BOOK REVIEW

DNA and ability to reproduce: the ‘Secret’ of evolution

DNA duplication and evolution

‘Genome duplication’ Edited by Melvin L DePamphilis and Stephen D Bell

ISBN: 978-0-4154-4206-0

Published by: Garland Science: 2010

RRP: £49.00/\$140.00

Alessandra Ferlini

European Journal of Human Genetics (2012) **20**, 244–245; doi:10.1038/ejhg.2011.165

The preface of this book opens with the premise that ‘nothing is more fundamental to life than the ability to reproduce’; indeed, this is the central theme of the book, which describes in great detail the mechanisms underlying the machinery of DNA replication/duplication and their evolutionary importance as a highly conserved biological process.

The authors begin with a state-of-the-art in genome(s) structure and organization. In Chapter 1, the architecture of genome(s), is very well described, with particular focus on the atomic three-dimensional topology of DNA. Chapter 2 introduces the three domains of life, namely Archaea, Bacteria and Eukarya, giving a highly comprehensive and pleasing description of the evolution of living organisms, from the prebiotic era (the primitive Earth, carbon- and nitrogen-based) through to the complex world of RNA.

In Chapters 3 to 6, the authors explore the *in vivo* of DNA replication. These four chapters are extremely well written, and adhere to the narrative principle of ‘What is true for replication forks in bacteria is also true for replication forks in elephants’ (Jacques Monod). Among its themes, the replication-fork factories (roughly 1000, completing replication every 45 min during an 8-h S phase) are minutely described. These factories, of which the impressive number of 10 000 are found per cell, represent the articulated protein/nucleic acids complexes operating during fork replication. Chapters 5 and 6 place special focus on the proteins involved in DNA replication (helicase, binding proteins, polymerase, topoisomerase), as well as those priming DNA synthesis (primase, ligase) and termination (replication-fork barriers and

telomerase). Of particular interest are the sections on dynamic processivity (fine coordination of the events involved in replication over time; it is intriguing how the synthesis of leading and lagging strands coordinate) and the evolutionary perspective (see the absorbing section on DNA polymerase fidelity and molecular evolution, which concludes with the sentence ‘The goal of DNA replication and DNA repair is to achieve a balance between genomic stability and genetic mutation that allows species both to survive and to evolve,’ one of the central themes of this book).

DNA is also chemically modified and invariably reorganized in a DNA–protein complex, a process called chromatin assembly and remodeling.

Chapter 7 is dedicated to this topic, and the authors ‘travel through’ Chapters 3–6, reinterpreting the previously described fork-replication mechanisms in light of the chromatin assembly-disassembling processes. This chapter is very up-to-date and easy to read, despite the complexity of its content.

The treatment of replicons, replication origins, origin paradigms and initiation (Chapters 8–11) attest to the strong scientific background of the authors (they ‘play at home’). Nevertheless, although experts in this field will thoroughly enjoy this detailed description, the general readership (such as myself) may have difficulty following these chapters.

Again, the themes discussed are unfailingly contextualized in the evolutionary perspective; see, for instance, the explanation and ‘history’ of the DNA-helicase loader mechanism. This is a single universal mechanism, chosen by evolution for all living organisms,

and consists of an initiator protein that both binds the DNA replicator and uses it as a platform for recruiting and assembling itself into a DNA helicase (helicase loader). Chapter 12 (cell cycles) is a pleasingly written, evolution-oriented account of the mechanisms of cell division. The authors succeed in guiding the reader through these processes, enriching previously discussed topics with novel information (see the link between initiator/replicator as triggering genome duplication and heavily interfering with the cell cycling, by sequestering, inactivating and depleting specific proteins).

The concluding paragraphs of ‘Parallel pathways’ are appropriate for a wide readership, providing an integrated view on cell cycles and replication, ‘Functional redundancy’ (highlighting the evolutionary pressure on these processes) and ‘Development programmed polyploidy’, a truly interesting read due to its repercussions in medical genetics (human aneuploidies).

Chapter 12 also explores the cell-cycle checkpoints, originally defined and named by Leland Hartwell in 1989. The sophistication of this surveillance mechanism is particularly evident in Eukarya (six checkpoints instead of the two present in bacteria), and reflects the complexity of their genome architecture and shape.

As this articulated and multi-tasking surveillance system fails in cancer, its elucidation is fundamental to understanding the neoplastic cascade and to the design of innovative therapeutic approaches.

As regards Chapter 14 (Human Disease), I felt this chapter was a little lacking in detail; no doubt this feeling was influenced by my background in medical genetics, but, nonetheless, I would have preferred a more in-depth approach. Indeed, the title of the book, not to mention its subtitle ‘Concepts, Mechanisms, Evolution, and Disease’, led me to expect a thorough treatment of this issue, but this aspect appeared to be marginalized.

Indeed, the first part of this chapter is dedicated to infectious diseases before moving swiftly on to discuss cancer; in these paragraphs, the authors provide a clear summary on human diseases caused by oncogene/oncosuppressor mutations and detailing some underlying mechanisms.

I thoroughly enjoyed the final paragraph on heritable diseases, with particular reference to the ‘Seven Deadly Sins’ of DNA replication, which brought to mind the seven Horcruxes of the Harry Potter saga (objects which a dark magician uses as a vessel to contain a fragment of their, thereby immortal soul) in reverse, that is, the seven

sins can lead to cell death. These seven 'sins' are the generation of (1) genetic mutations and (2) secondary structures, the promotion of (3) DNA breakage and (4) DNA recombination, (5) the activation of DNA damage response, (6) the alteration of gene expression by disrupting the methylation pattern, and (7) the alteration of gene expression by disrupting chromatin assembly. This is an appealing vision of both the etiology of cancer and the impact of replication errors, which place tremendous stress on the mechanisms that prevent or repair DNA damage. Examples of the actions of these sins in

several diseases are provided (particularly effectively in the case of nucleotide-repeat disorders) and a brief look at medicines targeting DNA replication errors, including antivirals (HIV and HBV therapies) and anti-cancer drugs (topoisomerase inhibitors and others) is described.

The final chapter offers an overview of 'DNA and ability to reproduce: the 'Secret' of evolution', the pivotal theme of the book. This chapter opens novel perspectives on various topics such as the move from RNA to the more complex world of DNA, the role of viruses in the evolution of DNA genomes,

the gene invasion from viruses, the intron expansion, the variegate multiple origins of replication in Eukarya, and the deeper significance of viruses (are they fossil records of evolution?).

This book, on the other hand, is very comprehensive and up-to-date, and will be of particular interest to molecular biologists and human geneticists ■

*Dr A Ferlini is at the Section of Medical Genetics, University of Ferrara, Via Fossato di Mortara 74, Ferrara, Ferrara 44100, Italy.
E-mail: fla@unife.it*

A useful guide for your practice

Practical, brief, yet comprehensive – highly recommended book for practitioners

'Lysosomal Storage Diseases: Early Diagnosis and New Treatments' Edited by Rossella Parini and Generoso Andria

ISBN: 978-2-7420-0779-0

Published by: Mariani Foundation Paediatric Neurology 23: Montrouge, France, Editions John Libbey Eurotext, 2010, 186pp, Hardback, €70 (approx.)

Alessandra Ferlini

European Journal of Human Genetics (2012) **20**, 245; doi:10.1038/ejhg.2011.117

I was very pleased to discover a very practical and comprehensive material, containing updated information on basic and clinical research in the field of lysosomal storage diseases, a field that has witnessed an extraordinary evolution in the last 15 years.

The material is structured in four major parts: 'general aspects', 'clinical presentations in detail', 'mucopolysaccharidoses from the specialists' point of view' and 'specific treatments for lysosomal storage diseases', each of them rich in practical data, reflecting the author's experience in the field. A remarkable aspect is that all the presentations concentrate on early recognition and diagnosis, specific therapies being more efficient in incipient stages.

The first part introduces lysosomal storage diseases, discussing common features that suggest the presence of a storage disorder, as well as specific features that make the difference between entities. The next section (epidemiology, biochemistry and genetics) illustrates how to read and interpret biochemical and molecular tests. Suddenly, the complex field of

metabolic disorders becomes very understandable after reading this material. This part also presents organizational and ethical aspects of newborn screening, as well as pathophysiological aspects of lysosomal storage disorders in a very comprehensive, yet realistic way. Even if the text is clear, I think some schemes and graphs are necessary to illustrate biochemical pathways, pathophysiology and interpretation of lab results.

The next section remarkably discusses two of the most complex lysosomal storage diseases – mucopolysaccharidoses and Anderson–Fabry disease. Illustrative photographs and imagistic investigations appropriately complete the text for both of them. In my opinion, the value of this material is given by the discussion in detail of early signs and symptoms, separately for different fields involved (dysmorphology, ENT, musculoskeletal, etc). Updated data are included and the most important mechanisms and theories are discussed.

The third part refers to mucopolysaccharidoses from the specialists' point of view. Once you start reading this section, you

cannot put it away – you become more and more eager to discover something new about the next specialist's opinion. Classical features are mentioned, but here, the accent is put on practical issues that practitioners have to solve in their daily activity – epilepsy, psychological assessment and support, radiological findings, anesthesia, as well as neurosurgical complications and their management. The rich selection of illustrations makes the material practical and instructive.

Physicians should not miss the last part referring to specific treatments for lysosomal storage diseases. In addition to the presently used enzyme replacement therapy and hematopoietic stem cell transplantation, other therapeutic approaches are discussed (eg, allogeneic stem cell transplantation and hematopoietic stem cell gene therapy). Each of the chapters included in this section is a state-of-the-art description in the field. I am convinced that readers will appreciate the therapeutic goals and the follow-up and management indications added to the classical presentation of therapy.

The bibliography is remarkable – it includes hundreds of very interesting articles, some historical, most of them recent ones.

In conclusion, this is an excellent book that should be available in every medical service that deals with lysosomal storage disorders (pediatric and neurological wards, medical genetics centers, and medical school libraries). The material is dense, but provides you with comprehensive and updated data in the field ■

*Dr C Rusu is at the Medical Genetics Department, University of Medicine and Pharmacy, Street Universitatii 16, Iasi 700115, Romania.
E-mail: abcrusu@gmail.com*