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Meeting Report

Synthetic biology: an EFB Microbial Physiology Section initiative

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The BioBricks Foundation in the USA has pioneered the dissemination of information about developments in synthetic biology. Despite the immense interest in this topic within the biotechnology community, Europe has been less organised in building comprehensive links between the biotechnology industrial sector and fundamental research. Indeed, many colleagues in Europe are still asking for a clear definition of 'Synthetic Biology', which might read: Synthetic Biology is a bottom up approach that aims to redesign a cell, organism, or components from them to achieve specific objectives. It thus complements systems biology, which adopts a top-down approach to determine all of the interacting components of a biological system. In reality many research objectives will be achieved only with the appropriate combination of both approaches.

Last summer the Microbial Physiology Section of the European Federation of Biotechnology (EFB) anticipated that there might be a need to form a new group within the Section to promote advances in synthetic biology. A questionnaire was circulated to the more than 110 companies and research institutes that are Institutional Members of EFB and to its 13,000 Personal Members enquiring whether there is a need for a pan-European meeting focusing on how the currently fragmented scientific advances in the area of microbial systems biology could be linked to the needs of European biotechnology industries. The response was unexpectedly positive, so much so that the EFB Section immediately organised a symposium in Barcelona spread over three days from 6 to 8 February 2012. The meeting was arranged by staff at the EFB Central Office in Barcelona, and partners included Novozymes, BioCat, the UK Society of Chemical Industry and the UK Engineering and Physical Sciences Research Council.

The 35 oral presentations included 7 invited lectures that spanned synthetic biology of antibiotic production, cost reduction in bioprocessing, plants with increased resistance to abiotic stresses, plants producing terpenoids of pharmaceutical interest, metabolic and genetic engineering to generate improved strains, industrial platform development and the potential of lantibiotics to replace antibiotic therapy. The following are some of the many take-home messages from the meeting.

- Despite substantial interest in synthetic biology in some parts of Europe, not every country has embraced the biotechnological potential of the new techniques stemming from this field.
- There is a continuum between top-down systems biology at one extreme, and bottom up approaches to novel bioprocesses developed by systems biology: successful processes will benefit from input from both approaches, which are interdependent.
- Mathematical modelling can identify bottlenecks and provide effective cost–benefit analysis only when combined with adequate experimental data.
- Metabolic engineering lies at the heart of much synthetic biology.
- Metabolomics offers fantastic potential, but is hampered by the lack of a single analytical method that can identify every metabolite in a cell, culture or environment.
- There is an urgent need to replace currently used antibiotics that are increasingly becoming ineffective. Two slightly inconsistent messages were sent. One view is that combinatorial biosynthesis offers very little solution to the problem of antibiotic resistance, so a synthetic biology approach is urgently required to produce novel compounds, for which Europe is taking the key role. Alternatively, combinatorial genetics (gene shuffling) is well established in Europe and offers a realistic possible solution to the problem of antibiotic resistance.
- Lantibiotics are produced ribosomally, but then extensively post-translationally modified to generate short, disulphide-bonded peptides: they are extremely toxic to bacteria, and may become a sound approach to the replacement of traditional antibiotics.
- New agents for whole-cell biocatalysis and bioremediation can be designed by merging forward genetic engineering with combinatorial approaches (e.g. gene shuffling).
- Rational – often automated – assembly of genetic modules from a range of micro-organisms allow production of valuable compounds that are intractable to chemical synthesis.
- Public awareness of synthetic biology is still very limited. We need proactively to approach and educate the public on this topic and show that it is not creating a danger to the community.
- There are too few funding opportunities within Europe for collaborative projects, especially on applied synthetic biology. We need this funding to strengthen the field where we are lagging behind compared to the US and China.

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Various presentations focused on: the commercial potential of *Pichia* yeast as a production platform; nanoparticles for the purification of difficult membrane proteins; tailor-made ligands for affinity separation processes and protein engineering using synthetic amino acids and alternative genetic codes. The following specific example illustrates the flavour of the meeting, which incorporated both microbial and plant synthetic biology.

Despite the alarming increase in resistance to all of the antibiotics currently in clinical use, no major new group of antibiotics has been brought to market in the past 20 years. Synthetic biology offers two exciting approaches to solving this problem. Both of them rely on bioinformatic analysis of genomic databases to identify relevant genes followed by conventional genetic engineering approaches to combine synthetic modules from different natural sources. The first approach would be to recombine polyketide synthase modules to generate products that pathogenic microbes have never encountered naturally. While this combinatorial approach has an element of a 'spray and pray' approach, it is amenable to high throughput robotic screening of resulting clone libraries. Critics argue that because each of the modules to be recombined occur naturally, it will only be a matter of time before a resistance mechanism to the final product emerges. Others argue that such a fear is unfounded because the final products can be structurally so different from those currently found naturally.

An alternative approach described by several speakers was the development of new lantibiotics for which nisin provides a useful case study (see, e.g., [1]). Lantibiotics are genetically encoded peptides that are so extensively post-translationally modified that the final compounds are difficult to recognise as products of ribosomal synthesis. Bioinformatic analysis of genome sequence data now allows recognition of modules for lantibiotic synthesis, even if their expression is suppressed. As for the polyketide antibiotic example above, new antimicrobial peptides could therefore be generated by recombinatorial genetics into expression vectors.

Planning for a follow-up meeting will begin soon. If you or your organisation would like to become involved, please contact the author of this report.

Reference

1 Ruhr, G. and Sahl, H.G. (1985) Mode of action of the peptide antibiotic nisin and influence on the membrane potential of whole cells and on cytoplasmic and artificial membrane vesicles. *Antimicrob. Agents Chemother.* 27, 841–845

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