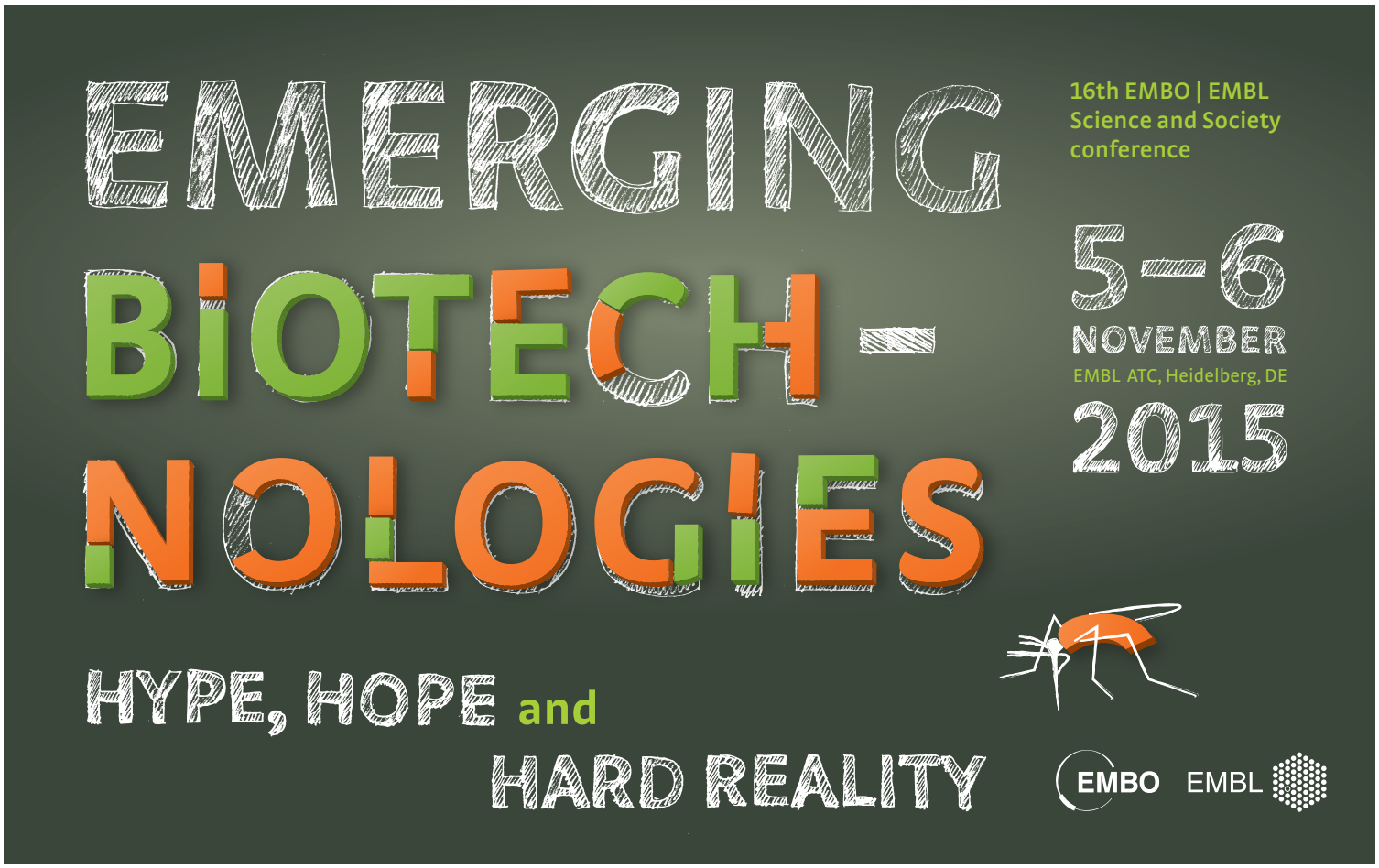

Conference report
Introduction

The 21st century has been called the "century of biology" because scientific knowledge in the life sciences and in related technologies offers potential contributions to nearly all research and consumer sectors to tackle and solve many past and present challenges.

The 16th event in the EMBO | EMBL Science and Society conference series focussed on the impacts on society of innovative biotechnologies in the fields of human health and the environment, two areas presenting urgent societal challenges. An interdisciplinary and international group of 17 speakers and chairs and about 200 participants from all over Europe and beyond gathered for two days in the auditorium of the Advanced Training Centre on the EMBL | EMBO campus to discuss the potential benefits as well as risks and concerns associated with the use of biotechnology applications in these areas. Topics included the roles and responsibilities of different actors to realize the potential economic and societal benefits of these technologies. Issues including governance, patenting, and innovation were discussed.

Biotechnologies for human health

Modern medical biotechnology includes the use and modification of genetic material for the benefit of human health. It is the most important area of application of biotechnologies to many people and a number of talks were dedicated to it. The speakers in this area illustrated the potential benefits of these applications for patients compared to existing therapies, and highlighted their limitations and the challenges to bring them to the market.

The emerging technology for gene editing CRISPR/Cas9 was a focus of the conference. *Dirk Heckl* from the Hannover Medical School in Germany presented and discussed the many potential applications of what has been defined as the game changer in genome editing. Due to its simplicity, efficiency and low cost, the CRISPR/Cas9 system can be used in all fields of biomedicine, from basic research to clinical applications. Moreover, in agriculture, CRISPR/Cas9 can be used to modify crops without mixing DNA from different species.

Along with the enthusiasm about its potentialities, CRISPR/Cas9 genome editing has also raised concerns within and outside the scientific community. These concerns relate in particular to its potential use in editing the human germline, resulting in changes being passed on to future generations. More research is needed to demonstrate that the technology is safe and genome edits occur in the desired position. Moreover, the possible application of CRISPR/Cas9 to germline editing has revived international ethical and policy discussions about whether research involving

the human germline should be allowed at all, and about the role and the responsibilities particularly of scientists, and of the public, in taking decisions on the use of this technology.

Regenerative medicine is a field where new technologies are constantly in development. *Luigi Naldini*, Director of the San Raffaele Telethon Institute for Gene Therapy in Milan presented his ground-breaking work using a novel combination of old technologies, stem cell therapy and gene therapy: the development and application of HIV-based vectors to deliver blood stem cell gene therapies. Gene-transfer efficacy and safety have been the major problems for gene therapy for a long time, but Professor Naldini's team developed new techniques that seem to have overcome these problems and recently produced results in two clinical trials for the treatment of rare diseases in children, raising hopes, and expectations, for cures for devastating genetic diseases.

Emerging stem cell technologies are used also in the field of paediatric regenerative medicine, as *Paolo De Coppi*, from the Institute of Child Health, University College London, illustrated in his talk. They can be used to either repair existing organs or build new ones in the lab. The most promising experimental therapies being developed by his group involve the use of human amniotic fluid stem cells (AFSC) to treat malformations in foetuses or in newborns, on whom it is nearly impossible to do surgery. AFSC have characteristics between embryonic and adult stem cells, but with the advantage that rejection by the host would be avoided.

The development of these new technologies with potential applications in human health has raised expectations and hopes among researchers and patients, but at the same time also concerns, in particular related to safety. Some concerns are common in research using human subjects, such as how to ensure appropriate informed consent from research participants. In this field, however, these concerns are exacerbated by the fact that the research participants are also patients and often they have life-threatening diseases, for which there might be no other therapeutic options. There is often a tension between patients, their families, scientists and doctors who are eager to test research advances in the clinic as soon as possible to treat some otherwise lethal diseases, and regulators, who in order to protect patients may take a cautious approach and often impose controls that are thought to slow down progress. Some of these emerging medical technologies can actually be used in the clinic by employing a compassionate use mechanism, which allow therapies to be given to seriously ill patients who do not have other treatment options without previous marketing approval. This mechanism is an exception to the rules on the process and the speed for the approval of experimental technologies to the clinic.

Another concern in this area relates to the costs of developing these complex therapies that benefit a relatively small number of individuals with rare diseases. A central question is who should decide on funding priorities. This is complicated by that fact that private industry plays an important role in bringing these therapies to the market. Only through collaborations between academia and industry is it possible to meet the high costs of the development process, as Luigi Naldini explained and is doing for the therapies developed by his group. In this situation conflicts of interests could easily arise, for example if a researcher involved in a clinical trial has a financial interest in the company funding the trial. Thus the role of hospital ethics committee is of paramount importance in taking decisions on these issues, and in carrying out a thorough analysis of the benefits and the risks for the patients.

A different set of possible benefits and risks is linked to other medical applications of technologies, such as the development of genetically modified mosquitoes to stop the spread of devastating diseases such as dengue fever, for which there is currently no cure. As *Simon Warner*, CSO of the British company Oxitec, explained, the benefits of this technology over existing ones, such a the use of pesticides, is that it only targets the insects for which it is developed (such as *Aedes aegypti*), so no harm is done to other animals, and it does not pollute the environment. Problems deriving from insects developing resistance to pesticides would be avoided. On the other hand, environmental questions about possible consequences of the disappearance of these mosquitos for the ecosystem remain open, such as 'Would it have any consequences for the animals that feed on these mosquitos?'

As with any new biotechnological applications, all possible benefits and risks deriving from this technology will have to be weighted to take decisions on whether to allow its use or not. In countries like Brazil, where dengue fever is endemic and has serious consequences in terms of public health and economic costs, the Oxitec mosquitos have been approved for release.

Biotechnologies and the environment

Another area of promised outcomes from new biotechnologies is the improvement of ecological management. While discussions about biotechnology have focussed largely on possible negative impacts on the environment, the same tools hold large potential for environmental protection and sustainability. From the use of genetically modified microorganisms for environmental interventions aimed at preventing or remediating environmental pollution, to the use of genetic markers to assess genetic variability within and between species for monitoring and, possibly, for restoration, biotechnology solutions have been developed and used to sustain the environment.

Synthetic biology is one of the technologies used in this area. As *Victor de Lorenzo*, from the National Centre for Biotechnology in Madrid, explained, this "extreme genetic engineering", matched with the recent development of very fast and accurate DNA sequencing, has increased scientists' ability to exploit existing and new-to-nature microbial activities in ways that were not

even envisioned just a few years ago. For example, Professor de Lorenzo works on re-engineering bacteria giving them new-to-nature characteristics to make them able to remove dangerous chemicals from the environment.

Synthetic biology techniques have also been used to reproduce or enhance properties of plants such that they can be exploited more easily and on a larger scale for industrial production. One example is the production of synthetic artemisinin, a drug against malaria, which is traditionally purified from the sweet wormwood plant. As explained by *Anne Osborn*, a project leader at the John Innes Centre in the UK who uses synthetic biology techniques, scientists have succeeded in producing synthetic artemisinin in yeast in much higher quantities and at lower prices than following traditional cultivation. Also *Sven Panke*, from ETH in Zurich, uses synthetic biology with the intent to design novel biological organisms that could be used in industrial manufacturing, energy production, and food and pharmaceutical processing.

Synthetic biology is still an emerging field with high potential for the production of a wide range of useful products for society in, among other areas, pharmaceuticals, vaccines, diagnostics, biofuels and cosmetics. These applications, though, are at an experimental stage, and it is difficult to predict how many of the promises will translate into products.

Despite the many potential benefits promised by synthetic biology, the risks associated with making new organisms and manipulating existing ones need to be assessed. There is a conjectured risk of the accidental production of something dangerous that cannot be controlled and that could accidentally be released in the environment. These concerns are similar to those raised by an already established technology, genetic modification. One difference is due to the interdisciplinary nature of synthetic biology: more stakeholders, like engineers, need to be aware and trained in biosafety issues. Moreover, there is the possibility that synthetized biological parts could be assembled for malign use, for example by terrorists. Professor De Lorenzo explained that while these risks need to be taken seriously, artificially created organisms would not win in the competition with natural organisms that have undergone natural selection and are stronger. Also, synthetic biologists have already thought of strategies that would make a crossing with naturally existing organisms nearly impossible. Nevertheless, careful consideration must be given to make sure that this technology is used in a responsible way. In terms of regulation, most of the experts in the field are of the opinion that GMO regulations will cover synthetic biology and that there is no need to modify current regulation systems.

Sometimes old or established technologies can be used in new fields, opening new possibilities and offering new solutions. Using genetic forensic technologies (e.g. genetic marker analysis), for example, *Carsten Nowak* from the Senckenberg Research Institute in Germany and his team study the recovery and distribution of large carnivores such as wolves and lynxes in Germany. DNA-based molecular analysis has become an essential tool in wildlife biology and conservation, allowing researchers to determine the species, population, origin, relationship or individuality of a sample, to support the protection of endangered species.

Although the risks inherent to technologies like genetic marker analysis are of little relevance, the possible consequences of restoration or reintroduction of species in a habitat might be severe on the environment and the ecosystems. For example, what might happen to other animals or even to humans that have taken over that habitat? And to the environment itself? While reintroducing native species in their natural habitat is often motivated by a desire to restore biological diversity, at the same time by natural selection species are superseded by other species all the time, so reintroducing species might be considered as unnatural.

Governance: how to realize the potential economic and societal benefits while minimising the risks

A session of the conference focussed on the governance of new technologies, which as *Kieron Flanagan* from Manchester University explained, is not simply a synonym for regulation, but rather refers to the process through which rules, norms and actions are produced, sustained, regulated and held accountable. Different actors are concerned with governance: scientists, policy makers and citizens. They might have different views on how to approach it, but the goal is the same for all: realizing the potential societal and economic benefits whilst minimizing the risks that could derive from the use of these technologies.

The necessity to take into consideration a wide range of points of views in the governance of technologies, including the possible uses of a technology in society, was highlighted by *Dirk Stemerding*, an expert in technology assessment from the Rathenau Institute in the Netherlands, in the case of antibiotic resistance. The current high level of antibiotic resistance is due to the combination of two problems: a natural phenomenon that happens in bacteria, and the widespread inappropriate use of antibiotics in society, mainly in health-care and in farming. The World Health Organization (WHO) has developed a comprehensive strategy to tackle this problem in their “global action plan”, aimed at developing scientific solutions, but also at promoting a responsible use of antibiotics in society.

The need for new governance systems for emerging biotechnologies where the interests and values of different groups are taken into consideration was also stressed by *Joyce Tait*, from the Innogen Institute in Edinburgh. More emphasis should also be given to an analysis of the costs and benefits of alternative options, and of the trade-offs between risks and benefits, rather

than mainly to the risks associated to new technologies. The current governance system for biotechnology, narrowly focused on the precautionary principle, has had as a consequence extremely high costs for marketing products of biotechnologies in Europe. As *Maureen McKelvey*, from the School of Business, Economics and Law at the University of Gothenburg in Sweden, explained, this system has created a "death valley" for innovation in Europe, while biotechnology innovation is concentrated essentially in North America, where the US is the cradle for 80% of all biological drugs.

Bernadette Bensaude-Vincent called for a new pragmatic approach to ethics in biotechnology and scientific research. In the current European Commission framework programme Horizon 2020 the concept of Responsible Research and Innovation (RRI) has reduced ethical aspects to a bureaucratic burden for scientists and equates society with the marketplace. Ethics has become a sort of police for scientists' behaviour, and scientists may see it as an intrusion in their work. Dr Bensaude-Vincent proposes to move beyond RRI, and to take a pragmatist approach to technology, as proposed by the philosopher John Dewey, which starts with the identification of underlying values and emotions of the stakeholders involved, and is followed by a subsequent evaluation of them.

Although the ability to patent an invention is often thought of as strictly a technical issue, there are a number of interesting governance concerns that emerge when they are looked at more closely. *Siobhán Yeats* from the European Patent Office explained that although there are widespread concerns about the limiting effects of patents on scientific research, in reality in Europe academic researchers are exempt from patent infringement. And while patenting in biotechnology has been seen as a limitation to innovation, it has the potential to drive innovation because it gives inventors commercial rights over their work, and at the same time it drives technology transfer and innovation by requiring disclosure of information about inventions. Also, without patents, governments would have to pay for the whole process from research to commercialization. Most patent requests come from universities or small and medium enterprises, not from big companies, and without the limited monopoly provided by patents, these companies could not carry out expensive research, as they need to safeguard their investment.

Governance and regulations are tightly related to public opinion, and the issue of how scientists should communicate relevant information to the public and to policy makers such that they can make informed decisions whether they want a technology or not was the subject of a number of questions during the panel discussions. The general sense was that more focus should be given to the trade-offs between benefits and risks of new technologies, and that scientists need to win public trust by engaging more in conversation with the public and understanding people's concern and points of view. However, it is hard to define who "the public" is, and concerns were expressed that too much weight might be given to opinions expressed by interest groups, which may often based on ideology rather than on evidence. All stakeholders involved, scientists, the public – including interest groups – and regulators should act in a responsible way and be aware of the possible consequences of their decisions.

Conclusions

The two days of the conference were focussed on innovative biotechnologies and their potential to provide solutions to relevant societal issues. Although the conference included "hype" in its title, the speakers were well aware of the "hard reality", the limitations and the risks that might stem from these technologies, and of the concerns related to them. There was no hype, but rather the acknowledgment that different points of view and concerns need to be taken into consideration and discussed. The conference was an example of how trust can be built and how technologies can be developed in a responsible manner. We hope that this model can play out in society more generally.

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For more information on the conference, including videos of the talks:
events.embo.org/science-society-conference/past/2015/

Contact:
EMBO Science Policy Programme: policy@embo.org

Text: S. Bendiscioli, Graphics: S. Krahl