CIPIP Annual Spring Conference 2020
Is IP Good for Your Health?

Mateo Aboy
Centre for Law, Medicine & Life Sciences

Co-Authors:
Kathleen Liddell, Cristina Crespo, Johnathon Liddicoat
Is the recent patent case-law “good” for precision medicine?

Mateo Aboy
Centre for Law, Medicine & Life Science

Co-Authors:
Kathleen Liddell, Cristina Crespo, Johnathon Liddicoat
Requested Talk from CIPIL

“Is the recent patent case-law ‘good’ for precision medicine?”

Parsing the research question

1) What do we mean by “precision medicine”? What is the relevant “recent case-law”? How does this emergent patent case-law affect precision medicine?

2) What has been the impact of these decisions on precision medicine?

3) How does this impact affect the different stakeholders (“good” for whom)?

Summary of my approach to address the above question on this talk

Share results from our published evidence-based IP studies analysing the impact of the key decisions affecting precision medicine innovation and let you reach your own conclusion (6 feature patent articles published in *Nature Biotechnology* 2016-2020)
“Is the recent patent case-law “good” for precision medicine?”

Parsing the research question

1) What do we mean by “precision medicine”? What is the relevant “recent case-law”? How does this emergent patent case-law affect precision medicine?

2) What has been the impact of these decisions on precision medicine?

3) How does this impact affect the different stakeholders (“good” for whom)?

Approach Summary

Share results from our published evidence-based IP studies analysing the impact of the key decisions affecting precision medicine innovation and let you reach your on conclusion (6 feature patent articles published in Nature Biotechnology 2016-2020)
Q1-Background on Precision Medicine

- Precision & Personalised Medicine (Spectrum of Personalisation)

- Tailoring of medical treatment to the individual characteristics of each patient (National Research Council)

- Explicit personalised medicine uses relationships between several types of biomarkers and medical responses to determine diagnoses and treatment plans.

- "Frequently, these biomarkers are genomic variations, and genetic diagnostic tests are correspondingly the most explored version of explicit personalised medicine. However, other sets of biomarkers — different “omics” — are also used in explicit personalised medicine, including measurements of RNA transcription levels (transcriptomics), the presence and level of various proteins (proteomics), levels of nonprotein small metabolic molecules (metabolomics), and the presence of DNA modifications that affect gene expression levels (epigenomics). These and other biomarkers can also help direct treatments of patients or improve the development process." (W. Nicholson Price II)

- Implicit Personalised Medicine: BlackBox Medicine

- Blackbox medicine is the next stage of personalised medicine. It differs from explicit personalised medicine in three principal ways. First, the information used to develop the relationships and predictions used in treatment recommendations comes from a much larger, broader set of information. Second, a large, rich dataset and machine learning techniques enable many predictions based on complex connections between patient characteristics and expected treatment results without explicitly identifying or understanding those connections. For example, […] a blackbox medicine prediction might be that patients who have a set of linked variations in a dozen different genes, smoke, and have middling high blood pressure might predictably respond better to one medication than another — even if those factors could not be explained or even explicitly identified. (W. Nicholson Price II)
How does emerging patent case law in the US and Europe affect precision medicine?

No topic in medicine garners more interest today than precision medicine, with its goal of better tailoring treatment to patient needs. It is not only patients who stand to benefit from better diagnosis, prognosis and treatment, but also the organizations investing in its research and development. According to one recent estimate, the global precision medicine market accounted for $78.85 billion in 2018 and is expected to reach over $216.75 billion by 2028, with a compound annual growth rate of 10.64% between 2018 and 2028.

Use in clinical trials or entered the clinic as diagnostic tools. Considerable R&D is still required, with associated expense and risk. The FDA/NIH BEST (Biomarkers, Endpoints, and other Tools) Resource provides examples for each category of biomarkers, including diagnostic, monitoring, pharmacodynamic/response, predictive and prognostic biomarkers. As an example, the Oncotype DX is a test based on a biomarker that assists doctors in determining proper cancer treatment. Precision medicine also builds on...

In truth, it is better to think of this as a spectrum of ‘opacity’ of the proverbial box. Medical correlations often reflect complex interactions of natural relationships at an individual or group level, rather than universal natural laws like E = mc². For instance, the Oncotype DX test is considerably more specific than a universal law and correlates various biomarkers to create a cancer Recurrence Score.

Starting first with the United States, followed by Europe, we examine how patent law developments in the areas of nature-
1) How do the US patent decisions affect precision medicine?

Fig. 1 | Application and impact of emergent patent case law to different categories of precision medicine, including biomarkers, diagnostics, and algorithms and AI.

(c) 2016-2020 :: Prof. Mateo Aboy, PhD, PE/CEng, MBA, CLP, RPA (USPTO), FIT (IAPP), CIPP/E, CIPM
Requested Talk from CIPIL
“Is the recent patent case-law “good” for precision medicine?”

Parsing the research question

1) How does emergent patent case-law in the US and Europe affect precision medicine?

2) What has been the impact of these decisions on precision medicine?

3) How does this impact affect the different stakeholders (“good” or “bad” for whom)?

Approach Summary

Share results from our evidence-based IP studies analysing the impact of the key decisions affecting precision medicine innovation and let you reach your on conclusion.
Evidence-based (Empirical) Patent Studies

*e.g., Impact of Legal or Regulatory Changes*

- Broad-level impact studies (before & after landscapes)
- Claim-level impact studies (before & after claims, claim scope)
- Prosecution-level studies (prosecution timelines, strategies, effects on types of entity)
- Wide-impact studies (side effects, ripple effects, unexpected consequences)
A) Empirical Patent Study on Myriad’s Impact
- ✓ Study I: Myriad’s Impacts on Gene-Related Patents - NBT 1
- ✓ Study II: Myriad’s Impact on Claim Drafting - NBT 2
- ✓ Study III: Myriad’s Impact on Patent Prosecution - NBT 3
- ✓ Study IV: Myriad’s Impact beyond Isolated DNA - NBT 3

B) Empirical Patent Study on Mayo’s Impact
- Study I: Mayo’s Impacts on Diagnostics Patents NBT 6
- Study II: Mayo’s Impact on Claim Drafting - NBT 6
- ✓ Study III: Mayo’s Impact on Patent Prosecution (Personalized Medicine) - NBT 4

C) Empirical Patent Study on Alice’s Impact
- Study I: Alice’s Impacts on Precision Medicine - NBT 5
- Study II: Alice’s Impact on Biotechnology Claim Drafting - NBT 8 (In prep)
The US Supreme Court held that “a naturally occurring DNA segment is a product of nature and not patent eligible merely because it has been isolated, but […] cDNA is patent eligible because it is not naturally occurring”

“In the United States … it now seems clear that gene patents are not only dead, but … really most sincerely dead”

“…it would be a mistake to assume that these decisions spell the end of patents in the [genetic] industry”
Guerrini et al. 49 Nature Biotechnol. 34 (2016)

What a surprise…Reasonable minds differ!
Highly experienced judges, patent examiners, attorneys, legal scholars, and commentators reach different conclusions based on the same statutory language and legal precedents…
Question:

Did Myriad result in a reduction of gene-related patents in general (i.e., beyond isolated DNA patents)?

[“good” or “bad” to whom?]
Myriad’s impact on gene patents

Mateo Aboy, Kathleen Liddell, Johnathon Liddicoat & Cristina Crespo

Three years later, the landmark Myriad decision on gene patents has led to some striking and unforeseen implications.

“The lawless science of our law, that codeless myriad of precedent, that wilderness of single instances…”

—Alfred, Lord Tennyson

In the three years since the United States Supreme Court’s decision in AMP v. Myriad1, there has been much debate and speculation about the impact of the case on the biotech industry, particularly on the standard of “different” from nature. The Federal Circuit applied this reasoning in a subsequent case in 2014 (ref. 3), concluding that Myriad’s patents over single-stranded DNA primers for detecting mutations in the BRCA genes were also invalid because such primers are unpatentable. Commentators offered a wide variety of opinions on the significance of the BRCA decisions. Sherkow and Greely said “In the United States...it now seems clear that gene accelerant trends that are already very much evident in the data,” and that the outcome was “likely to be less profound than either abolitionists or advocates seem to expect”6.

This prediction was based on their empirical findings that only 8,703 US patents were at risk of invalidation (of which only 3,535 were related to human medicine)6. Claims to isolated nucleotide sequences were, in the authors’ analysis, already a strongly diminishing category of patent.
Question:

What were the trends in “isolated gene patent activity” in the last 20 years?
Isolated Gene-Related Patents

(c) 2016-2020 :: Prof. Mateo Aboy, PhD, PE/CEng, MBA, CLP, RPA (USPTO), FIT (IAPP), CIPP/E, CIPM
Isolated Gene-Related Patents

(c) 2016-2020 :: Prof. Mateo Aboy, PhD, PE/CEng, MBA, CLP, RPA (USPTO), FIT (IAPP), CIPP/E, CIPM
Isolated Gene-Related Patents

(c) 2016-2020 :: Prof. Mateo Aboy, PhD, PE/CEng, MBA, CLP, RPA (USPTO), FIT (IAPP), CIPP/E, CIPM
Isolated Gene-Related Patents

(c) 2016-2020 :: Prof. Mateo Aboy, PhD, PE/CEng, MBA, CLP, RPA (USPTO), FIT (IAPP), CIPP/E, CIPM
Isolated Gene-Related Patents

Do you see any potential negative side effect?
Isolated Gene-Related Patents

Potentially negative effect to small entities
Questions:

Are there any indications that the patent system was already “self correcting” prior to Myriad?

Does Europe have a competitive advantage now (isolated DNA is subject-matter eligible in Europe but not in the US)?

Does the patent data tell us anything about what we may expect is the US Supreme Court had reached the opposite decision in Myriad?

[“good” or “bad” to whom?]
"…patent attorneys are developing strategies to ‘draft around’ Myriad and related cases to ensure their clients will withstand scrutiny going forward”

Guerrini et al. 49 Nature Biotechnol. 34 (2016)

What do you think?
Has it being easy for patent attorneys to ‘draft around’ Myriad?

The US Supreme Court held that “a naturally occurring DNA segment is a product of nature and not patent eligible merely because it has been isolated, but […] cDNA is patent eligible because it is not naturally occurring”

Profound impact vs

Myriad is of little practical importance because…

(c) 2016-2020 :: Prof. Mateo Aboy, PhD, PE/CEng, MBA, CLP, RPA (USPTO), FIT (IAPP), CIPP/E, CIPM
After *Myriad*, what makes a gene patent claim ‘markedly different’ from nature?

Mateo Aboy, Johnathon Liddicoat, Kathleen Liddell, Matthew Jordan & Cristina Crespo

Examining the types of claim amendments that have transformed isolated gene claims from patent-ineligible into eligible subject matter provides clarity into the threshold of eligibility for gene-related patents.

While nearly four years have passed since the US Supreme Court’s decision in *Association for Molecular Pathology v. Myriad Genetics*, its impact is still not fully understood. The Supreme Court held that “a naturally occurring DNA segment is a product of nature and not patent eligible merely because it has been isolated, but cDNA is patent eligible because it is not naturally occurring”\(^1\). The decision left open many questions and was “far from illuminating”\(^2\). The US Patent and Trademark Office (USPTO) has published eligible gene patents and what makes a claim “markedly different” from ineligible natural products\(^8,12,13\).

In a recently published empirical study\(^14\), we addressed questions about *Myriad’s* impact on gene-related patents (including but not limited to isolated gene-related patents). That study employed an automated search algorithm designed to analyze, in a broad way, *Myriad’s* impact by looking at granted gene-related patents using consistent search terms before and after the *Myriad* decision.

have transformed ineligible isolated nucleic acid claims into patent-eligible claims in examination proceedings before the USPTO and, relatedly, whether *Myriad* has failed to provide a workable legal test of subject-matter eligibility\(^18\). The answers to these questions are also important in debates about whether *Myriad* has caused a problem such that subject-matter legislation (35 USC §101) should be amended\(^19,20\).

Our research also highlights the operation of the USPTO Manual of Patent Examination
Claim-Level Analysis Methodology

**Patent Search Algorithm (S1)**

a) Search Strategy: claims:(seq id) AND ("isolated DNA"~5 OR "isolated gene"~5 OR "isolated nucleotide"~5 OR "isolated (deoxyribonucleic acid)"~5 OR "isolated (nucleic acid)"~5))

b) Dates: 2010-06-13 to 2013-06-13

- **Analysis I**
  - Step 1: Search isolated gene patents using automatic search algorithm
  - Step 2: Manual Classification

- **Analysis II**
  - Step 3: Simple Isolated DNA
  - Step 5: Excluded Applications

- **Analysis III**
  - Step 6: Determination of Patent Application Legal Status
  - Step 7: Granted
  - Step 8: Rejected/Abandoned

- **Analysis IV**
  - Step 9: Claim Analysis
  - Step 10: Claim Analysis

- **Analysis V**
  - Step 11: Analysis of Office Actions
  - Step 12: Analysis of Office Actions

- **Analysis VI**
  - Step 13: 35 USC 101 Myriad Rejection
  - Step 14: 35 USC 101 Myriad Rejection

- **Analysis VII**
  - Step 15: Expert Analysis of Applicant Responses
  - Step 16: Classification of Prosecution Actions

- **Analysis VIII**
  - Step 17: Results: Claim Amendment Typology

- **Analysis IX**
  - Step 18: Overall Results: Subject-Matter Eligibility
79.2% of the patents containing isolated DNA claims were abandoned or all the isolated DNA claims were canceled.

18.6% of the patents containing isolated DNA claims were successfully amended.

Table 1 Results of isolated DNA patent claim analysis

<table>
<thead>
<tr>
<th>Manual classification (M1 analysis)</th>
<th>N</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Simple isolated DNA (M1a)</td>
<td>653</td>
<td>50.5</td>
</tr>
<tr>
<td>Complex isolated DNA (M1b)</td>
<td>561</td>
<td>43.4</td>
</tr>
<tr>
<td>Excluded (M1c)</td>
<td>78</td>
<td>6.0</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>1,292</strong></td>
<td><strong>100%</strong></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Patent status of M1a applications</th>
<th>N</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Granted (M1aG)</td>
<td>313</td>
<td>47.9</td>
</tr>
<tr>
<td>Rejected/abandoned (M1aR)</td>
<td>311</td>
<td>47.6</td>
</tr>
<tr>
<td>Pending (M1aP)</td>
<td>29</td>
<td>4.4</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>653</strong></td>
<td><strong>100%</strong></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Patent claim analysis of M1aG applications</th>
<th>N</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Canceled (M1aGC)</td>
<td>183</td>
<td>58.5</td>
</tr>
<tr>
<td>Amended (M1aGA)</td>
<td>116</td>
<td>37.1</td>
</tr>
<tr>
<td>Unchanged (M1aGU)</td>
<td>14</td>
<td>4.5</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>313</strong></td>
<td><strong>100%</strong></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Fate of M1a patents</th>
<th>N</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>M1aR</td>
<td>311</td>
<td>49.8</td>
</tr>
<tr>
<td>M1aGC</td>
<td>183</td>
<td>29.3</td>
</tr>
<tr>
<td>M1aR+M1aGC</td>
<td>494</td>
<td>79.2</td>
</tr>
<tr>
<td>Amended isolated gene claims</td>
<td>116</td>
<td>18.6</td>
</tr>
<tr>
<td>Granted as originally filed (unchanged)</td>
<td>14</td>
<td>2.2</td>
</tr>
</tbody>
</table>
Is it easy to draft around *Myriad*? Our results indicate that in the years since *Myriad* there has been much less amending activity than some commentators expected. In over 79.2% of M1a cases, the simple isolated nucleic acid product claims were canceled. Claim amendments were attempted and successful in fewer than 18.6% of the cases. We found only 21 (3.2% of M1a) instances of successful amendments after receiving an explicit *Myriad*-based rejection. Furthermore, none of these retained the scope (breadth) of the original applications.

**Summary of Amendments:**
- Type 1: cDNA – 7
- Type 2: Nucleic acid with non-naturally occurring sequence variations – 5
- Type 3: Heterologous Recombination – 3
- Type 4: Label – 2
- Type 5: Recombination with non-specific regulatory nucleic acid – 1
- Type 6: Vector – 1
- Type 7: Type 2 and a negative-claim clause – 1
- Type 8: Short nucleotide – 1
- Type 9: Cancelled – 3 (183 total cancelations)

**Original & Amended Claims (along with 35 USC 101 arguments)** show specific examples of claim drafting required to “transform” the ineligible subject matter into patent eligible claims.
In the months immediately surrounding the decision, several academics heralded Myriad as a “narrowly crafted” decision “that delivered a surgical strike against patents that block development in genetics-based diagnostics while preserving protection for therapeutics, personalized medicine, and other fields of biotechnology”


- Was do you think?
  - Option 1: Narrowly crafted decision - surgical strike
  - Option 2: Wider impacts (affecting subject-matter eligibility beyond naturally occurring DNA)
PATENTS

Was the *Myriad* decision a ‘surgical strike’ on isolated DNA patents, or does it have wider impacts?

Mateo Aboy, Cristina Crespo, Kathleen Liddell, Johnathon Liddicoat & Matthew Jordan

Five years later, what are the wider impacts of the US Supreme Court’s *Myriad* decision on subject-matter eligibility and patent prosecution for nature-based products beyond isolated DNA?

On 13 June 2013, the US Supreme Court held in *Association for Molecular Pathology v. Myriad Genetics, Inc.* (*Myriad*) that “[a] naturally occurring DNA segment is a product of nature and not patent eligible merely because it has been isolated, but...” Other commentators, typically aligned with industry, were much less complimentary and warned that the decision would have broad, sweeping implications and chill investment in a wide variety of isolated molecules other than DNA, including RNA, antibodies, antibiotics causing a chilling effect on isolated natural products other than DNA. A third view is that the USPTO is applying *Myriad* beyond DNA but in a relatively narrow way and readily allowing nature-based products so long as the applicant identifies a functional difference between the...
Empirical Results

- 1) USPTO PAIR All Class Search ("Myriad" AND "Association for Molecular Pathology")
  - Research Results: 14,380 USPTO correspondence documents (14K)

- 2) Analysis of Office Actions & Responses
  - Examiner Office Actions: 10,052 Myriad citations (10K)
  - Applicant Counsel Responses: 3,795 Myriad citations (3K)
  - Appeal Documents: 533 Myriad citations (.5K)

- 3) Analysis of Patented, Abandoned & Pending
  - Patents Application with Myriad Rejections: 6,875 (Overall Allowance Rate: 48.5%; 35.6% allowed)
    - Abandoned: 2,449
    - Patented: 2,590
    - Pending: 1,846
Figure 1 Study results. (a) 85% of the Myriad-based rejections in our sample were directed to patent claims that extended beyond isolated DNA. (b) Upon receiving a Myriad rejection applicants advanced prosecution by either amending (71%), cancelling (27%) or providing legal and scientific/technical argument (2%) for these claims.
Reactions to Mayo—Good or Bad

- The *Mayo* Supreme Court’s decision was highly controversial.

- Nature Biotechnology spoke to patent attorneys who wholeheartedly agreed, calling it “the worst patent decision in the history of the Supreme Court” and “almost impossible to apply” [1].

- Litigating parties argued that it would “radically limit” patent protection and “fatally undermine the biomedical field” [2].

- Eisenberg opined that diagnostic technology was no longer patent eligible [3].

- Holman stated in 2016 that *Mayo* “threatens the availability of patent protection for some of the most innovative and meritorious applications” [4].

- As recently as 2017, it has been said that *Mayo* “resulted in whole swaths of health care inventions being unpatentable and existing patents being poured out of the courts as invalid” [5].

- **Q:** Is there any empirical evidence that *Mayo* has already swallowed or eviscerated patent law for precision medicine and diagnostics?

- **Q:** What do you think? Has its impact been as profound as predicted? Or is the speculative worry unsubstantiated?
Study B3-Research Questions

- After 6 years, what has been Mayo’s impact on patent applications related to biotech, diagnostics, and personalised medicine in the US?
  1) How many applications have received Mayo-based rejections over the last 6 years, and what has been the fate of these applications —were they eventually allowed, allowed with amendments, abandoned or still pending?
  2) What is the expected prosecution timeline of patent applications receiving a Mayo-based rejection?

- After Mayo where is the threshold of subject-matter eligibility employed by Examiners at the USPTO?
  1) What is the prevalence of 35 USC 101 rejections (pre- and post-Mayo)?
  2) How has the prevalence of 35 USC 101 subject-matter eligibility rejections changed over the six years since Mayo?
  3) What type of amendments have overcome Mayo-based (35 USC 101) rejections?
Mayo’s impact on patent applications related to biotechnology, diagnostics and personalized medicine

On the sixth anniversary of Mayo v. Prometheus, what impact has the US Supreme Court decision had on patent subject-matter eligibility and the prosecution of biotech-related patent applications before the US Patent and Trademark Office?

On 20 March 2012, nine judges of the Supreme Court of the United States held unanimously that “Prometheus” patents set forth laws of nature—namely, relationships between concentrations of certain metabolites in the blood and the likelihood that a dosage of a thiopurine drug will prove ineffective or cause harm.”

The Court recognized that it takes human action to trigger the metabolite/dosage concept (for example, law of nature) and (ii) if the answer is yes, then consider the elements of the claim to determine whether additional elements transform it into a patent-eligible application—that is, consider whether there is an element or combination of elements that ensure that the patent in practice amounts to significantly more than a patent directed to the ineligible concept itself (see Supplementary Data). Despite Supreme Court” and “almost impossible to apply,” litigating parties argued that it would radically limit patent protection and “fatal undermine the biomedical field.”

Eisenberg opined that diagnostic technology was no longer patent eligible. Minssen and Nilsson were one of the few voices in 2012 suggesting that Mayo would be highly significant but not necessarily devastating.
- **1) USPTO PAIR All Class Search (Mayo v Prometheus)**
  - Research Results: 72,990 USPTO correspondence documents; 21K applications (~73K; 21k)

- **2) Analysis of Office Actions & Responses**
  - Examiner Office Actions: 33,878 Mayo citations (~33K)
  - Applicant Counsel Responses: 34,417 Mayo citations (~34K)

- **3) Analysis of Patented, Abandoned & Pending (TC 1600)**
  - Overall Statistics: 9435 patent applications in TC=1600 (Biotech)
  - Abandoned: 4,650
  - Patented: 2,605
  - Pending: 2,180

- **4) Analysis of Prosecution Statistics & Art Units**
  - No. of Office Actions, RCEs, Appeals, Prosecution Time (Cont)
A3/4-Empirical Results

Increased legal uncertainty

Increased prosecution costs

Substantially lower proportion of small entities

“Crafty drafting”

[“Good” or “Bad”?]
One year after *Vanda*, are diagnostics patents transforming into methods of treatment to overcome *Mayo*-based rejections?

What impact have *Mayo* and *Vanda* had for applicants attempting to obtain patent protection for inventions involving methods of diagnosis and methods of treatment?

In 2012, the US Supreme Court issued its much-anticipated decision in the case of *Mayo Collaborative Services v. Prometheus Laboratories, Inc.* (*Mayo*). The Court concluded that a claim directed to a method of optimizing drug dosage for treatment of a disorder was patent-ineligible for being directed to a law of nature, namely "the correlations between thiopurine metabolite levels and the toxicity and efficacy of thiopurine drug dosages". This decision set the *Mayo/Alice* test. The claim in example 29 directed to a method of detection of the disease was considered eligible at step A (not "directed to" a law of nature). In contrast, other claims directed to methods of diagnosis and treatment were deemed to be directed to natural laws, and were eligible or ineligible based on whether or not they satisfied step B, the "significantly more" inquiry. It was against this background that, in light of the *Vanda* decision, the two-step *Mayo/Alice* test should have been applied differently in example 29 (Iulitis) of the USPTO guidance but would nonetheless eventually yield the same eligibility results. More specifically, the method of treatment claims should have been considered patent-eligible under Step A of the *Mayo/Alice* test.

Taken at face value, such developments could seem just a slight shift. But on closer inspection, the *Vanda* decision had the
Fig. 1 | **Study results.** **a**, Typology of patent application claims with *Mayo* rejections. **b**, Typology of granted patent claims after *Vanda*. The results indicate that a large proportion of diagnostic related claims are being amended to method of treatment claims to overcome *Mayo*-based rejections following the *Vanda* decision and corresponding USPTO examination guidance.
On June 19, 2014 the US Supreme Court held that “We hold that the claims at issue are drawn to the abstract idea of intermediated settlement, and that merely requiring generic computer implementation fails to transform that abstract idea into a patent-eligible invention.”

Focused on ‘abstract ideas’, affects business methods and software, **Does not affect biotech** vs **Impacts biotech patents** *(especially precision medicine)*

What do you think?
Alice Updated Results

- **Date:** 2019-08-07
- **Search:** Alice and CLS
- **General Results:** 232,007 documents citing *Alice*
  - Office Actions: 123,977
  - Responses: 92,858
  - Appeals: 14,272
  - Other: 820
- **Medical/Diagnostic Device Results:** 2,339 documents citing *Alice*
  - Art Units: 377X, 379X Medical Instruments, Diagnostic Equipment, Treatment Devices
  - Office Actions: 844
  - Responses: 1313
  - Appeal: 175
  - Other: 7

(c) 2017 :: Mateo Aboy, PhD, CLP, US Patent Agent
Alice Updated Results-Guidance Impact

- **Medical Results: 844 OA citing Alice**
  - Total Number of Applications: 514
  - Patented: 115
  - Rejected/Abandoned: 67

- **Disposition Period 1: 2014-2018**
  - Total Dispositions: 41
  - Patented: 16 (1+ RCE: 50%)
  - Rejected/Abandoned: 25 (1+ RCE: 32%)
  - Allowance Rate: 38%

- **Disposition Period 2: YTD2019 (Updated USPTO Guidance)**
  - Total Dispositions: 141
  - Patented: 99 (1+ RCE: 68.7%)
  - Rejected/Abandoned: 42 (1+ RCE: 52.4%)
  - Allowance Rate: 70.2%
1) How do the US patent decisions affect precision medicine?

Fig. 1 | Application and impact of emergent patent case law to different categories of precision medicine, including biomarkers, diagnostics, and algorithms and AI.
# US vs Europe Comparison

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Comparison of US and European patent subject matter eligibility of precision medicine inventions</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Patent eligibility comparison</strong></td>
<td><strong>Claims directed to</strong></td>
</tr>
<tr>
<td>Precision medicine inventions based on nature-based products</td>
<td>Isolated DNA</td>
</tr>
<tr>
<td></td>
<td>cDNA</td>
</tr>
<tr>
<td></td>
<td>Other nature-based products</td>
</tr>
<tr>
<td>Precision medicine inventions based on individual responses and correlations</td>
<td>Responses and correlations</td>
</tr>
<tr>
<td></td>
<td>Methods of detection</td>
</tr>
<tr>
<td></td>
<td>Methods of treatment</td>
</tr>
<tr>
<td></td>
<td>Method of diagnosis</td>
</tr>
<tr>
<td>Precision medicine inventions based on algorithms</td>
<td>Pure mathematical methods of algorithms (including AI) as such</td>
</tr>
<tr>
<td></td>
<td>Mathematical methods of algorithms (including AI) implemented in a computer or device</td>
</tr>
<tr>
<td></td>
<td>Mathematical methods of algorithms (including AI) directed to a technical application or specific technical implementation</td>
</tr>
</tbody>
</table>

(c) 2016-2020 :: Prof. Mateo Aboy, PhD, PE/CEng, MBA, CLP, RPA (USPTO), FIT (IAPP), CIPP/E, CIPM
Conclusion 1: Myriad & Isolated DNA

79.2% of the patents containing isolated DNA claims were abandoned or all the isolated DNA claims were canceled.
Conclusion 2: Myriad Wider Impact

Figure 1 Study results. (a) 85% of the Myriad-based rejections in our sample were directed to patent claims that extended beyond isolated DNA. (b) Upon receiving a Myriad rejection applicants advanced prosecution by either amending (71%), cancelling (27%) or providing legal and scientific/technical argument (2%) for these claims.
Alice (abstract idea), which was originally thought to primarily impact algorithms, software, and business methods, is also impacting biotech inventions.
Based on the results of our evidence-based IP studies, it appears that there is:

- **De minimis impact** on “isolated DNA patents” (the system had already self-corrected with novelty and inventive step);

- **Negative impact** on legal certainty (i.e., higher legal uncertainty) during prosecution and post-grant (validity);

- **Negative impact** the scope of claims (i.e., narrower claims) involving classical biomarkers (*Myriad*), “digital biomarkers” based on algorithms/relationships (*Alice*/*Mayo*);

- **Minimal impact** on large entities with sufficient resources to prosecute patent applications in an environment of high legal uncertainty;

- **Negative impact** on small entities working on biotech [higher prosecution times, cost, decrease in proportion of small entities];

- **Negative impact** on small entities that need to assert their patents [easier to invalidate]
Thank you

Any questions?