Biologics

Technical Manual

How to Design and Evaluate Bispecific Antibodies (BsAbs)?

- What is bsAb?
- How to develop bsAbs discovery strategies based on structure?
- How to evaluate bsAbs comprehensively based on MOA?
- How to select a suitable partner for bsAb discovery?

GenScript PROBIO

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What is bsAb?

What is bsAbs?

Discovery Overview

Bispecific antibodies (bsAbs) are artificial antibodies containing two specific antigen binding sites. It has acquired much attention as the next-generation strategy of antibody-target cancer immunotherapy due to its efficacy and safety concerns over monoclonal antibodies (mAbs) based on their MOAs. The current clinical results have been proven clinically effective and approved for applications in the treatment of malignancies.

Improving therapeutic efficacy

- Inducing T cell activation and killing
- Regulating receptor signaling pathways
- Simultaneously targeting multiple inhibiting receptors or immune checkpoints
- Targeting multiple epitopes to improve the neutralization

Increasing safety index

- Off-target binding rate decreased for less side effects

Reducing manufacturing cost

- Only manufacturing one molecule with reduction in manufacturing cost compared with the combination of two molecules.

Figure 1: Advantages of BsAbs

Discovery Process

A bsAb is generally composed of two parental mAbs, the functionality and the developability of which need to consider before constructing a bsAb molecule.

1. Building multiple bsAb candidates through gene synthesis and recombinant expression after obtaining desirable mAb molecules.

2.BsAbs screening: Through binding and blocking screening against two targets, bsAb leads with satisfactory affinity for both targets are obtained.

3.BsAbs validation: *in vitro* function assay and *in vivo* validation.

4. Early developability assessment to obtain the pre-clinical candidates (PCCs) of bsAbs for CMC.

The discovery period of bsAbs is approximately six months.

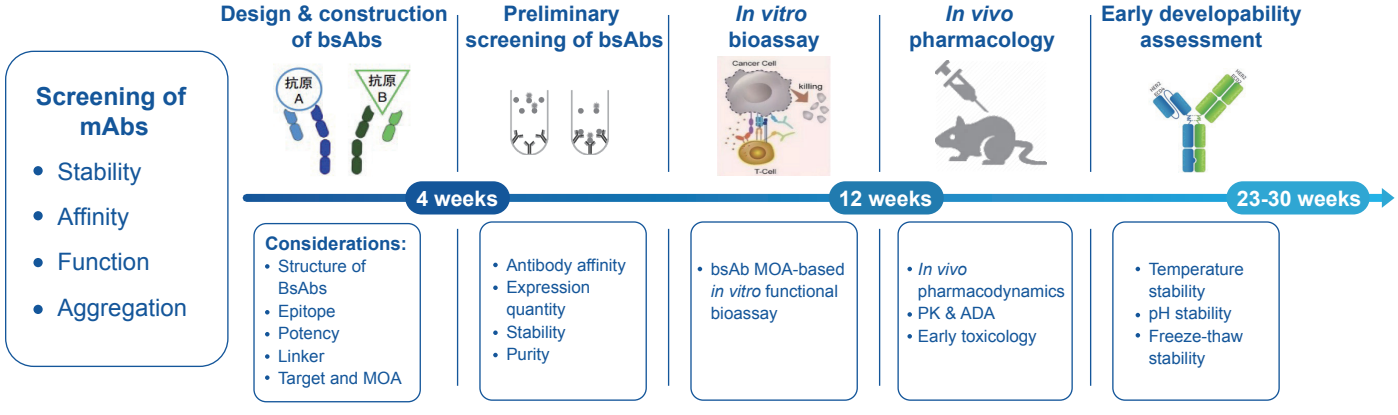

Figure 2: workflow of bsAbs discovery

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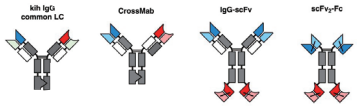
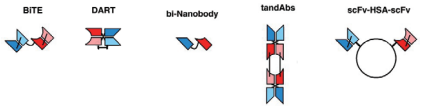
How to develop bsAbs discovery strategies based on structure?

How to develop bsAbs discovery strategies based on structure?

BsAbs Structure

During the past six decades, the technology of bsAb development has evolved rapidly. Over 100 bsAbs structures and approximately 40 distinctive bsAb platforms are available currently. The structure of bsAb is a critical factor in the development of bsAb drugs, which impacts its functionality and developability. Due to one of the discriminating features of the presence or absence of an Fc region, bsAbs can be classified into fragmented bsAbs with no Fc region and full-length bsAbs with the Fc region. The full-length bsAbs can be further divided into bsAbs assembled as IgG structures and bsAbs containing additional binding sites onto an existing IgG antibody. The different bispecific antibodies have either a symmetric or an asymmetric architecture. The bsAb with asymmetric architecture exhibits better flexibility regarding spatial structure. However, eliminating heterodimers through sequence engineering, or protein A purification is problematic. Secondary purification, such as ion exchange or hydrophobic exchange, is often required. The symmetric bsAbs solve the mis-paring of heavy and light, but the configuration may restrict the spatial flexibility of the MOA.

Table 1: Classification of common bsAbs

Structure types	Full-length bsAbs with Fc fragments	Fragmented bsAb without Fc fragments
Structure diagram		
Molecular characteristics	• Containing several chains with a high molecular weight • Longer half-life • Flexibility with ADCC and CDC effect	• Generally a single chain with a low molecular weight • Shorter half-life • No Fc effectors (e.g., ADCC/CDC)
Advantages	• Good stability • Good solubility • Easy to purify with the presence of Fc fragments	• Easy to manufacture with less by-products and a high yield • No mispairing of heavy and heavy chains
Disadvantages	• Transfection ratio of multiple chains to be investigated • Generally low expression level due to asymmetric structures • Low yield due to being prone to aggregation, mispairing and fragmentation	• Without Fc fragments; need special purification process and expression detection methods • Lyophilization process to be developed generally due to poor stability and easy aggregation

Considerations for BsAb Design

The choice of the bsAbs structure relies on the targets, MOA, and indications. The appropriate structure selection is on the basis of the following considerations:

How to develop bsAbs discovery strategies based on structure?

1	Affinity & potency	• Higher antibody affinity is not always better and should be considered in combination with the MOA. • The valency of bsAbs will affect their efficacy and safety. For example, a monovalent antibody is generally selected for CD3 due to its toxicity. The potency of antibody targeting tumor-associated antigen (TAA) should be determined according to its characteristics.
2	Linker	• The length, flexibility, and amino acid composition of the linker used to connect two antibodies, and the IgG hinge region is crucial for the efficacy of BsAbs.
3	Antigen epitope	• The distance between the antibody epitope and the target cell, as well as two different antigens, are the factors affecting the efficacy and safety of bsAbs.
4	Antibody size	• It is difficult for antibodies with large sizes and long half-life to infiltrate solid tumors. • Antibodies with small sizes and short half-life can enter solid tumors through vascular exudation.
5	Fc region	• Fc has effector functions, it is necessary to remove Fc region to prevent excessive T-cell activation. • The IgG1/IgG4 hinge region facilitates the formation of synapses between T cells and target cells by the bridging mechanism.
6	Parental antibody	• The parent monoclonal antibody is required to have good functionality and developability. • A cost-effective bsAb is designed according to the status of the existing mAbs.
7	Patent	• Choosing an FTO bsAb structure is preferable.

Figure 3: considerations for bsAbs design

BsAbs Screening

The efficacy of bsAb drugs is closely related to the targets, MOA, parental mAbs, and their structure. GenScript ProBio recommends constructing at least two bsAb molecules for subsequent screening. PCC molecules are obtained for CMC through 3 rounds of bsAb screening.

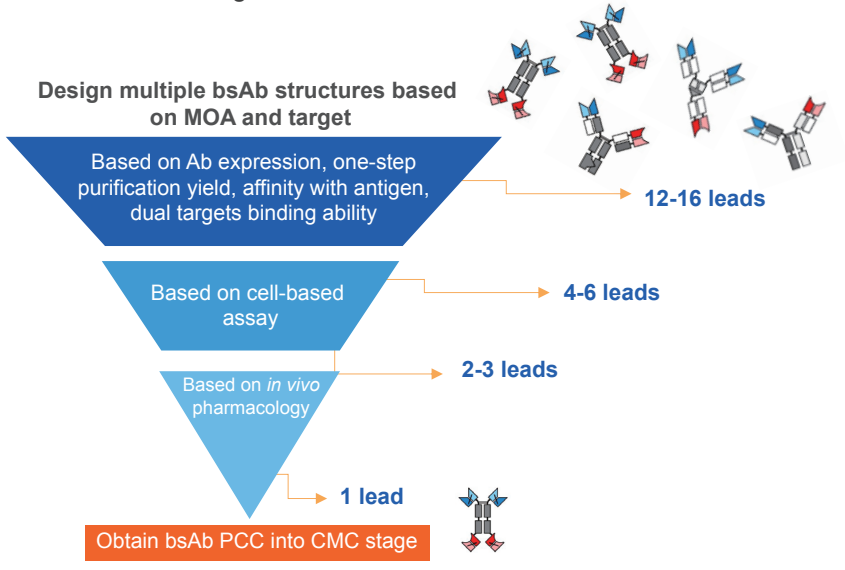


Figure 4: Screening and evaluation process of bsAbs

How to develop bsAbs discovery strategies based on structure?

Tip: How to design T cell bridging bsAbs

CD3 plays a role in information transmission in the T cell receptor (TCR)-CD3 complex. T cells recognize antigen peptides-major histocompatibility complex (MHC) molecular complex on tumor cells through TCR. The activation signal is transmitted to T cells through CD3 to activate T cells and hereby kill tumor cells. Tumor cells can escape the immune surveillance by down-regulation of MHC molecules. Anti-CD3×TAA bsAbs bridge T cells and tumor cells, activate T cells by anti-CD3 antibody, and specifically kill tumor cells through high expression of TAA. At present, bridging with T cells is one of the most important research directions of bsAbs.

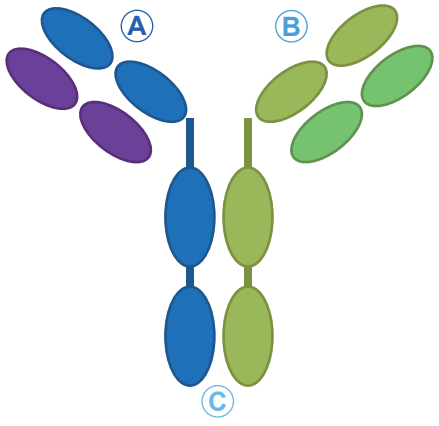


Figure 5: Considerations for design of anti-CD3×TAA bsAb structure

Ⓐ Target to TAA arm

- High target specificity to reduce the toxicity to non-targets
- The choice of BsAb structures due to antigen expression abundance and cell internalization efficiency
- Antigen-binding epitopes close to cell membrane for synapse formation (immunoscreening)
- Ligand/soluble target competition

Ⓑ Target to CD3 arm

- Affinity is crucial for efficacy and a prolonged therapeutic window
- CRS ranges from 50 to 200 nM with less T-cell depletion and tumor/PK distribution
- Tumor lysis syndrome is a dangerous signal
- Antibody having cross-reactions with cyno antigen

Ⓒ Fc domain

- Fc domain affects the spatial distance between the T cell and the target cell
- Fc domain binds to FcRn elongating half-life and silencing FcγR, which affects the developability, stability, and PK.
- Serious concerns about safety hazards from TCE protein aggregation

Dual-target CAR-T therapy:

CAR-T therapy has shown remarkable success in treating recurrent hematological malignancies but may be limited by the disadvantages of antigen escape and tumor recurrence. To address this, an intensively invested strategy is to use two hybrid CAR-T cells with different antigen binding specificities or a single CAR-T cell capable of targeting two antigens, enabling recognition of more than one TAA by dual-target CAR-T therapy. Popular antigen combinations in dual-target CAR-T therapy include CD19/CD20, CD19/CD22, and BCMA/CD38, while major CAR structures include single-target hybrid CAR, bivalent tandem CAR, bivalent circular CAR, and bicistronic CAR. Dual-target CAR-T cell therapy remains in the early stages of discovery, making it crucial to optimize the selection of CAR targets and structures through pre-clinical and clinical data.

References:

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2. Wang Q, Chen Y, Park J, et al. Design and production of bispecific antibodies[J]. Antibodies, 2019, 8(3): 43.

3. Current Status and Perspectives of Dual-Targeting Chimeric Antigen Receptor T-Cell Therapy for the Treatment of Hematological Malignancies. Cancers (Basel).2022 Jul; 14(13): 3230.

4. Ulrich Brinkmann & Roland E. Kontermann (2017) The making of bispecific antibodies, mAbs, 9:2, 182-212, DOI: 10.1080/19420862.2016.1268307

03

How to evaluate bsAbs comprehensively based on MOA?

How to evaluate bsAbs comprehensively based on MOA?

“Nonclinical studies are generally needed to characterize the pharmacology and toxicology of bispecific antibodies.”

-Bispecific Antibody Development Programs, FDA 2019

Previous studies suggested that bsAbs demonstrated a strong synergistic effect and offered a high efficacy and safety compared to monoclonal antibodies that directed against a single target. GenScript ProBio offers *in vitro* bioassay and *in vivo* pharmacology services to evaluate the efficacy and safety of bsAbs.

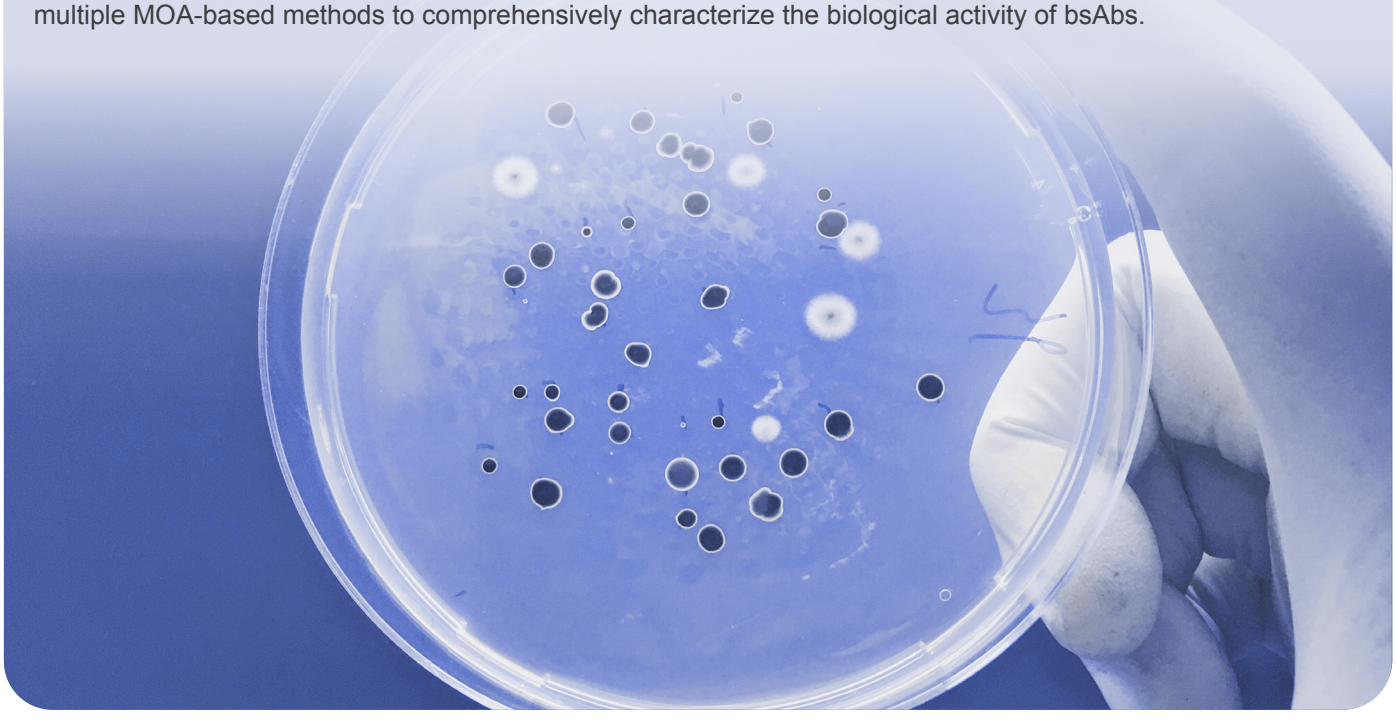
In vitro Bioassay

In vitro pharmacology evaluations provide early screening support and follow-up development of bsAbs. This works in two aspects:

1）Determination of the relative potency of mAb leads - a prerequisite to confirm the suitability for a component of bsAbs;

2）Functional analysis for bsAbs - a critical step to demonstrate the mechanism of action (MOA) of bsAbs and their advantages over mAbs.

The MOAs for bsAbs are classified as **cell bridging, dual-target blockade, immune cell activation, and in-cis protein bridging (binding to the same cell).** When evaluating bsAbs, the proposed MOA should be based on *in vitro* assay designs. Due to the complexity of *in vivo* system, an optimal *in vitro* pharmacology study design utilizes multiple MOA-based methods to comprehensively characterize the biological activity of bsAbs.



How to evaluate bsAbs comprehensively based on MOA?

1.Cell bridging

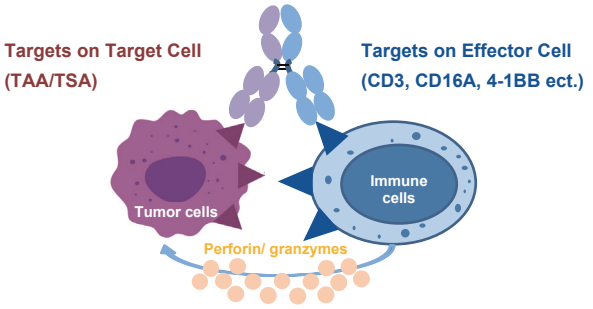


Figure 6. MOA of cell bridging

Cell bridging is a prevailing MOA for the bsAbs under investigation. BsAbs bind to the antigens on both the effector cells (immune cells, such as T cells, and NK cells) and target cells (tumor cells), activating the effector cells to kill the target cells.

Monitoring the expression of a reporter gene in an engineered cell line that mimics T or NK effector cells is one way to assess bsAb-mediated activation of in vitro cell bridging MOA. Additionally, isolated primary immune cells can be utilized as effector cells to evaluate the potency of bsAbs by killing tumor cells, similar to in vivo systems. However, it is importance to consider the bsAb-induced cytokine release for safety concerns, particularly for CD3-bsAbs, which may lead to a cytokine release storm (CRS) due to excessive activation.

Table 2. *In vitro* pharmacology methods for bsAbs adopting the MOA of cell bridging

Antibody type	Target cell	Target on target cell	Effector cell	Target on effector cell	*In vitro* functional assays
T cell bridging	• Engineered cell lines overexpressing TAA/TSA • Tumor cell lines	TAA/TSA	• Primary cells (T cells /NK cells/macro-phages /DC cells, etc.) • Reporter gene cell lines	CD3	• 1. Primary immune cell assay (TDCC, Cytokine release assay etc.) • 2. Reporter gene assay
NK cell bridging				NK cell activated receptors (CD16A, NKG2D, NKp46, NKp30, etc.)	• 1. Primary immune cell assay (NK cell-mediated tumor cell killing, etc.) • 2. Reporter gene assay
Anti-TAA x stimulatory immune checkpoint				Stimulatory immune checkpoints (CD40, 4-1BB, CD28, etc.)	• 1. Reporter gene assay • 2. Primary immune cell assay (immune cell activation, tumor cell killing, mixed lymphocyte reaction (MLR), etc.)
Anti-TAA x TAA/inhibitory immune checkpoint				NK cell activated receptor CD16A and macrophage activated receptor CD32A	• 1.Reporter gene assay • 2. Primary immune cell assay (ADCP, etc.)

- Tumor-associated antigen (TAA)
- Tumor-specific antigen (TSA)

How to evaluate bsAbs comprehensively based on MOA?

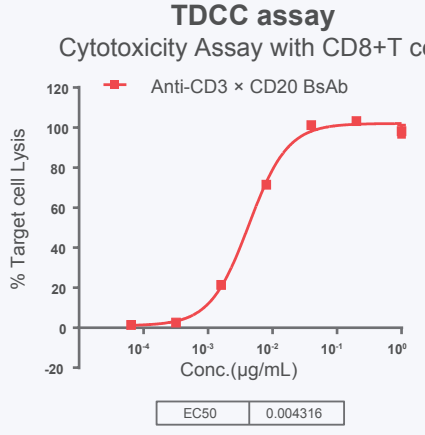
Anti-CD3 x TAA bsAb

T-cell engagers (TCEs) are one of the bsAbs that can connect a T cell via CD3 with a tumor cell via TAA, forming a TCR-independent artificial immune synapse and activating the cytotoxicity of T cells, thereby eliminating the tumor cells. These bsAbs activate tumor-infiltrating T cells and are preferred for treating "hot tumors" and hematological malignancies.

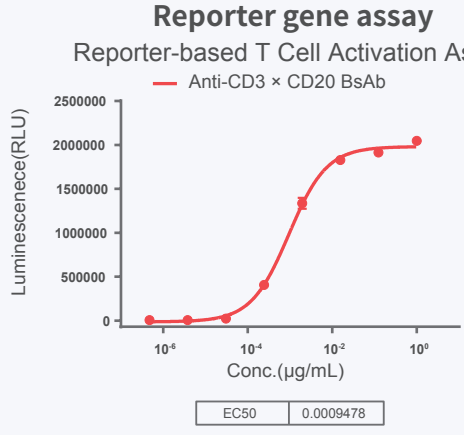
Case study:

Aspects for *in vitro* evaluation of in-house made anti-CD3 × CD20 bsAb:

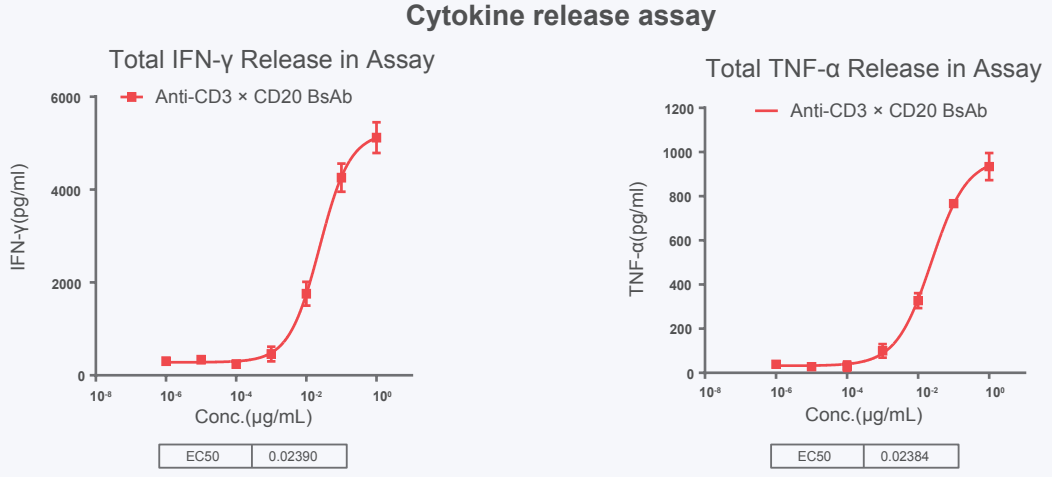
1. bsAb potency on T cell activation using proprietary reporter gene cell lines.
2. bsAb-mediated T-cell dependent cellular cytotoxicity (TDCC) against tumor cells using isolated primary CD8+ T cells.
3. Cytokine release (e.g., IFN-γ and TNF-α) upon bsAb-induced T cell activation.



Killing ability of primary CD8⁺ T cells against CD20⁺ tumor cells via anti-CD3×CD20 bsAb mediated TDCC effect.



Induction of the reporter gene through T cell activation upon engagement of effector cells and target cells via anti-CD3×CD20 bsAb.



Release of IFN-γ and TNF-α from primary CD8+ T cells induced by anti-CD3×CD20 bsAb.

Figure 7. *In vitro* functional evaluations of anti-CD3xCD20 bsAb

How to evaluate bsAbs comprehensively based on MOA?

bsAb and NK cell bridging

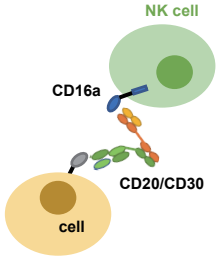


Figure 8. NK cell bridging

NK cell engagers are bsAbs that engage an NK cell via cytotoxic receptors (CD16A, NKG2D, NKp46, NKp30) and a tumor cell via TAA. These engagers activate NK cell and trigger the death of target tumor cells by releasing cytotoxic granules containing granzymes and perforin, as well as secreting chemokines and cytokines, such as IFN-γ. NK cell engagers show fewer adverse effects, such as cytokine release syndrome (CRS) and neurotoxicity compared to TCEs.

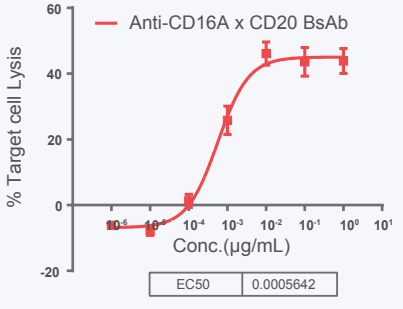
Case study:

Aspects for *in vitro* evaluation of in-house made anti-CD16A×CD20 bsAb:

1. bsAb potency on NK cell activation using proprietary reporter gene cell lines.
2. bsAb-mediated cytotoxicity against tumor cells using isolated primary NK cells.

NK cell-mediated tumor cell killing assay

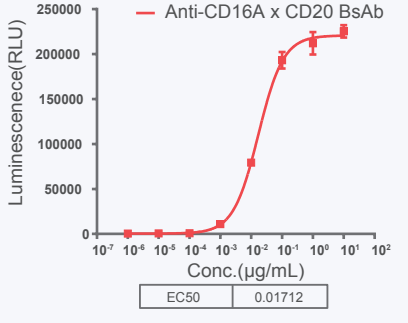
Cytotoxicity Assay with Primary NK



Cytotoxicity of primary NK cells against CD20⁺ tumor cells via anti-CD3×CD20 bsAb.

Reporter gene assay

Cell-based Reporter Assay for CD16A Activation



Induction of the reporter gene through cell activation upon engagement of effector cells and target cells via anti-CD16A×CD20 bsAb.

Figure 9. *In vitro* functional evaluation of anti-CD16A×CD20 bsAb

How to evaluate bsAbs comprehensively based on MOA?

Anti-TAA×stimulatory immune checkpoint bsAb

Co-stimulatory immune checkpoints, such as 4-1BB and CD40, are members of the tumor necrosis factor receptor superfamily (TNFRSF). Most of these receptors are expressed on the immune cells as T cells and DC cells and can be activated through cross-linking. When a bsAb bridges an immune cell and a tumor cell with a high TAA expression, this crosslinking mechanism limits the cytotoxic effect in the tumor microenvironment (TME). These bsAb additionally have better efficacy and safety to spare normal tissues compared to monoclonal antibodies.

Case study:

Aspects for in vitro evaluation of in-house made anti-4-1BB×PDL1 bsAb:

1. Potency measurement of the bsAb to activate T cells by 4-1BB reporter gene cell line.
2. Evaluation of clustering effect-dependent bsAb by 4-1BB reporter gene cell line cocultured with CHO-K1 or CHO-K1/PDL1 cells.

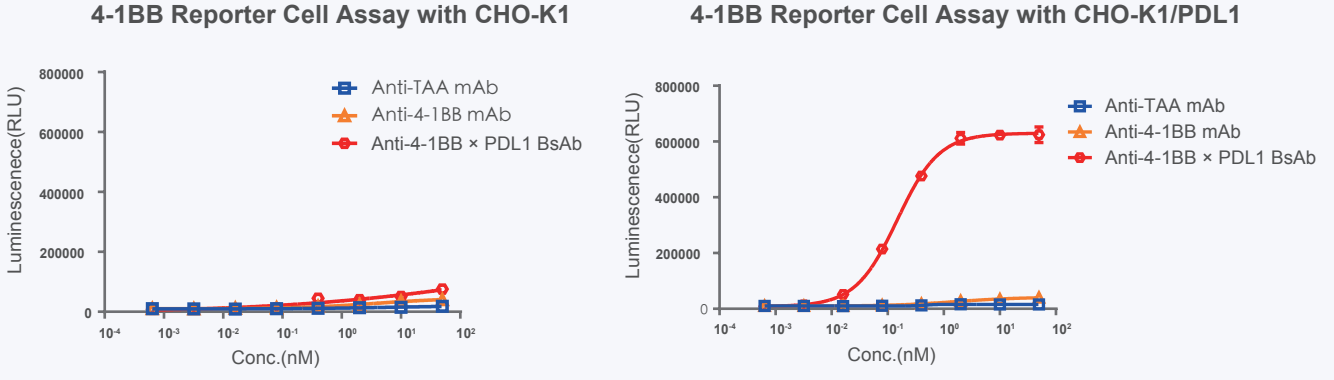


Figure 10. *In vitro* functional evaluation of anti-4-1BB×PDL1 bsAb.

The results showed that anti-4-1BB×PDL1 bsAb significantly activated 4-1BB signaling pathway only in the presence of CHO-K1/PDL1 cells instead of CHO-K1 cells, indicating this bsAb induced activation is dependent on the clustering effect.

How to evaluate bsAbs comprehensively based on MOA?

2.Dual-target blockade

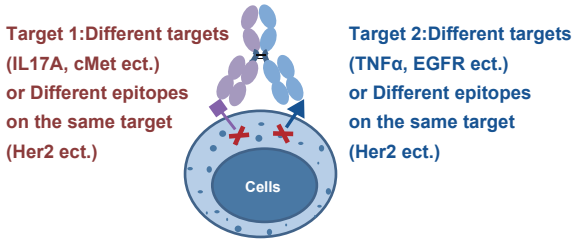


Figure 11. MOA of dual-target blockade

The dual-target blockade is a common targeting mechanism of bsAbs used in the treatment of tumors and autoimmune diseases. Tumor cells can develop drug resistance or undergo immune escape by switching signaling pathways or activating intracellular signals through homo- or heterodimerization between family members or different members. Therefore, bsAb drugs that target two signaling pathways simultaneously help overcome drug resistance and improve therapeutic efficacy.

To understand the MOA of the dual-target blockade in bsAbs, a customized *in vitro* assay should be designed. For example, a bsAb construct that targets the signaling pathways could be assessed using reporter gene assays, analysis of downstream protein phosphorylation, cytokine/chemokine release assays, and/or cell proliferation assays. For bsAbs targeting extracellular nucleotidases, such as CD39 and CD73, the effect on enzymatic activity could be an indicator of their functions. Some bsAbs targets may act as a TAA and mediate intracellular signaling pathways. Therefore, functional Fc domains are likely to be introduced in the design of bsAbs, and their functions can be evaluated by ADCC, CDC, etc.

Table 3. *In vitro* pharmacology evaluation for bsAbs adopting the MOA of dual-target blockage

Antibody type	Target combinations	*In vitro* functional assays
Antibody blocking angiogenesis/ tumorigenesis	VEGF & ANG2, Her2 & Her2, EGFR & c-Met, VEGF & DLL4, etc.	1.Signaling pathway assay 2.Reporter gene assay 3.Enzymatic activity assay 4.Cytokine/chemokine release assay 5.Antibody internalization assay 6.Cell proliferation assay 7.Primary cell assay (ADCC, MLR, etc.)
Antibody targeting TME	TGFβ & PDL1, TGFβ & CD73, TGFβ & CD39, etc.	
Antibody blocking inflammatory/ autoimmune disease pathway	TNFα & IL17A, IL4 & IL13, BAFF & IL17A, etc.	
Antibody blocking angiogenesis/ tumorigenesis & immune checkpoint inhibitor	VEGF & PD1, EGFR & PD1, Her2 & PD1, etc.	

bsAb blocking angiogenesis/tumorigenesis

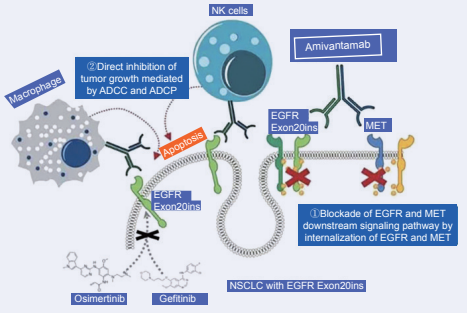


Figure 12. MOA of amivantamab

Angiogenesis is critical in tumor growth, progression, diffusion, and metastasis. Inhibition of angiogenesis is a promising therapeutic strategy for treating cancers. BsAbs can reinforce the anti-angiogenic effect by simultaneously blocking angiogenic pathways, EGFR, VEGFR, c-Met, and DLL4, Amivantamab, an EGFR&c-Met bispecific antibody used to treat metastatic non-small cell lung cancer (NSCLC), binds to EGFR and c-Met on the extracellular domain to inhibit ligand binding. It prevents receptor phosphorylation, thereby blocking the activation of both EGFR- and c-Met-mediated signaling pathways. By binding to each of the receptors, amivantamab can promote receptor-antibody complex endocytosis and degradation and induce Fc-dependent trogocytosis by macrophages and ADCC and ADCP effects by natural killer cells.

How to evaluate bsAbs comprehensively based on MOA?

3.Immune cell activation

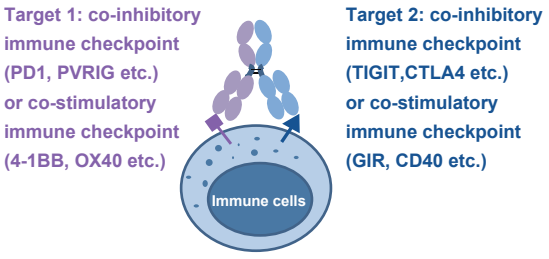


Figure 13. schematic diagram of the MOA of immune cell activation

Monoclonal antibodies such as PD1 have made a breakthrough in the development of immunotherapy. However, the objective response rate (ORR) of patients treated with anti-immune checkpoint mAbs still needs improvement. Therefore, bsAbs, with their synergistic effect of targeting dual targets on immune cells, have become a promising option to enhance immune cell activation. These bsAbs can be further categorized into **immune checkpoint inhibitor + immune checkpoint inhibitor, immune checkpoint inhibitor + immune checkpoint agonist, and immune checkpoint agonist + immune checkpoint agonist.**

One challenge in manufacturing bsAbs is the production of incomplete or mispaired bsAbs. To identify the properly paired bsAbs, the use of dual-target reporter gene cell lines is an optimal choice. The cell lines can accurately assess the bioactivity of bsAbs in one test. The cost-effectiveness of dual-target reporter gene cell lines is another advantage compared to using the combination of single-target reporter gene cell lines.

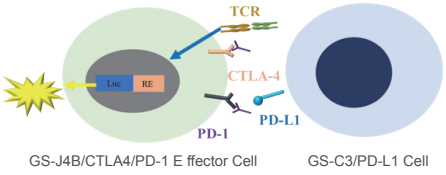


Figure 14. Advantages of dual-target reporter gene cell lines.

The measurements:

- Single-target and/or dual-target reporter gene cell lines can be applied to evaluate the activity of the immune cells mediated by bsAbs.
- The primary cell assay can be conducted to measure further the bsAbs immune potency to activate immune cells.

Table 4. *In vitro* pharmacology evaluations for bsAbs adopting the MOA of immune cell activation

Antibody type	Target combinations	*In vitro* functional assays
Immune checkpoint inhibitor & immune checkpoint inhibitor	PD-1 & TIGIT, PD-1 & CTLA4, etc.	1. Reporter gene assay 2. Primary immune cell assay (immune cell activation, MLR, etc.)
Immune checkpoint inhibitor & immune checkpoint agonist	PD-1 & 4-1BB, PD-1 & OX40, etc.	
Immune checkpoint agonist & immune checkpoint agonist	4-1BB & CD40, 4-1BB & OX40, etc.	

How to evaluate bsAbs comprehensively based on MOA?

4.bsAb activation by in-cis binding

BsAb can bind to the antigens expressed in cis, which can activate downstream signaling pathways by forming protein complexes. For instance, Emicizumab, a bsAb approved for marketing to treat hemophilia, simulates coagulation factor VIII by binding to both the activated coagulation factor IX and factor X, mediating the activation of the latter. This process enables blood coagulation to continue, reducing the bleeding rate of hemophilia patients. Some bsAbs can also recognize the TAA/TSA on tumor cells and bind to pro-apoptotic receptors in cis, inducing tumor cell apoptosis.

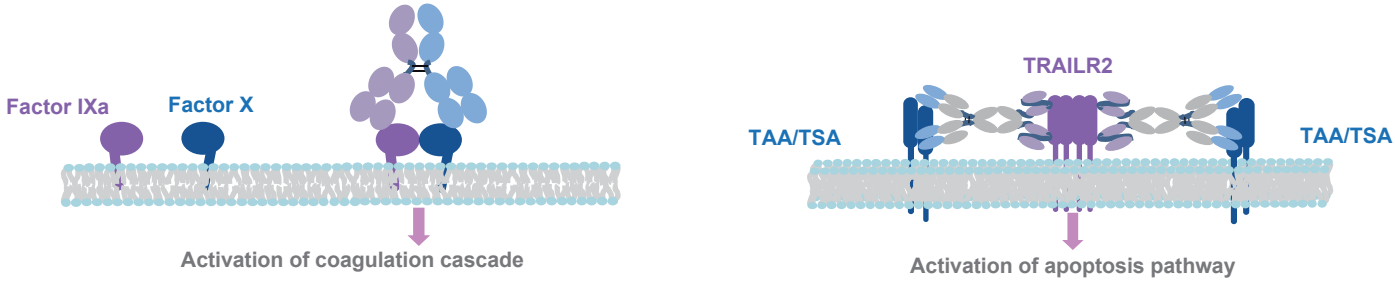


Figure 15. bsAb activation by in-cis binding.

The activity of bsAbs targeting coagulation factors can be evaluated by the coagulation time (left panel). The activity of bsAbs targeting TAA/TSA and pro-apoptotic receptors can be evaluated via apoptosis induction upon engagement (right panel).

Table 5. In vitro pharmacology evaluations for bsAb activation by in-cis binding

Antibody type	Target combinations	*In vitro* functional assays
Antibody mediated apoptosis	DR5 & TAA, etc.	Cell viability assay, etc.
Antibody mediated coagulation	Coagulation factor IXa & X, etc.	Coagulation time measurement, etc.

References:

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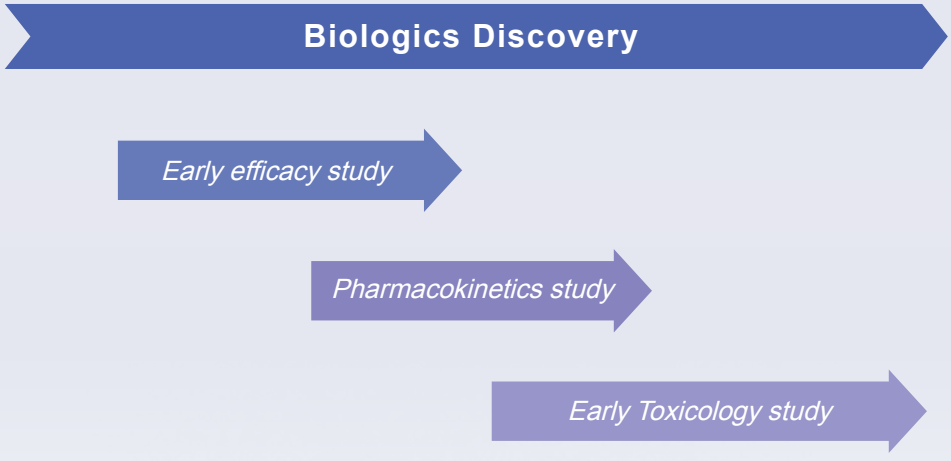
How to evaluate bsAbs comprehensively based on MOA?

In vivo Pharmacology

In vivo pharmacology study design for bsAbs based on the MOA of bsAbs is crucial. Similar to mAbs, bsAbs *in vivo* pharmacology strategy includes **early pharmacodynamics(PD) study, pharmacokinetics (PK) study, and early toxicology study.**



How to evaluate bsAbs comprehensively based on MOA?

Pharmacodynamics study

The syngeneic animal model is a suitable option for testing bsAbs that can cross-react between mice and humans or those with surrogate antibodies. Meanwhile, the immune humanized model is preferred for testing bsAbs that kill tumors by activating immune cells. The table below summarizes the animal models currently used for testing bsAbs with different MOA:

Table 6: Animal models suitable for bsAbs with different MOA

MOAs	Animal models
Targeting tumor cells and immune cells	1. Immune humanized model 2. Transgenic animal model
Targeting two different signaling pathways in the pathogenesis	1. Immune humanized model 2. Transgenic animal model 3. Subcutaneous xenograft tumor model in immunodeficient mice
Targeting different antigens or epitopes on the tumor cells	1. Transgenic animal model 2. Subcutaneous xenograft tumor model in immunodeficient mice 3. Patient derived xenograft (PDX) model

Pharmacokinetics study

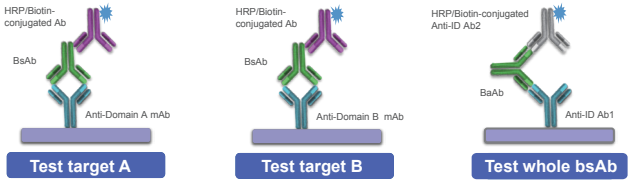


Figure 16: PK analysis strategy for bsAbs

Demonstrating the efficacy of bsAbs through pharmacokinetics strategies is more complex than with traditional monoclonal antibodies. To assess the binding affinity and specificity of the two different targets of bsAbs, the indirect ELISA method is commonly used. And the sandwich ELISA is used to analyze the complete bsAbs for the same parameters. Finally, three concentration-time curves are fitted and compared for agreement to determine the structural stability of the bsAb *in vivo*.

Early toxicology study

BsAbs constructions often encounters challenges such as proteolysis, aggregation, physical instability, and low yield. Additionally, bsAbs can induce anti-drug antibodies (ADA) in animals, which can have negative effects on long-term toxicology. Furthermore, some bsAbs may exhibit poor pharmacokinetic (PK) profiles and abnormal clearance, which can affect the toxicity of the drug. Therefore, conducting early toxicology studies is crucial during the development of bsAbs before entering the CMC stage.

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How to select a suitable partner for bsAb discovery?

How to select a suitable partner for bsAb discovery?

Maintaining functionality and improving the developability of bsAbs are two essential aspects that need to be considered throughout the discovery process. Selecting a reliable and accountable discovery partner is crucial to de-bottleneck production and increase capacity development, which can enhance the success of obtaining bsAb pre-clinical candidates. When choosing a partner, several elements should be considered, **such as their expertise in bsAb discovery, track record, and their ability to meet project timelines and goals.**

Experience	Dedicated researchers understand the targets and MOAs with the proof of multiple successful bsAb discovery projects.
Technology platform	Platforms cover target discovery, antibody generation, high-throughput screening, antibody engineering, *in vitro* bioassay, *in vivo* pharmacology, and developability assessment to facilitate customers obtaining the bsAb PCCs.
Turn-around time	Professional project management capabilities ensure a fast timeline.

With 20 years of experience in biologics discovery, GenScript ProBio is your optimal bsAb discovery partner!

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- 5 strategic partners
- Most advanced project is in clinical phase 1

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Comprehensive bsAb discovery platform

- One-stop solution from target to PCC
- Comprehensive antibody discovery platform
- *In vitro* bioassay and *in vivo* pharmacology solutions based on targets and MOAs

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