

foundations need to invest to turn validated targets and candidate drugs into actual treatments.

Our list of likely drug leads and their targets must be validated and extended using additional lines of evidence by computation and, most importantly, wet lab experiments. We are committed to helping other researchers add their protocols and analyses to the current kernel. For example, computational docking, biophysical analysis, activity assays, site-directed mutagenesis and synthetic chemistry could be performed for all predicted targets. Unfortunately, such techniques are usually very expensive and thus not feasible on a genomic scale by a single research group. The main goal of our exercise was to narrow down the number of targets and identify their putative ligands for experimental follow-up, so that the overall process is faster, more thorough and less expensive. The TDI kernel's list of 'hits' does not exhaust the ten target genomes. Researchers who want TDI to investigate additional candidates should contact us or engage in online discussions at our collaborative portal (<http://www.thesynapticleap.org/>).

Note: Supplementary information is available on the *Nature Biotechnology* website.

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## Of Newtons and heretics

### To the Editor:

In a commentary for *Nature Biotechnology* last year<sup>1</sup>, Joachim Boldt and Oliver Müller argue that synthetic biology poses ethical issues beyond those of traditional genetic engineering. This is because synthetic biology aims, among other things, to create biological systems with features that might never have been part of living organisms before. Moreover, the authors point out that synthetic biology represents a radical shift from manipulation to creation—a shift to organisms, “significant portions” of which are “designed by humans,” conferring new responsibilities on human beings as creators and questioning our understanding of life and living organisms. According to data we describe here, however, this interpretation contrasts with the views of the scientific community itself. As part of the European SYNBIOSAFE project on the ethics and safety of synthetic biology<sup>2</sup>, we have interviewed 20 European researchers working in synthetic biology to explore their ideas and attitudes regarding the ethical implications of their work, a discussion we hoped would contribute to the ethical, safety and regulatory discourse in Europe. To complement the discussion begun by Boldt and Müller, we present the results of this survey below.

The survey was carried out between June 2007 and January 2008 (see **Supplementary Methods** online), during which we interviewed leading scientists from the European synthetic biology community, which we defined as those persons and institutions that coordinate (or participate in) one of the EC-FP6-NEST<sup>3</sup>-funded synthetic biology projects. As the synthetic biology community in Europe was still, at

the time, defining its identity, we wanted to survey the opinions and expectations of researchers regarding their field. Moreover, given the past debates about biotechnologies in Europe, scientists here might have had, we believed, a significant contribution to make regarding the ethics, regulation and

perception of a new biotech that may or may not match the prevailing views in the US community. The survey took the form of an interview, in which we asked whether there were ethical issues associated with synthetic biology, whether the creation of artificial organisms posed ethical problems and whether synthetic biology ethical debates resembled those associated with earlier

biotechnologies (interested readers should contact us for a copy of the interview guide). Answers are listed in full in **Supplementary Methods** online.

According to most of the interviewees, and quite to the contrary of what Boldt and Müller suggest, the prevailing view was that synthetic biology raises no particular ethical issues in itself. Escaping the natural is part of what man does and many felt that where there are ethical questions, they are almost entirely restricted to unintended negative effects and intended misuse. Where respondents did recognize other moral implications, these were almost exclusively related to practical applications of synthetic biology. Some respondents, for example, felt that the only important issue was the application of synthetic biology to higher organisms or that the manipulation of the human genome should be prohibited. Others had more difficulty in pinpointing specific ethical issues but showed discomfort at bringing wholesale changes to the genome, worries perhaps related to the ‘instrumentalization’ of living organisms.



Related to this issue was the concern expressed by a few respondents about the new status synthetic biology gives to scientists as a consequence of enhanced possibilities, such as the creation of new types of living organisms. Scientists, one respondent noted, would now have a further responsibility to preserve the natural habitat, and the responsibility to decide what should or should not be created. However, in opposition to a few respondents' notion of increased responsibility, many seemed to equate ethical issues with what the public makes of them, suggesting that the only important ethical concerns would be those that arise from public fears, or the 'Frankenstein Factor'. This echoed the fear among scientists that synthetic biology may suffer from a similar backlash in Europe as genetically modified (GM) organisms. In a bid to avoid eliciting an adverse reaction from the public, one respondent proposed a form of semantic gymnastics in which synthetically created organisms would be recast as "self-replicating complex biological entities" instead of living organisms<sup>4</sup>.

We also tried to gather opinions on the issue of regulation of synthetic biology. Boldt and Müller as well as others<sup>5</sup> discuss the possibility for another Asilomar; indeed, at the Second International Conference on Synthetic Biology (SB 2.0) held at the University of California, Berkeley, in May 2006, the need for an ethical and regulatory framework was the subject of several sessions. Some commentators, however, disqualified this process as undemocratic and lacking transparency<sup>6</sup>. To further explore this topic, we offered our respondents four possible regulatory frameworks to choose from: international guidelines, national laws, self-regulation by scientists, and a participatory approach involving stakeholders, including civil societies. Contrary to our expectations, none of our respondents opted for self-regulation by scientists as the most favorable solution; rather, a large majority preferred a combined approach. Many liked the idea of an umbrella international guideline above a national law or self-regulation, but others feared that international harmonization would be difficult to reach. National regulation would be slow to catch up with the advances of synthetic biology, but it would provide the necessary heterogeneity among nations lacking when implementing international

guidelines only. The idea of a participatory approach drew various types of reaction, with one respondent dismissing it as a joke, others feeling that it would be the only way to avoid a GM-like backlash, and others still who liked the idea but were not sure how feasible this would be.

In their commentary, Boldt and Müller conclude with the suggestion that if we were to develop a code of ethics for synthetic biology, such a code should reflect how scientists understand their activity in the context of society and nature, beyond concerns of risks. According to the results of our survey, however, the main concerns of those interviewed relate to biosafety and biosecurity. The results also reflect an eagerness to appease public worries and to achieve sensible regulation without impeding scientific progress. Although the small group of researchers interviewed cannot be said to speak for the entire scientific community, the concerns raised here can be seen as indicators of the main areas that the European synthetic biology community may want to tackle.

Even so, we tend to concur with Boldt and Müller that it is unlikely that the ethical debate outside the scientific community will be limited to the commonly encountered risk-based discussion on emerging technologies. Be they hailed as 'Newtons of a blade of grass' or criticized as heretics<sup>7</sup>, synthetic biologists will probably have to engage in discussions that probe beyond risk and security assessments, into concepts of life, the status of new synthetic organisms and the responsibility that may arise from such acts of creation. Synthetic biology also tends to blur the traditional boundaries between life and machine, as well as the 'natural' and 'unnatural'. It forces us to question our understanding of the intrinsic and instrumental values present in nature and living organisms, resulting in a variety of possible implications for the normative discourse.

Having recognized the need to address societal issues at an early stage, the synthetic biology community has a great opportunity to deal with ethical issues more appropriately and expeditiously than proponents of previous technologies. From the interviews presented here and the general discussion on ethical and societal issues related to synthetic biology, we conclude that a comprehensive assessment of ethical issues in synthetic biology should address the philosophical questions mentioned

by Boldt and Müller as well as the existing and potential concerns of society and the position of scientists. Whereas it may well take some time to fully grasp the philosophical challenges that synthetic biology presents, it will be important to create the necessary space for an informed, participatory discourse to accompany the development of this discipline. Over the months since the interviews were conducted, the SYNBIOSAFE team has followed this approach by setting up an e-conference<sup>8</sup> and dialogs with different stakeholders. These efforts resulted in a priority paper, defining the topics in ethics, safety, security and science-public interface that might frame the societal discussion around synthetic biology. European and international scientists, as well as a variety of stakeholders have come forward to facilitate a discussion on this subject and have provided their insight and expertise to the paper. Although there remain many different and often opposing opinions concerning ethical and societal questions in synthetic biology, there is a general willingness among researchers to participate in a dialog, which is a favorable precondition for a constructive exchange of ideas and the ability to achieve rational, multi-stakeholder governance of the discipline.

Note: Supplementary information is available on the Nature Biotechnology website.

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