Small Cysteine-Rich Motif, Big Function—Metal-Driven Dimerization of the CopY C-Terminal Fragment

Autorzy

Aleksandra Hecel

Arian Kola

Alicia Domínguez-Martín

Daniela Valensin

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Transition metal homeostasis is essential for bacterial survival, especially under host-induced metal stress. The CopY repressor from *Enterococcus hirae* regulates copper levels through a conserved C-terminal CxCxxxxCxC motif, which binds metal ions such as Cu(I) and Zn(II) and modulates the DNA-binding activity of the protein. This work highlights the distinct coordination behaviors of Cu(I) and Zn(II) in the CopY C-terminal motif (Ac-ECNCIPGQCECKKQ) and sheds light on the structural basis of its metal-driven regulatory function. Using ESI-MS, potentiometry, UV–Vis, CD, NMR, and FT-IR, we show that this short sequence is sufficient for metal-driven dimerization and forms distinct complexes with Cu(I) and Zn(II). Cu(I) promotes the formation of binuclear (Cu_2L) and dimeric (Cu_4L_2) clusters, while Zn(II) favors monomeric (ZnL), bis-complex (ZnL_2), and minor dimeric (Zn_2L_2) forms. Metal binding induced significant structural rearrangements in the peptide, while the apo form was largely disordered; Zn(II) coordination stabilized more ordered conformations, and Cu(I) induced extensive conformational changes associated with the formation of distinct multinuclear complexes. These findings enhance our understanding of bacterial metallostasis and provide a molecular framework for future studies of metal-dependent gene regulation and antimicrobial strategies targeting metal homeostasis.

Słowa kluczowe

Equilibrium constant, Ions, Metals, Monomers, Peptides and proteins

Adres publiczny

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