DIMA BIOTECH
Recombinant mAbs and proteins

Custom Rabbit DimAb™ services

DIMA Biotechnology LTD

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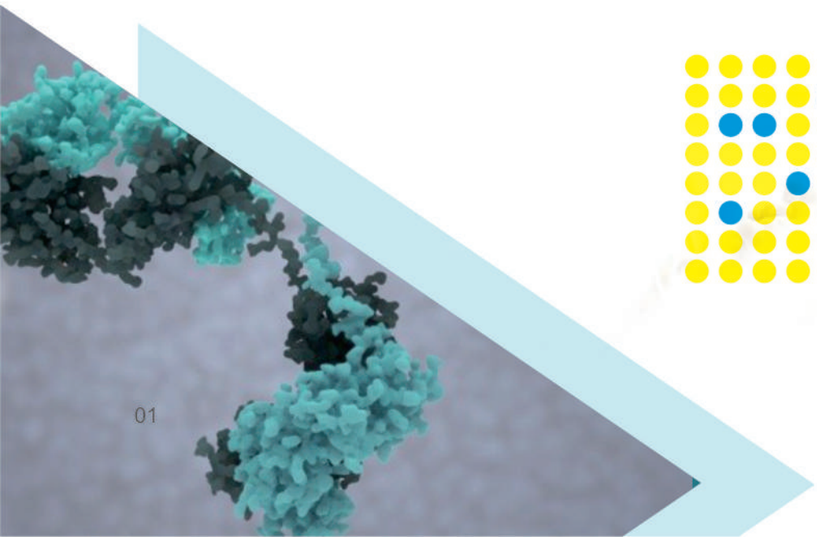
Custom Rabbit DimAb™ services

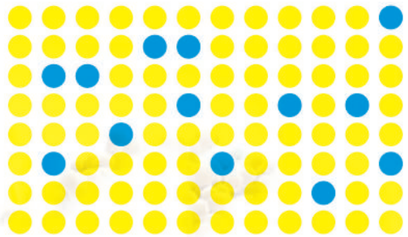
Our team has decades of experience on high quality monoclonal antibody development services. DIMA' s DimAb™ development platform is a revolutionary technology platform for monoclonal antibody development. Different from hybridoma fusion platform, we can directly isolate IgG genes from B cells of immunized animals.

The unique advantages of DimAb™ rabbit recombinant monoclonal antibodies

High cloning efficiency

DimAb™ can directly enrich, isolate and clone IgG genes from B cells of immunized animal. Therefore, the overall cloning efficiency is extremely high. We can easily obtain more than thousands of ELISA positive clones from a single immunized animal.





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More clones with high affinity and wide sequence diversity

Comparing with other animals, the rabbit has a unique B cell development process and is more distant from human than rodent. Besides these, rabbit B cells utilize a dual affinity maturation mechanism, including gene conversion and SHM (somatic hyper−mutation). At the same time, the rabbit IgG has a unique protein structure different from the mouse IgG, including one subtype of IgG, more noncanonical C−C for light chain, great variation in length and sequence for CDR3, etc. These differences might make rabbit produce antibodies with high affinity and wide diversity.

Suitable to develop antibodies against epitopes of hapten, point mutation or posttranslational modification antigen

The B cell maturation process between rabbit and mouse is quite different. Rabbit can express 5 different subtypes of CD1 molecules. However, mouse has only one subtype. Many experimental evidences indicate that rabbit is very good at producing immune responses against small molecule hapten antigens, or specific antibodies against posttranslational modification sites, including phosphorylation, methylation, Acetylation, etc.

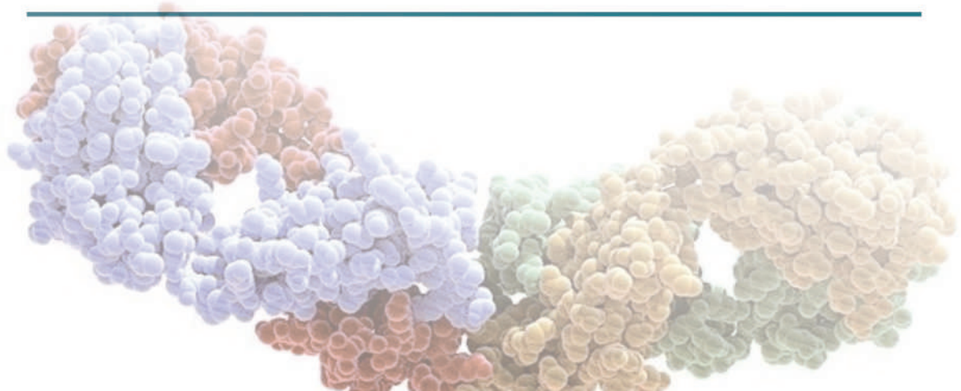
The applications of rabbit monoclonal antibodies

Application on therapeutic antibody drug development

On October 8th, 2019, the first rabbit monoclonal antibody derived drug Beovu® was approved by FDA for the treatment of wet age-related macular degeneration (AMD). Beovu® is a variable region fragment of humanized rabbit monoclonal antibody scFv targeting VEGF. This is also the 83rd antibody drug approved by FDA. Compared with other antibodies, rabbit recombinant monoclonal antibodies have higher affinity, which can not only reduce the clinical dosage of antibodies, but also reduce the side effects caused by the use of a large dosage. The success of Beovu has proved the therapeutic drug developability of rabbit monoclonal antibody.

Part of the FDA approved list of rabbit monoclonal antibodies for companion diagnosis

Concomitant diagnostic reagents	Antibody drug	Cancer	Detection platform
PATHWAY ANTI-HER -2/NEU (4B5)	HERCEPTIN (trastuzumab)	Breast cancer	IHC
VENTANA ALK (D5F3) CDx Assay	XALKORI(crizotinib)	Non-small cell lung cancer	IHC
PD-L1 IHC 28-8	OPDIVO(nivolumab)	Melanoma Non -small cell lung cancer	IHC
VENTANA PD-L1 (SP142) Assay	TECENTRIQ (atezolizumab)	Bladder cancer Non-small cell lung cancer	IHC
VENTANA PD-L1 (SP263) Assay	KEYTRUDA® (pembrolizumab)	mNSCLC	IHC



Application in clinical diagnosis

Recent evidences indicated that rabbit monoclonal antibody has clear advantages in immunohistochemistry application. Currently rabbit monoclonal antibodies become the favorite choices for pathologists. At present, FDA has approved 11 rabbit monoclonal antibodies for diagnosis, including companion diagnostic IHC antibodies for anti-PD-1 and anti-PD-L1 immunotherapy drug treatment, 4B5 clone for Herceptin treatment, etc.

Application in scientific research

With the advantages of high specificity and high affinity, rabbit monoclonal antibodies have been widely used in life science research. Due to its unique B cell development system, rabbit monoclonal antibodies have exhibited special strength in detecting subtle difference on small epitopes, such as post-translational modified amino acids within a protein.

Custom rabbit DimAb™ development procedure & deliverables

Step	Service details	Deliverables	Estimated production cycle (week)
Immunogen preparation	Plasmid construction, mammalian cell produced immunogens or supplied by customer		7-10 Weeks
Animal immunization	Immunize two rabbits against the same antigen	Crude sera and ELISA data on anti-serum titer test	5-8 Weeks
B cell isolation and amplification	PBMC collection and cryopreservation; target positive B cell enrichment and single B cell expansion	100ul B cell supernatant; B cell supernatant ELISA test data	2-3 Weeks
DimAb™ cDNA cloning, sequencing and storage	IgG gene cloning, Expression vector construction; small-scale antibody production and validation; select 1-2 positive clones for full-length IgG sequencing and sequence analysis	Sequencing report of one clone; ELISA data	3-4 Weeks
DimAb™ production and validation	Antibody production, purification and QC validation	1 mg purified recombinant antibody, antibody QC data	3-4 Weeks

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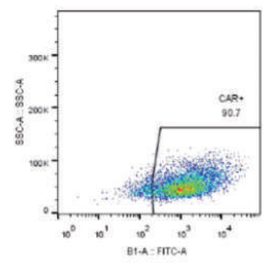
Service Case

The whole DimAb™ development procedure took around 3.5 months (delivered 8 flow working rabbit DimAbs to customer (Bioraid, a CAR−T company)

Flow data

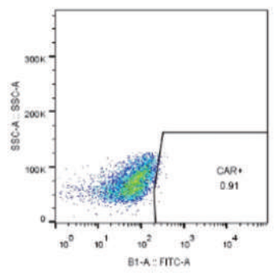
CLONE#	ELISA (OD_{450})	Flow Positive CAR cells
12D10	2.0	98.00%
13C5	2.6	98.20%
13E10	1.2	92.10%
14D11	1.0	91.90%
15E4	2.6	99.50%
15G3	2.7	98.50%
17G3	1.0	84.30%
20A11	2.3	98.60%

Flow data on K562-mCD30



CAR-T 14D11-3.0016 fcs
live
6793

Flow data on K562



WZM T 14D11-3.0015 fcs
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5073