

Gene editing – new technology, old risks?

In brief

- Thanks to a new technology, genetic alterations of organisms are now simpler, more precise and quicker than before.
- Taboos such as human germ line intervention are up for discussion again as are the foundations of how genetically modified organisms (GMOs) are regulated.
- In the future, genetic engineering might become more ubiquitous, which could bear potential for conflict whilst the need to reach political decisions is becoming more urgent.

What is it about?

Recombinant DNA technology is a matter of the past – now, with the help of gene editing technologies, researchers are able to change the genes of every organism more quickly, more easily and with more precision than before. Basic research becomes easier, genetic diseases can be treated, new therapies for, inter alia, AIDS will be developed and agricultural crops will be changed at will – such are the hopes. The significance of this new technology is being compared to that of the polymerase chain reaction, which revolutionised biotechnology in the 1980s. As a result, scientific and economic expectations are high. Such advanced options, however, put existing taboos up for discussion; at the same time, current legal definitions are eroding. Old contentious issues reappear, new ones arise.

Gene editing methods have been available for some time. A real breakthrough took place in 2012 with the CRISPR-Cas9 system. It exploits a natural mechanism used by bacteria to

defend themselves against viral infections: a special RNA detects viral DNA having entered the bacterium; an enzyme then cuts the viral sequences into pieces. This mechanism can be applied to deliberately introduce changes to every gene in the organism's genome. The recognising RNA detects the target gene; the enzyme cuts it and thus eliminates its function or changes it, thereby subjecting it to a mutation in a simple and cheap way. The new technique inspires a large number of potential applications such as:

- Quick alterations of agricultural crops without traceability;
- Combatting harmful organisms and pathogens;
- Interference with the human genome.

For many applications, gene editing is still not specific enough. The error rate is too high and there are too many unexpected off-target effects. Nevertheless, old debates on germ line therapy, ecological risks and the regulation of GMOs are becoming topical again.



Genetic alterations are now much simpler and quicker than before

Application and risk: Currently, an unresolved patent dispute might impede the wide distribution and application of the new method. Nevertheless, commercial companies already deliver ready-made and tailored gene editing systems at moderate prices. George Church, a pioneer in biotechnology, estimates that more than 30,000 persons had applied gene editing tools in 2015. Even small laboratories and companies can now tackle projects that appeared impossible not too long ago. This may turn into the democratisation of the technology; however, it could also raise concerns and controversy.

Since seemingly impossible projects now appear feasible, they may be implemented with little hesitation. For example, plant breeders hope for affordable niche products developed with the help of gene editing. Others, however, are afraid of the wide distribution of genetically modified varieties. Easy access to the technology may also lead to misuse, i.e. for example the development of dangerous organisms without adequate safety measures or for intentional harm. Military applications are to be considered as well.

Controversial questions

What should be classed as a GMO? Some genetic alterations through gene editing cannot be discerned from naturally occurring mutations. In a way, the genome is being altered 'without traces'. This raises the question whether the result, a new crop variety for example, should be seen as a genetically modified organism before the law. The German Federal Office of Consumer Protection and Food Safety says no because alterations might occur naturally as well and cannot be traced. In contrast, environmental protection organisations want the law on GMOs to be applied. Moreover, consumers tend to react negatively to a blurring of boundaries between genetically engineered and non-engineered products.

The EU Commission has announced that they will soon explain their position on how to deal with natural, genetically modified and edited organisms. In the US, it is mostly researchers and representatives of industry who demand a revision of existing GMO regulations which they consider contradictory and outdated. Proposals range from imposing strict laws to complete deregulation.



Genetically modified insects to be released into the environment?

Combatting disease carriers? The new 'gene drive' method has been advertised as a new means to combat threats such as the Zika virus. The idea is to genetically modify individual insects with CRISPR so that individual insects distribute a gene into the population, resulting in killing them all. The autonomous distribution of artificial genes has so far been rejected. Too little is known about the consequences, controls are difficult, and the technology is not precise enough. Experiments in the open are prohibited for the time being.

Altering the human genome? Human germ line gene therapies, in which the offspring would inherit the alteration, have been considered a taboo up until now. Gene editing, however, promises to eradicate severe genetic diseases such as muscular dystrophy, rendering the intervention more attractive. In 2015, the first experiments with human embryos took place. The authors of the report considered the method not mature enough yet; however, the inhibition threshold is clearly being lowered. The legal situation is ambiguous – some countries prohibit germ line therapy, others allow it, albeit on a case-by-case decision, but many lack legal frameworks. The scientific community is undecided. The US Academy of Sciences has announced that they are currently in the process of developing global guidelines on the matter.

What to do?

As the technology and its products become ubiquitous, definitions are slowly being eroded, taboos are disappearing and thus far purely theoretically-debated questions are becoming topical. As a result, regulatory decisions become indispensable, addressing:

- *A more adequate definition of what constitutes 'genetically modified organisms':* Genetic alteration by way of the new method often cannot be traced. Special regulations for the labelling of edited organisms could be an option.
- *A moratorium on interventions to the human germ line:* Many scientists recommend a moratorium as well as more research to render gene editing more precise.
- *Combatting pests through gene drive:* As long as the consequences for human health and the environment cannot be better assessed, outdoor applications remain highly problematic.
- *Globalisation:* As with tax evasion and medical tourism, individual countries are unable to act on their own. Regulatory pioneers could encourage others; nevertheless, in the long run, international cooperation is essential.
- *National competencies:* GMO regulation is a matter of responsibility for the European Union. Relevant individual member states' scopes of action have been widened; however, attempts by individual nations have rarely been very promising. Consequently, a revision of European GMO regulation may be necessary.

Further reading

CRISPR everywhere. A *NATURE* special issue.
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