

# How much can a large population study on genes, environments, their interactions and common diseases contribute to the health of the American people?

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## Abstract

I offer a critical perspective on a large-scale population study on gene–environment interactions and common diseases proposed by the US Secretary of Health and Human Services’ Advisory Committee on Genetics, Health, and Society (SACGHS). I argue that for scientific and policy reasons this and similar studies have little to add to current knowledge about how to prevent, treat, or decrease inequalities in common diseases, all of which are major claims of the proposal. I use diabetes as an exemplar of the diseases that the study purports to illuminate. I conclude that the question is not whether the study will meet expectations or whether the current emphasis on a genetic paradigm is real or imagined, desirable or not. Rather, the question is why, given the flaws of the science underwriting the study, its assumptions remain unchallenged.

Future research should investigate the reasons for this immunity from criticism and for the popularity of this and similar projects among laypersons as well as among intellectuals.

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## Introduction

Genetics is playing an increasingly important role in the diagnosis, monitoring, and treatment of diseases [...]. The potential for using genes themselves to treat disease—gene therapy—is the most exciting application of DNA science.

The Human Genome Project Information ([http://www.ornl.gov/sci/techresources/Human\\_Genome/medicine/medicine.shtml](http://www.ornl.gov/sci/techresources/Human_Genome/medicine/medicine.shtml))

In May 2006, a Task Force on Large Population Studies called upon by the US Secretary of Health and Human Services’ Advisory Committee on Genetics, Health, and Society (SACGHS) issued a report with the intention of evaluating the feasibility of a project to study “genes, environments, their interactions and common diseases” (Secretary’s Advisory Committee on Genetics, 2006). The report claimed that “characterizing human genetic variation and how genetic variants interact with environmental factors (physical, behavioral, and social) to influence health is currently *one of the most pressing goals* for scientists trying to unravel and understand the underlying causes of common diseases”, and

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that “scientists hope that *major clinical and public health advances will be realized by learning where variation among individuals lies within the genome, how it differs among healthy, predisposed, and sick individuals, and how particular variants of DNA interact with each other and diverse environmental factors*” (emphasis added, p. 4). The challenges of the project notwithstanding—involving a large number of research subjects, and consuming a considerable amount of the budget of the sponsoring agencies, the US Department of Health and Human Services (US DHHS) and the National Institutes of Health (NIH)—the SACGHS believed it had “the potential to generate significant health benefits” (Secretary’s Advisory Committee on Genetics, 2006, p. 10).

In June 2006, I received an invitation to comment on the project, yet what started as my reply developed into an analysis of two major claims of the proposal, namely, that examining gene–environment interactions is a pressing goal for scientists concerned with human health, and that this examination will generate significant health benefits. I divide this analysis into four parts: first, I discuss the geneticization debate, locating it within a broader nature–nurture debate, and argue that geneticization scholars have missed the target of their critiques, by failing to understand how the strengths and limits of genetic knowledge affect its potential contributions to human health; second, I examine the relevance of the proposal to primary, secondary, and tertiary prevention; third, I clarify key concepts in genetics; and fourth, I discuss the implications of the project for public health policy, and the resilience of what appears to be its underlying disease paradigm to be challenged on its own terms, even by critics.

This type of analysis, I believe, is lacking in both the medical and the sociological literatures, and in this paper I try to address this gap. I use type 2 diabetes (henceforth diabetes) as a paradigmatic “common disease” of the sort that the proposed project attempts to illuminate, yet I expect this analysis to be relevant to conditions comparable to diabetes in their pathophysiology, the environments promoting them, and the risks they pose to human health, such as common, multifactorial forms of cancer, hypertension, or heart disease. I imply all these when I refer to “common diseases”.

Diabetes today is common indeed, and there are many good reasons to be concerned about it. First,

if left untreated or if poorly treated, diabetes leads to disabling complications and to premature death. Second, rates of diabetes have increased epidemically over the last ten years, the increase is global, and its projected distribution is very uneven. By the year 2025, the number of people affected by diabetes will have risen to 300 million (from 135 million in 1995), and while the increase will be of 42% in the developed countries, it will reach 170% in developing countries (King, Aubert, & Herman, 1998). While these numbers do not discriminate among types of diabetes, at least 90% of the cases are presumed to be type 2, the real protagonist of the epidemic. Third, diabetes is very costly: in the United States alone, it imposes a toll of over 130 billion dollars—one out of every ten health-care dollars (American Diabetes Association, 2003). Last, rates of diabetes and diabetes complications are two to six times higher among minorities worldwide than among dominant groups (American Diabetes Association, 2001). Clearly, anything that contributed to fighting diabetes would be worth considering. And yet, I believe that a study of the sort proposed will achieve nothing to this effect—it would be redundant at best, while at worst it would distract from the real roots of, and solutions to, common diseases.

### **The Nature–Nurture debate: a reenactment**

The debate about which “part” of the range of anatomical, physiological, or behavioral features of human beings is caused by nature and which by nurture—or by some interaction of the two—is certainly not new. While for Plato, whether individuals were meant to be artisans, soldiers, or philosopher-kings, depended on their “essences” being bronze, silver, or gold (Bloom, 1968), for 19th century European aristocrats it was a matter of “blood”. Thus readers of *Oliver Twist* “knew” that the protagonist’s perfect English and manners, much like the defective English and manners of the Artful Dodger, were the result of nothing but biological pedigree (Lewontin, Rose, & Kamin, 1984). One incarnation of the “nature–nurture” debate, more suited to the modern world than “essences” or “blood”, is the “genes–lifestyle” debate, premised on the idea that genes contribute, at least in part, to conditions ranging from diabetes, to heart disease, to cancer, and that identifying this contribution is crucial to fighting these conditions (Chaufan, 2006).

And there is certainly no denying the fact that our genes contribute to them somehow, although how exactly and to what extent this contribution should concern us is less clear.

The overemphasis on genetic explanations of human differences is captured by Lippman's (1991) concept of *geneticization*, defined as “an ongoing process by which differences between individuals are reduced to their DNA codes”, with most physical, physiological and behavioral variations “defined, at least in part, as genetic in origin”, a process which encourages adopting genetic technologies to manage health problems (15).

Lippman's now classical statement initiated a lively debate, largely around whether the “geneticization” of human variation was increasing, and whether this increase was positive or negative. Thus, in a content analysis of newspapers and magazines spanning over 70 years Condit, Ofulue, and Sheedy (1998) concluded that there was no “statistically significant change in the relative proportion of physical phenomena attributed to genetic causes”, while Hedgecoe (1998) suggested that “it is not clear that the ideas put forward by Lippman, Nelkin and others are based on convincing empirical evidence rather than theory-derived polemic” — for both, geneticization was in the eye of the beholder, offering no reason for concern. In contrast, ten Have (2001) has argued that its increase is undeniable, and largely negative, while Shostak (2002) has concluded that whether genetic technologies will lead or not to “genetic reductionism, determinism, and individualization of risk” [...] “deserves continued scholarship and debate” (2339).

I have attempted to characterize an important field of inquiry—i.e., the impact of genetics on human affairs—ongoing for close to 20 years, in a paragraph, only to call attention to a key assumption of the controversy, namely, that the problem is the *overemphasis* on genetic variations (alleles) as causes of human variations, and the potential misuse of this knowledge. The possibility of *achieving* this knowledge is not disputed. Put otherwise, it is taken for granted that at least in theory, alleles causing, or influencing, diabetes, or depression, can be identified, and that their identification may lead to desirable outcomes, such as the development of personalized, optimal treatments, or to undesirable ones, such as the denial of health insurance on the basis of pre-existing “genetic susceptibilities”. Other outcomes might include the ability to identify at birth a host of such susceptibilities that will allow us

to select gene-specific environments that foster or impede the expression of traits based on their desirability, or even to engineer designer babies with traits “to order”.

But what if the very enterprise of understanding which variations in the human genome produce which variations in the vast majority of physical and mental conditions led nowhere? What if current knowledge of how gene variations contribute to observable variations, and of the conditions generally conducive to physical and mental health, indicated that whatever these variations, good physical and mental health require at least access to proper nutrition, decent housing, medical care, and so forth? What, in sum, if the attention to “variations within the genome” were a distraction from those factors well known to produce, on average, physically and mentally healthy individuals, whatever the gene variants?

The main point of this paper is to argue that SACGHS proposal is such a case, and that what it purports to illuminate, i.e., the “genetic predisposition” to common diseases, is at best a conceptually confused notion, at worst one that distracts from the real roots of ill-health, hence from truly effective interventions. This examination should be applicable to kindred projects that have been either conducted or proposed, at least in part, on the grounds of their potential to shed light on a variety of human problems, including what makes some people or groups more vulnerable to disease than others (Collins & McKusick, 2001; Drayna, 2006; Farahany & Bernet, 2006; Raffel et al., 1996).

### **Primary and secondary prevention: the “genes–lifestyle debate”**

Typically, the staggering rates of type 2 diabetes among racial and ethnic minorities have been attributed to an alleged genetic predisposition colliding with unhealthy lifestyles (American Diabetes Association, 2001). The proposed study is aimed precisely at unraveling the details of this predisposition, i.e., identifying gene variants that cause some individuals to develop diseases like diabetes while others do not, and the environments under which this genetic vulnerability becomes expressed. While the DNA sequence of any two people is 99.9% identical, as the report itself acknowledges, it also suggests that the 0.1% which varies “may greatly affect an individual's disease risk” (Secretary's Advisory Committee on Genetics,

2006). The assumption is that a better understanding of gene–environment interactions—which would require sequencing the genetic background of large number of individuals, and tracking with precision the interactions of these backgrounds with varying physical and social environments for prolonged periods of time—may lead to early diagnosis, genetically-tailored drugs, or even replacement of “defective genes” by “healthy” ones.

At first sight, the idea seems perfectly reasonable, and the extraordinary logistical challenge should be offset by the potential for savings in dollars and suffering for millions of individuals affected by, or at risk of, common diseases. After all, people are different in all sorts of ways, and one of these ways is their genetic makeup. Gene variations do contribute to biological variations and interact with environments in unique ways. Surely understanding the details of these interactions should enhance our capacity to fight disease. Or should it? The *prima facie* reasonableness of the approach conceals the fatal flaws of the questions it asks—which alleles will identify individuals more likely to develop disease X in the future? How much do these alleles contribute to X in general? What is the relative weight of environmental factors?—and makes of the enterprise a non-starter, for scientific and policy reasons.

Let me begin with the scientific ones, specifically those concerning *primary* prevention, i.e., how to avoid disease in the general population. First, *we already know which environments are optimal to prevent most of these common conditions*. Consider diabetes. There is well-established epidemiological and experimental evidence that the biological vulnerability to diabetes begins to develop in the womb and continues into early childhood, through a variety of mechanisms, including the effects of poorly controlled diabetes, or malnutrition, in the mother, or of malnutrition in the small child, on the endocrine pancreas, the producer of insulin.

High levels of blood glucose during pregnancy make the fetus more vulnerable to diabetes and other related conditions later in life (Freinkel, 1964, 1980; Jovanovic & Pettitt, 2001). The mechanism appears to be the burden placed on the developing pancreas by a uterine environment rich in glucose, as indicated by an observational study showing that fetuses responded to their diabetic mothers' high blood glucose levels by increasing their own secretion of insulin, hence overworking their fetal pancreases (Dabelea et al., 1998). Similarly, a

seminal study conducted during the Dutch famine in WWII (Ravelli et al., 1998) showed that participants born to mothers who had experienced hunger during mid- and late gestation (the period when pancreatic function develops), had the highest glucose concentration 2 h after a standard glucose load (an indicator of insulin-resistance or pre-diabetes). These observations have been interpreted as indicating the effect of interferences with early growth and development, or “fetal programming”, by *programming* meaning “a permanent or long-term change in the structure or function of an organism resulting from a stimulus or insult acting at a critical period of early life” (Barker & Osmond, 1986) (596).

Importantly, the effects of malnutrition on development do not stop at birth, but continue into the very first years of life. Stunting, the failure to thrive due to lack of basic nutrients in early childhood, currently impairs the adequate metabolic development of some 200 million children worldwide and predisposes them to heart disease, obesity, and diabetes (Branca & Ferrari, 2002), independently of ethnicity (Popkin, Richards, & Montiero, 1996), not merely in industrializing nations but in the wealthy ones such as the United States, where at least 12 million are at risk of hunger (Koch, 2000).

Disturbingly, the effects of maternal malnutrition or poorly controlled diabetes on the fetus, or of stunting in young children, on glucose metabolism, are bequeathed upon generations of newborns condemned to ill-health years before they are born. In a study examining the nutritional history of a native North American tribe, the Havasupai, in the context of the tribe's political history, researchers argued that the chronic under-nutrition caused by long-marches, forced relocations, concentration camp-like conditions of reservations, and loss of traditional livelihoods, produced several generations of malnourished Native women who gave birth to prone-to-diabetes babies. Post World War II, higher wages, welfare, and government nutrition programs increased the average calorie intake which triggered underlying insulin-resistant states, resulting in the staggering diabetes rates now observed in this and other Native populations. Currently, propose the researchers, the biological vulnerability to diabetes is reproduced by poorly controlled diabetes during pregnancy, compounded by the effects of high-calorie diets and low levels of exercise that individuals are exposed to at increasingly early ages (Benyshek, Martin, & Johnston, 2001).

Finally, animal experiments attempting to replicate the Havasupai's nutritional history have confirmed the developmental and multi-generational, non-genetic origin of these observations: These experiments showed that, when compared to a control group from the same breeding colony, pups born to mothers malnourished while pregnant were small at birth and became glucose intolerant as young adults. When these adult females themselves became pregnant they “passed down” this intolerance to their offspring even if they and their offspring consumed nutritionally adequate (control) diets. The glucose intolerance (and accompanying insulin resistance) of this younger (F2) generation was also extremely refractory to dietary manipulation (Benyshek, Johnston, & Martin, 2004). Incidentally, that there are critical periods during development when major organs can be permanently affected has been known, and accepted, since at least the 1920s (Maher Rasmussen, 2001) (74), and studies showing the effects of perinatal environmental exposures on adult health status go back at least to the 1960s (Dubos, Savage, & Shaedler, 2005).

It appears from this over seventy-year old tradition of research that there is little need to examine, let alone to genotype, *yet more* individuals who undergo “abnormal fetal environments” or are malnourished early in life to confirm that certain environments are bad for the health of either rats or humans. Moreover, in order to intervene upon these environments, no medical breakthroughs are needed. At least in the case of humans, sensible and equitable public health policies guaranteeing proper nutrition and medical care to women of child-bearing age and to young children would do much of the job, better still if they extend these guarantees over the life course. After all, genes do not interact with a *cross-section* of an environment but with a *sequence* of environments, and the cumulative effect of unfavorable environments appears to take a toll on human health, whatever the gene variants.

As to *secondary* prevention, i.e., interventions targeting those “at risk”, it is already well-established that “healthy lifestyles” prevent diabetes, irrespective of ethnic background (Tuomilehto, Lindstrom, & Eriksson, 2001). Since the mid-1980s, studies in China and Finland have showed substantial reductions of risk for diabetes with lifestyle changes (Pan et al., 1997) (Tuomilehto et al., 2001). Arguably the best study in the world

relative to secondary prevention, the Diabetes Prevention Program (DPP), showed that while pharmacological treatment reduced risk of diabetes by 31%, lifestyle changes did so *by* 58%. (Diabetes Prevention Program Research Group, 2002).

Given this evidence, why not just encourage healthy lifestyles as the main secondary prevention strategy? Because whatever individuals *ought* to do there is reason to believe that successful lifestyle changes are unlikely to be maintained once the support of clinical studies is no longer available. Studies tracking clinical successes such as weight loss showed that these successes disappear within five years of an intervention (Swinburn, Metcalf, & Ley, 2001; Wing, Venditti, & Jakicic, 1998). In fact, primary care physicians who made of health promotion the goal of their practice noted that the moment patients stopped seeing the exercise physiologist, the dietitian, or the counselor, they returned to their usual states of health—the lower their socioeconomic status, the faster their return was (Guthrie, 2001). The physicians concluded that “it is not patients who don’t understand, but we doctors who don’t” and that unless the social and economic pressures faced by “high risk groups” were addressed through social policies, “health promotion (will help) no one” (Guthrie, 2001, p. 997).

### **Tertiary prevention: its medical care, stupid!**

As to the usefulness of the proposal to tertiary prevention, i.e., the prevention of diabetes complications, there is little doubt that proper and timely medical treatment dramatically reduces them, irrespective of gene variants, ethnic background, or type of diabetes (American Diabetes Association, 2002a,2002b). In North America, the Diabetes Control and Complications Trial (DCCT) confirmed what the clinical community had long suspected: that tight control of blood glucose reduced microalbuminuria, a precursor of kidney failure, by 39%; neuropathy by 60%; and retinopathy by 76% in type 1 diabetes (The Diabetes Control & Complications Trial Research Group, 1993). Across the Atlantic, the UK Prospective Diabetes Study Group of type 2 diabetes showed a reduction of microvascular complications with intensive treatment of 25% (American Diabetes Association, 2002b).

In sum, the evidence is overwhelming. Quality and timely diabetes care prevents complications,

and lack of it leads to them. And there is little reason to believe that someone unlucky enough to have developed diabetes will be spared from needing treatment by yet-to-be-discovered protective alleles. And my 10 years of clinical experience lead me to believe that no sensible practitioner would recommend that patients let go of proper treatment betting on the fact that they might have just such alleles—at least with diabetes, it is unclear that there is anything to gain by studying the genetic background of those who receive or fail to receive medical care. And if the studies above are of any scientific value, it is even less clear that there is anything to gain by *further* studying the environments where diabetes complications are less likely to occur.

### What is in a DNA sequence? Reaction norm and common diseases

Let me now offer the second, and probably most important, scientific reason why the proposal is misguided: that organisms, including human ones, are the product of genes *and* environments is a truism that everybody agrees on, yet whose implications for human health are rarely acknowledged in searches of “diabetes genes”. Let us explore these implications briefly. A basic distinction in genetics is that between *genotype*, the material substratum of genetic inheritance, and *phenotype*, any structural, functional or behavioral trait of an organism. Phenotypes are the product of development, the result of complex interactions of genes, a historical sequence of environments, and developmental random noise (Lewontin, 2000).

The reaction norm, a property of the genotype known by geneticists for close to a century, represents the triadic relationship among genotypes, phenotypes and environments (Lewontin, 2004; Sarkar & Fuller, 2003). When, in elaborating the reaction norm for a given genotype, “environment” is plotted on the *x*-axis and “phenotype” on the *y*-axis, it becomes apparent that phenotypes vary as environments vary. It also becomes apparent that with the rare exception of naturally occurring or lab-produced mutants, the relationship between genotypes and phenotypes varies as sequences of environments vary.

For example, a plant with a genotype A may be taller than one with a genotype B at sea level, shorter than plant B at 3000 m, and equal to B at 1400 m. This relationship is illustrated by an

experiment where seven specimens from a California herb of the genus *Achillea*, each with a different genotype, were collected from the wild, and three cuttings were obtained from each one (Lewontin, 2000). Cuttings from each specimen (genetically identical) were planted at different altitudes. The genotype which grew the tallest at sea level was not the tallest at 1400 or at 3050 m. Similarly, the tallest at 3050 m was not the tallest at the other levels. In fact, no single genotype was consistently taller or shorter than all others over the range of environments examined.

This experiment, illustrating the reaction norm of different genotypes of a plant for height shows that expressions such as “alleles for X” or “a genetic tendency to X” are biologically empty until all relevant environments are specified. Tendencies do not occur in a vacuum: an “allele for tallness” at sea level may become one for shortness at 3050 m, and may be irrelevant to height differences at 1400 m. It also follows that one cannot compare two genotypes along any trait “in general”, much less when the conditions of development have differed.

That reaction norms of different genotypes cross each other in largely unpredictable ways reflects the *non-additivity* of gene, environment, and developmental random noise interactions, and the fact that genes contribute to the making of organisms through multiple feedback loops—organisms are open systems, continuously receiving external inputs (Lewontin, 2000). Non-additivity precludes any biologically meaningful quantification of the relative contribution of the “ingredients” (i.e. genes, environments, and random noise) of a trait in an individual (Lewontin, 1974). It also precludes the identification of alleles “for” a trait difference “in general”.

Reaction norms have been well studied in experimental organisms where genetic and environmental variables are easy to manipulate, traits are relatively easy to define and measure, and selective breeding possible and desirable. For instance, farmers can buy crops genetically modified for high vitamin content *under conditions* *x*, *y*, and *z*, or raise cows *selected* for their production of quality milk—incidentally, knowing nothing about “milk producing” alleles, but rather knowing the *heritability* of “high milk yield”.<sup>1</sup>

<sup>1</sup>For a discussion of the heritability concept that some authors (wrongly) interpret as a measure of the relative importance of genes in the etiology of diabetes I refer the reader to “Separating

Yet elaborating reaction norms for complex human traits presents at least three challenges: first, defining what counts as a trait; second, identifying all environments relevant to its development; and third, empirically manipulating these environments to study how they interact with trait-relevant genes, which ought to be identifiable from trait-irrelevant ones, otherwise the whole enterprise would collapse. With humans, securing genetically identical “specimens” to “grow” in controlled environments is logistically very difficult and ethically out of the question—controlled growth and selective breeding are not options.

If we take these biological facts seriously their implications for human health and for common diseases like diabetes are huge: it is clearly incorrect to claim that some individuals are more “genetically predisposed to diabetes” than others unless *both of them* have been compared along a scale of insulin resistance after exposure to *exactly the same range of environments relevant to insulin resistance in the course of its development*. And as I have argued, these environments are multiple, exposure to them begins very early in life, and the timing of the exposure is at least as important as the exposure itself—malnutrition does not have the same effect on insulin sensitivity in the very young child as in the grown adult. Of course what is usually *meant* by “some individuals are genetically predisposed to diabetes” is that their genes contribute to their diabetes *all other things being equal*. But this *ceteris paribus* clause is precisely the problem that has yet to be resolved, for the empirical and ethical reasons stated.

Now one thing that reaction norms teach about both herbs and human beings is that detailed knowledge of the DNA may teach us a lot about genomes, but not necessarily about phenotypic variations, such as why some individuals yet not others develop diabetes. And it certainly will not lead to knowledge about how to alter these variations, for example, to produce non-diabetic, or other “desired” phenotypes, unless the adequate sequence of environments can be secured over the life course. And the fact is, *we already know which environments are those that contribute to the*

(footnote continued)

nature and nurture” (Sober, 2001), to “Hereditarian scientific fallacies” (Bailey, 1997), to “Unpacking the heritability of diabetes” (Chaufan, 2007, unpublished), and to “Analysis of variance and analysis of causes”, Lewontin’s (1974) seminal paper which provides the analytic foundations to the others.

*most common “unhealthy” phenotypes, whatever the alleles:* as argued above, and exemplified by diabetes, it is those where individuals lack basic resources for health since conception.

### **Of birds and butterflies: single-gene and polygenic conditions**

Let me point out one more problematic aspect of the science underlying the proposal: rare, “single-gene” defects where medical genetics has had relative successes, such as phenylketonuria (PKU)—whose treatment, incidentally, is environmental—need to be distinguished from the vast majority of diseases, over 98%, that affect the human species (Strohman, 1995), at least in nations like the United States, and increasingly in developing ones. Assuming that knowledge of the genetics of rare (single-gene) forms of diabetes is useful to understanding the genetics of the “polygenic” type 2 form, as numerous studies do (Freeman & Cox, 2006; Gloyn, 2003), merely because both forms share one characteristic, high blood sugar (or insulin resistance), is like assuming that learning from birds will teach us about butterflies, merely because they both have wings. Taxonomically, birds and butterflies belong to different orders, classes and phyla, in ways that are relevant to their biology and to their evolutionary history. Likewise, single-gene and polygenic conditions belong to disease categories that differ in ways that are relevant both to their pathophysiology and to their treatment. Hence for methodological reasons, features of the first should not be used to infer features of the second.

While a full explanation of this difference is beyond the scope of this analysis, the thrust of it is that so-called single-gene or Mendelian traits are usually *phenotypically invariant*, i.e., there is usually no known sequence of environments under which the “undesirable”, diseased phenotype, will *not* be expressed. These “gene defects”, less than 2% of human ills, usually lead to alterations or changes in the concentration of a single protein, such as the enzyme to metabolize phenylalanine, which in and of themselves constitute the disease—phenylketonuria (Lewontin, 2000). Indeed, even if there existed single-gene defects leading to high blood sugar, the vast majority of cases of diabetes result from interactions between “several altered genes” (Tusie Luna, 2005) (211) and environmental factors (Freeman & Cox, 2006; Gloyn, 2003), hence do not fit the model of PKU.

To note, even with PKU the qualifier of “genetic” is environment-dependent: PKU was 100% “genetic” when the effects of dietary manipulations were unknown, yet is 100% “environmental” today, when we know that mental retardation can be prevented with a phenylalanine-free diet, yet cannot or will not make it available (Lewontin, 2000).

### **Quick fixes will not work: common diseases and public health policy**

Let me now offer the policy reasons why studies such as the one proposed are at best problematic: even if there were such thing as healthy or sickly genes to identify, and something to be gained by studying in detail their interactions with the *current* range of environments (which would say nothing about their interactions with *different*, or *future*, environments individuals may encounter in the course of their lives) it is unclear how this knowledge would translate into cost-effective public health policies. What else could result from these lines of research, other than massive programs of genetic engineering, or developments of “genetically individualized pharmaceuticals”? Either of these would at best break the back of an already vulnerable health care system, at worst be useless.

Moreover, it feels morally disturbing to invest millions in pharmaceuticals that might save *potential* lives when *actual* lives are being lost or greatly disabled by the current system’s inability to provide for basic medical needs, including the excellent, and affordable, pharmaceuticals already available to treat common diseases, whose benefits have been well tested over the years. These massive programs of genetic engineering would be no more cost-effective than whichever health promotion initiatives may follow from the same studies attempting to encourage socially deprived, “at risk for X” groups, to adopt healthy lifestyles, get timely health care, or follow medical recommendations with no attention to the socioeconomic constraints likely to have prevented them from staying healthy in the first place.

As to the claim that further knowledge of environments relevant to common diseases is needed, let me offer one last reason why the project would add nothing to current knowledge of which ones are health-promoting to most people on Earth, irrespective of their genotypes: the refractory-to-change link between socioeconomic and health statuses—higher status, better health—known for over two hundred

years (Frank, 2003) (1790), persists whatever the main causes of disease happen to be. In particular, Link and Phelan’s fundamental cause explanation (Link & Phelan, 1995) rearticulates what 19th century social epidemiologists had plenty of evidence for: that unfavorable social conditions breed disease.

The authors propose that knowledge, power, prestige, and beneficial social connections allow individuals to preserve or restore their health and that of their loved ones over and above contingent risk factors. Because a fundamental assumption of the theory is that knowledge, power, prestige and beneficial social connections enhance people’s ability to utilize whatever resources are *available* to preserve or restore their health, the theory also predicts that social disparities in health will tend to disappear when such resources do not exist—when a condition is not preventable, not curable, or inevitable (Phelan & Link, 2005)—and that patterns of disease will reverse as new and successful medical technologies are developed.

Indeed, the authors found that socioeconomic status made an important difference to deaths by chronic obstructive pulmonary disease and pneumonia, both highly preventable, a negligible one to pancreatic and prostate cancer, less preventable, and virtually no difference to mortality at or after 80 years of age (Phelan & Link, 2005). The theory also explains the reversal of the social distribution of diabetes, which in the past affected patients from “prosperous circles” (von Engelhard, 1995) (7), yet in our day disproportionately affects the poor (Chaturvedi, Jarrett, Shipley, & Fuller, 1998), provided they have access to enough calories.

In sum, whenever new knowledge or medical technologies increase our ability to control disease and postpone death, so increases the ability of those with money, power, prestige, and beneficial social connections to use it. Hence, *further* knowledge of gene–environment interactions, assuming it increased our therapeutic arsenal against common diseases, would at best *increase* disease disparities, by leaving behind those who cannot afford its fruits, and who probably lost their health for this reason in the first place.

### **The emperor has no clothes: what social scientists can do**

While it would be desirable that this or similar proposals improved the health of the American people, the evidence indicates that there is little

reason to believe they will. Improving the nation's health will require major changes in the public commitment to health, to eliminating health disparities, and probably to social justice. Further examination of gene–environment interactions will contribute little to this effect. Solutions to major health threats would certainly be complex, yet do not appear to require further medical knowledge, let alone knowledge plagued with confusions about genetics. Rather, they require adequate use of the overwhelming knowledge about health and disease already available, and to a great extent produced in the United States. Adequate use involves making the right policy and political choices with respect to how to distribute social, including medical, resources.

So what can social scientists contribute, given that the actual drafting of distributive policies depends not on them but on legislators? Part of the answer to this question, I believe, lies in understanding the details of the biological processes leading to health and disease enough to identify which uses of public moneys are worth supporting—it is in the biological details of disease processes that the sociological devil lies.

Scholars interested in human health need to understand whether or not certain lines of research promising great benefits are warranted. Only arguing that social factors deserve more attention than biomedical ones, even if warranted, can create false dichotomies. Social and biological factors are not antithetical, and anything affecting health ultimately acts upon bodies and minds. And effective biomedical tools will always be needed—a world free from disease or accidents requiring medical attention is a biological impossibility, and few would deny that the discovery of insulin, a true biomedical breakthrough, has saved millions of type 1 diabetics from a certain death. Furthermore, that health status depends on much more than biomedical interventions, as scholars have correctly pointed out (Daniels, Kennedy, & Kawachi, 1999; McKinlay & McKinlay, 1977), does not make these interventions unnecessary, as 18,000 perfectly preventable deaths resulting from lack of medical care in the United States, where this care is not a social right, attest (Institute of Medicine, 2003).

As to the frequent critique that special interests underwrite the search for genetic miracles, this alone does not make this search worthless. Indeed, if the alleles of Latinos and African Americans or the details of their environmental interactions mattered

to minorities' vulnerability to diabetes, as the *New York Times* reported when describing the diabetes epidemic in East Harlem as “an interplay of genetic and socioeconomic forces”—or conversely, if the alleles of Upper Westside residents shed light on why the prevalence of diabetes in their neighborhood is, as the same medium reported, “almost nil” (Santora, 2006) (1)—then there would be nothing wrong about studying them—how much time and money to invest would be a matter of judgment about cost-effectiveness.

But if there is little reason to believe that knowledge of gene variations can illuminate the vulnerability to common diseases, then it behooves us to ask what keeps the quest for this knowledge alive. Hence the goal of my analysis: to argue that this quest is at best redundant, because it cannot offer knowledge that we do not already have, at worst harmful, because it diverts attention and resources away from interventions that are well-known to prevent disease, and to provide reasons and evidence to help readers make a judgment. An ancillary goal is to propose that at least as important as asking whether geneticization is happening or increasing, and what its implications are for social practices, is to ask whether the emperor has any clothes. And if it turns out that he does not, then the question becomes: why do his subjects keep on praising them?

Current partnerships between government, the research community, the non-profit sector, and industry shed light on this question: in “*Conquering Diabetes: A Strategic Plan for the 21st Century*”, the Congressionally appointed Diabetes Research Working Group, consisting of a team of top medical experts, concluded that “the *only* way to reduce the tremendous burden of [diabetes] is through intensified biomedical research” (Diabetes Research Working Group, 1999) (emphasis added). Not that there is paucity of evidence showing that this “conquest” might lie elsewhere—that poverty and diabetes go hand in hand is hardly a matter of debate, is confirmed every time it is measured (Bachman et al., 2003; Chaturvedi et al., 1998; Evans, Newton, Ruta, MacDonald, & Morris, 2000; Forssas, Keskimäki, Reunanen, & Koskinen, 2003; Green, Hoppa, Young, & Blanchard, 2003), and is unlikely to be disconfirmed any time soon. Yet a search in the database of the American Diabetes Association (ADA), the largest non-profit in America involved in diabetes prevention and treatment, showed that most research projects,

many co-sponsored by the ADA, industry, and government, consisted of the searches of genes or their interactions at the heart of the SACGHS proposal (Chaufan, 2006). This search retrieved not a single project concerned with diabetes and poverty. This silence is worth investigating.

## Conclusions

In sum, our knowledge of common diseases is greater than our ancestors would have ever dreamed achievable, and whatever knowledge we still need is unlikely to be found in the genome. Hence the study proposed will not enhance our ability to conquer the vast majority of ills that affect the American people, and most likely other peoples. Rather, it will divert scarce resources away from urgently needed interventions.

As I noted at the beginning, scholars have examined the overemphasis on genetic explanations of human differences, including disease differences, yet have rarely challenged the science. What, if anything, explains the resilience of the underlying disease paradigm, immune even to intellectuals? There is likely to be more than one explanation of the paradigm's resilience, as there is more than one metabolic pathway leading to elevated blood sugar—and I am in no position to provide an answer. But resilience it is, as illustrated by the case of social scientists who use genetics to explain phenomena belonging to levels of analysis clearly different from that of the genome, such as the claim, in the feature article of a leading social scientific journal, that “political attitudes are influenced much more heavily by genetics than by...socialization” (Alford, Funk, & Hibbing, 2005) (164).

The quest for understanding complex diseases, attitudes or behaviors by scrutinizing genes severely distorts not merely psychological and social issues, but biological ones as well. While human societies, psyches, and bodies have to be *compatible* with our genes, much as they have to be compatible with the subatomic particles constituting matter, it does not follow that genetics or quantum physics will provide an “instruction book for human biology” (Collins & McKusick, 2001) (540), much less illuminate anything interesting about the human condition. Further research should investigate how the genetic paradigm exerts its fascination on intellectuals themselves. Failure to challenge it on its own term matters because it leaves beliefs

about its “potential” (or its imagined dangers) alive, legitimizing claims that grab the collective imagination and driving resources away from urgently needed social, economic, and public health policies.

We have known for years, and study after study confirms, which human environments will enable us to plot a reaction norm for any human genotype yielding the healthiest possible phenotype: reasonable access to healthy lifestyles, proper housing, living wages, safe neighborhoods, well-funded schools, equitable medical care, and so forth. None of these provide quick fixes. Yet improvements in any of them would be rational—based on sound evidence and good logic—and just—a step towards eliminating social inequities in health. We also know that when any of these human needs are not met health deteriorates: our human genes simply do not thrive—we are remarkably equal in this respect—and, frankly, this fact about human beings is unlikely to change. We do not live in Aldous Huxley's “Brave New World”. So let us not invent false questions to answer or imaginary problems to solve. There are plenty of real ones.

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