FOREWORD Biology's Love Affair with the Genome

Postgenomics is the unavoidable consequence of an intense love affair between biomedical scientists and the human genome. The discovery of the double-helical structure of DNA in 1953 lit the flame. The breathtaking rapidity with which this discovery lead to the entrenchment of the central dogma (DNA → RNA → protein), the cracking of the genetic code, the emergence of genetic engineering technology, and the early understanding of Mendelian diseases created an expectation of exponential increases in our ability to measure and interpret DNA information. DNA satisfies the compulsions of many scientists: measurable, discrete, molecular (yet apparently integrative), deterministic, and evolvable. If a little DNA sequence was good, then a lot—the genome—would be great. With the prospect of greatness, reasonable people are prone to hyperbole: save money, develop cures, predict disease, learn about our ancestors, and bring justice to all. It can be hard to judge harshly someone in love.

But even the most intense love affairs simmer and require nurturing. The breakneck speed of the courtship slows to a more reasoned set of discussions, negotiations, and settings of expectation. Some love affairs do not survive these adjustments, but others transition to a lifelong shared adventure. Postgenomics commences with an inventory of the successes and disappointments of the genome; we lift our heads, look around, and figure out what the future holds.

I do genomics, and I plan to do postgenomics. But this volume compels me to examine what I do and why I do it. The chapter authors combine a deep understanding of the history and technical content of modern genomic science with largely contrarian (to many genomicists, at least) interpretations of the significance and impact of the work. They expose significant biases in the way we formulate, justify, communicate, and defend work in genomics. Surprisingly, however, their analyses do not lead to despair, but to opportunity.

The chapters in this book highlight unrecognized and unexamined assumptions and suggest novel analyses and experiments. Evelyn Fox Keller refers to the "linguistic habits of geneticists"—habits that I have tried to master and also tried to avoid being fooled by. Keller reminds us that the genome's program is dynamic and reactive. John Dupré emphasizes that individuals are in fact combinations of multiple genomes. It is sometimes easy to overlook inconvenient facts that violate our abstractions, but as Mike Fortun celebrates in his marvelous meditation on "Toll!," an openness to the genome's surprises can gratify and motivate.

Adrian Mackenzie shows how as the genome's "shape" moves from linear to high dimensional, it provides more features than anyone can possibly interpret. In light of this, we may need to move to alternative representations of physiology that are more integrative. But, as Hallam Stevens makes clear in his analysis of network metaphors in postgenomics, the distinction between reductionist and holist is more complex than we thought. Epigenetics, for example, is thought to provide a nonreductionist mechanism for studying the interaction between gene regulation and the environment. As Sarah Richardson argues in her examination of maternal-fetal epigenetics, however, epigenetics claims often mirror classic genetic reductionist explanations in their focus on the mechanism of regulation of gene expression. Similarly, Sara Shostak and Margot Moinester point out that looking at environmental measures at multiple levels (molecular, cellular, tissue, organism) involves forms of reductionism that inevitably obscure some dimensions of the environment, including high-level environmental abstractions such as a neighborhood.

Intriguing questions about the reward and funding structure of the sciences accompany the postgenomic moment. One example is the increasingly dispersed nature of scientific knowledge production. As we integrate multiple databases, the legitimate coauthorship claims of data curators suffer from their distance (in both place and time) from the other authors. Rachel A. Ankeny and Sabina Leonelli explore how we can give credit to those who have shared and annotated data. Funders such as the National

Institutes of Health greatly benefit genome research, but funding focused principally on genomics can lead to distortions. Aaron Panofsky examines how certain areas of behavioral genetics have been "lavishly rewarded despite consistent failure to deliver," while Catherine Bliss looks at how genomics research in the field of race- and ethnicity-based health disparities may be crowding out public health and social science approaches.

Postgenomics: Perspectives on Biology after the Genome delivers important scientific and social messages. One scientific message is that the genome sequencing projects were neither unmitigated successes nor failures, but rather the start of a newly enabled era in which determining the sequence of four DNA bases is easy, but understanding its role in biological systems is incredibly challenging. One social message is that postgenomics should not be simply the playground of former genomicists now turned postgenomicists. Instead, there is a credible argument for a "reset" and evaluation of what the most promising and fruitful areas of investigation are likely to be. We should resist the temptation to merely declare the "obvious" next steps: epigenetics, environmental characterization, and large-scale population sequencing. Rather, we should pause and consider the range of societal and scientific responses to the past fifteen years of work and choose questions and strategies that allow us to marry discovery and its beneficial applications.

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January 2014