Benjamin Lewin

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# Genes VII

**Benjamin Lewin** 



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#### **Preface**

This edition of GENES marks the most significant reorganization for several editions. It is time to acknowledge that the power of direct analysis of the genome is making a significant difference to our approach. This is now recognized in the first part of GENES, which starts with the concept of the gene as a segment of DNA coding for protein and then proceeds directly to the characterization of the genome in terms of its content of genes.

The rapidity of our advance in analyzing the genome has led to some confusion about means and ends. A genome is no more than a sum of the genes it contains, although the number and complexity of these genes gives us important insights into the nature of their connection into regulatory networks. The focus of this book, as its name suggests, therefore remains firmly on the gene.

The thesis of GENES is that only by understanding the structure and function of the gene itself will we be able in turn to understand the operation of the genome as a whole. Although the emphasis has shifted to the characterization of eukaryotic genes, and therefore to their analysis by the direct techniques of molecular biology rather than the subtlety of genetics, the classical approach remains intellectually penetrating. It remains an aim of this book to integrate both approaches in the context of a unified approach to prokaryotes and eukaryotes.

We consider the gene from all aspects: the basic forms that it takes, the numbers and relationships among genes in a genome, their packaging into chromosomes, the process of gene expression from transcription through translation, the reproduction and safeguarding of the structure of the gene, and finally some aspects of the overall circuitry through which genotype determines phenotype.

Almost two decades after the first edition of GENES, this latest edition is a celebration of the remarkable progress during that time, and, I hope, an indication of the future to come.

B. L. Cambridge, Massachussetts January 2000

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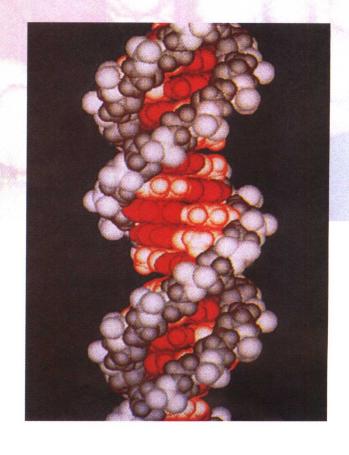
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## Genes




#### **Genes are DNA**

The basic nature 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 (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. The equivalence led to the discovery that chromosomes in fact carry the genes.

The next step was the demonstration that each chromosome consists of a linear array of genes. Mendel's laws predict that genes carried on different chromosomes will segregate independently. However, genes that are on the same chromosome show linked inheritance. The basic observation is that genes on different chromosomes recombine at random from one generation to the next, whereas genes that are linked show a reduction in recombination, that is, they tend to stay together.

Genetic analysis allows the construction of a linkage map that connects all the genes carried by one chromosome. The genetic map of a linkage group corresponds to the physical existence of the chromosome.

On the genetic maps of higher organisms established during the first half of this century, the genes are arranged like beads on a string. They occur in a fixed order, and genetic recombination involves transfer of corresponding portions of the string between homologous chromosomes. The gene is to all intents and pur-

poses a mysterious object (the bead), whose relationship to its surroundings (the string) is unclear.

The resolution of the recombination map of a higher eukaryote is restricted by the small number of progeny that can be obtained from each mating.

Figure 1.1 A brief history of genetics.

1865	Genes are particulate factors
1903	Chromosomes are hereditary units
1910	Genes lie on chromosomes
1913	Chromosomes contain linear arrays of genes
1927	Mutations are physical changes in genes
1931	Recombination is caused by crossing over
1944	DNA is the genetic material
1945	A gene codes for a protein
1953	DNA is a double helix
1958	DNA replicates semiconservatively
1961	Genetic code is triplet
1977	DNA can be sequenced
1997	Genomes can be sequenced