## **Microbial Cell Factories**



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## Old bugs for new tasks; the microbial offer in the proteomics era Antonio Villaverde

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Microbial transformations have been unnoticeably exploited by mankind for centuries especially in the context of early food industries. The modern biotechnology uses microbial cells in a more directed approach to produce enzymes, antibiotics, amino acids and other metabolites of economical interest. Food and mining industries are also sustained by natural microbial activities tailored in a way that favours the desired transformations. The birth of genetic engineering in the late 70's and its further technical expansion have provided molecular tools to engineer and produce hetereologous proteins in a diversity of microorganisms including bacteria, yeast and filamentous fungi, thus largely extending their manufacturing capabilities.

Nowadays, the main sources of proteins for research are genetically modified microorganisms. However, industrial production of such proteins has not been as successful as initially expected and in many cases, the yield of the processes is low and hard to justify, from an economical point of view, a large-scale recombinant production. Producer cells commonly suffer from protein-promoted toxicity, often resulting in slow growth, cell death and plasmid instability. On the other side, recombinant proteins, apart from overloading the cells with extra metabolic demands, often undergo proteolysis and/or aggregate as inactive polypeptides into inclusion bodies. These events derive from the incapability of foreign proteins, as produced at high non-physiological rates, to fold into their native conformation. Although the exploration of differ-

ent cell systems can permit to escape from the above listed obstacles (that on the other hand, are rather unpredictable for a given protein), some of them can be surmounted by genetic, protein and metabolic engineering approaches and/or by process and downstream optimisation. Intriguingly, the emerging need for a wide-spectrum, efficient protein production in the proteomics era has favoured a deeper analysis of the recombinant cell physiology. In this regard, scientists have turned their attention to the cells rather than merely observing the products. The Cell Factory concept is then completely structured through the examination of the metabolic capabilities of the producer cells in close relationship with the nature and features of the product (recombinant or not) and the production process itself. The consequent identification of main bottlenecks encountered during production, as well as the cell responses triggered under this situation reveals the integrated nature and complexity of the machinery involved in biosynthesis and quality control and also its connexions with the mechanisms coping with stress at both cellular and populational levels. Based on these findings, we can now better approach improved strategies to adapt old microbes to new production requirements for both natural and engineered products.

Experimental results relevant to both natural and recombinant microbial factories are dropping in microbiology, genetics, biotechnology, biochemistry, chemical engineering and environmental journals. Microbial Cell Factories [http://www.microbialcellfactories.com/start.asp], published online by BioMed Central [http://www.bi-

omedcentral.com/| since February 2002, offers a new forum for the fast publication of research in this field, addressing both product-focused and cell-focused aspects of the microbial production and transformations. The topics covered by the journal include recombinant DNA technologies, genetic engineering, plasmid construction and maintenance, gene cloning and expression, development of new expression systems, protein engineering, protein production, proteolysis and aggregation of recombinant proteins, cell stress responses, bioreactor design and operation, process control and monitoring, scale-up, downstream procedures, protein folding and refolding, production of natural substances, mutagenesis, strain improvement and screening, metabolic engineering, microbial transformations, food microbiology, extremophile biology and biosensors. Manuscripts submitted to Microbial Cell Factories through our online submission system [http://www.microbialcellfactories.com/manuscript/] are immediately sent to two external referees plus one member of the international editorial board [http://www.microbialcellfactories.com/edboard/], who are requested to respond within 15 days. Therefore, manuscripts showing sufficient merits for publication can be accepted only a few weeks after submission, depending on the speed of the authors to address eventual referees' concerns. After acceptance, the publication online is immediate and the manuscript is finally replaced by the definitive pdf form once the proofs have been approved by the authors. The inclusion in PubMed [http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=PubMed&cmd=Search&term=1475-2859] databases (with the journal abbreviation Microb Cell Fact) usually takes a few days. Costs of publication and maintenance of papers in databases are defrayed by the authors through reasonable processing charges. Waivers are considered upon request and authors who are members of institutions joining the BioMed Central membership programme [http://www.biomedcentral.com/info/instmembership.aspl are not charged. The publication of a manuscript in Microbial Cell Factories implies that it is immediately and freely available to all of the scientific community through the journal home site, the BioMed Central web site and PubMed databases. The authors retain the copyright of their research and manuscripts are permanently stored electronically by the research depository PubMed Central, which is run by the US National Institutes of Health (NIH). The publication policy [http://www.microbialcellfactories.com/info/faq/default.asp?txt\_faq\_no=1] supported by Microbial Cell Factories and its publisher BioMed Central represents a new and revolutionary approach on the road to the frictionless and worldwide spread of science. Microbial Cell Factories is now the fastest way for the broad communication of your experimental research, improved protocols or literature review in any facet of microbial production.