

## Comment

# An Asilomar moment

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“An Asilomar moment.” That’s what David Galas, who used to head the Human Genome Project in the US Department of Energy and is now Vice President of the Keck Graduate Institute in Claremont, California, called it. I believe the phrase has also been used by others, but I first heard it from him. I agree. As governments in the US and Europe contemplate legislation that would divert funding of some genomics-driven research to Offices of Homeland Security and the like, and that would restrict the freedom of biologists to publish and share some of their data, we of the scientific community are facing a crisis, brought on by fears of bioterrorism, that eerily mirrors the early days of recombinant DNA research.

The phrase refers to a meeting of molecular biologists that was held at the Asilomar Conference Center in Pacific Grove, California, in 1975. Asilomar - the name is a joining of two Spanish words meaning a ‘refuge by the sea’ - was designed by Julia Morgan, one of the first women architects in the US, who also designed the Fairmont Hotel in San Francisco, and San Simeon, the mansion of publisher William Randolph Hearst (the real-life model for *Citizen Kane*). Set amidst pine and redwood trees by the shore of the Pacific Ocean, the buildings of the Center were made of local stone and redwood, to integrate them with their surroundings. In addition, most of the buildings are low and horizontal, which connects them with the local landscape of sand dunes and horizon. They have projecting eaves and low-pitched roofs, porches, grouped casements, sloping foundations, and use local materials - split wood shingles, for example. This rustic setting has served as the site for many purely scientific symposia over the years, but the meeting in 1975 had a different purpose. It was convened by, as Robert Sinsheimer, one of the organizers, put it, “a bunch of academics - focused, idealistic, and often naïve - trying to do good, struggling to reconcile our conflicts, our apprehensions, our scientific ambitions our careers, our sometimes murky sense of obligation and emerge with a practical resolution.”

The resolution they were trying to reach was how to move forward safely with recombinant DNA technology. The earliest reports of techniques that allowed foreign genes to be expressed in bacteria had created a flurry of reports in the popular press, which in turn had raised a chorus of alarms, from both professional Luddites and concerned citizens. Some would-be recombinant-DNA researchers themselves were worried that they might, through ignorance, accidentally produce organisms that would turn out to be dangerous. No one was quite sure what could happen once the species barrier was breached in this way.

It was against this background that the Asilomar Conference was held. (For those who want to read more about it and the times that spawned it, I recommend Donald S. Fredrickson’s excellent book, *The Recombinant DNA Controversy: a Memoir*, published by ASM Press, Washington, DC, 2001). It was attended by both scientists and members of the press. The press, as Ronald Atlas, President of the American Society for Microbiology, has pointed out, “represented the public and provided the link between science and society.” During the three-and-a-half day meeting, the group of about 150, which included most of the leaders in the emerging field, debated the risks - known and unknown - of cloning and manipulating foreign genes and expressing them in bacteria. The meeting ended with a series of resolutions to the just-established NIH Recombinant DNA Advisory Committee (RAC) that set forth guidelines for the safe conduct of recombinant DNA experiments, and that endorsed the RAC as the instrument governing the implementation of the guidelines. The public participated in the formulation of these guidelines through open hearings, and the guidelines were given force by linking their compliance with obtaining federal funds for any such research. Sinsheimer says that this result was “A middle ground ... too restrictive for some, insufficiently restrictive for others ... but Asilomar surely helped in many ways to launch the complex world of biotechnology we know today.”

Twenty-seven years later, the world is very different. One reason the Asilomar process may have worked, as Atlas has noted, is “the relative small size of the scientific body and the fact that the technology had yet to be widely deployed.” Now nearly every biologist uses recombinant-DNA technology. Experiments that were originally mandated under safety precautions suitable for handling nuclear materials are now permitted in open laboratories, and can be done, legally and feasibly, in someone’s basement. We now understand that Nature breaches the species barrier constantly through the shuffling of mobile genetic elements, transposons, plasmids, and other vehicles for recombination and integration. Lateral gene transfer is acknowledged as a standard evolutionary mechanism. Much of what we feared had in fact been going on for millions of years. Most of the original guidelines have been relaxed, and some have been eliminated altogether.

It is in this climate of freedom of inquiry that the specter of bioterrorism has arisen. The ease of recombinant DNA materials and techniques, plus the availability of genomic data, even on human pathogens and known biowarfare agents, has made the creation of new weapons of mass destruction more feasible than ever before. This in turn has caused jittery governments to contemplate - and in some cases to attempt to implement - tight controls over the funding, conduct and publication of biological research. In the US, proposals under deliberation include one that would transfer control of funding for much of microbiology research, including all biodefense research, from the National Institutes of Health and the National Science Foundation to the newly created Office of Homeland Security, a non-science organization. Other proposals would require government review of essentially all papers in genomics, genetics, cell biology and biochemistry that deal with pathogens, their genes, or their gene products. These publications could be embargoed or could have portions of their data removed and classified. In July, the British Parliament passed a law allowing the government to restrict access to information that could be used to build nuclear, biological or chemical weapons. The Export Control Act covers information transmitted verbally, electronically or in print for the first time. Scientists were able to push through a last-minute amendment requiring any controls on research communications to be “no more than is necessary”, but the law might be used to bar publication of gene sequences that, in the judgment of the government, could be used to make bioweapons.

Those of us who lived through the Cold War era know what affronts to human rights and freedom can be committed in the name of ‘national security’. Yet it cannot be denied that almost every week the newspapers and scientific journals report some new biological horror in prospect. Australian researchers are reported to have cloned an immune system gene into mouse pox virus, creating a strain of such virulence that it kills not only naturally resistant mice but vaccinated ones as well. Japanese scientists have discovered that

deletion of a single gene in a chicken ‘flu virus makes it infectious to humans. Biologists at the State University of New York at Stony Brook have synthesized the entire genome of the polio virus, demonstrating that small pathogen genomes such as those of Ebola virus are accessible - and can be manipulated - by widely available methods. In response to such threats, it is hard to dismiss government efforts to control the flow of biological information as either a paranoid overreaction or an attempt to exploit a potentially dangerous situation to seize additional power, even though they might well be both.

Scientists are responding to these threatened restrictions in a number of ways. One is, of course, the traditional ostrich approach: bury one’s head in the sand and hope the problem goes away. A smaller group is calling for restrictions, whether voluntarily agreed-upon or governmentally imposed, on experiments and publications such as the polio virus synthesis. Others believe that broad accessibility to all forms of information is vital to preparing for and responding to bioterrorist actions. And many scientists are protesting that any barriers to free and open inquiry and exchange of information represent a dangerous precedent that cannot be allowed to happen.

No one is more wary of this slippery slope than I am. But it is interesting to note that the following experiments were prohibited under the Asilomar guidelines as first adopted: cloning of recombinant DNAs derived from the organisms in CDC biohazard classes; deliberate formulation of recombinant DNAs containing genes for the biosynthesis of toxins of very high toxicity (such as botulinum toxin); deliberate creation from plant pathogens of recombinant DNAs that are likely to increase virulence or host range; widespread or uncontrollable release into the environment of any organism containing a recombinant DNA molecule unless a series of controlled tests leave no reasonable doubt of safety; transfer of drug-resistant traits to organisms that are not known to acquire them naturally; and large-scale experiments (more than 10 liters of culture) with recombinant DNAs known to make harmful products. Many of these are precisely the sort of experiments we are worried about again today, not because we fear what might happen by accident, but because we now realize that evil or deluded people may attempt them deliberately. And the scientific community once accepted these restrictions, partly because they seemed prudent but partly because they had participated in drawing them up themselves.

I think the government is not the best object of our concern in this situation. In the free world, governments tend to be responsive to the wishes and fears of their people. The real danger here is that the age we live in, the age of genomics, is slowly terrifying the average person. Long before the anthrax-laced letters began arriving in the mail, the public was voicing concern about human cloning, designer babies,

and genetically modified foods. Bioterrorism is just the latest demon to arise from what the public sees as the Pandora's Box of modern biology. Governments may use this fear as an excuse to control research and restrict the flow of information, but in doing so they are responding to a public that is increasingly nervous about what we are doing and why we are doing it. Without that public anxiety, efforts at excessive regulation will fail.

Our aim as a community therefore should be to respond to this public concern, just as we did in 1975. And I think the best way we can do that is by agreeing as a community on a set of limited guidelines and restrictions, just as we did in 1975. If we ourselves act now to protect the public, we reassure them that we place our concern for their interest ahead of our self-interests. We also take away from those in government who would control every aspect of what we do both the moral high ground and the initiative.

I'm not alone in calling for a gathering of scientists and representatives of the public to debate these issues and come up with a set of recommendations that would try, as the Asilomar Conference did, to find a middle ground: too restrictive for some, not restrictive enough for others. D.A. Henderson, director of the Center for Civilian Biodefense at Johns Hopkins University, is just one of a number of voices to have suggested something similar. I'll offer some suggestions for how those recommendations might be implemented and enforced in my next article, but for now let's agree that this gathering must be held. It should at a minimum include the heads of all major life science societies, funding agencies and academies; deans of major medical schools; prominent researchers in microbiology, pathogenesis, immunology and virology; biodefense experts, both civilian and governmental; and the press as representative of the general public. As for the time, I suggest as soon as possible. And for the place, why not Asilomar? It served us well once before.