Best Practices in Patenting Precision Medicine

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Section 101 Patent Eligibility – State of Play

- **Courts**
  - Methods of treatment
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Claims at issue in *Vanda* and *Mayo*

Vanda Claim

1. A method for treating a patient with iloperidone, wherein the patient is suffering from schizophrenia, the method comprising the steps of:

determining whether the patient is a CYP2D6 poor metabolizer by:

obtaining or having obtained a biological sample from the patient; and performing or having performed a genotyping assay on the biological sample to determine if the patient has a CYP2D6 poor metabolizer genotype;

and if the patient has a CYP2D6 poor metabolizer genotype, then internally administering iloperidone to the patient in an amount of 12 mg/day or less,

and if the patient does not have a CYP2D6 poor metabolizer genotype, then internally administering iloperidone to the patient in an amount that is greater than 12 mg/day, up to 24 mg/day,

wherein a risk of QTc prolongation for a patient having a CYP2D6 poor metabolizer genotype is lower following the internal administration of 12 mg/day or less than it would be if the iloperidone were administered in an amount of greater than 12 mg/day, up to 24 mg/day.

Mayo Claim

1. 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.

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Claims at issue in *Vanda* and *Mayo*

Vanda Claim (patent eligible as applying a natural relationship)

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obtaining or having obtained a biological sample from the patient; and performing or having performed a genotyping assay on the biological sample to determine if the patient has a CYP2D6 poor metabolizer genotype;

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Mayo Claim (patent ineligible as directed to natural relationship)

1. A method of optimizing therapeutic efficacy for treatment of an immune-mediated gastrointestinal disorder, comprising:

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(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.

Certiorari Petition in *Vanda*

Question presented:

"Whether patents that claim a method of medically treating a patient automatically satisfy Section 101 of the Patent Act, even if they apply a natural law using only routine and conventional steps."

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Roche – Primer claim

- "A primer having 14–50 nucleotides that hybridizes under hybridizing conditions to an M. tuberculosis rpoB [gene] at a site comprising at least one position-specific M. tuberculosis signature nucleotide selected . . . from the group consisting of
  - [*one of 11 position-specific signature nucleotides*]."
- *Held*: patent ineligible
  - Claimed primers "have the *identical nucleotide sequences* as naturally occurring DNA"

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Claim 7 at issue in *Athena*

1. A method for diagnosing neurotransmission or developmental disorders related to [MuSK] in a mammal comprising the step of detecting in a bodily fluid of said mammal autoantibodies to an epitope of [MuSK].

7. A method according to claim 1, comprising

contacting MuSK or an epitope or antigenic determinant thereof having a suitable label thereon, with said bodily fluid,

immunoprecipitating any antibody/MuSK complex or antibody/MuSK epitope or antigenic determinant complex from said bodily fluid and

monitoring for said label on any of said antibody/MuSK complex or antibody/MuSK epitope or antigen determinant complex,

wherein the presence of said label is indicative of said mammal is suffering from said neurotransmission or developmental disorder related to [MuSK].

Policy considerations noted in *Athena*

- The dissent states much that one can agree with from the standpoint of policy, and history, including that "the public interest is poorly served by adding disincentive to the development of new diagnostic methods." . . . We would add further that, in our view, providing patent protection to novel and non-obvious diagnostic methods would promote the progress of science and useful arts. But, whether or not we as individual judges might agree or not that these claims only recite a natural law, . . . the Supreme Court has effectively told us in *Mayo* that correlations between the presence of a biological material and a disease are laws of nature, . . . and "[p]urely 'conventional or obvious' '[pre]-solution activity' is normally not sufficient to transform an unpatentable law of nature into a patent-eligible application of such a law"

Athena Diagnostics, Inc. v. Mayo Collaborative Servs., LLC, 915 F.3d 743, 753 n.4 (Fed. Cir. 2019)

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Draft Outline of Section 101 Reform

- Eliminate in Section 101 that any invention or discovery be both "new and useful."
- Statutorily abrogate judicially created exceptions to patent eligible subject matter in favor of exclusive statutory categories of ineligible subject matter, e.g., fundamental scientific principles; products that exist solely and exclusively in nature; pure mathematical formulas; economic or commercial principles; mental activities.
- Create a "practical application" test to ensure statutorily ineligible subject matter is construed narrowly.
- Make clear that eligibility is determined by considering each and every element of the claim as a whole and without regard to considerations properly addressed by 102, 103 and 112.

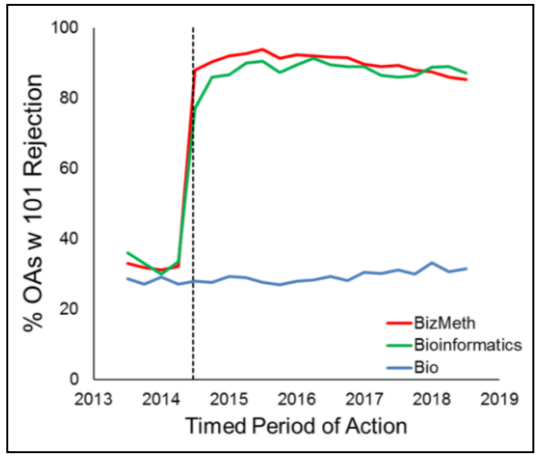
Patenting AI for Precision Medicine Diagnostics

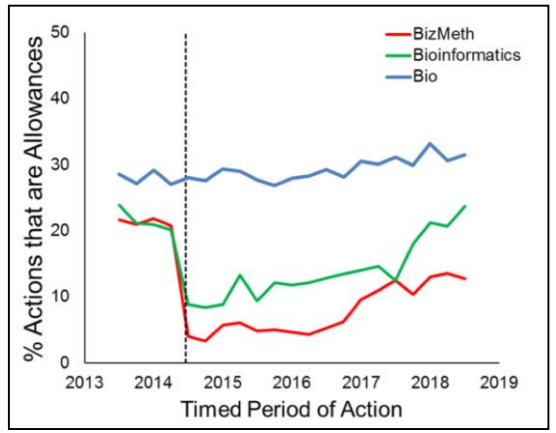
- **What are possible strategies to successfully patent Artificial Intelligence-[1] or Bioinformatics-based inventions for precision medicine?**
- Artificial Intelligence- and Bioinformatics-based patenting continues to evolve due to decisions by Federal Circuit and Supreme Court (and perhaps soon Congress[2]) and requires 'invention-specific' strategies including **i)** a description of technical obstacles and solutions for the 'intended practical use' of the invention, **ii)** carefully crafted claim language and **iii)** prioritization and balance of protection tools[3] and FTO objectives to guide, deploy and protect innovations.
- Patents do not provide the protection or the value they once did.

[1] Encompasses AI and Machine Learning
[2] Houses of Congress released identical draft outlines for Section 101 reform April 17, 2019
[3] Patents, Copyrights, Trade secrets, Trademarks, public disclosures, etc.

Challenges of Patenting AI and Bioinformatics in Diagnostics

- 35 U.S.C. § 101 and 112 rejections (first observed in business units then spread to software-related art units)[1]
- Requires deep understanding of patent precedent and ongoing office actions/decisions[2]
- Discoverability of infringing activities
- Comprehensive and clear description permitting 'enablement' of invention
- 'Black box' nature of most machine learning algorithms
- Alternative non-infringing machine learning strategies to accomplish same outcome (design arounds)
- Rapidly evolving technology that outdates prior strategies in a relatively short time frame
- Wealth of published machine learning technologies serve as precedent (prior art)
- May be difficult to integrate dynamic learning into machine learning invention claims





[1] Scope only includes 'patent eligibility'; 'injunctive relief' out of scope (eBay v. MercExchange (2006))

[2] For example, 2019 Revised Patent Subject Eligibility Guidance (35 U.S.C. § 101 and § 112 (a, b, and f))(Jan 4, 2019)). Ironically patent analytics use machine learning tools (e.g. Juristat)

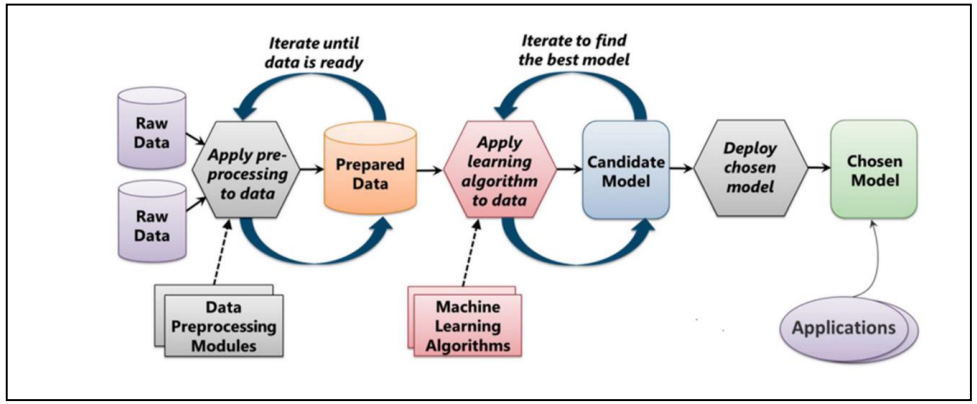
Computers as 'inventors' using machine learning out of scope of this content

Areas of AI Innovation

- Input data set selection, preparation and transformation (data engineering)
- Using domain knowledge of the data to develop covariates (feature engineering)
- Structure/architecture of the model (or ensemble (combination) or order thereof)
- Training process (optimization/loss function)
  - Counterfactuals
  - Linear effect and non-linear interaction effect of covariates
- Validation process (internal and/or external validation)
  - Discern causal covariates
- Interpretability of overall model
- Post-processing and interpretation of model output

Optimal diagnostic tests for Precision Medicine require integration of multiple covariates (e.g. molecular, phenotypic, etc.) to be maximally accurate and clinically relevant

The Machine Learning Process



Artificial Intelligence for IP Analytics

- IP Analytics can be used before, during and after patent prosecution
  - Craft claims
  - Manage office actions
  - Monitor competitor landscape
- All stakeholders can benefit from reviewing salient content
- Classic Big Data problem addressed with AI tools
- Custom searches and upload of bespoke data sets
- Broad individual and combined query capability
  - Filing volume by keyword, assignees, firms, class assignment, allowance rate by tech center and business unit, average office actions to disposition, examiner records, etc.
- Representative key word query: “Cancer” AND “Diagnostics” AND “Machine Learning” NOT “Imaging” (Jan 2014-Dec 2017)
  - ~3 yrs to disposition; ~50% allowed; major reasons for rejections were 101 and Alice; ~3 office actions per disposition

Thank you.

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