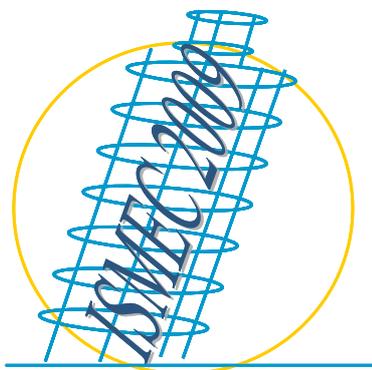




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BIDIMENSIONAL NMR REVEALS NEW FEATURES OF NICKEL(II) BINDING TO A FRAGMENT OF CAP43 PROTEIN

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Since its discovery, our research group chose Cap43 protein as an interesting subject for our studies because of its striking characteristic of being specifically induced by nickel(II) ions [1]. Nickel is a well known pollutant and carcinogenic agent, and the mechanisms involved in its toxicity are slowly being revealed [2]. Although Cap43 seems to participate in a number of events occurring inside the cell (like cell growth and differentiation, stress response, and hormone response, but also in cancerous states and metastasis suppression) we still do not know what its real function might be. However, the fact that Cap43 is specifically induced by nickel ions gives us a hint about its possible role as a detoxifying agent. In fact, in analogy with other proteins expressed after exposure to different metals and with the task of binding the dangerous ions to eliminate them from the cellular environment (like metallothioneins, for instance), we might think also Cap43 could exert a similar function towards nickel.

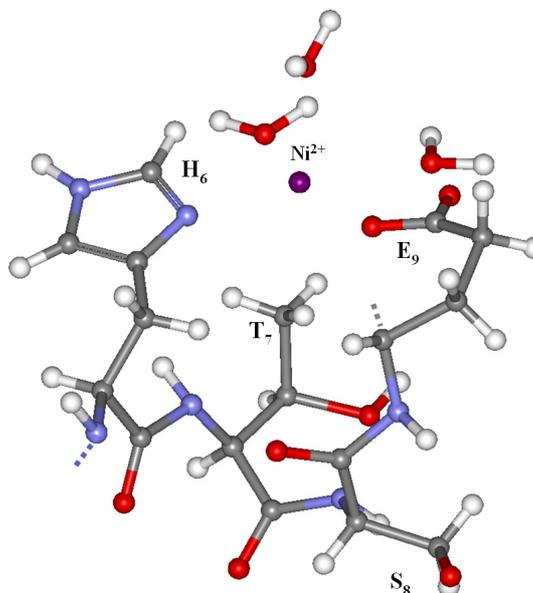


Figure 1: Three-dimensional scheme of the mono-histidinic fragment binding Ni(II) in a $1N\{N_{im}, COO\}$ coordination mode

In our previous studies we found that Cap43 has at its C-terminus an interesting sequence for metal binding, consisting in a mono-histidinic fragment of 10 aminoacids which is repeated consecutively three times [3,4]. We tested this sequence for nickel interaction at different pH values and metal concentration, and we found it can effectively bind up to three nickel ions.

In this contribution we would like to report our latest findings on this topic, unveiling the details of metal binding to the C-tail of Cap43 protein by the use of bidimensional NMR techniques.

[1] D. Zhou et al., *Cancer Res.*, **1998**, *58*, 2182-2189.

[2] M. A. Zoroddu et al., *Environ. Health Perspect.*, **2002**, *110*, 719-723.

[3] M. A. Zoroddu et al., *J. Inorg. Biochem.*, **2001**, *84*, 47-54.

[4] M. A. Zoroddu et al., *J. Inorg. Biochem.*, **2004**, *98*, 931-939.