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Enacting the molecular imperative: How gene-environment interaction research links bodies and environments in the post-genomic age

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ABSTRACT

Despite a proclaimed shift from 'nature versus nurture' to 'genes and environment' paradigms within biomedical and genomic science, capturing the environment and identifying gene-environment interactions (GEIs) has remained a challenge. What does 'the environment' mean in the post-genomic age? In this paper, we present qualitative data from a study of 33 principal investigators funded by the U.S. National Institutes of Health to conduct etiological research on three complex diseases (cancer, cardiovascular disease and diabetes). We examine their research practices and perspectives on the environment through the concept of molecularization: the social processes and transformations through which phenomena (diseases, identities, pollution, food, racial/ethnic classifications) are re-defined in terms of their molecular components and described in the language of molecular biology. We show how GEI researchers' expansive conceptualizations of the environment ultimately yield to the imperative to molecularize and personalize the environment. They seek to 'go into the body' and re-work the boundaries between bodies and environments. In the process, they create epistemic hinges to facilitate a turn from efforts to understand social and environmental exposures outside the body, to quantifying their effects inside the body. GEI researchers respond to these emergent imperatives with a mixture of excitement, ambivalence and frustration. We reflect on how GEI researchers struggle to make meaning of molecules in their work, and how they grapple with molecularization as a methodological and rhetorical imperative as well as a process transforming biomedical research practices.

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1. Introduction

In the decade after the Human Genome Project (HGP), genome scientists, medical geneticists, and science policy leaders worked to find new ways to identify and credibly establish the value of genomic science for medicine and public health. They did so by articulating the fields of genomic medicine, public health genomics, and precision medicine. These fields constituted new post-genomic combinations of techniques, methods, and disciplines that promised to yield more precise and robust explanations for disease and a future of personalized treatment and prevention. Gene-environment interaction (GEI) research emerged as one central formation of post-genomic science. GEI research examines genetically defined susceptibility to a range of exposures and the exposure-mediated regulation of gene expression (Frickel, 2004; Shostak, 2013). A shift from a "nature versus nurture" dichotomy to a focus on complexity and gene-environment interactions led to a growing "interactionist consensus" within post-genomic science (Landecker and Panofsky, 2013). This consensus required integrating knowledge about 'the environment' with genomics, and promised to empower researchers to leverage genomic science for public health. However, despite consensus about the existence of gene-environment interactions and their contribution to health and disease, researchers have found it challenging to define, measure, and analyze the environment in genomic science.

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What does 'the environment' mean in the practice of genomic research? What do GEI researchers think about when they think about the environment? Drawing on data from longitudinal qualitative interviews and participant observation at scientific meetings, we answer these questions by showing how GEI researchers enact the environment in NIH-funded research on complex diseases. This article offers a close-to-the-ground look at what GEI scientists involved in research on cancer, diabetes, and heart disease think about when they think about the environment. We examine how they incorporate and 'enact' the environment in their scientific practices, and how their efforts to do so are complicated by approaches that both exemplify, resist, and aspire to molecularization.

We first situate GEI researchers' practices and experiences within the shifting landscape of post-genomic science in the U.S. Next, we discuss the concept of molecularization and introduce our concept of epistemic hinges. We then describe how GEI researchers in our study operationalize and measure the environment in everyday practice. Their efforts reflect contemporary imperatives to personalize or individualize risk predictions, public health messages, and biomedical treatments. Thus GEI scientists' conceptualizations of the environment ultimately yield to the demand that they "go into the body" to most credibly capture the environment. We describe three different ways in which their practices re-work the boundaries and connections between human bodies and their environments. First, GEI researchers see bodies as environments in and of themselves and measure the impacts of various bodily attributes and lifestyles in terms of their effects on individuals' internal physiologies. Second, they see bodies as permeable—living in environments such that physical and chemical exposures of the external environment can be measured as chemical perturbations in the internal environment of the body. And third, bodies are seen as the materialization of social experiences, such that social phenomena like discrimination, inequality, and deprivation are manifested at the molecular level.

In each of these three modes, we demonstrate how GEI researchers create "epistemic hinges" between, on the one hand, social and environmental phenomena, and on the other hand, techniques for measuring the environment 'in the body,' measures of the body, and arguments about the body. The concept of an epistemic hinge highlights how GEI scientists conscript different disciplinary perspectives, methods and techniques, and even their own embodied experiences, to hinge 'social' and 'environmental' processes to 'biological' and molecular processes 'in the body.' These epistemic hinges thereby allow GEI scientists to pivot from their understandings of complex environments *outside* the body to their assessments of what occurs *inside* the body. Conceptually and methodologically, these epistemic hinges shift the focus 'into the body.'

However, some GEI scientists also questioned post-genomic promises of personalization. They find the molecular knowledge produced through GEI research to be quite distant from the practical applications and public health impacts that institutions like NIH and even they themselves hope to achieve. Yet, to garner credibility and manage complexity, our participants heeded the imperative to molecularize and replicate current ways of tracing the environment at the molecular level.

GEI scientists' encounters with the imperative to molecularize raise questions about what Shostak and Moinester have called the "political economy of perception"—the scientific and political questions of which "environments can be seen and which remain invisible" in post-genomic science (2015, p. 223). Paying attention to the politics of perceptibility—which risks we can see and how—can offer analysts and practitioners a lens for mapping how and why some technologies and methods for perceiving, operationalizing and measuring the environment may be "more or less social in nature" (Shostak and Moinester, 2015, p. 223). Some strategies for perceiving environmental exposures "include social institutions and processes, while others render 'the environment' an internal, individual attribute" (Shostak and Moinester, 2015, p. 223).

We argue that the dynamics we observed ultimately narrow the possibilities for understanding causal complexity rather than open up their potential. Epistemic hinges that rely exclusively on molecular methods and explanations ultimately narrow the causal spectrum in ways that limit what we can know about complex diseases and the social inequalities at their root. In particular, these findings raise questions for scholars and public health practitioners interested in the "upstream" social conditions—the "causes of causes"—that shape health inequalities in the U.S (Krieger, 2011; Phelan et al., 2010). While GEI researchers seek to integrate knowledge of 'biological' and 'social' causes of complex disease, the links they make also produce a specific trajectory of "causal accountability" (Krieger, 2008), in which responsibility for health risks resides within individuals. We also contribute to critiques of personalized or precision medicine (Tutton and Jamie, 2013) and other transformations that continue to individualize responsibility for managing health risks and preventing illness. First, recognizing the imperative to molecularize may create an opening for discussing the cultural authority of molecular knowledge and its privileged position over other ways of producing knowledge about complex disease. Second, understanding how scientists themselves are raising questions about the meaning and implications of molecular arguments, measures, and markers of risk may enable new ways of engaging with post-genomic scientists through critique as well as collaboration.

2. Post-genomic environments and molecularization at work

Scientific debates about gene-environment interactions date back to the early days of genetics (Tabery, 2014). More recently, GEI emerged as an orienting rubric for large-scale population studies and an area of institutional investment by federal research funders in the U.S. In the landscape of biomedical research funded by the U.S. National Institutes of Health (NIH), a few key milestones herald GEI research as emblematic of post-genomic science. Recent efforts led by the U.S. NIH explicitly sought to transform how biomedical researchers work with the environment and to alter the way U.S. citizens viewed their environment in relation to their health (Manolio et al., 2006; National Human Genome Research Institute, 2014; Olden et al., 2011). NIH leaders and senior investigators heralded a shift from "nature vs. nurture" to "genes and environment" (Khoury et al., 2011). Genome scientists increasingly acknowledged environmental complexity and turned their attention to a wider range of complicated causal processes that produce chronic diseases, including cancer, cardiovascular disease, and diabetes.

They did so by investing in genomic and molecular techniques and promoting ideas about personalizing biomedicine and public health. In particular, the National Institute of Environmental Health Sciences and the National Human Genome Research Institute launched the jointly organized Genes, Environment, and Health Initiative in 2006 (National Human Genome Research Institute, 2014). This collaboration sought explicitly to create a new vision of the environment that was more precise and more personalized, and less dependent on traditional methods now perceived to be indirect and insufficient, such as epidemiological questionnaires (Weis et al., 2005). After the Human Genome Project, then, the environment was increasingly viewed as a collection of individual attributes that should be measured at the molecular level. These

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