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Microbial Physiology of Nickel and Cobalt

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Abstract Nickel and cobalt are essential micronutrients for many microorganisms and serve as enzyme cofactors that catalyze a diverse array of reactions. One complication is that high concentrations of these transition metal ions are toxic to cells, leading some prokaryotes to evolve sophisticated homeostatic mechanisms to regulate their transmembrane uptake or efflux. The biosynthesis of nickel and cobalt metalloenzymes requires the intracellular allocation of the metals to the appropriate apoproteins, often in an intricate process that involves the cooperative activity of accessory proteins. Here, we highlight the molecular physiology of nickel and cobalt cation metabolism in *Escherichia coli* and summarize additional nickel- or cobalt-dependent processes and homeostatic mechanisms found in other microorganisms.

1 Introduction: Microbial Physiology of Nickel and Cobalt

Over 50 years ago a requirement for Co^{2+} or vitamin B_{12} was established in cyanobacteria that fix nitrogen or utilize nitrate (Holm-Hansen et al. 1954). A decade later, Bartha and Ordal noted that Ni^{2+} is needed for the growth of two hydrogen-oxidizing bacteria (Bartha and Ordal 1965). These micronutrients are transported into cells by highly specific uptake systems (Eitinger and Mandrand-Berthelot 2000; Eitinger et al. 2005). By contrast, microbes that grow at elevated concentrations of Ni^{2+} or Co^{2+} can utilize metal-specific efflux systems as a powerful resistance mechanism (Nies 2003). The Ni^{2+} or Co^{2+} uptake and efflux systems must be carefully regulated for optimal cell growth, and certain bacteria have devised ingenious mechanisms to sense the concentrations of these and other cations (see the work by Helman, Soosanga, and Gabriel, 2007, in this volume). Within the cell these metal ions are incorporated into specific metalloenzymes (see Table 1) by a process that often requires additional accessory proteins.

Our goals in this contribution are to illustrate in some detail the physiology of Ni^{2+} and Co^{2+} metabolism in *Escherichia coli*, in some cases extending to related better-studied systems, and to briefly review novel aspects of the physiology of these metal ions in other microorganisms. We cannot be comprehensive in our coverage of the microbial physiology of Ni^{2+} and Co^{2+}, so we refer to many key papers and more extensive reviews of these general topics.

2 Nickel and Cobalt Physiology of *E. coli*

Physiological studies of *E. coli* have been used to address the mechanisms of cell uptake of Ni^{2+}, Co^{2+}, and vitamin B_{12}, to provide evidence for a Ni^{2+} and Co^{2+} efflux transporter, and to examine for Ni^{2+} storage in these cells. Additional investigations in this microorganism have characterized the mechan-