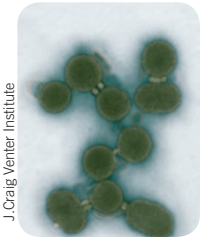
IN brief

Synthetic biology go ahead



J. Craig Venter Institute

M. mycoides, the first synthetic bacterial cell.

Synthetic biologists see freedom to operate in the new guidelines from the Presidential Commission for the Study of Bioethical Issues (PCSBI) published on 16 December 2010. "Measured" is the word being used by many researchers to describe the 18 recommendations put forward in New Directions: The Ethics of Synthetic Biology and Emerging Technologies (http://www.bioethics.gov/documents/synthetic-biology/PCSBI-Synthetic-Biology-Report-12-16-10.pdf). The new report relies on existing regulations while remaining vigilant for technological developments in this still-young field. Most current research in synthetic biology still resembles conventional genetic engineering, with typical commercial efforts focused on modification of cellular biosynthetic pathways. As such, it should be business as usual for companies such as Berkeley, California–based Bio Architecture Lab (BAL), which is reprogramming algae for biofuel production. "We have a lot of control, and the guidelines are very well articulated for industrial microbiology and industrial fermentation," explains co-founder Yasuo Yoshikuni, "so we don't see many obstacles." The response from scientists in academia and industry has been broadly positive. J. Craig Venter, whose headline-earning production of a *Mycoplasma* bacterium with a synthetically constructed genome this past May (*Science* **329**, 52–56, 2010) was a major driver for the PCSBI efforts, praised the report's findings as "wise, warranted and restrained" in a recent press release. Keeping guidelines current, however, will be a challenge in this rapidly moving area. Indeed, more than a third of the PCSBI recommendations are concerned with reviewing progress in the field over the next 18 months and the suitability of existing guidelines by scientists and policymakers, with the results to be made public. "At least in the present state of the field, the hype is far outpacing our capabilities," says James Collins, a researcher at Harvard's Wyss Institute for Biologically Inspired Engineering and one of dozens of guest speakers who gave presentations to the PCSBI, "and I think the Commission did a very good job of assessing current capabilities." Many see such efforts at transparency and combating hype—key themes of the report—as essential to the future of the field. Jay Keasling, of the University of California at Berkeley, says: "Scientists can't be so naive to think there won't be a possibility of bad things happening, but I think the public will grow to accept synthetic biology if we're able to talk about all of the great things that can be done with it."

Michael Eisenstein

not realistic for advancing compounds to the IND [investigational new drug] stage."

NCATS will bring "a centralized, more focused and collaborative approach" to NIH and "could really be a driving force to help generate innovative tools, ideas, and most importantly, embed the translational mindset into the scientific community more than it is today," says Laura Richman of MedImmune in Rockville, Maryland, where she is vice president, R&D, translational science. The new center, once established, "also will focus on training the next generation of translational scientists to perpetuate this mindset," she adds.

Richman's colleague Steve Projan, who recently became senior vice president R&D, Innovative Medicines and Head of Infectious Diseases & Vaccines at MedImmune, also is in favor of NCATS. "In my own view this is certainly a good idea," he says. "In my previous job at Novartis we had a strong focus on host targets for infectious diseases, and I think this could well be a useful focus of this enterprise at the NIH." Other researchers at biotech companies are also eager to advise NIH officials on how to tailor its programs to meet very specific needs. Ronald Farquhar, vice president, discovery biology at Cubist Pharmaceuticals in Lexington, Massachusetts, points out that many "translational gaps" still exist in antibacterials and analgesic research—areas pursued by the company.

For instance, in developing antibacterial drugs, Farquhar says it is possible to find potent inhibitors of targets, but understanding of drug penetration into [microbes] and efflux remains limited. "Can any one drug company address this question? We don't see it as compatible with company goals, but NIH could enable research into this problem," Farquhar notes.

In the pain field the knowledge gap is in the animal models, he continues, as many compounds that appear to work in animal models fail in the clinic. "The translational challenge with animal data is so great that it almost requires a leap of faith to go into the clinic, and that's a huge risk," he says. "Scoring" candidate drugs in clinical trials generates a further gap as there is an "enormous placebo effect," he adds. "If NIH takes this challenge on and made its findings available to industry, it would be a huge advance."

"There is a whirlwind of change affecting all major therapeutic areas, including infectious diseases, which is still the largest killer," says Lance Stewart, CEO of Emerald BioStructures on Bainbridge Isle, Washington. "There's a lot of work on antivirals, but the economics of developing antibacterial drugs don't add up. Where will the new drugs come from?" Although NIH recruited "talent" from pharma companies and started several centers aimed at filling such gaps, "overall that was not enough to get anywhere because it requires orders of magnitude more in resources," he says, adding, "I'm excited with the resources and interest behind [NIH Director] Collins's ideas. And, because I don't see drugs for infectious and neglected diseases coming from industry, this may be the only way."

The approach envisioned for NCATS could prove especially important if resources become scarcer, according to Stewart. "Teams with the right organization could get compounds to the clinic very rapidly, and it's possible to translate basic research into the clinic, but it's not inexpensive, especially for small companies," he says.

Many small companies see NIH mainly as a source for resources, according to Lynn Silver, a consultant based in Springfield, New Jersey. And many of those companies are worried about meeting regulatory requirements laid out by officials at the Food and Drug Administration, she says. "Maybe NIH can help with those worries, and get government science on the side of drug development and doing clinical trials."

Although Farquhar, Stewart and Silver suggest very specific needs to be addressed through the NIH proposal to form NCATS, others see it in much broader terms. Developing new therapeutics "requires trying new models," says Robi Blumenstein, president of Cure Huntington's Disease Initiative Foundation in New York, a not-for-profit clearinghouse whose research focus is Huntington's disease. "The process of developing drugs is very, very complicated, and many different types of organizations are needed. It needs a catalyst to bring institutions together, recognize the strengths of different people and bring them together to solve problems. Any single approach is doomed to failure. But if NIH can orchestrate an entire suite of activities, that's great."

Jeffrey L Fox, *Washington, DC*

IN their words

"Going from the germ theory of disease to antibiotics that saved people's lives took 60 years. We might beat that. But anybody who thought in the year 2000 that we'd see cures in 2010 was smoking something."

Eric Lander counters criticisms that the Human Genome Project and its potential were hyped. (*Technology Review*, Jan/Feb 2011)