

The Ethics of Translational Science: Imagining Public Benefit in Gene-Environment Interaction Research

SARA L. ACKERMAN¹

UNIVERSITY OF CALIFORNIA SAN FRANCISCO

KATHERINE WEATHERFORD DARLING

UNIVERSITY OF CALIFORNIA SANTA CRUZ

SANDRA SOO-JIN LEE

STANFORD UNIVERSITY

ROBERT A. HIATT

UNIVERSITY OF CALIFORNIA SAN FRANCISCO

JANET K. SHIM

UNIVERSITY OF CALIFORNIA SAN FRANCISCO

Keywords

post-genomic science; gene-environment interactions; translational research; ethics

Abstract

Biomedical research is increasingly informed by expectations of “translation,” which call for the production of scientific knowledge that can be used to create services and products that improve health outcomes. In this paper, we ask how translation, in particular the idea of social responsibility, is understood and enacted in the post-genomic life sciences. Drawing on theories examining what constitutes “good science,” and interviews with 35 investigators who study the role of gene-environment interactions in the etiology of cancer, diabetes, and cardiovascular disease, we describe the dynamic and unsettled *ethics of translational science* through which the expected social value of scientific knowledge about complex disease causation is negotiated. To describe how this ethics is formed, we first discuss the politics of knowledge production in interdisciplinary research collectives. Researchers described a commitment to working across

¹ Sara L. Ackerman, Email: sara.ackerman@ucsf.edu

disciplines to examine a wide range of possible causes of disease, but they also pointed to persistent disciplinary and ontological divisions that rest on the dominance of molecular conceptions of disease risk. The privileging of molecular-level causation shapes and constrains the kinds of knowledge that can be created about gene-environment interactions. We then turn to scientists' ideas about how this knowledge should be used, including personalized prevention strategies, targeted therapeutics, and public policy interventions. Consensus about the relative value of these anticipated translations was elusive, and many scientists agreed that gene-environment interaction research is part of a shift in biomedical research away from considering important social, economic, political and historical causes of disease and disease disparities. We conclude by urging more explicit engagement with questions about the ethics of translational science in the post-genomic life sciences. This would include a consideration of who will benefit from emerging scientific knowledge, how benefits will accrue, and the ways in which normative assumptions about the public good come to be embedded in scientific objects and procedures.

Introduction

How science can and should contribute to efforts to improve human health has long been an abiding concern among researchers studying the causes of common diseases. In the biomedical sciences of the early 21st century, the question of social responsibility has been recast as a call for "translational research." Commonly understood as the attempt to move scientific knowledge "from bench to bedside" in order to improve health outcomes (Zerhouni 2003; Zerhouni 2005), the notion of translation emerged in the 1990s at the US National Cancer Institute and became ubiquitous in biomedical research by the early 21st century (Butler 2008). More recently, biomedical researchers have made calls to extend the scope of translational research beyond the clinic to inform disease prevention strategies and efforts to reduce health disparities (van der Laan and Boenink 2015; Wallerstein and Duran 2010).

A defining feature of translational research is collaboration across disciplines with the goal of better understanding complex phenomena and rendering scientific knowledge more applicable to the real-world contexts of patient care and public health policy. We ask how social responsibility is understood and enacted in a context of intensified imperatives for interdisciplinary collaboration. How do contemporary life scientists think about how translational science ought to be done? What kinds of ethics do scientists articulate around making science "translational"? This paper addresses these questions by examining the potential applications of emerging knowledge about the complex causes of common diseases. We focus specifically on the study of gene-environment interactions (GEIs) by researchers working at the intersection of genomics and epidemiology. GEI research has become an important pathway towards potentially successful translations of scientific knowledge to efforts to reduce the burden of common, etiologically complex diseases.

The study of GEIs gained momentum after it became apparent that the sequencing of the human genome, and subsequent flurry of genome-scale studies, would not discover simple genetic culprits for most diseases. Most life scientists now approach the study of common disease

etiology with a growing understanding of, and explicit attempts to study, the many ways that bodies and environments are inextricably linked. Attempting to account for complex causation in their estimates of disease risk, genetic epidemiologists and other scientists study the “interactions” of genetic, behavioral, socioeconomic, and environmental variables (Beaty and Khoury 2000; Shostak 2003; Hunter 2005; Khoury et al. 2005). These researchers often work in large, interdisciplinary teams, amassing thousands of research participants across large geographical areas and using novel information technologies to compile and analyze vast quantities of biological and other data. The promise of these complex enterprises is that they will build better explanations of the numerous, interacting forces that shape disease incidence and distribution in human populations. Whether and how this knowledge will lead to clinical and/or public health benefit, however, is unclear for many scientists.

Drawing on interviews with 35 researchers studying GEIs related to common diseases, and observations at professional meetings where GEI studies are presented, we explore how particular ideas of public benefit inhere in the ways that researchers think about and conduct their work. We found that our participants’ accounts of everyday scientific practice, and their reflections on the value of GEI research, contained an *ethics of translational science* in which assumptions about the proper conduct of research, and a commitment to interdisciplinarity, were imbricated with claims about the social implications and value of GEI research. Researchers’ ethics of translation were flexible, helping them navigate a variety of cross-disciplinary collaborations, prevailing methodological norms guiding post-genomic knowledge production, and considerations of the possible uses and impact of their research on clinical and public health efforts to reduce the burden of disease.

The structure of our paper is as follows. First, we outline our theoretical framework, drawing on concepts from science and technology studies to consider how imaginaries of science for the public good are (re)shaped through the emergence of new technologies, procedures, and research collectives. Examining different conceptions of what constitutes “good science” (Thompson 2013; Shim and Thomson 2010), we invoke Madeleine Akrich’s (1992) notion of “scripts”—or expectations of future contexts of use embedded in scientific objects and knowledge—to understand how imaginaries of contributory science come to be formed and mobilized in a post-genomic era, with its emphasis on interdisciplinarity and the translation of scientific knowledge into broadly beneficial practices and policies.

Then, we compare the promise of interdisciplinarity with on-the-ground efforts to enact it in the pursuit of knowledge about the causes of common diseases. We describe how cross-disciplinary efforts are highly generative of new research objects and enterprises. At the same time, funding priorities and the dominance of genetic technologies and methodological standards

² Although the concept of “translation” has become ubiquitous in biomedical research, its meaning varies depending on the circumstances of its use (Woolf 2008; Mittra 2013). Here, we focus specifically on the multiple and contested ways that scientists imagine the potential uses and benefits of knowledge about gene-environment interactions.

³ We draw on George Marcus’ concept of “imaginary” as a socially and culturally embedded mode of sense-making that “looks to the future and future possibility through technoscientific innovation but is equally constrained by the very present conditions of scientific work” (Marcus 1995, 4).

often limit efforts to work across disciplines in more even-handed or bi-directional ways, and tend to privilege molecular understandings of how environments come to be embodied. These limitations result in the production of certain types of gene-environment interactions over others, and in the re-production of gene-environment *dichotomies* among scientists aiming to understand how the two domains are inextricably entangled. The result is research products that contain limiting assumptions about the scope of complex causality, the location of risk, and how etiological knowledge can and should be acted on.

Next, we discuss how researchers think with—and against—genomics in order to anticipate the potential clinical and public health benefits of the knowledge produced by GEI research. Drawing on the concept of “civic science,” which Kim and Mike Fortun describe as “historically and culturally specific ways of understanding how science can be fashioned to serve the public good,” we explore tensions between what counts as good science in the post-genomic context and the etiological problems that GEI researchers themselves consider to be “worthy of care and ethical attention” (Fortun and Fortun 2005, 44). Because GEIs are scripted with a molecularized understanding of disease causation and risk, some of our participants were concerned that GEI research is drawing attention away from important behavioral, social, economic, and political contributions to disease. Others expected knowledge about GEIs to be more beneficial for treating rather than preventing disease.

We conclude with a discussion of post-genomic science’s reshaping of what counts as social responsibility and how it can be enacted. Science’s responsibility to provide public benefit, we argue, is not simply a matter of translating research findings into beneficial messages, devices, or policies. Rather, GEIs’ potential contributions are conceived and made possible through the very categories, techniques, and objects of scientific practice, and through the ethical sensibilities of scientists, rather than simply in how the products of science might be put to use in the future.

Good Science

What is good science? Charis Thompson divides notions of the good into uses that are for the most part internal to science itself and those that are more external (Thompson 2013). In both domains, the good is both technical and social, moral and intellectual. However, internal deliberations about good science are primarily tied to judgments about the conduct of research, faithfulness to established procedures, accountability, and integrity. In the second, more external, domain, the term good science most commonly evokes the surveillance and regulation of scientific conduct by various ethical apparatuses, which Thompson argues have prioritized regulatory compliance over meaningful ethical deliberation—particularly public participation in debates about “a greater good or good unto itself” (Thompson 2013, 63)

Kim and Mike Fortun offer a related conception of good science with their notion of “civic science,” or science that serves the public good (Fortun and Fortun 2005). They focus on the field of toxicology, whose practitioners’ “civicness” was located historically in the creation of an applied science that underwrote regulations protecting public health. More recently, however, toxicology has been transformed by a growing awareness of the complexity of the human body,

prompted by the expansion of genomics into population sciences, and by informatics, which enables the production, movement, and organization of massive amounts of data [see also Stevens (2013) on the growing entanglement of biology with computers via bioinformatics].

Documenting how the field of toxicology positioned itself as socially responsive and responsible, the Fortuns argue that civic science is “enunciated” through specific, historically contingent ways of doing science and defining what counts as credible scientific knowledge. Civic science emphasizes the ways scientists’ identities as public servants or stewards of human and environmental health, for example, are fashioned in relationship to changing methods, disciplinary alliances, and institutional formations.

Understandings of science’s potential social contributions are also embedded in the procedures and technologies through which knowledge is produced, and in scientific knowledge itself. We draw on Madeleine Akrich’s idea that technological objects (and, similarly, technoscientific forms of knowledge) embody assumptions, or “scripts,” about the contexts in which they will be used, and about the relationship between an object and its future context(s) of use (Akrich 1992). The notion of script is not meant in a determinist sense, but rather as a set of expectations of future use(s)—expectations that will ultimately interact with, or be co-constituted by, the way the object is used. It is also important to note that users of scientific products or knowledge may opt for different roles than those (implicitly or explicitly) imagined for them in the design process, which means that the trajectories of scripted objects are not pre-fixed.

Here, we describe how GEIs hold scripts that signal particular understandings of causal complexity and how it can be acted on to prevent and treat common diseases. We found that these assumptions are formed and normalized through seemingly mundane decisions about research procedures and variables; suitable cross-disciplinary collaborators; and the use of information technologies to transform complex phenomena into data that can be quantified, standardized, and compared. In this way, ethical and advocacy positions are hidden in seemingly technical forms and processes, and science is enacted as “politics by other means” (Latour 1987, 228). We now explore two concepts—complexity and interdisciplinary—that lie at the heart of post-genomic translational research.

Complexity

“Complexity” is ubiquitous in post-genomic science, and in etiological research it usually refers to biological processes that are multifactorial, rather than having a single cause and effect. Looking more critically at the reliance on the notion of complexity, Nelson (2013, 2015) and Arribas-Ayllon and colleagues (2010) argue that evoking the complexity of human experiences and behaviors—such as stress, anxiety, and psychiatric disorders—is a rhetorical strategy to justify and explain the frequent failures of animal and human genetic studies, and works both to attenuate and to preserve optimism about future genetic research. Importantly for this paper, Arribas-Ayllon and colleagues (2010) also found that scientists’ emphasis on complexity, and its implications for interpreting study results and tempering expectations of future research, served as a means of performing cautious, sober, professional responsibility.

Other authors have pointed out that scientific efforts to understand complex causality often rely on—and are undermined by—research methods that embrace simplicity and control. For example, Suryanarayanan and Kleinman (2016) traced current knowledge—and ignorance—about honeybee declines and colony collapse to historically shaped norms and values governing field experiments on the impacts of agrochemicals on honeybee health. These standard practices favored “precision over validity and...simplicity over complexity” (Suryanarayanan and Kleinman 2016, 39). The values embedded in these ethical and experimental standards were compounded by the practical constraints of doing research in the field, which explicitly resisted scientists’ pursuit of “control-oriented” experimental designs and “clean” results. Such historical and practical barriers prevented scientists from being able to model, study, and understand the complex interactions among chemical exposures, agricultural practices, and honeybee health.

Questions about the fit between prevailing methodological norms and the study of complex systems also impacts the “truth value” of experimental research. Nelson (2015) found that during the 1990s in animal behavioral genetics, disciplinary differences in definitions of what constitutes “good” experiments led to contrasting ideas of whether and how to resolve issues that arose while using genetically modified mice in studies of animal behavior. Nelson found deep epistemological differences in how groups of researchers considered the role of genetically modified mice (termed “knockout mice”) in behavioral experiments. For some, such mice were an elegant way to demonstrate the significance of particular genes on physiology and in turn on behavior. For others, behaviors were the result of incredibly complex networks and interactions of genes and environments, such that any results from purportedly precise genetic modifications could not actually comment on the links between one modified gene and subsequent behavioral outcomes. Thus, Nelson argues that contrasting positions on how to conduct good animal experiments overlay onto differing epistemological positions on the nature of gene action in shaping behavior. Moreover, she found that resolving differences of experimental technique and process—or the “how” of laboratory work—could not settle disputes over the weight and interpretation given to experimental results. These contestations arose from deeply divergent ontological and epistemological assumptions stemming from disciplinary background and training. Thus, negotiations around how to study complexity “well” are often invoked or are caught up in debates about when and how disciplinary matters and when and how interdisciplinary research works.

Interdisciplinarity

Collaboration across disciplines is another sine qua non of post-genomic translational research, and is part of a broader trend in academic research (Jacobs and Frickel 2009). Frickel and colleagues note that one of the unspoken assumptions about interdisciplinarity is that “the traditional social order in the scientific field, characterized by turf wars among the disciplines, would be replaced by new arrangements that are unconstrained by boundary work and disciplinary hierarchies” (2017, 15). Yet, STS scholars have found that when researchers from different disciplines collaborate, their interactions are permeated by power asymmetries that take

disciplinary hierarchies and replicate them as “a new interdisciplinary order” (Frickel et al. 2017, 16; see also Albert et al. 2017). This new order may be characterized by persistent, but productive, tensions—or “collaboration without consensus”⁴ (Centellas, Smardon, and Fifield 2013). Moreover, scientific collaborators often do not share common understandings of the meaning of interdisciplinarity, and they instead mobilize the notion in strategic, and sometimes contradictory, ways.

Albert and colleagues (2017) interviewed social science and humanities scholars working in Canadian faculties of medicine that had taken interdisciplinarity as a mandate and strategic way forward. They found a disconnection between the idealized discourse of interdisciplinarity guiding institutional policies and the day-to-day practice of interdisciplinarity, which was characterized by entrenched power differences between disciplines and epistemologies. This “decoupling” (Bromley and Powell 2012) proved especially difficult for social science and humanities scholars, who had to adapt their research and align themselves to the emerging interdisciplinary order, even as their own disciplinary standards were devalued and they were subject to the prevailing evaluation criteria of medical science.

Translational Science

As a field of practice (Bourdieu and Johnson 1993) that embraces interdisciplinarity, and seeks to explain and act on etiological complexity, GEI research produces, and is shaped by, multiple ethics and practices of translation or “ethics of translational science.” This term builds on Shim and Thomson’s use of ethics to describe epidemiologists’ “contrasting definitions of social responsibility, views of epidemiological research priorities, and perspectives on professional jurisdiction and the proper conduct of good science” (Shim and Thomson 2010).

Ethics of translational science are situated at the intersection of academic research institutions, their obligations to public health, and transformations in the conduct of research. In our interviews, GEI investigators simultaneously problematized (or at least wondered about) the utility of the research they were engaged in, how and towards what ends that research ought to be conducted, and the contributions of science towards ameliorating larger societal concerns. We borrow from Karlin’s case study of the University of Chicago Medical Center’s reorganization of their research and biomedical activities, in which she argues that the “development of translational research and the reorganization of the research university came to inhabit the same problem space as the much longer history of the struggle to provide care and investment in underserved communities” (2013, 525). Similarly, our participants anticipated and negotiated the ethics of translational science by placing concerns about the practice of their research in the same problem space as epistemological or ontological concerns about the social, economic, and political determinants of health and illness.

⁴ The idea of “collaboration without consensus” builds on Star and Griesemer’s (Star and Griesemer 1989) theory of “boundary objects,” which are arrangements—or “organic infrastructures”—that arise and enable different groups to work together without consensus (Star 2010, 602).

In this paper, we demonstrate how scientists experienced different approaches to doing gene-environment interaction research, and, in turn, how these approaches script different “knowledge effects” (Landecker 2013). This means that translational research, as Landecker points out, is “not just a question of getting pure research to become applied to human life more quickly; rather it involves reshaping the very way research is done...knowledge is always already generated to be pipeline amenable” (2013, 498). We also find that “translational research is not a singular object” (Rajan and Leonelli 2013, 464), and researchers’ varying reactions to different approaches and effects articulate multiple ethics and practices of translational science. But although different definitions of good science and practices for conducting it were mentioned by our participants, translational science is commonly assumed to involve a linear process of innovation, in which the products of research are translated into use and, presumably, social benefit (van der Laan and Boenink 2015). This definition elides the ways in which scientific knowledge and technology reimagine societal problems and their solutions. Proponents of “public health genetics,” for example, claim that preventing common diseases with known environmental causes will require a new definition of “risk” that includes individual genetic susceptibilities as well as behavioral and environmental factors (Khoury et al. 2005; Khoury 1996). Critics have argued that this “reorientation of the field of public health towards genetic/genomic knowledge, technologies, and practices” may lead to greater attention to how particular social and material environments are embodied in biological processes [Shostak 2003, 2338; see also Niewohner (2011) on the “embedded body” and Lock (1993) on “local biology”]. However, imperatives for molecularization also create new forms of genetic reductionism that may further individualize received definitions of risk and prompt policies and prevention strategies that emphasize individual responsibility for health (Shostak 2003; Lippman 1991; Lock 2013; Darling et al. 2016).

Given these potential and complicated “knowledge effects” (Landecker 2013), and the ways in which varying definitions of and practices around understanding complexity and enacting interdisciplinarity both shape them and are invoked therein, we embarked on the present analysis of the ethics of translational science in post-genomic research.

Methods

This paper draws on findings from a larger project conducted in 2010-2014, in which we explored how gene-environment interaction researchers conceptualized and worked with categories of race, ethnicity, and ancestry. For that study, we recruited National Institutes of Health (NIH)-funded principal investigators whose research focused on one of three etiologically complex diseases: cancer, type 2 diabetes, and cardiovascular disease. Our interviews focused primarily on how researchers defined and measured race, ethnicity and ancestry (Shim et al. 2014). In the process, however, many of our participants also reflected on whether knowledge about GEIs had the potential to help alleviate health disparities and improve public health.

The investigators in our study were disciplinarily diverse. They reported affiliations with epidemiology, genetic epidemiology, molecular epidemiology, genetics, and interdisciplinary

fields such as cancer research. Most of our participants asked to speak off the record. To protect their anonymity, and prevent identification of their often highly specialized and therefore easily identifiable studies, we decided to remove or alter some identifying information and occasionally change disease information to more general terms (e.g., “cancer” instead of prostate cancer).

We conducted a total of 55 in-depth, semi-structured interviews, including 35 initial interviews and 20 follow up interviews approximately 12-18 months later. Interview questions focused on participants’ career paths, experiences working across disciplines, and opinions about the field of GEI research. We also asked for specific details about their past and current studies, how they selected their research topics, and what procedures were used to collect and analyze data. Concerns about the potential societal benefits of GEI research often arose unprompted during our conversations with researchers. Our findings also draw on over 200 hours of ethnographic observation and informal interviews at nine scientific meetings in the US. The study was approved by the institutional review boards at Stanford University and the University of California, San Francisco, and we obtained informed consent from all participants.

After being transcribed verbatim, all interview transcripts and fieldnotes were uploaded to the qualitative data analysis software ATLAS.ti. A codebook was developed based on close reading of the first eight interviews and the principles of grounded theory (Charmaz 2006). Codes were applied to all data, and we then extracted coded data relevant to our analysis for this paper (including “public health, societal, social implication,” “ethics,” “career trajectory” and “patterns/trends in genetics, epidemiology, or GEI”). We then engaged in repeated discussions to refine our interpretations of the coded data and its relevance to questions about the potential social benefits of knowledge about GEIs.

Identifying Gene-environment Interactions: A Model of Interdisciplinary Research?

Understanding that common diseases usually arise through complex interactions between biological, social, behavioral, and environmental forces is a basic assumption in GEI research. As one scientist put it, disease causality is all about how bodies respond to their surroundings: “genes...are really important in physiologic functioning, and...almost all genetic effects are contingent on some environment.” Or, as another of our participants explained,

I think it’s pretty clear from a lot of the work that has been done in common disease that it’s very unlikely that one factor is really going to explain the majority of the disease burden or the etiology...So if you’re interested in seeing the bigger picture, explaining the whole story, then you kind of have to go to this multi-pronged approach looking at genes and exposures and things like that.

In other words, this researcher argues, understandings of disease etiology will always be incomplete if scientists continue to focus on single causal variables in isolation from the full spectrum of possible influences on disease risk *and* the ways that these influences interact with each other to alter population-level risk patterns.

The commitment to studying etiology as multi-factorial and interactive was often articulated by our participants as a leave-no-stone-unturned approach to identifying and assessing the myriad forces that contribute to the development of common complex diseases. Almost any potential risk factor should be open to consideration, they insisted, from molecular-level differences between bodies to broadly defined social phenomena such as “discrimination.” A wide search for all possible sources of risk was a defining characteristic of good science. As a speaker at a scientific conference exhorted, “...let’s do good science. Let’s evaluate the diverse contributions of socioeconomic status, culture, discrimination, health behaviors, diet, environmental exposure, and genetics.”

Putting this exhortation into practice, however, is not simply a matter of performing science as usual, given that geneticists studying individual differences in DNA have until recently shared little epistemological and methodological common ground with epidemiologists studying social and environmental risk factors for common disease. Rather, the collaborative study of causal factors at multiple domains or “levels,” e.g. biological, behavioral, social, and economic (Galea, Riddle, and Kaplan 2010), requires scientists to enter unknown territory by forming new research collectives across “disciplines that weren’t even really talked about in the same circles,” in the words of one researcher.

GEI studies extend this project by bringing researchers together to measure variables at multiple levels while also identifying how these variables interact with each other to influence disease risk. Although there is no typical GEI research team, they often include investigators with diverse disciplinary and institutional affiliations and training. For example, an investigator who participated in our study had appointments in departments of medicine and environmental health sciences at an academic medical center. His GEI-related publications were co-authored with investigators affiliated with departments of epidemiology, biostatistics, radiology, cardiology, medical genetics, and public health genomics, among others, from at least eight academic institutions.

Some researchers described their embrace of interdisciplinary research as both a personal epiphany and a venturing forth from the bounds of the community of practice with which they had trained. A geneticist who studies type 2 diabetes recounted the shift in perspective that he and his colleagues have undergone:

I think we are taking a step back now and reflecting and saying, you know what, you can’t solve everything with a gene chip, you really, really need to understand the social, behavioral, environmental component as well.

Hoping to better understand how interactions between genetic variation and access to food and exercise contributed to diabetes risk, this researcher embraced, as he put it, the “merging” of the biomedical sciences and behavioral sciences. He and other researchers found what he called “that crossroads, that intersection” between genes and environment, and between researchers from different disciplines, to be exciting and full of potential for new approaches and directions. Other terms used by GEI researchers to simultaneously narrate and celebrate this

phenomenon included “cross-pollination” and “...diversity. Diversity of thought, diversity of ideas, diversity of directions.”

Inhabiting the “crossroads” between genetics and environment is not only exciting, but increasingly obligatory, for post-genomic researchers. For example, interdisciplinary collectives in GEI research often involve the incorporation of sociocultural variables, and the researchers who study them, into studies of genetic differences between individuals and their association with disease risk. Several genetic epidemiologists, for example, described their newfound conviction that genetics alone could not explain the etiology of common diseases. This understanding led them to introduce “social factors”—and social scientists—into their research:

I don't think we can ignore the social factors. And it does require coming together, bringing the best minds in the social sciences together. [...] And I think the sooner we recognize some of these things that we can't measure are important, then the sooner we'll be able to try to figure out ways to measure them.

In the same vein, a speaker at a professional meeting invoked the idea that a scientific revolution has enabled the compelling concept of “culture” to become a newfound subject of serious inquiry in the biosciences:

I'm talking about the paradigm shifting here...the dominant research method in this field has precluded an intensive exploration and integration of culture into our research, whereas the blended paradigms we're going to be talking about this morning will help us to increase our understanding of cultural difference.

Conversely, epidemiologists whose careers had been devoted to studying the risks of “lifestyle,” such as diet and exercise, often incorporated genetics—and geneticist collaborators—into their research projects. Recognizing the growing demand for a genetic component in epidemiologic research among both funders and their peers, these researchers described DNA analysis as a necessary addition to etiological research.

Thus, investigators from both “sides” of the gene-environment interaction used terms like “intersection,” “crossroads,” and “center” to suggest a new emphasis on interconnections between genes and environments and between scientists from previously distinct disciplines. However, in examining actual research practices, we found that interdisciplinary interactions, and those of genetic and environmental variables, were not characterized by a simple blending of compatible but previously separate entities. Nor are genes and environments, and scientists from different disciplines, necessarily equivalent in influence or activity. Rather, we learned that considerable work goes into ensuring that scientists and their objects of study perform and interact in ways that reliably produce credible knowledge, and determining which research questions and methods are considered legitimate. Below, we look closely at how interdisciplinarity operated on the ground—both in the production of knowledge about complex causality and in the ethics of translational science that scripted the anticipated applications of GEI science.

Interdisciplinarity in Action

Examining the daily work of interdisciplinarity, we found that scientists navigated infrastructures and norms that alternately encourage and undermine efforts to conduct collaborative studies of disease etiology. For example, the NIH now sponsors, and even expects, interdisciplinary, multi-sited studies of disease etiology. However, this endorsement runs up against institutional and professional norms that assign academic credit primarily to a project's lead researcher.³ One of our participants explained:

We're going to need to change the way our merit system is set up, in order to recognize the multidisciplinary input of a lot of different people on a collective problem...it has been like a me-me system. One person gets all the glory and credit. And that system in itself is antithetical to collaborations.

Epistemological and methodological differences across disciplines also shaped whether and how collaborative projects were pursued. As one of our participants described, researchers from different disciplines "speak different languages, they have different goals and standards for what is good research, you know, so having them be all in the same wavelength is very hard." This dilemma often led to the pursuit of more readily initiated collaborations among disciplinary "neighbors." Moreover, disciplines tend to focus their etiological gaze at different scales, which results in the production of distinct forms of knowledge and ideas about whether and how the products of research can be used for public benefit. For example, we interviewed an epidemiologist who could more readily see the social utility of the "macro level" work engaged in by population science colleagues than her own "genomic level" collaborations with geneticists:

I like to collaborate with my geneticist friends. I very much enjoy learning about the biology involved and disease causation...I am in a population science environment, so there are some investigators here who are very interested in media and on its influence on environment and risky behaviors...I think what they are doing has a huge impact. In terms of my own research it's a little harder to translate what that is into what I am doing...the scale is totally different...it's at the macro level and we're kind of at the genomic level.

On the other hand, some epidemiologists argued, these different levels can and should be bridged through multi-level modeling and combining metrics and variables across disciplines. The real problem, as they understood it, was that genetics researchers do not make enough of an effort to collaborate with scientists who have expertise in, as one researcher put it, the "environmental side" of GEI interactions. "Geneticists have not invested a huge amount in bringing environmental scientists into their cohorts," said an epidemiologist. The result, several epidemiologists argued, is either an exclusive focus on genetic factors in etiological research, or a

³ See Shim and Thomson (2010) for an extended discussion of the push and pull of "transdisciplinarity" among researchers studying the epidemiology of complex diseases.

pairing of highly sophisticated measures of genetic difference with, in the words of one investigator, “very poor” or “really trivial measures or representations” of the environment in geneticist-led GEI studies. Disputes about how to approach the GEI equation point to two key aspects of GEI research that are relevant to our notion of the ethics of translational science. First, there is a contradiction built into the very premise of GEI research: that common diseases are caused by inextricably linked phenomenon that must be de-linked in order to be studied. Second, an increasing emphasis on molecular-level measurement of risk is shaping broader conversations about the potential public health impacts of post-genomic science.

Genes vs. Environments

The study of the interactions of genes and environments is based on a paradoxical assumption: that forces and materials that are enmeshed and inseparable in individual bodies can be separated into discrete, measurable variables. In other words, as Evelyn Fox Keller explains, the very idea of a GEI depends on a “presupposition of disjunction on which conjunction rests” (2010, 17; see also Grace 2008). Keller also reminds us that population genetics research (including GEI studies) is concerned with the contributions of genes and environments to variation within a population, not to individual traits such as the propensity to develop disease (2010). However, population-level estimates of risk variance and individual disease risk are often conflated in scientific discourse, demonstrating a common conceptual and linguistic slippage that, Keller argues, serves to perpetuate longstanding nature/nurture dualisms. In GEI research, this dualism perpetuates a myth of gene/environment equivalence, or the idea that a vastly complex “environment” can and should be reduced to discrete variables that can be measured and compared with the effects of suspicious genetic variants.

This reductionism was apparent even among researchers who embraced the importance of complex causality and had successfully assembled interdisciplinary research teams. This is because the narrowing of the environment had become embedded in the norms guiding scientific practice. In particular, decisions about appropriate study variables and data collection methods were driven less by an agnostic consideration of all relevant etiological variables, than by circumstances that at first glance seem to be unrelated to political and ethical considerations, such as funding agency priorities, data collection constraints, prior research findings, available technologies, and prevailing methodological standards. For example, a researcher described the difficulties of narrowing down the environmental variables in a study of GEIs related to cancer that brought together investigators from nutritional epidemiology, genetics and immunology:

...it was bringing multiple disciplines together...so we had of course DNA and serum, but we also collected vacuum cleaner bags and then measured pesticides in the vacuum cleaner bags. We took water samples...So it was sort of hitting it from multiple angles with multiple people coming from different backgrounds to put a study together. [...] You can imagine the train crash...when everybody submitted what they wanted on the exposure assessment. It would have taken like five days to collect all [the data on the

questionnaire]. So it's sort of an arm wrestling to get it down [to a realistic number of questions].

The “arm wrestling” consisted of negotiations led by the principal investigator in order to shrink the scope of inquiry and the length of the questionnaire, given that a “five-day” questionnaire was simply not feasible, while maximizing the statistical power of the study and preserving the “non-negotiable” variables required by the funding agency. These seemingly straightforward technical problems of questionnaire design guided researchers away from potentially important phenomena that they had hoped to include in the study, and elided considerations of which environmental risk factors would be likely to have the most significant public health impact if intervened on. Thus, the necessity of collecting DNA was taken for granted, whereas potentially more changeable risk factors—such as environmental pollutants—were open to negotiation and exclusion.

Routine decisions thereby contributed to producing and maintaining norms governing what counts as credible—and potentially actionable—knowledge about GEIs. Interestingly, many of the researchers we interviewed were reflexive about this process and their role in it. The researcher quoted above, for example, went on to describe that what *can* be learned about his disease of interest does not necessarily align with what *should* be learned:

Well, obviously, the pressure and the—now the tech—the ability to do it and the technology is there right now with the genetic side, so that seems to have a potential to overwhelm. But I think when people step back, they sort of start understanding it's a—you know, environment has to be—one of the major drivers here, and so we really need to understand it...but you know it's a lot of work to characterize people from an environmental point of view.

The implication is that the methodological imperative to seek molecular knowledge is prompted by the availability of new technologies that produce increasingly precise, fine-grained data. This results in pressures to generate findings that are amenable to emerging, molecular standards of scale and measurement.⁴ More often than not, variables that yielded more readily to precise measurement gained traction over those that were messier and “a lot of work.” This is how scientific norms were created, reinforced, and sometimes resisted, through everyday decisions about the conduct of research and how a geneticized understanding of disease risk became embedded—or scripted—in knowledge about GEIs.

As a consequence, GEI research runs the risk of further intensifying the “biomedical individualism” that has long underwritten epidemiologic understandings of complex causality and that emphasizes risk factors that can be measured and addressed at the individual level (Krieger 1994). This trend was expressed by some of our participants as an ethics of translational science in which risk is known—and can and should be mitigated—through the genetic profiling

⁴ See also Ackerman et al.'s (2015) analysis of the politics of quantification in GEI research, and Darling et al. (2016) on how GEI research “molecularizes” the environment.

of individuals. Not all GEI researchers, however, unequivocally embraced the reconceptualization of risk as a molecular phenomenon. We now turn to a discussion of the different ways that the potential public benefits of knowledge about GEIs are imagined by our participants. Their narratives highlight how an ethics of translational science depends not only on cross-disciplinary collaboratives and the practice of “good science,” but also on imaginaries of how to enact social responsibility as a post-genomic scientist.

Why GEIs Matter: Scientists Weigh in on the Social Contributions of GEI Research

As mentioned earlier, our participants all conducted research on heart disease, cancer, or type 2 diabetes, conditions for which strong environmental risk factors have been identified. A classic example is the now-undisputed causal link between smoking and lung cancer, which has prompted countless smoking cessation interventions and anti-smoking laws. GEI studies of smoking and lung cancer focus on small variations in risk between smokers with minute genetic differences, and may predict higher or lower lung cancer risk among smokers with a particular genetic variant(s) than among smokers without the variant(s). In this way, disease risk is parsed into tiny slivers that can only be known on a molecular level.

As researchers consider and debate how to apply the knowledge they are producing, the molecularization of understandings of disease processes and disease risk that inhere in GEIs shapes the possibilities and limits of translation. Among most of our participants, GEIs were assumed to be actionable, or potentially actionable, either by way of genotyping individuals, or by elucidating the molecular mechanisms of disease. In other words, genotyping has become essential to credible etiological research and increasingly animates considerations of how science can and should contribute to efforts to prevent and treat disease. Here, we consider how reconceptualizing disease risk via genotyping shapes GEI researchers’ ethics of translational science and the potential futures that it conjures.

Genotyping as a Public Health Strategy

Although epidemiologic risk factors are conventionally defined as self-directed behaviors or environmental factors outside of individual control, post-genomic etiological research has shifted risk further into the body. Researchers often discussed risk as something that is located in DNA and “triggered” by different environments: “gene-environment interaction is that some genotypes [persons sharing the same genetic variant or group of variants] are better or worse off than other genotypes in the same environment,” said one investigator.

This way of understanding risk lends itself to approaches to disease prevention that target genotyped individuals or groups to change behavior or alter environments so that the genetic variant(s) in question will/will not be triggered or “activated.” Moreover, many of the environmental variables in GEI studies are imagined to be under individual control. The scripting of GEIs as readily applicable to geneticized, self-directed individuals prompted some of our participants to anticipate possible disease prevention campaigns in which individuals or

groups would be informed about their genotype and whether it puts them at increased or decreased risk in the presence of a particular, individually-controllable environmental exposure. One example offered by a researcher involved "...telling people and families that already have a mutation that makes them prone to having a melanoma that they shouldn't get into a tanning booth." Another researcher described how knowledge about a GEI could influence dietary behavior: "20 percent of people have a deletion in GSTM1, and to get a beneficial effect from, say, broccoli, they would have to eat like may be one-tenth of the amount. That'd be nice for people to know."

These examples illustrate a translational imaginary that scripts a particular kind of receiving public that can benefit from knowledge about GEIs. We argue that this public does not simply exist outside of the scientific research enterprise, waiting for new knowledge or tools to emerge. Rather, the beneficiaries of post-genomic science are constituted, or "made up," through the very construction of GEIs themselves (Hacking 1986). Specifically, the public is conceived as an aggregate of individuals, each of whom will be prompted to act more prudently after receiving knowledge about their genotype. In this way, it is imagined, public health will be maximized, genotype by genotype.

Clinical and Social Benefits of Knowing How Diseases Work

Other researchers shared the faith in the public health potential of genotyping, but they did not think it would be useful for disease prevention efforts. Although they wanted their findings to have a broader impact on public health, they anticipated that the molecular emphasis of GEI research would be most valuable for improving knowledge about disease prognosis or the development of clinical therapeutics tailored to genotyped individuals or groups. A researcher studying cancer, for example, suggested that GEI findings could be useful for developing targeted treatments, such as those promised by "precision medicine" (Collins 2015; National Research Council 2011), but lamented that the parsing of minute differences between bodies and their exposures to environmental toxins may be too individualized for broader public health strategies:

If there's absolutely unique things for every different cancer, then how do you make a public health message out of that? I think that's more relevant for the treatment side rather than the prevention side...that raises the issue of where we're going to go with genetics and prevention. And I don't have a great answer for that yet.

Conversely, other researchers argued that molecular-level knowledge about how diseases occur could potentially contribute to disease prevention efforts, but that genotyping would put the onus of change on individuals. These investigators expected that GEI research would improve scientific knowledge about the biological mechanisms of disease, which could in turn be used to influence public policy—in particular legislation or regulations to clean up unhealthy environments. For example, an investigator studying the links between heart disease

and air pollution warned against using genetic information to hold individuals responsible for changing their “personal” environments. Much like the researchers championing the individual benefits of genotyping, he articulated an ethics of translational science that was based on the molecularization of disease and disease risk. However, he argued that knowledge about GEIs should contribute to collective efforts to clean up unhealthy environments, rather than create new forms of individual responsibility:

So when this research was done in the mid-90s [with] groundbreaking data that’s showing that the long-term exposure to air pollution is related to cardiovascular mortality, people didn’t really believe it...and so every piece of evidence that you get is sort of a chink in the armor of trying to strengthen this case...these are high stakes business because we’re talking about regulations that have cost the industry in the, you know, tens of billions, hundreds of billions of dollars a year...We’re not going to say that people who have a variant in the angiotensin receptor gene should all move away from big cities...I don’t think we should go there.

Resisting the Turn to Molecular Risk

A vocal subgroup of our participants—many, but not all, identifying as epidemiologists—expressed ambivalence about the molecularization of risk being mobilized by post-genomic research, and they doubted the value of GEI research for broad efforts to prevent disease and reduce disparities in disease distribution. They agreed that knowledge about GEIs might contribute to better explanations of disease “pathways,” or how diseases occur and develop, and that this knowledge could be used to develop more effective treatments for common diseases. However, these investigators argued that any such future treatments were more likely to yield commercial products than widespread public health benefits: “[Genomics research] will benefit the drug companies more than anybody else,” said one of our participants.

One of the arguments we heard most often centered on the claim that genetics and GEI research diverts funding and attention from behavioral and environmental factors that are known to significantly increase population-level disease risk, regardless of genetic differences between individuals. For example, a researcher who described himself as an observational epidemiologist agreed that disease causation is complex and involves both genetic and environmental influences. However, he insisted that separating people by genotype results in the prioritization of searching for “little causes,” or “little slivers” of the etiological pie, rather than attempting to address non-genetic risk factors that are already well understood and could potentially be intervened on. To illustrate, he described a Native American community with a prevalence of diabetes close to fifty percent:

Some people think, “oh, they must have some kind of really bad gene,” [but] it’s totally environmental. And they do genetic research in the [name of Native American tribe]...I don’t understand why personally...the public health value per dollar spent, it’s not worth it. Zero or close to it...it doesn’t matter what their genotype is. It’s just they’re not taking care of themselves.

Not all of our participants shared this investigator's emphasis on individual responsibility for health, and many offered a more expansive definition of the environment that included social, historical, and economic conditions. Nonetheless, they agreed that genomics has shifted attention and resources away from efforts to prevent disease based on existing knowledge about more macro-level forces. We heard nostalgic calls for a return to traditional epidemiologic research focused on "modifiable," i.e. non-genetic, risk factors and disease prevention. "I'm really wanting to get back to identifying how we can prevent cancer," said a researcher. In taking a stand against the seemingly inexorable dominance of genomics, they wrenched apart the provisional unification of genes and environment, and genomics and epidemiology. In so doing, they affiliated epidemiology with an ethos of public service and disease prevention, and genomics with disease treatment, or "bench to bedside" translational research. As one research put it, "...just philosophically, I'm more of a public health person than a genetics person."

Yet all of the investigators in our study pursued GEI research, and they recognized that including genetic analysis in epidemiologic studies of disease etiology is increasingly expected by funders, journal reviewers, and their colleagues. Although many expressed a sense of moral conflict regarding the life sciences' turn to genomics, they were also pragmatists with careers on the line. One of our participants bluntly phrased his compromise this way: "If I was God, yes...genetics wouldn't be on the top of my list. It would be education, access to health care, clean water...but we are in a political system..." Like this researcher, few of our participants had abandoned the inclusion of DNA analysis in their studies. However, in articulating a commitment to a notion of non-molecular risk, or "what really matters...in your behavior, your environment, that sets off that gene..." they were attempting to rewrite the individualization embedded in GEIs in order to cast light on the more mutable behavioral, social, and environmental forces that epidemiology has long attempted to understand and influence.

We found, therefore, considerable ambivalence among GEI researchers about the potential social contribution of their findings. On the one hand, they embraced and benefitted from the post-genomic approach to complex causality, in which interdisciplinary collectives work with "big data" to expand and transform etiological research. On the other hand, they recognized that GEIs embody a shift in how risk is conceptualized and produced, and that this shift may undermine policies and interventions aiming to prevent disease at the level of populations and environments, even if these interventions may be stymied by powerful political and economic forces. A researcher summed up the conundrum in this way:

I sometimes wonder why people are doing research on [the] genetics of nicotine addiction, when if we just raise the tobacco tax, which we failed to do, you know, just recently...we'd have a much bigger impact than trying to identify people who because of some genetic reason seem to be more prone to be addicted to nicotine.

The previous quote highlights the dilemma and tension that many GEI researchers seem to feel are inherent to the post-genomic research enterprise. Scientists' activities were shaped by

funding priorities, career advancement opportunities, and norms guiding the proper conduct of research, all of which require an ever-closer scrutiny of molecular processes. However, there was a sense—among many of our participants (but certainly not all) that genotyping may do more harm than good. GEI researchers' ethics of translational science, therefore, were strategically flexible—with aspirations of broad public benefit sitting side by side and in tension with the routine production of artifacts (GEIs) that may ultimately be more beneficial to select individuals than to populations.

Conclusion

Post-genomic etiological research is premised on the formation of interdisciplinary collectives and the notion that the causes of common, complex diseases are an intricate tangle of biological, behavioral, and environmental influences. These ways of thinking and working, alongside the emergence of information technologies enabling the collection and analysis of vast quantities of biological information, have transformed how research on complex diseases is conducted and how risk is understood. In this paper, we have examined the routine scientific procedures through which “genes” and “environments” are understood as distinct, interacting, and differently valued entities. These everyday practices, and the interactions of researchers from different disciplines, shape potential applications of GEIs. We have described three dimensions of GEI researchers' ethics of translational science—or how scientific knowledge can and should be used to improve human health: the scope and limits of interdisciplinary research teams; norms and practices constituting “good science;” and understandings of science's social responsibility.

Empirical studies of interdisciplinary efforts have mostly investigated cases where new interdisciplinary methods are introduced into existing research endeavors with their often powerful organizational interests (e.g., Albert et al. 2017) or are being imagined anew (e.g., Downey et al. 2017). Our case seems to be something of a hybrid: while gene-environment interaction research is touted as a different model and approach for studies of disease, many such collaborations are launched by genetic researchers seeking to incorporate environmental determinants in their studies, or researchers who typically study environmental and behavioral determinants seeking to incorporate genetics. Thus, as we found, what began as full-faith efforts to treat both sides of the interaction on equal terms often came with the disciplinary trappings of one or the other.

Although our findings do not suggest that researchers' ethics of translational science were directly linked to disciplinary affiliations or backgrounds, we did find that ostensibly interdisciplinary identities and alliances created epistemological and moral fault lines. These fault lines were also reinforced by implicit commitments to “data-driven” or “theory-driven” research—a distinction that continues to divide epidemiology into those who would separate science from “advocacy” and those who espouse that etiological research be guided by existing evidence about the (primarily social) domains responsible for most population-level disease variance (Shim and Thomson 2010).

However, GEI researchers' understandings of their social responsibility was more

flexible, or situated, than the data-driven/theory-driven distinction would suggest, mobilizing personalized prevention, biomedical innovation, public policy, and etiological knowledge as the potential contribution(s) of science. Nonetheless, enhancing self-knowledge and responsibility in individuals, and developing targeted drugs for genetically similar groups, emerged as the most imaginable “translations” of GEI research findings. The common thread linking these potential contributions was GEIs’ embodiment of an individualistic understanding of risk in which genetic differences, or “genotypes,” are tied to individually measured behaviors or exposures.

Therefore, while broad agreement about the relative value of the promised benefits of GEIs was lacking, post-genomic research on disease etiology has moved conceptions of disease and disease risk further into individual bodies, making tailored therapeutics and individual-level preventions strategies the more likely applications of GEI knowledge (rather than social, economic and public health policies) (Chaufan 2007). This emphasis on the individual is concerning to us for two reasons. First, it points to a mismatch between the promise and reality of interdisciplinary knowledge production, with molecular-level inquiry marginalizing other ways of knowing. Second is the vexing question of whether the study of gene-environment interactions can be fashioned as science that contributes to the public good, when “public” is envisioned as a citizenry rather than an aggregate of individuals, each responsible for their own well being. We urge more open engagement with questions about interdisciplinarity and the knowledge effects of post-genomic research in the life sciences. These questions should address who will benefit from emerging scientific knowledge, how they will benefit, and how assumptions about public benefit—and the very definition of “the public”—are reconfigured through the routine procedures, technologies, interactions, and products of science itself.

Author Biographies

Sara L. Ackerman is a medical anthropologist and assistant professor in the Department of Social and Behavioral Sciences at the University of California, San Francisco. Her research interests include the sociocultural and ethical implications of emerging biomedical technologies. She is currently studying the use of genome sequencing for patients with advanced cancer and the production of uncertainty in “precision medicine.”

Katherine Weatherford Darling is Assistant Director of Research and Academic Programs at the Science and Justice Research Center and Adjunct Assistant Professor of Sociology at the University of California, Santa Cruz. Dr. Weatherford Darling’s current book project traces how and why HIV became a chronic illness and remains an ongoing crisis in the US. Her collaborative research traces visions of health, risk, and care in California’s emerging “biohub.”

Sandra Soo-Jin Lee is a medical anthropologist and senior research scholar at the Stanford Center for Biomedical Ethics, and teaches in the Program in Science, Technology and Society at Stanford University. Her research interests are in the sociocultural and ethical dimensions of emerging genomic technologies and their translation into biomedical practice. Dr. Lee leads

studies on the governance and use of biospecimens and data in research and the ethics of identifying race, ethnicity and ancestry in studies of human genetic variation.

Robert A. Hiatt is professor and chair of the Department of Epidemiology and Biostatistics, University of California, San Francisco, and associate director for Population Science of the UCSF Helen Diller Family Comprehensive Cancer Center. His research interests include cancer epidemiology, health services and outcomes research, and the social determinants of cancer.

Janet K. Shim is professor of sociology in the Department of Social and Behavioral Sciences, University of California, San Francisco. Her current research focuses on analyzing the science of health disparities and the production of health care inequalities. She is the author of *Heart-Sick: The Politics of Risk, Inequality, and Heart Disease* (2014, NYU Press).

Acknowledgements

We extend our thanks to the researchers who generously gave their time to answer our questions. We are also grateful for the attention of the editors, Daniel Lee Kleinman and Katie Vann, and two anonymous reviewers. Their thoughtful suggestions greatly improved the manuscript. Research reported in this publication was supported by the National Human Genome Research Institute's Ethical, Legal, and Social Implications Research Program of the National Institutes of Health under award number R01HG005848. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

References

- Ackerman, Sara L, Katherine W Darling, Sandra S J Lee, Robert A Hiatt, and Janet K Shim. 2016. "Accounting for Complexity: Gene-Environment Interaction Research and the Moral Economy of Quantification." *Science, Technology & Human Values* 41(2): 194-218. doi:10.1177/0162243915595462.
- Albert, Mathieu, Elise Paradis, and Ayelet Kuper. 2017. Interdisciplinary fantasy: Social scientists and humanities scholars working in faculties of medicine. Pp. 84-103 in *Investigating Interdisciplinary Collaboration: Theory and Practice Across Disciplines*, edited by Scott Frickel, Mathieu Albert, and Barbara Prainsack. New Brunswick, NJ: Rutgers University Press.
- Akrich, M. 1992. "The De-Scriptio of Technical Objects." In *Shaping Technology/Building Society*, edited by W. Bijker and J. Law, 205-224. Cambridge, MA: MIT Press.
- Arribas-Ayllon, Michael, Andrew Bartlett, and Katie Featherstone. 2010. "Complexity and Accountability: The Witches' Brew of Psychiatric Genetics." *Social Studies of Science* 40 (4): 499-524. doi:10.1177/0306312710363511.
- Beaty, T. H., and M. J. Khoury. 2000. "Interface of Genetics and Epidemiology." *Epidemiologic Reviews* 22 (1): 120-25.
- Bourdieu, Pierre, and Randal Johnson. 1993. *The Field of Cultural Production*. New York, NY:

Columbia University Press.

- Bromley, Patricia, and Walter W Powell. 2012. "From Smoke and Mirrors to Walking the Talk: Decoupling in the Contemporary World." *The Academy of Management Annals* 6 (1): 483–530. doi:10.1080/19416520.2012.684462.
- Butler, Declan. 2008. "Translational Research: Crossing the Valley of Death." *Nature* 453 (7197): 840–42. doi:10.1038/453840a.
- Centellas, Kate M, Regina E Smardon, and Steven Fifield. 2013. "Calibrating Translational Cancer Research: Collaboration Without Consensus in Interdisciplinary Laboratory Meetings." *Science, Technology & Human Values* 39 (3): 311–335. doi:10.1177/0162243913505650.
- Charmaz, Kathy. 2006. *Constructing Grounded Theory: A Practical Guide Through Qualitative Analysis*. London: Sage Publications.
- Chaufan, Claudia. 2007. "How Much Can a Large Population Study on Genes, Environments, Their Interactions and Common Diseases Contribute to the Health of the American People?" *Social Science & Medicine* 65(8): 1730–41. doi:10.1016/j.socscimed.2007.05.049.
- Collins, Francis S, and Harold Varmus. 2015. "A New Initiative on Precision Medicine." *N Engl J Med* 372(9): 793–95. doi:10.1056/NEJMp1500523.
- Darling, Katherine Weatherford, Sara L Ackerman, Robert H Hiatt, Sandra Soo-Jin Lee, and Janet K Shim. 2016. "Enacting the Molecular Imperative: How Gene-Environment Interaction Research Links Bodies and Environments in the Post-Genomic Age." *Social Science & Medicine* 155: 51–60. doi:10.1016/j.socscimed.2016.03.007.
- Downey, Gregory J., Naoh Weeth Feinstein, Daniel Lee Kleinman, Sigrid Peterson, and Chisato Fukuda. 2017. The frictions of interdisciplinarity: The case of the Wisconsin Institutes for Discovery. Pp. 47-47-64 in *Investigating Interdisciplinary Collaboration: Theory and Practice Across Disciplines*, edited by Scott Frickel, Mathieu Albert, and Barbara Prainsack. New Brunswick: NJ: Rutgers University Press.
- Fortun, Kim, and Mike Fortun. 2005. "Scientific Imaginaries and Ethical Plateaus in Contemporary U.S. Toxicology." *American Anthropologist* 107(1): 43–54. doi:10.1525/aa.2005.107.1.043.
- Frickel, Scott, Mathieu Albert, and Barbara Prainsack. 2017. Introduction: Investigating Interdisciplinarity. Pp. 5-26 in *Investigating Interdisciplinary Collaboration: Theory and Practice Across Disciplines*, edited by Scott Frickel, Mathieu Albert, and Barbara Prainsack. New Brunswick: NJ: Rutgers University Press.
- Galea, Sandro, Matthew Riddle, and George A Kaplan. 2010. "Causal Thinking and Complex System Approaches in Epidemiology." *International Journal of Epidemiology* 39 (1). Oxford University Press: 97–106. doi:10.1093/ije/dyp296.
- Grace, Victoria. 2008. "Human Genome Epidemiology: Reviewing the Stakes." *International Journal of Health Services* 38(1): 143–59. doi:10.2190/HS.38.1.h.
- Hacking, Ian. 1986. "Making Up People." In *Reconstructing Individualism: Autonomy, Individuality, and the Self in Western Thought*, edited by T.C. Heller, D.E. Wellbery, and M. Sosna, 222–236. Stanford, CA: Stanford University Press.
- Hunter, David J. 2005. "Gene-Environment Interactions in Human Diseases." *Nature Reviews*

- Genetics* 6 (4). Nature Publishing Group: 287–98. doi:10.1038/nrg1578.
- Jacobs, Jerry A, and Scott Frickel. 2009. "Interdisciplinarity: a Critical Assessment." *Annual Review of Sociology* 35 (1): 43–65. doi:10.1146/annurev-soc-070308-115954.
- Karlin, Jennifer. 2013. "Loss and Gain in Translation: Financial Epidemiology on the South Side of Chicago." *Public Culture* 25 (3 71). Duke University Press: 523–50. doi:10.1215/08992363-2144634.
- Keller, Evelyn Fox. 2010. *The Mirage of a Space Between Nature and Nurture*. Duke University Press.
- Khoury, Muin J. 1996. "From Genes to Public Health: the Applications of Genetic Technology in Disease Prevention. Genetics Working Group." *American Journal of Public Health* 86(12): 1717–22.
- Khoury, Muin J, Robert Davis, Marta Gwinn, Mary Lou Lindegren, and Paula Yoon. 2005. "Do We Need Genomic Research for the Prevention of Common Diseases with Environmental Causes?" *American Journal of Epidemiology* 161(9): 799–805. doi:10.1093/aje/kwi113.
- Krieger, Nancy. 1994. "Epidemiology and the Web of Causation: Has Anyone Seen the Spider?" *Social Science & Medicine* 39(7): 887–903.
- Landecker, Hannah. 2013. "Postindustrial Metabolism: Fat Knowledge." *Public Culture* 25: 495–522. doi:10.1215/08992363-2144625.
- Latour, Bruno. 1987. *Science in Action*. Cambridge, MA: Harvard University Press.
- Lippman, A. 1991. "Prenatal Genetic Testing and Screening: Constructing Needs and Reinforcing Inequities." *American Journal of Law & Medicine* 17(1-2): 15–50.
- Lock, Margaret. 1993. *Encounters with Aging: Mythologies of Menopause in Japan and North America*. Berkeley, CA: University of California Press.
- Lock, Margaret. 2013. "The Epigenome and Nature/Nurture Reunification: a Challenge for Anthropology." *Medical Anthropology* 32(4): 291–308. doi:10.1080/01459740.2012.746973.
- Marcus, George. 1995. *Technoscientific Imaginaries: Conversations, Profiles, and Memoirs*. Chicago, IL: University of Chicago Press. doi:10.1016/0898-1221(95)90189-2.
- Mittra, J. 2013. "Repairing the Broken Middle of the Health Innovation Pathway: Exploring Diverse Practitioner Perspectives on the Emergence and Role of Translational Medicine." *Science and Technology Studies* 26(3): 103–23.
- National Research Council. 2011. "Toward Precision Medicine: Building a Knowledge Network for Biomedical Research and a New Taxonomy of Disease." Washington, D.C.: The National Academies Press.
<http://eutils.ncbi.nlm.nih.gov/entrez/eutils/elink.fcgi?dbfrom=pubmed&id=22536618&retmode=ref&cmd=prlinks>
- Nelson, Nicole C. 2013. "Modeling Mouse, Human, and Discipline: Epistemic Scaffolds in Animal Behavior Genetics." *Social Studies of Science* 43(1): 3–29. doi:10.1177/0306312712463815.
- Nelson, Nicole C. 2015. "A Knockout Experiment: Disciplinary Divides and Experimental Skill in Animal Behaviour Genetics." *Medical History* 59(3): 465–85. doi:10.1017/mdh.2015.30.
- Niewohner, Jörg. 2011. "Epigenetics: Embedded Bodies and the Molecularisation of Biography and Milieu." *BioSocieties* 6 (3): 279–98. doi:10.1057/biosoc.2011.4.
- Rajan, KS, and S Leonelli. 2013. Introduction: Biomedical trans-actions, postgenomics, and

- knowledge/value. *Public Culture* 25(3 71): 463-75. doi:10.1215/08992363-2144607.
- Shim, Janet K, and L Katherine Thomson. 2010. "The End of the Epidemiology Wars? Epidemiological 'Ethics' and the Challenge of Translation." *BioSocieties* 5(2): 159-79. doi:10.1057/biosoc.2010.6.
- Shim, Janet K, Katherine Weatherford Darling, Martine D Lappe, L Katherine Thomson, Sandra Soo-Jin Lee, Robert A Hiatt, and Sara L Ackerman. 2014. "Homogeneity and Heterogeneity as Situational Properties: Producing - and Moving Beyond? - Race in Post-Genomic Science." *Social Studies of Science* 44(4): 579-99. doi:10.1177/0306312714531522.
- Shostak, Sara. 2003. "Locating Gene-Environment Interaction: at the Intersections of Genetics and Public Health." *Social Science & Medicine* 56(11): 2327-42. doi:10.1016/S0277-9536(02)00231-9.
- Star, Susan Leigh, and James R Griesemer. 1989. "Institutional Ecology, Translations and Boundary Objects - Amateurs and Professionals in Berkeleys-Museum-of-Vertebrate-Zoology, 1907-39." *Social Studies of Science* 19(3): 387-420. doi:10.1177/030631289019003001.
- Star, Susan Leigh. 2010. "This Is Not a Boundary Object: Reflections on the Origin of a Concept." *Science, Technology & Human Values* 35(5): 601-17.
- Stevens, Hallam. 2013. *Life Out of Sequence*. Chicago, IL: University of Chicago Press.
- Sunder Rajan, Kaushik, and Sabina Leonelli. 2013. "Introduction: Biomedical Trans-Actions, Postgenomics, and Knowledge/Value." *Public Culture* 25: 463-75. doi:10.1215/08992363-2144607.
- Suryanarayanan, Sainath, and Daniel Lee Kleinman. 2016. *Vanishing Bees*. New Brunswick, NJ: Rutgers University Press.
- Thompson, Charis. 2013. *Good Science*. Cambridge, MA: MIT Press.
- van der Laan, Anna Laura, and Marianne Boenink. 2015. "Beyond Bench and Bedside: Disentangling the Concept of Translational Research." *Health Care Analysis* 23: 32-49. doi:10.1007/s10728-012-0236-x.
- Wallerstein, Nina, and Bonnie Duran. 2010. "Community-Based Participatory Research Contributions to Intervention Research: the Intersection of Science and Practice to Improve Health Equity." *American Journal of Public Health* 100 (S1): S40-S46. doi:10.2105/AJPH.2009.184036.
- Woolf, Steven H. 2008. "The Meaning of Translational Research and Why It Matters." *JAMA* 299(2): 211-13. doi:10.1001/jama.2007.26.
- Zerhouni, Elias. 2003. "Medicine. the NIH Roadmap." *Science* 302(5642): 63-72. doi:10.1126/science.1091867.
- Zerhouni, Elias A. 2005. "US Biomedical Research: Basic, Translational, and Clinical Sciences." *JAMA* 294 (11): 1352-58. doi:10.1001/jama.294.11.1352.