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Review

Unraveling the genetic basis of microbial metal resistance: Shift from Mendelian to systems biology

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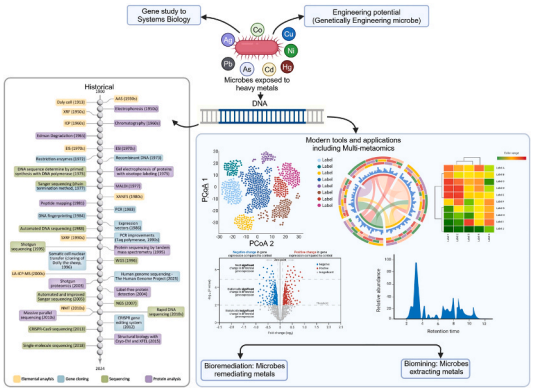
HIGHLIGHTS

- Bacteria evolve traits to tolerate toxic metals, impacting bioremediation.
- Molecular biology and metaomics accelerate metal resistance gene characterization.
- Omics reveal regulatory networks and evolution in microbial metal stress responses.
- The study evolved from Mendelian genetics to systems biology with advanced tools.
- Metal resistance insights help engineer microbes to regulate metal homeostasis.

GRAPHICAL ABSTRACT



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ABSTRACT

Microbial metal resistance, a trait that enables microorganisms to withstand high levels of toxic metals, has been studied for over a century. The significance of uncovering these mechanisms goes beyond basic science as they have implications for human health through their connection to microbial pathogenesis, metal bioremediation, and biomining. Recent advances in analytical chemistry and molecular biology have accelerated the discovery and understanding of genetic mechanisms underlying microbial metal resistance, identifying specific metal resistance genes and their operons. The emergence of omics tools has further propelled research towards a comprehensive understanding of how cells respond to metal stress at the systemic level, revealing the complex regulatory networks and evolutionary dynamics that drive microbial adaptation to metal-rich environments. In this article, we present a historical overview of the evolving understanding of the genetic determinants of metal resistance in microbes. Through multiple narrative threads, we illustrate how our knowledge of microbial metal resistance and genetics has interacted with genetic tools and concept development. This review also discusses how our understanding of microbial metal resistance has progressed from the Mendelian perspective to the current systems biology viewpoint, particularly as omics approaches have considerably enhanced our

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