Great Bay Bio
AI Advance Bioprocessing

CASE STUDY

Nano Bispecific Antibody Achieved a Titer of 15.6 g/L Within 3 Months

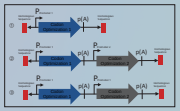
Background

Company B (Co. B) is a biopharmaceutical company focused on innovative immuno-oncology therapies. Using its proprietary next-generation antibody platform, it develops multifunctional antibody drugs. During the development of a nano bispecific antibody product, Co. B (along with several CRO partners) adopted a single open reading frame (ORF) design with random integration for cell line development. However, the resulting expression levels remained too low to support industrial-scale production.

This nano bispecific antibody project faced a critical deadline: the titer needed to exceed 5 g/L within 3 months, or the project risked termination.

GBB's Solution

Great Bay Bio (GBB), leveraging the world's first commercialized site-specific integration cell line development platform (AlfaCell), utilizes site-specific integration technology for multi-plasmid simultaneous screening. Combined with advanced instruments such as FACS, VIPS, and Octet, we efficiently complete cell line sorting, single-cell plating, monoclonality analysis, as well as analytical and purification process development. This enabled Co. B to rapidly establish high-yield, stable cell lines suitable for industrial production.



▲ Site-specific integration with multi-plasmid design

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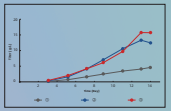
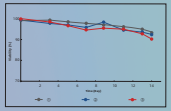
· Site-Specific Integration for High-Yield & Stable Cell Line Development

Through site-specific integration (SSI)-mediated homologous recombination, the target gene is precisely inserted into hot spots that are stable, high-titer, and of high quality. This enables the rapid development of high-yield and stable cell lines, while avoiding the gene expression variability caused by random integration.



▲ 14-day fed-batch titer profile

In this project, two sets of codons were optimized based on the molecular characteristics of the protein, and three different plasmids were constructed using distinct plasmid arrangements. Stable cell line development was carried out in parallel using all three plasmids, and monoclonal cell lines were obtained within 1.5 months. Subsequent fed-batch shake flask studies revealed significant differences in expression levels among the three plasmid designs.



▲ 14-day fed-batch viability profile

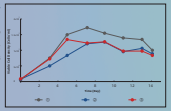
· HTP Cell Sorting, Detection, and Monoclonality Analysis Instruments

Stable integration ensures consistency in key quality attributes (CQAs), including charge heterogeneity and glycosylation modifications, across production batches.

FACS
Cell sorting

VIPS
Monoclonality analysis

Octet
HTP cell screening



▲ 14-day fed-batch viability profile

Results

Plasmid Design	14-day Fed-batch Titer (g/L)
	4.54
	13.1
	15.6

Within just 3 months, GBB completed stable cell line development for Co. B's nano bispecific antibody. The top-performing cell line achieved a titer of 15.6 g/L, successfully meeting and exceeding the industrial production target.