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SYNTHETIC BIOLOGY: OPPORTUNITIES AND GOVERNANCE

Abstract: Synthetic biology is already producing results that may have far-reaching implications in such sectors as biomedicine and agriculture.

However, with research and development advancing quickly, new techniques accessible and affordable to many, and the potential for harm as well as for good, synthetic biology is raising a number of issues in the fields of ethics and responsible research.

In 2014, IAP published its 'Statement on Realising Global Potential in Synthetic Biology: Scientific Opportunities and Good Governance', calling for capacity building in the field of synthetic biology so that its benefits can be exploited, responsible research, and encouraging its member academies and others to communicate with scientists, social scientists, ethicists, regulators and users (including the public) and to debate the ethical implications of synthetic biology.

Key words: *Synthetic biology, CRISPR-Cas 9, gain of function, responsible research, bioethics, science advice, science academies*

INTRODUCTION

In March this year, representatives of academies of science, engineering and medicine agreed to establish an umbrella organization, the InterAcademy Partnership[1].

The decision took place at the IAP — the global network of science academies, general assembly in South Africa that was held immediately after a 3-day conference on the issue of 'Science Advice'[2].

The InterAcademy Partnership brings together some 130 national, regional and global academies. At the general assembly, academy representatives also agreed on a structure for the Partnership (Fig. 1), as well as a strategic plan.

The strategic plan builds on the activities and track record of the three constituent networks of the InterAcademy Partnership that have been active since 1993 in

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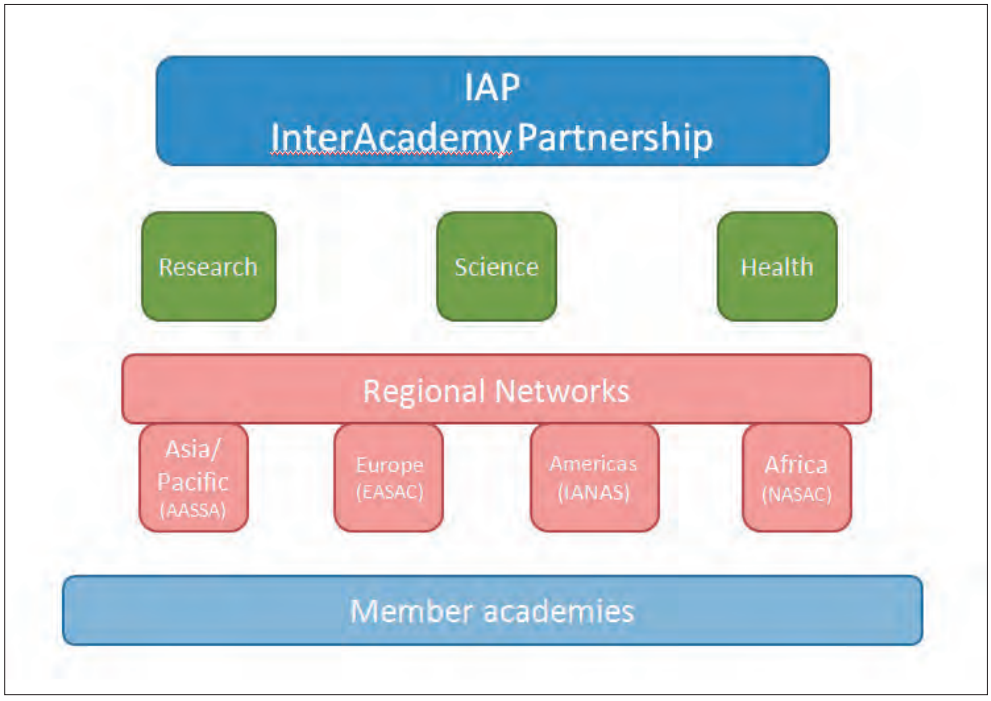

Figure 1. The structure of the newly-established InterAcademy Partnership

the case of IAP (now re-named IAP for Science), and since 2000 for the InterAcademy Medical Panel (now re-named IAP for Health) and the InterAcademy Council (now IAP for Research). It focuses on four thematic areas:

— Provide evidence-based advice and perspectives on global issues;
— Build a scientifically literate global citizenry;
— Strengthen the global scientific enterprise;
— Strengthen the global network of academies, including establishing new academies in countries where they do not currently exist.

Academies are typically independent, self-perpetuating national institutions that recognize excellence and achievement. They are merit-based, with members selected from among the leading scientific, medical and engineering minds within a country.

This gives academies the credibility to review, analyse and synthesise the latest scientific findings and to present the outcomes of their deliberations — which are independent of vested interests — to policy-makers at both national and international levels. In other words, the InterAcademy Partnership (IAP) is able to harness the power, authority and credibility of its member academies and to access their combined scientific talent.

Indeed, among the activities of IAP networks to date have been the production of statements and reports that aim to inform policy and provide recommendations to decision-makers. Likewise, the aforementioned conference held from 28 Febru-

ary to 1 March 2016 in South Africa focused specifically on different mechanisms and modalities of providing science advice[2].

One such area in which IAP and its member academies and regional networks have got involved is that of synthetic biology.

SYNTHETIC BIOLOGY

Synthetic biology is defined as the deliberate design and construction of customized biological and biochemical systems to perform new or improved functions. While the field is still in its infancy, it is already producing results that may have far-reaching implications in such sectors as biomedicine and agriculture.

Research and development are also advancing quickly. Already a major milestone in synthetic biology has been reached — that of defining the genome requirements for a minimal cell, which should pave the way for the construction of novel organisms[3].

However, it could be that genome editing will prove to be a simpler route to achieving various goals using synthetic biology.

Techniques such as CRISPR-Cas 9, for example, are becoming standard procedures in hundreds of laboratories worldwide. The accessibility of these techniques, combined with their potential — including the possibility of altering germlines, and use for harm as well as for good — are raising a number of issues in the fields of ethics and responsible research.

CRISPR-Cas 9 can be used to induce targeted mutations in somatic cells and germline cells alike. Unlike traditional genetic modification techniques that involve transferring DNA across species boundaries, CRISPR-Cas 9 can be used to modify organisms without introducing 'foreign' DNA. Not only is this a powerful technique, but it also has legal implications regarding the status of the resulting organism, especially given that the modification cannot be detected using the processes typically used to identify genetically modified organisms (GMOs).

Indeed, a number of plant, animal and fungal varieties produced using gene editing techniques are already, or soon will be, commercially available. In September 2015, for example, scientists in China announced the development of dwarf pigs using TALENs (transcription activator-like effector nucleases) — initially designed to make it more economical to carry out medical tests on pigs, but also allowing the institute that developed the so-called Bama pigs to raise funds by selling them as pets[4].

This followed on from the commercialization in the USA in 2015 of the first ever non-transgenic genome-edited crop, SU Canola™, designed to be resistant to a herbicide[5], followed by release in Canada in 2016[6]. And more recently, the US Department of Agriculture (USDA) ruled that a gene-edited mushroom designed to stay white longer — made by using CRISPR-Cas 9 to delete a few base pairs of DNA, so disrupting the activity of an enzyme that causes browning — does not need to be regulated as a GMO would. According to *Nature*, the „mushroom did not trigger USDA oversight because it does not contain foreign DNA from 'plant pests' such as viruses or bacteria. Such organisms were necessary for genetically

modifying plants in the 1980 s and 1990 s, when the US government developed its framework for regulating GMOs."[7]

Synthetic biology can also be used for the production of high-value biological chemicals, especially in instances where yields obtained by cultivating the source plant cannot keep up with demand. This is the case with the anti-malarial compound artemisinin[8], for example, as well as ginenosides[9], the sought-after active ingredients of the Chinese medicinal plant, ginseng. However, transferring production of such compounds to microbiological fermentation systems can have knock-on effects, for example on the livelihoods of farmers who may lose the market for their crops. For these reasons, Friends of the Earth, the ETC Group and others have called for a moratorium on synthetic biology until a number of principles are put in place[10].

Another area in which synthetic biology may play a part is in gain-of-function experiments. Among the most controversial to date were two parallel sets of trials which introduced specific mutations into the H 5 N 1 virus that causes avian influenza[11,12]. The researchers were criticized as they were able to create a strain of the virus that, unlike the original H 5 N 1, could be transmitted via aerosols. If such experiments were carried out under less-than-ideal isolation conditions (in this case, all biosecurity regulations were observed), such a virus could potentially cause a severe human epidemic, and there was a heated open debate on whether or not the research should be made public[13].

But perhaps the genome-editing advance that has caused most consternation is that reported by Gantz and Bier[14]. Working with CRISPR-Cas 9 in *Drosophila*, they developed a system whereby a mutation in one chromosome (a heterozygous individual) was duplicated into the second chromosome, making individuals homozygous for the mutation. In this way, a desired mutation can quickly spread through an entire population, an effect known as 'mutagenic chain reaction' (MCR) or 'gene drive'. One idea is to generate a mutation in disease-transmitting mosquitoes that would make them incapable of reproducing and developing normally. Such a mutation linked to a gene-drive mechanism could, theoretically, wipe out an entire population or even a species.

„Failure to take stringent precautions could lead to unintentional release of MCR organisms into the environment," warn the authors of the paper, who add their voice to a call or „a dialogue on this topic [to] become an immediate high-priority issue" and recommending the consideration of „biosafety measures and institutional policies appropriate for limiting the risk of engaging in MCR research while affording workable opportunities for positive applications of this concept."

Indeed, in a subsequent paper, the authors of the original MCR paper joined with 25 others to consider „safeguarding gene drive experiments in the laboratory" — one of a number of publications demonstrating that the scientific community is tackling such issues and that dialogue and careful consideration are already taking place.[15]

In addition, such is the relative simplicity and accessibility of various synthetic biology techniques, a 'movement' of DIY synthetic biologists has been established — students and others who are buying DNA 'building blocks' off the internet and

recombining them into such organisms as bacteria and yeast in efforts to develop microbes with new functionality. The iGEM (International Genetically Engineered Machine) competition, for example, has introduced students, increasingly from high schools and colleges in Asia and Africa as well as from Europe and the Americas, to the principles and practices of synthetic biology[16].

IAP STATEMENT

The recommendations made by Gantz and Bier[14] and others mirror those made by IAP in its 2014 'Statement on Realising Global Potential in Synthetic Biology: Scientific Opportunities and Good Governance'[17].

The Statement called for capacity building in the field of synthetic biology so that its benefits can be exploited. At the same time, however, IAP also raised the issues of responsible research, global regulation (that would not be too restrictive and deny society any potential benefits), and called on its member academies and others to debate the ethical implications of synthetic biology.

Such IAP statements are developed by a working group of experts nominated by IAP member academies. Once a final version is approved by the IAP executive committee, it is sent out to all member academies for their endorsement. If a majority of academies endorse the statement, then it is released. The IAP Statement on synthetic biology reached the required level of endorsement by IAP members and was released on 7 May 2014.

In a parallel Worldview column in *Nature*, IAP co-chair Volker ter Meulen noted: „The topic is, however, controversial, and that is jeopardizing its promise. Environmental groups argue that it poses risks to health and the environment and have called for a global moratorium. We have been here before: exaggerated fears and uncritical acceptance of claims of the risks of genetic modification led to excessively cautious regulation and a block on innovation that not only slowed the development of new products, but also deterred basic science."[18]

Since they were first commercialised in 1996, GM crops have been planted across a cumulative total of 2 billion hectares in 28 countries, providing benefits to farmers of more than US$150 billion. Indeed, nearly 18 million farmers now grow GM crops each year, 90% of whom are small, resource-poor farmers in developing countries. In Europe, however, the „excessively cautious regulation" that ter Meulen warns about has confined the growth of GM crops to a little over 110,000 hectares in just five countries[19].

INTERNATIONAL ENGAGEMENT

The release of the IAP Statement was timed to coincide with the scheduled 18th meeting of the Convention on Biological Diversity's (CBD) Subsidiary Body on Scientific, Technical and Technological Advice (SBSTTA-18), which met in Montreal, Canada, in June 2014 to review potential positive and negative impacts of synthetic biology on biodiversity and was under pressure from some environmental groups to impose a moratorium on synthetic biology research and development[10].

Two years later and the CBD is still discussing the issue of synthetic biology. Indeed, its latest documents have developed a new „operational definition" of synthetic biology: „Synthetic biology is a further development and new dimension of modern biotechnology that combines science, technology and engineering to facilitate and accelerate the understanding, design, redesign, manufacture and/or modification of genetic materials, living organisms and biological systems."[20]

This definition was the result of deliberations of a specially-implemented Ad Hoc Technical Expert Group (AHTEG) on Synthetic Biology and a moderated online forum. Again, IAP submitted its Statement for deliberation by the forum and AHTEG, one of 27 submissions received by the CBD[21]. Members of the IAP Statement Working Group were also proposed as members of AHTEG. Although none were eventually selected, academies did have one voice in the group, nominated by the Royal Society, UK.

AHTEG members also concluded that „living organisms developed through current and near future applications of synthetic biology are similar to LMOs (living modified organisms) as defined in the Cartagena Protocol"[20] — so paving the way for the same kinds of regulation as GMOs (equivalent to LMOs), which goes against the text of the IAP Statement. However, the AHTEG did also encourage Parties to the CBD, other Governments and relevant organizations to: „Conduct research on the positive and negative impacts of synthetic biology, on biodiversity, with a view to filling knowledge gaps and identifying how those impacts relate to the objectives of the Convention and its Protocols,"[18] and: „Promote and enable public and multi-stakeholder dialogues and awareness-raising activities on the potential positive and negative impacts of synthetic biology on biodiversity, taking into account ethical considerations in the context of the three objectives of the Convention, with the full engagement of indigenous peoples and local communities."[20] These two points are in line with the IAP Statement and steer well clear of any proposed moratorium.

It is also clear that, by requesting additional research and multi-stakeholder engagements, the discussions surrounding synthetic biology are far from over.

In addition to the CBD, IAP is also engaged with the Biological and Toxin Weapons Convention (BWC). An IAP Biosecurity Working Group (BWG) comprising representatives of academies from Australia, China, Cuba, Egypt, India, Nigeria, Pakistan, Russia, the United Kingdom and the United States and currently chaired by the Polish Academy of Sciences has been engaging with the BWC for several years, in particular feeding into various meetings of experts, providing up-to-date scientific information for deliberation.

Most recently, IAP provided input into the Meeting of Experts that convened in Geneva, Switzerland on 10–14 August 2015, which discussed various recent rapid advances in the life sciences (including synthetic biology), along with 'warnings' from regional and global outbreaks of infectious diseases including SARS, bird flu and Ebola.

However, there are worries that the current processes of the Convention do not adequately take into account developments in science and technology. In addition, many of the 173 States Parties that have signed up to it also argue that there is not enough at-

tention being paid to strengthening cooperation and assistance, especially to developing nations — something that signatories to the Convention have undertaken to do.

Speaking at the Meeting of Experts in August 2015, the author highlighted IAP's role in supporting the activities of the BWC to promote responsible research practices and build awareness of dual-use research[22]. Among these activities are the publication of a report, 'Responsible Conduct in the Global Research Enterprise: A policy report'[23], and, more recently, the release of a guide for teachers, 'Doing Global Science: A guide to responsible conduct in the global research enterprise'[24]. As well as such projects carried out by the IAP itself, IAP also supports projects carried out by its member academies. One recent example was implemented by the Pakistan Academy of Sciences and involved reaching out to biotechnology students in remote areas of the country[25].

Indeed, in his intervention on behalf of the IAP BWG to the Meeting of Experts in Geneva, Ryszard Slomski of the Polish Academy of Sciences called for more awareness-raising activities to be implemented, for example, by engaging with national agencies such as academies of science[22].

Immediately prior to the Meeting of Experts, the IAP BWG, and especially the US National Academies of Sciences, organized an information-sharing workshop on 'Advances in Design and Use of Microbial Production Systems: A workshop for the BWC community'. Workshop speakers reviewed the implications of advances in bioscience research and in the industrial bioscience sector.

As Piers Millett (Biosecure Ltd., UK) summed up: „Advances in areas such as tool and platform development, automation, and experimental analysis are leading to progress on multiple fronts in design and development of biological production processes. However, the field is not yet at a stage in which a researcher could simply enter a desired end product into a software package, have the system map out the metabolic pathways, and robotically conduct the experiments necessary to achieve the desired result. A significant role remains for tacit knowledge and specialized resources. Practical challenges also remain in scale-up from laboratory to industrial-scale production of relevant microorganisms. Complex system aspects must be controlled, making it difficult for someone to switch from one route of production to another, whether that would entail use of a new organism, feeding an organism a new feedstock, or trying to produce a new end product. Each synthetic scheme would require intense optimization to achieve robustness and cost-effectiveness."[26]

Such conclusions should provide some reassurance to those who worry that wider access to DNA sequences and synthetic biology technology will make it is easier for rogue scientists to weaponise viruses or develop ways of mass-producing biological toxins.

These and other deliberations of members of the IAP BWG are being taken forward to the 8th BWC Review Conference scheduled for late 2016.

GAIN OF FUNCTION

Academies continue to engage with governance issues that involve science, as reflected by recent activities on the gain-of-function (GOF) issue. As stated before,

GOF is one possible target of synthetic biology research, and also something that could be used for good or potentially also for harm.

In October 2015, EASAC (IAP's regional network for Europe) published its report, 'Gain of Function: Experimental applications relating to potentially pandemic pathogens'[27]. Among the recommendations of the report was the proposal for self-regulation among scientific institutions in parallel with raising the awareness of researchers regarding their responsibilities. It was also pointed out that risk assessment cannot be a 'once and for all' calculation, but that there is a need for continuing evaluation.

The issue of public engagement was also tackled, with strong recommendations on building a climate of trust and openness, with scientists, their institutions — and academies of science — involved in public dialogue to discuss the objectives of research projects, potential risks and benefits, as well as informing about the biorisk management practices that are in place.

Elsewhere, following a series of avoidable incidents involving biohazard materials in the USA, in October 2014 the White House announced the suspension of federal funding for certain types of GOF research pending a review of procedures. The US National Academy of Science was tasked with convening experts from different disciplines to undertake the review through a series of workshops and other mechanisms, overseen by a newly-established National Science Advisory Board for Biosecurity (NSABB). The discussions of the second such workshop have just been published[28], with the final report of the NASABB due for publication by the end of May 2016.

CONFERENCE ON SCIENCE ADVICE

As the examples above clearly demonstrate, there is a role for academies of science and medicine to play in providing advice to governments. Academies are unique in that they are able to bring together the best minds in each country and are independent from political or commercial interests. However, around the globe, different national governments have developed different mechanisms for receiving science advice — from the appointment of a single expert science advisor, to ad hoc committees. In addition, how advice is presented can vary depending on whether there is time to deliberate and debate a particular topic, or whether there is an emergency situation.

Such issues were discussed at the IAP Conference on Science Advice (South Africa, February/March 2016).

Indeed, the conference dedicated a session to 'Science Advice in the International Arena with a Special Focus on Synthetic Biology'.

Among the outcomes of this session was the opinion that research into synthetic biology is moving quickly, but that regulatory oversight is failing to keep pace. In addition, participants raised the concern that products derived via synthetic biology could be seen as equivalent in all respects to genetically modified organisms (GMOs). In this case there is a need to work with social scientists on ways to engage the public in outreach and debate so that the benefits of synthetic biolo-

gy are not curtailed or over-regulated as they have been with GMOs in some parts of the world (see above). It was also noted that many synthetic biology practitioners are operating outside academia, so it is difficult to ensure responsible and ethical research. For these reasons, it was proposed to engage more with these informal groups so that potential misuse of research can be spotted early and averted[2].

CONCLUSION

DIYbio. org is an online hub for people interested in pursuing DIY biology, and which lists more than 80 local groups and communities around the world. The website (www.diybio.org) also has sections where people can review a code of ethics that has been developed, or ask an expert about biosafety issues. Todd Kuiken, a US-based researcher and co-founder of DIYbio. org, notes that the DIY biologists „proactive culture of responsibility is an advance on the post hoc scrambling that often occurs within the scientific establishment," and highlights that „the current culture of responsibility among DIY biologists, their collaborative style of working and the fact that community labs are open spaces in which everyone can see what is going on reduce, if not eliminate, doomsday scenarios of mutant organisms escaping from basements and causing harm."[29]

Such considerations, allied with the outcome of the IAP Conference on Science Advice, have prepared the ground for collaboration between academies of science — representing the scientific establishment — and the DIY biologists. Indeed, discussions are already under way to bring the two groups together, especially with the involvement of the Global Young Academy.

As well as these efforts, as prescribed by several of the papers and reports presented here, including the IAP Statement[14,15,17,18,27], there is a need for engaging the wider community, including social scientists, ethicists and science communicators, and being open and transparent with the general public when it comes to explaining the rationale for, and benefits and potential risks of, synthetic biology experiments.

To this end, IAP encourages its member academies to take another look at the 2014 Statement and to promote the recommendations therein within their nations and to join with IAP and its regional networks in promoting them internationally. For its part, IAP will continue to engage with international processes such as the Convention on Biological Diversity and the Biological and Toxin Weapons Convention.

IAP is also providing financial support to the Federation of European Academies of Medicine (FEAM) for a project that is reviewing the European landscape for human genome editing, comparing and contrasting current national legislation, again with the aim of developing Europe-wide recommendations for presentation to the European Commission, while EASAC (IAP's regional network for Europe) is undertaking a separate project looking at all genome editing applications.

The fact remains, as outlined in the IAP Statement, that „by applying the principles of systems biology, engineering and chemical design to biological systems, synthetic biology will lead to new applications of considerable societal value. Proof-

of-concept has already been demonstrated in establishing less expensive ways of producing pharmaceuticals and other high-value chemicals and there are likely to be other early achievements in the generation and optimal use of biofuels. Further ahead there are possible applications of this biological toolbox in biomedicine, agriculture, land and water decontamination, biosensing, new materials, nano-machines and novel approaches to information processing."[17]

Thus, the benefits of synthetic biology are likely to be enormous, but they must be achieved in a responsible and transparent manner if governments and the public are to be persuaded to accept whatever risks will need to be constrained as new products are developed and commercialised.

REFERENCES

[1] International networks of academies create umbrella organization. 2 March 2016. http://www.interacademies.net/News/PressReleases/29843.aspx
[2] Summary of the IAP Conference on Science Advice. 4 March 2016.http://www.interacademies.net/News/29857.aspx
[3] Hutchison III, C. A. *et al.* (2016) Design and synthesis of a minimal bacterial genome. Science, 351: 6280. 25 March 2016. http://science.sciencemag.org/content/351/6280/aad6253.full
[4] Gene-edited 'micropigs' to be sold as pets at Chinese institute. *Nature*. 29 September 2015. http://www.nature.com/news/gene-edited-micropigs-to-be-sold-as-pets-at-chinese-institute-1.18448
[5] Cibus and Rotam announce launch of their first non-transgenic commercial product. Press release, 19 November 2014. http://www.cibus.com/press/press111914.php
[6] Sulfonylurea-tolerant canola eyed for 2016 launch. 26 March 2014. http://www.agcanada.com/daily/sulfonylurea-tolerant-canola-eyed-for-2016-launch
[7] Gene-edited CRISPR mushroom escapes US regulation. *Nature*. 14 April 2016. http://www.nature.com/news/gene-edited-crispr-mushroom-escapes-us-regulation-1.19754
[8] Paddon, C. J. *et al.* (2013). High-level semi-synthetic production of the potent antimalarial artemisinin. *Nature*, 496, 528–536, 25 April 2013.
[9] Dai, Z. *et al.* (2013). Metabolic engineering of *Saccharomyces cerevisiae* for production of ginsenosides. *Metabolic* Engineering, 20, 146–156.
[10] Friends of the Earth, CTA and ETC Group (2012). The Principles for the Oversight of Synthetic Biology. http://www.etcgroup.org/content/principles-oversight-synthetic-biology
[11] Herfst, S. *et al.* (2012). Airborne transmission of influenza A/H 5 N 1 virus between ferrets. *Science*, 336: 6088, 1534–1541. http://science.sciencemag.org/content/336/6088/1534.full
[12] Imai, M. *et al.* (2012). Experimental adaptation of an influenza H 5 HA confers respiratory droplet transmission to a reassortant H 5 HA/H 1 N 1 virus in ferrets. *Nature,* 486: 7401, 420–428. http://www.nature.com/nature/journal/v486/n7403/abs/nature10831.html
[13] Work resumes on lethal flu strains. *Nature*, 493: 460. 24 January 2013. http://www.nature.com/news/work-resumes-on-lethal-flu-strains-1.12266
[14] Gantz, V. M. and Bier, E. (2015). The mutagenic chain reaction: A method for converting heterozygous to homozygous mutations. *Science*, 348: 6233, 442–444.

[15] Akbari, O. S. *et al*. (2015). Safeguarding gene drive experiments in the laboratory. *Science*, 349: 6251, 927–929. http://science.sciencemag.org/content/349/6251/927
[16] http://igem.org
[17] IAP — the global network of science academies. 7 May 2014. 'Statement on Realising Global Potential in Synthetic Biology: Scientific Opportunities and Good Governance'. http://www.interacademies.net/10878/Scientific_Opportunities_and_Good_Governance.aspx
[18] ter Meulen, V. (2014). Time to settle the synthetic controversy. *Nature*. 7 May 2014. http://www.nature.com/news/time-to-settle-the-synthetic-controversy-1.15169
[19] ISAAA Brief 51–2015: Top ten facts about biotech/GM crops in their first 20 years, 1996 to 2015. http://www.isaaa.org/resources/publications/briefs/51/toptenfacts/default.asp
[20] Convention on Biological Diversity, Subsidiary Body on Scientific, Technical and Technological Advice, 20th meeting, Montreal, Canada, 25–30 April 2016, Item 6 of the provisional agenda, Synthetic Biology.
[21] Convention on Biological Diversity. http://bch.cbd.int/synbio/submissions/
[22] Meeting of Experts (10–14 August 2015). http://www.unog.ch/__80256ee600585943.nsf/%28httpPages%29/46cac219b57f8b49c1257db20030bce8?OpenDocument&ExpandSection=9#_Section9. See also 'Biological and toxic weapons': http://www.interacademies.net/News/27904.aspx
[23] IAP (2012). Responsible Conduct in the Global Research Enterprise: A policy report. www.interacademies.net/file.aspx?id=19789
[24] IAP (2016). Doing Global Science: A guide to responsible conduct in the global research enterprise. www.interacademies.net/File.aspx?id=29738. Princeton University Press.
[25] IAP (2015). Annual Report 2014, 'Dual-use education in Pakistan' (p. 40–41) http://www.interacademies.net/Publications/27799.aspx
[26] IAP BWG, S. Mueller and K. Bowman, rapporteurs (2015). Advances in Design and Use of Microbial Production Systems: A Workshop for the BWC Community. http://www.iapbwg.pan.pl/index.php?option=com_content&view=category&layout=blog&id=9&Itemid=111
[27] EASAC (2015). Gain of function: experimental applications relating to potentially pandemic pathogens. http://www.easac.eu/home/reports-and-statements/detail-view/article/easac-report-1.html
[28] National Academies Press (2016). Millett, P., Husbands, J., Sharples, F. and Thevenon, A., rapporteurs. Gain-of-Function Research: Summary of the second symposium, March 10–11, 2016. http://www.nap.edu/catalog/23484/gain-of-function-research-summary-of-the-second-symposium-march
[29] Kuiken, T. (2016). Governance: Learn from DIY biologists. Nature 531, 167–168, 10 March 2016. http://www.nature.com/news/governance-learn-from-diy-biologists-1.19507