

BESTcell

www.theantibodylab.com



BESTcell: revolutionizing biologics development using high-yield, stable cell lines for research and biomanufacturing

The Antibody Lab's proprietary cell line development technology enables drug developers to move seamlessly from preclinical discovery to manufacture of the biologic for clinical testing. BESTcell clonal Chinese hamster ovary cell lines can be rapidly generated to enable preclinical testing of multiple biologic drug candidates. After selection of the final candidate, the respective cell line can be used to manufacture master cell banks. This revolutionary approach shortens timelines and reduces the reproducibility risk associated with changing the source of the biologic during research and development.

Developing biologic drug candidates that can be manufactured for clinical testing and commercial launch is not a trivial exercise and is both time consuming and hugely expensive. Creating and testing drug candidates for lead selection routinely uses traditional approaches such as transient expression, followed by the generation of stable cell pools and research cell lines for manufacture of the clinical candidate. This process can take 4–6 months to produce a research cell bank (RCB) and a further 6 months or more to produce a master cell bank (MCB), with costs ranging from a few hundred thousand dollars to more than half a million. The Antibody Lab, an antibody technology company based in Vienna, Austria, has developed its BESTcell technology to offer a radical solution for the complete research and development process, cutting timelines and consequently reducing overall costs.

"We have been developing the technology for a number of years and have, with partners, worked on more than 50 projects developing high-yield Chinese hamster ovary (CHO) cell lines expressing mainly antibodies but also other polypeptides and difficult-to-express proteins," explained Anton Bauer, The Antibody Lab cofounder and COO.

Companies looking to develop protein drugs such as monoclonal antibodies will usually create and manufacture a number of variants of the molecule for preclinical testing using transient transfection, and only after lead candidate selection will they go to a contract manufacturer with the chosen sequence to generate a clonal cell line. This is then the traditional starting point to create the associated RCB and MCB.

The BESTcell approach

With BESTcell (www.bestcellmabs.com), The Antibody Lab is offering a novel and much more streamlined approach. "We are proposing that companies let us make the clonal cell lines for their preclinical candidates. As we start with quality control documented cell lines in our state-of-the-art facilities, that same cell line can be used later to create the MCB and enable them to go straight to current good manufacturing practice (cGMP) manufacture. Given

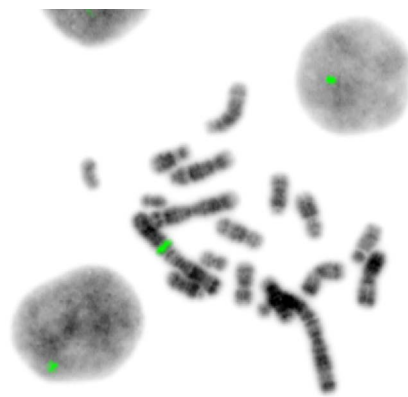


Fig. 1 | Staining of a high copy number recombinant BESTcell CHO cell line by FISH. This demonstrates a single integration site of the transgenic loci in the host cell chromosome. CHO, Chinese hamster ovary; FISH, fluorescence in situ hybridization.

the speed and economics of our system, BESTcell offers a great alternative to the current approach so drug developers can skip the need to use transient transfection, stable cell pools or research-only cell lines," added Bauer.

The Antibody Lab explained that it takes about 6 weeks to develop the RCB. "Our CHO cell lines have been shown to express up to 6 grams per litre. Even with difficult-to-express proteins, our technology—which involves inserting multiple copies of the gene of interest into the expressing cell—can boost yields up to 20-fold," added Bauer.

BESTcell is underpinned by targeted cloning into an expression hotspot—rather than specified simple genetic elements. Stable integration of multiple copies of large genetic loci (up to 200 kb) into a single site within the host cell chromosome results in extremely high product yields and can be used for the expression of complex glycoproteins and monoclonal antibodies in CHO or human embryonic kidney cells. The regulatory elements of the transferred loci prevent downregulation of expression and confer epigenetic stability independent of the integration site.

High copy number clones are stable immediately and thus do not require additional stabilization steps, which is key to the dramatic reduction in timelines. The Antibody Lab's cell line development service provides clients with stable cell clones, RCBs and the potential to manufacture the MCB.

"We believe that this is a groundbreaking technology for the whole biologics development process, including manufacture of clinical trials material and the development of production cell lines. One contract manufacturing organization, which is currently using the BESTcell technology, has material in clinical testing. As it is already approved in a human setting, we do not anticipate any regulatory issues for material produced from our platform," Bauer claimed. The contract manufacturer has secured a nonexclusive license to use the BESTcell platform.

Branching out into manufacturing

In addition to developing cell lines for client companies, The Antibody Lab is now offering a discrete manufacturing capability following the opening of its first new facility at the Vienna BioCenter. "We can provide customers with high-quality proteins from the clonal cell lines—up to multiple gram quantities—for preclinical research, in vitro diagnostics or veterinary use" Bauer explained. Indeed, plans are already in place to expand the facility substantially in 2019 while broadening the panel of host cell lines.

"Our aim is to offer our customers exactly what they need at their respective development stage: initially maybe just 100 mg for initial preclinical studies, then a few grams, and when they are decided to start a clinical program, they may acquire the cell line and finally the respective documentation for cGMP. And the protein will always be from the same source," he added.

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