Microbial Cell Factories

Editorial

Recombinant protein production in the new Millennium

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In 2000, the Microbial Physiology Section of the European Federation of Biotechnology gathered the academic and industrial community involved in the production of heterologous proteins for an update on physiological aspects governing protein production in prokaryotic and eukaryotic cells. While there was common understanding that the limits of efficiency in productivity and quality had by far not been reached, that meeting concentrated on a comparative description of physiological events, from genetic stability via transcription and translation to protein folding and secretion [1]. Despite the progressive comprehension of physiological limitations and cellular stresses in producing cells, there were only few examples of cell engineering towards improved expression systems.

In a biannual rhythm, the 4th conference of this series was held in Barcelona in 2006, setting out to compile the achievements of novel genome wide analyses on the understanding and engineering of protein producing cell factories. Microbial Cell Factories provided then a forum for the publication of novel research presented at this conference, publishing all of the more than 100 abstracts presented in the conference [2] and selected papers. It became obvious that research in the field has made a major leap since 2000, from mere analytical approaches to complex and targeted cell engineering.

The development of a novel yeast vector was described in detail [3] and novel insight of plasmid/host interactions in *Escherichia coli* was presented [4]. At the transcript level, RNA stability was engineered in *E. coli* by downregulation of RNaseE [5], and novel regulatory mechanisms of transcription by estradiol in yeast were described [6]. While several authors studied heterologous protein secretion in a more general way [7,8], Resina et al. concentrated on induction of the unfolded protein response in yeasts [9]. As the production and secretion of many proteins is obviously still handicapped, there is still significant research on new, non-conventional expression systems, like psychrophilic bacteria [10], gram-positive bacteria [11] or fungi [3]. Being molecular physiology a key parameter for protein overexpression, one should not overlook the impact of process control. Maurer et al. have resolved a widely debated question – the dependence of specific productivity on cell growth – for protein secreting yeasts, and applied this information to predict an optimum feed rate profile for maximum productivity [12].

But future will not wait: the next Recombinant Protein Production conference is scheduled for 24th–28th September, 2008, in Sardinia, Italy. In the way to explore cell physiology applied to improved protein production, successful cell engineering based on thorough – at best quantitative – understanding of the physiological limitations will be discussed: energy metabolism related to heterologous protein production, latest data on transcription and translation control, stress responses, protein folding and assembly, glycoengineering, and process development, stability and analytics in the light of host physiology. The Microbial Physiology Section of EFB will again welcome the Recombinant Protein Production community to a scientifically outstanding and stimulating meeting. More

information will be found at the web site of the 5th Recombinant Protein Production Meeting [13].

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