

## Highlight

# Twenty one important things you should know

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In the March *Microbial Biotechnology* special issue on bioremediation, a new feature called 'Crystal Ball 2009' was published. In this section leading researchers in the field of microbial biotechnology looked into their crystal balls and speculated on the technical and conceptual developments that will drive innovative research and open new vistas over the next few years. Twenty one separate articles were presented, which contained information and ideas that every microbiologist should know.

Aharoni (2009) suggests in 'Mining for new enzymes' that the clue for cheaper, stronger and cleaner industrial processes is to dig through metagenomic libraries for the identification of novel biological catalysers. To overcome current screening limitations, either in efficiency and/or coverage, diverse high-throughput screening methods based on cell-surface display or *in vitro* compartmentalization are proposed. Additionally, finding the appropriate host organisms to express the desired enzymes is still a difficult issue, however, one that could be solved using the plethora of newly isolated environmental organisms.

When dealing with global approaches in 'The microbial reactome', Ferrer (2009) emphasizes the importance of holistic methodologies in unravelling metagenomic, proteomic, metabolomic and reactomic analyses. He suggests that in order to fully exploit our current abundance of 'omic' data, we need to concentrate on a systems biology approach, using many, if not all of the available technologies to fully annotate the data. This approach would allow us to garner more potentially useful information that could be directly applied to biotechnology. More views on global

analysis and systems biology come from Dr Svein Valla's article 'The future is artificial' that deals with different issues relating to synthetic biology; because of the reduced cost of gene construction, he predicts an increase in the design of new *in silico* optimized microbes and the production of super-bugs, not only for use as traditional cell factories, but also to fight against climate change. Valla (2009) wrote: 'if I am going to be really brave I might predict that developments in System and Synthetic Biology will become a major turning point in the history of man'. He also suggests that systems biology will allow us to understand complex processes, such as ageing and consciousness.

In 'Building bugs', Panke (2009) deals with the impact of biological systems engineering on biotechnology via the availability of cheap *de novo* DNA synthesis. He focuses on the need to elucidate the components that participate in the organization of genomes to boost success in artificial construction. Previously known information has become available in the Registry of Standard Biological Parts (<http://partsregistry.org>). Again, as in Aharoni (2009) emphasis is also placed on the need to unearth appropriate hosts or developing efficient *in vitro* systems.

In 'Food and gut microbes for thought', Arigoni and Brüssow (2009) discuss the previous, current and potential uses of both bacteria and bacteriophage in the fight against infectious pathogens and both chronic and acute disease states. Emphasis is placed on some previous applications, such as the use of bacteriophage in wound cleaning and dressing by the Red Army, but also the current uses of commensal bacteria impacting on host physiologies, metabolism and drug pharmacokinetics.

In 'Predictions: evolutionary trajectories and planet medicine', Baquero (2009) deals with two different integrative approaches, both complex but worthwhile. In the first one, the hope is set in the application of novel mathematical methods (such as Prices equation derivatives) to predict biological evolution that even in 'simple' organisms requires the unravelling, integration and hierarchical ranking of multiple elements. In the second future integrative approach, planet earth is considered as an individual, and microbiologists will play a pivotal role in predicting and treating environmental problems through modification of microbial diversity.

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Brock (2009) discusses in 'Back to the roots' the fact that although 'omic' sciences represent a major scientific breakthrough in the identification of new genes and proteins, they also generate many hypothetical and inconclusive data. He illustrates these limitations with the isocitrate lyase 2 from *Saccharomyces cerevisiae*. Identified by genetic homology, this enzyme exhibits no activity towards isocitrate but to methylisocitrate. The author emphasizes that 'old' biochemical and functional assays with proteins are still indispensable.

In the chapter called 'Microbial genomics as pursuit of happiness', Galperin (2009) continues the debate regarding the value of genomic sequences and places a positive view on the possible future usefulness of the acquired information. Touching on the expanding use of microbes in the bioremediation of environmental contaminants, the author expands the view by stating that soon microbial metabolic engineering will be used to improve food supply, solve the energy crisis and fight global warming.

In 'Optimising rational vaccine design', Guzman (2009) tackles the current roadblocks in vaccine development. It appears that we face at least three: (i) a somewhat fragmentary knowledge of the effector mechanisms required for pathogen clearance, (ii) a lack of tools for the stimulation of predictable immune responses and (iii) the large gap between initial development and the translation of vaccines to human trials. The author considers that all three will be overcome in the next few years, by rational vaccine design using in-depth studies of natural infections, development of well-defined, highly efficient adjuvants with different biological properties and the implementation of cost-effective small animal models, such as mice engrafted with human immune components.

McInerney (2009) discusses recent developments in research regarding microbial communication and interactions in his chapter on 'Listening to microbial conversations'. As many available genomes contain cryptic gene clusters, it is considered likely that these may encode for complex chemical pathways, some of which are used as signalling molecules by bacteria. Emphasis is placed on the technologies to understand how microbial populations respond to each other, computational approaches to unravel the available data and potential uses of signal manipulation in control of bacteria in biotechnology and medicine.

'Measurements versus understanding: the (metabol)-omics dilemma' by Sauer (2009) deals with the ever-broadening gap between data generation from -omics platforms and the ability of us as microbiologists to interpret and exploit the available data. It is believed that our present computing methods that rely on logical reasoning will not be sufficient to cope with metabolomics data.

The author puts out an open call to his colleagues for the development of intelligent computational methods and suggests that improved initial experimental design and the use of specific follow-up experiments may be our foremost option of success. Continuing on the topic of computational solutions to system-level understanding is the chapter on 'Predictive microbial ecology' by Zhou (2009). Dr Zhou points out that extensive microbial community modelling studies are lacking because our current methods of microbial ecology analysis are essentially descriptive. It appears that we need to increase the availability of community-wide spatial and temporal information by following the lead of recent developments in high-throughput sequencing (Sogin *et al.*, 2006; Hamady *et al.*, 2008) and their related metagenomics technologies (He *et al.*, 2007). With these methodologies in hand, along with rigorous experimental design and high-performance computational tools, microbial ecologists will be able to answer a slew of ecological questions. The answers will usher in a new era in quantitative predictive microbial ecology and allow a system-level perception.

As remediation of polluted sites by free-living microbes is frequently unsuccessful, Ramos, Molina and Segura discuss the alternative use of plant root associated microorganisms in 'Removal of Organic Toxic Chemicals in the Rhizosphere and Phyllosphere of Plants'. Failures in microbial bioremediation are commonly due to a limited proliferation of the microorganisms and/or to lack of activity of catabolic pathways. To overcome this last point, the authors suggest placing catabolic genes under the control of recently described promoters that are induced by root metabolites (Ramos *et al.*, 2009). Areas that need improvement are related to the pollutants low bioavailability, the generation of unwanted chemicals by plant metabolism or the detoxification of contaminants that prevent plant growth.

Furthermore, de Vos (2009) in 'Mining the Microbes – the Human Microbiome as a Model', focuses on potential applications of metagenomic data from microbes living inside human beings, especially in intestinal habitats. Despite that the isolation, identification and growth of these microorganisms are still a difficult tasks, he predicts that in a short time microbiome-based diagnosis will be available.

Human biome biotechnology and the personalization of odour profiles by Timmis (2009), deals with the potential use of body odours in personalised medical treatments and in the cosmetic industry. From a clinical point of view, the identification of compounds and microbes present on our skin could be used for the search of physiological and/or mental illness biomarkers. Nevertheless, to achieve this, vast advances in physiological determinants, epidermal secretion and skin microbial

flora knowledge are required, together with the development of ultrasensitive analytical procedures. The article also considers how skin chemistry could modulate the elimination of undesirable volatiles and favour the desirable ones, opening the door to customized perfumes and cosmetics.

The cell surface is the barrier that limits the microbe's living territory. The study of the complex set of interactions between surface proteins, sugars and other surface components is difficult, and only recently the developments in cryo-electro microscopy have enabled us to solve some aspects of flagellum and Type IV pili structure. Covacci and Rappuoli (2009) in this Crystal Ball section predict that the use of sortases – bacterial enzymes that catalyse the attachment of proteins to cell surfaces, together with new advances in high-resolution fluorescence and scanning microscopy will allow the specific tagging of target proteins based on different colour shadings for use in high throughput data capture and real-time expression.

Rosenberg (2009) deals with a theme of enormous interest related to climate change: coral microbiology. He expects knowledge on coral microbes to allow us to understand current coral diseases, to decipher the environmental factors that contribute to the diseases and their spread, and to define the positive role microbes play in coral life. Evolutionary forces that come into play, including the role of coral viruses are expected to shed light on this fundamental environmental problem.

Of no less interest is the proposal by Lovley (2009) on microbial cell fuels and, most particularly, their potential to generate energy. The relevance of the theme is such that the following issue of *Microbial Biotechnology* has a thematic section on bioenergy. Murell and Smith (2009) bring forward a hot topic for discussion: the value of hidden microbial diversity and its genetic reservoir to the understanding of ecosystem function and a way to mine for valuable biochemical diversity for the production of added-value products. They predict that the combination of stable isotope probing technology and expression metagenomic libraries of <sup>13</sup>C-enriched DNA will enable us to close the gap between biocatalysis and biodiversity. This, combined with high-throughput *in vitro* technologies will set up the basis for the accelerated evolution of enzymes of interest.

Handlesman (2009) challenges us with the term *metagenetics*, the genetics of the community of microbes. In this article there are a number of reflexions on the role of 'classic' genetics in the definition of biochemical pathways and networks over the last 50 years and predictions of the full understanding of community genetics in the next 50 years. Some approaches are envisaged, for instance to knock out all homologues of a particular gene in all members of the community or the inactivation of a given

gene in a family of bacteria. This will require new specific homing devices that should work at the community level. The impact of metagenetics on microbial ecology will enable a better understanding of the phenotypes found in the communities.

Thompson (2009) tackles the manipulation of microbes *en masse* through new engineering approaches that challenge microbes to fight against global climate change. The new approaches include techniques for moving bacteria through soil, manipulation of biofilm formation via electrokinetics and methods to stimulate biodegradation through the use of new nanomaterials. He also predicts that the new generation of microbiologists need to be more multidisciplinary than ever. Young microbiologists will need to work harder than ever, but the optimistic future in the field warrants such efforts.

These 21 points and ideas that have been brought to the table by leading biologists in our field are both diverse and timely. They also provide important insight into the future of research in microbial biotechnology and to the potential future uses of our discoveries.

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