

NMR investigations of metal interactions with unstructured soluble protein domains.

Autorzy

Riccardo de Ricco

Sławomir Potocki

Henryk Kozłowski

Daniela Valensin

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Streszczenie

Essential main-group elements [e.g., Na(I) and Ca(II)] and transition metal ions [e.g., Cu(II)/Cu(I), Fe(III)/Fe(II), Zn(II), and Ni(II)] play key roles in the structural organization and biological function of many macromolecules such as proteins, DNA, and RNA. Healthy conditions require tight regulation of metal concentrations inside and outside cells, and both metal deficiency and overload can lead to cellular dysfunction. Altered metabolism of transition metal ions is implicated in severe and chronic diseases, including cancer, neurodegenerative disorders, and microbial infection. Nature has developed a sophisticated machinery to balance the content of transition metal ions. Many enzymes, transporters, and chaperones are involved in these complex processes and control metal uptake and delivery to specific cellular domains. Many efforts have been devoted to clarifying metal interactions with amyloidogenic proteins, metal transporters, and metal storage proteins via different spectroscopic techniques. In this review we describe the application of NMR to determine the metal coordination spheres and structural features of flexible and disordered regions of proteins that are either involved in neurodegenerative processes or are derived from metal chaperones. The systems investigated include (i) copper, iron, and zinc binding to unstructured regions of prion protein, α -synuclein, and amyloid β ; (ii) zinc binding to extracellular domains of ZIP proteins; and (iii) zinc and nickel binding to the loop region of HypA, HspA, and SlyD proteins. The NMR behavior of these systems is compared and discussed. The benefits and drawbacks of the methodology are addressed by stressing the tricks and pitfalls encountered.

Słowa kluczowe

NMR, transition metal ions, disordered proteins,
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