# Using single B platform to develop a CAR T-cell therapeutic solution for a GPCR target



Kaikai Zeng\*, Antao He\*, Shujuan Hong\*, Fen Mei\*, Meng Cai\*, Chong Dai\*, Min Luo #, Guangchao Li #, Donghui Ma\*

\*Wuhan institute of Biotechnology B7, Biolake No.666 Gaoxin Road, Wuhan, Hubei, China,

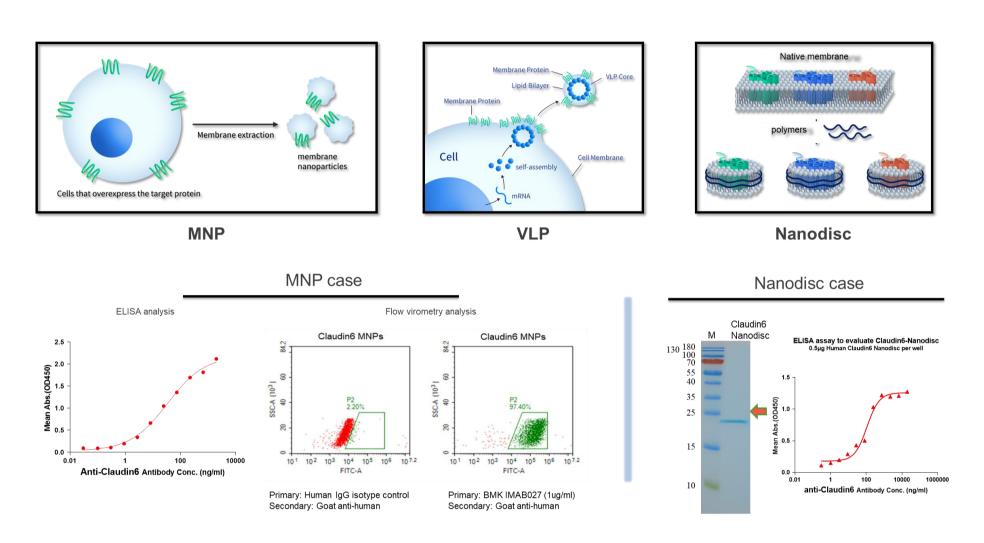
# Guangzhou Bio-gene Technology Co., Ltd 206 Kaiyuan Blvd, Huangpu Qu, Guangzhou City, Guangdong Province, China

### **Abstract**

To expedite antibody-based drug development, DIMABio developed more than 5000 on-shelf lead antibody molecules on 500+ druggable targets with its DimAb® single B platform. In this presentation, we will elaborate DimAb® platform and showcase how we developed anti-GPRC5D CAR T-cell therapy constructs from leads to IIT clinical trial stage with our collaborator. The preliminary data from ongoing clinical trial exhibits astonishing clinical efficacy on RRMM patients.

# **Experimental approach**

## Membrane protein purification platform



**Figure 1.** DiMPro™ multi-pass transmembrane production and purification platform. Dima biotech has established a plethora of technology platforms to produce functional membrane proteins as immunogen for therapeutic antibody development.

# DimAb® single B cell platform

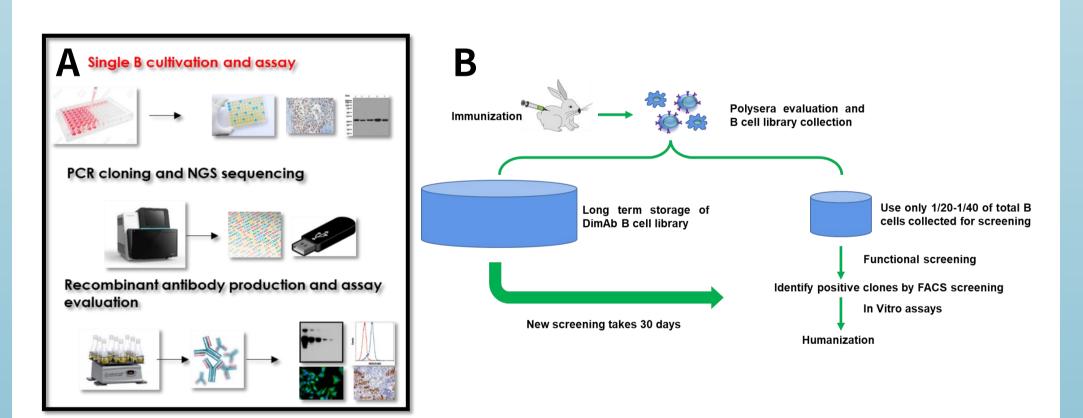


Figure 2. (A) DimAb® single B cell workflow. Dima B® takes advantages of unique B cell culture method, which allows fast and precise isolation of positive antibody sequences. (B) DimAb® B cell library. The unused B cells from immunized animal can be stored in liquid nitrogen for long term. More lead antibody molecules can be screened by initiating a new round of screening and cloning, which the whole process takes only 30 days.

#### DiLibrary™ antibody humanization platform

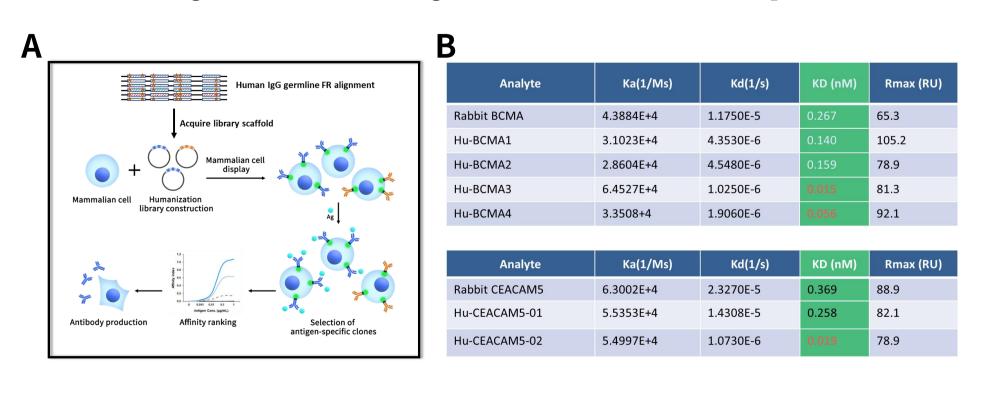
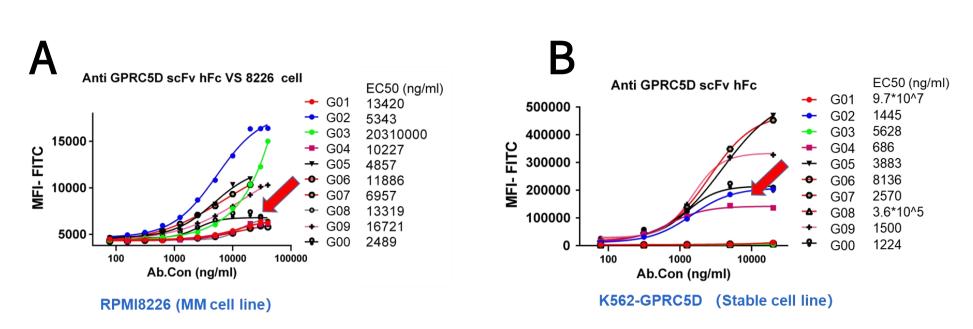
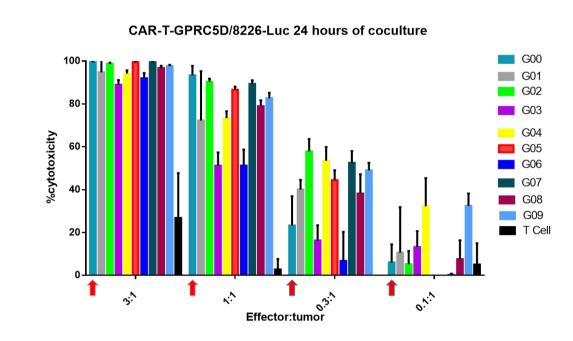


Figure 3. (A) The work flow of DiLibrary™ antibody humanization. CDRs from parental antibody are first grafted onto a FR library constructed from a number of selected human IgG germline sequences. The final antibody library will be displayed on HEK293 cell surface, and the best binders can be isolated through FACS sorting with target protein. (B) Examples of two humanization experiments.

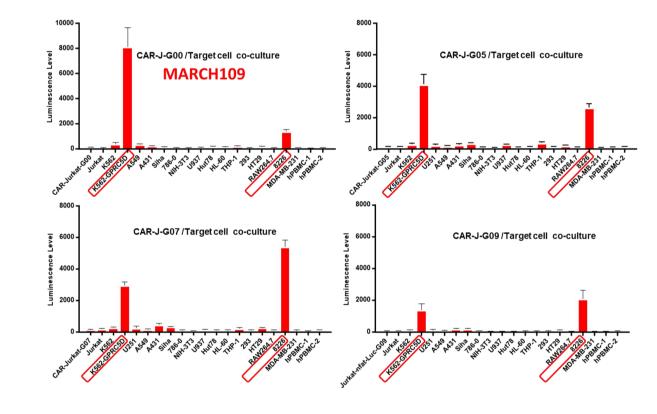
## Results



**Figure 4.** Affinity ranking of 9 humanized anti-GPRC5D DimAbs through flow assay. Comparing to BMK antibody (G00) pointed by red arrow, derived from a CAR construct currently in phase I clinical trial, 4 out of 9 DimAbs exhibit stronger binding affinity on both RPMI8226 or K562-GPRC5D stable cell line.



**Figure 5. In Vitro tumor cell cytotoxicity assay.** The experimental data showed that several of CARs constructed from DimAbs exhibit stronger cytotoxic capacity than bench-mark CAR (G00), pointed by red arrows, especially under low Effector:Tumor ratio.



**Figure 6. The selected CAR constructs exhibit high specificity on target cells.** We examined target cell specificity of G00, G05, G07, and G09 CAR constructs. Through a CAR-Jurkat assay, all CAR constructs show exclusive target cell specificity.

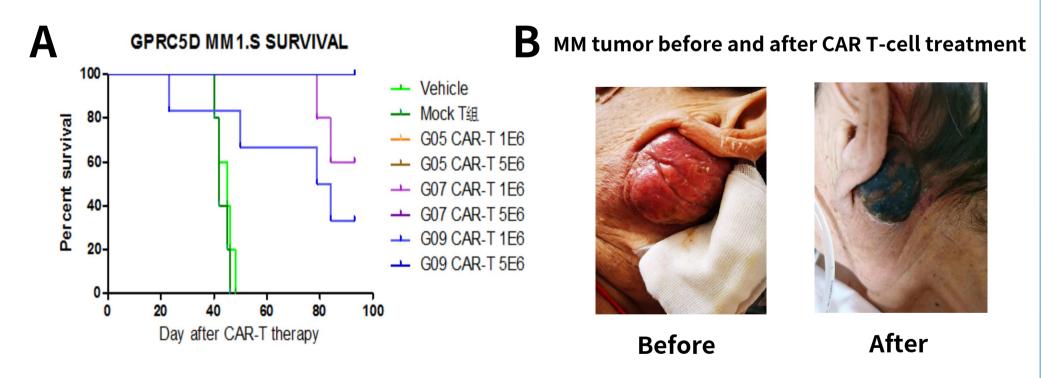


Figure 7. Animal survival data and early IIT clinical trial data. A. MM model mice infused with two dosage of CAR T-cells exhibit elongated survival time comparing with control groups. B. A RRMM patient relapsed from BCMA CAR T-cell therapy was treated with our anti-GPRC5D CAR T-cells. A big tumor mass behind patient ear disappeared in 10 days after CAR T-cells infusion. (Currently our collaborators are recruiting more patients.)

#### Conclusion

DIMA Bio. is a biotech company dedicated on hit to lead stage therapeutic antibody discovery. Currently we have obtained more than 5000 IgG molecules on 500+ targets. In this anti-GPRC5D CAR T-cell project, we showcased how we developed 3 lead stage DimAbs and then chose one to push into IIT clinical trial. For this project, our collaborator is planning to recruit 18 patients for IIT and the clinical data will be reported separately.