Genetic Frontiers:
Unraveling the Impact and Anticipating Future Challenges of SYNBIO

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In the evolving technological era of large-scale combat operations and multidomain operations, the U.S. Army is facing a most complex problem of simultaneously meeting and overmatching its competitors and enemies across multiple domains of warfare. Adding to this challenge, the People's Republic of China declared biology to be "a new domain of war" and announced plans to make China the global leader in technologies like genetic engineering.[1]

Advances in synthetic biotechnology, including gene-editing technologies such as clustered regularly interspaced short palindromic repeats (CRISPR), promise protection—and even cures—from diseases, but they also create new security risks. Research scientists can use CRISPR technology to selectively modify an organism's deoxyribonucleic acid (DNA) by incorporating foreign DNA into a living host cell. Five years ago, a Chinese scientist used CRISPR technology to create the first gene-edited babies, for which he faced international accusations of violating medical ethics. While this technology can potentially be used to cure genetic diseases, it also has the potential to edit bacterial or viral genomes to create enhanced pathogens. The 2022 "National Biodefense Strategy and Implementation Plan for Countering Biological Threats, Enhancing Pandemic Preparedness, and Achieving Global Health Security"[2] categorizes biological threats among the most severe threats to the United States and calls for bold approaches to transforming the Nation's biodefense program.

Due to the increasing ubiquity and simplicity of synthetic technologies, the chemical, biological, radiological, and nuclear (CBRN) profession and enterprise must be prepared to encounter its use on future battlefields. Raising awareness of this technology should begin in the classroom through modernization of the biodefense program of instruction to include information on synthetic biology (SYNBIO).

SYNBIO is a multidisciplinary field that is centered on creating and modifying organisms and their genetic material to produce novel phenotypic traits previously unseen in their natural predecessors. Advances in the field have allowed humankind to modify pathogens for desired functionality, resurrect eradicated viruses, and synthesize novel pathogens. Due to the technological advancement rate and the scope of application, SYNBIO poses a significant threat to national security. Advances in SYNBIO have created tools that could enable a state, group, or individual to produce novel viruses that are intentionally or unintentionally capable of impacting large groups of people.[3] Weapons resulting from SYNBIO would enable state actors to have a serious effect on an area—specifically, on the people, plants, and livestock in the area—while leaving critical infrastructure primarily untouched. For example, in 2002, scientists at Stony Brook University, New York, used SYNBIO to construct a live polio virus from genetic information publicly available on the Internet.[4] Using SYNBIO, scientists can also modify existing organisms so that they possess abilities they would not naturally exhibit, allowing potential adversaries to develop new or enhanced agents.[5] CRISPR is but one of several types of gene-editing technologies that allows for exact genome edits; it is so efficient and cost-effective that it has significantly increased the threat of SYNBIO to national security.

CRISPER is the most-discussed gene-editing technology during national and international security debates[6] because it does not require sophisticated knowledge, specialized equipment, or the time that was needed for earlier gene-editing technologies.[7] CRISPR uses a guide ribonucleic acid (RNA) strand to locate a desired target gene in the DNA, where enzymes cause a break in the double-stranded DNA, allowing the gene to be modified.[8] In short, scientists can cut and paste segments of DNA at desired locations within the genome. With CRISPR, any double-stranded DNA sequence in human cells and pathogenic invaders can theoretically be targeted. This allows for the technology to be used for beneficial purposes; and in December 2023, the U.S. Food and Drug Administration approved the first-ever gene-editing therapy for humans. CRISPR can now be used to treat sickle cell disease, a blood disorder caused by a single gene mutation.[9] However, gene-editing technology can also

be used for nefarious purposes—and CRISPR accessibility, affordability, and efficiency make it an attractive vehicle for biowarfare. Furthermore, CRISPR efficiency increases when paired with artificial intelligence, which can make use of machine learning to predict the effect of specific gene editing on an organism, avoiding time-consuming laboratory experiments and testing cycles.[10]

Because gene editing allows scientists to edit and shape whole genomes of bacteria and viruses with new properties,[11] concerns about its possible future use have been raised. U.S. scientists who were researching CRISPR modified the mousepox virus by inserting a gene for a natural immunosuppressant, originally intending to increase antibody production; instead, it turned off the part of the immune system that usually fights the virus, creating a more deadly form of mousepox.[12] These experiments suggest that it is possible to produce a smallpox variant that is resistant to the vaccines that are such an integral part of any deterrence strategy since vaccines reduce the incentive for adversaries to release certain agents by rendering attacks unsuccessful.[13]

CRISPR might also be used to edit genes of entire populations of disease-spreading animals, like mice and mosquitoes.[14] Researchers have attempted to modify the DNA of these animals so that future generations cannot spread disease. That objective is dangerously close to modification of their DNA so that future generations can more efficiently and effectively spread disease.

The implications of future use of these scientific advancements should be considered in terms of their significance to international security with regard to proliferation, deterrence, and unconventional weapon development. Several nations have engaged in covert biological weapons programs in the past,[15] and many nations openly conduct research that would be illegal in the United States. In the People's Republic of China, He Jiankui used CRISPR to edit genes in a human embryo in an attempt to create a baby that was immune to the human immunodeficiency virus (HIV); this sparked fears that he had opened the door to further embryo modification, such as the creation of "designer babies," for which parents could leverage gene-editing technology to select traits they value for their offspring.[16] Chinese scientists also used CRISPR to remove genes that inhibit muscle and hair growth in goats, successfully increasing yields of meat and wool.[17] Geneticist Denis Rebrikov, of the Pirogov Russian National Research Medical University, Moscow, Russia, plans to use CRISPR to genetically modify embryos to treat inherited deafness.[18] His research has been widely condemned as unethical, as these germline edits can be passed to future offspring. Despite the backlash, Rebrikov is still seeking approval to move forward.

Although China permits germline gene editing for research purposes, edited human embryos are not allowed to be used to establish a pregnancy. He Jiankui, therefore, spent 3 years in a Chinese prison for his embryo modifications that resulted in twin girls, but he has since been released. He is again working with CRISPR—this time in an attempt to cure Duchenne muscular dystrophy, a hereditary degenerative disease of the muscles. There are lingering concerns among experts about his motives as well as the motives of the Chinese government in allowing him to continue his research in the field.[19]

In addition to state-sponsored laboratories with the technology necessary to reengineer existing organisms or genomes for defined purposes, the affordability and accessibility of SYNBIO technology allows anyone with the right equipment and a crude laboratory to create a vaccine-resistant virus or make existing bacteria more dangerous.[20] They could even resurrect an eradicated virus, perhaps by turning the easily obtained cowpox virus into smallpox.[21] Because these gene-edited pathogens are unfamiliar, manifestations of these biothreats are unpredictable, creating additional monitoring and detection challenges.[22]

To further complicate matters, no international legal, ethical, or moral framework for determining a common understanding of the safe use of SYNBIO exists. Likewise, there is no international oversight committee for gene editing and no agreement on the ethical boundaries within which CRISPR may be used.[23] The Oviedo Convention on Human Rights and Biomedicine is the only legally binding international protocol that addresses gene editing; Article 13 of the Oviedo Convention allows gene editing for prevention, diagnosis, or treatment—but only if there is no modification in descendants' genes.[24] It prohibits the type of germline modifications that scientists in China and Russia are attempting to conduct. The Oviedo Convention, was not signed by the United States, China, or Russia.

With new technology comes the genuine possibility of new and more sophisticated threats. The field of SYNBIO has been expanding the possibilities of biowarfare for several decades, and recent advances in biotechnology are making it even easier to develop and use biological weapons. With the advent of more-straightforward, cheaper, and more-accessible gene-editing technology like CRISPR, the danger has become more urgent. This will undoubtably expand the scope and diversity of the biological threat landscape. In order to help the Department of Defense (DoD) achieve and maintain its biodefense goals, our defense capabilities must evolve alongside these changes. The *2023 Biodefense Posture Review*[25] calls for the modernization of operations to sustain readiness and resilience against burgeoning threats. We must implement the plan outlined in the *National Biodefense Strategy* by pursuing innovative approaches, encouraging learning, and linking stakeholders with new tools and ideas,[26] starting with our student Soldiers at the U.S. Army Chemical, Biological, Radiological, and Nuclear School (USACBRNS), Fort Leonard Wood, Missouri. When a CBRN Soldier understands that there may be altered or combined biological threats, then he or she realizes the limitations that can be imposed by traditional knowledge of diseases and, thus, can provide more flexible and dynamic recommendations to ground force commanders.

Endnotes:

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