The biological century: coming to terms with risk in the life sciences

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Although the life sciences promise huge benefits, the possibility of doing harm from deliberate misuse of knowledge is an increasingly worrisome issue. Discussion and mitigation of these risks by life scientists must be encouraged.

As the world hurtles through the early years of the 21st century, there are increasingly frequent reminders of how exciting it is to be a life scientist. Never before in history has an area of science offered as much potential for novel insight and predictive understanding of the world, as well as opportunities for enhancing the human condition, as have the life sciences. Genomics, microbial metabolic re-engineering, stem cell biology and molecular immunology provide ready examples of revolutionary advances in capability and newfound understanding. For example, in the past decade, scientists have learned to read and interpret microbial genomes and have an early understanding of how to reprogram the differentiation patterns of human cells. In recognition of such advances this has been called the 'Biological Century'[1]. For the sake of the subsequent discussion, the fundamental perspective is that nearly all activities in the life sciences serve a beneficial purpose.

One purpose of this commentary is to explore the nature of the risk that the life sciences pose and to review strategies for minimizing risk while preserving the health of the research enterprise. An equally important purpose is to highlight the role of life scientists in risk management. A large number of policy proposals and pending legislative and executive actions in the United States, with broad and deep ramifications for the life-sciences research community, deserve greater attention by biologists at the present time (documents available online from the National Science Advisory Board for Biosecurity and the Senate Homeland Security and Governmental Affairs Committee (http://hsgac.senate.gov/public/index.cfm?FuseAction=Press.MajorityNews&ContentRecord_id=E359917B-5056-8059-76CB-4180E2541F2E))[2,3].

Recognition of the potential risk for misuse of the life sciences to cause harm is longstanding, although it is not nearly as widely accepted in this field as it is in nuclear physics. In fact, there is a wide spectrum of opinion among life scientists today about the importance and magnitude of risk that the life sciences pose; many scientists discount any substantial risk of misuse out of hand, and others minimize the importance of this issue or seek to deflect discussion of risk to social scientists or policymakers. The infectious-disease and immunology communities in particular should be taking a more proactive role in the present policy discussion.

Risks from and misuse of the life sciences

Terms such as 'threat' or 'risk' are used widely with many different intended meanings. For the purposes of the discussion here, the 'threat' of misuse of the life sciences for causing harm is dependent on both intent (to misuse or do harm) and capability (of misusing or doing harm), and the 'risk' of misuse is dependent on threat, vulnerability and consequence (**Fig. 1**). Although some have labored to express these relationships in a mathematical format, such efforts are sometimes distracting and often misplaced. It is more important to recognize that multiple factors give rise to threat and risk and that each suggests different strategies for risk management and mitigation.

First, I will start with one component of risk, which is intent. For most life scientists, the concept of intentionally using biology to cause harm is contrary to the ethical and moral principles by which they lead their lives. Hence, it may be difficult to accept the assertion that others will cross this moral line.

However, there are several classes of people that should raise concern. First, it is increasingly clear that there are individual people and groups throughout the world determined to harm others, even at the cost of their own lives or those of their compatriots. Acts of terrorism are unfortunate features of the present international landscape. Evidence that these people and groups are willing to exploit the life sciences to achieve their goals is less obvious, but examples can be found in the open literature. Documents retrieved from an al Qaeda training camp in Afghanistan in 2001 highlight the interest of this group in developing biological weapons and reveal their awareness of at least one professional scientific society in the United Kingdom with relevant expertise[4]. Subsequent findings have documented a relatively sophisticated effort to acquire a biological weapons capability for harming tens or hundreds of thousands of people[5]. The appeal of such inexpensive, powerful and easy-to-hide weapons may gain further acceptance.

A second consideration is that there are even more individual people or groups with expertise in the life sciences who might be vulnerable to coercion or unwitting manipulation and thereby aid others who wish to exploit the life sciences to do harm than there are those with self-acknowledged intent to do harm. Third

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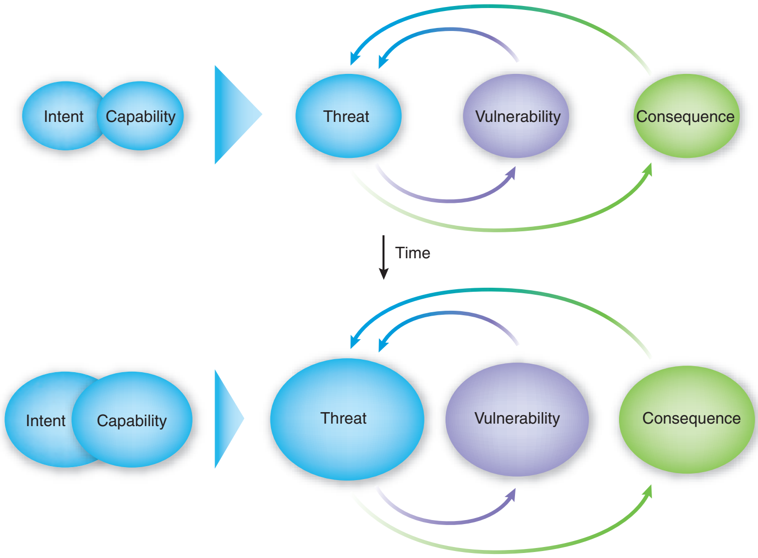

Figure 1 Risk of harm from misuse of the life sciences: components and trends. Risk is a function of threat, vulnerability and consequence. Threat, in turn, is a function of intent and capability and the overlap between the two. Because all five of these terms are growing in magnitude over time, it can be argued that risk of harm from misuse of the life sciences is increasing. Threat, vulnerability and consequence are not independent of each other. For example, awareness of vulnerabilities and the consequences of misuse may motivate intentions, and threat awareness may lead to improved countermeasures and hence lower vulnerabilities and consequences.

is the concern about people or groups who conduct research in a careless or irresponsible manner and, by so doing, cause harm. This class includes those who might, for example, publish a detailed method for subverting a critical medical countermeasure without an obvious beneficial purpose[6]. As segments of the world's population become stressed by political, social or economic disturbance, the size of the first class grows. And although the resources and knowledge of each of these classes may vary, the capabilities of life scientists are expanding across the board at an accelerating rate and will continue to do so for the foreseeable future.

Like other types of scientists, life scientists are a highly heterogenous population. Perspectives on the magnitude and nature of the risks of misuse vary widely. For example, infectious-disease researchers or those who receive biodefense funding perceive risks differently than do those who work in other areas. Likewise, the perceptions of risk by those who work on basic biological mechanisms are distinct from the perceptions of risk of those who do not. This diversity of perspectives on risk, in turn, has important implications for education and risk communication and management.

Although nearly all aspects of the life sciences have some potential for use to cause harm, some aspects hold greater risk. Among others, the generation of novel genetic diversity, manipulation of the genetic programs of living organisms in the laboratory, design and selection of new biological properties and subversion of critical aspects of host defense will probably magnify the risk. Regardless of how much risk the life sciences pose today, trends suggest these risks will increase with time. A report from the US National Research Council in 2003 described so-called "experiments of concern" as kinds of research that should warrant a greater degree of scrutiny[6]. These experiments include, for example, work that would enhance microbial virulence or enhance host susceptibility to infectious disease. The subsequent creation of the National Science Advisory Board for Biosecurity provided a forum for further deliberation about criteria for dual-use research of concern and guidance for oversight and education about these and related issues. The present capabilities in the life sciences are already substantial and are increasingly commercialized, prepackaged and globally dispersed[7].

Despite those substantial and growing capabilities, some life scientists have argued that the only agents of considerable biological threat are those that have naturally evolved with particular biological characteristics and that scientists cannot create agents as harmful as those. However, those arguments are based on the assumption that the breadth of naturally occurring genetic diversity and the importance of long-term survival determine the potential diversity and success, respectively, of pathogens. Such assumptions may not be appropriate[7]. For example, the expression of cytokines by recombinant poxviruses[8] and the derepression of naturally occurring hypervirulence genes in bacterial pathogens[9] lead to unexpected virulence-associated phenotypes in the laboratory that might not otherwise occur.

The other risk components, vulnerability and consequence, also warrant further discussion among life scientists. Vulnerability to microbial pathogens reflects host genetic factors, as well as functional immune status and a wide variety of other host and environmental factors. Many of these factors are dynamic in both individual people and whole populations. For example, the increasing global prevalence of acquired immune deficiencies, chronic persistent infectious diseases (such as tuberculosis) and population-based factors, such as crowding, conflict and migration, suggests that humans, animals and plants are becoming more vulnerable to infectious agents[10]. Public health preparedness and the availability of diagnostics and biological countermeasures (regardless of whether humans, animals, plants or other hosts are at risk) determine the magnitude of the effect (that is, the consequence) posed by misuse of the life sciences. The strength of the public health infrastructure varies worldwide, but nowhere is it as strong as might be wished. It is also important to note that threat, vulnerability and consequence are not independent factors. Heightened awareness of vulnerability and consequence may motivate those who might not have otherwise done so to pursue use of the life sciences for harmful purposes[4]. It can also have the opposite effect: although the discovery of an unusually important host immune-regulatory molecule and an easy, potent method for its disruption might serve to motivate potential evil-doers, a new technology for the rapid, generic production of vaccines might serve to dissuade them.

Managing and reducing risks

The immense potential benefits of biological research demand a judicious approach for reducing and managing the risks of misuse. And the globally distributed, rapidly evolving and inherently open nature of biological research requires a realistic approach. Each of the factors that give rise to risk—intent, capability, vulnerability and consequence—has different sets of possible responses. Moreover, the responses will need to be tailored for different subpopulations of the life-sciences community. All may be necessary, at least for consideration, whereas none will be sufficient alone. Between 2001 and 2008, US biodefense policy emphasized the need to strengthen the national ability to recognize and respond to acts of bioterrorism[11,12]. Subsequent US national security policy has emphasized the importance of anticipating and preempting misuse of the life sciences and thus of preventing or reducing biological threats[13]. Although strategies for threat reduction and risk management at the national and international levels are important, the ongoing revolution in the life sciences is a distributed, local phenomenon. The most important day-to-day activities take place at the level of the individual person. So how does national policy achieve meaning and relevance for the individual scientist?

Role of scientists

First and foremost, individual scientists must embrace and reinforce a culture of awareness and responsibility in the life sciences that their work not be subverted or misused. In recognition that all acts of good intentions are fraught with some risk, physicians swear that they will keep their patients from harm. Norms of responsible behavior in the life sciences are less well codified than they are in the practice of medicine, but they do find historical precedent, for example, with the International Congress on Recombinant DNA Molecules held at the Asilomar Conference Center in Pacific Grove, California, in 1975, at which early leaders in this emerging technology suggested self-restraint and risk assessment[14], and they are certainly no less relevant today. However, many of today's life-science students are not familiar with this history. Norms are most effective when taught early in life and should be reinforced throughout a scientist's career through case studies and local discussion and by example from respected leaders of the community. Role models are important in this; however, given the diversity of disciplines, backgrounds and kinds of work in the life sciences, multiple types of role models are required. Behavioral norms in the conduct of the life sciences will be most effectively promulgated in the local workplace using the language and sensitivities of the local scientific culture rather than through legal mechanisms or obligations imposed from outside the community.

How can awareness be instilled that some scientists might seek to do harm or that some might be susceptible to coercion and unwitting manipulation, and what are the kinds of responses that should be encouraged from individual scientists? Trusted thought leaders in science need to initiate discussions with their colleagues about the nature of risk, the primacy of doing no harm and the importance of such discussions throughout the research enterprise. Discussions about the risk of misuse for causing harm might be interwoven with discussions about fraud, plagiarism, unethical use of human or animal subjects, and other forms of research misconduct. The risk of misuse should be viewed as no less relevant to the daily practice of the life sciences as these other forms of misconduct.

A sensitized community of scientists constitutes a distributed, self-reinforcing, and adaptive protection system. Thus, it is more effective than any piece of legislation or regulation. A scientist who works in the same field of study and in the same local research community is more likely to detect aberrant behavior or activity, be privy to inadvertent leaks, or by some other means recognize the purpose of a person or group with harmful intentions than is someone without the same background, expertise, access or understanding of the local community. Yet because the practice of science is in part personal and is almost always undertaken for beneficial purposes, and because creative science may involve 'aberrant' behavior, it is inherently difficult to recognize the signs of misuse of science for harmful purposes.

Recognition of a threat demands a response, and the response must be measured, appropriate and sensitive. At this time, in 2010, many scientists are naturally concerned about erroneous, disproportionate or inappropriate responses that will only serve to polarize and antagonize the scientific community. Thus, local networks must be created among scientists who can be trusted and understand these risks and who will calibrate various possible responses appropriately depending on the level of concern. Individual scientists also need to engage in educational outreach efforts with students, the general public and their political representatives.

Role of institutions

Local academic institutions have an important supporting role in educating about risk and providing a conducive environment for associated discussions. However, institutions are much more likely to be effective in this role if they emphasize openness, quality in science, partnership and relationship-building rather than restrictions, enforcement, risk avoidance and excessive concern about liability. Local institutions could help by facilitating discussion among life scientists about their concerns and by providing a safe environment for these discussions without provoking misattribution or a dysfunctional response.

Beyond the local level, federal institutions and professional societies have responsibilities in reducing the risk of misuse in the life sciences. The principles of an effective strategy are similar to those for academic institutions: partnership, relationship-building and guidance, rather than regulation. Education and outreach are key areas for investment and should include the development of teaching tools. In

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Misuse of the life sciences poses an ever increasing risk. The infectious-disease and immunology communities in particular should be taking a more proactive role in formulating policy to circumvent this risk.

particular, caution should be exercised in the promulgation of the personnel-reliability measures now being discussed by the US federal government. The effectiveness of many of these measures is unproven, but the potential harm to the research enterprise is real.

At the national level, which is the most difficult arena, an overlooked but important component of any strategy for countering and reducing biological threats is a productive, working relationship between the life-sciences research and national security communities. Each of these communities, in some sense, needs the other. At a fundamental level, these two communities, despite having widely disparate cultures and styles, share common goals (for example, the prevention of harm from misuse of the life sciences and the promotion of a robust defense against natural and deliberate biological threats). Yet each has a different understanding of the global life-sciences landscape, uses different criteria for defining and interpreting incongruities in this landscape and takes a different approach in exploring the unknown. For example, with respect to the last point, each designs experiments and uses controls in different ways and for somewhat different purposes. A number of publications and reports have already described some of the steps that might enhance relationships between the life-sciences and national security communities[7,15]. Working groups composed of members from each community can greatly enhance each other's understanding of the risks of misuse, recognize trends, minimize unnecessary concerns, and help develop more effective interventions. At the end of the day, the cultural divide can be bridged only by sustained partnerships based on mutual trust.

Finally, international engagement is critical for reducing the risk of misusing biological research, given that this science is globally distributed and has an effect on and relevance for every member of every society. Although treaties, conventions and dialog between national governments and among international agencies are valuable, any meaningful progress will require relationships built on existing interactions of mutual trust and respect between individual scientists worldwide. Even though local public-health priorities and perceptions of the nature of biological threat vary widely across the globe, it is in everyone's interest to maximize the potential benefit and minimize the potential harm associated with biological research.

Concluding remarks

Given the accelerating rate at which insights have been gained and benefits have been realized in the life sciences, it is not surprising and is even understandable that many life scientists ignore or minimize the potential risks from misuse of this science. Yet with acquisition of capabilities and power comes responsibility. It would behoove life scientists to engage in a wider discussion about the nature of these risks and to consider a variety of measures and approaches for managing and reducing these risks. Such discussion will need to be accompanied by outreach and relationship-building with local institutions and government. Openness and transparency by both scientific and national security communities will go a long way toward promoting trust and ensuring a more robust, safe, and beneficial life sciences enterprise.

COMPETING FINANCIAL INTERESTS
The author declares no competing financial interests.

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