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Nickel toxicity in *Saccharomyces cerevisiae*: mutant analysis of the Ni uptake system. The transcriptional and phenotypic responses of the *Saccharomyces cerevisiae* yeast Sac4/Nic1p transporter to Ni, Zn and Cd were investigated using a new Ni-sensitive yeast strain. Exposed cells accumulated Ni and Zn, and exhibited higher levels of oxidative damage than Cd-exposed cells. A cDNA for the Sac4p transporter was expressed in Sac4p-negative cells and cell growth and Ni accumulation were assessed. Growth was dramatically slowed in the presence of Ni, but not of Cd or Zn. This suggests that Ni uptake and toxicity occur independently of the Sac4p transporter. Mutants defective in yeast uptake systems for Ni, Zn and Cd were generated by replacement of five genes (SOC1, VTC1, ZRT1, ZRT2 and NAT1) encoding essential transporters with the kanamycin cassette. Cells were exposed to Ni, Cd or Zn and the concentrations of the metals that inhibited growth by 50% (IC50) were determined. These results show that the yeast Ni uptake system lacks overlapping specificity with the Zn or Cd transport systems and the uptake system for Cu. Furthermore, the results confirm previous biochemical and kinetic data for the relationships between Ni, Zn and Cd transport in *S. cerevisiae* cells.

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