What Genes Can't Do

by Lenny Moss
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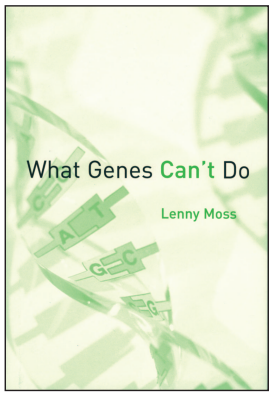
Understanding the principles of inheritance is, arguably, the greatest achievement in biology. Central to this is the concept of a gene, a replicating unit subject to mutation and Darwinian selection. This paradigm has transformed medicine and society: we now know the cause of more than 1,000 single-gene disorders; we have identified DNA alterations associated with cancers; we are making great strides in understanding common diseases, such as heart disease, diabetes and schizophrenia; and we have the power to 'engineer' plants and animals.

In *What Genes Can't Do*, Lenny Moss, a cell biologist turned philosopher, tells us that we have it wrong.

Moss says that about 100 years ago, there was an unfortunate "phenotypic turn" that led to an unbalanced, gene-centered orientation of biology. The notion that genes determine traits and constitute blueprints for development is "scientifically unwarranted and socially destructive," he says. His book attempts to examine the historical basis of the gene-centered view and to illustrate with selected examples how biologists have been led, by a "rhetorical glue," down a misguided path.

Moss organizes his arguments into five chapters. The first attempts to retrace the historical origins of the gene's ascendancy. His analysis reveals a "phylogenetic turn," sparked by Darwin and Mendel, that marked "the movement away from ontogeny toward phylogeny" as an explanation of biologic form, resulting in a new "genetic preformationism". The second chapter continues the historic perspective, focusing on Schrödinger's attempt to explain life, using quantum-mechanical arguments, that promoted a hereditary code-script. Moss is sympathetic to postmodernist critics of science such as Richard Doyle, and he argues that the gene-centered orientation of biology is based on the metaphors we have chosen to aid in our understanding of nature (such as Mendel's exemplars).

In chapter 3, Moss cites a number of experimental and theoretical studies backing his assertion that "the claims for the primacy of a hereditary code-script must be rejected." He emphasizes the importance of membranous compartments, protein complexes and DNA modification (he calls these "parallel epigenetic systems") in explaining the nature and continuity of organisms. To support the idea that heritable information does not reside entirely in DNA, he cites the classic example of epigenetic inheritance in *Paramecium*. The chapter does not, however, discuss in any detail the many thousands of experiments, beginning with the classic study of Avery, McCarty and MacLeod in 1944, that have linked genetic information with DNA.



Chapter 4 begins with a history of oncology, from the Greeks to the somatic mutation hypothesis of Bovari in 1914 to the identification of oncogenes and tumor suppressor genes in the 1980s. This is followed by a vociferous, multi-pronged attack on the importance of genes in cancer. Moss dismisses the oncogenes discovered by J. Michael Bishop, Harold Varmus and others 25 years ago as largely irrelevant to human cancer, citing evidence that cancer is primarily a disease of the extracellular organization. He argues (unconvincingly) that the mutations associated with cancers may be the result, rather than the primary cause, of cancer. He concludes that the evidence indicates the somatic mutation hypothesis has failed and that "the question of the driving force of carcinogenesis either cannot be answered at the level of genetic analysis or perhaps is just not the right question at all."

How is it that the current consensus has strayed so far from the truth? Moss suggests that the genomic model of cancer has taken center stage not only because of the "phylogenetic turn" but also because of the influence of the marketplace on the biomedical research agenda.

The last chapter focuses on data from the Human Genome Project, citing the unexpectedly low number of genes in the human genome and new evidence for the importance of chromatin organization and gene splicing in higher organisms. Moss claims that these data cap the "decay and demise of the gene as the bedrock of biological explanation."

Some of these unorthodox conclusions result from Moss' confusion about aspects of genetics and biology. He says only some, perhaps "comparatively superficial," traits are decomposable in their inheritance (namely, mendelian traits such as cystic fibrosis). These, he argues, are primarily loss-of-function aberrations that shed little light on biologic mechanisms. Moss seems to be unaware of the concept, about 100 years old and supported by considerable evidence, that non-mendelian traits result from the aggregation of multiple genetic factors mediated by environment.

The book has many other errors, some minor ("proteasome" is confused with "proteome"), others important (DNA methylation is considered a fundamental developmental mechanism for *all* multicellular organisms). The chapter on cancer is particularly flawed, consisting in large part of outdated or marginal studies, or results taken out of context. Experiments inconsistent with Moss' arguments—such as studies of transgenic mice in which specific cancers could be repeatedly induced or regressed by turning an oncogene on or off—are not mentioned.

I suspect that Moss' arguments are tainted by his apparent distaste for the deterministic nature of a gene-centered view of biology. In the introduction, he says his purpose in writing this book was "to contribute to freeing the 'naturalizing' enterprise from the unnecessary burdens of preformationistic baggage and thereby better to allow for the re-embedding of the self-understanding of human language and knowledge in contingent social and developmental processes." I have no reason to believe that Moss is insincere in this treatise, but I can't help being reminded by this book of some biologists of the 1970s, such as some members of 'Science for the People,' who bent science to accommodate their political and ideological beliefs.

This is one of those books that may have some value in saying to us that maybe, just maybe, we need to rethink some of our views. Unfortunately, it is a rambling, pretentious synthesis based on a poor understanding of the biologic research literature.