

Zrozumienie homeostazy jonów metali u mikroorganizmów szansą na nowe strategie obrazowania i terapii zakażeń = Understanding metal ion homeostasis in microorganisms as a chance for new imaging and therapeutic strategies for infections

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Streszczenie

In the age of rising antibiotic resistance among various pathogens, the search for alternative antimicrobial strategies has become a pressing scientific challenge. Metal ions are indispensable to life, participating in a vast range of structural and catalytic roles across all forms of biology. The Biological Inorganic Chemistry Group explores the fundamental chemistry of metal ions in biological systems, focusing on their role in host-pathogen interactions. In this article we aim to focus on four aspects, representing the main scientific interests of our group. Metal homeostasis and assimilation chapter explores the coordination chemistry of biologically essential Mn(II) and Fe(II) ions using model peptides and fragments of metal transport proteins. By varying the number and position of His, Asp, and Glu residues, the study revealed how sequence composition governs metal-binding strength and selectivity. Studies on bacterial Fe(II) transporters, such as FeoB, identified potential metal-binding regions and mechanisms of ion transfer, deepening our understanding of metal recognition and transport in biological systems.

To better understand iron uptake in pathogens, we explored synthetic siderophore analogs as tools for studying this process. Ferrichrome mimics effectively chelated Fe(III) and were taken up by *Pseudomonas putida* and *Escherichia coli*. Fluorescent labeling allowed visualization of these complexes in cells. Ferrioxamine E analogs showed promise as ^{68}Ga -labeled imaging agents. The ability of various siderophores to bind metal ions such as Cu(II), Zn(II), Ni(II), Bi(III), and Zr(IV) has also been studied.

One of the chapters focuses on chaperonins and metalloproteinases as bacterial virulence factors. GroEL1, a chaperonin present e.g. in *Mycobacterium*, binds metal ions like Cu(II) via its unstructured His-rich C-terminal tail, helping

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bacteria survive under toxic metal conditions. Peptide studies showed that specific His residues position affects metal complex stability, and various metals create distinctly different complex geometries. Bacterial metalloproteinases need Zn(II) for activity. Research on peptide models revealed how Cu(II) and Ni(II) can inhibit these enzymes by displacing Zn(II). Studies on human MMP-14 enabled the identification and detailed characterization of the metal-binding site, as well as the elucidation of the interactions between peptide-based inhibitors, the catalytic metal ion, and the enzyme active site. Detailed knowledge of virulence proteins may enable their use as a potential target for novel drugs.

Membrane proteins are vital for transport, signaling, and maintaining membrane integrity. However, their studies are challenging due to poor solubility and detergent sensitivity. Lipoprotein nanodiscs (NDs) has revolutionized research on these proteins, by providing a soluble, stable, and physiologically relevant environment for membrane protein reconstitution. Their defined size, high stability, and compatibility with structural and functional studies make NDs a powerful tool for investigating membrane transporters, ion channels, and receptors.

This article highlights the key aspects of metal interactions with siderophores, transport and chaperone protein fragments, and metalloproteinases, and demonstrates how nanodiscs can advance the study of membrane proteins.

Słowa kluczowe

metal homeostasis, siderophores, metalloproteins, metalloproteinases, nanodiscs

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