Potential impacts of genome editing on climate adaptation and mitigation

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EXECUTIVE SUMMARY

Climate change poses an enormous challenge to plant agriculture. Crops will need to endure weather extremes, including heat, drought and excess precipitation. New pathogens will also emerge as ecosystems adapt to new climate norms and the geographic range of insects and fungal and bacterial pathogens are altered.[1] There is clearly a need for new crop varieties that can withstand these abiotic and biotic challenges. Further, these new varieties will need to rely on fewer inputs, such as water and fertilizer, as such inputs will become increasingly costly and difficult to attain.[2]

Whereas some new plant varieties will help to weather the storm, others can actually mitigate the climate problem. Plants naturally fix carbon from the atmosphere, and even a modest increase in the amount of carbon that is captured by major row crops and converted to biomass equates to millions of metric tons of fixed CO2 per year.[3] Further, if the increase in biomass occurs in the roots in the form of biomolecules that are slow to degrade, then captured carbon will only slowly be released back into the atmosphere.[4]

Over the past 120 years, plant breeders have made remarkable progress in developing new crop varieties with novel traits, including increased productivity.[5] However, the pace and scale of climate change will make it difficult for traditional breeding methods to generate the varieties needed to sustain food security and ameliorate the problem of increased CO2. New tools are available to help tackle this problem. In the past decade, powerful gene editing technologies have been developed that give us control over the plant's genetic blueprint.[6] Gene editing makes it possible to introduce precise changes to the plant genome, accelerating the production of new crop varieties, including those that better withstand the stresses induced by a changing climate as well as those that capture and store excess atmospheric CO2.

GENETIC DIVERSITY UNDERLIES CROP IMPROVEMENT

Since the advent of agriculture, humans have advanced plant varieties that provide an abundant, healthy source of food.[7] Species have been transformed by iteratively identifying the best performing individuals and then propagating them in the next generation. A modern crop such as maize, for example, barely resembles its ancestral, grassy relatives in both plant architecture and productivity. Plasticity in plant form and function arises from changes in the plant's genome brought about by spontaneous mutation, genome duplication or crosses with distant relatives. The diverse array of fruits and vegetables in the produce aisle of our grocery stores is the result of human selection imposed upon genetic diversity that occurs naturally. Modern breeding still relies heavily on genetic diversity that exists in the gene pool or arises spontaneously.

In the last century, methods have been developed to deliberately create genetic variation of value to augment the variation that occurs naturally by happenstance. For example, novel genetic variation can be created by exposing plants to mutagenic chemicals or high energy radiation, both of which alter the alter the plant's genome.[8] A drawback to this form of mutagenesis is that it provides no control; large mutant populations of plants must be generated, planted and screened in the hope of identifying genetic variation of value. Additionally, mutagens typically alter multiple loci, sometimes creating unwanted genetic changes that necessitate multiple rounds of crossing to isolate desired DNA sequence modifications in a preferred genetic background.

More recently, biotechnology has been used to create new traits of value. Transgenesis involves the addition of new genes to plant genomes that confer traits such as insect tolerance or herbicide resistance.[9] These genes typically originate from distantly related organisms, such as bacteria, and therefore cannot be introduced into the plant genome by crossing. Plants with foreign DNA in their genomes are considered genetically modified organisms (GMOs). To date, transgenesis has only been deployed in a handful of high-value row crops. Transgenic crops are highly regulated, and clearing the regulatory process is costly.[10] Further, consumer-driven concerns over GMOs have limited the widespread use of this technology globally.

THE ERA OF GENE EDITING

With the advent of gene editing, it is now possible to create genetic variation with a high degree of precision and specificity. No longer are we reliant on genetic variation that already exists within a species' gene pool, arises spontaneously, or is induced by chemical or radiation mutagenesis. Further, the genetic variation created through gene editing does not necessitate introducing foreign DNA into the plant's genome, thereby gene editing does not create a GMO.

The science behind gene editing

Once a gene editing reagent finds its site in the genome, it introduces DNA damage, the repair of that damage results in the desired DNA sequence modification. Native CRISPR systems, for example, break both strands of the DNA double helix.[13] The broken chromosomes are rejoined by cellular enzymes, but sometimes the repair is imprecise, and bases are lost at the cut site. [14] If imprecise repair occurs within a gene's coding sequence, the result can be loss of gene function. Alternatively, DNA repair templates can be provided that carry sequence information to be copied to the break site. This allows for a variety of DNA sequence changes to be incorporated into the genome, from single base changes to the insertion of thousands of base pairs. Some specialized CRISPR reagents chemically modify DNA bases at the target site without introducing a DNA double strand break.[15] Repair of these modified bases results in predictable single base changes. The suite of targeted CRISPR gene editing reagents continues to grow, providing increased control over the number and types of DNA sequence changes that can be readily accomplished.

How does gene editing work? Gene editing is based on DNA targeting; that is, the delivery of molecular reagents to specific sites in complex genomes. The maize genome, for example, is comprised of 2.3 billion bases – the G's, A's, C's and T's that make up the DNA code.[11] To create a trait of value, perhaps only one or a few bases need to be altered. Gene editing reagents must be able to scan the 2.3 billion bases and home in on the bases that need to be changed. DNA targeting was first achieved by engineering DNA binding proteins to recognize specific DNA sequences.[12] In 2012, the discovery of RNA-guided DNA targeting by CRISPR systems made identifying specific sites in complex genomes simple, inexpensive and easy to achieve.[13] CRISPR opened up a new era of biology in which imagined genetic variation could be realized.

The advent of gene editing closely follows the era of Next Generation Sequencing (NGS) – a period of more than a decade in which our capacity to sequence genomes grew exponentially. We now have high quality genomes for most domesticated crop species and numerous wild plants.[16] Coupled with DNA sequence information are enormous datasets documenting gene expression and metabolite profiles in various tissues throughout the life cycle of many plant species. Gene editing makes it possible to test hypotheses generated from analysis of this data to gain a better understanding of how plant genomes dictate growth and development and respond to abiotic and biotic stresses. This information, in turn, can be harnessed to develop new crop varieties through gene editing with improved traits, including those that can better withstand a changing climate.

OPPORTUNITIES FOR GENE EDITING IN THE FACE OF A CHANGING CLIMATE

Although deployment of gene editing for crop improvement is still in its infancy, in the decade since the discovery of CRISPR, remarkable progress has been made. Applications of the technology to help plants respond to climate change are abundant and clear, as are opportunities to design plants to slow the pace of climate change.

Abiotic stress. Crops of the future will need to be highly resilient to intense heat and changing patterns of precipitation. In some species, such as rice, genes have been identified in certain accessions that confer flooding tolerance, and with the genetic basis for tolerance understood, gene editing could be used to distribute this trait more broadly.[17] For most plants, however, drought, heat and flooding tolerance are conferred by the action of multiple genes.[18] Basic research being conducted in species such as sorghum and millet will help us understand how these genes operate.[19, 20] Gene editing can determine the genetic underpinnings of these tolerance traits, and then we can introduce the relevant genetic information into crop varieties to increase abiotic stress tolerance.

Resistance to pests and pathogens. Increased abiotic stress will make plants more susceptible to biotic stresses, such as insect, fungal and bacterial pathogen attack.[1] Further, warmer temperatures will increase the abundance of some pathogens and alter their geographic distribution. Crop varieties resistant to fungal and bacterial pathogens are typically developed by crossing resistance genes from non-elite varieties or wild relatives into commercial cultivars.[21] The hybrids are then backcrossed to the susceptible parent for multiple generations to ultimately achieve disease resistant, elite germplasm. Such breeding programs require considerable time – up to a decade for some species – which is perilously slow considering how rapidly the climate is changing. In as little as a year, gene editing has introduced tolerance to fungal pathogens of wheat [22] and bacterial pathogens of rice [23] by modifying genes important for pathogen resistance and response. One can imagine a future where gene editing obviates the current time-consuming approaches to create disease resistant cultivars through breeding.

Carbon sequestration. Plants naturally capture carbon from the atmosphere and sequester it in the above- and below-ground portions of the plant. Unfortunately, this form of carbon storage is often temporary. After plants die and decompose, the carbon is returned to the atmosphere.[3] Gene editing could be used to shunt captured carbon into compounds more resistant to decomposition, such as suberin, a carbon-rich compound found in the roots of many plants.[24] Further, root architecture could be changed to increase the below-ground biomass and thereby increase the amount of carbon that can be stored.[25] Even a very small increase in the amount of carbon stored in soil by the major row crops could result in millions of metric tons of carbon being scrubbed from the atmosphere.[3]

Increasing efficiency of carbon capture. Whereas all plants perform photosynthesis to capture CO2 from the atmosphere, some plants have evolved much more efficient photosynthesis mechanisms. The so-called C4 plants, such as maize and sugarcane, are up to 50% more photosynthetically efficient than C3 plants, such as rice and wheat.[26] Efforts are underway to engineer C3 plants to perform C4 photosynthesis.[26, 27] To enable the C4 trait, gene editing will be needed to alter the genome to implement changes in leaf architecture and metabolism. If successful, it is estimated that rice yields could be boosted significantly, and since native C4 plants consume less water, the engineered C4 plants will likely be more drought tolerant.

De novo domestication. Remarkably few plant species provide the food that sustains humankind. Through the process of domestication, changes in the expression and activity of a handful of regulatory genes have resulted in the remarkable physical transformation of wild progenitors into the highly productive modern crops we rely on for food. [7, 28] As the climate changes, we will benefit from cultivating new species that can tolerate extremes of weather or flourish on marginal lands. Gene editing can greatly accelerate the domestication of these species by modifying key regulatory genes to enhance their productivity. One candidate for domestication is tef – a cereal staple of Ethiopia and Eritrea. Tef productivity is hampered by seed loss that occurs upon lodging. Gene editing has already succeeded in creating semi-dwarf varieties of tef that promise to have increased yield.[29] Traditional breeding methods were unable to obtain semi-dwarf varieties of tef, despite decades of effort.

Redesigning seed biochemistry for sustainability. Grain harvested from row crops provides the carbohydrates, fats and proteins that sustain humankind. Different crops vary in the composition of one or more of these three macronutrients, making each crop valuable for specific food applications.[30] For example, the oil from sunflower is high in mono-unsaturated fats, which is ideal for frying, whereas palm oil is high in poly-unsaturated fats, making it a preferred choice for margarines and spreads. More than 51% of the world's sunflower oil comes from Russia and the Ukraine, whereas 84% of the palm oil comes from Malaysia and Indonesia.[31] In the U.S., the primary oil crop is soybean. Gene editing has already been used to make soybean varieties that produce a cooking oil equivalent in fatty acid composition to sunflower oil.[32] Why not also make a soybean variety that makes a palm oil equivalent? If soybean varieties were made through gene editing that meet our needs for different types of cooking oil, then the U.S. would have a domestic source of these products, minimizing the ongoing deforestation of Southeast Asia required to sustain palm oil cultivation and obviating the fuel-intensive shipping required to move these commodities around the world.

RECOMMENDATIONS

To fully realize the opportunity gene editing provides to help address the climate crisis, it will be important to produce edited plants faster, with less cost, and at scale. Research should focus on overcoming technical bottlenecks to achieve high throughput editing, so multiple genetic changes can be made simultaneously to optimize gene function and achieve climate tolerance. Further, a concerted, global effort is required to establish a science-based regulatory framework, so that deployment of the technology is not impeded by discordant regulatory policies.

Realizing the full potential of gene editing

Scaling the production of gene edited plants. Most gene edited plants are produced from single cells grown aseptically in Petri dishes, which requires up to 6-12 months. Further, the approach only works well with a handful of plant species, and frequently unintended changes occur in the plant genome. It would be ideal if the Petri dish could be avoided entirely, and gene editing reagents were delivered directly to the cells that give rise to flowers and seed, making it possible to produce gene edited seed in a single plant generation. Regardless of the ultimate technical solution, high throughput methods that generate heritable gene edits in diverse plant species are needed if this technology is to live up to its potential.

Trait discovery through gene editing. As described above, we still have a rudimentary understanding of the genetic basis for many traits – such as drought and flooding tolerance – that are needed to help crop plants withstand a changing climate. As gene editing methods become more robust, the technology can be used to accelerate our understanding of the genetic basis of these traits. Identifying key genes will be achieved by integrating data from genetic mapping studies, gene expression analyses and other phenotypic readouts, coupled with sophisticated computational approaches to refine predictions of gene function. Accelerating trait discovery will, in turn, accelerate the production of climate resilient crops.

Harmonizing global regulatory policy. The types of changes made to plant genomes through gene editing are typically no different than the types of genetic changes that arise spontaneously in nature. Further, gene editing can be performed without the addition of any foreign DNA, so that the end product is a non-GMO. A science-based regulatory policy is needed that assesses plants with traits created through gene editing to ensure their safety to the environment and to the humans and livestock that consume them. Ideally, this policy would be harmonized so that gene edited crops can be grown and distributed on a global scale without impediment.

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