Metallobiolomics

Analysis, Function, Clinical Trials

Edited by
Antonios Kyriakopulos
Bernhard Michalke
Alexandra Graebert
Dietrich Behne

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Preface

Biochemical and biological conferences, 50 years earlier, rarely covered the topic of the role of metal and metalloid ions in living systems. Many years have elapsed since intensive discussions began regarding the subject of biologically active molecules with low and/or large molecular masses containing metals and/or metalloids. Studies of metals in biological systems began after several genomes, as well as prokaryotic and eukaryotic systems were elucidated. More than a decade ago scientific reports, in the field of proteins, concentrated partly on the subject of metals and biologically active molecules. It can now be assumed that the biological significance of most essential metals and metalloids is due to their functions in metalloproteins and other metal containing molecules.

The investigation of the relationships between these essential elements and proteins is a promising approach which is yielding initial information on the existence of metalloproteins and other metal containing molecules. Some other elements assumed to have biological effects also might act as constituents of metalloproteins and have therefore been included in this meeting. Discussions were held at the recent conference regarding analysis procedures of elements by AAS, ICP-MS, laser ablation ICP-MS, micro-SRXRF and other analytical methods. The structure and function of metal containing proteins and other micro-molecules and their clinical application were reported on as well.

The most interesting highlight of the conference was the attendance, and especially the active involvement, of many young scientists such as PhDs and postdocs, who reported their latest results and problems concerning topics of analysis, structure, function and clinical application of metal and metalloidproteins, and other metal-containing molecules. The presentation by 20 posters of several European countries is also worth mentioning here. Due to the high quality of the posters represented at the conference awarding the prize for the two best posters was a very difficult decision. Finally, the poster commission decided to award a prize to four posters.

We hope that by holding this conference new ideas will emerge in the field of metallobiolomics, and especially be a useful source of information, which is always indispensable for further studies.

The editor wishes to thank all contributors for submitting their articles. Last but not least a special thank you goes to Alexandra Graebert, Gabriele Beschnidt and the colleagues of the dept. SF6 for their really splendid and friendly cooperation, as well as the great overall effort made in managing the conference.

Dr. Antonios Kyriakopoulos
(Senior Researcher)

Berlin, February 2007

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CLINICAL TRIALS

Metalloid- and Metalloproteins – visualized with Neutrons and Photons

Markus Kühbacher [1], Gerald Falkenberg [2], Ulrich Schade [3], Jürgen Bartel [1], Igor Grbavac [1], Gregor Bukalis [1], Dorothea Alber [1], Dietrich Behne [1], Antonios Kyriakopoulos [1]

[1] Hahn-Meitner-Institut Berlin, Department of Molecular Trace Element Research in the Life Sciences, Glienicker Str. 100, 14109 Berlin, Germany
[2] Hamburger Synchrotronstrahlungslabor HASYLAB at Deutsches Elektronen-Synchrotron DESY, Notkestr. 85, 22603 Hamburg, Germany
[3] Berliner Elektronenspeicherring-Gesellschaft für Synchrotronstrahlung m. b. H. BESSY, Albert Einstein-Str. 15, 12489 Berlin, Germany
*e-mail: kuehbacher@hmi.de

Introduction

In this overview the concept of the complementary use of radiotracers produced with neutrons at the reactor of the Hahn-Meitner-Institut (Berlin) and photons produced at the synchrotron facilities BESSY (Berlin) and HASYLAB (Hamburg) for 2D and 3D chemical imaging of metal- and metalloid-containing proteins in specific tissues - in particular in the central nervous system - is discussed. Metals and metalloids are known to be involved in various cerebral metabolic processes. The determination of their spatial distribution within tissues in health and disease may help to identify their specific sites of action and to elucidate their biological roles. Possibilities and limits of the synchrotron techniques are shown in relation to the application of radiotracers used for specific labeling of those metal- and metalloid containing proteins, which are then detectable, by autoradiography.

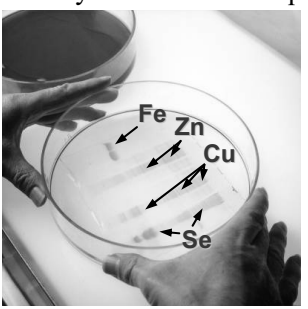

Figure 1: Metalloid- and Metalloproteins after electrophoretic separation.

Synchrotron radiation X-ray fluorescence analysis (SRXRF) allows the determination of the metal distribution in cryosections of tissues while

synchrotron radiation-based Fourier transform infrared (SRFTIR) spectromicroscopy may provide information on the chemical composition of the sections of interest. These methods can therefore be used as valuable tools in studies on the role of metalloproteins in health and disease.

Localization of Metalloid- and Metalloproteins with µ-SRXRF

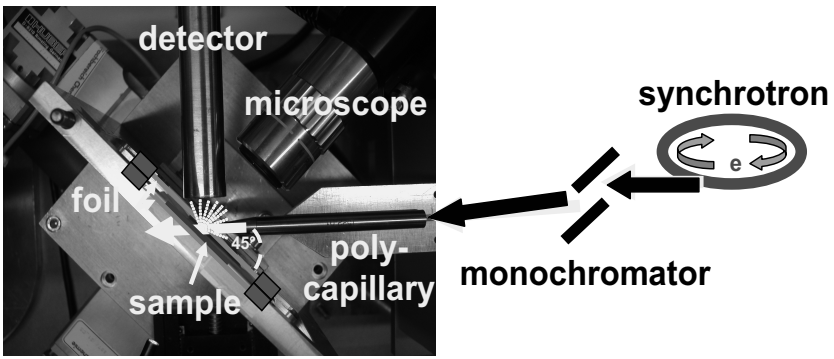

Figure 2: Experimental set-up employed at HASYLAB beamline L for µ-SRXRF.

The µ-SRXRF technique at HASYLAB and the BAMline at BESSY was applied as a bio-analytical tool in the investigation of the distribution of several elements in different neurodegenerative disorders of the central nervous system like Alzheimer's disease or Transmissible Spongiform Encephalopathy. Metals and metalloids are known to be involved in various cerebral metabolic processes. Changes caused by oxidative stress are thought to be important factors in their pathogenesis, and in these processes, several metals seem to play crucial roles. Metals are known to be involved in the production of free radicals and peroxides, but also in the protective systems against these oxidants.

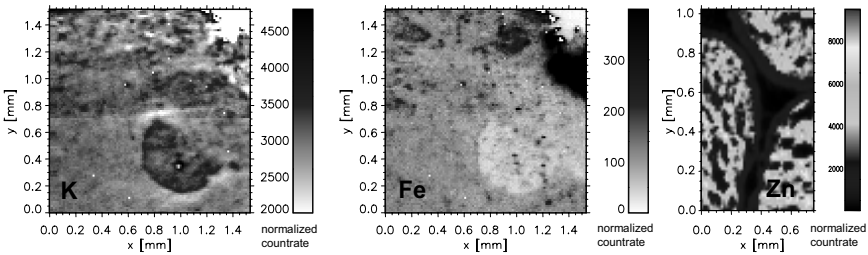

Figure 3: Element maps of K (left) and Fe (center) of brain tissue and Zn (right) of testis tissue. The color bar at the right indicates the count rate per second.

Characterization of Metalloid- and Metalloproteins with µ-XANES and SRFTIR-Spectromicroscopy

The pathological changes of the chemical pattern in a morbus Alzheimer affected brain section was investigated with SRFTIR-Spectromicroscopy.

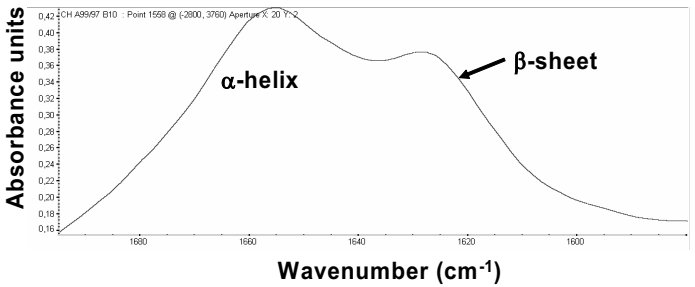

Figure 4: Amide I band in the IR spectrum and chemical map of a morbus Alzheimer affected brain section. The obtained spectrum from a senile plaque shows the beta-sheet assembly of ß-Amyloid, a metalloprotein.

While the spectroscopic use of infrared light allows insights into the conformation of the whole protein, the spectroscopic use of x-ray absorption, called x-ray absorption near edge structure (XANES) focuses on the metals inside the proteins. The figure 5 shows the possibility to employ this method with a spatial resolution in the micrometer range.