Gene therapy

Andrzej Stasiak

The New Healers

by William R. Clark

Oxford University Press, Oxford, UK
256 pages, UK£ 10.99 Paperback, UK£ 17.99
Hardcover
ISBN 019 513084 7

As molecular biologists we frequently face the challenge of explaining the social value of our research to the lay public. A sincere answer, trying to explain the cognitive value of fundamental studies of living matter, usually does not convince our sceptic interlocutors. In such a case, the best argument is to tell them about the possible medical applications of our work. But then, we may not easily find convincing examples and experience difficulties in answering a flood of further questions from our interlocutors who suddenly become very interested in the subject.

William R. Clark's book provides us with almost all the answers and arguments we need for such a debate. If our interested interlocutors are good friends or family members we should even present them this book as it contains a good and gripping science story that can be easily understood by readers who are not specialists in the field. Indeed, Clark,

Professor Emeritus of Immunology at the University of California, Los Angeles, knows very well how to present complex scientific subjects in genetics, medicine and molecular biology to non-expert readers. First, he lays out or refreshes the relevant scientific background before he progressively moves on to subjects such as hereditary diseases, AIDS, cancer and gene therapy. The reader learns interesting details of the molecular etiology of such hereditary diseases as cystic fibrosis and severe combined immunodeficiency disease (SCID) and is introduced to various approaches to gene therapy. Viral delivery vectors are well described so the reader learns, for instance, about the advantages and inconveniences of retroviruses and adenoviruses. Although the book was written before the tragic death of 18 year old Jesse Gelsinger in 1999 due to a high dose of adenovirus vectors applied during gene therapy trials at the University of Pennsylvania's Medical Center, the author stresses potential complications resulting from patients' immune response to adenovirus administration.

The reader learns about different methodologies of gene therapy and also gets familiar with individual patients, their doctors and the scientific teams supporting them. Thus we get to know Ashanti DeSilva, the first patient cured by gene therapy, and French Anderson who planned and performed her treatment in 1990. This reminds me of the famous medical event in 1967 when Christiaan Barnard performed the first heart transplantation to treat Louis Washkansky. The difference is, that Washkansky—then 55 years old and suffering from a fatal heart disease—survived only 18 days, whereas DeSilva is today a 15 year old healthy girl. But in both cases, new perspectives in medicine were opened. Today, organ transplantation is frequently performed to save lives, due to ensuing development of anti-rejection drugs, and we expect the same to happen soon with gene therapy.

However, the way from the laboratory demonstration that the introduction of a

given gene corrects a given hereditary defect to a clinical application is long and difficult. Here, the book explains various technical and ethical hurdles that need to be overcome before trials with patients could start. The reader is informed about the requirements that the US Recombinant DNA Advisory Committee and the US Food and Drug Administration demand to approve a new treatment. Indeed, both institutions use different criteria before they give the green light for a new experimental protocol to be applied on humans. One would think that all these hurdles posed by RAC and FDA are counterproductive. However, the story of Jesse Gelsinger, who could have treated his OTC disorder through diet and medications, tells us that perhaps we should proceed even more carefully.

Although the book aims at a general readership, scientists in related fields can also profit from it. But specialists in molecular biology and genetics may be disturbed by some mistakes. For example, Clark repeatedly uses the term gene replacement to describe the procedure that introduces one or more copies of a given gene into a cell without replacing the faulty copy. Indeed, it is a pity that real gene replacement methods are not discussed although they are potentially the most promising. Clark also writes that only a coding strand constitutes a gene, but, in fact, both DNA strands make up a gene and only one strand is coding. Figures and their legends have frequent mistakes, so for example the gene for the cystic fibrosis transmembrane conductance regulator is presented as having 1480 base pairs. In fact, the gene is circa 250,000 base pairs long and codes for a protein composed of 1480 amino acids. Such mistakes do not spoil the story, but our confidence in the author's expertise gets diminished. Clark or Oxford University Press should have asked molecular biologists to proofread the manuscript.

The author is at the University of Lausanne, Switzerland. E-mail: Andrzej.Stasiak@lau.unil.ch

DOI: 10.1093/embo-reports/kve059