

Gene expression and the concept of the phenotype

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Abstract

While the definition of the ‘genotype’ has undergone dramatic changes in the transition from classical to molecular genetics, the definition of the ‘phenotype’ has remained for a long time within the classical framework. In addition, while the notion of the genotype has received significant attention from philosophers of biology, the notion of the phenotype has not. Recent developments in the technology of measuring gene-expression levels have made it possible to conceive of phenotypic traits in terms of levels of gene expression. We demonstrate that not only has this become possible but it has also become an actual practice. This suggests a significant change in our conception of the phenotype: as in the case of the ‘genotype’, phenotypes can now be conceived in quantitative and measurable terms on a comprehensive molecular level. We discuss in what sense gene expression profiles can be regarded as phenotypic traits and whether these traits are better described as a novel concept of phenotype or as an extension of the classical concept. We argue for an extension of the classical concept and call for an examination of the type of extension involved.

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1. Introduction

‘To give a new concept’ can only mean to introduce a new employment of the concept, a new practice. (Wittgenstein, 1978, p. 432)

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Our central aim in this article is to present a current extension in the way the concept of the phenotype is being applied, namely its becoming more comprehensively quantitative and grounded in complex molecular level properties. This development is driven by the increasing power of molecular measurement technologies. We observe that practitioners in biology and medical genetics currently extend the classical notion of the phenotype to include measurable levels of gene expression. To better understand the current developments in the concept of the phenotype, we note the changes that took place in the concept of the genotype within the context of the transition from Mendelian to molecular genetics. This transition has brought about a radical transformation in our conception of genes: from functional and informational unit to structural molecular one. While heredity units were already presupposed in Mendel (1865) and an explicit distinction between soma and germ cells was made by Weismann (1889 [1885]), genotypes were first defined by Johanssen (1909) as abstract accounting or calculating units. Such units were postulated by Morgan (1917) and his colleagues to be ‘physical genes lined up on the chromosomes in the fruit fly’s nucleus’ (Harman, 2006), while others, especially in Germany, considered them to be holistic and/or vitalistic entities located both within and outside the nucleolus (Harwood, 1993, pp. 49–52; Harrington, 1996, pp. 49–51).

Abstract or physical, mechanical or vitalistic, however divergent conceptions of genes were employed in the classical period of genetics, (that is, until the early nineteen fifties), genes were defined according to the phenotypic trait they were responsible for. In the molecular period, the genome was identified with the DNA molecule and genes came to be defined as segments on the DNA molecule. The genome thus came to be seen as a molecular entity defined by its sequence of nucleotide base pairs.¹ Yet, in practice, the definition of gene as a segment on the DNA molecule is not purely structural but also functional. A ‘gene’ is typically defined as the segment coding information for the production of a polypeptide chain of a functional protein (see Stotz & Griffiths, 2004). In fact, our current understanding of cellular regulatory mechanisms implies that an accurate definition of genes requires an accommodation of a plurality of DNA segments as well as disjunctive functions. For example, Berg & Singer (1992) define a gene as ‘a combination of DNA segments that together constitute an expressible unit—that is, a unit whose expression leads to the formation of either a functional RNA or a polypeptide’ (*ibid.*, p. 135).

While the concept of the gene is not defined in current molecular genetics in purely structural and chemical terms (that is, as entirely independent of its function and activity), and even if this concept is quite ambiguous (Moss, 2002), it is beyond doubt that the molecular conception of the genotype has proven to be immensely fruitful. Moreover, Falk (1986) has convincingly argued that the functional/structural ambiguity has itself been very fruitful and influential. The molecular approach, with its definition of the genome as the complete sequence of DNA and genes as segments on the DNA sequence, is likewise the current definition in the minds of working scientists (see Stotz

¹ As Lewontin nicely points out ‘a complete description of the DNA sequence is identical with a complete specification of the genotype. . . the developments of techniques of observing the phenotype have been revolutionary for genetic analysis, precisely because they solve the problem of inferring genotype from phenotype by eliminating development. All genotypes, irrespective of their influence on development, can be unambiguously discriminated at the molecular level [of the phenotype]’ (Lewontin, 1992, p. 143).

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