

BACTERIAL HEAVY METAL RESISTANCE: New Surprises

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Abstract: Bacterial plasmids encode resistance systems for toxic metal ions including Ag⁺, AsO₂, AsO₄³⁻, Cd²⁺, Co²⁺, CrO₄²⁻, Cu²⁺, Hg²⁺, Ni²⁺, Pb²⁺, Sb³⁺, TeO₃²⁻, Tl⁺, and Zn²⁺. In addition to understanding of the molecular genetics and environmental roles of these resistances, studies during the last few years have provided surprises and new biochemical mechanisms. Chromosomal determinants of toxic metal resistances are known, and the distinction between plasmid resistances and those from chromosomal genes has blurred, because for some metals (notably mercury and arsenic), the plasmid and chromosomal determinants are basically the same. Other systems, such as copper transport ATPases and metallothionein cation-binding proteins, are only known from chromosomal genes. The largest group of metal resistance systems function by energy-dependent efflux of toxic ions. Some of the efflux systems are ATPases and others are chemiosmotic cation/proton antiporters. The CadA cadmium resistance ATPase of gram-positive bacteria and the CopB copper efflux system of *Enterococcus hirae* are homologous to P-type ATPases of animals and plants. The CadA ATPase protein has been labeled with ³²P from ⁻³²P-ATP and drives ATP-dependent Cd²⁺ uptake by inside-out membrane vesicles. Recently isolated genes defective in the human hereditary diseases of copper metabolism, Menkes syndrome and Wilson's disease, encode P-type ATPases that are more similar to the bacterial CadA and CopB ATPases than to eukaryote ATPases that pump different cations. The arsenic resistance efflux system transports arsenite, using alternatively either a two-component (ArsA and ArsB) ATPase or a single polypeptide (ArsB) functioning as a chemiosmotic transporter. The third gene in the arsenic resistance system, *arsC*, encodes an enzyme that converts intracellular arsenate [As (V)] to arsenite [As (III)], the substrate of the efflux system. The three-component Czc (Cd²⁺, Zn²⁺, and Co²⁺) chemiosmotic efflux pump of soil microbes consists of inner membrane (CzcA), outer membrane (CzcC), and membrane-spanning (CzcB) proteins that together transport cations from the cytoplasm across the periplasmic space to the outside of the cell. Finally, the first bacterial metallothionein (which by definition is a small protein that binds metal cations by means of numerous cysteine thiolates) has been characterized in cyanobacteria.