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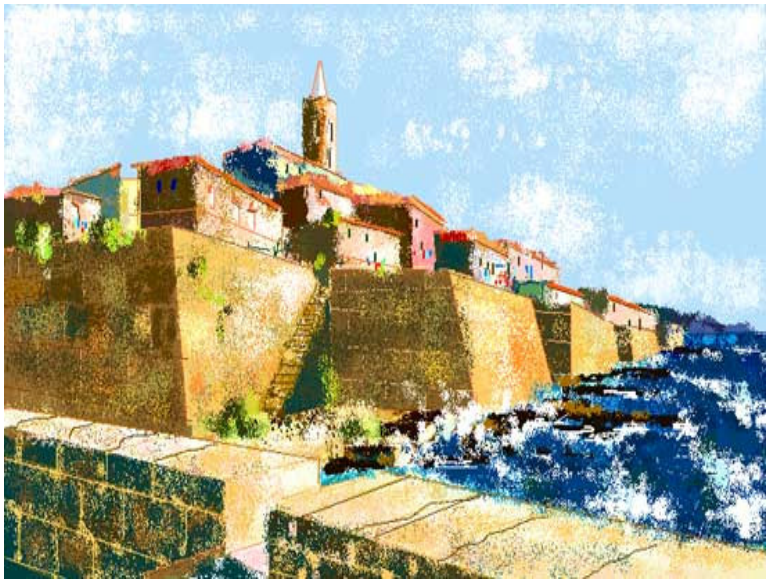

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CAP43 PROTEIN: AN ATTRACTIVE MOTIF FOR Ni(II) IN THE C-TERMINAL DOMAIN

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The carcinogenicity of nickel compounds has been confirmed by numerous epidemiological studies in humans and animals.[1] 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.[2] Cap43 is one of these genes, and it expressed a 3.0-kb mRNA encoding a Mr 43,000 protein.[3] 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: Calcium protein 43,000. The peculiarity of protein Cap43 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.

The present work supports the existence of an interesting binding site for Ni(II) at the C-terminal domain of Cap43 protein.

References

[1] IARC, Lyon, France Monographs on the evaluation of carcinogenic risks to humans, Vol. 49, Chromium, Nickel and Welding, (1990)
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