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Book Reviews

The RNA World. Second Edition. Edited by GESTELAND, CECH and ATKINS.

The second edition of the RNA world provides a welcome update and expansion of the topics covered in the original. One of the major problems facing modern biologists is to find a plausible (or least unlikely) hypothesis that explains the origin of life. In the absence of any clear historical record and, as a consequence, no real idea of the conditions prevailing on earth as the first life forms were evolving, these hypotheses remain speculative. However, cumulative evidence from various aspects of RNA biology supports the hypothesis that the first primitive life forms from which we are all descended had RNA genomes and that RNA-based enzymes provided many of the functions that are carried out by proteins in today's cells.

The chapters of the book are divided into several subsections that take us from the origin of the RNA world and evolve through catalytic RNAs to modern day ribonucleoprotein particles where protein components have become essential for function. Most of the chapters are very well written and the inclusion of WWW sites by the authors for supplementary material ensures that the book does not become too unwieldy. Two chapters stand out: one describing the 'Genomic Tag Hypothesis', originally proposed by Weiner & Maizels (1987) and brought up to date by the same authors (Chapter 3, pp. 79–111). The critical observation for this hypothesis is that tRNAs are composed of two halves which have the possibility to evolve independently. They argue that tRNA like molecules were first used in replication of linear RNA genomes where they marked the 3′ end and ensured that material was not lost during replication. As the RNA world gave way to the ribonucleoprotein world the tRNA like structures could evolve into the many similar structures that we see today involved in seemingly diverse processes such as protein translation and telomerase activity. The second outstanding chapter is by Lambowitz *et al*. (Chapter 18, pp. 451–485), where they describe the fascinating world of group I and II self-splicing introns and how they have evolved to using protein co-factors for splicing both intron encoded and also host encoded factors. This may help us to understand how the more complex spliceosome was able to evolve.

The only minor criticism is that alternative and sex specific splicing of pre-mRNAs is not covered in any great detail where great advances have been made in our understanding of these processes.

I would recommend The RNA World not only to anyone working in the RNA field but also to those who have an interest in biology and evolution. The book provides a fascinating insight into the many faces of RNA and its biology and like any good book raises more questions than it answers- a good sign for RNA research!

Weiner, A. M. and Maizels, N. 1987. 3′ Terminal tRNA-like structures tag genomic RNA molecules for replication: Implications for the origins of proteins synthesis.

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The Development of Gene Therapy. Edited by T. FRIEDMANN. CSHL Press, 1999. ISBN 0-87969-528-5.

The Cold Spring Habor monograph series has been running for just under 30 years, and many earlier volumes have become classic reference works. The likes of 'The Lactose Operon' and 'The Bacteriophage Lambda' appeared in less frantic times and their editors largely succeeded in compiling comprehensive and timely *vade-mecums*. With the huge expansion in scale and pace of molecular biology in the intervening years, a monograph is destined to be out-of-date the moment it is printed. Such a fate has befallen the present volume, a minor but inevitable fault. What is striking and less excusable, however, is its lack of breadth, a major failing in what is intended to become a historical milestone of molecular biology. The selection of topics is idiosyncratic and their compilation under the given title cannot help but convey a misleading overall impression of the field.

What science is to be found here? On the vehicle side, viral vectors are given most prominence in a series of chapters. The targets for gene therapy covered range from the haematopoietic system through cancer to viral infections. Matt Cotten and Ernst Wagner's review of receptor-mediated delivery is excellent, John Wolff gives a good account of naked DNA therapy, and Eric Kmiec and colleagues survey the provocative approach of mediating gene correction using RNA/DNA oligonucleotides.

Of potential readers, those active in the field might dip into it for reviews on a variety of topics. They may perhaps be startled by the omissions, but will be happy at least to scan what does appear for useful (if dusty) summary data and references. Those new to gene therapy, workers in other fields, or students might be attracted to the book in the understandable supposition that it presents a balanced and comprehensive summary of the state of the art. They would be mistaken. For example, only one of the 25 chapters is devoted specifically to non-viral delivery systems: in contrast, there are eight on viral systems. A naive reader might form the opinion that research into non-viral delivery is a peripheral area. Nothing could be further from the truth: in fact, there is significant and growing interest in the approach – even in the US.

Another example: cystic fibrosis gene therapy is hardly mentioned. This is a lamentable oversight, the equivalent of a book on the development of powered flight referring to the Wright brothers only in a footnote. CF has been from the outset a paradigmatic candidate disease for gene therapy and remains a major international research front. In the 1992–1996 period, 31% of all peer-reviewed gene therapy publications were on CF, so it is frankly unforgivable for there to be no chapter solely devoted to the disease.

As I work on CF gene therapy research using non-viral delivery systems, these omissions particularly rankle, but they are not the only ones. Other well-studied target diseases are not given adequate exposure and there is not chapter summarising the results of the many clinical trials that have taken place worldwide.

On the positive side, it is encouraging to see chapters on public policy and ethical issues in a book such as this. Ted Friedmann reminds us in his thoughtful opening chapter how some eminent geneticists in the first third of this century flirted favourably and openly with the ideas of eugenics, many of which were predicated on the sorts of crude racial stereotyping that led directly to medical malpractice and genocide. More recently, controversy surrounding the pioneering gene transfer work of Martin Cline and colleagues in the 1970s (conducted without ethical approval) culminated in the setting down of strict guidelines for the conduct of human gene therapy research. Lay concern about the implications of gene therapy research is thus entirely understandable and it is incumbent on the scientists involved to engage the public in open discussion on the ethical and other implications of their work as it progresses.

To sum up, my concerns are not with the constituent chapters, which live up to the high standards of the series as a whole, but with the glaring omissions and lack of balance. As a result, the book falls far short of providing a comprehensive synopsis of human gene therapy development.

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