Reshaping life

Key issues in genetic engineering

G. J. V. Nossal and Ross L. Coppel

THIRD EDITION

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For our children

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Preface to the third edition

Genetic engineering and related areas of biotechnology continue to advance at an astonishing pace. Since the second edition of *Reshaping Life* was published, there has been a great leap forward in the form of the human genome project, which had been barely discussed then but now has reached virtual completion with the release on Monday 26 June 2000 of a 'first draft' of the full DNA sequence of humans. As a result, the large field of functional genomics has been born. Similar automated approaches to sequencing the genome of pathogenic bacteria and parasites have proven very useful. Study of gene function has been greatly aided by techniques in which genes can be 'knocked out' in mice—this is now a routine research tool. The 'DNA industry' has broadened in a commensurate fashion, now comprising at least 3000 companies.

As research intensifies, so society's concerns have increased. The debate about the use of genetically modified organisms as crops is lively. In 1998, there was a referendum in Switzerland which sought to ban all research on genetically modified animals. Though it was defeated by a two to one majority, it dominated the media for weeks. Subsequently, release of modified plants and contamination of seed stocks has been widely publicized. The extraordinary research leading to the cloned sheep Dolly has raised the possibility, feared by many, that humans may one day be cloned. It is not just DNA research which worries people, but reproductive, cellular and genetic research generally. Much of this technology is being rushed into widespread use, with little time to debate or educate the public. This makes it all the more important that the key issues

of modern biotechnology are outlined in a simple yet authoritative way. Powerful technologies can be used wisely or unwisely. Moreover, perceptions as to what is ethically acceptable change with time. While it is prudent to question some uses of the new biology, it is also vital to appreciate the vast potential for good. The third edition seeks to make a contribution to a vital societal debate. At the dawn of the new millennium, we attempt to summarize a complex and rapidly moving field in a way which, we hope, the non-expert can follow with interest.

We have been aided by friends and colleagues in the writing of this book and we would like to acknowledge the assistance of Pamela Dewhurst and Beth Harrison during the writing and revising of this book. The artwork has been supplied by Peter Maltezos and we thank him for his sterling efforts. Finally the time to ponder and write is increasingly precious in the harried environment of today's universities. We would like to thank David Lipman and the staff of the National Center for Biotechnology Information in Washington DC for providing the opportunity to think about where biotechnology and the life sciences have been and where they are going.

GJVN
RLC
Melbourne, November 2001

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The genie is out of the bottle

When historians look back on the twentieth century, they will conclude that its first half was shaped by the physical sciences but its second by biology. The first half of the century brought the revolution in transportation, communications, mass production technology and the beginnings of the computer age. It also ushered in nuclear weapons and an irrevocable change in the nature of warfare. All these changes and many more rested on physics and chemistry. Biological science, too, was stirring over those decades. The development of **vaccines** and antibiotics and advanced crop **genetics** to feed a hungry world represented proud achievements. Yet the public preoccupation with the physical sciences and technologies, and the immense upheavals in the human condition which these brought, meant that biology and medicine could only move to centre stage somewhat later. Moreover, the intricacies of living structures are such that their deepest secrets could only be revealed after the physical sciences had produced the tools—electron microscopes, radioisotopes and chemical analysers—required for penetrating study. Accordingly, it is only over the last quarter century that the fruits of biological science have jostled their way to the front pages.

In the eye of the storm we find **DNA**. This long but essentially rather simple **molecule** is the key to the puzzle of life. It embodies what each biological **species** looks like, how long it lives, what the limits of its potential are. It specifies in the minutest detail what each plant or animal, and indeed each **cell** in each plant or animal, can do. For this reason DNA has been termed the thread of life; the progressive elucidation of its structure and function have rightly been biology's central preoccupation since 1950. If this is so, why

the unique excitement about DNA over the last twenty-five years? What is so new, so special?

For a quarter of a century between 1950 and 1975, DNA was thought by most scientists to be like a remote dictator within a fortified stronghold—inviolate, sacrosanct, issuing orders but itself still and unchanging. Then came the genetic engineers, who with a speed that was truly breathtaking, changed the image of DNA. They made it accessible to a whole new generation of investigators, unafraid of its big reputation. DNA contains the **genes**, the fundamental units of inheritance, the blueprints for the cell's work. Genetic engineers split DNA open, cut out individual genes, transplanted them into **bacteria** or other cells, reproduced them a billion times. They created hybrids in the test tube unlike anything that three and a half billion years of **evolution** had accomplished. Within less than a decade, it became clear that **genetic engineering** and related technologies represented the biggest single advance in the life sciences this century. Genetic engineering held the key to a deeper understanding of human diseases, including cancer. It offered glittering prizes to industry. It promised to free agriculture from constraining requirements for fertilizers and pesticides. There seemed no limits to what the genetic engineers would dare. The genie was out of the bottle.

Unlike the atomic age, which was born in secrecy during a world war, the DNA age began amidst the fiercest blaze of publicity. An unprecedented act of global self-censorship by the scientific community, which in 1974 placed a brief moratorium on genetic engineering research until potential hazards could be assessed, was predictably misinterpreted by society. Scaremongers abounded, and much of the public debate created more heat than light. In the event, patience and sanity prevailed and the research was resumed in 1975 under stringent safeguards that, with hindsight, proved unnecessarily elaborate. It is to the enduring credit of both scientists and their critics that the legislative framework permitting continued advance relied more on regulatory guidelines than on proscriptions and sanctions. As a result, genetic engineering research has infiltrated virtually every nook and cranny of biomedicine. The DNA industry was born and, as we shall see, irrevocably changed the way that pharmaceutical companies did their work. Philosophers and jurists have discovered a new cause,

and bioethicists constitute a new professional group. Governments have developed various schemes to nurture the **biotechnology** industry, a source of employment and export income. Above all, journalists of both print and electronic media have exploited the new wonder for stories both of 'breakthroughs' and 'cures', and of conjectural hazards and disasters.

Why, then, another book on genetic engineering? What could possibly remain to be said? The need for this book has dawned on us gradually. In the normal course of work as we interact with many segments of society, many of our lay contacts display a lively interest in research. However, we had been so saturated with gaudy press releases on the one hand, and weighty technical tomes on the other, that we had missed a central point about genetic engineering. Those of us within science who have witnessed the birth of this amazing development, those of us who sit on the endless government committees and write the dry technical reports, even those of us who honestly strive to brief young journalists on their first scientific assignment, have all been too close to the problem. We have forgotten how alien the concepts of genes and cells and molecules are to the layperson. We use our own special language, unconsciously slipping in unfamiliar technical terms, and we soon lose even a hard-working listener. Yet it is vitally important that the potential and also the limitations of genetic engineering be made accessible to a wide public, the more so as its central concepts are really simple. Therefore, the aim of this book is to present the essential elements of genetic engineering within a slim volume in a manner requiring no background in biology and for a readership with no technical expertise in the field. The target audience includes decision-makers at many levels: politicians, financiers and industrialists, community leaders, and academics in non-biological fields. We also hope to stimulate a diversity of people from all walks of life interested in informing themselves about a key development which, slowly but surely, will reshape many aspects of their children's lives. Our greatest wish is to stir the interest of the young, for example the school leaver pondering a career, so that the fascination of the field may tempt a few to become its future devotees. It is not possible to talk about science without using some technical terms. We have tried to keep these to a minimum and have provided simple definitions in the glossary. The first uses

of words glossed are given in **bold type** to indicate that they occur in the glossary.

Genetic engineering cannot be intelligently approached without some reference to basic biology. In the next chapter the bare bones of biological organization will be described. Following that, we discuss how genetic engineering works. These two chapters get us over the toughest hurdles; thereafter we deal with practical fruits and social implications of this extraordinary turning point in humanity's affairs. Despite our target of a general audience, the concepts involved in Chapters 2 and 3 are of a more technical nature and may be demanding for readers with a non-scientific background. If a quick scan of them seems formidably daunting to you, we suggest you skip over them and go straight to Chapter 4. This explains the concept of the **genome** and discusses the **human genome project**, one of the most audacious and potentially most rewarding scientific adventures ever essayed. Chapter 5 takes us to the now more familiar ground of how new drugs and products might arise from our new knowledge. This chapter explains how **hormones** and other human **proteins** of use in the treatment of serious diseases can be mass-produced by genetic engineering. Chapter 6 describes how purified genes can help to diagnose hereditary and other diseases, and Chapter 7 goes on to speculate about how, in the future, good genes might be able to be substituted for bad ones right within the body of the patient. We also discuss stem cell therapy and the new developments of **cloning** whole organisms with their awesome implications for the future of our species. Chapter 8 examines some disease problems of the tropical developing countries, with special reference to new vaccines made through genetic engineering. Chapter 9 looks at genetic engineering from an industrialist's viewpoint, and discusses genetically modified organisms and their potential uses in areas such as agriculture, chemistry, mining and waste disposal. The last chapters of the book concentrate on the broader areas of the economics of genetic engineering and some societal issues of the new technology. However, many implications of the new technology have been discussed in Chapters 6, 7 and 9 in particular.

Since the last edition of this book, developments have emphasized the power of recombinant DNA technology and its importance to modern biology. We have seen the molecular study

of genes assume absolute centre stage. There is no branch of biomedical research that has not been profoundly altered by the use of these techniques, and problems that were insoluble a decade ago now routinely yield their secrets. Our understanding of key areas of medicine such as the causes of cancer and of **autoimmune** diseases has been greatly enhanced as a consequence. In this revised edition we cover some of the most exciting developments in basic biology. The discovery of **oncogenes**, genes implicated in the disordered growth characteristic of cancer, and the discovery of **growth factors**, chemical messengers that pass between cells and stimulate growth, are two examples.

A further major development in the last five years has been that this technology has stepped out of the laboratory into the outside world. It is beginning to touch every facet of our lives. Patients are treated with new drugs that were mere laboratory curiosities a short time ago. These proteins, normally present in such small amounts in the body that they could never have been obtained in any other way, are being synthesized and used in routine clinical practice to treat heart disease and other disorders. In the legal arena court cases are being decided on the basis of evidence provided by **genetic fingerprinting**. In commerce, gene companies such as Amgen and Biogen now market products made by recombinant DNA techniques and they are the darlings of the stock exchange. Many food products and additives are produced in increased yield using techniques of biotechnology. New organisms, containing mixtures of genes that as far as we know have never existed before, are in widespread use in agriculture producing substantial amounts of soy bean and corn. We have included sections on these new developments in the book in Chapter 9.

The utilization of these techniques is not without controversy, however. **Transgenic** animals (animals with new genes injected into their cells) have been constructed and we are developing ways to introduce genes into plants and fish. We have allowed limited release of novel micro-organisms into the environment. The technology behind these modified life forms and considerations concerning their release into the world are discussed in Chapter 9. We now have the ability to identify every individual on the basis of their own unique DNA sequences. We will soon have the ability to predict who will be likely to develop heart disease at a young age

and who may be cancer-prone. The individual's right to privacy will run smack up against the demands of insurance companies, business and government. Such far-reaching issues require new safeguards to protect the rights of individuals while allowing us to reap the benefits of these techniques. The technology of genetic engineering, like all powerful tools, can be used for good or abused and it is society as a whole that will decide how it is to be applied. We believe that an informed public is a crucial prerequisite to ensuring the technology is used appropriately and in a humane manner.