

Speicher • Antonarakis • Motulsky

VOGEL AND MOTULSKY'S HUMAN GENETICS

Problems and Approaches

Fourth Edition

Speicher Antonarakis Motulsky

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Problems and Approaches

Fourth, Completely Revised Edition

With 343 Figures and 76 Tables

 Springer

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In memory of Friedrich Vogel

The editors

*To my wife, Irene, and our children,
Alexander and Julia.*

Michael R. Speicher

*To my parents, my wife, Grigoria, and
our children.*

Stylios E. Antonarakis

*To the memory of my wife, Gretel, and
to my children.*

Arno G. Motulsky

Preface

The first edition of *Human Genetics, Problems and Approaches*, was published in 1970 by human geneticists Friedrich Vogel and Arno Motulsky as sole authors. The aim was broad coverage and in-depth analysis of both medical and human genetics with an emphasis on problems and approaches with occasional historical comments. This point of view was fully explained in an introductory chapter of the three previous editions (1970, 1976, 1997). The book acquired an excellent reputation as an advanced text of human genetics and has been translated into Italian, Japanese, Russian, Chinese, and Portuguese. Our general aims for the fourth edition remain similar and together with novel developments are now set out in the Introduction of this new fourth edition.

Around 2004/2005, both Friedrich Vogel and Arno Motulsky, as well as the publishers, felt that the book should be continued with a new fourth edition in the same spirit and coverage as earlier editions, but should now include additional expert authors. After some delay and the death of Friedrich Vogel in the summer of 2006, a new editorial team consisting of Michael R. Speicher of the Medical University of Graz, Austria, Stylianos E. Antonarakis of the University of Geneva Medical School, and Arno G. Motulsky of the University of Washington School of Medicine, was constituted for the fourth edition of the Vogel/Motulsky book in the spirit of the original work.

An outline of the fourth edition's contents was developed and various internationally known geneticists, including the new editors, were selected to write the individual chapters. The resultant titles are listed in the table of contents. Most chapters are entirely new, while only three chapters (1, 5, and 6) utilize the third edition with appropriate, up-to-date revisions. Entirely new chapters include the description of the human genome, epigenetics, pharmacogenetics, genetic epidemiology, human evolution, genetics of mental retardation, autism, alcoholism and other addictions, consanguinity and related matters, gene therapy, cloning and genetic aspects of global health. Multiple chapters of various animal models used in the study of human and medical genetics are novel as are Databases and Genome Browsers as well as Databases Used in Human and Medical Genetics. The final content of the book was the result of many e-mails and conference calls. This new, updated, and totally revised edition does not contain some important and historically interesting chapters on certain topics. These can be found in the third edition of the book published in 1997, which was exclusively authored by F. Vogel and A.G. Motulsky. These topics were: enzymes in Chap. 7 (pp. 258–299); mutation rates in Chap. 9 (pp. 393–413); and mutation induction by ionizing radiation and chemicals in Chap. 11 (pp. 457–493).

The staff of Springer was most helpful in giving us extensive and firm aid in getting the book finished. We thank particularly Doris M. Binzenhöfer-Walker for her work during the early stage of the project and Isabella Athanassiou for her efficient help later. Andrea Pillman was a strict task mistress, who encouraged us to finish the book expeditiously.

The editors of the fourth edition want to express their intellectual indebtedness to Friedrich Vogel for having conceived of and played a major role in the first three editions of this book. Arno Motulsky particularly misses his discussions with Friedrich on human genetics and its role in science and medicine.

The cover illustration portrays a marble statue of Asclepius, the Greek god of healing, grasping a serpent-encircled staff as a symbol of medicine. The double helix of DNA joined to Asclepius symbolizes the applications of basic genetics to medicine.

4th edition
June 28, 2009

Michael R. Speicher, Graz
Stylianos E. Antonarakis, Geneva
Arno G. Motulsky, Seattle

Preface to the First Edition

Human genetics provides a theoretical framework for understanding the biology of the human species. It is a rapidly growing branch of science. New insights into the biochemical basis of heredity and the development of human cytogenetics in the 1950s heightened interest in this field. The number of research workers and clinicians who define themselves as full-time or part-time human and medical geneticists has increased sharply, and detailed well-founded knowledge has augmented exponentially. Many scientists and physicians are confronted with genetic problems and use concepts and methodology of human genetics in research and diagnosis. Methods developed in many different fields of the biologic, chemical, medical, and statistical sciences are being utilized toward the solution of genetic problems. The increasing number and sophistication of well-defined and elegantly solved problems helps to refine an extensive framework of genetic theory. These new conceptual insights in their turn lead to solutions of new questions. To mention only one example, the structure of hemoglobin genes has been elucidated using methods derived from protein chemistry and DNA technology. It is an exciting experience to participate in these developments!

Moreover, scientific progress in genetics has practical implications for human well-being. Improved knowledge of the genetic cause of an increasing number of human diseases helps to refine diagnosis, to find new therapeutic approaches, and above all, to prevent genetic diseases. So far, human genetics has had less of an impact on the behavioral and social sciences. It is possible that genetic differences involved in shaping personality structure, cognitive faculties, and possibly human social behavior may be at least as important as genetic variation affecting health and disease. The data, however, are less clear and more controversial. These problems are discussed in detail in the text. The rapid progress of human genetics in recent decades has attracted – and is still attracting – an increasing number of students and scientists from other fields. Various elementary textbooks, more advanced monographs of various branches of the field, and the original journal literature are the usual sources of introduction to human genetics. What seems to be lacking, however, is a fairly thorough and up-to-date treatise on the conceptual basis of the entire field of human genetics and its practical applications. Often, the absence of a broadly based background in the field leads to misunderstanding of its scope, unclear goals for research, improper selection of methods, and imbalanced theoretical discussions. Human genetics is based on a powerful theory, but this implicit conceptual foundation should be made explicit. This goal is the purpose of this book. It certainly is a formidable and possibly even too audacious task for two sole authors. However, both of us have been active in the field for more than 25 years.

We have worked on various problems and with a variety of methods. Since the early years of our careers, we have met occasionally, followed each other's writings, and were often surprised by the similarity of our opinions and judgments despite quite different early medical and scientific backgrounds. Moreover, our knowledge of the literature turned out to be in part overlapping and in part complementary. Since we are working in different continents, AGM had a better knowledge of concepts and results in the USA, while FV knew more of the continental European literature. Moreover, both of us have extensive experience as editors of journals in human genetics and one (FV) published a fairly comprehensive textbook in Germany some time ago (*Lehrbuch der allgemeinen Humangenetik*, Springer 1961), parts of which were still useful for the new book. We finally decided to take the risk, and, by writing an "advanced" text, to expose our deficiencies of knowledge, shortcomings of understanding, and biases of judgment.

A text endeavoring to expose the conceptual framework of human genetics cannot be dogmatic and has to be critical. Moreover, we could not confine ourselves to hard facts and well-proved statements. The cloud of conjectures and hypotheses surrounding a rapidly growing science had to be depicted. By doing so, we face the risk of being disproved by further results.

A number of colleagues helped by reading parts of the manuscript on which they had expert knowledge and by making useful suggestions: W. Buselmaier, U. Ehling, G. Flatz, W. Fuhrmann, S. Gartler, Eloise Giblett, P. Propping, Laureen Resnick, and Traute M. Schroeder. They should not be held responsible for possible errors. J. Krüger was of supreme help in the statistical parts. Our secretaries, Mrs. Adelheid Fengler and Mrs. Gabriele Bauer in Heidelberg, Mrs. Sylvia Waggoner in Seattle, and Mrs. Helena Smith in Stanford gave invaluable aid. The figures were drawn by Edda Schalt and Marianne Lebküchner. Miriam Gallaher and Susan Peters did an expert job of copy editing. The authors are especially grateful to Dr. Heinz Götze and Dr. Konrad F. Springer, of Springer Publishing Company, for the excellent production. The work could not have been achieved had the two authors not been invited to stay at the Center for Advanced Study in the Behavioral Sciences at Stanford (California) for the academic year of 1976/1977. The grant for AGM was kindly provided by the Kaiser Family Foundation, while the Spencer Foundation donated the grant for FV.

The cover of this book shows the mythical first human couple, Adam and Eve, as imagined by Albrecht Dürer (1504). They present themselves in the full beauty of their bodies, ennobled by the genius and skill of a great artist. The drawing should remind us of the uniqueness and dignity of the human individual. Human genetics can help us to understand humanity better and to make human life happier. This science is a cardinal example of Alexander Pope's statement. "The proper study of mankind is man."

Spring 1979

Friedrich Vogel, Heidelberg
Arno G. Motulsky, Seattle

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