

Specific metal ion binding sites in unstructured regions of proteins.

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In this review, we summarize the most recent observations on some very effective binding sites (e.g. ATCUN motif, poly-His, poly-Cys, or Met-containing sequences) for biologically relevant metals in proteins and peptides. In addition, the influence of the specific sequence on the binding stability, besides the donor atoms, is described (e.g. Pro residues as in PrP or poly-Gln sequences).

It is well known that some disorders are connected with proteins which need metal ions for biological activity. Often metal ions coordinate to binding sites located in loops or unstructured regions of those proteins. These rather recent discoveries make metal ion binding to proteins slightly more enigmatic than in the case of an insertion of metal into an “organized” site. Although in the latter cases, we still may need chaperons helping to select the proper metal ion, some selectivity is provided by the pre-organized structure of the donor site itself in the protein. The metal ion binding usually exerts a distinct impact on the binding pocket structure due to the secondary or tertiary structure donors from the residues being often very far away in the peptide sequence. Recently, several metallo-proteins were discovered whose structures are rather disordered (e.g. α -synuclein, prions or β -amyloid peptide involved in Alzheimer disease). Also some specific metal chaperons, consisting of long poly-His sequences being very effective binders of metals, do not show any specific secondary structure. Examples of these might be bacterial nickel accessory proteins, involved in the complicated pathway of metal uptake, delivery and regulation in microorganisms. Recently, several observations were reported on the homeostasis of nickel in *Helicobacter pylori*, a Gram-negative bacterium that colonizes the gastric mucosa in humans, and is the causative agent of acute and chronic gastritis, peptic ulcer disease, gastric carcinoma, and gastric lymphoma. The homeostasis of nickel is crucial for the survival of this bacterium in the extremely acidic environment of the stomach; the metal is delivered to urease and hydrogenase by a set of accessory proteins. Zinc often plays a structural or regulatory role in those nickel chaperones. It can also be one of the metal ion which interferes with the homeostasis of Ni^{2+} , since the affinity of the two metals toward His- and Cys-rich sequences can sometimes be comparable.

Słowa kluczowe

α -synuclein, Cys-Cys binding sites, Cysteines, Histidines, Extra stability effects, Met containing regions, Metal ion binding, Polyhistidine sequences, Prion protein, Unstructured binding sites, ZIP and Znt transporters

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