Y-Biologics
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Y-Biologics: utilizing innate assembly mechanisms in cell lines to create bispecific antibodies

Through its innovative, bispecific antibody platform ALiCE, Y-Biologics is discovering and developing next-generation immuno-oncology therapeutics.

Bispecific antibodies combine two therapeutic antibodies into one, simultaneously utilizing the effect of both to benefit patients. However, currently available technologies to produce these two-for-one therapeutics rely on mutating the structure of the original antibody to promote heterodimerization—a process that can result in many different and undesirable dimers in the expression medium. Antibodies generated this way contain mutated structures or linkers, are hard to purify, and are likely to have high immunogenicity that can cause antibody antidrug effects.

Y-Biologics, an emerging biotechnology company headquartered in Daejeon, South Korea, offers a superior and more natural alternative by developing novel bispecific antibodies using its proprietary platform technology ALiCE.

Y-Biologics' journey toward the discovery of novel antibody therapeutics began in 2007. Initially, the company focused on creating and validating its 10^{11} diverse phage-display human antibody library, Ymax-ABL. Having established itself as an antibody and novel biologics expert through successful discovery partnerships with Korean biotech firms, Y-Biologics then set about transforming into an immunotherapy company with its own pipeline and proprietary platform technology.

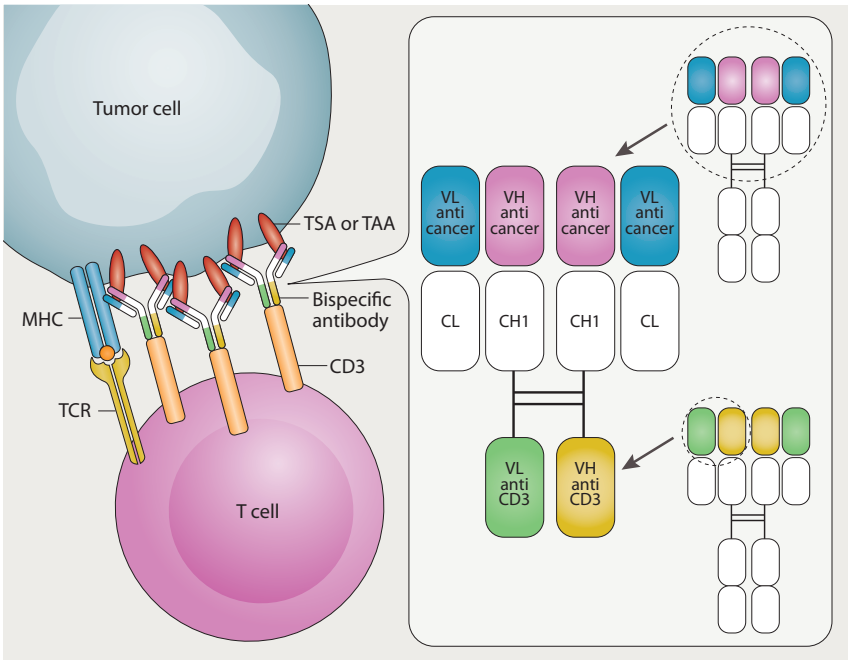

Fig. 1 | The ALiCE platform. Diagram shows both the structure of the ALiCE antibodies and their mechanism of action against tumor cells.

Introducing ALiCE

During that time, explained Seil Jang, antibody engineering team lead at Y-Biologics, the drawbacks of the mutation-based engineering system typically used to create bispecific antibodies became apparent. "Recognizing this significant unmet need and utilizing our expertise and in-depth knowledge of antibodies, our scientists came up with a new technology that overcomes these hurdles," he said. "We have developed ALiCE—which stands for Antibody-Like Cell Engager—a novel bispecific antibody platform with a unique structure and assembly mechanism."

In contrast to mutation-based engineering, ALiCE harnesses innate assembly mechanisms in cell lines, elegantly utilizing the innate affinity of the heavy chain–light chain variable domains (V_H–V_L) to induce heterodimerization of the heavy chains. This enables preservation of the antigen-binding fragment (Fab) structure of the parental antibody and substitution of the crystallizable fragment (Fc) region with a monovalent variable fragment (Fv) to secure an additional binding arm.

The resulting ALiCE antibodies—which have two different heavy chains and one light chain assembled into an architecture that preserves the native domain structures of a natural antibody, comprising two Fab regions and a hinge region—bind to tumor cells with two binding arms but activate T cells with only one binding arm to minimize off-target toxicity. "Our antibodies bind to specific antigens on the tumor surface while simultaneously engaging T cells in the tumor microenvironment. But the higher avidity for tumor cells means that although the immune system is activated to destroy the tumor, there is less off-target toxicity," explained Bum Chan Park, Y-Biologics' COO. "While there are no guarantees, we expect our ALiCE antibodies to be very efficacious but with relatively less toxicity."

Furthermore, because they rely on innate assembly mechanisms in cell lines rather than mutations, ALiCE antibodies are relatively easy and efficient to purify and manufacture. "Only homogenous ALiCE antibodies are secreted into the culture medium and they can be easily purified from there with traditional affinity chromatography—the quality control is highly regulated," said Bum Chan Park. "Moreover, while other bispecific antibodies end up with mutated structures or linkers, our manufacturing mechanism results in bispecific antibodies composed of only natural elements."

Platform and partnering

Using its ALiCE platform, Y-Biologics has identified novel T cell-engaging bispecific antibodies for lymphoma and currently has five candidates in late-stage discovery. The company has an open innovation business model and is amenable to various partnerships, including outlicensing, research collaborations, and codevelopment, particularly with companies experienced in clinical development.

"Our ALiCE antibodies are produced through mutation-free manufacturing procedures, are easy to purify, have a natural antibody-like structure, and a better safety profile," said Seil Jang. "We are looking for partners to covalidate this unique platform and realize the enormous potential of these transformative bispecific antibodies, which could profoundly benefit patients."

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