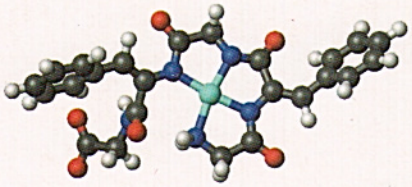
International Symposium
METALS, ENVIRONMENT, HEALTH



Book of Abstracts

Wroclaw Medical University
Faculty of Chemistry, University of Wroclaw

Szklarska Poręba, Poland
June 24-27, 2004

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BOOK OF ABSTRACTS

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Ni(II) CARCINOGENESIS AND BINDING TO CAP43 PROTEIN

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Nickel compounds are well known as human carcinogens. [1] The carcinogenicity of nickel compounds has been confirmed by numerous epidemiological studies in humans and animals. The leading concepts in nickel carcinogenesis involves oxidative promutagenic DNA damage and epigenetic effects in chromatin resulting from nickel binding inside the cell nucleus. [2-5]

A possible way to better understand the molecular mechanisms implicated in toxicity and carcinogenicity of nickel compounds is to study the characteristics of the proteins expressed by the genes specifically induced by these carcinogens.

Cap43 is an excellent tumor marker recently discovered. Exposure to either soluble or insoluble nickel compounds strongly activated several hypoxia-inducible genes.[6] Cap43 is one of these genes, and it expressed a 3.0-kb mRNA encoding a M_r 43,000 protein.[7] The primary signal for its induction is an elevation of free intracellular calcium ion caused by nickel ion exposure in cultured human cells; for this reason is named Cap43 : *Ca*lcium *p*rotein *43*,000. The peculiarity of Cap43 protein is its new mono-histidinic motif consisting of ten amino acids *TRSRSHTSEG* repeated three times in the C-terminus.

We have analyzed, for Ni(II) binding, the 30-amino acid C-terminal fragment of the protein, by a combined pH-metric and spectroscopic study. The fragment showed to bind one, two and three metal ions depending on the metal to ligand molar ratio.

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LECTURES

Nickel Carcinogenesis and Binding to Cap 43 Protein

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