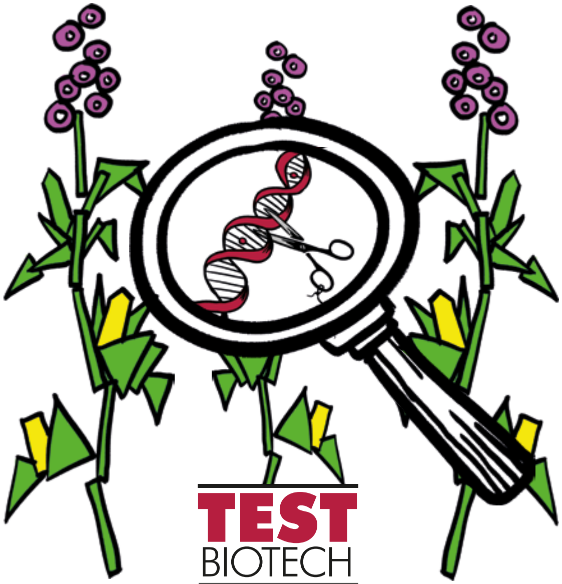
WHAT IS (NOT) GENETIC ENGINEERING?

It is often claimed that new genetic engineering methods like CRISPR/Cas only do what continuously happens in nature anyway. Is this really true?



TESTBIOTECH

In 2012, the discovery of CRISPR/Cas technology led to a new boom in the biotechnology sector. Interested parties saw a new chance of making genetic engineering in agriculture socially acceptable in Europe.

With this in mind, it is often claimed that new methods of genetic engineering, such as CRISPR/Cas, only do what continuously happens in nature anyway. Is this really true?

This booklet explains the differences between

I. CONVENTIONAL BREEDING

II. »OLD« GENETIC ENGINEERING

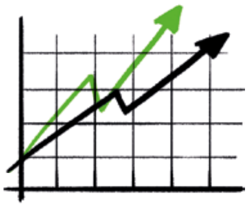
III. NEW GENETIC ENGINEERING

In addition, the RISKS are explained and a CONCLUSION is drawn on how to handle new genetic engineering.

BACKGROUND

IN 2012, the discovery of CRISPR/Cas technology led to a new boom in genetic engineering. This was because new techniques – collectively known as »genome editing« – enabled intervention into the genetic code in a completely new way.

Since then many interested parties – from the economy as well as from science – have seen a new chance to make genetic engineering in European agriculture socially acceptable. In the past, it was met with widespread condemnation: even now, almost no genetically engineered plants are cultivated in Europe.[1]



Stakeholders have long wanted to change that. Therefore, ever since the discovery of the new methods, they have been careful to use the appropriate »wording« to create the desired »framing« for the technology: no more talk of »genetic engineering«. Instead, the new techniques are referred to as »precision breeding« or simply »new breeding techniques«.

The argument put forward: the technology can be applied without inserting new genes and the changes (mutations) are indistinguishable from natural ones. Therefore, it is not genetic engineering.

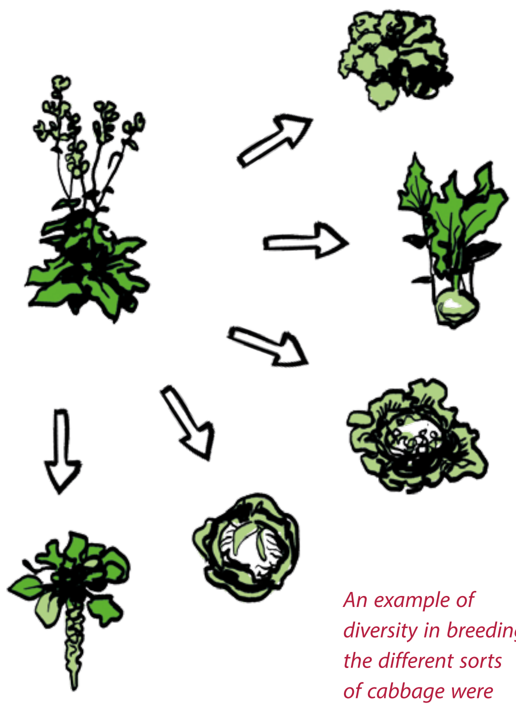
Is this really true? Are conventional breeding and the new genetic engineering techniques the same thing? What are the differences? And which risks should be considered?

[1] There is one exception: genetically engineered maize (MON810) is occasionally grown on a small scale (https://kurzelinks.de/pits)

I. NOT GENETIC ENGINEERING:

Conventional breeding

CONVENTIONAL BREEDING HAS BEEN used for thousands of years to improve crops and farm animals. It uses the mechanisms and processes of evolution; new varieties emerge, in particular, from further crossing and selection.



An example of diversity in breeding: the different sorts of cabbage were bred without genetic engineering, through spontaneous mutations, selection and further crossing.

Different »tricks« can be used to trigger mutations and increase genetic diversity, e.g. plants can be brought into contact with chemical substances to accelerate the processes of evolution. Subsequently, new mutations and new traits emerge.

Conventional breeding does not intervene directly at the level of the genome. The natural mechanisms of inheritance and gene regulation are not bypassed.

At this stage, it cannot be predicted where the changes, i.e. mutations in the genome will occur. At the same time, it is not purely coincidental. Rather, the changes underlie the natural rules of inheritance and gene regulation. Evolution has developed many diverse mechanisms to protect the preservation of species and still allow changes. These include, amongst others, repair processes in the cells and the creation of »back-up copies«. Interdependencies between plant genes and their interactions with the environment have developed and been proven over millions of years.

Conventional breeding always uses the whole cells of plants and animals that have emerged from evolutionary processes. It does not intervene directly at the level of the genome. The natural mechanisms of inheritance and gene regulation are not bypassed.

Further information in our video-series:

„What is genetic engineering?“
on: www.testbiotech.org/en/videos

II. »OLD« GENETIC ENGINEERING:

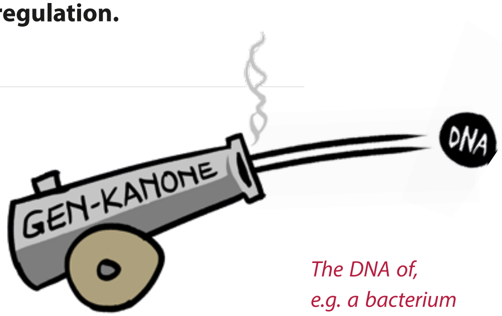
Transgenic plants

UNTIL NOW, GENETIC ENGINEERING has aimed to introduce specific new traits into plants. It involves the insertion of »foreign« genes into the plant genome.

For example, a »gene gun« can be used to introduce a gene from a bacteria into the plant genome. The aim is to, e.g. force a bacterial trait in the plant and make it resistant to weed killers. However, other unintended changes and interactions frequently occur. The risks associated with these changes need to be thoroughly investigated.

Genetic engineering of plants and animals reduces them to the functions of individual »gene building blocks« and bypasses the natural mechanisms of inheritance and gene regulation.

Genetic engineering of plants creates organisms with biological traits that have not been proven in evolutionary processes.



The DNA of, e.g. a bacterium is inserted into the genome of a plant with a so-called »gene gun«.

Genetic engineering: plants and animals are reduced to the function of individual »gene building blocks«.

Transgenic plants are created with technical procedures that intervene directly in the genome. Plants and animals are not seen as a »whole«, but reduced to the function of individual »gene building blocks«. The natural mechanisms of inheritance and gene regulation are bypassed.

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III. NEW GENETIC ENGINEERING:

Genome editing (CRISPR/Cas etc.)

NEW GENETIC ENGINEERING TECHNOLOGY makes it possible to change the plant genome in a completely new way. Similarly to the way word processing programs on computers allow us to arbitrarily rewrite texts, genome editing supposedly enables us to arbitrarily »rewrite« the code of life.

The most important tools in this process are enzymes which serve as »gene scissors«. With the help of so-called »guides«, they target locations in the genome that are to be »reconstructed«. This reconstruction can affect small or large, single or multiple sections of the genome. The gene-scissors can be used to delete genes, alter their function or insert additional genes.

New genetic engineering technology makes it possible to change the plant genome in a completely new way. New biological properties as well as new risks can be the result.

The possibilities for the application of CRISPR/Cas are much more extensive than single point mutations, e.g. multiplexing: genome editing makes it possible to alter several (identical or different) genes at the same time. Such alterations can result in new combinations of genetic material that are not possible with conventional breeding. Even if the changes only affect small sections of the DNA, they can lead to significant alterations and completely new traits in the organisms.

»Precision« is a term often referred to in the discussion on the safety of the new procedures: unlike conventional breeding, in which breeders have no influence on where in the genome mutation(s) occur, geneticists can use genome editing to predefine both the location and kind of mutation. However, it cannot therefore be concluded that this process is safe; this always depends on interactions with other genes and the environment. Precision editing of single gene-sequences does not by any means automatically imply safety. A targeted, precision edit could – depending on the context – also lead to serious harm to the affected organism and its ecosystem.

New methods of genetic engineering also bypass the natural mechanisms of inheritance and gene regulation.

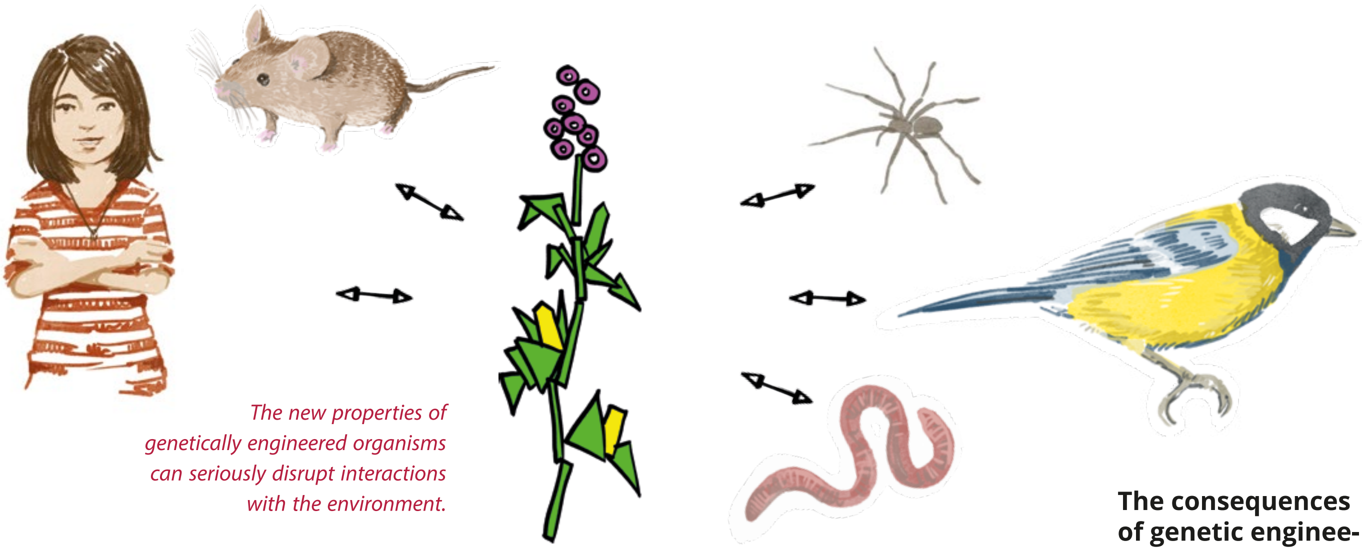
Furthermore, gene-editing techniques are prone to mistakes: it has been observed that gene-scissors can cut at the wrong place (off-target-effects), or that the wrong DNA fragments are unintentionally inserted (on-target-effects).[2]

Even if everything goes according to plan, the use of gene-scissors still leads to specific patterns of genetic change that generally differ from those in conventional breeding.[3]

Just like the »old« methods of genetic engineering, genome editing also intervenes directly in the genome. The natural mechanisms of inheritance and gene regulation are bypassed. The biological traits and risks of gene edited plants can therefore differ significantly from plants emerging over the course of evolution or from conventional breeding – even if no additional genes are inserted.

² https://kurzelinks.de/39ru
³ https://kurzelinks.de/glj6

RISKS



The new properties of genetically engineered organisms can seriously disrupt interactions with the environment.

EVEN MODERN BIOSCIENCES are still a long way from completely understanding vital biological and evolutionary processes. Often there is more interest in making a profit rather than prioritising in-depth research into natural interdependencies.

Genetic engineering applications can create the impression that a living organism is nothing more than the sum of its genes. The complex evolutionary processes of change and development are reduced to changes in the genetic code.
Both the »old« and »new« methods of genetic engineering can substantially override the natural rules of gene regulation and inheritance. These technical applications can lead to changes that are dangerous for the environment. Amongst others, there is no process of mutual adaptation in the environment as there would be over the course of evolution.
The long-term effects of the release of genetically engineered organisms and their uncontrolled spread in the environment cannot be predicted. The properties of genetically engineered organisms that propagate in the environment and hybridize with natural populations can differ significantly from those tested in the laboratory or in trial releases. Unexpected effects can lead to a significant disturbance of interdependencies in the ecosystems, as well as endanger biodiversity and species preservation.

The consequences of genetic engineering are often difficult to predict because life cannot be reduced to the sum of its individual gene sequences.

Therefore, the protection of people and the environment must be prioritised over economic interests. In addition, risks should only be taken if effective controls exist.

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CONCLUSION

IT IS CERTAINLY NOT as if nature per se is »good« and – on the other hand – technology »bad«. That said, it is clear that in nature the process of inheritance of traits to following generations follows specific rules. The new genetic engineering methods are very powerful tools; in contrast to conventional breeding methods, they make it possible to change the genetic code by bypassing the natural mechanisms of inheritance and gene regulation.

Nature has developed many different mechanisms of gene regulation to allow a balance between the emergence of new biological diversity and securing the stability of species. If mutations occur, they are not targeted, but neither are they completely random. The same applies to genetic exchanges between different species: this only works in nature under specific conditions.

In addition, there are natural processes of selection and adaptation that extend over extremely long periods of time. It is not only the change in DNA, i.e. genetic material, that is important in defining which traits are created in which organisms, but also the interactions between DNA, cells, the organism and the environment.

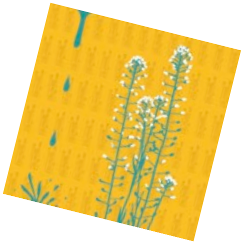
Nature works with many small steps which are subject to numerous controls. Thus, changes are possible whilst maintaining the stability of species. Perfect adaptation is the result.

Conventional breeding works with the mechanisms of natural gene regulation and inheritance. It operates within the existing rules governing natural biodiversity.

If these natural mechanisms of gene regulation and inheritance are bypassed using technical methods, then ecosystems and people could be seriously harmed.

Organisms created by technical methods, such as genome editing, should therefore undergo thorough testing. Studies show that unwanted effects and side effects often occur. Risk assessment must also take the effects that the desired properties in genetically engineered organisms and their altered biological properties have on humans, the environment, ecosystems and the preservation of species into account.

Examples showing the need for strict regulation of organisms derived from genome editing:



„INEDIBLE CAMELINA“

In the US and the EU, there is a great deal of interest in the potential use of Camelina (Camelina sativa) in genetic engineering applications. The main focus is on the production of agro-fuels and animal feed. In the US, the plants are already deregulated, even though 18 sites on the genome were altered using CRISPR/Cas gene scissors. As a result, these plants show new patterns of genetic changes and gene combinations as well as a change in oil composition, which would hardly be possible or even impossible to achieve using conventional breeding.

Camelina is one of the oldest domesticated plants in Europe. The plants can persist and propagate in the environment; they might also cross into natural populations. Experts have warned of risks to food webs caused by genetically engineered plants producing seeds with a changed oil composition: for example, some of the fatty acids produced in genetically engineered plants such as Camelina, can alter the growth and fecundity of the wild species feeding on them. This might also become a problem for consumers if the kernels are unintentionally mixed into food and feed. A mandatory approval process is needed to gather the data needed to identify the plants and prevent them from spreading into the environment. Otherwise, great masses of disharmonious gene patterns could be introduced into the natural populations and inedible agro-fuels might end up in food plants.[4]

THE „MONARCH FLY“

A gene in fruit flies (*Drosophila melanogaster*) was adjusted to a similar gene of the monarch butterfly. Just three tiny changes in individual base pairs within a gene can make the fruit flies resistant to toxins produced by specific plants. As a consequence, the flies ingest the toxin and thereby become toxic to other animals feeding on them. Releasing the flies into the environment may have detrimental effects on the food web and interconnected ecosystems. This example shows: little tiny changes in the genome can have huge effects and cause severe risks for nature, even when no additional genes are inserted. If such genetically engineered organisms are not strictly regulated, they might be released unnoticed into the environment.[5]

„HORNLESS CATTLE“

Gene-editing errors in the genome may also be overlooked. This was the case with cattle that were genetically engineered with gene scissors to prevent the growth of horns. DNA originating from genetically engineered bacteria used in the process was unintentionally inserted into their genome. Several years later, researchers found complete DNA sequences conferring antibiotic resistance in the genome of the cattle. This example shows that the process used to genetically engineer organisms has to be the starting point for mandatory risk assessment. Otherwise, side effects caused by the process itself are likely to be overlooked.[6]

For references see:

[4] Testbiotech (2019) Am I Regulated? (www.testbiotech.org/node/2345)

[5] Karageorgi et al., (2019) Genome editing retraces the evolution of toxin resistance in the monarch butterfly, Nature, (https://doi.org/10.1038/s41586-019-1610-8)

[6] Norris et al., (2019) Template plasmid integration in germline genome-edited cattle, bioRxiv preprint doi: (http://dx.doi.org/10.1101/715482)

„Everything is interconnected-ness."

Alexander von Humboldt

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