Preface

Mammalian cell cultures are the dominating production system of today's biopharmaceutic products. The increasing emphasis on product quality and the demand for greater cost-efficiency and process robustness call for better fundamental understanding on cell, process and product. Whereas physiological manipulation and bioprocess renovation have played a pivotal role to the success of cell culture biomanufacturing in the past, genomic and systems approaches will drive the next innovations in mammalian cell culture technology. Genome-wide analysis of the genetic information, gene expression, signaling network and metabolism, along with the integration of vast experimental data and mathematical tools will afford a holistic and quantitative understanding of cellular processes and lead to quality products and robust processes. Although somewhat lagging behind life sciences and biomedicine, systems biology application to cell culture technology is gaining its momentum.

In this volume, we have gathered nine chapters written by authors from both academia and industry which present recent development and different facets of genomic and systems-biological approaches applied to mammalian cell cultures. The first two chapters by Stahl et al. and by Castro-Melchor et al. deal with transcriptomic analysis and methodologies of systems biology analysis of static and dynamic gene expression data, respectively. Examples of their uses in mammalian cell cultures are presented. The next two chapters by Gerdtzen and by Niklas and Heinzle describe strategies and available tools for the modeling of metabolic pathways and networks of mammalian cells, especially the method of metabolic flux analysis. The following chapter by Schaub et al. presents an interesting framework of advanced data analysis consisting multivariate data analysis, metabolic flux analysis and pathway analysis for mapping of large-scale gene expression data. This integrated data analysis approach was successfully applied to the analysis and improvement of cultures of Chinese hamster ovary cells in an industrial bioproduction process. For the production of recombinant pharmaceuticals in mammalian cells the glycosylation of the recombinant proteins is of paramount importance for their functions and efficacy. The next two chapters by Berger et al. and by Hossler review the recent developments of analytic tools for

the characterization of protein glycolylation, strategies for protein glycosylation control in production processes and perspectives of genomics and systems biology for understanding and enhancing protein glycolsylation control. For glycosylation and many other key cellular processes in mammalian cells intracellular transport and compartmentation are two key aspects which are however still not well understood, at least not quantitatively and in mathematical models. The chapter by Jandt and Zeng summarizes recent developments in simulation methods and frameworks for describing intracellular transport processes. In the last chapter of this volume Botezatu et al. describes methods for targeted genetic perturbation of mammalian cells which is an essential part of an utmost systems biology approach, namely the iterative process of perturbation, data generation, modeling, hypothesis generation and verification by perturbation again. The authors go a step beyond this by combining a synthetic biology approach for targeted and predictable modification of cellular networks. Indeed, a combined systems analysis and synthesis approach will lead to the next level of advances of mammalian cell cultures.

We thank the authors for their excellent contributions and hope that this volume will give some impulse and inspiration to the genomics and systems biology of mammalian cell cultures.

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