

# Introduction . . . The Journey Inward

*by Betty S. Pace*

*The true science and study of man, is man himself.*

*Pierre Charron, 1541–1603*

Scientific exploration and discovery are, at their core, a perpetual journey for truth. To know and understand the essence of one's being is the ultimate revelation of that truth. But the boundaries surrounding the quest for this truth have certainly come under great challenge and scrutiny.

Recently, there have been intense discussion and debate around the sanctity of life and the ethical issues raised by efforts to clone humans, or to alter the genetic makeup of children by design. Who would have thought in 1949, when Linus Pauling published the seminal paper declaring “Sickle cell anemia, a molecular disease,” followed in 1977 by the demonstration of a point mutation in the  $\beta$ -globin gene, that less than 30 years later the ethics of human cloning would be the focal point of discussion — while we have not yet acquired the knowledge required to cure the *first* genetic disease, sickle cell anemia?

Since that critical discovery of 1977, the scientific community has completed a fantastic voyage to sequence the entire three billion base pairs in the human genome under the leadership of Dr. Francis Collins, Director of the National Human Genome Research Institute, and Dr. Aristides Patrónis, Director of the Department of Energy Human Genome Program. The first draft of the entire human genome sequence was published in February 2001, followed by a high-quality, reference sequence in April 2003. Yes, the Human Genome Era was born, bringing new hope for a cure not only for sickle cell anemia, but for other genetic disorders as well. The quest to sequence the human genome was a “journey inward,” in the words of Dr. Collins, to the essence of life, so we invite you to join us as we chronicle the journey on the pages of this historic book.

As we embark upon this journey, it is important to stay the course, from beginning to end, for behind every chapter you will find a fresh perspective on research efforts toward improving outcome and producing a cure for sickle cell disease. Four major groups, including family and community, the National Institutes of Health, healthcare providers, and researchers are essential for establishing the inter-disciplinary team that will find the universal cure for any disease. All elements must be acknowledged and balanced to provide a successful healthcare program for individuals affected with genetic disorders. Sickle cell anemia was the *first* genetic disease, and therefore is a perfect paradigm

to establish standards for curing monogenic diseases. We will explore sickle cell disease from a contemporary perspective by addressing questions such as the impact of the human genome project on new approaches to an old disease in *the genomic era*.

Here is a sneak preview:

Part I will cover the history of sickle cell disease, the progress and missteps that have been made along the way, the role of the federal government in the success we now enjoy, and future research directions. A picture of progress made with genetic diseases will be painted on the canvas of the Human Genome Project, with a focus on the global implications and impact of this ground-breaking research at home and abroad.

In Part II, we will delve into the heart of the matter: What have we accomplished over the last 50 years to truly improve the quality of life for individuals and families living daily with the burden of sickle cell disease? How can the lessons learned apply to other genetic disorders? Traversing the winding road of genetic research from a clinical perspective, we will discuss everything from the impact of Comprehensive Care Centers to the organized multi-center drug trials that finally led to Hydroxyurea, the *first* specific therapy released by the Federal Drug Administration in 1985 for sickle cell disease. From the very beginning, the control of painful vaso-occlusive episodes was, and remains, a central issue for improving function of those living with sickle cell disease. Indeed, some 50 years later, the passion for progress in meaningful intervention still burns. That passion is inescapably fueled by the voices of those crying out for help. Further, we will take an in-depth look at how state-of-the-art technology has impacted stroke management and transfusion therapy. This will be contrasted with the ongoing efforts to develop more tolerable approaches to control the iron overload secondary to chronic transfusion.

In Part III, we will journey deep into the progress that has been made toward understanding the molecular mechanisms that control globin gene expression during development, to aid efforts to produce a gene therapy cure. It is important to note that a cure for sickle cell disease had been hindered by our inability to accurately isolate bone marrow stem cells prior to the 1990s, or to produce effective gene therapy vectors that transport a normal hemoglobin gene into stem cells and produce protein on a permanent basis. Most fearful are the untoward ill effects associated with random integration of engineered DNA molecules into the human genome, and the potential for activation of deleterious proteins or inactivation of vital genes that may lead to cancer. This risk must be eliminated.

And finally, in Part IV we will explore the progress and great knowledge gained from the perspective of affected individuals, the most important focus of our efforts. These people remain courageous and hopeful despite fear and frustration. We will dare to explore and expose the heart of the African-American community as it relates to sickle cell disease — those fears that may remain based on past experiences with research in America, and the cultural acceptance of genetic therapy. The reader will be enlightened on the recommendations of the Ethical, Legal and Social Implications Committee established by the National Human Genome Research Institute to address concerns over individual rights to privacy, the use of genetic information, forensic profiling, and the impact of genetic testing on healthcare delivery in the United States.

This is a unique document, produced by a diverse group of contributors, with a common goal of improving healthcare and ultimately curing sickle cell disease. We have melded together the successes and failures of the past, the technical and the not-so-technical knowledge, and the human spirit, to produce a complete picture of the impact of genetic diseases in our society. Somehow, the role that sickle cell disease has played in this story has varied from front and center to supporting cast.

However, with the dawn of the Human Genome Era, reawakened interest in the *first* genetic disease will hasten the journey to the final destination, a cure. *Renaissance of Sickle Cell Disease Research in the Genomic Era* will enlighten and empower you to make your personal, inward exploration. You will discover how the Human Genome Project ignited a revolution in genomics and genetics that will change the face of medicine in the 21st century.