

## The Environmental Genome Project: Ethical, Legal, and Social Implications

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The National Institute of Environmental Health Sciences is supporting a multiyear research initiative examining genetic influences on environmental response. Proponents of this new initiative, known as the Environmental Genome Project, hope that the information learned will improve our understanding of environmentally associated diseases and allow clinicians and public health officials to target disease-prevention strategies to those who are at increased risk. Despite these potential benefits, the project presents several ethical and social challenges. Of immediate concern is the protection of individual research participants. Other ethical issues relate to the application of research results and how study findings could affect social priorities. Clarifying these emerging areas of concern, many of which have not received adequate attention in the existing bioethics literature, is an important step toward minimizing potential research-related risks and defining research needs. *Key words:* Environmental Genome Project, environmental genomics, ethics, genetic susceptibility, human subjects research, informed consent. *Environ Health Perspect* 108:279–281 (2000). [Online 14 February 2000] <http://ehpnet1.niehs.nih.gov/docs/2000/108p279-281sharp/abstract.html>

The National Institute of Environmental Health Sciences recently launched a new research initiative known as the Environmental Genome Project (EGP) (1–3). The EGP will examine how genetic variation affects response to environmental exposures. Initially, the project will identify polymorphic variation in genes that appear to play an important role in environmentally associated diseases. Having identified these genetic polymorphisms, researchers then will examine their functional implications more carefully (4). These functional studies will be multidisciplinary in approach, incorporating research methodologies from biochemistry, epidemiology, genetics, pharmacology, and toxicology (5).

Proponents of the EGP hope that the information learned will be instrumental in improving public health (6). A better understanding of genetic influences on environmental response could lead to more accurate estimates of disease risks and provide a basis for disease prevention and early intervention programs directed at individuals and populations at increased risk (7). Identifying functionally significant polymorphisms also could shed light on disease pathways and suggest targets for therapeutic intervention (8,9).

As with all research, these potential benefits must be weighed against possible risks. Following the precedent developed in connection with the Human Genome Project (10,11), there are plans to support research on the ethical, legal, and social implications of the EGP (12). By examining these issues, we may be able to anticipate problems before they arise and develop policies that maximize the benefits of the EGP while minimizing its risks (13).

In this paper we highlight several ethical, legal, and social issues raised by the EGP. These issues are presented in the order that they likely will present themselves to researchers, beginning with the protection of research participants and concluding with potential long-term implications of environmental genomic research. Our goal in providing this overview is to draw attention to future research needs and encourage others to join us in thinking about these difficult and complex issues.

### Current Issues: Protecting Research Participants

The most immediate ethical, legal, and social issues raised by the EGP relate to the protection of individual research participants (14–16). Genetic studies often present special challenges in protecting human subjects because genetic research frequently poses psychosocial risks that may be difficult to anticipate and convey to prospective participants (17). These risks can include possible discrimination or stigmatization, disrupted relationships between family members, and adverse effects on a participant's self-image (18).

The presentation of research-related risks to participants is especially troublesome in connection with the EGP because of the many uncertainties surrounding the study of genetic hypersensitivities to environmental exposures. Studies of gene–environment interactions often do not allow for precise quantification of the respective genetic and environmental contributions to disease (19). As a result, research findings may be difficult for researchers and participants to interpret. A study may identify a genetic polymorphism that appears to play a role in environmental response, but the extent to which its

effects are mediated by environmental factors often will remain unclear. Without more information on an individual's genome and past environmental exposures, the detection of such a polymorphism is of uncertain value in predicting future disease. These uncertainties complicate the process of informed consent, particularly the communication of potential risks and benefits to prospective participants (20). The inability to quantify the precise extent to which a particular polymorphism increases disease risks also makes it difficult to determine whether research results should be disclosed to participants, and if so, in what manner (21).

If study results are conveyed to participants, still other complications present themselves (22). In many genetic studies, specially trained genetic counselors discuss findings with participants. This approach helps minimize potential psychosocial risks. Although genetic counselors could be used to convey results obtained in connection with the EGP, the current shortage of these professionals likely would make this a practical impossibility. Moreover, if many laypersons overestimate the predictive value of genetic information (23), it may be difficult to present findings on genetic hypersensitivities to environmental exposures in a manner that avoids placing too much emphasis on genetic contributions to disease. It is more likely that information on increased susceptibility to environmentally associated diseases will be viewed fatalistically, prompting some to infer that because they have a genetic predisposition to a disease, they will eventually develop that condition. Such misunderstandings are a concern in presenting study results to individual participants, as well as in presenting research findings more generally.

Other immediate ethical, legal, and social issues relate to the breadth of the consent obtained in connection with EGP studies (24). Associations between individual alleles and particular environmental exposures are difficult to identify. As a result, researchers are interested in designing studies that look at possible associations between many different allelic variants and many

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different exposures concurrently. Although such studies increase the likelihood of identifying functionally significant polymorphisms, they complicate the consent process. As more genes and exposures are considered simultaneously, it becomes increasingly difficult to anticipate the potential risks and benefits of the research (25,26). Hence, it also becomes more difficult to ensure that individual participants are fully informed about the possible risks and benefits of their participation. At the extreme, the worry is that individual consent becomes a blanket permission for genetic research in general (27). These broad permissions are considered morally problematic because it is unclear how participants could be fully informed about such a wide range of potential research uses (28).

A related concern is that current policies governing informed consent could place inappropriate restrictions on research in environmental genomics (29). Although the present standards for informed consent in genetic research may be appropriate for studies of highly predictive alleles, they may be overly demanding for studies of genetic hypersensitivities to environmental exposures, particularly because such studies generally present more limited risks to individual participants. Thus the challenge facing the EGP is to establish consent procedures that allow individuals to make genuinely informed choices about their participation in studies that examine many different alleles and multiple exposures concurrently. The permissions granted by participants should be broad enough to permit diverse research interests, yet specific enough to allow individual participants to assess the possible risks and benefits of their participation.

### Emerging Issues: Protecting Socially Identifiable Groups

Many of the ethical, legal, and social issues surrounding the EGP are familiar to experienced researchers and Institutional Review Boards. Although the EGP complicates these familiar areas of concern, studies of genetic influences on environmental response also introduce other less familiar ethical and social considerations. These concerns will become more prominent as research in environmental genomics expands and information on common genetic hypersensitivities becomes more widely available.

One such issue is the protection of socially identifiable groups, including racial and ethnic populations. Some allelic variants are more common in certain populations and less common in others. As specific genetic polymorphisms are associated with increased susceptibility to environmental exposures, it is likely that some genetic hypersensitivities will be associated with particular social

groups (30). The association of genetic hypersensitivities with race or ethnicity could threaten the employment and insurance opportunities available to entire groups of individuals, not just those who choose to participate in research (31,32). Members of these populations also could encounter broader forms of discrimination and stigmatization, for example, in child custody disputes or adoption efforts (33,34). In this regard, the association of Ashkenazi Jews with *BRCA1* mutations (and increased risk of breast cancer) is suggestive of the type of risks presented by studies of genetic influences on environmental response (35,36).

In response to these research-related risks, some have proposed that members of study populations be involved directly in the review of proposed research (37,38). Involving community representatives early in the design of research protocols could help identify potential risks that otherwise could go unnoticed (39). This approach has been controversial and the effectiveness of these supplemental protections has been questioned (40,41). Additional discussion and empirical research are needed to determine how best to incorporate the perspectives of study populations in the review of genetic research (42).

### Long-Term Issues: Shifting Social Priorities and Responsibility for Health

Although it is difficult to speculate on the long-term consequences of any area of research, there are a number of broad social considerations suggested by the EGP. One such concern is that research on genetic influences on environmental response could affect how we view an individual's responsibility for his or her overall health. It seems reasonable to suggest that individuals with known genetic hypersensitivities to particular exposures are responsible for avoiding those adverse exposures. Individuals who know that they are particularly susceptible to the toxins found in cigarette smoke, for example, should quit smoking. What is less clear, however, is how far this moral obligation extends.

For instance, suppose an individual has a known hypersensitivity to an environmental exposure that is very common and difficult to avoid—exposure to low levels of direct sunlight, for example. An individual may be able to avoid such adverse exposures, but only by taking extraordinary measures. Although preventive interventions are available, it is unclear how we should view those individuals who fail to take such extraordinary measures to lower their risk of disease. Insurers, for example, may claim that individuals who do not minimize their exposure to these agents are responsible for any subsequent illness

because they knowingly placed themselves at risk. Employers asked to pay for health costs through workers' compensation may refuse based on the idea that it was the individual who knowingly took a job that placed him or her at increased risk. In contrast, individuals with heightened genetic sensitivities may seek protection under the Americans with Disabilities Act or state legislation protecting against genetic discrimination (43). Currently, it is unclear how to resolve such disputes or the extent to which information on genetic hypersensitivities might be inappropriately used to avoid responsibility for illness. In part, these disputes concern possible discriminatory uses of genetic information, but the more fundamental issue is how information on genetic risks will alter our views on personal responsibility for one's health (12).

Other examples suggest further complications to the notion of personal responsibility. Suppose gene-modification techniques become more effective than they are at present. When certain genetic polymorphisms help protect against adverse exposures, individuals may wish to alter their genetic makeup to increase their tolerance to these exposures. Given the scarcity of medical resources, such applications of gene-manipulation techniques are unlikely to become commonplace. However, because these genetic enhancements could be purchased by wealthy individuals, their availability would contribute to existing health disparities between the rich and the poor. Genetically enhanced millionaires could live recklessly, engaging in unhealthy behaviors, whereas the poor would be held to a higher standard of accountability for their health.

Related to these considerations regarding medical responsibility are concerns about the effect the EGP and projects like it may have on how we view at-risk, but currently asymptomatic, individuals. As with other known genetic susceptibilities to disease, some individuals who are at increased risk of developing environmentally associated diseases will view themselves, and will be viewed by others, as ill—even though they may not be exhibiting any symptoms of the disease and may never develop the illness in question (44). If associations between particular polymorphisms and specific diseases prove difficult to quantify, the EGP could foster such fatalistic attitudes by making it difficult to specify the precise extent to which an individual is at increased risk.

Other long-term considerations relate to increased emphasis on the genetic causes of disease. This trend, which has been described as the geneticization of disease (45), could foster the belief that social problems are primarily the result of genetic causes. This reduction of social problems to biological

problems could change how we think about social priorities. For example, employers may be viewed as less responsible for improving workplace conditions, with the focus of disease causation shifting from the hazardous workplace to the predisposed worker. Similarly, research funding may be diverted away from preventive strategies for improving public health, moving instead to approaches stressing genetic influences on disease (46).

### Areas for Future Research

It is expected that as the EGP develops, a wide range of ethical, legal, and social issues will emerge as important areas for additional consideration. There is already extensive literature examining the social implications of genetic research, much of which is directly relevant to the EGP. All too frequently, however, policy recommendations focus on rare alleles that are highly predictive of disease. It is unclear whether these moral and legal perspectives are appropriate guides when the alleles under investigation are much more common and less predictive of future disease (47,48).

In many ways, the EGP is representative of a new type of genetic research program, with its emphasis on the incorporation of detailed genomic information into our understanding of disease susceptibility and individual response to environmental exposure. Thus, it is not surprising that the social implications of the project have not been adequately discussed in the existing bioethics literature. As the field of environmental genomics develops, researchers, legislators, and policy makers will need to consider the extent to which traditional bioethical perspectives apply to this new area of research. Thoughtful discussions of the ethical, legal, and social implications of environmental genomic research are critical to the overall success of projects like the EGP. We hope that this paper plays a role in fostering those discussions.

For additional information on the ethical, legal and social implications of the EGP, visit the project's web site (49).

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