**Introduction**

The hereditary nature of every living organism is defined by its genome, which consists of a long sequence of nucleic acid that provides the *information* needed to construct the organism. We use the term "information" because the genome does not itself perform any active role in building the organism; rather it is the sequence of the individual subunits (bases) of the nucleic acid that determines hereditary

features. By a complex series of interactions, this sequence is used to produce all the proteins of the organism in the appropriate time and place. The proteins either form part of the structure of the organism, or have the capacity to build the structures or to perform the metabolic reactions necessary for life.

The basic behavior of the gene was defined by Mendel more than a century ago. Summarized in his two laws, the gene was recognized as a "particulate factor" that passes unchanged from parent to progeny.

A gene may exist in alternative forms. These forms are called alleles. In diploid organisms, which have two sets of chromosomes, one copy of each chromosome is inherited from each parent. This is the same behavior that is displayed by genes. One of the two copies of each gene is the paternal allele (inherited from the father), the other is the maternal allele (inherited from the mother). The equivalence led to the discovery that chromosomes in fact carry the genes.

Each chromosome consists of a linear array of genes. Each gene resides at a particular location on the chromosome. This is more formally called a genetic locus. We can then define the alleles of this gene as the different forms that are found at this locus.

The key to understanding the organization of genes into chromosomes was the discovery of genetic linkage. This describes the observation that alleles on the same chromosome tend to remain together in the progeny instead of assorting independently as predicted by Mendel's laws. Once the unit of recombination (reassortment) was introduced as the measure of linkage, the construction of genetic maps became possible.

Understanding the process by which a gene is expressed allows us to make a more rigorous definition of its nature. Figure 1.2 shows the basic theme of this book. A gene is a sequence of DNA that produces another nucleic acid, RNA. The DNA has two strands of nucleic acid, and the RNA has only one strand. The sequence of the RNA is determined by the sequence of the DNA (in fact, it is identical to one of the DNA strands). In many, but not in all cases, the RNA is in turn used to direct

production of a protein. Thus a gene is a sequence of DNA that codes for an RNA; in protein-coding genes, the RNA in turn codes for a protein.



**DNA is the genetic material of bacteria**

The idea that genetic material is nucleic acid had its roots in the discovery of transformation in 1928. The bacterium *Pneumococcus* kills mice by causing pneumonia. The virulence of the bacterium is determined by its *capsular polysaccharide.* This is a component of the surface that allows the bacterium to escape destruction by the host. Several types (I, II, III) of *Pneumococcus* have different capsular polysaccharides. They have a smooth (S) appearance.

Each of the smooth *Pneumococcal* types can give rise to variants that fail to produce the capsular polysaccharide. These bacteria have a *rough* (R) surface (consisting of the material that was beneath the capsular polysaccharide). They are avirulent.

They do not kill the mice, because the absence of the polysaccharide allows the animal to destroy the bacteria. When smooth bacteria are killed by heat treatment, they lose their ability to harm the animal. But inactive heat-killed S bacteria and the ineffectual variant R bacteria together have a quite different effect from either bacterium by itself. **Figure** shows that when they are jointly injected into an animal, the mouse dies as the result of a *Pneumococcal* infection. Virulent S bacteria can be recovered from the mouse postmortem. In this experiment, the dead S bacteria were of type III. The live R bacteria had been derived from type II. The virulent bacteria recovered from the mixed infection had the smooth coat of type III. So some property of the dead type III S bacteria can *transform* the live R bacteria so that they make the type III capsular polysaccharide, and as a result become virulent.

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**DNA is the genetic material of viruses**

Having shown that DNA is the genetic material of bacteria, the next step was to demonstrate that DNA provides the genetic material in a quite different system. Phage T2 is a virus that infects the bacterium E. coli. When phage particles are added to bacteria, they adsorb to the outside surface, some material enters the bacterium, and then -20 minutes later each bacterium bursts open (lyses) to release a large number of progeny phage. Figure 1.5 illustrates the results of an experiment in 1952 in which bacteria were infected with T2 phages that had been radioactively labeled either in their DNA component (with 32P) or in their protein component

(with 35S). The infected bacteria were agitated in a blender, and two fractions were separated by centrifugation. One contained the empty phage coats that were released from the surface of the bacteria.

The other fraction consisted of the infected bacteria themselves. Most of the 32P label was present in the infected bacteria. The progeny phage particles produced by the infection contained ~30% ofthe original 32P label. The progeny received very little less than 1%—of the protein contained in the original phage population. The phage coats consist of protein and therefore carried the 35S radioactive label. This experiment therefore showed directly that only the DNA of the parent phages enters the bacteria and then becomes part of the progeny phages, exactly the pattern of inheritance expected of genetic material.



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**DNA is the genetic material of animal cells**

When DNA is added to populations of single eukaryotic cells growing in culture, the nucleic acid enters the cells, and in some of them results in the production of new proteins. When a purified DNA is used, its incorporation leads to the production of a particular protein.

Figure 1.6 depicts one of the standard systems. Although for historical reasons these experiments are described as “**Transfection”** when performed with eukaryotic cells, they are a direct counterpart to bacterial transformation. The DNA that is introduced into the recipient cell becomes part of its genetic material, and is inherited in the same way as any other part. Its expression confers a new trait

upon the cells (synthesis of thymidine kinase in the example of the figure).

At first, these experiments were successful only with individual cells adapted to grow in a culture medium. Since then, however, DNA has been introduced into mouse eggs by microinjection; and it may become a stable part of the genetic material of the mouse .

Such experiments show directly not only that DNA is the genetic material in eukaryotes, but also that it can be transferred between different species and yet remain functional.

The genetic material of all known organisms and many viruses is DNA. However, some viruses use an alternative type of nucleic acid ribonucleic acid (RNA), as the genetic material. The general principle of the nature of the genetic material, then, is that it is always nucleic acid; in fact, it is DNA except in the RNA viruses.

