

Book Review

Gene Regulation: A Eukaryotic Perspective, 4th Edition

David Latchman.

Nelson Thomes, Cheltenham, UK. 2002. 368 pp. £30.00.

The 4th edition of David Latchman's book *Gene Regulation: A Eukaryotic Perspective* is a very methodical presentation of the current knowledge about regulation of gene expression. The book opens with the central question of how organisms generate their diversity of cell and tissue types by differential and combinatorial expression of genes present in an identical genome. It begins by presenting how the abundance of certain proteins produced by each cell type is reflected in the pool of transcription products. From there the author lists the large collection of factors known to influence the initiation of transcription from the genome to mRNA pool.

Latchman takes a systematic approach to introduce the levels of complexity underlying the factors that influence gene expression during development. My favorite aspect of the book is how Latchman introduces new concepts by explaining the key experiments that led to the insights and how he uses very clear and abundant graphics to illustrate each point. Another high point in the book is the chapter on changes in chromatin structure and the resulting impact on DNA binding by regulatory proteins. The author addresses the fascinating question of how differentiated cells maintain their state, but I looked in vain for a discussion of how changes of chromatin structure might be maintained across successive cell divisions. Are these structural changes maintained through successive rounds of chromatin condensation during cell divisions? Do regulatory protein complexes ride the chromosomes through mitosis? Latchman's book is good about presenting facts, but much less so about triggering the reader's curiosity and stressing the important unknowns.

The author's methodical approach comes at a certain price. I repeatedly felt like I was reading an endless list of yet another factor involved in gene regulation in important ways. Early on we are told that transcriptional initiation is the key level of gene regulation and that alternative mechanisms such as gene loss, gene amplification, or gene rearrangements are exceptions arising from peculiar functional constraints such as space (in mammalian erythrocytes), rapid production of protein (*Drosophila* salivary gland), or generation of diversity (vertebrate immunoglobulin and T-cell receptor genes). As an organismal biologist, I was struck by the detachment of the discussion of gene regulation phenomena from the organisms in which these are observed. The author seems to have forgotten Dobzhansky's famous reminder that "nothing in biology makes sense except in the light of evolution." While enjoying the precision and detail in Latchman's discussion of various levels of gene regulation, I was disappointed by the almost complete absence of an evolutionary perspective.

For example, a discussion of why one level of regulation would have become favored through evolution, or a consideration of whether one can discern trends in the complexity of mRNA splicing in certain taxa would be helpful. Even though we cannot definitively answer such questions, they appear to be the kind of questions that drive many biologists. I realize that the book is on gene regulation and not on genomic evolution, but that is no justification for not addressing the typically eukaryotic organization of genes into exons and introns, and why this may represent an important evolutionary innovation. Many aspects of genome evolution undoubtedly matter for an understanding of why certain mechanisms of regulation have evolved. Similarly one of the hallmarks of eukaryotic genomes, the presence of numerous copies of cytoplasmic mitochondrial and/or chloroplast genomes and the coordinated expression of cytoplasmic genes with their counterparts and complements in the nuclear genome is not addressed.

At a more molecular level, I was disappointed by the neglect of the other classes of molecules constituting major fractions of eukaryotic organisms. Early on, Latchman discusses the "dogma" of molecular biology that DNA produces RNA which produces proteins. As useful as this dogma has been, one can argue that it may also be limiting. Latchman addresses posttranslational modification in one or two sentences, as when mentioning o-glycosylation and phosphorylation of transcription factors. The world he paints is a world consisting almost exclusively of proteins, irrespective of the fact that lipids and carbohydrates play crucial roles in modifying proteins and their functions.

If Latchman succeeded in illustrating the complexity of activators, coactivators, and repressors, their complicated interactions, and their role in fine-tuning the regulation of multiple genes, he missed a great opportunity to add examples of how certain proteins (e.g., glycosyl transferases) change the structure and function of many other proteins (including transcription factors such as steroid receptors) which they glycosylate.

The book would have greatly benefited from more discussions such as the one about the novel possibilities of eukaryotic genomes due to the existence of unlinked genes that can be coexpressed to varying degrees due to the existence of common promoters, in contrast to single operons linking the function of multiple genes as in bacteria. I also looked in vain for a discussion of gene regulation processes possibly due to the threat of integrating genomic parasites such as transposable elements or retroviruses. Are there regulatory mechanisms that were co-opted from initial mechanisms of interference with genomic parasites? Could methylation have evolved primarily as a means of silencing

parasitic elements and only been co-opted much later by mammals for silencing of genes capable of causing conflicts between maternal and paternal genomes?

It was not until the last chapter on regulation and disease that one encounters this type of discussion. Unfortunately the last chapter also presents a classic dichotomy of "normal" and "diseased," and there is no mention of the possibility that much of the variation observed may be part of adaptive variation allowing different reactions to the same type of environmental stimuli.

Latchman gives a few examples of environmental determinants, such as the presence of copper for yeast metallothionin gene induction or changes in temperature for heat shock proteins. I was hoping for a discussion of the overwhelming importance of environmental stimuli in changes in gene expression, be they pressure, gravity, light, exogenous molecules, or even interactions with other organisms. Moreover, apart from being fairly tedious to read, the text regularly conveyed a certain teleological sense, such as in the sentence "Thus, different activating factors or different molecules of the same activating factor could contact different targets within the basal transcriptional complex, so ensuring the great enhancement of transcriptional activity which is the ultimate aim of activating molecules" (p. 251).

Gene Regulation: A Eukaryotic Perspective is a useful book full of precious information, but I cannot say that I found it particularly inspiring.

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