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Gene-Editing. New Genetic Engineering Techniques, Yes or No? “Who’s Thinking Outside the Box?”

Award-winning Article Gives Both Sides of the Gene-editing Debate. Leading German publication quotes the warnings of critical scientists and experts

By Angela Lieber and GMWatch
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The following article from the German weekly newspaper Der Freitag is a vanishingly rare example of both sides of the debate about new GM techniques getting coverage in the mainstream media.

All too often journalists allow GM promoters to determine the narrative on topics like gene editing while the concerns of critical scientists go unreported.

The problem with that, as Dr Michael Antoniou notes in the article, is that, “Those who work on the development of such plants seem to believe almost blindly in their own propaganda regarding the precision and predictability and thus in the safety of their products – without the necessary studies to prove their position.”

The author of the Der Freitag article, Angela Lieber, was awarded the Salus-Medienpreis (Salus Media Prize) 2019 for her work on this article.

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Who’s thinking outside the box?

by Angela Lieber
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English translation of German language article by Deepl/Google Translate/GMWatch

Gene editing: The ruling of the European Court of Justice divides the agricultural sector. What potential do new genetic engineering techniques hold for plant breeding?

Virus-resistant cucumbers, allergen-free peanuts, and maize that better withstands drought and heat: The list of current research projects is long, as are the advantages that breeders and seed companies around the world hope to see from the use of new biotechnological processes in agriculture. With the help of so-called “genome editing methods” such as the gene scissors CRISPR/Cas, the genome of useful plants can be changed precisely and in the shortest possible time. It’s not only in this country that farmers and consumers could benefit from such types of fruit and vegetables.

Globally, an important contribution to the nutrition of the growing world population would be made – according to the advocates of the new technologies. In addition, pesticide use could

be reduced and food ingredients could be changed as needed. Holger Elfes, press spokesman for Bayer CropScience, summarizes the potential of the new technologies: “We expect a drastic acceleration in the breeding of new varieties that are less susceptible to diseases, pests or drought – and of course achieve a higher yield” – a process that in conventional breeding can take up to ten years or longer could be halved with the new methods. “This enables farmers to react more quickly to emerging plant diseases or changing climate cycles.”

From sick apples …

In view of these promising possibilities, even some representatives of the organic industry have recently raised the question of whether the use of the new methods should be rejected in principle – especially since their intervention in the genetic material is less serious than that in the context of classic genetic engineering. Because, in the latter case, DNA from bacteria or animals was sometimes introduced into the genome of maize, oilseed rape or soybean, foreign DNA is rarely used in the new technologies. Instead, you can change genes in a targeted manner or transfer genes from related species into the plant’s genetic makeup. Urs Niggli, Director of the Research Institute for Organic Agriculture (Fibl) in Switzerland, also recently spoke in favour of using the CRISPR/Cas gene scissors to make apples resistant to apple scab – one of the most important apple diseases worldwide. For this purpose, he suggested that the resistance gene of the Japanese crab apple (malus floribunda) be introduced into today’s cultivated apples. (Lebensmittelzeitung 06/2018).

For orchardist and apple grower Hans-Joachim Bannier from Bielefeld, looking at the history of modern apple cultivation, it would become clear that this idea – “to believe that a single gene can save a species that has long since developed in a risky direction” – is fundamentally wrong, says Bannier. He explains: “For around 80 years, almost only five apple varieties and their descendants have been grown worldwide: Golden Delicious, Cox Orange, Jonathan, McIntosh and Red Delicious. The reason these varieties are so popular is because they bloom more often and therefore deliver higher yields – but only if you spray them heavily. ”The apples are actually highly susceptible to disease. And only since the chemical industry began supplying the appropriate pesticides in 1930 did it suddenly become possible to grow them on a large scale.

“When the varieties were used in organic farming in the 1980s, it quickly became clear that they were infected by pathogens far too often,” Bannier continues. But instead of going back to the old, somewhat less productive, but much more robust apple varieties, [breeders] simply crossed the already known resistance gene of the Japanese crab apple in the classic way [by breeding] into the disease-prone cultivated apples. “It is exactly the same gene that now they want to transfer back into the genome – but using genetic engineering,” says Bannier, shaking his head. To start with, the tactic with the resistance gene worked, but today the apple scab is back in many places. “Once the fungus has eluded the gene by mutation, the immunity of the apples collapses – and also because their rest of the genome is so susceptible: not only to apple scab, but also to mildew and other diseases.”

Short-term “solutions”

Bannier is therefore very concerned about current developments in plant breeding. Even with other fruits and vegetables, the main focus today is on disease-prone varieties that are only successful with the continuous use of pesticides. “This is a conflagration! And now the genetic engineers want to go in there and clear it bit by bit, by putting individual genes in

an otherwise sick and genetically impoverished strain!" Of course, you could always offer and sell 'solutions' in this way: "But such resistances don't last long. They break through pests and pathogens pretty quickly."

It is different with many traditional varieties that can still be found in orchards today. "With these varieties, several genes are almost always responsible for immunity, for example with the 'Seestermüher lemon apple'. It is not only productive, but also multi-resistant to scab, powdery mildew and fruit tree cancer."

For Bannier, the fact that these apples are hardly known to any breeder today is a real mistake:" We have well-trained molecular geneticists, but they no longer know the old varieties," he scolds. "You can no longer study them at a university or institution of applied sciences" – one of the many reasons why the apple grower fights against the disappearance and forgetting of the old varieties. He regularly takes visitors through his orchard, where more than 300 varieties, some of which have been forgotten, thrive – and all without pesticides. Bannier is convinced: "What we need today is a return to locally adapted and genetically diverse varieties. Clearly, this breeding path is tedious. But the supposedly faster genetic engineering will not be able to solve the problems of modern agriculture in the long term!"

Felix zu Löwenstein, organic farmer and chairman of the organic umbrella association for the organic food industry (BÖLW) also criticizes the "tunnel vision of the genome" – as he puts it. When he first heard about CRISPR, there was talk of trying to keep a banana virus at bay through genetic engineering. "At that time, no one asked how smart it is that we are traveling around the world with a single type of banana that is also grown in huge plantations – banana, banana, banana, banana," said Löwenstein. "We have created incredibly unstable systems with industrial agriculture. And if we now save them a little bit more by tinkering with the genetics of plants, then we will ignore the real problem."

For him, it is therefore not a question of whether genome editing is good or bad in principle. The question is rather whether a technology is suitable for creating ecologically stable systems. "Quite apart from the fact that there are also risks that have to be assessed with great caution."

Genetic engineering – yes or no?

It was precisely those potential risks that caused the judges of the European Court of Justice (ECJ) in Luxembourg at the end of July to rule that all genome editing processes must be subjected to European genetic engineering law and that all resulting products (plants and animals) must be regulated as genetically modified organisms (GMOs). For months there had been speculation about whether the new technologies would be classified as conventional breeding methods and would therefore be released without safety assessment and labelling. Martin Häusling, Member of the European Parliament and agricultural policy spokesman for the Greens/EFA Group, is pleased with the clear verdict: "Now all plants that are bred with the new methods must be checked for possible risks before they are approved."

In addition, there is a labelling requirement, thus retaining the freedom of choice for consumers to buy such products or not. "I am relieved that the ECJ made a decision based on the precautionary principle and verifiability," said Häusling. "Consumers can now no

longer be sold hidden genetically modified products and breeders know what material they are dealing with."

At the Federal Association of German Plant Breeders (BDP), on the other hand, enthusiasm is limited. "The judgment surprised us. We have always advocated a differentiated assessment of the new breeding methods, according to which genetically modified organisms arise in some cases, but not in others," said association chairwoman Stephanie Franck. In the run-up to the ECJ ruling, there was a fierce discussion about whether there could be exceptions in the event of regulation. In some cases, genome editing only triggers point mutations – similar to a natural mutation (e.g. caused by UV light) or mutations in the context of traditional breeding methods. And as long as a genome-edited product cannot be distinguished from a product from traditional breeding, it does not have to be regulated separately, or so the proponents argued.

For Michael Antoniou from King's College in London, this debate has worrying features: "Genome editing is always a laboratory-based, genetic modification process and therefore per se leads to a genetically modified organism," says the scientist, who has worked in the field of genetic research for human medicine for more than 30 years. Claims that one only has to look at the result and not the process by which a product is created are anything but scientific and are potentially dangerous. The particular method is absolutely crucial in science. "If you move away from this principle, possible side-effects and their consequences will be completely ignored!" And the molecular geneticist is convinced that there can be such side-effects.

Lack of risk research

Regardless of whether ZFN, TALEN, ODM or CRISPR/Cas is used, all genome editing processes follow a similar principle. First, the site that is to be changed must be found in the massive genome of the plant. For this purpose, special "probes" are constructed in the laboratory, which search the genetic material in order to dock onto the target sequence identified. The DNA double strand is then cut open with the aid of an enzyme coupled to the probe (hence the term "gene scissors"). In response to the cut, the plant's own cell repair mechanisms come into force to "patch" the DNA break again. And it is precisely this process that is now used to bring about the desired change – for example, a point mutation or the inhibition or activation of a specific gene.

But although most genome editing processes change the gene structure at a predetermined point and are therefore very precise and targeted, there are potential sources of error – as scientist Antoniou explains. In addition to cuts at unintentional locations in the genome, neighboring genes can also be disrupted in addition to the actual target site. In addition, even intended changes could lead to unforeseen biochemical reactions. "All of this can change the nutritional profile of a plant from scratch – up to possible toxin and allergen production."

Christoph Then, Managing Director of Testbiotech, an institute in Munich that critically examines the new biotechnology processes, also fears potential risks: "Of course, it is theoretically possible that genome editing can also result in plants that do no harm." However, what is decisive are the possibilities that the system offers. "You can also use it to switch off entire synthetic routes or delete entire gene families that previously were not accessible via breeding." And he doesn't find convincing the argument that classical mutagenesis (breeding techniques that work with chemicals or radiation) that has been

permitted [in conventional breeding] since the 1970s would change the genetic code much more extensively: “[In classical mutagenesis] you still use the mechanisms that evolution has developed for mutations. With the new genetic engineering, on the other hand, we intervene directly at the level of the DNA – that is another level of intervention,” says Then, who criticizes the lack of risk research in Germany in particular: “There are currently almost no government research programs on this.”

This is a fact that molecular geneticist Antoniou also criticizes on an international level: “Those who work on the development of such plants seem to believe almost blindly in their own propaganda regarding the precision and predictability and thus in the safety of their products – without the necessary studies to prove their position.” From his point of view, the ECJ judgment is therefore clearly to be welcomed – especially for the consumer: “Because there is now an adequate regulation and safety assessment of these products.”

In the patent jungle

But what does the ECJ decision mean for small and medium-sized plant breeders in Europe? After all, many of them had high hopes for the new technologies – not least because they are much cheaper to use than the methods of classic genetic engineering. It suddenly seemed possible to keep up with the big seed companies. Accordingly, after the verdict was pronounced, the Bund Deutscher Plant Breeders were disappointed: “Now all plants that are developed with the help of the new breeding methods have to go through the time-consuming and financially complex approval process,” said association chairman Franck. Against this background, plant breeders see little prospect of using the methods in the development of new varieties.

“It’s true that EU approval for genetically modified plants costs time and money,” admits Christoph Then, “but I don’t think this is an absolute market obstacle for smaller companies if they calculate that they will have products afterwards that are actually in demand by farmers and consumers.” However, these small companies are not able to survive in the context of patents. In contrast to traditional breeding methods, all genome editing applications are in principle patentable. “And this is where the large corporations are currently massively laying down their claims: DowDuPont has already submitted around 50 international applications, ‘Baysanto’ around 30, and Calyxt, Syngenta and BASF are also actively involved.” Only a few patents have so far been registered by smaller breeders.

For Heike Moldenhauer, formerly Head of Genetic Engineering at the Federation for the Environment and Nature Conservation (BUND), this is a clear indication that deregulation of the new technologies would not have strengthened the competitiveness of small breeders – on the contrary: “The little ones could research and develop, but as soon as they brought a variety to the market and wanted to offer it commercially, they would have to deal with the patent question – and in the best case would have to pay license fees or in the worst case a patent infringement fee.” In general, the patent system, which involves expensive lawyers and litigation, could only be afforded by large corporations with the appropriate financial resources.

Christoph Then also believes this and refers to the example of the USA: “There, the patents in connection with classic genetic engineering have contributed to the fact that the medium-sized plant breeders have almost completely disappeared.” So whoever really wants the new gene-editing processes to be used by smaller breeders, must first abolish the patents. Heike Moldenhauer therefore advocates a corresponding amendment to the EU patent

directive: “To do this, however, the EU Commission would have to take the initiative – but there is too little pressure from the member states. Or too much lobbying from those who profit from the status quo.”

Future challenges

So what’s going to happen in the future? Is gene editing, with its potential opportunities, but also risks, now being slowed down in Europe? Heike Moldenhauer is convinced that it will be more difficult for agricultural companies to sell gene-edited seeds in Europe. “Because they now have to be labelled as ‘genetically modified’ and marketed just like the plants and products that result from them.” A fact that will also have consequences for the import sector. In the USA, for example, a few genome-edited products have already been released without regulation and safety assessment. For a corresponding approval in Europe, their genetically engineered origin will now have to be communicated openly – including transparent detection procedures. “The ruling by the European Court of Justice obliges the EU Commission to enforce the laws applicable to Europe against our trading partners,” comments Moldenhauer. “Anything else would be a clear violation of the law.”

As far as plant growing itself is concerned, the new technologies can of course continue to be used for research and breeding – also in Europe. “The judges didn’t give an evaluation for or against gene editing. They only correctly stated that the processes and products fall under the currently applicable genetic engineering law,” explains Felix zu Löwenstein. And there are already a number of promising projects that point to the future potential of new technologies, for example in the area of drought and heat tolerance of crops. For example, researchers in the United States have succeeded in increasing the tolerance of maize to water shortages, as well as that of soybeans. However, Heike Moldenhauer remains skeptical: “Not a single new crop with these properties is yet on the market.”

Tolerance features in particular are highly complex and are based on the interplay of numerous genetic factors. For this reason, conventional, holistic cross-breeding is more suited to achieving such traits. “The reality of the products developed so far with genome editing is a herbicide-resistant oilseed rape that increases the use of chemicals in the field, and a non-browning mushroom that you can no longer tell when it is old,” says Moldenhauer. Therefore she personally does not believe that the new genetic engineering can provide the solution to current and future challenges in agriculture – a view shared by molecular geneticist Antoniou: “Genetic engineering earns more because it is patented. However, it is not what we have been waiting for – not even with a view to the rest of the world population.” Especially in the poorer regions of Africa and Asia, genetic engineering leads above all to the certainty that the centuries-old knowledge of regional varieties would be wiped out and dependency of farmers on patents would further increase. This is different from ecological management methods, which do not require any patented technologies. Using such methods, the skills and knowledge of the local farmers are preserved. “And that is the real basis for global food security.”

Need for discussion

Heike Moldenhauer of BUND does not believe that the last word has been spoken with the judgment of the European Court of Justice: “For large companies, it is a billion dollar business. So I suspect that they will push to change the genetic engineering regulations to suit them and to introduce a new genetic engineering definition that excludes gene-edited plants. “Christoph Then from Testbiotech also remains thoughtful:” A large part of the

population is still critical of genetic engineering, but so far we have had relatively little discussion about the new methods. It remains to be seen whether and how genetic engineering will prevail in Europe," says Then – and adds:" We are only at the beginning and not at the end of the necessary social debate!"

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