



**DNA: The Secret of Life.** James D. Watson and Andrew Berry. Arrow Books, London, 2004. 487 pp. Price: £8.99.

*In the absence of selective pressure to change, cellular organisms do not innovate and so bear many imprints of the evolutionary past. A process may be carried out in a certain way simply because it first evolved that way, not because that is absolutely the best and most efficient way (p. 81).*

The book under review is a commemoration of the 50th year of discovery of the DNA double helix. J. D. Watson, F. H. C. Crick, M. Wilkins and R. Franklin elucidated the structure of DNA in 1953, for which they were awarded the Nobel Prize in Physiology or Medicine in 1962 (Franklin was not awarded the prize as she had died). Within a period of the next twenty years of this discovery, the ground mechanisms of cell functioning were found out, which implied that activities of different organisms are simply chemistry-based and that DNA is the carrier of information. Manipulation of DNA *in vitro* in the 1970s gave birth to the new era of recombinant DNA technology or genetic engineering. The successful production of human insulin in bacteria using this technology led to the concept of biotechnology. Later this technology was used to generate transgenic plants. Today the DNA molecule is used in common practices like prenatal diagnosis for genetic disorders, DNA fingerprinting technique in forensic science to identify criminals and to resolve paternity disputes, etc. The application of gene therapy technology in incurable genetic diseases gave a new dimension to human health. Recently, news of human genome sequencing has drawn the attention of the whole world and many people look at this achievement with great expectations. It is not that all the developments brought about by DNA technology got public appreciation. In spite of its tremendous potential, genetically modified (GM) food is a contentious issue

now, as these might have negative impacts on our health and environment. The prenatal diagnosis for genetic disorders in human is also considered as ethically wrong. Within a short span of fifty years of the discovery of the double helix, the revolutionary advancements of DNA science in practical, social and ethical fronts are amazing. DNA is the most familiar biomolecule among scientists and non-scientists today. In this book, Watson himself, the co-discoverer of the double-helix structure, talks about all these developments. Though Watson and Berry have written this book, the style has been maintained throughout as if Watson is telling this fascinating journey of DNA science to a lay reader.

The book consists of thirteen chapters, excluding introduction and the last commentary of the authors. The introduction gives an idea on Watson's thought about the discovery of the DNA double-helix structure with Crick. This discovery solved the long-standing mystery regarding the origin of life and united the three important independent theories proposed in the nineteenth century: the cell theory, the theory of natural selection and the laws of heredity. It becomes obvious, that chemistry is the basis of life, and that life operates through the information contained and perpetuated by the DNA molecule.

The first chapter describes briefly the inheritance of characters in organisms, theories of evolution and the eugenics movement. Development of eugenics was more associated with political and biased scientific minds than logical thinking and experimentation. This led to a disaster however, as exemplified by the killing of thousands of Jews by Nazis in Germany.

The second chapter one gets a better insight into the incidents associated with the elucidation of DNA double-helix structure than that of Watson's earlier book *The Double Helix*. We get to know here the reason for Avery not being awarded the Nobel Prize for discovering DNA as the genetic material in 1944. 'Avery's candidacy for Nobel Prize was blocked by the Swedish physical chemist Einar Hammarsten – who continued to insist that Avery should not receive the Prize until after the mechanism of DNA transformation had been completely worked out. Avery died in 1955; had he lived only few more years, he would almost certainly have gotten the prize' (p. 39). Hammarsten was biased towards considering the protein as the genetic material and not DNA.

The third chapter describes discoveries and inventions that revealed the ground mechanisms of cell functioning: DNA–RNA–protein, the central dogma of life. The function of RNA as an intermediate in the flow of genetic information from DNA to proteins is being described here as a reminiscence of the RNA world. 'RNA is an evolutionary heirloom. Once natural selection has solved a problem, it tends to stick with that solution, in effect following the maxim "if it ain't broke, don't fix it." In other words, in the absence of selective pressure to change, cellular organisms do not innovate and so bear many imprints of the evolutionary past. A process may be carried out in a certain way simply because it first evolved that way, not because that is absolutely the best and most efficient way' (p. 81).

The fourth chapter describes the starting of the recombinant DNA technology by Cohen *et al.* and the concerns raised by different scientists about the possible dangers that this new technology might create. The fifth chapter describes the initiation of the first biotech companies of the world, Genentech and Biogen, with the help of two molecular biologists, Boyer and Gilbert respectively, to produce insulin for diabetes patients. Genentech was the first to produce the life-saving drug insulin, which was followed by the production of other important drugs for humans such as Epoetin, human growth hormone and tissue plasminogen activator by different biotech companies. This chapter also introduces different cancers and various attempts made by biotech industries in their fight against this dreadful disease.

The sixth chapter describes the movements against chemical pesticides and the development of transgenic plants that are resistant to insects and specific herbicides. A good description of host–parasite relationship has been given here. This chapter also describes GM food and anti-GM food movements. The authors mention that such movements are unnecessary and transgenic food is a solution for the food crisis in the world today with a large population. The seventh chapter elucidates in detail, circumstances of the initiation of the human genome project, its execution and completion. It is interesting to note here that the idea to sequence the whole genome was an outcome of a proposal to build a telescope given by University of California in the 1980s.

The eighth chapter describes the genomes of different organisms. Organisms whose genomes have been completely

sequenced are that of several archaea, many bacteria, unicellular eukaryotes like *Saccharomyces cerevisiae*, multicellular organisms like *Caenorhabditis elegans*, *Drosophila melanogaster*, *Arabidopsis thaliana*, *Oryza sativa*, *Homo sapiens*, etc. Genomic studies of these organisms are important from the point of evolution, development, adaptation to extreme environments, health and food production. This chapter describes the emergence of new biology to study the whole genome, known as genomics, transcriptomics and proteomics. An important description in relation to evolution of different organisms is given as follows: 'once evolution solves a particular problem – for example, designing an enzyme to catalyze a particular biochemical reaction – it tends to stick with that solution. This kind of evolutionary inertia is responsible for the centrality of RNA in cellular processes: life started in an "RNA world", and the legacy remains with us to this day. And the inertia extends to the biochemical details: 43% worm proteins, 61% fruit fly proteins, 75% of fugu proteins have marked sequence similarities to human proteins. Some 90% of the domains that have been identified in human proteins are also present in fruit fly and worm proteins. In effect, therefore, even a protein unique to humans is likely nothing more than a reshuffled version of one found in *Drosophila*' (p. 218). Here the authors give an interesting explanation between gene number and intelligence in humans.

The ninth chapter describes human evolution. Though there is no written record of our evolution, we all carry the history written in our DNA as mentioned: 'Prehistory by definition refers to the period prior to written records, and yet we find written in every individual's DNA sequences a record of our ancestors' respective journey' (p. 252). This chapter describes by analysing the Y chromosome as well as mitochondrial DNA from different human populations; the patrilineal and matrilineal origin of human population respectively, is being traced in Africa. Denaturation and renaturation studies of DNA molecules revealed that the chimpanzee is the closest organism to humans and that the human genome is different from that of the chimpanzee by only 1%. In fact, the chimpanzee is closer to humans than to gorillas. The authors describe 'humans are, I suspect, simply great apes with a few unique – and special – genetic switches' (p. 266). The tenth chapter de-

scribes the contribution of DNA fingerprinting in forensic science today, to identify criminals and sort out paternity disputes. Many incidents have been cited in this chapter that were solved by DNA fingerprinting, which signifies the importance of this technology. The eleventh chapter introduces different genetic diseases of humans that are inherited by simple or complex traits. The authors describe the difficulties that lie in cloning human genes and successful stories of cloning genes for several diseases like Huntington's disease, Duchene's muscular dystrophy, cystic fibrosis and breast cancer.

The twelfth chapter describes methodologies used to detect genetic disorders by prenatal diagnosis and the ethics involved. This chapter also introduces gene therapy technology and several incidences where this has been used. The thirteenth chapter describes the importance of nature (gene) and nurture (environment) in the development of human behaviour. This chapter also describes Lysenko and his pseudoscience, Lysenkoism. The last chapter is correlated with the first chapter in that both nature and nurture have to be given importance in studying human behaviour. In conclusion, the authors emphasize that great potential lies with DNA-based technology, which should be used judiciously for making our future safe and healthy. There are several sentences in the book written in an amusing manner, e.g. describing Pauling's wrong model of DNA: 'the world's best known, if not best, chemist had gotten his chemistry wrong. In effect "Pauling had knocked the A off of DNA"' (p. 50). Each chapter of the book also contains several anecdotes, which keep the reader engrossed.

Overall this a wonderful book!

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This is a compilation of seventeen reviews which are categorized under the following subjects for ease of discussion: Drug

metabolism, Signalling, Receptors and Proteases. Chapters written by experts are educative for those who are new to pharmacology, while experts in the area are likely to appreciate the grand scope of the volume.

Drug metabolism: Five complementary review articles deal with drug metabolizing enzymes and multi-drug transporters. The cytochrome P450 (CYP) enzymes have been well characterized for their efficacy in the breakdown and clearance of drugs. They also generate carcinogens from otherwise harmless chemicals. Altered levels and activity of these enzymes due to mutation or polymorphism lead to drug resistance in diseases. As a consequence, there is either a decrease in the bioavailability of drugs or drug-induced xenotoxicity. Activity of the enzymes and their isotype distribution are important criteria in the pharmacokinetic administration of the drug. Although some cancers can be cured with current-day drugs, the major impediments towards a complete cure are innate or acquired drug resistance, toxicity and relapse. These aspects are reviewed in the context of childhood leukaemia by Cheok *et al.* Treatment regime has to take into account the genetic background and associated polymorphism. To recapitulate these and to overcome the often disparate results obtained using animal models, generation of humanized animal models appears to be mandatory. The article by Gonzales and Yu covers current status of such humanized mouse models for CYP and xenobiotic receptor humanized mice. Tying neatly with these articles is the related topic on the role of drug-metabolizing enzymes in inflammation (Regulation of drug metabolizing enzymes and transporters in inflammation). The chapter focuses on regulation of CYP, the major enzyme involved in this process with brief notes on flavin monooxygenase (FMO), phase II enzymes and hepatic transporters. Apart from chronic inflammatory cases, due to the role of inflammation in sepsis and cancer, this article will have a wider impact. Cashman and Zhang cover basic aspects of FMO, the lesser studied of the detoxifying enzymes. Isoform distribution and tissue-specific expression are particularly well covered. These authors predict further expansion of knowledge about these enzymes. The focus would be to distribute the drug load between CYPs and FMOs, and the design of pro drugs that can be metabolized specifically by the FMOs into their clinically potent active forms.