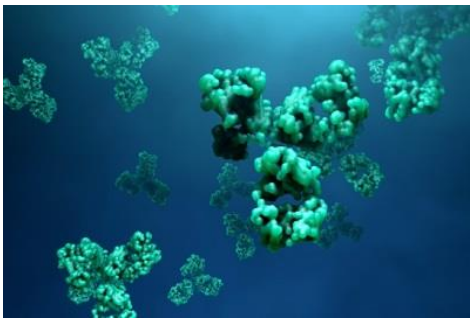
In Pursuit Of Biological Specificity

Which culture method is best to generate reagents with native biological specificity?

Cell culture methods vary a lot with respect to their ability to produce secreted proteins and antibodies that possess true biological specificity. Culture methodology is therefore a critical consideration where serological test specificity is a priority. To this end a key goal would be to meet minimum physiological criteria for uniform and consistent protein glycosylation via the optimisation of culture conditions. A practical, easy-to-implement approach that can mimic *in vivo* conditions is therefore highly desirable.

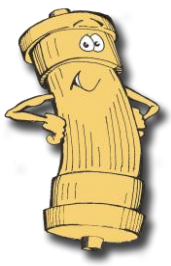


Imagine a large mass of cells in continuous 3D culture, capillarized and continuously nourished and oxygenated in such a way as to resemble living tissue. Imagine regularly harvesting the proteins secreted by this cultured mass of cells: now you have just visualised how hollow fiber cell culture works. By maintaining constant culture conditions, free of shear stress on the cells, with a continuous supply of oxygen and nutrients coupled with the elimination of waste metabolites and ammonia, a hollow fiber bioreactor recapitulates the homeostatic *in vivo* milieu that will most certainly be absent or poorly-represented in other less *in vivo*-like culture methods. Hollow fiber bioreactors have demonstrated complete and uniform post-translational modifications over extended periods of time making them ideal as a way to generate the highest affinity antibodies and difficult-to-express recombinant proteins. Consequently, for diagnostic kit manufacturers who may urgently be seeking ways to enhance monoclonal antibody avidity, hollow fiber cell culture can offer a significant "natural advantage".

A hollow fiber bioreactor is very compact, easy to install, easily scalable and very affordable. Left, is a photo of a set consisting of 4 pumps and 8 hollow fiber cartridges capable of generating 2 grams of mAb per week with a good hybridoma, or 400 mg per week of recombinant protein.

Other advantages include the ability to operate with a simple and inexpensive media formulation based on DMEM, reduced host cell protein contamination, reduced endotoxin, and the generation of target product that is highly concentrated.

Recommended Reading: ***Adaptive antibody diversification through N-linked glycosylation of the immunoglobulin variable region****: Fleur S. van de Bovenkamp et al.; PNAS, 2018, 115 (8) 1901-1906.*
Optimal and consistent protein glycosylation in mammalian cell culture*: Hossler, P. et al.* Glycobiology*, Volume 19, Issue 9, September 2009, Pages 936–949*
https://doi.org/10.1093/glycob/cwp079



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