

DECENTERING THE CONSUMING SELF: PERSONALIZED MEDICINE, SCIENCE, AND THE MARKET FOR LEMONS

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I. INTRODUCTION

Until the Food and Drug Administration (“FDA”) initiated an investigation of potentially misleading marketing claims against 23andMe in 2014, the start-up company provided a thriving business in through-the-mail medical diagnostics of genetic samples.¹ Whether a fledgling market will survive, and how, are the questions at issue in the ongoing FDA investigation. Although this Article does not promise a prediction of this dispute’s resolution, it does present an analysis of the economic, legal, and policy issues underlying the emerging institutions of personalized medicine.

Understood broadly, the promise of personalized medicine is a simple one. Medical diagnostics and therapies can be individualized to the personal family, genetic, and environmental history of a patient.² Proclivities to chronic and fatal diseases are identified early, and the informed patient can use the information

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1. See Warning Letter from Alberto Gutierrez, Dir., Office of In Vitro Diagnostics & Radiological Health, Food & Drug Admin., to Ann Wojcicki, CEO, 23andMe, Inc. (Nov. 22, 2013), available at <http://www.fda.gov/ICECI/EnforcementActions/WarningLetters/2013/ucm376296.htm> (accessed November 10, 2014).

2. See *About*, PERSONALIZED MED. COALITION, http://www.personalizedmedicinecoalition.org/About_Us/About_PMC (last visited Jan. 29, 2015).

to make wise and meaningful lifestyle and medical decisions. If a patient receives a positive diagnosis of a medical condition, health care professionals can use the patient's history to target treatment for more effective recovery and responsive palliative care, and health care outcomes improve. Diagnosis and treatment can be even more precise and scientific, and consumers of health services will be better off.

Underlying the promise of personalized medicine is an understanding of how deeper knowledge of an individual's genetic record can aid in medical diagnosis and treatment that goes beyond the traditional examination of symptoms and recognition of disease pathways. For the purposes of diagnosis, much of this understanding is based on statistical correlation that allows reading genetic sequences and identifying statistical correlations with the incidence of disease.³ As for therapeutics, the correlations are between identified genetic sequences and responses to specific pharmaceutical treatments. One scholar has described this scientific understanding as a "black box," suggesting that all the causal pathways may not be fully understood.⁴ Instead, medical professionals have a sense of what works and use their judgment as a guide in identifying and treating disease.

The characterization of personalized medicine as a black box examines the need for regulation to protect consumers as medical professionals tailor medical response to disease.⁵ But traditional, non-genetic based medical practice is not premised on a full understanding of the biological and chemical pathways for either the spread of disease or response of disease to medical

3. See W. Nicholson Price II, *Incentives, Intellectual Property, and Black Box Personalized Medicine*, 28 HARV. J. L. & TECH. (forthcoming 2015), available at https://www.law.berkeley.edu/files/Price_Nicholson_IPSC_paper_2014.pdf.

4. *Id.*

5. See, e.g., Mari Edlin, *More Evidence Needed Before Genetic Tests Become Mainstream: It's Your Genes*, MANAGED HEALTHCARE EXECUTIVE (Aug. 1, 2013), <http://managedhealthcareexecutive.modernmedicine.com/managed-healthcare-executive/content/tags/diagnostic-test/more-evidence-needed-genetic-tests-become?page=full>. For another example of personalized medicine marketing, this one involving do-it-yourself diagnostic tests of blood samples, see Ken Aulette, *Blood, Simpler: One Woman's Drive to Upend Medical Testing*, THE NEW YORKER (Dec. 15, 2014), available at <http://www.newyorker.com/magazine/2014/12/15/blood-simpler>.

treatment. As with many types of judgments, decisions by medical professionals do not require complete knowledge of the underlying science.⁶ Instead, treatment and diagnosis often involve practical guesswork based on experimentation and empirical observation.⁷ The challenge is identifying how much uncertainty is tolerable.⁸ What is tolerable in turn depends on whom the decisionmaker is. A health care provider makes decisions within the parameters of the profession and its standard of care for patients.⁹ A regulator, such as the FDA, may have slightly different parameters for tolerating uncertainty with the goal of protecting the health, safety, and welfare of consumers. These potentially conflicting parameters are tested with the introduction of any new medical technology.¹⁰ Not surprisingly, this tacit conflict is central to the FDA's investigation of 23andMe.

At the heart of the promise of personalized medicine is an idealized notion of science and technology. The ideal of the autonomous individual, whether caregiver or patient, shapes the dream of gaining better information that provides control and more meaningful choice over health care decisions. Personalized medicine can improve not only medical decision making but decisions related to the consumption of medical services. Whether companies like 23andMe thrive will determine how the health care marketplace takes shape. For purveyors of personalized medicine, the marketplace can only improve with better information, even if the information is not perfect and completely accurate. Skeptics and regulators are concerned that what is being sold by personalized medicine companies is not, in fact, information that supports meaningful decision making. Instead, what passes as information is actually deception. While one can question whether this deception is intentional, and rises to fraud, one may still wonder what the black box is telling us and why consumers should trust it and pay large sums for the oracle.

Between the extremes of scientific and instructive information and pure unadulterated deception lies the reality of

6. See JEROME GROOPMAN, *HOW DOCTORS THINK* 77–79 (2008).

7. *Id.*

8. See, e.g., Andrew Hresko & Susanne B. Haga, *Insurance Coverage Policies for Personalized Medicine*, 2 J. PERSONALIZED MED. 201, 202 (2012).

9. *Id.*

10. See HERBERT HOVENKAMP, *THE OPENING OF AMERICAN LAW: NEOCLASSICAL LEGAL THOUGHT 1870-1970* 144–45 (2014).

many markets where information is the key commodity being sold. This reality entails asymmetries of information where the two sides of a market may have different information on the nature of a commodity.¹¹ This asymmetric information problem is described as the “lemons problem,” made famous by Nobel Prize winning economist George Akerlof in his seminal article, “The Market for Lemons.”¹²

According to Akerlof, if a supplier may be better informed about product attributes than the demander, the market may fail to arise because demanders would be wary about contracting with a supplier that has superior information.¹³ If products differ in quality, demanders will be willing to pay for only the product of average quality.¹⁴ Suppliers who know that their product is above average will not supply to the market, forcing the average quality expected by demanders down further.¹⁵ To solve this problem of market failure (really, market collapse), suppliers need to be able to make credible statements about product quality so that consumers will be able to identify the level of quality they seek for the product. Warranties, government certification, or other institutions resolve the lemons problem.¹⁶

What should be emphasized is that there are several solutions to the lemons problem. The solution policymakers choose is a question of institutional choice. With food and drugs, the United States has designated an administrative agency, the FDA, to police the marketplace.¹⁷ Critics of the FDA question whether this is the most appropriate response. The debate over health care regulation, including the emerging market of personalized medicine, rests on which legal and economic institutions are the most desirable for consumers of health care services. This description of the regulatory debate serves as the starting point for the analysis in this Article, particularly in

11. See George A. Akerlof, *The Market for ‘Lemons’: Quality Uncertainty and the Market Mechanism*, 84 Q.J. ECON. 488, 489 (1970).

12. *Id.* at 490.

13. *Id.* at 492.

14. *Id.*

15. *Id.*

16. See, e.g., George L. Priest, *A Theory of the Consumer Product Warranty*, 90 YALE L.J. 1297, 1308 (1981).

17. See, e.g., Susanna Hornig Priest, *Risk Communication for Nanobiotechnology: To Whom, About What, and Why?*, 37 J.L. MED. & ETHICS 759, 768 (2009) (describing FDA regulatory process).

Sections III and IV, which present the regulatory responses to personalized medicine.

While the lemons problem frames the policy analysis, the case of personalized medicine clearly goes beyond the problem of asymmetric information that informs Akerlof's seminal article. In that piece, Akerlof focuses on the market for cars, in which some cars function for a long time, and some, like lemons, do not function at all.¹⁸ The underlying science of how a car functions is not relevant for his argument. Professor Akerlof extends this analysis to the credit market in which some borrowers are solvent and others are not.¹⁹ Within the credit market, the solvency of the borrower can be ascertained through identifying attributes such as personal attributes of the borrower.²⁰ In short, for the lemons problem, information about quality can be verified. Either the car runs or it does not. Either the debtor has collateral or he does not.

Personalized medicine, however, suffers not only from the problem of asymmetric information but also from the problem of uncertainty.²¹ The supplier of personalized medicine services knows the underlying statistical model that provides the basis for the prediction. Of course, this model may be shared with the purchaser of the services. This sharing of information, however, does not address the black box which generates the underlying correlations that form the basis for the prediction. Information can be revealed, but it cannot be verified in the same way that it can with a car or with the creditworthiness of a borrower. With medical treatment, the patient cannot know whether the diagnosis or treatment is correct until the disease either does not arise or there is full recovery.²² In other words, personalized medicine markets are more fraught with information problems than the canonical market for lemons. The implication is that the choice of regulatory regime is even more complicated.

18. Akerlof, *supra* note 11, at 493.

19. *Id.* at 497.

20. *Id.* at 499.

21. NESSA CAREY, *THE EPIGENETICS REVOLUTION: HOW MODERN BIOLOGY IS REWRITING OUR UNDERSTANDING OF GENETICS, DISEASE, AND INHERITANCE* 77–79 (2012) (discussing the ongoing uncertainty over environment and genetics in shaping disease proclivity).

22. *See* Price, *supra* note 3, at 10 (explaining that specified treatments based on biological subpopulations are more targeted and thus, more effective).

With this information as a foundation, the next point is a full analysis of the law and policy of personalized medicine regulation. Section II presents some basic background on the law and business surrounding personalized medicine. Section III addresses the information problems afflicting personalized medicine markets. Section IV considers policy responses. Section V provides a brief conclusion.

II. CASE STUDIES OF PERSONALIZED MEDICINE

This section provides the business background of several companies from the personalized medicine industry: Myriad, Nitromed, Genetic Technologies Limited, and 23andMe. These companies are the subject of news stories as well as several legal disputes. The purpose of this section is to present a background for readers unfamiliar with the legal and business background to personalized medicine.

A. Myriad, Nitromed, and the Types of Personalized Medicine

Two types of inventions feed the market for personalized medicine. The first type consists of inventions based on identification of genetic markers for the diagnosis and treatment of diseases.²³ The second consists of diagnostics and treatments that are targeted at particular demographics.²⁴ Myriad's patent illustrates the first; Nitromed's patent on treating hypertension in a black patient, illustrates the second.²⁵ What both types share is research and development pertaining to human persons. If companies seek to patent these inventions, agencies, courts, and legislatures must confront turning human persons or attributes of persons into legally protected property. This section presents background information about how these two companies entered and shaped the market for personalized medicine.

On January 30, 2013, the United States Patent and Trademark Office ("USPTO") published a pending application submitted by Myriad, Inc., a Utah-based genetic research and

23. SHUBHA GHOSH, IDENTITY, INVENTION, AND THE CULTURE OF PERSONALIZED MEDICINE PATENTING 39 (2012).

24. *Id.*

25. *Id.*

medical diagnostic company.²⁶ The application contained a description of a process for detecting susceptibility to breast cancer among individuals of “Ashkenazi-Jewish ancestry.”²⁷ Proposed claims one, five, and seven cover:

1. A method comprising determining whether a plaintiff’s tumor sample has BRCA deficiency and, if there is somatic BRCA [gene] deficiency, determining whether the patient has germline BRCA deficiency.

5. The method of claim 1, wherein said patient is identified as lacking any significant risk factors for germline BRCA deficiency.

7. The method of claim 5, wherein said patient lacks any of the following: breast cancer at less than 40 years; bilateral breast cancer; breast cancer at less than 50 years and a close relative with breast cancer at less than 50 years; Ashkenazi Jewish ancestry with breast cancer at less than 50 years old; breast or ovarian cancer at any age and two or more close relatives with breast cancer at any age; a first or second degree relative that meets at least one of the above criteria.²⁸

A patent application is published in the United States roughly eighteen months after the filing date.²⁹ Myriad filed the United States patent application on November 5, 2010, and an accompanying international application under the Patent Cooperation Treaty (“PCT”) on the same date.³⁰ The antecedent

26. Compositions and Methods for Determining Cancer Susceptibility, U.S. Patent Application Serial No. 20,130,029,926/20130029926 (filed Nov. 5, 2010) (published Jan. 31, 2013).

27. *Id.*

28. *Id.*

29. 35 U.S.C § 122(b)(1)(A) (2012). Certain exceptions exempt an application from publication after the standard eighteen months, including when an application is no longer pending or it is subject to a secrecy order. *Id.* § 122(b)(2)(A).

30. See U.S. Patent Application Serial No. 20,130,029,926/20130029926, *supra* note 26.

to this pending patent application is European Patent 0785216B2, “Chromosome 13-linked breast cancer susceptibility gene BRCA2,” which was granted by the European Patent Office (“EPO”) on January 8, 2003, and reissued on June 7, 2006, with new specifications after an opposition.³¹ As stated in the “Summary of Invention,” the patent covers a method “for diagnosing a predisposition to breast cancer in Ashkenazi-Jewish women *in vitro*.”³²

One difference between the granted European patent and the United States application is that the application refers to many factors other than Ashkenazi-Jewish heritage and the claim is worded in relation to persons of “Ashkenazi-Jewish heritage” rather than just “Ashkenazi-Jewish women.”³³ These changes may have to do with inventing around the prior art of the European patent, which could serve to make the invention disclosed in the patent application non-novel or obvious. Both granted patent and application, however, illustrate the use of an ethnic category to identify the proprietary invention.³⁴

The patents owned by Nitromed illustrate another approach to personalized medicine. Specifically, the patent underlying the pharmaceutical compound, BiDiI, reads as follows:

1. A method of reducing mortality associated with heart failure, for improving the oxygen consumption, for improving the quality of life or for improving exercise tolerance in a black patient comprising administering to the black patient a therapeutically effective amount of at least one hydralazine compound of Formula (I) or a pharmaceutically acceptable salt thereof, and at least one of isosorbide dinitrate and isosorbide mononitrate,

31. New European Patent Specification No. EP 0 785 216 B2, Chromosome 13-linked Breast Cancer susceptibility gene BRCA2 (granted Jan. 8, 2003).

32. *Id.* at 5.

33. See U.S. Patent Application Serial No. 20,130,029,92620130029926, *supra* note 26; New European Patent Specification No. EP 0 785 216 B2, *supra* note 31.

34. See generally U.S. Patent Application Serial No. 20,130,029,92620130029926, *supra* note 26; New European Patent Specification No. EP 0 785 216 B2, *supra* note 31.

wherein the hydralazine compound of Formula (I) is ##STR2##

wherein a, b and c are each independently a single or a double bond; R.sub.1 and R.sub.2 are each independently a hydrogen, an alkyl, an ester or a heterocyclic ring; R.sub.3 and R.sub.4 are each independently a lone pair of electrons or a hydrogen, with the proviso that at least one of R.sub.1, R.sub.2, R.sub.3 and R.sub.4 is not a hydrogen.

2. The method of claim 1, wherein the black patient has a less active renin-angiotensin system relative to a white patient.

3. The method of claim 1, wherein the black patient has hypertension.³⁵

Like the Myriad patents, the Nitromed patent is restricted to a particular racial category, in this case a “black patient.” Unlike the Myriad patent, Nitromed’s claim is not written in terms of a genetic marker. Instead, the patent uses the term “black” as a sociological term not connected to an isolated gene sequence. Both companies use the respective patents to develop a business model marketing the relevant products to the subpopulation seeking either diagnosis or treatment of a medical condition. In the case of Myriad, the market is for diagnosis of proclivities towards breast and uterine cancers. In the case of Nitromed, the market is for a pharmaceutical compound that clinical trials, as explained below, showed was especially beneficial for the subpopulation.

The science underlying Myriad’s and Nitromed’s patents also offers some contrasts. Myriad identified the gene sequence associated with breast and uterine cancers by aggregating genealogical data and the gene sequences of individuals.³⁶ By

35. US Patent No. 6,465,463 (Filed 6465463 (Oct. 15, 2002)).

36. Ass’n for Molecular Pathology v. U.S. Patent & Trademark Office, 689 F.3d 1303, 1314 (Fed. Cir. 2012) (“Relying on a large set of DNA samples from families with

constructing medical histories, researchers at Myriad could identify prevalence of cancer in families.³⁷ Researchers could identify genetic markers that are statistically associated with the prevalence of certain forms of cancer.³⁸ By contrast, Nitromed's patent derived from research by Dr. Jay Cohn, a medical researcher at the University of Minnesota.³⁹ Dr. Cohn obtained a patent in 1989 on a pharmaceutical compound that would treat hypertension not restricted to "black patients."⁴⁰ Unfortunately for Dr. Cohn, the FDA denied marketing approval for the patented drug in 1997, citing deficiencies in the clinical data on safety and efficacy for treating patients.⁴¹ That same year, Nitromed began to support Dr. Cohn's research on hypertension on patients in veterans' hospitals. Dr. Cohn discovered a combination of compounds that were particularly effective on African American patients. These compounds were the basis for the 2002 patent cited above. The FDA approved these compounds for treatment of African Americans in 2004, and Nitromed marketed the drug as BiDil until 2008, when the company deemed the drug to be unprofitable.⁴²

Both Myriad and Nitromed base their personalized medicine products on findings of correlation that identify a statistical link between a patient characteristic and a particular diagnosis (in the case of Myriad) or a particular treatment (in the case of Nitromed). Myriad looks at the genetic characteristics of a patient while Nitromed focuses on the phenotypic characteristics (in the case of BiDil, identification as African American). These correlations with personal characteristics in turn become the basis for claiming the inventions in respective patents. This background on the science underlying the inventions and patents will be important for discussion of the need for regulation in the rest of this paper.

inherited breast and ovarian cancers, the inventors correlated the occurrence of cancer in individual family members with the inheritance of certain marker DNA sequences.”).

37. *Id.*

38. *Id.*

39. See US Patent No. 6,465,463, *supra* note 35, listing Dr. Cohn as an inventor and Nitromed as an assignee from Dr. Cohn.

40. US Patent No. 4,868,197 (Sept. 19, 1989) (“Method of reducing mortality associated with congestive heart failure using hydralazine and isosorbide dinitrate.”).

41. GHOSH, *supra* note 23.

42. See David Armstrong, *Nitromed Halts Marketing of Drug*, WALL ST. J., available at <http://www.wsj.com/articles/SB120044147052292697>.

Several legal implications follow from the business models for personalized medicine exemplified by Myriad and Nitromed. These questions include the validity of the patents, the statistical inferences drawn from the correlations as they translate into information for patients on the diagnoses and treatments they are receiving, and the research and development choices made by companies engaged with personalized medicine. This Article now turns to the legal treatment of personalized medicine inventions, drawing on the business experiences of Nitromed, Myriad, and some emerging companies.

*B. Legal Treatment of Personalized Medicine Inventions:
The Cases of Nitromed and Myriad*

This section examines two salient legal issues raised by personalized medicine. The first is the validity of patents under the nonobvious doctrine. The second is the policy issue raised by the patenting natural phenomenon. The third problem raised by personalized medicine concerns the claims made by firms selling diagnoses and treatments. It will be the focus of the remaining sections of this paper.

i. Nonobvious Personalized Medicine Patents

For a patent to be validly issued by the USPTO and upheld by the courts, the invention must be nonobvious. Intuitively, this requirement means that an invention must be different from prior technology and that these differences are not trivial as gauged by a person with ordinary skill in the field of technology. Congress codified the non-obviousness requirement in Section 103 of the Patent Act, which states that differences between an invention and the prior art must be nonobvious to a person having ordinary skill in the art, or a PHOSITA.⁴³ Personalized medicine patents raise potential problems of obviousness. In this section, Nitromed will serve as the primary example of these potential problems. But the experience of Myriad briefly illustrates analogous problems, discussed in the following subsection.

The main difference between the Nitromed patent duplicated in part above and the prior art is the limitation to black patients. For example, notice that Nitromed's 2002 patent cited a

43. See 35 U.S.C. § USC 103.

1989 patent issued to one of the inventors for a “Method of Reducing Mortality associated with Congestive Heart Failure Using Hydralazine and Isosorbide Dinitrate.”⁴⁴ The patent expired in 2003.⁴⁵ It is instructive to read the first claim of the 1989 patent and compare it with the more recent ones:

A method of reducing the incidence of mortality associated with chronic congestive heart failure in a patient with impaired cardiac function and concomitant reduced exercise tolerance, comprising the oral administration to said patient in need of the same of a combination of (a) between about 75 and about 300 milligrams of hydralazine, or a pharmaceutically acceptable acid addition salt thereof, per day, and (b) between about 40 and about 160 milligrams of isosorbide dinitrate, per day.⁴⁶

The two differences between the 1989 claim and the 2002 claim are the dosages and the absence of any racial limitations. Would these differences be nonobvious to a person having ordinary skill in the art, as required under Section 103? By itself, discovering a different dosage level of a chemical compound would not be enough to satisfy the nonobvious requirement of patentability, unless there was some “unexpected result” from what was in the prior art.⁴⁷ Examiners have found these changes to be common sense to someone with knowledge in the field.⁴⁸ The unexpected result in the case of BiDil is the identified effectiveness in black patients. A review of how Nitromed was able to persuade the USPTO to grant its 2002 patent illustrates this point. On December 5, 2001, the patent examiner rejected the race-specific claims in the application supporting the 2002 patent

44. See US Patent No. 4,868,197, *supra* note 40.

45. This is based on the fourteen year patent term under the law in effect in 1989. See 35 U.S.C. § USC 154(a)(2).

46. See US Patent No. 4,868,197, *supra* note 40.

47. See, e.g., *Ortho-McNeil Pharmaceuticals v. Kali Laboratories, Inc.*, 482 F. Supp. 2d 478 (noting that the change in dosage level was not sufficient for nonobviousness).

48. See *Tyco Healthcare Grp. LP v. Mut. Pharm. Co.*, 642 F.3d 1370, 1377 (Fed. Cir. 2011).

for being obvious in light of the 1989 patent.⁴⁹ The patent applicant responded on May 6, 2002, arguing that there was nothing in the 1989 patent that would “disclose or suggest” the race-specific claims.⁵⁰ In addition, the applicant argued that the efficacy in the African American population was an “unexpected result” which supported a conclusion of nonobviousness.⁵¹ The patent examiner accepted this argument, and in an office action on May 18, 2002, the examiner concluded that the claims were nonobvious in light of the unexpected result.⁵²

Should the efficacy of a new dosage level in a demographic subgroup count as an unexpected result for nonobvious purposes? This policy question has been explored in related scholarship. For the purposes of this Article, focus will remain on how this question is at the heart of personalized medicine patenting, especially as companies seek to tailor existing inventions to specific groups. As argued elsewhere, the nonobvious requirement creates incentives for inventions. If personalized tailoring is the basis for invention, the concern would be that companies might make trivial variations in order to obtain a patent. The patent system may want to police against this possibility by adopting a higher standard of nonobviousness for personalized medicine patents.

ii. Gene Sequences and the Patentability of Nature

On June 13, 2013, the United States Supreme Court addressed the question of the patentability of DNA sequences in a challenge to Myriad’s breast cancer gene patent brought by the Association of Medical Pathologists.⁵³ The Court’s answer seems straightforward. Isolating a naturally occurring DNA sequence does not give rise to patentability while creating a synthetic DNA sequence might be patentable.⁵⁴ While this response seems clear

49. Memorandum from Raymond Henley, Jr. Primary Examiner, to Edward D. Grieff, Registration No. 38,898 (December 5, 2001) (on file with author).

50. Memorandum from Edward D. Grieff, Registration No. 38,898 to Raymond Henley, Jr., Primary Examiner (May 6, 2002) (on file with author).

51. *Id.*

52. Memorandum from Raymond Henley, Jr. Primary Examiner, to Edward D. Grieff, Registration No. 38,898 (May 18, 2002) (on file with author).

53. *Ass’n for Molecular Pathology v. Myriad Genetics, Inc.*, 133 S. Ct. 2107 (2013).

54. *Id.* at 2119–20.

cut on the surface, some might find the decision devastating for the pharmaceutical and biotechnological industries.

In 1997 and 1998, Myriad Genetics was granted three patents related to identifying genetic sequences associated with susceptibility to breast and ovarian cancer.⁵⁵ These patents covered the isolated gene sequence as well as complementary DNA sequences (“cDNA”), both useful for identifying the presence of the various strains of the cancer gene in patients and diagnosing the susceptibility to breast and ovarian cancers.⁵⁶ Myriad marketed a diagnostic test for detecting the presence of the gene sequences.⁵⁷

Myriad’s practices became the subject of media scrutiny. Medical practitioners, patient rights advocates, and health care access proponents raised critical issues of high medical costs and a patient’s right to know in questioning Myriad’s business and litigation strategies. In 2009, the Association for American Pathologists sued Myriad, challenging the validity of its patents.⁵⁸

Spring 2010 marked the district court’s decision in the Myriad litigation and a turning point for biotechnology patenting. Judge Sweet of the Southern District of New York ruled that all of Myriad’s patents on DNA sequences were not patentable.⁵⁹ The ruling rested on established, if somewhat vague, precedent that natural phenomena are not patentable. Judge Sweet reasoned that all DNA sequences, whether isolated or synthetic, were products of nature, indistinguishable from naturally occurring DNA sequences.⁶⁰ Therefore, Myriad’s patents should never have been granted.

Judge Sweet may have tapped into anti-patent sentiment. In June 2010, the Supreme Court published its long awaited decision in *Bilski v. Kappos*, dealing with business method patents.⁶¹ While there was unanimity as to holding invalid the

55. *Id.* at 2113.

56. *Id.* at 2112–13.

57. *Id.*

58. “The Complaint in this action was filed on May 12, 2009.” Ass’n For Molecular Pathology v. U.S. Patent & Trademark Office, 669 F. Supp. 2d 365, 370 (S.D.N.Y. 2009).

59. Ass’n for Molecular Pathology v. U.S. Patent & Trademark Offices, 689 F.3d 1303, 1314 (Fed. Cir. 2012), *aff’d in part, rev’d in part sub nom.*; Ass’n for Molecular Pathology v. Myriad Genetics, Inc., 133 S. Ct. 2107 (2013).

60. *Id.*

61. *Bilski v. Kappos*, 561 U.S. 593 (2010).

particular business method at issue (a method for hedging risk in commodities markets), four of the justices would have gone further and ruled that all business methods are unpatentable.⁶² In 2012, the Supreme Court reviewed a patent on a medical diagnostic procedure to treat Crohn's Disease held by the company Prometheus, who was alleging patent infringement by the Mayo Clinic.⁶³ The Court ruled that the patent was invalid because it entailed using a correlation that would be an unpatentable law of nature.⁶⁴ Judge Sweet's 2010 ruling foreshadowed these developments. Upon appeal to the Federal Circuit in 2011, which hears appeals of patent cases, Judge Sweet's decision was overturned with respect to the nonpatentability of the isolated DNA sequence.⁶⁵ Upon further appeal to the Supreme Court, the case was sent back to the Federal Circuit in 2012 for reconsideration in light of the Court's ruling in *Mayo v. Prometheus*.⁶⁶

This back and forth of a case is not atypical in controversial areas of law. In 2012, the Federal Circuit once again upheld the patentability of the DNA sequences identified by Myriad.⁶⁷ In its second review of the Myriad patents, the judges agreed that cDNA, or synthetic DNA sequences, would be patent eligible since they were not natural phenomena.⁶⁸ The basis for this ruling was the finding that research scientists at Myriad had to engage in inventive activity in constructing the synthetic DNA sequence.⁶⁹ Two of the three Federal Circuit judges ruling on the case also found that there was inventive activity in isolating the DNA sequence from its naturally occurring state.⁷⁰ One of the three, however, reasoned there was no difference between the isolated

62. *See id.* at 626 (Justice Stevens, with whom Justice Ginsburg, Justice Breyer, and Justice Sotomayor join, concurring in judgment).

63. *Mayo Collaborative Servs. v. Prometheus Labs., Inc.*, 132 S. Ct. 1289 (2012).

64. *Id.* at 1294.

65. *Ass'n for Molecular Pathology v. U.S. Patent & Trademark Office*, 653 F.3d 1329, 1334 (Fed. Cir. 2011).

66. *Ass'n for Molecular Pathology v. Myriad Genetics, Inc.*, 132 S. Ct. 1794 (2012) (granting cert. to remand).

67. *Ass'n for Molecular Pathology v. U.S. Patent & Trademark Office*, 689 F.3d 1303, 1309 (Fed. Cir. 2012).

68. *Id.* at 1326.

69. *Id.* at 1349 (discussing how Myriad's patents transform natural phenomenon).

70. *Id.* 1348 (describing Myriad's patent as being "inspired by nature" and the steps needed to create the isolated DNA sequence).

DNA sequence and the naturally occurring sequence.⁷¹ Therefore, one dissenting judge concluded that isolated DNA sequences were not patentable.⁷² The Supreme Court decided to review this opinion and issued its own, final opinion in June 2013.⁷³

Two words describe the 2013 Supreme Court opinion: anticlimactic and frustrating. The anticlimax was in the Court's conclusion that isolated DNA was not patentable while synthetic DNA could be. This conclusion followed as a matter of course from the Court's precedent. What is frustrating is the reasoning supporting this conclusion.

In 1948, the Supreme Court ruled, in a case called *Funk Brother v. Kalo Inoculant Co.*, that a patent covering a combination of bacteria that facilitated nitrogen fixation in plants was a product of nature and therefore unpatentable.⁷⁴ The purported inventor in that case had simply combined naturally occurring substances and had not invented anything.⁷⁵ This ruling was important in the Court's 1980 decision, *Diamond v. Chakrabarty*, in which the Court addressed the question of whether a genetically modified bacterium was an unpatentable product of nature or a patentable invention.⁷⁶ The Court held that the inventor had modified the organism to create a new life form that did not exist in nature.⁷⁷ Therefore, the new organism could be patented.⁷⁸ The *Diamond* decision is famous for the oft-repeated line that "anything under the Sun made by man" is potentially patentable.⁷⁹

The *Myriad* decision is a logical extension of these precedents. The Court had to determine whether the DNA sequences at issue were natural phenomena or man-made.⁸⁰ Its conclusion was that isolated DNA is a natural phenomenon and

71. *Id.* at 1353.

72. *Id.* at 1356.

73. *Ass'n for Molecular Pathology v. Myriad Genetics, Inc.*, 133 S. Ct. 2107 (2013), *aff'g in part, rev'g in part* *Ass'n for Molecular Pathology v. U.S. Patent & Trademark Office*, 689 F.3d 1303 (Fed. Cir. 2012).

74. *Funk Bros. Seed Co. v. Kalo Inoculant Co.*, 333 U.S. 127, 132 (1948).

75. *Id.* at 130.

76. *Diamond v. Chakrabarty*, 447 U.S. 303, 307 (1980).

77. *Id.* at 309–10.

78. *Id.* at 310.

79. *Id.* at 309 (quoting Senate hearings).

80. *Ass'n for Molecular Pathology v. Myriad Genetics, Inc.*, 133 S.Ct. 2107, 2111 (2013).

synthetic DNA is man-made.⁸¹ What is puzzling is how the nine justices came to this conclusion. The Court seems to rely on expert scientific testimony that was part of the record.⁸² The opinion is steeped in a summary of the underlying science. Interestingly, Justice Scalia refused to sign onto the scientific exegesis although he agreed with the result.⁸³ What lesson is learned, then, for future cases about DNA sequences, whether human, animal, or plant?

Two possibilities emerge from the opinion. One is a comparison between the claimed DNA sequence and its natural counterpart. If they are identical, then the claimed sequence is a natural phenomenon and unpatentable. The Court seemingly engages in this mind numbingly complex comparison. This approach is similar to how courts attempt to determine whether one software program has been copied from another in a copyright infringement case. As with copyright, the Court seems to be using a substantial similarity approach to comparing DNA sequences with their naturally occurring counterpart. Although there is language in the opinion implying that such comparison is the appropriate methodology, this approach leaves open the question of how much similarity is enough.

The second possible approach to determining when a DNA sequence is patentable is to focus on the method for uncovering the sequence.⁸⁴ The Court emphasizes that isolating DNA sequences entails snipping the relevant sequence from its natural state, like extracting a mineral from the earth.⁸⁵ Constructive synthetic DNA involves scientific activity. With respect to the isolated DNA, the Court rejects the approach of the Federal Circuit that a researcher has to determine where to snip the natural sequence in order to derive the isolated one.⁸⁶ That

81. *Id.* at 2111.

82. *Id.* at 2111–12.

83. *Id.*

84. See JUSTINE PILA, THE REQUIREMENT FOR AN INVENTION IN PATENT LAW 356–60 (2010).

85. *Ass'n for Molecular Pathology v. Myriad Genetics, Inc.*, 133 S. Ct. 2107, 2119 (2013).

86. *Ass'n for Molecular Pathology v. U.S. Patent & Trademark Office*, 653 F.3d 1329, 1365 (Fed. Cir. 2011) *cert. granted, judgment vacated sub nom*; *Ass'n for Molecular Pathology v. Myriad Genetics, Inc.*, 132 S. Ct. 1794, *opinion vacated, appeal reinstated sub nom*; *Ass'n for Molecular Pathology v. U.S. Patent & Trademark Office*, 467 F. App'x 890 (Fed. Cir. 2012)).

decision was enough to make the isolated sequence man-made for the Federal Circuit. The Supreme Court, however, does not view that decision as inventive enough. Extraction is not invention, while synthesizing is.⁸⁷ That distinction seems to be the most clear answer the Supreme Court provides for distinguishing naturally occurring sequences from man-made ones.⁸⁸

In short, the Supreme Court applied a predictable and recognized rule in reaching its decision in *Myriad*. But it is far from clear how this rule is to be applied in practice. On the day the Supreme Court opinion was announced, within hours, the USPTO issued a short memorandum to patent examiners summarizing the decision.⁸⁹ The memo tracks the Supreme Court's reasoning by stating that patents would not be issued for merely isolating DNA sequences, but patents were available for synthetic sequences.⁹⁰ The USPTO promises to issue further guidelines in the future.⁹¹

One can hope that the USPTO provides some clarification on how to proceed. Needless to say, there are some in the field who view the *Myriad* decision as devastating to biotechnology. Some of this speculation is overwrought. Since the Supreme Court concluded that patents on synthetic DNA are available, the future is not as gloomy as some foresee. While it is true that merely identifying natural DNA sequences cannot be the basis for a patent, researchers and inventors will have to put more effort in creating synthetic forms and in developing inventions that tap the DNA sequences that have been mined. Arguably, such efforts can only enrich the industry and make the field more competitive and innovative. More devastating would have been the *Myriad* decision issued twenty-five years ago when identification of genomes, human, animal, and plant, was in its infancy. At that earlier point of time, limitations on patenting, as seen in *Myriad*, may have

87. Ass'n for Molecular Pathology, 133 S. Ct. at 2117 (2013).

88. See PILA, *supra* note 84, at 6–7.

89. See Memorandum from Andrew H. Hirshfeld, Deputy Comm'r for Patent Examination Policy, U.S. Patent and Trademark Office, to Patent Examinationg Corps (June 13, 2013), available at http://www.uspto.gov/patents/law/exam/myriad_20130613.pdf.

90. *Id.*

91. See Memorandum from Andrew H. Hirshfeld, Deputy Comm'r for Patent Examination Policy, U.S. Patent and Trademark Office, to Patent Examinationg Corps (Mar. 4, 2014), available at http://www.uspto.gov/patents/law/exam/myriad-mayo_guidance.pdf.

altered the field. But because the future is in synthetic DNA and in applications of isolated sequences,⁹² two areas of invention left untouched by the opinion, the Supreme Court may have shut the barn door when the naturally occurring horse has been let loose. Instead of bemoaning lost patents, attention should turn towards the future. In that way, the *Myriad* decision may actually be ushering in the next stage of the genomic revolution.

One indication of the controversy over the Supreme Court's decision in *Myriad* is the 2014 opinion by the Australian High Court in New South Wales, rejecting the Supreme Court's analysis in favor of the Federal Circuit's in a challenge to *Myriad's* Australian patent on the isolated breast cancer gene.⁹³ The High Court (the equivalent of a district court in the United States) quoted the Supreme Court's language that "such important and useful genes had never been located or isolated from surrounding genetic materials."⁹⁴ In finding invention in the identification and isolation of the gene mutation, the High Court rejected the Supreme Court's emphasis on the information content of the isolated gene sequence.⁹⁵ Even if the information content in the isolated and naturally occurring genes were identical, the High Court concluded that the chemical compositions of the two sequences were different.⁹⁶ Citing the Federal Circuit majority opinion, the Australian High Court concluded that the chemical difference was enough to make the isolate sequence patentable.⁹⁷ Although this case is only one lower court opinion from a foreign jurisdiction, the analysis of the Australian High Court indicates that the role of patents in the personalized medicine industry may still be vital.

C. Other Notable Developments in the Law of Personalized Medicine

While the business practices and legal strategies of Nitromed and *Myriad* are the most prominent examples of the

92. See, e.g., Eyal Karzbrun et al., *Programmable On-Chip DNA Compartments as Artificial Cells*, 345 SCIENCE 829 (2014).

93. D'Arcy v. *Myriad Genetics Inc.* [2014] FCAFC 115.

94. *Id.* at para. 135.

95. *Id.* at para. 155.

96. *Id.* at para. 149.

97. *Id.* at para. 211–12.

challenges to the field of personalized medicine, several other less publicized cases illustrate the variegated dimensions of developing marketable technologies for tailoring medical treatment to genetic and other characteristics of the individual patient.

In 2012, the Supreme Court ruled on the patentability of a therapeutic method for the treatment of Crohn's disease in a dispute between patent owner Prometheus Labs and alleged infringer the Mayo Clinic.⁹⁸ The patent covered the adjustment of dosage for a drug therapy in response to biometrics taken from a Crohn's patient obtaining treatment.⁹⁹ As a therapeutic method, the patent directly covered a method of administering personalized medicine since the adjustment in dosage was based on specific biometric characteristics of the patient, namely the level of vitamin B-12 measured after an initial administration of the drug.¹⁰⁰ The Court invalidated the patent on the therapeutic method because the claims covered a law of nature, specifically the statistical correlation between the amount of drug administered and the level of vitamin B-12.¹⁰¹ The Court also expressed concerns with the policy of interfering in medical treatment by limiting the ability of the medical practitioner to calculate a correlation in her head while treating a patient.¹⁰²

One example of the compounding effects of *Myriad* and *Mayo* is provided by the 2014 decision in the United States District Court for Delaware, invalidating a patent for identifying and selecting genetic characteristics associated with athletic ability. Owned by the Australian company, Genetic Technologies Limited, the patent covered "a method to predict potential springing, strength or power performance in a human."¹⁰³ The claims consist of identifying specific alleles in genes and making a prediction about athletic ability based on the presence of the alleles in the identified genetic sequence.¹⁰⁴ On a motion to dismiss, the court ruled that there was no plausible basis for the patentability of this

98. *Mayo Collaborative Servs. v. Prometheus Labs., Inc.*, 132 S. Ct. 1289 (2012).

99. *Id.* at 1295.

100. *Id.* at 1296.

101. *Id.*

102. *Id.* at 1302.

103. *Genetic Tech. Ltd. v. Lab. Corp. of Am. Holdings*, No. 12-1736-LPS-CJB, 2014 WL 4379587, at *3 (D. Del. Sept. 3, 2014).

104. *Id.*

claim under the standards of *Mayo* and *Myriad*.¹⁰⁵ The magistrate judge recommended that the claims covered laws of nature and natural phenomena, and the inventor had added little inventiveness beyond the identification of a correlation between a naturally occurring sequence and athletic ability.¹⁰⁶

What is striking about the Delaware court's opinion is its ruling on a pretrial motion to invalidate the patent. The magistrate's decision rested on the plausibility of the invention being patentable in light of the Supreme Court's limitations on patentable subject matter.¹⁰⁷ This decision is one of the few applying the *Twombly-Iqbal* standard¹⁰⁸ for motions to dismiss for failure to state a claim in the patent context.¹⁰⁹ While the plausibility ostensibly rests on applying the legal standard for patentability,¹¹⁰ implicit is an assessment of the scientific basis for the invention. In other words, given the science, the court was examining the claimed invention in light of the scientific background to conclude the viability of the patent owner's claim of ownership of patentable subject matter. The role of background science in personalized medicine is the subject of Sections III and IV, where the market failures rising from information asymmetries and uncertainty provide the basis for designing regulation of personalized medicine markets.

The problems with knowledge and information in personalized medicine also offers the basis for the FDA's investigation of 23andMe, a company that provides through the mail prognoses of proclivities to disease based on personalized genetic samples.¹¹¹ The case of 23andMe was the motivating

105. *Id.*

106. *See id.* at 26 (explaining that merely pointing out that someone will have relatively greater performance due to the presence of the genetic variation does not amount to an "application of the law of nature to a *new and useful end*").

107. *Id.* at 9.

108. *See* *Ashcroft v. Iqbal*, 556 U.S. 662, 678 (2009).

109. *See* Arthur R. Miller, *From Conley to Twombly to Iqbal: A Double Play on the Federal Rules of Civil Procedure*, 60 DUKE L.J. 1, 14 (2010); *see also* Chris Morrison & J. Patrick Elsevier, *Macronix Ruling Revives Twombly Questions in Patent Cases*, LAW360 (Mar. 25, 2014, 1:34 PM), http://www.law360.com/articles/520186/macronix-ruling-revives-twombly-questions-in-patent-cases?article_related_content=1 (explaining that, in the context of patent cases, the strict *Twombly/Iqbal* standard has not been regularly used).

110. *See* Damon C. Andrews, Note, *Iqbal-ing Seagate: Plausibility Pleading of Willful Patent Infringement*, 25 BERKELEY TECH. L.J. 1955, 1967–68 (2010).

111. *See* Warning Letter from Alberto Gutierrez, *supra* note 1.

example in the introduction to this Article and serves as the final example of the travails of personalized medicine companies.

Until a complaint was brought by the FDA in November 2013, 23andMe, Inc. sold personal genomic testing.¹¹² The Mountain View, California company, founded in 2006, operates at the intersection of biotechnology and information technology by combining “potential of personal genetic information and web-based interactive tools” to “empower individuals to access and understand their own genetic information while also holding the potential of accelerating research in the field of genetics.”¹¹³

To what extent does such a company empower individuals? The ideal is one of providing individuals with personal information about their genetic ancestry and disease proclivities. An individual armed with such information can make better decisions about health care over one’s lifetime. The information includes a tracing of genetic ancestry and identification of proclivities to disease based on ethnicity.¹¹⁴ However, empowerment comes at a cost. 23andMe, Inc. collects the information into a database that would arguably be proprietary. The construction and use of such a database creates issues of privacy as well as ownership over data. Furthermore, a company like 23andMe, Inc. largely determines how the genetic information is packaged and communicated to the consumer. In turn, the packaging of information shapes how individual consumers and the medical profession may understand the health characteristics of patients. Industry marketing and packaging shape the vocabulary for personal identity in genetic categories.

In a letter to 23andMe, published on the FDA website, the agency stated that “even after these many interactions with 23andMe, we still do not have any assurance that the firm has analytically or clinically validated the PGS [Personal Genome Service] for its intended uses, which have expanded from the uses that the firm identified in its submissions [for marketing approval].”¹¹⁵ According to the agency, there is no scientific support for the claims made by 23andMe in its advertising for

112. *Id.*

113. Matthew Rimmer, *23andMe Inc.: Patent Law and Lifestyle Genetics*, 22 J. L., INFO., & SCI. EAP 1, EAP 2 (2012).

114. *Id.* at EAP 4.

115. See Warning Letter from Alberto Gutierrez, *supra* note 1.

diagnosing or informing consumers about the predictions made from genetic testing.¹¹⁶

The lack of scientific basis and explanation for the reports made by the company is echoed in a complaint filed by a nationwide class of consumers against 23andMe shortly after the FDA complaint. The class action plaintiffs alleged that the company advertises that it provides “‘health reports on 240+ conditions and traits[,] ‘drug response[,] ‘carrier status[,] among other things, when there is no analytical or clinical validation for the PGS for its advertised uses.”¹¹⁷ The class action complaint further alleges that 23andMe “uses the information it collects from the DNA tests consumers pay to take to generate databases and statistical information that it then markets to other sources and the scientific community in general, even though the test results are meaningless.”¹¹⁸

Because of these complaints, 23andMe ceased providing health related reports, but continues to provide ancestry reports and raw genetic data based on the samples provided by customers.¹¹⁹ As with the other examples of personalized medicine related companies, the story of 23andMe demonstrates the differences in information between companies and consumers and the controversies over the underlying science supporting the services being advertised and provided. These two concerns—information differences and uncertainty as to the science—define the market failures providing the basis for policy reform. They are the focus of the next section of the Article.

III. LEMONS, SCIENCE, AND MARKETS: A THEORETICAL FRAMEWORK

The market for personalized medicine is subject to two types of market failures that justify policy intervention. What form this intervention should take is an open-ended question and will be the subject of Section IV. The discussion in this Section,

116. *Id.*

117. Class Action Complaint at 1, *Casey v. 23andMe, Inc.*, No. 13-CV-2847-HJMA, 2013 WL 6687874 (S.D. Cal. Nov. 27, 2013).

118. *Id.* at 2.

119. *Welcome*, 23ANDME, <https://www.23andme.com> (last visited Jan. 28, 2015) (displaying company’s disclaimer at the top of the website that health-related genetic reports are no longer provided).

however, informs the larger question of institutional design and the market rules that can aid in constructing a market for personalized medicine that is responsive to the needs of consumers.

A. *The Market for Lemons*

A market transaction arises from someone seeking a particular commodity and another person attempting to give up a particular commodity. If these two persons can meet and negotiate, they can arrive at agreed upon terms for transferring the commodity from the second person to the first. As described, the exchange is voluntary, but structuring it is a set of rules that protect each side of the exchange.¹²⁰ Property law defines basic rules of exclusion permitting the exchange, and contract law ensures the enforcement of all promises made during the exchange.¹²¹ In addition, tort law can address liability arising from any injuries stemming from the underlying commodity, such as physical injury, or from the underlying negotiation, such as fraud.¹²²

One dimension of a market that shapes its success is the information available to the participants in market transactions.¹²³ The word “information” here is used broadly to include data relevant to a transaction (such as what is being sold or characteristics of the seller or buyer), information in the strict sense as an inference drawn from the data (such as the inference that a first time seller may not have much experience with the marketplace), and knowledge as the systematic aggregation of information into conclusions (such as German cars are more reliable than Italian cars).¹²⁴ The available information in a marketplace, and its distribution, shapes how markets will operate.

120. See generally JAMES BOYLE, SHAMANS, SPLEENS, AND SOFTWARE: LAW AND THE CONSTRUCTION OF THE INFORMATION SOCIETY 88–89 (1996) (explaining that without rules, the market would not exist); JOHN MCMILLAN, REINVENTING THE BAZAAR: A NATURAL HISTORY OF MARKETS 5–6 (2002) (stating that participants in the market make decisions that reflect their own preferences within the market’s rules).

121. See Alan Schwartz & Robert E. Scott, *Contract Theory and the Limits of Contract Law*, 113 YALE L.J. 541, 543, 559 (2003).

122. See JULES L. COLEMAN, MARKETS, MORALS, AND THE LAW 34–35 (1998).

123. See MCMILLAN, *supra* note 120, at 54–55.

124. See Anthony Liew, *Understanding Data, Information, Knowledge, and Their Inter-Relationships*, ALLIANCE INC. (June 2007), <http://www.tlainc.com/articl134.htm>.

George Akerlof's market for lemons, discussed in the Introduction, famously illustrates how asymmetric information results in market failure and how policy can respond to cure asymmetric information.¹²⁵ Suppose the simple example from above is complicated by introducing a quality dimension for the commodity. A commodity may self-explode after a few months or last for several years. Each seller knows what type of commodity he is trying to sell, but no buyer knows beforehand what kind of commodity he is about to purchase. While negotiation may resolve this problem of asymmetric information, there may be no fully successful way to make information symmetric. If a buyer asks the seller how long the commodity will last, the seller holding a poor quality commodity will lie. While potential liability for fraud or misrepresentation may limit the seller's ability to lie, lying may not be completely deterred. Furthermore, a purchaser may not be able to determine the longevity of the commodity through inspection or a test-drive. Under these conditions, the existence of lemons in the marketplace leads to the complete breakdown of a market for the commodity, absent some corrective to the rules of the game for the market institution.

The last statement is a strong one, but the argument in its support is a straight-forward and elegant one.¹²⁶ Because each seller knows the quality of the commodity he holds, a seller holding a high quality good will ask for a higher price than one who has a low quality good. A potential purchaser, however, cannot distinguish between a low quality and high quality good and would be willing to pay some average price for the good. But, by definition, the average price will be lower than the seller's asking price for the high quality commodity and greater than the asking price for the low quality commodity. As a result, only low quality goods, or lemons, will enter the market. Because bad products will drive out good products, purchasers will not enter the market to begin with.

The argument's logic may belie market realities. Shoddy goods exist in a marketplace alongside quality ones. Markets exist despite differences in information. The point behind the market for lemons is to illustrate the dynamics of information in shaping market transactions. Recognizing asymmetric information in

125. See Akerlof, *supra* note 11, at 489–90.

126. *Id.* at 494.

transactions poses challenges to the ideal of *laissez-faire*. Specific commodities illustrate the problem as well as potential solutions. Professor Akerlof introduced the market for lemons in terms of the used car market, but the principles apply more strongly to financial markets, where underlying characteristics about buyers or sellers may be unobservable.¹²⁷ Adverse selection, the technical term for the bad driving out the good in a marketplace, is prevalent in certain markets where information is asymmetric and may be difficult to verify.¹²⁸

Adverse selection is addressed in part by creating a correlative market for reputation.¹²⁹ The analysis of the market for lemons rested in part on the price dynamics for the market. Market collapse arose from buyer's willingness to pay only an average price which caused high quality suppliers to abandon the market for low quality suppliers. But market transactions operate not only through negotiations over price but through variables such as reputation and product quality. While product quality may not always be verified before the transaction is closed, reputation might be.¹³⁰ In the market for cars, a buyer might seek a third party to verify the condition of the automobile or request information about the vehicle's history to further refine the prediction that a car will be of high quality or low quality. In addition, a buyer might look at the characteristics of the seller, such as reports from other consumers, brands, and past practices. A solution to the market for lemons is found in institutions which facilitate forms of non-price competition through markets for reputation that are secondary to the market for the commodity.

Certain rules for the marketplace can promote markets for reputation. Implied warranty terms under contract law guarantee that products would have to meet a certain quality standard before they are brought to market. Such assurances, if credible, would restore trust in a market with asymmetric information and lead buyers to engage in market transactions. Furthermore, the legal requirement would raise the costs of entering a market for

127. See MCMILLAN, *supra* note 120, at 41–50.

128. See Akerlof, *supra* note 11, at 489–90.

129. See JOE MARCONI, REPUTATION MARKETING: BUILDING AND SUSTAINING YOUR ORGANIZATION'S GREATEST ASSET 35–37 (2002).

130. See Thomas Noe, *A Survey of the Economic Theory of Reputation: Its Logic and Limits*, in THE OXFORD HANDBOOK OF CORPORATE REPUTATION 114, 114–15 (Michael L. Barnett & Timothy G. Pollock eds., 2012).

suppliers and serve as a filter between high and low quality suppliers.¹³¹ Pre-market clearance through government agencies may also provide an analogous screen with the agency serving a third party auditor of the goods being brought to market.¹³² What the story of the market for lemons teaches is not that asymmetric information dooms all markets, but the need for identifying institutional correctives that can promote trust in markets for commodities when quality is difficult to verify.

While the discussion in this Section has been abstract, the implications for personalized medicine markets should be apparent. Companies that provide personalized medicine services have better information about the service they provide than the patients receiving the service.¹³³ This statement is perhaps true for all medical services. Medical practitioners have more information about disease and pharmaceuticals than patients.¹³⁴ But information asymmetries between doctor and patient are certainly addressed through reputational filters, such as affiliation with certain hospitals, third party auditors such as medical boards, and even insurance companies, and credentialing through medical schools.¹³⁵ Companies like Nitromed, Myriad, and 23andMe cannot fully rely on a well-developed reputational market to resolve the asymmetric information problem.¹³⁶ As a result, one might predict that the market for personalized medicine might collapse absent some institutional mechanisms that regulate the transactions through addressing the informational asymmetries.

What exacerbates the lemons problem in personalized medicine is the added uncertainty introduced by the black box technology used to apply personalized medicine diagnostics and therapeutics. While some dimensions of quality can be verified, such as the durability of an automobile engine or the existence of manufacturing or design defects, the quality of service provided by personalized medicine companies may not be verifiable. What these companies offer is a prediction, and the strength of the

131. See MCMILLAN, *supra* note 120, at 54.

132. See, e.g., Virginia Haufler, *New Forms of Governance: Certification Regimes as Social Regulations of the Global Market*, in SOCIAL AND POLITICAL DIMENSIONS OF FOREST CERTIFICATION 237, 237–47 (Errol Meidinger, et al. eds., 2003).

133. See Price, *supra* note 3, at 18.

134. See PAUL STARR, *THE SOCIAL TRANSFORMATION OF AMERICAN MEDICINE* (1982).

135. See *id.* at 77–79.

136. See GHOSH, *supra* note 23, at 43–51; Rimmer, *supra* note 113, at 28.

forward-looking statements about the likelihood of developing diseases rests on the strength of the underlying model used to make a prediction. But if this model is truly a black box, then no one can attest to its true strength. Are the correlations on which 23andMe's health reports were based a Delphic Oracle? If so, the market may be doomed to failure. But before jumping to that pessimistic conclusion, one should examine the problem of fundamental uncertainty in market design.

B. "Unknown Unknowns" and the Screen for Lemons

At the heart of the lemons problem is the discrepancy in knowledge between the seller and the buyer about the quality of the product or service that is the subject of the transaction. Resolutions to the lemons problem involve equalizing the information between buyer and seller so that low quality commodities can be identified. But what if there is fundamental uncertainty as to the quality of a product or service? How should the existence of such uncertainty affect regulation of the marketplace?

In many instances, the existence of uncertainty would not affect the lemons problem. A car may break down for no cognizable reason. All the buyer cares about is whether it does break down, not why. Furthermore, a product, such as a hair coloring gel, might work perfectly in giving the buyer the right shade of a particular color. But neither the buyer nor seller may know why it works so well. What matters is that it does work as the buyer desires.

Certainty is not required for information problems to be resolved. More often than not, there will always be some basic data about a product or service that will be uncertain to a buyer, seller, or both. To refer to the language of contract law, what is relevant is the expectations of the transacting parties.

But the existence of uncertainty is relevant when a company is selling a diagnosis or a therapy for a disease. The purchaser wants to know whether she has or is likely to have a disease. Whether a treatment is working to fight a disease is the relevant question to the purchaser, with some degree of certainty. The diagnostic or therapeutic seller may only be providing an expectation, not a guarantee, but how is that expectation to be communicated to the patient? What does it mean to say that we

can say with ninety-five percent confidence that there is a sixty percent chance that you will have breast cancer after the age of forty? How much should one be willing to pay for that information?¹³⁷

Assessing these questions requires a more in depth consideration of the granularity of information. What does it mean to know something as true? When is information—pardon the glibness—actually informative? The reader might be reminded of the economic arguments over the role of advertising in providing information to potential consumers. One noted legal scholar quipped that an economist is someone who thinks advertising is about information.¹³⁸ The point behind this jab is that advertising serves a persuasive function that has nothing to do with providing information about a product. The goal is to convince the unwitting to buy what they otherwise might not want or need. Similarly, information might often provide very little certainty or knowledge.

Information consists of data that is known and data that is unknown. For example, information about a product would include knowledge about how it functions under various conditions as well as uncertainty about product attributes under conditions that have not been tested, such as how it fares in outer space or under water. To use some popular terminology, we can refer to information about “knowns” and “unknowns.”¹³⁹ Adding another level to our understanding of information, we can refer to “known knowns” and “known unknowns.” The former are data we feel confident about with some tolerance for uncertainty. The latter are data about things we yet need to find out.¹⁴⁰

The focus here is on “unknown unknowns.” This category refers to information that we think we know but only with a high level of uncertainty. The point is that personalized medicine involves this category of information, predictions about the future whose level of uncertainty is in a debatable area of certainty. From

137. For a discussion of the need to verify and test assumptions, see Daniel M. Hausman, *Why Look Under the Hood?*, in *THE PHILOSOPHY OF ECONOMICS: AN ANTHOLOGY* 183 (Daniel M. Hausman ed., 3d ed. 2008).

138. See BOYLE, *supra* note 120, at 44 n.35 (attributing quote to Robert Gordon).

139. Donald H. Rumsfeld, Dep’t of Def., News Briefing (Feb. 12, 2002), *available at* <http://www.defenselink.mil/transcripts/transcript.aspx?transcriptid=2636>.

140. NASSIM NICHOLAS TALEB, *THE BLACK SWAN: THE IMPACT OF THE HIGHLY IMPROBABLE* 127 (2007).

a regulatory perspective, the tension is between the confidence of the company in making a prediction and the concerns with the regulator of imposing too much uncertainty on the consumer. From the perspective of the lemons problem, the issue is one of coming up with an acceptable measure for determining when a product or service is of low quality or high quality.

To take a concrete example, suppose a company promises to provide a diagnosis for proclivity to prostate cancer based on an examination of a gene sample. A consumer accepts the promise and submits the payment and a swab. The report comes back that there is seventy-five percent chance of developing prostate cancer in the next twenty years. The company says that its results are deemed to be ninety-five percent reliable, meaning that there is a five percent chance that the diagnosis is false. How is a consumer to ascertain whether this information was worth the fee? How should the information influence behavior?

A central problem is that statistical statements are about groups, not individuals.¹⁴¹ That point may belie the notion of personalized medicine. But the implication of the diagnosis is that of the population having the genetic profile shared by the individual consumer: seventy-five percent developed prostate cancer within the twenty year period, with a ninety-five percent level of confidence. How an individual responds to these statistical possibilities depends on attitudes towards risk (which very likely will vary among individuals sharing a similar genetic profile).¹⁴² Therefore, different individuals may be willing to pay different amounts for the same information.

Looking from the seller's perspective, the other looming problem is that such statistical information is the product of a black box. The statistical prediction is based on an examination of epidemiological data and the prevalence of disease within identified populations.¹⁴³ There is no claim being made for the mechanism through which disease arises. Instead, the statement is about a large group of individuals having a profile similar to the patient who purchased the information. Information quality is as

141. Richard F. Taflinger, *Statistics*, PROBLEMS WITH STATISTICS (June 5, 1996), <http://public.wsu.edu/~taflinge/evistats.html>.

142. See PAUL BREST & LINDA H. KRIEGER, PROBLEM SOLVING, DECISION MAKING, AND PROFESSIONAL JUDGMENT: A GUIDE FOR LAWYERS AND POLICYMAKERS 459–60 (2010).

143. See Price, *supra* note 3.

good as the statistical models and data that generate it. This uncertainty, however, does not undermine the value of the information but requires us to approach the information with the appropriate level of knowledge to assess its value.

Unknown unknowns¹⁴⁴ exacerbate the lemons problem and make it harder to resolve asymmetric information in the marketplace. If there is uncertainty in the measure of quality, the buyer and seller not only have different information about the quality of a commodity but have different cognitive approaches to assessing quality. Institutional solutions to the lemons problem cannot fully resolve these differences in information and how to assess information. Warranties would be impossible to enforce because of the difficulties in arriving at a common standard for determining quality. Third party verifiers may add to the problem by introducing yet another approach to assessing the uncertainty. Not surprisingly, market failure and solutions to market failure are more intractable in the presence of asymmetric information and in fundamental disagreement about how to interpret and assess information.

The economist Frank Knight proposed an important market solution in the presence of risk and uncertainty.¹⁴⁵ Risk, he defines, as quantifiable uncertainties,¹⁴⁶ akin to “known unknowns.” Markets and institutions correlative to markets can arise in the presence of risk. Insurance companies and financial instruments, such as hedges, can allow for mitigation of systematic risk. Unsystematic risk can be controlled through diversification. Government regulation and third party intermediaries can serve a role in assessing these risks and communicating information about them to the marketplace.

Uncertainty, on the other hand, is unquantifiable risk. It is synonymous with unknown unknowns, reflecting dimensions of information that we do not know about with particularity but do know exist at a general level. A natural disaster would be one example. Another might be unforeseeable hazards of a new technology. Because, by definition, these hazards are unquantifiable, market or regulatory mechanisms cannot resolve

144. For the use of this phrase, see Dina Fine Maron, *When DNA Means “Do Not Ask,”* SCIENTIFIC AMERICAN, Jan. 2015, at 28.

145. FRANK H. KNIGHT, RISK, UNCERTAINTY, AND PROFIT (1921).

146. *Id.* at 19.

unknown unknowns. Instead, according to Frank Knight, particularly risk-seeking individuals, whom he calls entrepreneurs, undertake these activities, either blind to the potential unchartable downside or attracted to the immeasurable riches.¹⁴⁷ In the Age of Discovery, explorers like Magellan and Balboa would be examples of these entrepreneurs. In the modern world, entrepreneurs are ones who seek to commercialize new technologies through willingness to enter an uncertain future, from a risk-loving personality.

While Frank Knight offers a fruitful explanation for the supply side of a potential market with unknown knowns, one had to ask about the demand side. Presumably, there is a group of purchasers who are willing to accept the uncertainty associated with a new technology. These early adopters, like the entrepreneurs, have a more liberal tolerance to risk and are willing to accept the uncertainties associated with a largely untested and unexplored new product or service.¹⁴⁸ Such mutual risk-taking can allow for the development of a new market, which once established, can allow for the entry of more sheepish firms and consumers.

Note that these brave new markets might also suffer from the lemons problem. Even if a consumer is highly risk-loving, he may be hesitant to buy a new technology if the seller might be pushing off a lemon. The point here is that the lemons problem can be resolved through institutions described above, allowing high risk-loving consumers to enter a new market and trade with high risk-loving suppliers. What the presence of unknown unknowns suggests is that the personality of suppliers and purchasers will jumpstart the market for a new technology once the lemons problem is resolved.

Companies like Nitromed, Myriad, 23andMe, and the others described in Section II represent the Knightian entrepreneurs, companies that are willing to enter uncertain territory and develop new markets. The problem is the highly risk-loving consumers. Should they serve as guinea pigs for the new personalized medicine technologies? As the case studies in Section II illustrate, the success of these new ventures vary depending on

147. See HOVENKAMP, 1970 *supra* note 10, at 144–45 (describing entrepreneurship in Knight's view of risk and uncertainty).

148. *Id.* at 144–46 (discussing technology and risk management).

the underlying services and technologies. Nitromed's failure stemmed from a form of ill-defined personalized medicine.¹⁴⁹ Myriad's woes stemmed from business practices that seemed exploitative involving patents that were questionable. Finally, the future of 23andMe rests on how the FDA assesses the health predictions that it sells to consumers. While each of these companies illustrates the shared dreams of entrepreneurship, although with different strategies, the common question is whether the legal system should tolerate risk-loving consumers to serve as test subjects for the adventurous companies. The answer, not surprisingly, is no.

The need for consumer protection stems more from a sense of paternalism on the part of regulators. If one accepts the premise that personalized medicine entails unknown unknowns, then there is a legitimate regulatory concern in mitigating consumer harms to health and safety arising from medical diagnostics and therapeutics. While there might be a considerable upside to new medical technologies through the saving of lives, there is also a considerable downside to new technologies that might exacerbate suffering and introduce new risks to disease mitigation. A consequentialist approach supports precaution in the introduction of the new medical technology.

Underscoring these arguments for regulation of personalized medicine is the existence of "ambiguity aversion," identified by Professor Daniel Ellsberg.¹⁵⁰ Presented in his economics doctoral dissertation, the Ellsberg paradox demonstrates that individuals may prefer to avoid situations of uncertainty in favor of ones with identified risks. Because of ambiguity aversion, consumers prefer situations of quantifiable risks rather than unquantifiable ones.

The scenario for the Ellsberg paradox is a straightforward one. Consider an urn that contains ninety marbles, thirty of which are red and sixty of which are either black or yellow. Because it is unknown how many of the non-red balls are black and how many yellow, these represent situations of unquantifiable risk. Now consider two different situations. In one situation, a person has to pick between Gamble A of winning one hundred dollars if he picks a red ball and Gamble B of winning one hundred dollars if

149. See GHOSH, *supra* note 23, at 61.

150. Daniel Ellsberg, *Risk, Ambiguity, and the Savage Axioms*, 45 Q.J. ECON. 643 (1961).

he picks a black ball. In this situation, people tend to pick Gamble A over Gamble B. Now consider another choice between Gamble C of winning one hundred dollars if he picks a red or yellow ball and Gamble Y of winning one hundred dollars if he picks a black or yellow ball. When confronted with this choice, the same people surveyed tend to pick Gamble Y over Gamble X. These two choices are inconsistent with each other. Hence, the paradox.¹⁵¹

The explanation for this paradox is that people tend to prefer quantifiable risks to non-quantifiable ones.¹⁵² In the first choice, the probability of picking a red ball can be calculated to be one-third. But the probability of picking a black ball cannot be measured with exactness. It is something less than two-thirds. Similarly, in the second choice the probability of picking a ball that is black or yellow (or non-red) is two-thirds. On the other hand, the probability of picking a red or yellow ball is something greater than one-third and less than two-thirds. In short, when confronted with a choice of unquantifiable risk or quantifiable risk, individuals prefer the outcome whose risk can be quantified.¹⁵³

The Ellsberg paradox is also referred to as the “phenomenon of ambiguity aversion” to reflect a preference for exact quantification rather than numerical ambiguity.¹⁵⁴ There are two implications for the regulation of personalized medicine from this observation. First, risk-loving consumers might be more readily taken in when a company presents the uncertainties associated with its diagnoses and therapies through exact

151. To see the paradox, note that if someone chooses Gamble A over Gamble B, he must be thinking that it is more likely to get a red ball than to get a black ball. However, if the same person choose Gamble Y over Gamble X, he must be thinking that it is more likely to get a black ball than to get a red ball. That is the paradox. This analysis assumes that the chooser makes decisions in order to maximize expected utility (or expected well-being). However, that assumption may be the source of the paradox. The assumption of expected utility rests on the view that a chooser values outcomes, but not the method of obtaining that outcome. If utility depends not only on outcomes, but also on probabilities, so that a person may value a low outcome more than a high outcome if it is more certain, then Ellsberg’s result may not be paradoxical at all. The challenge is to understand more clearly the behavior of individuals in situations involving risk and uncertainty.

152. See BREST & KRIEGER, *supra* note 142, at 505–07.

153. Craig R. Fox & Amos Tversky, *Ambiguity Aversion and Comparative Ignorance*, 110 Q.J. ECON. 585, 599 (1995) (noting that ambiguity aversion is impacted by new information).

154. See Colin Camerer & Martin Weber, *Recent Developments in Modeling Preferences: Uncertainty and Ambiguity*, 5 J. RISK & UNCERTAINTY 325, 333 (1992).

numerical probabilities.¹⁵⁵ Regulation needs to police against misleading and groundless statements about risk. Second, regulation serves to verify the underlying statistical models used by companies to determine the diagnostic statements and therapeutic recommendations they make. Furthermore, regulation serves to communicate to a consumer the relevant risks so that they can be assessed in making decisions regarding responses to and treatment of medical diagnoses.¹⁵⁶ Through these two goals, regulation can address both the lemons problem and the problem of uncertainty. Oversight of how a personalized medicine company derives its predictions can address the asymmetric information problem. The government regulator can serve as a third party auditor. In addition, translating the information derived by the provider of personalized medicine services into understandable probabilities can help to quantify the unknown knowns and address the issue of ambiguity aversion.

This section has presented an analysis of the various market failures associated with the market for personalized medicine and the need for regulation. However, regulation can take many forms, all with their own benefits and costs. In light of this section, Section IV addresses various regulatory responses to the market failures in the provision of personalized medicine. The key focus of the next section is how best to promote the science underlying personalized information and its ability to generate information about services that benefit consumers.

IV. POLICY RESPONSES: THE CHALLENGE FOR WARRANTIES, DISCLOSURE, AND THE DEVELOPMENT OF SCIENCE

Two common responses to the problem of asymmetric information in markets are warranties and requirements of disclosure. Both attempt to resolve information problems by either compensating the consumer for failed expectations from the purchase of a product or by informing the consumer about known risks before a sale occurs. Neither approach can effectively

155. Jacquelyn Burkell, *What Are the Chances? Evaluating Risk and Benefit Information in Consumer Health Materials*, 92 J. MED. LIBR. ASS'N 200 (2004) (examining contractual and other bases for liability).

156. See generally Mark A. Rothstein, *Physicians' Duty To Inform Patients of New Medical Discoveries: The Effect of Health Information Technology*, 39 J.L. MED. & ETHICS 690 (2011) (providing one example of disclosure model).

address the lemons problem in the context of personalized medicine. This lack of effectiveness stems from the nature of the service and the problem of uncertainty that exacerbates the problem of asymmetric information. Instead, the traditional solution of warranties and disclosure may need to be supplemented by policies that aid in promoting and developing a more scientific understanding of the phenomenon of personalized medicine. The promotion of science can occur through patent law reform as applied to the burgeoning market for personalized medicine.

Warranties create contractual and tort liability for a seller of a product or service that fails to meet the expectations of the purchaser as to the quality of the commodity.¹⁵⁷ Although a buyer and seller can contract for terms regarding the quality of the product or service being provided, the presence of asymmetric information will make it impossible for a willing buyer to identify desirable terms to require the seller to provide a requisite level of quality. Article Two of the Uniform Commercial Code reads into all contracts for the sale of goods implied warranties of merchantability and fitness of purpose that impose obligations on the seller to deliver goods of the requisite quality.¹⁵⁸ Furthermore, any express representations about the nature of the contracted for good created express warranties that are terms of the contract.¹⁵⁹ Breach of these express and implied warranties gives the buyer a cause of action for damages and possible restitution of the product.¹⁶⁰

Article Two applies only to the sale of goods and therefore has limited application to personalized medicine, which often involves the sale of services.¹⁶¹ Professor Walter Robinson, however, points out that personalized medicine services, such as the collection of individual medical data is increasingly integrated into products through the “internet of things.”¹⁶² This technological possibility suggests how personalized medicine

157. See generally David A. Rice, *Product Quality Laws and the Economics of Federalism*, 65 B.U. L. REV. 1, 11 (1985) (discussing warranties).

158. U.C.C. § 2-314 (2012).

159. U.C.C. § 2-313 (2012).

160. See, e.g., *Burr v. Sherwin Williams Co.*, 268 P.2d 1041, 1044 (Cal. 1954).

161. See U.C.C. § 2-102 (2012).

162. See W. Keith Robinson, *Economic Theory, Divided Infringement and Enforcing Interactive Patents*, 67 FLA. L. REV. (forthcoming 2015).

services may become embodied into products. Contracts for the sale of such goods would include the relevant express and implied warranties. But through-the-mail diagnoses or therapies would not be covered by the warranty provisions of Article Two. Some states, such as Texas, have expanded the reach of implied warranties under the UCC to the provision of services.¹⁶³ Despite the decisions in these states, service contracts are unlikely to have robust and predictable consumer protections through warranties as exist in contracts for the sale of goods. Warranty claims in contract are the basis for tort claims, such as products liability, and the analogy might apply to alleviate harms caused by personalized medicine.¹⁶⁴ Therefore, the potential for compensation exists even though many doctrines may have to be revived or modified in the context of personalized medicine markets.

A problem with warranties is determining a finding of wrongdoing by the seller. Breach of warranty occurs if there is less than a perfect tender of the product or service.¹⁶⁵ But if the seller provides only a prediction of what might happen, it may be impossible to determine that the seller has provided a service that fails to meet the expectations of the buyer. Under a tort theory, the injured party would have to show that the seller of the personalized medicine service fell below a standard of care, either strict liability or negligence.¹⁶⁶ Unless personalized medicine is classified as an ultra-hazardous activity, for which strict liability would apply, the standard of liability will be one of negligence.¹⁶⁷ While the potential exists for the plaintiff to show that the defendant acted unreasonably in providing a particular probability of contracting a disease or providing a therapy with a particular probability of treatment, it is highly unlikely that the plaintiff can show the defendant acted in an unreasonable manner in making the diagnosis or providing the treatment.¹⁶⁸

163. See *Melody Home Mfg. Co. v. Barnes*, 741 S.W.2d 349, 353 (Tex. 1987).

164. See 1 HAWKLAND U.C.C. SERIES § 2-314:6 (describing the relationship between implied warranty and tort claims).

165. See, e.g., *Leitchfield Dev. Corp. v. Clark*, 757 S.W.2d 207, 209 (Ky. Ct. App. 1988) (perfect tender rule applied to breach of contract or breach of warranty).

166. See HOVENKAMP, *supra* note 10, at 150 (holding that the perfect tender rule applies in breach of contract).

167. *Id.*

168. *Id.* at 146–47 (discussing role of risk-utility analysis in risk management over new technologies).

Reforms in medical malpractice would make it even more difficult for the plaintiff to prevail, especially if the standard of care is defined by a nascent industry as opposed to the national standards of the medical profession.¹⁶⁹

By contrast to warranties, disclosure solutions provide a remedy that is imposed before the contract is formed. As with the sale of securities, the sale of personalized medicine might be accompanied by strong obligations to disclose information about the underlying services, diagnoses, and therapies. This information would allow the consumer to assess whether to purchase the particular service from the specific seller. Where disclosure solutions often fail is in providing details on what must be disclosed, in what manner, and with degree of clarity. For example, securities disclosures are required to be presented in plain English. As pointed out above, the highly probabilistic nature of personalized medicine disclosure may make it difficult for an ordinary consumer to assess the underlying probabilities and the level of statistical confidence with which the prediction is presented. In theory, it should be possible to find a pellucid way to communicate the probabilities. But these standards for disclosure would require extensive upfront administrative costs for implementation.

In the case of personalized medicine, the failure of disclosures to have information value is particularly critical. More verbiage about the underlying predictions may provide neither heat nor light. One way to resolve this problem is to make disclosures more communicative by providing simple rubrics that are easily understandable by consumers. For example, graphics might illustrate disease proclivity at different ages and might provide guidance on what steps might be taken to diminish disease susceptibility. Furthermore, information may be better presented as probabilities, or quantified risks, in order to address the problem of ambiguity aversion by consumers. Disclosures in terms of risks may alert many consumers to take proper steps, in conjunction with a medical professional, to make lifestyle and healthcare choices.

169. See, e.g., Crocker v. Roethling, 675 S.E.2d 625, 631 (2009) (discussing national and community standards in medical malpractice cases); see also Scott DeVito & Andrew W. Jurs, "Doubling-Down" for Defendants: The Pernicious Effects of Tort Reform, 118 PENN ST. L. REV. 543, 548 (2014).

At the heart of both warranty and disclosure solutions is a better grasp by companies, consumers, and government regulators on the science underlying personalized medicine. Currently, the field is one of black box prognoses and therapies. In the future, however, better models and empirical evidence may strengthen the correlations on which the field lies. The government can play a role in promoting such scientific inquiry by making stringent demands on companies to provide more clinical data and experiments that support the claims of personalized medicine. The FDA complaint against 23andMe is the correct step towards this goal of better science.

In addition, the intellectual property system can promote better science consistent with the constitutional mandate of promoting progress in science and the useful arts. The Supreme Court's current skepticism towards patents in the medical area, as shown in its *Prometheus* and *Myriad* decisions, is a healthy one. Although the *Myriad* decision is a controversial one because of the Court's dubious engagement with science, the *Prometheus* decision is more promising. In this latter case, the Court strikes down a patent on diagnosis and therapy involving personalized medicine treatment of Crohn's disease.¹⁷⁰ The basis for the invalidation was the claim's coverage of a relation among natural objects that exist independent of human action; the Court describes this claimed relation as a law of nature.¹⁷¹ Put simply, the Court concluded that a mere mental correlation to adjust treatment was not patentable. Instead, medical practitioners are free to gauge correlations and make adjustments in pharmaceutical dosage.

The Court's decision in *Prometheus* is a promising one for developing the science of personalized medicine. By allowing researchers and practitioners to be free of proprietary rights in identified statistical relationships, the Court allows scientists to communicate and refine their medical findings. In this way, freedom to experiment and apply scientific findings is promoted, and the field can move towards identification of risks and benefits from treatment. As information flourishes in personalized medicine, disclosures for consumers can become more meaningful and provide guidance in how to respond to identified

170. *Mayo Collaborative Servs. v. Prometheus Laboratories*, 132 S. Ct. 1289, 1294 (2012).

171. *Id.*

disease proclivities and risk. This more liberal patent regime, combined with disclosure solutions, may provide the best set of regulations to allow the market for personalized medicine to mature and the field to progress for the benefits of patients.

V. CONCLUSION

Personalized medicine currently takes many forms and covers many areas of medical diagnosis and therapy. What the many forms have in common is a troubling maldistribution of information between companies and consumers and an underdeveloped understanding of the science underlying predicted disease proclivities and prescribed therapies based on an assessment of genetic profiles. As a result, the burgeoning market for personalized medicine suffers from the lemons problems and the problem of uncertainty. Regulation is clearly needed to address these market failures. This Article has examined the potential shape and scope of the appropriate regulation. What is needed is a regulatory environment that nurtures the development of science and the communication of its findings to companies, consumers, and government regulators. In this way, sunshine might be cast on the current black box technology, and the problem of personalized medicine can flourish and come into fruition.