

## Bakteryjne strategie wykorzystania jonów metali - kulisy chemii koordynacyjnej = Bacterial strategies for the use of metal ions - backstage of coordination chemistry

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### Streszczenie

In the Biological Inorganic Chemistry Group we are inspired to better understand metal ions acquisition and homeostasis in pathogenic bacteria, and in this review we present three different approaches to the role of these processes. The growing importance of a full understanding of the iron transport system in pathogens prompted us to study synthetic analogs of siderophores, used as structural probes in the process of iron uptake by microorganisms. The ferrichrome biomimetic analogs allowed efficient Fe(III) chelation under biological conditions and were recognized better by *P. putida*. than *E. coli*, suggesting differences in uptake mechanisms. Addition of a fluorescent probe to the compound allowed to track biological fate of studied complexes [1,2]. Biomimetics of ferrioxamine E revealed their potential as radioactive  $^{68}\text{Ga(III)}$ -based probes [3], and studies of Zr(IV) complexes permitted to explain the *in vivo* behavior of desferrioxamine B as  $^{89}\text{Zr(IV)}$  radionuclide carrier [4], as well as design better chelators for this metal ion [5]. One of the possible mammalian immune system responses to mycobacterial infection is the increase of Zn(II) concentration in phagosomes to a toxic level [6-8]. The mycobacterial SmtB protein is a transcription regulator that in the presence of high concentrations of metals, dissociates from DNA and activates the expression of metal efflux proteins. We focused on  $\alpha$  5Zn(II) binding domains of SmtB/BigR4 proteins [9], looking at the coordination modes and their thermodynamic of their Zn(II) and Ni(II) complexes. The study points out the specificity of metal-ligand interactions and the effect of mutations on the coordination properties of studied systems. The project can be considered as an introduction to the new strategies in tuberculosis treatment based on Zn(II)/Ni(II)-sensitive mechanisms.

*F. nucleatum* is an anaerobic bacteria present in the plaque. It leads not only to periodontal diseases but also, angina,

purulent inflammation of the lung tissue or reproductive organs [10]. Moreover, *F. nucleatum* promotes colon cancer growth [11]. This bacteria strain promotes inflammation and tumorigenesis by modulating the tumor immune microenvironment [12, 13]. Microbial pathogens drive tumorigenesis in 15–20% of cancer cases [14]. However, not only microorganisms are considered a major risk factor, but also metal ions play an important role in tumor promotion [15, 16]. Therefore, our primary research goal is to investigate the effect of metal ions coordination on the activity of outer-membrane proteins from *F. nucleatum* and to answer whether these proteins increase the prooxidative activity of Cu(II) and Fe(II) ions [16-18].

Słowa kluczowe

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metal homeostasis, metalophores, metalloproteins, metal toxicity

homeostaza metali, metalofory, metalloproteiny, toksyczność metali

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