

Licensing for profit *and* for good

The Broad Institute's enlightened licensing approach to CRISPR-Cas9 intellectual property stands out in the otherwise regrettable spat for patent rights over the foundational technology.

The latest salvo in a long-running battle surrounding intellectual property (IP) for CRISPR-Cas9 was heard last month. This time, the Patent Trial and Appeal Board of the US Patent and Trademark Office [decided](#) in favor of the Broad Institute, Massachusetts Institute of Technology and Presidents and Fellows of Harvard College (collectively, 'Broad') in their dispute over who 'invented' gene-editing in eukaryotic cells with the Regents of the University of California (UC), the University of Vienna, and Nobel co-laureate Emmanuelle Charpentier. The ruling is [not likely](#) to be the last word in the tussle between these academic institutions for supremacy over CRISPR IP. But it does have implications for CRISPR companies' [freedom to operate](#). And it reinforces Broad's position at the center of the CRISPR patent landscape — not a bad thing, given the institute's judicious and progressive approach to IP licensing.

Research breakthroughs like CRISPR-Cas9 are rare. Based on the chronology of previous breakthroughs — [recombinant DNA technology](#), [monoclonal antibodies](#), [the polymerase chain reaction](#), [viral gene therapy](#), [human embryonic stem cells](#), [RNA interference](#) and [induced pluripotent stem cells](#) — they come along only once or twice every decade.

These technologies tend to be quickly recognized because they immediately create a buzz among researchers. They are rapidly reproduced in different labs and open up new lines of investigation, often with immediate applications in biomedicine, agriculture or industry. Often, they can turn into cash cows for the academic institutions in which they were discovered; in the case of the Broad's license to Editas Medicine, the company currently owes \$12.5 million in [milestone payments](#), which could mount up to \$125 million.

Patents grant their inventors a limited (20-year) monopoly over a technology in return for disclosing the details of its workings. In theory, they are meant to promote technology dissemination by allowing others to build on it, spurring further innovation. Indeed, in biotech, the huge investments needed for companies to

develop new products over multiple years would not be possible without patent protection.

But patents don't always facilitate research and innovation — in practice, they can do the reverse. They can be written opaquely to prevent those reasonably skilled in the art from reproducing the work or to include more than what was actually invented. They can be [evergreened](#) — an endeavor pursued with gusto by the drug industry. They can be 'trolled' by entities not seeking to reduce an invention to practice but instead extort fees from organizations that do (as in the [case](#) of the Alzheimer's Institute of America and Jackson Laboratory). And they can be written with overbroad claims — a problem that has been highlighted for certain [CRISPR patents](#).

Beyond the patents themselves, perhaps the most damaging problem is exclusive licensing of IP to companies that litigate it in an overly aggressive or restrictive manner. For example, [Roche](#) was accused of ham-fisted handling of the licenses to academic and clinical labs when it acquired the rights to PCR from Cetus; and [Sangamo Therapeutics'](#) restrictive licensing of IP and materials surrounding zinc-finger technology prompted academics to form an open-science alternative, the [Zinc Finger Consortium](#).

These days, with more and more universities forming startups, an exclusive license is becoming the almost universal path to IP transfer to a newly formed venture. In such cases, the university negotiates the largest payout possible while the venture seeks to get the broadest rights possible to build a dominant IP position. When these licenses are sublicensed to other companies, the academic institution gets a slice of the fees.

This is not a problem in itself. But all too often, such 'surrogate' licenses are written in a manner whereby the university gives away the farm. This can happen when the license terms cede all fields of use, fail to outline appropriate diligence milestones (which set out timelines for development of the technology) or omit clawback clauses (whereby the university can retrieve rights to the IP if the original licensee fails to develop it).

In the case of CRISPR, the Broad and UC Berkeley deserve credit for waiving IP licenses for academic and non-profit research. But according to [one analysis](#), for commercial research, their licensing strategies diverge.

Apart from its license with Editas covering human therapeutics, the Broad grants a non-exclusive license to any company wishing to use CRISPR in tool development. It also is willing to join patent pools like [MPEG LA](#); in 2017, it created a [joint licensing framework](#) with DuPont Pioneer for agriculture; and two years later, it did the same with [MilliporeSigma](#) for biological research.

In contrast, UC Berkeley and the University of Vienna gave one exclusive license for all fields of research and application to a single company: Caribou Biosciences (which has since exclusively sublicensed IP for human therapeutics to Intellia Therapeutics). And Emmanuelle Charpentier gave her rights exclusively to two companies (without any clawback terms): CRISPR Therapeutics for human therapeutics and ERS Genomics for everything else.

Of course, not all academic institutions have the resources of the Broad, so delegating IP license management and waiting for the money to roll in from surrogate license and sublicenses is an easy solution. But for a foundational technology like CRISPR, giving an exclusive license to just one or two companies seems wrong — especially if the licenses don't contain terms to claw back IP so that other companies can develop uses neglected by the original licensee.

The question is whether university deans and presidents care enough about IP (beyond the cash it brings in) to give their tech transfer offices the requisite resources to audit exclusive commercial licenses on a regular basis. Given that their duty is "[to ensure the expeditious and wide dissemination of university-generated technology for the public good](#)," perhaps they should. □

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