

Future gene drive applications: concerns, regulations, and communication

Overview

We are now living in a period of the Information Age where enough data about the biosphere has been gathered, granting us the knowledge and power to synthesize lives, enhance humans, eradicate species, or even redesign nature. However, who will or who can permit us to do so? This review examines a specific case of gene-editing technology whose development entails as many promises as value conflicts and ethical debates: gene drive, a biotechnology that aims at modifying the genome of an entire species by introducing bias to the inheritance frequency of a genetic marker in organisms' progeny, usually through engineering heritable genomic integration systems into organisms capable of sexual reproduction. The nature of gene drive deployment's irreversible, cross-generational, and global-scale impacts on nature demands our careful consideration of not only the ecological concerns but also the ethical and cultural values of all living communities of both the current generation and future generations.

Potential applications and concerns: Multiple perspectives

The several debated gene drive applications can be divided into four categories based on their deployment purposes: 1) disease eradication, such as suppressing the population of mosquitoes to prevent the spread of dengue, malaria, and other mosquito-borne diseases, or modifying rodents, ticks' hosts, to eradicate Lyme's disease; 2) agricultural and sustainability enhancements, such as reversing herbicide or pesticide resistance in weeds and pests to reduce the use of toxic chemicals; 3) control of invasive species, such as the black rats and brown rats in the United States; and 4) preservation of endangered or threatened species, presumably enhancing the species' resistance to certain diseases aside from controlling other species threatening their survivals (Esvelt, 2014).

Surrounding these proposals to deploy gene drives, many have questioned whether they are in line with certain communities' ethical and cultural values. One moral objection raised against the use of gene-drive technologies to eradicate certain species is the "sanctity of life" argument, which argues no animal should be driven to extinction because all lives are sacred. Another is the "Promethean aspirations" critics, which argue that altering nature to satisfy certain human desires destroys our appreciation for the given nature and reserves no options for future generations to apply their own cultural and ethical values (Pugh, 2016). These generalized ethicists' viewpoints have been countered by both ethicists and scientists. Dr. Pugh (2016) argued that the eradication of certain species, like mosquitoes, could be justified based on the moral status of mosquitoes and the availability of alternatives in serving humans' benefits. He

claimed that as individual mosquitoes do not have noteworthy moral status, moral status cannot be an emergent property of the species as a whole. He further equated the elimination of mosquitoes to the elimination of the smallpox virus by the vaccination program, while distinguishing mosquitoes from other common pets or farm animals whom most deem as having certain levels of moral status because of their sentient and conscious state. Similarly, Dr. Esvelt (2018) held the view that certain forms of life are not meant to be valued. He also claimed that evolution was essentially amoral and cruel in the sense that it neither cares about nor optimizes the well-being of creatures. Thus, his lab intended to sculpt evolution and justified alleviating the sufferings of the more sentient beings at the sacrifice of certain pests or vectors among the lower species, such as the New World screwworms, which infect millions of mammals and domestic animals annually and lead to excruciating deaths. Both Dr. Esvelt and Dr. Pugh pushed for continued research and trials and considered the benefits of lifting the global disease burden to outweigh certain moral concerns or the adverse outcome of potential ecological risks.

However, those more cautious about the technology also bring up the possibility of damaging the culture of certain communities that will not be spared by the gene drive deployment. Kuzma and Rawls (2016) gave an example of the Hawaiian feral wild pig, a population central to Native Hawaiian communities' cultural events and food. The reduction of this population cannot be approved based on the ecological benefits alone. They also evaluated gene drives from the perspective of social and intergenerational equity, stating the need to conserve access, quality, and options for future generations when it comes to natural resources. Based on such principles, their evaluations concluded that decisions and policies regarding gene drives must be made on a purpose-specific basis. In general, there is more tolerance for the irreversibility and uncertainties of gene drive technologies aiming at downsizing invasive species and preserving endangered or threatened species than those aiming at enhancing agriculture and eradicating human disease-related species. The criterion is whether the intention considers the non-use values of nature and whether the burden of risks is placed on future generations while the current generation enjoys the primary benefits.

Comparing gene drives and other traditional gene-editing technologies, we see similar constantly recurring debates, such as whether there might be gene transfers into non-target organisms or irreversible replacement of wild types by engineered varieties. Yet, we cannot develop an accurate risk-benefit analysis for gene drives at present without sufficient field trials. However, what makes gene drives riskier than other gene-editing also brings promises: gene drive implementation is cross-generational and cross-national; thus as Dr. Esvelt (2018) commented in an interview, every gene drive application strictly requires the acceptance of all communities, and commercial interests are hard to find roots in this business, making gene drive more an open science than other gene-editing technologies.

Current biological risk assessments

Since gene drive technologies are under lab research, the existing related governance remains as biological risk assessments aiming at countering any accidental release of gene drives into the wild by recognizing and containing biological hazards - organisms that might have harmful effects on the environment and health.

European nations are among the first to develop and adopt biological risk assessment guidelines for gene drive technologies ("IGEM", 2020). Similar to other genetic modifications done on plants and animals, gene drives are usually deployed in specific species in individual deployments. Thus, van der Vlugt et al. (2018) proposed a biological risk assessment framework for gene drive technologies based on previous EU directives on genetically modified organisms (GMOs). The process of assessment includes the identification of key elements relevant to the gene drive implanted organisms: the nature of the potential adverse impacts on health and environment, both the severity and the likelihood of these adverse impacts once realized, and the characteristics of the organisms. Following these case-specific evaluations, one of the three risk classes is assigned to each case. Likewise, Germany's position statement on gene drive risk assessments (2016) is built upon their existing ZKBS biosafety standards. Gene drive experiments are identically assigned containment level 2, which laboratories operating on pathogenic agents typically fall under. Arguably upholding a stricter precautionary principle, the evaluation only considers the possibility of gene drives escaping the laboratory no matter the implanted organisms' likelihood or consequences of survival in the wild. The UK has only made an HSE eBulletin announcement (2016) to all genetic engineering research groups so far, promoting a somewhat similar "tiered strategic approach" that recommends collecting data from "gene-drives in contained use" to inform future applications and conducting case-specific evaluations. Besides, there have been initiatives to discuss gene drives in both Australia and the United States in recent years ("Factsheet", 2018).

Among the existing biological risk assessments, the main difference between those for typical GMOs and gene drive implanted organisms are the adverse effects concerned. While most GMOs need to be examined for their toxic or pathogenic effects, gene drive cassettes often reduce rather than induce the implanted organisms' toxicity or pathogenicity. Therefore, the discussions of gene drives' biosafety mainly circle around the environmental aspect rather than health, especially since the release of gene drives into the environment usually leads to permanent changes to the ecological system in the future. The existing frameworks thus assign effective lab containment policies primarily according to the consequences and possibility of "the establishment or dissemination" of gene drives in the environment and "the natural transfer of inserted genetic materials" to non-target species (Van der Vlugt et al., 2018, pp. 26-27). Currently, the Netherlands has the most complete and independent guidelines for gene drive risk assessments. Germany and the UK incorporate gene drives research regulation into that of genetic engineering, with Germany providing more detailed categorization on the type of gene drive constructs and enforcing formal containment

level requirements. Although gene drive application remains in its womb, risk assessments still need cross-border collaboration, because once released, the spread of gene drive can only be contained by the natural boundary of the cassette's habitats, instead of the man-drawn national borders.

Addressing future challenges: public communication

Decision-making regarding the use of gene drives to control and suppress certain species involves more than biological risk assessments. Aside from the health and ecological concerns, communities' moral values and culture should also be taken into account. Thus, to facilitate the safe and acceptable use of such technology, we must come up with an effective means of communicating the efficacy and risks of the technology. As pointed out by Bossard et al (2019), gene drive is essentially a case of post-normal science: "facts are uncertain, values are in dispute, stakes are high, and decisions are urgent" (pp. 7695). Some fundamental principles have been suggested on how public engagement should be carried out to find the solution for gene drive deployment: Journalism and media coverage should communicate both scientific facts and ethical questions responsibly without creating false hope or false alarm. In addition to reporting the promises and problems of future applications, there should be updates on the current progress, including new regulations, debates within the scientific communities, emerging commercial interests, government research funding, and public health project initiatives. The communication should not be one-way between researchers and the lay public: keep in mind that the assumption about the "knowledge deficit" of laypeople is erroneous. Simply revealing the technical aspects of gene drives does not garner support or trust from the public. Researchers should adopt narratives that best address different communities' concerns based on understandings of their values which decide how they perceive risks and efficacy differently from the scientific community (Bossard et al., 2019).

Public engagement is essential to post-normal science applications like gene drives: to make progress, the technology needs further research and trials, which then needs the approval of the public. Before that, the scientific community needs to gain trust by having constructive discussions with the public, clearing misconceptions, and increasing transparency.

V. Conclusion

The gene drive technology is a powerful idea that has yet to be realized, but its irreversible, broad, and long-lasting impacts imply a responsibility for case-specific communication and evaluation before any attempts at deployment. For each case, we must identify what modifying the target species means to different communities. With biological risk assessments, we have only addressed health and environmental concerns. To address different cultural and ethical judgments of risks and efficacy, researchers should ask for the opinions of more communities. Gene drive is another force that will

bring gene-editing to the level of post-normal science, at which we redefine the boundary between nature and non-nature amidst uncertainties, interest conflicts, and value clashes. Thus, to make the technology "right" for the future world, we must first make the technology "clear", especially to the younger generation whose lives might be the one with actual gene drives. Based on the current debates and regulations regarding potential gene drive deployment, this review proposes that gene drive technologies require case-specific risk assessments, collaborative supervision among different communities, and strong public engagement from development to deployment.

Work Cited

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