Making sense of the battle for the CRISPR-Cas9 patent rights

MARCH 15, 2021 11 MIN READ

Related Expertise

- Intellectual Property
- Pharmaceuticals and Life Sciences

Authors: Felicia Lozon, Vincent M. de Grandpré

Updated March 18, 2021

On October 7, 2020, the Royal Swedish Academy of Sciences awarded the Nobel Prize in Chemistry to Professors Emmanuelle Charpentier and Jennifer Doudna for their immense contribution to the CRISPR-Cas9 gene-editing technique.[1] This technology is at the source of a true biotechnological revolution that holds the promise of fabulous innovations in medicine, agriculture and many other fields. One would think that the two award-winning scientists and the institutions to which they belong are poised to reap the huge economic rewards of their invention when its many applications are marketed throughout the world. It is not that simple, however: beyond the accolades, a legal battle has been ongoing for years over the intellectual property (IP) relating to the CRISPR-Cas9 technology. While these disputes are far from being resolved, recent developments suggest that most of the benefits of this invention may be slipping away from the two Nobel laureates.

What is CRISPR-Cas9?

In June 2012, the two geneticists wrote a scientific paper describing a new tool capable of simplifying genome editing, a mechanism called CRISPR-Cas9.[2] The tool, otherwise known as "molecular scissors," allows researchers to cut DNA at a specific location and modify existing genes.[3] This technology has the potential to edit genes in organisms to correct mutations at specific locations to treat genetic diseases and defects.[4] Researchers have used CRISPR-Cas9 to genetically modify mosquitoes so that they do not carry the malaria parasite, in addition to eliminating HIV in infected mice.[5] CRISPR-Cas9 editing has also restored the efficacy of front-line chemotherapies for lung cancer, and these are just a few of the many transformative applications of CRISPR-Cas9. [6]

The patent race

History is full of cases in which several researchers have found the same or similar inventions almost simultaneously. This is the case with CRISPR-Cas9.

In May 2012, Professor Doudna's team at the University of California, Berkeley (UC Berkeley) rushed to the U.S. patent office to file its first patent application for CRISPR-Cas9, the first of many to follow.[7] The UC Berkeley group actually includes Professors Charpentier (then at Umeå University in Sweden and now affiliated with the Max Planck Institute in Berlin) and Doudna of UC Berkeley, who are collaborating on the project.[8] A mere few months later, in December 2012, a research group at the Broad Institute affiliated with MIT and Harvard

University (the Broad Institute) also filed its first patent application for CRISPR-Cas9.[9] As is usually the case in these types of situations, the institutions filed a multitude of patent applications which remained secret for 18 months.[10] Only when the curtain was lifted did the institutions realize that they have filed competing patent applications.

The same drama played out at the same time in Europe. In March 2013, UC Berkeley filed a patent application with the European Patent Office (EPO) claiming priority from its U.S. patent application filed in May 2012.[11] Shortly thereafter, in December 2013, the Broad Institute filed a competing application with the EPO claiming priority from its own application filed in the United States in December 2012.[12] The universities also remained in limbo in Europe as they awaited the publication of their respective applications.

As of 2016 in the United States, UC Berkeley and the Broad Institute launched priority proceedings to be granted the exclusive rights to CRISPR-Cas9 technology in the form of patents for invention.[13] And the saga continues to this day. It may be surprising that universities are competing in this way. This is probably a reflection of the inestimable potential of this new genome-editing technique.

International ramifications, including in Canada

The legal battle that ensued was of global proportions: the international patent system is based on a system of priorities. Inventors can file a single patent application in any member country of the international system in order to benefit from a priority date that they can claim in any other related patent application,[14] hence the importance of rushing to the patent office when an invention is being developed in order to obtain an earlier priority date than those of potential competitors. But even then, it has to be the same invention. Whether an inventor can take advantage of an earlier priority application than those of competitors requires defining the inventions to which the patent applications relate.

In this particular case, the question was whether UC Berkeley's patent application for the use of CRISPR-Cas9 in any living cell made the Broad Institute's more narrowly worded invention, the use of CRISPR-Cas9 in eukaryotic cells (i.e., animal and plant cells) in particular, obvious and thus invalid.[15]

In an initial appeal on February 15, 2017, the U.S. Patent Trial and Appeal Board (PTAB) stated that there was no conflict between the Broad Institute's application and UC Berkeley's application.[16] This is because the researchers described and qualified their respective inventions in different ways. The UC Berkeley researchers, winners of the Nobel Prize in Chemistry, described their invention in general terms, applying to all kinds of DNA. In contrast, the Zhang team at the Broad Institute described its invention as a method for correcting DNA sequences in animal and plant cells. According to the PTAB, there was no "interference-in-fact" between the parties' patent claims.[17] UC Berkeley filed an appeal from the U.S. patent board's decision, but that appeal was dismissed by a U.S. Court of Appeals.[18]

As a result, the Broad Institute took the lead in the United States. In 2018, UC Berkeley filed new U.S. patent applications including claims intended to create a new patent interference, specifically new claims directed to the use of CRISPR-Cas9 in eukaryotic cells.[19] This second interference led the U.S. Patent Office to directly compare the claims of competing inventors to assess which research group had provided the best evidence that the CRISPR-Cas9 technique works in eukaryotic cells.[20]

On September 10, 2020, the U.S. Patent Trial and Appeal Board rejected UC Berkeley's arguments, assigning UC Berkeley a filing date of January 28, 2013, and the Broad Institute an earlier filing date of December 12, 2012 — corresponding to the filing dates of their respective provisional patent applications.[21] This decision confirms that, at this time, the Broad Institute has priority in the use of the CRISPR-Cas9 technique in animal and plant cells where arguably the greatest potential benefits of the technique lie. UC Berkeley, on the other hand, has priority in applying the technique to other cells, such as bacterial cells.

In addition, the PTAB also announced that a third hearing would be required to determine the priority of the patent filings.[22] All jurisdictions in the world where patent applications claim priority from either UC Berkeley's or the Broad Institute's U.S. patent applications are therefore awaiting the outcome of the U.S. proceedings to determine which competing patent applications may be granted.

Europe favours the Nobel Prize winners

The saga is playing out differently at the EPO, where a technical error resulted in the Broad Institute's patent applications having a later date than UC Berkeley's. The Boards of Appeal of the EPO ruled that the initial revocation of the Broad Institute's patent for lack of novelty was correct.[23] As a result, in Europe, the UC Berkeley group holds all of the first-generation patents on CRISPR-Cas9.

What about in Canada?

In Canada, as in many other countries, the validity of the parties' respective patent applications will depend on the validity of priority patent applications filed in the United States. The outcome of appeals in the U.S. will influence the decisions of stakeholders in Canada and the decisions of examiners at the Canadian Intellectual Property Office (CIPO). In the meantime, there are more than 1,200 patent applications pending before CIPO relating to CRISPR-Cas9.[24]

A complicated commercial landscape

For researchers and interested parties, this state of play creates thorny issues around where to obtain the rights to use the CRISPR-Cas9 technique. In order to commercialize new CRISPR-Cas9 technologies and applications, interested parties will need to obtain commercial licences to the basic CRISPR-Cas9 patents. However, this task is complicated by the fact that licences must be obtained from different sources. The owners of the core patent applications have granted their rights exclusively to marketing companies, with the mandate to grant exclusive or non-exclusive licences to private companies willing to invest in developing applications using CRISPR-Cas9.[25] For example, for the development of human therapies, rights must be obtained from CRISPR Therapeutics, Intellia Therapeutics and Editas Medicine.[26] CRISPR Therapeutics obtained its exclusive rights from Emmanuelle Charpentier, Intellia Therapeutics from UC Berkeley and the University of Vienna, and Editas Medicine from the Broad Institute. For all other areas, the companies holding the relevant rights are ERS Genomics, Caribou Biosciences and the Broad Institute.[27] ERS Genomics obtained its exclusive rights from Emmanuelle Charpentier, Caribou Biosciences from UC Berkeley and the University of Vienna, while the Broad Institute licenses CRISPR IP non-exclusively for commercial research or to companies wishing to sell tools and reagents for genome editing.[28]

To this day, no entity has been granted licences for all CRISPR-Cas9 IP rights, whether held by one research group or the other. While this is likely to have minimal impact on basic research using these tools (since this type of research is exempt from the patent infringement regime under national laws or condoned by the institutions holding the patent rights), any therapeutic or commercial opportunities will have to wait until legal controversies are resolved, unless interested universities and researchers agree on a one-stop shop for licensing their potential IP rights.

Since 2017, the Broad Institute has been taking steps to create a single pool of CRISPR-Cas9 intellectual property rights, first under the auspices of a rights management entity called MPEG LA and subsequently, in June 2019, in a new collaboration with MilliporeSigma. The Broad Institute's apparent withdrawal from the MPEG LA group and its launch of an alternative project with MilliporeSigma, as well as UC Berkeley's silence on both initiatives, suggest that the creation of a CRISPR-Cas9 patent pool is not (yet) in the cards.[29] We will therefore have to wait for a commercial agreement between the holders of potential IP rights on CRISPR-Cas9 or for the outcome of the U.S. legal proceedings. In the meantime, scientific research using this revolutionary technique continues to make great strides.

---

[1] The Royal Swedish Academy of Sciences, press release, "The Nobel Prize in Chemistry 2020" (October 7, 2020), online: https://www.nobelprize.org/prizes/chemistry/2020/press-release/.

[2] Martin Jinek et al., "A Programmable Dual-RNA-Guided DNA Endonuclease in Adaptive Bacterial Immunity" (2012) 337 SCIENCE 816.

[3] Agence France-Presse, "Le Nobel de chimie décerné à une Française et à une Américaine" (October 7, 2020), online: *Radio-Canada* https://ici.radio-canada.ca/nouvelle/1739314/prix-nobel-chimie-science-2020.

[4] Patrick Neville, "MPEG LA's Use of a Patent Pool to Solve the CRISPR Industry's Licensing Problems" (2020) 2020:2 Utah Law Review p. 535-536 [Neville].

[5] "CRISPR-Cas9: Timeline of key events" (2020), online: *What is biotechnology?* https://www.whatisbiotechnology.org/index.php/timeline/science/CRISPR-Cas9 [Biotechnology].

[6] Biotechnology.

[7] Catherine Jewell, "The battle to own the CRISPR-Cas9 gene-editing tool" (April 2017), online: *WIPO* https://www.wipo.int/wipo_magazine/en/2017/02/article_0005.html [Jewell].

[8] Neville p. 548.

[9] *Ibid.*

[10] USPTO, "Public Patent Application Information Retrieval", online: *USPTO, Application Numbers 61/652,086 and 61/736,527* https://portal.uspto.gov/pair/PublicPair.

[11] European Patent Office, "EP2800811" (November 10, 2020), online: *European Patent Office*

https://register.epo.org/application?lng=fr&number=EP13793997.

[12] European Patent Office, "EP2771468" (November 10, 2020), online: *European Patent Office* https://register.epo.org/application?lng=fr&number=EP13818570.

[13] Jon Cohen, "The latest round in the CRISPR patent battle has an apparent victor, but the fight continues" (September 11, 2020), online: *Science* https://www.sciencemag.org/news/2020/09/latest-round-crispr-patent-battle-has-apparent-victor-fight-continues [Cohen].

[14] World Intellectual Property Organization, "Protecting your Inventions Abroad: Frequently Asked Questions About the Patent Cooperation Treaty (PCT)" (April 2020), online: *WIPO* https://www.wipo.int/pct/en/faqs/faqs.html.

[15] Nathaniel Lipkus, "The nascent CRISPR-Cas9 patent landscape in Canada" (September 14, 2018), online: *Osler* https://www.osler.com/en/resources/regulations/2018/the-nascent-crispr-cas9-patent-landscape-in-canada.

[16] *Broad Institute, Inc.* v. *Regents of the University of California*, No. 106,048, (P.T.A.B., February 15, 2017).

[17] *Ibid* p. 49.

[18] *Regents of the University of California* v. *Broad Institute, Inc.*, No. 2017-1907 (Fed. Cir. September 10, 2018).

[19] Louis Lieto et al., "Patent Trial and Appeal Board Hears Argument in CRISPR Patent Priority Dispute" (May 21, 2020), online: *JDSUPRA* https://www.jdsupra.com/legalnews/patent-trial-and-appeal-board-hears-96548/#3; "Methods and Compositions for RNA-Directed Target DNA Modification and for RNA-Directed Modulation of Transcription", U.S. Patent Application No. 15/981,807 (May 16, 2018), clm 156.

[20] Cohen.

[21] *Regents of the University of California* v. *Broad Institute, Inc.*, No. 106,115, (P.T.A.B., September 10, 2020) p. 109-110; Kevin E. Noonan, "PTAB Decides Parties' Motions in CRISPR Interference" (September 11, 2020), online: *Patent Docs* https://www.patentdocs.org/2020/09/ptab-decides-parties-motions-in-crispr-interference.html; Jon Cohen, "The latest round in the CRISPR patent battle has an apparent victor, but the fight continues" (September 11, 2020), online: *Science* https://www.sciencemag.org/news/2020/09/latest-round-crispr-patent-battle-has-apparent-victor-fight-continues.

[22] *Ibid.*

[23] Broad Institute, Inc., et al., Application No. 13 818 570.7 (E.P.O. March 26, 2018); Clara Rodriguez Fernandez, "Broad Institute Loses Appeal on European CRISPR Patent" (January 24, 2020), online: *Labiotech* https://www.labiotech.eu/crispr/crispr-patent-europe/; Decision of Technical Board of Appeal 3.3.08

of January 16, 2020, T 1726/15 (Heterologous FPPS/University of California) of 13.8.2020 online: https://www.epo.org/law-practice/case-law-appeals/pdf/t151726eu1.pdf

[24] Canadian Intellectual Property Office, "Search Results" (October 10, 2020), online: *CIPO* https://www.ic.gc.ca/opic-cipo/cpd/eng/search/results.html?query=%28%22CRISPR-Cas9%22%29+AND+%28current-status%3APending+Applications%29&start=1&num=10&type=advanced_search&newSearch=0.

[25] Timothé Cynober, "CRISPR: One Patent to Rule Them All" (February 11, 2019), online: *Labiotech* https://www.labiotech.eu/in-depth/crispr-patent-dispute-licensing/ [Cynober].

[26] *Ibid.*

[27] *Ibid.*

[28] See also: Walter Isaacson, "CRISPR rivals put patents aside to help in fight against Covid-19" (March 3, 2021), online: https://www.statnews.com/2021/03/03/crispr-rivals-put-patents-aside-fight-against-covid-19/

By statnews.com and Broad Institute, "Information about licensing CRISPR systems, including for clinical use", online: https://www.broadinstitute.org/partnerships/office-strategic-alliances-and-partnering/information-about-licensing-crispr-genome-edi.

[29] Neville.