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

Armored Globo H-Specific CAR-T Cells to Attack Cancer

Institute of Biologics
Development Center for Biotechnology

Presenter：Yu-Hsun Lo, Ph.D.

2020/04/23 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

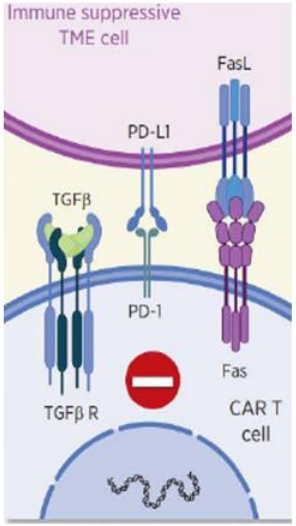
T E A M

Principal Investigator Yu-Hsun Lo, Ph.D.	La Jolla Institute FOR IMMUNOLOGY	T cells signaling Antibody Generation
Li- Shuang Ai, Ph.D.		Molecular Virology Cell therapy
Ru-Lin Cheng, Ph.D.	UNIVERSITÄT BONN	T cells signaling Cell therapy

New Challenges to Develop Effective CAR-T Cells Therapy for Solid Tumor

- In patients with solid tumors, objectives response to CAR-T cells are still limited.
- The hurdles of CAR-T cells in solid tumor:

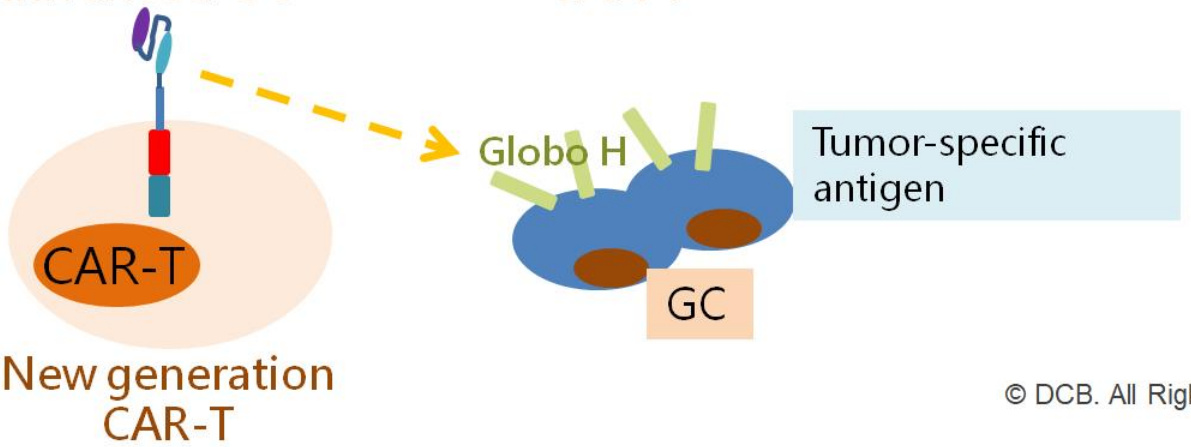
  - Tumor specific antigens , expression level(Heterogeneity), and susceptibility to CAR-T cells.
  - Physical barriers in solid tumors.
  - CAR-T dysfunction in Immunosuppressive tumor microenvironment.



Clin Cancer Res

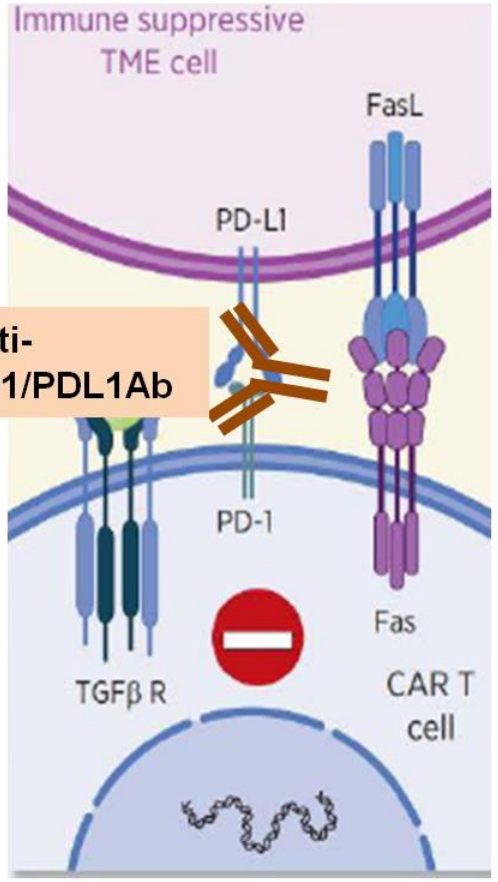
Globo H as a Target Antigen on Solid Tumors

- Globo H is highly expressed on several type of malignancies, including gastric, breast and lung cancer.
- For gastric cancer: 1,000,000 new cases/year; 780,000 deaths/year.
- The most patients belong to advanced GC and the 5-year survival rate is 5%.
- The treatment options for advanced gastric cancer are limited.
- The identification of novel therapeutics for the treatment of advanced GC>>>>>>>CAR-T



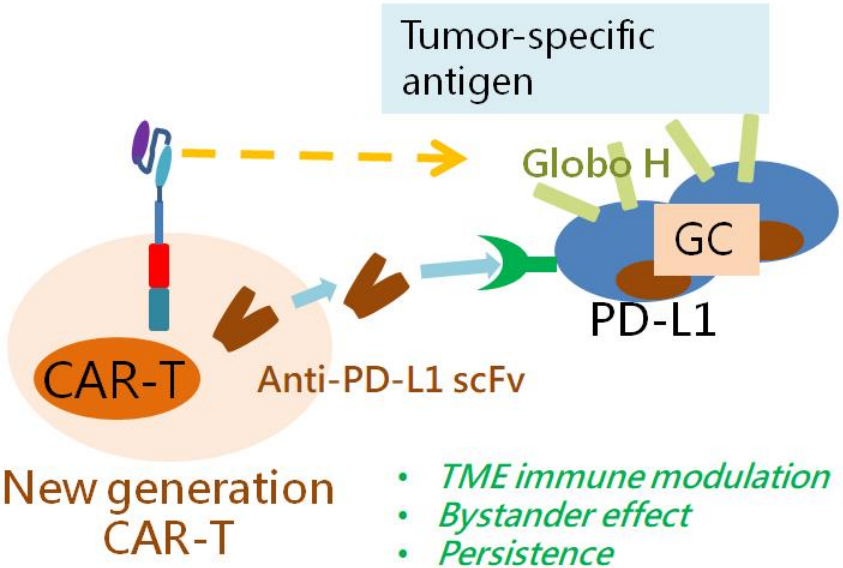
Combination of CAR-T Cells and PD1/PD-L1 Blockade in Clinical Trials

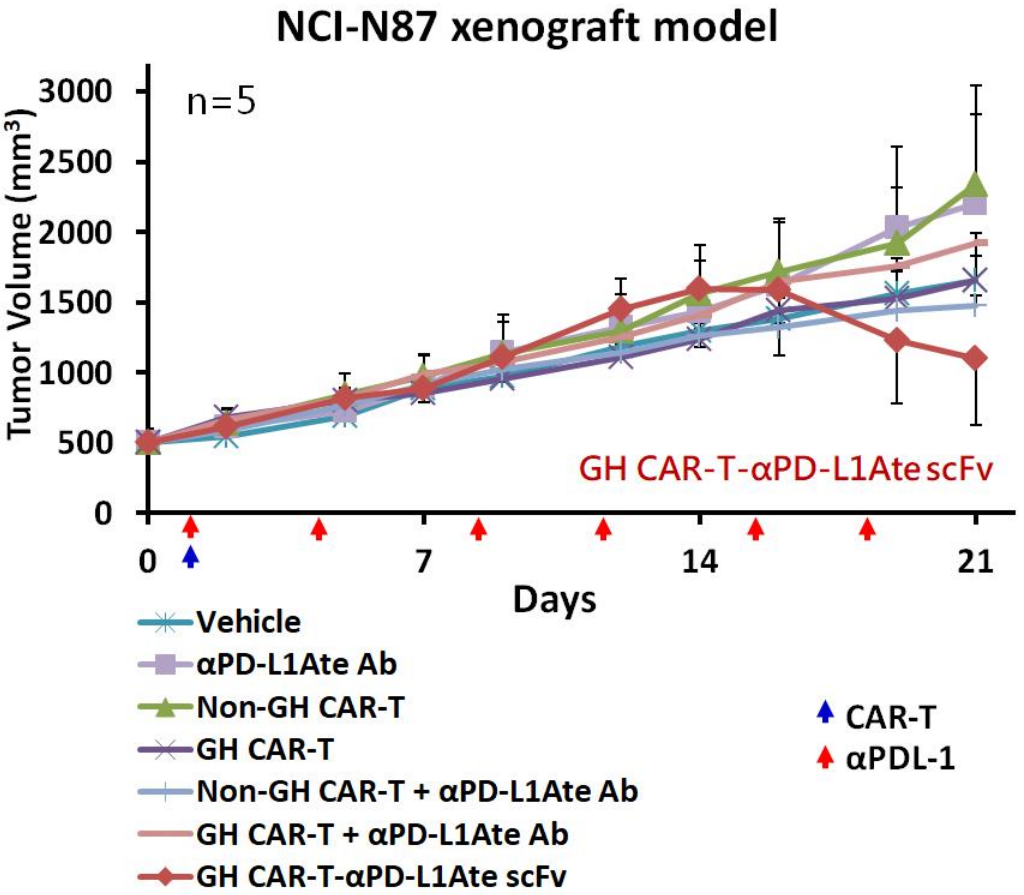
	Study Title	Conditions	Phase
1	**PD-1** Antibody Expressing CAR T Cells for **Mesothelin** Positive Advanced Malignancies	⊙Solid Tumor, Adult ⊙Advanced Cancer	**I/II** February 15, 2017
2	**CTLA-4** and **PD-1** Antibodies Expressing MUC1-CAR-T Cells for **MUC1** Positive Advanced Solid Tumor	⊙Advanced Solid Tumor	**I/II** June 7, 2017
3	**CTLA-4** and **PD-1** Antibodies Expressing EGFR-CAR-T Cells for **EGFR** Positive Advanced Solid Tumor	⊙Advanced Solid Tumor	**I/II** June 7, 2017
4	**CTLA-4** and **PD-1** Antibodies Expressing Mesothelin-CAR-T Cells for **Mesothelin** Positive Advanced Solid Tumor	⊙Advanced Solid Tumor	**I/II** June 7,
5	Study of CRISPR-Cas9 Mediated **PD-1 and TCR Gene-knocked Out Mesothelin**-directed CAR-T Cells in Patients With Mesothelin Positive Multiple Solid Tumors.	⊙Solid Tumor, Adult	**I** March 1, 2018
6	Safety and Efficacy of **iPD1 CD19** eCAR T Cells in Relapsed or Refractory B-cell Lymphoma	⊙Relapsed or Refractory B-cell Lymphoma	**I** June 21, 2017
7	**CD19/22** CAR T Cells (AUTO3) for the Treatment of Diffuse Large B Cell Lymphoma (ALEXANDER)	⊙Diffuse Large B Cell Lymphoma ⊙Relapsed Diffuse Large B-Cell Lymphoma ⊙Refractory Diffuse Large B-Cell Lymphoma ⊙DLBCL	**I/II** September 5, 2017
8	3rd Generation **GD-2** Chimeric Antigen Receptor and iCaspase Suicide Safety Switch, Neuroblastoma, GRAIN (GRAIN)	⊙Neuroblastoma	**I** August 2013



Clin Cancer Res

Increasing Anti-tumor Efficacy of Golob H CAR-T by *in situ* expression of anti-PD-L1 scFv





GH CAR-T cells-mediated inhibition of tumor growth was moderately increased upon αPD-L1 scFv secretion in N87 xenograft model.

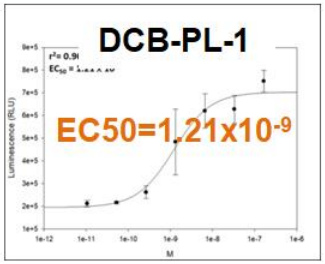
Anti-PD-L1 Antibodies in DCB

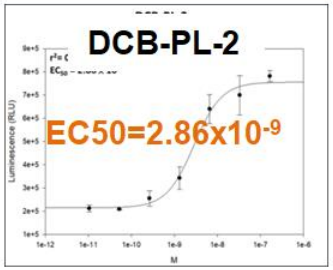
High affinity for PD-L1

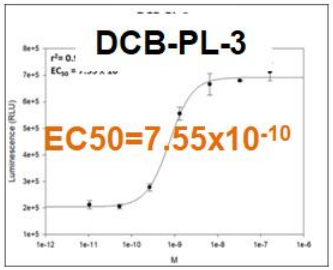
αPD-L1	affinity KD
DCB-PL-1	1.474e-010
DCB-PL-2	2.674e-010
DCB-PL-3	2.241e-010
DCB-PL-4	8.110e-011

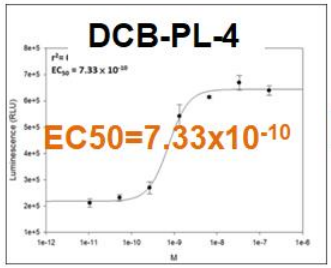
KD: 10^{-10}M

High potency for T cell activation



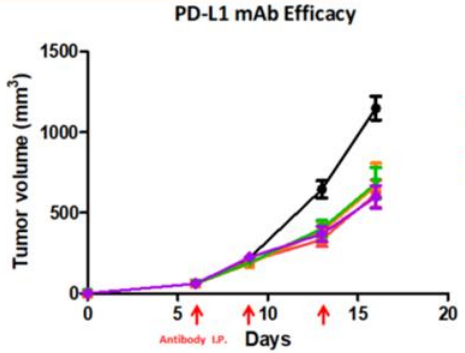






EC50: 10^{-9}~10^{-10}M

Tumor Inhibition



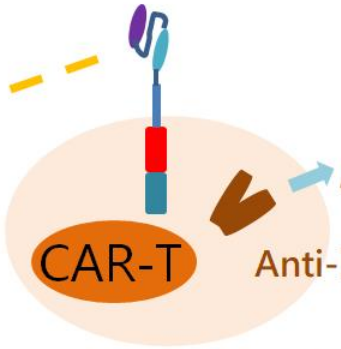
TGI:~30%

MC38 HuCELL® Model in C57BL/6 Mouse

Possibility, Status, and Strategy

IP

- Anti-Globo H mAb :
  - ✓PCT/US2018/034469
  - ✓TW 107117759



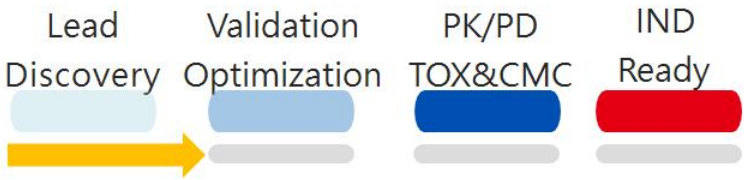
- Anti-PD-L1 mAb :
  - ✓PCT/US2019/041747
  - ✓TW108124494

New generation CAR-T

Partnership

Exclusive License
Co-development

Development status



Novel Globo H CAR-T/IO Blocker Design

Globo H CAR-T-αPD-L1 scFv

- Potential cell therapy for Globo H^+ solid tumor.
- Overcome PD-L1-mediated immune suppression on CAR-T cells in tumor microenvironment.
- Anti-PD-L1 scFv is able to induce bystander effect during Globo H CAR-T cell treatment.

BD Contact

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Thank you for your attention