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Association for Responsible Research and Innovation in Genome Editing

IN THIS ISSUE

EDITORIAL

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President of ARRIGE

CRISPR tools have shown their great versatility and adaptability to many different applications during this COVID-19 pandemic. Besides the known and widespread uses for genome editing purposes, CRISPR can also be used as diagnostic tools. Since 2017 we know, thanks to Feng Zhang (BROAD Institute) and other researchers, the existence of Cas nuclease variants isolated from diverse bacteria with different properties. In particular, the Cas13 series displays RNA-guided endogenous RNAse activity. The specificity of these Cas13 nucleases (at least Cas13a and Cas13b) is lost upon finding the complementary RNA target. Thereafter, the nucleases proceed in vitro and digest all RNA molecules in the assay tube. This unexpected behaviour was converted into an opportunity and led to the development of SHERLOCK, the acronym of the fist CRISPR-derived diagnostic application. Jennifer Doudna's lab (UC Berkeley) reported a similar behaviour from Cas12a and Cas12b nucleases, whose target is double strand DNA (dsDNA), but which also lost the specificity and began cutting single strand DNA (ssDNA) upon being activated after finding the complementary sequences. This discovery led to the development of DETECTR, an alternative CRISPR-derived diagnostic application. The addition of reporter short RNA or ssDNA bound to fluorescent markers that shine upon those molecules being digested was the key, eventually transformed into reactive stripes easier to read. SHERLOCK was soon applied to detect the SARS-CoV-2 coronavirus RNA genome, followed by several similar DETECTR developments.Other researchers explored analogous activities with Cas3 resulting in the CONAN diagnostic application. The combination of SHERLOCK with nanofluidic technologies led to CARMEN, a strategy to detect the coronavirus in thousands of patients at once, or more than hundred different viruses into a limited number of subjects.

On the other hand, in 2018 a more specific Cas13d variant was isolated, whose target specificity was not lost upon activation. The use of Cas13d targeting the RNA genome of SARS-CoV-2 was explored in vitro successfully, through a method called PACMAN, leading to suggest this approach as a potential antiviral application. Most recently, the targeting specificity of SARS-CoV-2 and influenza virus RNA genomes by Cas13a was demonstrated in vivo, in mice and Syrian hamsters, further documenting the potential therapeutic role of CRISPR tools not only for detecting but also for inactivating the coronavirus.

In this new issue of the ARRIGE newsletter you will find contributions provided by international experts working in various settings, on the applications of CRISPR in relation to the COVID-19 pandemic.

FREE COMMENTARIES

Tackling COVID-19 with the CRISPR toolbox

Rodolphe BARRANGOU & Kevin DAVIES, The CRISPR Journal, New Rochelle, New York, USA

One year into the severe acute respiratory syndrome CoronaVirus (SARS-CoV-2) pandemic, it is still unclear when and how we will globally reach a semblance of normalcy, following unfathomable human and economic casualties. The (mis)handling of the pandemic in too many parts of the world has been exacerbated by the stench of scientific denialism and political opportunism. The reliance on scientific solutions to our medical woes is a reminder of our need to fuel the science enterprise to enable the medical community.

In a more optimistic vein, scientists in general and the CRISPR community in particular are discovering ingenious ways to solve the daunting therapeutic and diagnostic challenges that lie before us.

Within weeks of the COVID-19 pandemic onset in 2020, hundreds of groups in industry and academia launched programs to develop vaccines, encompassing both classical and innovative approaches. Building off 200 years of vaccine development, many groups pursued time-tested approaches focusing on protein-based, attenuated and inactive viruses. Others bet on modern biotechnologies hinging on nucleic acid-based modalities and vector-based engineering. Academia, industry and governmental agencies feverishly embarked on a race against time to develop a vaccine that would prove safe and efficacious, as well as affordable and manufacturable at scale.

Developing classical therapeutics with new modalities

Diligent efforts on both sides of the Atlantic have yielded multiple vaccines that were approved less than a year after launch. Nearly 100 million individuals have already been dosed with Moderna, Pfizer-BioNTech, Johnson & Johnson, and AstraZeneca vaccines. Although distribution challenges remain, especially for under-developed nations, the safety, efficacy and success of RNA vaccines especially will be an enduring highpoint of the COVID-19 pandemic. The success of these RNA-based modalities - ushering a new era of reliance on and exploitation of RNA molecules - has proven more versatile and programmable than many anticipated.

The design, manufacture and exploitation of RNA-based solutions is a new dogma that is surely here to stay, enabled by a powerful synthetic biology toolbox. CRISPR-based genome editing technologies also showcase the versatility of RNA – so often in the shadow of its deoxy cousin - at the forefront of the biotechnology wave. For example, CRISPR-based screens have identified factors involved in viral targeting and infection (Daelemans 2021 Nat Gen paper).

Besides preventative vaccines, there is also a need to develop therapeutic antivirals, and the CRISPR toolbox, besides the popular DNA-manipulating effectors Cas9 and Cas12, also encompasses programmable Cas13 nucleases that target RNA.

Last year, Stanley Qi and colleagues at Stanford showed that CRISPR, a natural bacterial antiviral system, can be reprogrammed to target human RNA viruses including COVID-19 (Qi 2020 Cell paper). More recently, it was shown that the aforementioned mRNA approach can be used to deliver Cas13-based antivirals that have therapeutic potential to fend off COVID-19 lung infections in rodents (Santangelo 2021 NBT paper). While this is promising, time will be needed to develop this technology clinically and assess its potential in humans. Nevertheless, the speed at which CRISPR-based therapeutics are being developed is truly exciting.

Next-generation diagnostics are here to stay

Although vaccines and antiviral therapeutics might get the bulk of the attention, a bona fide diagnostic revolution is underway. Indeed, we are witnessing CRISPR-based detection methods being developed at amazing speed that combine unprecedented flexibility and affordability. In fact, the well-documented programmability of Cas effectors – validated by the 2020 Nobel Prize in Chemistry – enables design flexibility and specificity that opens avenues for targeting of any sequence of interest. Thus, any viral sequence, including fast-arising variants, can be readily targeted through flexible redesign of the guide RNA that directs Cas13 (Sabeti Mol Cell paper).

Critically, the cost of development, manufacturing, distribution and paper-based read out make this a potential game changer. Recognizing diagnostic challenges early on, some CRISPR pioneers quickly developed and tested Cas-based diagnostics that went from a lab-scale test to commercial prototypes: Mammoth Biosciences (co-founded by Jennifer Doudna) and Sherlock Biosciences (co-founded by Feng Zhang) developed assays called DETECTR (Chiu 2020 NBT) and one-pot STOPCovid, respectively (Zhang NEJM 2020). These two CRISPR diagnostics start-ups have attracted significant venture capitalist interest, and partnered with big pharma to pave the way for affordable virus diagnostics.

As infectious diseases encompass both viruses and bacteria, there is little doubt that CRISPR-based diagnostics will soon be developed to target a plethora of pathogens. Given the explosion of our understanding of the impact of the virome and microbiome on health and disease, we surmise that home-based testing of viruses and bacteria are on the horizon. Furthermore, besides human applications, these biome-monitoring approaches also hold potential for tracking viruses and bacteria of relevance to food, livestock feed, and agriculture, globally enabling the monitoring of problematic pathogens. We see this potential not only for point-of-care use but also for home deployment and supply chain-wide usage. This brings the CRISPR technology to our homes.

Genome editing & COVID-19

Ayola Akim ADEGNIKA, Board of Directors of the Centre de Recherches Médicales de Lambaréné (cermel.org) in Gabon, member of ARRIGE Scientific Committee

The genome editing is a novel tool to control for infectious diseases and is a potential revolutionary step in the medicine. However, the contribution of genome editing in genetically born disease was helpful and straightforward. When infectious diseases are concern the results seem less promising with several barriers including ethical, environmental, issues. COVID-19 causing by the SARS-Cov 2 virus lead to unprecedented pandemic may seek, the use of genome editing to overcome the pandemic in theme of vaccine development, control of pathogenesis, reducing the severity of the diseases, as well as in the controlling the development and a spread of new variant. Such contribution will be likely accepted by affected community, though the weighting of risk against benefice may tend immediately to the benefice if one come to compare the lost at human and economic levels by the pandemic.

At ethical level, the main concern may arise with a possibility of new variant to be severe more than existing one or a vaccine to be less effective or less safe. The question of how to mitigate such risk need to be addressed.

In developing countries, the genome editing may face the potential interaction with pre-existing pathogens including parasites, bacteria and virus. Yet some cases of pre-existing SARS-Cov2 antibodies have been reported in several African countries (Immun Inflamm Dis. 2021 Mar; 9(1):128-133. doi: 10.1002/iid3.367. Epub 2020 Dec 15.PMID: 33320447; Science. 2021 Jan 1;371(6524):79-82. doi: 10.1126/science.abe1916. Epub 2020 Nov 11.PMID: 33177105). These preexisting antibodies may be less specific to SARS-Cov-2. The recent report from Germany indicated more false positive serological tests in Africa compared to Europe (Trop Med Int Health. 2021 Mar 5. doi: 10.1111/tmi.13569. Online ahead of print.PMID: 33666297).

At environmental level no one can predict the effects, since there is not yet data available on the effect of the pandemic of the environment. The genome editing of SARS-Cov 2 can also take this in account by imposing the safer variant across the world.

At clinical level, the genome editing can help mitigate the symptoms and reduced the lethality.

Altogether, more thoughts and research are need ahead before starting the genome editing of COVID-19 at ethical, environmental and clinical levels.

The Potential of Genome Editing as a response to COVID-19 – some ethical and legal considerations

Sheetal SONI, School of Law, University of KwaZulu-Natal, South Africa

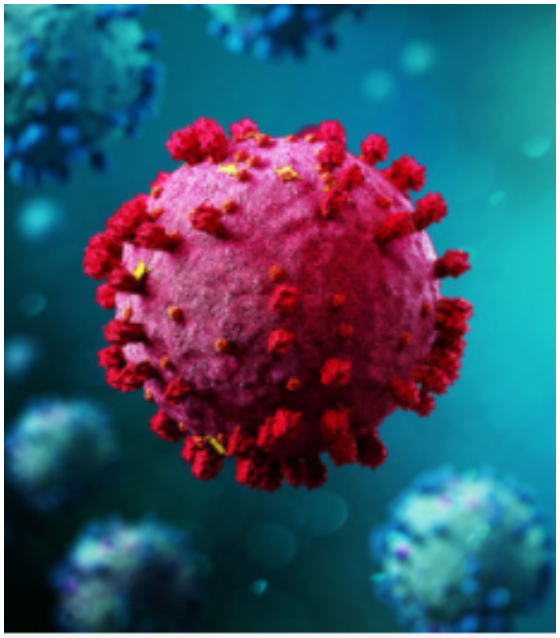
One year ago, the World Health Organization declared that the world was in a pandemic. SARS-CoV-2, now known as COVID-19, is caused by a novel coronavirus. This called for established as well as novel responses. The worldwide Solidarity clinical trial began, and countries around the world initiated vaccine clinical trials. With the pandemic reaching all parts of the world, time was of the essence, however, the search for a cure cannot come at the expense of an ethical approach. The International Bioethics Committee and the World Commission on the Ethics of Scientific Knowledge and Technology issued a joint statement calling for an interdisciplinary dialogue among scientific, ethical and political stakeholders. The joint statement did not describe specific treatment options, but called on the research community to work together to find a cure using a bioethics and ethics of science and technology perspective which is rooted in human rights.

One of the methods researchers have explored to combat COVID-19 is genome editing. Genome editing could potentially be used on the genome of the virus that causes COVID-19, to make it harmless by performing an edit. It could be used to develop better testing kits, and could even be used to edit the human genome to prevent people from being infected by the virus. But gene editing is associated with a range of ethical issues such as safety, equal access and consent. Bioethicists and researchers believe that genome editing in humans must be proven to be safe before it can be offered as a treatment option. There are also other issues, such as equal access to treatment, which must be considered.

CRISPR genome editing

Scientists have considered the possibility of CRISPR (or clustered regularly interspaced short palindromic repeats) technology being used to address the COVID-19 pandemic. CRISPR may help fight COVID-19 in three ways:

1 - Using CRISPR to edit the SARS-CoV-2 genome



CRISPR has the potential to disable the virus that causes COVID-19 by editing its genome so that it is, in effect, made harmless. Using a strategy called PAC-MAN (Prophylactic Antiviral Crispr in huMAN cells), researchers have shown that CRISPR has the ability to attack the SARS-CoV-2 genetic makeup and reduce the amount of virus in a test solution by 90%. Research is ongoing, but it's thought that this approach is so effective, it might have the potential to stop the disease in people. In October 2020, the study was published in Nature Methods. Principal investigator Joseph Bondy-Denomy, PhD, associate professor in the UCSF Department of Microbiology and Immunology described the CRISPR tool as a motor– after finding its specific DNA target, "it runs on DNA and chews it up like a Pac-Man." There would be no barrier to such research as long as researchers abide by the ethical and legal guidelines that apply to their institution and country.

2 - CRISPR-based COVID-19 tests

Genome editing tools have the potential to improve testing rates and could be used to create COVID-19 testing kits and alleviate the global testing burden. Apart from being a genome editing tool, CRISPR is also a diagnostic tool, and can be used to detect infection in cells. The Food and Drug Administration approved a CRISPR-based COVID-19 diagnostic test by a Cambridge biotech start-up on 8 May 2020. The test can provide results within an hour, and the company making it claims that more than 1 million tests can be performed in a week. In October 2020, it was reported that Jennifer Doudna's lab had created a CRISPR-based test which yielded results in five minutes. In order for these tests to be legally made available for use, they would need to be approved by the appropriate regulatory authority, such as the Food and Drug Administration in the US, or South Africa's Health Products Regulatory Authority.

3 - Using CRISPR to make people resistant to infection

CRISPR creates the potential to edit the human genome to make people resistant to infection. The idea is that if we cannot stop the virus from infecting people, can we stop ourselves from getting infected? Gene editing in humans takes one of two forms: somatic cell editing and germline editing. Somatic cell editing affects a person's body cells, while germline editing involves editing the DNA in sperm, eggs or embryos, resulting in genetic changes in an individual's descendants. There are a number of somatic cell CRISPR clinical trials being undertaken and some treatments have been successful. But germline editing is more ethically controversial and over 40 countries prohibit it in their law. When the Chinese scientist He Jiankui used CRISPR to edit the genomes of two children, he was criticised as acting unethically, since the safety and efficacy of germline editing has not been established. Scientists around the world called for a five-year moratorium on it. He Jiankui was sentenced to three years in prison in 2019. There are also laws which will obstruct this potential use of CRISPR. Article 3 of the Oviedo Convention states that "an intervention seeking to modify the human genome may only be undertaken for preventive, diagnostic, or therapeutic purposes and only if its aim is not to introduce any modification in the genome of any descendants". This has been interpreted as expressly forbidding germline gene editing. National law can also prohibit this. For example, section 57 of South Africa's National Health Act states that "a person may not manipulate any genetic material, including genetic material of human gametes, zygotes or embryos". Section 57 was enacted to specifically prohibit human reproductive cloning. But this law was enacted before CRISPR even existed and it mimics the approach taken in international law against genetic manipulation of gametes and embryos.

There are licensed somatic cell CRISPR therapies available. But there are potential legal barriers to the lasting protection which germline CRISPR intervention would give us. It is important to note that CRISPR genome editing is not specifically mentioned in these national and international laws, however we must remember that genome editing was not possible at the time that these laws were written. One of the many methods of legal interpretation involve a consideration of the objective or purpose of a legal prohibition. When we consider the various legal provisions, it is clear that heritable genome editing has been prohibited in these laws. Some authors argue that the Convention does not prohibit genome editing for basic research purposes, but only its clinical application on human embryos to be transferred into a womb. They therefore recommend a revision of Article 13.

We must also consider the question of whether it is ethically viable that we use genome editing to modify the human genome to be resistant to infection by the novel coronavirus.

Way forward

There is always pressure on researchers to develop safe and effective treatment and vaccines. CRISPR technology has been used in a number of ways, but it raises a series of ethical and legal issues with regard to its potential use in humans. So far, scientists have been cautious about putting CRISPR technology to use in humans. Should CRISPR be considered as a legitimate weapon in the fight against the pandemic, knowing that time is of the essence? CRISPR genome editing has potential to be used effectively in the context of the pandemic, however we must ensure that we act within the parameters of the law, with a consideration of ethics.

Listening to the society: multiple pathways for a common goal

Hervé Chneiweiss, Vice President of ARRIGE

On March 3rd 2021, I had the great opportunity to be the moderator of the third roundtable on the ethics of genome editing organized by UNESCO and entitled « Voices From Society ». Like most of our meetings, and contrary to the first two roundtables that took place at UNESCO's headquarter in Paris, this one adopted the COVID-19-imposed format of a webinar via Zoom gathering more than 200 people on-line and that has now been uploaded to You Tube (https://youtu.be/-hG7cvPd3Xc). It focused on public engagement in decision-making as regards the introduction of new technologies into society, duly considering their impact on the values and cultures of each society.

In her opening remarks, Gabriela Ramos, Assistant Director General, Social and Human Sciences Programme, UNESCO, emphasized the mission of United Nation bodies such as UNESCO to promote both science and education with a special need to understand the impact on the society of emerging technologies such Artificial Intelligence or Genome Editing. Interestingly, from its inception, the International Bioethics Committee of UNESCO constitutes a forum which, in a transdisciplinary perspective, keeps abreast of progress in biomedical sciences, particularly genetics. As soon as the end of 2015, in its report on Updating Its Reflection on the Human Genome and Human Rights, the IBC underlined the importance of genome editing but also emphasized its careful use considering the many uncertainties, particularly when it comes to heritable human genome editing, and called at that time for a moratoria in the latter application. She also mentioned as of paramount importance of listening to the society and the crucial role of non-governmental organizations such ARRIGE.

Then Yoshiaki Ishida Deputy Secretary-General, Japanese National Commission, UNESCO, recalled the engagement of the Japanese government and its support to the organization of the three UNESCO roundtables.

We had then a splendid panel of three major players that presented highly complementary approaches to th etopic. Sonya Pemberton spoke first. She is a documentary filmaker specialized in Science (GenepoolProductions, Australia). Sonya is a leading documentary filmmaker, an Emmy Award recipient and record-breaking five-time winner of the prestigious Eureka Prize for Science Journalism. Her forte is finding ways to engage the general viewer in controversial conversations, while satisfying the rigors of effective scientific communication. Sonya recalled her presence at the 2nd International Summit in 2018 in Hong-Kong and how she was astonished by the dense crowd of journalists before He Jiankui's speech and no more the following day for the break-out sessions. There originated the idea to call for a citizen deliberation and make it global, which became the Global Citizen's Assembly on genome editing. Because public mistrust is building, hard decisions need to be made. Who gets to decide? The demand to place the public at the center of the discussion is growing. But what kind of global dialogue can take place? We live in an era of disinformation and political polarization, of conspiracy theories and declining trust in scientific institutions. Is a meaningful discussion on complex technologies and moral disagreements possible? The Global Citizens' Assembly will bring together at least one hundred participants representing different countries across all continents most affected by genome editing. Participants will take part in five days of deliberation about the global principles of governance of genome editing. They will have access to eminent scientists at the forefront of genomic research, ethicists, and other stakeholders. They will have the ear of decisionmakers at national and global levels. Of note, several active ARRIGE members are part of the process and signed the paper in Science announcing its launch . The process is now taking place in several countries such as Australia, France or the US, despite difficulties encountered during the COVID-19 pandemia, and the final gathering is still scheduled in the summer 2022.

The second speaker was Kevin Esvelt, Assistant Professor at the MIT Media Lab, Cambridge, United States. Kevin invents new ways to study and influence the evolution of ecosystems within the Sculpture Evolution Group. In 2013, he was the first to identify the potential for CRISPR "gene drive" systems to alter wild populations in an evolutionarily stable manner. Kevin is an advocate of open science to accelerate discovery and improve safety. He has worked to ensure that community discussions always precede and guide the development of technologies that will impact the shared environment. He reported his experience in Nantucket and Martha's Vineyard to use gene-drive to fight Lyme disease and the many deliberations he had with a "highly educated population, highly motivated by a strong community culture". He also reported a very different experience with Maori people in New Zealand and didn't hide the mistakes he made along this innovative path. He called for a global code of conduct that should be respected by all scientists working on such a sensitive question considering the potential impact on both the environment and the local culture .

Finally, we heard from Tesi Aschan, Senior Legal Adviser, National Board of Health and Welfare (Socialstyrelsen), Sweden. Tesi's main areas within medical law include the legislation on the donation of organs, tissues, and cells, medical devices, assisted reproduction technology, genetic testing, genome editing and end-of-life treatment. Formerly Chair of the Committee on Bioethics (DH-BIO) of the Council of Europe, Tesi Aschan has been the Swedish representative to the named committee since 2012. She shared with us the making of and the content of the "Guide to the public debate in human rights and biomedicine" approved by DH-BIO in November 2019, and already translated in seven languages . She recalled that Article 28 of the Convention creates an obligation on member States to offer members of the public the opportunity to make their opinions count in the field of biomedicine. It says: "Parties to this Convention shall see to it that the fundamental questions raised by the developments of biology and medicine are the subject of appropriate public discussion in light, particularly, of relevant medical, social, economic, ethical and legal implications, and that their possible application is made the subject of appropriate consultation." Even if only 29 countries ratified the Oviedo Convention, it should applied everywhere.

The ensuing discussions were friendly and enlightened, allowing for a very rich 2-hour panel time that we highly recommend the reader to enjoy.

COMMUNITY CONTRIBUTIONS

Statement on the regulation of gene editing for crop breeding

Statement promoted by the ARRIGE Scientific Committee and endorsed by ARRIGE

The possibility to introduce targeted genomic changes through site-directed nucleases platforms or prime editors (i.e. gene editing) has revolutionized the research on the genetic basis of biological processes and has also opened the door to a wide range of applied uses. Among them the use of gene editing for plant breeding has been one of the fastest to be developed. This is in part because gene editing in plants does not raise the ethical questions that its use in animals, and in particular in humans, raises, but also because of the high potential these techniques have to improve, facilitate and accelerate plant breeding.

Humans have continuously selected those plants or combined different species to obtain plants better adapted to their needs since Neolithic times and plant breeding has allowed the successful improvement of crops that are the basis of world food production. The changes introduced in traits such as plant architecture, requirements for optimal growth, fruit size and composition and flowering time, are so important that cultivated plants could be considered as human inventions. Plant breeding relies on the use of available gene variants to introduce desired traits into cultivated varieties. Breeders have always used the best science to maximize the variability they can use, expanding the available gene pool to related species that are not spontaneously interfertile and, since the middle of the last century, inducing additional random mutations with physical or chemical agents. Random mutagenesis has been widely used and there are thousands of plant varieties derived from these techniques available in our markets **(1)**. However, these techniques require the genetic screening of large mutagenized populations to search for the desired mutation, and a process of breeding out the undesired mutations that is long and tedious, and frequently incomplete. This is even more difficult for polyploid crops, where several gene copies have to be mutated to result in a new phenotypic trait. In addition, the randomness of these techniques makes it difficult to obtain new traits that require the introduction of precise genetic changes. Against this background, the possibility that gene editing technologies offer the selective introduction of precise nucleotides changes, constitutes a real advancement in the field.The genomic changes introduced are of the same nature than the ones resulting from spontaneous mutations or random mutagenesis and therefore, in general, no additional risks are foreseen linked to the process of gene--editing

The first products obtained from gene-edited crops reached the US market in 2019, and there are already an important number of crops approaching approval in different countries and that will reach the market soon. However, as it has already happened in the past with other biotechnology innovations in crop breeding, such as the use of transgenic plants, the development of gene-edited crops is not progressing at the same pace worldwide.

Although the commercialization of gene-edited crops requires a notification through a process that differs from country to country, and many of them decide on a case-by-case basis, most processes do not require an extensive safety analysis of plants containing only few nucleotide changes. This is the case of Canada and USA but also of Argentina, Brazil, Australia, Japan and India among others **(2)**.

In the European Union (EU), discussions among Member States to decide on the legal status of gene-edited crops started as early as 2008, but no consensus on the regulation of gene-edited crops was reached. Following a request of different French organizations, the European Court of Justice (ECJ) issued a ruling on July 2018, which consider that the GMO Directive 2001/18/EC is also applicable to organisms obtained by mutagenesis techniques that have emerged since its adoption. As a consequence,and in contrast with the procedure for randomly mutagenized plants, gene-edited crops would have to follow the long and expensive GMO risk assessment process as a pre-requisite for commercial approval. This decision has generated an intense debate among scientists and stakeholders.

First, there is the claim that these costs will seriously limit these techniques to high commercial value traits developed by big-enough companies that can afford the high costs associated with the approval process.Among the scientific community there is also the concern of the lack of scientific basis justifying regulating different mutations obtained by random mutagenesis or gene-editing that are similar or actually identical. Notably, the GMO EU Directive 2001/18/EC requires the development of a specific detection method for each GMO as a pre-requisite for approval, which, as mutations introduced through gene-editing are indistinguishable from spontaneous mutations, renders the GMO EU Directive 2001/18/EC is impossible to apply, as such, to gene-edited crops.

For these reasons, the Group of Chief Scientific Advisors of the Scientific Advice Mechanism of the European Commission recommended revising the existing GMO EU Directive 2001/18/EC to reflect current knowledge and scientific evidence, in particular on gene editing and established techniques of genetic modification **(3)**. There is ample consensus in the scientific community that the GMO legislation is not fit-for-purpose. For example, ALLEA, the European Federation of Academies of Sciences and Humanities, which represents more than 50 academies from over 40 EU and non-EU countries, considers that continued policy restrictions may hamper the selection of more productive, diverse, and climate-resilient crops with a reduced environmental footprint, and urges for a revision of the legal framework that considers both potential benefits and risks **(4)**.

As a first step to redefine the legal status of gene-edited crops in the EU, the Council of the European Union requested on October 2019 the European Commission to submit a study to clarify the situation and propose a possible way out by April 30 2021.

European scientists and stakeholders are waiting for this study to be published and the EU-SAGE network, representing researchers from 133 leading European plant science institutes and learned societies have recently sent a letter to the President of the European Commission and to several Commissioners that points to the need that the study will promote a proportionate, non--discriminatory regulatory status of genome-edited crops under Union law and to the requirement of an internationally harmonized approach to the regulation of gene-edited crops **(5)**.

ARRIGE is an international non-governmental organization that promotes the development of genome editing technologies within a safe and ethical framework for individuals and for our societies. ARRIGE agrees with the content of the EU--SAGE letter and advocates for a proportionate and science--evidence based regulation, which focuses more on the characteristics of the final product and less on the technique used to develop it. This decision does not only affect the EU, but it may also have impacts on international trade and cooperation with developing countries, and very likely, also on the EU research and innovation landscape. This regulation should ensure the safety of the products while facilitating the use of gene--editing to help breeding the best possible crop varieties needed for a sustainable and equitable food production in the context of global population growth and climate change.

8 April 2021

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(3) Statement by the Group of Chief Scientific Advisors. A Scientific Perspective on the Regulatory Status of Products Derived from Gene Editing and the Implications for the GMO Directive, 13 November 2018
(4) Academies' report reviews debate on genome editing for crop improvement. 29 October 2020
(5) EU-SAGE letter to the President of the European Commission and to several Commissioners, February 2021

Recent News & Publications

- Sheetal Soni, *Covid-19 and gene editing: ethical and legal considerations*, published in The Conversation (https://theconversation.com/covid-19-and-gene-editing-ethical-and-legal-considerations-138164)
- Bonginkosi Shozi, *Does human germline genome editing violate human dignity? An African perspective*, published in the Journal of Law and the Biosciences (https://doi.org/10.1093/jlb/lsab002)
- Francine Ntoumi, *What if tropical diseases had as much attention as COVID?* Nature 587, 331 (2020) (https://doi.org/10.1038/d41586-020-03220-5)
- Hervé Chneiweiss and Dr Jusaku Minari from Kyoto University were invited to participate in a scientific program on Genome editing for the NHK public television in March 2021.
- Sheetal Soni has been appointed as a member of the Gene Editing Technology Initiative (GETI) Working Group, organized by the Network of African Science Academies and Africa Harvest.

More information available at https://arrige.org/

You can register to ARRIGE here

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