III Conferenza Organizzativa
Inquinamento da metalli pesanti: la biodisponibilità

Sassari
5 e 6 maggio 2005
Polo didattico - Facoltà di Scienze
Via Vienna
MOLECULAR MECHANISMS OF NICKEL CARCINOGENESIS: NICKEL BINDING TO HISTONE H4 AND CAP43 PROTEIN

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The carcinogenicity of nickel compounds has been confirmed and corroborated by numerous epidemiological studies in humans and carcinogenesis bioassays in animals [1].

Although the mechanisms of nickel-induced carcinogenesis are not well-known, they are believed to involve genetic and epigenetic routes. Nickel compounds influence carcinogenesis by interfering with a variety of cellular targets. We found that nickel is a potent inhibitor in vivo of histone H4 acetylation, in both yeast and mammalian cells [2]. It has preference to specific lysine residues in the N-terminal-S1GRGK5GGK5GLGK12GGAK18RH18RKVL22 histone H4, in which the sites of acetylation are clustered.

The metal ion is able to bind histidine H18 in the N-terminal which protrude out from the nucleosome [3].

We also found that an excellent tumour marker recently discovered and specifically induced by nickel, Cap43 protein, has a new mono-histidinic motif consisting of ten amino acids TRRSHTSEG repeated three times in the C-terminus which is able to bind several metal ions in a cooperative way [4,5].

References

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References