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CHO-cell based manufacturing: A 30-year success story of DNA, cells, bioreactors and high value products.

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Abstract

CHO cells are the hosts for high value proteins with pharmaceutical applications that generate income in excess of 50 Billion US $ annually. This success story, surpassing by far even microbial systems for manufacturing, is surprising in many ways and was not anticipated, even by insiders. This talk will summarize historic and scientific insights and will argue why CHO cells have become the gold-standard for manufacturing of complex proteins. The story started with a glycosylated blood enzyme, the human tissue plasminogen activator (Activase®-TPA), approved for sale by Genentech in 1986.

While Activase®-TPA was required in quantities of about 50 kg annually to satisfy the market, some of today's blockbuster antibodies, given in multigram doses to patients repeatedly, require hundreds of kilogram (even exceeding the ton-range) to be produced.

Today's CHO cells can achieve specific productivities of 50-100 pg/cellxday and will provide, in highly optimized, proprietary processes, volumetric yields of 3-10 g/L. These productivities are not the result of better expression vectors or superior genetic engineering of these cells, but due to a deep understanding of their genetics and physiology in conjunction with the very unique chemical engineering challenges when cultivating these delicate cells in specially designed bioreactors.

Besides summarizing the overall strategies to obtain high yielding manufacturing processes, my talk will also provide insights into the pedigree of immortalized CHO cells, cultivated the first time in 1953. The challenge for the future will be to obtain more predictable performance of CHO processes, understanding all aspects – cells, culture specifics and reactors.

Biography

Florian M. Wurm was trained as Biologist/Molecular Geneticist in Germany. He worked in industry (Behringwerke AG, Marburg and Genentech Inc., San Francisco) for 15 years during the earlier parts of his career. His work contributed to the generation of several high-value products, such as Herceptin, Pulmozyme and TNKase TPA. In 1995 appointed Professor for Biotechnology in Lausanne, Switzerland, he also founded ExcellGene in 2001. Florian is past Chairman of the European Society of Animal Cell Technology. He has published more than 200 papers and filed more than 30 patents, covering aspects of expression and manufacture of clinical proteins using mammalian cells in bioreactors.