

## Transporters for Nickel and Cobalt – Experimental Evidence and Comparative Genomic Analyses

Thomas Eitinger<sup>1</sup>, Dmitry A. Rodionov<sup>1,2</sup>, Peter Hebbeln<sup>1</sup>, and Julien Maurel<sup>1,3</sup>

<sup>1</sup>*Institut für Biologie/Mikrobiologie, Humboldt-Universität zu Berlin, Germany,* <sup>2</sup>*Institute for Information Transmission Problems, Russian Academy of Sciences, Moscow, Russia,*

<sup>3</sup>*Department of Biochemistry, Université Paris VII, France*

NiCoTs are a family of secondary membrane transporters for nickel and cobalt ions in prokaryotes and fungi. Systems which are distantly related to NiCoTs and are known or predicted to function in metal ion transport are widespread in bacteria and in plants [1]. Experimental analyses [2] have confirmed *in silico* predictions [3] that the genomic localization of NiCoT genes and the presence of regulatory sites in the upstream region are a reliable indication of the substrate preference of the corresponding permeases.

Primary nickel transporters (NikABCDE) which cluster phylogenetically with members of the peptide/opine ABC transporter (PepT) family were characterized in a few bacteria. Genome-wide searches for (i) binding sites for the nickel-dependent transcriptional repressor NikR and (ii) coenzyme B<sub>12</sub>-dependent riboswitch elements suggest that metal transporters with preference for either nickel or cobalt are contained in the PepT family.

CbiMNQO proteins are considered to mediate uptake of cobalt for incorporation into the corrin ring during coenzyme B<sub>12</sub> biosynthesis. Although CbiO contains the signatures of ABC proteins, the complex does not resemble typical ABC transporters and a solute-binding protein has not been identified. The genes for related transporters (NikMNQO, NikKLMQO) with a predicted role in nickel uptake are located adjacent to genes for nickel-dependent enzymes and/or are preceded by NikR binding sites.

We predict a function in Ni and Co transport across the outer membrane for a group of TonB-dependent receptors in certain gram-negative bacteria, based on genomic linkage to genes for Ni/Co transporters in the cytoplasmic membrane and on the presence of regulatory elements.

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