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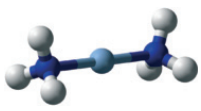
BOOK OF ABSTRACTS



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NI(II)-HISTONE H4 INTERACTIONS : STRUCTURAL MODIFICATIONS

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It is known that nickel participates to carcinogenic processes through mechanisms interfering with several cellular targets; among them, histone H4 has been recently identified. Histones are nuclear proteins that package and organize DNA into nucleosomes and chromatin, but they are also involved in gene regulation and transcription. By undergoing post-translational modifications, such as acetylation, methylation and phosphorylation, they change chromatin structure helping gene transcription or inhibition. Nickel showed to be *in vivo* a potent inhibitor of histone H4 acetylation. Acetylation causes important structural modifications in histones : for instance, it increases the α-helix content, thus decreasing the length of the histone tail and affecting the transcription mechanisms.

Following these indications, we studied how nickel interacts with the histone H4 tail, investigating the coordination mode of this metal to the the N-terminus of H4 where the sites of acetylation are clustered. [L. Broday et al., 2000], [M.A. Zoroddu et al., 2000, 2002, 2007]

Lately we have expanded the scope of our research to the structural modifications involving the whole protein. [M.A. Zoroddu et al., 2010]

From the study carried out by the use of several spectroscopic techniques (multidimensional NMR, CD) we found that nickel is able to induce a secondary structure in the protein; in particular, nickel induces an increase in α-helical conformation of the non-acetylated histone H4.

References

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