

# Introduction to the Special Issue on Society and Genetics

Guang Guo

*University of North Carolina at Chapel Hill*

Until recently, while studying individual traits and behaviors such as cognitive development, educational achievement, occupational attainment, mental health, binge drinking, smoking, and illegal drug use, sociologists have either assumed that individuals are the same at birth or have treated the differences across individuals at birth as a black box. When treated as a black box, intrinsic individual differences are typically subsumed by unobserved heterogeneity. Although it is possible to exercise some control over it via statistical methods (e.g., fixed effect models), unobserved heterogeneity is considered generally impenetrable and incomprehensible.

The spectacular advances in molecular genetics over the past few decades have made it possible to begin to decipher the black box. Evidence is mounting that substantial genetic variation exists across individuals. The year 2007 saw an unparalleled succession of discoveries in the genomics of complex traits (e.g., Frayling et al. 2007; Scott et al. 2007; Sladek et al. 2007; Steinthorsdottir et al. 2007; Zeggini et al. 2007). These studies identified genetic variants associated with acute lymphoblastic leukemia, obesity, type 2 diabetes mellitus, prostate cancer, breast cancer, and coronary heart disease.

Genetic association results had been plagued with false-positive results. Earlier findings that were aimed at linking genetic variants and human outcomes often suffered from small sample sizes, population admixture, issues of multiple testing, and nonreplication (Cardon and Palmer 2003; Ioannidis et al. 2001; Ioannidis et al. 2003). It is important that these recent discoveries were made via more sophisticated methodological approaches, which made a point of basing analysis on at least several thousands of individuals, applying state-of-the-art techniques to control for potential population

---

**Author's Note:** Please address correspondence to Guang Guo, University of North Carolina, Department of Sociology, 155 Hamilton Hall CB #3210, Chapel Hill, NC 27599-3210; e-mail: [guang\\_guo@unc.edu](mailto:guang_guo@unc.edu).

admixture, addressing multiple testing, and replicating in at least a number of large and independent samples. A newly acquired confidence in the scientific community had developed in the genetic findings for complex human traits, and the American Association for the Advancement of Science chose human genetic variation as *Science's* breakthrough of the year of 2007 (Pennisi 2007).

If individuals do differ in genetic propensities for human diseases, it would be logical to predict that individuals also differ in genetic propensities for other human traits and behaviors. If individuals do have differential genetic propensities for cognitive development, educational achievement, occupational attainment, mental health, binge drinking, smoking, and illegal drug use, sociologists will be compelled to reevaluate many long-standing sociological assumptions and strategies.

The reevaluation will likely center on the question of how genetics may advance sociology. Incorporating genetics will advance at least three aspects of sociology. First, if genetic variants influence human traits and behaviors, incorporating genetics will improve predictions of sociological models. Second, taking into account genetic effects will yield more accurate estimates of social environmental effects on human traits and behaviors. For example, there is good reason to suspect that some of the key measures of social origin, including parental education and parental occupation, may contain components of both social-environmental influences and influences of genetic transmission. Proper adjustment of genetic effects will yield purer effects of social origin. Third, introducing genetic influences into sociological analysis may reveal gene-environment interactions, in which social-environmental influences may be present only in a subgroup (defined by genetic variants) of the analysis sample (Caspi et al. 2002). Without interacting with genetic variants, the social-environmental influence would be invisible.

Recent progress in epigenetics has disclosed a close interdependence between genes and environment. Epigenetics are biochemical instructions for gene activity, and epigenetics do not alter DNA sequences (Tsankova et al. 2007). Epigenetics is particularly interesting to sociologists because it promises to be the key to understanding the mechanisms of how gene expression is regulated in response to environment. Methylation, a process in which DNA sequences are chemically modified by acquiring methyl groups to cytosine bases, is a main component of epigenetics. Methylation is an important mechanism for gene-environment interaction. DNA methylation has been shown to play an important part in the regulation of gene expression. Mounting evidence shows that the silencing of tumor

suppressor genes by DNA methylation is a typical process in cancer development (Baylin et al. 2001).

Meaney, Szyf, and Seckl (2007) demonstrated an epigenetic case of the interplay between the maternal behavior of mother rats and the glucocorticoid receptor gene for offspring's responses to stress. In the study, mother rats are classified into low or high licking/grooming (LG) and arched-back nursing (ABN). The latter is characterized by a mother rat nursing her offspring with her back arched and legs splayed outward. The offspring of low LG-ABN mothers were found to grow up more fearful and abnormally sensitive to stress than offspring of high LG-ABN mothers. Cross-fostering studies, in which pups born to low LG-ABN mothers and high LG-ABN mothers were switched at birth, exclude the possibility of a direct transmission of maternal care to offspring stress responses (Francis et al. 1999).

Meaney and colleagues (Weaver et al. 2004) discovered that rats' maternal behavior alters the dynamics of methylation and demethylation of the promoter in offspring's glucocorticoid receptor genes. In response to stress, this receptor protein helps bring about gene expression in the brain. Methylation is observed in the gene promoter only shortly after birth (not before birth) and among offspring of low LG-ABN mothers. It is hypothesized that low LG-ABN nursing causes the methylation, which leads to lowered levels of gene expression and produces more stressful animals. These biochemical and behavioral changes are stable and tend to last for the remainder of an animal's life.

Incorporating genetics into sociological analysis is challenging. Sociological outcomes such as socioeconomic status, educational achievement, and longevity tend to be further removed from the effects of specific genes than some of the medical measures such as breast cancer, hypertension, and LDL cholesterol. These sociological outcomes have more measurement errors; their genetic effects (if any) are likely to be mediated by more complicated social-environmental influences, and the financial support for research on these sociological outcomes is far more scarce. Although the large sample size of many social science surveys would provide excellent statistical power to detect the effects of genetic variants, social science surveys almost always include individuals from many different ethnic backgrounds. Greater ethnic diversity generally leads to more serious problems of population stratification (Cardon and Palmer 2003). Few sociologists have received the training in genetics, and the payoff for undertaking such training is uncertain.

The four articles in this special issue provide a brief introduction to the vast literature on the methods of statistical genetic analysis, including

gene–environment interaction analysis. Guo offers an intuitive, nontechnical introduction to the basic concepts and techniques in molecular and statistical genetics that are used to establish statistical connections between genetic variants and human outcomes. The article by North and Martin focuses on gene–environment interaction from the perspective of genetic epidemiologists. They describe the concept of gene–environment interaction, the tools that are used to perform gene–environment interaction analysis, and the potential complications in that analysis. Cherny presents the variance-component statistical methods that have been developed to combine the methods of linkage and association analysis: two main methods of finding genetic variants responsible for human outcomes. In the final article, Henderson addresses the ethical, legal, and social issues of gene–environment studies.

The development of contemporary molecular genetics has created challenges and opportunities for sociology. Meeting those challenges and opportunities will advance our understanding of how individual traits and behaviors are affected by social processes. I hope this special issue on society and genetics will serve as a useful introduction for our colleagues who are persuaded to rise to the occasion and meet these challenges and opportunities.

## References

- Baylin, S. B., M. Esteller, M. R. Rountree, K. E. Bachman, S. Schuebel, and J. G. Herman. 2001. "Aberrant Patterns of DNA Methylation, Chromatin Formation and Gene Expression in Cancer." *Human Molecular Genetics* 10:687–92.
- Cardon, L. R. and L. J. Palmer. 2003. "Population Stratification and Spurious Allelic Association." *Lancet* 361:598.
- Caspi, A., J. McClay, T. E. Moffitt, J. Mill, J. Martin, I. W. Craig, et al. 2002. "Role of Genotype in the Cycle of Violence in Maltreated Children." *Science* 297:851–4.
- Francis, D., J. Diorio, D. Liu, and M. J. Meaney. 1999. "Nongenomic Transmission Across Generations of Maternal Behavior and Stress Responses in the Rat." *Science* 286:1155–8.
- Frayling, T. M., N. J. Timpson, M. N. Weedon, E. Zeggini, R. M. Freathy, C. M. Lindgren, et al. 2007. "A Common Variant in the FTO Gene Is Associated With Body Mass Index and Predisposes to Childhood and Adult Obesity." *Science* 316:889–94.
- Ioannidis, J., E. Ntzani, T. Trikalinos, and D. Contopoulos-Ioannidis. 2001. "Replication Validity of Genetic Association Studies." *Nature Genetics* 29:306–9.
- Ioannidis, J. P. A., T. A. Trikalinos, E. E. Ntzani, and D. G. Contopoulos-Ioannidis. 2003. "Genetic Associations in Large Versus Small Studies: An Empirical Assessment." *Lancet* 361:567.
- Meaney, M. J., M. Szyf, and J. R. Seckl. 2007. "Epigenetic Mechanisms of Perinatal Programming of Hypothalamic-Pituitary-Adrenal Function and Health." *Trends in Molecular Medicine* 13:269–77.
- Pennisi, E. 2007. "Breakthrough of the Year: Human Genetic Variation." *Science* 318:1842–3.

- Scott, L. J., K. L. Mohlke, L. L. Bonnycastle, C. J. Willer, Y. Li, W. L. Duren, et al. 2007. "A Genome-Wide Association Study of Type 2 Diabetes in Finns Detects Multiple Susceptibility Variants." *Science* 316:1341–5.
- Sladek, R., G. Rocheleau, J. Rung, C. Dina, L. Shen, D. Serre, et al. 2007. "A Genome-Wide Association Study Identifies Novel Risk Loci for Type 2 Diabetes." *Nature* 445:881–5.
- Steinthorsdottir, V., G. Thorleifsson, I. Reynisdottir, R. Benediktsson, T. Jonsdottir, G. B. Walters, et al. 2007. "A Variant in CDKAL1 Influences Insulin Response and Risk of Type 2 Diabetes." *Nature Genetics* 39:770–5.
- Tsankova, N., W. Renthal, A. Kumar, and E. J. Nestler. 2007. "Epigenetic Regulation in Psychiatric Disorders." *Nature Reviews Neuroscience* 8:355–67.
- Weaver, I. C. G., N. Cervoni, F. A. Champagne, A. C. D'Alessio, S. Sharma, J. R. Seckl, et al. 2004. "Epigenetic Programming by Maternal Behavior." *Nature Neuroscience* 7:847–54.
- Zeggini, E., M. N. Weedon, C. M. Lindgren, T. M. Frayling, K. S. Elliott, H. Lango, et al. 2007. "Replication of Genome-Wide Association Signals in UK Samples Reveals Risk Loci for Type 2 Diabetes." *Science* 316:1336–41.

**Guang Guo** is a professor of sociology and a faculty fellow at the Carolina Center for Genome Sciences at the University of North Carolina at Chapel Hill. He has made sustained and focused efforts to integrate social sciences and genetics in his career. He is a guest editor of a special issue for two major sociology journals (*Social Forces* and *Sociological Methods & Research*) on sociology and biology/genetics, and he served recently on the National Committee on Gene–Environment Interaction for Health Outcomes at the Institute of Medicine, National Academies 2005–2006. In addition to publications in sociological literature, he has published numerous articles in genetics journals.