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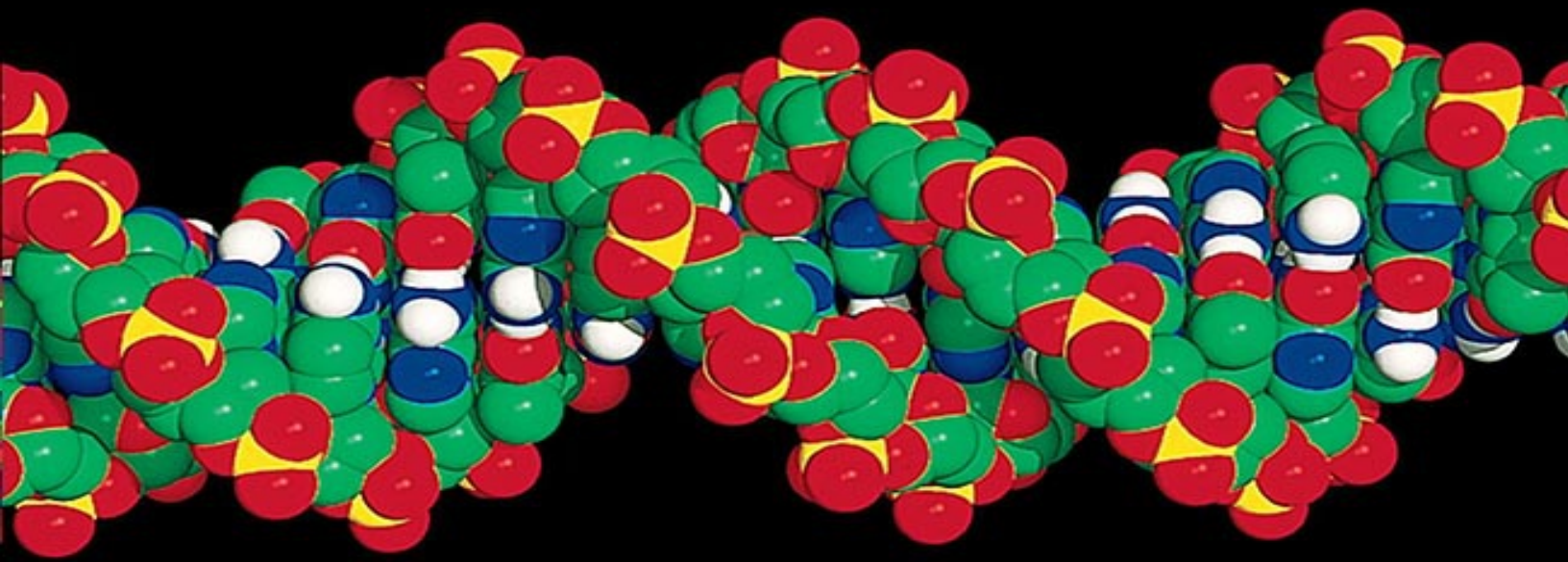
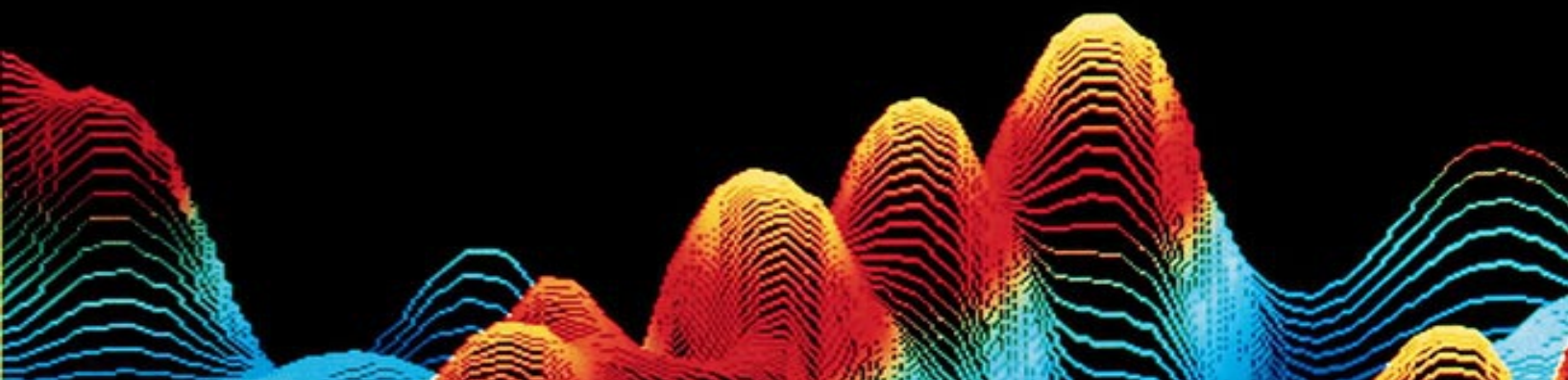
GENOME



THE AUTOBIOGRAPHY OF A SPECIES IN 23 CHAPTERS

MATT RIDLEY

AUTHOR OF *THE RATIONAL OPTIMIST*



GENOME

THE AUTOBIOGRAPHY OF A SPECIES IN 23 CHAPTERS

MATT RIDLEY

HARPER PERENNIAL

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Preface

When I began to write this book, the human genome was still a largely unexplored landscape. Some eight thousand human genes had already been roughly located, and I mention a few of the most interesting ones in the book, but the rapid acceleration towards the reading of the entire genome still lay in the future. Now, only a little over a year later, that gargantuan task is complete. Scientists all over the world have deciphered the entire human genome, written down its contents and distributed them on the Internet to all who wish to read them. You can now download from the Internet the near-complete instructions for how to build and run a human body.

The revolution was swift. In early 1998, the publicly funded scientists who made up the Human Genome Project still predicted that they would take another seven years at least to read the entire human genome, and they had barely read ten per cent of it by then. Then, suddenly a joker was thrown on the table. Craig Venter, a flamboyant and impatient scientist now working in the private sector, announced that he was forming a company and would do the job by 2001 for a fraction of the cost: less than £200 million.

Venter had made such threats before, and he had a habit of delivering results. In 1991, he had invented a quick way to find human genes when everybody said it could not be done. Then in 1995, he received a withering reply to his request for a government grant to map a whole bacterial genome using a new ‘shotgun’ technique. The technique would never work, said the officials. The letter arrived when the job was already almost complete.

So it would be a foolish person who bet against Venter a third time. The race was on. The public project was reorganised and refocused; extra funding was poured in and a goal was set to complete a first draft of the entire genome in June 2000. Venter soon set his sights on the same deadline.

On June 26, 2000, President Bill Clinton in the White House and Tony

Blair in Downing Street simultaneously announced that the rough draft was complete. This is therefore an astonishing moment in human history: the first time in the story of life on earth that a species has read its own recipe. For the human genome is nothing less than the instructions for how to build and run a human body. Hidden within it, as I have tried to show in the book, lie thousands of genes and millions of other sequences that constitute a treasure trove of philosophical secrets. Most of the research into human genes is driven by the urgent need to find cures for both inherited diseases and the more common diseases like cancer and heart disease, whose origins are abetted or enhanced by genes. A cure for cancer would, we now know, be virtually impossible if we did not understand the role of cancer genes and cancer-suppressing genes in the progress of tumours.

Yet there is much more to genetics than medicine. As I have tried to show, the genome contains secret messages from both the distant and the recent past — from when we were single-celled creatures and from when we took up cultural habits such as dairy farming. It also contains clues to ancient philosophical conundrums, not least the question of whether and how our actions are determined and what is this curious sensation called free will.

The completion of the genome project has done little to change this picture, but it is gradually adding more examples to the themes I explore in this book. As I wrote, I was conscious that the world was rapidly changing; genetic knowledge was exploding all about me in the scientific literature. I could do no more than capture the first glimpse of some of these exciting debates. But many great insights still lie in the future. Science, I believe, is the search for new mysteries rather than the cataloguing of old facts. I have little doubt that there will be astounding surprises in store for us over the next few years. We are realising for the first time just how little we know about ourselves.

What I could not have foreseen is how dramatically the debate over genetics would have invaded the public media. With controversy raging over genetically modified organisms and with speculation growing about cloning and genetic engineering, the public is demanding the right to be heard. Quite correctly it does not want these decisions left only to the experts. But most geneticists are too busy mining nuggets of intellectual gold from the laboratory to give up their time to explaining their science to the public. So it falls to commentators like me to try to translate the arcane stories of genes

into something more like entertainment than education.

I am an optimist. As will be clear from this book, I think knowledge is a blessing, not a curse. This is especially true in the case of genetic knowledge. To understand the molecular nature of cancer for the first time, to diagnose and prevent Alzheimer’s disease, to discover the secrets of human history, to reconstruct the organisms that populated the pre-Cambrian seas — these seem to me to be immense blessings. It is true that genetics also brings the threat of new dangers - unequal insurance premiums, new forms of germ warfare, unanticipated side effects of genetic engineering - but most of these are either easily dealt with or extremely far-fetched. So I cannot subscribe to the fashionable pessimism about science nor can I warm to the idea of a world that turns its back on science and the unending assault on new forms of ignorance.

Introduction

The human genome - the complete set of human genes - comes packaged in twenty-three separate pairs of chromosomes. Of these, twenty-two pairs are numbered in approximate order of size, from the largest (number i) to the smallest (number 22), while the remaining pair consists of the sex chromosomes: two large X chromosomes in women, one X and one small Y in men. In size, the X comes between chromosomes 7 and 8, whereas the Y is the smallest.

The number 23 is of no significance. Many species, including our closest relatives among the apes, have more chromosomes, and many have fewer. Nor do genes of similar function and type necessarily cluster on the same chromosome. So a few years ago, leaning over a lap-top computer talking to David Haig, an evolutionary biologist, I was slightly startled to hear him say that chromosome 19 was his favourite chromosome. It has all sorts of mischievous genes on it, he explained. I had never thought of chromosomes as having personalities before. They are, after all, merely arbitrary collections of genes. But Haig's chance remark planted an idea in my head and I could not get it out. Why not try to tell the unfolding story of the human genome, now being discovered in detail for the first time, chromosome by chromosome, by picking a gene from each chromosome to fit the story as it is told? Primo Levi did something similar with the periodic table of the elements in his autobiographical short stories. He related each chapter of his life to an element, one that he had had some contact with during the period he was describing.

I began to think about the human genome as a sort of autobiography in its own right - a record, written in 'genetish', of all the vicissitudes and inventions that had characterised the history of our species and its ancestors since the very dawn of life. There are genes that have not changed much

since the very first single-celled creatures populated the primeval ooze. There are genes that were developed when our ancestors were worm-like. There are genes that must have first appeared when our ancestors were fish. There are genes that exist in their present form only because of recent epidemics of disease. And there are genes that can be used to write the history of human migrations in the last few thousand years. From four billion years ago to just a few hundred years ago, the genome has been a sort of autobiography for our species, recording the important events as they occurred.

I wrote down a list of die twenty-three chromosomes and next to each I began to list themes of human nature. Gradually and painstakingly I began to find genes that were emblematic of my story. There were frequent frustrations when I could not find a suitable gene, or when I found the ideal gene and it was on the wrong chromosome. There was the puzzle of what to do with the X and Y chromosomes, which I have placed after chromosome 7, as befits the X chromosome's size. You now know why the last chapter of a book that boasts in its subtide that it has twenty-three chapters is called Chapter 22.

It is, at first glance, a most misleading thing that I have done. I may seem to be implying that chromosome 1 came first, which it did not. I may seem to imply that chromosome 11 is exclusively concerned with human personality, which it is not. There are probably 30,000—80,000 genes in the human genome and I could not tell you about all of them, partly because fewer than 8,000 have been found (though the number is growing by several hundred a month) and partly because the great majority of them are tedious biochemical middle managers.

But what I can give you is a coherent glimpse of the whole: a whistle-stop tour of some of the more interesting sites in the genome and what they tell us about ourselves. For we, this lucky generation, will be the first to read the book that is the genome. Being able to read the genome will tell us more about our origins, our evolution, our nature and our minds than all the efforts of science to date. It will revolutionise anthropology, psychology, medicine, palaeontology and virtually every other science. This is not to claim that everything is in the genes, or that genes matter more than other factors. Clearly, they do not. But they matter, that is for sure.

This is not a book about the Human Genome Project — about mapping and sequencing techniques — but a book about what that project has found.

On June 26, 2000, scientists announced they had completed a rough draft of the complete human genome. In just a few short years we will have moved from knowing almost nothing about our genes to knowing everything. I genuinely believe that we are living through the greatest intellectual moment in history. Bar none. Some may protest that the human being is more than his genes. I do not deny it. There is much, much more to each of us than a genetic code. But until now human genes were an almost complete mystery. We will be the first generation to penetrate that mystery. We stand on the brink of great new answers but, even more, of great new questions. This is what I have tried to convey in this book.

PRIMER

The second part of this preface is intended as a brief primer, a sort of narrative glossary, on the subject of genes and how they work. I hope that readers will glance through it at the outset and return to it at intervals if they come across technical terms that are not explained. Modern genetics is a formidable thicket of jargon. I have tried hard to use the bare minimum of technical terms in this book, but some are unavoidable.

The human body contains approximately ioo trillion (million million) CELLS, most of which are less than a tenth of a millimetre across. Inside each cell there is a black blob called a NUCLEUS. Inside the nucleus are two complete sets of the human GENOME (except in egg cells and sperm cells, which have one copy each, and red blood cells, which have none). One set of the genome came from the mother and one from the father. In principle, each set includes the same 30,000-80,000 GENES on the same twenty-three CHROMOSOMES. In practice, there are often small and subtle differences between the paternal and maternal versions of each gene, differences that account for blue eyes or brown, for example. When we breed, we pass on one complete set, but only after swapping bits of the paternal and maternal chromosomes in a procedure known as RECOMBINATION.

Imagine that the genome is a book.

here are twenty-three chapters, called CHROMOSOMES.
ach chapter contains several thousand stories, called GENES.