UCLA Journal
of
Law & Technology

RNAI TECHNOLOGY COMPATIBILITY IN THE US AND EU—COMPARISONS AND FUTURE PERSPECTIVES

Izabella Higson*

ABSTRACT

This paper discusses the differences in patent eligibility in the US and the EU, and how the resulting inconsistencies have specifically affected RNAi research and patents.

Courts around the world have struggled with defining clear distinctions between patentable and unpatentable biotechnological inventions. Gene-editing technology is unlike anything patent systems have seen before and the field continues to rapidly evolve. The changing technology thus challenges both legislators and the judiciary as they attempt to keep patent rules balanced and current. In the landmark case *Association for Molecular Pathology v. Myriad Genetics*, the US Supreme Court found that naturally occurring DNA sequences were unpatentable. European courts, however, have not yet followed suit, with the European Directive on the Protection of Biotechnological Inventions noting that isolated DNA sequences are patentable subject matter. In fact, the corresponding European patents at issue in *Myriad* remained valid in the EU despite various oppositions.

RNAi-based research and technology is still in the early stages of its evolution. Thus the relative ease or difficulty of protecting RNAi IP is likely to have a large effect on the growth of this new class of therapeutics.

* Patent Litigation Associate at Marshall, Gerstein & Borun LLP. Thanks to the JOLT team for their brilliant comments and edits.

TABLE OF CONTENTS

INTRODUCTION

Developments in the field of biotechnology have brought many new and divisive challenges to intellectual property legislation. Particularly, courts have struggled with defining clear distinctions between patentable and unpatentable gene-related inventions. Over the past decade the US Supreme Court has issued several decisions resulting in a shift in gene-related patent eligibility. These decisions culminated in the landmark case *Ass'n for Molecular Pathology v. Myriad Genetics* ("*Myriad*"), where the Supreme Court found that naturally occurring DNA sequences were unpatentable under USC 35 §101 despite the discovery of their association with certain cancers.[1] European courts have not yet followed suit, with the European Directive on the Protection of Biotechnological Inventions 98/44/EC noting that isolated DNA sequences are patentable subject matter.[2] In fact, Myriad's corresponding European patents, though narrow, remained valid in the EU despite various oppositions.[3]

This paper discusses the effect that differences in patent eligibility on either side of the Atlantic have had on RNAi research and patents. Given that the first ever RNAi-based therapeutic (Onpattro) was only approved by the FDA in 2018, this field is still very much in the early stages of its evolution.[4] The relative ease or difficulty of protecting RNAi IP is likely to have a huge effect on the growth of this new class of therapeutics.

I. RNAi Technology

Ribonucleic acid interference (RNAi) is a naturally occurring, sequence-specific gene silencing mechanism. Double-stranded RNA molecules (dsRNAs) are processed by an enzyme called Dicer to produce short, single-stranded RNA molecules termed small interfering

---

[1] Ass'n for Molecular Pathology v. Myriad Genetics, Inc., 569 U.S. 576, 596 (2013).

[2] Directive 98/44/EC, of the European Parliament and of the Council of 6 July 1988 on the Legal Protection of Biotechnological Inventions 1998 O.J. (L 213), 13, 18.

[3] *See* Johnathon Liddicoat et al. *Continental Drift? Do European Clinical Genetic Testing Laboratories Have a Patent Problem?*, 27 EUR. J. HUM. GENETICS 997 (2019); *see also* Gert Matthijs et al., *The European BRCA Patent Oppositions and Appeals: Colouring Inside the Lines*, 31 NATURE BIOTECH. 704, 709 (2013).

[4] *See* News Release, U.S. Food & Drug Admin., FDA Approves First-of-Its Kind Targeted RNA-Based Therapy to Treat a Rare Disease (Aug. 10, 2018), https://www.fda.gov/news-events/press-announcements/fda-approves-first-its-kind-targeted-rna-based-therapy-treat-rare-disease.

ribonucleic acids (siRNAs).[5] These siRNAs are loaded onto a second enzyme, Argonaute, to form the RNA-induced silencing complex (RISC). RISC uses the siRNA as a guide to find complementary mRNA and cleave it. This results in gene silencing (the gene is "switched off") as the mRNA is degraded, which can be useful in treating diseases that are caused by harmful gene expression.[6]

In the context of therapeutics, scientists design duplexes made up of a desired siRNA guide and a complementary second strand, thus resembling natural dsRNAs.[7] Scientists then introduce these duplexes into a cell where the Dicer and Argonaute enzymes process the duplex, as if it were natural dsRNA.[8] After processing, the designed siRNA guide selectively silences genes which have complementary mRNA to that strand. Thus, the therapeutic payload of RNAi technology is extremely similar to the native cellular process, with the main difference being the source of the double-stranded RNA, which is later processed by Dicer and Argonaute to result in single stranded siRNA.[9]

II. Patentable Subject Matter

A. United States

i. General Patent Eligibility

Section 101 of the Patent Act states that there are four categories of patentable subject matter: processes, machines, articles of manufacture, and compositions of matter.[10] Case law further restricts patentability within these categories by stating that "laws of nature, natural phenomena, and abstract ideas" are also not patentable subject matter.[11] These restrictions on patentability were

---

[5] David Bumcrot et al., *RNAi Therapeutics: A Potential New Class of Pharmaceutical Drugs*, 2 NATURE CHEM. BIOLOGY 711 (2006), https://doi.org/10.1038/nchembio839.

[6] Nat'l. Ctr. For Biotech. Info., *RNA Interference (RNAi)*, NAT'L LIBR. OF MED., https://www.ncbi.nlm.nih.gov/probe/docs/techrnai/ (last visited Nov. 5, 2022).

[7] Anastasia Khvorova et. al., *Functional siRNAs and miRNAs Exhibit Strand Bias*, 115 CELL 209 (2003), *available at* https://doi.org/10.1016/s0092-8674(03)00801-8.

[8] Queta Boese et al., *Mechanistic Insights Aid Computational Short Interfering RNA Design*, 392 METHODS ENZYMOLOGY, 74-75 (2005), https://doi.org/10.1016/S0076-6879(04)92005-8; *see also* Bumcrot et al., *supra* note 5 at 711.

[9] Bo Hu et al., *Therapeutic siRNA: State of the Art*, 5 SIGNAL TRANSDUCTION TARGETED THERAPY 101, 101 (2020), https://doi.org/10.1038/s41392-020-0207-x.

[10] 35 U.S.C. § 101 (1952).

[11] *See* Diamond v. Diehr, 450 U.S. 175, 185 (1981).

created in order to prevent patenting of standard scientific research methods.[12] Because the purpose of patents is to "promote the progress of science and useful arts,"[13] patenting a basic research tool may over-reach and in fact stunt and impede the growth of innovation.

But reading the restrictions too broadly would undermine the patent system altogether because, at some level, all new inventions are based around "laws of nature."[14] Consequently, the Supreme Court created a two-step test to determine whether an invention, despite falling into one of the case-law restrictions, consists of patentable subject matter.[15]

First, the court must determine whether the invention is *directed to* a natural law, natural phenomenon, or abstract idea. Almost anything strongly related to naturally occurring cellular processes fails this first step. In the first step, the court also looks to whether a natural product has been sufficiently transformed or is markedly different from the naturally occurring product.[16]

Second, the court asks if the "process has additional features" that distinguish the process from natural law.[17] In this step, the court must determine if there is an 'innovative concept.'

ii. Nucleotide Patent Eligibility

In *Myriad*, the defendant Myriad discovered the precise location and sequence of the BRCA1 and BRCA2 genes, mutations of which can substantially increase the risk of breast and ovarian cancer.[18] The key claims were for the full sequences of the two genes and the complementary DNA (cDNA) of the transcribed mRNA of the genes.[19] If valid, Myriad's patents would give them the exclusive rights to isolate the genes and to synthetically create BRCA cDNA. Because gene isolation is a required step during genetic testing, such a patent would in-effect give Myriad a monopoly on all diagnostic applications using the two genes to test for breast cancer susceptibility. The court

---

12 *See e.g. PharmaStem Therapeutics, Inc. v. ViaCell, Inc.*, 491 F.3d 1342, 1363 (Fed. Cir. 2007) (invalidating a patent because the researchers had "merely used routine research methods").

13 U.S. CONST. art. I, § 8, cl. 8.

14 Mayo Collaborative Servs. v. Prometheus Lab'ys, Inc., 566 U.S. 66, 71 (2012).

15 Alice Corp. Pty. v. CLS Bank Int'l, 573 U.S. 208, 217–18 (2014).

16 *Mayo Collaborative Servs.*, 566 U.S. at 72–73, 81 (describing that a successful patentee "transformed the process into an inventive application of the formula").

17 *Id.* at 77.

18 Ass'n for Molecular Pathology v. Myriad Genetics, Inc., 569 U.S. 576, 582–83 (2013).

19 *Id.* at 583–85.

found that the location and sequence of the naturally occurring genes was unpatentable subject matter, but conversely found that the cDNA sequence was patentable.[20]

The full length BRCA1 and BRCA2 genes were unpatentable because neither discovering the chromosomal location of a gene nor separating the gene from its surrounding genetic material is a valid invention. On the other hand, cDNA "is distinct from the DNA from which it was derived" because it is reverse transcribed from mRNA and thus must be produced synthetically. As a result, cDNA is not a "product of nature" and the court therefore found it was patent eligible under § 101.[21] The court also noted, however, that if a sequence of cDNA was so short as to have an identical sequence to a stretch of the gene, it would be unpatentable.[22]

In a different case concerning Myriad's patents, *University of Utah Research Foundation v. Ambry Genetics*, the Federal Circuit noted that claims to short nucleotide primers were invalid under §101 of the Patent Act.[23] Although short single stranded DNA sequences, such as the primers at issue, are not naturally occurring, the court relied on the Supreme Court's dicta from *Myriad* that identical sequences to the genomic DNA are unpatentable. Specifically, the Federal Circuit explained that because they contain the exact same sequence, "primers do not have [a unique] structure and are patent ineligible."[24]

B. European Union

i. General Patent Eligibility

The European counterpart of 35 USC §101 (patentable subject matter) is Article 52 of the European Patent Convention (EPC) (Patentable Inventions). Unlike the US where the Patent Act states what "is" patentable, the EU's Article 52 lists what "shall not be regarded as inventions."[25] The European list corresponds strongly to the US case-law exceptions to patentability. Specifically, the US's exception for "laws of nature, natural phenomena, and abstract ideas"[26] mirrors Art. 52(2)(a), which states that

---

[20] *Id.* at 591, 594–95.
[21] *Id.* at 595.
[22] *Id.* (noting that if a strand of cDNA was so short so as to only include a single exon—i.e., with no introns to remove—it "may be indistinguishable from natural DNA").
[23] *In re* BRCA1- & BRCA2-Based Hereditary Cancer Test Pat. Litig., 774 F.3d 765 (Fed. Cir. 2014).
[24] *Id.* at 761.
[25] The European Patent Convention art. 52, EUROPEAN PATENT OFFICE (Nov. 29, 2000), https://www.epo.org/law-practice/legal-texts/html/epc/2020/e/ar52.html.
[26] *See* Diamond v. Diehr, 450 U.S. 175, 185 (1981).

"discoveries, scientific theories and mathematical methods" are not patentable.[27]

As noted earlier, all new inventions have, at some level, a basis in scientific discovery or mathematical method. Thus, the difficulty in determining patentable matter is deciding when something crosses the line from a discovery to an invention. In case G 2/88, the European Patent Office (EPO) Board of Appeals explained that the essential step in this consideration is determining the claim's "technical features."[28] If after this determination it remains "clear that the claimed invention relates to […] excluded subject-matter" then it should be excluded.[29] In case T 1538/05, the EPO Board of Appeals added that to avoid exclusion under Art. 52(2), the invention must be "of a technical character" and "solve a technical problem" using "technical means."[30] This language creates a very low hurdle to overcome, as almost any invention can be explained as being of technical character and solving a technical problem. As such, it is easier to get around the issue of unpatentable subject matter than in the US, as long as there is enough proof of a *technical effect* of the invention.[31]

ii. Nucleotide Patent Eligibility

IP protection for biotechnological inventions in the European Union is governed by three main documents: the Biotech Directive, the EPC and the EPO Guidelines.[32]

The Biotech Directive covers the patentability of 'biological material' and thus governs all genetic material patents – including siRNA. Article 3 specifically notes that "biological material which is isolated from its natural

---

[27] *Id.*

[28] Mobil Oil Corp. v. Chevron Rsch. Co., G 2/88, Decision, Eur. Pat. Off. Enl. Bd. App., 22 (Dec. 11, 1989) ("The technical features of the invention are the physical features which are essential to it […] the technical features of a claim to a physical entity are the physical parameters of the entity, and the technical features of a claim to an activity are the physical steps which define such activity."), https://www.epo.org/law-practice/case-law-appeals/recent/g880002ex1.html.

[29] *Id.*

[30] T 1538/05, Decision, Eur. Pat. Off. Tech. Bd. App., ¶ 4 (Aug. 28, 2006), https://www.epo.org/law-practice/case-law-appeals/recent/t051538eu1.html.

[31] *Case law of the boards of appeal:Problem and solution approach*, EUR. PAT. OFF., *available at* https://www.epo.org/law-practice/legal-texts/html/caselaw/2019/e/clr_i_d_2.htm.
Siva Thambisetty, *Alice and 'Something More': the Drift Towards European Patent Jurisprudence*, J. of L. and Biosciences, 691, 694 (2016).

[32] Directive 98/44/EC, *supra* note 2, at 13. Note that Court of Justice judgments on the interpretation of the Directive are not binding on the EPO. T 276/99, Decision, Eur. Pat. Off. Tech. Bd. App., ¶ 14 (Sep. 26, 2001), https://www.epo.org/law-practice/case-law-appeals/recent/t990276eu1.html.

environment or produced by means of a technical process *may be the subject of an invention* even if it previously occurred in nature" (emphasis added).[33]

In the case of *human* biological material, there are several extra hurdles for patentability.[34] For instance, mere discovery of a sequence is not enough.[35] Additionally, the discovery must reveal a technical effect (for instance determining that a gene makes a specific protein) or produce the sequence with a technical process (for instance creating cDNA).[36] In essence, this extra requirement serves to raise the bar for patentability by focussing on industrial application, which is additionally a required disclosure for any gene sequence related inventions.[37] This requirement directly relates to the requirement of a technical effect in the overall patentability rules under EPC Art. 52(2).

III. RNAi Technologies

A. The Effect of Subject Matter Patentability

RNAi therapeutics have only recently emerged, with several clinical trials ongoing and the first FDA/EMA-approved RNAi drug, Onpattro, approved in 2018.[38] As of yet, there are no court interpretations of subject-matter patentability as applied specifically to RNAi

---

[33] Directive 98/44/EC, *supra* note 2, at 19. Article 2 defines biological material as "any material containing genetic information and capable of reproducing itself or being reproduced in a biological system."

[34] European Patent Convention, *supra* note 25, at art. 53https://www.epo.org/law-practice/legal-texts/html/epc/2020/e/ar53.html. *See also* Eur. Pat. Off., *Guidelines for Examination*, pt. G, Chapter II, 5.3, https://www.epo.org/law-practice/legal-texts/html/guidelines/e/g_ii_5_3.htm

[35] Josie Miller, *Patenting of Gene and Protein Sequences: an EU and US Perspective*, TAYLOR WESSING: SYNAPSE (Oct. 2019), https://www.taylorwessing.com/synapse/ti-patenting-gene-sequences.html. *See also* Directive 98/44/EC, *supra* note 2, at art. 5.

[36] Eur. Pat. Off., *Guidelines for Examination*, pt. G, Chapter II, 5.2, https://www.epo.org/law-practice/legal-texts/html/guidelines/e/g_ii_5_2.htm.

[37] Eur. Pat. Off., *Guidelines for Examination*, pt. G, Chapter III, 4, https://www.epo.org/law-practice/legal-texts/html/guidelines/e/g_iii_4.htm.

[38] U.S. Food & Drug Admin., *supra* note 4 (announcing approval of Onpattro for use in the United States); https://www.fda.gov/news-events/press-announcements/fda-approves-first-its-kind-targeted-rna-based-therapy-treat-rare-disease; *see also Onpattro Information Page*, EUR. MED. AGENCY, https://www.ema.europa.eu/en/medicines/human/EPAR/onpattro (last visited Nov. 5, 2022) (providing information regarding Onpattro's authorization in the European Union).

technology in either the United States[39] or Europe.[40] But based on the existing patent landscape, the United States is a more hostile environment for such technologies because the legal standard is more unpredictable.[41]

Under *Myriad* and *Ambry*, composition of matter claims for RNAi technology are unlikely to be patent-eligible subject matter. In order for RNAi technology to perform its gene silencing function, the siRNA guide strand must have exact or near-exact complementarity to the mRNA that is to be degraded.[42] That is, the siRNA guide strand will have a sequence made up of the directly complementary bases of the naturally occurring mRNA.[43] The *Myriad* decision noted that if a sequence of cDNA had an identical sequence to a stretch of the DNA from which it was derived, it would be unpatentable.[44] The Supreme Court specified that this would mostly occur in the context of very short segments of genes where there are no intervening "intron sequences" to remove.[45] siRNA *appears* to pass muster under this standard because unlike a short strand of cDNA, which can be identical to a stretch of a gene, guide siRNA does not have an identical sequence to mRNA due to its requirement for exact complementarity (i.e., the sequence is based on the directly opposing base pairs).

In the context of therapeutics, the siRNA guide must be introduced into a cell in double-stranded form, and for the duplex to remain stable, the siRNA guide must have a near exact complementary second strand. Thus, the complementary strand is likely to be the same as the mRNA that the siRNA guide is designed to bind with.

---

[39] *See* Alexander M. Walker, *Silencing Innovation: The Patent Eligibility of siRNA Therapeutics*, 21(2) MINN. J.L. SCI. & TECH. 333, 349 (2020) (discussing federal circuit decisions and PTAB proceedings that came closest to reaching this issue).

[40] *See* Maggie Lynch, *Alnylam Settles 'Inherently Unpredictable' Patent Litigation over Onpattro*, BIOPHARMA-REPORTER (Aug. 12, 2019), https://www.biopharma-reporter.com/Article/2018/12/19/Alnylam-settles-inherently-unpredictable-patent-litigation-over-Onpattro (describing a case of alleged RNAi patent infringement that settled before trial).

[41] Jessica C. Lai, Myriad Genetics *and the BRCA Patents in Europe: The Implications of the U.S. Supreme Court Decision*, 5 U.C. IRVINE L. REV. 1041, 1065 (2015) (arguing that the *Myriad* holding is unworkable for anything other than eukaryotic cDNA made up of multiple exons).

[42] *See* NAT'L LIBR. OF MED., *supra* note 6. https://www.ncbi.nlm.nih.gov/probe/docs/techrnai/.

[43] *See, e.g.*, Jenny K.W. Lam et al., *siRNA Versus miRNA as Therapeutics for Gene Silencing*, 4 MOLECULAR THERAPY NUCLEIC ACIDS, no. 252, 2015, at 2, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4877448/pdf/mtna201523a.pdf.

[44] *See In re* BRCA1- & BRCA2-Based Hereditary Cancer Test Pat. Litig., 774 F.3d 755, 760-761 (Fed. Cir. 2014).

[45] *Id.* at 760.

Thus, a court would likely find that the second complementary strand of an RNAi therapy duplex is unpatentable because it has 100% identicality to naturally occurring mRNA. The Federal Circuit's holding in In re BRCA1- & BRCA2-Based Hereditary Cancer Test Pat. Litig. that even primers—which are short complementary nucleotide sequences that are not necessarily naturally occurring—are patent ineligible further supports the premise that siRNA would be unpatentable in the US.[46]

Under the European standard of solving "a technical problem" using "technical means," RNAi technology is likely patent-eligible subject matter. This is especially probable when the RNAi technology is claimed in conjunction with a particular therapeutic effect. Unlike in the US, the European system is less concerned about whether a biological invention is found in nature and is more focused on the so-called technical-effects. For most RNAi technology, the technical effect is the ability to silence a particular gene.[47] Thus, it is akin to discovering that a particular gene codes for a particular enzyme, which is patentable under the technical-effect standard. RNAi technology also resembles the technical process required to create cDNA through its requirements for complementarity. As such, RNAi easily fits into the patentable subject matter restrictions of the EPO and Biotech directive.

B. The Tuschl Patents

One of the most well-known RNAi patent families is made up of the "Tuschl patents" – named for their common original assignee Thomas Tuschl. Alnylam Pharmaceuticals, the producer of Onpattro, is the exclusive licensee of the Tuschl patent No. 8,362,231, and its related patents.[48] U.S. Pat. No. 8,895,721, which was issued on Nov. 25, 2014, is a continuation of the '231 patent. As part of the '721 Patent's prosecution, the U.S. Patent and Trademark Office issued a non-final office action rejecting one of its claims, among others, under *Myriad* because the "claims read on naturally occurring molecules that are a product of nature."[49] The same office action noted that some of the claims that "require modifications to the molecule" were not rejected under *Myriad*.[50] But those claims were still rejected under §112 of the Patent Act because the

[46] *Id.*
[47] *See* NAT'L LIBR. OF MED., *supra* note 6. https://www.ncbi.nlm.nih.gov/probe/docs/techrnai/.
[48] Alnylam Pharm., Inc., Annual Report (Form 10-K) (Feb. 13, 2015).
[49] Official Action on U.S. Patent Application No. 13/725,262 at 2 (filed Dec. 21, 2012).
[50] *Id*. at 2.

specification only enabled RNA duplexes that were "100% identical to a target mRNA," while the claims in the '721 Patent were much broader.[51] Crucially, the office action noted that "even single nucleotide mismatches between the siRNA duplex and the target mRNA abolish interference."[52] Thus, although "modifications" could overcome the test in *Myriad*, those modifications may destroy the molecule's potency as a therapeutic if said modifications include a lowering of nucleotide identity.[53] Therefore, in order to comply with *Myriad*, the applicant needed to further narrow the independent claim in a way that may have resulted in a lower efficacy. In response to the office action, the applicants amended claim 1 of the '721 Patent to include the new clauses underlined in the excerpt below.

> 1. An isolated double-stranded RNA molecule, comprising:
>
> (i) a sense strand and an antisense strand that form a double-stranded region consisting of 14-24 base pairs;
>
> (ii) at least one strand having a single-stranded 3'-overhang; <u>and</u>
>
> <u>(iii) at least one nucleotide analogue,</u>
>
> wherein said RNA molecule is non-enzymatically processed and is capable of target-specific RNA interference, <u>and said sense strand has an identity in the double-stranded region of at least 85 percent to a target RNA molecule</u>.[54]

The Tuschl patent family is extensive and therefore has many continuations, divisionals, and counterparts. A European counterpart to the '721 Patent is the EP3199631B1 Patent. Compared to the '721 Patent, which ended up with an arguably narrow independent claim 1, the '631 Patent's claim 1 is extremely broad (see excerpt below).[55] Notice that this claim does not refer to any analogues (i.e., modifications) nor specific sequence identity because those limitations are claimed separately in dependent claims.

> 1. Isolated double-stranded RNA molecule, wherein each RNA strand has a length from 19-25 nucleotides and at least one strand has a 3'-overhang from 1-5 nucleotides, wherein said RNA molecule is capable of target-specific RNA interference.[56]

---

[51] *Id.* at 3.

[52] *Id*. at 4.

[53] Sayada M. Elbashir et al., *Functional Anatomy of siRNAs for Mediating Efficient RNAi in Drosophila Melanogaster Embryo Lysate*, 20 EMBO J. 6877, 6878 (2001).

[54] U.S. Patent No. 8,895,721 B2 (filed Dec. 21, 2012). Note this was also the final form of the claims.

[55] European Patent Office [EPO], *European Patent Specification*, Patent No. 3199631 B1 (filed 29.11.2001) (issued Jan. 30, 2019).

[56] *See, e.g.*, *id.* at 49 l. 34-44.

In Europe, there is less need to show that the technology involves nucleotide sequences *different* from those found in nature. Thus, the EPO makes it easier to claim RNAi technology because the claim language is less affected by the patentability issues present in the US.

C. Has *Myriad* Generated a Shift in Where RNAi Technologies are Patented?

The USPTO receives about three times more patent applications than the EPO.[57] Europe also tends to grant fewer nucleotide-based patents than the United States, seemingly due to the fact many applicants do not follow through with their applications.[58] Based on absolute numbers alone, it is unclear whether the US Supreme Court decisions on §101 patentability have had much effect on where petitioners decide to apply for patent protection.

To more readily compare the relative trajectories of RNAi related patenting, I created a moving annual coefficient to simulate the number of patents the EPO would have granted had the same percentage of RNAi patents from the EPO been granted as a fraction of total US patents.[59] As shown in Figure 1, the relative numbers of RNAi patents granted by the EPO compared to the US split dramatically between 2010 and 2017. Perhaps the US Supreme Court decision in *Myriad* (2010) contributed to this marked effect, given that the judgment made patentability for nucleotide-based inventions much more uncertain.[60]

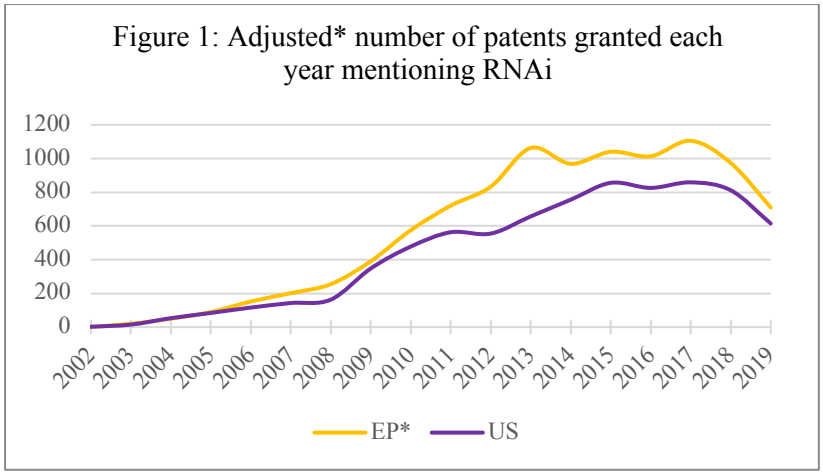

***Figure 1**: Graph depicting the number of patents granted per year by the USPTO and EPO* that mention "RNAi" or "siRNA" in*

[57] WORLD INTELL. PROP. ORG., WORLD INTELLECTUAL PROPERTY INDICATORS 2019, at 13 (2019).

[58] *See* Isabelle Huys et al., *Legal Uncertainty in the Area of Genetic Diagnostic Testing*, 27 NATURE BIOTECHNOLOGY 903, 908 (2009).

[59] Each year's coefficient was calculated as a ratio of the total number of EPO patents, relative to the total number of US patents granted that year.

[60] *See* Lai, *supra* note 39.

*their title/abstract/claims. Data source: Lexis TotalPatent One. * EPO patent data has been multiplied by an annual coefficient to account for differences in total number of patents granted by the USPTO and EPO.*

It is likely however, that these differences are grounded more in the perceptions of inventors and investors about which jurisdictions are more nucleotide-patent friendly.[61] Investors are a key factor driving the directions of innovation and IP, so their opinions on the patentability of a technology is fundamentally intertwined with this data.[62]

Conclusion

The European patent rules make it easier to identify RNAi therapeutics as patent eligible as compared to the US Patent Act. Public perception can have a marked impact on how and where RNAi patents are registered. The aftermath of the COVID-19 pandemic and the publicity it has brought for patent systems around the world may bring further unexpected developments. It is possible that the EPO will shift towards a more constrained perspective on biotechnological patents, thus closing the gap between the US and Europe. Alternatively, the US Supreme Court may update the patentability test for Section 101 in the context of biotechnological patents. In any case, striking the balance between overreaching patents on standard tools and techniques and exceedingly narrow patents is always going to be a difficult line to tread. This is especially true where the technology itself is rapidly changing and growing. Perhaps, instead of any one jurisdiction finding an appropriate middle ground, the fact that there are territorial discrepancies in patentability is itself a balance. The field of RNAi therapeutics is, however, still in the early stages of its evolution and given the lack of definitive court rulings on the topic, it will be interesting to see how the field progresses into the future.

[61] *Id.* at 1071.
[62] Dietmar Harhoff, *The Role of Patents and Licenses in Securing External Finance for Innovation*, 14 EIB PAPERS 74, 80–82 (2009).