6. Gene-editing technology is owned and controlled by big corporations

MYTH

Gene editing, and the CRISPR tool in particular, puts the power of genetic engineering into the hands of hundreds of thousands of scientists, including those working in publicly funded institutes and small companies.

REALITY

Gene editing technology for agricultural use is already firmly under the control of the multinationals that dominate the seed and agrochemicals markets. Corteva has become the main gatekeeper of CRISPR patents in the agricultural arena.

Advocates claim that gene-editing techniques, especially those using the CRISPR/Cas system, can democratise genetic engineering because they are cheaper and easier to apply than older genetic modification techniques. Jennifer Doudna, one of CRISPR's inventors, said the technology "became a democratising tool that allowed labs to do experiments that in the past had been prohibitive for various reasons, whether due to expense or just technical difficulty".[1] Bayer calls CRISPR the "most 'democratic'" gene-editing tool, which is so "cheap and simple" that it can be used by "universities and institutes that do not have major research budgets".[2]

It is further argued that if gene editing were exempted from the EU's burdensome and expensive-to-comply-with GMO regulations, it would be removed from the control of the big agbiotech multinationals and be made available to public research institutes and universities, non-profit organisations, and small and medium-sized enterprises (SMEs).[3,4] The seed industry claims that GMO regulations "prevent most of Europe's plant breeding companies from developing and using these methods".[5]

TECHNOLOGY PATENTS

Claims of democratisation through new GM techniques must be viewed in the light of the fact that these techniques are patented, as are their products – the plants and animals developed using them. Patents are monopoly rights. Patent holders have the right for up to 20 years to prohibit others from exploiting the patented invention or to charge royalties for its use. This is not just about limiting commercial exploitation, but also further innovation. Exclusive patent rights prohibit others from building on the protected invention, as research exceptions to patent rights are usually very strictly formulated.

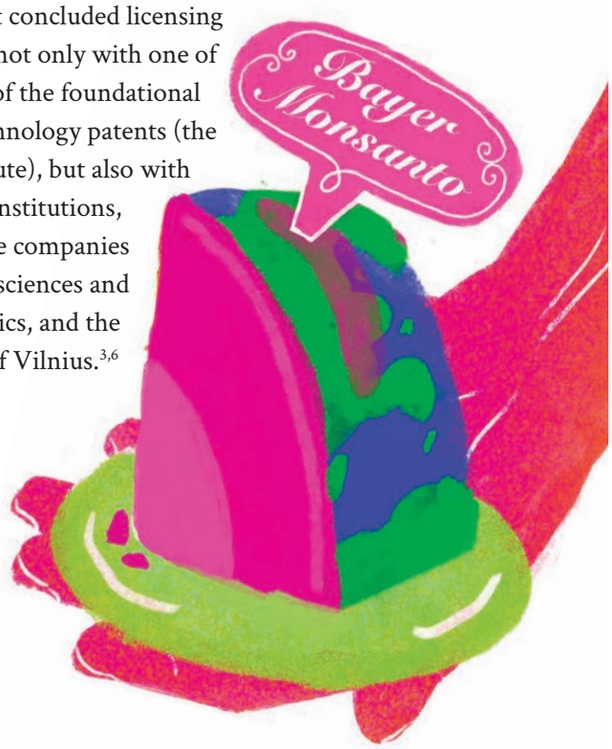
> Patent holders have the right for up to 20 years to prohibit others from exploiting the patented invention or to charge royalties for its use

The Broad Institute of MIT and Harvard, the University of California, the University of Vilnius in Lithuania, and the University of Vienna are the main institutional "inventors" of CRISPR technology.[6,7,8,9] Between them they have filed (and fought each other over[9]) hundreds of foundational patents, some of which have already been granted in Europe.[6]

LICENSING AGREEMENTS

Once technology patents are granted, patent owners can conclude licensing agreements with companies allowing them to use the technology in certain areas or in a specific application. These agreements can be exclusive or non-exclusive. Other companies can obtain licensing agreements only if the rights to use the patents are granted non-exclusively to a licensee. An overview of CRISPR-based gene-editing technology licensing agreements was published in Science in 2017.[8]

In the areas of CRISPR gene-edited plants and livestock, licensing agreements reached by patent owners, the Broad Institute and the University of California (or its spinoff company Caribou Biosciences), with licensees DowDuPont (now Corteva) and Bayer/Monsanto, are particularly important.[6,8] DowDuPont concluded licensing agreements not only with one of the holders of the foundational CRISPR technology patents (the Broad Institute), but also with all relevant institutions, including the companies Caribou Biosciences and ERS Genomics, and the University of Vilnius.[3,6]



CARIBOU BIOSCIENCES AND ERS GENOMICS

Corteva (the agricultural division spun off from DowDuPont) is the main gatekeeper for CRISPR patents in the agricultural arena[10] and has gained unprecedented market power due to its ability to grant access to this patent pool.[6] To understand why, we need to learn the history of the CRISPR licensing agreements.

> The story begins with two biotech startups co-founded by the inventors of CRISPR technology

The story begins with two biotech startups co-founded by the inventors of CRISPR technology. The first, Caribou Biosciences, was co-founded in 2011 by one of the inventors of CRISPR-based gene-editing technology, Jennifer Doudna from the University of California. The second, ERS Genomics, was co-founded in 2013 by another CRISPR technology inventor and patent owner, Emmanuelle Charpentier, as a "licensing engine" that "exists to make the [CRISPR] technology more broadly available under appropriate commercial licences". ERS Genomics has signed non-exclusive and exclusive licensing agreements with companies operating in different fields.[8]

DuPont (later DowDuPont and now Corteva) concluded its licensing agreement with Caribou Biosciences in 2015. In the deal, DuPont received exclusive rights for CRISPR technology applications in major row crops and non-exclusive rights in other agricultural

applications.[11] In 2016 Caribou reached a deal with the company Genus in which the latter received an exclusive licence to use CRISPR technology in certain livestock species.[12]

DuPont also reached an exclusive licensing agreement in 2018 with ERS Genomics. The agreement gave DuPont exclusive rights to use CRISPR technology in the agricultural area. ERS Genomics also granted sub-licensing rights to DuPont. DuPont's agricultural division was spun off in 2019 as an independent entity named Corteva. Thus Corteva achieved its dominance of the CRISPR technology in the agricultural field.

DEMOCRATISATION OR PATENT CARTEL?

Jean Donnenwirth of DowDuPont (now Corteva) presented the company's agreements on 5 November 2018 at a meeting between the EU Commission and various interest groups, according to Dr Christoph Then of Testbiotech, who was present. According to Donnenwirth, DowDuPont succeeded in combining 48 basic patents into a common patent pool (35 patents from the Broad Institute, 4 from the University of California, 2 from the University of Vilnius, and 7 from DowDuPont).[6]

Donnenwirth said that access to this number of patents is necessary for full use of the technology in plant breeding. DowDuPont can offer bundled, non-exclusive licenses giving access to this patent pool. The conditions include appropriate fees, reporting obligations, compliance with guidelines, and confidentiality.[6] The first company to licence CRISPR technology under these conditions in 2018 was the US company Simplot, which develops GM potatoes.[13] In 2019, a French company, Vilmorin & Cie, followed.[14]

Christoph Then commented, "DowDuPont has unprecedented market power thanks to the possibility of granting access to this patent pool: What is on the one hand touted as a 'democratisation' of patent law turns out, on closer examination, to be a means of controlling competitors and protecting a dominant position. DowDuPont becomes, so to speak, the gatekeeper of an international patent cartel."[6]

PATENTS ON "NEW GM" CROPS DOMINATED BY DOWDUPONT, BAYER/MONSANTO

The 'democratic' credentials of gene editing are determined not only by access to the technologies but also by access to their products – gene-edited crops and seeds. But just like the technologies, the products are circumscribed by intellectual property rights.

According to Christoph Then, patent applications involving new and old genetic engineering relate to plants with modified growth and yield, composition, or resistance to disease, as well as technical modifications of the nucleases. As a rule, the patents cover methods, seeds, plants and often also the harvest.[6]

Both Bayer/Monsanto and DowDuPont have applied for patents on glyphosate-tolerant plants produced with the CRISPR-mediated gene-editing process. This means that the core agricultural GMO business – the marketing of herbicide-tolerant plants such as soy, corn, oilseed rape/canola and cotton – can continue to be protected by new patent applications in the future.[6]

Both Bayer/Monsanto and DowDuPont have applied for patents on glyphosate-tolerant plants produced with the CRISPR-mediated gene-editing process

The owners of the patents are largely the same multinationals that dominate the GMOs and agrochemicals markets. Christoph Then wrote in 2019 : "DowDuPont leads the field in the new genetic engineering methods for crops, with around 60 international patent applications, while Bayer/Monsanto follows in second place with more than 30. Calyxt… comes in at more than 20. Syngenta and BASF are also involved, and a few patents have also been applied for by traditional breeding companies such as Rijk Zwaan and KWS."[6]

A 2016 review of the intellectual property rights landscape by Egelie and colleagues found that "larger industry players, with Dow and DuPont at the forefront, already appear to be more in control of the technology's agricultural and food applications."[15]

LOST ACCESS TO TRADITIONAL CULTIVARS

In a discussion dominated by concerns about gaining access to CRISPR technology, it is easy, as pointed out by Maywa Montenegro de Wit of the University of California, to forget the crucial issue of farmers "losing access to traditional cultivars that might be displaced with expanded markets in new biotech crops, or mined as genetic resources for breeding gene-edited varieties".[1] There is a danger that farmers will be forced to pay for access to gene-edited seeds and breeds, but lose access to non-GM seeds and breeds in the process.

ACCESS TO THE TECHNOLOGY FOR SMES ACTING ALONE IS ILLUSORY

Could the de-regulation of gene editing help empower small and medium size enterprises (SMEs) to develop the gene-edited crops and foods that will enable us to meet the challenges of climate change?[4,16]

This prospect is highly unlikely, according to molecular geneticist Dr Michael Antoniou, who has many years' experience of developing patented biotech products for medical research with SMEs and larger companies.[4]

He explained that different types of licences exist for technologies like CRISPR gene editing, which industry-based researchers (including those working in SMEs) must take out at different stages of product development. These include evaluation, research, and commercial licences. Evaluation licenses are granted to researchers by the patent owners or their sub-licensing affiliate companies to allow the researchers to do preliminary work to see if the technology could be useful. If the researchers want to pursue a particular application, they can apply to the patent owners for research licenses.[4]

Evaluation and research licences are often granted quite cheaply, and fees can even be waived altogether, since the technology owners want it to be used to develop a product that can be commercialised.
Even when evaluation and research licence fees are charged, a typical SME could afford them.[4] But at the commercialisation stage, things can quickly get very expensive, with technology patent holders demanding high payments for use of the technology, in the form of commercial licence fees and royalty payments on product sales.

As an example, Corteva has made a commitment to allow free access to the CRISPR technology for "universities and nonprofit organizations for academic research". The company has claimed that this will put the CRISPR technology "in the hands of many", resulting in "a wide array of benefits for the global food supply".[3] But scientists will only be able to use CRISPR for basic non-commercial research, not for developing commercial products. Maywa Montenegro de Wit concluded: "Despite the opening up of CRISPR IP [intellectual property] for non-commercial research, CRISPR's commercial development remains tightly bound up in patents and licensing agreements – a landscape already showing strong signs of agroindustry dominance."[1]

> "Despite the opening up of CRISPR IP for non-commercial research, CRISPR's commercial development remains tightly bound up in patents and licensing agreements"
> - Maywa Montenegro de Wit

Plant breeders using conventional breeding to develop a new plant variety can protect it through plant breeders' rights. But if they decide to use CRISPR (whether or not the technology is regulated as GM), they will need to learn to navigate a far more complex and expensive process. They will have to compensate the CRISPR patent holder(s) both at the research and development stage and also at the commercialisation stage.
Patent and licensing fees will raise the cost of variety development considerably.

Patenting fees can easily accumulate to six-figure sums, since patents must be applied for – and patent lawyers engaged – in each territory where intellectual property rights are sought. The patenting process can drag on for years, with lawyers' fees rising all the while.[4]

GAME FOR BIG PLAYERS

Due to the expense involved, SMEs on their own will never be able to afford the patents and commercial licensing agreements that govern gene editing. So the system in the agricultural biotech market is, and will remain, that researchers based in small companies or universities, often with industry funding, "invent" a GMO and partner with investors and/or a large company to patent the product, obtain regulatory approval, and bring it to market. The inventors and their institutions enjoy a profit-sharing arrangement with the investors or large partner company. Often in this process, the SME is bought up by larger companies.[4]

At the end of the day, gene editing is a game for big players and will remain so

This business model is not considered a cause for lamentation. On the contrary, it is celebrated as a path to success for all involved, including the individuals and SME that invented the product.[4]

However, at the end of the day, gene editing is a game for big players and will remain so. The notion that CRISPR will grant small players access to the technology is a myth.

PATENTS THE DRIVING FORCE OF OLD AND NEW GENETIC ENGINEERING

Experience with genetic engineering to date shows that patent law has been the driving force behind development. The advent of genetic engineering marked the first time that patent law was systematically applied to plant breeding. Large agrochemical companies, which had previously protected their pesticides with patents, now also applied for patents on GM seeds and at the same time bought up many plant breeding companies.[17]

The advent of genetic engineering marked the first time that patent law was systematically applied to plant breeding

With new genetic engineering techniques, this strategy has continued and been expanded. Already, corporations such as Corteva and Bayer/Monsanto control large parts of the seed market.[17] Patented genetic engineering techniques such as CRISPR gene-editing technology help them extend and deepen this control.[6]

Therefore gene-editing technology will not make genetic engineering accessible to publicly funded breeding programmes, but will further consolidate power within the big multinationals.

REFERENCES

1. Montenegro de Wit M. Democratizing CRISPR? Stories, practices, and politics of science and governance on the agricultural gene editing frontier. Kapuscinski AR, Fitting E, eds. Elementa: Science of the Anthropocene. 2020;8(9). doi:10.1525/elementa.405

2. Bayer. Here are the facts about agriculture and nutrition. Published online November 2018. https://release.ace.bayer.com/sites/default/files/2020-04/here-are-the-facts-about-agriculture-and-nutrition-brochure.pdf

3. Cameron D. DuPont Pioneer and Broad Institute join forces to enable democratic CRISPR licensing in agriculture. Broad Institute. Published October 18, 2017. Accessed December 4, 2020. https://www.broadinstitute.org/news/dupont-pioneer-and-broad-institute-join-forces-enable-democratic-crispr-licensing-agriculture

4. Robinson C. Why regulation of gene editing will not hurt small and medium size companies. GMWatch. https://gmwatch.org/en/news/latest-news/19239. Published November 28, 2019.

5. Euroseeds. Position: Plant Breeding Innovation. Euroseeds; 2018. https://www.euroseeds.eu/app/uploads/2019/07/18.1010-Euroseeds-PBI-Position-1.pdf

6. Then C. Neue Gentechnikverfahren und Pflanzenzucht: Patente-Kartell für große Konzerne. Forum Umwelt & Entwicklung. Published online February 2019:10-11. https://tinyurl.com/y5hcu996

7. University of California Office of the President. University of California's foundational CRISPR-Cas9 patent portfolio reaches 20 total U.S. patents. prnewswire.com. Published December 31, 2019. Accessed December 7, 2020. https://www.prnewswire.com/news-releases/university-of-californias-foundational-crispr-cas9-patent-portfolio-reaches-20-total-us-patents-300980003.html

8. Contreras JL, Sherkow JS. CRISPR, surrogate licensing, and scientific discovery. Science. 2017;355(6326):698-700. doi:10.1126/science.aal4222

9. Wagner JK. Disputes continue over foundational patents for gene editing. The Privacy Report. Published online April 18, 2017. Accessed January 12, 2021. https://theprivacyreport.com/2017/04/18/disputes-continue-over-foundational-patents-for-gene-editing/

10. O'Malley M. CRISPR's licensing landscape decoded. Intellectual Property Magazine. Published online January 2, 2018.

11. DuPont. DuPont and Caribou Biosciences announce strategic alliance. BioSpace.com. Published October 8, 2015. Accessed December 7, 2020. https://www.biospace.com/article/dupont-and-caribou-biosciences-announce-strategic-alliance-/

12. Caribou Biosciences. Genus and Caribou Biosciences announce exclusive collaboration for leading CRISPR-Cas9 gene editing technology in livestock species. cariboubio.com. Published May 18, 2016. Accessed December 7, 2020. https://cariboubio.com/in-the-news/press-releases/genus-and-caribou-biosciences-announce-exclusive-collaboration-leading

13. Nosowitz D. Potato company Simplot licenses DowDuPont's gene editing tech. Modern Farmer. Published August 7, 2018. Accessed December 7, 2020. https://modernfarmer.com/2018/08/potato-company-simplot-licenses-dowduponts-gene-editing-tech/

14. Michalopoulos S. Corteva signs first major gene editing deal with European company. EurActiv.com. Published online December 10, 2019. Accessed January 12, 2021. https://www.euractiv.com/section/agriculture-food/news/corteva-signs-first-major-gene-editing-deal-with-european-company/

15. Egelie KJ, Graff GD, Strand SP, Johansen B. The emerging patent landscape of CRISPR–Cas gene editing technology. Nature Biotechnology. 2016;34(10):1025-1031. doi:10.1038/nbt.3692

16. Foote N. MEPs slam gene-editing court ruling as damaging for SMEs. www.euractiv.com. https://www.euractiv.com/section/agriculture-food/news/meps-slam-gene-editing-court-ruling-as-damaging-for-smes/. Published November 22, 2019. Accessed December 9, 2019.

17. Howard PH. Global seed industry changes since 2013. Philip H. Howard. Published December 31, 2018. Accessed December 4, 2020. https://philhoward.net/2018/12/31/global-seed-industry-changes-since-2013/