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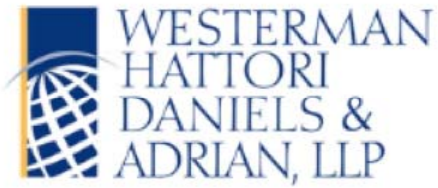
Gene Patenting:

The *Myriad* Genetics case

遺伝子特許取得の問題: ミリアド事件



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Intellectual Property Law

The Case：事件の概要

- ✓ *Association for Molecular Pathology, et al. v. U.S. Patent and Trademark Office, et al.*
  - ✓ Summary Judgment; Decided March 29, 2010
  - ✓ U.S. District Court, Southern District of New York
  - ✓ Judge Robert Sweet

- ✓ The case is also commonly known as:
  - ✓ *AMP v. USPTO*
  - ✓ *"the gene patent case"*
  - ✓ *"the Myriad case"*
  - ✓ *ACLU v. Myriad* (but, the ACLU is not a party)
- ❑ The case has been appealed to the CAFC（控訴裁判所に控訴中）
- ❑ Decision at: http://www.aclu.org/files/assets/2010-3-29-AMPvUSPTO-Opinion.pdf

The Parties (Plaintiffs)　原告：特許反対派

- ✓ Represented by the American Civil Liberties Union (ACLU) and Public Patent Foundation (PubPat)
- ✓ Four Non-profit scientific organizations（非営利科学団体）:
  - ✓ Association for Molecular Pathology
  - ✓ American College of Medical Genetics
  - ✓ American Society for Clinical Pathology
  - ✓ College of American Pathologists

PUBPAT

ACLU
AMERICAN CIVIL LIBERTIES UNION

- ✓ Eight doctors, professors and clinicians（医者等）:
  - ✓ Dr. Haig Kazazian: Professor at University. of Pennsylvania School of Medicine
  - ✓ Dr. Arupa Ganguly: Professor at University of Pennsylvania Hospital
  - ✓ Dr. Wendy Chung: Professor at Columbia University
  - ✓ Dr. Harry Ostrer: Professor at New York University School of Medicine
  - ✓ Dr. David Ledbetter: Professor at Emory University School of Medicine
  - ✓ Dr. Stephen Warren: Professor at Emory University
  - ✓ Ellen Matloff: Director of Yale Cancer Genetic Counseling Program
  - ✓ Elsa Reich: Genetic counselor at New York University
- ✓ Two advocacy groups（乳ガン研究等を支援する運動家等）:
  - ✓ Breast Cancer Action: Breast cancer advocacy group
  - ✓ Boston Women's Health Book Collective: nonprofit women's health education group
- ✓ Six cancer patients（ガン患者）:
  - ✓ Lisbeth Ceriani, Runi Limary, Genae Girard, Patrice Fortune, Vicky Thomason, Kathleen Raker

The Parties (Defendants) 被告：特許賛成派

- ✓ U.S.P.T.O.（米国特許庁）
- ✓ Myriad Genetics（被告会社）
  - ✓ Publicly-traded corporation based in Salt Lake City, Utah
  - ✓ Owner or co-owner of patents in question. Sole provider of BRCA1/2 gene testing in the United States
- ✓ University of Utah Research Foundation（大学）
  - ✓ Owner or co-owner of patents in question

The *Amici* (Support Plaintiff) 特許反対派をサポートする意見書

- ✓ Five professional organizations（プロフェッショナル団体）:
  - ✓ American Medical Association, American Society of Human Genetics, American College of Obstetricians and Gynecologists, American College of Embryology, The Medical Society of the State of New York
- ✓ Six disease research organizations（研究団体）:
  - ✓ March of Dimes, Claire Altman Heine Foundation, Breast Cancer Coalition, Massachusetts Breast Cancer Coalition, National Organization for Rare Disorders, National Tay-Sachs and Allied Diseases Association
- ✓ Five women's health organizations（ウーマンヘルス団体）
  - ✓ National Women's Health Network, Asian Communities for Reproductive Justice, Center for Genetics and Society, Generations Ahead, Pro-Choice Alliance for Responsible Research
- ✓ Three miscellaneous organizations（他の団体）:
  - ✓ The International Center for Technology Assessment, Indigenous People Council on Biocolonialism, Greenpeace
- ✓ Interesting side note: Susan G. Komen for the Cure, the largest breast cancer advocacy/education organization in the United States, does not appear to have an official position.

The *Amici* (Support Defendant) 特許賛成派をサポートする意見書

- ✓ Six biotech companies（バイオテックカンパニー）:
  - ✓ Rosetta Genomics
  - ✓ Genomic Health, Inc.
  - ✓ Qiagen
  - ✓ Target Discovery, Inc.
  - ✓ XDx, Inc.
  - ✓ Celera Corp
- ✓ Three trade organizations（貿易団体）
  - ✓ Biotechnology Industry Association
  - ✓ BayBio
  - ✓ The Coalition for 21st Century Medicine
- ✓ Four patent law groups and scholars（特許法関係団体、大学教授等）
  - ✓ Boston Patent Law Association
  - ✓ George Mason University
  - ✓ Dr. Kenneth Chahine: Law professor at University of Utah
  - ✓ Dr. Kevin Noonan: Patent Attorney, publisher of “PatentDocs” blog

Grounds for Lawsuit　訴えの根拠

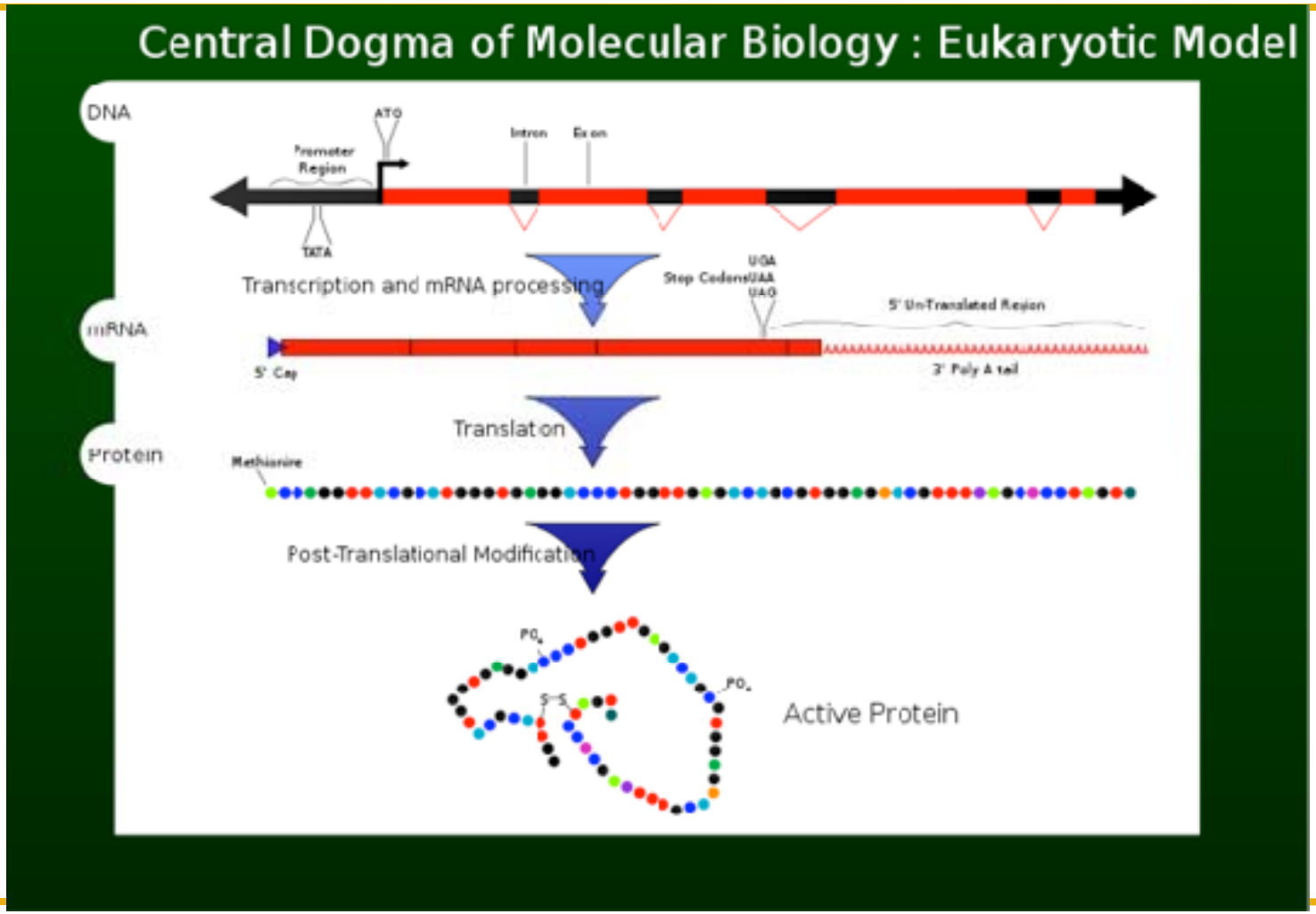
- ✓ Violates 35 U.S.C. §101（特許法101条の解釈に反する）
  - ✓ “Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.”

- ✓ Violates U.S. Constitution, Article I, Section 8, Clause 8（憲法違反：科学技術の進歩に反する）
  - ✓ “Congress shall have the 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....”

- ✓ Violates U.S. Constitution, 1st and 14th Amendments（憲法違反：表現の自由に反する）
  - ✓ 1st Amendment “Congress shall make no law respecting an establishment of religion, or prohibiting the free exercise thereof; or **abridging the freedom of speech**, or of the press; or the right of the people peaceably to assemble, and to petition the Government for a redress of grievances.”
  - ✓ Summary of 14th Amendment: Protects rights against state infringements, defines citizenship, prohibits states from interfering with privileges and immunities, requires due process and **equal protection under the law**, punishes states for denying vote, and disqualifies Confederate officials and debts.

- ✓ But, do plaintiffs have standing?　-　しかし、原告（特許反対派）に当事者適格はあるのか？

The Technology



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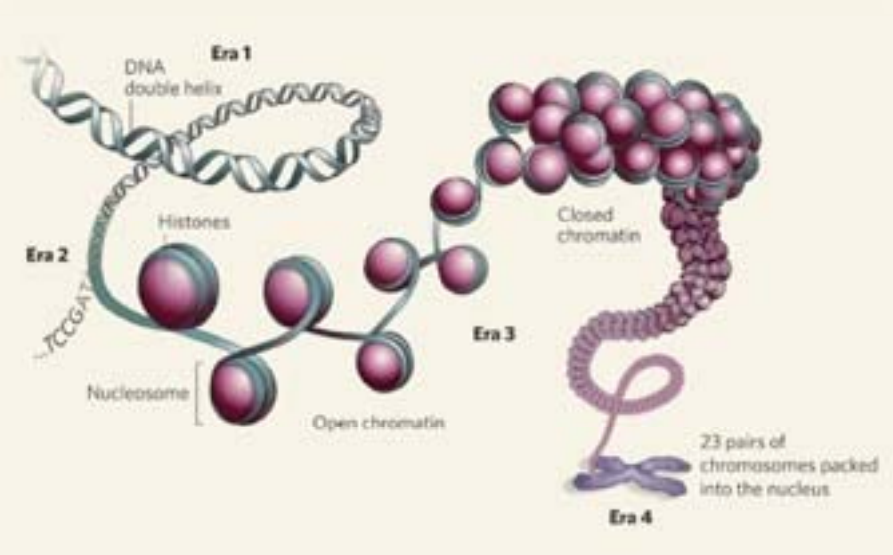
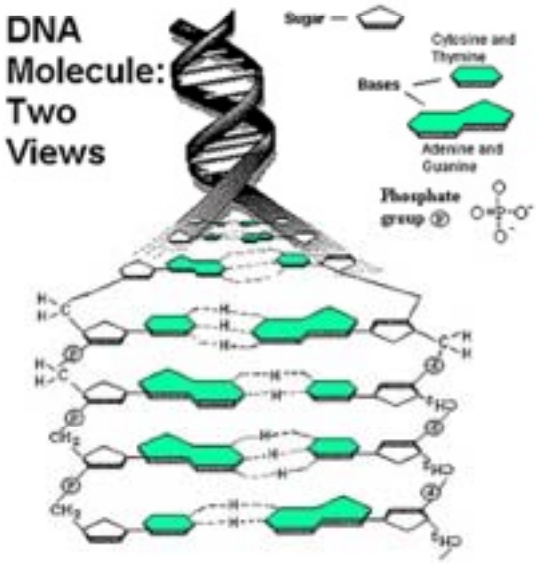
The Technology

- ✓ Genomic or “natural DNA”





- ✓ “Isolated DNA” is obtained using known laboratory techniques to lyse (open) cells, separate DNA from proteins and other cellular matter, and isolate DNA. Isolated DNA can also be artificially generated.
- ✓ Detection/diagnosis methods are performed by using isolated DNA as a “probe” to determine the genomic DNA in a patient.

Patents in Issue　争われている特許

- ✓ U.S. Patent No. 5,747,282 (claims 1, 2, 5, 6, 7 and 20)
- ✓ U.S. Patent No. 5,837,492 (claims 1, 6, and 7)
- ✓ U.S. Patent No. 5,693,473 (claim 1)
- ✓ U.S. Patent No. 5,709,999 (claim 1)
- ✓ U.S. Patent No. 5,710,001 (claim 1)
- ✓ U.S. Patent No. 5,753,441 (claim 1)
- ✓ U.S. Patent No. 6,033,857 (claims 1 and 2)

Representative Claims　代表的なクレーム

- Composition Claims (claim 1 of ‘282 patent) ： 組成物クレーム
  - An isolated DNA coding for a BRCA1 polypeptide, said polypeptide having the amino acid sequence set forth in SEQ ID NO: 2.

Representative Claims 診断方法のクレーム

- "Diagnosis" Method Claim (claim 1 of '999 patent)

- A method for detecting a germline alteration in a BRCA1 gene, said alteration selected from a group consisting of the alterations set forth in Tables 12A, 14, 18, or 19 in a human which comprises
  - ***analyzing*** a sequence of a BRCA1 gene or BRCA1 RNA from a human sample or
  - ***analyzing*** a sequence of BRCA1 cDNA made from mRNA from said human sample with the proviso that said germline alteration is not a deletion of 4 nucleotides corresponding to base numbers 4184-4187 of SEQ ID NO: 1.

Representative Claims 診断方法のクレーム

- "Diagnosis" Method Claim (claim 1 of '441 patent)
  - A method for screening germline of a human subject for an alteration of a BRCA1 gene which comprises
    - ***comparing*** germline sequence of a BRCA1 gene or BRCA1 RNA from a tissue sample from said subject or a sequence of BRCA1 cDNA made from mRNA from said sample with germline sequences of wild-type BRCA1 gene, wild-type BRCA1 RNA or wild-type BRCA cDNA,
    - wherein a difference in the sequence of the BRCA1 gene, BRCA1 RNA or BRCA cDNA of the subject from wild-type indicates an alteration in the BRCA1 gene in said subject.

Representative Claims

薬物スクリーニング
方法のクレーム

- "Drug Screening" Method Claim (claim 20 of '282 patent)

  - A method for screening potential cancer therapeutics which comprises:
    - ***growing*** a transformed eukaryotic host cell containing an altered BRCA1 gene causing cancer in the presence of a compound suspected of being a cancer therapeutic,
    - ***growing*** said transformed eukaryotic host call in the absence of the compound,
    - ***determining*** the rate of growth of said host cell in the presence of said compound and the rate of growth of said host cells in the absence of said compound and
    - ***comparing*** the growth rate of said host cells,
    - wherein a slower rate of grow of said host cell in the presence of said compound is indicative of a cancer therapeutic.

Public Perception　　新聞報道

- ✓ Patent law usually not discussed in mainstream U.S. media. However, this case has been discussed in:

The New York Times
Expect the World®

THE WALL STREET JOURNAL.

USA TODAY

The Washington Post

Newsweek

Public Perception　ニュース番組での特集

- Featured on “60 Minutes,” which is the most highly rated news TV program in the U.S.
  - http://www.cbsnews.com/video/watch/?id=6362525n
    - (might not work in Japan)

- Quotes/points from “60 Minutes” program:
  - Unequal time given to each side (~11 min for anti-patent vs. ~2 min for pro-patent)
  - “A vital part of who you are belongs to someone else” (reporter)
  - “It’s a simple blood test. It’s not a complicated procedure.” (patient)
  - “No one invented my gene” (patient)
  - “In most of Europe and Canada, where Myriad’s patents are ignored, the tests are given for a fraction of the $3200 that Myriad charges.” (reporter) But, note that those countries have nationalized medicine systems.
  - Is this a patent issue, or an insurance coverage issue?

ACLU's Arguments
原告の主張

- Composition claims（組成物のクレーム）
  - Isolated DNA is the same as genomic DNA in the body, and thus is a non-patent eligible "product of nature."
  - Even if isolation of DNA is a complex process, the end result is still a DNA sequence made not by man, but by nature.
  - Cited the U.S. Supreme Court in the 1948 case of *Funk Brothers Seed Co. v. Kalo Inoculant Co.*, which held that a patent cannot be granted for "one of the ancient secrets of nature now disclosed."
  - Analogized isolated DNA to gold extracted from a mine. Also, others have raised the "leaf plucked from a tree" or "organ removed from the body" analogy.

Myriad's Arguments
被告の主張

- Composition claims（組成物のクレーム）
  - There is no explicit prohibition on patenting of "products of nature"…Only "laws of nature, physical phenomena and abstract ideas."
  - Isolated DNA is different than genomic DNA in the body, and thus is not a "product of nature."
  - Isolation of DNA is a complex process, the end result is a DNA sequence which is structurally distinct from the natural form.
  - Isolated DNA sequences do not exist in nature!
  - No legislation banning gene patenting, so Congress' intent must be to permit it.
  - USPTO examination guidelines approve of isolated DNA claims.

ACLU's Arguments
原告の主張

- Method claims（方法のクレーム）
  - The method claims of the patents violate the First Amendment because they appear to cover the mere act of (1) looking at one sequence of letters and another sequence of letters, and (2) thinking about or saying whether they appear to be the same.
  - ACLU argued that this stifles the sharing of information between researchers.
  - ACLU also argues that this is an obstacle which prevents researchers from building upon existing research and potentially developing cures or treatments for BRCA1- and BRCA2-related cancers.
  - Under this reasoning, the patents do not "Promote the Progress of Science and the useful Arts" under Article I, Section 8, Clause 8.
  - Claims do not meet the "machine-or-transformation" test of *Bilski*.

Myriad's arguments
被告の主張

- Method claims（方法のクレーム）
  - The claims include a transformation (removing cells from body, opening cells, introducing DNA probes, probes attaching to complementary DNA), and therefore pass the "machine-or-transformation" test of *Bilski*.
  - As to First Amendment issue, the claims are not about intangible information, but rather are about physical molecules. Thinking or talking about the DNA sequences is not precluded by the patents.

Judge Sweet's Decision

地裁判事の判断

- Composition claims（組成物のクレーム）

  - It has been the longstanding practice of the U.S.P.T.O. to grant patents on gene sequences as long as the claim recites an *isolated* nucleic acid.
  - As to the composition claims reciting "an isolated DNA," Judge Sweet ruled that these were not patentable subject matter, because the isolated DNA is not "markedly different" from a product of nature.
  - Although the decision frequently cites to Supreme Court decisions predating the 1952 Patent Act, Judge Sweet also relies heavily on *Diamond v. Chakrabarty*, a Supreme Court decision from 1980 which authorized the patenting of living organisms (genetically-engineered oil eating bacteria).
  - Judge Sweet cites a passage of *Chakrabarty* which states that: "the patentee has produced a new bacterium with markedly different characteristics from any found in nature."

Judge Sweet's Decision

地裁判事の判断

- "Markedly different characteristics"
  - The Supreme Court in *Chakrabarty* did not explicitly state that a compound must be "markedly different" from nature to be patentable.
  - However, Judge Sweet establishes this as a legal test for patentability.
  - Judge Sweet concludes that the isolated DNA is not "markedly different" from the DNA found in nature. This determination relies in large part on the question of the dual nature of DNA as ***encoding information*** and as a ***physical compound***.
  - Judge Sweet appears to believe that DNA is special due to its encoding information, which is the same in the natural and isolated forms. Thus, Judge Sweet regards claims directed at isolated versions of naturally-occurring gene sequences as being unpatentable subject matter under 35 U.S.C. §101 as reciting **a product of nature**.

Judge Sweet's Decision

地裁判事の判断

- "Diagnosis" method claims（診断方法のクレーム）
  - For these claims, Judge Sweet relies heavily on the CAFC's *Bilski* decision. Note that this decision was issued before the Supreme Court issued their *Bilski* decision, stating that "machine-or-transformation" test is not the **only** test for whether a method is patent-eligible.
  - Essentially, Judge Sweet states that even if steps such as isolating and sequencing are required as a practical matter in order to perform the claimed method, such steps are not claimed.
  - Judge Sweet basically interprets the "diagnosis" method claims as including only mental steps of comparing sequences of data. However, Judge Sweet further states that even if the claims did include the steps of isolating and sequencing, these would merely be "data-gathering steps."
  - Judge Sweet regards claims directed at comparing gene sequences as being unpatentable subject matter under 35 U.S.C. §101 as reciting **a mental process**.

Judge Sweet's Decision

地裁判事の判断

- "Drug Screening" method claims（薬物スクリーニング方法のクレーム）
  - Only discussed very briefly in the decision.
  - Judge Sweet acknowledges that this method includes transformative steps, but avoids a discussion of *Bilski* and instead discusses "the essence of the claims."
  - Judge Sweet argues that the claimed process "is, in fact, the scientific process itself," and that the claims recite a scientific principle. Judge Sweet concludes that the transformative steps are merely data gathering steps.
  - Thus, Judge Sweet regards claims directed at screening therapeutics as being unpatentable subject matter under 35 U.S.C. §101, apparently as reciting **a mental process and a scientific principle**.
  - The *Bilski* test only requires a machine-or-transformation. Thus, it would appear that claims including transformative steps should be patent-eligible. However, in this section of the decision, Judge Sweet did not apply the full *Bilski* test.
  - Judge Sweet appears to believe that there is a *pre-emption* issue.

Judge Sweet's Decision

地裁判事の判断

- ✓ Does not comment on Constitutional arguments.
- ✓ Relies on the "Doctrine of Constitutional Avoidance," which states that a court should avoid ruling on Constitutional issues if possible.

What's next?　今後の見通し

- ✓ Already appealed to CAFC（既に連邦控訴裁判所に控訴）
  - ✓ U.S. Dept. of Justice filed *amicus* brief mostly taking anti-patent position!
- ✓ Good chance that the CAFC will overturn at least a portion of the decision.
- ✓ Possible that the CAFC's decision will eventually be appealed to the Supreme Court, at least with respect to the isolated DNA sequences.
- ✓ If the Supreme Court agrees to hear the case, it is very difficult to predict the outcome.

Countermeasures 実務上の対策

- ✓ Continue to file claims reciting isolated nucleic acids, polypeptides, etc. USPTO policy will **not** change until the Federal Circuit issues a decision.

- ✓ File claims reciting artificial compositions which include an isolated nucleic acid or polypeptide, if applicable. For example, for gene therapy, recite a delivery construct including the isolated nucleic acid. As another example, recite a cell culture medium including the isolated polypeptide. As another example, recite a vector including the nucleic acid sequence. This should be done even if the subject matter other than the nucleic acid or polypeptide is not novel.

- ✓ As to method claims, file claims which include any arguably ***transformational*** steps, even if those steps are not novel themselves. For example, explicitly recite steps of isolating and sequencing nucleic acids or polypeptides. Do not rely only on "comparing" and "analyzing" steps.

Countermeasures 実務上の対策

- ✓ When possible, recite methods which include an “action step” after a determination has been made. For example, recite a method including comparing DNA sequences, determining that a mutation is present, and treating the patient with a medicine, even if the medicine is known.

- ✓ As always, we recommend including many dependent claims, so that a broad-to-narrow range of patent scope can be claimed.

Other cases to be aware of　関連事件の動き

- *Prometheus v. Mayo* (on CAFC docket). Was appealed to Supreme Court but returned to CAFC after *Bilski* decision.
- Representative claim:
- A method of optimizing therapeutic efficacy for treatment of an immune- mediated gastrointestinal disorder, comprising:
  - (a) ***administering*** a drug providing 6-thioguanine to a subject having said immune-mediated gastrointestinal disorder; and
  - (b) ***determining*** the level of 6-thioguanine in said subject having said immune-mediated gastrointestinal disorder,
  - wherein the level of 6-thioguanine less than about 230 pmol per $8x10^8$ red blood cells indicates a need to increase the amount of said drug subsequently administered to said subject and
  - wherein the level of 6-thioguanine greater than about 400 pmol per $8x10^8$ red blood cells indicates a need to decrease the amount of said drug subsequently administered to said subject.

  - Previously: CAFC held that this claim complies with §101 and passes pre-Supreme Court *Bilski* "machine-or-transformation" test.

Other cases to be aware of　関連事件の動き

- ✓ *Classen v. Biogen* (on CAFC docket). Was appealed to Supreme Court but returned to CAFC after *Bilski* decision.
- ✓ Representative claim:

- ✓ A method of determining whether an immunization schedule affects the incidence or severity of a chronic immune-mediated disorder in a treatment group of mammals, relative to a control group of mammals, which comprises
  - ✓ ***immunizing*** mammals in the treatment group of mammals with one or more doses of one or more immunogens, according to said immunization schedule, and
  - ✓ ***comparing*** the incidence, prevalence, frequency or severity of said chronic immune-mediated disorder or the level of a marker of such a disorder, in the treatment group, with that in the control group.

  - ✓ Previously: CAFC held that this claim does not comply with §101 and does not pass pre-Supreme Court *Bilski* "machine-or-transformation" test.

Summary

- ✓ Patenting of isolated versions of naturally-occurring DNA is at risk. This could have far-reaching effects on the biotechnology industry.
- ✓ For now, continue to file claims directed at isolated DNA, proteins, etc.
- ✓ If possible, include claims which recite an artificial composition of, for example, DNA and another element (*i.e.*, vector, etc.).

- ✓ Claim drafting of method claims should be done carefully.
- ✓ If possible, explicitly recite a physically transformative step and an "action" step after decision is made.

- ✓ CAFC will hear all of *AMP v. USPTO*, *Prometheus v. Mayo* and *Classen v. Biogen* in the coming year.

Thank you for listening! Questions?

- ✓ WHDA Biotech Team:

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