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## Surveying The CRISPR Patent War

By **Michael Stramiello** (May 3, 2018, 12:56 PM EDT)

Following this week's oral argument at the U.S. Court of Appeals for the Federal Circuit, there has been a surge of interest in the long-running CRISPR[1] patent dispute between the Regents of the University of California (with collaborators the University of Vienna and Emmanuelle Charpentier) and the Broad Institute (with collaborators Harvard and MIT). This article summarizes the broader patent war between those two sides and addresses its potential implications for others seeking to use CRISPR-based technologies.



Michael Stramiello

### Battlefields

#### ***United States***

The CRISPR spotlight in the U.S. is currently fixed on the Federal Circuit as it decides whether the Patent Trial and Appeal Board properly dissolved the now-famous interference contest between UC and Broad. The PTAB terminated that proceeding upon accepting Broad's argument that its claims pertaining to eukaryotic cells are patentably distinct from UC's claims for use in any environment, meaning there was no "interference in fact," a threshold requirement rooted in 37 C.F.R. § 41.203(a).[2] UC appealed, and both sides expressed optimism in light of this week's oral argument.[3] They now await the Federal Circuit's decision, which may not come until August or September.

Though the PTAB did not cancel or finally refuse any claims when terminating the interference, its decision triggered speculation that UC might eventually take U.S. rights to use in prokaryotes, with Broad taking them in eukaryotes.[4] While that may eventually come to pass, much remains to be seen before then, even at the U.S. Patent and Trademark Office. For instance, the UC v. Broad interference panel suspended (and the PTAB may soon act on) an anonymously requested ex parte re-examination targeting one of Broad's patents at issue.[5] In addition, the PTAB has yet to respond to two ToolGen suggestions of interference against five Broad-owned patents at issue in the UC interference on appeal,[6] and at least one other UC-owned application has been referred to the PTAB for another potential interference.[7] It is also possible that key rights on either side will become targets for inter partes and post-grant review, though would-be petitioners might prefer to hold back petitions until they can establish Article III standing (e.g., by filing marketing applications) in order to lessen any risk of nonappealable loss.[8]

#### ***Europe***

Broad's stateside success came to a screeching halt at the European Patent Office in the face of oppositions to EP2771468, a European counterpart to its interference-tested rights in the U.S. In January, the EPO's Opposition Division considered whether priority rights had been properly transferred to Broad at the time of its application — a critical determination in assessing whether Broad's claims are sufficiently novel over intervening art. Ultimately, the OD found a defective chain of priority.[9] Broad appealed, requesting accelerated review because "[t]he same questions of law, and the same factual situation ... also arise[] in opposition proceedings pending in relation to at least five patents in the same family." [10] Broad will also face oppositions to EP3009511, which is directed to CRISPR-Cpf1 (now called Cas12a) systems. Relative to Cas9-based technologies, these systems reportedly have the potential to simplify the design and delivery of CRISPR tools.[11] Like Broad's recently revoked Cas9 patent, the application leading to the '511 patent survived third-party

observations during examination, and nothing suggests that it will meet a similar fate on opposition (i.e., revocation due to defective priority).

The stage is also set for UC to defend foundational CRISPR rights at the OD with respect to EP2800811. Like UC's appeal-embroiled rights in the U.S., the '811 patent covers use of CRISPR-Cas9 systems for gene editing in a wide range of environments, including eukaryotic cells. Though UC will have the option of pursuing narrower claims during the opposition process,[12] its patent has withstood various third-party observations — including a 25-page note from Broad that took aim at UC's disclosure as not properly enabling use in eukaryotic cells.[13] In addition, UC may face opposition to EP3241902, its recently granted patent covering use of CRISPR-Cas9 systems for gene regulation. Like UC's '811 patent, it covers use in a wide range of environments, again including eukaryotic cells.[14] One party has already signaled its intent to oppose.[15]

## **China**

Most work in the CRISPR field is being done in the U.S. and China, say the experts at IPStudies,[16] and China has emerged as the world's second-busiest landscape for CRISPR-related priority patent applications.[17] Accordingly, China's State Intellectual Property Office may eventually host its own CRISPR patent disputes, but the UC-Broad rivalry has been relatively quiet on this front. The lone public dust-up played out shortly after SIPO awarded UC a patent broadly covering CRISPR-Cas9 gene-editing methods and compositions,[18] when Broad ominously reminded the world that, "[i]n China, patents are subject to invalidation proceedings after they are issued." [19] When such a challenge might occur is anyone's guess, as post-grant challenges in China need not be initiated within a nine-month window like certain counterparts in the U.S. (i.e., PGRs) and Europe (oppositions).[20]

## **Safe Zones**

As battles rage among the few who seek foundational patent rights, the many who simply wish to use and develop CRISPR have enjoyed an active licensing landscape. One of Broad's named inventors, Feng Zhang, even suggested that research has not been slowed "at all" by the uncertainty, [21] and he may be right: The National Institutes of Health (the federal government's leading funder of medical research), stated in June 2017 that it "ha[d] not received any inquiries or complaints about lack of access to the CRISPR-Cas9 technology for research or commercial development from those who are in a position to use the technology." [22] That lack of immediate concern may be because hundreds of researchers (including named inventors from Broad and UC) have shared access to CRISPR via AddGene, a nonprofit organization that archives and distributes materials to academic and nonprofit users at low cost and subject to agreements that purportedly offer intellectual property and liability protection to providers.[23]

Commercial licensees have not been left out in the cold, but the cost of shelter may be steep. This is particularly true in human therapeutics, where businesses generally expect exclusivity to protect their massive investments in rigorous clinical trials.[24] For instance, one pharmaceutical company made an up-front commitment of \$105 million (including a \$30 million equity investment) as part of a deal for exclusive rights to license up to six new CRISPR-Cas9 treatments aimed at genetic causes of human disease.[25] And that may be a mere drop in the bucket, given the potentially enormous breadth of underlying patent rights whose certainty value as of February 2017 was estimated at \$100 million to \$265 million.[26] Lingering doubts about pending or disputed patent claims may provide fertile ground for prospective licensees seeking discounts, and some have secured licenses from competing rights holders, perhaps expecting to encounter overlapping patents once the dust settles. [27]

Increasing supply and demand for CRISPR patent rights may create a favorable environment for joint licensing platforms (also known as patent pools), especially outside the realm of human therapeutics. In theory, these pools provide means for separately owned, complementary rights to be licensed together through a single, nonexclusive deal with predictable terms and minimal transaction costs. [28] Such arrangements could be useful for commercializing overlapping foundational rights, or those pertaining to a particular use of CRISPR. Though Broad and others have announced their interest in a pool,[29] UC reportedly has concerns about potential conflicts with its existing licenses.[30] Some have questioned whether a pool without UC would be commercially successful,[31] but that question might become moot if UC joins before contributors finalize pool-license terms — a process that could

take years.[32] Either way, consolidating transactions may make sense for potential licensees looking to control costs, even if they will also need to seek supplemental rights outside the pool.

## Conclusion

Regardless of how the Federal Circuit decides the UC v. Broad appeal, the CRISPR patent war seems unlikely to end soon. There are now battles raging on multiple fronts, particularly in Europe, with several more on deck at the USPTO, and maybe even in China. Fortunately, the technology is reportedly widely accessible, and potential licensees may eventually benefit from an elegant, one-stop platform for securing whatever rights they need for commercialization. CRISPR watchers, stay tuned.

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*Michael A. Stramiello, Ph.D., is an associate in the Washington, D.C., office of Paul Hastings LLP.*

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[1] By way of background, “CRISPR” is short for clustered regularly interspaced short palindromic repeats—the genetic signatures of particular bacterial immune systems that scientists have hijacked into a broad range of biological tools for potential use in medicine, agriculture, and beyond. This article uses the term to refer to those tools (not to the repeats themselves), which are especially well known for their ability to edit the genome (i.e., the DNA-based instruction manuals from which all living things are built and maintained).

[2] Broad Inst., Inc. v. Regents of Univ. of Cal., No. 106,048, 2017 WL 657415 (P.T.A.B. Feb. 15, 2017).

[3] Lisa M. Krieger, UC vs. Harvard: Round 2 in CRISPR Fight, The Mercury News (Apr. 30, 2018), <https://www.mercurynews.com/2018/04/30/uc-vs-harvard-round-2-in-crispr-fight/>.

[4]. See, e.g., Jef Akst, UC Berkeley Receives CRISPR Patent in Europe, Scientist (Mar. 24, 2017), <https://www.the-scientist.com/?articles.view/articleNo/48987/title/UC-Berkeley-Receives-CRISPR-Patent-in-Europe/>.

[5] Order – Suspension of Reexamination, at 2, Broad Inst., Inc. v. Regents of Univ. of Cal., No. 106,048 (P.T.A.B. May 12, 2016), <https://acts.uspto.gov/ifiling/PublicView.jsp?identifier=106048&identifier2=null&tabSel=4&action=filecontent&replyTo=PublicView.jsp> (Doc. No. 49).

[6] Preliminary amendments in U.S. Patent Application Nos. 14/685,568 and 14/685,510, dated Apr. 13, 2015.

[7] Office Communication in U.S. Patent Application No. 15/435,233, dated Dec. 19, 2017.

[8] Benjamin Jackson & Jordan Engelhardt, Fed. Circ. Case May Change Biosimilar IPR Strategy, Law360 (Apr. 12, 2018), <https://www.law360.com/ip/articles/1032699/fed-circ-case-may-change-biosimilar-ipr-strategy>.

[9] Dana A. Elfin, European Patent Office Revokes Broad’s Gene-Editing Patent, Bloomberg Law (Jan. 19, 2018), <https://www.bna.com/european-patent-office-n73014474373/>.

[10] <https://register.epo.org/application?documentId=E1GB5DVU0273DSU&number=EP13818570&lng=en&npl=false>

[11] Bernd Zetsche et al., Cpf1 Is a Single RNA-Guided Endonuclease of a Class 2 CRISPR-Cas System, Cell 163, 759–711 (2015).

[12] Akst, supra note 4.

- [13] <https://register.epo.org/application?documentId=EXZCLOG31855FI4&number=EP13793997&lng=en&npl=false>
- [14] <http://www.ersgenomics.com/news-press-release-20180228.php>
- [15] <https://register.epo.org/application?documentId=E1NRYQQ04706132&number=EP17163434&lng=en&npl=false>
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- [23] <https://help.addgene.org/hc/en-us/articles/206150325-What-is-a-Material-Transfer-Agreement-MTA-and-why-do-I-need-one>
- [24] See, e.g., Kevin O'Connor, Making a Splash in the CRISPR Patent Pool, Life Sciences Intellectual Property Review (Sept. 15, 2017), <https://www.lifesciencesipreview.com/article/making-a-splash-in-the-crispr-patent-pool>.
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- [26] Jacob S. Sherkow, How Much Is a CRISPR Patent License Worth? Forbes (Feb. 21, 2017), <https://www.forbes.com/sites/jacobsherkow/2017/02/21/how-much-is-a-crispr-patent-license-worth/#7af1e6af6b77>.
- [27] See, e.g., Taconic, <https://www.taconic.com/genetically-engineered-animal-models/> (last visited Feb. 21, 2018); Catherine Hagan, In the Fight Over the CRISPR Patent, JAX Customers Win, The Jackson Laboratory, <https://www.jax.org/news-and-insights/jax-blog/2017/january/crispr-patent> (last visited Feb. 21, 2018).
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[31] See, e.g., Sophie Lawrance & Francion Brooks, The Competition Law Issues of the CRISPR Patent Pool, Lexology (Feb. 16, 2018), <https://www.lexology.com/library/detail.aspx?g=62ef2525-a34c-4e5e-b401-ea0c90082374>.

[32] Leung, *supra* note 32.

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