

Molecular Genetics - An Overview

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Editorial

The term molecular genetics is now redundant because contemporary genetics is thoroughly molecular. Genetics is not made up of two sciences, one molecular and one non-molecular. Nevertheless, practicing biologists still use the term. When they do, they are typically referring to a set of laboratory techniques aimed at identifying and/or manipulating DNA segments involved in the synthesis of important biological molecules. Scientists often talk and write about the application of these techniques across a broad swath of biomedical sciences. For them, molecular genetics is an investigative approach that involves the application of laboratory methods and research strategies. This approach presupposes basic knowledge about the expression and regulation of genes at the molecular level [1,2].

Philosophical interest in molecular genetics, however, has centered, not on investigative approaches or laboratory methods, but on theory. Early philosophical research concerned the basic theory about the make-up, expression, and regulation of genes. Most attention centered on the issue of theoretical reductionism. The motivating question concerned whether classical genetics, the science of T. H. Morgan and his collaborators, was being reduced to molecular genetics. With the rise of developmental genetics and developmental biology, philosophical attention has subsequently shifted towards critiquing a fundamental theory associated with contemporary genetics. The fundamental theory concerns not just the make-up, expression, and regulation of genes, but also the overall role of genes within the organism. According to the fundamental theory, genes and DNA direct all life processes by providing the information that specifies the development and functioning of organisms [3,4].

Techniques

Forward genetics: Forward genetics is a molecular genetics technique used to identify genes or genetic mutations that produce a certain phenotype. In a genetic screen, random mutations are generated with mutagens (chemicals or radiation) or transposons and individuals are screened for the specific phenotype. Often, a secondary assay in the form of a selection may follow mutagenesis where the desired phenotype is difficult to observe, for example in bacteria or cell cultures. The cells may be transformed using a gene for antibiotic resistance or a fluorescent reporter so that the mutants with the desired phenotype are selected from the non-mutants.

Mutants exhibiting the phenotype of interest are isolated and a complementation test may be performed to determine if the phenotype results from more than one gene. The mutant genes are then characterized as dominant (resulting in a gain of function), recessive (showing a loss of function), or epistatic (the mutant gene masks the phenotype of another gene). Finally, the location and specific nature of the mutation is mapped

via sequencing. Forward genetics is an unbiased approach and often leads to many unanticipated discoveries, but may be costly and time consuming. Model organisms like the nematode worm *Caenorhabditis elegans*, the fruit fly *Drosophila melanogaster*, and the zebrafish *Danio rerio* have been used successfully to study phenotypes resulting from gene mutations [5].

Reverse genetics: Reverse genetics is the term for molecular genetics techniques used to determine the phenotype resulting from an intentional mutation in a gene of interest. The phenotype is used to deduce the function of the un-mutated version of the gene. Mutations may be random or intentional changes to the gene of interest. Mutations may be a mis-sense mutation caused by nucleotide substitution, a nucleotide addition or deletion to induce a frameshift mutation, or a complete addition/deletion of a gene or gene segment. The deletion of a particular gene creates a gene knockout where the gene is not expressed and a loss of function results (e.g. knockout mice). Mis-sense mutations may cause total loss of function or result in partial loss of function, known as a knockdown. Knockdown may also be achieved by RNA interference (RNAi). Alternatively, genes may be substituted into an organism's genome (also known as a transgene) to create a gene knock-in and result in a gain of function by the host. Although these techniques have some inherent bias regarding the decision to link a phenotype to a particular function, it is much faster in terms of production than forward genetics because the gene of interest is already known.

Conflict of Interest

None.

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