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ΣΕΜΙΝΑΡΙΟ Μ.Υ. ΣΕΜΙΝΑΡΙΟ Μ.Υ.

ΟΜΙΛΗΤΗΣ: κ. Σπύρος Βερναρδής

Υπεύθυνη Διατριβής: Dr. Μαρία Κλάπα

ΘΕΜΑ: Η μεταβολομική σαν εργαλείο ευαίσθητης μοριακής ανάλυσης στη μηχανική κυτταροκαλλιεργειών.

Metabolomics as a sensitive molecular analysis tool in industrial cell culture engineering.

ΤΟΠΟΣ: Αίθουσα Σεμιναρίων ITE/ΕΙΧΗΜΥΘ

ΗΜΕΡΟΜΗΝΙΑ: Τετάρτη, 21 Δεκεμβρίου 2011

ΩΡΑ: 12:00

ΠΕΡΙΛΗΨΗ:

Mammalian cell cultures have been widely used for the production of therapeutic proteins. The primary objective of most current programs for the development of therapeutic protein production processes is the rapid development of bioreactor cultures that are characterized by high product yield and consistent product quality. In addition, due to the high manufacturing cost of these processes, the identification and use of accurate and sensitive controls for cell cultivation robustness is desirable. These controls could provide early warnings of problems in protein productivity and/or final quality before the end of the cultivation. Today, both bioreactor monitoring and process improvements are based primarily on cell growth, metabolic activity and protein productivity data. While useful, the limitations of this cell specific rate-based approach have been recognized. There is a clear need for the development and application of methods that enable the comprehensive characterization of the physiological state of mammalian cell cultures. Moreover, utilized in the context of programs for industrial process improvement, which allow for experimentation with various cell lines and physiological conditions, these methods could contribute to enhancing our overall understanding of the protein production and manufacturing processes. Such developments could lead to the identification of targets for process improvements. In the systems biology era, holistic analysis of the physiology of biological systems at various molecular levels of cellular function has become possible through the high-throughput “omic” technologies. Metabolomics, referring to the simultaneous quantification of the (relative) concentration of the free small metabolites, i.e. the molecules used as reactants or products in the metabolic reactions, is the most recently



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introduced high-throughput method for the measurement of the metabolic fingerprint of a biological system. Considering the role of metabolism in the context of the overall cellular function, it is easily understandable why quantifying a complete and accurate metabolomic profile is foreseen to have a major positive impact in cell culture engineering research. My research has focused in establishing the usefulness of metabolomics as a sensitive molecular analysis tool in cell culture engineering. I will present application of Gas Chromatography-Mass Spectrometry metabolomics to monitor and analyze industrial mammalian cell culture systems in high cell density perfusion reactors, which are used by our industrial collaborator, Bayer HealthCare, CA, USA, for the manufacturing of therapeutic proteins. It will be shown that metabolomics indeed enables the differentiation between cell cultures based on cell age and subtle changes in cell culture growth parameters, while these differences are not directly observable based on the conventional monitoring toolbox.