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

PD-L1/TIM-3/CSF-1R antibody in preclinical studies for Cancer Immunotherapy

Institute of Biologics
Development Center for Biotechnology

Liao, Chu-Bin Ph.D.
HO, Chen-Hsuan Ph.D.
Yu, Cheng-Chou Ph.D.

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

Principal Investigator
Tsai, Shih-Chong Ph.D.

E

Biology Leader
Liao, Chu-Bin Ph.D.

A

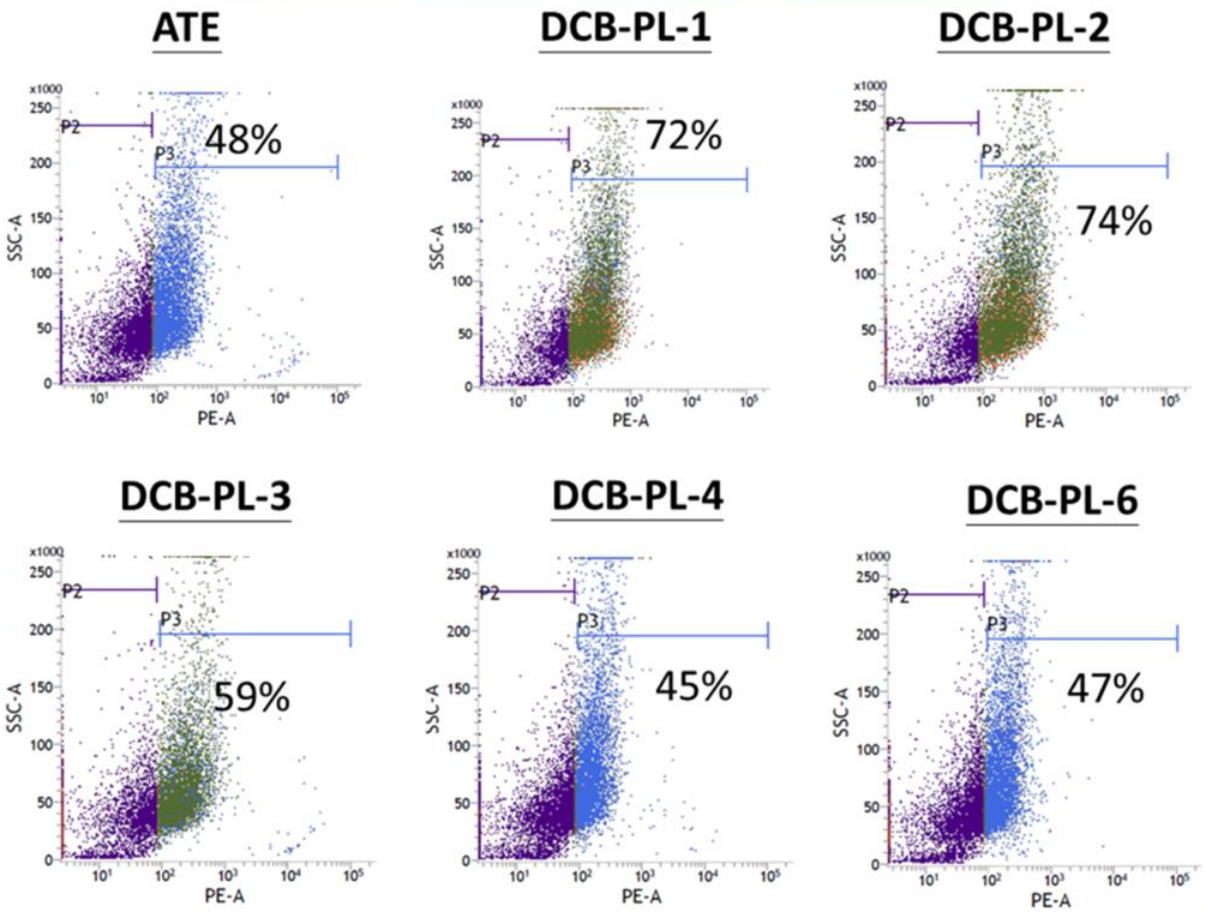
Biology Leader
HO, Chen-Hsuan Ph.D.

M

Chemistry Leader
Yu, Cheng-Chou Ph.D.

DCB’ s PD-L1 mAbs Show High Affinity Property

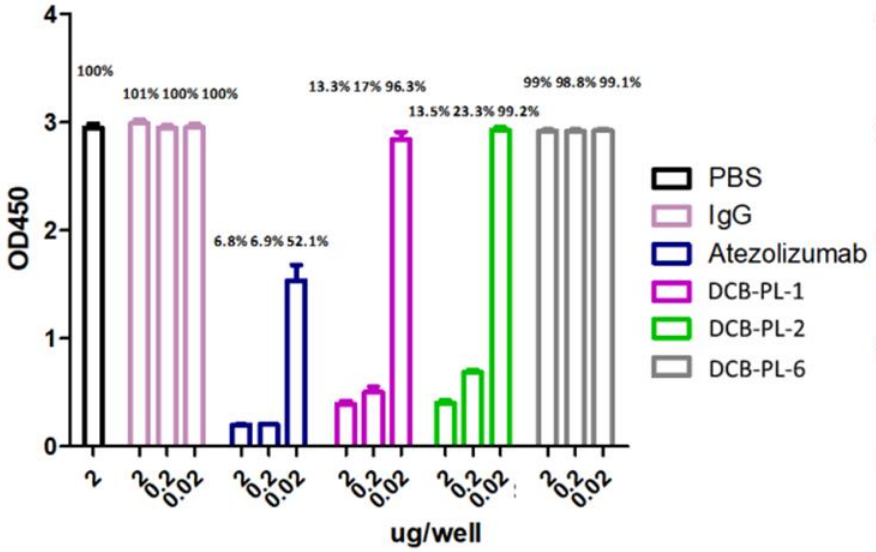
DCB’s anti-PD-L1 mAbs bind to HCC827 cells

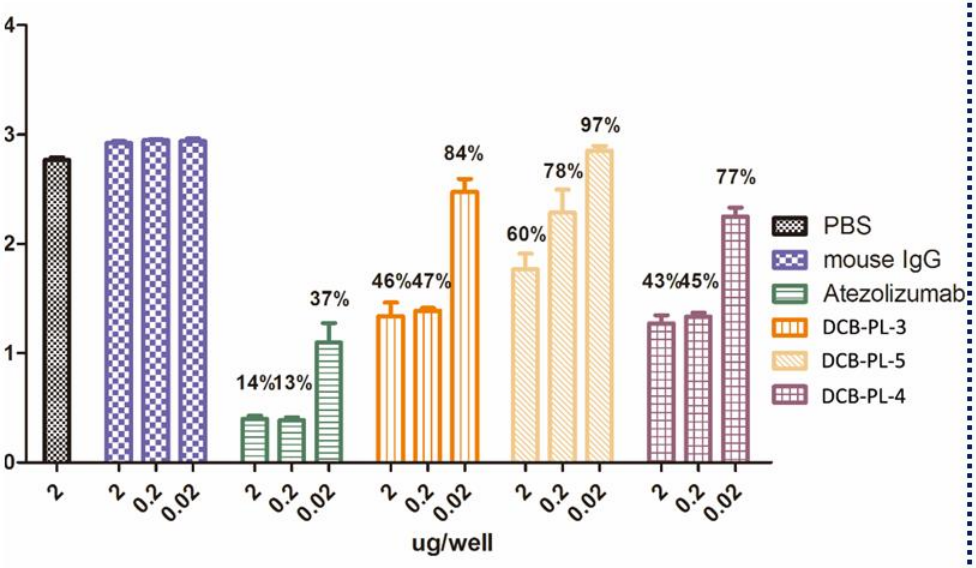


αPD-L1	EC_{50}
DCB-PL-1	4.506×10^{-10}
DCB-PL-2	4.342×10^{-10}
DCB-PL-3	3.491×10^{-10}
DCB-PL-4	5.309×10^{-10}
DCB-PL-5	1.652×10^{-9}
DCB-PL-6	3.896×10^{-10}

DCB’ s anti-PD-L1 mAbs Effectively Block PD-1/PD-L1 Interaction

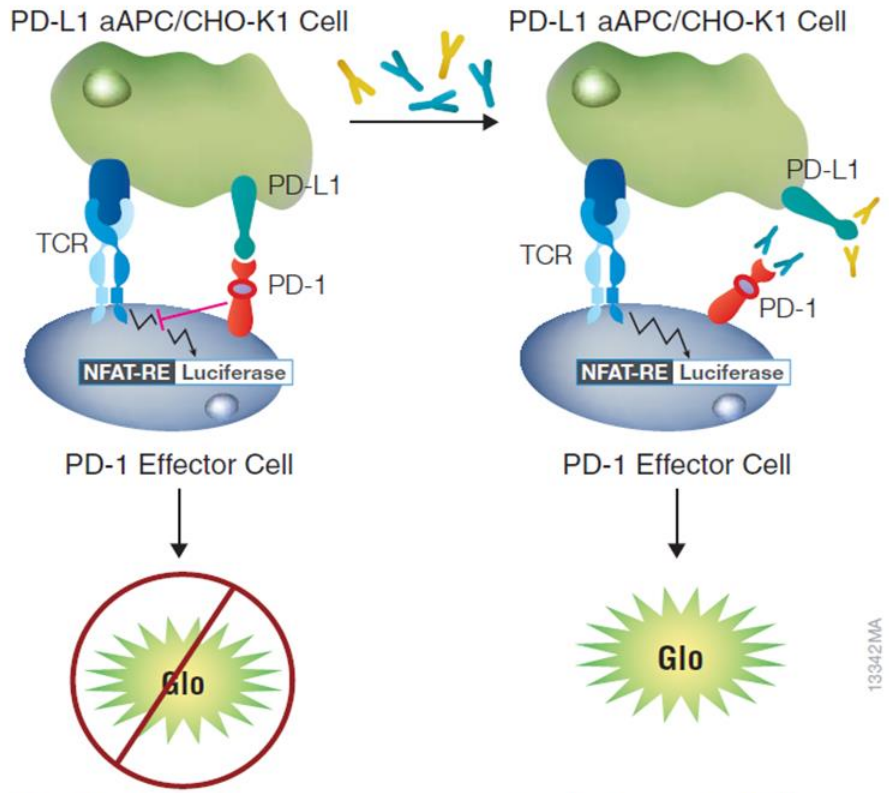
PD-1/PD-L1 blocking assay (ELISA based)





DCB’ s Anti-PD-L1 mAbs Show Good PD-1/PD-L1 Blocking Bioactivity

PD-1/PD-L1 Blockade Assay (Cell based)



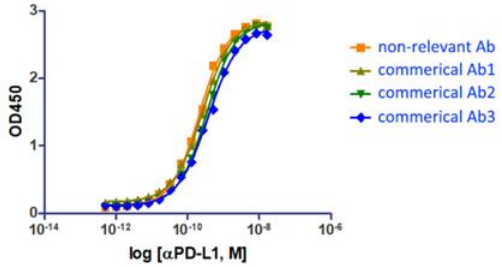
https://worldwide.promega.com/c/global/biologics-toolkit/#popup29

mAb	EC_{50} (g/mL)
BCB-PL-1	1.83×10^{-7}
BCB-PL-2	4.33×10^{-7}
BCB-PL-3	1.14×10^{-7}
BCB-PL-4	1.11×10^{-7}

The Binding Epitopes of DCB's PD-L1 mAbs Are not Overlapped with Commercial Antibodies

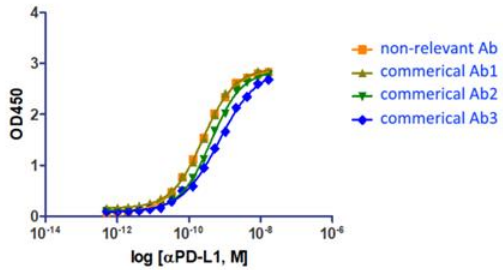
Competitive Binding Assay

DCB-PL-1



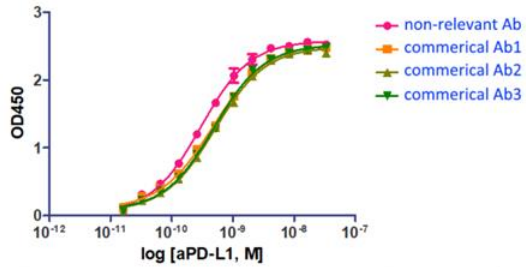
	non-relevant Ab	commerical Ab1	commerical Ab2	commerical Ab3
EC50	2.148e-010	2.658e-010	3.400e-010	3.790e-010

DCB-PL-2



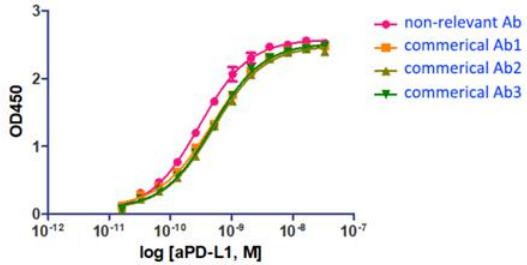
	non-relevant Ab	commerical Ab1	commerical Ab2	commerical Ab3
EC50	2.266e-010	2.527e-010	4.168e-010	7.013e-010

DCB-PL-3



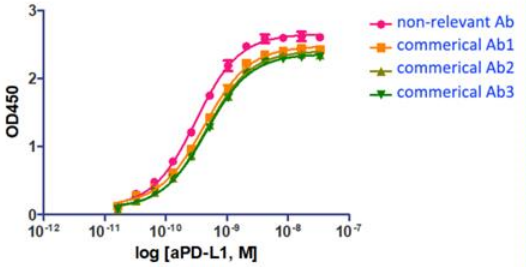
	non-relevant Ab	commerical Ab1	commerical Ab2	commerical Ab3
EC50	3.009e-010	4.718e-010	5.091e-010	4.893e-010

DCB-PL-4



	non-relevant Ab	commerical Ab1	commerical Ab2	commerical Ab3
EC50	3.009e-010	4.718e-010	5.091e-010	4.893e-010

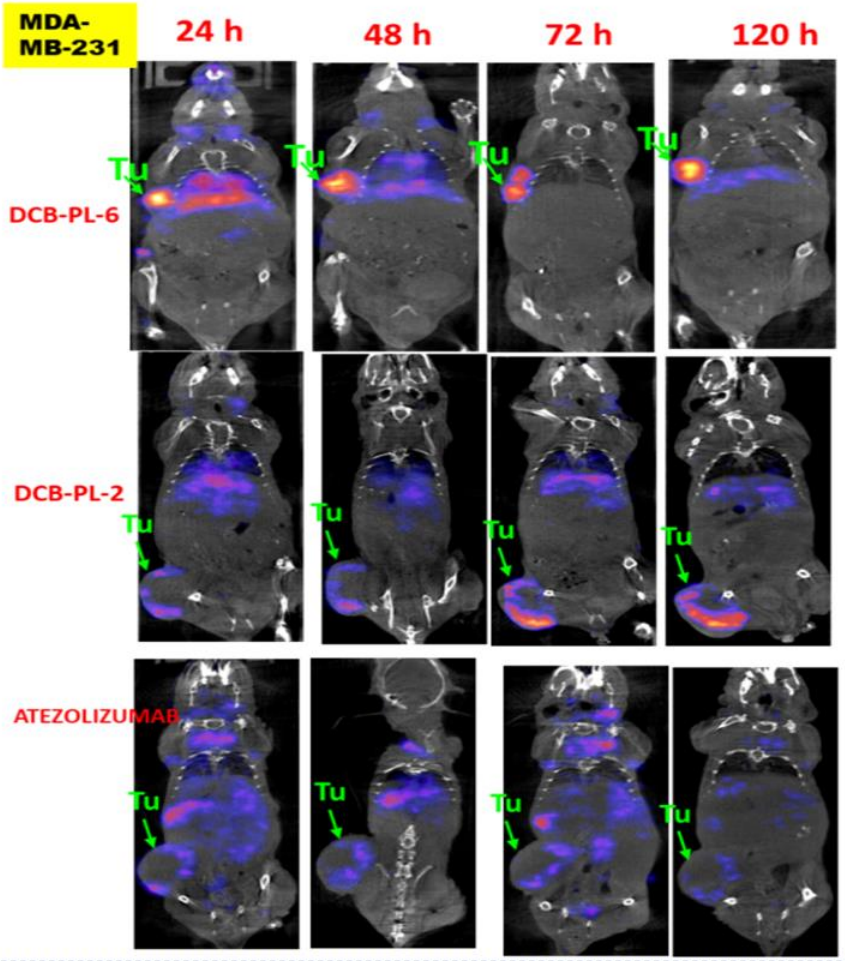
DCB-PL-5



	non-relevant Ab	commerical Ab1	commerical Ab2	commerical Ab3
EC50	3.093e-010	4.249e-010	4.577e-010	4.612e-010

DCB’ s anti-PD-L1 mAbs Can Specifically Detected PD-L1 Expression Tumor

Tissue Distribution



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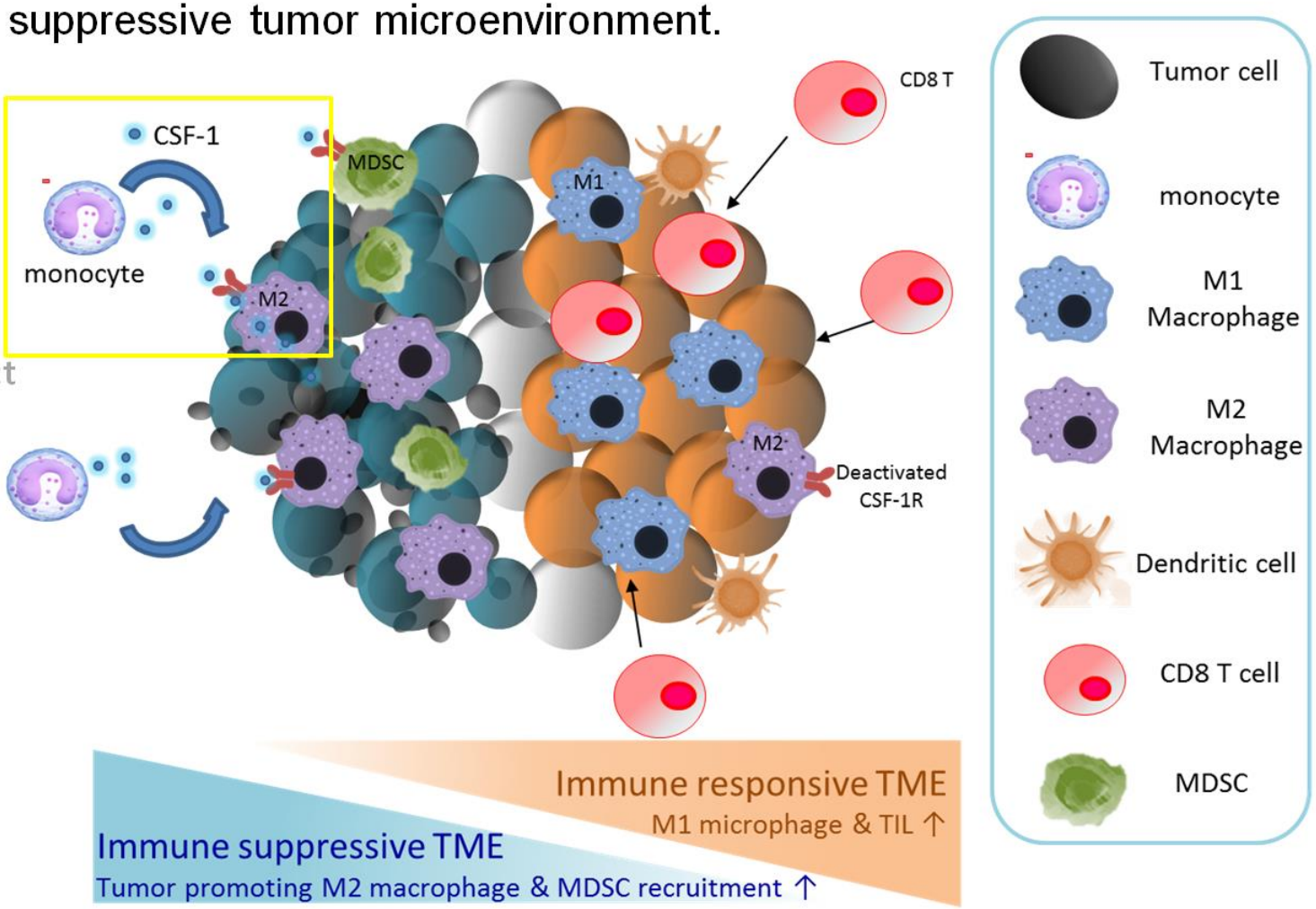
Development of CSF-1R Antibody Drug to Target Tumor-Associated Macrophage for Cancer Immunotherapy

Institute of Biologics
Development Center for Biotechnology

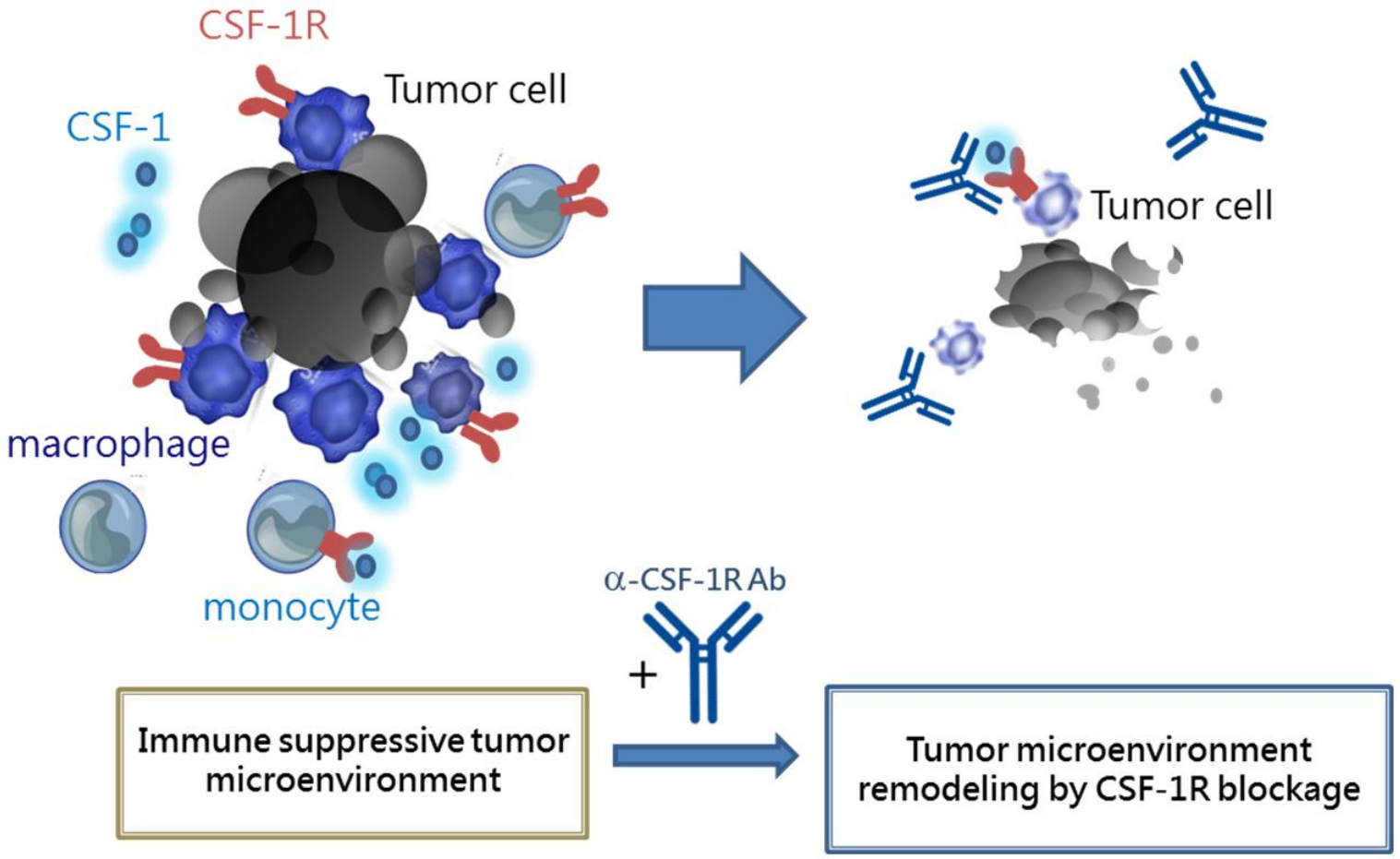
OOOO/OO/OO Updated

CSF-1 Signaling Induces Monocyte Differentiate into M2 Macrophage in Tumor Microenvironment

In a tumor tissue, there are not only tumor cell, but also many immune cell, fibroblast and stromal cell. All of these constitute an immune suppressive tumor microenvironment.



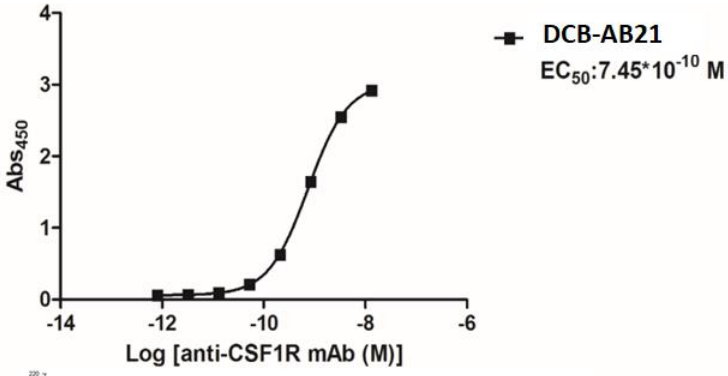
Remodeling the Immunosuppressive Tumor Microenvironment via anti-CSF-1R Antibody

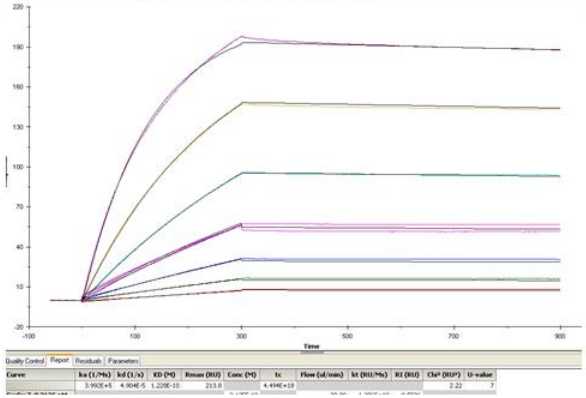


- anti-CSF-1R Ab can remodeling the tumor microenvironment from immune suppressive to immune responsive.

DCB-AB21 Binds to CSF-1R and Blocks the Interaction Between CSF-1 and CSF-1R

Binding Property

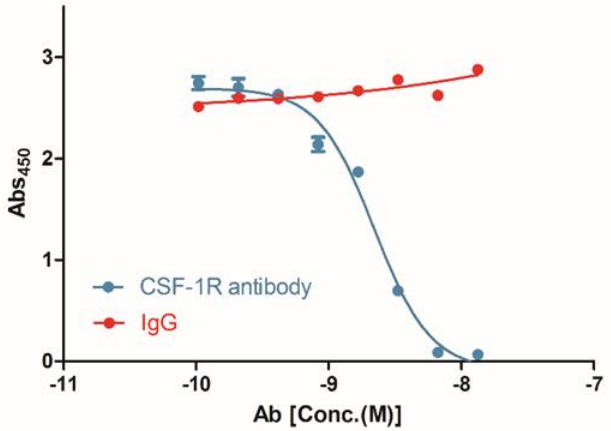


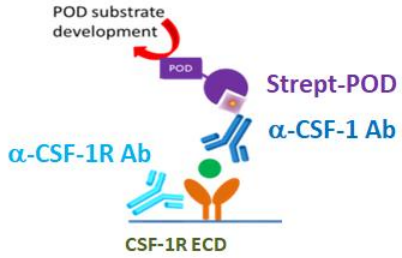


ka(1/Ms)	kd(1/s)	KD(M)	Rmax(RU)	Chi²(RU²)
3.992E+5	4.904E-5	1.228E-10	213.8	2.22

High affinity (around sub-nM level)

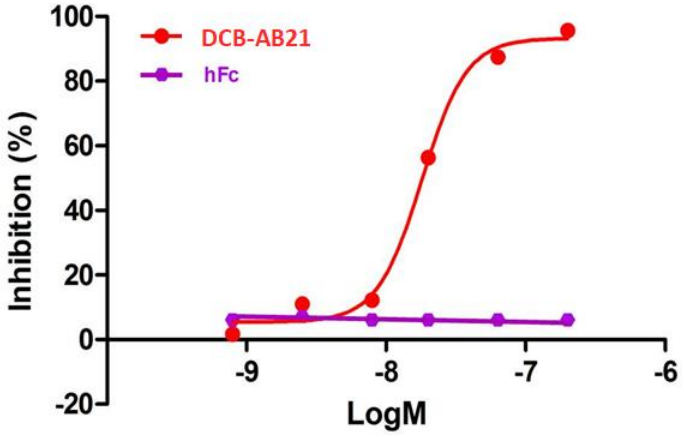
Blocking Property

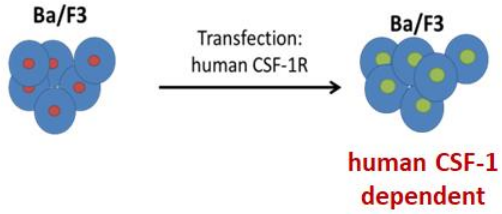




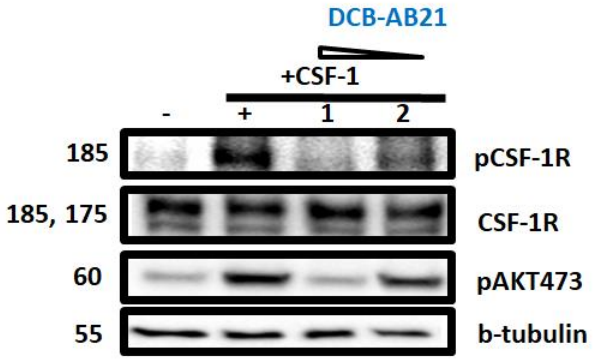
DCB-AB21 Inhibits Ligand–Dependent Cell Growth and Downstream Signaling

Ligand-dependent Cell growth Inhibition





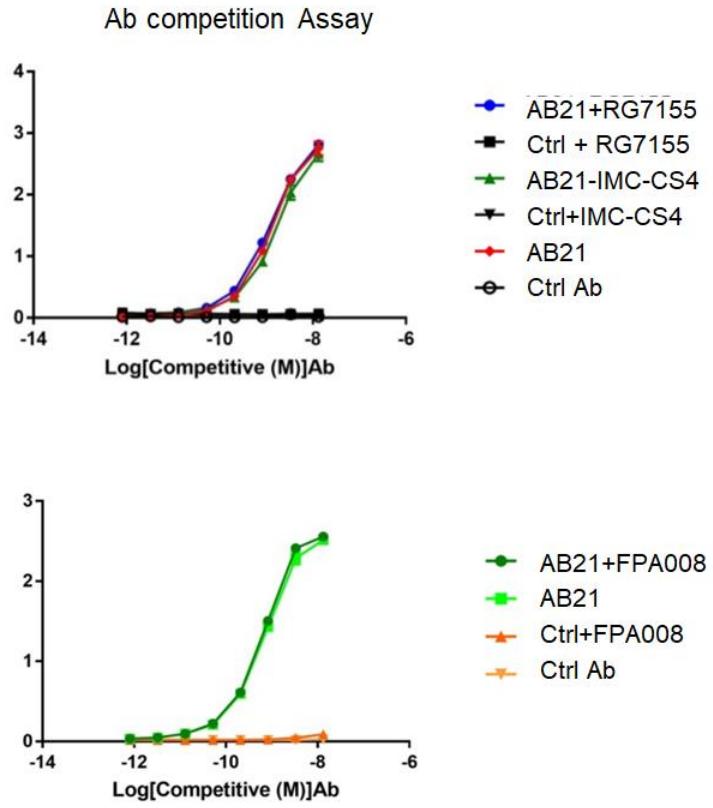
CSF-1 downstream signaling



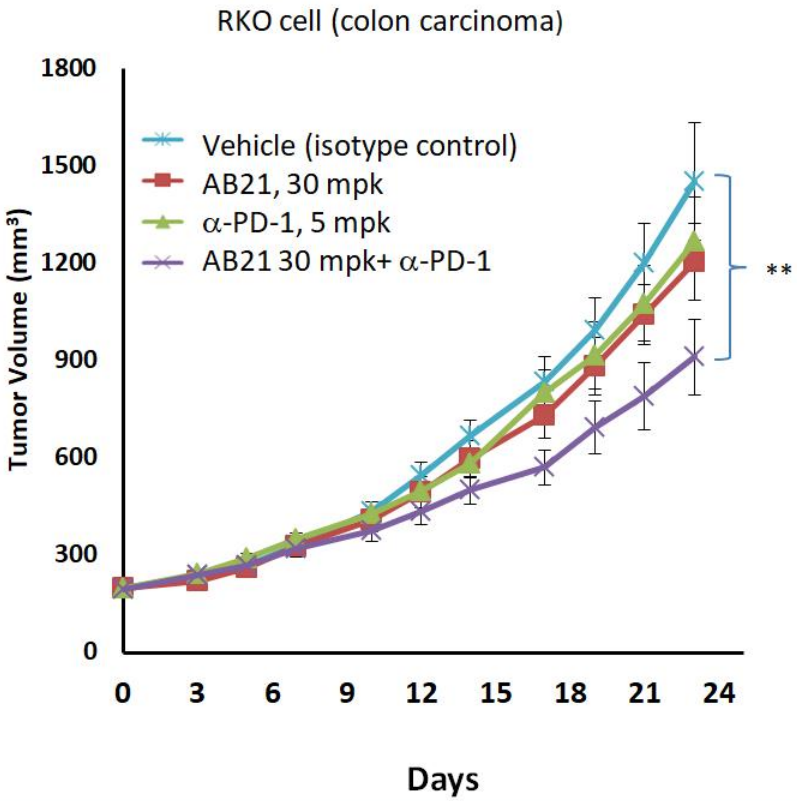
- : Negative control (THP-1 only)
+: Positive control (+ CSF-1)
1: + CSF-1R Ab 5 ug/ml
2: + CSF-1R Ab 0.5 ug/ml

DCB-AB21 Owns Unique Epitopes and Could Generate Clinical Benefits

Non-Overlapping Epitopes



Anti-tumor activity



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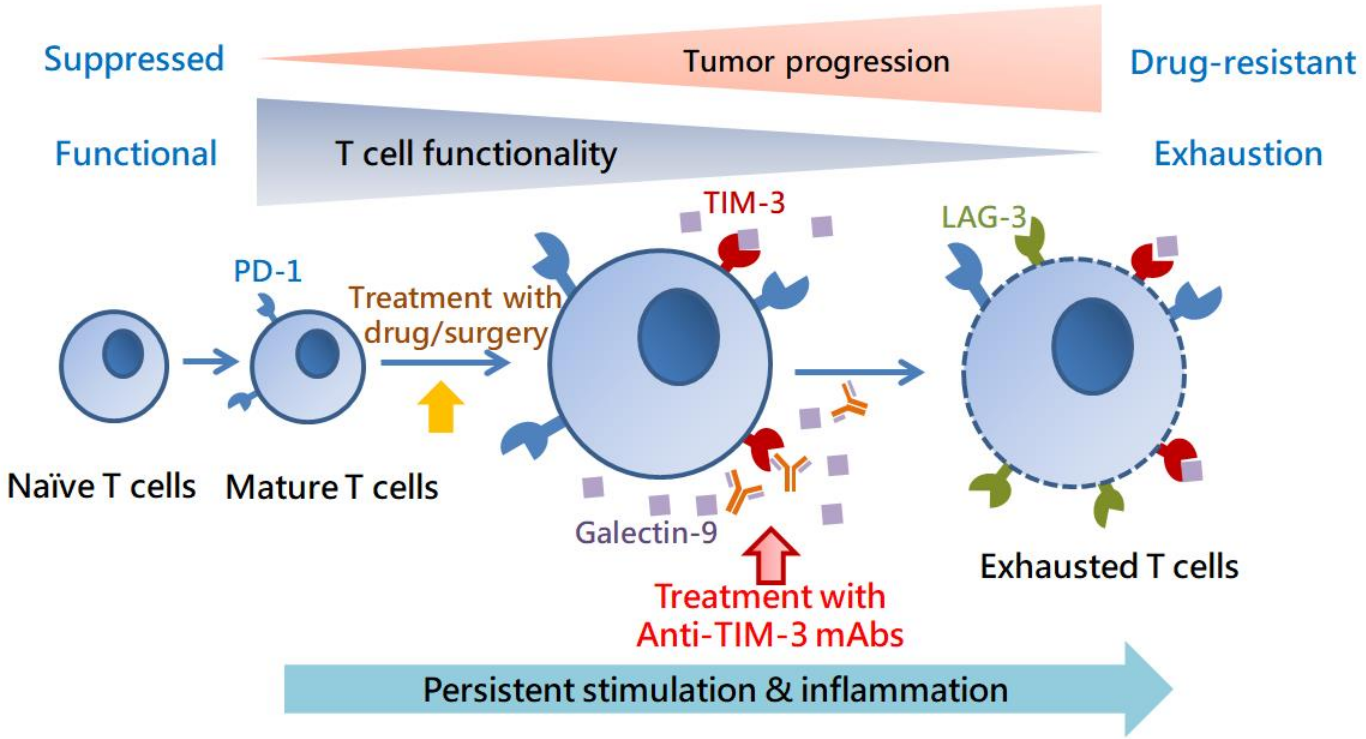
Therapeutic TIM-3 Antibody for Cancer Immunotherapy

Institute of Biologics
Development Center for Biotechnology

OOOO/OO/OO Updated

TIM-3 is a Second Wave Immune Checkpoint after PD-1/PD-L1

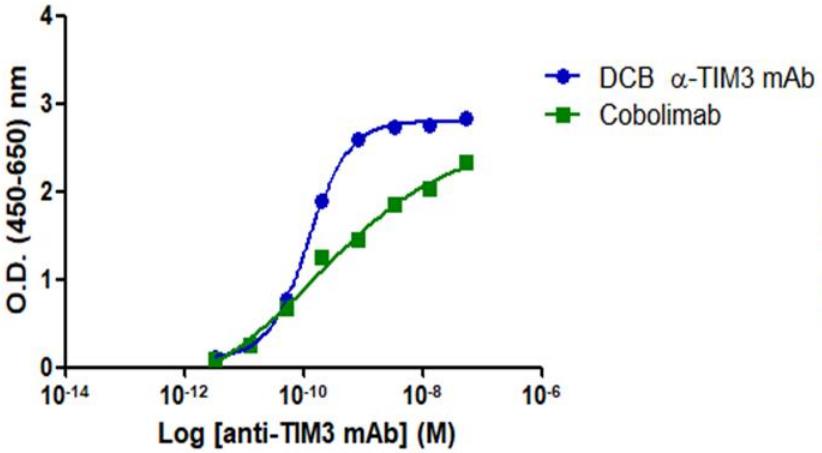


- Low response rate is still the limitation of cancer immunotherapy
- Co-inhibitory receptor Tim-3 is associated with acquisition of T cell exhaustion
- TIM-3 antibody can increase the T cell activity, and inhibit the tumor growth

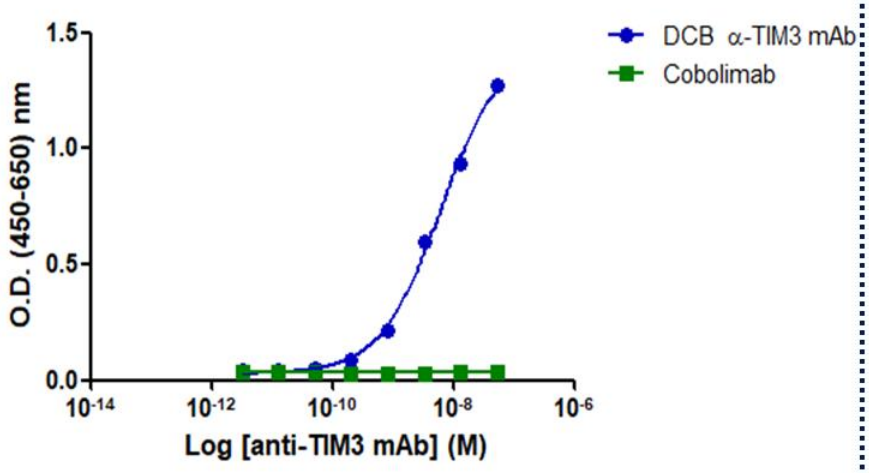
α-TIM3 mAb Can Bind to TIM-3 with High Affinity

Binding Property

Anti-human TIM-3 ELISA



Anti-mouse TIM-3 ELISA

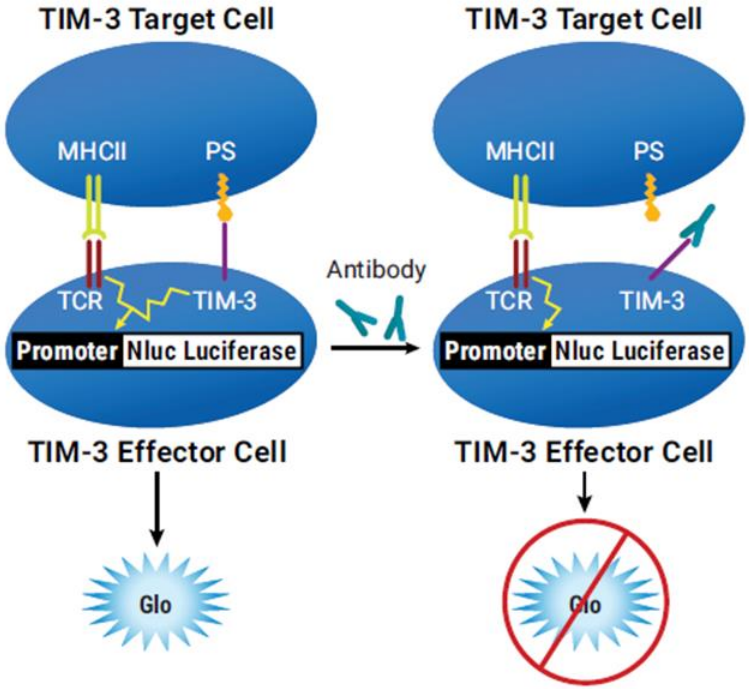


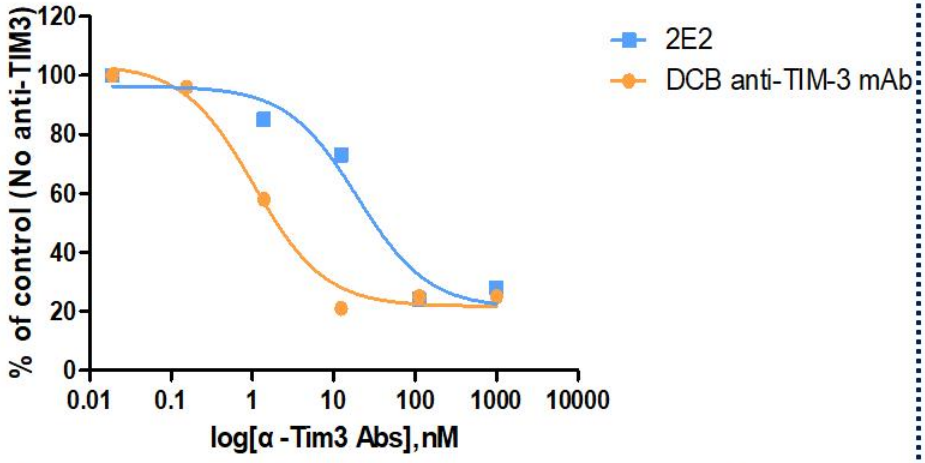
Cobolimab is an anti-TIM-3 mAb in clinical trial phase II

- The fully human anti-TIM-3 antibody binds to human TIM-3 with high affinity and shows cross-species binding ability to mouse TIM-3

α-TIM3 mAbs Block TIM-3 in TIM-3 Functional Bioassay Study

TIM-3 Bioassay





	EC_{50} (nM)
Reference Ab (2E2)	17
DCB's a-TIM-3 mAb	1.04

Possibility, Status, Strategy

CSF-1R

IP

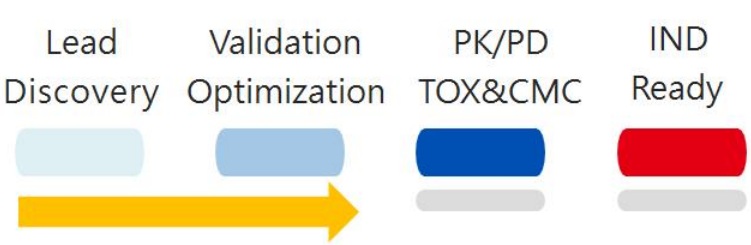
PCT (PCT/US2019/066384), 2019

Taiwan patent (No.108145750) 2019

Partnership

Exclusive License

Development status



PD-L1

IP

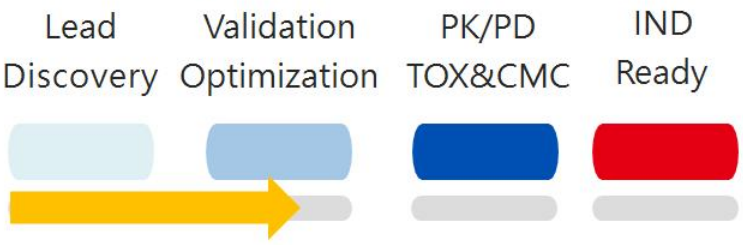
PCT/US2019/041747, 2019

TW108124494, 2019

Partnership

Exclusive License

Development status



Summary

1. DCB's have identified novel anti-PD-L1, anti-CSF-1R, and anti-TIM3 mAbs with high affinity and are highly functional.
2. They have unique CDR sequences and different binding epitopes from competitors.
3. CSF-1R Ab have proved anti-tumor activity when combine with immune checkpoint inhibitors.
4. Patents of CSF-1R and PD-L1 antibodies are filed. We are searching for exclusive license or cooperation opportunity.

BD Contact

Adam Deyao Wang Ph.D
Deyao.wang@dcb.org.tw
+886-2-77003800 #5240

Thank you for your attention