Genetics and Toxic Torts

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"In biology, one rarely deals with classes of identical entities, but nearly always studies populations consisting of unique individuals."[**]

INTRODUCTION

Legal analysis of genetics has so far focused primarily on DNA forensic evidence used in criminal cases[1] and potential discriminatory uses of genetic information in employment or insurance contexts.[2] Toxic torts is another area of the law that will both use, and be transformed by, genetic information. Genetic data have many potential applications to toxic torts, such as in proving or disproving causation or establishing the appropriate amount of damages to injured plaintiffs.[3] Genetic variations that affect the individual susceptibility and hence relative risk of exposed persons, or genetic changes which provide objective, quantitative proof of exposure, can greatly reduce much of the uncertainty and arbitrariness that currently hinders toxic tort litigation. Through these and other applications, genetic evidence may be beneficial to either plaintiffs or defendants in particular lawsuits.

Genetic information potentially relevant to toxic tort litigation can be divided into two major categories. The first involves inherited genetic

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[**] ERNST MAYR, THE GROWTH OF BIOLOGICAL THOUGHT 55 (1982).

[1] *See, e.g.*, D.H. Kaye, *The Admissibility of DNA Testing*, 13 CARDOZO L. REV. 353 (1991).

[2] *See, e.g.*, Melinda B. Kaufmann, *Genetic Discrimination in the Workplace: An Overview of Existing Protections*, 30 LOY. U. CHI. L.J. 393 (1999); Mark A. Rothstein, *The Use of Genetic Information for Nonmedical Purposes*, 9 J.L. & HEALTH 109 (1994-95).

[3] Gary E. Marchant, *Genetic Susceptibility and Biomarkers in Toxic Injury Litigation*, 41 JURIMETRICS J. 67 (2000); *see also* Mark S. Ellinger, *DNA Diagnostic Technology: Probing the Problem of Causation in Toxic Torts*, 3 HARV. J.L. & TECH. 31 (1990); Susan R. Poulter, *Genetic Testing in Toxic Injury Litigation: The Path to Scientific Certainty or Blind Alley?*, 41 JURIMETRICS J. 211 (2001); Bob Van Voris, *Tort Lawyers Discover the Power of Genetics: Some Store DNA Samples Now for Lawsuits in Future*, NAT'L L.J., Sept. 14, 1998, at A1.

variations that affect an individual's susceptibility to disease as a result of toxic exposures. The second consists of genetic changes that occur in individual cells as a result of toxic exposures during the person's lifetime. These mutations are usually not passed on to future generations (unless they occur in reproductive cells), but can provide useful biomarkers of exposure or the early stages of the disease process in the exposed individual. As discussed below, both types of genetic information have multiple potential applications in toxic tort litigation, and indeed are already beginning to be applied in individual cases.

I. GENETIC MARKERS OF SUSCEPTIBILITY

A. Scientific Developments

One of the first pay-offs of the Human Genome Project and companion efforts to analyze the human genome is the identification of a growing number of genetic variations that affect individual susceptibility to foreign substances.[4] The most common of these genetic variations, which exist in the human population at a frequency of at least one percent, are termed "polymorphisms." A consortium of pharmaceutical companies, known as the SNP Consortium, has mapped over one million "single nucleotide polymorphisms" ("SNPs"), which are common single-base pair genetic variations in human DNA.[5] Many other genetic variants are present at much lower frequencies in the human genome, and some of these also have biological significance.

Many of the most frequent genetic polymorphisms that have been identified in the human gene pool appear to affect our individual susceptibility to disease from exposure to toxic substances.[6] Our bodies

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[4] *See, e.g.*, William W. Au et al., *Usefulness of Genetic Susceptibility and Biomarkers for Evaluation of Environmental Health Risk*, 37 ENVTL. & MOLECULAR MUTAGENESIS 215, 215 (2001); N. Rothman et al., *The Use of Common Genetic Polymorphisms to Enhance the Epidemiologic Study of Environmental Carcinogens*, 1471 BIOCHEMICA ET BIOPHYSICA ACTA C1 (2001).

[5] The SNP Consortium's website is at http://snp.cshl.org/ (last visited Oct. 1, 2001). Only some of the SNPs may influence susceptibility directly, but others may be closely linked to susceptibility genes and therefore serve as a marker that can be used to map and select such genes in scientific studies. *See* Howard L. McLeod & William E. Evans, *Pharmacogenomics: Unlocking the Human Genome for Better Drug Therapy*, 41 ANN. REV. PHARMACOLOGY & TOXICOLOGY 101, 108 (2001).

[6] Kenneth Olden & Janet Guthrie, *Genomics: Implications for Toxicology*, 473 MUTAGENSIS RES. 3, 3-4 (2001). Two types of susceptibility genes can be distinguished. *Id.* at 8. One category, which includes genes such as BRCA1 which predispose the carrier to breast cancer, increase the risk of one or more diseases independent of any environmental exposure. The second category of susceptibility genes, which are the primary focus of this present paper, are those that increase the risk of disease from exposure to particular toxic agents. *See* Neil Caporaso & Alicia Goldstein, *Cancer Genes: Single and Susceptibility:*

metabolize foreign compounds that enter the body ("xenobiotics") through a series of enzymes coded by genes now known to be highly polymorphic (or variable) in humans.[7] These enzymes convert the xenobiotic through a series of reactions into both reactive and inert metabolites as part of the process for detoxifying and removing the foreign compound from the body.[8] The variations in the genes coding for these metabolic enzymes can greatly affect the dynamics of the metabolic process, increasing or decreasing the rates of detoxification and production of reactive intermediates and their associated risks.[9] Each person will thus react to exposure to a particular substance in a different way depending on the set of metabolic gene variants they are born with.

For example, about ten percent of the Caucasian population carries a variant of one cytochrome p450 gene (*CYP1A1*) that increases the rate of metabolism of certain substances and thus the formation of reactive metabolites. This genetic variant has been associated with increased lung cancer risk in smokers in some (but not all) studies.[10] In approximately fifty percent of the Caucasian population, a gene (*GSTM1*) coding for one in another set of metabolic enzymes (the glutathione S-transferases) is completely deleted, which is associated with an increased risk of bladder and lung cancer from exposure to several toxic substances normally detoxified by the *GSTM1* enzyme.[11]

The variations in the genes coding for metabolic enzymes can at least partly explain why only some individuals incur illness from particular toxic exposures, such as lung cancer from smoking.[12] As a consequence of these same genetic variations, most pharmaceuticals are ineffective in some individuals and cause toxic side-effects in others.[13] For example, the popular allergy drug Seldane was withdrawn from the market when it was found to cause, when taken with certain other drugs such as erythromycin, potentially fatal heart problems in people with a mutation in a particular

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Exposing the Difference, 5 PHARMACOGENTETICS 59 (1995).

[7] Olden & Guthrie, *supra* note 6, at 5.

[8] *See* Au et al., *supra* note 4, at 216.

[9] *See id.* at 216; Olden & Guthrie, *supra* note 6, at 5. Genetic polymorphisms in the genes coding for these metabolic enzymes can result in more than a 10,000-fold variation in enzyme activity. *Id.*

[10] *See* J.A. Indulski & W. Lutz, *Metabolic Genotype in Relation to Individual Susceptibility to Environmental Carcinogens*, 73 INT'L ARCHIVES OCCUPATIONAL ENVTL. HEALTH 71, 72-74 (2000).

[11] *See* Radim J. Sram, *Effect of Glutathione S-transferease M1 Polymorphisms on Biomarkers of Exposure and Effects*, 106 ENVTL HEALTH PERSP. 231, 231-32 (Supp. 1 1998).

[12] Olden & Guthrie, *supra* note 6, at 5; Rothman et al., *supra* note 4, at C2-C3.

[13] McLeod & Evans, *supra* note 5, at 103 ("Interpatient variability in response to drug therapy is the rule, not the exception, for almost all medications.").

gene coding for a metabolic enzyme in the cytochrome p450 family.[14] Similarly, ten to fifteen percent of the approximately 2400 children in the United States who each year develop the deadly cancer, acute lymphoblastic leukemia have mutations of the thiopurine S-methyltransferase (TPMT) gene that causes them to metabolize the lifesaving drug used to treat the disease either too fast or slow, resulting respectively in either lack of therapeutic benefit or potentially lethal accumulation of the drug.[15] Pre-treatment genetic testing is now being used to select the appropriate dosage for the medication depending on which versions of the gene the individual child carries.[16] In addition to these polymorphisms in metabolism genes, individuals also differ in their response to foreign substances due to other genetic variations affecting functions such as DNA repair, cell cycle control, receptors, and immune function.[17]

Notwithstanding the tremendous progress that has been made in understanding genetic susceptibility over the past few years, attempts to define the genetic susceptibility of an individual are nevertheless complicated by several factors. To begin with, most of the genes affecting susceptibility are probabilistic rather than deterministic in that they only increase the risk of disease and are neither necessary nor sufficient to cause disease.[18] The susceptibility genes are generally quite frequent in the population, but the increased (or decreased) risk in any one individual carrier is relatively modest.[19] Moreover, research on genetic susceptibility markers often produces inconsistent results, with some studies finding a significant increased (or decreased) risk of disease from a particular gene-environment interaction, while other studies report no such effect.[20]

Even when a susceptibility genetic marker has been unambiguously identified, its effects can vary across individuals for a variety of reasons. Some increases in susceptibility are dose-dependent, in that they primarily increase an individual's susceptibility to a toxic agent relative to the general population only at low or high doses. Certain associations appear to be ethnic-dependent, in that the susceptibility associated with a particular

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[14] *See* David Brown, *P450: Enzymes with the Answers on Drug Risks*, WASH. POST, Apr. 10, 2000, at A9.

[15] *See* Marc Wortman, *Medicine Gets Personal*, MIT'S TECH. REV, Jan./Feb. 2001, at 72, 74.

[16] *Id.*

[17] Rothman et al., *supra* note 4, at C3.

[18] Olden & Guthrie, *supra* note 6, at 5. The susceptibility genes are therefore different than deterministic disease-causing genes such as those that cause cystic fibrosis, Tay-Sachs disease, or Huntington's Disease.

[19] *See* Caporaso & Goldstein, *supra* note 6, at 60.

[20] Au et al., *supra* note 4, at 215-17.

gene appears to be limited to particular ethnic groups and is not seen in other groups even when the same gene is present.[21] The distribution of gene frequencies also varies significantly between different ethnic groups.[22] Finally, individual susceptibility to potentially toxic agents is rarely determined by a single genetic locus, but rather is the combined influence of many different genes (as well as non-genetic factors).[23] Thus, even if testing identifies a specific gene variant with a significant effect on individual susceptibility to a particular agent, the magnitude and nature of the susceptibility conferred by the gene may vary depending on the other gene variants present in a given individual.

Notwithstanding these complications, recent findings identifying and characterizing genetic markers of susceptibility demonstrate that there are substantial inter-individual differences in responses to, and risks from, toxic exposures. Perhaps even more important than the knowledge of the existence of frequent genetic heterogeneity within the population is the increasing capability to identify individuals who are more or less susceptible.[24] The potential to genetically profile individual susceptibility has many potential applications in toxic tort litigation, as discussed next.

B. Tort Applications of Genetic Susceptibility

In the past, necessitated largely by ignorance, the tort system has for the most part treated all individuals as identical black boxes with respect to their risk from potentially tortious exposures. There have been some limited exceptions, such as for highly vulnerable "egg-shell skull" plaintiffs,[25] but generally there has been no basis for discerning individual risk factors from the risks to the general population. Now, with the growing capability to genetically characterize individual susceptibility to toxic agents, every individual—and thus each plaintiff—has a unique genetic risk profile. Both plaintiffs and defendants are likely to try to capitalize on this information in a number of different ways.

1. Genetically Susceptible Plaintiff at Higher Relative Risk

A plaintiff has the burden of proof to demonstrate that it was more likely than not that exposure to defendant's product caused the injury for

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[21] *Id.* at 217.

[22] *Id.* at 217-19.

[23] *See* Au et al., *supra* note 4, at 217; Wendell W. Weber, *Effect of Pharmacogenetics on Medicine*, 37 ENVTL. & MOLECULAR MUTAGENESIS 179, 182 (2001). In addition to genetics, other factors affect individual susceptibility, including age, gender, health status, nutritional and economic status, and past exposures and employment. *See* Olden & Guthrie, *supra* note 6, at 6.

[24] *See* Weber, *supra* note 23, at 179.

[25] *See infra* note 57 and accompanying text.

which the plaintiff seeks compensation. In toxic tort and pharmaceutical product liability cases, the plaintiff must usually meet this burden of proof using epidemiological evidence showing a doubling of risk (*i.e.*, relative risk >2) from exposure to the agent in question.[26] The rationale for this requirement is that only when the incidence of the disease is at least twice as high in the exposed population as the background rate in the general population is it more likely than not that the exposure caused the disease.

Many harmful substances do not double the risk of disease at any exposure level, especially those that cause diseases that are common in the background population, such as lung cancer.[27] For such common ailments, only the most hazardous agents such as tobacco smoke will meet the legal causation standard of doubling background risk. Accordingly, many plaintiffs will be denied recovery because they cannot show that it is more likely than not that the toxic exposure caused their disease. A plaintiff may be able to overcome this evidentiary hurdle if she can show that she has genes that make her more susceptible to the exposure in question than the "average" person. Even if the general population has a relative risk less than two, an individual plaintiff may have a higher relative risk that meets the legal "more likely than not" standard because of her genetic susceptibility.

Such an argument has already been advanced in several cases, albeit with limited success to date because of the lack of evidence showing that the specific plaintiff carried genes conferring genetic susceptibility. For example, in litigation brought by residents surrounding the Hanford nuclear facility in Washington State, the plaintiffs claimed that radioactive exposures from the facility were responsible for their thyroid cancers.[28] For their claims to survive summary judgment, the court ordered the plaintiffs to produce evidence that they had received a "doubling dose" of radiation—a dose that would double the background rate of thyroid

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[26] *E.g.*, Daubert v. Merrell Dow Pharms., Inc., 43 F.3d 1311, 1321 (9th Cir. 1995); *In re* "Agent Orange" Prod. Liab. Litig., 597 F. Supp. 740, 833-34 (E.D.N.Y. 1984), *aff'd*, 818 F.2d 145 (2d Cir. 1987). *See generally* Russellyn S. Carruth & Bernard D. Goldstein, *Relative Risk Greater Than Two in Proof of Causation in Toxic Tort Litigation*, 41 JURIMETRICS J. 195 (2001). "Relative risk" is the risk for exposed individuals relative to the unexposed general population. A relative risk of two, for example, means that the frequency of the relevant disease in the exposed group is twice the rate observed in the general population.

[27] *See* Frederica P. Perera, *Environment and Cancer: Who Are Susceptible?*, 278 SCIENCE 1068, 1072 (1997) ("In epidemiology, it has been difficult to detect relative risks of 1.5 or even 2.0."); Gary Taubes, *Epidemiology Faces Its Limits*, 269 SCIENCE 164, 165 (1995) (only a few of the potential cancer risks reported in scientific journals and the media over the past eight years have "come close to fulfilling [the] criteria" of a twofold increased risk).

[28] *In re* Hanford Nuclear Reservation Litig., No. CY-91-3015-AAM, 1998 WL 775340, at *9-10 (E.D. Wash. Aug. 21, 1998).

cancer—in order to meet the legal "more likely than not" standard. In calculating the level of radiation that would represent such a doubling dose, the plaintiffs' expert reduced the dose expected to double the cancer rate in the general population by a factor of five to account for the existence of genetic susceptibility within the plaintiffs. This approach was rejected by the court because the plaintiffs' expert applied the genetic susceptibility factor to every plaintiff,[29] and had failed to introduce specific evidence quantifying the susceptibility of any particular plaintiff to radiation.[30]

Some silicone breast implant plaintiffs also argued that they were genetically susceptible to silicone in an attempt to overcome epidemiological studies showing no, or at most very small, increases in the relative risk of autoimmune disease in breast implant recipients generally.[31] At least one published scientific study suggested that women with a particular genotype might be more susceptible to adverse health effects from silicone.[32] While these claims of genetic susceptibility were presented to the jury in some cases, other courts rejected the introduction of such evidence because the plaintiffs had failed to show that they carried the specific genes allegedly conferring susceptibility.[33]

Attempting to establish causation based on unusual susceptibility has succeeded in at least one case. In *Collins v. Hygenic Corp. of Oregon*,[34] a state appellate court held that even though a worker was exposed to a commercial chemical (1,1,1 trichlorethane) at a level two orders of magnitude below its recognized safety level, the chemical nevertheless caused the worker's illness due to his unusual susceptibility. The court did

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[29] *Id.* at *66-68. The court noted that to the extent there are some unusually susceptible individuals in the population, there must necessarily be some people less sensitive than the population average. *Id.* at *68. The court noted that:

> If [plaintiffs' expert] wants to adjust these baseline risk estimates for persons of greater susceptibility, then he must first remove them from the underlying epidemiological studies, because their inclusion skews the risk estimates upwards due to their greater susceptibility. Once the hypersensitive individuals are factored out of the underlying studies, the risk estimates for the remaining population should drop, and the doses necessary to prove generic causation should rise.

Id. (citing defendant's brief with approval).

[30] *Id.* at *70 (use of five-fold susceptibility factor 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").

[31] *See* Ernest H. Hornsby & Dianna Pendleton, *Plaintiffs' Mounting Case Against Silicone Gel Breast Implants*, 6 No. 4 MED.-LEGAL ASPECTS OF BREAST IMPLANTS, Mar. 1998, at 5.

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

[33] *See, e.g.*, Hall v. Baxter Healthcare Corp., 947 F. Supp. 1387, 1456 (D. Or. 1996).

[34] 739 P.2d 1073, 1076-77 (Or. Ct. App. 1987).

not require the plaintiff to provide specific evidence demonstrating his unique susceptibility, but rather relied on the testimony of an expert that "there is a spectrum of sensitivity in all industrially associated product exposure" and that "there are a number of products which were considered to be in safe concentrations in years past which have subsequently been found to cause sensitivity in a certain number of individuals in the workplace."[35] The expert testified to a "high clinical suspicion" that the worker's illness was related to a potential susceptibility to the chemical in question, although no definite diagnosis with objective data was possible.[36]

The lessons from this limited case law to date, in which plaintiffs have tried to rely on their genetic susceptibility to establish causation, are that this general approach is sound and feasible in principle, but to succeed will likely need to be supported by specific evidence showing that the plaintiff carries a relevant genetic susceptibility gene. Such a showing will usually require genetic testing of the plaintiff. Such testing may carry other risks for the plaintiff, however. Not only may the testing reveal the absence of the appropriate susceptibility gene, which could make it harder for the plaintiff to recover, but the genetic testing might reveal other genetic information that the plaintiff may not wish to know herself, or have others (such as insurance companies or the defendant) know. Finally, while most susceptibility genes to date increase susceptibility, some may result in reduced susceptibility (or increased resilience) to a toxic exposure.[37] Defendants may be able to capitalize on this information to argue that plaintiffs carrying such genes have a lower relative risk than the general population, and thus have an even higher hurdle in establishing causation. As more genes conferring reduced susceptibility are identified, defendants will have a growing incentive to routinely seek genetic testing of plaintiffs to determine if they carry such genes.

2. Duty to Warn Genetically Susceptible Individuals

A manufacturer of a product has a duty to warn of potential hazards of that product. Failure to provide an adequate warning can result in liability for failure to warn. The growing knowledge of inter-individual genetic

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[35] *Id.* at 1074.

[36] *Id.* at 1074-75. The lenient standard applied by the court in upholding the worker's claim in this case can likely be attributed to the less rigorous standard for proving causation in workers' compensation cases than in tort cases. *See infra* note 66 and accompanying text.

[37] *See* Frederica P. Perera, *Uncovering New Clues to Cancer Risk*, SCI. AM., May 1996, at 54, 61 ("[C]ertain genetic traits may protect against one type of cancer, but may predispose to another."); Martyn T. Smith & Luoping Zhang, *Biomarkers of Leukemia Risk: Benzene as a Model*, 106 ENVTL. HEALTH PERSP., 937, 940 (Supp. 4 1998) (describing an inherited polymorphism in the *MPO* gene that when homozygous appears to lower the risk of benzene toxicity).

differences in susceptibility to chemicals, pharmaceuticals, and other products raises the issue of to what extent must a manufacturer provide a warning about specific susceptibilities. In the past, the existence of different susceptibilities to toxic side-effects of a product within the population could only be inferred, and *ex ante* identification of susceptible individuals was difficult and rare.[38]

The general rule is likely to be that a manufacturer is required to provide a warning for readily knowable susceptible subgroups, at least when susceptible individuals represent a significant proportion of product users. After all, many product warnings for pharmaceuticals today warn of side-effects that we now know likely occur primarily or exclusively in people with certain susceptibility genes. The only difference is that we now know that such side-effects are concentrated in sub-populations carrying relevant susceptibility genes, rather than occurring randomly throughout the entire population. This should not change the present requirement to warn of side-effects that occur in a non-trivial percentage of the population. Indeed, to the extent that susceptible individuals can identify their susceptibility, the case for a warning grows stronger, since a warning will now better help susceptible individuals to avoid the product.

The potential to identify individuals who are genetically susceptible to adverse side-effects from a pharmaceutical or other product, and for those individuals to take preventive action to avoid the product based on an adequate warning, may allow some products that would otherwise be banned to enter or return to the market. For example, some pharmaceuticals are beneficial for the majority of the population, but have had to be removed from use because they cause adverse effects in a small percentage of consumers.[39] If we can now genetically identify those susceptible individuals, and warn them not to take the product, the pharmaceutical could be resurrected and allowed back on the market.[40]

Even if the general rule is that a product manufacturer has a duty to warn susceptible individuals, several parameters of that duty remain undefined. For example, does the duty to warn apply regardless of how infrequent the susceptibility gene is present in the population? There are contradictory holdings on whether a product manufacturer has a duty to warn of very rare idiosyncratic reactions to a product, such as allergic

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[38] In a few cases, susceptible individuals could be identified by non-genetic methods, such as by inference from physiologic, biochemical, pharmacologic, or toxicologic features. *See* Weber, *supra* note 23, at 180. Such cases were the exception, however, and in most cases the susceptible individuals could only be identified *ex post* by their adverse reaction to the product.

[39] *See supra* note 15 and accompanying text.

[40] *See* Weber, *supra* note 23, at 179; Geeta Anand, *Big Drug Makers Try to Postpone Custom Regimens*, WALL ST. J., June 18, 2001, at B1.

reactions to cosmetic products.[41] The most frequent genetic polymorphisms with a frequency of one percent or more in the population would appear to trigger a warning requirement, whereas such a requirement for less frequent genetic susceptibilities is less clear. Genetic variants affecting susceptibility that are extremely rare in the population may not require a warning.

Another issue is whether the warning requirement depends on the product users' capability to determine their individual susceptibility. A relevant factor may be whether a genetic test is commercially available to allow potential product users to evaluate their susceptibility and avoid the product if they carry the relevant susceptibility genes.[42] Without an available method for product users to self-identify those that are susceptible, a product warning may not have practical utility, since most people are unlikely to take precautions to avoid the product unless they know they are susceptible. On the other hand, providing the information about the susceptibility trait in the population, even without the capability to identify which individuals carry the gene, may provide relevant information that will allow physicians and their patients to make probabilistic risk management decisions on whether to take the risk of a possible adverse effect. In addition, the provision of a warning indicating that people with a certain genotype may experience adverse side effects may provide useful information to a person who does not know his or her genotype, but starts to experience the side effects in the warning after using the product. Such a person would then have increased reason to suspect that they carry the susceptibility gene, and forego further use of the product.

An even more complex issue is the level of knowledge that product manufacturers will be expected to have about genetic susceptibility to their products. Courts have imposed a general duty on manufacturers to adequately test their products.[43] Will this duty to test include a duty to test the product on individuals with different genetic susceptibilities? This issue is just now beginning to be addressed in the regulatory approval of

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[41] *See infra* notes 62-63 and accompanying text.

[42] One company is planning to soon sell a home test kit in drugstores and supermarkets that will allow consumers to test themselves to see if they carry one particular susceptibility gene (coding for the cytochrome p450 2D6 enzyme) that is present in seven to ten percent of the population and results in improper metabolism of up to one-quarter of all drugs on the market, including many popular painkillers and cough medicines. *See* Wortman, *supra* note 15, at 78.

[43] *E.g.*, Borel v. Fibreboard Paper Prods. Corp., 493 F.2d 1076, 1090 (5th Cir. 1973) ("[A] manufacturer has a duty to test and inspect his product."); RESTATEMENT (THIRD) OF TORTS: PRODUCTS LIABILITY § 2 cmt. m (1997) ("[A] seller bears responsibility to perform reasonable testing prior to marketing a product and to discover risks and risk-avoidance measures that such testing would reveal.").

pharmaceuticals, where the application of genotype-stratified testing is now being considered.[44] Surely, a product manufacturer cannot be tasked with testing its product on every possible genotype—such an undertaking would not be feasible. Some type of "reasonableness" standard will therefore be needed—such as requiring testing and a warning when the manufacturer has a reasonable basis to suspect that its product would uniquely affect one or more specific genotypes.[45]

Factual disputes and complexity will further complicate this type of claim. A particular gene conferring susceptibility to a product will have variable effects depending on other factors such as the individual's nutritional status, genetic background, ethnicity, exposures to other toxic agents, and the level and duration of exposure to the product in question.[46] Moreover, the scientific data on whether a particular gene confers susceptibility to a particular type of exposure is often ambiguous, disputed, or contradictory.[47] The litigating parties are likely to disagree on whether a particular genetic variant results in susceptibility to a product and justifies a warning. The courts will be called upon to resolve these scientifically complex questions.

These types of complications are illustrated in a pending class action against the drug manufacturer SmithKline Beecham (now GlaxoSmithKline) alleging that the company's LYMErix vaccine causes illness in people with a particular genetic variant.[48] The complaint alleges that the vaccine, intended to inoculate against lyme disease, causes a chronic autoimmune reaction described as "treatment-resistant Lyme Arthritis" in people carrying the HLA-DR4+ gene variant, which is found in approximately thirty percent of the general population.[49] The complaint

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[44] *See* James N. Czaban, *Pharmacogenomics: The Uncertain Path to Decoding the Regulatory Genome*, FDLI UPDATE, May/June 2001, at 1, *available at* http://www.fdli.org/pubs/Update/2001/Issue3/Czaban/article.html (last visited Oct 10, 2001) ("Although there is no formal office within FDA specifically charged with oversight of pharmacogenomics per se, regulators here and abroad have been focusing closely on this field and its implications."); Wortman, *supra* note 15, at 75 ("Within five years, genetic tests identifying individuals at risk for an adverse reaction will very likely be a more routine part of how new drugs are developed . . . .").

[45] *See, e.g.*, Hawkinson v. A.H. Robins Co., 595 F. Supp. 1290, 1308 (D. Colo. 1984) (describing standard as that of a "reasonably prudent" manufacturer); W. PAGE KEETON ET AL., PROSSER AND KEETON ON THE LAW OF TORTS § 99 at 697 (5th ed. 1984) ("There will be no liability unless manufacturer failed to take the precautions that a reasonable person would take in presenting the product to the public.").

[46] *See supra* notes 21-23 and accompanying text.

[47] *See supra* note 20 and accompanying text.

[48] *See* Holcomb B. Noble, *Concerns Grow Over Reactions To Lyme Shots*, N.Y. TIMES, Nov. 21, 2000, at F1 (discussing class-action lawsuits filed in New Jersey, New York, and Pennsylvania).

[49] Plaintiffs' Amended Class Complaint at 10, Cassidy v. SmithKline Beecham, No. 99-

alleges that the company should be held liable for failing to screen participants for the DR4+ genetic trait in the safety studies for the vaccine, for failing to warn of the increased risk of treatment-resistant Lyme Arthritis to consumers who are HLA-DR4+, and for failing to recommend preliminary screening of potential LYMErix users for the HLA-DR4+ gene.[50]

The company denies that the vaccine causes any adverse effects, in genetically susceptible individuals or otherwise, and claims that the extensive clinical trials and post-marketing surveillance for the vaccine indicate no association with arthritis or any other adverse effect.[51] The FDA approved the LYMErix vaccine as safe and effective in 1998, but has requested a follow-up study by the manufacturer to further investigate the possibility of adverse reactions in genetically susceptible groups.[52] If a genetic susceptibility to the LYMErix vaccine is found, the FDA may require the vaccine label to be revised to require genetic testing of all patients prior to administration of the vaccine.[53]

While the conflicting factual claims in this particular lawsuit remain to be resolved by the courts, it likely represents the first in a new wave of lawsuits in which plaintiffs allege that a product manufacturer failed to test for and warn of genetic susceptibilities to the product. If courts begin to apply liability in such cases, product manufacturers may be forced to test their products for differential effects on people with different potential genetic susceptibilities, and recommend that product users be genetically screened for any such known susceptibilities before using the product.

3. No Duty on Defendant to Prevent Illness to Unusually Susceptible Plaintiff

Defendants may be able to exploit the same information about the plaintiff's genetic susceptibility to argue that it has no duty to protect a genetically hyper-sensitive individual. In particular, if the defendant's product is safe for the "normal" population, but only harms individuals that are genetically susceptible to the exposure, the defendant may be able to assert an "idiosyncratic response" defense.[54] The idiosyncratic response

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10423 (Ct. Com. Pls., Chester County, Pa.).

[50] *Id.* at 38, 48.

[51] Susan Okie, *Lyme Disease Vaccine's Safety Is Questioned*, WASH. POST, Apr. 8, 2001, at A3; Wendy Todaro Thanassi & Robert T. Schoen, *The Lyme Disease Vaccine: Conception, Development, and Implementation*, 132 ANNALS INTERNAL MED. 661 (2000) (describing development and testing of LYMErix vaccine).

[52] Okie, *supra* note 51, at A3.

[53] Czaban, *supra* note 44, at 2.

[54] *See* Marchant, *supra* note 3, at 80-84; *see also* John Gerald Gleeson, *Idiosyncrasy: A Developing Defense in Drug and Hazardous Substances Litigation*, FOR THE DEFENSE, Apr.

defense has been applied most often in cases involving allergenic responses to cosmetic products, but would also appear to apply to cases where a plaintiff was harmed due to a rare genetic susceptibility by a product that is otherwise harmless to the general population. Under such circumstances, it can be said that the hyper-susceptibility of the plaintiff, rather than some defect in the product, is the proximate cause of the plaintiff's injury.[55]

The idiosyncratic response defense appears inconsistent with the maxim that the defendant takes the plaintiff as he finds her, otherwise known as the "eggshell skull" doctrine.[56] Under this doctrine, a tortfeasor is liable for the full damages to an unusually susceptible or fragile plaintiff, even if the extent of those damages were unexpected and would not occur in a "normal" person. However, the "eggshell skull" doctrine applies only in the negligence context, where the defendant's wrongdoing is established separate and prior to reaching the issue of damages.[57] In such cases, policy favors saddling a defendant who has already been proven to be a wrongdoer with the risk of unexpected or extraordinary damages resulting from its negligent actions. In most toxic tort and product liability cases involving products such as pharmaceuticals, in contrast, the inquiries into liability and damages merge, in that the manufacture and distribution of an otherwise beneficial product is only tortious to the extent it causes harm.[58] Courts are thus squarely presented with the question of whether injury to a few susceptible individuals without any other wrongdoing is sufficient harm to justify liability and perhaps force a beneficial, and generally harmless, product off the market.

The idiosyncratic response defense represents a policy judgment that a non-negligent manufacturer should not be held liable for producing a product that is beneficial and harmless to most persons, even if it may injure a small number of unusually susceptible individuals. As one court put it, "[a] manufacturer has no duty to withhold its product from the market merely because the product may pose a risk to certain hyper-sensitive individuals."[59] To apply liability in such circumstances may unduly burden commerce, since there may be some susceptible individuals

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1989, at 9; Joseph J. Ortego et al., *Idiosyncratic Reactions: A Limitation on the Duty to Warn*, MEALEY'S LITIG. REP.: TOXIC TORTS, Oct. 20, 1999, at 29.

[55] *See* Adelman-Tremblay v. Jewel Cos., Inc., 859 F.2d 517, 522 (7th Cir. 1988).

[56] *See* Vosburg v. Putney, 50 N.W. 403, 404 (Wis. 1891) (noting "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).

[57] *See* Bahr & Graham, *supra* note 56, at 409 ("[T]he thin skull principle is uniformly restricted to cases of personal injuries in negligent torts . . . .").

[58] *See* Marchant, *supra* note 3, at 83-84.

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

for any product. For example, individuals suffering from multiple chemical sensitivity (MCS) claim to be injured by many products in everyday use, such as perfumes and cosmetic products, many cleaning products, and "off-gassing" from furniture, carpeting and new cars.[60] If manufacturers of these common and generally safe products could be held liable to hyper-sensitive MCS patients, many useful products would likely be forced off the market. Likewise, product manufacturers held liable for harm to individuals with rare genetic susceptibilities may be forced to remove beneficial products.

The idiosyncratic response doctrine applies most clearly to protect against design defect liability. Courts are more divided over whether an idiosyncratic response also provides a defense to failure to warn liability. Some courts have limited the idiosyncratic response defense to design defects, and still require an appropriate warning if the manufacturer had reason to know that there is an "identifiable class of sensitive users" of the product.[61] Other courts have not required a warning when the susceptibility is sufficiently rare.[62] A warning is more likely to be required the higher the frequency at which the susceptibility marker occurs in the population.

The idiosyncratic response defense creates a potential trap for the plaintiff. If the plaintiff introduces evidence of genetic susceptibility to try to show a higher relative risk in order to establish causation, she may open the door to a defendant's argument that there should be no liability even if causation is proven, given that it would be unreasonable to expect manufacturers to protect such unusually susceptible individuals. This is exactly what happened in *Cavallo v. Star Enterprise*,[63] in which a homeowner claimed to be "highly susceptible" to fuel vapors to support her claim that she had been injured from inhaling fuel vapors from a spill at a nearby petroleum distribution terminal. The Fourth Circuit Court of Appeals held that only those adverse effects that would be suffered by a "normal" person are cognizable, and thus plaintiff's own allegation that she was "highly susceptible" to fuel vapors precluded her recovery.[64]

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[60] While the existence and etiology of MCS remains controversial, a significant number of people claim to suffer from such a condition and report symptoms of illness from exposure to many household products. *See generally* NICHOLAS A. ASHFORD & CLAUDIA S. MILLER, CHEMICAL EXPOSURES: LOW LEVELS AND HIGH STAKES (1991).

[61] *See, e.g.*, Adelman-Tremblay v. Jewel Cos., Inc., 859 F.2d 517, 521-22 (7th Cir. 1988).

[62] *See, e.g.*, Kaempfe v. Lehn & Fink Prods. Corp., 249 N.Y.S.2d 840, 845-46 (1964) (noting "in the case of a useful and reasonably safe product, in general use, the supplier owes no special duty of warning to the unknown few who constitute a mere microscopic fraction of potential users who may suffer some allergic reaction not common to the ordinary or normal person").

[63] 100 F.3d 1150 (4th Cir. 1996).

[64] *Id.* at 1154.

The "idiosyncratic response" defense will generally not apply in cases brought under state workers' compensation laws for job-related health problems. Workers' compensation statutes typically provide compensation when a workplace exposure is a "substantial" or "contributing" factor in bringing about the disability, a more lenient standard than the causation requirement that applies in tort law.[65] Under this substantial factor standard, courts in most states have held that a workplace exposure that aggravates or accelerates a pre-existing genetic condition qualifies for compensation.[66] This result is often justified by the beneficial purpose of the workers' compensation laws.[67] An employer will generally only prevail if it can show that the pre-existing genetic condition or predisposition was the exclusive cause of the disability, and would have occurred independent of any workplace exposure.[68]

4. Genetics and Alternative Causation

A defendant could not only contend that a plaintiff's illness resulted from an unusual genetic susceptibility to its product, but could also argue in the alternative in appropriate cases that the plaintiff's disease resulted solely from a genetic predisposition totally unrelated to the defendant's product. For example, if a plaintiff alleges that exposure to a chemical manufacturer's product caused her breast cancer, the company could argue that the plaintiff developed cancer solely as a result of the BRCA1 gene she carried, which dramatically increases the risk of breast cancer independent

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[65] *See, e.g.*, ARTHUR LARSON, THE LAW OF WORKMEN'S COMPENSATION § 41.64(c) (1991) ("Preexisting disease or other predisposition does not prevent compensability. The employer takes the worker as he finds him. It is not necessary that the employment conditions be the sole cause, or dominant cause, so long as they are a contributing cause.").

[66] *See, e.g.*, DeYonge v. NANA/Marriott, 1 P.3d 90, 96 (Alaska 2000) (upholding workers' compensation claim because workplace factors have not been excluded as a substantial factor in producing the disability, even though the court found that the evidence "tend[s] to demonstrate that a non-work-related factor—DeYonge's genetic predisposition for arthritis and its natural degenerative progression—caused DeYonge's underlying impairment."); Cagle v. Brock & Blevins, Inc., 723 So. 2d 65, 68 (Ala. Civ. App. 1998) (noting that "[i]f the employment aggravates, accelerates, or combines with a latent disease or infirmity to produce disability, the pre-existing disability does not disqualify the employee's claim under the 'proximate cause' requirement . . .").

[67] *See, e.g.*, *Cagle*, 723 So. 2d at 68 ("The Workers' Compensation Act is to be liberally construed in order to effectuate the beneficent purposes of the Act.").

[68] *See, e.g.*, Lopez v. Adm'r Pub. Employees' Ret. Sys., 20 P.3d 568, 572-73 (Alaska 2001) (denying occupational disability benefits for back condition attributed to "natural progression of a degenerative arthritis with genetic predisposition" rather than work-related injury); Smith v. Serv. Tire Truck Ctr., Inc., No. 98A-03-013-WCC, 2000 WL 145817, at *4 (Del. Super. Jan. 19, 2000) (denying workers' compensation claim for latex allergy triggered by workplace exposure because "according to Claimant's own experts, he had an inherited, allergic predisposition that merely needed something to trigger it").

of any chemical exposure.[69] In other words, the defendant could argue that genetics was an alternative cause.

Defendants in toxic tort cases have often suggested that heritable factors could be an alternative cause of a plaintiff's illness, although such claims have rarely been accompanied by specific genetic evidence of such predispositions. The change brought about by recent scientific advances in genomics is that it may now be possible to medically test the plaintiff for an increasing number of identified genetic traits and predispositions that may explain a plaintiff's illness. Thus, an alternative causation defense based on genetics will become more common and effective to the extent it is supported by objective test data. As one genetics expert noted, "When a person sues a company and says an exposure caused a birth defect or some other problem, the company has every right to request genetic testing. That should be standard practice."[70]

A recent example in which such a defense was asserted was a case in which a mother of a mentally retarded son sued the supplier of chemicals to her employer, alleging that her occupational exposure to those chemicals while pregnant caused her son's condition.[71] The defendant argued that the boy's symptoms resembled a genetic disorder called Fragile X Syndrome, and successfully petitioned the court to require genetic testing of the boy. When a blood sample was later about to be taken from the boy, however, he put up such a violent struggle that the treating physician refused to take the sample.[72] No sample from the boy was taken, and when the parties next appeared before the judge, the mother's attorney stated that genetic tests of the mother revealed no Fragile X chromosome, thus ruling out the condition in the son.[73] The issue of genetic testing was set aside for a later stage of the trial, and the case settled after the plaintiff prevailed on other issues in the first leg of a bifurcated trial.

In another recent case receiving considerable publicity, the Equal Employment Opportunity Commission (EEOC) sued the Burlington Northern Railway for secretly genetically testing some of its workers.[74]

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[69] *See* Patricia Kahn, *Coming to Grips with Genes and Risk*, 274 SCIENCE 496, 496-97 (1996).

[70] 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).

[71] *See* Sally Lehrman, *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 (discussing case of Severson v. KTI Chems. Inc.).

[72] Interview with Kevin Mayer, counsel for Defendant KTI Chemicals, Inc. (Apr. 7, 2000).

[73] *Id.* Because a male receives his only X chromosome from his mother, if the mother's X chromosomes don't carry the particular genetic variant responsible for the Fragile X syndrome, then the son will not have the condition.

[74] Equal Employment Opportunity Comm'n v. Burlington N. Santa Fe R.R., No. C01-

The company genetically tested several workers who had applied for workers' compensation for carpal tunnel syndrome, apparently looking for a rare genetic variant that may cause carpal tunnel syndrome. The EEOC contended that the company's secret genetic testing of the workers was a violation of the Americans with Disabilities Act (ADA), which the EEOC contends bars genetic testing in such a manner.[75] The case was settled after the company agreed to stop the testing and destroy the test results, as well as to take no retaliatory action against the workers.[76]

These attempts by defendants, even though mostly unsuccessful to date, to demonstrate that a complainant's illness was caused by genetics are unlikely to be the last, although companies asserting such a defense will be well-advised to seek court-ordered genetic testing rather than secretly attempting the genetic testing themselves.

5. Assumption of Risk

The availability of genetic tests to determine susceptibility to particular substances may open the door to more frequent assertion of the assumption of risk (or contributory negligence) defense. A defendant could argue that a plaintiff knew, or should have known, that she was genetically susceptible to a particular agent and accordingly should have taken greater precautions to avoid exposure. Such a defense would be strengthened to the extent that it was common knowledge that people with certain genetic traits are susceptible to a particular product, and that genetic testing was available to ascertain one's genetic susceptibility.[77] A relevant precedent is provided by judicial decisions finding assumption of risk or contributory negligence when a plaintiff failed to take a "patch test" for allergic reactions to a cosmetic product as recommended by the manufacturer.[78]

4013 MWB, slip op. (N.D. Iowa, Apr. 17, 2001). *See* Tamar Lewin, *Commission Sues Railroad to End Genetic Testing in Work Injury Cases*, N.Y. TIMES, Feb. 10, 2001, at A10.

[75] The application and requirements of the ADA with respect to occupational genetic testing remains controversial, and is largely untested by the courts. *See, e.g.*, Mark S. Dichter & Sarah E. Sutor, *The New Genetic Age: Do Our Genes Make Us Disabled Individuals Under the Americans with Disabilities Act?*, 42 VILL. L. REV. 613 (1997); Charles B. Gurd, *Whether a Genetic Defect Is a Disability Under the Americans with Disabilities Act: Preventing Genetic Discrimination by Employers*, 1 ANNALS HEALTH L. 107 (1992).

[76] Press Release, The U.S. Equal Employment Opportunity Commission, EEOC Settles ADA Suit Against BNSF for Genetic Bias (Apr. 18, 2001), *available at* http://www.eeoc.gov/press/4-18-01.html.

[77] *See supra* note 24 and accompanying text.

[78] *E.g.*, Quiroz v. Max Factor, Inc., 264 So. 2d 263, 266 (La. Ct. App. 1972); Thomas v. Gillette Co., 230 So. 2d 870, 876 (La. Ct. App. 1970); Arata v. Tonegato, 314 P.2d 130, 133 (Cal. Ct. App. 1957).

The assumption of risk defense has less force in the occupational context, because often workers are economically compelled to undertake risks that are an integral part of their job. Nevertheless, there may be circumstances where the assumption of risk defense may apply to workers. For example, individuals carrying a particular genetic trait are at an increased risk of developing potentially fatal chronic beryllium disease (CBD), also sometimes known as berylliosis, from occupational exposure to beryllium.[79] Genetic tests for beryllium sensitivity have now been developed and are being offered on a voluntary basis to beryllium-exposed workers.[80] Studies have suggested that genetic screening and exclusion of genetically susceptible workers may provide a cost-effective approach for further reducing CBD.[81] If a prospective worker undertakes the genetic test and tests positive for beryllium susceptibility, but nevertheless chooses to undertake employment that involves significant beryllium exposure,[82] the worker may be barred by the assumption of risk doctrine from suing the employer or the beryllium supplier if he subsequently develops beryllium disease.[83]

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[79] Luca Richeldi et al., *HLA-DPB1 Glutamate 69: A Genetic Marker of Beryllium Disease*, 262 SCIENCE 242 (1993) (ninety-seven percent of the workers tested who developed berylliosis carry a particular susceptibility gene consisting of a specific mutation in the HLA-DPB1 marker). Beryllium is an important metal used in the computing, space and other high tech industries because of its high strength and light weight. While efforts to control occupational exposures to beryllium have to date focused primarily on reducing exposures through engineering controls, work practices, and personal protective equipment, such measures are unlikely to eliminate the very low levels of beryllium dust that can cause CBD in genetically susceptible workers.

[80] *See* Stephanie Armour, *Could Your Genes Hold You Back?*, USA TODAY, May 5, 1999, at B1 (reporting that 800 employees of largest beryllium supplier have voluntarily been tested as part of genetic research program); Kristen Davenport, *Lab Offers Genetic Testing to Beryllium Workers*, SANTA FE NEW MEXICAN, Nov. 15, 2000, at A7 (describing voluntary genetic testing offered to workers exposed to beryllium at the Los Alamos National Laboratory).

[81] Scott M. Bartell et al., *Risk Estimation and Value-of-Information Analysis for Three Proposed Genetic Screening Programs for Chronic Beryllium Disease Prevention*, 20 RISK ANALYSIS 87 (2000); Mark Nicas & Geoffrey P. Lomax, *A Cost-Benefit Analysis of Genetic Screening for Susceptibility to Occupational Toxicants*, 41 J. OCCUPATIONAL & ENVTL. MED. 535 (1999).

[82] The majority of workers with the susceptibility gene for beryllium do not develop CBD when exposed to beryllium. Up to 30% of workers carry the susceptibility gene, but only 2-5% percent of exposed workers develop CBD. Lee S. Newman, *To Be2+ or Not to Be2+: Immunogenetics and Occupational Exposure*, 262 SCIENCE 197, 198 (1993). Thus, the presence of the susceptibility gene in the worker signifies only an increased risk, and not the certainty, of being adversely affected by beryllium exposures.

[83] Lawsuits by an employee against his employer for personal injury are generally barred by workers' compensation laws, although in most states such suits can proceed if the employer acted intentionally, recklessly, or even knowingly in imposing an unreasonable health risk on a worker. *See infra* note 133 and accompanying text.

The Supreme Court's *Johnson Controls*[84] decision suggests that the assumption of risk defense may indeed apply in such employment contexts. In that case, the employer attempted to exclude all women capable of bearing children from jobs with potential exposure to lead, purportedly to protect any developing fetuses in those women from the toxic effects of lead.[85] The Supreme Court struck down this policy as facially discriminatory against women, and found no bona fide business necessity for such a fetal exclusion policy.[86] In briefly addressing the company's concern about potential tort liability from allowing fertile women in the workplace, the Court suggested in passing that as long as the employer "fully informs the woman of the risk," and does not act negligently, it should be protected from tort liability.[87]

This dicta suggests that if an employer provides adequate warning to workers of the potential risks from occupational exposures, including the existence of susceptibility genes within the population that enhance such risks, a susceptible worker who nevertheless accepts the job and assumes the risk may be precluded from suing for any resulting health impacts. Many sub-issues are likely to be raised in applying the assumption of risk defense to genetically susceptible workers. For example, how certain and large must the risk to genetically susceptible workers be for the assumption of risk defense to apply? Will it matter if the employer had other available options (such as engineering controls) for reducing worker risks? Is it relevant how expensive those controls would be? How much information must the employer provide the worker for the defense to apply? Must the employer make genetic testing available to the worker? If the employer provides for voluntary genetic testing, but the worker elects to not be tested and therefore remains ignorant of her individual risk, would the assumption of risk defense still apply? May the employer mandate genetic testing, or require access to the test results? These and other issues are likely to be confronted in future litigation.

6. Opposing Certification for Genetically Heterogeneous Class

A defendant in a toxic tort case may be able to use the existence of genetic variation in a putative class of plaintiffs to argue against certification of that class. The prerequisites for class certification include a requirement that the issues in common within the class must "predominate"

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[84] Int'l Union, United Auto., Aerospace, and Agric. Implement Workers of Am., UAW v. Johnson Controls, 499 U.S. 187 (1991).

[85] *Id.* at 192.

[86] *Id.* at 198-208.

[87] *Id.* at 208.

over individual issues.[88] If one of the principal issues in the litigation is the causation of health effects by the defendant's product or actions, the defendant may be able to successfully argue that genetic differences affecting the individual's response to the agent in question may require individualized assessment of causation. This precise argument has been successfully applied by defendants in arguing against class certification in several cases. For example, a New Jersey court denied the certification of a proposed class consisting of all New Jersey smokers in a suit against the tobacco industry, in part because the determination of whether smoking caused a smoker's illness will require an assessment of each individual smoker's medical and genetic history.[89] A California court denied 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.[90]

7. Discounting Damages for Plaintiff's Genetic Predispositions

Defendants can also use the plaintiff's genetic susceptibility to argue for a reduction in damages even after the defendant has been found liable for the plaintiff's injury. There are two forms of this argument. The first is when the plaintiff has a genetic predisposition for the same condition that she ultimately developed in response to defendant's actions or product. In such a case, the defendant will likely try to argue that it was the genetic predisposition, rather than the defendant, that caused the plaintiff's illness.[91] Even if this argument fails, however, and the defendant is found liable, the defendant may be able to reduce its damages by arguing that the plaintiff would likely have developed the same condition eventually because of her predisposition. Thus, the amount of damages should be discounted to compensate the plaintiff only for the time period for which the defendant's actions accelerated her development of the inevitable disease.[92]

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[88] FED. R. CIV. P. 23(b)(3).

[89] Cosentino v. Philip Morris Inc., No. MID-L-5135-97, slip op. (N.J. Super. Ct. Feb. 11, 1999) (opinion denying plaintiffs' motion for reconsideration of motion for class certification); *see also* Reed v. Philip Morris Inc., Civil No. 96-5070, Mem. Op. and Order (D.C. Super. Ct. July 23, 1999) (denying class certification of all District of Columbia smokers for similar reasons).

[90] Lockheed Martin Corp. v. Superior Court, 94 Cal. Rptr. 2d 652, 658 (Cal. Ct. App. 2000).

[91] *See supra* notes 70-77 and accompanying text.

[92] For example, in *Kegel v. United States*, 289 F. Supp. 790 (D. Mont. 1968), the court found that the accident resulting from defendant's negligence was the legal cause of the plaintiff's herniated disc. However, the court also found that in the absence of the accident, the plaintiff's disc would have ruptured within two years because of a preexisting condition.

The second and more troubling form of the argument for reducing damages would be for the defendant to seek to uncover a genetic predisposition for any disease condition that could shorten or diminish the quality of the plaintiff's life. Any such evidence of diminished life expectancy or quality could be used to support reduced damages. Because this argument is not limited to the specific disease condition that the plaintiff actually has, it could involve a very broad and intrusive search into the plaintiff's medical and genetic history, and perhaps even comprehensive genetic testing. Such "fishing expeditions" have been criticized on the ground that they represent excessive intrusion into the personal privacy of the plaintiff, with the potential to unveil genetic information that the plaintiff herself may not want to know or which may be used by insurers or employers to discriminate against the plaintiff in the future.[93] Yet, courts have allowed defendants to require testing of plaintiffs for HIV for the purpose of reducing damages based on the plaintiff's diminished life expectancy due to AIDS.[94] It remains to be seen how lenient courts will be in allowing defendants to obtain genetic testing of plaintiffs for the purpose of calculating life expectancy for damages assessment.

II. GENETIC MARKERS OF EXPOSURE AND EFFECT

A. Scientific Developments

The second major category of genetic biomarkers potentially useful for toxic tort litigation are genetic changes that occur in an individual's cells as a result of exposure to toxic substances. These genetic changes can provide a useful qualitative or quantitative measure of exposure or provide an early diagnostic measure of disease development prior to the development of clinical symptoms. Unlike the in-born genetic susceptibility markers discussed in the previous section, genetic biomarkers of exposure and effect occur in only some cells of the person, and are not

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Id. at 795. The court therefore 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. *Id.* at 796-97.

[93] 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, 900-01 (1996).

[94] 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 (2000) (discussing court-ordered HIV and genetic testing).

passed on to future generations (unless the genetic alterations occur in the reproductive cells).

The presence of this type of biomarker in only some cells of the body creates additional complications compared to genetic susceptibility markers. It is not possible to genetically sample all cells in the body, and indeed it is usually only feasible to examine a relatively limited number of easily accessible cells. The failure to observe genetic changes in the sampled cells is therefore not conclusive as to whether other of the trillions of cells in the body have undergone such changes. Moreover, cells from the blood or urine are much more accessible and available than cells from internal organs such as the liver or brain. These frequently sampled cells may or may not be reliable indicators of the presence of genetic changes in the cells in the target tissues in which the disease is most likely to develop. Yet another complication is that many genetic biomarkers of exposure and effect are not stable over time, and are gradually eliminated by repair mechanisms or cell death. The timing of the surveillance is therefore a critical parameter for such biomarkers.

Notwithstanding these complications, rapid progress has been made in identifying and in some cases validating potential genetic biomarkers of exposure and effect.[95] Some of the most promising biomarkers of exposure and effect are DNA adducts, in which a toxic substance or its metabolites binds with DNA to form a stable and characteristic chemical complex. The formation of DNA adducts is believed to be an initial step in the mutation process, although not all adducts necessarily result in mutation. Several hundred different carcinogen-DNA adducts have been identified to date, with many carcinogens forming distinct patterns of adducts with respect to type and location on the DNA macromolecule.[96] DNA adducts can therefore provide a sensitive and specific biomarker of exposure and perhaps effect.[97]

Cytogenetic changes also provide a potentially useful biomarker of exposure and effect, and generally are considered the best validated genetic

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

[96] *See* Christopher P. Wild & Paola Pisani, *Carcinogen DNA and Protein Adducts as Biomarkers of Human Exposure in Environmental Cancer Epidemiology*, 22 CANCER DETECTION & PREVENTION 273, 276-77 (1998).

[97] *See* Frederica P. Perera, *Molecular Epidemiology: On the Path to Prevention?*, 92 J. NAT'L CANCER INST. 602, 603 (2000); Herman A.J. Schut & Kathleen T. Shiverick, *DNA Adducts in Humans as Dosimeters of Exposure to Environmental, Occupational, or Dietary Genotoxins*, 6 FASEB J. 2942 (1992); Chunyan Zhao et al., *DNA Adducts of 1,3-Butadiene in Humans: Relationships to Exposure, GST Genotypes, Single-Strand Breaks, and Cytogenetic End Points*, 37 ENVTL. & MOLECULAR MUTAGENESIS 226, 229 (2001) (study showing that DNA adducts provide a sensitive and specific biomarker of exposure to 1,3-butadiene).

biomarkers with regard to predicting risk.[98] Cytogenetic changes refer to gross rearrangements within or between chromosomes, resulting from breakage and rejoining of chromosomes after exposure to an agent capable of causing chromosome breaks. The resulting chromosome aberrations can be observed under a light microscope after a staining of the chromosomes. Chromosomal aberrations are non-specific in that the same aberration can potentially be caused by many different agents,[99] and therefore these markers are most useful for confirming or quantifying exposure to individuals who are known to have been, or are suspected of having been, exposed to a specific toxic agent.

Monitoring cells of exposed individuals for mutations in specific genes can also provide useful biomarkers of effect or exposure, and several "reporter gene" assays have been developed to monitor mutational rates in blood cells. For example, an assay that measures mutations of the hypoxanthine-guanine phophoribosyl transferase (*hprt*) gene in a person's white blood cells is frequently employed to monitor a person's exposure to mutagenic substances. This *hprt* assay has been used to monitor mutations in workers occupationally exposed to butadiene, an important chemical known to cause leukemia, which can both help to assess risks from various exposure levels as well as potentially to identify exposed, at-risk workers.[100] The *hprt* mutations identified in this research persist for long periods of time, enhancing their usefulness as a biomarker of exposure and effect.[101]

Even more specific and informative assays may soon be available for toxic agents that induce chemical-specific mutational "fingerprints" or "spectra" at precise sites in specific genes. For example, several mutagens including UV exposure, aflotoxin B and vinyl chloride have been found to induce characteristic mutational spectra in the important tumor suppressor gene *p53*.[102] The *p53* gene plays a critical role in controlling cell division,

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[98] Perera, *Molecular Epidemiology*, *supra* note 97, at 605.

[99] *Id.* at 604.

[100] Jonathan B. Ward et al., *Assessment of Butadiene Exposure in Synthetic Rubber Manufacturing Workers in Texas Using Frequencies of* hprt *Mutant Lymphocytes as a Biomarker*, 135-136 CHEMICO-BIOL. INTERACTIONS 465 (2001) (*hprt* mutations are a biomarker of butadiene exposure). *But see* Richard J. Albertini et al., *Biomarkers for Assessing Occupational Exposures to 1,3-Butadiene*, 135-136 CHEMICO-BIOL. INTERACTIONS 429 (2001) (finding no association between *hprt* mutations and butadiene exposure).

[101] Ward et al., *supra* note 100, at 478.

[102] 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).

and mutated *p53* genes are found in half of all human tumors.[103] The detection of a characteristic genetic change in the *p53* gene might indicate the initiation of the cancer process, and perhaps the specific cause of that event. Such mutational spectra have, to date, only been identified for a few gene-mutagen combinations, and even the mutations in these spectra may not be exclusive to a single agent.[104] Nevertheless, the findings of chemical-specific mutational spectra raises the possibility that these mutational fingerprints could be used to ascertain whether a specific agent caused a tumor in a particular individual.

B. Tort Applications of Biomarkers of Exposure and Effect

Thousands of potential biomarkers have now been identified that could potentially serve as surrogates of exposure or disease progression. Most of these biomarkers have yet to be fully validated scientifically, yet that may not prevent their use in toxic tort litigation. Toxic tort litigants (especially plaintiffs) are usually one-time players in a high-stakes game, and are not likely to forgo reliance on potentially relevant and useful data just because some uncertainty about their relevance and reliability remain.

1. Exposure Dosimeter

In many toxic tort cases, plaintiffs face great difficulty in proving the fact and quantity of exposure to a toxic agent. Many of these cases involve exposure scenarios that are highly uncertain and contested—such as the amount of exposure from groundwater contamination, accidental or routine pollutant air releases from a nearby facility, living near a toxic waste dump, or pesticide applications in the home or at a business. In many of these cases, plaintiffs have no objective exposure data, and modeling attempts often involve little more than speculation. It is therefore not surprising that plaintiffs' claims are often dismissed for failure to prove sufficient exposure to the agent that allegedly caused their disease.[105]

Biomarkers of exposure can provide objective qualitative or quantitative evidence of a plaintiff's exposure to a hazardous agent. For

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[103] Curtis C. Harris, *p53: At the Crossroads of Molecular Carcinogenesis and Risk Assessment*, 262 SCIENCE 1980, 1980 (1993).

[104] *See* Andrea Hartwig et al., *The Potential Use of Mutation Spectra in Cancer Related Genes in Genetic Toxicology: A Statement of a GUM Working Group*, 473 MUTATION RES. 263, 264 (2001).

[105] *E.g.*, Shudel v. Gen. Elec. Co., 120 F.3d 991, 997 (9th Cir. 1997); *see also* Decaprio, *supra* note 95, at 1842 (noting plaintiffs "typically introduce indirect measures, such as ambient air or other environmental media analyses, job and process descriptions, or chemical usage and disposal records as evidence for significant exposure. Defense counsel generally challenges such evidence as unreliable, nonspecific, or incidental to the disease in question").

example, the presence of chemical-specific DNA adducts in the plaintiff's blood cells might provide a reliable quantitative measure of exposure.[106] Such biomarkers may greatly assist plaintiffs in the future to overcome the burden of proving adequate exposure. On the other hand, defendants may likewise be able to rely on the absence of the appropriate DNA adducts in the plaintiff to demonstrate that the plaintiff did not receive significant exposure.

Cytogenetic markers can also provide quantitative measures of exposure. Cytogenetic biomarkers of radiation exposure figured prominently in the Three Mile Island (TMI) litigation, where the "critical issue" was the inability of nearby residents to prove that they were exposed to sufficient radiation doses from the TMI nuclear accident to cause their cancers.[107] Plaintiffs lacked direct exposure measurements or adequate modeling to demonstrate significant radiation exposure. Plaintiffs instead relied on the frequency of chromosome aberrations known as a "dicentric chromosomes" in their lymphocytes as a biomarker of radiation exposure. The Third Circuit Court of Appeals endorsed in principle the use of such biomarkers as a "biological dosimeter" of exposure: "counting the number of dicentrics 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."[108]

The court also found, however, that dicentric chromosomes are unstable and therefore can only provide an accurate indicator of dose when assayed within one or two years of exposure, not fifteen years after exposure as occurred with the TMI plaintiffs.[109] The court found that an alternative cytogenetic biomarker also relied on by the plaintiff—chromosome translocations measured by the FISH (Fluorescent In Situ Hybridization) method—provided a better and more stable biomarker of radiation exposure.[110] However, plaintiffs had introduced their evidence on cytogenetic biomarkers of exposure using the FISH technique only after the deadline for new evidence had passed. Excluding the dicentric biomarker evidence as unreliable and the FISH results as untimely, the court granted summary judgment for defendants.[111] Despite the rejection of the plaintiff's cytogenetic evidence on technical grounds, this Court of Appeals

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[106] *See supra* note 98 and accompanying text.

[107] *In re* TMI Litig., 193 F.3d 613, 622-23 (3d Cir. 1999), *cert. denied*, 120 S. Ct. 2238 (2000).

[108] *Id.* at 690.

[109] *Id.* at 691-92.

[110] *Id.* at 692-93.

[111] *Id.* at 692-93, 717-722, 729.

opinion provides strong endorsement in principle for the general use of appropriate cytogenetic biomarkers to demonstrate and quantify exposure.

Other types of genetic biomarkers are also likely to be increasingly relied on to demonstrate exposure in the near future. For example, assays that detect "mutational fingerprints" of a specific toxic substance can provide compelling evidence of exposure.[112] One testing company, Benchmark Genetics, offers to collect and archive DNA samples from persons concerned about exposure to hazardous substances to establish a "genetic benchmark" that serves as a pre-exposure baseline, which can then be used in future litigation to demonstrate genetic changes as a result of subsequent occupational or other exposures.[113]

2. Chemical-Specific Markers of Effect

A toxic tort plaintiff must not only demonstrate sufficient exposure to an agent that is capable of causing her disease (general causation), but must also show that the agent did in fact cause the disease in that individual plaintiff (specific causation). The existence of chemical-specific genetic changes that are part of the etiology of a plaintiff's disease can provide compelling objective evidence of specific causation.

Although there are no published cases involving the use of *genetic* biomarkers to identify plaintiffs that have been harmed by a particular product, there have been closely analogous cases involving other types of biomarkers. For example, silicone breast implant plaintiffs relied prominently on studies claiming that various antibody and other biological markers of physiological response to silicone could be used to identify breast implant recipients with autoimmune disorders caused by their leaking implants.[114] By purporting to establish an objective biological relationship between silicone and an immunological response (represented by the presence of the biomarker), this evidence appeared to play a critical role in the decisions of several juries to award large damages to silicone breast implant plaintiffs.[115]

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[112] *See supra* note 103 and accompanying text.

[113] The company charges $50 for the storage of DNA samples. The company's materials advertise that "[b]y establishing a genetic benchmark now, if you should ever become ill you can have comparative DNA studies done to demonstrate that the genetic damage was not present prior to exposure. This information could be critical in establishing workers compensation or liability issues." BENCHMARK GENETICS, OCCUPATIONAL EXPOSURE TO HAZARDOUS CHEMICALS IS NO ACCIDENT, *at* http://www.benchmarkgenetics.com (last visited Oct. 15, 2001).

[114] *E.g.*, Hopkins v. Dow Corning Corp., 33 F.3d 1116, 1125 (9th Cir. 1994); Baxter HealthCare Corp. v. Grimes, No. 05-95-01682-CV, 1998 WL 5487729, at *2, *6-8 (Tex. Ct. App. Aug. 31, 1998).

[115] *See* Gary Taubes, *Silicone in the System*, DISCOVER, Dec. 1995, at 65, 66.

Many if not all of the alleged silicone biomarkers were scientifically suspect. For example, a private physician, suspicious about one silicone sensitivity test that was relied on in numerous court cases, sent to the laboratory that developed the test twelve blood samples from women who never had breast implants, but whose medical records were fabricated to indicate breast implantation. The laboratory reported that eleven of the twelve women tested positive for silicone.[116] Another silicone biomarker test used extensively in litigation could not be replicated by independent laboratories and was the subject of a warning letter from the Food and Drug Administration.[117] Large, independent epidemiologic studies failed to find any association between silicone breast implants and the various biomarkers relied on by plaintiff experts, and several expert scientific reviews concluded that such silicone biomarkers were not valid or reliable.[118] As the scientific doubts about the biomarker evidence accumulated, courts have refused to admit expert testimony based on such evidence in more recent cases.[119]

Biomarkers of effect can also be used by the defendant. If, for example, the plaintiff's cells contain genetic changes that are characteristic of exposure to other toxic agents, the defendant could argue that those agents are the alternative causes of the plaintiff's disease. The absence of any biomarkers of effect can be also used by a defendant to argue against causation. A defendant corporation successfully used the absence of a genetic biomarker to defend against liability in a Texas case in which the family of a deceased worker alleged that occupational exposure to benzene caused the worker's acute myelogenous leukemia (AML). While it was undisputed that benzene is capable of causing AML, the jury delivered a verdict for defendant after its expert testified that benzene only causes AML with specific cytogenetic markers—breaks in the fifth and seventh chromosomes—which were not present in the worker's DNA.[120] Although

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[116] V. Leroy Young, *Testing the Test: An Analysis of the Reliability of the Silicone Sensitivity Test (SILS) in Detecting Immune-Mediated Responses to Silicone Breast Implants*, 97 PLASTIC & RECONSTRUCTIVE SURGERY 681, 682 (1996).

[117] *See* Taubes, *supra* note 115, at 74.

[118] *E.g.*, INSTITUTE OF MEDICINE, SAFETY OF SILICONE BREAST IMPLANTS 198-214 (2000); SUBMISSION OF RULE 706 NATIONAL SCIENCE PANEL REPORT, CHAPTER II, CLINICAL IMMUNOLOGY; *IN RE*: SILICONE BREAST IMPLANT PRODUCTS LIABILITY LITIGATION (MDL 926) (N.D. Ala. Nov. 30, 1998); INDEPENDENT REVIEW GROUP, SILICONE GEL BREAST IMPLANTS (1998), *at* http://www-silicone-review.gov.uk (last visited Oct. 21, 2001) (scientific panel established by UK Chief Medical Officer).

[119] *E.g.*, Allison v. McGhan Med. Corp., 184 F.3d 1300, 1317-19 (11th Cir. 1999); Kelley v. Am. Heyer-Schulte Corp., 957 F. Supp. 873, 882-83 (W.D. Tex. 1997), *aff'd*, 139 F.3d 899 (5th Cir. 1998); Minnesota Mining & Mfg. Co. v. Atterbury, 978 S.W.2d 183, 201 (Tex. App. 1998).

[120] *See Expert Testimony: Jury Returns Verdict for Oil Company After Testimony on Missing Disease Marker*, 22 CHEM. REG. REP. (BNA) 193 (1998) (reporting jury verdict in

successful in the Texas case, this identical defense was subsequently rejected by other courts on the ground that the cytogenetic marker theory is "nothing more than an untested, unsupported hypothesis cloaked in the aura of scientific knowledge."[121] While breaks in the fifth and seventh chromosomes may be probative of benzene-induced leukemia, there is no published scientific evidence that the absence of such biomarkers in a leukemia patient definitively excludes benzene as a possible cause of that leukemia.[122]

These examples provide several lessons. First, biomarkers of effect, by purporting to provide an objective diagnostic link between exposure to a toxic substance and disease, can be extremely helpful to plaintiffs in establishing causation. Second, the absence of such biomarkers can also be used by defendants to argue persuasively against causation. Finally, as both the breast implant litigation and Texas benzene cases demonstrate, the reliability and medical significance of biomarkers are likely to be controversial, and litigants may be prone to exaggerated or premature reliance on biomarker evidence.

3. Recovery for Latent Risk

Perhaps the greatest impact of genetic biomarkers of effect will be in giving greater traction to plaintiffs' claims for recovery for latent risk. A "latent risk" is an increased probability of developing a future disease having a latency period between the time of exposure and the manifestation of symptomatic disease. Latent risk claims include recovery for increased risk of future disease, fear of developing future disease, and medical monitoring costs. These claims are all premised on the belief that the plaintiff has likely incurred genetic or other subcellular injury as a result of toxic exposures and is at an increased risk of future disease as a result of the expected progression of those present injuries.

Proof of latent risk has tended to be highly speculative, and allowing such claims may open a floodgate of additional legal claims. The courts have accordingly limited recovery for latent risks by establishing, in the words of the Supreme Court, "recovery-permitting categories the contours of which more distantly reflect [these] abstract general policy concerns."[123] For example, most courts have limited recovery for increased risk and fear of future disease to plaintiffs who can demonstrate a present injury,

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Wells v. Shell Oil Co., East Texas District Court, Mar. 2. 1998).

[121] *See, e.g., Benzene: Defense Experts' Opinions Inadmissible, Not Based on Reliable Methodology*, 22 CHEM REG. REP. (BNA) 613 (1998) (discussing Lavender v. Bayer Corp., No. 93-C-226-K, slip op. (W. Va. Cir. Ct. May 29, 1998)).

[122] *See* Marchant, *supra* note 3, at 98.

[123] Metro-North Commuter R.R. Co. v. Buckley, 521 U.S. 424, 436 (1997).

and many have also required plaintiffs to demonstrate a sufficiently large quantum of increased risk.[124] These recovery-limiting requirements are intended to ensure that latent risks are both substantial and objectively ascertainable. At the same time, these requirements impose a high threshold to recovery that most plaintiffs cannot presently surmount.

Genetic biomarkers of disease precursors may assist plaintiffs in meeting these evidentiary requirements. Such biomarkers would provide objective proof that would help to alleviate concerns about speculative or fraudulent claims, and would also validate a plaintiff's anxiety and medical need for ongoing monitoring. Conversely, the absence of biomarkers of effect, especially when such biomarkers would normally be expected, may allay the plaintiffs' fear of future cancer, as well as bar recovery for latent risk.

The use of biomarker evidence to identify large numbers of people who can objectively demonstrate that they are at an increased risk has the potential to swamp the litigation system. Given that over one-third of the population will eventually develop cancer, and that every human likely carries accumulated mutations that could eventually lead to cancer if the person lived long enough, it may be that with improved diagnostic capabilities of such mutations, every person could be a potential plaintiff claiming to be at an increased risk of cancer.[125] While resolving the need for objective proof of latent risk in many cases, biomarkers are therefore likely to create new challenges and problems for the courts.[126]

4. Duty to Conduct Genetic Tests

The rapid development and validation of numerous biomarkers of exposure and effect may create a legal duty for employers to genetically test their employees for such biomarkers as part of their duty to provide a safe workplace. The Occupational Safety and Health Administration (OSHA) has included a medical monitoring requirement in some occupational exposure standards for toxic substances, but such standards only exist for a handful of occupational exposures and to date have not

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[124] *E.g.*, *In re* Paoli R.R. Yard PCB Litig., 916 F.2d 829, 852 (3d Cir. 1990) (requiring showing of "significantly increased risk" for medical monitoring damages); Adams v. Johns-Manville Sales Corp., 783 F.2d 589, 591-93 (5th Cir. 1986) (requiring present injury); Potter v. Firestone Tire & Rubber Co., 863 P.2d 795, 807-16 (Cal. 1993) (requiring showing that disease is more likely than not to recover for fear of future disease); Ayers v. Township of Jackson, 525 A.2d 287, 308 (N.J. 1987) (refusing recovery for *unquantified* increased risk of future disease).

[125] *See* Donald T. Ramsey, *The Trigger of Coverage for Cancer: When Does Genetic Mutation Become "Bodily Injury, Sickness, or Disease?"*, 41 SANTA CLARA L. REV. 293, 329 (2001).

[126] For further discussion of the policy issues presented by biomarkers with respect to latent risks, see Marchant, *supra* note 3, at 84-88, 104-05.

required monitoring for genetic biomarkers.[127] An employer may have a common law duty to provide broader monitoring if it could help detect workers who may be beginning to develop chronic disease and who could be protected from developing the full disease by taking appropriate remedial measures to reduce their exposure.

In *Sbrusch v. Dow Chemical Co.*,[128] a chemical manufacturer has recently been sued by the widow of a deceased employee for failure to conduct cytogenetic testing that may have detected early biomarkers of her husband's leukemia, which allegedly resulted from benzene exposure in the workplace.[129] The plaintiffs relied on the fact that Dow had conducted cytogenetic monitoring of its workers in the 1970s, and had apparently found an association between benzene exposure and an increased frequency of chromosomal aberrations.[130] However, because Dow ceased its cytogenetic monitoring program in the late 1970s, Robert Sbrusch "was one of many benzene-exposed workers who was denied cytogenetic testing" which in his case allegedly "would have caught his cancer early."[131]

Such lawsuits contending that employers have a legal duty to genetically test their workers must circumvent the bar in state workers' compensation laws against workers suing their employers for occupational injuries, but an employee may be able to get to court by arguing that an employer was knowingly foregoing the opportunity to prevent potentially fatal diseases by failing to conduct such testing. That is precisely what the plaintiff has argued in the *Sbrusch* case, by relying on a Texas statute that allows the family of a deceased worker to recover exemplary damages from an employer who caused the worker's death "by an intentional act or omission of the employer or by the employer's gross negligence."[132]

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[127] *See* Michael Baram, *Genetic Testing for Susceptibility to Disease from Exposure to Toxic Chemicals: Implications for Public and Worker Health Policies*, 41 JURIMETRICS J. 165, 171-72 (2001).

[128] Sbrusch v. the Dow Chem. Co., Cause No. 12782*BH00, First Amended Original Petition (Dist. Ct., Brazoria Cty, TX, filed Jan. 10, 2001) (hereinafter Sbrusch Petition). The case was initially filed in state court, was successfully removed to the federal court based on diversity by the defendant, and then remanded to the state court because the case arose under the workman's compensation laws of Texas, which do not permit removal based on diversity. Sbrusch v. Dow Chem. Co., 124 F. Supp. 2d 1090,1091 (S.D. Tex. 2000).

[129] *See* Steve Olafson, *Suit Claims Dow Shirked Duty on Cancer-Testing of Workers*, HOUSTON CHRON., Aug. 12, 2000, at 33.

[130] *See* Sbrusch Petition, *supra* note 128, at 4.

[131] *Id.* at 6, 1.

[132] TEX. LAB. CODE ANN. § 408.001(b) (Vernon 2001). *See Sbrusch*, 124 F. Supp. 2d at 1091 (remanding case back to state courts because the claim arose under Texas Labor Code § 408.001(b)).

This potential new duty to genetically monitor their workers may put employers in a Catch-22 situation. Genetic testing of workers has been strongly criticized by the media, the government, and scholars.[133] Employers may also resist any requirement to genetically monitor their workers because such tests may provide evidence that support workers' compensation claims or even tort claims for knowing endangerment.[134] Moreover, a patchwork of state laws restricting genetic testing may prohibit genetic testing of employees in some locations.[135] On the other hand, employers may be legally forced to conduct such testing to avoid being sued for failing to provide a safe workplace by genetically monitoring their employees.

5. Improving Hazard Identification and Risk Assessment

Perhaps the most significant benefit of genetic biomarkers for toxic tort litigation in the long term will be the use of such biomarkers in studies to understand and demonstrate the capability of various agents to cause adverse effects. Of the more than 70,000 chemicals in commerce, only a small fraction have been thoroughly tested for toxicity.[136] The development of new test methods utilizing biomarkers of exposure or effect can lead to the toxicological screening of more chemicals in a shorter time period.[137] Biomarkers also have many applications in risk assessment of toxic substances, including providing more accurate exposure data for epidemiology studies, providing more sensitive indicators of toxic response in animal studies, improving understanding of the mechanism of toxicity

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[133] *See* Lillian Trettin et al., *Genetic Monitoring in the Workplace: A Tool Not A Solution*, 10 RISK: HEALTH SAFETY & ENV'T 31, 34 (1999) (concluding "workplace screening to ensure employee health and safety is out of favor with legislators, regulators and many business leaders").

[134] *See id.* at 38. The plaintiff in the *Sbrusch* case claimed that the reason that Dow discontinued its genetic monitoring program in the 1970s was precisely because the testing was generating evidence of occupational health risks. *See* Sbrusch Petition at 4-7. *See also* ELAINE DRAPER, RISKY BUSINESS 57 (1991) (quoting anonymous Dow official expressing concern that as a result of cytogenetic monitoring program "[w]e may even become the target of litigation and unfavorable publicity").

[135] Over twenty states have enacted laws restricting genetic testing that impose varying requirements. See http://www.gene-watch.org/programs/GD_Long_state_00.html (last visited on August 30, 2001), for the text of each State's legislation. Several bills proposing to restrict genetic testing by employers are also pending in Congress.

[136] *See* Perera, *Molecular Epidemiology*, *supra* note 97, at 609; Ken Olden, *The Role of the NIEHS in the Development of a National Program for Environmental Health Science Research*, *in* BIOMARKERS AND OCCUPATIONAL HEALTH: PROGRESS AND PERSPECTIVES 25 (M. Mendelsohn et al. eds., 1995).

[137] Olden, *supra* note 136, at 29-32.

caused by specific agents, and providing better information for extrapolating human risks from animal studies.[138]

The National Institute of Environmental Health Sciences (NIEHS) has recently established a National Center for Toxicogenomics that will use "gene chip" technology[139] to characterize and classify the body's response to different toxic substances.[140] This approach is intended to identify the human genes that are involved in the body's response to environmental exposures, and to differentiate patterns of gene expression that are associated with different mechanisms of toxicity from such exposures.[141] This information can then be used to rapidly screen untested chemicals to determine if they trigger a toxic response characteristic of one of the identified mechanisms of toxicity. The rapidly growing database of toxicological information from toxicogenomics should assist tort litigants in identifying toxic agents and proving the presence or absence of causation.

CONCLUSION

There are many potential applications of genetic biomarkers in toxic tort litigation. Many of these applications will fit easily within existing doctrinal templates, and should help to achieve a more informed and just outcome in many lawsuits. For example, biomarkers can be used to quantify an individual's exposure (or lack of exposure) to a toxic agent, or to provide an objective link between such exposure and the development of a disease process. Such applications can greatly contribute to overcoming some of the critical evidentiary gaps in many toxic tort suits. Similarly, the use of biomarkers of susceptibility to calculate relative risks based on the individual plaintiff's own specific susceptibility, rather than on some overall population average, can provide a more precise and just adjudication of causation.

Other potential applications of genetic biomarkers in toxic tort litigation will raise or amplify difficult doctrinal and policy issues that the tort system will be forced to address. For example, the genetic dissection of individual susceptibilities will present the issue of whether a manufacturer or employer has the duty to protect hyper-susceptible

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[138] Decaprio, *supra* note 95, at 1841; Perera, *Environment and Cancer*, *supra* note 27, at 1073.

[139] A gene chip, also known as a gene microarray, is a small glass slide, nylon filter or silicon wafer with up to thousands of different genes arranged on its surface that can be used to simultaneously screen for the existence or activity of many different genes in a cell. *See* McLeod & Evans, *supra* note 5, at 102.

[140] Olden & Guthrie, *supra* note 6, at 7.

[141] *Id.*

individuals, perhaps at the cost of withdrawing many otherwise beneficial products from the market. The use of biomarkers of effect to identify large numbers of people in which the disease process has been initiated or primed as a result of exposure to toxic agents will give greater credibility to claims for increased risk, and require decision-makers to balance the costs and benefits of giving greater recognition to latent disease claims.

The widespread use of genetic biomarkers in toxic tort cases will increase the challenge that trial courts already face in dealing with complex scientific information. The scientific basis for most genetic biomarkers will be complex, with the likelihood of conflicting and sometimes ambiguous data, confounding by factors such as ethnicity, genetic background, dose level and other exposures, and in the case of biomarkers of exposure and effect, the critical relationship between the time of exposure and the time of sampling.[142]

Given the apparent objectivity and certainty that biomarkers can provide, there will be a strong incentive for exaggerated or premature reliance on genetic biomarkers by tort litigants. Such premature or exaggerated use has already been seen in the breast implant and benzene examples discussed above.[143] The high stakes and one-shot dynamics of tort litigation provide compelling incentives for litigants to use any available biomarker evidence that is potentially helpful to their case, unlike the more cautious, science-based approach that regulatory agencies are likely to follow in incorporating this new type of information into their decisions. Courts will therefore be challenged to perform their role as scientific gatekeepers in screening the reliability and relevance of biomarker evidence, and juries will be challenged to understand and properly apply the scientific and probabilistic aspects of biomarker evidence.[144]

Some tort applications of genetic biomarkers are likely to raise other concerns relating to privacy and confidentiality. Many of the genetic biomarkers that are most relevant to evaluating a plaintiff's genetic susceptibility to a toxic agent will be very relevant to the individual's future health status and life expectancy, and may include sensitive information that the plaintiff herself may not want to know, or does not want others such as employers and insurers to know. Unlike the DNA forensic evidence used in criminal cases, which involves the use of markers that have no known biological relevance, genetic markers will be useful in

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[142] *See supra* notes 18-23 and accompanying text.

[143] *See supra* notes 115-123 and accompanying text.

[144] Jurors may be prone to giving too much weight to "objective" genetic evidence, failing to adequately appreciate the probabilistic nature of such evidence. *See* Marchant, *supra* note 3, at 106.

tort litigation only to the extent that they are relevant to the individual's health.

A blanket prohibition on use of plaintiffs' genetic data in tort cases seems ill-advised, given that the information will often be directly relevant to the issues in contention, and may in different cases help plaintiffs as often as it benefits defendants.[145] If a plaintiff can benefit from her own genetic susceptibilities in some cases, it would be unfair to preclude a defendant from obtaining and using similar genetic information in a case where it would benefit the defense. A general presumption in favor of using genetic information should therefore apply in tort cases, with judges exercising case-by-case review under Federal Rule of Civil Procedure 35 to protect against abuse or fishing expeditions that lack no reasonable cause.[146] Plaintiff's attorneys may also have an ethical duty to notify their clients that they may be subject to genetic testing in appropriate cases.

[145] A recent report by an international environmental group predicts that genetic susceptibility markers will be a boon to plaintiffs in toxic tort cases who will be able to use such information to prove that they have been injured by chemical companies and other businesses. FRIENDS OF THE EARTH, CRISIS IN CHEMICALS 42 (2000).

[146] Rule 35 provides for medical examination of a party upon a showing of good cause, which typically involves a case-by-case review by the trial or magistrate judge of the reasonableness of the medical testing request. This rule, and its state equivalents, will govern request for genetic testing of plaintiffs. *See* Marchant, *supra* note 3, at 106-07; Niedwiecki, *supra* note 94, at 299-309; Rothstein, *supra* note 93, at 889-91.