



Aragen's Cell Line Development capabilities for difficult to express proteins

Many proteins are extremely difficult to produce in mammalian expression systems for a variety of reasons, and intracellular processing is required to eliminate expression bottlenecks. The most common problem is that it can often be challenging for a foreign host to correctly fold a protein it does not normally produce. In some cases, intrinsic properties of the protein represent challenges for the expression host to express the protein in its native form. For example, some membrane proteins with multiple domains might not properly fit into the lipid bilayer of the host expression system, or a protein might not be expressed in a fully soluble form. Additionally, many proteins require post-translational modifications (e.g., glycosylation or phosphorylation) that are absent or significantly different in the expression host.

An efficient cell line development process employing resilient host cell lines is one of the ways through which a range of biologics are produced. When the biologic in consideration is difficult to express, the most important factor is identifying a thoroughly optimized and well-established host cell line platform. Some of the most important variables include the cell line's capacity to produce the biologic in adequate yield and purity, its immunogenic posttranslational modification mechanism, its selection mechanism, and its ability to scale-up production at various bioreactor levels, etc. If the wrong cell line is chosen, it results in a high cost of performing the optimization cycle in different cell lines, as well as extending the timelines for IND applications.

Aragen assists its customers in their protein expression projects from the early stages and agrees on the host cell line after considering all the physical and chemical properties of the protein. Some of our platforms, including CHO-DG44, CHO-GS and Asimov are very popular among our clients for expressing a broad range of molecules, including antibodies, bi-specifics, and fusion proteins. This, coupled with Aragen's Cell Line Development (CLD) expertise using a royalty-free and regulatory-friendly platform, makes Aragen your partner of choice.

Range of host cell lines for difficult to express proteins

Aragen Life Sciences is working on cell line development platforms for more than 20 years and already has many research cells banks (RCBs) producing a variety of biologics for therapeutics, diagnostics, and research reagents. These RCBs can efficiently express molecules like multi-domain proteins, antibodies, vaccines, fusion proteins in excellent quality and titers in optimum time frames.

Our royalty free CHO-GS platform, which is based on CHO cell lines can efficiently express numerous molecules. It was successfully tested for a protein that acts as a prodrug for many diseases and has a cleavable mask. Evaluation of the titers demonstrates almost 1.9g/L of the protein on day 14th of the subculturing and 80 percent cell viability. CHO-GS platform is also suitable for the expression of bispecific monoclonal antibodies which are difficult to express due to mispairing of light and heavy chains. When expressed in our CHO-GS platform the titer obtained is around 5.9 g/L at day 14 with 80 percent of cells surviving.

In another study, the proprietary CHO-DG44 platform was utilized for producing a trimeric viral protein with a molecular weight of around 700 kDa. Multimeric proteins are heavy proteins and are difficult to produce recombinantly. Our superior experimental methodologies and the DG44 platform's resilience allowed us to produce the heavy protein in a decent titer within the ideal time frame. After day 12 of the subculturing, the titer equivalent to 1g/L was achieved with 75 percent of cell survival rate.

We also optimized our DG44 cell lines to produce antibody cytokine fusion proteins. CHO-DG44 is most favorable cell line for the expression of fusion proteins because they adapt well to serum-free culture, offer high-titer expression, and facilitate scale-up. Results showed 0.3g/L concentration of the titer after 13 days of subculturing with a 65 percent of cell survival rate.

At Aragen, before conducting the expression experiment, the physicochemical properties of the concerned biologic are studied thoroughly. Expert scientific teams are responsible for the designing of primers and for the selection of vectors. Aragen's proprietary expression vector systems are flexible tools carefully designed to facilitate enhanced, stable expression of the inserted genetic material while minimizing any secondary effects on the host cells. We ensure our clients with the greatest quality product at the most competitive costs.

If you are interested in learning more about our cell line development facilities or want to scale up the manufacturing of your biologic, please contact our technical team, and we'll take it from there.

Let's begin the
Conversation

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