

Biologicznie aktywne metalopeptydy (BAM): od homeostazy metali u patogenów do precyzyjnego dostrajania aktywności peptydów przeciwdrobnoustrojowych =
Biologically active metalloptides (BAM): from pathogen metal homeostasis to controlled switching of antimicrobial peptide activity

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Streszczenie

The increasing resistance of bacteria and fungi to antimicrobial agents demands therapeutic strategies with higher target selectivity and a lower risk of rapid resistance development. The Biologically Active Metalloptides (BAM) group develops an approach based on the controlled interaction of metal ions with peptides and pathogen-derived proteins. In our work, metal ions (including Cu(II)/Cu(I), Zn(II), and Ni(II)) are treated as functional modules: they stabilize peptide structure, induce defined conformations and aggregation states, conditionally activate antimicrobial activity, and modulate the pathogen's access to essential micronutrients. We elucidate the mechanisms of metal uptake and homeostasis in pathogens (including Cu and Zn acquisition systems, zincophores, and metal chaperones), identifying protein fragments that can act either as therapeutic targets or as targeting domains for the selective delivery of antimicrobial agents (a "Trojan horse" strategy). In parallel, we investigate antimicrobial peptides and endogenous peptides in the presence of metal ions, demonstrating that coordination of Cu(II) and Zn(II) can markedly enhance their bactericidal or antifungal activity by enforcing active conformations, inducing aggregation (e.g. fibril formation), and promoting the generation of reactive oxygen species locally at the infection site. Building on these principles, we design selective targeted antimicrobial peptides (STAMPs, ang. specifically targeted antimicrobial peptides) and chemically stabilized peptide and glycopeptide constructs with improved biological stability and tissue selectivity. We show that metal ion coordination chemistry can serve as a platform for engineering a new class of selective antimicrobial therapeutics.

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Licencja otwartego dostępu

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