

Los Alamos Science

LOS ALAMOS NATIONAL LABORATORY





The human genome presents us with a vast, largely unexplored frontier containing answers to many mysteries about how we evolved, how we are related to other living things, and how we differ from one another. The Human Genome Project is an attempt to open up this territory to our understanding. As scientists and the public anticipate the new knowledge, physicians, lawyers, social scientists, and philosophers are trying to anticipate the impact of the information on our institutions and on our lives. We all stand at the brink of an increased awareness of our human limitation and potential.

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“It’s all in the genes!” When I was a child I listened to my father repeat those words again and again as the definitive explanation for certain physical disorders or personality traits of his patients, his friends, our relatives—even me and my sisters. It was why some people were prone to colds and others not; why some people were good at numbers, or business, or music and others not. It was why I had curly hair and crooked teeth and a mean temper. It was also why I couldn’t take no for an answer. So I was told.

My father was a physician trained in the late 1920s during the heyday of classical genetics. Mendel’s laws of inheritance and their extensions were being applied to plants, animals, and also to human beings. Physicians were taught that the information in our genes determines a good deal about our health and physical well-being and maybe even our behavior. That idea had a profound influence on my father and his contemporaries. Two decades later, it became more fashionable to believe that much of what we are is learned—that we all start with more or less the same blank slate and through learning and experience the slate is etched with patterns and connections determining our abilities, character, and behavior.

Now, in the late twentieth century, the Human Genome Project is beginning to gather the data needed to determine once and for all what is—and what is not—in our genes and thereby disentangle the contributions of nature and nurture. Will that information also mean we’ll be able to alter our genes or choose the genes of our offspring? Are we on the brink of tampering directly with human evolution? It’s easy to let the imagination run wild when thinking about the Human Genome Project. It’s also easy to get trapped into an oversimplified notion of genetic determinism.

Popular descriptions of the Human Genome Project tend to focus not on the Project itself but on its long-range implications for ameliorating genetic diseases, for improving health care in general, and even for altering an individual’s genetic makeup. Few presentations delve into the inherent complexity of the human genome, its mutability, our present state of ignorance, and the difficulties of gathering and interpreting data about DNA.

This volume is an exception. Here we have attempted to get beneath the hyperbole associated with selling the Project and deal head-on with the technical challenges of rapidly gathering reliable data on human DNA and facilitating the interpretation and practical use of that information.

The human genome is a vast new frontier. It is estimated to contain between fifty thousand and a hundred thousand genes—only about a hundred of which have been isolated and sequenced. Locating and sequencing all the remaining human genes is the overriding priority of the Project. But the development of tools to find and sequence those genes will lead to the exploration of many related questions. How are the genes organized along the DNA molecule in each human chromosome? What coded messages control gene expression so that the right proteins are made in the right cells in the right amounts at the right times? Why do vast regions of the genome appear to have no function at all? Why is the human genome so similar to the mouse genome? The human genome is a product of millions of years of evolution, so, in a sense, to study the human genome is to study evolution.

The roots of the Human Genome Project, extending back over 150 years, are presented in "Understanding Inheritance." This piece covers important topics in both classical genetics and molecular biology, the two fields that, through the Project, are in the process of becoming one.

Our centerpiece, a frank discussion among some of the major participants in the Project, reveals their dream of accomplishing a revolution in biology and the very real technical and logistic problems of carrying out that dream. Talents from many institutions and many fields of science, including biology, physics, mathematics, computer science, and engineering, are being combined in the attempt to scale up the old techniques and invent new ones for cloning and analyzing DNA. Focusing these efforts on the big goals of the project—on constructing physical and genetic-linkage maps for the entire genome, on sequencing long continuous stretches of DNA covering a large fraction of the genome, and on building a large public database of genome information—is a formidable job. It's not easy for a physicist or mathematician or computer scientist to understand the language, the techniques, and the methodology of the molecular biologists—and vice versa. Consequently even communication among the various camps is a big challenge.

Now after two years of a proposed fifteen-year effort, the results of the Project are becoming tangible. Results emanating from the Los Alamos Center for Human Genome Studies are presented in the second half of this volume. These articles are notable for the quality of the research—for example, a reliable map of chromosome 16 is almost complete—and for the fine attempts to convey the basic ideas and challenges behind the research. We hope the emphasis on pedagogy will help not only the casual reader but also scientists from all fields who are becoming involved in this sprawling, multidisciplinary effort.

The Human Genome Project is already generating large quantities of information about what's in our genes and through genetic testing that information will affect the lives of many of us in the near future. Therefore the Project has taken the unprecedented step of studying its own ethical, legal, and social implications. That effort, known as ELSI, is designed to help prepare society for evaluating and using the information in ways that benefit everyone. We close this volume with two discussions of ethical issues. The development of genetic literacy is probably the most important ingredient in assuring that genetic information is used fairly and appropriately. It is our hope that this volume will contribute to that most essential goal.

The *Los Alamos Science* staff wants to thank all those who participated in preparing this volume. Their enthusiasm was catching—it must be in the genes!

A handwritten signature in black ink, reading "Kevin Grant Cooper". The signature is written in a cursive style with a large, prominent 'K' and 'C'.