

PERSONALIZED MEDICINE AND TOXIC EXPOSURE

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I. INTRODUCTION

In 1990, a global coalition of scientists embarked on the Human Genome Project. The group's ambitious goal was to identify all of the genes in human DNA and to sequence the three billion chemical base pairs of which DNA is composed. Thirteen years and \$300 million later, the project succeeded in fully sequencing a human genome for

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the first time.¹ The project's success was rightly hailed as a watershed event in scientific history.² But as the National Human Genome Research Institute's (NHGRI) own website notes: "[E]xploration of the genome is just beginning."³ An important step in this exploration is developing the ability to map additional genomes more quickly and less expensively. Today, advancements in this realm are proceeding at a rapid pace,⁴ with processes available that can read chemical bases thousands of times faster and at a fraction of the cost than previously possible.⁵

These scientific and technological advances have given rise to the emerging field of "personalized medicine," which focuses on tailoring preventive health strategies and treatment options to people based on their unique molecular profile.⁶ While much of personalized medicine, at least so far, is based on genomic information, it also includes the analysis of measurable proteins and metabolites

¹ See *Superfast Genomes Move a Step Closer to Reality*, <http://www.admin.cam.ac.uk/news/dp/2008112003> (Nov. 20, 2008) [hereinafter *Superfast Genomes*] (providing \$300 million figure).

² See Carl T. Hall, *Bringing Biotech Into Real World No Neat Fit Between Lab Work And Road To Lucrative Patents*, S.F. CHRON., June 13, 2004 at J1 ("Completion of the Human Genome Project, he said during an interview, was the watershed event that set the field in motion, fueled by the advent of high-speed gene analysis, three-dimensional protein imaging and easy Internet access to all sorts of raw data.").

³ See NHGRI, *supra* note 1 ("Researchers now have a pretty good list of parts: the human genome sequence. But they still need to figure out exactly where each part is located, how different parts interact with each other and how the parts work together to contribute to health and disease.").

⁴ *Superfast Genomes*, *supra* note 3 (describing novel technology that allows researchers to read and sequence chemical bases thousands of times faster than previous methods and at a cost that could fall to \$10,000 per genome by 2010).

⁵ These advances are based on improvements in information technology that allow for the storage and analysis of extremely large amounts of data. See Adam W. Culbertson, Stephen J. Valentine & Stephen Naylor, *Personalized Medicine: Technological Innovation and Patient Empowerment or Exuberant Hyperbole*, DRUG DISCOVERY WORLD, Summer 2007, at 18, 21. The techniques are improving so quickly that the commercially-available \$1,000 genome sequencing may soon be available. *Superfast Genomes*, *supra* note 3. ("This research takes another step towards the aim of the \$1,000 genome that could allow each of us to discover our unique genome that could lead to tailor made treatments for a wide range of diseases."); Richard Powers, *The Book of Me*, GQ MAG., Nov. 2008, at 220, 225. ("The magic target of the \$1,000 genome ... may be no more than a few years away.").

⁶ See Culbertson et al., *supra* note 7, at 18.

unrelated to genetics.⁷ This collection of information is then analyzed with sophisticated software algorithms to help explain the complex interplay between genetics and the environment in the development of disease.⁸

The goal of personalized medicine is to use knowledge derived from the study of this molecular information to improve public health and the health of individuals. In pursuit of this goal, academic scientists, public health authorities, and private companies have begun collecting human biological samples and associated health data to speed the advance of personalized medicine. These collections have supported a flourishing market of products that receives little federal or state regulation or oversight.⁹ Each of these developments will impact numerous aspects of our legal system.

This article considers one important issue—how personalized medicine might affect the legal system’s ability to address the consequences of human exposure to toxic substances. The article’s first section describes some of the current scientific, clinical, and public health uses of information in pursuit of the goals of personalized medicine. The article’s second section goes on to consider the potential impact of proliferating personal molecular information on toxic tort litigation, including the role of courts in addressing sub-cellular damage caused by toxic exposures. In the end, our goal is not to resolve all of the issues that might come to the fore, but instead, to identify some challenges ahead and contribute to an ongoing and evolving conversation.

⁷ Proteomics, for instance, is the study of proteins in the body. “[E]very organ in the body constantly releases hundreds of different proteins into the bloodstream. Around 50 of these are unique to each organ, and make up what scientists call a ‘protein fingerprint’ for the organ.” The Institute for Systems Biology in Seattle, Washington, for instance, is developing a “simple blood test . . . to allow people to screen themselves for life-threatening diseases, including a variety of cancers and dementias, before they develop any symptoms.” Ian Sample, *Kit to Spot Serious Illness Early May Be Just Ten Years Away*, GUARDIAN (London), Nov. 14, 2007, at 14, available at (<http://www.guardian.co.uk/science/2007/nov/14/medicalresearch.health>). The website for the Institute for Systems Biology in Seattle, Washington is available at <http://www.systemsbiology.org/>.

⁸ Culbertson et al., *supra* note 7, at 21 (citing A. Kalyanaram et al., Proceedings, 20th International Parallel and Distributed Processing Symposium 10 (2006)).

⁹ For a description of some of the products and services available, see *id.* at 26, 28-29. The regulation of these products will be described below, *infra* Section I.A.

II. CURRENT CLINICAL, WELLNESS, AND PUBLIC HEALTH USES OF PERSONALIZED MEDICINE

A. Clinical Uses

Scientists and medical researchers are collecting and studying human biological samples that will be useful in gaining a better understanding of how genes interact with the environment in the development of disease and how to tailor therapies to individuals based on their genetic qualities. When tests are developed and validated, the resulting information can be used in a clinical setting to identify individuals at risk of developing certain diseases in the future. In addition, a test may “detect[] . . . changes in a patient’s disease state prior to the manifestation of deterioration or improvement of the current status.”¹⁰ When an individual needs medication after developing disease, the field of pharmacogenomics (the scientific study of how genomics affects human response to medication) provides data about a person’s genes that might allow doctors to target drug prescriptions to patients most likely to be helped by the treatment, and conversely, to avoid giving drugs to those predisposed to harmful side effects.¹¹ Pharmacogenomics is one of the most promising applications in personalized medicine and can already save lives, reduce suffering, and save money.¹²

Although the number of available tests and tools continues to grow, clinical practitioners use only a very small percentage—and for good reason. Laboratories that perform such tests are regulated by the Clinical Laboratory Improvement Amendments,¹³ but there is no

¹⁰ Culbertson, et al., *supra* note 7, at 21 (citing K. Gunter & A. Tarnok, *Cytomics in Predictive Medicine*, 53B *Clinical Cytometry* 1, 1-3 (2003)).

¹¹ *See*, Powers, *supra* note 7, at 227.

¹² Barbara J. Evans, David A. Flockhart & Eric M. Meslin, *Creating Incentives for Genomic Research to Improve Targeting of Therapies*. 10 *NATURE MED.* 1289, 1289 (2004).

¹³ *See* Centers for Medicare and Medicaid Services, Overview Clinical Laboratory Improvement Amendments, available at <http://www.cms.hhs.gov/clia> (“The Centers for Medicare & Medicaid Services (CMS) regulates all laboratory testing (except research) performed on humans in the U.S. through the Clinical Laboratory Improvement Amendments (CLIA). In total, CLIA covers approximately 200,000 laboratory entities. . . . The objective of the CLIA program is to ensure quality laboratory testing. Although all clinical laboratories must be properly certified to receive Medicare or Medicaid payments,

government oversight regarding whether the test is performed properly or whether the test actually “detect[s] or predict[s] the associated disorder.”¹⁴ This lack of oversight is particularly problematic as researchers have attempted to connect the results of genetic testing to a wide range of conditions. Early genetic tests focused on rare disorders that were often very closely associated with a particular disease and were, therefore, highly predictive of future disease.¹⁵ Today, however, tests have proliferated, particularly in the area of common diseases like diabetes, heart disease, and cancer. These diseases are thought to be caused by several genetic variants, their interactions, and interactions between genes and the environment.¹⁶ As researchers recently noted in the *New England Journal of Medicine*, “What we have now is recognition of a limited number of variants associated with relative risks of diseases on the order of 1.5 or lower. Risk factors with this level of relative risk clearly do a poor job of distinguishing people who will develop these diseases from those who will not.”¹⁷

Even though many of these tests have not yet passed the threshold of being useful in clinical care by physicians, people seeking wellness care provide test-makers with a potential market. Dozens of companies, for example, are already marketing direct-to-consumer genetic tests aimed at analyzing the small portion of the genome known to have a correlation to human disease. The company 23andMe offers a product for individuals with a wide variety of desires, “from adoptees who want to learn where their ancestors came from and fill in the gaps in an unknown family medical history, to seniors who want to leave a genetic legacy for future generations, to the health conscious who want to learn about their genetic propensities for various conditions.”¹⁸ For \$399, 23andMe will

CLIA has no direct Medicare or Medicaid program responsibilities.”).

¹⁴ David J. Hunter, Muin J. Khoury & Jeffrey M. Drazen, *Letting the Genome Out of the Bottle – Will We Get Our Wish?* 358 *NEW ENG. J. MED.* 105, 106 (2008).

¹⁵ Kathy L. Hudson, M.K. Holohan & Francis S. Collins, *Keeping Pace with the Times – The Genetic Information Nondiscrimination Act of 2008*, 358 *NEW ENG. J. MED.* 2661, 2661 (2008).

¹⁶ See Hunter et al., *supra* note 16, at 106.

¹⁷ *Id.* at 105-06.

¹⁸ Press Release, 23andMe, *23andMe Democratizes Personal Genetics* (Sept. 9, 2008) (<https://www.23andme.com/about/press/20080909b/>).

analyze 580,000 locations on an individual's genome and provide information regarding 90 diseases, conditions, or traits an individual may be predisposed to developing.¹⁹ Other companies offer molecular profiling services direct-to-consumer and for use with a physician's order. PPM, for instance, is a company located in Bloomington, Indiana, that "is the first company to discover and provide an individual's health bioprofile."²⁰ PPM uses a blood sample to measure thousands of biomarkers that can provide "actionable" information related to cardiovascular health, diabetes, metabolism, and nutrition.²¹ In a best case scenario, personalized medicine tests can improve the health of individuals by providing them with tools to evaluate and monitor their risk factors for certain diseases or their exposure to toxic substances, which may lead to a more proactive approach to health.

Although the science shows great promise for the future, questions also remain about the current usefulness of data from these tests for clinical practice and preventive health measures. For these complex diseases, it is unclear whether identifying a genomic susceptibility is currently more helpful than taking a family history or if it would lead to medical advice different than what is already routinely given—patients should exercise, eat a healthy diet, and refrain from smoking.²² Virtually no data exists to suggest that people become more vigilant about their health when they learn that they have an increased risk of a complex disease. In the meantime, the information collected may be used in ways that threaten discrimination in employment and insurance contexts.²³

¹⁹ See 23andMe, *Beyond Genetic Testing, How It Works*, <http://www.23andme.com/howitworks/> (last visited Apr. 18, 2009).

²⁰ Viveda Health Assessments, PPM website, *Our Capabilities*, http://www.ppmwellness.com/our_capability.html (last visited June 6, 2009).

²¹ Viveda Health Assessments, PPM Home Page, <http://www.ppmwellness.com>. The information is "actionable" because these are areas of health that individuals can change through behavior, such as improving diet and exercising. *Id.*

²² Viveda Health Assessments, *Our Capability*, http://www.ppmwellness.com/our_capability.html (last visited Apr. 18, 2009).

²³ See, e.g., Hudson et al., *supra* note 17, at 2663. The Genetic Information Nondiscrimination Act (GINA) of 2008 will protect against discrimination in employment and insurance contexts for genetic information but does not protect against discrimination based on information derived from non-genetic markers like proteins. Genetic Information

B. Public Health

Personalized medicine can also serve the goal of public health. For instance, public health might improve if personalized medicine enables widespread early screening that prevents the development of a chronic disease such as diabetes,²⁴ or if biological sampling of members of a geographic community identifies environmental toxins that the government can regulate in a more effective fashion.²⁵

These tools can be used in conjunction with information derived from the burgeoning field of toxicogenomics—the study of the interaction between genes and toxins like chemicals and radiation.²⁶ As with all new applications of genomic science, available information will increase exponentially in the coming years due to the mapping of the human genome, the development of new methods of screening for many chemicals at once (called “high throughput” microarrays), and more sophisticated biostatistical methods.²⁷ This science can provide information about chemicals that cause changes in DNA, and it can also “identify genes important in making people susceptible to environmentally induced diseases.”²⁸ Like the associations demonstrated between genes, other biomarkers, and complex diseases, it is important to note that toxicogenomics will produce information that is suggestive but not currently definitive.²⁹

Public health will not only be served by looking at

Nondiscrimination Act of 2008, Pub. L. No. 110-233, § 2, 122 Stat. 881, 882-83 (2008).

²⁴ See, e.g., Steven Pinker, *My Genomic Self*, N.Y. TIMES MAG., 24, Jan. 11, 2009, at 24L; Powers, *supra* note 7.

²⁵ California has found a public health use for this molecular information and has created a voluntary program to identify toxic chemicals “present in the bodies of Californians.” CAL. HEALTH & SAFETY CODE § 105441 (2007).

²⁶ See National Institute of Environmental Health Sciences, Toxicogenomics Research Consortium, <http://www.niehs.nih.gov/research/supported/centers/trc> (last visited June 7, 2009).

²⁷ *Id.*

²⁸ See Thomas P. Redick, *Twenty-first Century Toxicogenomics Meets Twentieth Century Mass Tort Precedent: Is There a Duty to Warn of a Hypothetical Harm to an ‘Eggshell’ Gene?* 42 WASHBURN L.J. 547, 552 (2003).

²⁹ These associations will be reported as hypotheses in the scientific literature, and “[l]awyers and carefully chosen experts will . . . take hypothetical genetic susceptibilities into court for the consideration of juries” before they are accepted in relevant scientific communities. See *id.* at 552.

susceptibilities, but also by comparing signs of exposure to toxic substances with the development of diseases of interest. The Centers for Disease Control and Prevention ("CDC") began a nationwide sampling process in 2001 that "provides an ongoing assessment of the U.S. population's exposure to environmental chemicals using biomonitoring. Biomonitoring is the assessment of human exposure to chemicals by measuring the chemicals or their metabolites in human specimens such as blood or urine."³⁰ The CDC plans to issue reports every two years.³¹ This national data is very important, but in order to make clinically useful assessments about associations between these levels and prevalence of diseases, the data have to be collected and studied on a regional, or even local, level.

California is attempting to address these very questions by performing biomonitoring on Californians. In 2006, the California legislature passed the California Environmental Contaminant Biomonitoring Program ("CECBP") that "shall utilize biological specimens, as appropriate, to identify designated chemicals that are present in the bodies of Californians."³² The CECBP is run by the California Department of Health Services and will collect human biological specimens such as blood, urine, and breast milk from donors, and then identify and measure chemicals present and their metabolites.³³ The program will begin with a statewide sample of participants but hopes to expand to high risk groups which might include agricultural workers, people living near highways and busy roads, and populations that consume large amounts of fish from local waters.³⁴ Among the public health purposes that could be served by this program are:

³⁰ See Centers for Disease Control and Prevention, National Report on Human Exposure to Environmental Chemicals, <http://www.cdc.gov/exposurereport/default.htm>.

³¹ So far, it was done in 2001, 2003, 2005, and the next is expected in early 2009. *Id.* at http://www.cdc.gov/exposurereport/results_reporting_process.htm (last visited Mar. 29, 2009).

³² See CAL. HEALTH & SAFETY CODE § 105441 (2007).

³³ *Id.* See CALIFORNIA DEPARTMENT OF HEALTH SERVICES, CALIFORNIA BIOMONITORING PLAN 6 (2003), available at http://www.cdph.ca.gov/programs/Biomonitoring/Documents/CDHS_Biomonitoring_Plan.pdf [hereinafter CBP].

³⁴ *Id.* at 7.

To determine which potentially harmful chemicals are in Californians' bodies, and at what concentrations; . . . [t]o establish reference ranges that can be used by physicians and scientists to determine whether a person or group has an unusually high exposure; . . . [t]o determine whether exposure levels are higher among children, women of childbearing age, or other potentially vulnerable groups; . . . [t]o set priorities for action to protect the public's health.³⁵

Biomonitoring will occur on a voluntary basis,³⁶ and any data that is made publicly available will "be provided in a summary format to protect the confidentiality of program participants."³⁷ If the participant chooses, program staff will return a sample analysis results that "indicate[s] a significant known health risk" ³⁸ The staff will have experience "communicating biomonitoring results," and will "consult with the individual and recommend follow up steps, as appropriate."³⁹

As with the wellness products and analyses, California's biomonitoring program will put information in the hands of people exposed to toxic substances before they experience any noticeable symptoms. The government's purpose in pursuing this program is to gain information to help it regulate industry wisely and educate its citizens effectively on ways to avoid disease (or avoid passing substances on to others, like nursing infants). But the information might have other uses as well. For example, what might individuals accomplish with this information if they are engaged in litigation, seeking compensation for health-related consequences of toxic exposure against those responsible for the exposure? The following section considers the possibilities.

III. USE IN LITIGATION

Genetic science has been used in courtrooms for some time in efforts to prove or disprove what caused a plaintiff's injury, but

³⁵ *Id.* at 5.

³⁶ See CAL. HEALTH & SAFETY CODE § 105441 (2007).

³⁷ *Id.* at § 105459.

³⁸ See *id.* at § 105443.

³⁹ *Id.*

personalized medicine ups the ante. People now have the possibility of gaining information about individual health risks and environmental exposure, in some cases even before they manifest any symptoms of disease.⁴⁰ This new information might offer attorneys new opportunities to argue on behalf of clients from both sides of a lawsuit. Plaintiffs, for example, will look to expand the concept of compensable harm. Defendants, on the other hand, will look for data to suggest that a claimant's disease process was well underway before a toxic exposure took place. This section will consider how personal molecular information might find its way into courts, particularly in response to questions about susceptibility, exposure, and causation.

A. Susceptibility

The tools of personalized medicine can provide information about whether a person who develops an exposure-related injury had a genetic susceptibility to that disease.⁴¹ On the one hand, this would appear to be a positive piece of information for a defendant accused of causing the plaintiff's disease. After all, if an individual already had a high likelihood of developing a particular disease, proving that a defendant's actions were its specific cause is difficult.⁴² On the other hand, the development of associations between genetic characteristics, toxic exposures, and the path to disease might implicate particular exposures in toxic tort cases.⁴³ Even if the data is not yet convincing to scientists, "companies will be in the distinctly uncomfortable position of knowing, to a reasonable degree of scientific certainty, that their product may be harming a small group of users."⁴⁴ In addition, employers might face difficult questions, including "whether workers should be allowed to remain in a potentially risky position in the workplace."⁴⁵ Attempts to protect

⁴⁰ See generally James P. Evans et al., *The Complexities of Genetic Testing*, 322 BMJ 1052 (2001).

⁴¹ See Redick, *supra* note 30 at 552.

⁴² See *infra*, notes 60-2 and accompanying text.

⁴³ See *infra* notes 50-54.

⁴⁴ See Redick, *supra* note 30, at 549.

⁴⁵ *Id.* at 550.

workers from injury based on their genetic susceptibilities may run into violations of Title VII, gender discrimination, and even the new Genetic Information Nondiscrimination Act.⁴⁶

B. Exposure

The tools of personalized medicine can also be used in litigation to address the issue of exposure—that is, whether the plaintiff was exposed to a toxic substance in high enough concentration that it might have caused the alleged injury. Biomonitoring can provide either certain or suggestive information about a particular individual's exposure to a toxic substance. Some types of biomonitoring simply measure concentrations of toxic substances in human biological samples, such as urine or hair, with techniques that have been in use for a long time. For example, testing children for lead exposure by analyzing urine for lead metabolites can provide very reliable information about whether children have been exposed to lead. In other cases, the science is suggestive, but not yet accepted by relevant scientific communities. A newer technique is to use genetic biomarkers to demonstrate an individual's exposure to a toxin, or in some circumstances, to show progression of the disease process before actual symptoms appear. Today, scientists can observe these biomarkers at the molecular level, permitting the detection of "previously undetectable, intermediate events" between exposure and disease.⁴⁷ In addition, there are some claims that exposure to certain substances leaves "signatures" that allow the triggering substance to be identified.⁴⁸ A recent article in the ABA Journal featured a medical toxicologist, Dr. Bruce Gillis, who claims that every chemical triggers a unique release of cytokines.⁴⁹ The testing he

⁴⁶ See, e.g., *Int'l Union v. Johnson Controls Inc.*, 499 U.S. 187 (1991); Press Release, U.S. Equal Employment Opportunity Comm'n, EEOC Settles ADA Suit Against BNSF for Genetic Bias (Apr. 18, 2001) (<http://www.eeoc.gov/press/4-18-01.html>).

⁴⁷ See Jamie A. Grodsky, *Genomics and Toxic Torts: Dismantling the Risk-Injury Divide*, 59 STAN. L. REV. 1671, 1687 (2007).

⁴⁸ Mark Hansen, *DNA Poised to Show Its Civil Side*, 94 ABA J. 18, 18 (Mar. 2008).

⁴⁹ *Id.* Cytokines are "hormone-like proteins, secreted by many cell types, which regulate the intensity and duration of immune responses and are involved in cell-to-cell communication." STEDMAN'S CONCISE MEDICAL DICTIONARY FOR HEALTH PROFESSIONS, ILLUSTRATED 212 (3d ed. 1997).

developed, known as MSDS1, can “determine what chemical, if any, triggered the identical release pattern in an individual’s DNA.”⁵⁰ Gillis claims that his test has “been used in more than two dozen workers’ compensation cases in California.”⁵¹ He reports that:

[s]ome cases have been dropped after the test showed that an applicant had not been injured by exposure to the chemical from which he or she was alleging harm. Other cases have been settled after the test showed that the applicant was injured by exposure to a chemical present in the workplace.⁵²

C. Causation

Even if a plaintiff has demonstrated exposure to the toxic substance in question by demonstrating a change at the molecular level, that information alone is not sufficient to prove that the substance caused the plaintiff’s disease.⁵³

To focus our conversation, imagine the following scenario. Suppose ten years from now, Alice, a 30-year-old woman, purchases a full genome sequencing from a private company, GenesRU, Inc. The reading is accompanied by a graphic representation of Alice’s chromosomes, coded to show known areas of elevated risk. Suppose further that the evaluation shows no elevated genetic risk for lung cancer and that Alice has no other leading risk factors for the disease—she has never smoked, nor has she been exposed to asbestos or other workplace chemicals known to cause lung cancer.

After receiving her report, Alice buys and moves into a house in Iowa. At the time, the seller installed a radon remediation system in the home’s basement. Ten years later, Alice is diagnosed with lung cancer. Subsequent investigation determines that the radon remediation system was defective and that Alice had been exposed to potentially dangerous levels of radon during the past decade. Alice files a lawsuit against the manufacturer of the radon remediation

⁵⁰ See Mark Hansen, *supra* note 50, at 19.

⁵¹ *Id.*

⁵² *Id.*

⁵³ See *infra* notes 56-69 and accompanying text (discussing what plaintiffs must prove to establish causation).

system, seeking to connect her disease to the radon exposure.

A major hurdle—indeed, *the* major hurdle—in Alice’s lawsuit will be proving a causal connection between her cancer and the radon exposure. Doing so will require a three-step process. First, as noted above, Alice must prove a significant level of radon exposure. Next, she must prove general causation—that is, that radon can cause cancer.⁵⁴ She also must prove specific causation—that is, she will have to show by a preponderance of the evidence that she would not have developed lung cancer but for the exposure to radon in her Iowa home.⁵⁵ In our hypothetical, we can assume that Alice was exposed to a significant amount of radon. But even in cases where significant exposure is less clear, post-exposure genetic testing can help clarify the issue.⁵⁶

Regarding general causation, the law typically has relied on scientific evidence, often based on extrapolation or group probabilities.⁵⁷ The most important discipline that lawyers have relied upon for this purpose is epidemiology, which is concerned with disease distribution and determinants among human populations.⁵⁸ For tort law purposes, the critical measurement in

⁵⁴ Radon is considered the second-leading cause of lung cancer, after cigarette smoking. See <http://www.cancer.gov/cancerTopics/factsheet/Risk/radon>.

⁵⁵ See RESTATEMENT (THIRD) OF TORTS: LIAB PHYSICAL HARM § 28 cmt. c (Proposed Final Draft No.1, 2005); Michael D. Green, *The Future of Proportional Liability: The Lessons of Toxic Substances Causation*, in *EXPLORING TORT LAW* 342-45 (M. Stuart Madden ed., 2005); Gary E. Marchant, *Genetic Data in Toxic Tort Litigation*, 14 J.L. & POL. 7, 23 & n.54 (2006).

⁵⁶ See *supra* notes 49-54 and accompanying text.

⁵⁷ Regarding extrapolation, courts have looked particularly to toxicology studies to understand the consequences of substance exposure. However, because toxicological tests do not provide direct evidence of how a substance impacts humans, courts have been reluctant to rely on toxicology studies for proof of causation in a tort action. See Andrew R. Klein, *Causation and Uncertainty: Making Connections in a Time of Change*, 49 JURIMETRICS J. 5, 26, n.124 (2008).

⁵⁸ *Id.* at 26 (“Two types of epidemiology studies have the most relevance to toxic tort cases—‘cohort’ and ‘case-control’ studies, both of which consider the statistical effects of exposure within a population. Case-control studies are retrospective in nature, comparing the history of those with disease (‘cases’) to those without (‘controls’). . . . Cohort studies, by contrast, are prospective, tracking the incidence of disease among groups of people who were exposed to a particular substance and comparing it to the rate of those who were not.”) (citing Gerald W. Boston, *A Mass-Exposure Model of Toxic Causation: The Content of Scientific Proof and the Regulatory Experience*, 18 COLUM. J. ENVTL. L. 181, 231-34 (1993)); see also Albert C. Lin, *Beyond Tort: Compensating Victims of Environmental Toxic Injuries*, 78 S. CAL. L. REV.

epidemiology studies is relative risk. Relative risk can be defined as $R1/R2$ where $R1$ equals the rate of disease among the exposed population and $R2$ equals the rate of disease in the non-exposed population.⁵⁹ If relative risk equals one, the study suggests no association between exposure and disease, as the risk is identical in both the exposed and the non-exposed group. If relative risk is greater than one, the study might well support an association, as those exposed to the toxin are statistically more likely to suffer disease than those in the non-exposed group.⁶⁰

But proving general causation is not enough. To succeed in a tort action, a plaintiff needs to prove specific causation—that the exposure more likely than not led to her individual disease. Here, even the existence of strong epidemiological evidence might not be sufficient. For example, what of a situation where the relative risk among a population is between 1.0 and 2.0, suggesting an association but not a connection “more likely than not”? Where epidemiological studies show a relative risk greater than 2.0, how should a court deal with individual factors that might impact the likelihood of causation in a given case? For example, suppose Alice *had* been a smoker in addition to being exposed to radon. It is in the area of specific causation that personalized medicine might have its greatest impact in a toxic tort action.

1439, 1448-49 (2005) (“Courts tend to view epidemiological studies, which apply statistical techniques to explain variations in disease rates of human populations, as the most persuasive and acceptable type of general causation evidence in toxic tort cases.”).

⁵⁹ See Joseph L. Gastwirth, *The Need for Careful Evaluation of Epidemiological Evidence in Products Liability Cases: A Reexamination of Wells v. Ortho and Key Pharmaceuticals*, 2 LAW PROBABILITY & RISK 151, 156-57 (2003); Michael D. Green, *Expert Witnesses and Sufficiency of Evidence in Toxic Substances Litigation: The Legacy of Agent Orange and Bendectin Litigation*, 86 NW. U. L. REV. 643, 647 (1992).

⁶⁰ See Klein, *supra* note 59, at 26-27 & nn. 130-32 (“In more complex situations, where the exposure is only one of multiple risk factors, evaluations become more complicated. Some interactions, for example, are only additive, while others might have a synergistic or multiplicative effect on the possibility of future disease. For an excellent explanation, see also Susan R. Poulter, *Genetic Testing in Toxic Injury Litigation: The Path to Scientific Certainty or Blind Ally*, 41 JURIMETRICS J. 211, 223-31 (2001) (“One well-known example of ‘synergistic causation’ is seen in cases where smokers are exposed to causation. In general terms, occupational exposure to asbestos increases the risk of lung cancer five times the background rate. A significant level of smoking increases the risk at least 10 times the background rate. Together, however, the increase is not fifteen percent—it is 50 percent above background rates.”).”).

Personalized medicine creates the potential for evidence that is highly tailored to an individual plaintiff. In the case of Alice's hypothetical, the GenesRU test results would seem quite helpful—they eliminate the defendant's argument that genetic predisposition led to the lung cancer, making her radon exposure a more likely culprit. The evidence would be particularly strong if combined with post-exposure DNA tests showing structural changes specific to radon exposure. In such a case, Alice would seem to have evidence of both exposure and the consequences of that exposure at a very personal level.⁶¹ But what if the test result had come out the other way, showing that Alice had a high genetic risk of contracting the disease, even before her radon exposure? This might suggest that the disease was likely to manifest even in the absence of radon exposure. If so, proving that the exposure "more likely than not" led to the cancer becomes harder, if not impossible.

One final issue merits at least a quick mention. What if a person like Alice is asymptomatic, but genetic testing suggests that her exposure to radon has increased her risk of contracting lung cancer in the future?⁶² Current tort doctrine leaves a "pre-manifestation" plaintiff with few options for recovery, absent present physical harm.⁶³ However, genetic information, such as gene expression data, has the potential to alter the legal landscape by forcing courts to reconceptualize the notion of injury.⁶⁴ This is particularly true for the

⁶¹ See, e.g., Klein, *supra* note 59, at 33.

⁶² Perhaps gene expression data can be viewed as an impact at a subcellular level, even though she remains technically cancer free. See, e.g., *Rainer v. Union Carbide Corp.*, 402 F.3d 608, 611-13 (6th Cir. 2005); Grodsky, *supra* note 49, at 1692-93; Marchant, *supra* note 57, at 27-28. See also James A. Henderson, Jr. & Aaron D. Twerski, *Asbestos Litigation Gone Mad: Exposure-Based Recovery for Increased Risk, Mental Distress, and Medical Monitoring*, 53 S.C. L. REV. 815, 817 (2002) (discussing individuals exposed to asbestos who have physical evidence of exposure, but no manifestation of disease).

⁶³ See Grodsky, *supra* note 49, at 1693; Marchant, *supra* note 57, at 28. For one of this paper's author's suggestions on how tort law might compensate for increased risk of harm, see Andrew R. Klein, *Fear of Disease and the Puzzle of Future Cases in Tort*, 35 U.C. DAVIS L. REV. 965, 970 (2002); Andrew R. Klein, *A Model for Enhanced Risk Recovery in Tort*, 56 WASH. & LEE L. REV. 1173, 1174-75 (1999).

⁶⁴ See Marchant, *supra* note 57, at 29 ("Gene expression data can potentially help at-risk plaintiffs to demonstrate both a present injury and a sufficient increase in risk in appropriate cases. Courts have adopted different approaches for defining 'present injury,' but at least some jurisdictions permit an asymptomatic, subclinical effect to qualify as a

remedy of medical monitoring, which has been accepted by a number of jurisdictions as a way to provide asymptomatic plaintiffs with recovery for the costs of medical surveillance after tortious exposure to a toxic substance.⁶⁵

Recently, Professor Jamie Grodsky considered this issue at length and argued for a reinvigoration of medical monitoring in light of recent developments in genetic science.⁶⁶ In particular, Professor Grodsky argued that restricting medical monitoring recovery to situations where plaintiffs have clinical injury might stifle the tort system's ability to deter and prevent future harm: "The argument for early detection will gain added currency as medical breakthroughs open up new possibilities for cellular-level intervention. . . . The emerging field of 'nanomedicine' aims to translate discoveries arising from genomics and proteomics into techniques to detect, prevent, and treat disease at a molecular level."⁶⁷

As Professor Grodsky suggests, developments in science and health care cannot be ignored as we consider their impact on tort law. Developments in tort law will undoubtedly mirror developments in other areas that will be impacted by personalized medicine, such as public health regulation and clinical practice. This, of course, is the point we have been trying to make all along.

IV. CONCLUSION

The proliferation of individual, molecular information through new and evolving tools of personalized medicine poses both risks and rewards. Along the path to its goals of improving health at the individual and population levels, personalized medicine also will impact litigation involving toxic exposures. This is not to suggest that the potential for future tort actions should drive the development of personalized medicine. But it does mean that it makes sense to consider some predicate issues that might arise in these early days of the industry. One must acknowledge that some products currently

present injury.").

⁶⁵ Klein, *supra* note 59, at 46 & n.241.

⁶⁶ See Grodsky, *supra* note 49, at 1717.

⁶⁷ *Id.* at 1713-14.

aimed at personal wellness uses are based on relatively weak associations that have not yet convinced scientists of their validity. Clinicians are often left scratching their heads trying to figure out how, if at all, they can use the information derived from these products to help their patients. Despite these concerns, however, personalized medicine will inevitably find its way into toxic tort litigation. As we have discussed, this will have implications for showing exposure. But toxic tort litigation's most important use might be in helping to clarify vexing issues of causation and providing mechanisms for defining legal injury even before the manifestation of disease. In the early days of applying these tools, courts may spend an inordinate amount of time trying to sort through the science and validity of each particular personalized medicine test that has been used to prove susceptibility, exposure, or causation. But as the science matures, our society may benefit both from a decreased burden of disease caused by toxic exposures as well as clearer answers in the courtroom.