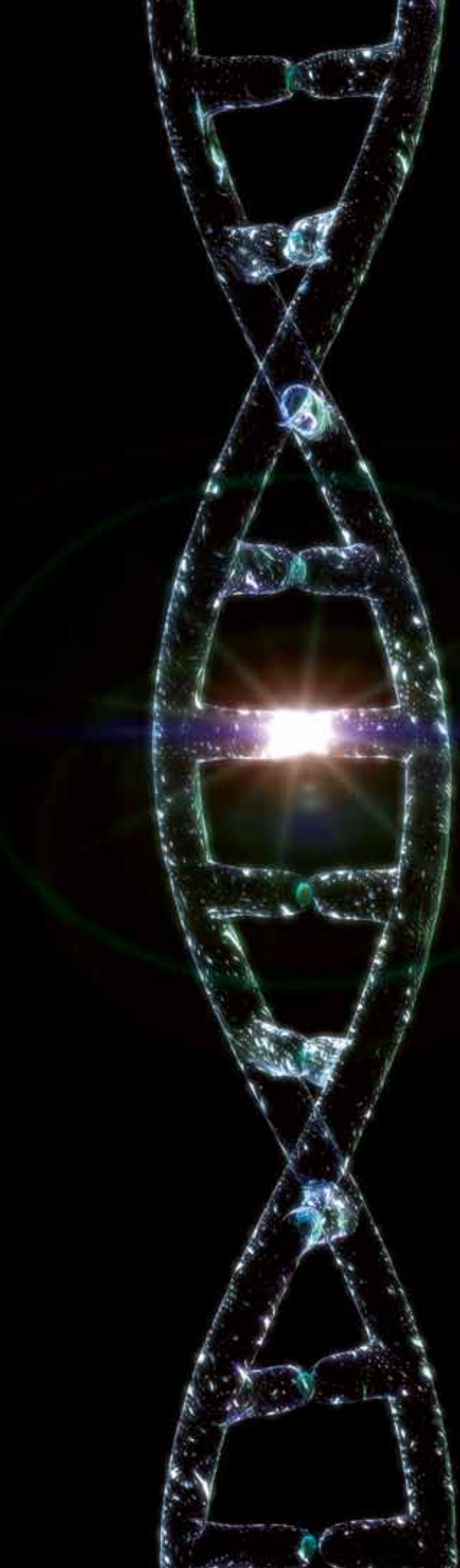

Genetic Data in Toxic Tort Litigation

BY GARY E. MARCHANT

Genetic data are rapidly transforming health care, criminal forensics, paternity disputes, and pathogen tracking. Toxic tort and personal injury litigation may be next. New types of genetic data can help to address the major data gaps and uncertainties about the health risks of most potentially toxic substances, and even more importantly, whether a particular toxic agent caused the injury incurred by a plaintiff in a toxic tort or personal injury lawsuit. Until now, there has usually been no direct evidence of causation, leaving judges and juries to infer causation using crude and highly inexact indirect evidence and statistical assumptions. Moreover, even though it has been well known for many decades if not centuries that people differ dramatically in their susceptibility to toxic exposures, the courts have had no information or mechanism to identify such sensitivities in individual plaintiffs, resulting in the legal system essentially ignoring the scientific fact of interindividual variability in toxic response.

New genetic methods and data potentially may make toxic tort litigation more accurate and fair but also more complex, contentious, and ethically problematic.

New genetic methods and data have the potential to fill these scientific uncertainties and data gaps in toxic tort litigation, thus making toxic tort litigation both more accurate and fair. At the same time, these same genetic data have the potential to make toxic tort litigation even more complex, contentious, and ethically problematic. Two types of genetic data are likely to have the biggest impact in toxic tort litigation: (1) data on genetic susceptibility of individual plaintiffs, and (2) genetic biomarkers of exposure and effect. This article explores the potential applications of these two types of genetic information in toxic tort litigation, as well as the potential benefits and risks of such applications.

Genetic Susceptibility Data

The genes that code for enzymes involved in the metabolism of foreign substances entering the body, including pollutants and other toxic substances, are highly variable between individuals.[1] Genetic variations (or "polymorphisms") that affect susceptibility have been identified for most toxic substances that have received significant regulatory scrutiny.[2] Some of these polymorphisms are very common in the population, while others are rare. For example, almost 50 percent of Caucasians lack a functional copy of the gene coding for the important metabolic enzyme glutathione S-transferase M1, increasing their risks to toxic substances such as polycyclic aromatic hydrocarbons (PAHs) and aflatoxin.[3] The Environmental Genome Project has identified over 500 putative environmental susceptibility genes.[4] As discussed below, these variations in genetic susceptibility have many potential applications to toxic torts.

Proving or disproving causation. Plaintiffs in toxic tort lawsuits must prove that the toxic substances to which they were exposed caused their illness. To satisfy this causation requirement, some (but not all) courts require that plaintiffs demonstrate that the defendant's action doubled their background risk (i.e., relative risk > 2.0) such that the exposure was "more likely than not" the cause of the illness in the individual.[5] Plaintiffs often cannot meet this demanding requirement. Evidence of genetic susceptibility, however, may assist some susceptible individuals in overcoming this hurdle. Even if epidemiology studies show that the relative risk in the general population is less than 2.0, genetically susceptible plaintiffs could argue that their individual risk is higher than the general population due to their unique susceptibility, and indeed may exceed the twofold legal threshold.[6]

In several cases, plaintiffs have already advanced claims of genetic susceptibility to try to circumvent causation barriers to recovery. For example, some silicone breast implant plaintiffs relied on a published study allegedly identifying a gene variant conferring susceptibility to silicone[7] to argue they may have been harmed by silicone leaking from their implants even if epidemiology studies showed no significant increase in disease associated with silicone breast implants in the general population.[8] Similarly, thyroid cancer victims living near the Hanford nuclear facility argued their background risk doubled from exposure to radioactive wastes from the facility when their alleged genetic susceptibility to ionizing radiation was factored in. Specifically, they claimed this genetic susceptibility justified a fivefold reduction in the exposure levels necessary to double background risk.[9] These claims have generally failed to date because the plaintiffs simply pointed to evidence of a genetic susceptibility in the general population without

TIP
Counsel may soon have an ethical duty to notify plaintiffs whose health is at issue that pursuit of a claim may require them to submit to genetic testing.

introducing evidence that they themselves carried the relevant susceptibility-conferring gene.[10] To prevail on such arguments in the future, plaintiffs will likely need to undergo genetic testing to substantiate their claims of genetic susceptibility.

Alternatively, the defense may argue that the lack of a susceptibility gene undercuts a plaintiff's causation argument. In *Easter v. Aventis Pasteur, Inc.*,[11] the plaintiff alleged that thimerosal, a mercury preservative in the defendant's pediatric vaccines, caused her son Jordan to develop autism. Although large studies had shown no association between thimerosal and autism in the general population, the plaintiff contended that "some children are genetically susceptible to mercury poisoning and cannot excrete or otherwise eliminate the mercury in the vaccine preservative."[12] Unfortunately for the plaintiff in this case, genetic testing revealed that Jordan did not have the pertinent genetic susceptibility. As described by the court, the plaintiff "conceded that [she] cannot prove, in Jordan's case, that his autism was caused by thimerosal . . . because Jordan does not meet the genetic profile for children who . . . are at increased risk for developing autism caused by thimerosal."[13] This concession was "[t]he beginning and the end" of the court's ruling to exclude the testimony of the plaintiff's causation expert.[14]

In some cases, defendants could seek to test plaintiffs for other genetic traits that might predispose the plaintiffs to the illnesses they have developed. For example, recent findings indicate that a gene mutation known as BAP1 can strongly predispose a carrier to mesothelioma.[15] Defendants in asbestos liability cases have sought genetic testing of plaintiffs and argued in a number of pending cases that the BAP1 gene mutation and not exposure to asbestos was the cause of the plaintiff's mesothelioma.[16]

A plaintiff may argue that a manufacturer had a legal duty to warn product users that they may be genetically susceptible to the manufacturer's product.

In another case, the defendant obtained genetic testing of a plaintiff whose birth defect was allegedly caused by prenatal exposure to Benlate, and based on the test results, demonstrated to the satisfaction of both the plaintiff's lead expert and the court that the disability was caused by a specific inherited genetic mutation rather than chemical exposure.[17] These cases illustrate that plaintiffs' genetic traits, which increase susceptibility for a particular toxic substance or create a predisposition to disease without any environmental exposure, can be used to argue for or against causation. Given the potential usefulness of such genetic data for either proving or disproving causation, it is likely that both plaintiffs and defendants will increasingly seek to obtain and introduce such evidence in future toxic tort cases. One expert has even suggested that it should become "standard practice" for defendants to seek genetic testing of plaintiffs in order to identify potential alternative causes.[18]

Duty to protect or warn genetically susceptible plaintiffs? Another set of legal issues will revolve around the duty of a product manufacturer to protect or warn genetically susceptible individuals in the population. Defendants are likely to argue that they should have no duty to protect individuals with rare genetic susceptibilities to their products, perhaps invoking a doctrine known as the "idiosyncratic response" defense.[19] This defense has traditionally been applied to protect a manufacturer from liability for a product such as a cosmetic that appears safe to the general population but may cause an unusual response in individuals with a rare allergy or sensitivity to the product. As one court stated, "[a] manufacturer has no duty to withhold its product from the market merely because the product may pose a risk to certain hypersensitive individuals."[20]

An example of how the idiosyncratic response defense could be applied to genetically susceptible individuals is provided by *Cavallo v. Star Enterprise*.[21] In that case, a resident living near a petroleum distribution terminal claimed she became ill from inhaling fuel vapors released by a spill from the facility.[22] The plaintiff alleged that she was "highly susceptible" to fuel vapors, in part to explain why she

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was adversely affected while many of her neighbors were not.[23] The Fourth Circuit Court of Appeals held that liability can only be imposed for adverse effects that would be suffered by a "normal" person, and thus the plaintiff's own allegation that she was unusually susceptible precluded her claim.[24]

While defendants may be able to use the existence of unusual genetic susceptibility to escape legal liability in some cases, plaintiffs may be able to use such susceptibilities to impose additional duties on manufacturers in other cases. Specifically, a plaintiff may argue that a manufacturer had a legal duty to warn product users that they may be genetically susceptible to the manufacturer's product. The first such cases have already been filed, alleging that the LYMErix vaccine, the only biologic approved to protect against Lyme disease, caused a chronic autoimmune reaction in approximately 30 percent of the population who carry a specific genetic polymorphism.[25] The lawsuits argued that the manufacturer had a legal duty to not only warn vaccine users that a potential genetic susceptibility to the vaccine is prevalent in the population, but also recommend that vaccine users should obtain a genetic test for the susceptibility gene before taking the vaccine.[26] Although both the manufacturer and federal regulators disputed the factual premises of the lawsuit,[27] the cases were settled before trial and the vaccine was subsequently removed from the market. These cases are the first in what is likely to become an increasingly frequent type of legal claim in which a plaintiff contends that a manufacturer has a duty to identify and warn about possible genetic susceptibilities to its products.

Other potential applications of genetic susceptibility data. There are several other potential applications of genetic susceptibility data in toxic tort litigation. One such use is for defendants to cite to the genetic heterogeneity within the population with respect to susceptibility to a product or substance at issue in arguing against class certification of plaintiffs in a potential class action lawsuit. Some defendants have successfully argued that differences in genetic susceptibility to a product require individualized assessments of risk and causation, thereby helping to defeat the requirement that common issues predominate, resulting in denial of class certification.[28]

Judges may allow juries to use information on a plaintiff's genetic predisposition to disease to determine the damages to be paid to a plaintiff who has prevailed on the merits of a lawsuit. A defendant could try to exploit the plaintiff's genetic predisposition to disease by arguing that the damages should be discounted due to the plaintiff's increased risk of disease. In other words, a plaintiff injured by the defendant's actions who happened to have a genetic predisposition that reduced his or her life expectancy independent of the tortious injury may have the damages discounted accordingly.[29] The most closely analogous precedent are cases where courts have ordered HIV testing of plaintiffs to determine if their damage awards should be discounted due to their reduced life expectancy based on their future development of AIDS.[30] Courts will have to determine whether, and under what circumstances, defendants can request genetic testing of plaintiffs for the purpose of determining genetic risks affecting life expectancy.[31]

Genetic Biomarkers of Exposure or Effect

Genetic biomarkers of exposure or effect are the second major type of genetic information that is likely to be used in toxic tort litigation. A biomarker is a molecular change in blood or some other tissue of a person exposed to a toxic substance that can be used to qualitatively or quantitatively prove exposure or causation.[32] Several types of genetic biomarkers exist, including chromosomal rearrangements,[33] mutational spectra,[34] or gene expression patterns.[35] Some potential tort applications are discussed below.

Proving or disproving exposure. One promising application of genetic biomarkers in toxic tort litigation is in demonstrating and even quantifying exposure. Many toxic tort cases involve sudden unexpected or previously undetected chronic environmental exposures, such as exposure to contaminated drinking water, hazardous chemicals released into the air, or hazardous worksites. Plaintiffs often are unaware that they are being exposed until after the fact, and frequently there are no direct measurements of the exposure that occurred. Yet, courts often insist that plaintiffs must adequately demonstrate and quantify their exposure to move forward with their claims.[36]

An iconic case demonstrating the potential for using genetic biomarkers to prove exposure is the litigation resulting from the 1979 Three Mile Island nuclear reactor accident.[37] The plaintiffs, nearby residents who developed cancer, lacked any direct or modeling evidence to quantify exposure to an alleged plume of radioactive release they contended caused their tumors. Instead, they sought to demonstrate exposure using expert evidence purporting to show that the residents had an increased frequency of a specific chromosomal aberration (dicentric chromosomes) that is characteristic of radiation exposure. The Third Circuit Court

of Appeals validated the general approach of using such biomarkers to prove exposure, holding that such use of genetic markers "is an accepted method, not simply for determining if the subject of the analysis was irradiated, but also for estimating radiation dose to the individual."[38] But the court ultimately held that the evidence could not be used to prove exposure in that case because the validity and reliability of dicentric chromosomes as a quantitative marker of radiation exposure "decrease as the time gap between the alleged irradiation and the dicentric count increases."[39] According to the court, dicentric chromosomes only provide an accurate indicator of dose within one or two years of exposure, but the plaintiffs attempted to use dicentric chromosome evidence collected over 15 years after the exposure occurred, which may no longer be reliable.[40] This case thus stands for the proposition that genetic markers can, in principle, be used to demonstrate and quantify exposure to a toxic agent, but the temporal dimensions of when the exposure occurred and when the exposure biomarkers were assayed will be critical to the admissibility of such evidence.

Causation. Genetic biomarkers can also be useful in providing direct evidence on whether or not a particular toxic agent caused the plaintiff's disease. Except for genetic data, there are no types of evidence that can directly evaluate causation. In the words of one court, "science cannot tell us what caused a particular plaintiff's injury."[41] Consequently, the tort system currently relies on crude, inexact methods to evaluate specific causation, such as "differential diagnosis"[42] or statistical inferences.[43]

Genetic biomarkers can address the lack of direct evidence of causation. For example, parties have used the association between specific chromosome rearrangements and leukemia caused by benzene (as opposed to other causes) to argue for or against specific causation. In several cases, the defendant successfully argued that the plaintiff lacked the specific types of genetic biomarkers that would allegedly be present if the defendant's activities had caused the disease. For example, in one case, the plaintiff claimed that benzene from the defendant's refinery caused his acute myelogenous leukemia (AML), but the jury was convinced by the defendant's argument that when benzene causes AML it does so via breaks in chromosomes five and seven, which were absent in this particular plaintiff.[44] Alternatively, when the specific chromosomal change indicative of benzene causation is present in a leukemia plaintiff, the plaintiff can utilize that evidence to support causation.[45]

The epigenetic "revolution" will present new applications and opportunities for such data in toxic tort litigation.

The gene expression profile of a tumor can also be probative of causation. In a recent case, a plaintiff claimed her thyroid cancer was caused by exposure to "naturally occurring radioactive material" (NORM) associated with the defendant's operations.[46] A defense expert used gene expression profiling to demonstrate the plaintiff's "gene signature" for sporadic thyroid cancer rather than for radiation-induced thyroid cancer.[47]

By shifting the specific causation inquiry from statistical rules of thumb or subjective medical assessments to genetic changes within the plaintiff's own cells, genetic biomarkers such as gene expression signatures have the potential to make specific causation significantly more objective and reliable.

Recovery for "latent risks." Another toxic tort area where genomic biomarker data could potentially have a large impact is in support of claims brought by plaintiffs who are at an increased risk of disease as a result of toxic exposures, but who have not yet manifested clinical disease. These "latent risk" claims can seek compensation for an increased risk of disease, fear of developing disease, or medical monitoring. Whether and when to allow recovery for latent risks has been described as the most difficult problem confronting toxic torts.[48] Courts have generally imposed stringent prerequisites for such claims, based on policy considerations such as the need to prevent courts from being flooded with claims, many of which might be "trivial" or "comparatively unimportant," as well as to protect defendants from being subjected to "unlimited and unpredictable liability."[49] In increased risk and fear of disease claims, for example, most courts require the plaintiff to demonstrate a "present injury"[50] as well as to quantify a sufficient increase in risk.[51] Many plaintiffs exposed to toxic substances are unable to make these demonstrations with the types of scientific evidence presently available, and their claims are accordingly precluded.[52]

Genetic biomarkers are creating new challenges and opportunities in defining and detecting "injury."[53] Courts have adopted different approaches for defining

"present injury," but at least some jurisdictions permit an asymptomatic, subclinical effect to qualify as a present injury.[54] In those jurisdictions, genetic changes may provide a powerful new tool for demonstrating subcellular injury. A critical issue in this application of genomic data will be in distinguishing subcellular changes that are truly representative of a toxic response as opposed to a reversible adaptive response that is not associated with an increased risk to the individual. Increased risk and fear of disease claims will likely become more objective and sustainable in future cases due to the potential of genetic biomarkers to help plaintiffs overcome evidentiary hurdles to these types of claims.

Genetic biomarkers are also likely to spur more medical monitoring claims, which are already recognized in many (but not all) states.[55] While different states have adopted slightly different criteria for such claims, most states require that plaintiffs pursuing such claims demonstrate an increased risk of disease from their exposure, that this increased risk makes periodic diagnostic medical examinations reasonably necessary, and that monitoring and diagnostic methods exist that make early detection and treatment of the disease both possible and beneficial.[56]

Genetic biomarkers could potentially provide a valuable diagnostic test that could be used for medical monitoring. Alternatively, the abnormal results of a genetic monitoring test could be used to support a medical monitoring claim requesting continuous traditional clinical testing. By providing a sensitive and objective preclinical marker of risk, genetic biomarkers have the potential to greatly expand the number of plaintiffs with valid medical monitoring and other latent risk claims. To the extent that the increased frequency and precision of medical monitoring can better identify at-risk individuals and provide more effective preventive or therapeutic interventions, this technology has great potential for reducing disease and suffering. To the extent other types of latent risk claims, such as increased risk and fear of disease, can provide compensation to deserving plaintiffs who might otherwise be precluded from recovery when latent diseases manifest years or decades later, such claims might enhance the corrective justice and deterrence goals of tort law.[57]

On the other hand, one concern with an increased number of such claims is the limited capacity of courts to handle these cases.[58] The Sixth Circuit Court of Appeals recently noted such "floodgate" concerns in refusing to recognize chromosomal damage objectively demonstrated by chromosome tests on blood samples from plaintiffs who had been exposed to radioactive substances at a uranium-enrichment plant:

> [T]he most persuasive reason to deny the plaintiffs' claims in the present case comes from public policy considerations. . . . Given that negligently distributed or discharged toxins can be perceived to lie around every corner in the modern industrialized world, and their effects on risk levels are at best speculative, the potential tort claims involved are inherently limitless and endless. Accepting the plaintiffs' claim would therefore throw open the possibility of litigation by any person experiencing even the most benign subcellular damage. Based upon the average American's exposure to chemically processed foods, toxic fumes, genetically modified fruits and vegetables, mercury-laden fish, and hormonally treated chicken and beef, this might encompass a very large percentage of the total population.[59]

Thus, as genetic science increasingly provides plaintiffs the tools to meet the factual prerequisites for latent disease claims under current law, the legal evidentiary and risk thresholds for bringing such claims may need to be tightened even further to avoid overrunning the courts with such claims and to ensure judicial and defendant resources are focused on the most meritorious claims.

Epigenetics

Another important area of genetic research that is likely to have a major impact on toxic tort litigation is epigenetics. "Epi" means above, and so epigenetics refers to modifications above the genetic code. Specifically, epigenetic changes are changes to the DNA molecule or associated proteins that affect gene expression without changing the genetic code itself. The best-studied epigenetic changes are methylation of the cytosine base in DNA, which tends to suppress gene expression. The important significance for toxic tort litigation is that environmental exposures exert epigenetic changes that could affect the exposed individual's risk of future disease, and may even impact the disease risks of future generation progeny of the exposed individual.[60]

The epigenetic "revolution" will present many new applications and opportunities for such data in toxic tort litigation.[61] Epigenetic data have already been successfully introduced in some cases. For example, in litigation involving the drug Actos, the plaintiff's expert referred to an epigenetic mode of action to explain why the plaintiff's tumor may have arisen so quickly after exposure.[62] Moreover, epigenetic markers can be used to quantify past exposures to

toxic substances,[63] which will no doubt be applied in toxic tort cases to prove or disprove both exposure and causation.

Reflections and Recommendations

The many potential applications of genomic data in toxic tort litigation will not be without controversy and obstacles. One challenge will be the incentives for the premature use of genomic data that has not been adequately validated. Given the often substantial stakes and one-time nature of toxic tort litigation, litigants will likely seek to use potentially helpful data even if its significance is not yet adequately understood. Trial judges will need to carefully evaluate the admissibility of genomic data under the criteria provided in the U.S. Supreme Court's *Daubert* decision, including whether the data have been peer reviewed and published, the rate of error of the methods, the "fit" or relevance of the data to the issue being litigated, and the general acceptance of the methodology.[64] The National Academy of Sciences has recently issued guidelines to assist courts in evaluating toxicogenomic data in toxic tort cases.[65] One of the key recommendations is that while caution and vigilance will be needed to guard against premature use of genomic data in tort litigation, such data should not be subjected to a higher standard of admissibility than other toxicological data currently used to prove or disprove exposure, causation, and damages, which are often of poor reliability and accuracy.[66]

Latent disease claims will grow as capabilities develop to detect with genetic markers individuals who were exposed to toxic substances.

Genomic data could also have important consequences for the types of claims brought in toxic tort cases.[67] As the capability to identify our individual genetic differences in susceptibility to toxic substances increases, there is likely to be a growing number of cases arguing that product manufacturers have a duty to test for, warn about, or protect against genetic susceptibilities to their products.[68] While it seems unreasonable to require that a manufacturer must protect the most ultrasusceptible individual in the entire population, it also seems unreasonable that a manufacturer could simply ignore differences in susceptibility within the population especially as such variations become better known and established. How the limits of manufacturer responsibility should and will be drawn remains to be seen. Latent disease claims will also probably grow exponentially as we develop the capability to detect with objective, genetic markers of exposure and effect in individuals who have been exposed to toxic substances. Courts and legislatures will likely face difficult choices about whether and how to limit such claims in order to avoid overwhelming both court dockets and manufacturer financial resources while also fulfilling the tort goals that such claims are intended to advance.[69]

Another important set of issues raised by the utility of genomic data are the privacy, discrimination, and disclosure risks for plaintiffs whose genetic information is placed into evidence.[70] Genetic information is personal and sensitive, and often

individuals do not want to know their own genetic traits, never mind having other people gaining access to such information.[71] In toxic tort litigation, the plaintiff, whose genetic information is relevant, will almost always bear the privacy risks involved, because the case centers on the plaintiff's health status. Nevertheless, a blanket prohibition on any use of genomic data in order to protect plaintiffs' confidentiality would be unwise, because both plaintiffs and defendants can benefit from such data in appropriate cases. Furthermore, plaintiffs who put their health status at issue by bringing the litigation cannot expect such a blanket prohibition.

Focused and scientifically justified genetic inquiries and tests can help to resolve some lawsuits. For example, in the Benlate litigation discussed above, the defendant identified a specific genetic trait it believed caused the plaintiff's injury, and then sought and obtained judicial permission to genetically test the plaintiff for that specific trait, which resolved the case.[72] In contrast, broader and more intrusive "fishing expeditions" into the plaintiff's genome that lack any probable cause in terms of having a reasonable basis for investigating a specific gene or trait are likely to create more mischief than insight needed to resolve a case. Courts must use their discretion, therefore, to determine which genetic tests and data are justified, and also to provide for protective orders in appropriate cases to prevent disclosure of a plaintiff's genetic information to nonparties.

Another issue is that genetic discovery of a plaintiff's genome may reveal important information that could affect the health of a plaintiff and his or her family, which may warrant appropriate screening or prophylactic measures. Who has the responsibility to counsel the plaintiff about these risks and opportunities? The physician who collected the blood or saliva for genetic testing usually does not have a doctor-patient relationship with the plaintiff, and the attorneys, judge, and expert witnesses involved in the case will lack the requisite expertise and responsibility to counsel the plaintiff on the medical significance of the revealed genetic information. Finally, as the use of genomics in toxic torts begins to accelerate, plaintiffs attorneys may soon have an ethical duty to notify their clients whose health is at issue that they may be required to submit to genetic testing in pursuing their claims. In sum, genetic data will present courts with both great opportunities and serious challenges to ensure that such information is used in a sound, effective, and ethical manner.

Conclusion

Genomic data have the potential to transform toxic tort doctrine and practice. There are many potential applications of genomic data in toxic tort litigation, and the doctrinal templates and analogies for most of these applications already exist. We can therefore expect genetic data to be introduced more frequently in future toxic tort cases, especially as the use of genetic information in health care continues to accelerate. By replacing crude assumptions, subjective guesses, and "toxic ignorance" with objective and individualized data on a particular plaintiff's exposure, toxicity response, and susceptibility, genomic data have enormous potential to make toxic tort litigation more informed, consistent, and fair. At the same time, the widespread use of genomic data in toxic tort litigation will create a number of doctrinal, ethical, and institutional dilemmas for courts and toxic tort attorneys. ■

Notes

1. *See* Federica Gemignani et al., *A Catalogue of Polymorphisms Related to Xenobiotic Metabolism and Cancer Susceptibility*, 12 Pharmacogenetics 459 (2002).

2. Gary E. Marchant, *Genomics and Toxic Substances: Part II—Genetic Susceptibility to Environmental Agents*, 33 Envtl. L. Rep. 10,641, 10,644–45 (2003).

3. *See* Lawrence S. Engel et al., *Pooled Analysis and Meta-Analysis of Glutathione S-Transferase M1 and Bladder Cancer: A HuGE Review*, 156 Am. J. Epidemiology 95 (2002).

4. *See* Jocelyn Kaiser, *Tying Genetics to the Risk of Environmental Diseases*, 300 Sci. 563 (2003).

5. *See* Russellyn S. Carruth & Bernard D. Goldstein, *Relative Risk Greater Than Two in Proof of Causation in Toxic Tort Litigation*, 41 Jurimetrics J. 195 (2001).

6. *See, e.g.*, Daubert v. Merrell Dow Pharm., Inc., 43 F.3d 1311, 1321 n.16 (9th Cir. 1995).

7. V. Leroy Young et al., *HLA Typing in Women with Breast Implants*, 96 Plastic & Reconstructive Surgery 1497, 1508 (1995).

8. Gary E. Marchant, *Genetic Susceptibility and Biomarkers in Toxic Injury Litigation*, 41 Jurimetrics J. 67, 91–92 (2000).

9. *In re* Hanford Nuclear Reservation Litig., No. CY-91-3015-AAM, 1998 WL 775340 (E.D. Wash. Aug. 21, 1998).

10. *Id.* at *70; Hall v. Baxter Healthcare Corp., 947 F. Supp. 1387, 1456 (D. Or. 1996).

11. 358 F. Supp. 2d 574 (E.D. Tex. 2005).

12. *Id.* at 575.

13. *Id.*

14. *Id.* at 579.

15. *See* Yoshie Yoshikawa et al., *Frequent Inactivation of the BAP1 Gene in Epithelioid-Type Malignant Mesothelioma*, 103 Cancer Sci. 868 (2012).

16. Heather Isringhausen Gvillo, *Asbestos Defendants Say BAP1 Gene Mutation Causes Predisposition to Mesothelioma*, Madison Rec.

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17. Bowen v. E.I. Du Pont de Nemours & Co., No. 97C-06-194 CH, 2005 WL 1952859 (Del. Super. Ct. Aug. 5, 2005).

18. Diane E. Lewis, *Under a Genetic Cloud: The Benefits of DNA Testing Come with a Potential for Abuse*, Boston Globe, Aug. 14, 1994, at A1 (quoting Philip Reilly).

19. *See* John Gerald Gleeson, *Idiosyncrasy: A Developing Defense in Drug and Hazardous Substances Litigation*, For the Def., Apr. 1989, at 9.

20. Bingham v. Terminix Int'l Co., 896 F. Supp. 642, 645 (S.D. Miss. 1995).

21. 100 F.3d 1150 (4th Cir. 1996).

22. *Id.* at 1153.

23. *Id.* at 1154.

24. *Id.*

25. Amended Complaint at ¶ 10, Cassidy v. SmithKline Beecham Corp., No. 99-10423, 1999 WL 33645128 (Pa. Ct. Com. Pl. Dec. 14, 1999).

26. *Id.* ¶¶ 38, 48.

27. *See* Sarah L. Lathrop et al., *Adverse Event Reports following Vaccination for Lyme Disease: Dec. 1998–July 2000*, 20 Vaccine 1603 (2002).

28. *See, e.g.*, Estate of Mahoney v. R.J. Reynolds Tobacco Co., 204 F.R.D. 150, 161 (S.D. Iowa 2001).

29. *E.g.*, Kegel v. United States, 289 F. Supp. 790 (D. Mont. 1968).

30. *See* Anthony S. Niedwiecki, *Science Fact or Science Fiction? The Implications of Court-Ordered Genetic Testing under Rule 35*, 34 U.S.F. L. Rev. 295, 295 (2000).

31. Mark A. Rothstein, *Preventing the Discovery of Plaintiff Genetic Profiles by Defendants Seeking to Limit Damages in Personal Injury Litigation*, 71 Ind. L.J. 877, 889–91 (1996).

32. Anthony P. DeCaprio, *Biomarkers: Coming of Age for Environmental Health and Risk Assessment*, 31 Envtl. Sci. & Tech. 1837, 1838 (1997).

33. *See* James D. Tucker, *Use of Chromosome Translocations for Measuring Prior Environmental Exposures in Humans*, *in* Biomarkers: Medical and Workplace Applications 117 (Mortimer L. Mendelsohn et al. eds., 1998).

34. *See* Jan C. Semenza & Lisa H. Weasel, *Molecular Epidemiology in Environmental Health: The Potential of Tumor Suppressor Gene p53 as a Biomarker*, 105 Envtl. Health Persp. 155, 155–56 (Supp. 1 1997).

35. *See* Marilyn J. Aardema & James T. MacGregor, *Toxicology and Genetic Toxicology in the New Era of "Toxicogenomics": Impact of "-omics" Technologies*, 499 Mutation Res. 13 (2002).

36. *E.g.*, Wright v. Willamette Indus., Inc., 91 F.3d 1105, 1107 (8th Cir. 1996).

37. *In re* TMI Litig., 193 F.3d 613, 622 (3d Cir. 1999).

38. *Id.* at 690.

39. *Id.* at 692.

40. *Id.*

41. Merrell Dow Pharm., Inc. v.

Havner, 953 S.W.2d 706, 715 (Tex. 1997).

42. *See* Joseph Sanders & Julie Machal-Fulks, *The Admissibility of Differential Diagnosis Testimony to Prove Causation in Toxic Tort Cases: The Interplay of Adjective and Substantive Law*, 64 Law & Contemp. Probs. 107, 108–09 (2001).

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45. Harris v. KEM Corp., No. 85 Civ. 2127(WK), 1989 WL 200446 (S.D.N.Y. 1989).

46. Guzman v. Exxon Mobile Corp., No. 693-606 (La. 24th Jud. Dist.), *cited in* Howard E. Jarvis, E. Paige Sensenbrenner & Laura K. Whitmore, *Genetics and Genomics: Making the Invisible Visible*, For the Def., Apr. 2015, at 64, 66.

47. Jarvis, Sensenbrenner & Whitmore, *supra* note 46, at 79.

48. Geoffrey C. Hazard Jr., *The Futures Problem*, 148 U. Pa. L. Rev. 1901, 1901 (2000).

49. Metro-North Commuter R.R. Co. v. Buckley, 521 U.S. 424, 433 (1997).

50. *E.g.*, Adams v. Johns-Manville Sales Corp., 783 F.2d 589, 591–93 (5th Cir. 1986).

51. *E.g.*, Ayers v. Twp. of Jackson, 525 A.2d 287, 308 (N.J. 1987).

52. *See* Andrew R. Klein, *A Model for Enhanced Risk Recovery in Tort*, 56 Wash. & Lee L. Rev. 1173, 1179 (1999).

53. *See* Jamie A. Grodsky, *Genomics and Toxic Torts: Dismantling the Risk-Injury Divide*, 59 Stan. L. Rev. 1671 (2007).

54. *See, e.g.*, Bryson v. Pillsbury Co., 573 N.W.2d 718, 720–21 (Minn. Ct. App. 1998).

55. *See* Badillo v. Am. Brands, Inc., 16 P.3d 435, 438–39 (Nev. 2001).

56. *See, e.g.*, Hansen v. Mountain Fuel Supply Co., 858 P.2d 970, 979 (Utah 1993).

57. *See, e.g.*, Christopher H. Schroeder, *Corrective Justice and Liability for Increasing Risks*, 37 UCLA L. Rev. 439 (1990).

58. *See, e.g.*, Metro-North Commuter R.R. Co. v. Buckley, 521 U.S. 424, 442 (1997) ("[T]ens of millions of individuals may have suffered exposure to substances that might justify some form of substance-exposure-related medical monitoring.").

59. Rainer v. Union Carbide Corp., 402 F.3d 608, 621 (6th Cir. 2005) (citations omitted) (internal quotation marks omitted).

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64. Daubert v. Merrell Dow Pharm., Inc., 509 U.S. 579, 580 (1993).

65. Nat'l Research Council, Applications of Toxicogenomic Technologies to Predictive Toxicology and Risk Assessment 191–95 (2007).

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67. *See* Steve C. Gold, *The More We Know, the Less Intelligent We Are? How Genomic Information Should, and Should Not, Change Toxic Tort Causation Doctrine*, 34 Harv. Envtl. L. Rev. 369 (2010).

68. *See* Thomas Parker 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 (2003).

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70. *See* Diane E. Hoffmann & Karen H. Rothenberg, *Judging Genes: Implications of the Second Generation of Genetic Tests in the Courtroom*, 66 Md. L. Rev. 858 (2007).

71. *See* Ronald M. Green & A. Mathew Thomas, *DNA: Five Distinguishing Features for Policy Analysis*, 11 Harv. J.L. & Tech. 571, 572 (1998).

72. Bowen v. E.I. DuPont de Nemours & Co., No. 97C 06-194, 2005 WL 1952859, at *5 (Del. Super. Ct. Aug. 5, 2005).