Platinum and Biological Systems

Metal Ions in Biological Systems, Volume 32: Interactions of Metal Ions with Nucleotides, Nucleic Acid, and Their Constituents

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Nucleotide- and nucleic acid-metal ion interactions have been a major focus of research for over forty years. Many of the enzymes involved in RNA and DNA biochemistry utilise metal ions. Metal ions affect the stability of the three dimensional structures of nucleic acids and nucleic acid-protein complexes, and indeed, the platinum-based anticancer drugs exert their effect by interaction with DNA. This volume and Volume 33 (to be reviewed in a future issue) bring together international experts who review the present status of research in this field.

The book can be subdivided into four sections, with the first ten chapters covering the interaction of metal ions with the low molecular weight nucleotides. Chapters 11 to 15 review interactions with high molecular weight ligands, such as nucleic acids and nucleic acid-protein complexes. These chapters provide the background for two chapters on the role of metals in gene regulation. The final chapters examine the interaction of the platinum anticancer drugs with nucleic acids.

Interactions of naturally occurring metals (with biological systems) are a key feature of this volume, and though not of direct relevance to this journal, their significance should not be overlooked. The chapters on gene regulation are at the leading edge of an important area in modern inorganic biochemistry.

The platinum group metals feature strongly throughout the book. The interactions of metal ions and nucleic acids can be studied in the solid state using X-ray diffraction, or in solution using techniques such as NMR or UV-Visible spectroscopy. The use of platinum complexes as probes for these techniques forms sections in Chapters 4, 6 and 11. In Chapter 3, R. B. Martin describes the use of palladium complexes to provide the empirical basis for a discussion of metal ion binding to purines. In Chapter 9, T. Rau and R. van Eldik, and in Chapter 10, J. Arpalahti, describe the kinetics of palladium(II)- and platinum(II)-nucleobase interactions.

An important reason for studying metal-DNA interactions is to understand the mechanism of the platinum anticancer drugs. A review of the current status of structure-activity relationships of platinum anticancer drugs, is presented by N. Farrell in Chapter 18, focusing on recent work on the biological activity and unique DNA interactions of *trans*-platinum complexes, previously thought not to have activity as anticancer drugs. In Chapter 19, M. J. Bloemink and J. Reedijk review the mechanism of cisplatin binding to DNA from both a structural and a kinetic perspective, and discuss the significance of this for new platinum complexes.

The still unanswered question of how cisplatin-DNA binding leads to tumour cell death is addressed by J. P. Whitehead and S. J. Lippard in Chapter 20, who describe the current understanding of the repair of platinum lesions on DNA. They discuss the binding of a DNA damage-recognition protein, leading to the formation of a platinum-DNA-protein ternary complex, and its involvement in platinum-induced cell death. Since the discovery of cisplatin many laboratories have attempted to identify other metal-based anticancer drugs, and in Chapter 21, M. J. Clarke and M. Stubbs discuss the interaction of experimental ruthenium and rhodium metallopharmaceuticals with DNA.

Metal ions play an important role in many biological processes – the rationale for this long running series. This is an excellent book and maintains the high standards set by this series. There are occasional overlaps between chapters, perhaps only to be expected in such a long book; however, this is offset by the quality and topical nature of the contributions, making this a valuable addition to bioinorganic literature. S.P.F.