Ab Studio
www.antibodystudio.com

Innovative antibodies with better safety, efficacy and manufacturability balance

Ab Studio combines traditional approaches with computer-aided design to speed development of therapeutic antibodies.

Not all antibodies that bind their intended target also have the right properties to become safe and effective drugs that are easy to manufacture. In traditional antibody drug development, these properties may only be assessed after considerable time and investment. Ab Studio is combining its expertise in established antibody discovery methods with computer-aided antibody design (CAAD) to smooth the path to the clinic.

Using in silico tools, Ab Studio interrogates primary and tertiary antibody sequences and models to understand, select and optimize candidate antibody properties, notably affinity, stability, immunogenicity and manufacturability (Fig. 1). These early in silico results can guide decision-making without the need to first produce and purify large quantities of antibody, accelerating timelines and increasing the likelihood of clinical success.

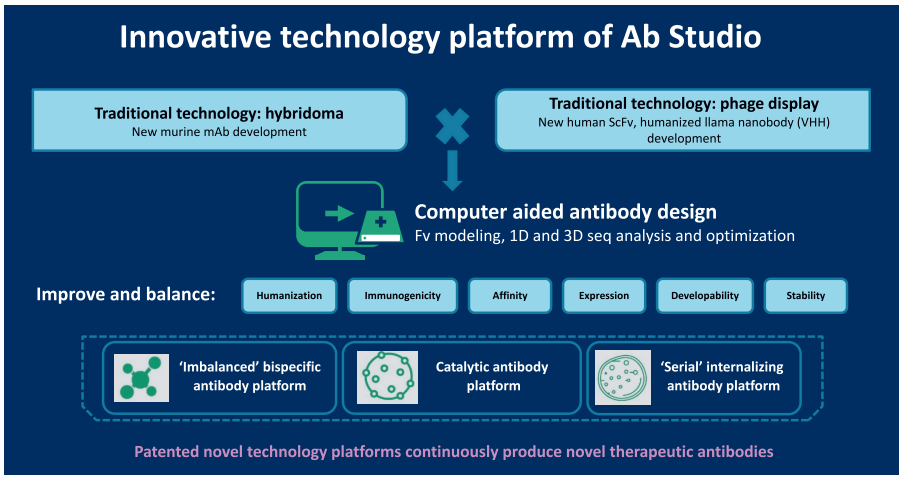

Fig. 1 | Technology platform at Ab Studio. Ab studio offers expertise in traditional discovery and in silico computer-aided antibody design to optimize antibody properties and intellectual property on three novel antibody technology platforms. mAb, monoclonal antibody; VHH, humanized llama nanobody; ScFv, single-chain variable fragment.

Therapeutic antibody platforms

In addition to offering antibody discovery and CAAD-based optimization services, Ab Studio has developed three proprietary therapeutic antibody platforms (Fig. 1). These technologies can be used to produce bispecific or multispecific antibodies with unique properties; create 'serial' internalization antibodies, i.e. antibodies with tailored binding and internalization properties; or generate catalytic antibodies, or catabodies, with a 'catalytic' function, e.g. proteolysis. Since its founding in 2017, the company has completed more than 60 antibody discovery and optimization projects and created a spin-out, Antibody Therapeutics, in partnership with JHBP. The deal also included out-licensing a pipeline of five preclinical programs.

Ab Studio's 'imbalanced' bispecific antibodies (BsAbs) are strategically designed with two distinct antigen-binding arms, each with differentiated binding affinities. The technology also incorporates a unique engineered Fc domain with complementary 'knob into hole' design that favors formation of the desired bispecific heterodimer over homodimers.

Using this patented platform, Ab Studio designed a novel BsAb, GB261. GB261 combines the well-established anti-CD20 cancer drug rituximab with an anti-CD3 antibody arm. The CD3 affinity is engineered to be 100-fold lower than typically used clinically, and this is expected to result in reduced cytokine production and lower the risk of triggering cytokine release syndrome. In preclinical studies, GB261 showed enhanced tumor cell killing relative to anti-CD20 monospecific antibodies and enhanced safety–efficacy balance relative to a positive control BsAb, likely due to the synergy of multiple mechanisms: T cell activation, antibody-dependent cellular cytotoxicity and complement-dependent cytotoxicity. GB261 has been licensed to JHBP holding and will enter into phase 1 clinical trials soon.

The design of multispecific antibodies is also possible, as illustrated by ABS-VIR-001, a trispecific antibody designed as a prophylaxis and therapeutic against SARS-CoV-2 infection. Using in-house phage libraries of naïve and synthetic humanized llama nanobodies (VHH), the Ab Studio team rapidly identified VHHs against the SARS-CoV-2 spike protein (S1). Using CAAD and epitope binning, multiple VHHs binding to different predicted epitopes on S1 were combined and fused to a human IgG1 Fc domain. In preclinical studies, ABS-VIR-001 shows more potent S1 binding, blocking of S1–ACE2 interaction and SARS-CoV-2 neutralization than a combination of individual monoclonal VHH-Fcs. These data support the idea that ABS-VIR-001 may prove more effective clinically than multi-antibody cocktails, while being simpler to manufacture, and may maintain greater activity versus variants.

Targeting cancer-associated antigens

Ab Studio has defined antibodies against cancer-associated antigens that undergo high levels of internalization. This intellectual property underpins its serial internalization antibody platform. Using this platform, Ab Studio can design a BsAb with one arm targeting a cancer-associated antigen, expressed at high levels on tumor cells and low levels on normal cells, with internalizing ability and the other arm targeting a cancer-specific antigen, exclusively expressed on tumor cells, which alone possesses low or no internalizing ability. GB262 offers a proof-of-concept that this strategy can confer co-internalization. GB262 combines a high-affinity anti-PDL1 arm with a weakly binding antibody specific for CD55.

As reported in a poster at the American Association for Cancer Research[1] internalization of CD55 drove co-internalization and downregulation of PDL1 and stimulated pancreatic cancer cell killing via T cell activation, antibody-dependent cellular cytotoxicity and complement-dependent cytotoxicity, as well as antibody–drug conjugation, when GB262 is conjugated to saporin (a plant toxin). This case study highlights the potential to design new BsAb–ADCs targeting new internalizing antigen combinations.

Ab Studio plans to continue developing novel therapeutic antibodies based on their patented platforms in partnership with biopharma partners, as well as independently.

1. Poster presented at the American Association for Cancer Research. Chaudhary, A. K., 2021.

CONTACT
Ab Studio Inc.
Hayward, CA, USA
Tel: +1-510-397-6439
Email: abstudio.info@antibodystudio.com