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Abstracts

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Nickel interaction with metal binding sequences of histone H4

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Nickel compounds are well known as human carcinogens.[1] 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] The nuclear proteins, and in particular the most abundant among them, the histones, are able to compete for metal ions with even higher affinity metal binding sites in other less abundant nuclear proteins or smaller molecules. Phagocytosis of insoluble particles of Ni_3S_2 by either macrophages or epithelial cells causes buildup of very high levels of nickel inside the cells after its intracellular dissolution catalyzed by the acidic pH of endocytic vacuole, thus providing a continuous source of Ni(II) ions.[6]

We investigated the issue of Ni(II) binding within the histone octamer. Using histone sequences in conjuction with the structural data we identified a binding site for Ni(II) ions located in the N-terminal tail of the histone H4.

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370

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