



Genetic Frontiers : Unraveling the Impact and Anticipating Future Challenges of SYN BIO

基因前沿:剖析合成生物學的影響及預測未來的挑戰(譯)

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本文

In the evolving technological era of large-scale combat operations and multi domain 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.

在大型戰鬥行動與多領域作戰技術演進的時代，美國陸軍正面臨一項極其複雜的問題，需於多個作戰領域中同時應對並超越其競爭對手與敵人。更增挑戰的是，中華人民共和國已宣布生物學是戰爭的新領域，並計畫使中國成為基因工程等技術的全球領導者。

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” categorizes biological threats among the most severe threats to the

United States and calls for bold approaches to transforming the Nation's biodefense program.

合成生物技術的進步，包括基因編輯技術，例如成簇的規律間隔短回文重複序列(CRISPR)，有望預防甚至治癒疾病，但也帶來了新的安全風險。研究人員可利用 CRISPR 技術，透過將外來去氧核糖核酸(DNA)植入活體宿主細胞，選擇性地改造生物體的 DNA。五年前，一位中國科學家運用 CRISPR 技術創造出首例基因編輯嬰兒，因而面臨國際間對其違反醫學倫理的譴責。雖然此技術可望用於治療遺傳疾病，卻也可能被用來編輯細菌或病毒基因，以製造強化型病原體。美國於 2022 年發布的《國際生物防禦戰略和實施計畫：應對生物威脅、強化疫情準備與實現全球健康安全》中，將生物威脅列為對其最嚴重的威脅之一，並呼籲採取大膽行動以重塑國家生物防禦體系。

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).

隨著合成技術日益普及與操作容易，化學、生物、放射、核子(CBRN)專業領域必須做好準備，以因應未來戰場上這些技術的應用。應從教學端開始提高對此技術的認識，透過現代化生物防禦課程將合成生物學(SYNBIO)納入教學內容中。

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. 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. Using SYN BIO, 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. 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 SYN BIO to national security.

SYN BIO 是一門跨學科領域，核心在於創造與改造生物體及其遺傳物質，以產生自然狀態下未曾見過的新表現型特徵。此領域的進展已使人類能依需求改造病原體功能、復活已根除的病毒，及合成新型病原體。由於技術發展的速度與應用範圍，SYN BIO 對國家安全構成重大威脅。SYN BIO 的進展已產生工具，足以使國家、團體或個人製造出新型病毒，無論是有意或無意，皆可能對大量人群造成影響。由 SYN BIO 所衍生的武器可使國家行為者對某一地區造成嚴重影響-特別是對該地區的人員、植物與牲畜-而不損害關鍵基礎設施。例如，2002 年紐約州石溪大學的科學家利用 SYN BIO 技術，根據網路上公開取得的基因資料，構建出活體小兒麻痺病毒。此外，科學家也可利用 SYN BIO 改造現有生物體，使其具備自然狀況下不會表現出的能力，讓潛在對手研發出新型或強化型生物戰劑。CRISPR 是多種基因編輯技術之一，它可精確進行基因體編輯，其高效率與低成本，大幅提升 SYN BIO 對國家安全構成的威脅。

CRISPR is the most-discussed gene-editing technology during national and international security debates because it does not require sophisticated knowledge, specialized equipment, or the time that was needed for earlier gene editing technologies. 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. 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. However, gene-editing technology can also be used for nefarious purposes—and CRISPR accessibility, affordability, and efficiency make it an attractive vehicle for bio warfare. 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.



CRISPR 是在國內外安全辯論中最具討論度的基因編輯技術，因其不需要複雜知識、特殊裝備或早期基因編輯所需的繁複技術。CRISPR 利用一段嚮導核糖核酸(RNA)，定位 DNA 中的目標基因位置，並由酶切斷雙股 DNA，使基因得以被改造。簡而言之，科學家可在基因組內指定位置進行 DNA 片段的剪貼操作。藉 CRISPR，理論上可針對人體細胞與病原體中的任一雙股 DNA 序列進行編輯。這項技術可用於正面用途，例如 2023 年 12 月美國食品藥物管理局已核准全球首項針對人類的基因編輯療法。如今，CRISPR 可用於治療鐮刀型紅血球貧血症，這類由單一基因突變所引起的血液疾病。然而基因編輯技術亦可被用於不法用途，且 CRISPR 因容易取得、低成本與高效率等特性，成為具吸引力的生物戰工具。此外，當 CRISPR 與人工智慧結合時，其效率會更加提升，可運用機器學習預測特定基因編輯對生物體的影響，減少耗時的實驗與測試流程。

Because gene editing allows scientists to edit and shape whole genomes of bacteria and viruses with new properties, concerns about its possible future use have been raised. U.S. scientists who were researching CRISPR modified the mouse pox 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. 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.

由於基因編輯能讓科學家編輯及塑造細菌與病毒的整個基因體，使其具新特性，而對其未來潛在用途的憂慮不斷升高。美國研究 CRISPR 的科學家曾改造鼠痘病毒，將一段天然免疫抑制基因插入原病毒中，原本是為了增加抗體產量，因而關閉了免疫系統中對抗病毒的部分機制，製造出更致命的鼠痘病毒。這些實驗顯示可能製造出對疫苗具抗性的天花變異株，而疫苗為任何威懾策略不可或缺的部分，因為它們能降低敵方釋放特定戰劑的動機，藉此使攻擊失效。

CRISPR might also be used to edit genes of entire populations of disease-spreading animals, like mice and mosquitoes. 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.



CRISPR 也可能被用來編輯整個會傳播疾病的動物族群的基因，例如老鼠與蚊子。研究人員已嘗試改造這些動物的 DNA，使其後代無法再傳播疾病。但這目標與改造其 DNA 讓後代更有效率且更具傳染力之行為，已極為接近，且風險高。

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, 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. Chinese scientists also used CRISPR to remove genes that inhibit muscle and hair growth in goats, successfully increasing yields of meat and wool. 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. 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.

這些科學進展未來可能的應用，應從國際安全的角度來看，特別是與擴散、防衛嚇阻及非常規武器研發相關的面向。過去已有一些國家參與了秘密的生物武器計畫，而現在多個國家公開進行在美國是違法的研究。在中華人民共和國，賀建奎曾使用 CRISPR 編輯人類胚胎的基因，試圖創造對人類免疫缺陷病毒(HIV)具免疫力的嬰兒；此舉引起了擔憂，認為他開啟了進一步改造胚胎的大門，例如「設計寶寶」，讓父母利用基因編輯技術為子女挑選他們偏好的特徵。中國的科學家也曾使用 CRISPR 移除山羊體內抑制肌肉和毛髮生長的基因，成功提高了肉和羊毛的產量。於俄羅斯，一位來自莫斯科皮羅戈夫國立醫學研究大學的遺傳學家丹尼斯.雷布里科夫計畫使用 CRISPR 編輯胚胎基因來治療遺傳性耳聾。他的研究涉及胚胎生殖細胞的改造，而這些變化會傳給下一代，因此被廣泛認為不符合倫理。儘管受到反彈，雷布里科夫仍在尋找批准繼續推進這項研究。

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.

雖然中國允許在研究目的下進行生殖系統的基因編輯，但被編輯過的人類胚胎不得使用於建立妊娠。因此賀建奎因進行胚胎基因改造並誕生了一對雙胞胎女嬰，而在中國服刑三年，目前他已出獄。他現在再次投入 CRISPR 的研究，這次是為了嘗試治療杜興氏肌肉萎縮症，一種遺傳性的肌肉退化疾病。不過，許多專家仍對他的動機，以及中國政府允許他繼續從事這類研究的背後用意，持續感到疑慮。

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

除了由國家資助、具備改造既有生物體或基因組以達特定目的的實驗室外，SYN BIO 技術本身的低成本及高可及性，讓任何擁有適當設備與簡易實驗室的人，都可能製造出對疫苗具抗性的病毒，或讓現有的細菌變得更具危害性。他們甚至可能重建已被消滅的病毒，例如將容易取得的牛痘病毒轉化為天花病毒。因為這些經基因編輯的病原體屬於未知類型，其表現的生物威脅難以預測，而為監控與偵測帶來更多挑戰。

To further complicate matters, no international legal, ethical, or moral framework for determining a common understanding of the safe use of SYN BIO exists. Likewise, there is no international oversight committee for gene editing and no agreement on the ethical boundaries within which CRISPR may be used. 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. 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.

更複雜的是目前國際上並無一套法律、倫理或道德層面的框架，能用來建立對 SYN BIO 安全使用的共同認知。同樣的也無專責的基因編輯國際監督機構及無對 CRISPR 可使用範圍的倫理界線達成共識。《歐維多公約》是目前唯一具法律約束力、針對基因編輯的國際協議。其中第 13 條允許預防、診斷或治療目的進行基因編輯，但前提是不得對後代的基因造成改變。該公約明確禁止中國與俄羅斯科學家正試圖進行的這類生殖細胞基因改造。不過《歐維多公約》並未獲得美國、中國與俄羅斯的簽署。

With new technology comes the genuine possibility of new and more sophisticated threats. The field of SYN BIO has been expanding the possibilities of bio warfare 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 undoubtedly 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 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, 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.

隨著新技術的出現，帶來了新型且更具複雜威脅的可能性。SYN BIO 這領域在過去數十年中持續拓展生物戰的可能性，且近期生物科技的進展使得發展與使用生物武器變得更加容易。隨著如 CRISPR 這類更簡單、成本更低且取得更容易的基因編輯技術出現，此一風險愈顯迫切，生物威脅的範圍與樣態也必將擴大。為了協助國防部(DoD)達成並維持其生物防禦的目標，我們的防禦能力必須隨著這些改變演進。《2023 年生物防禦態勢檢討報告》呼籲作戰現代化，以



維持面對新興威脅的備戰能力與應變韌性。我們必須依《國家生物防禦戰略》中的規劃加以貫徹，採取創新方式、鼓勵持續學習，並透過新工具及新想法整合各方利益相關者，而這應從我們在密蘇里州李奧納伍德堡的美國陸軍化學、生物、放射與核子訓練學校(USACBRNS)中學習的學員開始。當一名化生放核士兵瞭解未來可能面對經改造或複合的生物威脅時，他或她就能體認傳統疾病知識在應對時的侷限，進而向地面部隊指揮官提供更具彈性與動態性的建議。