



MONIB ZIRVI, MATTHEW LUBIN, MARIA KEMPE and NORMAN GERRY,

Petitioners,

v.

JAY T. FLATLEY, ILLUMINA INC., DAVID R. WALT, STEPHEN P.A. FODOR, KEVIN GUNDERSON, JIAN BING FAN, MARK CHEE, AFFYMETRIX, D/B/A AS PART OF THERMO FISHER SCIENTIFIC, APPLIED BIOSYSTEMS, D/B/A BRAND OF THERMO FISHER SCIENTIFIC, ROBIN M. SILVA and JOHN R. STUEPLNAGEL,

Respondents.

On Petition for a Writ of Certiorari to the United States Court of Appeals for the Second Circuit

BRIEF OF AMICUS CURIAE CHARLES CANTOR, Ph.D. IN SUPPORT OF PETITIONERS

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TABLE OF CONTENTS

Page

TABLE O	F AUTHORITIES	ii
STATEME CHARLES	ENT OF INTEREST OF AMICUS CURIAE S R. CANTOR	1
SUMMAR	Y OF ARGUMENT	4
ARGUME	NT	
I.	RESEARCH SCIENTISTS' INNOVATION IS VITAL TO THE NATION AND THE WORLD	6
II.	<i>KOCH V. CHRISTIE'S</i> IS AN INAPPROPRIATE STANDARD FOR COMPLEX INTELLECTUAL PROPERTY CASES	9
III.	NEGATIVE TRADE SECRETS HAVE INDEPENDENT ECONOMIC VALUE	
CONCLUS	SION	

TABLE OF AUTHORITIES

Cases:

Ariosa Diagnostics, Inc. v. Illumina, Inc., Case IPR2014-01093 (U.S.P.T.O. Jan. 7, 2016)	2
Coda v. Goodyear,	
916 F.3d 1350 (Fed. Cir. 2019)	
Dow Corning Corp. v. Xiao,	
283 F.R.D. 353, 354 (E.D. Mich. 2012)	
Halo Electronic, Inc. et al. v Pulse Electronics, Inc., et al.,	
(Nos. 14-1513 and 14-1520) at page 5	
Koch v. Christie's Int'l PLC,	
699 F.3d 141 (2d Cir. 2012)	
Zirvi v. U.S. Nat'l Institutes of Health et al.,	
No. 3:20-cv-07648-MAS-DEA (D.N.J.)	

Other Authority:

The Paradox of Source Code Se	ecrecy,	
104 Cornell L. Rev. 1183 (2019)	11 - 12

Page

STATEMENT OF INTEREST OF AMICUS CURIAE CHARLES R. CANTOR¹

Amicus Curiae Charles R. Cantor was the Chief Scientific Officer at Sequenom, Inc. in San Diego, California from 1998 through 2013. He currently is Professor Emeritus of Biomedical Engineering at Boston University, where he was a Chair of the Biomedical Engineering Department from 1995-1998. He also currently serves as a Distinguished Adjunct Professor in Physiology and Biophysics at the University of California, Irvine. He also serves as a board member, an advisor, or a consultant to about 20 different biotechnology companies.

During his career, he has held many other academic positions, including Professor of Molecular Biology at the University of California, Berkeley from 1989-1992; Director of the Human Genome Center at Lawrence Berkeley Laboratory from 1988-1990; Professor and Chairman of Genetics and Development at Columbia University College of Physicians & Surgeons from 1981-1989; and Professor of Chemistry, with a joint appointment in Biological Sciences, at Columbia. University from 1972-1981.

He received his B.A. (summa cum laude) in Chemistry from Columbia University in 1963, and his Ph.D. in Biophysical Chemistry from the University of California, Berkeley in 1966. He has published more than 450 peer-reviewed articles, and has co-authored a three-volume textbook on biophysical chemistry. Charles R. Cantor

¹ Counsel for all parties have consented to the filing of this brief. Counsel for Petitioners assisted in drafting this brief, are retained and compensated by Petitioner, and represent amicus herein. *See* Rule 37.

& Paul R. Schimmel, Biophysical Chemistry, W.H. Freeman (1980). He also co-authored the first genomics textbook. Charles R. Cantor & Casssandra L. Smith, Genomics: The Science and Technology of the Human Genome Project, John Wiley & Sons (1999). This textbook, among other topics, discusses analysis of DNA sequences by hybridization, polymerase chain reaction, and strategies for large-scale DNA sequencing.

Dr. Cantor is a co-inventor of over 130 U.S. and foreign patents, including inventions related to nucleic acid hybridization, labeling, such as non-radioactive labeling with biotin, and detection of nucleic acid sequences. He was elected Fellow of the National Academy of Inventors for his contributions to science.

He is an elected member of the National Academy of Sciences, the American Academy of Arts and Sciences, and a Fellow of the American Association for the Advancement of Science.

Dr. Cantor developed parallel approaches to address the same problems in the art addressed by U.S. Patent No. 7,955,794 ("the '794 patent"). He has received patents directed to his own approaches.

He has also been an expert witness for plaintiffs Roche/Ariosa in multiple trials in which respondent Illumina, Inc. ("Illumina") was the defendant including trials specifically involving U.S. Patent 7,955,794.² However, at the time, he was unaware of many of the fraudulent acts that Petitioners alleged in the instant lawsuit.

² See generally Final Written Decision, Paper No. 69, Ariosa Diagnostics, Inc. v. Illumina, Inc., Case IPR2014-01093 (U.S.P.T.O. Jan. 7, 2016), reh'g denied, Paper No. 83 (U.S.P.T.O. Sept. 29, 2016), aff'd in part and dismissed in part, 705 Fed. Appx. 1002 (Fed. Cir. 2017), cert. denied, 139 S. Ct. 2740 (2019).

In the lawsuit which originated this appeal, Petitioner alleged that Illumina and its purported arch-rival, respondent Thermo Fisher Scientific ("Thermo Fisher") colluded to secretly purloin his genetic-testing inventions by stealing trade-secret intellectual property, including so-called "negative know-how" or "dead-end" trade secrets, re-patent them as their own invention, and defraud the petitioners of their rightful royalties. Illumina, having commercialized this wrongly obtained intellectual property, today (with Thermo Fisher), control greater than 90 percent of the market in DNA microarrays and DNA sequencing instruments and consumables, and they have made billions of dollars in profits.

Amicus curiae Dr. Cantor has an interest in this case because his decades of experience in academic scientific research, as well as his experience in the development and commercialization of genetic innovations, compel him to support Petitioners in their efforts to obtain this Court's review of the lower courts' dismissal of their claims. Dr. Cantor believes that the lower courts applied the wrong standard in considering whether Petitioners had constructive (or actual) notice of Respondents' wrongdoing, thus starting the statute of limitations clock. The simplistic *Koch v*. *Christie's* standard has no proper application to intellectual property cases involving highly complex scientific trade secrets and a decades-long scheme of fraudulent concealment by sophisticated corporate actors against individual inventors. Furthermore, the lower courts utterly misunderstood the important concept of negative trade secrets, wrongly concluding that they *per se* lacked economic value once the related innovation had been patented or publicized. These errors violate the fundamental intellectual property rights enshrined in the Constitution and threaten to undermine longstanding legal protections given to inventors. If this Court does not intervene and grant certiorari, the scientific innovation fueling the economy of the Nation -- and indeed the well-being of the world -- will ultimately suffer.

SUMMARY OF ARGUMENT

The federal courts' adoption of the Second Circuit's constructive notice standard – where complex and voluminous patent filings, which contain intentionally buried and obfuscated evidence of stolen intellectual property, are deemed to constitute "storm warnings" putting the inventor on notice and starting the statute-of-limitations clock – would gravely harm the scientific research community and unjustly deprive inventors of the fruits of their labor. In contrast, the Federal Circuit's decision in *Coda v. Goodyear*, 916 F.3d 1350 (Fed. Cir. 2019) recognized that an individual or small-business inventor cannot reasonably be expected to comb through scores of complex patent filings over years to divine evidence of trade secret misappropriation by a sophisticated corporate wrongdoer. *Koch v. Christie's Int'l PLC*, 699 F.3d 141 (2d Cir. 2012) involved the far more pedestrian (and far more easily discoverable) fraud of fake wine being peddled as historically important artifacts, a fraud that had been widely reported in the media. The Petitioners' Universal Array and Zip code design inventions enabled key advances in detecting the human gene changes responsible for cancers, genetic defects, and infectious diseases. Yet, the media have never reported Illumina's intellectual property theft nor Illumina's fraudulent collusion with Thermo Fisher. For the Second Circuit to impose the simplistic *Koch* analysis on the complex genetic-mapping technology and sophisticated, years-long corporate fraud underlying this case was at best inappropriate, and at worst threatens the most basic Constitutional protections of intellectual property.

Further, the lower courts' conclusion that so-called "negative trade secrets" *per se* have no economic value once an invention is patented, commercialized and/or otherwise publicized, lacks scientific foundation, legal basis, or simple common sense. Universities (as well as corporations) spend billions of dollars to fund scientific research and development. That experimentation leads to knowledge not only of successful innovations, but also to knowledge of what rabbit-holes lead to dead ends. That knowledge is equally protected as intellectual property and can be equally if not more valuable than the inventions themselves.

ARGUMENT

I. RESEARCH SCIENTISTS' INNOVATION IS VITAL TO THE NATION AND THE WORLD

The Constitution expressly recognizes and broadly protects intellectual property:

"The Congress shall have Power to promote the Progress of Science and useful Arts, by securing for limited Times to Authors and Inventors the exclusive Right to their respective Writings and Discoveries."

U.S. Const. Art. I, sec. 8, cl. 8. This provision has formed the basis for the entire scope of intellectual property development and protection, not only in the United States but as the standard for the developed world. This has been accomplished not only via patent protection of innovation by the United States Patent and Trademark Office, but also through the identification and protection of trade secrets. Much of the innovation over the last two centuries in many fields has originated in universities through the tireless efforts not only of professors, but also of graduate students and post-doctoral fellows. As Adam Mossoff stated in his Amicus Curiae Brief in *Halo Electronic, Inc. et al. v Pulse Electronics, Inc., et al.* (Nos. 14-1513 and 14-1520) at page 5, the practice of firms paying to license patents and otherwise compensate inventors for their innovations (instead of inventors commercializing their own intellectual property) "has achieved tremendous efficiencies through the division of labor and has been essential to America's flourishing innovation economy."

Corporations – honest ones -- thus provide much of the necessary capital or financial liquidity for universities and individuals to engage in ongoing research and development. Second, and more important, paying rightful royalties creates efficiencies in converting an invention in a university or another laboratory into real-world products that are sold in the marketplace. If companies are allowed to illegally purloin the inventions of others, and subsequently to commit fraud to ensure they never pay rightful royalties to the true and original innovators, then this will surely stifle innovation and diminish both national and global economic prosperity over the long term.

Innovation is easy to stifle and difficult to promote. To quote Stephen Haber of the Hoover Institution at Stanford University:

We began this essay by inquiring into the question of why some societies are much more innovative than others, and thus much more prosperous. We hope that at least one implication is now fixed in the reader's mind: innovation is not an event, it is a process. It happens when individuals take risks because they know that risk taking will be rewarded. Without a common belief that individuals will share in the rents from innovation, the necessary complementary skills, laws, and technologies do not come into existence. We hope, as well, that at least one secondary implication is jostling about in the reader's mind: it is that innovation and the prosperity it brings are not manna from heaven. They are equilibrium out-

7

comes of a complex combination of political structures, laws, judicial systems, stocks of human capital, and belief systems. As such, they are fragile plants.

S. Haber, Innovation, not Manna from Heaven, Hoover Inst. (available at hoover.org)

Our nation is at the dawn of a new era of genome-driven healthcare, one where capabilities such as early diagnosis of cancer, personalized medicine, and mRNA vaccines are turning from science fiction into reality. All these advances are now possible because of the pioneering innovation in DNA sequencing, microarrays, and mRNA biology conducted by researchers at American universities.³ Petitioners' Universal DNA Array, comprising both universal and unique Zipcodes both in solution and on the Array, has revolutionized the way DNA is sequenced and genetic diseases are analyzed. The Universal Zipcode Array and other important concepts and procedures that Petitioners conceived of, developed, and proved in the Barany Laboratory in the mid-to-late 1990's, as well as exact DNA sequences that are used in these procedures, have been instrumental in this revolution.

³ Four-color DNA sequencing by synthesis using cleavable fluorescent nucleotide reversible terminators. Ju J, Kim DH, Bi L, Meng Q, Bai X, Li Z, Li X, Marma MS, Shi S, Wu J, Edwards JR, Romu A, Turro NJ. Proc Natl Acad Sci U S A. 2006 Dec 26;103(52):19635-40. doi: 10.1073/pnas.0609513103, available at <u>https://pubmed.ncbi.nlm.nih.gov/17170132</u>/; Universal DNA microarray method for multiplex detection of low abundance point mutations, Gerry NP, Witowski NE, Day J, Hammer RP, Barany G, Barany F.J Mol Biol. 1999 Sep 17;292(2):251-62. doi: 10.1006/jmbi.1999.3063, available at <u>https://pubmed.ncbi.nlm.nih.gov/10493873/</u>; Incorporation of pseudouridine into mRNA yields superior nonimmunogenic vector with increased translational capacity and biological stability, Karikó K, Muramatsu H, Welsh FA, Ludwig J, Kato H, Akira S, Weissman D. Mol Ther. 2008 Nov;16(11):1833-40. doi: 10.1038/mt.2008.200. available at <u>https://pubmed.ncbi.nlm.nih.gov/18797453/</u>.

Upholding the dismissal at the pleading stage of Petitioners' lawsuit would establish a harmful or even dangerous precedent. Not only would it harm universities, professors, graduate students, and post-doctoral fellows, but it would also harm the entire innovation economy by stifling future innovation not only in the original technique but also as these lead to breakthroughs in fields such as cancer early detection and combating infectious diseases. Ultimately, this precedent would be contrary to the Patent Clause of the United States Constitution. The Framers of that Clause would never have intended the important allegations in this action to be so unjustly and trivially dismissed.

II. KOCH V. CHRISTIE'S IS AN INAPPROPRIATE STANDARD FOR COMPLEX INTELLECTUAL PROPERTY CASES

Both the Southern District of New York and the Second Circuit Court of Appeals appear to have applied the wrong standard in their analysis in dismissing petitioners' complaint as being untimely under the applicable statutes of limitations. They cited Koch v. Christie's Int'l Pub. Ltd. Co., 699 F.3d 141 (2d Cir. 2012), a case involving the authenticity of wine, as a similar matter. Applying that analysis it is not only inappropriate, but also it is a dangerous precedent to utilize this as the standard in complex intellectual property matters.

It is simply unreasonable to expect individual inventors – in this case, practicing physicians who are busy tending to patients and saving lives -- to endlessly scour the vast array of patents being filed continually by numerous large companies (and/or attempting to obtain copies of corporate submissions to government agencies via FOIA requests, *see, e.g., Zirvi v. U.S. Nat'l Institutes of Health et al.*, No. 3:20-cv-07648-MAS-DEA (D.N.J.)) to ensure that their intellectual property is not secretly being stolen. The same is true for university professors and faculty who are busy teaching and training the next generation of scientists, engineers, programmers, and inventors who will be needed to solve critical problems facing our Nation and indeed the world.

A timely example of the national and global benefits of university-based research is the mRNA vaccines developed over the course of decades of research at the University of Pennsylvania. Dr. Drew Weissman, MD, PhD, a professor of Infectious Diseases in the Perelman School of Medicine at the University of Pennsylvania, and Katalin Kariko, Ph.D., an adjunct associate professor at Penn and currently a senior vice president at BioNTech, discovered in the early 2000s that introducing certain chemical modifications into messenger ribonucleic acid (mRNA) molecules can greatly increase their therapeutic potential. This discovery played a critical role in the development of two of the leading COVID-19 vaccines produced by Moderna and Pfizer/BioNTech that rely on the use of modified mRNA. Both of these researchers were appropriately credited for their research and received rightful royalties for their contribution. Consider if Moderna and/or Pfizer/BioNTech had secretly purloined these scientists' inventions, secretly used them to obtain patents, and then developed and commercialized the COVID vaccines, reaping billions in profits. Then posit that Moderna and Pfizer blithely dismissed the inventors' claims for just recognition and remuneration by telling them they should have been reviewing every patent filing by every biotechnology or pharmaceutical company in the field over the past two decades, and should have detected their fraud years ago. Fortunately, Moderna and Pfizer did not do this to Drs. Weissman and Kaliko. But this is precisely what Illumina and Thermo Fisher did to Petitioners.

III. NEGATIVE TRADE SECRETS HAVE INDEPENDENT ECONOMIC VALUE

The very nature of basic research in universities requires scientists to devote innumerable hours to experimental trial and error, resulting in incremental increases in the human knowledge base. Basic research is painstaking work which generates not only breakthroughs in innovation and invention but – much more often – knowledge about what approaches lead to suboptimal results or even dead ends. This so-called "negative know-how" (a/k/a negative trade secrets) is invaluable to competitors. It can save significant time and effort to know what directions to avoid in future research and development needed to bring products to market.

Negative trade secrets have independent economic value for genetic-analysis innovations such as ZipCode Sequences and ZipCode arrays just as they do for computer software. See, e.g., Dow Corning Corp. v. Xiao, 283 F.R.D. 353, 354 (E.D. Mich. 2012) (citing Apple iPhones as a hypothetical example and observing that "[t]he availability of the iPhone 4S does not render the trade secrets associated with the iPhone 4 of 'no economic value"). *See also generally* Sonia K. Katyal, *The Paradox of Source* *Code Secrecy*, 104 Cornell L. Rev. 1183 (2019) (discussing the implications of increased reliance on trade secrecy to protect algorithms).

In this case, the lower courts gravely misunderstood this important intellectual-property concept. If left standing, this precedent would have far-reaching detrimental effects on science and industry. For example, pharmaceutical companies as well as pharmaceutical and biochemistry research laboratories at universities often invest millions, if not billions, of dollars in research, and the results of those experiments – whether positive or negative -- constitute immensely valuable trade secrets which must be protected. It should be a matter not only of law but of plain common sense that knowing what scientific experiments lead to dead ends can be equally if not greater in economic value than knowing which ones lead to a successful innovation. To conclude as a matter of law (at the pleading stage, moreover) that negative trade secrets are no longer valuable once an innovation is patented and/or enters the public domain is misinformed and simply wrong.

CONCLUSION

For the foregoing reasons, Amicus Curiae Charles R. Cantor respectfully re-

quests that the Court grant Petitioners' writ of certiorari in this matter.

Respectfully submitted,

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