2018

The CRISPR Patent Decision Didn't Get the Science Right. That Doesn't Mean It Was Wrong

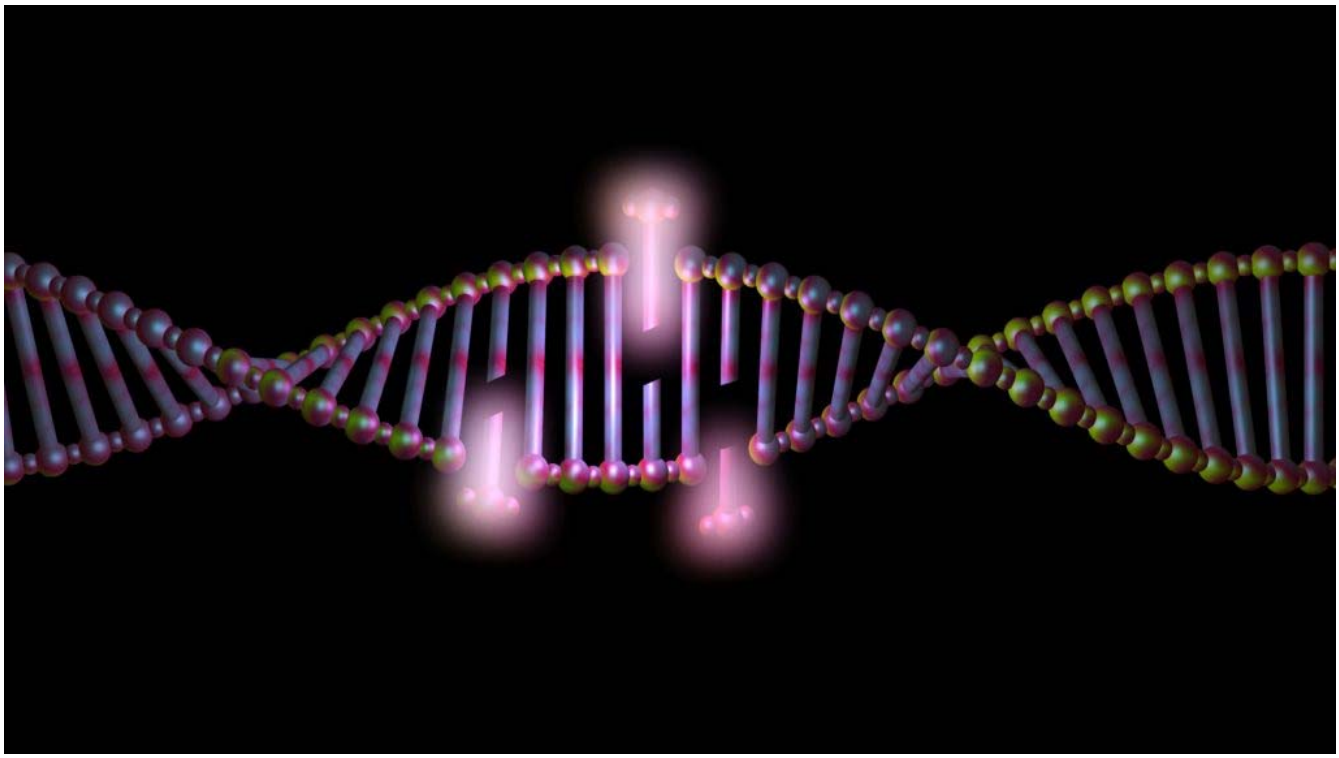
Jacob S. Sherkow
New York Law School, jacob.sherkow@nyls.edu

STAT

The CRISPR patent decision didn't get the science right. That doesn't mean it was wrong

By Jacob S. Sherkow

September 11, 2018



Adobe

The CRISPR patent dispute[1] between the University of California, Berkeley, and the Broad Institute is finally over[2]. As almost everyone following the case predicted, the U.S. Court of Appeals for the Federal Circuit affirmed Monday the U.S. patent office's decision[3] that there was "no interference-in-fact" between UC Berkeley's patent application and more than a dozen Broad patents. In plain English: Broad researcher Feng Zhang's CRISPR patents were sufficiently inventive over the UC Berkeley's patent applications with Jennifer Doudna and Emmanuelle Charpentier.

Many scientists disagree with the decision, believing that it fails to comport with how molecular biology is actually practiced. I agree with them. But that doesn't make the Federal Circuit's decision wrong. In fact, I think its decision is absolutely correct.

The reason has to do with standards of review — the standards courts use to weigh evidence, limit their authority, and make decisions. Like criminal law's "beyond a reasonable doubt" standard, standards of review are *incredibly* important for many legal cases. They're how much one side needs to prove something and, failing that, who should win.

The standard of review in the CRISPR patent dispute was the "substantial evidence" standard: whether a reasonable trier of fact (one or more people who determine the facts in a legal proceeding) based its opinion on substantial evidence. To be clear, that doesn't mean the trier of fact got things correct, or even whether there was more evidence for the other side. Rather, the substantial evidence standard means only that a fact-finder based its decision on substantial *enough* evidence to be reasonable.

Related: [1]
Appeals court upholds CRISPR patents awarded to the Broad Institute [1]

And there *was* substantial enough evidence for the Patent Office to determine that Zhang's application of Doudna and Charpentier's CRISPR-Cas9 system, which they developed in bacteria, to more complex eukaryotic cells (cells like human cells that have nuclei) constituted a significant enough advance to be its own invention. The patent office considered the scientific difficulties in getting other nucleic acid gene-editing systems to work in eukaryotes; statements submitted by experts from both sides, such as UC Berkeley's own expert[4] saying that there was "no guarantee that Cas9 would work effectively on a chromatin target or that the required DNA-RNA hybrid can be stabilized in that context," and ultimately statements by Doudna herself that called the gap between bacteria and human cells a "huge bottleneck."[1]

I, and many scientists[5] as well, think that holding these offhanded statements against Doudna is both unfortunate and bad as a matter of policy. But they were evidence, and the patent office was correct to consider them as such. Considered as a whole, those statements, the testimony of experts, and scientific difficulties in getting previous gene-editing systems to work in eukaryotic cells represent at least substantial evidence.

This doesn't mean I agree with the patent office's interpretation of the science. In its original decision, the patent office wrote that moving previous gene-editing systems from bacteria to eukaryotic cells suffered from numerous problems: "differences in gene expression, protein folding, cellular compartmentalization, chromatin structure, cellular nucleases, intracellular temperature, intracellular ion concentrations, intracellular pH, and the types of molecules in prokaryotic versus eukaryotic cells."

These problems were real and shouldn't be discounted. But, as I wrote in article for EMBO Reports[6] last year, they were widely known to scientists at the time who could have solved each with a road map of solutions. "[D]ifferential gene expression can be controlled by selecting appropriate promoters; protein folding can, in some instances, be made uniform by certain optimization techniques; chromatin structure can be altered by histone modification; nucleases can be blocked; temperature can be regulated; pH can be buffered; and so on," I wrote. As a matter of patent law, however, this experimental road map isn't enough — it does not provide, in patent parlance, a "reasonable expectation of success."

This illustrates, I think, a classic disconnect between the legal standards of patent law and the realities of scientific research. There are others, which I have also written about at length: on how science and patent law treat reproducibility[9]; how they treat genetic datasets[10]; on what, exactly, is a "law of nature."[11]

You could say that as a former laboratory scientist turned patent law professor, this is a particular academic interest of mine. But my view of what's best is not the same as what the law actually is. The CRISPR patent decision may not have gotten the science right. But that doesn't make it wrong as a legal matter.

If you don’t agree with the Federal Circuit’s decision, you may be in good company. The law can sometimes be wrong as a matter of both policy and practicality. But, at least ideally, the law provides a previously agreed-upon, neutral set of rules to decide disputes. When the law no longer works, it’s ultimately the job of Congress to change the law. And although this ideal is routinely flaunted in practice, it’s still a model to live by.

In fact, it’s something scientists themselves should be familiar with. When the facts stop fitting the model, you change the model, not the facts. You dust yourself off, come up with new hypotheses and new experiments to explain the world, and try again.

Jacob S. Sherkow, J.D., is professor of law at the Innovation Center for Law and Technology[12] at New York Law School.

About the Author

Jacob S. Sherkow

@jsherkow[13]

Tags

Links

1. https://www.statnews.com/2018/09/10/appeals-court-upholds-crispr-patents-awarded-to-broad-institute/
2. https://t.co/uVWyHBwvV2
3. https://e-foia.uspto.gov/Foia/RetrievePdf?system=BPAI&flNm=fd106048-02-15-2017-1
4. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3437577/
5. http://www.michaeleisen.org/blog/?p=1981
6. https://papers.ssrn.com/sol3/papers.cfm?abstract_id=2993133
7. https://www.statnews.com/signup/
8. https://www.statnews.com/privacy/
9. https://papers.ssrn.com/sol3/papers.cfm?abstract_id=2735181
10. https://papers.ssrn.com/sol3/papers.cfm?abstract_id=2928241
11. https://papers.ssrn.com/sol3/papers.cfm?abstract_id=2268180
12. https://www.nyls.edu/innovation-center-for-law-and-technology/
13. https://twitter.com/jsherkow
14. https://www.statnews.com/tag/biotechnology/
15. https://www.statnews.com/tag/crispr/
16. https://www.statnews.com/tag/legal/