FOREWORD

Preventive medicine, individual healthcare, and public health are increasingly dependent on our rapidly advancing knowledge of human molecular genetics and genomics. For many years, we have been aware of several devastating "single gene" diseases like sickle-cell anemia and cystic fibrosis. It has become clear, however, that for most diseases and disorders the genetic causes are rarely this simple. In some cases, genetics play a major role in either the vulnerability to develop a specific disease, or in the body's protection against disease development. It is also increasingly evident that gene-environment reactions are of seminal importance. Scientists now recognize that our genetic composition does not represent predestination or predetermination, but rather sets the stage for the interaction between genes and an array of factors in our individual and shared environments. This relationship can influence our risks of developing any disease or disorder. In another area of importance, our world food supply is increasingly dependent on our ability to manipulate genes of plants and animals of all types, desirable in many cases, but controversial in others.

The new science of genomics is having a growing impact on our lives. However, the public's knowledge about genes, molecular genetics, and human genomics is extraordinarily limited, both in the United States and throughout the world. This knowledge gap is not surprising, both because of the technical nature of genomics and since many of the critical developments in this field have been made only recently and, thus, after the years of any formal education of the majority of adults. Even for those who may have had the privilege of learning about the fundamental aspects of molecular biology, molecular genetics, or genomics in their formal high school or college education, it is difficult to keep up with the enormous volume of new information and its applications and implications. Therefore, a book such as this one, *Welcome to the Genome: A User's Guide to the Genetic Past, Present, and Future*, provides a welcome primer for individuals of diverse ages, educational backgrounds, and current interests.

The story told here, that is, the story of molecular genetics and genomics, is well over a century old. In 1869, Friedrich Miescher discovered and elucidated the

chemistry of nucleic acids, which was a critical first step in this story. However, it was not until the extraordinary work in the early nineteen-forties of Oswald Avery, Maclyn McCarty, and Colin MacLeod (briefly detailed in this book), working at The Rockefeller University, that there was the first proof that nucleic acids are the centerpiece of the transmission of "traits between generations" and, thus, that nucleic acids are the "fundamental elements of life." (Dr. Maclyn McCarty recently celebrated his ninety-third birthday and is vigorous and actively participating in the intellectual ferment of The Rockefeller University community, many of whose members are working in either molecular biology or molecular genetics, including studies related to the human genome and its global implications.) In 1953, the pivotal studies of James Watson and Francis Crick, along with colleagues in England and in the United States, unraveled the structure and the function of DNA. Since that time, all biological science has been radically changed and is undergoing rapid evolution, a process which will undoubtedly continue for many years to come.

In the human genome, we now appreciate that all of humankind living today is extraordinarily similar. On an individual level our large genomes differ by only 0.1%. Or, in other words, we are 99.9% genomically alike. However, variants of specific genes which play important roles in our biology are neither "good" nor "bad," but simply variations in the human genome. Although these differences do not reflect the ways in which we have historically divided humankind, they are proving scientifically and medically significant. For instance, studies of the human mu opioid receptor gene, where many of our "endorphins" bind, as well as where pain medications (such as morphine) and drugs of abuse (such as heroin) act, have allowed us to identify a genetic variant which plays an enormous role in many different aspects of human physiology. The physiological changes that may result from one copy of a variant can be measured objectively, are substantial in magnitude, and may have implications for development of specific diseases. Despite the "sameness" of human kind, there is obvious diversity. Increasingly, we appreciate that this diversity may have implications, not only for diseases, but also for response to medications and possibly for understanding our own physiology.

Many readers may have concerns about the ethical issues surrounding genomic science. These concerns may increase as the reader learns of the many areas where genetics and genomics are beginning to play a role in our lives. At the personal level, and with respect to each of our own genetic information, many or most of us would like to have knowledge of our own genome if it can make us healthier. At the same time, most of us would also want to be assured that no negative consequences result from that knowledge. It is absolutely essential that no "reprisals," or unenlightened negative actions, be taken based on genetic information, such as the presence of genetic variants that may contribute to cancer, cardiovascular disease, depression, or an addictive disease. It is essential that there be national and international legislation and, hopefully, international standards and ethical constraints

by which no denial of insurance or inappropriate escalation of insurance fees, nor denial of access to education, employment, or advancement therein be based on genetic composition. As you will learn in this book, a majority of U.S. states offer varying protections against genetic discrimination, and the U.S. Senate in 2003 passed bipartisan legislation making genetic discrimination in health insurance and employment illegal. Each individual adult needs to understand the scientific basis, including clinical implications, of genetic information. Each individual also has to contemplate, on the one hand, the personal "desire to know", as well as the "need to know" by physicians and other healthcare providers and, in that context, the question of who has the "right to know." Similarly, debates are ongoing nationally and internationally concerning the use of genetically modified foods. It is important to have these debates. However, they need to be based on a fundamental base of information and knowledge. Again, this book offers an overview and highlights elements of the ethical and other controversies that have been engendered by rapid developments in the field. *Welcome to the Genome,* provides a wonderful resource of information. While I am sure this will be one of many books for the lay public on this topic to be published in future years, DeSalle and Yudell offer a uniquely informative perspective on the genomic revolution.

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