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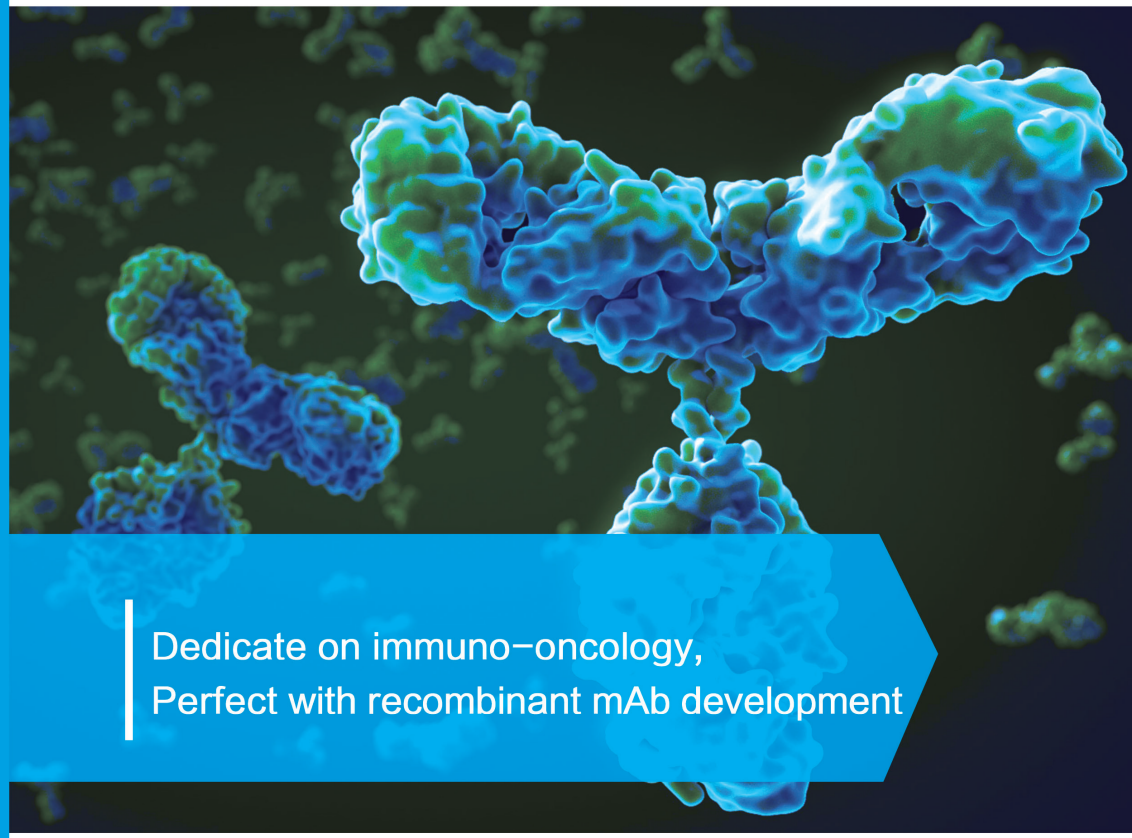
DIMA BIOTECH
Recombinant mAbs and proteins



Dedicate on immuno-oncology,
Perfect with recombinant mAb development

DIMA Biotechnology LTD

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The introduction of DIMA Biotechnology LTD

DIMA Biotechnology LTD is a research and development company focusing on immune oncology products and services. DIMA’s proprietary B cell cloning and recombinant monoclonal antibody monoclonal antibodies in high throughput. The R&D team has many years of experience in monoclonal antibody development. We provide solutions for scientific research, clinical diagnosis and therapeutic R&D.

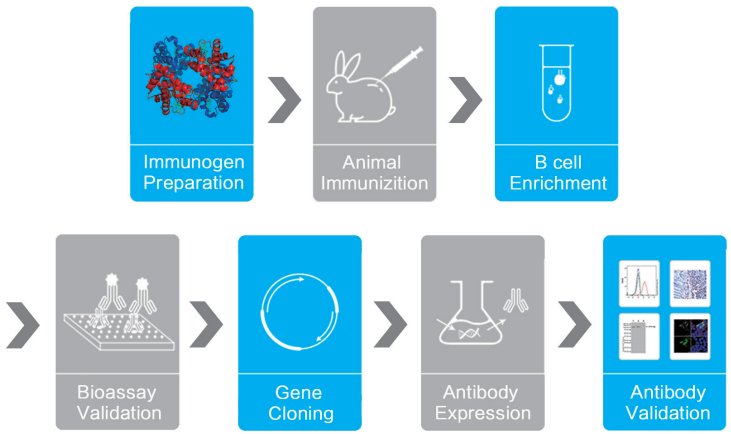
The corporate culture is integrity, pragmatism, innovation and focus. The mission for the company is to apply advanced biotechnology to provide new and effective solutions for cancer diagnosis and treatment.

DIMA BIOTECH
Recombinant mAbs and proteins

DimAb™ recombinant monoclonal antibody development platform

DimAb™ recombinant monoclonal antibody development platform is considered as a technology revolution for monoclonal antibody development. Compared with traditional hybridoma based monoclonal antibody development platform, this new technology platform can directly obtain IgG gene sequences from immunoreactive B cells without the need of hybridoma fusion. From our data, we can easily isolate more than 1000 immunoreactive B cell clones from a single immunized animal. The success rate for downstream application is far higher than the traditional hybridoma platform. With large number of positive clones, it will give us better chance to screen out monoclonal antibodies with high specificity, high sensitivity and high affinity.

DimAb™ platform workflow



The unique technology advantages of DimAb™ development platform

Platform comparison

With the limited availability of myeloma cell lines, most of the monoclonal antibody development is restricted to mouse mAbs. DimAb™ has completely broken this boundary and enable us to explore mAbs from many species.

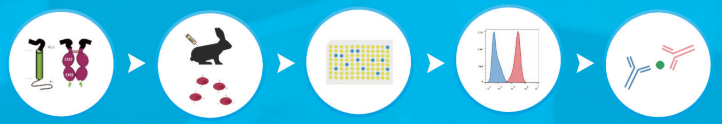
Comparison Items	DimAb™ antibody preparation platform	Hybridoma Platform
Success Rate	High project success rate (80-90%)	Low project success rate (50%)
Storage mode	The antibody gene sequence is obtained directly, and the antibody information is easy to store and transmit	The cost of hybridoma cell preservation is very high, which requires a lot of liquid nitrogen and cell storage equipment
Screening efficiency	In theory, every antibody secretion B cells can be screened and isolated	The fusion efficiency of hybridoma is a limiting factor, and many B cells cannot form stable fusion clones
Antibody quality	Recombinant antibody with DNA sequence available	Hybridoma cells are unstable, which may lead to the loss of antibody genes
Availability of mAbs from different kinds of animal species	Recombinant mAbs from different kinds of animal species can be obtained	Due to intellectual property, only mouse monoclonal antibodies are widely avialble
Preparation process	The preparation process is fast and antibody genes can be obtained directly	The quality and stability of antibodies secrected from hybridoma cells are highly unstable.
Animal ethics	No need to kill animals	Need to sacrifice animal to obtain splenocytes

Development of Flow DimAbs

It is difficult to develop flow mAbs on membrane protein targets. The main challenges come from the production of high quality immunogens that can mimic the native conformation of its targets on membrane. In DIMA Biotech LTD., we adopted a robust HEK293 mammalian expression system to produce highest quality proteins for immunization and screening.

Right now, we have successfully developed a number of flow antibodies by utilizing DimAbTM platform. Here is an example how we developed anti-BCMA flow DimAbs from scratch.

The developmental flow chart



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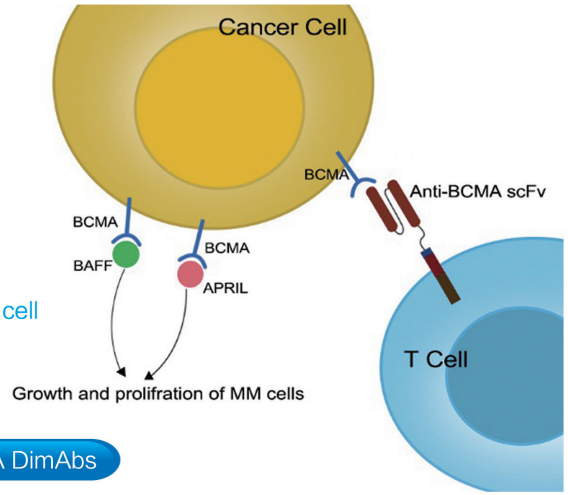
Recombinant mAbs and proteins

BCMA is a tumor cell target for CAR-T cell therapy on Multiple Myeloma (MM)



The flow data exhibition for anti-BCMA DimAbs

Functional proteins developed as immunogens

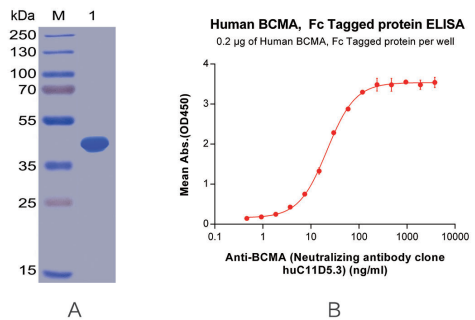


Figure1.
A. Human BCMA, mFc-His Tag on SDS-PAGE under reducing condition.
B. ELISA plate pre-coated by 2 μg/ml (100 μl/well) Human BCMA , hFc-His tagged protein (PME100001) can bind Anti-BCMA (Neutralizing antibody clone huC11D5.3) in a linear range of 3.71-22.29 ng/ml.

Phylogenetic analysis of CDRs on 6 different anti-BCMA flow DimAbs

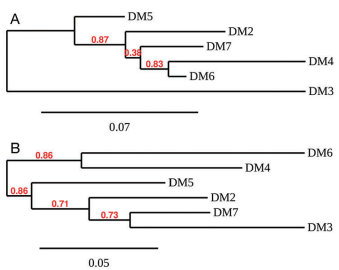


Figure2.
Phylogenetic analysis of different Anti-BCMA DimAb clones. A) heavy chain and B) Light chain.

Flow cytometry analysis and affinity ranking on different Anti-BCMA DimAb clones

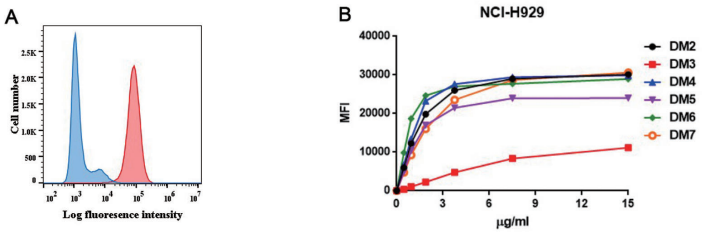


Figure 3.
A. Flow cytometry analysis with anti-BCMA (DM2) (Red histogram) or rabbit control antibody on NCI-H929 cells (Blue histogram).
B. Affinity ranking of different DimAb clones by titration of rabbit antibody concentration onto NCI-H929 cells. Different concentrations of various anti-BCMA DimAb clones were incubated with NCI-H929 cells at 4℃. Bound rabbit IgG was detected in flow cytometry analysis. The Y-axis represents the mean fluorescence intensity (MFI) while the X-axis represents the concentration of IgG used.

Epitope binning analysis

5 DimAbs exhibit different binding epitope from BB2121

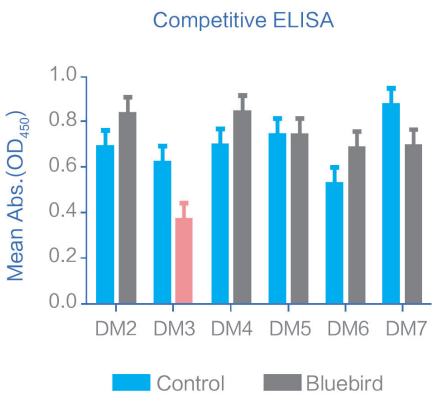
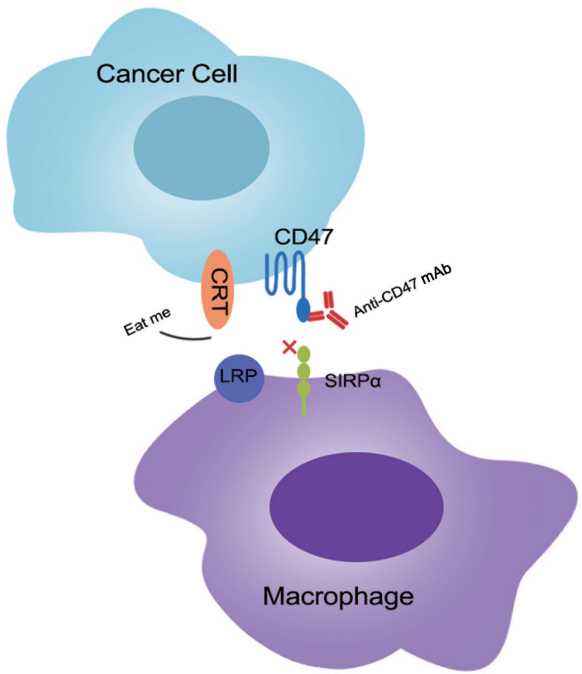


Figure 4.
ELISA plate was coated with recombinant BCMA-hFc fusion protein, followed by pre-blocking with **huC11D5.3** antibody (Grey bar) or rabbit control IgG (Blue bar) and then different rabbit DimAbs antibodies were added to check the competitive inhibition of **huC11D5.3**. DM3 clone exhibits the strongest inhibition (Red bar). This data indicated that DM3 binds to the same epitope as bb2121.

Using DimAb™ platform to develop neutralizing antibodies for cancer therapy

Tumor cells and immune cells can actively interact with each other in tumor micro-environment. Through specific receptors and ligands located on the membrane surface of tumor or immune cells, immune cells can be either inhibited or activated to kill tumor cells. Therapeutic monoclonal antibodies with neutralizing activities can exert therapeutic effects through blocking the specific receptor-ligand interactions.



The development of functional proteins for CD47 and SIRPα

Protein Purity

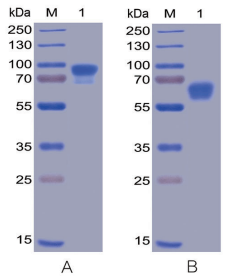


Figure 1.
Human SIRPα, hFc – His Tag (A)and CD47, mFc-His Tag (B) on SDS- PAGE under reducing condition.

Receptor-ligand interaction

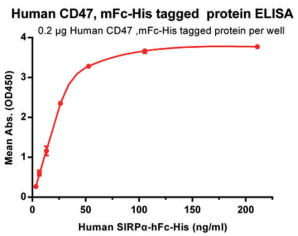


Figure 2.
ELISA plate pre- coated by 2 μg / ml (100 μl / well) Human CD47, mFc- His tagged protein (PME100008) can bind its native ligand Human SIRPα, hFc- His tagged protein (PME100009) in a linear range of 3.3- 26.37 ng/ml.

Biosimilar interaction

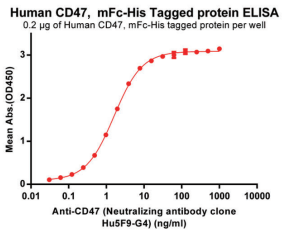
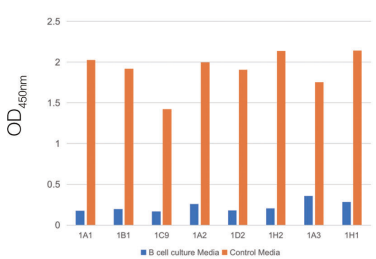


Figure 3.
ELISA plate pre- coated by 2 μg / ml (100 μl / well) Human CD47, mFc- His tagged protein (PME100008) can bind Magrolimab (Neutralizing antibody clone Hu5F9- G4) in a linear range of 0.061-1.606 ng/ml.

Screening anti-SIRPα DimAbs with neutralizing activities



SIRPα neutralizing DimAbs screening
(Clone 1C9 was cloned and also works on flow validation.)