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Human Genome Epidemiologic Reviews: The Beginning of Something HuGE

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This issue of the *Journal* contains the first two published Human Genome Epidemiologic (HuGE) reviews, which are systematic, structured, peer-reviewed synopses of epidemiologic aspects of human genes in relation to specific diseases. In the first review, Cotton et al. (1) evaluate the relations between glutathione *S*-transferase polymorphisms and colorectal cancer. In the second review, Rasmussen and Friedman (2) assess epidemiologic aspects of the neurofibromatosis 1 (*NF1*) gene and its relation to the relatively common Mendelian condition. As such, these reviews represent the spectrum of the relations between genes and diseases (from single gene disorders to multifactorial conditions). Both HuGE reviews illustrate the range of methodological problems likely to occur when reviewing data from investigations of the relations between other genes and other diseases. Even for the single gene disorder, neurofibromatosis type 1, there is wide variation in the clinical phenotype, even in individuals with the same *NF1* gene mutation. It seems that many of the other factors involved in determining clinical manifestations have not yet been determined. In addition, although a protein truncation test for *NF1* mutations is commercially available, its sensitivity, specificity, and predictive value have not been established. With regard to glutathione *S*-transferase polymorphisms and colorectal cancer, many of the published studies have been subject to selection and participation bias, and some have had limited statistical power, particularly for subgroup analyses. It is difficult to assess how much these methodological problems may account for the inconsistencies in the results. The limited statistical power of small studies to detect associations between genotype and disease is particularly important with regard to effect modification, and as yet, few studies have investigated interactions between glutathione *S*-transferase genotypes and environment.

These articles are among 40 or so such reviews currently in preparation after the announcement in 1998 of the formation of the Human Genome Epidemiology Network (HuGE Net) and the partnership between the *American Journal of Epidemiology*, *Epidemiologic Reviews*, and the Centers for Disease Control and Prevention in seeking and publishing such peer-reviewed articles (3). This partnership reflects the increasing recognition by the editors of the *American Journal of Epidemiology* and *Epidemiologic Reviews* of the role of genetics in epidemiologic research.

In brief, HuGE Net represents a global collaboration of individuals and organizations from diverse backgrounds who are committed to the development and dissemination of population-based human genome epidemiologic information. The goals of such an endeavor are 1) to establish an information exchange network that promotes global collaboration in the development and dissemination of peer-reviewed epidemiologic information on human genes; 2) to develop an updated and accessible knowledge base on the World Wide Web; and 3) to promote the use of this knowledge base by health care providers, researchers, industry, government, and the public for making decisions involving the use of genetic tests and services to improve health and prevent disease. Additional information about this "virtual" collaboration can be found on the HuGE Net website (4).

The term HuGE denotes an evolving field of inquiry that uses systematic applications of epidemiologic methods and approaches in population-based studies of the impact of human genetic variation on health and disease (3). Human genome epidemiology can be viewed as the intersection of genetic epidemiology (primarily concerned with finding genes), molecular epidemiology (primarily concerned with using genetic markers in epidemiologic studies of risk), and applied epidemiology (primarily concerned with health services research on the impact of genetic tests and services). With the impending completion of the human genome project and the identification of the 50,000–100,000 human genes in the next few years

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Abbreviations: HuGE, human genome epidemiology; HuGE Net, Human Genome Epidemiology Network.

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(5), there will be a "huge" need for an epidemiologic approach to evaluate the role of gene variants in the occurrence of various human diseases (6).

Since the formation of HuGE Net, a wide array of medical and public health professionals have voiced concerns about the increasing gap between gene discovery and the implementation of disease prevention measures in which information on genetic variation might be used. The translation from gene discovery to disease prevention depends to a large extent on rapidly developing the scientific information by means of conducting high-quality, population-based investigations on gene-disease relations, including study of gene-environment interactions, integration of the evidence from these investigations, and evaluation of disease interventions. This is the approach that HuGE represents.

HuGE Net has also witnessed a growing membership roster, a liaison board, and a recently formed editorial board (4). It is widening its collaborative base with several journals, including *Genetics in Medicine*, *Teratology*, and *Emerging Infectious Diseases.*

We hope readers will find these reviews pertinent, timely, and helpful, especially in evaluating the currently existing gaps of information. We also hope readers will contribute to the building of this knowledge base by collaborating and conducting HuGE reviews of their own.

REFERENCES

1. Cotton SC, Sharp L, Little J, et al. Glutathione *S*-transferase polymorphisms and colorectal cancer: a HuGE review. Am J Epidemiol 2000;151:7–32.
2. Rasmussen SA, Friedman JA. *NF1* gene and neurofibromatosis type 1: a HuGE review. Am J Epidemiol 2000:151: 33–40.
3. Khoury MJ, Dorman JS. The Human Genome Epidemiology Network. Am J Epidemiol 1998;148:1–3.
4. Centers for Disease Control and Prevention. The Human Genome Epidemiology Network (HuGE Net). 1999. http://www.cdc.gov/genetics/hugenet/default.htm (1 November 1999).
5. Collins FS. Shattuck lecture—medical and societal consequences of the Human Genome Project. N Engl J Med 1999; 341:28–37.
6. Shpilberg O, Dorman JS, Ferrell RE, et al. The next stage: molecular epidemiology. J Clin Epidemiol 1997;50:633–8.

For further information about submitting articles, please refer to "Revised Guidelines for Submitting HuGE Reviews," which follows this editorial.