Genetic Data in Toxic Tort Litigation

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There are major data gaps and uncertainties about the health risks of most potentially toxic substances. When the question focuses in on whether a particular toxic substance caused injury in a specific individual, the data gaps and uncertainties are even greater. Most disease conditions have multiple potential etiologies, and there is usually no direct evidence of which possible cause produced the disease in a specific individual. Moreover, each person is unique in his or her susceptibility to toxic agents, further complicating the inquiry into what caused illness in that individual. Yet, it is precisely into this black hole of ignorance and uncertainty that judges and juries must venture to resolve whether a particular exposure caused an individual plaintiff’s illness. Not surprisingly, the outcome in such toxic tort cases is often uncertain, contentious and unjust.

New genetic methods and data have the potential to fill some of the scientific uncertainties and data gaps in toxic tort litigation, thus making toxic tort litigation more credible, accurate, and fair. At the same time, these same genetic data also have the potential to make toxic tort litigation even more complex, contentious and ethically problematic. One thing is certain, genetic data have the potential to fundamentally transform toxic tort litigation, and is likely to do so over the next decade. Two types of genetic data are likely to have the biggest impact in toxic tort litigation – (i) data on genetic susceptibility of individual plaintiffs, and (ii) genetic biomarkers of exposure and effect. The potential applications of these two types of genetic information in toxic tort litigation, and the potential benefits and risks of such applications, are the subject of this paper.
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, appear to be highly variable between individuals. Genetic variations (“polymorphisms”) that affect susceptibility have been identified for most toxic substances that have received significant regulatory scrutiny. Some of these polymorphisms are very common in the population, while others are rare. For example, almost fifty percent of Caucasians lack a functional copy of the gene coding for the important metabolic enzyme glutathione S-transferase M, increasing their risks to toxic substances such as polycyclic aromatic hydrocarbons (PAHs) and aflatoxin. The Environmental Human Genome Project has identified over 500 putative environmental susceptibility genes, and is now in the process of fully characterizing mutations in these genes conferring susceptibility or resilience to toxic substances in individuals carrying the genes. As discussed below, these findings of genetic susceptibility have many potential applications to toxic torts.

1. Proving or Disproving Causation

Plaintiffs in toxic tort lawsuits must prove that the toxic substances they were exposed to 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. Plaintiffs often cannot meet this demanding requirement, but evidence of genetic susceptibility may assist some susceptible individuals to overcome this hurdle. Even if epidemiology studies show that the relative risk in the general population is less than two, genetically susceptible plaintiffs could argue that their individual risk is higher than the general population due to their susceptibility, and may exceed the two-fold legal threshold.

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1 INTERNATIONAL AGENCY FOR RESEARCH ON CANCER (IARC), METABOLIC POLYMORPHISMS AND SUSCEPTIBILITY TO CANCER, IARC Scientific Publications No. 148 (P. Vineis et al. eds., 1999); Frederica Gemignani et al., A Catalogue of Polymorphisms Related to Xenobiotic Metabolism and Cancer Susceptibility, 12 PHARMACOGENETICS 459 (2002) (identifying 313 known experimentally confirmed polymorphisms in 54 candidate genes affecting cancer susceptibility from exposure to toxic substances).
6 See, e.g., Hall v. Baxter Healthcare Corp., 947 F. Supp. 1387, 1398 n.26 (D. Or. 1996) (even when statistical study shows relative risk less than 2, some plaintiffs may still recover if they can “demonstrate that they differ in some significant way from the subjects of the statistical study”); Daubert v. Merrell Dow Pharmaceuticals, Inc., 43 F.3d 1311, 1321 n.16 (9th Cir. 1995) (“A statistical study showing a relative risk of less than two could be combined with other evidence to show that it is more likely than not that the accused cause is responsible for as particular plaintiff’s injury,” but in that particular case the “plaintiffs’ experts did not seek to differentiate these plaintiffs from the subjects of the statistical studies.”).
Claims of genetic susceptibility have already been advanced by plaintiffs in several cases 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 residing near the Hanford nuclear facility argued that an alleged genetic susceptibility to ionizing radiation justified a five-fold relaxation in the exposure levels they had to prove they were exposed to which corresponded to a doubling of their 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 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.\(^11\)

A case which demonstrates this approach and its potential, even though the result (both scientific and legal) in this particular case was not favorable to the plaintiff, is Easter v. Aventis Pasteur, Inc.\(^12\) The plaintiffs in this case alleged that thimerosal, a mercury preservative in the defendant’s pediatric vaccines, caused Jordan Easter’s autism. The plaintiffs contended that “some children are genetically susceptible to mercury poisoning and cannot excrete or otherwise eliminate the mercury in the vaccine preservative.”\(^13\) Unfortunately for the plaintiff in this case, genetic testing revealed that he did not have the pertinent genetic susceptibility. As described by the court, the plaintiff concedes that he “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 by thimerosal.”\(^14\) This concession was “the beginning and the end” of the court’s ruling to exclude the testimony of the plaintiff’s causation expert.\(^15\) Here then, the genetic test results were decisive for a decision adverse to the plaintiffs, whereas a genetic test result showing that the plaintiff did carry the alleged susceptibility-conferring gene may well have produced a different outcome.

As demonstrated by the Easter case, the absence of the pertinent susceptibility genes in a plaintiff could be used by defendants to buttress their arguments against causation. In addition to testing for the absence of a particular susceptibility gene, a defendant might also seek to test a plaintiff for the presence of other genetic traits that might

\(^7\) V. Leroy Young et al., *HLA Typing in Women with Breast Implants*, 96 PLASTIC & RECONSTRUCTIVE SURGERY 1497, 1508 (1995).


\(^9\) In re Hanford Nuclear Reservation Litig., 1998 WL 775340 (E.D. Wash. 1998), rev’d on other grounds, 292 F.3d 1124 (9th Cir. 2002). See Marchant, supra note 8, at 90-91.

\(^10\) In re Hanford Nuclear Reservation Litig., 1998 WL 775340 *70 (E.D. Wash. 1998), rev’d on other grounds, 292 F.3d 1124 (9th Cir. 2002) (use of susceptibility factor to calculate plaintiffs’ risk from radiation exposure must be rejected because “of the present reality that there is no way to identify persons who are allegedly more susceptible to radiation-induced thyroid cancer, nor can alleged differences in susceptibility be quantified.”); Hall v. Baxter Healthcare Corp., 947 F. Supp. 1387, 1456 (D. Or. 1996). (rejecting introduction of evidence of genetic susceptibility to silicone because the breast implant plaintiffs had failed to show that they carried the specific genes allegedly conferring susceptibility).

\(^11\) See, e.g., Woolf v. Consolidated NDE, Inc., 796 A.2d 906, 908, 912 n.1 (Super. Ct. N.J. 2001) (worker’s compensation claimant successfully demonstrated that occupational exposures most likely caused his leukemia in part by showing that he carried a chromosomal abnormality known as a “Philadelphia chromosome” which made him genetically predisposed to developing leukemia).

\(^12\) 358 F.Supp.2d 576 (E.D. Tex. 2005).

\(^13\) Id. at 575.

\(^14\) Id.

\(^15\) Id. at 579.
predispose the plaintiff to the illness they have developed. Such a finding would support an alternative causation argument, namely, that the plaintiff’s own genotype rather than exposure to the defendant’s toxic substances caused or contributed to the plaintiff’s illness. Such an alternative causation defense based on genetic susceptibility has already been asserted in many cases, but like many genetic claims by plaintiffs, often fails because the claim is not supported by specific evidence that the individual plaintiffs at issue had the relevant genetic variant.16

There are, however, a few known examples where defendants have sought genetic testing of plaintiffs for the purpose of showing potential alternative causes of the claimants’ condition.17 In one case, for example, a chemical company defendant successfully obtained a court order to test for the genetically-determined fragile X syndrome in a mentally-retarded child whose condition was allegedly caused by his mother’s workplace exposure to defendant’s solvents.18 In another case, the defendant obtained genetic testing of a plaintiff whose birth defect was allegedly caused by prenatal exposure to Benlate and 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.19

Genetic traits increasing susceptibility for a particular toxic substance, or creating a predisposition to disease without any environmental exposure, can be used by plaintiffs and defendants respectively to argue for or against causation. The lesson from attempts to use such genetic claims or defense to date is that to be successful, such arguments must be supported by genetic test data from the individual plaintiff showing the presence or absence of the genetic trait at issue. Given the potential usefulness of such genetic data in both 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.20

2. **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

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16 See, e.g., Davanzo v. Fisher, 758 N.Y.S.2d 49, 50 (Sup. Ct. 2003) (upholding dismissal of defendant’s “genetic predisposition defense” because “there was no evidentiary basis for the defense”); Dombrowski v. Gould Electronics, 85 F. Supp.2d. 456, 477 (M.D. Pa. Feb. 3, 2000) (“There is a distinct lack of credible testimony ... showing that genetics or family environments did, in fact cause the difficulties suffered by these individual Plaintiffs.”); Willey v. Ketterer, 869 F.2d 648 (1st Cir. 1989) (defendant’s argument that genetic predisposition caused plaintiff’s cerebral palsy rather than medical malpractice was not supported by valid evidence and hence prejudicial to jury).


18 See Sally Lehman, Pushing Limits of DNA Testing: Suit Prompts Study Into Whether a Birth Defect Was Inherited or Caused by Toxics, S.F. EXAMINER, June 5, 1994, at A1; Marchant, supra note 8, at 99-100. This case settled on terms favorable to the plaintiff when genetic testing of the mother indicated that she did not carry the fragile X trait, and thus the son with the disability who necessarily received his X chromosome from his mother also could not have had the fragile X trait. Id.


“idiosyncratic response” defense. 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.” This defense only applies in strict liability cases, because in negligence cases where the defendant has separately been shown to have acted unreasonably, it is held liable for the unforeseen harm to an unusually susceptible individual under the “eggshell skull” doctrine.

An example of how the idiosyncratic response defense could be applied to genetically susceptible individuals is provided by *Cavallo v. Star Enterprise*, even though the case does not involve genetic susceptibility and does not cite the idiosyncratic response defense by name. In this case, a resident living near a petroleum distribution terminal claimed to be made ill from inhaling fuel vapors released by a spill from the facility. The plaintiff alleged that she was “highly susceptible” to fuel vapors, in part to explain why she was adversely affected while many of her neighbors were not. 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.

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, could cause a chronic autoimmune reaction in approximately thirty percent of the population who carry a specific genetic polymorphism. 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 that vaccine users should obtain a genetic test for the susceptibility gene before taking the vaccine. Although both the manufacturer and federal regulators disputed the factual premises of the lawsuit, the cases were settled before trial and the vaccine was subsequently removed from the market.

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23 See Vosburg v. Putney, 50 N.W. 403, 404 (Wis. 1891) (“the rule of damages in actions for torts . . . [is] that the wrongdoer is liable for all injuries resulting directly from the wrongful act, whether they could or could not have been foreseen by him.”). See also Gary L. Bahr & Bruce N. Graham, *The Thin Skull Plaintiff Concept: Evasive or Persuasive*, 15 LOY. L.A. L. REV. 409 (1982). The eggshell skull doctrine applies only where the defendant has been negligent, and does not apply in strict liability cases. *Id.* at 409; Dahlen v. Gulf Crews, Inc., 281 F.2d 487, 495 (5th Cir. 2002). See also Marchant, supra note 8, at 81-84.
24 100 F.3d 1150 (4th Cir. 1996).
25 *Id.* at 1154.
26 Cassidy v. SmithKline Beecham, Amended Complaint, Class Action, ¶ 10, No. 99-10423, Court of Common Please, Chester County, Pa.) See Holcomb B. Noble, *Concerns Grow Over Reactions To Lyme Shots*, N.Y. TIMES, Nov. 21, 2000, at S1 (class-action lawsuits have also been filed in New York and New Jersey in addition to the original Pennsylvania suit).
27 Cassidy v. SmithKline Beecham, Amended Complaint, ¶¶ 38, 48.
28 Centers for Disease Control and Prevention, *Recommendations for the Use of Lyme Disease Vaccine: Recommendations of the Advisory Committee on Immunization Practices (ACIP)*, 48 (No. RR-7) MORBIDITY & MORTALITY WEEKLY REP. 1, 8 (June 4, 1999) (recognizing potential for autoimmune arthritis reaction in some patients but finding no evidence of such a response in pre-marketing clinical studies); Sarah L. Lathrop et al., *Adverse Event Reports Following Vaccination for Lyme Disease: December 1998-July 2000*, 20 VACCINE 1603-1608 (2002) (Centers for Disease Control and Prevention post-marketing analysis found no increase in adverse reactions from LYMErix vaccine).
These cases are likely the first in what is likely to become an increasingly frequent type of legal claim in which plaintiffs contend that a manufacturer has a duty to identify and warn about genetic susceptibilities to its products.

3. **Other Potential Applications of Genetic Susceptibility Data**

There are several other potential applications of genetic susceptibility data in toxic tort litigation, some of which have already commenced. 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 a potential class action lawsuit to argue against class certification of plaintiffs. Class certification is often critical for a lawsuit to proceed as a practical matter, but requires a finding that common issues that apply to the entire putative class must “predominate” over individual issues. Some defendants have successfully argued that differences in genetic susceptibility to a product requires individualized assessments of risk and causation, thereby helping to defeat the requirement that common issues predominate and resulting in denial of class certification. These initial successes in citing to genetic differences in susceptibility are likely to lead to more common reliance on such an argument by defendants in potential class actions.

Information on a plaintiff’s genetic predisposition to disease could also be used in determining the damages to be paid to a plaintiff that has prevailed on the merits of a lawsuit. A defendant could try to exploit the plaintiff’s genetic predisposition to disease to argue that the damages it must pay 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 their damages discounted accordingly. The most closely analogous precedent are cases where courts have ordered HIV testing of plaintiffs to determine if their life expectancy, and hence damages to which they are entitled, should be discounted because of the likely development of AIDS. Courts will have to determine, likely on a case-by-case basis, whether and under what circumstances defendants can request genetic testing of plaintiffs for the purpose of determining genetic risks affecting life expectancy.

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29 See Manufacturer Discontinues Only Lyme Disease Vaccine, FDA CONSUMER, May 2002, at 5 (“Initially, hundreds of thousands of people received the vaccine. However, sales plummeted after highly publicized reports that some users suffered arthritis-like symptoms, muscle pain and other ailments following vaccination”).


31 Cosentino v. Philip Morris Inc., No. MID-L-5135-97, Opinion of Plaintiffs’ Motion for Reconsideration of Class Certification (Superior Ct. N.J., Feb. 11, 1999) (denying class certification because issue of whether smoking caused a smoker’s illness will require an assessment of each individual smoker’s medical and genetic history); Mahoney v. R.J. Reynolds Tobacco Co., 204 F.R.D. 150, 157 (S.D. Iowa 2001)(denying certification to class of long-time smokers with lung cancer); Reed v. Philip Morris Inc., Civil No. 96-5070, 1997 WL 538921 (D.C. Sup. Ct, Aug. 18, 1997) (denying class certification of all District of Columbia smokers); Lockheed Martin Corp. v. Superior Court, 94 Cal.Rptr.2d 652, 657, 658 (Ct. App. 2000), aff’d, 29 Cal. Rptr.2d 1 (Cal. 2003) (denying class certification for medical monitoring claims brought by residents allegedly put at increased risk from chemical contamination of groundwater, in part because of potential individual differences in health backgrounds of the plaintiffs, including genetic predispositions).

32 E.g., Kegel v. United States, 289 F. Supp. 790 (D. Mont. 1968) (after finding that the plaintiff would have developed the same condition within two years because of a preexisting condition, the court discounted the plaintiff’s recovery to the lost income and pain and suffering that the plaintiff will incur in the two year period immediately following the accident).


34 A trial judge has the discretion to order genetic testing of a plaintiff under Rule 35 of the Federal Rules of Civil Procedure if good cause for such testing is shown. Mark A. Rothstein, Preventing the Discovery of Plaintiff KCP-4455414-1
Genetic Biomarkers of Exposure or Effect

The second major type of genetic information that is likely to be used in toxic tort litigation are genetic biomarkers of exposure or effect. A biomarker is a molecular change in blood or some other tissue of a person exposed to a toxic substance which can be used to qualitatively or quantitatively diagnose the individual’s exposure (biomarker of exposure) or the early, pre-symptomatic progression of the disease process (biomarker of effect). Several types of genetic biomarkers exist. The most commonly used and best-validated, but the least agent-specific, genetic biomarker are chromosomal rearrangements such as translocations. Another type of biomarker involves specific mutations in the genes of an exposed person, which in at least a few cases may be informative of the specific agent that caused the mutation. The most promising types of genetic biomarkers for the future, because of both their potential sensitivity and specificity, are toxicogenomic changes consisting of changes in gene expression, protein concentrations, or metabolite profiles. The discussion below will focus primarily on gene expression changes, whereby toxic chemicals produce characteristic changes in which genes get turned on or off in cells, which can be measured using “microarrays” that measure or compare changes in gene expression following an external stimulus.

1. Proving or Disproving Exposure

Perhaps the most 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 survive summary judgment. For example, in one recent case a New York court dismissed the claims of a gas station worker who developed leukemia after being exposed to benzene in gasoline on a daily basis for seventeen years because he lacked any direct scientific data to quantify his exposure over that time period.

A case demonstrating both the potential and pitfalls of using genetic biomarkers to prove exposure is the litigation brought by residents who developed cancer they claimed was caused by the 1979 Three Mile Island nuclear reactor accident. The plaintiffs in that case 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.”41 Yet, the court ultimately held that the evidence could not be used to prove exposure in that case because while “[r]adiation dose estimation based on dicentric enumeration is a valid and reliable scientific methodology,” the “validity and reliability decrease as the time gap between the alleged irradiation and the dicentric count increases.”42 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 fifteen years after the exposure occurred, which may no longer be reliable.43 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.44

Based on such precedents, gene expression data using microarrays holds considerable promise for helping litigants prove or disprove that sufficient exposure occurred to cause the plaintiff’s injuries.45 Gene expression assays of the plaintiffs’ blood or skin cells may demonstrate the presence (or absence) of gene expression “fingerprints” that are characteristic of the toxic substance to which the plaintiff was allegedly exposed. Such an assay might even be capable of quantifying the level and duration of plaintiff’s exposure. Before being used for this purpose, it will be necessary to adequately validate the gene expression signature, including how such responses vary between different individuals, different tissues within the same individual, different microarray platforms made by different vendors, and different time courses of exposure. For example, most microarray experiments to date have only evaluated the effects of toxic exposure on gene expression for a few days after exposure. Longer-term studies will be needed to validate the gene expression changes that can be expected over many months or years of exposure, which are common for some chronic environmental exposures.46 Notwithstanding these caveats, gene expression microarrays have tremendous potential to provide objective, individualized data on exposure, which both plaintiffs and defendants will be able to use in appropriate cases.

2. General and Specific Causation
Gene expression biomarkers have the potential to help prove or disprove both general and specific causation. Plaintiffs often fail to establish general causation because they are unable to introduce valid scientific data that links the specific toxic agent to which the plaintiff was exposed with the exact health endpoint he or she developed. In the absence of such data, plaintiffs often attempt to use available data that might show that a related substance causes the specific health effect incurred by the plaintiff, or data showing that the toxic agent the plaintiff was exposed to causes other adverse health effects that might involve similar etiologies as the health endpoint that is present in the plaintiff. These attempts to extrapolate general causation from closely related agents or endpoints usually fail as courts require direct evidence linking the specific health endpoint with the specific toxic agent at issue.

The challenge facing plaintiffs in proving general causation is thus much more daunting than, for example, the challenge facing a regulatory agency attempting to regulate the same substance. The regulatory agency need only show that the chemical might cause any adverse health effect in some people. In contrast, a toxic tort plaintiff has the burden of proof to show that the chemical did cause a specific adverse effect (i.e., that from which plaintiff suffers) in a particular individual. “Toxic ignorance,” or the lack of adequate testing data for many potential toxic substances, thus severely limits a plaintiff’s ability to introduce the required data on a specific chemical-health endpoint linkage, given that data evaluating many such potential linkages will often be non-existent.

Gene expression biomarkers may be able to provide the direct evidentiary link needed to extrapolate results from analogous exposures or health endpoints. Unlike traditional toxicological studies such as a chronic bioassay, which can cost millions of dollars and take years to complete, gene expression assays can be undertaken for a few hundred dollars within a day or two. Such quick and inexpensive assays could be used to show that two related substances induce similar toxicological responses at the molecular level, or that two different toxicological endpoints such as two different types of tumors involve similar molecular pathways that can be altered by the same toxic chemical. If valid data using traditional well–accepted toxicological assays exist for the related toxic agent or health endpoint, concordance in gene expression results may allow a related agent or endpoint at issue in a specific lawsuit to “piggyback” on those existing data by showing that the two are indeed related.

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47 General causation concerns whether the toxic agent at issue has the potential to cause a particular health effect in the general population. Specific causation inquires as to whether the toxic agent produced by defendant did in fact cause the adverse health effect in a specific plaintiff.


49 See, e.g., Allen v. Pennsylvania Eng. Corp., 102 F.3d 194, 197 (5th Cir. 1991) (studies showing that a chemical causes cancer in blood cells cannot be used to argue that same chemical causes brain cancer); Lockheed Litigation Cases, 23 Cal.Rptr.3d 762, 774 (Ct. App. 2005) (epidemiology studies showing one group of organic solvents causes disease cannot be used to support conclusion that the solvent plaintiffs were exposed to caused their disease in absence of evidence showing that the solvents share common chemical properties and toxicities); Lynch v. Merrell-National Labs., 830 F.2d 1190, (1st Cir. 1987) (rejecting expert’s reliance on toxicological studies with “analogous chemicals” to show causation); General Electric Co. v. Joiner, 522 U.S. 136, 144 (1997) (study finding that PCBs cause alveologenic adenomas at high concentrations in mice cannot be used to show that PCBs caused plaintiff’s small-cell carcinoma). But see Donaldson v. Central Illinois Public Service Co., 767 N.E.2d 314, 327 (Ill. 2002) (Illinois permits extrapolation between similar but not identical cause and effect relationships in the “limited instances” where science unable to directly establish cause of disease).


52 Courts in several cases have indicated that such extrapolations would be possible if a plaintiff can show that two health endpoints involve similar molecular pathways. See, e.g., Christophersen v. Allied-Signal Corp., 939 F.2d 1106, 1116 n. 10 (5th Cir. 1991) (plaintiff’s attempt to argue, based “on the nature of the biochemical reaction,” that defendant’s chemicals can cause small-cell carcinoma of the lung would be relevant to show the same chemicals can also cause small-cell carcinoma of the colon from which plaintiff suffered rejected because plaintiff
Gene expression data may also be helpful in assessing specific causation. There are no existing types of data that can directly demonstrate that a toxic agent caused illness in a specific individual.53 In the words of one court, “science cannot tell us what caused a particular plaintiff’s injury.”54 Consequently, the tort system currently results on crude, inexact methods to evaluate specific causation such as “differential diagnosis”55 or rules of thumb that an epidemiology study must demonstrate a relative risk greater than two before it will be inferred that it is more likely than not as a statistical matter that the exposure caused the illness incurred by a specific plaintiff.56

Gene expression data may be able to provide for the first time direct data linking exposure to a specific individual with the development or manifestation of a resulting toxic effect in that same individual. Initial studies have demonstrated that toxic substances produce a “unique expression profile.”57 The detection of the specific expression profile in a plaintiff who claims to have been injured by exposure to the relevant toxic substance could provide compelling evidence of specific causation. Alternatively, the failure to detect such a profile in the plaintiff, or the discovery of gene expression profiles for other toxic agents, would argue against specific causation. Defendants have already successfully argued in some cases that the absence in an individual plaintiff of specific types of genetic biomarkers that would allegedly be expected if defendant’s activities were the cause of the plaintiff’s disease vindicates the defendant as not being the cause of the plaintiff’s illness.58

failed to introduce sufficient evidence supporting this alleged biochemical relatedness); Austin v. Kerr-McGee Refining Corp., 25 S.W.2d 280, 288 (Tex. Ct. App. 2000) (plaintiff could not rely on evidence that benzene causes one type of leukemia to show that benzene must also cause a different type of leukemia because plaintiff had failed to show adequately that the two types of leukemia derived from the same genetic mutation).

53 For so-called “signature” diseases that are almost always caused by the same specific exposure, the question of what caused the disease in a particular individual is elementary. Such signature diseases are uncommon, however, and examples include mesothelioma caused by asbestos or clear cell adenocarcinoma caused by the drug DES. See Daniel A. Farber, Toxic Causation, 71 MINN. L. REV. 1219, 1251-52 (1987).

54 Merrell Dow Pharmaceuticals, Inc. v. Havner, 953 S.W.2d 706, 715 (Tex. 1997). See also In re”Agent Orange” Product Liability Litigation, 597 F. Supp. 740, 834 (E.D.N.Y. 1984) (“it may be impossible to pinpoint which particular person’s cancer would have occurred naturally and which would not have occurred but for exposure to the substance.”); Steve Gold, Causation in Toxic Torts: Burdens of Proof, Standards of Persuasion, and Statistical Evidence, 96 YALE L.J. 376, 379 (1986) (“Cancers and mutations provide no physical evidence of the inducing agent, so direct observation of individual plaintiffs provides little or no evidence of causation in many instances.”).

55 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, 1201-29 (2001). Differential diagnosis was described by one court as follows: “a physician begins by ‘ruling in’ all scientifically plausible causes of the plaintiff’s injury. The physician then ‘rules out’ the least plausible causes of injury until the most likely cause remains. The final result of a differential diagnosis is the expert's conclusion that a defendant's product caused (or did not cause) the plaintiff’s injury.” Glastetter v. Novartis Pharmaceuticals Corp., 252 F.3d 986, 989 (8th Cir. 2001).


58 For example, in Wells v. Shell Oil Co., the plaintiff claimed that benzene from defendant’s refinery caused his acute myelogenous leukemia (AML), but the jury was reportedly convinced by 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. See Expert Testimony: Jury Returns Verdict for Oil Company After Testimony on Missing Disease Marker, 22 CHEM. REG. REP. (BNA) 193 (1998).
By shifting the specific causation inquiry from statistical rules of thumb or subjective medical assessments to molecular changes within the plaintiff’s own cells, genetic biomarkers such as gene expression signatures have the potential to make specific causation much more objective and reliable. It may even obviate the need for general causation, because if a party can directly show using gene expression markers that a particular toxic agent caused (or did not cause) his or her toxic response, causation is established without any need to make a separate general causation finding.  

3. 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. 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 “frivolous” or “comparatively unimportant,” as well as to protect defendants from being subjected to “unlimited and unpredictable liability.” For increased risk and fear of disease claims, for example, most courts require the plaintiff to demonstrate a “present injury” as well as to quantify a sufficient increase in risk. 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.

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 present injury. In those

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59 Similarly, there is no general causation requirement in most traumatic injury cases because the general propensity of the technology or action involved is beyond dispute, and the only contested issue is whether it did cause the injury in the specific case. See AMERICAN LAW INSTITUTE, RESTATEMENT OF THE LAW TORTS: LIABILITY FOR PHYSICAL HARM (BASIC PRINCIPLES), TENTATIVE DRAFT NO. 2 (MARCH 25, 2002), § 28 at 102 (“In cases involving traumatic injuries, such as a broken bone following an automobile accident, the absence of other causal sets and better understanding of the causal mechanisms involved moots the necessity for independent proof of general causation beyond the ‘specific causation’ evidence in the case.”).


63 E.g., Ayers v. Township of Jackson, 525 A.2d 287, 308 (N.J. 1987) (rejecting claim for unquantified enhanced risk of disease because of speculative nature of unquantified risk); Abuan v. General Electric Co., 3 F.3d 329, 334 (9th Cir. 1993)(recovery for increased risk only where plaintiff shows that toxic exposure will more likely than not result in disease); Gideon v. Johns-Manville Sales Corp., 761 F.2d 1137-38 (5th Cir. 1985) (increased risk of cancer must be more likely than not to occur for claim to be recognized).


jurisdictions, gene expression changes will provide a powerful new technology for demonstrating subcellular injury. A critical issue in this application of toxicogenomic data will be in distinguishing subcellular changes that are truly representative of a toxic response as opposed to a reversible adaptive response that are not associated with an increased risk to the individual. In the near future, the type and degree of gene expression changes may also be able to be used quantify an individual’s increased risk, thus potentially also helping plaintiffs to meet this requirement much more frequently. The potential of toxicogenomic data to help plaintiffs overcome the existing evidentiary hurdles to increased risk and fear of disease claims is likely to make such claims more viable in many more cases.

Genetic biomarkers are also likely to spur more medical monitoring claims. This type of claim, already recognized in at least seventeen States and the District of Columbia, permits individuals or classes of individuals who have been exposed to a hazardous agent to obtain funds from the responsible defendant to pay for ongoing medical monitoring tests to detect earlier, and hopefully treat more successfully, the onset of clinical disease. While different states have adopted slightly different criteria for such claims, most states require that plaintiffs pursuing such claims must 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.

Gene expression assays could potentially provide a useful diagnostic test that could be used for medical monitoring, or alternatively the abnormal results of a gene expression assay could be used to support a medical monitoring claim involving ongoing monitoring using a more traditional clinical test. In the first situation, the claim would be for funding of ongoing monitoring of gene expression changes that are the early indications that a serious toxicological response is progressing as a result of exposure to a hazardous substance. The gene expression changes of interest here would not be chemical-specific biomarkers of exposure, but rather biomarkers of effect that represent the early manifestations of disease. Detecting the development of such disease at the early, pre-clinical stage in exposed persons would be of value if it permitted more effective and timely interventions.

In the second situation, the gene expression assays would be to identify individuals who had received a hazardous exposure for inclusion within a class of plaintiffs seeking medical monitoring. The relevant biomarker here would be chemical-specific markers of exposure. Individuals who could demonstrate with this type of objective evidence a toxic exposure might qualify for inclusion in a class of individuals seeking financial support for medical monitoring. Individuals lacking the biomarker as revealed by gene expression assays might be excluded from such recovery. In this way, gene expression assays may provide a more accurate and fair measure for determining who should be included in medical monitoring classes and who should not. Of course, the medical monitoring would only be justified under the existing legal standards if the plaintiffs were able to show that the gene expression changes they experienced represented a sufficient increased risk, and if there were a useful diagnostic test available for monitoring the clinical development of disease in such individuals.

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By providing a sensitive and objective pre-clinical marker of risk, gene expression assays 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. And, to the extent other types of latent risk claims (e.g., increased risk and fear of disease claims) can provide compensation to deserving plaintiffs who might otherwise be precluded from recovery when latent diseases manifests years or decades later, such claims might enhance the corrective justice and deterrence goals of tort law.

On the other hand, the increased number of such claims may tax the capacity of courts to handle these cases. 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 the 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.

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 over-running the courts with such claims and to ensure judicial and defendant resources are focused on the most meritorious claims.

Discussion

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 cases, and once such data have been ruled admissible and have affected the outcome in a few notable cases, there is likely to be a flood of

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cases utilizing such data. 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 will create a number of doctrinal, ethical and institutional dilemmas for courts. 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. Judges might look to policy statements on genomic data issued by federal regulatory agencies such as the Environmental Protection Agency and Food and Drug Administration which are currently starting to utilize such data themselves. In addition, the National Academy of Sciences is currently examining potential applications of toxicogenomics, and judges may find guidance provided by this authoritative scientific organization helpful in making admissibility decisions. 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.

Genomic data could also have important consequences for the types of claims brought in toxic tort cases. 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. While it seems unreasonable to require that a manufacturer must protect the most ultra-susceptible 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, scientific evidence 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 coffers while also fulfilling the tort goals that such claims are intended to advance.

Another important set of issues raised by the utility of genomic data are the privacy and discrimination risks to plaintiffs whose genetic information is placed into evidence. 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

74 The NAS project is entitled “Applications of Toxicogenomic Technologies to Predictive Toxicology,” and is expected to issue its report by mid-1996. See http://www4.nas.edu/cp.nsf/Projects%20_by%20PIN/BEST-K-03-09-A?OpenDocument. The author of this article is a member of this NAS committee, but the opinions expressed herein are the author’s individual views and do not necessarily represent the committee’s views.
75 The current controversy over latent risk claims relating to asbestos exposure gives a flavor of the difficult issues to be faced by the proliferation of latent risk claims. See, e.g., 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 (2002) (discussing how the “massive, never-ending que of claimants” litigating latent risk claims for asbestos exposure has “become a tragic chapter in American jurisprudence” and “will remain so unless courts put an end to the madness.”)
There is a certain asymmetry in who would incur these risks in toxic tort litigation in that it will almost always be the plaintiff and not the defendant whose genetic information is relevant, because the cases center on the plaintiff’s health status. Nonetheless, 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, and because plaintiffs have put their health status at issue by bringing the litigation.

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. 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 non-parties. Enactment of pending legislation to provide legal protection against discrimination based on genetic data would also be helpful. 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.

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76 See Ronald M. Green & A. Mathew Thomas, DNA: Five Distinguishing Features for Policy Analysis, 11 Harv. J. L. & Tech. 571, 572 (1998) (describing “informational risks” from finding out genetic information about one’s self that a person may prefer not to know).

77 See supra notes 12-15 and accompanying text.

78 Id. The trial judge initially denied defendant’s motion for genetic testing of the plaintiff, but then agreed to the testing over the plaintiff’s objection on a motion for reconsideration. Bowen v. E.I. Dupont, 2005 WL 1952859 *5.

79 See Marchant, supra note 8, at 106-108; Rothstein, supra note 34, at 900-01; Niedwiecki, supra note 33, at 345-46.

80 H.R. 1227, the Genetic Information Nondiscrimination Act of 2005.