Programmed for defence

Waging the immunological campaign against the gamut of wily pathogens.

The War Within Us: Everyman's Guide to Infection and Immunity
by Cedric Mims
Academic: 2000. 228 pp. $39.95, £24.95

Fred Rosen

On the eve of the presidential election, *The New York Times* found some small space in its editorial columns to praise the Bill & Melinda Gates Foundation for its attempts to lessen the burden of infectious diseases throughout the world. With US$21 billion in assets, the foundation could easily have distributed computers rather than vaccines to the remotest parts of the developing world. But as Bill Gates said: "The mothers are going to walk right up to that computer and say, 'My children are dying, what can you do?'. They're not going to sit there and, like, browse eBay or something." It was as if Gates had just finished reading Cedric Mims' *The War Within Us*.

Mims has written an attractive and brief overview of the current understanding of immunity and infectious disease. The book is clearly intended for educated lay readers with a minimal background in science. The first third of the book is a reasonably accurate and simple discourse on the components of the immune system and how they work. Although rendered in plain English, it is not oversimplified to the point of introducing gross inaccuracies. The remainder of the text discusses various infectious diseases and the wily pathogens that cause them. Although the way in which immunological specificity is generated must be among the greatest wonders of the natural world, it always evokes striking images of war, and attack and defence, and a whole vocabulary more appropriate to the Pentagon or any other government war ministry. Mims has totally succumbed to this type of imagery. Perhaps he feels it makes the contents more dramatic, and maybe it does.

Scattered throughout the text the reader will find boxed vignettes of fascinating bits of history: how the cook who became known as Typhoid Mary, and who was herself immune to the typhoid bacillus, infected a long succession of her unwitting employers; how Carelton Gajdusek brazenly entered the New Guinea highlands and discovered kuru; how Ignasz Semmelweis, who introduced antisepsis into medical practice, died in an insane asylum of the very disease he spent his life trying to eradicate; and how the physician John Snow traced the source of a London cholera outbreak to the Broad Street water pump.

Those of us who grew up before the Second World War have vivid memories of the summer terrors brought on by polio epidemics, of relatives and neighbours dying of tuberculosis, of the ravages of syphilis among the gentry, and of children with whooping cough who were obliged by the health department to wear red armbands. Mims reveals in the course of this book his own medical history, from his mother's death from puerperal sepsis to the time he contracted rift valley fever in the laboratory. His interest in infection and immunity is, it seems, well founded.

Life in all its vulnerability: Hans Baldung's *The Three Ages of Man and Death.*

ARCHIVO ICONOGRAPHICO/CORBIS

Rather disappointingly, no more than two pages of the book are devoted to a discussion of AIDS. Targeted as it is to a lay audience, the book might have been a good vehicle for saying more about the subject. Nonetheless, the reader is left with a broad understanding of the insidious destructiveness of infectious diseases, and also, no doubt, with a new appreciation of the Gates Foundation's efforts. ■

Fred Rosen is at the Center for Blood Research, Warren Alpert Building, 200 Longwood Avenue, Boston, Massachusetts 02115, USA.

Gene games of the future

Engineering the Human Germline: An Exploration of the Science and Ethics of Altering the Genes We Pass to Our Children
edited by Gregory Stock & John Campbell
Oxford University Press: 2000. 169 pp. £19.95, $29.95

Veronica van Heyningen

The relegation of sex from being procreational to purely recreational may be premature, but Gregory Stock, one of the editors of this volume, believes that the production of designer babies will eventually take over from normal reproduction.

Altering the human genome in a permanently heritable manner (germline gene therapy) is highly controversial, and in many countries it is prohibited. As with most controversial subjects, though, much can be gained from a thorough discussion of the possible applications, both now and, more speculatively, in the future. This volume is the record of a symposium held at the University of California at Los Angeles in March 1998. It was hosted by Stock, director of the university's Program on Medicine, Technology and Society, and his fellow editor John Campbell, who is professor of neurobiology. The participants, mostly drawn from US academic institutions, fall into three categories: eminent practising scientists; panellists, including James Watson, the co-discoverer of the structure of DNA; and commentators — scientists, ethicists and theologians.

The book paints a futuristic picture of the 'practical aspects' of genome manipulation. Engineering proposals include the use of artificial chromosomes possessing multiple 'docking' sites for introducing several desirable genes simultaneously into recipient cells. Sophisticated chromosomal vectors may be available within a decade. These could, for example, deliver resistance-conferring anti-HIV RNA to helper T cells of

the immune system, which are susceptible to attack by HIV. One unanswered question is how the unpaired artificial chromosome will behave at meiosis, when maternal and paternal chromosomes pair up before separation.

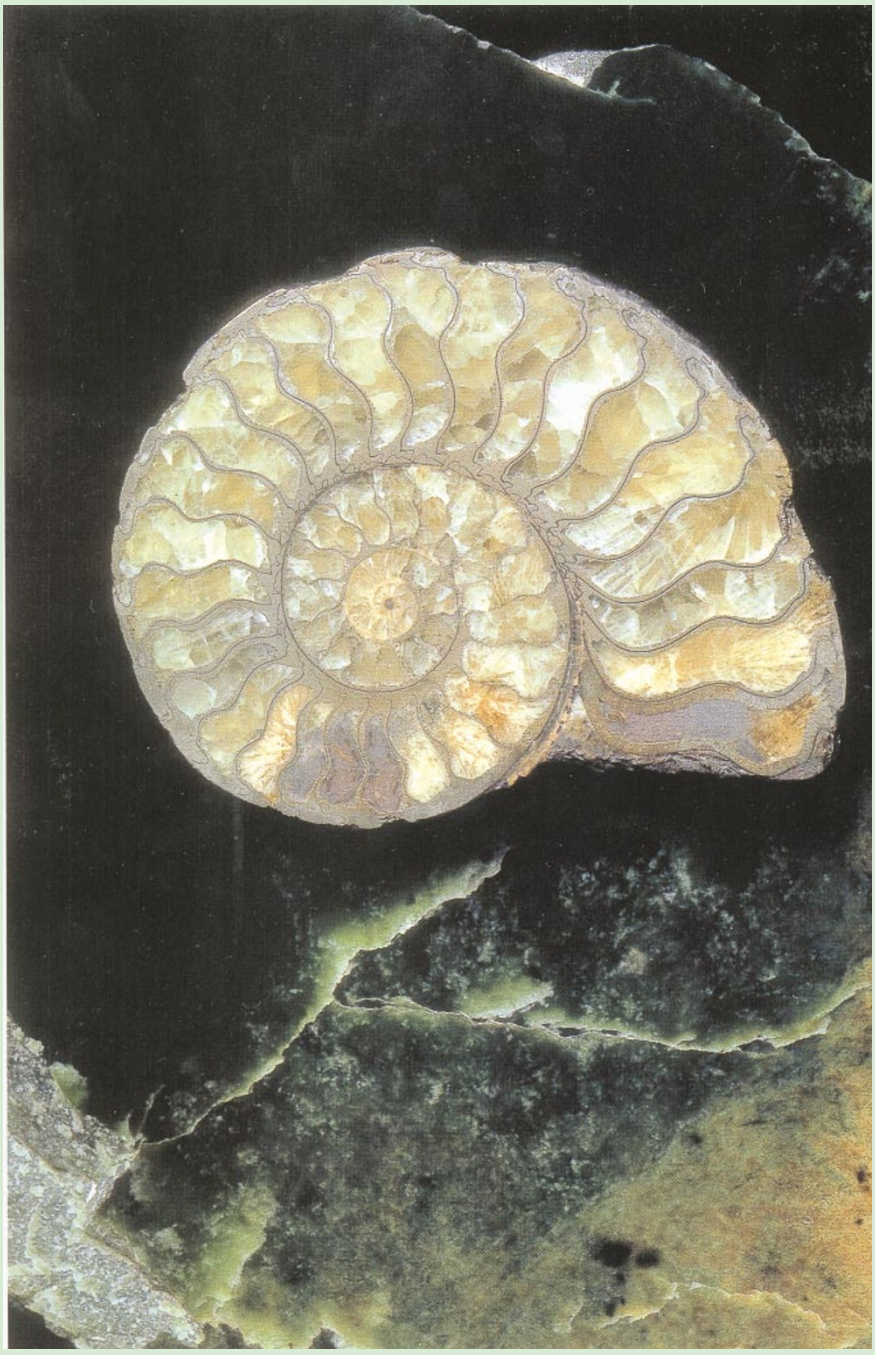
Another suggested application of germline gene therapy is the prevention of prostate or breast cancer. According to this stratagem, a toxin gene would be inserted which would be active only in certain tissues and would be expressed only in response to a specific external trigger should the tissue turn cancerous. Similar schemes are envisaged for preventing cell death in neurodegenerative diseases — once the protective genes have been defined. The resident gene would have to be silenced to ensure the correct 'dosage' and to prevent any interference when the inserted gene was turned on — a difficult molecular control task. But, assuming that such technology can be implemented, there is the problem of how we would select individuals for prophylactic engineering that would be carried out decades before the disease developed.

Lee Hood predicts that gene manipulation will be used to 'enhance' desirable traits such as emotional stability, intelligence and longevity, once we conquer the biology sufficiently to understand how these complex traits are controlled. But this may take 50 years. That gives us time to assess whether we can alter gene regulation with the degree of fine control required in these cases. Much of the technology for manipulating DNA already works in model systems, although there have been very few reports of changes to specific nucleotides — the building blocks of genes — and certainly not simultaneously at multiple gene positions as envisaged for engineering aimed at human enhancement.

Because we are starting to identify genes that affect ageing, it has been suggested that we might be able to prevent ageing by delivering a cocktail of beneficial genes using artificial chromosomes. However, not all participants at the symposium were keen to extend their children's lifespan, since quality of life is perceived to be more important than its duration. And there was some concern about the changes in population dynamics that increased longevity would create.

Jim Watson's view that no novel ethical dilemmas are raised by the concept of gene therapy on the germ line — the set of genes that are passed on to the next generation — is being taken up by some. They believe that the germ line is not particularly sacrosanct; if people think they can safely improve it using new technologies they should be allowed to do so. Watson is particularly eloquent about the moral imperative of seizing any opportunity to redress the genetic inequalities evident in all populations. However, only one or two participants mentioned the tremendous economic costs of such procedures. These would inevitably reinforce and exacerbate the inequalities that already plague us — or, more precisely, that plague the United States, since most of the discussion was centred on the free enterprise, no-federal-interference North American system. The predilection for state regulation in European countries is seen as undue squeamishness which hampers the development of robust, affordable new technology.

Although it seems that the ethical problems raised by germline gene therapy can be dealt with in our current moral framework, as a geneticist I feel strongly that the technological difficulties of safe but



Scientifically speaking

Crossing Over: Where Art and Science Meet **(Crown, $27.50) is a collection of essays by Stephen Jay Gould and photographs by Rosamund Wolff Purcell which aims to present science and art in conversation. In this context, a gibbon and Fred Astaire — "brothers under the hair" — are juxtaposed, and a tin toy illustrates the role of bilateral symmetry in creating complexity. The fossil ammonite shown above, cut, polished and set against a slab of jade, is a symbol of the arbitrariness of extinction and survival — ammonites survived two major mass extinctions, only to succumb to the catastrophe that obliterated the dinosaurs.**

effective intervention in the genome have been underestimated. Complications such as genetic control elements that act over a long distance, and overlapping gene domains, make clean genomic intervention difficult. The use of model systems and molecular analysis of human disease is giving us insight into the complexities of gene regulatory mechanisms, and it seems premature to tinker with many of these delicate systems. The amazing thing about mammalian development is not that it sometimes goes wrong, but that it ever succeeds. ■

Veronica van Heyningen is in the MRC Human Genetics Unit, Western General Hospital, Edinburgh EH4 2XU, UK.

Extremophiles in the raw

The Surprising Archaea: Discovering Another Domain of Life
by John L. Howland
Oxford University Press: 2000. 214 pp. £19.95, $29.95

P. G. Willmer

Life just keeps on multiplying. When we were very young there were Animals and Plants, which Carolus Linnaeus happily confirmed for us, but which grew into three 'kingdoms' when we had to add on the unicellular things. At school we learned to recognize that unicells came in eukaryotic and prokaryotic versions, those respectively with or without their DNA packaged in a nucleus. A little later, and we had barely learned to love Lynn Margulis' definitive five kingdoms when the molecular lobby started to tell us that the two 'simplest' of these were each in themselves multiples of many kinds of unicellular life-forms. Now the evidence of molecular biologists is forcing us to recognize that not only can life be categorized into five, or even more, kingdoms, but also according to a parallel system of three 'domains' (Eukaryota, Bacteria and Archaea). John Howland's book takes us on a tour of the third domain, the Archaea. Prokaryotic, but not bacterial, they pursue their peculiar lifestyles in the more extreme environments of Earth, as they may have done for perhaps 3.5 billion years.

This biography of their discovery, and the gradual revelation of their unique biochemistry and adaptability, tells a fascinating story. The 'Surprising' of the title hardly does them justice; these creatures are genuinely amazing, and we all need to know more about them. This short book works as an introduction, but it could have been so much better if its target audience had been more carefully defined, without the jumps from chatty informality (reflected in sub-headings) to stilted academic prose. Some strange choices have been made about what needs careful explaining for the general reader and what is assumed knowledge, while biologists will find the background excessive and the repetition irritating. And instructions on how to obtain archaeal cultures are surely pointless for anyone.

Above all, the book badly needs improved illustration. The few figures are mainly of technical points; photographs don't appear until 80 pages in, and the quality is then so poor as to make them almost useless. The Archaea may not be very photogenic, but surely line drawings would give us a picture image to hang our thoughts around. Descriptions just won't do, unless they are brilliantly written; here, the narrations of the weird archaean cell structures, and their modes of division, are sometimes quite impossible to figure out.

The crucial question for me was how the Archaea differ from the other two domains. The key answer lies with molecular phylogeny; comparative ribosomal RNA analyses put them quite separate from Eubacteria — the other prokaryotes — and the eukaryotes (perhaps nearer the latter). But we are not told about the other key features of Archaea until the fourth chapter, and even then it is easy to get lost; I had to struggle to assemble my own list of what makes these organisms different. This wasn't helped by an unusually high error rate in text and captions; most are trivial and obvious, but when we are told that archaeal lipids contain "either" bonds instead of "ether" bonds, it only adds to the confusion. (And while we are quibbling, only genera and species should be italicized; here, the domains and sometimes the phyla get italics, perpetuating the muddle.)

The book comes into its own, though, in taking us through the breathtaking range of lifestyles and metabolisms of the Archaea. They are the real extremophiles — living in soda and salt lakes (where they pump chloride and nitrate out across their unique — sometimes purple — version of the cell membrane); in anoxic muds, animal guts and the rocky pillars of deep-sea vents (where they metabolize sulphides and release methane to compound greenhouse warming); and in hot springs in excess of 90 °C (where they manage to keep proteins and membranes functioning against all precedent). One species lives, bizarrely, only in the hot, deep wastes of coal mines, which can have only existed as a habitat for a few hundred years.

Later chapters give us real insight into the importance of the Archaea, and what they may tell us about the Earth's original chimaeric, gene-exchanging life-forms, and possibly about potential life-forms deep within the apparently barren rocks of other extraterrestrial objects.

I had wanted to know more about the Archaea, and now do. And most biologists concerned with life's beginnings, the phylogeny of modern taxa and the adaptability of cellular machineries will appreciate this volume. The final chapter, on the future of the Archaea, should be compulsory reading, not just for those interested in genes, evolution and biodiversity, but also for fuel scientists, chemical engineers and pharmacologists, who may well find that the Archaea have already solved some of their problems for them. But we might have learned more, and more easily, if its text had been shortened to reduce repetition, and the space devoted to tabulations, flow diagrams and drawings. Let's hope that some publisher hears this plea to multiply the media, as well as the taxa. ■

P. G. Willmer is in the School of Biology, University of St Andrews, Fife KY16 9TS, UK.

New in paperback

Air Apparent: How Meteorologists Learned to Map, Predict, and Dramatize Weather
by Mark Monmonier
University of Chicago Press, £11, $17
"The targeted readership includes both cartographic historians and weather enthusiasts drawn predominantly from the United States. Monmonier's approach is that of the academic cartographer, and this particular slant both gives the book its charm and defines its weaknesses." Huw C. Davies, *Nature* **400,** 523–524 (1999)

Classification of Mammals: Above the Species Level
by Malcolm McKenna & Susan K. Bell
Columbia University Press, $50, £31
"The classification of extant and fossil mammals by McKenna and Bell will be the classic reference work for all investigators interested in mammalian evolutionary biology." Jean-Louis Hartenberger, *Nature* **392,** 350–351 (1998)

The Search for Life on Mars
by Malcolm Walter
Perseus Books, $15
"Throughout, Walter expresses his feelings about the joy of science, the thrill of the hunt, the difficulty of being sure about anything in the complex geobiological setting, and the frustrations of being half-right, or even wrong, as the work has proceeded." Kenneth Nealson, *Nature* **406,** 936–937 (2000)

Speaking in the Air: A History of the Idea of Communication
by John Durham Peters
University of Chicago Press, $16, £10.50