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GENETIC DATA IN TOXIC TORT LITIGATION

*Gary E. Marchant**

INTRODUCTION

There are major data gaps and uncertainties about the health risks of most potentially toxic substances. When the question in a toxic tort case is 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,

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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 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. Courts can expect this significant transformation to take place 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. This paper 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.

I. 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.¹ Genetic variations (“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 fifty percent of Caucasians lack a

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).

² Gary E. Marchant, *Genomics and Toxic Substances: Part II - Genetic Susceptibility to Environmental Agents*, 33 ENVTL. L. REP. 10641, 10644-45 (2003) [hereinafter Marchant, *Genomics and Toxic Substances*].

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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.³ 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.⁴ 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 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

³ 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); Radim J. Sram, *Effect of Glutathione S-Transferase M1 Polymorphisms on Biomarkers of Exposure and Effects*, 106 ENVTL. HEALTH PERSP. 231, 231-32 (1998). Polycyclic aromatic hydrocarbons (PAHs) are a group of over 100 different chemicals that are formed from the incomplete combustion of coal, oil, gas, garbage, tobacco and charbroiled meat. Aflatoxins are naturally occurring carcinogens produced by certain species of fungus that are toxic and carcinogenic to animals, and can contaminate nuts, cereal grains, and spices, as well as the milk of cows that eat contaminated crops.

⁴ Jocelyn Kaiser, *Tying Genetics to the Risk of Environmental Diseases*, 300 SCIENCE 563 (2003); Julie Wakefield, *Environmental Genome Project: Focusing on Differences to Understand the Whole*, 110 ENVTL. HEALTH PERSP. A757, A758 (2002). The website for the Environmental Genome Project is at <http://www.niehs.nih.gov/envgenom/home.htm>.

⁵ See, e.g., *Daubert v. Merrell Dow Pharm., Inc.*, 43 F.3d 1311, 1321 (9th Cir. 1995); *Hall v. Baxter Healthcare Corp.*, 947 F. Supp. 1387, 1403-04 (D. Or. 1996). See Russellyn S. Carruth & Bernard D. Goldstein, *Relative Risk Greater Than Two in Proof of Causation in Toxic Tort Litigation*, 41 JURIMETRICS J. 195

requirement.⁶ 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 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.⁷

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 silicone⁸ 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.⁹ Similarly, thyroid cancer victims living near the Hanford nuclear facility argued that 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 five-fold reduction in the exposure levels necessary to double background

(2001) (listing cases that require relative risk > 2.0 and those that do not).

⁶ Carruth & Goldstein, *supra* note 5.

⁷ See, e.g., *Hall*, 947 F. Supp. at 1398 n.26 (stating that even when statistical study shows relative risk less than two, some plaintiffs may still recover if they can “demonstrate that they differ in some significant way from the subjects of the statistical study”); *Daubert*, 43 F.3d at 1321 n.16 (“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 this particular case the “plaintiffs’ experts did not seek to differentiate these plaintiffs from the subjects of the statistical studies.”).

⁸ V. Leroy Young et al., *HLA Typing in Women with Breast Implants*, 96 PLASTIC & RECONSTRUCTIVE SURGERY 1497, 1508 (1995).

⁹ See *Hall*, 947 F. Supp. at 1456; Ernest H. Hornsby & Dianna Pendleton, *Plaintiffs’ Mounting Case Against Silicone Gel Breast Implants*, 6 MEDICAL-LEGAL ASPECTS OF BREAST IMPLANTS 4, 5 (1998); Gary E. Marchant, *Genetic Susceptibility and Biomarkers in Toxic Injury Litigation*, 41 JURIMETRICS J. 67, 91-92 (2000) [hereinafter Marchant, *Genetic Susceptibility*].

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risk.¹⁰ 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.¹¹ To prevail on such arguments in the future, plaintiffs will likely need to undergo genetic testing to substantiate their claims of genetic susceptibility.¹²

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 Pastuer, Inc.*¹³ The plaintiffs in this case alleged that thimerosal, a mercury preservative in the defendant's pediatric vaccines, caused their son, 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."¹⁴ 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

¹⁰ *In re Hanford Nuclear Reservation Litig.*, 1998 WL 775340 (E.D. Wash. 1998). See Marchant, *Genetic Susceptibility*, *supra* note 9, at 90-91.

¹¹ *Hanford*, 1998 WL 775340, at *70 (explaining that the 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).

¹² See, e.g., *Woolf v. Consolidated NDE, Inc.*, 796 A.2d 906, 908, 912 n.1 (N.J. Super. Ct. 2001) (holding that the 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).

¹³ 358 F. Supp. 2d 576 (E.D. Tex. 2005).

¹⁴ *Id.* at 575.

children who . . . are at increased risk for developing autism by thimerosal.”¹⁵ This concession was “the beginning and the end” of the court’s ruling to exclude the testimony of the plaintiff’s causation expert.¹⁶ In this case, the genetic test results were decisive for a decision adverse to the plaintiffs, whereas genetic test results showing that the plaintiff did carry the alleged susceptibility-conferring gene may well have produced a different outcome.

As demonstrated by the *Easter* case, defendants might use the absence of the pertinent susceptibility genes in a plaintiff to buttress their arguments against causation. Additionally, defendants could also seek to test plaintiffs for the presence of other genetic traits that might predispose the plaintiffs to the illnesses they have developed. Defendants would use such findings to support alternative causation arguments, namely, that the plaintiffs’ own genotypes, rather than exposure to the defendants’ toxic substances, caused or contributed to the plaintiffs’ illnesses. Some defendants have already asserted such alternative causation defenses based on genetic susceptibility, but like many genetic claims by plaintiffs, these defenses often fail because the claims are not supported by specific evidence that the individual plaintiffs at issue had the relevant genetic variant.¹⁷

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.¹⁸ In one

¹⁵ *Id.*

¹⁶ *Id.* at 579.

¹⁷ *See, e.g.,* Willey v. Ketterer, 869 F.2d 648 (1st Cir. 1989) (finding that the 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); 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 Elecs., 85 F. Supp. 2d. 456, 477 (M.D. Pa. 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.”).

¹⁸ In one high-profile case, the Burlington-Northern Railway secretly genetically tested workers for a genetic trait that allegedly could be an

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case, 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.¹⁹ 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.²⁰

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. The lesson learned from attempts to use such genetic claims or defenses 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

alternative cause of the workers' carpal tunnel syndrome. See Equal Employment Opportunity Comm'n v. Burlington N. Santa Fe R.R., No. C01-4013 MWB, settlement reached (N.D. Iowa, Apr. 17, 2001); Tamar Lewin, *Commission Sues Railroad to End Genetic Testing in Work Injury Cases*, N.Y. TIMES, Feb. 10, 2001, at A10. See also Bourkney v. New York Infirmiry-Beekman Downtown (N.Y. Sup. Ct. 2002), reported at 228 N.Y.L.J. 18 (Nov. 19, 2002) (granting defendant hospital's motion to compel genetic testing of plaintiff in medical malpractice case).

¹⁹ See Sally Lehrman, *Pushing Limits of DNA Testing: Suit Prompts Study Into Whether a Birth Defect Was Inherited or Caused by Toxics*, SAN FRANCISCO EXAMINER, June 5, 1994, at A1; Marchant, *Genetic Susceptibility*, *supra* note 9, 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.*

²⁰ Bowen v. E.I. Du Pont de Nemours & Co., No. Civ. 97C-06-194 CH, 2005 WL 1952859 (Del. Super. Ct. Aug. 5, 2005).

defendants to seek genetic testing of plaintiffs in order to identify potential alternative causes.²¹

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 “idiosyncratic response” defense.²² 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

²¹ 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, a lawyer/doctor who at the time was Executive Director of the Eunice Kennedy Shriver Center for Mental Retardation and is now CEO of Interleuken Genetics, Inc.).

²² See Marchant, *Genetic Susceptibility*, *supra* note 9, at 80-84; John Gerald Gleeson, *Idiosyncrasy: A Developing Defense in Drug and Hazardous Substances Litigation*, FOR THE DEFENSE, Apr. 1989, at 9; Joseph J. Ortego et al., *Idiosyncratic Reactions: A Limitation on the Duty to Warn*, 8-14 MEALEY'S EMERGING TOXIC TORTS 35, Oct. 20, 1999. The idiosyncratic response 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. See *Vosburg v. Putney*, 50 N.W. 403, 404 (Wis. 1891) (“[T]he 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.

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hypersensitive individuals.”²³

An example of how the idiosyncratic response defense could be applied to genetically susceptible individuals is provided by *Cavallo v. Star Enterprise*,²⁴ though the case itself 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 she became ill from inhaling fuel vapors released by a spill from the facility.²⁵ 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.²⁶ The Court of Appeals for the Fourth Circuit 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.²⁷

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 thirty percent of the population who carry a specific genetic polymorphism.²⁸ The

²³ *Bingham v. Terminix Int’l Co.*, 896 F. Supp. 642, 645 (S.D. Miss. 1995). In this case, a homeowner who allegedly developed asthma as a result of termiticides applied in his home alleged that the manufacturer and applicator of the termiticide had a duty to protect “hypersensitive” individuals such as himself. *Id.*

²⁴ 100 F.3d 1150 (4th Cir. 1996).

²⁵ *Id.* at 1153.

²⁶ *Id.* at 1154.

²⁷ *Id.*

²⁸ Amended Complaint at ¶ 10, *Cassidy v. SmithKline Beecham Corp.*, No. 99-10423, 2003 WL 22216528 (Pa. Com. Pl. July 1, 2003). *See also* Holcomb B. Noble, *Concerns Grow Over Reactions To Lyme Shots*, N.Y. TIMES, Nov. 21,

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.²⁹ Although both the manufacturer and federal regulators disputed the factual premises of the lawsuit,³⁰ the cases were settled before trial and the vaccine was subsequently removed from the market.³¹ 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.

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 arguing against

2000, at F1 (reporting that class-action lawsuits have also been filed in New York and New Jersey in addition to the original Pennsylvania suit).

²⁹ Amended Complaint at ¶¶ 38, 48, *Cassidy*, No. 99-10423.

³⁰ See CENTERS FOR DISEASE CONTROL AND PREVENTION, *Recommendations for the Use of Lyme Disease Vaccine*, MORBIDITY & MORTALITY WEEKLY REP.: RECOMMENDATIONS & REPORTS 1, 8 (1999), available at <http://www.cdc.gov/mmwr/PDF/RR/RR4807.pdf> (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: Dec. 1998-July 2000*, 20 VACCINE 1603-08 (2002) (describing how the Centers for Disease Control and Prevention post-marketing analysis found no increase in adverse reactions from LYMERix vaccine).

³¹ See *Manufacturer Discontinues Only Lyme Disease Vaccine*, FDA CONSUMER, May-June 2002, at 5, available at http://www.fda.gov/fdac/departs/2002/302_upd.html#lyme (“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.”).

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class certification of plaintiffs in a potential class action lawsuit. As a practical matter, class certification is often critical for a lawsuit to proceed, but certification requires a finding by the court that the common issues that apply to the entire putative class “predominate” over individual issues.³² 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, resulting in denial of class certification.³³ These initial successes in citing to genetic differences in susceptibility will likely result in more defendants relying on such arguments in future potential class actions.

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 that 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 their damages discounted accordingly.³⁴ The most closely analogous precedent are cases

³² FED. R. CIV. P. 23(b)(3).

³³ *Mahoney v. R.J. Reynolds Tobacco Co.*, 204 F.R.D. 150, 161 (S.D. Iowa 2001) (denying certification to class of long-time smokers with lung cancer); *Lockheed Martin Corp. v. Super. Ct.*, 94 Cal. Rptr. 2d 652, 657-58 (Cal. Ct. App. 2000) (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); *Cosentino v. Philip Morris Inc.*, No. MID-L-5135-97, 1998 WL 34168879, at *10 (N.J. Super. Ct. Feb. 11, 1999) (Opinion of Plaintiffs’ Motion for Reconsideration of Class Certification) (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); *Reed v. Philip Morris Inc.*, Civil No. 96-5070, 1997 WL 538921 (D.C. Super. Ct. Aug. 18, 1997) (denying class certification of all District of Columbia smokers).

³⁴ *E.g.*, *Kegel v. United States*, 289 F. Supp. 790 (D. Mont. 1968) (holding that the plaintiff’s recovery should be discounted to the lost income and pain and

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.³⁵ 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.³⁶

II. 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 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).³⁷ 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.³⁸ Another

suffering that the plaintiff will incur in the two year period immediately following the accident after finding that the plaintiff would have developed the same condition within two years because of a preexisting condition).

³⁵ *Pettyjohn v. Goodyear Tire & Rubber Co.*, No. Civ.A. 91-CV-2681, 1992 WL 105162 (E.D. Pa. Apr. 29, 1992) (ordering HIV testing); *Agosto v. Trusswal Sys. Corp.*, 142 F.R.D. 118 (E.D. Pa. 1992) (ordering disclosure of HIV test results). See also 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).

³⁶ 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 Genetic Profiles by Defendants Seeking to Limit Damages in Personal Injury Litigation*, 71 IND. L.J. 877, 889-91 (1996); Marchant, *Genetic Susceptibility*, *supra* note 9, at 106-07.

³⁷ Anthony P. Decaprio, *Biomarkers: Coming of Age for Environmental Health and Risk Assessment*, 31 ENVTL. SCI. & TECH. 1837, 1838 (1997).

³⁸ James D. Tucker, *Use of Chromosome Translocations for Measuring Prior Environmental Exposures in Humans*, in BIOMARKERS: MEDICAL AND WORKPLACE APPLICATIONS 117-32 (Mortimer L. Mendelsohn et al., eds., 1998),

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type of biomarker involves specific mutations in the genes of an exposed person, which may be informative of the specific agent that caused the mutation.³⁹ 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.⁴⁰ The discussion below focuses 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 compare changes in gene expression following an external stimulus.⁴¹

1. Proving or Disproving Exposure

Perhaps the most promising application of genetic biomarkers in toxic tort litigation is in demonstrating and even quantifying

available at <http://www.nap.edu/openbook/0309064228/html117/html>. A translocation involves the breakage and removal of a large segment of DNA from one chromosome, followed by the segment's attachment to a different chromosome. See NATIONAL INSTITUTES OF HEALTH, NATIONAL HUMAN GENOME RESEARCH INSTITUTE TALKING GLOSSARY OF GENETIC TERMS, <http://www.genome.gov/glossary.cfm?key=translocation>.

³⁹ See, e.g., Ian 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); Steven J. Smith et al., *Molecular Epidemiology of p53 Protein Mutations in Workers Exposed to Vinyl Chloride*, 147 AM. J. EPIDEMIOLOGY 302, 302–03 (1998). See generally Gary E. Marchant, *Genetics and Toxic Torts*, 31 SETON HALL L. REV. 949, 971-72 (2001).

⁴⁰ 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); NAT'L RESEARCH COUNCIL, TOXICOGENOMIC TECHNOLOGIES AND RISK ASSESSMENT OF ENVIRONMENTAL CARCINOGENS: A WORKSHOP SUMMARY (2005), available at <http://www.nap.edu/openbook/0309097002/html/R1/html> [hereinafter *Impact of “-Omics” Technologies*].

⁴¹ Emile F. Nuwaysir et al., *Microarrays and Toxicology: The Advent of Toxicogenetics*, 24 MOLECULAR CARCINOGENESIS 153 (1999); *Impact of “-Omics” Technologies*, *supra* note 40, at 13.

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.⁴² 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.⁴³

A case demonstrating both the potential for, and pitfalls of, using genetic biomarkers to prove exposure is the litigation involving the 1979 Three Mile Island nuclear reactor accident.⁴⁴ The plaintiffs, nearby residents who developed cancer,⁴⁵ 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 Court of Appeals for the Third Circuit 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

⁴² *E.g.*, *Mitchell v. Gencorp Inc.*, 165 F.3d 778, 781 (10th Cir. 1999); *Allen v. Pa. Eng’g Corp.*, 102 F.3d 194, 197 (5th Cir. 1996); *Wright v. Williamette Indus., Inc.*, 91 F.3d 1105, 1107 (8th Cir. 1996). *But see* *Westberry v. Gislaved Gummi AB*, 178 F.3d 257, 264 (4th Cir. 1999) (holding that plaintiff is not required to quantify toxic exposures because “only rarely are humans exposed to chemicals in a manner that permits a quantitative determination of adverse outcomes”).

⁴³ *Parker v. Mobil Oil Corp.*, 793 N.Y.S.2d 434, 437-38 (N.Y. App. Div. 2005).

⁴⁴ *In re TMI Litigation*, 193 F.3d 613, 622 (3d Cir. 1999).

⁴⁵ *Id.*

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for estimating radiation dose to the individual.”⁴⁶ 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.”⁴⁷ 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.⁴⁸ 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.⁴⁹

⁴⁶ *Id.* at 690.

⁴⁷ *Id.* at 692.

⁴⁸ *Id.*

⁴⁹ As biomarkers become more available, courts are increasingly likely to require such evidence to prove exposure. In one recent unreported California case, the court (arguably somewhat over-exuberantly) suggested just such a requirement for biomarker evidence:

According to [defendant’s expert] Dr. Ordog, there are biological tests (biomarkers) that measure the levels of chemicals in the body to reveal whether these levels can exceed expected or accepted levels. Biomarkers can be performed utilizing blood, urine or fat samples taken from a live patient or at autopsy. Such markers can test for 180,000 different chemicals, including the chemicals to which plaintiffs claim Mr. Cord [the plaintiff] was exposed resulting in his cancer. Dr. Ordog testified that because no such tests were performed on Mr. Cord, ‘it is impossible to determine to a medical certainty’ whether Mr. Cord’s exposure, absorption or toxicity to benzene or other chemicals exceeded normal and expected levels. In other words, existing tests were available to measure whether Mr. Cord in fact had excessive exposure to benzene and other chemicals, but plaintiffs’ experts did not use them.

Cord v. City of Los Angeles, 2004 WL 2189182, at *9 (Cal. App. Sept. 30, 2004).

Based on such precedents, gene expression data using microarrays holds considerable promise for helping litigants prove or disprove that sufficient exposure occurred to cause particular injuries.⁵⁰ 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.⁵¹ Such an assay might even be capable of quantifying the level and duration of plaintiff's exposure.⁵² 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.⁵³ 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.

⁵⁰ See Gary E. Marchant, *Toxicogenomics and Toxic Torts*, 20 TRENDS IN BIOTECH. 329, 330 (2002) [hereinafter Marchant, *Toxicogenomics and Toxic Torts*].

⁵¹ Matthew Bartosiewicz, Sharron Penn & Alan Buckpitt, *Applications of Gene Arrays in Environmental Toxicology: Fingerprints of Gene Regulation Associated with Calcium Chloride, Benzo(a)pyrene, and Trichloroethylene*, 109 ENVTL. HEALTH PERSPECT. 71, 73-74 (2001); Hisham K. Hamadeh et al., *Prediction of Compound Signature Using High Density Gene Expression Profiling*, 67 TOXICOL. SCI. 232 (2002).

⁵² Marchant, *Toxicogenomics and Toxic Torts*, *supra* note 50, at 330.

⁵³ See Carol J. Henry et al., *Use of Genomics in Toxicology and Epidemiology: Findings and Recommendations of a Workshop*, 110 ENVTL. HEALTH PERSPECT. 1047, 1049 (2002) [hereinafter *Findings and Recommendations of a Workshop*] ("An additional challenge [of toxicogenomic methods] is to examine gene expression at the time period that is relevant to the health outcome of interest.").

GENETIC DATA IN TOXIC TORT LITIGATION 23*2. General and Specific Causation*

Gene expression biomarkers have the potential to help prove or disprove both general and specific causation.⁵⁴ 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.⁵⁵ 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.⁵⁶

⁵⁴ 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.

⁵⁵ See Daniel J. Capra, *The Daubert Puzzle*, 32 GA. L. REV. 699, 715-19 (1998).

⁵⁶ See, e.g., *Gen. Elec. Co. v. Joiner*, 522 U.S. 136, 144 (1997) (discussing a 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); *Allen v. Pa. Eng'g Corp.*, 102 F.3d 194, 197 (5th Cir. 1991) (discussing studies showing that a chemical causes cancer in blood cells cannot be used to argue that same chemical causes brain cancer); *Lynch v. Merrell-Nat'l Labs*, 830 F.2d 1190, 1194 (1st Cir. 1987) (rejecting expert's reliance on toxicological studies with "analogous chemicals" to show causation); *Lockheed Litig. Cases*, 23 Cal. Rptr. 3d 762, 774 (Cal. Ct. App. 2005) (stating that 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). *But see Donaldson v. Cent. Ill. Pub. Serv. Co.*, 767 N.E.2d 314, 328 (Ill. 2002) (explaining that Illinois permits extrapolation between similar but not identical cause and effect relationships in the "limited instances" where science is unable to directly establish cause of disease).

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.⁵⁷ In contrast, a toxic tort plaintiff has the burden of proving that the chemical *did* cause a *specific* adverse effect (i.e., that from which plaintiff suffers) in a particular individual. “Toxic ignorance,”⁵⁸ 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.

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.⁵⁹ Plaintiffs could use such quick and inexpensive assays 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, the plaintiff may be able to ‘piggyback’ on those existing studies. Concordance in gene

⁵⁷ For example, EPA may regulate a toxic chemical under the Toxic Substances Control Act (TSCA) if it finds that there is “a reasonable basis to conclude” that the chemical “presents or will present” an “unreasonable risk” of injury to members of the public. 15 U.S.C. § 2605(a) (2005).

⁵⁸ ENVTL. DEFENSE FUND, TOXIC IGNORANCE, THE CONTINUING ABSENCE OF BASIC HEALTH TESTING FOR TOP SELLING CHEMICALS IN THE UNITED STATES (1997), http://www.environmentaldefense.org/documents/243_toxicignorance.pdf; GOV’T ACCOUNTABILITY OFFICE, CHEMICAL REGULATION: OPTIONS EXIST TO IMPROVE EPA’S ABILITY TO ASSESS HEALTH RISKS AND MANAGE ITS CHEMICAL REVIEW PROGRAM (2005), <http://www.gao.gov/new.items/d05458.pdf>.

⁵⁹ See Gary E. Marchant, *Genomics and Toxic Substances: Part I—Toxicogenomics*, 33 ENVTL. L. REP. 10071, 10082-83 (2003).

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expression results may show that the related agent or endpoint at issue in plaintiff's case is indeed related to the better studied related agent.⁶⁰

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.⁶¹ In the words of one court, "science cannot tell us what caused a particular plaintiff's injury."⁶² Consequently, the tort system currently relies on crude, inexact methods to evaluate specific causation. For example, courts rely on "differential

⁶⁰ 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.16 (5th Cir. 1991) (rejecting 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, because plaintiff failed to introduce sufficient evidence supporting this alleged biochemical relatedness); Austin v. Kerr-McGee Refining Corp., 25 S.W.3d 280, 288 (Tex. Ct. App. 2000) (holding that the 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).

⁶¹ For so-called signature diseases, which 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).

⁶² Merrell Dow Pharms., Inc. v. Havner, 953 S.W.2d 706, 715 (Tex. 1997). *See also In re "Agent Orange" Product Liab. Litig.*, 597 F. Supp. 740, 834 (E.D.N.Y. 1984) ("[I]t 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.").

diagnosis,”⁶³ or require that an epidemiology study demonstrate a relative risk greater than two, before the fact finder can infer that it is more likely than not as a statistical matter that the exposure caused the illness incurred by a specific plaintiff.⁶⁴

Gene expression data may be able to provide for the first time direct data linking a specific individual’s exposure to 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.”⁶⁵ 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, supports arguments against specific causation. In at least one case, a defendant successfully argued that the plaintiff lacked the specific types of genetic biomarkers that would allegedly be present if

⁶³ 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). 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 Pharm. Corp.*, 252 F.3d 986, 989 (8th Cir. 2001).

⁶⁴ Edward J. Imwinkelried, *The Admissibility and Legal Sufficiency of Testimony about Differential Diagnosis (Etiology): of Under- and Over-Estimations*, 56 BAYLOR L. REV. 391, 397-405 (2004); Carruth & Goldstein, *supra* note 5, at 195-202.

⁶⁵ See, e.g., Jeffrey F. Waring et al., *Microarray Analysis of Hepatotoxins in Vitro Reveals a Correlation Between Gene Expression Profiles and Mechanisms of Toxicity*, 120 TOXICOL. LETT. 359, 367 (2001). See also Hisham K. Hamadeh et al., *Prediction of Compound Signature Using High Density Gene Expression Profiling*, 67 TOXICOL. SCI. 232 (2002) (discussing how microarray analysis was able to correctly identify 22 of 23 blinded chemicals based on their gene expression profiles).

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defendant's activities had caused the disease.⁶⁶

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 significantly 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, that party establishes causation without any need to make a separate general causation finding.⁶⁷

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

⁶⁶ For example, in *Wells v. Shell Oil Co.*, the plaintiff claimed that benzene from defendant's refinery caused his acute myleogenous 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).

⁶⁷ 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 RESTATEMENT (THIRD) OF TORTS: LIABILITY FOR PHYSICAL HARM (BASIC PRINCIPLES), § 28 cmt. c(3) (Tentative Draft No. 2, March 25, 2002) ("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.").

described as the most difficult problem confronting toxic torts.⁶⁸ 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.”⁶⁹ In increased risk and fear of disease claims, for example, most courts require the plaintiff to demonstrate a “present injury”⁷⁰ as well as to quantify a sufficient increase in risk.⁷¹ 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.⁷²

⁶⁸ Geoffrey C. Hazard, *The Futures Problem*, 148 U. PA. L. REV. 1901, 1901 (2000) (“Perhaps the most difficult problem in addressing mass torts is that of future claimants.”); Richard W. Wright, *Causation, Responsibility, Risk, Probability, Naked Statistics, and Proof: Pruning the Bramble Bush by Clarifying the Concepts*, 73 IOWA L. REV. 1001, 1067 (1988) (“[T]he most problematic area of current tort practice [involves] cases involving liability for risk exposure.”).

⁶⁹ *Metro-North Commuter R.R. Co. v. Buckley*, 521 U.S. 424, 433 (1997) (explaining how courts generally deny recovery for latent risk claims because of policy concerns about defendants being subjected to “unlimited and unpredictable liability” and courts being overwhelmed with a “flood of comparatively unimportant claims”).

⁷⁰ *E.g.*, *Adams v. Johns-Manville Sales Corp.*, 783 F.2d 589, 591-93 (5th Cir. 1986); *Anderson v. W.R. Grace & Co.*, 628 F. Supp. 1219, 1226-27 (D. Mass. 1986).

⁷¹ *E.g.*, *Abuan v. General Elec. Co.*, 3 F.3d 329, 334 (9th Cir. 1993) (holding that recovery is possible 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 1129, 1137-38 (5th Cir. 1985) (holding that increased risk of cancer must be more likely than not to occur for claim to be recognized); *Ayers v. Twp. of Jackson*, 525 A.2d 287, 308 (N.J. 1987) (rejecting a claim for unquantified enhanced risk of disease because of speculative nature of unquantified risk).

⁷² *See, e.g.*, *Brafford v. Susquehanna Corp.*, 586 F. Supp. 14, 18 (D. Col. 1984) (“[T]he inability to precisely quantify the extent of present damage to the chromosomes is a function of medical technology’s inability to make such a measure.”); Andrew R. Klein, *A Model for Enhanced Risk Recovery in Tort*, 56 WASH. & LEE L. REV. 1173, 1179 (1999) (examining how threshold

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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.⁷³ In those 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 is not associated with an increased risk to the individual.⁷⁴ In the near future, the type and degree of gene expression changes may be used in quantifying an individual’s increased risk. Increased risk and fear of disease claims will likely become more sustainable in future cases due to toxicogenomic data’s potential to help plaintiffs overcome evidentiary hurdles to these type claims.

Genetic biomarkers are also likely to spur more medical monitoring claims, which are already recognized in at least seventeen States and the District of Columbia.⁷⁵ In order to make

requirements imposed by courts create “a nearly insurmountable barrier for enhanced risk plaintiffs”).

⁷³ See, e.g., *Anderson*, 628 F. Supp. at 1226-27 (explaining that a present injury must be “manifested by objective symptomatology,” but subcellular injuries could meet this standard if they were “objectively evidenced”); *Brafford*, 586 F. Supp. at 17-18 (denying summary judgment against plaintiff who relied on an inference that he must have incurred subcellular chromosomal damage from radiation exposure); *Bryson v. Pillsbury Co.*, 573 N.W.2d 718, 720-21 (Minn. Ct. App. 1998) (noting that asymptomatic, subcellular injury may constitute a legally recognized present injury). Other jurisdictions have held that subclinical effects cannot constitute a present injury. See, e.g., *Dodge v. Cotter Corp.*, 203 F.3d 1190, 1202 (10th Cir. 2000) (requiring evidence of “a chronic objective condition caused by their increased risk of developing cancer” to permit recovery for emotional distress damages); *Schweitzer v. Consolidated Rail Corp.*, 758 F.2d 936, 942 (3d Cir. 1985) (holding that subclinical injury insufficient for recovery); *In re Hawaii Federal Asbestos Cases*, 734 F. Supp. 1563, 1567 (D. Hawaii 1990) (requiring “an objectively verifiable functional impairment”).

⁷⁴ *Findings and Recommendations of a Workshop*, *supra* note 53, at 1049.

⁷⁵ See *Badillo v. Am. Brands, Inc.*, 16 P.3d 435, 438-39 (Nev. 2001)

such a claim an individual or class of individuals must have been exposed to a hazardous agent.⁷⁶ A successful plaintiff is typically awarded 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.⁷⁷ 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.⁷⁸

Gene expression assays could potentially provide a valuable diagnostic test that could be used for medical monitoring. Alternatively, the abnormal results of a gene expression assay could be used to support a medical monitoring claim requesting continuous traditional clinical testing. 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 valuable if it permitted more effective and timely interventions.

In the second situation, individuals whose gene expression assays identified them as having been hazardously exposed would be included within a class of plaintiffs seeking financial support for medical monitoring. The relevant biomarker here would be

(surveying medical monitoring case law).

⁷⁶ Victor E. Schwartz, Leah Lorber & Emily J. Laird, *Medical Monitoring: The Right Way and the Wrong Way*, 70 MO. L. REV. 349, 350 (2005).

⁷⁷ *Id.* at 353-54.

⁷⁸ See, e.g., *In re Asbestos Cases*, 265 F.3d 861, 866 (9th Cir. 2001); *In re Paoli R. Yard PCB Litig.*, 916 F.2d 829, 852 (3d Cir. 1990); *Hansen v. Mountain Fuel Supply Co.*, 858 P.2d 970, 979 (Utah 1993).

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chemical-specific markers of exposure. 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 the disease in such individuals.

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. 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 manifests years or decades later, such claims might enhance the corrective justice and deterrence goals of tort law.⁷⁹

On the other hand, one concern with an increased number of such claims is the limited capacity of courts to handle these cases.⁸⁰ The Court of Appeals for the Sixth Circuit recently noted

⁷⁹ See, e.g., David Gerecke, *Risk Exposure as Injury: Alleviating the Injustice of Tort Causation Rules*, 35 MCGILL L. J. 797 (1990); Christopher H. Schroeder, *Corrective Justice and Liability for Increasing Risks*, 37 UCLA L. REV. 439 (1990). But see Stephen R. Perry, *Risk, Harm, and Responsibility*, in PHILOSOPHICAL FOUNDATIONS OF TORT LAW 321, 330-39 (David G. Owen ed., 1995) (arguing against cause of action for risk in absence of symptomatic injury).

⁸⁰ 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.”); *In re Rezulin Prod. Liab. Litig.*, 365 F. Supp. 2d 268, 275

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.⁸¹

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 deserving claims.

(S.D.N.Y. 2005) (declining to recognize asymptomatic subcellular harm as a present injury in part because of concerns about impacts on the legal system’s limited resources); *Henry v. The Dow Chem. Co.*, 701 N.W.2d 684, 696 (Mich. 2005) (rejecting recognition of medical monitoring claims in Michigan because of potential for flood of litigation and harm to the state’s economy).

⁸¹ *Rainer v. Union Carbide Corp.*, 402 F.3d 608, 621 (6th Cir. 2005) (quotations and citations omitted). *See also* Andrew R. Klein, *Fear of Disease and the Puzzle of Futures Cases in Tort*, 35 U.C. DAVIS L. REV. 965, 966 n.2 (2002) (collecting statistics on large percentages of population who have been exposed to various toxic agents); Arvin Maskin, Konrad L. Cailteux & Joanne M. McLaren, *Medical Monitoring: A Viable Remedy for Deserving Plaintiffs or Tort Law’s Most Expensive Consolation Prize?*, 27 WM. MITCHELL L. REV. 521, 528 (2000) (listing toxic exposures which most Americans have experienced).

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III. 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 any 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,⁸² 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.⁸³ 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.⁸⁴ 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.⁸⁵ 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

⁸² *Daubert v. Merrell Dow Pharm., Inc.*, 509 U.S. 579 (1993).

⁸³ *Id.* at 580.

⁸⁴ SCIENCE POLICY COUNCIL, U.S. ENVIRONMENTAL PROTECTION AGENCY, INTERIM POLICY ON GENOMICS (June 25, 2002), <http://www.epa.gov/osa/spc/pdfs/genomics.pdf>; FOOD AND DRUG ADMINISTRATION, GUIDANCE FOR INDUSTRY: PHARMACOGENOMIC DATA SUBMISSIONS (March 2005), <http://www.fda.gov/cder/guidance/6400fnl.pdf>.

⁸⁵ The NAS project is entitled "Applications of Toxicogenomic Technologies to Predictive Toxicology," and is expected to issue its report by mid-2006. See <http://www4.nas.edu/cp.nsf/Projects%20by%20PIN/BEST-K-03-09-A?OpenDocument>.

accuracy.⁸⁶

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 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 coffers while also fulfilling the tort goals that such claims are intended to advance.⁸⁷

⁸⁶ Carl F. Cranor & David A. Eastmond, *Scientific Ignorance and Reliable Patterns of Evidence in Toxic Tort Causation: Is There a Need for Liability Reform?*, 64-AUT LAW & CONTEMP. PROBS. 5, 7 (2001) (scientific ignorance and the slow accumulation of knowledge make proving causation difficult). None of the major types of evidence introduced in toxic tort cases are capable of “proving conclusively a cause and effect relationship between plaintiff’s exposure to defendant’s product and plaintiff’s impaired health” and thus “[e]vidence of this kind is inherently subject to considerable uncertainty and inconclusiveness.” PETER W. HUBER, *GALILEO’S REVENGE: JUNK SCIENCE IN THE COURTROOM* (1991) (arguing that too much “junk science” is being relied on in toxic tort litigation). *See, e.g.*, *Sterling v. Velsicol Chem. Corp.*, 855 F.2d 1188, 1208 (6th Cir. 1988) (clinical ecology evidence that plaintiffs relied on lacked sufficient scientific basis to permit an opinion on the plaintiffs’ immune system dysfunction).

⁸⁷ 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,

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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 information.⁸⁸ 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,⁸⁹ 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.⁹⁰ 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

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.").

⁸⁸ 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).

⁸⁹ See *supra* note 20 and accompanying text.

⁹⁰ *Bowen v. E.I. Dupont*, No. Civ. A. 97C 06-194, 2005 WL 1952859, at *5 (Del. Super. Ct. June 23, 2005). 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. *Id.*

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.⁹¹ Enactment of pending legislation to provide legal protection against discrimination based on genetic data would also be helpful.⁹² 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 cases, and once such data have been ruled admissible and have affected the outcome in a few notable cases, there will likely be a flood of 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 and toxic tort attorneys. These issues will have to be managed effectively before the

⁹¹ See Marchant, *Genetic Susceptibility*, *supra* note 9, at 106-08; Niedwiecki, *supra* note 35, at 345-46; Rothstein, *supra* note 36, at 900-01.

⁹² Genetic Information Nondiscrimination Act of 2005, H.R. 1227, 109th Cong. (2005).

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promise and potential of genomic data in toxic tort litigation will be realized.