

New methods of genetic engineering: The 'CRISPR Mushroom'

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Biotechnology

A possible future scenario

Testbiotech's work is based on exacting scientific standards. Nevertheless, in our video clip on the 'CRISPR mushroom' we go beyond what can be considered to be scientific knowledge and present a possible future scenario. The clip uses 'scientific fiction' to narrate a well-known pattern: it starts with a mysterious incident in the year 2025 and goes on to tell the story

So why was this clip produced? What is the reality? What is the future scenario?

Why have we made this video-clip?

Currently, a highly dynamic process is ongoing in the field of genetic engineering. New tools such as the 'DNA scissor' (nuclease) CRISPR-Cas have become cheaper and more efficient than previous methods. This means that many more plants and animals can be genetically engineered within shorter periods of times than has been the case until now. These new methods enable not only additional DNA sequences to be inserted, but also the deletion natural genes - this is a process known as genome editing in which the DNA of plants and animals undergoes genetic engineering using tools such as CRISPR-Cas. These techniques can be used to target specific regions in the genome to delete or change them.

The technical potential of genome editing goes far beyond what has ever been achieved with previous methods of genetic engineering: radical changes in the genome and the usage of synthetic DNA with no natural template has become reality. In addition, there are plans to use so-called 'gene drives' to genetically engineer natural biodiversity, including insects, wild plant populations and mammals.

Some of these genetic changes are said to be to be very small and precise. Our video clip is about such 'small' and targeted genomic changes where no additional DNA sequences are inserted.

Why is genome editing such an important issue for the general public?

Industry as well as various users and developers of the technology want to exclude plants and animals with so-called 'small' changes to their genome so that they do not have to undergo an approval process and are not subject to mandatory risk assessment if no additional genes are inserted.

However, if no approval process is required, the companies do not need to present any data on risk assessment. Consequently, independent experts will not be able to examine the risks in detail. Furthermore, if labelling is not required, consumers will no longer have any choice. And, importantly, if no methods of detection are available, the organism can spread undetected into the environment.

Conclusion: without a mandatory approval process, there is less safety, less transparency and no possibility of controlling these organisms. Protection of human health and the environment will be put at risk.

What are the differences between genome editing and conventional breeding?

Even if no additional genes are inserted, there are substantial differences between conventional breeding and genome editing. The application of nucleases, such as CRISPR-Cas, is not subject to natural control mechanisms of gene regulation and heredity to the same extent as conventional breeding. The DNA scissors can also change genetic conditions in ways that would not be expected under natural conditions. Furthermore, unlike conventional breeding, genome editing always changes all the copies of a gene at the same time. Whereas conventional breeding usually means that there are still some backup copies present in the genome that can compensate the effects of random mutations. Under some circumstances, plants can use these backup copies to repair the mutated gene function or, for example, specific enzymes can still be produced even if one copy of the gene is lost at another site in the genome.

As a result, with genome editing there is in most cases a very specific pattern of change in the plant genome. This means that plants and other organisms can be created with changes not only in their genetic structure, but with unintended biological effects and risks that are clearly different to conventional breeding. Therefore, Testbiotech is strongly calling for these plants to be subjected to mandatory risk assessment before a decision is made on agricultural usage or release into the environment.

Why have we chosen this mushroom as an example?

The specific mushroom presented in our video clip was manipulated with CRISPR so that it does not turn brown after being cut or during storage. Consequently, the mushrooms will look fresher than they actually are. For this purpose, several copies of one specific gene were deleted in the genome. This gene is necessary to produce an enzyme which is involved in browning and that is part of the natural degradation process of mushrooms. Thus, although no additional genes were inserted, several copies of one natural gene were destroyed. This is very typical of CRISPR plant applications: only very few genes exist in just one copy in the genome, many food plants have huge genomes with several sets of chromosomes. There has been very little research on the genome of mushrooms, but from the information available on the CRISPR mushroom one has to conclude that the targeted gene is available in several copies in the genome.

This mushroom is an important precedent case:

- It is the first CRISPR organism that was approved for food production in the US. Because no additional genes were inserted, the regulatory authorities did not request a detailed risk assessment and declared that the mushroom does not need to be regulated if used in food.
- It is an example of the expansion of genetic engineering applications. So far there have been never been any genetically engineered mushrooms (mushrooms are neither plants nor animals).
- Penn State University that developed the mushroom has also been filing patents on CRISPR technology and resulting organisms. In Europe, big companies in particular are filing more and more patents in this area. The overall development is largely dominated by their interest in short-term profits.

How plausible is this future scenario?

The story tells of people falling ill from eating the mushrooms, especially with diarrhoea. The effects on the health of particularly vulnerable groups in the population (children and the elderly) are shown to be severe.

The scenario starts with a simple observation: The browning of the mushrooms has something to do with the processes of its natural degradation. These processes can also be involved in their digestibility. If this enzyme is blocked, it might also have implications for nutritional quality.

Furthermore, the production of enzymes within the organisms often involves feedback mechanisms: if one enzyme is lacking, the cells in response might try to balance their metabolism by overproduction of other compounds. This process can also impact the nutritional quality of the mushrooms.

Conclusion: In the case of the CRISPR mushroom, it would be necessary to examine whether the metabolism in the mushroom was changed unintentionally. The risk assessment cannot be confined to the level of DNA and the question of whether genes were inserted or not. The composition of the mushroom components also has to be investigated. However, no such investigations were carried out in the US, so it is therefore not possible to draw any conclusions on their safety. There are neither scientific publications nor independent scientific investigations. Existing experience is also unhelpful since it is not likely that mushrooms with these specific genetic conditions ever existed before.

Therefore, the future scenario proposed in the video cannot be ruled out. How probable it really is, nobody can say. And this is precisely the problem. This is why Testbiotech is demanding that reliable data are made available and the risks are examined in all relevant details before any decision is made on the market approval of products such as this mushroom.

Would it be possible for these mushrooms to enter the EU market under CETA?

As yet, these mushrooms are not on the market either in the US or in Canada. But it would be possible to bring them onto the markets in the US. The US regulatory authorities have already declared that no further regulation is needed. Very often, in the case of genetically engineered organisms, the Canadian authorities make similar decisions to those in the US.

The free trade agreement CETA foresees alignment of future regulation of genetically engineered organisms. If Canada and the EU do not establish clear regulation for products such as CRISPR, it may well be that the mushrooms will enter the EU market unnoticed.

Is Testbiotech scaremongering?

The video clip is meant to provoke controversial debates. Civil society should broadly discuss the new developments in the area of genetic engineering. Should CRISPR mushrooms, plants and animals be allowed to enter the market without detailed examination or labelling, and should they be released into the environment?

We look forward to an informed and controversial debate.

Further information:

www.testbiotech.org/en/limits-to-biotech/mushroom/basic_paper

www.testbiotech.org/en/limits-to-biotech/what-is-genetic-engineering

www.testbiotech.org/en/node/2198