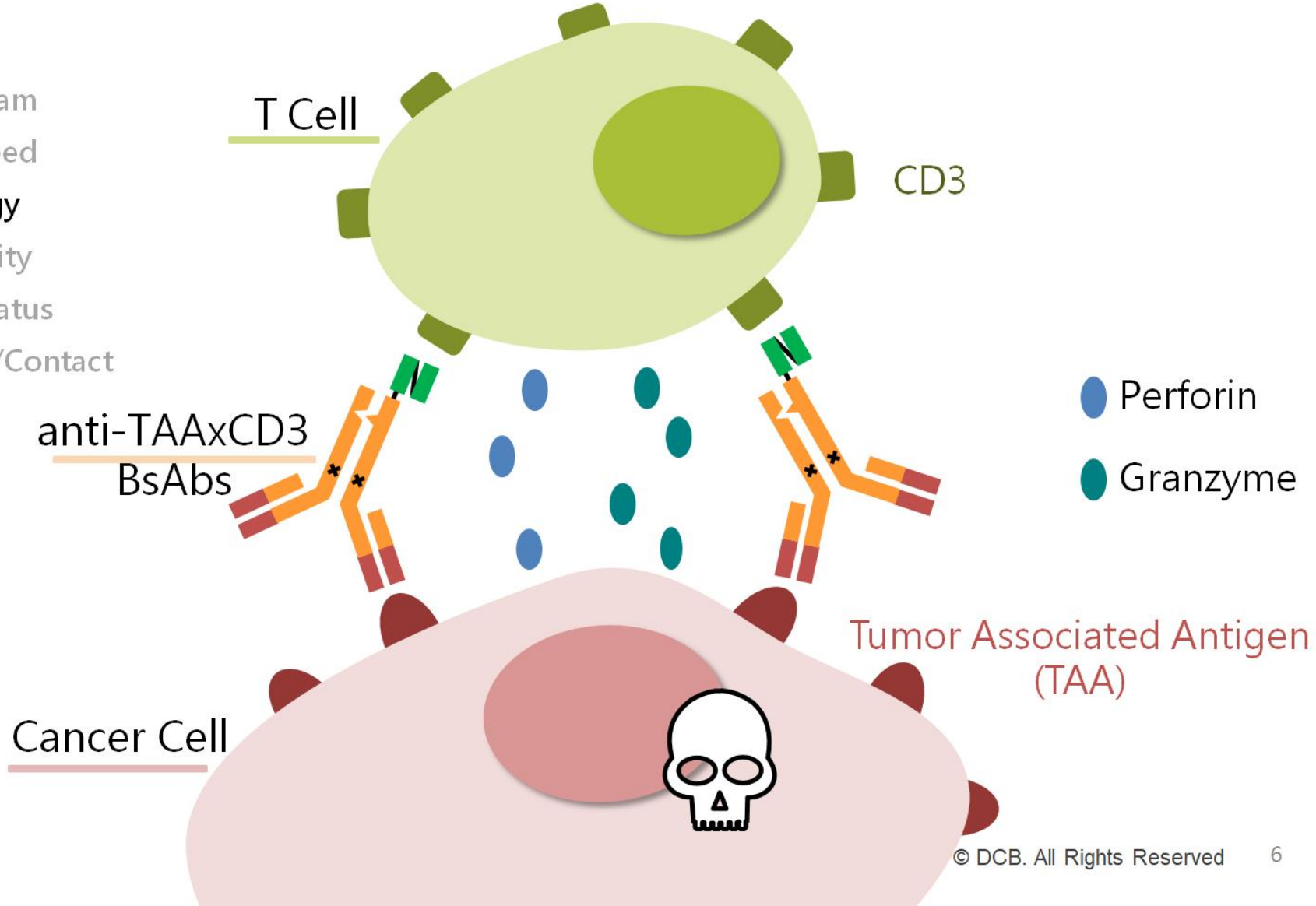
Purity & Heterogeneity Analysis of BsAbs by Non-Reduced CE-SDS (Anti-TAAxCD3 BsAb)





No.	Sample	LC	HC	H+L	2H	2H1L	NG	Intact
1	*Anti-TAAxCD3 BsAb Batch#1*	0.49%	--	--	--	2.57%	--	96.93%
2	*Anti-TAAxCD3 BsAb Batch#2*	0.45%	--	--	--	2.21%	--	97.34%

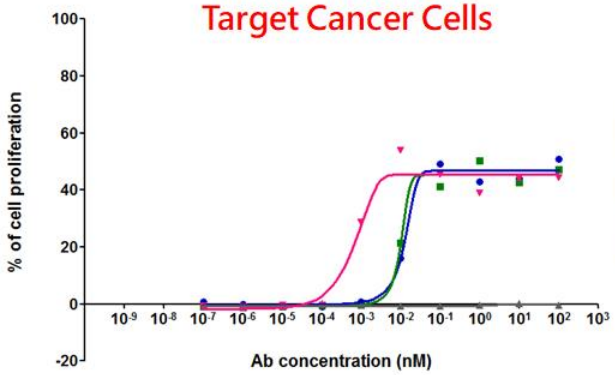
Mechanism of Action



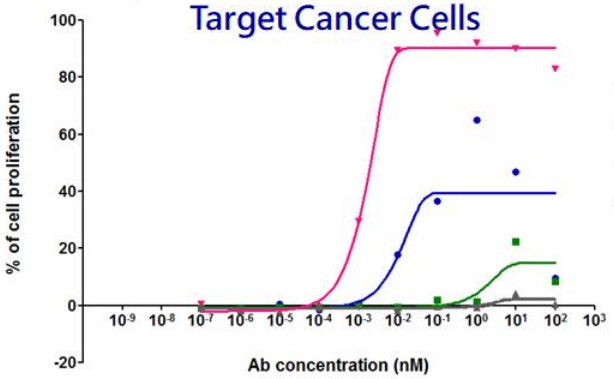
Target-dependent T Cell Activation (Anti-TAAxCD3 BsAb)

Proliferation of CD8 T cells

In the Presence of Target Cancer Cells



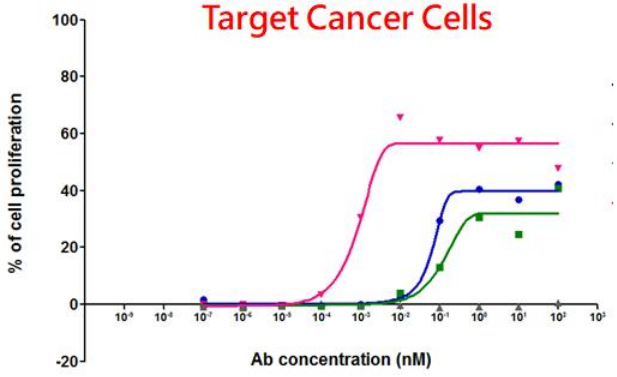
In the Absence of Target Cancer Cells



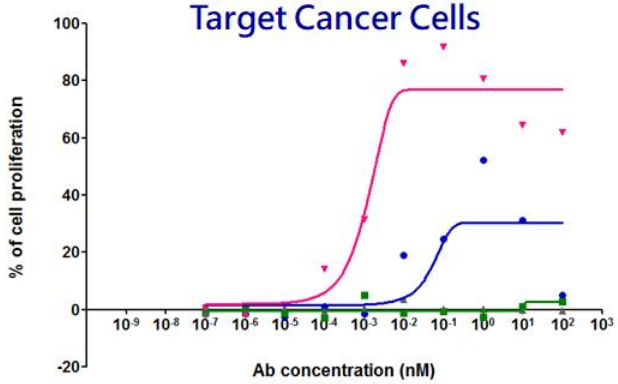
- Anti-TAAxCD3 BsAb (Fc WT)
- Anti-TAAxCD3 BsAb (Fc Mut)
- Anti-TAA mAb
- OKT3

Proliferation of CD4 T cells

In the Presence of Target Cancer Cells

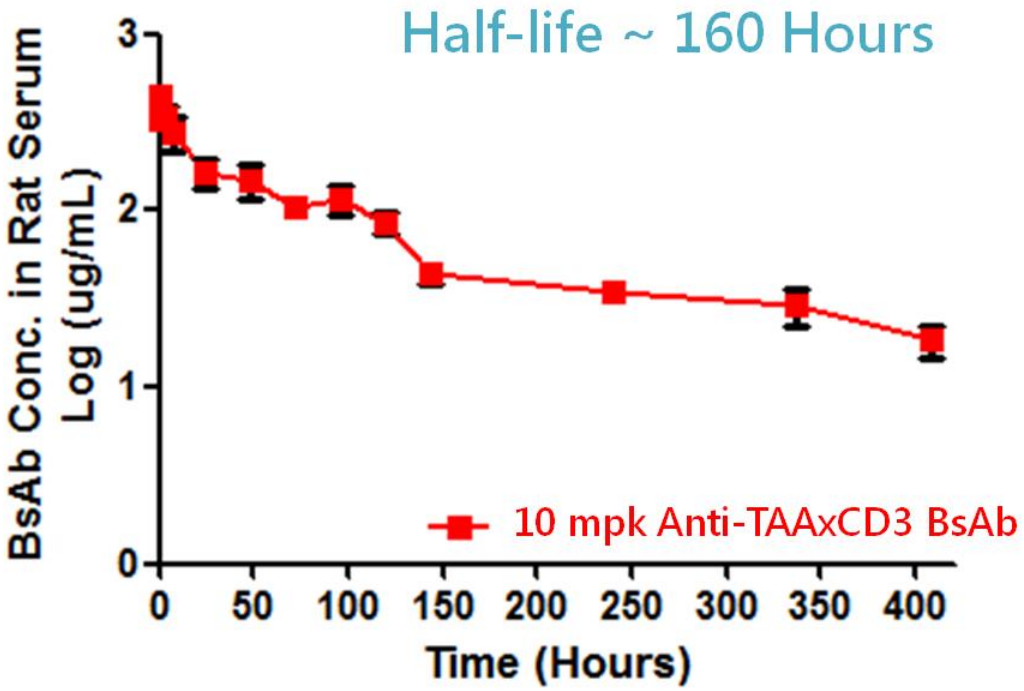


In the Absence of Target Cancer Cells



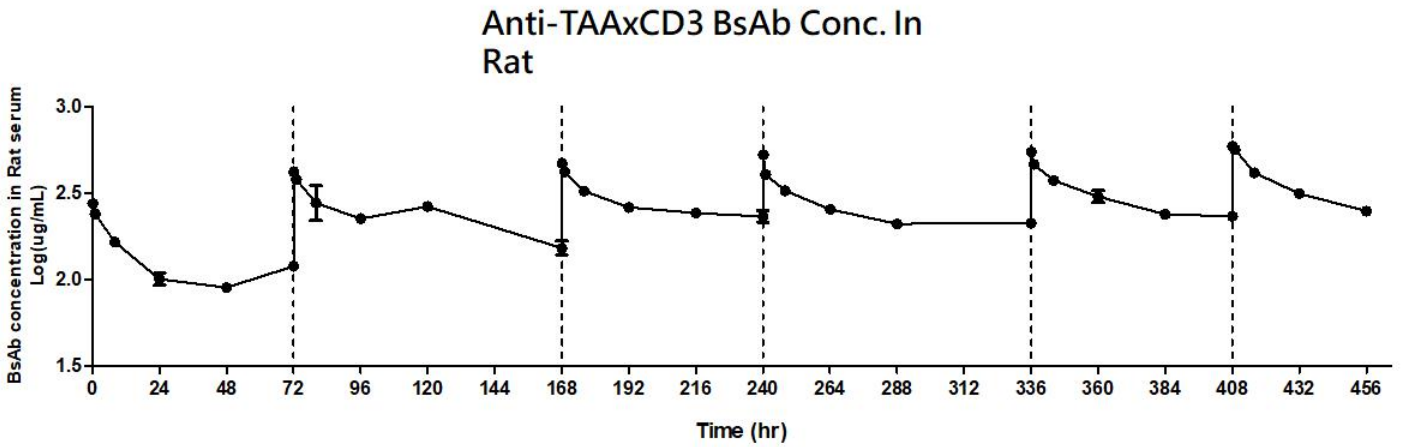
- Anti-TAAxCD3 BsAb (Fc WT)
- Anti-TAAxCD3 BsAb (Fc Mut)
- Anti-TAA mAb
- OKT3

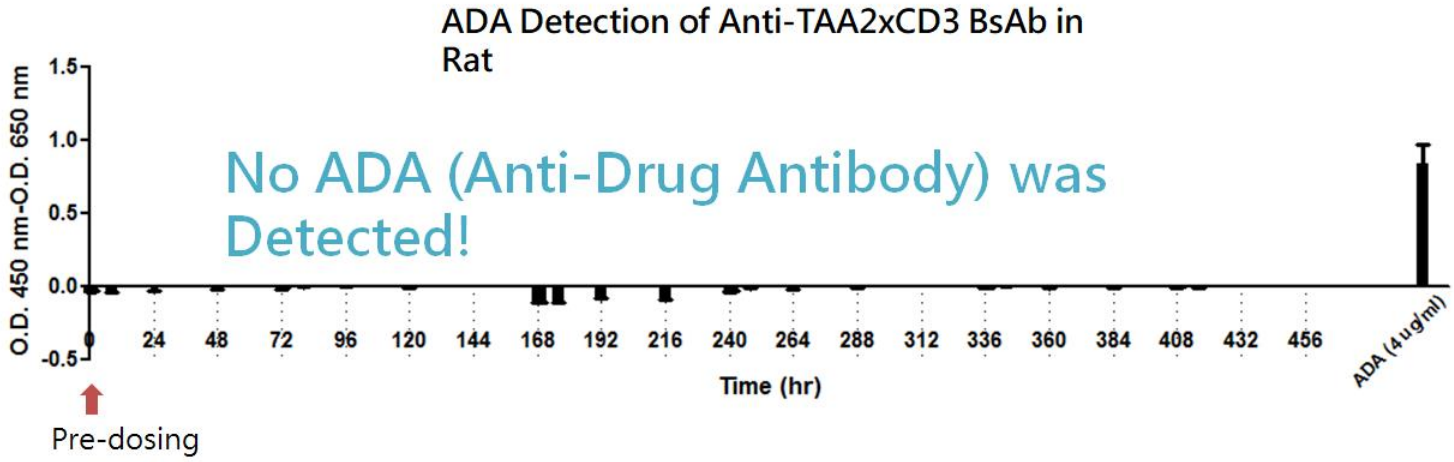
Long *in Vivo* Half-life -comparing to BiTE



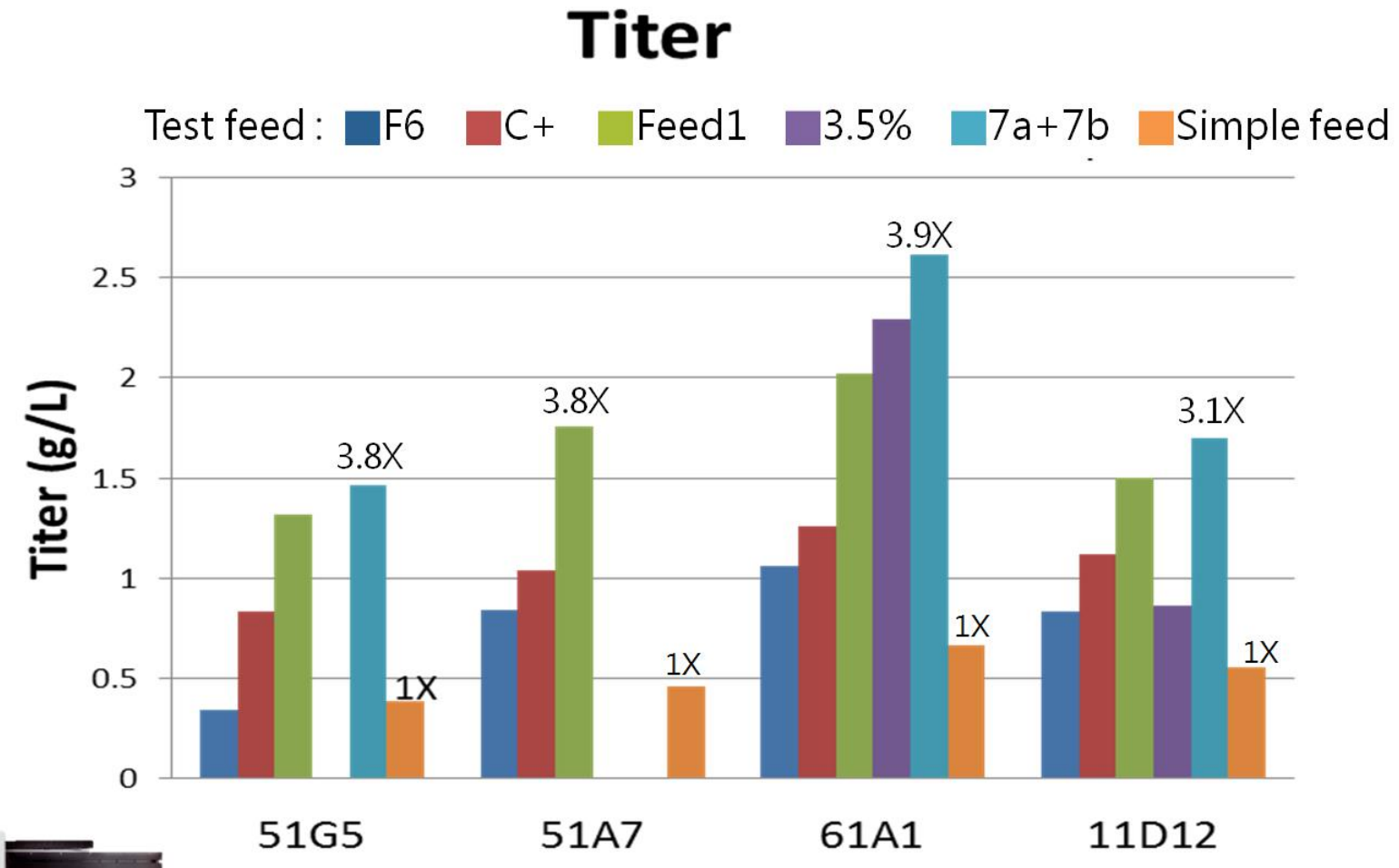
Rat Single Dosing PK	Dose (mg/Kg)	C_0 (mg/mL)	$AUC_{(0\text{-last})}$ (mg*hr/mL)	$AUC_{(0\text{-}\infty)}$ (mg*hr/mL)	MRTinf (hr)	$t_{1/2}$ (hr)	CL (mL/min/Kg)	V_{ss} (L/Kg)
Anti-TAAxCD3 AIS BsAb	10	465±31.3	28114±3645	32569±5425	187±32.0	162±45.7	0.01±0.001	0.06±0.01

Low Immunogenicity of Anti-TAAxCD3 BsAb in Rat





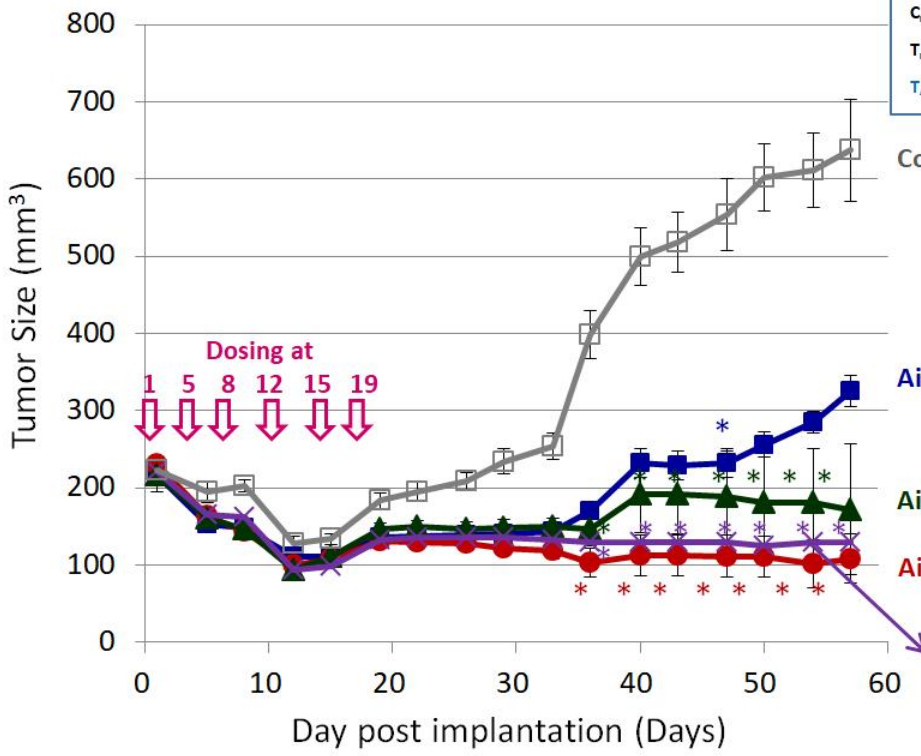
High Production Yield of The Anti-TAAxCD3 BsAb CHO-S Cell Line



- Anti-TAAxCD3 BsAB Process by AMBR (NUambr02)

Therapeutic Effect of Anti-TAA2xCD3 BsAb in HCC1428 Xenograft Mice

HCC1428 breast cancer cells xenograft animal model in female NOD/SCID mice



Tumor growth was calculated as T/C (treatment/control) x 100%.

$T/C = (T_n/C_n) \times 100\%$

C_n: Tumor size measured on Day n in the control group

T_n: Tumor size measured on Day n in the treated group

T/C value ≤ 42% was considered significant antitumor activity (*).

Control: PBS only

Aig-T01, 3 mpk (2/w, 3wks) PBMC 1, 14, 22

Aig-T01, 3 mpk (2/w, 3wks) PBMC 1, 8, 14, 22

Aig-T01, *10 mpk* (2/w, 3wks) PBMC 1, 14, 22

Taxol, 10 mpk (1/w, 3wks)

n=5

Possibility, Status, and Strategy

IP

PCT (2018), US (2018), and TW (2018) Patents Applied

Partnership

- Non-exclusive Licensing
- Co-development
- Other Ways of Partnership

Expect in the Future

- Comparing this novel BsAb platform to other existing technologies

Summary and Contact

DCB's Bispecific Antibody

- Easy to Make
- High Correct Pairing (>95%)
- Target cell-dependent T cell activation (Better safety profile)
- Long *in vivo* half-life($T_{1/2}$~ 160 Hours)
- Low immunogenicity in rats (No detectable ADA)
- High production yield (Yield= 2~3 g/L)

BD Contact

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Thank you for your attention