HUMAN GENETICS

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PRENTICE-HALL, INC. / ENGLEWOOD CLIFFS, N.J., 07632

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Library of Congress Cataloging in Publication Data

Rothwell, Norman V (date)

Human genetics.

Bibliography: p.
Includes index.
1. Human genetics. I. Title.
QH431.R853 573.2'1 76-26701
ISBN 0-13-445080-9

Printed in the United States of America

10 9 8 7 6 5 4 3 2 1

Prentice-Hall International, Inc., *London*
Prentice-Hall of Australia, Pty. Limited, *Sydney*
Prentice-Hall of Canada, Ltd., *Toronto*
Prentice-Hall of India Private Limited, *New Delhi*
Prentice-Hall of Japan, Inc., *Tokyo*
Prentice-Hall of Southeast Asia Pte. Ltd., *Singapore*
Whitehall Books Limited, *Wellington, New Zealand*

HUMAN GENETICS

PRENTICE-HALL BIOLOGICAL SCIENCES SERIES

William D. McElroy and Carl P. Swanson, *Editors*

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To Robert F. Lewis / friend and colleague

PREFACE

The basic objective of this book is to present the major concepts and problems of human genetics in a manner that can be readily understood by a reader with little or no background in the subject. Specific topics and examples were selected with two major audiences in mind: First, for "non-science" college students who wish to become familiar with biological principles that will remain pertinent to their everyday affairs. To satisfy that need, several schools offer a variety of courses in specific areas of the life sciences, among them human genetics intended for the non-science undergraduate. The number of such courses is increasing because of a growing awareness of human genetics problems. This book is also written for persons preparing for careers as nurses, physicians' associates, clinical technicians, and social workers concerned with communicating genetic information to community groups. The demand for physicians' associates and other allied medical personnel continues to increase with advances in human genetics, particularly as related to prenatal diagnosis, detection of carriers in high-risk groups, and the manipulation of environmental factors.

In fact, any person who desires to understand the genetic and environmental components that interact to produce the human being will find this book of value. No attempt is made to satisfy the requirements for a course in general genetics; instead we deal almost completely with the human organism. Examples from other species are given only when they best serve to make a major point. No plant genetics is included nor are microorganisms explored as genetic systems. However, references to bacteria and viruses are made throughout the text because of the insights these groups provide as to the nature of the gene and molecular interactions. Phage replication and the prophage concept are also included to explain their relation to environmental and genetic interactions and the triggering of diseases.

Technical nomenclature is minimized but the reader is not "talked down to" by substituting awkward phrases in place of common genetic expressions. All the elementary genetic terms are given such as homozygous, heterozygous, genotype, allele. All terms are explained thoroughly and used continually so as

to integrate them with a reader's vocabulary without requiring rote memorization.

Certain elementary mathematical principles are stressed, mainly those applying to the concepts of probability. Nowhere are these concepts more important than in their application to problems in human genetics. Failure to understand the principles of probability as they relate to simple genetic ratios and gene frequencies in populations can lead to naive and unfortunate interpretations of the facts. The person who encounters genetic problems in daily life must understand the simple fundamentals of probability. The necessary, elementary mathematical concepts are carefully developed here and applied to specific examples of the human organism.

Genetic counseling is reviewed within the framework of recent ideas that attempt to define the role of counseling teams. The material on counseling is intended for the reader with a medical orientation or anyone who may be unaware of the role of this essential service. The chapter on pedigree analysis shows the dependence of the genetic counselor on probability.

Although the specific genetic disorders included are rather extensive this book is not a clinical text. These disorders are afflictions that are familiar to some persons (such as cystic fibrosis, sickle cell anemia, Tay-Sachs disorder). Others which may be less well known (such as glycogen storage diseases) are explained in regard to the information they provide on gene expression and the manipulation of the environment. Certain subjects are treated (homosexuality, for example) even though no genetic bases may have been established for them. The controversial topic of sex-role inheritance is also included. Such material is intended to answer questions which occur to a reader who often finds such topics omitted from basic genetics texts.

The presentation assumes no familiarity with biology or other sciences beyond that encountered in most high school curricula. Chemistry is kept to the essentials needed to appreciate the nature of gene action and of molecular disorders, their detection, and diagnosis. Mitosis and meiosis are stressed in relation to the transmission and maintenance of balanced sets of genetic information. Names of meiotic substages are not given nor are any other terms that are unnecessary for an appreciation of the biological significance of nuclear divisions. The concepts of linkage and crossing over, difficult ones for many students, cannot be eliminated from any text on human genetics without the danger of presenting a distorted viewpoint and an incomplete picture of the relationship between genes and chromosomes. Moreover, our knowledge of human linkage groups and chromosome maps is rapidly growing and will continue to be applied more routinely to the prenatal diagnosis of human afflictions. The treatment of these topics here is kept as simple as possible and is always tied to familiar situations and practical applications.

A glossary, which follows the last chapter, includes all terms defined and used in the text, as well as elementary biological expressions that may not be familiar to the student with little science background.

Norman V. Rothwell

Brooklyn, New York

ACKNOWLEDGMENTS

The author expresses his appreciation to the following individuals and sources for permission to reproduce the material cited below:

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chapter 1

SOME FUNDAMENTAL GENETIC PRINCIPLES

In some families, one child may combine features of both parents, whereas another resembles only the mother or the father. And then, there are those cases in which the offspring bear no physical resemblance to any family member. What accounts for such variations as these? Obviously, parents must transmit hereditary material to their children, but exactly what is being passed down? It must be something which carries the information required to guide the formation of a human being. All living things must carry specific information which can be transmitted to the next generation. This transfer of information insures that cats give rise to cats, dogs to dogs, oak trees to oak trees, and similarly for all forms of life. The science of *genetics* encompasses a study of the nature of the hereditary material, how it is transmitted, and how it interacts with the environment to bring about an effect on a cell or an individual. A knowledge of genetics helps us to explain why an individual may resemble both parents, one of them, or neither.

The Human and Other Species in Genetic Analysis

Most of the information on patterns of inheritance and the action of the hereditary material has been assembled from forms of life lower than the human. It is true that well before the turn of the century certain simple patterns of inheritance in humans were known. While it was appreciated that such traits as the presence of extra fingers (polydactyly) and colorblindness occur in a characteristic fashion in human pedigrees, the basis for the transmission was not well understood. Pioneer investigators utilized both plants and animals in their genetic studies. More recently, elegant analyses employ-

ing bacteria and viruses as genetic tools have provided an insight into the very nature of the hereditary material and the way in which it acts in the cell. The basic principles established in these lower groups have been found to apply to the human. Since it is the human species which concerns us most, why is it that biologists have not concentrated solely on the human to obtain fundamental genetic information? The human is not the ideal creature for such research, and the reasons become clear when we consider several factors which are essential to a detailed study of inheritance patterns.

Extremely important to such research is the need to follow not just one or two, but several generations in order to determine the way in which a particular trait occurs among members of a family line. The span of a human generation is long, in the vicinity of 25 years. Consequently, not many generations of one family can be followed in the lifetime of an investigator. Moreover, the average person can contribute little to a study of his family, since he knows little about his ancestors.

Another requirement for genetic analysis is the existence of a number of clear-cut traits in the organism being used as a genetic tool. Suppose we wanted to study the inheritance of eye color, a characteristic of all humans which occurs in many forms: blue, gray, brown, hazel, etc. Each of these alternatives is considered a *trait,* a variant form of a characteristic [Fig. 1-1(A)]. To gain information on the inheritance of any characteristic, it must exist in variant forms. If everyone had brown eyes, it might be appreciated that brown eye color has a hereditary basis; but lacking an alternative to brown, not much could be surmised about the transmission of information for the color characteristic. Moreover, the best traits for genetic study are those which are easy to recognize and to describe. Eye color in humans is a characteristic whose traits meet this requirement. In contrast, a characteristic such as height presents difficulties [Fig. 1-1(B)]. While persons may be classified into general categories such as tall, short, and medium, such groups are separated by ill-defined boundaries. Many persons would not fit precisely into any one of them. A further complication entails the influence of the environment on height. Poor diet can stunt the growth of any individual, who might otherwise be able to grow taller. A complex characteristic such as

Figure 1-1. Characteristics and traits. (A) A characteristic is a general attribute of an individual which may occur in 2 or more well-defined forms. Characteristics such as the first six noted above are obvious ones whose traits can be recognized by casual inspection. Many characteristics such as color vision or blood grouping demand closer inspection or special techniques before their variant forms can be recognized. Nonetheless, for each of these characteristics, rather sharply defined categories are apparent. (B) Height is a characteristic in which the variation is not distinct. No clear-cut traits exist. Instead, the variation describes a continuum from one extreme to the other. Such characteristics present more difficulties in genetic analysis than those in which the variant forms are clearly defined.

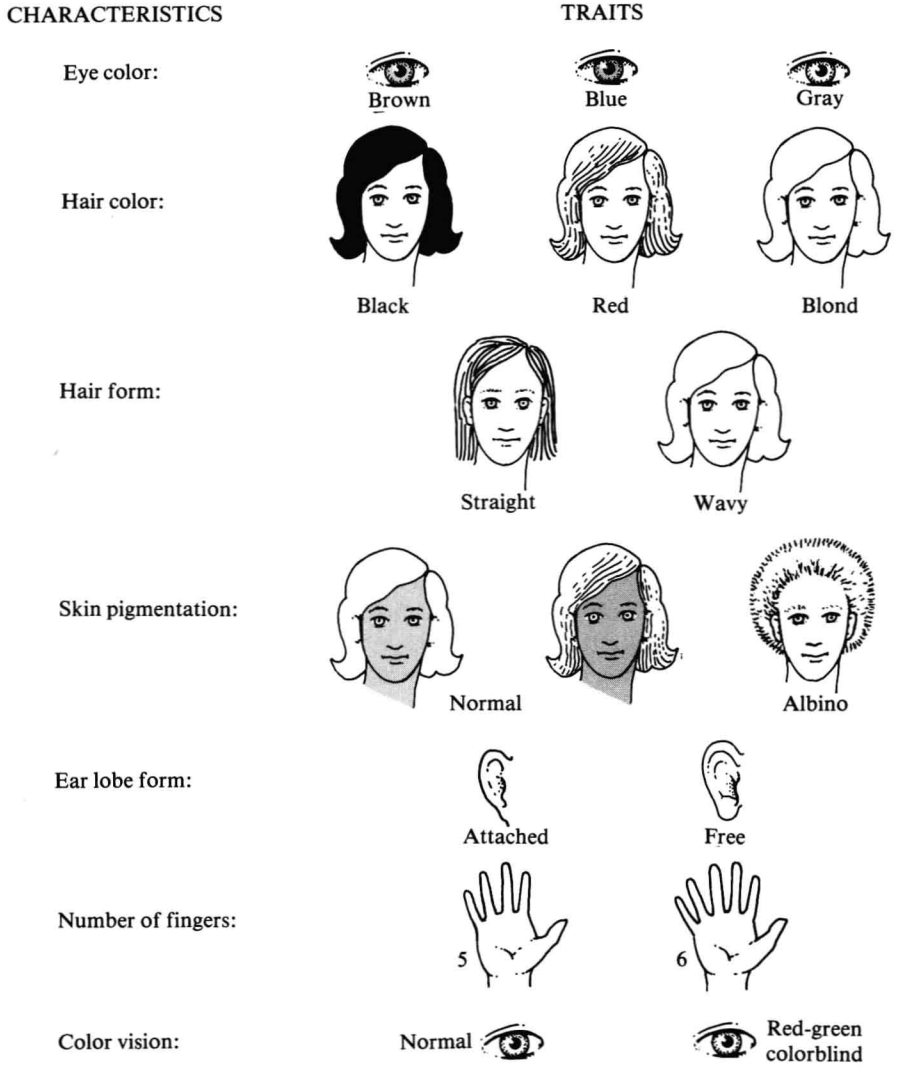

Figure 1-1