The Antibody Lab GmbH
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The Antibody Lab

Reliable mammalian cell expression

The Antibody Lab is launching BESTcell, a new system to make fast, stable mammalian cells for bioproduction.

Time is money in the research and development of biologics and therapeutics. Researchers need high-quality products for reproducible results. When the team at The Antibody Lab needed a reliable and fast technology to produce antibodies and other recombinant proteins using mammalian cells, they struggled to find a system to fit their needs. "We needed quick generation of a stable cell line with high yield," said Gottfried Himmler, co-founder and CSO of The Antibody Lab. "We tried various systems, but they weren't satisfying us. So we optimized our own to fit our needs."

Enter BESTcell, or BAC-based Expression System Technology in mammalian cells. This new system can go from transfection to isolated high-productivity clones in three weeks. "Until now, researchers would shortcut the process with transient expression with reasonable quality," Himmler noted. "Companies would spend hundreds of thousands of dollars to develop a cell line producing the protein of interest with high quality and reasonable yield in over three months. BESTcell produces both high-quality and high-quantity clones with a time saving of at least two months in the generation of cell lines."

Himmler's group is researching secretory immunoglobulin A (SIgA) for early therapeutic purposes. "During that work we had some problems with expression levels of mammalian cells. Secretory IgA is difficult to express, and we need large amounts," Himmler said, explaining that the current average yield is 3–5 grams per liter for production cell lines, but not for difficult-to-express proteins. "With this new technology, we observed a tenfold rise in specific productivity as compared with conventional systems with such difficult proteins." The Antibody Lab uses BESTcell in-house for its SIgA and other diagnostic projects.

Building on an established platform

The BESTcell system is based on the use of bacterial artificial chromosomes (BACs) as expression vectors. According to Anton Bauer, the COO of The Antibody Lab, BACs have been widely used in the mouse transgenic field for some time. "We are the first to apply this established mouse technology to the recombinant protein production field," he said. "It enables us to quickly produce a cell line that remains stable over many generations for the production of the particular protein." Bauer and colleagues published a 2015 paper on the use of BAC technology to produce two difficult-to-express proteins, the HIV-1 glycoprotein CN54gp140 and the HIV-1-neutralizing PG9 antibody[1]. In that work, the industrial applicability of production using BESTcell was evaluated and validated.

BACs can accommodate an entire locus owing to their large cloning capacity of 200–300 kilobases. All elements that control the expression of a gene remain intact—that is, the full locus of a mammalian transcription hotspot, comprising all chromatin and gene regulatory elements, which are further enhanced by a strong promoter. "We take a 200-kilobase gene fragment, transfect this into a host cell line and get several copies integrated in that production cell line," explained Bauer. "We have, in effect, what happens with a knock-in approach, but in our case we can bring in 50 to 100 copies of a specific locus for protein expression instead of one or two."

BESTcell creates clones through the integration of the gene of interest in multiple copies into the host cell in one or two days instead of a couple of months. No gene-amplification steps are required. "Due to the stability of the system we have the clones from the beginning, in the first week after transfection," said Himmler.

The BESTcell system is universal and can be used for any mammalian production cell line. It is versatile enough for small companies that need reliable materials quickly at a reasonable cost. It also produces clones that remain stable during upscaling in a bioreactor, which is required for large companies with high production volumes.

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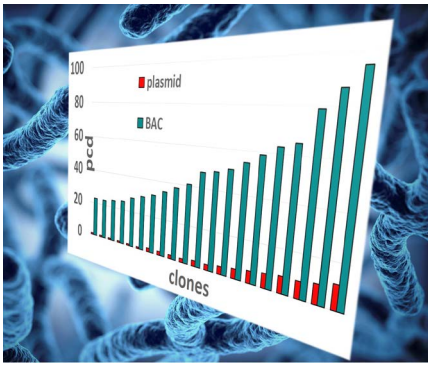
Quality-driven research

Himmler explained that research is often stumped by long wait times and low-quality materials that cause irreproducible results. He co-founded The Antibody Lab to bring together the expertise needed to create reliable products. BESTcell arose from the company's need for a reliable mammalian cell expression system.

Based in Vienna, Austria, Himmler has over 30 years of experience in engineering antibodies for clinical research and diagnostics. He joined forces with veteran research scientist Wolfgang Woloszczuk in 2009 to form BDF, a company with a strong reputation as a business-to-business supplier of immunoassays for research and *in vitro* diagnostics, including screens for pre-eclampsia in pregnant women.

Himmler and Woloszczuk renamed the company The Antibody Lab in 2015 when Bauer—who invented the BESTcell technology—joined as COO.



Clonal distribution of cell pools.

Bauer has a PhD in biochemistry, a global eMBA and a strong background in research and development and antibody technologies.

Future partnerships

The Antibody Lab is evolving its business model and is poised to discuss partnership opportunities with regard to BESTcell, for which the company holds worldwide intellectual property rights. "We have a robust technology that can relieve a bottleneck for biotech companies during development of biologics," said Himmler. "We are beta-testing a service business offering stable cell line development and protein production at a small scale for preclinical research."

For potential partners producing under good manufacturing practice (GMP), BESTcell can form the basis to produce efficient cell lines with yields of 10 grams per liter. "We are evaluating currently various business model options," Bauer said. "The Antibody Lab is open for discussions on partnerships."

The Antibody Lab will be represented at upcoming conferences, including BIO 2016 in San Francisco, California, in June; BioJapan in Yokohama, Japan, in October; and BIO-Europe in Cologne, Germany, in November.

1. Zboray, K. *et al. Nucleic Acids Res.* **43**, e102 (2015).

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