Metalloproteins and Metalloidproteins

Analysis, Function, Clinical Trials

Edited by
Antonios Kyriakopoulos
Bernhard Michalke
Alexandra Graebert
Dietrich Behne

Herbert Utz Verlag · München

Biochemie

Bibliografische Information Der Deutschen Bibliothek:
Die Deutsche Bibliothek verzeichnet diese Publikation in der Deutschen Nationalbibliografie;
detaillierte bibliografische Daten sind im Internet über http://dnb.ddb.de abrufbar.

ISBN 3-8316-0576-9

Printed in Germany

Herbert Utz Verlag GmbH, München
089-277791-00 · www.utzverlag.de

CONTENTS

REVIEW

D. Behne and A. Kyriakopoulos
Metals und metalloids as binding partners of proteins 1

ANALYSIS

M. Kühbacher, G. Falkenberg, U. Schade, J. Fischer, T. Donath, F. Beckmann, B. Grünewald, D. Behne and A. Kyriakopoulos
Selenomics and Metalloproteomics using Synchrotron Radiation - Frequently Asked Questions - different Animal Models, different Methods, different Answers 11

R. Krivanek, H. Dau and M. Haumann
Photothermal spectroscopy to investigate the energetics of photosynthetic water oxidation 18

P. Schmieder
NMR in the structure elucidation of natural products - the Hassalidins..... 25

S. Hann, M. Sulyok, M. Popp and G. Koellensperger
Hyphenation of CIM® mini DEAE disks to ICP-MS for studying protein adducts of the cancerstatic Ru compound KP1019 32

S. Overkamp
ProteomeLab™ IgY – digging deeper than ever into the plasma proteome..... 40

K. Bukalis, C. Wolf, D. Alber, D. Behne and A. Kyriakopoulos
Combination of biochemical and analytical methods in the studies on trace elements and trace-element-containing proteins in the lung and trachea of the rat 44

N. Hertkorn, R. Benner, M. Frommberger, Ph. Schmitt-Kopplin, M. Witt, K. Kaiser, A. Kettrup and I. J. Hedges
Characterization of a New and Major Refractory Component of Marine Organic Matter..... 57

H. Dau, M. Haumann, P. Liebisch, C. Müller, M. Grabolle, M. Barra, P. Loja and O. Kirilenko
Photosynthetic O_2-Production at the tetra-manganese complex of photosystem II tracked by novel X-ray absorption experiments 62

FUNCTION

B. Stahl, G. Fleissner, G. Falkenberg and G. Fleissner
Magnetite nanoparticles alone are not able to explain iron mineral-based magnetoreception in homing pigeons 69

I. Hamann, T. Schwerdtle, G. Jahnke and A. Hartwig
Copper overload decreases genomic stability by distinct mechanisms 75

D. Kümmel, A. P. Turnbull, J. J. Müller, Y. Rosk and U. Heinemann
Structural Studies of the Human Tethering Complex TRAPP Involved in Vesicular Transport..... 80

S. Boxhammer, S. Glaser, A. Kühl, A. Wagner and C. L. Schmidt
The Rieske iron-sulfur proteins of *E. coli* – unknown and uninteresting? . 85

U. Wollenberger, N. Bistolas, C. Jung, M. Richter and F. W. Scheller
Studies on direct reduction of nitric oxide synthase 98

CLINICAL TRIALS

B. Michalke
Selenium speciation in human serum of cystic fibrosis patients compared to serum from healthy persons 101

C. Schmutzler, I. Hamann, A. Bacinski and J. Köhrle
Endocrine disruptors disturb the metabolism of the essential trace element iodine and interfere with thyroid hormone biosynthesis..... 112

W. Windisch
Nutritive Bioavailability of Zinc from Zinc Amino Acid Formulations Using Zinc Glycinate as a Model 117

POSTER PRESENTATION

H. Bertelsmann, H. Sieme, H. Bollwein, D. Behne and A. Kyriakopoulos
Zinc and Iron in Equine Semen and Semen Fractions 127

L. Dalla Puppa, N. E. Savaskan, A.U. Bräuer, D. Behne and A. Kyriakopoulos
Effect of Selenium on hydrogen peroxide-induced apoptosis 134

I. Grbavac, N. Wenda, C. Wolf, M. Kühbacher, D. Alber, D. Behne and A. Kyriakopoulos
Distribution of metals- and metalloids and related proteins in the prostate 139

A. Kyriakopoulos, I. Grbavac, C. Wolf, A. Plotnikov, M. Kühbacher, A. Graebert and D. Behne
Isolation and characterization of a copper-binding protein 148

A.-G. Lenz, H. Hinze-Heyn, M. Brielmeier, K. Bukalis, A. Kyriakopoulos, H. Schulz and K. L. Maier
Effect of selenium-depletion on lipidperoxidation and oxidation of proteins in tissue of mice and rats 153

A. Plotnikov, H. Bertelsmann and A. Kyriakopoulos
Scanning Laser Ablation Inductively Coupled Plasma Mass Spectrometry of Proteins after 1D-Separation by Gel Electrophoresis and Subsequent Western Blotting: Theoretical Basics, Optimization and Practical Applications to the Analysis of Se-Containing Proteins..... 159

A. Richter, T. Pohl, C. Wolf, A. Plotnikov, I. Grbavac, D. Behne and A. Kyriakopoulos
Selenium in the cardiovascular system of the rat 169

N. Wenda, I. Grbavac, C. Wolf, A. Plotnikov, M. Kühbacher, D. Behne and A. Kyriakopoulos
Prostate and the essential trace element Selenium..... 175

C. Wolf, U. Schweizer, K. Bukalis and D. Behne
Investigations of metallo- and metalloid proteins by element specific detection methods 181

AUTHOR INDEX 189

REVIEW

Metals und metalloids as binding partners of proteins

D. Behne and A. Kyriakopoulos

Hahn-Meitner-Institut, Department "Molecular Trace Element Research in den Life Sciences", Glienicker Str. 100, D-14109 Berlin, Germany

Summary

It can be assumed that the biological significance of most essential metals and metalloids is due to their functions in metalloproteins. The investigation of the relationships between these essential elements and proteins is therefore a promising approach to obtain first information on the existence of metalloproteins not yet identified. Some other elements assumed to have biological effects might also act as constituents of metalloproteins and should therefore be included in these studies. In this overview the metals and metalloids are discussed which should be taken into consideration as potential binding partners of proteins and which are therefore of interest in metalloprotein research.

It has been suggested that many of the proteins present in the mammalian organism require a metal or metalloid to be biologically effective. However, only relatively few of these compounds are known so far, and the identification of novel metalloproteins is at present one of the main tasks in metalloprotein research. Our knowledge of metalloproteins not yet identified is restricted to the fact that they contain a metal or metalloid. First information on the existence of such compounds can therefore be obtained when we choose appropriate elements and carry out studies to find out whether they are present in the organism in form of specific protein complexes.

There are numerous metals and metalloids to choose from for these investigations. However, obviously one should start with those most likely to be constituents of proteins.

Several of the elements listed in the periodic table (s. Fig. 1) can be excluded from the list of potential protein binding partners. Among them are the noble gases, the non-metals such as hydrogen, carbon, nitrogen, oxygen, phosphorus, sulfur and the halogens, the non-naturally occurring

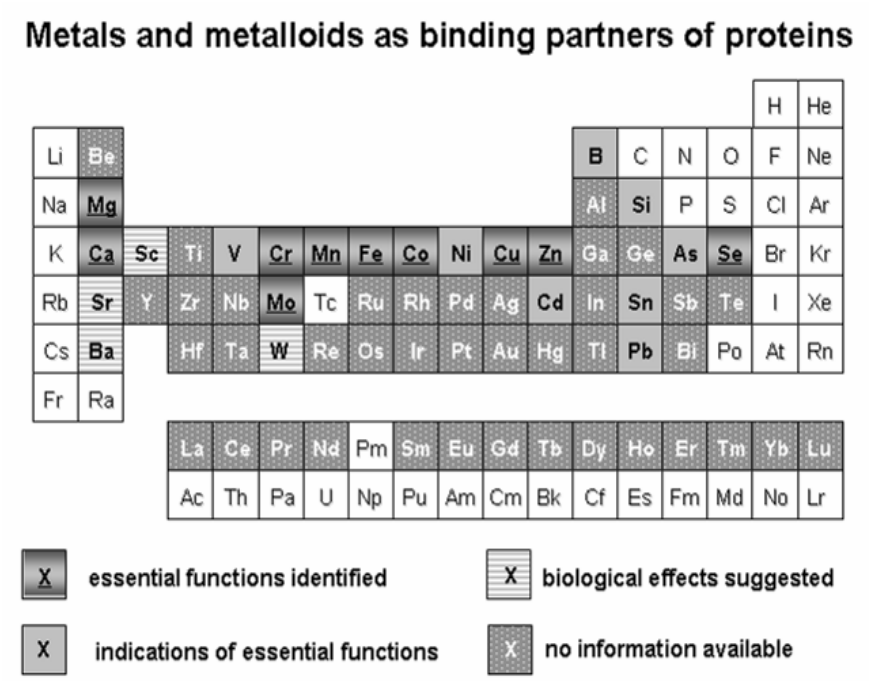

Fig. 1: Overview of metals and metalloids which, as is suggested by their biological effects and chemical characteristics, might function as constituents of metalloproteins and should therefore be taken into consideration when novel metalloproteins are to be identified.

elements including technetium, promethium and the transuranium elements and also the elements with naturally occurring radioisotopes. The highly electropositive alkali metals, with the great tendency of their cations to dissociate in solution, do not form stable metalloproteins and can likewise be disregarded.

The most promising way is to choose metals and metalloids with known essential functions as it may be assumed that in most cases their effects are due to their presence in specific protein complexes. The question of which of the elements of the periodic table belong to this category has not yet been completely solved. According to the traditional criteria an element is considered essential for a certain species when a decrease in its intake below a certain level leads to functional or structural anomalies in these organisms which can be avoided by sufficient supply of the element or the element in a certain chemical form. A more modern version includes as second possibility that the element is part of an organic structure with an

important function in these organisms. All of the essential metals and metalloids listed in Fig. 1 have been identified by the traditional criteria by means of investigations of deficiency states. It is very probable that, with further studies in metalloprotein research and the detection of additional elements as constituents of physiologically important proteins, the group of essential elements will be increased.

Here the most likely candidates are metals and metalloids for which indications of essential effects were obtained in deficiency studies but for which the results were not unambiguous enough to justify their definite classification. This group is specially marked in Fig 1.

Some of the metals and metalloids with known essential functions have been shown to be biologically active in the form of numerous metalloproteins. In the case of **zinc**, for instance, we already know a large number of enzymes that require this metal, and from searching sequence bases for possible zinc-binding sites hundreds of catalytic zinc sites and thousands of structural zinc sites are predicted in the mammalian proteomes [1]. Detailed information on numerous specific metalloproteins has also been obtained for **iron** [2,3], **copper** [2,3] and **selenium** [4,5], although their number is considerably smaller than the zinc compounds. In the case of **manganese** [2,3], **molybdenum** [2,3] and **cobalt** [2,3] only a few metalloenzymes have so far been detected in the mammalian organism and it is very likely that there are further protein complexes of these metals to be identified. A special case in the group of the essential elements is **chromium**. It was shown to play a role in the insulin metabolism, and chromium deficiency resulted in impaired glucose tolerance in humans and rats [6]. However, so far only one biologically active chromium-containing oligopeptide has been described, the so-called “low molecular weight chromium-binding substance“ [7]. This would be the only case where an essential metal is present in form of only a single biomolecule, and the clarification of the question of the existence of further biologically active chromium compounds is therefore of great interest.

The group of elements for which in deficiency studies indications of essential functions have been obtained includes boron, silicon, vanadium, nickel, arsenic, cadmium, tin and lead.

Several parameters were found to be affected in animals [8] and also in humans [9] after insufficient **boron** supply. They include bone calcification, calcium and magnesium metabolism and plasma alkaline phosphatase. It has been suggested that boron affects the mineral metabolism via steroid hormones but so far its biochemical function is still unknown.

Growth stimulation by administration of **silicon** was demonstrated in rats fed a low silicon diet [10]. This element was shown to be necessary for the

normal development of bone and connective tissue. It is a constituent of the enzyme prolylhydroxylase [11] and probably has structural functions in glycosamino-protein complexes [12].
Goats with v**anadium** deficiency were shown to have a higher abortion rate. The off-springs had skeletal deformations and a higher mortality [13]. In rats a low vanadium intake led to an enlarged thyroid and disturbances in the iodine metabolism [14]. Vanadium-dependent haloperoxidases have been identified in lower forms of life [3].
Effects of **nickel** deprivation have been found in several mammalian species. Severe nickel deficiency resulted in disturbances in growth and haematopoiesis. The effects were enhanced by insufficient iron supply [15]. Several nickel-containing enzymes were found in plants and micro-organisms [3] and there is the possibility that similar enzymes exist in mammals, too.
Suggestions on essential functions by means of deficiency studies have also been obtained for some elements such as arsenic, cadmium, tin and lead, which so far were best known for their toxic effects.
It was found in several mammalian species that a low **arsenic** intake resulted in impaired growth rates. Other effects observed in goats were a decreased conception rate, an increased abortion rate and a higher mortality of mothers and off-springs which could have been caused by a cardiomyopathy [16]. The biochemical function of arsenic is not yet known. First indications of the existence of several arsenoproteins have been obtained in a recent investigation (K. Bukalis et al., in preparation).
Deficiency studies on **cadmium** in rats [17] and goats [18] indicated that small doses of the element are required for optimal growth of the animals. No information is as yet available on the biochemical function responsible for this effect and on the existence of biologically active cadmium proteins.
In the case of **tin**, too, deficiency studies showed depressed growth of rats that suggested an essential function of the element [19,20]. Other effects of zinc deprivation were alopecia and changes in the mineral concentrations in the tissues [20]. A role of tin in the formation of the tertiary structure of proteins was hypothesized [19] but so far no biochemical function of the element has been found.
Lead is another element that is mainly known for its toxicity but might have an essential function. Lead deficiency was found to affect the growth of rats [21,22]. The deficient animals had an impaired iron absorption and anaemia [23]. Here, too, nothing is known about the biochemical role of the element and the existence of specific lead proteins.
The third group comprises elements for which biological effects have been suggested. Some of the candidates, which may be of interest in this respect, are marked in Fig. 1. Experiments carried out in the late 1940s on guinea