



# Membrane Proteins and Monoclonal Antibodies

DIMA's products and services for your drug target research

### **DIMA's Mission**

DIMA harnesses cutting-edge technologies to provide a fully integrated solution for the preclinical research and development of antibody drugs and membrane proteins.

### **DIMA's Vision**

Empowering our customers to accelerate their preclinical research and development in antibody drug discovery.

### **About DIMA**

DIMA Biotechnology Ltd. is a biotech company offering products and services for BioPharma companies for their preclinical research need. Different from other traditional CRO companies, we provide on-shelf pre-stocked and validated hit-to-lead stage antibody molecules for BioPharma companies.

Currently we have over 5000 on-shelf lead antibody molecules for around 300 drug targets with verified sequences and validation data. In the next couple of years, we plan to develop lead antibody molecules for all druggable targets. Our purpose is to help BioPharma companies speed up their antibody-based drug discovery process.

Over the years, DIMA Biotech has been deeply engaged in developing and optimizing various technology platforms for antibody-based drug development. Here is a summary of our technology platforms:

1. DiMPro<sup>™</sup> membrane protein production platform: We use mammalian cell expression system to prepare and purify various membrane proteins including single and multi-pass membrane proteins. Right now, we are offering over 1000 on-shelf functional validated druggable target proteins. For multi-transmembrane proteins, such as GPCRs and ion channels, we have successfully utilized five different technology solutions, i.e., Membrane Nanoparticle (MNP), Virus-Like Particle (VLP), Exosome (EXO), Detergent and Nanodisc, to produce and purify active full length membrane proteins. As of now, we have made more than 50 multi-transmembrane full-length proteins in Nanodisc format, all of which can be shipped by the next day. 2. DimAb<sup>®</sup> single B-cell lead antibody molecule discovery platform: Using this platform, DIMA Biotech has completed hit-to-lead discovery for around 300 druggable targets and obtained over 5000 antibody molecules with IgG sequence information. Our DimAb<sup>®</sup> B cell library platform can help customers easily obtain more than 10,000 positive hits in as short as a month's time.

3. DiLibrary<sup>™</sup> mammalian display based antibody engineering platform: DIMA developed its proprietary mammalian display platform for antibody engineering. DiLibrary<sup>™</sup> mammalian display platform can be utilized for antibody humanization, affinity maturation or other antibody engineering applications. As opposed to phage or yeast display platforms, the developability of molecules engineered from our system could be much better since we use a mammalian cell-based system during development.

Our products and services are widely recognized. A number of top-tier BioPharma companies already in-licensed DimAb<sup>®</sup> lead antibody molecules from DIMA Biotech. We offer flexible partnership models tailored to your needs.



Suzhou

Wuhan

# **Technology Platform**

#### ■ DiMPro<sup>™</sup> platform for functional membrane protein preparation

One of the key requirements for antibody development is to utilize protein immunogens that best mimic native state of target protein. Most druggable targets for antibody-based therapy are membrane proteins, which are notoriously hard to express. DIMA biotech has created multiple solutions for membrane protein production. Human proteins are produced using HEK293 secretion expression system, so that they can have a good chance to keep their native conformation and modifications. To find the best production strategy, we individually study and design the expression construct for every membrane protein target.

For single transmembrane protein, we use the well-designed ECD to mimic its functional domain. For full length multi-transmembrane proteins, such as GPCR and Claudin series proteins, we invested heavily on new expression and extraction technologies, and developed 5 different solutions to extract different targets, e.g. VLP, Exosome, MNP, Detergent and Synthetic Nanodisc.



#### **Key advantages**

- Mammalian cell expression system with authentic post-translational modifications
- Serum free medium culturing system to minimize host cell contamination
- Function validated proteins
- Custom protein and large batch production available

#### **Key applications**

- Native immunogens for therapeutic antibody drug development
- Native ligand and receptor identification
- Therapeutic drug In Vitro functional test
- In Vitro protein functional test
- Cell based assays

#### Extra Cellular Domain (ECD) Protein

- Ideal for the single transmembrane druggable targets
- Over 1000 on-shelf ECD-Fc fusion proteins
- HEK293 mammalian expression system for production

#### Multi-pass Transmembrane Protein (MTP)

5 different platforms in 2 categories:

- Multi-transmembrane proteins in native membranous vesicles: Membrane Nanoparticles (MNPs), exosome (EXO) and Virus-like particles (VLPs).
- Purified proteins: Detergent and Nanodisc platforms.

#### DimAb<sup>®</sup> single B-cell lead antibody discovery

DimAb<sup>®</sup> 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 10,000 immunoreactive B cell clones from a single immunized animal. The success rate for downstream application is far higher than the traditional hybridoma platform. Therefore, we have a good chance to find monoclonal antibodies with high specificity and high affinity. With IgG sequence available, we can directly edit, optimize and identify antibodies for downstream applications, such as humanization, affinity maturation, CAR-T, etc.

Since DimAb<sup>®</sup> preparation process no longer depends on the availability of myeloma fusion partner, it is possible for us to use this platform to develop monoclonal antibodies from different species. Therefore, DimAb<sup>®</sup> offers a unique solution for the antigens with high homology and weak immunogenicity by using different hosts for immunization. At present, we have optimized the highthroughput development process on rabbit and mouse derived recombinant monoclonal antibodies.



#### Comparison Between DimAb® Platform and Hybridoma Platform

COMPARISON ITEMS	DIMAB <sup>®</sup> ANTIBODY PREPARATION PLATFORM	HYBRIDOMA PLATFORM
Success Rate	High (80-90%)	Low (50%)
Storage mode	Digital information; easy to store and transfer	Hybridoma cells: high cost for preservation, difficult to store and transfer
Screening efficiency	High	Low
Antibody quality	Recombinant antibody with DNA sequence available	Hybridoma cells are unstable, which may lead to the loss of antibody genes
Host species	Various animal species	Mostly mouse mAb
Preparation procedure	Fast and antibody genes can be obtained directly	slow
Animal ethics	No need to kill animals	Need to sacrifice animal to obtain splenocytes

#### ■ DiLibrary<sup>™</sup> mammalian display platform for antibody engineering

Antibody humanization is important for therapeutic antibody development, especially for the candidate antibodies derived from animal sources. DIMA Biotech has developed a proprietary mammalian display platform for antibody humanization and affinity maturation, DiLibrary™ antibody engineering platform. With this platform, we can deliver a panel of humanized variants with improved affinity than its parental antibody. In addition to improved affinity, the engineered clones also exhibit improved developability for downstream development, such as high expression level and low aggregation tendency. Therefore, DiLibrary™ system is a superior antibody engineering platform to help us optimize antibody molecules with better developability.





At least 3x increase in

affinity



Finish in 48 days





**Powerful** One-step process for humanization, optimization



Flexible Custom designed mAb library for your needs



Fast Deliver humanized mAb sequences and data in 48 days.



#### Complete

One stop shop from antibody discovery , optimization to functional evaluation.

& developability assessment



**Risk Free** Guarantee affinity after humanization

#### **Platform Workflow**



#### Case Studies: Humanization of Anti-BCMA rabbit mAb

By using DiLibrary<sup>™</sup> display platform, we have successfully obtained humanized antibodies with increased binding affinity (Hu-BCMA3 shows around 18-fold increase).

Analyte	Ka(1/Ms)	Kd(1/s)	KD (nM)	Rmax (RU)
Rabbit BCMA	4.3884E+4	1.1750E-5	0.267	65.3
Hu-BCMA1	3.1023E+4	4.3530E-6	0.14	105.2
Hu-BCMA2	2.8604E+4	4.5480E-6	0.159	78.9
Hu-BCMA3	6.4527E+4	1.0250E-6	0.015	81.3
Hu-BCMA4	3.3508+4	1.9060E-6	0.056	92.1











## All Druggable Targets (ADT) lead discovery program

To help Biopharma accelerate its pace on pre-clinical antibody drug lead selection and optimization, DIMA, equipped with its proprietary single B cell discovery platform, launched an "All Druggable Targets (ADT)" lead discovery program. The goal is to provide on-shelf pre-stocked and pre-validated hit-to-lead stage antibody molecules for all druggable targets. Currently, we have completed around 300 druggable targets and obtained over 5000 antibody molecules with IgG sequence information and antibody validation data. The complete list of our available targets can be found on our website (www.dimabio.com/lead-antibody-molecule).

Featured Cancer Targets										
2B4	4-1BB	4-1BB-L	5T4	ACE2	ADAM9	ADORA2A	AFP	ALB	AMHR2	
ANGPTL3	AXL	B71	B72	B7H2	B7H3	B7H4	B7H6	BAFF	BAFF-R	
BCL2L1	BCMA	BTLA	BTN3A1	CA9	CB1	CCR8	CD10	CD112	CD114	
CD117	CD123	CD138	CD155	CD171	CD19	CD200	CD21	CD22	CD24	
CD27	CD28	CD30	CD30L	CD33	CD34	CD36	CD37	CD38	CD40	
CD40L	CD43	CD45	CD46	CD47	CD48	CD5	CD56	CD7	CD70	
CD73	CD96	CD99	CEACAM5	CLDN18.2	CLEC12A	CS1	CSF1R	CTLA4	CXCR3	
DKK1	DNAM1	EGFR	EPCAM	EPHA2	EPHA3	FAP	FCGR3A	FCRL5	Galectin9	
GFAP	GITR	GITR-L	GM-CSF	GPC3	Her3	HVEM	IFNAR1	IL11RA	IL13RA1	
IL15RA	IL17RA	IL18RA	IL2	IL21R	IL2RA	IL4RA	IL-5	IL-6	IL6R	
IL7RA	JAM-A	KLRG1	LAG3	LGALS1	LIGHT	Methoselin	MICA	MICB	NEFL	
NKP30	NTB-A	OX40	OX40L	PCSK9	PD-1	PD-L1	PDL2	PGF	PSCA	
ROR1	ROR2	SCF	SELP	SELPLG	SIRPA	S-RBD	TACI	THEP	TIGIT	
TIM-3	TNFRSF10B	TNFSF11	TNFSF12	TREM2	TROP-2	UCHL1	VEGFA	VEGFR2	VSIG4	

Contact us for the complete list of targets!

## **Products for Drug Target Research**

DIMA Biotech has developed many on-shelf high-quality bioreagents including ECD membrane proteins, Full length membrane proteins, DimAb monoclonal antibodies and Biosimilar antibodies to support the discovery and development of drug targets.

Drug target research is crucial in mechanism-based drug discovery and development. Currently, we have over 2000 on-shelf products covering almost 900 drug targets, including many G protein-coupled receptors (GPCRs), CD markers, receptors, and enzymes et al. Please contact us for your R&D needs on new therapeutic targets.

#### **DimAb® Rabbit mAbs**

- 300+ Drug Targets
- Good specificity & affinity

#### Full-length Membrane Proteins

- Multiple choices for difficult protein targets
- Bioactive proteins with near native protein structures

On-shelf Availability

#### **Biosimilar Reference Abs**

- 150+ verified reference antibodies
- Used for functional testing of therapeutic protein targets

#### **ECD Bioactive Proteins**

- 1000+ bioactive ECD proteins
- Produced in mammalian cell expression system

## **Custom Services for Pre-clinical Research**

Empowered by the cutting-edge technologies in proteins and antibodies, DIMA biotech can easily deliver many mAb molecules for your druggable targets. We offer multiple on-shelf mAb molecules for each target protein (On-shelf Lead mAbs Service), and pre-validated B cell libraries for further screening of good candidates. We also provide a comprehensive services from antigen preparation (Custom Protein Production) to Lead mAbs Discovery Service and Antibody Engineering Service.



# **DIMA Biotechnology LTD**

Dedicate on immuno-oncology, Perfect with recombinant mAb development



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