

# New Disciplines, Challenges Emerge at Interface of Genetics and Public Health

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As the year 2099 turns into 2100, historians will surely consider the completion of the sequencing of the human genome in 2000 as the first significant scientific milestone of the twenty-first century. And we can only begin to imagine the profound revolution ahead for human health.

With the new genetic technologies and information available today, we are already in the early stages of a transformation of public health practice, research, and education. A new specialty — public health genetics — has recently emerged at the interface of these two disciplines. It is the application of advances in genetics and molecular biotechnology to improving public health and preventing disease.

In the coming decade, we will see an increasing integration of genetics into public health research, policy, and program development. Public health sciences will have an important role in elucidating the significance of newly identified human genetic variation and of the interplay between genetic and environmental influences. Public health professionals will increasingly use genetic information and technologies for the prevention and treatment of disease.

This article briefly reviews the trends as they are unfolding for public health research and education and the implications for communities and consumers.

## Research Trends

The explosion of genetic knowledge and technology has created a growing need for multidisciplinary and cross-disciplinary research related to public health and genetics. We can see these influences at work transforming the following areas of public health science and related fields.

### Genetic and Molecular Epidemiology

Genetic epidemiology seeks to identify genetic characteristics, and their interactions with environmental exposures, that influence

the distribution of disease among families and within diverse human populations. The goal is to improve early prediction of disease among high-risk persons and families and to design more effective interventions. For example, the tools of genetic epidemiology helped to identify a susceptibility gene for non-insulin-dependent (type 2) diabetes mellitus on chromosome 2 in a study of 330 Mexican-American sibling pairs (Hanis et al. 1996) and on chromosome 20 in a sample of Finnish sibling pairs (Ghosh et al. 1999).

Rapid advances in molecular biology are providing new tools for epidemiologic studies. Molecular epidemiology has increased understanding of the transmission and pathogenesis of infectious diseases. For example, a comparison of the genetic profile of *E. coli* shared between sex partners allows the identification of genes associated with transmission of uropathogens (Foxman et al. 1997). Genetic fingerprinting techniques for *E. coli* O157:H7, developed at the University of Washington, have helped epidemiologists quickly pinpoint food-borne or waterborne sources of contamination and halt spread of disease.

Furthermore, the emerging field of human genome epidemiology (HuGE) applies epidemiologic methods and approaches in population-based studies investigating the impact of human genetic variation on health and disease. Investigators are addressing a spectrum of topics ranging from research on gene variants to risk assessment and evaluation of genetic tests and services.

To further these efforts, a collaboration of individuals and organizations recently launched the Human Genome Epidemiology Network (HuGE Net). This global effort seeks to: (1) promote collaboration in developing and disseminating peer-reviewed epidemiologic information on human genes; (2) develop an updated and accessible knowledge base on the World Wide Web; and (3) promote 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 for disease prevention and health promotion.

### ***Pathobiology and Infectious Diseases***

Advances in genotyping technology and sequence analysis hold remarkable potential for better understanding susceptibility and resistance to infectious diseases. For example, a recent report based on five AIDS cohorts revealed a significant association between HLA class I heterozygosity and slower disease progression to AIDS among both Caucasians and African Americans and also identified two specific alleles associated with disease progression (Carrington et al. 1999). These findings demonstrate that host susceptibility and resistance to infectious diseases can be genetically mediated.

Concurrently, genome sequencing of microbes is advancing rapidly and leading to the identification of microbial gene products implicated in the infectious process, the screening for "pathogenicity islands" that influence virulence, and the identification of molecular targets for new therapeutic agents (Jenks 1998). Even more important is the possibility of characterizing the diversity of host-pathogen genomes, their interactions, and their roles in infectious diseases.

### ***Ecogenetics and Pharmacogenetics***

In the context of environmental health sciences, ecogenetics focuses on the role of gene-environment interactions in relation to health and disease. A recent and intriguing study shows that persons with a genetic trait that decreases the ability to metabolize nicotine were less likely to be tobacco-dependent (Pianezza et al. 1998). Further, those who were already tobacco-dependent were likely to smoke fewer cigarettes. These results raise the possibility for more effective disease prevention strategies targeted to those with specific genetic susceptibilities.

Pharmacogenetics has recently focused on the apparent interaction between use of oral contraceptives and a specific genetic mutation that causes resistance to a potent anticoagulant protein that limits clot formation. Among women who *do not use* oral contraceptives, those with the mutation have a six times greater risk of thrombosis compared to those who do not have the mutation. For women

who *use* oral contraceptives, those with the mutation have a 12 times greater risk of thrombosis compared to those who do not have the mutation (Vandenbroucke et al. 1994). Such synergistic effects between the mutation and oral contraceptive use have implications for screening policies.

### ***Statistical Genetics and Population Genetics***

The development of new methods for statistical analysis of genetic data is advancing rapidly and will be essential for understanding the data emerging from the Human Genome Project. These methods include gene mapping and positional cloning based on family studies and linkage analysis. Statistical genetics contributes to optimal sampling designs, to the development of better methods of statistical genetic analysis, and to the application of these methods to specific diseases. Another analytic challenge is the simultaneous consideration of many genes in conjunction with environmental exposures.

Population genetics is a closely related field that investigates genetic variation due to population structure, migration, mutation, and natural selection. It provides an important tool for identifying regions of the genome involved in disease susceptibility.

### ***Bioinformatics***

Acceleration in the volume of data generated by the Human Genome Project and numerous other research efforts will require deciphering genetic information and translating it into meaningful data that can be used in public health settings. Bioinformatics, an emerging field combining molecular biology and computer science, is furnishing the new hardware and providing efficient algorithms for symbolic analysis, scientific computation, graphical interpretation, and data management. These developing tools, along with epidemiologic information on human genes, will help to translate sequences of thousands of genes into functional and clinically relevant information that can advance our understanding of genetic susceptibility to disease.

### ***Consumers, Communities, and Conundrums***

Advances in genetic knowledge have generated ethical and legal conundrums

involving individuals and communities, both in research and in health care. The basic ethical principles of biomedical and public health research — respect for participants, beneficence and nonmaleficence, and justice — are applied through the process of informed consent, risk-benefit analysis, and appropriate selection and recruitment of study subjects, respectively. Considerable controversy surrounds the use of DNA samples for genetic research, especially those collected and stored without specific informed consent. Some investigators have proposed the informed consent process consider participants as “limited partners” in research rather than as “study subjects.”

Issues of privacy and confidentiality are reflected in recent concern about the publication of pedigrees in biomedical journals, and in the creation of a genetic database for the entire country of Iceland. These issues demonstrate that ethics is not just an abstract intellectual discipline. It is about the conflicts that arise in trying to meet real human needs and values and is of central importance in public health genetics.

Hand in hand with debates on biomedical ethics are questions of tort liability (e.g., medical malpractice, product liability, invasion of privacy, damage to business relationships), regulation of genetic technologies and products, and legal enforcement of “rights” to genetic information and services. For example, given that genotypes provide information about relatives of the patient or research subject, do third parties have a right to know this important information? Does this right gain legal vitality when such critical information might be able to prevent illness or death? What are the ethical and legal duties of the patient or health provider to warn the third party?

Other legal issues include the applicability of antidiscrimination laws (Americans with Disabilities Act, Fair Housing Act, Individuals with Disabilities Education Act), civil rights laws (Title VII of the Civil Rights Act), and common law (divorce and custody laws) to alleged genetic discrimination.

Furthermore, testing for genetic diseases can have profound psychological effects that alter health behavior. Education regarding the role of genetics in health and disease is needed, both for the public and for public health professionals.

## *Cultural Contexts and Considerations*

Genetics research in public health is, by nature, conducted in the context of communities and populations. The commercialization of body tissue, including DNA, as a resource to be “mined or harvested” and the patenting of DNA also create legal issues, but these questions are not merely ethical and legal in nature. They frequently collide with well-developed cultural mores. For example, the recent implementation of a genetic database composed of samples from the entire Icelandic population would be anathema to some Native American tribes, who strongly oppose such comprehensive invasion of their genome.

One proposed and controversial policy solution is the concept of community or group consent for genomic research (Weijer and Emanuel 2000), an approach that will require considerable honing to move from theory to public health practice. In a recent study involving two Native American tribes, the authors concluded that community review facilitates the development of partnerships between researchers and communities, thereby enhancing participant recruitment and retention in studies.

## *Population Testing and Access to Services*

Population-based genetic testing for disease presence and susceptibility is one of the most important potential applications of the deviancies in molecular biotechnology to public health. Such testing raises difficult policy decisions. For example, an expert panel convened at the Centers for Disease Control and Prevention in 1997 declined to endorse genetic testing for hereditary hemochromatosis due to uncertainties about prevalence and penetrance of gene mutations, the optimal care of asymptomatic people carrying the mutation, and the potential for stigmatization and discrimination (Burke et al. 1998). Such recommendations will need to be reevaluated as new genetic information becomes available, and as specific guidelines are developed regarding the criteria for conducting genetic testing in a population setting.

Each new test for disease susceptibility focuses more attention on issues of access to genetic services, including the availability of

genetic counseling. For example, the obligation for genetic service providers to recontact former patients about advances in research takes on new dimensions. A recent survey of geneticists and genetic counselors did not reflect a consensus about the benefits and burdens of such a practice. Although the respondents indicated that it was desirable to recontact patients, they did not perceive it as a practical goal within the current health care system (Fitzpatrick et al. 1999).

### *Education and Professional Training*

For many years schools of public health have offered courses with genetic content or that address associated ethical, legal, and social issues. Given the broad impacts of expanding genetic knowledge and technology, it is important that more, if not all, public health students be exposed to the fundamentals of public health genetics. Such education needs to address a variety of audiences, including traditional public health graduate students and practitioners, students from related disciplines, and health care professionals.

The University of Washington recently implemented new programs focused specifically on the application of the advances in human genetics and molecular biotechnology (sidebar). These programs differ from past efforts in that they deliberately link courses in a multidisciplinary approach to genetics in public health.

The rapid expansion in knowledge of human genetics strains the ability of the public health workforce, including practitioners, researchers, laboratorians, and policy makers to keep abreast of new information and its potential implications. Systematic, continuing education is needed to provide these varied audiences with the knowledge and skills necessary to use genetics information in public health programs that prevent disease and improve health. The Centers for Disease Control and Prevention offers several training programs, including short introductory and advanced courses in genetics and disease prevention, online training materials, lectures, and newsletters. In addition, faculty of the University of Michigan, the University of Washington, and the Johns Hopkins University are developing a multi-institution effort to plan and implement continuing education courses for genetics in public health.

The emerging field of public health genetics will increasingly involve interactions among a broad range of disciplines. New technologies and information will accelerate scientific advances, which must be evaluated in a societal context. Breslow (1999) proposes that genetic research should include efforts to identify “genetic indicators of longer and better lives,” not just markers of disease susceptibility. Such efforts will necessitate collaborations among scientists, social scientists, ethicists, and legal and policy experts. One of the biggest challenges for society and for public health professionals will be to develop policies and procedures that maximize health benefits derived from genetic advances while ensuring that genetic information is not misused.

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## UW Institute for Public Health Genetics

The Public Health Genetics (PHG) program at the University of Washington, established in 1997, offers both a two-year graduate program leading to a Master of Public Health (MPH) degree in Public Health Genetics and a graduate certificate program. The program is supported by the President's University Initiatives Fund (UIF) and involves the schools of Public Health and Community Medicine, Law, Medicine, Nursing, and Pharmacy, the College of Arts and Sciences, and the Daniel J. Evans School of Public Affairs. In addition, active collaborative relationships involve the Washington State Department of Health and the Fred Hutchinson Cancer Research Center.

The MPH degree track in Public Health Genetics is the only such degree program in the country. In addition to course requirements in all the public health disciplines and a practicum experience, the core curriculum consists of a series of courses that introduce students to each of the disciplines integral to PHG, including genetic epidemiology, legal, ethical, and social issues, and biotechnology, bioinformatics, and ecogenetics. Students are drawn from diverse backgrounds ranging from molecular biology to social science, and can select specially developed electives from numerous university departments.

The graduate certificate program is designed for students in other UW graduate programs who wish to take a set of core PHG courses. To date, students from Environmental Health, Epidemiology, Pharmacy, and Public Policy have earned the PHG certificate.

In addition to academic training, the Institute for PHG has initiated two major projects to facilitate relevant research: "Genetic Testing in the Workplace: Implications for Public Policy," and "Assessing Genetic Knowledge and Attitudes in Two Populations." The first project explores ethical, legal, social, and economic implications of advances in human genetics and molecular biotechnology for occupational health. The investigators have examined how this information is used in the workplace and what public policies promote the use of genetic information to appropriately balance the interests of workers, employers, and the general public. The second project will increase understanding of salient cultural features that may influence individual and family attitudes about participating in genetic research. The investigators developed an assessment tool and tested it through interviews with members of the Japanese American and the Pacific Islander communities.

The Institute for PHG has a multifaceted collaboration with the UW Center for Ecogenetics and Environmental Health (CEEH), funded as a Center of Excellence by the National Institute of Environmental Health Sciences of the National Institutes of Health. CEEH focuses on understanding gene-environment interactions that lead to chronic diseases of public health importance. Thus, the goals of the CEEH are highly complementary to those of the Institute for PHG. The second five-year award for the CEEH includes a new initiative to develop a series of cases studies on the Ethical, Legal and Social Implications (ELSI) of Ecogenetics Research.

The PHG Web address is: <http://depts.washington.edu/phgen>.

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