Pharmaceutical BIOPROCESSING

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EuroSciCon meeting on bioprocess miniaturization: development and optimization
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The impetus to accelerate process development in the biopharmaceutical industry is driven by reducing costs and time to market. Shortening development times is critical to the success of the industry [1]. The miniaturization of bioprocessing assists in the generation of quantitative data, fast and efficiently. This helps inform bioprocess design and speeds translation to the manufacturing scale. The meeting reviewed individual operations in the bioprocess workflow highlighting the state-of-the-art in technology and research and innovation. A brief overview of the themes covered is discussed below.

Miniaturized bioreactors

Two micro-bioreactors for early stage process characterization and optimization were presented, the BioLector® (m2p-labs) [2,3] and AMBR™ (TAP Biosystems) [4] fermentation systems. Both support parallel fermentations to screen a wide variety of parameters with each unit containing sensors to monitor and control biomass, pH and dissolved oxygen. A significant difference between the instruments is the fermentation volume. The AMBR system has a single use micro bioreactor permitting culture of volumes between 10–15 ml while the BioLector systems use FlowerPlates® with a volume range of 800–1500 µl. Both systems have successfully demonstrated bioprocess scale up from micro to laboratory scale.

Bioprocess optimization, intensification & scaling up

To facilitate sustainable production with a lower carbon footprint research and development in recent years has focussed on the optimization and intensification of bioprocessing at the microscale [5]. Ideally, process intensification would enable a continuous laboratory-scale process to replace a production plant. A technique for process intensification in a microfluidic environment was presented by a member of the Galip Akay group from the University of Newcastle. Here, a polymer with a well characterized and uniform micro-architecture was used as a 3D support matrix for cell culture [6,7]. This material is synthesized using a high internal phase emulsion polymerization. Pore sizes can be modified, by varying the chemical composition of the emulsion and the processing conditions, from sub-micron range to several hundred microns. Cells were immobilized on the matrix and the micropores facilitated a continuous culture.

Typically, during the scale-up procedure the bioprocess information generated increases but the throughput decreases. The Austrian Center of Industrial Biotechnology presented their results on scaling up using the BioLector Basic. The aim was to screen a wide variety of parameters and identify those protocols that led to the most efficient protein production. The results demonstrated that once optimized the process was transferable to a 20 l reactor. However, a major bottleneck was the downstream processing and analytics. For each experiment performed in the well plate the product had to be extracted, prepared, quantified and characterized before the outcomes of the optimization could be evaluated.

Downstream processing

One of the last steps of the bioprocess workflow is freeze-drying or lyophilization. This

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is the process of removing of water from a frozen solution by vacuum sublimation and it is a commonly used process for long-term storage of a product generated from a bioprocess. Over the last few decades the biopharmaceutical industry has concentrated on understanding and characterizing the quality attributes of a freeze dried product. The current system of characterization is semi-qualitative preventing comparison between research laboratories or even materials. The meeting reviewed a novel mechanical compression test presented by Daryl Williams from Imperial College London [8]. This test allows the freeze-dried product to be quantitatively assessed within the sample vials without further sample preparation.

The improvements to speed and throughput facilitated by miniaturization of bio-reactors have transferred the bottleneck further downstream to product analysis. Both product quality and quantity has to be evaluated for each screen. Analytical techniques like capillary electrophoresis [9,10] and liquid chromatography [11] were among the first to be miniaturized. Furthermore, other biological assays such as ELISAs have also been translated to the microscale, making them more efficient, faster and less labour intensive. The hyphenation of these systems will help realize the potential of a bioprocess lab-on-a-chip.

Outlook

The meeting demonstrated that the use of miniaturized bioreactor systems can accelerate bioprocess development and facilitate its translation to laboratory-scale production in a fast and comprehensive way. However, further reduction in the size of the bioreactor, to strictly operate at the microliter scale, requires a greater understanding of the surface effects and changes in cell behavior in this environment. It is known that 3D cultures better mimic the growth conditions of cells and will lead to improvements in protein production [12]. Moreover, interfacing with downstream analytics will help with real-time monitoring of the bioprocess and accelerate process development.

This meeting was organized by Euroscicon [13]. The next meeting, titled 'Bioprocess development: Discussing facilitation of industrial uptake', will take place on 19 June 2014 [14].

Financial & competing interests disclosure

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