The N-terminal domain of *Helicobacter pylori's* Hpn protein: The role of multiple histidine residues.

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Rok wydania

2021

Czasopismo

Journal of Inorganic Biochemistry

Numer woluminu

214

Strony

111304/1-111304/12

DOI

10.1016/j.jinorgbio.2020.111304

Kolekcja

Naukowa

Język

Angielski

Typ publikacji

Artykuł

Streszczenie

Helicobacter pylori is a gram-negative bacterium with gastric localization that can cause many gastrointestinal disorders. Its survival in the host environment strictly requires an efficient regulation of its metal homeostasis, in particular of Ni(II) ions, crucial for the synthesis of some essential enzymes. Hpn is a protein of 60 amino acids, 47% of which are histidines, expressed by *H. pylori* and avid for nickel, characterized by the presence of an ATCUN (Amino Terminal Cu(II)- and Ni(II)-binding) motif and by two further histidine residues which can act as additional metal anchoring sites. We decided to deepen the following aspects: (i) understanding the role of each histidine in the coordination of metal ions; (ii) comparing the binding affinities for Cu(II), Ni(II) and Zn(II) ions, which are potentially competing metals in vivo; (iii) understanding the Hpn ability of forming ternary and poly-nuclear complexes. For these purposes, we synthesized the Hpn N-terminal “wild-type” sequence (MAHHEEQHG-Am) and the following peptide analogues: MAAHEEQHG-Am, MAHAEEQHG-Am, MAHHEEQAG-Am and MAHAEEQAG-Am. Our results highlight that the histidines in position 4 and 8 lead to the formation of Cu(II) binuclear complexes. The ATCUN motif is by far the most efficient binding site for Cu(II) and Ni(II), while macrochelate Zn(II) complexes are formed thanks to the presence of several suitable anchoring sites (His and Glu). The metal binding affinities follow the order Zn(II) < Ni(II) < < Cu(II). In solutions containing equimolar amount of wild-type ligand, Cu(II) and Ni(II), the major species above pH 5.5 are hetero-binuclear complexes.

Słowa kluczowe

Copper, Nickel, Zinc, Metal complexes, Hpn protein, ATCUN motif