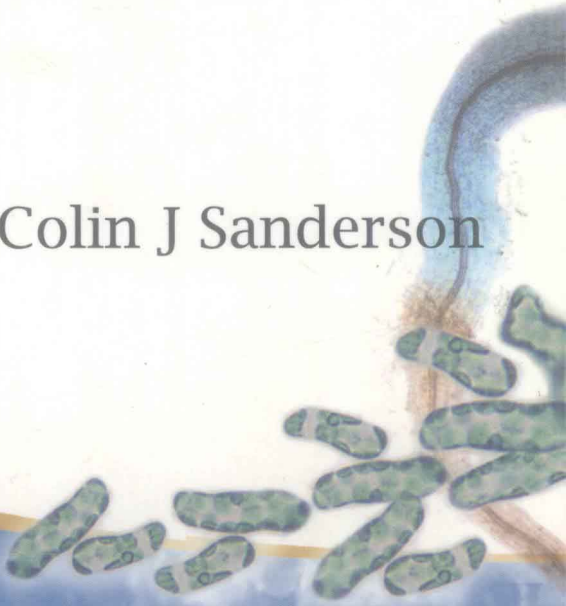
Understanding GENES and GMOs



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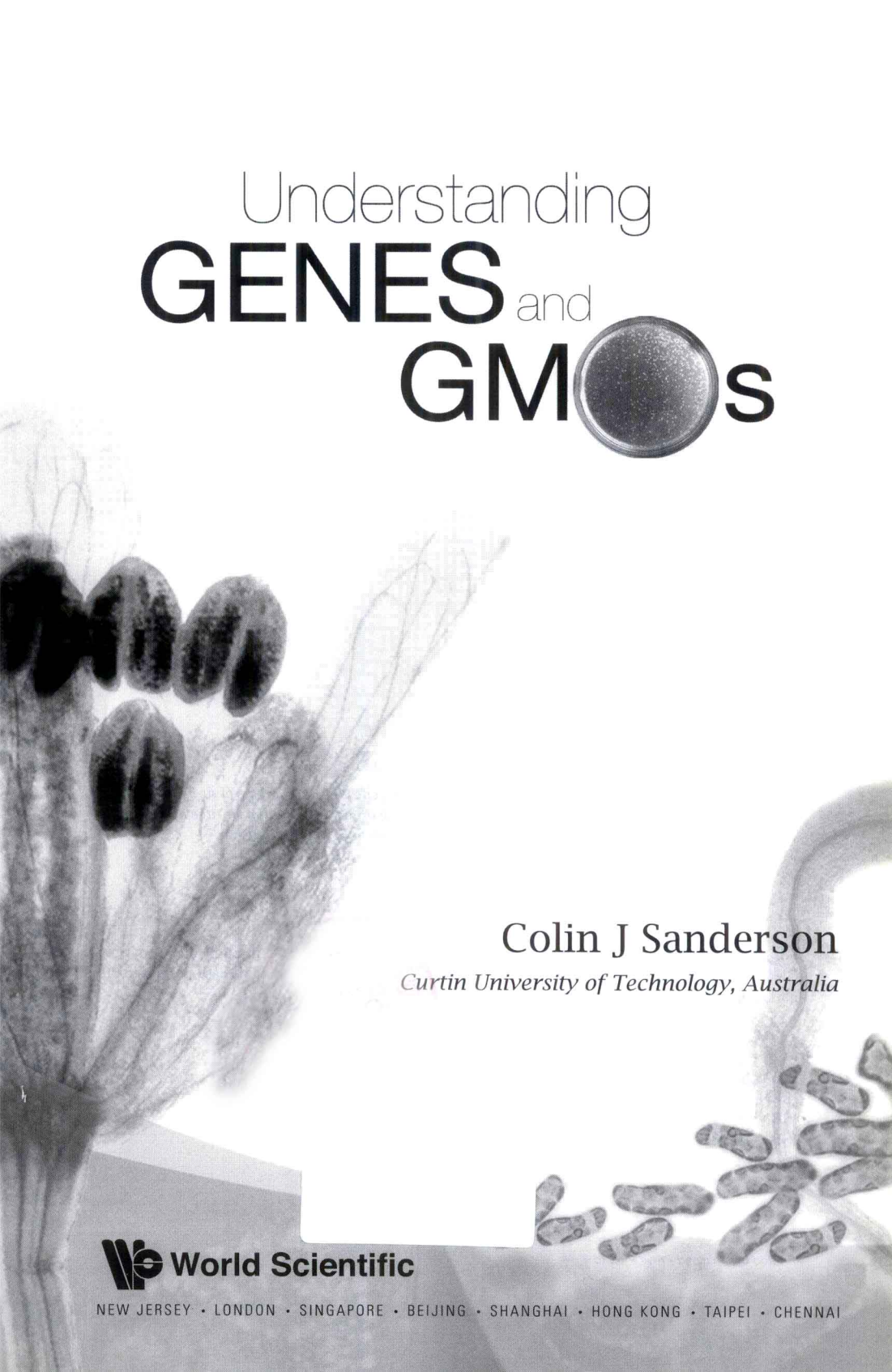

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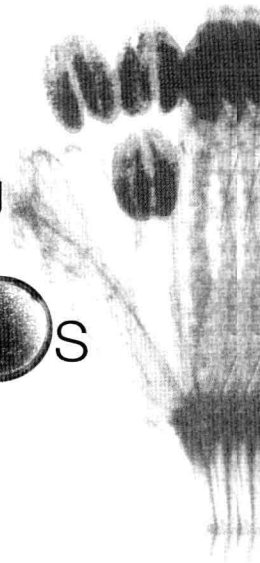

To

Pamela Elizabeth

&

Zoë Beth

Two strong and courageous women who have been an important influence in my life.

Preface

How to read this book.

My aim is to give a general introduction to genetics for a wide readership. This will mean different things to different readers. I sometimes give detail or use terminology for the more specialist readers, which others will not need to know about. The first two chapters are basic biology, chapters 3 to 7 describe the technology, and chapters 8 to 13 contain the more detailed discussions.

For readers with little background in biology or genetics, it is important to get a basic understanding about genes and how they work. However, some of my readers found parts of the technical chapters heavy going. If you have the same problem, scan read the hard parts so you know what is covered, pick up the important things in "Take-Away Message" and move on. I cross-reference the basic techniques in the later chapters, so you can come back to them to refresh your memory.

Some readers will have had little exposure to the jargon so to help separate the wheat from the chaff, words which I think you need to know about will be in ***bold italics.*** Conversely, jargon that is not in ***bold-italics*** is not necessary for a general understanding of the book or of genetic engineering. I do this because it is better to define and use the accepted scientific word than to invent yet another word for the same thing. Sometimes a full explanation comes a bit later than the first use of a word, so if a new word is all gobbledegook to you, hang in there because the explanation will come. Keep a good modern dictionary, at least 5cm thick beside you. It will contain a surprising amount of scientific jargon.

For a quick reference the glossary has definitions of most of the jargon used in this book.

I am often referring to things that come in very large numbers. Don't take these numbers too literally as it makes little difference to a general understanding whether it is millions, billions or trillions. It's a good idea to be clear about scientific notation where numbers are expressed to the power of 10. Thus 1,000 is written 10^3 (think of it as 1 and three zeros) and conversely 1/1000 is written 10^{-3} (thus 1 millimetre is 10^{-3} metres). A million is 10^6. A billion is a thousand million (10^9) and a trillion is a thousand billion (10^{12}). For evolutionary time I use 1,000 years ago (kya) or a million years ago (mya). The magnification of images is indicated by X (100X, indicates a magnification of 100 times).

A few years ago it was estimated and generally accepted that the human genome encoded 70-80,000 genes. The Human Genome Project reduced this to about 30,000. More recently many of these genes have been found to be inactive relics of previously active genes and the number of active genes estimated at about 21,000. To keep things simple, I use the round figure of 20,000.

Acknowledgements.

I wish to thank the following who provided valuable feedback on the drafts of the book: Don Bradshaw, Brendan Burns, Belinda Dally, Teresa Espanol, David Giles, Margot Gloger, Christine Harrison, Jo Hummerston, Tom Saggers, Jeanette Trent.

I have minimized the number of references on the basis that few people will have the time or the library access to look them up. I acknowledge people, publications or websites where they have been a major source of my information and where possible have chosen recent papers which will give the more specialist reader an introduction to the scientific literature. In the index I list only pages that contain an explanation about a word, not every use of the word. I only index the first page of longer explanations, so always check the following page as well.

It will also be clear that many aspects of genetics I write about, I do so with no personal research experience. I have depended heavily on

published material, as well as help from scientists with special expertise. I acknowledge these specialist sources in the text. I have used many graphic images provided by other scientists: diagrams and photographs without acknowledgement are my own work. Where necessary for clarity, I have enhanced graphic images using graphics software, probably sometimes beyond what would be acceptable in a scientific paper.

The Protein Data Bank (PDB, *www.pdb.org*) provided the three dimensional structures. The database is run by the publicly funded Research Collaboratory for Structural Bioinformatics. I give the PDB number for each structure, so anybody can go to the website and look up the full references, and play with the structures. There are links to free software for visualising the molecules. I have mainly used Protein Explorer by Eric Martz (*http://proteinexplorer.org/*)

Valuable sources of information.

The internet is an amazing resource, but search engines look for words and cannot evaluate the information. You will get thousands of hits, and it is sometimes difficult to sort out the gems from the rubbish. Sometimes the very thing you are looking for comes up in the first page of hits, but more often it's a matter of sorting through a large amount of irrelevant or misleading information. The important thing is to put in a combination of key words to restrict the hits so you get the ones you want on the first few pages. For example, if you doubt my statements on the effect of banning DDT on malaria, type in "ddt malaria" and you will find a lot of good information on the first few pages of hits. Many of the large universities and government agencies have good information on their websites. "Encyclopedia Britannica" and "Wikipedia" can be useful, but are sometimes unreliable or incomplete as anybody can contribute information.

Searching for names can be problematical. I found I had to put in "Colin Sanderson", "CJ Sanderson", and "C.J. Sanderson" to get a cross section of my own work. Don't forget the " ", otherwise you get all the other Colin's as well as all the other Sanderson's.

The main problem for the non-expert is to decide which information is misleading, and to find the gems that exist on a server somewhere. With all the available information, my role has been to edit, interpret, and present it in a readable form. For me researching this book has been a steep and very rewarding learning experience that has taken me far from my own medical research. Here are some of my main sources of information:

The AgBioWorld (*www.agbioworld.org*) a non-profit Foundation based in Alabama, USA. They provide regular science-based information on agricultural biotechnology via a free email newsletter.

Bioscope (*www.bio-scope.org*), an information group based in Germany, collecting and relaying news and press items from around the world.

Food and Agriculture Organisation (FAO, *www.fao.org*) publishes a wide variety of information and hosts online discussion groups on many topics important to food and agriculture.

International Service for the Acquisition of Agra-biotech Applications (ISAAA, *www.isaaa.org*). Based in the Philippines, it provides annual global reviews of commercialised transgenic crops.

The Scientist (*www.the-scientist.com*), started as a new generation free access scientific journal. Unfortunately access to some material requires a paid registration.

Affiliations

I abbreviate my own affiliations: I refer to myself as CJS; WA, Western Australia; CUT, Curtin University of Technology (Perth, WA); UWA, University of Western Australia (Perth, WA); NIMR, The National Institute for Medical Research (Mill Hill, London).

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Contents

Chapter 1

Getting Started

If politics is the art of the possible, research is surely the art of the soluble. Both are immensely practical-minded affairs.

The human mind treats a new idea the same way the body treats a strange protein; it rejects it.

Peter B Medawar, *The Art of the Soluble (1967)*

Everybody wants a better life for themselves and following generations. It is not difficult to agree on the necessity to improve the quality and availability of health care; that many people do not have enough to eat; our environment is a mess; that production of high quality food is important. Can gene technology help with any of these problems, or will it make things worse? Peter Medawar was awarded the Nobel Prize for his work on the rejection of foreign proteins by the immune system. He points out that people treat new ideas in the same way. Thus, the responsibility to change public opinion rests with people who understand the technology. This is a daunting task but there is an urgent need for everybody to have a better understanding of this new technology. Genetics is telling us more about evolution, the migration of ancient people across the globe and providing a new level of accuracy in forensic applications. We now face the prospect of treating genetic diseases by gene therapy. What are the risks to the individual and future generations? Farmers, for centuries, have been very good at breeding to improve their crops and stock and have done this without a detailed knowledge of how genes work. The advent of genetically modified plants has put them in a dilemma. Do they grow them or not? If they do, will it threaten their environment? Will they be able to sell the product? I will not answer all these questions because there is not always a simple answer, but an

understanding of the basics of genes and genetic engineering will help in these decisions.

The two quotes from Peter Medawar give an indication of his writing, which has been very influential amongst my generation of scientists. His simple clear prose changed the way many of us think about science. Although the perceptions have remained the same, things have moved on since Medawar was writing and we start this book in the midst of a genomics revolution. This is a coordinated effort to unravel the details of all the genes in the genome of different microbes, plants and animals. A massive volume of information is accumulating and spawning new words with the suffix *-omics*. This information is being assembled in super computers with information about proteins (proteomics) and metabolic pathways (metabolomics) and many other aspects of life in what the boffins call *systems biology*. This aims to bring together all aspects of life into an integrated overview, which can be interrogated to provide a basis for modification by drugs, chemicals or management to improve the quality of life. The science is exciting and challenging, and is indeed an immensely practical minded affair. Medawar would have loved to be involved in this new technology and the public debate, which surrounds it.

Prince Charles, future King and head of the Anglican Church with a corresponding large influence on public opinion in the UK, and the owner of a large company producing organic food, said only God should modify genes. It is hardly credible that he would seek to stop research to understand how genes work, which requires the production of a very large number of modified genes. Would he argue against modified genes, which can improve the life of children with hereditary diseases? After all, his family in an attempt to keep a pure "royal" lineage have had too many consanguineous marriages resulting in a higher frequency of genetic diseases. What about genetic modifications that can help clean up industrial pollution? Genes are continually being changed or ***mutated***, by random errors in the normal copying of genes from one generation to the next. Mind you, it is not a big deal, mutations are very rare and only mutations in germ cell DNA is passed on to the next generation. This provides a basis for natural selection in evolution, and for the breeding of new crops and domestic animals. This natural change was not fast

enough for plant and animal breeders and so, before genetic engineering, genes were modified by exposing organisms to chemicals or irradiation. This increased dramatically the rate of ***mutation***, and new traits appeared more frequently. Any useful traits could be selected by traditional breeding, but of course, there would be many mutations and traditional breeding would not separate completely the desirable from the undesirable. Genetic engineering allows this to be carried out in a targeted and precise manner, which means organisms can be modified in a shorter period of time and with less likelihood of unwanted genetic changes.

We have to face the fact that, like Prince Charles, many politicians and activists have not had an education in science, and yet are involved in making or negating policy. The Prince visited the Institute where I worked in Perth. Instead of trying to learn from the group of medical experts around the table, he insisted on pushing the value of "alternative medicine". It did not go over well with the group of clinical scientists who spend their lives assessing new treatments in controlled clinical trials. None of us have a problem with "traditional medicine" which has given the world a number of important chemicals such as the antimalarial drug quinine and the insecticide pyrethrum, and there are undoubtedly many more to come. The problem is that very few have been submitted to proper clinical trial. I am astonished that there are many people who worry about the health effects of genetically modified plants, which are submitted to detailed safety analysis, but will include alternative medicines in their diets that have not undergone any testing.

Coming from a medical research background, my interest in genes was widened when I became the owner of a small farm near Albany on the south coast of WA. I joined a small group called the Rainbow Coast Commercial Horticulturists. While the name is reminiscent of something from a Gilbert and Sullivan operetta ('rainbow coast' refers to the beautiful climate of this region), the group is serious and reflects the way farmers across the world get together to share experiences. This group includes a cross section of farmers from organic (organicos) to high tech (technicos). My own farming efforts in viticulture, and visits to farms where families earn a living producing food, brought home to me that most consumers have little idea how food is produced, and how precarious is the production of this most important product. It also taught me a

little about the balance between the environment and food production and stimulated my interest in sustainable agriculture and the relevance of GM plants. I will argue that the sustainability credentials of certified organic farmers is somewhat exaggerated. It is a pity they have not encompassed GM plants, many of which will surpass their best intentions of achieving sustainable farming. Unfortunately, the organic movement provides much of the anti-GM activism and as such, I think it is important to scrutinise their claims and to counter their arguments, which, especially in relation to GMOs, are not based on balanced information.

The final decision to write this book came when I attended a high profile biotechnology conference in the USA. A large number of anti-biotech demonstrators were expected and an army of police were there with anti-riot gear and automatic weapons. They far out-numbered the demonstrators who were herded into a compound with a high fence, where they sat under a large black balloon with GENE painted on it and sang songs and shouted slogans. In the face of this intimidation, I felt sympathy towards them. They want what we all want: to make the world a better place for our kids. Unfortunately, for them, the balloon was a bit simplistic and their slogans made little impact. Sadly, many people have opinions, but little knowledge, on everything from genes to nuclear power.

I have been close to the coalface of genes and genetic engineering in medical research, and have seen the technology evolving at a rapidly increasing pace. It's hard to keep up with, even when directly involved in research. This technology is impinging on all aspects of our lives and is too important to be left to professional lobbyists and activists. We all need a basic understanding, and it is not difficult. I am an enthusiast for the potential of genetic engineering. I regard it as another step in the long history of human endeavour, but like many technical developments has the potential to be used both wisely and unwisely. Everybody who wants to have an input into the debate needs to be able to present an informed argument. Slogans are not enough. If at the end of the book you are against genetic engineering, but can admit to a better understanding of the issues, then I have achieved my aim.