UNDERSTANDING GENETICS

Third Edition

NORMAN V. ROTHWELL

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PREFACE

This third edition of *Understanding Genetics*, like the first and second, presupposes only a passing familiarity with basic genetic principles and little contact with molecular biology. During twenty-six years of teaching, I have tried several approaches in my undergraduate genetics course, and I remain convinced that the best is the one which assumes no more than a nodding acquaintance with the language of genetics. Advanced biology majors often admit a complete lack of understanding of various elementary concepts such as linkage and crossing over. Many critical topics can be slighted as the student is plunged into the details of molecular biology and sophisticated genetic research. Even graduate students who are familiar with details of the chemistry of genetics sometimes have no inkling of the biological significance of such information. It seems to me that a clear, concise approach encompassing the details of classical genetics best enables students to appreciate the excitement of today's research. Moreover, the strides in human genetics that present hope and challenge to today's society demand a firm grasp of basic genetic principles along with the elements of probability and statistics.

Therefore, the sequence of topics in this book starts from the "beginning" and leads to some of the latest advances reported in the literature at the time of writing. In the development of basic topics, elementary or historical points are associated wherever possible with modern ideas and current problems. Certain material included in the second edition has been eliminated in order to direct attention to topics such as the processing of eukaryotic mRNA, transposons, DNA sequencing, and other subjects which reflect significant advances in our understanding of genetic phenomena. Certain chapters, which

deal with matters such as genetic manipulation and nonchromosomal genetic information have been rewritten and extended to include discussions of findings and techniques which are giving us deeper insights into the genetic constitution of all living forms and viruses. The coverage of population genetics has been expanded from one to two chapters.

A solid foundation in the basics of molecular genetics is essential for any biology student today. Most of the Chapters from 11 through 20 now contain additional material relating to this ever-changing field, and I believe they provide sufficient depth to serve as a point of departure for reading the research literature. The questions at the end of each chapter, many of them new to this edition, are intended as a study guide that will show students how well they have grasped the contents.

Understanding Genetics can be used in a one-semester course or as a guide for two semesters, depending on the specific goals and the preparation of the students. The following chapters would appear to be essential to a one-semester presentation: 1–8, selected parts of Chapter 10, and Chapters 11 through 15. If Chapters 1 through 7 are to be assigned solely for review, the course could begin with Chapter 8. I recommend the inclusion of Chapter 8 regardless of the background of the students, since the fundamentals of linkage and crossing over are critical to genetic analysis.

Essential to the understanding of scientific concepts in any textbook is the illustrative material. I was very fortunate in this respect to work along with Mrs. Diane Abeloff, a talented artist whose efforts have formed an important part of the completed book. Deep appreciation is due to Dr. Robert F. Lewis, a friend and colleague of many years, for his encouragement and suggestions. More than a word of gratitude must be extended to those at Oxford University Press who have taken a personal interest in completion of the work. I am particularly indebted to my editor Mr. Michael Cook and to Ms. Brenda Jones, an outstanding copyeditor, whose patience with detail and constant attention eased many anxieties and helped to improve the original manuscript.

While this book has been written for an introductory, undergraduate course in genetics, I feel that the treatment of most topics can also be of use to many advanced students. Although I do not consider this work to be a technical reference, I am confident that it can aid both the student and the teacher who want to clarify many genetic points.

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FOUNDATIONS OF GENETICS

The accomplishments of many brilliant biologists throughout the years have established the foundations upon which classical genetics, modern genetics, and the science of molecular biology rest. These contributions tell the story of the logical development of genetic principles. Familiarity with some of the major efforts is needed to provide a background in the concepts of heredity. Such knowledge can provide insight into the challenge which genetic phenomena present to us today.

Achievements before 1900

Before 1900, the history of the science of heredity was closely interrelated with that of cytology, the discipline concerned with cellular structure and function. The origin of both sciences can be traced to the discovery of the cell. This landmark is credited to Robert Hooke, who in 1665 described cellular entities in sections of cork. In the following decade, Leeuwenhoek described many interesting cell types, recognizing many free-living forms in addition to those cells which are associated to form tissues. However, more than a hundred years were to pass before any other significant observations would be made. We can appreciate the main reason for this standstill when we consider the fact that before the nineteenth century, there were no notable advances in the development of optical tools. Very little could actually be seen inside the cells. As a result, cell walls and cell boundaries were stressed rather than contents of the cell. It was essential to distinguish the subcellular components before the location of the genetic material could be established.

In 1831, Brown called attention to a body within the cell which he recognized as a regular, constant cellular element. This structure was the nucleus. A few years later (1838–1840), another important contribution was made, the proposal of the "cell theory" by Schleiden and Schwann. This concept is considered by many to be the most significant, all-encompassing generalization in biology: all living things are composed of one cell or more and their products. Schleiden and Schwann were not the first to recognize the cellular nature of organisms; however, they were able to present the idea very convincingly by compiling their own observations with those of others. Once the cell was accepted as the unit of life, several biological disciplines emerged. In addition to cytology, such fields as physiology,

embryology, and pathology were to undergo rapid advances.

Even though cytologists were now concentrating on cellular components, not too much was seen before 1850. This resulted from the still limited optical instruments and the lack of appropriate stains and fixatives. Most of the important improvements in this area occurred in Germany after a government subsidy of the dye industry. In the 1870's, development of the aniline dyes led to better staining methods. About this time, Abbé developed the condenser and the oil immersion lens. Aided by these advances, microscopists were able to see and describe in some detail the nucleus and changes associated with it.

At this time a large number of highly significant descriptions of the chromosome and its behavior suddenly appeared. Several investigators noticed the presence of threads in the nucleus of the cell and reported that these threads became split. Flemming, a zoologist, reported that the halves of the split threads separate, and in 1882, he gave the name "mitosis" to the process. The botanist Strasburger was the first to give a complete description of mitotic events. During this period, some biologists were paying special attention to the germ cells. By 1879, fertilization had been recognized in plants by Strasburger and in animals by Hertwig and Fol.

The observations made on mitosis eventually led to the establishment of the "chromosome theory of heredity." In 1884–1885, four different investigators (Hertwig, Kolliker, Weismann (all zoologists), and the botanist Strasburger) concluded independently that the physical basis of inheritance is in the nucleus and that the hereditary material is in the substance which makes up the chromosomes. To these workers as well as others, it was apparent that the separation of nuclear threads at mitosis is a very accurate procedure. In contrast to this, other portions of the cell are not so precisely distributed at cell division. Moreover, the cells uniting at fertilization, sperm and egg, differ immensely in size, primarily due to non-nuclear material. So, although cytoplasm can vary greatly in amount, the nuclei of gametes are quite similar. The larger sized female gamete does not contribute more nuclear material than the male. Inasmuch as heredity appeared to be equal from both parents, it seemed logical to assume that the hereditary material was in the nucleus, carried in the chromosomes. Although the chromosomes seemed to disappear in the "resting phase," they were still somehow carried along from fertilization on and distributed accurately from one cell to the next when the nucleus divided.

Therefore, in the 1880's, there were strong suggestions that the chromosomes are the carriers of hereditary material, because only they are quantitatively divided. The word "chromosome" was coined in 1888 by Waldeyer. However, there was still no real proof of the chromosome theory. Chromosomes can be seen only when the cell is dividing; therefore, it was essential to obtain evidence that they persist throughout all stages of the cell cycle, even when they are not visible. Also needed was some evidence to correlate chromosome behavior with the inheritance pattern of specific traits. Such confirmation was to be presented in the next few decades through the work of several outstanding scientists.

Of the four original proponents of the chromosome theory, Weismann was the one who recognized its additional implications. He reasoned that if the chromosome theory were correct, then the germ cells of one generation must supply the chromosomes for both the body cells and the germ cells of the next generation. These germ cells in turn give rise to still other body cells and germ cells (Fig. 1-1*A*). From such reasoning, Weismann formulated the idea of the "continuity of the germ plasm." According to this concept, it is the germ cells which connect one generation to the next. Although they provide the body cells as well as other germ cells with chromosomes, the body cells (or somatoplasm) do not form a continuum from one generation to the next; they are a "dead end," so to speak. Any hereditary effect, therefore, must come through the germ plasm, *not* the body cells. Such an idea argued against acquired characteristics, a theory which had been proposed in 1809 by Lamarck and which has been a popular one even in the twentieth century. According to this concept, a change in the body, resulting from an environmental influence during an individual's lifetime, can be passed on to the next generation. Most of us have heard the familiar story of the lengthening of the neck of the giraffe as the re-