1.1: Introduction to Genes

Introduction

Species share many traits in common from generation to generation. The bluebird nestlings in the box in my yard will look much like their parents when they are full-grown. The tomato plants that we set out will produce fruits that look, and hopefully taste, like those of their parents. Observable features of organisms, like color, size, and shape, comprise their phenotype. Adult male bluebirds share the phenotype of blue wings and a red breast.

A phenotype can be determined by inherited factors, by the environment, and often by both. For example, you are similar to your parents in many aspects of your appearance, your intelligence, and your susceptibility to some diseases, but you are not identical to them in all aspects of these traits. These three traits are clearly the product of both inherited and environmental factors. Considering appearance, I have crooked lower teeth and thinning gray hair, just like my father, but unlike me, neither of my parents has a scar on their knee from a childhood cut. The hair phenotype is inherited, whereas scars are from environmental influences. Quantitative studies show that intellectual capacity is about equally influenced by genetic and environmental factors. Susceptibility to diabetes is partially inherited, but a viral infection may trigger the autoimmune response at its core.

The genetic determinants of the inherited component of a phenotype are called genes. The set of genes that make up an organism is its genotype. In practice, we will consider only a small subset of the genes in an organism, which comprise a partial genotype. Likewise, an organism’s phenotype is all the traits it possesses, but we will only consider partial phenotypes, such as the blue wings of a bluebird or the color of the eyes of a fly.

This chapter will explore some of the basic characteristics of genes, and the experimental evidence for them. Some of the major points include the following.
• Genes are the units of heredity
• They are arranged in a linear fashion along chromosomes.
• Recombination can occur both between and within genes.
• Mutations in different genes required for a phenotype will complement each other in a diploid. This is the basis for genetic dissection of a pathway.
• A gene is composed of a series of mutable sites that are also sites for recombination (now recognized as nucleotides).
• One gene encodes one polypeptide.
• The gene and the polypeptide are colinear.
• Single amino acids are specified by a set of three adjacent mutable sites; this set is called a codon.

In considering experimental evidence for these points, some general genetic techniques as well as genetic techniques for bacteria and phage will be discussed. The first experiments that eventually hypothesized the existence of genes were conducted by Gregor Mendel (see Mendel's Laws).

Genes are mutable

We know that genes are mutable because they appear in different forms, called alleles. An allele that encodes a normal, functional product (found in nature or a standard laboratory stock) is called the wild type allele. Other alleles are altered in a way such that the encoded product differs in function from the wild type. This type of allele is mutated or mutant (adjective). The alteration in the gene is a mutation, and an organism showing the altered phenotype is a mutant (noun). Many mutated alleles encode a product that is nonfunctional or less functional than is the wild type, or normal, product; it is easier to break something than to improve it. A loss-of-function allele usually shows a recessive phenotype, which means that when it is present in the same cell as an allele that produces a different phenotype, the phenotype of the other allele is obtained. If no functional product is made, this loss-of-function allele is a null mutation; this can result from no expression or expression of a completely nonfunctional product. Other loss-of-function mutants make less than the normal amount of product, these are called hypomorphs. Another class of mutated allele encodes a product that provides an altered or new function. These gain-of-function mutations usually show a dominant phenotype; e.g. when the gain-of-function allele is in the same cell as a loss-of-function allele, the phenotype of the gain-of-function allele is observed. Another class of gain-of-function mutants makes more than the normal amount of product; these are called hypermorphs.

Within a population, the number of alleles at a given locus can vary considerably. Mutant alleles that cause a loss or detrimental change in the function of a gene are selected against, and they are rare in a wild population. In the laboratory, one can utilize growth conditions that select for certain mutants or that maintain mutants, so mutant organisms that would be rare or non-existent in the wild are encountered quite frequently in the laboratory. In many cases, however, alternate forms of genes, i.e. different alleles, have no particular effect on gene function. These variants can be found quite frequently in a population. One common examples of such genetically determined, apparently neutral variation is the ability of some persons to "roll" their tongue. In general, these common alleles are roughly equivalent in function to the wild type allele. Thus they are not providing a strong selective advantage or disadvantage. All the common alleles can be considered the wild type allele. Variant alleles that occur in greater than 5% of population are called polymorphisms. The term variant includes all alternative forms of a gene, whether they have an effect on function or not. The term mutant allele sometimes implies an altered function for the gene.
As will become clearer when we study the fine structure of genes, it is possible to change the structure of the gene (the nucleotide sequence in DNA) without changing the structure of the encoded polypeptide (the amino acid sequence). These **silent substitutions** also generate different alleles, but they can only be detected by examining the structure of the gene; the phenotypes of alleles that differ by silent substitutions are usually identical.

Another possibility is that a mutant allele not only causes a loss of function of the encoded protein, but this altered protein interferes with the activity of other proteins. One way this can happen is by the polypeptide product forming a complex with other polypeptides (e.g. in a heteromultimeric enzyme complex). Sometimes the mutant polypeptide will prevent formation of an active complex with the partner, even in the presence of wild-type polypeptide, thereby leading to a **dominant negative** phenotype. These are of considerable utility now in designing mutant genes and proteins to try to disrupt some cellular function. They are most commonly made in a vector that will drive a high level of expression of the mutant gene, and usually **over-expression** is needed to generate the dominant negative phenotype.