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Book review

Metallothioneins and Related Chelators Series: Metal Ions in Life Sciences , Vol. 5. A. Sigel, H. Sigel, R.K.O. Sigel (Eds.), 2009, 514 p., Hardcover, ISBN: 978-1-84755-899-2.

This book of 481 pages plus a detailed index, brings together 29 expert researchers who are authors and coauthors of 15 chapters. The content concerns the biological origins, *in vivo* properties, and physicochemical properties of a wide range of metallothioneins (13 chapters), with two chapters focusing on related chelators. Overall, an excellent book that clearly and with considerable detail describes the current state of much research into the metal binding properties of different metallothioneins. Indeed, a welcome aspect of this book is the focus on metallothioneins from sources other than mammals. The chapters on bacterial MT (Blindauer), and MTs from plants, particularly the wheat MTs (Freisinger), earthworms (Sturzenbaum), and aquatic organisms (Vergani) admirably fill a gap in the generally available literature on metallothioneins studied by researchers world-wide.

A brief summary of some highlights of selected chapters illustrates the variety and value of the contents of this new book. The first chapter by Monica and Gunnar Nordberg is an excellent beginning as these researchers have been key contributors to the development of the whole field since their first contributions in the 1970s and they bring a depth of knowledge to this chapter. The inclusion in this opening chapter of the connection between metallothioneins and disease and the effects of aging on metallothionein synthesis and metal status brings us to subjects of present day research. The book next turns to the genetic control of cellular metal concentrations through control of metallothionein synthesis. In this chapter, Balamurugan and Schaffner introduce an excellent survey of the complexity of the genetic control of metal homeostasis. Their description of the control of copper is particularly interesting.

The focus on genetic control is extended in Chapter 6 to metallothioneins in Drosophila by Atrian, and earthworms and nematodes by Sturzenbaum (Chapter 7). The chapter on bacterial metallothioneins (Chapter 3) introduces not only the occurrence of a metallothionein that uses histidine as well as cysteine to coordinate the metals, but also the value of NMR and mass spectrometry in the characterization of the metal binding properties. The detailed and clear comparisons of the heteronuclear correlation spectra with the 1D ^{111}Cd NMR spectra allows the reader to appreciate the power of these tools for systems as complicated as those where multiple-metal binding takes place. The use of the combination of NMR and ESI-MS techniques to follow the metal-induced folding also provides an excellent guide to the use of these tools to answer complex questions. Dolderer, Hartmann and Weser in Chapter 4, describe the only new X-ray structure of a metallothionein, that of the copper-containing yeast MT. Of considerable importance is the proof that copper can bind with mixed-coordination, both digonal and trigonal coordination by sulfur is found in the structure of this Cu_8-yeast MT.

While most metallothioneins studied over the last 60 years have been from mammals or yeasts, metallothioneins have been reported recently from algae and plants. The metallothioneins from plant sources have received little attention until recently, so that Chapter 5, "Metallothioneins in Plants", by Freisinger is a very welcome contribution. In this chapter she provides a detailed and wide-ranging review assembling much information not normally available in one place including a introduction to the problems of predicting metal-thiolate cluster structures in the absence of X-ray diffraction data or detailed NMR spectral studies. Detoxification of metals or cellular protection from toxic metals is the focus of chapters on MTs from earthworms and nematodes (Chapter 7), aquatic organisms (Chapter 8), freshwater animals (Chapter 9), and in mammalian metallothioneins (Chapter 12). These chapters lead naturally to studies of the role of metallothioneins in the central nervous system and the brain (Chapters 10 and 11) and finally to inorganic-induced carcinogenesis (Chapter 13).

The metals typically referred to with respect to metallation of metallothioneins are zinc, copper and cadmium. However, a much wider range of metals bind to the thiolate cysteines of the metallothionein binding site, as to be expected from the inorganic coordination chemistry of these donor atoms. While bismuth, mercury, silver, gold, platinum, iron, and nickel have been well studied, arsenic, chromium, and lead are relative newcomers. In this respect, reactions of arsenic with metallothioneins are discussed in Chapters 7, 12, 13, and 15 in this book.

The last two chapters concern proteins (Chapter 14) and peptides (Chapter 15) unrelated to the chemical and structural characteristics of the metallothioneins, namely, predominantly thiolate coordination of d^{10} metals and metal-induced folding from the near to random coil of the metal-free protein. The content of these two chapters provides a window on to a wider world of metal coordination. The thioredoxin family of proteins is characterized by significant structure in the metal-free form, and a role quite distinct from that of the metallothioneins. The phytochelatins (Chapter 15) were long considered to be the 'plant MT'. However, phytochelatins are not metallothioneins, they are small peptides formed by polymerization of glutamic acid, cysteine, and glycine, essentially, polymeric glutathione. As such, these peptides also bind the d^{10} metals of the metallothioneins, cadmium, zinc and copper.

Of interest to this reviewer is the very wide range of techniques that now comprise the tools of research into the metallothioneins that are showcased throughout this volume. Multinuclear NMR has played a major role in structure elucidation from the first reports in the 1970s, and with the routine availability of techniques such as HSQC (Chapter 3 and 8) we see structural information being made possible with much shorter instrument times and lower concentrations. Electrospray mass spectrometry is also now a vitally important tool and data are presented in detail in Chapters 3, 5 and 6.

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I have one minor complaint. It would be nice if the editors had ensured that the metal-oxidation state nomenclature was consistent throughout the book (for example, the nomenclature for copper changes from chapter to chapter).

In summary, "Metallothioneins and related Chelators" is a well-written, well-illustrated, and well-referenced book that will be invaluable to researchers interested in not only the *in vivo* biochemistry of metal regulation and homeostasis but also the new techniques used to determined the chemically important structural and mechanistic properties of these remarkable molecules. Because metallothioneins have been found in every organism and because metals control many of the processes of life, understanding the biochemistry and chemistry of metallothionein will continue to be challenging and important research.

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