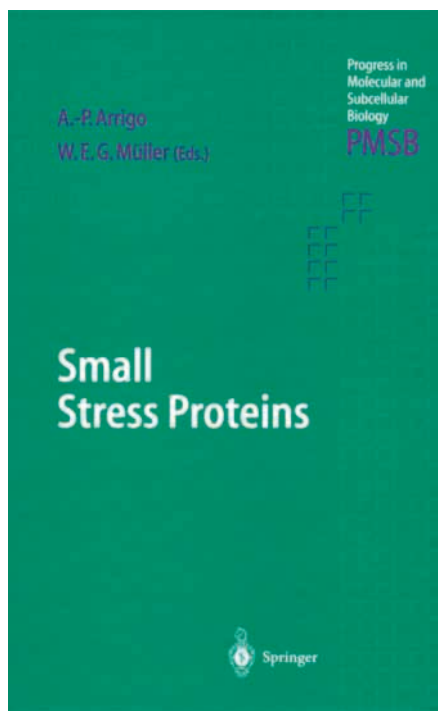


sHsps: the neglected chaperones



Progress in Molecular and Subcellular Biology, Vol. 28: Small Stress Proteins

edited by A.-P. Arrigo and W. E. G. Müller

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 €90.50/\$139

Arrigo and Müller provide an excellent resource summarizing the recent research on small heat shock proteins (sHsps) conducted in many of the most prominent laboratories in the world. The directions for future research in molecular biology, biochemistry, developmental and neurobiology are defined clearly for scientists interested in the biomedical potential of sHsps and molecular chaperones.

The broad significance of the sHsps can be assumed from the extraordinary diversity of the alpha crystallin domain throughout the plant and animal kingdoms from prokaryotes to man. Current results discussed in the chapter by Kappe et al. suggest that the functional importance of sHsps, and possibly the secondary, tertiary and

quaternary structure of the core alpha crystallin domain, may have been retained, although the primary sequence has become highly variable in individual proteins across phyla. The extraordinary significance of sHsps in normal cells and tissues is further reinforced in a chapter by Davidson et al., who summarize reports demonstrating the presence of sHsps at key stages of development, including apical projections of endometrial epithelium during implantation, neural crest cell migration, myocyte differentiation and developmental specialization of endodermal lineages in the bladder pharyngeal epithelium. Norris and Hightower's specific analysis of two sHsp families in the desert fish, *Poeciliopsis*, characterizes the complex evolutionary history of sHsps. With their broad phylogenetic representation and strong linkage to essential processes of normal development, it should not be surprising that the sHsps appear to have functional significance in biological mechanisms involving apoptosis and oxidation (discussed by Arrigo et al.), cellular signaling (discussed by Gaestel) and the organization of the cytoskeleton. With regard to the last point, single-site mutations in the sHsp alpha crystallins are revealed to be linked with cataracts and cardiomyopathies in humans (covered in the chapter by Quinlan). Nowhere is the biomedical significance of sHsps more obvious than in the example of sHsps and the cytoskeleton, where the importance and therapeutic potential in human disease is implicit in many of the studies described. Very basic functional questions that have been solved for other heat shock proteins, including GroEl and Hsp70, remain unresolved for the sHsps. The key problems of chaperone function of sHsps include the mechanism(s) of assembly of a functional complex, binding of substrate/target proteins, and the regulation and kinetics of chaperone activity, which are reviewed in the chapter by Haslbeck and Buchner.

Chapters by Candido and Michaud reveal that the regulation of sHsp expression is under investigation in *C. elegans* and *Drosophila*, respectively. It seems that the diversity of the family of proteins containing the core alpha crystallin domain may be associated

with a common set of functions or may suggest new as yet unidentified tissue-specific functions. The unanswered questions about sHsps are not limited to constitutive and spatially restricted patterns of expression, however. Even the functional and structural significance of phosphorylation remains to be elucidated (discussed by Kato et al.). While the field of sHsps appears to be neglected, we can expect that further advances in research will reveal the functional origins of sHsps and lead to clarification of the role of sHsps in cancer (discussed by Ciocca and Vargas-Roig), neuropathy, cardiac ischaemia (discussed by Latchman) and aging (discussed by Krueger-Naug et al.).

From the fascinating evolutionary diversity of sHsps in prokaryotes to specific protective effects resulting from overexpression of sHsp in neurons and cardiomyocytes, the book is an exciting read for those of us interested in sHsps and their involvement in to protein folding, apoptosis, cytoskeletal assembly, aggregation diseases, phosphorylation and chaperone structure and function. Each chapter is generally well referenced, although the index could be more detailed. The recent crystal structure of the eukaryotic Hsp16.9 (van Montfort et al., 2001) and its similarity with Hsp16.5 is not included. Overall the writing is clear. Both established theories and novel concepts about the interactions between sHsp subunits and target proteins are included. Many chapters contain figures that summarize the major points relevant to future research on sHsp function. Pathways involving oxidation, signaling and stress responses are presented clearly. The need for such a reference book is obvious from the start, when sHsps are introduced as "forgotten chaperones" in spite of the fact that each chapter demonstrates another significant fundamental cellular function for the sHsps in a variety of important biomedical problems from neurodegeneration to infectious disease, where potential for therapeutic intervention exists. Anyone, from senior investigator to student, concerned with sHsps and their functional importance to major research problems needs to have at least one copy of this fine and understandable reference in their library.

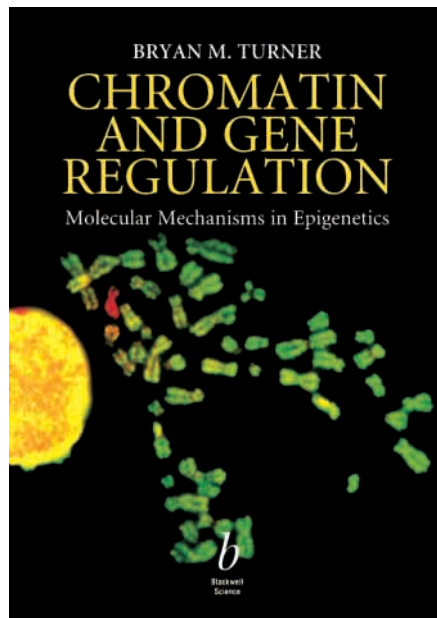
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John I. Clark

University of Washington, Seattle, WA, USA

New recipes for the story of a relationship: DNA packaging and gene expression



Chromatin and Gene Regulation: Molecular Mechanisms in Epigenetics

Bryan M. Turner

Blackwell Science (2001) 284 pages. ISBN 0-865-42743-7
£27.50

Bryan Turner engaged himself in a very

challenging task with the writing of a book on a topic that is evolving at a considerable rate and has seen an incredible amount of information accumulate in recent years. The most important aspect of this book is that it is aimed at a student and nonspecialist readership, and thus a real effort has been made in the writing style to present chromatin and gene expression as a story. To this end, Bryan introduces his book by setting the stage and the key players: the helpless gene, which in different cell types is the same but differently expressed, and its packaging into chromatin, a very influential partner. The story of the relationship can then begin.

As a specialist, I do not fall into the target audience; yet I enjoyed reading the book, mostly for the general picture and the colourful comparison with daily life. The metaphor that he borrowed from Richard Dawkins, which compares our genes to a recipe used to bake a cake, is particularly well developed: "even if we leave our cookery book open at the right page in a well-equipped kitchen with all the right ingredients close by, a cake is unlikely to appear. Unless, that is, a sympathetic friend who can take a hint happens to enter the kitchen. Then a cake may materialize". This allows him to make an important point, which is that there is information beyond just the recipe itself. In other words, this opens the discussion as to what conditions genes require in order that the information they contain can be 'converted' into a living organism.

The story is developed over twelve chapters. First, a brief overview is given of the basic principles involved in controlling transcription in prokaryotes. He next introduces the problems of complexity (genomic and cellular) in eukaryotes. The basic unit of chromatin, the nucleosome and its protein component, histones, is presented with a specific emphasis on the histone tails

and their various post-translational modifications. The less-defined aspects of higher-order chromatin structure and nuclear organization are also considered. The way in which transcription occurs in the context of chromatin is then discussed. The recent concepts of 'chromatin remodeling machines' are highlighted to explain newly refined control mechanisms. A chapter is dedicated to heterochromatin, thus raising the issue of long-term silencing of gene expression. The final part consists of a comparison of mechanisms used for dosage compensation in different organisms (mammals, *Drosophila* and *C. elegans*). This section is not meant to provide a real end to the story but rather to stimulate the imagination. It illustrates how ideas developed throughout the text can come together to help in our understanding of the fascinating mechanisms underlying the coordinated regulation of gene expression across an entire chromosome. Like any good relationship, the story has no end, but surely has the potential for much future development.

Aside from some pictures taken from original publications, a series of schematic figures, mainly grayscale line drawings adapted from various sources, are provided, and their major asset is their simplicity as useful teaching aids.

In conclusion, and to get back to the culinary metaphor (which rang a chord with me as a French reader), it seems that reading this book could be likened to a good appetizer - it should stimulate students to be curious about the rest of the meal and, therefore, run off and read up on more specific information on the individual aspects of the story.

Genevieve Almouzni

Institut Curie, Paris, France

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