Genetically engineered "micropigs" were on display at the 2015 China Hi-Tech Fair in Shenzhen city.

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GENETIC ENGINEERING

Tinkering with evolution

A comprehensive tome explores the far-reaching implications of genome editing

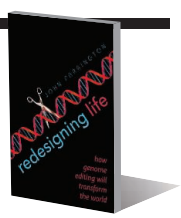
By **Adrian Woolfson**

We have an ambivalent relationship with nature. On the one hand, we acknowledge that it begat and nurtures us, while on the other, we are quick to denounce its shortcomings and sulk at the inconveniences of disease, mortality, and inadequacies of human existence.

That we should have attempted to improve our lot is unsurprising. Indeed, the history of humankind is a chronicle of deeply ingrained and incremental attempts to liberate ourselves from the embarrassments of the natural situation. The recent discovery that components of the bacterial immune system can be harnessed to edit genomes with great speed and precision, coupled with the emerging science of synthetic biology, has ratcheted these possibilities up to a new level. We have, as a result, reached a watershed in the history of our species and of life itself—a moment where critical issues pertaining to the relationship between natural and artificial, the sanctity of human nature, and the future of humankind must be addressed.

John Parrington's new book, *Redesigning Life*, is a comprehensive digest of the extraordinary scientific material relevant to this topic. Parrington presents himself as the trusted tour guide of the latest developments in this rapidly advancing area of investigation, lacing his accounts with a number of charming analogies and anecdotes. These include his description of bacterial CRISPR/Cas9 repeat sequences as "genetic sandwiches" and their display of bacteriophage sequence spacer fragments as a "molecular most-wanted gallery."

Redesigning Life
How Genome Editing Will Transform the World
John Parrington
Oxford University Press, 2016. 364 pp.



Although somewhat humdrum at times, the book achieves its stated aim, which is to provide readers with the basic factual information necessary to comprehend the enormity and potential effect of these unprecedented technologies. Parrington economically covers a huge swath of material, including a discussion of artificial genetic materials, and successfully communicates the excitement and relentless pace of the developments in this field. But there are some notable omissions, including the potential importance and effects of microbiome editing.

It was bacteria that provided the first basic tool kit for modifying genomes in the form of restriction enzymes, the catalytic proteins used to cut the DNA of invading viruses. Parrington gives an entertaining account of their discovery, weaving the story of American microbiologist Hamilton Smith's career with colorful descriptions of his moth-eaten sweaters and thick-rimmed glasses. Smith, we learn, was incredulous when he was informed that he had been awarded a Nobel Prize for his work, which he and others had viewed as esoteric and obscure. This provides a poignant reminder of how basic scientific investigations can deliver profound and unexpected insights of immense significance.

Parrington reminds us that humans have been indirectly modifying genomes for many thousands of years and that many aspects of our "natural" surroundings have arisen as a result of these activities. Cabbages, for example, were originally so toxic that they were only eaten in small quantities for their medicinal properties.

Using modifiable computer text as the metaphor for the genomic information of organisms, Parrington aspires to inform the reader of the risks and potential benefits of gene editing. It is disappointing, however, that he offers no framework or personal perspective on this critical issue.

Such is the speed of developments that the concerns about human germline editing expressed by Edward Lanphier and colleagues in March 2015 (*1*) are already being undermined by next-generation CRISPR/Cas9 gene-editing technologies that are more efficient, have fewer off-target effects, and have the potential to reduce genetic mosaicism (*2*). It is hard, then, to imagine why we would not want to edit the germ line to correct monogenic disease genes. The deep history of our formation and the tinkering nature of the evolutionary process have, however, riddled human nature with a host of interdependencies, paradoxes, inconsistencies, and constraints, making the results of complex interventions difficult to predict. As such, the repair of polygenic diseases is likely to be far more challenging.

The fact that many proteins perform more than one function does not make the prospect of redesign any easier. We have seen recently, for example, how variants of the complement protein C4 of the primitive immune system are implicated in the pathology of schizophrenia, most likely through their supplementary role in synaptic pruning (*3*).

The rate-limiting step in any grand design to reconfigure our genomes is likely to be the ability to model any proposed rewrites or edits. Equally important, however, will be the need to ensure that any changes align with our conception of what it means to be human. ■

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