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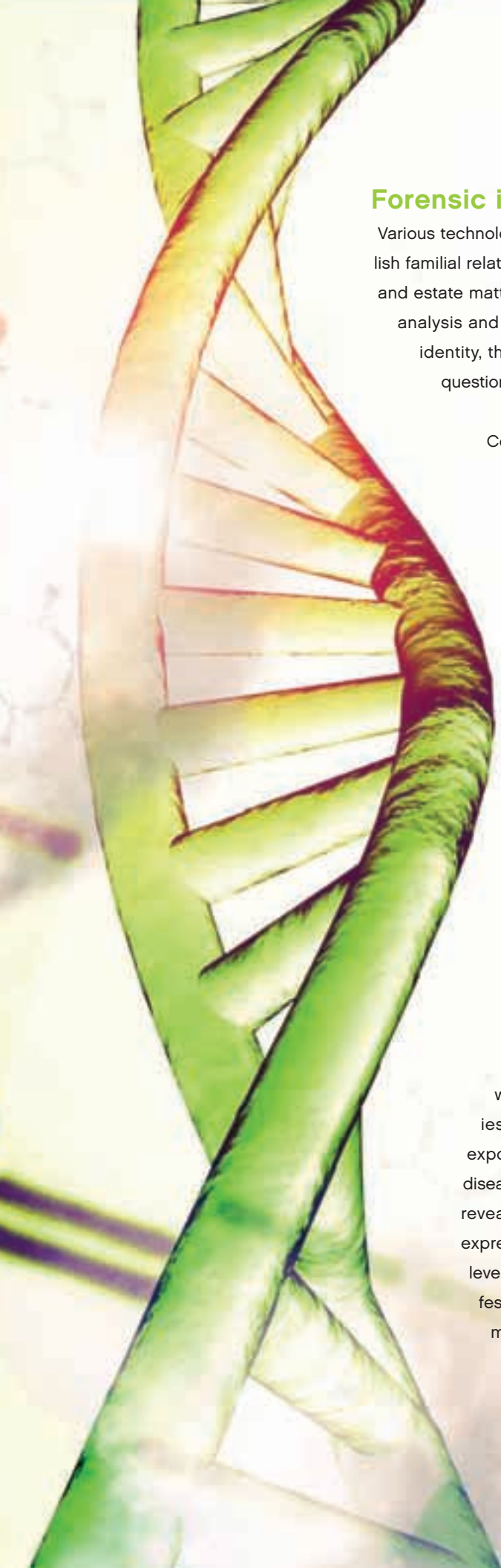
GENES FOR JUSTICE?

USING GENE EXPRESSION ANALYSIS TO **IDENTIFY** THE MOLECULAR FOOTPRINTS OF ENVIRONMENTAL **HAZARDS**



Forensic identification techniques have a long history.

Various technologies have been used to identify criminal defendants or their victims, establish familial relationships for paternity and immigration matters, prove authorship in contract and estate matters, and so on. But although conventional technologies such as fingerprint analysis and blood typing have long been accepted as reliable means of establishing identity, their uses beyond that are limited, and their reliability has been called into question as more advanced technologies have become more widely accessible.[1]

Conventional forensic identification techniques met their match in 1984 when British geneticist Sir Alec Jeffreys unexpectedly discovered the 0.1 percent of human DNA[2] that makes individuals unique. His discovery paved the way for DNA profiling, which is the use of DNA to identify an individual by the unique features of his or her genetic material. DNA profiling caught on rapidly and is now the gold standard in many courtrooms for proving or disproving identity. However, the use of DNA technology is hardly limited to identifying people by the invisible "footprints" left behind in their blood, hair, and skin cells. As science and technology have advanced, scientists have harnessed DNA technology to learn more about disease and human development.

Most recently, DNA technology developed by scientists at the University of Illinois College of Medicine and marketed through the Cytokine Institute offers the possibility of identifying the unique molecular footprints that environmental hazards leave behind in our bodies. This technology, which studies changes in the expression of genes, works to identify the unique series of chain reactions set off within a person's DNA when he or she is exposed to a toxic substance.

This DNA technology attempts to fill the critical gap left by epidemiology, which focuses primarily on the risk factors for disease as reflected in studies of the human population at large. Epidemiology provides evidence that exposure to a particular hazard is generally associated with or causes certain diseases. But it can be argued that only a study of the individual could definitively reveal the complex pathways of a disease or injury within that individual. Gene expression analysis thus has the potential to enable us to see, at the molecular level, how an individual was injured by outside forces long before the injury manifests itself in cognizable disease symptoms. Having the ability to unlock these molecular "bread crumbs" may well enable practitioners to determine whether an exposure has occurred in the absence of measurable quantities of the substance within the body or before the manifestation of a disease.

THE PROOF IS IN THE PUDDING

DNA is essentially a blueprint that contains the instructions necessary for cells to build and sustain life. Gene expression, in contrast, is the process by which the information contained in the blueprint is translated into the machinery of life. For example, the expression of many genes results in the formation of proteins, which then perform various cell functions.

The technology of gene expression analysis attempts to identify the impact of toxic substances by studying how gene expression changes in response to a particular exposure. There are three possible reactions to an exposure at the DNA level: a gene is up-regulated, which is when the genetic material "turns on" and increases the expression of the gene (*i.e.*, more protein is produced); the genetic material is down-regulated, which is when the genetic material "turns off" and decreases the expression of the gene (*i.e.*, less protein is produced); or the gene is unaffected. Through the use of computers, this technology makes it possible to study the expression of tens of thousands of genes at the same time. This, it is said, results in a detailed view of how toxic substances affect the translation of our DNA into life functions. In building the detailed picture, a unique footprint emerges for each toxic substance.

For example, some scientists report that exposure to benzene alters the expression of genes that regulate protein metabolism, electron transport, and the antigen-processing functions of leukocytes, or white blood cells, which form part of the immune system and defend against disease.[3] Likewise, exposure to hexavalent chromium is said to affect the expression of genes related to cellular metabolism, immune response, intracellular signaling, and other functions of certain blood cells.[4] Results of this technology may allow scientists to identify the unique genetic footprints that exposure to benzene and hexavalent chromium leaves behind before the injurious effects of these substances become apparent as illness or disease.

GENE EXPRESSION ANALYSIS IN THE COURTROOM

The proponents of this technology hope that gene expression analysis will enable medical professionals and scientists to understand the roles that DNA plays in disease. A better understanding of this relationship could lead to better treatments. And, although it is in its infancy, gene expression analysis could affect many aspects of product liability, insurance, workers' compensation, and personal-injury litigation. For example, a plaintiff or prospective plaintiff alleging toxic exposure might be tested to determine whether his or her cells contain the unique genetic footprint for the alleged substance. Defense independent medical examiners might use the technology to negate disability. For plaintiffs and defendants alike, gene expression analysis (much like DNA fingerprinting before it) potentially offers the opportunity to present persuasive evidence of exposure—or the absence thereof—by an impartial, scientific means. The technology could also play a gatekeeping role in class certification by limiting class membership to those individuals who bear the unique signature of a particular toxin. In so doing, gene expression analysis could reduce the number of frivolous cases and prevent unnecessary damage awards.

AN END TO MEDICAL MONITORING?

In medical monitoring cases, plaintiffs who present no physical injury or symptom of disease, but who have an increased risk of future disease due to exposure to a hazardous substance, may be entitled to recover for medical screening tests to detect the early onset of a targeted disease. Gene expression analysis may prove useful in developing the sort of evidence needed to move away from an award of damages based on uncertain, pre-injury claims for future medical monitoring.

By way of example, in *Potter v. Firestone Tire & Rubber Co.*, 863 P.2d 795 (Cal. 1993), four landowners who lived next to a landfill alleged that Firestone's practice of disposing its industrial waste there, including the known carcinogen benzene, subjected them to prolonged exposure to carcinogens. *Potter*, 863 P.2d at 975, 801–02. None of the plaintiffs had developed cancer; instead, they alleged that they were at risk for developing cancer in the future. *Id.* at 975. The California Supreme Court awarded medical monitoring damages, finding that plaintiffs in a negligence action need only prove that the need for future monitoring is a reasonably certain consequence of their toxic exposure and that the recommended monitoring is reasonable. *Id.* at 825. However, the California court noted that the medical monitoring would be "unnecessary if the particular plaintiff had not been wrongfully exposed to pollutants." *Id.* at 822.

Enter gene expression analysis. This technology could potentially be used by defendants in such cases to show that the

plaintiffs did not bear the hallmark footprint of exposure to benzene and that medical monitoring was therefore definitively unnecessary. *See*, *e.g.*, *Sheridan, et al. v. NGK Metals Corp., et al.*, 2010 WL 2246392 (3d Cir. June 7, 2010) (affirming dismissal of medical monitoring classes in beryllium cases absent genetic markers). On the other hand, once an injury is known—*i.e.*, once the footprint is found—a plaintiff may be more likely to be awarded damages for testing to monitor the status of the exposure and its potential to develop into disease or injury. Although this would, of course, provide plaintiffs another means of stating a claim, it could also have the collateral benefit to all parties of mitigating the potential effects of the resulting disease as soon as they become apparent. Bottom line: If successfully utilized, gene expression analysis could be a valuable aid in more accurately determining the need for medical monitoring and setting damage awards.

WORKPLACE MONITORING

Gene expression analysis could also be used in the workplace to monitor workers for occupational exposure to process chemicals or their byproducts. For example, steel mills and textile manufacturers that use hexavalent chromium could utilize the technology as part of a workplace-monitoring program to track potential exposures beyond what are considered to be safe levels. Such a program might establish baseline exposure by testing new employees for the unique footprint; it would then retest the workers over time, administering the final test at the conclusion of their employment. This technology has the potential to be a valuable aid in monitoring worker safety and could provide early notice of exposure, enabling manufacturers to institute measures to mitigate damages once exposure becomes apparent. It could also be used to substantiate or refute later allegations of workplace injury when presented in either individual or collective actions.

But the use of this technology for workplace monitoring may raise countervailing privacy and genetic-discrimination concerns.[5] Employees may object to the collection of blood samples and may view gene expression analysis as an invasion of the right to privacy. In addition, Title II of the Genetic Information Nondiscrimination Act ("GINA") of 2008, which took effect on November 21, 2009, prohibits employers from discriminating against any employee with respect to compensation, terms, conditions, or privileges of employment on the basis of the employee's genetic information. *See* 42 U.S.C. § 2000ff-1(a). GINA defines "genetic information" as information gained from an individual's genetic tests. *Id.* § 2000ff(4)(A). "Genetic test," in turn, is defined as "an analysis of human DNA, RNA, chromosomes, proteins, or metabolites that detects genotypes, mutations, or chromosomal changes." *Id.* § 2000ff(7)(A). The "analysis of proteins or metabolites that does not detect genotypes, mutations, or chromosomal changes" is expressly excluded from the definition of "genetic test." *Id.* § 2000ff(7)(B). Similarly, "genetic monitoring" is defined as "the periodic examination of employees to evaluate acquired modifications to their genetic material . . . that may have developed in the course of employment due to exposure to toxic substances in the workplace." *Id.* § 2000ff(5).

Whether gene expression analysis is covered by GINA, however, has yet to be decided. Proponents of the technology in the workplace will attempt to characterize it as simply a test of how an individual's DNA is translated—rather than a test of the composition of or changes to the DNA itself, which is regulated by GINA. Opponents, on the other hand, might argue that any procedure that looks for changes in genetic expression—up-regulation or down-regulation—is exactly the type of test contemplated by Congress.

Yet even if the use of gene expression analysis is considered "genetic monitoring" or a "genetic test" under GINA, under limited circumstances an employer may be permitted by GINA to collect genetic information within the context of a workplace-monitoring program. *Id.* § 2000ff-1(b)(5) (allowing genetic monitoring of the biological effects of toxic substances in the workplace). The employer must provide written notice of the monitoring to the employee; the employee must provide authorization for the monitoring or, alternatively, the monitoring must be required by federal or state law; the monitoring must be in compliance with federal or state regulations on genetic monitoring; the employee must be informed of the monitoring results; and the results must be presented to the employer in aggregate terms that do not disclose the identity of specific employees. *Id.* § 2000ff-1(b)(5)(A)–(E). Results reflecting specific employee identities may be provided to a licensed health-care professional or board-certified genetic counselor only. *Id.* § 2000ff-1(b)(5)(E).

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However, there are open questions about whether and how that information may be made available to employers, as well as what action employers may take upon receiving the information. If an employer is restricted from obtaining individually identifiable information, then a monitoring program may be of little use. An employer seeking to identify affected employees in order to take action to mitigate their injuries would be hampered in its efforts. And while the fact of an exposure presumably could be used to alter workplace conditions as a whole, it is of lesser use to the exposed individual. Whether, and to what extent, this information could be used to substantiate or refute later allegations of workplace injury remains unsettled. However, one could argue that GINA does not seem to prohibit an employer from keeping individual test results for later use in litigation, as long as the employer does not apprise itself of an individual's test results prior to the pending or threatened litigation.

CAUSATION AND INJURY REMAIN ELUSIVE

Gene expression analysis has two important limitations. First, as the technology now stands, it does not definitively prove *causation*. It is simply a test for *exposure*. A worker who alleges that his leukemia was caused by occupational exposure to benzene, and who exhibits the identified footprint for benzene exposure, cannot use the gene expression analysis test to definitively prove that his leukemia was caused by benzene as opposed to some other factor. The technology may provide some evidence of causation, but it would not exclude other possible causes, such as genetic predisposition or exposure to radiation. Moreover, it would not exclude other possible sources of benzene exposure—a different employer or household or other environmental exposure. On the other hand, gene expression analysis may definitively disprove causation if the person is found *not* to exhibit the unique footprint of exposure. Thus, proof of exposure is only one link in the causal chain. The existence of the unique footprint for a particular toxin must be linked to the disease or condition itself.

Second, gene expression analysis does not prove injury. Although it provides a vehicle to identify change within the body, such change is not necessarily harmful. Many parallels can be drawn to toxic trespass litigation, in which plaintiffs allege injury from the mere presence of chemicals in their bodies. In toxic trespass actions, courts have taken a variety of approaches in deciding whether a change that does not cause harm—or causes no more harm than that to which the general population is exposed—is compensable as a legal wrong. In the absence of the manifestation of an apparent injury to the exposed individual, defendants will have a strong defense that compensation is improper.

CONCLUSION

Gene expression analysis offers the promise of impartial, scientific evidence of exposure, even in the absence of measurable quantities of the substance in the body or the manifestation of apparent disease. However, gene expression analysis is not without limitations. The technology is relatively new, and its potential applications and benefits are still being explored. Employers seeking to implement workplace-testing or -monitoring programs will need to confront barriers raised by privacy and GINA's limitations on the use of genetic information. Parties seeking to use the technology in litigation will bear the burden of establishing its relevance and reliability, and they will still be required to prove or refute causation and injury. ■

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[1] *See, e.g.*, *United States v. Llera Plaza*, 188 F. Supp. 2d 549 (E.D. Pa. 2002) (Pollak, J.) (vacating earlier ruling preventing expert fingerprint analysts from offering opinions on whether latent prints matched a particular person because of the subjective nature of rendering such opinions); Michael J. Saks, "Merlin and Solomon: Lessons from the Law's Formative Encounters with Forensic Identification Science," 49 *Hastings L.J.* 1069, 1100–06 (1998).
[2] Deoxyribonucleic acid, one of two types of molecules that encode genetic information.
[3] Bruce Gillis et al., "Identification of Human Cell Responses to Benzene and Benzene Metabolites," 90 *Genomics* 324, 327 (2007).
[4] Igor M. Gavin et al., "Identification of Human Cell Responses to Hexavalent Chromium," 48 *Environmental & Molecular Mutagenesis* 650, 654 (2007).
[5] *See* Jeremy Smerd, "DNA Technology May Curb Bogus Disability Claims," *Workforce Management* (Sept. 18, 2007).