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BIOLOGY OF METALS

Editorial

The title of this journal shows that emphasis will be placed on the biology of metals; contributions dealing with the biology of ionized, complexed or protein-bound metals will be presented and discussed. However, this is not a plea in favour of a biological, chemical or physical view of metals. In principle, there is no difference between these disciplines as far as biological systems are regarded, since the fields together contribute to our understanding of the molecules and forces that finally make an organism function as a living organism. Instead, our aim in selecting a title such as *Biology of Metals* was to bring together experts who can elucidate the diverse biological structures containing metals or metal ions and scientists who are investigating the sophisticated metabolic and genetic events developed to insert, use or process the various metal ions. Many techniques and methods are currently available to study the basic questions of the biology of metals: spectroscopy, electrophoresis, chromatography, electron microscopy, chemistry and a variety of novel molecular biological methods, all of which represent important tools in modern biology. Biologists, chemists and physicists work on the same project in order to improve or develop methods that enable us to understand the basic principles of life.

The study of metal ions in biological systems requires knowledge of the chemistry of metal ions, their redox states, electronic properties and their binding constants to various ligands, as well as detailed knowledge of the composition, function and metabolism of the cell. However, very few scientists will approach this ideal. Therefore, we need a community of experts in different fields with a common interest in biology. Several groups have been established recently with similar purposes, aims and scopes that underline the increased interest in metal ions in biology. A variety of symposia and meetings will be held this year and next year, in which the properties of metal-containing compounds isolated from cells will be discussed: XXVIth International Conference on Coordination Chemistry, 28 August to 2 September, 1988, in Porto, Portugal; the XXVII Conference in 1989 in Australia; Metal Active Sites in Biology and Their Synthetic Analogues, 6-8 October, 1988, in Le Bischenberg Bas Rhin, France; the Fourth International Conference on Bioinorganic Chemistry, 24-28 July 1989, Cambridge, Massachusetts, USA; Ninth International Conference on Proteins of Iron Storage and Transport, 9-13 July, 1989, Brisbane, Australia. Further meetings have been announced dealing with the genotoxicity of metals: Symposium on Ruthenium and Other Non-platinum Metal Complexes in Cancer Chemotherapy, 30 June to 1 July, 1988, Triest, Italy; First International Meeting on Molecular Mechanisms of Metal Toxicity and Carcinogenicity, 19-22 September, 1988, Urbino, Italy.

Moreover the increasing interest in this area of biology is also documented by the volumes on metalloproteins, the toxicity of inorganic compounds, conference proceedings and book series on metal ions in biological systems, as well as reviews on metal ions and metal ion environments. Metal complexes that target DNA sites, zinc fingers representing novel motif for nucleic acid binding, *cis*-platin complexes, calcium-binding proteins, calmodulins, metallothioneins and metalloenzyme catalysis are some of the predominant themes in the current literature. Still under study or in the process of being intensively analyzed using newly developed spectroscopic methods are the active centers of enzymes containing iron, molybdenum, copper, manganese, nickel and zinc with roles in dinitrogen fixation, photosynthesis, oxidative phosphorylation, methane production, cytochrome-P-450-dependent oxidation or proteolysis. The various iron-sulphur proteins and their function in electron transfer and diverse metabolic processes, as well as their metabolic connection to flavins, hemes and other metal containing centers, have all provided new insight, followed by questions concerning the biological significance.

Iron certainly plays a prominent role in respiration, oxygen transport, detoxification (catalases, peroxidases, superoxide dismutases) and the hydroxylation reactions of all aerobic organisms. An increasing amount of literature has evolved covering the various chemical and biological aspects of iron, and this will probably be documented in further contributions in this journal. The finding that microbes and, to a certain extent, also plants can synthesize iron-sequestering molecules (siderophores) designed to capture environmental iron has led to intense chemical, genetic and transport studies. Copper is often associated with iron when electrons are transferred to molecular oxygen (cytochrome c oxidase), but it also substitutes for iron in certain enzymes. The functions of zinc involve catalytic, structural and regulatory processes. In all areas mentioned detailed knowledge of the structures of metal centres is a prerequisite to the understanding of their biological function. However, it is the biological function that often needs to be elaborated upon in more detail, and one of the aims of this journal is to foster the study of regulation, biosynthesis, interaction and function of metal centres, the recognition of metal environments and their genetic regulation. After a new structure of a metal-containing compound isolated from biological material is elucidated, further questions arise — for example, its biological function, the transport systemes involved, the factors regulating biosynthesis, the intracellular content and incorporation of the metal ion. Do we really know the mechanisms through which essential ions are taken up and distributed to the various compartments of the cell? In *Escherichia coli,* the biosynthesis of iron transporting ligands (siderophores) and the biosynthesis of their corresponding outer membrane receptors and regulation of ferric hydroxamate uptake by the *fur*-protein have been analysed at the genetic level. The *fur*-protein has been cloned and its expression studied. In fungi information is available on the structure/activity relationship of siderophores and the corresponding transport system(s), indicating that the iron centre and the surrounding functions of siderophores are essential for recognition by membrane-located transport systems.

Metal deficiencies greatly affect the growth of plants. The mineral composition of the soil is regarded as crucial for optimal growth. Iron chlorosis is a worldwide problem, particularly in semiarid regions containing calcareous soils. Although most soils contain enough iron, the amount available to the plant is dependent on factors such as iron species and plant genotype. Biologists distinguish between Fe-efficient and Fe-inefficient plants, indicating that some plants can overcome a decreasing iron content at the root surface by compensating mechanisms. The deficiency of several other metal ions exerts serious metabolic defects in plants that have not been analysed in detail.

In animals and humans transferrin and ferritin represent the most important iron proteins. Although much information is currently available on the structure and function of both molecules, intense research has been initiated to study their intracellular fate. Uptake, transport and metabolism of metals are essential functions in all cells. However, only a dozen metallic elements are considered essential, and a variety of others are regarded as toxic or even carcinogenic. For example, copper deficiency has been reported to result in cardiovascular, gastrointestinal, hepatic hematopoietic and neurological disorders in animals. The underlying molecular events are only partly understood. Zinc is essential for numerous metabolic processes, and zinc deficiency affects the endocrine, gastrointestinal, integumentary, musculoskeletal, nervous and reproductive systems. Thus, a single deficiency can produce several physiological symptoms which, in turn, may be caused to a single metabolic defect. The distribution and toxicity of various heavy metals have been studied in individuals residing in polluted areas. Human nutrition and metal toxicity, as well as the assessment of metal ion toxicity and metal carcinogenicity, are of utmost importance today. Thus, cadmium toxicity is greatly influenced by the presence of the low-molecular-weight (MG 6000–7000) cysteine-rich proteins called metallothionein, as they can protect cells from cadmium overload. Renal dysfunction is regarded as the most serious effect of cadmium in mammals. Certain heavy metals have been definitively correlated with carcinogenic activities, crystalline nickel sulfide being the most carcinogenic compounds. This short survey on some of the important aspects of the biology of metals is not intended to be comprehensive but instead should be regarded as a stimulant and an invitation to various scientists in the field and several existing societies and groups to cooperate in this exciting biological field, regardless of the fact that certain metal-containing structures must be discussed in terms of pure chemistry and physics.

Therefore, I cordially welcome all readers interested in the various aspects of metal ions in biology and invite all scientists working on the elucidation of metal-containing structures, their environments, and their genetic and metabolic regulation to cooperate in the study of the *Biology of Metals*.

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