Gene-editing tech

Gene editing has the potential to revolutionise dairy breeding. It allows researchers to accurately adjust DNA. But is the technique as promising as it sounds and what about the ethics surrounding the technology, not to mention the public perception of this controversial science? We spoke to some leading geneticists to find out more.

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Imagine that the polled gene could be added to dairy cattle DNA, making disbudding a thing of the past. Or suppose that by simply adjusting a gene a genetic defect could be repaired. With gene editing these scenarios could become reality, according to Henk Bovenhuis, who is professor of breeding and genetics at Wageningen University, in The Netherlands.

"Gene editing is a precision tool to change the DNA," he explains. "Towards the end of the 1980s, it was already possible to alter the genome. The genetically-engineered bull Herman was an example of this, but then a much more basic or primitive method was used. It was very much a case of 'wait and see' where an extra gene ended up. Now scientists can work more specifically, and the technique is also much easier to implement."

The discovery of the CRISPR-Cas technique was what really allowed the gene editing technique to take off. "The technique is not as simple as cutting and pasting on a computer, but CRISPR-Cas certainly makes gene editing much easier, whether you're talking about a plant, an animal, or a human being."

European ban

That said, this technology is still banned from use in practice in Europe. It can be used for research purposes, but nothing more. The European Court of Justice recently confirmed that gene editing falls under current GMO regulations. "The technique could also be used, for example, to add a gene from a different animal species. That is genetic modification, of course," says CRV's innovation manager Sijne van der Beek.

Even though gene editing technology is not yet permitted, or indeed ready, for use by the dairy industry right now, scientists are already thinking about what it could deliver. For example, it is possible to repair genetic defects, such as BLAD and CVM. Improving production traits is also a possibility.

But Wageningen University's breeding and genetics researcher John Bastiaansen is still skeptical. "The potential for genetic progress through gene editing is currently very small. This is because most of the traits in breeding, such as milk production, are influenced by many genes. And all of these genes, some of which we have yet to even identify, have a small effect. "Even if all the genes are known, the question is whether you can add all these effects together. It is likely that interactions will take place, an interaction between genes."

More realistic, according to Mr Bastiaansen, is the adaptation of an individual allele – a certain variant of a gene – through gene editing. "Naturally polled is a good example of this. Adapting just one gene will result in polled animals."

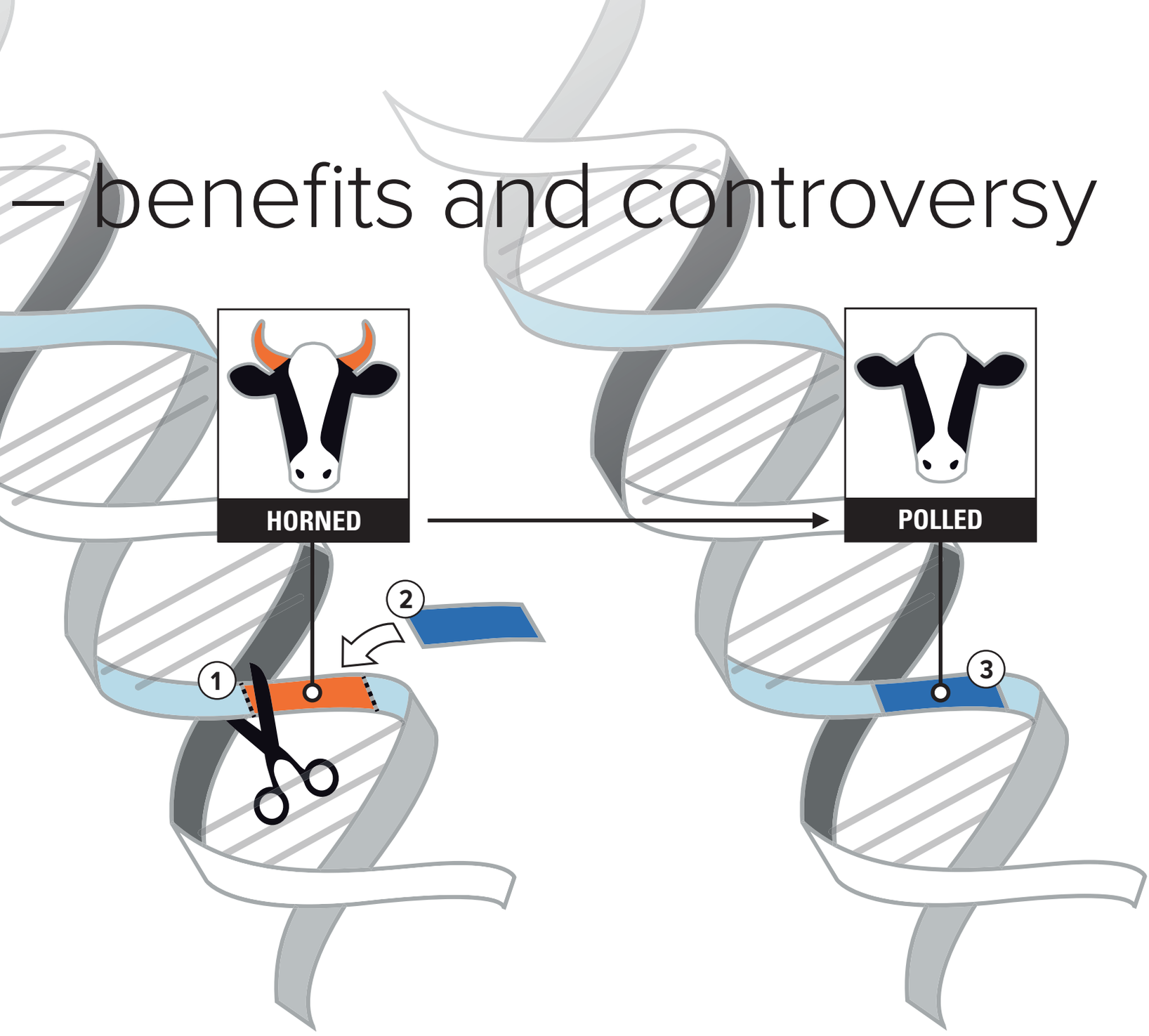
With this in mind, he set up a simulation study, together with his colleagues professor Bovenhuis

Genus gene editing update

Genus is exploring applications for gene editing technology, including a project in the early stages of development intended to address Bovine Respiratory Syndrome (BRD), with various collaborators including the University of Missouri, Roslin Institute and with Caribou Biosciences. The company is engaged with the appropriate regulatory bodies in several countries to understand the regulatory requirements necessary for approved use of gene editing technology in food-producing animals. And it has taken leadership roles in several cross-industry and cross-species gene editing coalitions. These coalitions are dedicated to advocating for the responsible use, regulation of, and communication around gene editing.

Genus has also begun work to ensure consumer acceptance for this technology, building alliances with key stakeholders, compiling a comprehensive outreach plan to engage with our food chain partners, and working to understand consumer perceptions of modern agriculture and this technology.

– benefits and controversy



Gene-editing example: **from horned to polled**

Gene editing is a precision instrument for adjusting the DNA at a specific location.
By opening DNA in a cell (1), the gene for horns can be removed for example (2) and then replaced by the gene for polled (3).

and Han Mulder. “Imagine that ethical and practical dilemmas do not play a role, what does gene-editing in the case of polled cattle mean?”
Their work is examining how many generations it would take for a population to be 100% polled, assuming a starting population with 1% polled animals. Even without gene editing, it is possible to breed a 100% polled population.
If there is pure selection for polled – and not for traits such as milk production, fertility or udder health – it would take about four generations before all animals in the population would be polled. “That’s quite quick, but in this instance the genetic progress for other important traits is significantly lower,” says Mr Bastiaansen. “If we do consider those previously mentioned traits, genetic progress would be higher. But then it also takes longer – in this study up to 19 generations – before all animals are polled.’
And if gene editing is applied? The researchers assumed that gene-editing was carried in 10% of the animals, and

Gene-editing technology could be used to replace the gene for horns with the gene for polled cattle

that all edits were successful, and they found that it was still vital to select for polled animals.

"If not, it will take around 13 generations through gene-editing before the gene is recorded in the population," explains Mr Bastiaansen. "That's a very long time. The advantage is that you do not lose out on genetic progress for the other traits. But a disadvantage is the cost of gene editing."

With the current technology, there has to be a selection pressure for polled in gene editing. "But we have found that if you apply a small amount of selection pressure to the trait, that immediately helps a lot. The trait is then 'tied up' faster and fewer 'edits' are required."

Mr Mulder also points out that the assumption that all 'edits' are successful, is a bit too optimistic. "In reality, gene editing is currently only successful in a tiny percentage of cases. For example, editing does not always work or there are no live-born offspring."

Thorough debate

Although scientists slightly temper the enthusiasm about gene editing, several breeding organisations are already working on gene editing. Genus announced a partnership with the US-based biotech company Caribou a few years ago. And in 2017 Semex announced a partnership with Recombinetics, another American biotech company. Together they are working on building in the gene for polled animals, so that producers will no longer have to disbud calves.

CRV is not currently investing in gene editing. "But we're keeping an eye on developments. We have already discussed the subject with our members and with our ethics committee," says Mr van der Beek. He certainly sees the advantages of this technology.

"Gene editing is a powerful technique that has the potential, for example, to result in a polled cattle population more quickly. This application is, in fact, similar to extremely targeted breeding."

But, before that happens, he says some questions still have to be answered. "Do the benefits of gene editing adequately outweigh the risks? We're assuming that if one gene at one specific location is changed then nothing else will change. But is that really the case?"

Under what conditions the technique may be applied is another question. "Can you also use the technique, for example, to improve production or only to improve animal welfare?"

Perhaps even more important, Mr van der Beek believes that a careful debate about gene editing is necessary. "That must certainly take place as far as CRV is concerned. And not only with researchers and stakeholders, but also with wider society. How does society view gene-editing?"

His role is to ensure that the issue of gene editing stays on CRV's agenda. "It's something that should be discussed each year, to stay up to date, because the technology is developing quickly."

Potential 'snags'

Gene editing is sometimes presented as the 'golden goose'. Professor Bovenhuis does not want to go that far. "There's a lot of hype around gene editing, but we only have knowledge about a handful of genes at the moment. In the longer term, gene editing may well be a 'game changer' in cattle improvement, but there are still many potential 'snags'."

Mr Van der Beek agrees. "It will take a while before gene editing is sufficiently safe, reliable and efficient. And that was also the case with genomic selection", he says. "But it is possible to imagine the technology's potential. If we know that there's a certain place in the DNA where there's a gene occurs in an undesirable form. Then we can imagine what could change if we we're able to 'edit' that gene to a more desirable form. Technological progress begins when you're able to imagine how things could be different and how to change them." |