Bioeconomy BW

CRISPR/Cas9 and genetic engineering laws

Transgene-free plant breeding using genome editing

Plant geneticists from Tübingen have used genome deletion to breed a variety of tomato that is resistant to powdery mildew. The CRISPR/Cas9 technology that they used enabled them to achieve this in a relatively short period of time. They also demonstrated beyond any doubt that the new tomato variety contains no foreign DNA and is indistinguishable from naturally occurring deletion mutants. The research provides convincing evidence that the European Court of Justice's decision to subject new breeding techniques such as genome editing to the requirements of genetic engineering laws is unrealistic and goes against scientific progress. This decision should be revised.

Powdery mildew on a tomato leaf
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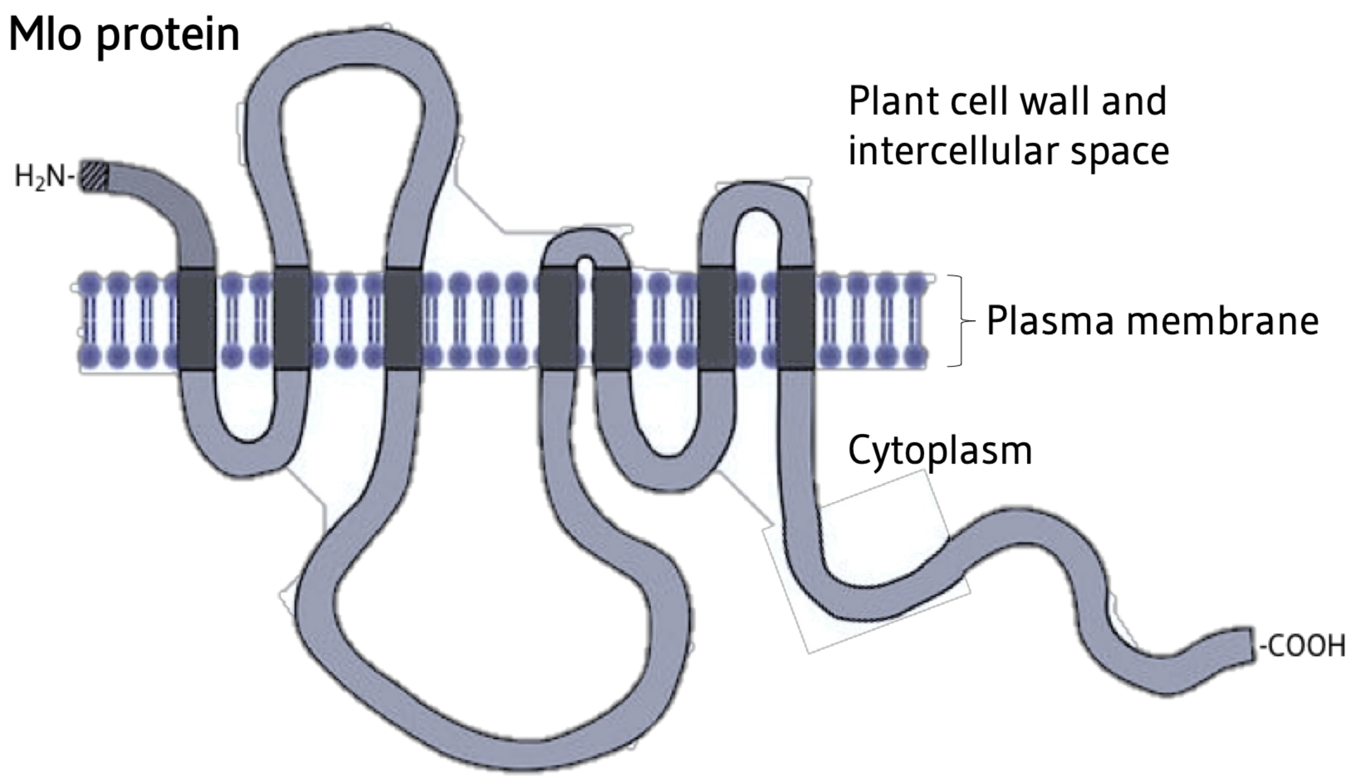
Against the current background of global climate change and the limitations and progressive destruction of natural resources, it is doubtful whether agricultural production can be sufficiently expanded to cater for a growing world population. It is therefore vital to grow crops that are better adapted to challenging environmental conditions such as elevated temperatures, lower precipitation, saline soils or new pest epidemics. Plant geneticists attempting to confront these challenges have high hopes for the new, relatively cheap and easy-to-use genome editing methods for targeted and precise gene modification. These new techniques are far superior in terms of efficiency, cost and speed to conventional plant breeding methods.

Powdery mildew-resistant tomato using genome editing

In a very short space of time, CRISPR/Cas9-based genome editing has become a world-renowned method for exploring genes and growing plants with properties that enable them to grow better in a changing environment. The gene modifications (mutations) created using CRISPR/Cas9 do not necessarily differ from mutations that can be created with classical breeding methods. But while CRISPR/Cas9 inserts the mutations at a specific desired site in the genome, mutations created using classical plant breeding methods occur at random (often induced by radioactive radiation) and need to be selected through backcrossing experiments, a time-consuming process that usually takes many years to complete. The huge advantage of the new technology is described below using the example of the powdery mildew resistance of tomatoes.

Powdery mildew is a widespread fungal disease in plants - including many important crops - and is mainly controlled in agriculture through chemical fungicides. Plant researchers are working on developing and growing powdery mildew-resistant plant varieties so that the application of fungicides can be reduced. This was achieved for barley a long time ago when a powdery mildew-resistant barley mutant was discovered and subsequently mutagen-induced. Powdery mildew (Oidium neolycopersica) was detected for the first time on tomatoes in 1992 and has since spread across the globe. It occurs mainly in greenhouse crops, but increasingly also in field-grown tomatoes, and causes enormous damage.

The parasite interacts with the host plant via the Mlo (mildew resistant locus O) protein, a highly conserved, integral membrane protein that winds like a snake seven times across the plasma membrane. While its biochemical activity is unclear, it is known that the protein confers susceptibility to fungi that cause powdery mildew diseases. Loss-of-function mutations therefore result in resistance to powdery mildew. Quite a number of such genes in the genomes of all higher plants are known. In tomatoes



Schematic showing the Mlo protein in the plasma membrane of a plant cell.
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(Solanum lycopersicum), the gene SlMlo1 is the main culprit behind susceptibility to mildew. Scientists have also found naturally occurring SlMlo1 mutations that make the gene dysfunctional and cause powdery mildew resistance. However, the transfer of such mutations using classical breeding methods such as hybridisation and backcrossing to produce economically high-quality tomato varieties is an extremely tedious and laborious process.

In 2017, Prof. Dr. Detlef Weigel, plant geneticist and director at the Max Planck Institute for Developmental Biology in Tübingen, described how he and his British colleagues managed to create a powdery mildew-resistant tomato ("Tomelo") in less than ten months. The powdery mildew-resistant tomato has a deletion in the SlMlo1 gene. This work is significant for two reasons. Firstly, because it demonstrates how precise CRISPR/Cas9 is, and how fast and how efficiently it can be used to create a new crop variety. And secondly, because the new variety, which was created by deleting 48 base pairs in the SlMlo1 gene, contains no foreign DNA at all and is totally indistinguishable from corresponding, naturally occurring deletion mutants. Weigel and his colleagues were able to clearly demonstrate this using whole genome sequencing.

The European Court of Justice rules on the Tomelo

The Tomelo is a genetically engineered but not transgenic organism. No "natural species barrier" was crossed during the process. According to American legislation, the new type of tomato is not a GMO (genetically modified organism) nor is it a GMO according to the definition of the German Genetic Engineering Act, which classifies an organism as GMO "if its genetic material has been altered in a way that does not happen under natural conditions by crossing or natural recombination." It therefore bears emphasising once again that DNA changes achieved by editing the genome of plants are similar to those created in traditional breeding by mutagenesis using chemicals (for example, ethyl methanesulfonate, EMS) or radioactive radiation. While mutations created with traditional breeding methods are completely random, genome changes produced using CRISPR/Cas9 are highly specific. Nevertheless, the European Court of Justice (ECJ) ruled on 26 July 2018, that all mutants resulting from genome editing are to be regarded as GMOs and thus subject to the strict requirements of the Genetic Engineering Act. Contrary to the recommendations of expert commissions and even the assessment of the Attorney General at the ECJ, the Luxembourg chief justices ruled that the method used to produce the organism and not the result led to their decision.

It seems that the ECJ judges made scant effort to understand molecular genetic relationships. If it is impossible to discern whether a mutation in a new plant variety was created by CRISPR/Cas9 or by natural breeding, no law can realistically prevent the application of genome editing in plant breeding. However, the judges' decision may well demotivate scientists and hinder excellent plant research in Europe. Countries such as the USA, Canada and Israel have more pragmatic legislation: if the plant variety in question is not a transgenic organism (i.e. the "natural species barrier" has not been crossed) and no major gene segments have been introduced, the new plant variety may be cultivated and traded in the same way as plant varieties produced using the standard method. In the USA, Canada and Israel, nations that export agricultural produce along with Brazil, Argentina and Australia, plant breeders want to be able to grow genome-edited plant varieties, and export them. How can these plant varieties therefore be stopped from entering Europe unrecognised?

Prof. Dr. Detlef Weigel, Director of the Department of Molecular Biology at the Max Planck Institute for Developmental Biology, Tübingen
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After recovering from the initial shock of the ECJ ruling, scientists and research organisations have called for a revision of the Genetic Engineering Law that takes into account the scientific facts and the state of knowledge. Agricultural and food industry associations, as well as politicians have since signalled their support. Theresia Bauer, the Baden-Württemberg Minister of Science, has called for "a differentiated regulation of genetic engineering. The same things have to be regulated in the same way, and different things have to be regulated differently" (quoted from the weekly newspaper DIE ZEIT, 24th October 2019). The minister stressed that even the Green Party can no longer ignore the opportunities offered by genetic engineering.

Weigel and his co-workers have demonstrated with the Tomelo that the way a genome-edited plant variety is bred is comparable to that of a "natural" plant variety, and this convincingly demonstrates that the ECJ ruling of 26 July 2018 was wide of the mark. It should be revised as a matter of urgency. Unfortunately, high-court jurisdictions are known for their determination and stubbornness, and this is likely to take a long time. But let’s hope that the facts will win out in the end.

Prof. Dr. Detlef Weigel

The German-American Detlef Weigel is one of the most renowned plant geneticists in the world. He is an elected member of high-profile scientific societies such as the National Academy of Sciences of the United States, the Royal Society, the German Academy of Sciences Leopoldina and the European Molecular Biology Organisation. Weigel's many awards include the 2019 Barbara McClintock Prize for Plant Genetics and Genome Studies, given in memory of one of the most important women in the sciences in the 20th century.

References:

Nekrasov V, Wang C, Win J, Lanz C, Weigel D, Kamoun S: Rapid generation of a transgene-free powdery mildew resistant tomato by genome deletion. Scientific Reports 7:482. DOI:10.1038/s41598-017-00578-x(2017)

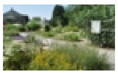
Article

27-Nov-2019
Dr. Ernst-Dieter Jarasch

Further information

- Original publication (Nature)
- Top-class plant research in Tübingen
- Natural genetic engineering

The article is part of the following dossiers



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