



ELSEVIER

# The ultimate rendezvous: microbial ecology meets industrial biotechnology

Editorial overview

Margaret McFall-Ngai and Victor de Lorenzo

**Current Opinion in Microbiology** 2007, 10:205–2061369-5274/\$ – see front matter  
Published by Elsevier Ltd.

DOI 10.1016/j.mib.2007.06.002

## Margaret McFall-Ngai

Department of Medical Microbiology and Immunology, University of Wisconsin, Madison, WI 53706, USA  
e-mail: mjmcfallngai@wisc.edu

Margaret McFall-Ngai is a professor in the symbiosis faculty cluster at the University of Wisconsin. The research of her laboratory focuses upon the role of beneficial bacteria in the promotion of health and the prevention of disease. She uses the squid–*Vibrio* model to characterize the onset, progression and persistence of a symbiotic association.

## Victor de Lorenzo

Centro Nacional de Biotecnología (CNB), Consejo Superior de Investigaciones Científicas, Campus de Cantoblanco, Madrid 28049, Spain  
e-mail: vdlorenzo@cnb.uam.es

Victor de Lorenzo leads the Environmental Microbiology Laboratory of the CNB in Madrid. His lab has developed many genetic tools for designing bacteria destined for environmental release in bioremediation. He has exploited transcriptional control of catabolic promoters of *Pseudomonas putida* for refactoring genetic circuits responsive to environmental pollutants.

One of the central questions of our time is how long our planet will be able to cope with the mounting deterioration of the environment brought about by the plethora of emissions associated with industrial growth. At the same time, economic progress is associated with a greater demand for pharmaceuticals and bioactive molecules to cover basic health needs, as well as specialized treatments. One way or another, any plausible sustainability of our developed/developing societies and economies shall depend on the discovery and exploitation of new biological catalysts able to perform, at a minimal energy cost and in an environmentally friendly manner, synthesis and degradation reactions that have been so far the near exclusive realm of industrial and chemical engineering. The prokaryotic world is the largest reservoir of enzymatic activities in the biosphere, but >95% of it is hard to access because of our current inability to culture its microbial constituents. Although explored since the mid-1980s, knowledge of non-culturable bacteria was little more than a matter of academic curiosity until the advent of metagenomics in the late 1990s. This new conceptual and technological framework will not only permit biologists to archive the genetic pool of complete microbial ecosystems, but also it has already granted us entry into altogether new worlds of biocatalysts and biomolecules.

The well-publicized campaigns for collection and sequencing of metagenomes worldwide currently yield  $>10^6$  new genes (or open reading frames) per year. But, paradoxically, the accelerated production of large volumes of DNA sequence occurs along with a virtual lack of discovery of new biochemical reactions and the finding of a very few novel bioactive compounds. In other words, our ability to sequence new genes goes exceedingly faster than the identification of new functions, molecules and reactions applicable both to synthesis of chemical species of interest and to biodegradation of toxic environmental pollutants, both of which are badly needed by industry. How do we, as researchers in this field, overcome this impasse? In the series of reviews compiled under this section, we have attempted to provide a landscape of current research at the interface between outstanding ecological questions and likely, as well as actual, applications for environmental, industrial and health-related biotechnology.

As a most exciting introduction, Ferrer *et al.* describe the state-of-the-art technologies available to the biotechnologist for mining enzymatic activities from unusual environments. It is a fact that, despite many successes in recent years, the dearth of suitable screening tools and the limitations of the available hosts for metagenomic libraries are a major bottleneck for identifying extraordinary biological activities in environmental DNA. The more

these technical problems are solved, the more enzymes with novel capabilities are likely to be exposed. In the meantime, what niches are worth targeting? In a fascinating article, [Grozdanov and Hentschel](#) report the current status of studies on the complex microbial community that associates with marine sponges, as revealed by metagenomic approaches. Many of the genes found in such scenarios are known or suspected to encode proteins involved in the production of small bioactive molecules that mediate a complex symbiotic interplay. Being players in interactions between such primitive life forms, such molecules are likely to be — *per se* or as precursors — of extraordinary interest to the pharmaceutical industry. But one does not need to go that far and that complex to find amazing cases of intricate (bio)chemical signaling between as few as one eukaryote and one prokaryote that play symbiotic partners. The exciting case of the interactions between *Wolbachia* and its insect host is addressed in a dedicated article by [Iturbe-Ormaetxe and O'Neill](#). The issue at stake here is how the bacteria manage to alter the host reproductive biology drastically, including the conversion of genetic males into fully functional phenotypic females and the induction of parthenogenesis. The chemical language involved in this process remains virtually unknown, although the availability of *Wolbachia* genomes might help to clarify the issue. That such chemicals or their derivatives might turn into a gold mine for a large number of applications requires little justification. Another equally spectacular but less widespread symbiotic partnership is discussed later by [Goodrich-Blair](#). In this case, the bacterium *Xenorhabdus nematophila* colonizes a discrete region of a specific developmental stage of the nematode *Steinernema carpocapsae*. The question at stake here is not only how bacteria discriminate the host (for which they are extremely specific) but also how the prokaryotic partner distinguishes between different developmental steps. It is fortunate that, as discussed in this article, mutants of the two partners can be generated and tested for the maintenance of the symbiosis. Again,

interesting small molecules are likely to be players in the phenomenon.

But current molecular technologies allow going much further than 'naturally occurring bacteria' and 'natural catalytic systems'. From existing interspecies associations, the paper by [Hendrickx and Mergeay](#) moves into current proposals for assembling minimal microbial consortia for life support. This notion originates in current research on conditions for exploratory space travel, or the settling of human habitats in extreme environments. Akin to ongoing exercises to assemble a minimal genome, some researchers pose the enticing question of requirements essential for the smallest, viable, self-sustained ecological partnership. This somewhat man-made, artificial scenario opens the way for the last two articles of the section, focused on forward engineering of biological processes. In one case, [Menzella and Reeves](#) recapitulate recent work in the area of combinatorial biosynthesis of polyketides, one of the research areas where the power of generating and shuffling gene libraries was first shown. This is because these antibiotics are non-ribosomal peptides typically produced by multimodular enzymes that can be randomly, or directly, combined and then screened with high-throughput technology. The amazing feature of these systems is the generation of non-natural combinations of modules, and thus the creation of altogether new compounds. Yet, the ultimate frontier for designing industrial processes is spelled out in the closing article by [Meyer, Pellaux and Panke](#) on the design of catalytic complexity by means of synthetic biology approaches. Recent advances in DNA synthesis are paving the way to rationally design and efficiently exploit such systems of enzymes for a large variety of beneficial applications. This last article thus closes the circle that runs from biological activities found in multi-partner environmental niches to the production of valuable goods, products and biomolecules. It is legitimate to say that the rendezvous between Microbial Ecology and Industrial Biotechnology is off to a highly promising start.