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

Development of Therapeutic Antibodies for Multi-Drug Resistant *Klebsiella pneumoniae*

Institute of Biologics
Development Center for Biotechnology

Presenter：Chia-Wei Wang, Ph.D.

2020/03/30 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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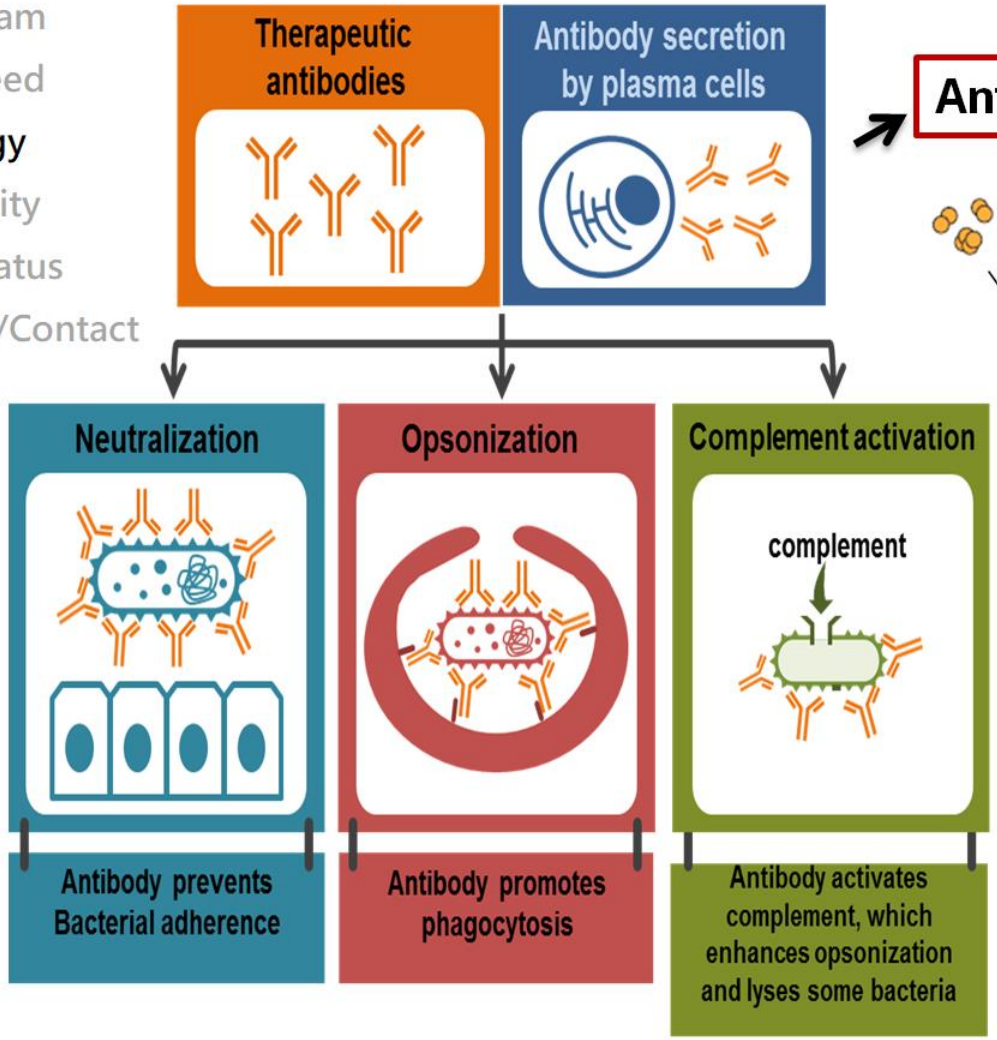
Multiple Drug Resistant (MDR) Bacteria

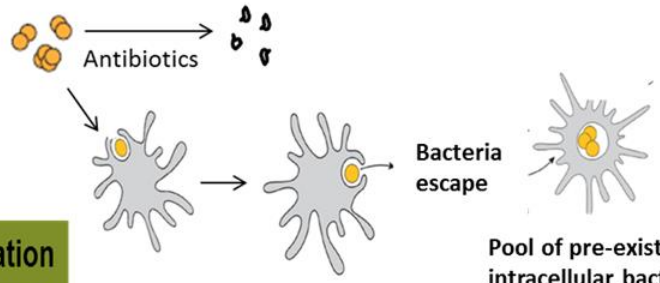
- MDR bacteria are estimated to account for 700,000 deaths of people each year currently, and expected for 10 million deaths by 2050.
- The treatment of multi-drug resistant bacteria urgently needs new antibiotics or new therapeutic methods.—Tom Friden (CDC director, USA)
- WHO publishes list of bacteria for which new antibiotics are urgently needed.

	Bacteria	Antibiotic-resistant
CRITICAL	*Acinetobacter baumannii*	carbapenem-resistant
	Pseudomonas aeruginosa	carbapenem-resistant
	Enterobacteriaceae (*Klebsiella pneumoniae* and *Escherichia coli*)	carbapenem-resistant, ESBL-producing
HIGH	*Enterococcus faecium*	vancomycin-resistant
	Staphylococcus aureus	methicillin-resistant, vancomycin-intermediate and resistant
	Helicobacter pylori	clarithromycin-resistant
	Campylobacter spp	fluoroquinolone-resistant
	Salmonellae	fluoroquinolone-resistant
	Neisseria gonorrhoeae	cephalosporin-resistant, fluoroquinolone-resistant

Targeting MDR Bacteria with Different M.O.A



Antibody-Antibiotic Conjugate



Intracellular bacteria eliminated by **AAC**

In vitro Activity of Anti-*K. pneumoniae (KP)* Antibodies in Clinical Strains

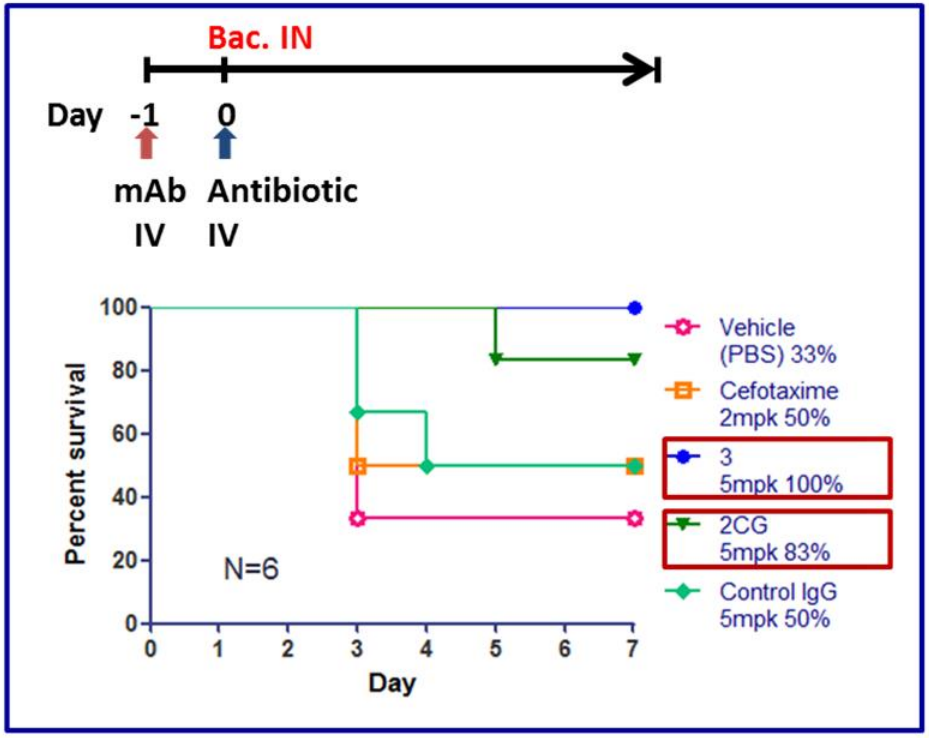
Clone Name	Aggregation	Complement-Mediated Cytotoxicity	Opsonophagocytosis
hIgG	-	-	-
3	++++	25%	20%
16	++	60%	70%
2CG	++	55%	45%
3CG	++	10%	20%

- Antibody-Induced agglutination and inhibited bacteria adhesion to host cell.
- Antibody-Induced complement-mediated cytotoxicity.
- Antibodies mediate opsonophagocytosis by monocytes.

Anti-KP Antibodies Provide Protection against K.P. Infection in the Prophylactic Animal Model

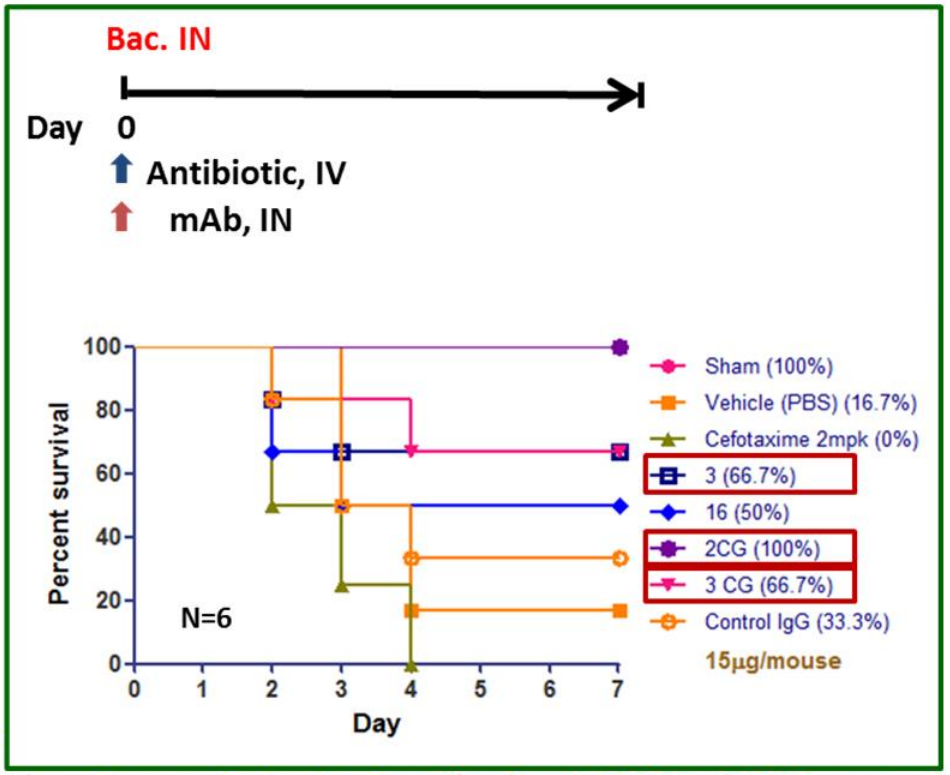
BCRC 13B0218 Lung infection model

Ab IV treatment



- The survival rate of antibodies 3 and 2CG were 100 and 83%, respectively. The survival rates of Cefotaxime and control antibody group were 50%, on the seventh day after infection.

Ab IN treatment

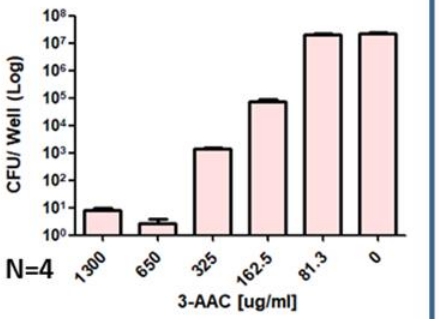


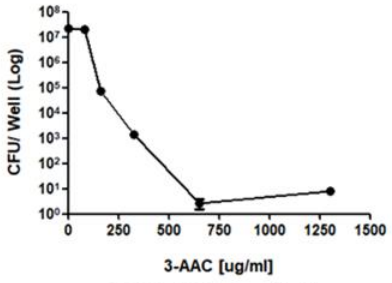
- The survival rate of antibodies 3 ,3CG and 2CG were 66.7 and 100%, respectively. The survival rate of Cefotaxime and control antibody group were 0 and 33%, respectively on the seventh day after infection.

AAC (Antibody–Antibiotic Conjugates) Shows Dose Dependent Intracellularly Bactericidal Potency in CG43 (K2 strain) and A5011 (K1 strain)

A549 cells infected by KP CG43

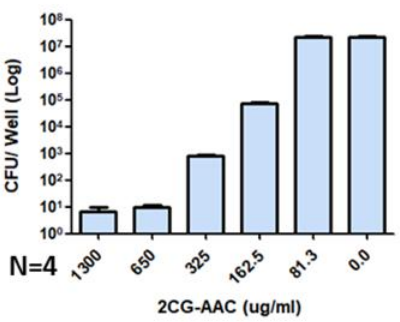
3-Meropenem

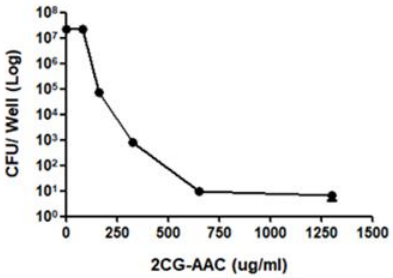




IC50=117.2ug/ml

2CG-Meropenem

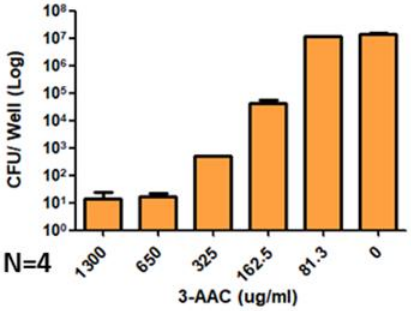


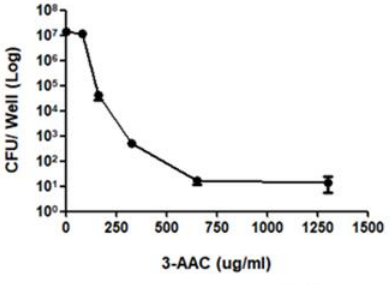


IC50=160ug/ml

A549 cells infected by KP A5011

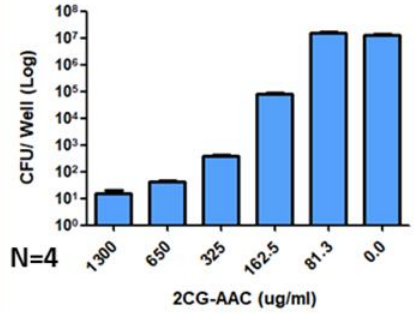
3-Meropenem

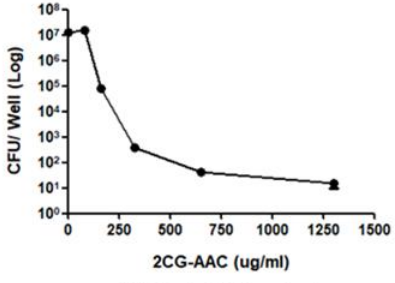




IC50=113.6ug/ml

2CG-Meropenem

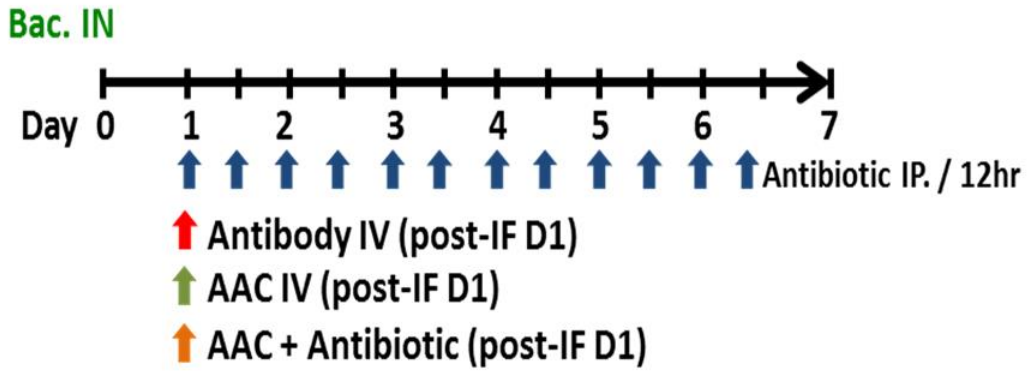


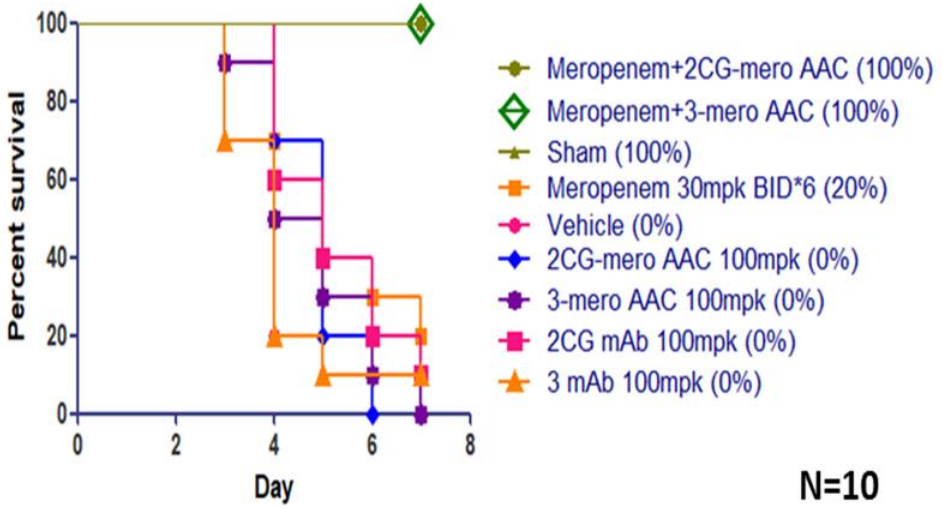


IC50=114.7ug/ml

Anti-KP Antibody 3-AAC and 2CG-AAC Show Therapeutic Effect in KP Lung Infection Animal Model

A5011 (K1), lung infection model





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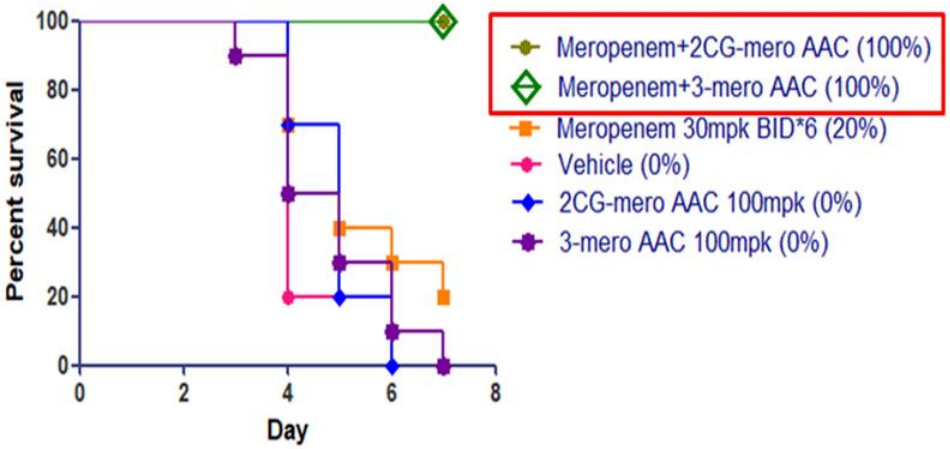


Opportunity and Development Status

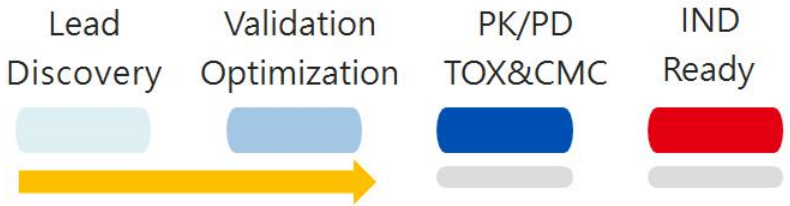
IP

US Provisional application in progress

Partnership

Exclusive License or Co-development

Development status



Future work

- Treatment of MDR bacteria infected patients

Summary

Anti-MDR KP Therapeutic antibodies :

- The Binding Affinity : KD $8x10^{-10}$ ~10^{-11}M.
- Antibody-Induced Complement-Mediated Cytotoxicity.
- Antibodies Mediate Opsonophagocytosis by Monocytes.
- Antibodies Providing Protection against K.P. Infection.

Anti-MDR Bacteria Therapeutic AAC :

- Two AACs (3- and 2CG-Meropenem) show dose dependent intracellularly bactericidal potency in MDR K1 and K2 strain.
- Anti-K.P. AAC provides the Protection against K.P. Infection.

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Thank you for your attention