

## **Nur, a Nickel-Responsive Regulator of the Fur Family in *Streptomyces coelicolor***

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In *S. coelicolor*, nickel represses and induces production of Fe-containing and Ni-containing SODs, respectively, primarily at the transcriptional level. We identified the nickel-responsive regulator (Nur), a Fur homologue, which binds to the promoter region of the *sodF* gene encoding Fe-SOD in the presence of nickel. Simulated structure based on crystal structure of *Pseudomonas* Fur showed that positions of metal-determining sites in Nur would be distinct from those in other Fur homologues. Disruption of the *nur* gene caused constitutive expression of FeSOD and no induction of NiSOD in the presence of nickel. The intracellular level of nickel was higher in  $\Delta$ *nur* mutant than in the wild type, suggesting that Nur also regulates nickel uptake in *S. coelicolor*. A putative nickel-transporter gene cluster (*nikABCDE*) was identified in the genome database. Its transcription was negatively regulated by Nur in the presence of nickel. Purified Nur protein bound to the *nikA* promoter region in a nickel-dependent way. Disruption of *nikA* caused reduced uptake of nickel compared to wild type in the absence of additional nickel, consolidating the prediction that this operon serves as a high-affinity nickel uptake system. These results support the action of Nur as a regulator of nickel homeostasis and anti-oxidative response in *S. coelicolor*, and add a novel nickel-responsive member to the list of versatile metal-specific regulators of Fur family. Sequence comparison, deletion analysis, and random screening of binding oligomers revealed a putative Nur-binding DNA motif of an imperfect inverted repeat which is different from the classic Fur-binding sequence.