therapeutic strategies in small molecules treatment, substrate-reduction therapy, enzyme replacement, modifiers and epigenetic factors, and RNA-mediated molecular therapy approaches.

Understandably, the part dealing with 'classical' gene therapy is very briefly described, with some examples as haemophilia.

Chapters 7–9 report on the best-described arguments in the book. These are those related to cancer or cancer-related genetic disorders and possible treatments. It emerges clearly that the major achievements in translational research have been those reached in this field. Mendelian cancer-related disorders such as tuberous sclerosis, neurofibromatosis and Peutz–Jeghers syndrome are described with novel therapeutics already translated in clinical trials. DNA-repair diseases and toxicogenomics are also reported. Finally, the therapies on cancer disorders are updated and clearly described, very well showing the translational application of basic research data. The author also overviews novel techniques, such as expression profiling in cancer for disease diagnosis and prognosis, and proposes 'guidelines' for cancer prognosis and therapy.

Chapter 10 recapitulates the novelties in pharmacogenetics and pharmacogenomics. These two fields of investigations will probably represent the mainstay of medical genetics in the near future, considering the possible impact they may have in predicting frequent diseases' susceptibility, drugs response, drug design, preventing side effects in therapies, and at the end, designing '*ad hoc*' therapeutics. This brings us towards the concept of personalised medicine. This is a concept clearly emerging not only for genetic diseases but also for other frequent disorders, for which genetic factors may influence the disease course and the therapy efficacy. This consideration drives us to the last Chapter, summarising the phenomic world interfacing with genetics and genomics. To this belong all the approaches aiming at organising OMIC databases (phenomic, genomic, proteomic), biobanks and genetic services.

The interaction between all these disciplines and sciences will fill the gap, allowing us to improve the translation of genetic sciences into medical genetics.

This is a very comprehensive and up-to-date book, recommendable both for young medical geneticists, but in particular to other physicians, such as neurologists, cardiologists, paediatricians and to all specialists working close to genetic disorders ■

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'Me, Myself, and Why. Understanding your own genome and evolutionary history'

Understanding human genome complexity

'Handbook of Human Molecular Evolution' Edited by David N Cooper, Hildegard Kehrer-Sawatzki
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At a time when reading through your own complete genome will be technically feasible soon, it also becomes important to have access to information that will help understand your own genome complexity and genetic history in more general terms. Acquiring a fast understanding of the many essential aspects of human molecular evolution was nearly impossible because a lot of information was scattered over many different sources. With the Handbook of Human Molecular Evolution in hand (literally a challenge in itself, unless you are a professional weightlifter), you have all the information for grabs.

The handbook comes in two volumes with, combined, 1717 pages. It has a total weight of 4866 g, is the product of 377 contributors, and is edited by Cooper and Kehrer-Sawatzki.[1] Its format is somewhat different from that of many other handbooks. There are 12 different sections: Vol 1 with General Concepts in Evolutionary Genetics; Mutation, Adaptation and Natural Selection; Evolutionary and Population Genetics; Human Evolution; and Human Genome Evolution; Vol 2 with Evolution of Human Gene Structure and Function; Evolution of Gene Expression; Mitochondrial Genome Evolution; Chromosomal Evolution; Comparative Genomics; Evolution and Disease Susceptibility; and Analysis of Ancient DNA. These sections contain 282 articles with levels of scientific complexity varying from Introductory, Advanced to Keynote. This makes this handbook accessible for different groups of readers, and reflects the editor's main ambition of covering the complete range of human molecular evolution studies for every scholar, from undergraduate to the experienced professional.

This handbook is a real treasure trove, because there are new facts and figures literally everywhere for everyone. For the experienced geneticist, the articles describing human evolution from a paleo-anthropological perspective are very helpful. For the archeologist, the articles introducing the structural complexity of genomes and population genetic statistics are very illuminating. Most sections have a very logical structure; other sections seem to contain haphazardly chosen articles. In this respect, one could wonder why in the section Human Evolution (Vol 1, pp 345–563) there are articles describing the genetic diversity of the German population and the British population, but not, for example, the Dutch, French or Greek. This seemingly lack of structure of this handbook, however, works very well for the reason that it introduces some repetition of facts. This cannot be avoided when editors choose for so many overlapping articles instead of distinctly cohesive chapters. As an example, the

importance and details of the concept of Hardy–Weinberg equilibrium, and the derived formula, are explained by different authors in different articles (in Vol 1 and Vol 2) with different levels of clarity, and it simply works because they do not contradict, instead support each other.

How should one use this handbook? Should it be read from cover to cover or should you follow the grazing strategy? I would recommend a combination of both. The first section of Vol 1, General Concepts in Evolutionary Genetics, provides a limited number (13) of very concise and well-balanced introductory discussions of nearly all essential topics of human evolution dealt with in much more detail in many of the following articles. Once done with this section, you are on your own. I subsequently read those parts of the handbook that are close to my heart (which is essentially the entire Vol 1). Here I have two distinct favorite sections. Despite the many necessary formulas, the second section, Mutation, Adaptation and Natural selection, is as clear is it should be. Especially, Dan Graur's article on Mutational Change in Evolution (Vol 1, pp 98–107) will be very difficult to improve, and is an absolute 'must read' and is brilliant in its simplicity. The section on Human Evolution is a 218-page long very clear treatise of human migration from a multidisciplinary perspective and is among the best that I have read.

The nice thing about reviewing such a handbook is that you are forced to also focus on those topics you normally have no time for. For me, that comes down to most of Vol 2. I admit here that I have not read it in full, but I have learned many facts that I wish I had picked up earlier. The article describing the comparative evolution of the human and chimpanzee transcriptome (Vol 2, pp 1242–1249) contained for me one of the most interesting illustrations (one that is also reproduced in full color as plate 42 in that volume). It shows the relative differences in gene expression between humans and chimpanzees. Although it is specifically discussed that the expression of many genes in the human brain is markedly elevated compared with the expression of these genes in other organs, this picture immediately draws your attention to something completely different: have a look at the expression of testis genes: what a difference with the other organs and between human and chimp! If this does not trigger further reading, nothing else will. It is also in Vol 2 that I find some of the weak points of this handbook. The article on members of the low-density lipoprotein receptor family (Vol 2, pp 1051–1055) is beyond comprehension for the uninitiated, if only because of lack of crucial illustrations. I also do not find it realistic (or simply unjust?) to cover the importance and complexity of the MHC complex in a mere nine pages (Vol 2, pp 1055–1063). Another clearly missed opportunity is the article describing the fascinating topic of the 'thrifty genotype hypothesis' (Vol 2, pp 1625–1629). It is, especially for a handbook, crucial to inform the readers not only that Neel[2] was among the first to introduce this term but also that he was the first to describe that the concept could be erroneous, at least when it is used to explain type 2 diabetes.[3] This article lacks a proper reference (and a more detailed explanation) of the 'thrifty phenotype hypothesis', introduced, for example, by Hales and Barker,[4] and there is no mention of a third alternative and an equally challenging hypothesis called 'the predation release hypothesis'.[5] More generally, I find the centrally placed two sets of color illustrations quite annoying. I understand that for reducing printing costs this had to be done, but I would have preferred them to be included as a separate insert, set apart from the major binding. This would have allowed a flexible cross-referencing while reading.

Notwithstanding these few criticisms, the editors have clearly been able to fulfill their ambition. It is worth every penny, and should be on the desk (not on the dusty shelves) of many readers of this journal. There is simply too much to read and digest, and for this, David and Hildegard, thank you very much ■

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