Pharmaceutical
BIOPROCESSING

News

Highlighting the latest news in Pharmaceutical Bioproccessing

Pharm. Bioprocess.
(2014) 2(1) 13–15

Study sheds light on nonessential amino acids in cell culture

Researchers from Amgen (WA, USA) have recently demonstrated that depletion of nonessential amino acids plays a role in the onset of the stationary phase of production processes and coincides with growth suppression. The results help elucidate the biological response of cells to nonessential amino acids depletion.

The team studied the depletion of two nonessential amino acids, asparagine and glutamine, in a CHO cell line expressing a recombinant antibody. During fed-batch production processes asparagine and glutamine levels in cell culture were depleted, which coincided with phenotypic changes in cellular growth.

The study demonstrated that depletion of asparagine or glutamine activates the amino acid response, a transcriptional program, which leads to cell cycle arrest while maintaining high levels of protein translation and culture viability. However, essential amino acid depletion (AAR), which also causes cell cycle arrest, leads to decreased levels of protein translation and culture viability.

Speaking to *Pharmaceutical Bioprocessing*, Jeffery McGrew, a researcher on the study, explained the significance of these findings, "This can explain, at least in part, the observation that during fed-batch processes, depletion of asparagine or glutamine precedes cell cycle arrest, but the cells remain viable and can continue to produce proteins at a high rate. In contrast, depletion of essential amino acids quickly leads to a reduction in protein production and culture viability."

McGrew continued, "These results provide some biological understanding of the fed-batch process, and will help provide some guideposts in developing protein production processes. For example, ensuring amino acid excess during the growth phase of cell culture will allow rapid growth, but utilizing controlled limitations of nonessential amino acids to halt growth during production phase. Furthermore, our results support previous suggestions that production cell lines with robust AAR are good candidates for production cell lines, and that cellular engineering of this pathway could provide a method to fine tune this response."

Looking to the future, the team are planning to study other amino acids to evaluate their interaction with cell responses and bioreactor performance. In addition, McGrew explained that the team are also hoping to utilize their findings during cell line selection to identify clones with robust AAR.

– Written by Jessica Thorne

> ...during fed-batch processes, depletion of asparagine or glutamine precedes cell cycle arrest, but the cells remain viable and can continue to produce proteins at a high rate.

Source: Fomina-Yadlin D, Gosink JJ, McCoyR *et al.* Cellular responses to individual amino-acid depletion in antibody-expressing and parental CHO cell lines. *Biotechnol. Bioeng.* doi:10.1002/bit.25155 (2013) (Epub ahead of print).

FUTURE SCIENCE

10.4155/PBP.14.2 © 2014 Future Science Ltd ISSN 2048-9145

Novel use of 3D *in vivo* imaging for monitoring of bioreactor performance

A group of researchers, from TAP biosystems (Hertfordshire, UK) and Loughborough University (Leicestershire, UK) have reported a novel use of a 3D *in vivo* imaging technique to visualize medium flow and cell distribution.

The team successfully utilized 3D *in vivo* imaging to study a hollow-fiber bioreactor, a complex culture platform, demonstrating the potential of this technique to monitor bioreactor performance.

Speaking to *Pharmaceutical Bioprocessing*, Elizabeth Ratcliffe, a researcher on the study from Loughborough University, explained the aim of the study, "The work aims to encourage research to address the dearth of technology and methods to aid process characterization, control and scale-up of complex culture platforms, an area that is integral to the authors' continuing research and collaborative opportunities are welcomed."

Ratcliffe explained the potential of their findings, "Imaging of labeled medium distribution and cell populations in this manner could be particularly useful for early detection of heterogeneity within complex 3D cell culture platforms and aid engineering of operational parameters to improve process performance and control prior to scale-up. The technique may also be useful for providing richer data to inform modeling experiments as well as for other hollow-fiber technology applications or processes (e.g., cell immobilization)."

– Written by Jessica Thorne

Source: Ratcliffe E, Thomas RJ, Stacey AJ. Visualizing medium and biodistribution in complex cell culture bioreactors using *in vivo* imaging. *Biotechnol. Prog.* doi:10.1002/btpr.1840 (2013) (Epub ahead of print).

Investment into early biotechnology start ups announced

In a recent press release, New York City Economic Development Corporation (NYCEDC) has announced the launch of the Life Sciences Funding Initiative, a US$100 million public–private initiative to support early biotechnology start ups in New York City. The initiative is hoped to help New York City establish itself as a dominant capital for life sciences innovation.

Robert Steel, the Deputy Mayor for Economic Development commented, "This funding initiative is a testament to the strength of the City's life sciences community. We have seen an unprecedented level of leadership from our local academic leaders in recent years. Today's announcement marks the beginning of a united front across the academic and commercial life sciences sectors in New York City."

As reported in the press release, funding is to be provided by NYCEDC, Celgene, GE Ventures, and Eli Lilly and Company. The collaboration of these companies aims to raise a minimum of $50 million to support early biotechnology start ups.

Steel concluded, "We are pleased to see Celgene, Lilly and GE Ventures place their full confidence in the future of New York City's life sciences ecosystem. With their support, and in close partnership with our local research institutions, New York City will become a formidable force in life sciences innovation."

– Written by Jessica Thorne

Source: Deputy Mayor Steel and NYCEDC announce two new initiatives to dramatically grow city's life sciences sector: www.nycedc.com/press-release/deputy-mayor-steel-and-nycedc-announce-two-new-initiatives-dramatically-grow-citys

Alvotech announces biosimilars investment

In a recent press release Alvotech, the sister company of Alvogen, has announced the investment of US$250 million to develop their biosimilar monoclonal antibody portfolio. Alvotech has several follow-on antibodies that will come onto the market in 2018.

Currently, Alvotech are building a 11,800 m^2 development and manufacturing facility at the science park of the University of Iceland (Reykjavik, Iceland). The new facility, which is reported to be fully operational in 2016, will enable Alvotech's own biologic production.

Andreas Herrman, Chief Executive Officer of Alvotech, explained the initiative behind the investment, "At Alvotech we are inspired to help patients around the world by increasing the accessibility and affordability of high-quality biopharmaceuticals. By combining Alvotech's development and manufacturing excellence with Alvogen's global marketing platform, we are taking a significant step toward becoming a major player in the biopharmaceutical industry and bringing valuable investment to support our growth."

Robert Wessman, Chairman and Chief Executive Officer of Alvogen also commented on the announcement, "The alliance with Alvotech will allow us to leverage our global commercial network in over 30 countries and is an important step for both companies towards becoming leaders in the biopharmaceutical industry. The partnership is a valuable addition to our current biosimilar business."

– Written by Jessica Thorne

Source: Alvotech invests US$250 million in biopharmaceuticals: www.alvogen.com/News/NewsArticle/alvotech-invests-250-million-in-biopharmaceuticals

New manufacturing platform installed at JHL Biotech's Research Center

GE Healthcare Life Sciences, a provider of transformational medical technologies and services and JHL Biotech, an emerging biopharmaceuticals company, have announced the completion of their FlexFactory™ biomanufacturing platform at JHL Biotech's Research Center and manufacturing plant (Hsinchu, Taiwan).

FlexFactory is an "a-centrally automated, flexible biomanufacturing platform," that enables rapid and easy establishment of biopharmaceutical manufacturing capacity. FlexFactory aims to enable biomanufactures, including JHL Biotech, to respond rapidly to local healthcare needs and to aid rapid introduction of new treatments to the market.

Co-founder, President and Chief Executive Officer of JHL Biotech, Racho Jordanov, commented, "JHL Biotech will make world-class biopharmaceuticals affordable to more people by utilizing innovations such as FlexFactory."

Olivier Loeillot, General Manager of Enterprise Solutions at GE Healthcare Life Sciences, also remarked on the biomanufacturing platform, "Our offering of tools, technologies and services for biomanufacturing has strength in both breadth and depth. For JHL Biotech we have been able to take an approach which recognizes the differing requirements of multiple sites, whilst at the same time allowing them to replicate processes."

– Written by Jessica Thorne

Source: GE Healthcare Life Sciences to build KUBio modular biopharmaceutical factory for JHL Biotech in China: www.jhlbiotech.com/news_detail.php?cid=46&ckid=7&pageno=1

Collaboration announced for rapid manufacture of biologics

In a recent press release, Rensselaer Polytechnic Institute (NY, USA) have announced that two of their chemical engineering professors, Steven Cramer and Pankaj Karande, have teamed up with academia, industry and the federal government to develop a method for rapid manufacture of biologics.

The Defense Advanced Research Projects Agency (DARPA) has invested US$10.4 million in the project, which is part of 'DARPA's Biologically derived Medicines On Demand programme.'

The collaboration, led by Christopher Love from the Massachusetts Institute of Technology (MA, USA), is focusing on developing novel purification technologies for biologic production. The project aims to develop specialized materials to allow highly selective and highly specific protein binding, and therefore, reduce the number of purification steps required during biologic production.

Cramer commented, "In this project, we are looking at ways of significantly simplifying and condensing several key steps of drug manufacturing and quality control."

The collaboration aims to enable military medics to rapidly produce drugs, as explained by Cramer, "Our goal is to be able to create a small, easy-to-carry system that can synthesize needed drugs in 24 h, instead of the 6–12 months it usually takes to create the same drugs in an industrial setting."

Karande commented on the potential of the collaboration, "The potential implications of this technology are far-reaching, as it will provide rapid access to drugs in remote settings, and have a direct effect in saving lives."

– Written by Jessica Thorne

Source: Chemical engineers at Rensselaer Polytechnic Institute collaborate to advance battlefield biomanufacturing technology: http://news.rpi.edu/content/2013/12/02/chemical-engineers-collaborate-advance-battlefield-biomanufacturing-technology

The editorial team welcomes suggestions for timely, relevant items for inclusion in the news. If you have newsworthy information, please contact:
Alice O'Hare, Commissioning Editor, Future Science Ltd, Unitec House, 2 Albert Place, London, N3 1QB, UK
Tel.: +44 (0)20 8371 6090; E-mail: a.ohare@future-science.com