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Genome editing as a national security threat

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Summary

Testimony from the intelligence community in the United States connecting genome editing with national security threats was a noted departure from past assessments of the implications of modern enabling biotechnologies. Rarely are individual biotechnologies included on lists of potential security threats. When they are, a broad range of advances are usually considered collectively – in terms of both risks and benefits. Given the classified nature of the rationale as to why gene editing tools were singled out, we are unlikely to fully understand for several decades what prompted this statement. This paper considers three ways in which these tools might impact national security: *i)* enabling the development of advanced biological weapons; *ii)* facilitating the development of new bioweapons based on ecological applications of genome editing, and *iii)* enhancing future generations of people in ways which could have an indirect impact on security, for example by improving a nation's cognitive ability and/or the physical endurance of its soldiers. Their implications are different and so are the possible policy and regulatory responses.

Keywords

Biorisk – Biosecurity – Biotechnology – Gene editing – Genome editing – Security.

Introduction

On 9 February 2016, the debate about the risks and benefits of genome editing took a new turn when the Director of National Intelligence in the United States (US), James Clapper, labelled it a national security threat (1). In the intelligence community's annual report to the Senate Armed Services Committee, genome editing was specifically highlighted (Box 1) – putting emerging capacities to manipulate genetic material on a par with North Korean weapons of mass destruction and chemical weapons in Syria and Iraq.

> **Box 1**
> **The Director of National Intelligence's testimony on genome engineering before the Senate Armed Services Committee, 9 February 2016**
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> 'Research in genome editing conducted by countries with different regulatory or ethical standards than those of Western countries probably increases the risk of the creation of potentially harmful biological agents or products. Given the broad distribution, low cost, and accelerated pace of development of this dual-use technology, its deliberate or unintentional misuse might lead to far-reaching economic and national security implications. Advances in genome editing in 2015 have compelled groups of high-profile US and European biologists to question unregulated editing of the human germline (cells that are relevant for reproduction), which might create inheritable genetic changes. Nevertheless, researchers will probably continue to encounter challenges to achieve the desired outcome of their genome modifications, in part because of the technical limitations that are inherent in available genome editing systems.'

Genome engineering has been previously considered an enabling technology in international security settings. It has seldom been viewed as a stand-alone threat. For example, the 2015 Meeting of States Parties to the Biological Weapons Convention, as part of its work to review relevant developments in science and technology, recognised the potential benefits of the technology for the fight against biological weapons and agreed that there was a need to share information on, and understanding of, advances in immunology and various other enabling technologies. The report of the meeting referred specifically to genome editing tools, including 'those derived from bacterial "immune systems", such as CRISPR [clustered regularly interspaced short palindromic repeats], as well as those related to continuing progress in synthetic biology' (2).

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Genome engineering is one approach that might be key for speeding up the development of new and more streamlined approaches to dealing with disease, such as those envisaged by the Coalition for Epidemic Preparedness Innovations (CEPI), recently launched at the World Economic Forum (3).

James Clapper's statement left members of the science policy community that focuses on these issues confused as to why this particular technology had been singled out and which national security threats were envisaged (4). The problem with a public summary from a restricted report is that much of the reasoning is redacted. Reflection suggests that concerns over genome editing could have been prompted by three different threats: its potential to accelerate development of traditional biological weapons, its potential to create new types of bioweapons by altering wild ecosystems, or the long-term security implications of its application in humans.

Advanced biological weapons

Perhaps the most obvious way a development in the life sciences could become a security threat is by direct application to bioweapons technology. Both the life science and security communities have long recognised that 'almost all biotechnology in service of human health can be subverted for misuse by hostile individuals or nations' (5). The challenge has been finding ways to further research and development for protective, prophylactic or other peaceful purposes while minimising risks of accidents or deliberate malign use. To help support international efforts to achieve this delicate balance, the global scientific community helps track relevant trends in science and technology. In September 2015, the Global Network of Science Academies, better known as IAP (the InterAcademy Partnership), convened an international workshop in Warsaw, Poland, to identify recent advances of import (6). Genome editing was highlighted as an important development which had the potential to strengthen capacities to deal with disease, regardless of origin, but which could also be used to develop more advanced bioweapons. In general, it was considered as one of a raft of enabling technologies that were making it easier, faster and cheaper to use biology as a manufacturing platform. Language from the testimony on 'the broad distribution, low cost, and accelerated pace of development of this dual-use technology' frames the security concerns from genome editing in a similar manner.

The Workshop participants identified three ways in which genome editing might be directly applied to the development of bioweapons:

– designing and constructing novel agents

– enhancing the virulence of naturally occurring pathogens

– modulating vector susceptibility to drugs and control methods.

They also determined that applying such advances would not be easy, noting that they are 'expensive and complicated to acquire and deploy successfully' and that 'making use of them for prohibited purposes would probably require the resources of a state'. This suggests that the malicious application of genome editing by terrorists is unlikely in the near future.

Nevertheless, however unlikely they are in the short term, perhaps such direct applications to weapons development were the threats envisaged by the US intelligence community. If so, genome editing might potentially be added to the list of 'experiments of concern' drawn up by the National Academies of Sciences, Engineering, and Medicine in 2004 (5). This list influenced the Federal Policy for Oversight of Life Sciences Dual Use Research of Concern, which places additional oversight requirements on certain types of research involving certain pathogens (7). If deemed of sufficient concern, could a subset of experiments involving genome editing be added to this list? Given the lack of focus on genome editing technologies in contemporary efforts to revise oversight arrangements, this seems unlikely (8). For example, there was little mention of genome editing technologies at a recent meeting of the National Academies to review US government policy options for oversight of 'gain-of-function' experiments (i.e. those that manipulate biological agents and introduce changes that confer new functions on the pathogen) (8).

It also seems unlikely that genome editing will be added to the Control List of Dual-Use Biological Equipment and Related Technology and Software (9) drawn up by the Australia Group (an informal forum of countries established in 1985 to ensure that exports do not contribute to the development of chemical or biological weapons). The Group notes that such controls on technology 'do not apply to information "in the public domain" or to "basic scientific research" or the minimum necessary information for patent application', suggesting that much of genome editing will likely fall outside its remit.

Ecological applications of genome editing

The IAP workshop also addressed the possibility that gene drive systems might be used as bioweapons. A gene drive is a naturally occurring phenomenon in which genetic elements promote the inheritance of a particular gene so that it spreads through populations even if it does not benefit individual organisms. The development of CRISPR genome editing has enabled researchers to build gene drive systems based on CRISPR with comparative ease. First described in 2014, the technology has been successively demonstrated in yeast, fruit flies, and two species of malarial mosquitoes (10, 11). One of the systems used for mosquitoes is a 'suppression drive' intended to reduce or possibly eliminate the target mosquito population. The potential use of this form of drive system to target organisms that are beneficial to the ecosystem or economy is particularly concerning, because its effects are invisible until a handful of generations before population collapse.

However, gene drive systems are easily countered by releasing 'immunising reversal' drives that overwrite earlier changes and patch the vulnerability in unaffected populations (10). Because CRISPR-based systems would still be identifiable via high-throughput DNA sequencing, ecological monitoring can provide early warning, while slow geographic and generational spread provides time to build, raise, and release organisms with a suitable immunising reversal drive. Combine this with the comparative inability of drive systems to affect long-lived organisms or those whose genetics are carefully monitored, such as humans and most crops, and it appears that gene drive technology inherently favours efforts to prevent misuse – rather than empowering those who would cause deliberate harm.

From a policy perspective, this underscores the importance of funding appropriate monitoring efforts, but also of ensuring that all gene drive research is conducted in the open. Here, security interests and ethics coincide: requiring open gene-drive science would benefit efforts to monitor ecosystems, create countermeasures, and accelerate development. It would also help to ease concerns about the technology and help build popular support among the communities that would be affected by particular applications, e.g. applications aiming to eliminate vector-borne diseases.

Enhancing future generations

Clues from Clapper's testimony suggest that the threat to national security to which he is referring is the application of genome editing to humans, not to biological agents or wild populations. He highlights risks from 'unregulated editing of the human germline (cells that are relevant for reproduction), which might create inheritable genetic changes'. So how could the ability to engineer inheritable traits be of security concern?

An obvious possibility is the engineering of enhanced combat soldiers. There have been claims that genome editing technologies could be applied to increase a soldier's resistance to sleep deprivation or their ability to go for prolonged periods with little food (12). There have been studies in mammals that showed that gene editing increased muscle mass (13, 14). However, modern warfare has been moving inexorably away from direct human involvement; in addition, changes made today would not have an impact for nearly 20 years, with no guarantee the resulting babies would become suitable soldiers. Somatic cell gene therapy applied to current combat soldiers could avoid these problems, but changes to these cells are not inherited.

Perhaps the most puzzling section of the testimony was the connection between genome editing and 'far-reaching economic and national security implications'. A focus on far-reaching implications suggests that the issues being considered are not those that might be reasonably expected to be deliverable over the coming decades. Rather, it suggests concern over a possible advance that is anticipated to have a long-term impact, perhaps one relevant to economic competitiveness.

One possible advance that could affect economic performance would be the development of a biotechnology in another country which would enable that country to erode the US lead in technology. Regulatory decisions taken elsewhere in the world to allow basic research prohibited in the US could allow rivals to develop more advanced biotechnologies, which could have profound economic implications, given the increasing importance of the bioeconomy. However, this is a general concern in any field, and it is unclear why genome editing would warrant such special attention.

It is perhaps more likely that the concern relates to the consequences of applying genome editing technologies to the general population. Early applications would certainly focus on easing the disease burden faced by many advanced economies; given rising healthcare costs, this could prove a tremendous economic benefit. Genome editing of gamete-producing cells or embryos could correct genetic disorders; for example, significant steps towards addressing specific forms of muscular dystrophy were reported earlier this year (15, 16, 17). Whilst genetic disorders are hugely costly (18), they are dwarfed by costs imposed by chronic conditions whose prevalence is linked to genetic susceptibility, including obesity, diabetes, cardiac disease, and dementia. In the longer term, it may even be possible to increase resistance to cancer by providing redundant copies of tumour suppressors, the same strategy employed by large cancer-resistant animals such as whales.

More controversially, genome editing could open the door to enhancing the population, for example by improving cognitive ability, rather than simply removing undesirable traits. There has been economics-based research demonstrating that human capital is important for economic growth, and that cross-cultural IQ tests provide a measure of human capital (19). Although there have been suggestions that cognitive skills, as measured by IQ scores and maths tests, have only a 'modest influence on individual wages', they have been found to be 'strongly correlated with national outcomes' (20). While the causal relationship is unclear, it suggests that an ability to increase a nation's average cognitive ability could have far-reaching economic and therefore security implications.

Studies have demonstrated that, while cognition is likely governed by a complex interplay of factors, there are single point mutations associated with educational achievement, even if no single allele has a particularly large impact (21). Moreover, *de novo* variants causing intellectual disability could conceivably be removed by editing (22); whether using this method to reduce overall mutational load would substantially enhance cognition in the absence of disability-causing variants is less clear (23). Either strategy would need to edit a large number of alleles to achieve a substantial impact. Whether near-future editing capabilities will be able to accomplish this, especially in a high-throughput manner, is unclear. Moreover, predicting which edits should be made is well beyond current genetics, although this may be feasible once large cohorts with comprehensive ability and health data, such as US military personnel, undergo whole-genome sequencing.

There are, however, alternative approaches not involving genome editing that could provide similar benefits. Current methods of *in vitro* fertilisation, embryo sequencing, and selective implantation are already in use and do not pose safety or ethical concerns from potential off-target effects or, especially, the potential insertion of sequences never previously found in humans. Siblings typically differ by roughly one standard deviation in adult cognitive ability, more than half of which is genetic. If sequencing could reliably predict which embryo to implant in order to maximise health and performance, this method could conservatively improve the cognitive ability of entire future generations by half a standard deviation.

Should any of these germline alteration strategies prove as effective as predicted – a substantial caveat – nations that offer them for free to willing citizens would enjoy tremendous economic and therefore security advantages relative to nations that forbid them or leave access to the marketplace. Perhaps the US intelligence community was making such a long-term strategic assessment and embracing more nuanced concepts of national security than found elsewhere in the report.

Whether the issue is the engineering of pathogens, wild organisms, or our societies more broadly, it is clear that genome editing technologies are powerful tools with great promise for beneficial applications. It is also apparent that they will raise a host of ethical, legal and social implications that we must address collectively. A recent meeting of the US National Academies examined principles underpinning clinical, ethical, legal, and social implications of human gene-editing technologies but did not consider security implications (24). It will be increasingly important to work more closely with our security colleagues to strive to find ways to maximise the benefits from technologies such as genome editing whilst minimising the risks.

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L'édition du génome en tant que menace à la sécurité nationale

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Résumé

Une récente déclaration de la communauté du renseignement des États-Unis d'Amérique, associant l'édition du génome à des menaces à la sécurité nationale, a marqué une prise de distance par rapport aux évaluations antérieures concernant les effets des biotechnologies modernes d'appui. Il est rare que des biotechnologies particulières figurent sur la liste des menaces potentielles de sécurité. Lorsque c'est le cas, il s'agit plutôt d'un large éventail d'innovations, généralement considérées comme un tout tant pour ce qui concerne les bénéfices qu'elles apportent que pour les risques qui leur sont associés. Étant donné que les raisons pour lesquelles les outils d'édition génomique font l'objet d'un traitement particulier sont classées secrètes, il est peu probable que nous sachions avant plusieurs dizaines d'années ce qui a suscité une telle affirmation. Les auteurs envisagent trois types d'effets que ces outils pourraient avoir sur la sécurité nationale : *i)* permettre la mise au point d'armements biologiques de pointe ; *ii)* faciliter la mise au point d'armes biologiques dérivées de l'application de l'édition génomique à l'échelle écologique ; *iii)* introduire dans les futures générations des traits d'amélioration pouvant avoir un effet indirect sur la sécurité, par exemple en renforçant les capacités cognitives d'une nation et/ou les capacités d'endurance physique de ses soldats. Leurs conséquences respectives sont différentes, de même que les réponses qui pourront leur être apportées en termes de politiques et de réglementation.

Mots-clés
Biosécurité – Biotechnologie – Édition de gènes – Édition du génome – Risque biologique – Sécurité.

La edición genómica, considerada una amenaza para la seguridad nacional

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Resumen
La declaración de los servicios de inteligencia de los Estados Unidos en que se vinculaba la edición del genoma con amenazas para la seguridad nacional constituyó una notoria novedad con respecto a anteriores evaluaciones de las consecuencias de las modernas biotecnologías instrumentales. Es raro que se individualice una biotecnología en particular para incluirla en una lista de posibles amenazas para la seguridad. Cuando se da el caso, en general se tiene en cuenta, desde el punto de los riesgos que conllevan y los beneficios que aportan, todo un ramillete de avances distintos. Dado el carácter confidencial de los motivos que llevaron a considerar las herramientas de edición génica por separado del resto, lo más probable es que pasen varios decenios antes de que podamos entender cabalmente la lógica en que reposa semejante declaración. Los autores plantean tres posibilidades en cuanto al modo en que estas herramientas pueden afectar a la seguridad nacional: *i)* podrían propiciar la creación de armas biológicas avanzadas; *ii)* podrían facilitar la obtención de nuevas armas biológicas basadas en las aplicaciones ecológicas de la edición genómica; y *iii)* podrían ser utilizadas para conferir a las generaciones venideras características que tengan efectos indirectos en la seguridad, por ejemplo porque mejoran las aptitudes cognitivas de una nación y/o la resistencia física de sus soldados. Las consecuencias de cada una de estas posibilidades son distintas, como lo son las posibles respuestas políticas y normativas frente a ellas.

Palabras clave
Biotecnología – Edición génica – Edición genómica – Riesgo biológico – Seguridad – Seguridad biológica.

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