Five Ways to Kill the Biotech Industry (and One to Help It Prosper)

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Addressing groups of industrial or academic experts goes with my job as editor in chief of *Scientific American*, and I enjoy it, but I confess that it inevitably feels peculiar. The audience consists of people who, almost by definition, have expertise or experience in the subjects of discussion. Why should anyone listen to me? I am a journalist—what do I know?

That question always makes me remember advice I heard years ago about the difference between public relations and journalism: If someone would pay you to say it about him, it's P.R. If someone would pay you *not* to say it about him, it's journalism. So for this reason, journalism is generally and rightly associated with unpleasantness.

Which, of course, brings to mind another adage: If you see journalists running in your direction, then flee for your life—because either something bad is about to happen (and you'll be in the middle of it) or something bad has already happened (and you're being blamed for it).

Thus, journalism is associated with risk and catastrophe. Consequently, when I tried to think of useful, constructive topics for discussion here, I drew a blank.

Perhaps that is a blessing in disguise. A lot of well-placed authorities can offer good advice about how to advance the biotech industry. Better for me to stick with what I as a journalist know best—risk and catastrophe. So, I will discuss what seem to me, from my outsider perspective, to be five ways to kill the biotech industry.

I am not arguing that there are *only* five ways to kill biotech, and I am also not claiming that these are the five *surest* ways to kill biotech. There are undoubtedly plenty of other ways even worse, and I sincerely hope that nobody finds any of them. These are just some of the ways that stand out to me, as a sympathetic, casually informed observer. Some of my points are items that you as individuals can address. Some are much bigger issues that you can best address as an industry.

Just to show that my heart is in the right place, though, at the end of the article I toss in one way to help biotech prosper. But let us begin with the first way to kill the biotech industry.

Ignore the Fears of the Public—It Clearly Doesn't Know What It's Talking About

As I am sure you are all frustratingly aware, the public is horribly ignorant about biology and biotechnology, and this ignorance breeds fear. Let's face

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it, the three people who have probably done the most to raise public awareness of DNA in the past 50 years are James Watson, Francis Crick, and O. J. Simpson—O. J., because his high-profile case brought DNA fingerprinting to everybody's attention. Suddenly, you could be fairly sure that everybody knew at least vaguely about DNA because standup comics on "The Tonight Show" could make jokes about it.

People certainly had some awareness of genetics and genetic engineering before the O. J. case, but what they knew did not provide a lot of reassurance. Thanks to television and movies, in their minds genetic engineering was synonymous with scary mutant animals, devastating bioweapon plagues, and races of arrogant supermen who looked like Ricardo Montalban and were bent on taking over the world.

Obviously, there were and are real success stories. Genetic screening for Tay-Sachs and other hereditary diseases, for example, has immeasurably improved the lives of countless people. You would think the biotech industry would get more credit for accomplishments like that, and yet I do not think it does.

The standard solution for addressing this problem (and one that involves popular magazines like *Scientific American*) is to try to educate the masses better—and this is simply mandatory. It is in society's best interests to make sure as many people are well educated as we can possibly arrange. But that is the wrong way to solve the problem from the perspective of business people—education is *hard*, and it is *slow*, and businesses have to be run *now*.

It would be wonderful if people were always smart and reasonable, but they aren't. Instead, they are often going to be irrationally disturbed—fearful that new technologies are dangerous, even if they cannot quite put their finger on why.

Consider what has happened with genetically modified (GM) crops. In Europe, it is quite easy to find people who claim that GM crops, notwithstanding years of studies clearing them, are just too much of a menace. And those people will then puff on their unfiltered Gauloise cigarettes and zip down the autobahn at 120 mph. You can show them that GM crops have been scrutinized for effects on human health more thoroughly than natural crops have been. You can point to the absence of evidence that the proper introduction of GM crops upsets any natural equilibrium in the ecosystem and that, in some situations, GM crops might be less disruptive than normal crops would be. You can demonstrate that more extensive genetic recombinations occur in nature all the time, or that many familiar crops are hybrids that involve "unnatural" combinations of traits. It won't really matter.

Why? Because, as 20/20 hindsight makes so clear, people have certain unreasonable fears about anything that smacks of somebody tampering with their food. "We are what we eat," so people have phobias about their food being altered. More generally, people cannot really see what genetic modifications to crops might be doing (or not doing), so they are suspicious about why businesses and scientists seem so eager to unleash them.

How do you combat that kind of fear? I don't know. Long term, you try to get to the roots of it through education. But shorter term, I think you need to demonstrate that checks and balances are in place—that industry and government believe and accept the scariness of GM products as a *fact* and have taken redundant measures to stop potential problems before they get out of control.

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Unfortunately, establishing credibility as a sentinel can be tough, and it is easily shattered. I am firmly convinced that, in Europe, much of the fear of GM foods is tied up with memories of how the British government failed to adequately prevent the spread of mad cow disease—even though mad cow disease has absolutely nothing to do with GM foods. And when GM corn plants are allowed to accidentally infiltrate other lots, or when pollen from GM fields drifts onto other supposedly pristine fields, it really does not matter that the demonstrable level of harm done is zero. Your credibility as trustworthy custodians of a frightening technology suffers.

I am nevertheless optimistic that, over time, the public will come around. But it is ironic that, if the first commercial application of genetic modification had been a somatic medical therapy, something in which people's own body tissues were being altered at the genetic level, there probably would have been less resistance than there has been to altering foods and other crops. People by and large trust their doctors to take care of them, but they have no such trust of industry. Maybe as medical biotechnologies continue to grow in acceptance, other varieties of biotechnology will benefit, too.

Let us move on to the second way to kill the biotech industry.

Let Fear of Terrorism Squash Research Progress

At a recent gathering of the Science Coalition in New York, 20 university presidents spoke with clear agitation about how new "homeland security" measures were interfering with the ability of foreign-born students and faculty to cross international borders, to be involved in sensitive projects, and so on. The problem sapped at manpower, it sapped at administrative resources, and, of course, it slowed down the work itself. Biomedical research was very much at the center of these new security concerns.

Several specific events or actions frame our current view of tensions between biomedical research and security. One, of course, is the Al Qaeda attack on the World Trade Center and the Pentagon. Another is the mailing of weapons-grade anthrax, which took place on the heels of September 11 and which has never been conclusively attributed to any culprit.

In addition to those acts of terrorism, we also have two acts of research. In 2001 Australian researchers were genetically modifying mousepox virus with the intention of developing a contraceptive vaccine to curtail the rodent population explosion. To their amazement and dismay, they found that inserting an interleukin gene inadvertently converted relatively mild mousepox into a mouse superpathogen. The publication of that work prompted worries that some would-be bioterrorist who could not obtain a sample of smallpox might create his own disease instead. Then, in 2002, Eckard Wimmer of the State University of New York at Stonybrook published a paper showing that it was possible to synthesize poliovirus from scratch, using the publicly available sequence of the viral genome.

Finally and most recently, we have an act of policy on scientific communication. In mid February 2003, the editors of more than 30 journals announced that they would adopt a voluntary policy of self-policing biology papers for information that might be useful to terrorists. Nobody likes to talk about this as self-censorship, but the distinction is in many ways a matter of semantics.

How serious or significant will this self-policing by the journals be? Edi-

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tors who have commented on this decision publicly say that they expect that only one or two papers a year may run afoul of these restrictions. They claim a commitment to making sure that the flow of essential scientific information will not be impeded, and I think they deserve the benefit of the doubt. It is likely that the editors felt that if they did not censor their own publications voluntarily, they would eventually encounter more ham-fisted outside review by the government.

My perspective on the new journal policy is that, in practice, it is not going to interfere much with scientific communication. So, even though as a journalist I am predisposed to be a First Amendment absolutist, I am not going to wring my hands about how the journal policy will wreck or cripple science. On balance, if the editors were really feeling heat from the government, or feared with good reason that it was about to be turned up, they were probably wise to take this on themselves. There is every good chance that, if the editors are dedicated to making good research public, this self-policing will become a nonissue over time.

On the other hand, for roughly the same reasons, I think the policy is going to do almost nothing to further national security.

After all, how much do newly published research results help terrorists, anyway? The most sophisticated approach to bioterror ever taken was the weaponized anthrax attack through the mail almost two years ago—and my understanding is that nobody has ever published a paper about how to weaponize anthrax.

Much of the information that budding bioterrorists might want is already in the public domain. Intelligence experts all fear that legions of underemployed researchers with experience making secret bioweapons in the former Soviet Union are potentially available to terrorists with cash. And of course, nature itself is already full of nasty pathogens—Ebola virus, anyone?

It is reasonable to worry about how new biological research could be of service to terrorists, but before society cracks down too hard on open research and discovery, it should make a stronger case that new research really abets terrorism. Moreover, before government's protective iron hand closes too tightly on research, it should do more to sensibly govern the commercial availability of actual materials that could be put to malicious ends. Controlling materials may be easier than controlling information, while doing more direct good. Such restrictions should not fall more heavily on biological materials than on chemical or radiological ones, given their tremendous potential for misuse.

In November 2001, *Scientific American* demonstrated how easy it was to obtain dangerous chemicals. At a time when the whole country was on alert against terrorists, we picked up the phone, called a chemical supply company, and conspicuously ordered all the ingredients needed to make the nerve gas sarin. These chemicals were delivered through the mail to an office in midtown Manhattan, no questions asked. Theoretically, I had enough material in my office to kill thousands of people.

For all the fearful emphasis on bioweapons, chemical weapons, and radiological weapons, it is still most likely that terrorist attacks will continue to employ conventional explosives. Ordinary explosives are cheap and easy to make. The Oklahoma City bomber made a truckload out of fertilizer. Of course, explosives are only one of the mundane weapons potentially available. The terrorists of September 11 killed thousands of people by hijacking and crashing airplanes. In 2003, the D.C. snipers spread fear across

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several states by killing individuals with rifles, over and over again.

Some limits on biomedical research are prudent and appropriate and do not infringe on liberties essential to progress. But before we adopt more severe limits, we must insist that the case be made that they are truly necessary.

Let us turn now to the third way to kill the biotech industry.

Let Intellectual Property Skirmishes Squash Research Progress

Patents and other forms of intellectual property protection are crucial for providing incentives for innovation in biotech and every other part of industry. In the short run they serve the individual interests of the innovators, but in the long run they serve everyone's interests. But we should not let the leverage provided by patents become a stranglehold on progress.

Since 1997, Jeremy Rifkin and Stewart Newman have repeatedly filed for a patent on a means of combining embryonic cells to create chimeras—organisms that would be part human and part animal. The latest version of this application is currently pending, I believe. Rifkin and Newman do not want to produce chimeras—quite the opposite. They want ownership of the patent so that they can stop anyone else from making chimeras, even ones useful to research, because they consider such organisms to be unnatural abominations.

When self-designated enemies of biotech do something like this, it is easy to see it as Luddism. But what about when biotech innovators do it? Harvard University, the Massachusetts Institute of Technology, and the Whitehead Institute for Biomedical Research jointly hold a very broad patent on methods of treating disease by regulating the activity of the protein Nuclear Factor Kappa B (which is involved in the genetic regulation of inflammation, cell division, and many other processes). Those institutions have informed more than 50 companies that they are seeking licensing fees or royalties for their research or commercialization of drugs that act on this pathway. For example, they have filed suit against Eli Lilly, charging that its drugs for treating osteoporosis and sepsis infringe on that patent. In effect, the patent now serves as a tollbooth blocking the way of anyone who wants to work on a biochemical pathway involving Nuclear Factor Kappa B. As an article in the journal *Law and Contemporary Problems* put it, "In this case, as in many others, upstream patents issued to academic institutions serve as a tax on innovation, diluting rather than fortifying incentives for product development."

I am not knocking Harvard or M.I.T. for this; they were granted the patent and they are acting within their rights. One might suppose they could be more forgiving or broadminded in their administration of the patent, but I suspect their attorneys advise that failure to press these cases will compromise the integrity of the patent.

The fault, I think, lies with the patent office itself, for granting a patent that may be too broad for the common good. It goes way beyond providing incentives for the development of specific drugs. This is why some observers are calling for wholesale reforms of the Bayh-Dole Act of 1980, which helped spur universities to seek patents and commercialize their research. That law has had an overwhelming effect in pouring the fruits of academic research into industry: Between 1979 and 2000, the number of university patents increased 14-fold, and about half of those were for biomedical discoveries. It is hard not to see the general effect of the law to have

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been good. But if bad administration of patents is now going to start choking off whole lines of progress, then we need to somehow fix the system before serious damage is done.

The problem is not restricted to "upstream patents" held by the basic research institutions. In fact, it can go precisely the other way, too. Historically, university-based research has been seen as exempt from claims of patent infringement because it was noncommercial. However, last year, the Court of Appeals for the Federal Circuit issued a ruling that could make this exemption for researchers so narrow as to be useless. In effect, the court said that, because academic research furthers the "legitimate business objectives" of universities, there should not be an exemption on university research unless it was purely for "amusement to satisfy idle curiosity, or for strictly philosophical inquiry."

How great will the fallout from this ruling be? It is hard to know. Some legal observers are not too worried because, in practice, few patent holders may want to bring suit against academics. Still, some investigators fear that they are going to have to spend more and more of their time clearing a path on rights issues instead of doing experiments.

Let me now turn to the fourth way to kill the biotech industry.

Let Crazy Nanotechnology People Do All the Talking

I want to make a crucial distinction: not all nanotech people are crazy. A lot of serious, reputable, valuable research into nanotechnology is going on. In fact, *Scientific American* published its 2001 single-topic issue on nanotech. Nanotech holds tremendous potential for people working in biotech, as a genuinely overlapping field of endeavor. After all, cells were the original nanotechnologists. They pioneered the manipulation of individual molecules for useful ends.

The crazy people I am warning you away from are, for better or worse, many of the ones most often touted as "leading visionaries" of nanotechnology. The ones who say that someday fleets of microscopic robots will cruise through your body, fixing damaged cells as they go, so that you can live forever. Or that trillions of these "molecular assemblers" will settle like clouds onto junk heaps and rearrange the atoms into Porsches while you wait.

Perhaps I lack imagination, but to me this sounds farfetched. Still, these "visionaries" do a great job of getting press for themselves. When *Scientific American* has criticized them for losing a grip on reality, their reply has been, given that we have not proved that "microrobots" won't someday be possible, they must be right.

Let us put aside the whole question of whether they are right or wrong. Here is why you do not want those spokespeople too closely associated with biotechnology: If you let the talk about "microrobots" run wild, you will end up terrifying the public with the possibility that nanobiotech will go berserk and destroy the world. Take a look at Bill Joy's famous essay from a few years ago or Michael Crichton's best-selling novel *Prey*. You will face a possibility of severe backlash, and biotech has enough P.R. problems already.

It is all well and good to say that biotechnology has the potential to change the world, but never forget that some people out there *like* the world just fine as it is, and they do not trust you to retailor it for them. In short, fear your own hype—someone may take it seriously!

Finally, here is the fifth way to kill the biotech industry.

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Hand Over Superiority in Stem-Cell and Human-Cloning Technologies to Other Countries without a Fight

These subjects have been in the news so frequently, I need not elaborate much on them. Here in the United States, work on human embryonic stem cells and on human cloning is mired in a political, religious, and ethical struggle that has its roots far outside any of the concerns that biologists and biotechnologists commonly address. It is a struggle that goes to the heart of what the United States stands for, including the separation of church and state but also our sense that we have a good, moral society. *Scientific American* has repeatedly taken the position that these techniques are extremely valuable, that they need to be studied to learn their full potential, and that the ethical objections are surmountable. From an economic standpoint, it would be disastrous for the United States to lose its natural lead in the development of these technologies to other countries.

Stem cells and cloning really ought not to be lumped together so often because, for all their connections, they are very different. In the interest of maintaining perspective, it is worth reminding ourselves that so far we do not really know how much we can do with either of these technologies. It is entirely possible that the dream of using embryonic stem cells to fix any and all types of tissue damage will in practice fall apart. We may not get good enough at prompting the stem cells to become truly normal differentiated cells that can integrate themselves into the body in a reliable way. Some medical conditions may not be conducive to the use of stem cells.

As for human cloning, it is still an open question whether it can even be done, or whether it may be impossible past a certain primitive level. Many opponents of human cloning say we need to have these debates now, before the technology overtakes our ethical deliberations, but the cart is getting ahead of the horse. Although the biomedical community keeps stressing that it is only interested in cloning to generate cell lines, the public discussion always slips over into reproductive cloning and the almost unhinged level of fearful speculation about what that would mean. Scientists have loudly said that they would accept a ban on reproductive cloning as long as it allowed therapeutic cloning, but some lawmakers insist the only way to prevent reproductive cloning is to ban any kind of cloning.

Scientific American supports the scientists' position, but lately I have begun to wonder whether this argument should not be turned on its head. Maybe no human cloning should be banned. Maybe it should all be kept expressly legal so that it can be regulated to within an inch of its life. That way, we could choose not to allow reproductive cloning for as long as we had doubts about its safety or ethicality and still clone therapeutically as much as we saw fit.

Whatever the case, the United States needs to stay on top of human stem cells and cloning. I can only urge the biotech industry to continue to make that case to the public and to our lawmakers.

Now, as promised, here is one way to help the biotech industry prosper.

Make the Industry Disappear

I look forward to the disappearance of biotechnology—and before you lynch me, let me explain why.

When I talk about the disappearance of biotechnology, I am making an analogy to the stated goals of information technologists who talk about "invisible computing" or "pervasive

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computing." They are referring to a time—one to which we are getting closer all the time—when computers are so ubiquitous that they fade into the background. Sure, you have a computer on your desktop, but maybe you also have a PDA in your pocket. You carry a sophisticated cell phone that does things only a computer could do some years ago. Your car is full of microchips. So is your microwave oven, along with most of the appliances in your house. You may have chips in your clothes or embedded in your pet's ear for identification. Computers in the form of microprocessors are on a steady, unstoppable rise, and why? Because you don't even think of them as computers anymore.

So, as biotech grows and becomes more pervasive, that "bio" prefix will matter less because it will say less that is distinctive. Biotechnology effectively disappears when every technology starts to contain biological elements or is the result of biological processes.

Consider that biological polymers can replace some inorganic materials. Researchers have shown that DNA can be harnessed to solve computational problems. There is interest in using the molecule as a structural element in nanoscale devices. Whole cells and organelles are being linked to microprocessors as intelligent sensors. Enzymes can sometimes replace caustic inorganic chemicals in industrial processes. Genetic analysis promises to become a routine part of medical practice, and genetic therapies might follow close behind.

Assuming that the biotech industry can safely navigate all the ways in which it might wreck itself, the time will come when biotech will be integrated into every aspect of manufacturing and services, just like plastics and alloys. There is so much opportunity to turn the capabilities of living things and their components to our further advantage. I cannot imagine an industry that has more potential, and I wish you all the very best success in realizing it.

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