

Additional Methods used in Supplemental Data

Anaerobic Growth in Anoxomat

Plates were pre-incubated in an Anoxomat chamber (Advanced Instruments), which creates an anaerobic environment in roughly 5 minutes. Bacteria were grown to an O.D. of 0.1, serially diluted onto the pre-incubated plates, and incubated in the Anoxomat chamber under anaerobic conditions. CFUs were counted after 18 hours of growth.

Modeling

The structure of NrdF from *E. coli* (pdb: 3N37) was aligned with a Phyre 2 model of NrdF from TIGR4 by using MacPyMOL.⁵⁴

Supplemental Figure Legends

Supplemental Figure 1. Copper decreases nucleotide synthesis. (A) Aerobic nucleotide synthesis genes increase during copper stress. $p < .05$ compared to $\Delta copA$ alone by using Student's *t*-test. (B) CFUs of $\Delta nrdD$ mutant in aerobic, anaerobic GasPak jar, and Anoxomat chamber conditions. Aerobically grown bacteria at O.D. 0.3; bacteria at 620 nm were plated on blood agar plates in aerobic, anaerobic GasPak jar, or Anoxomat conditions $n = 4$ (C) Additional transition metals do not change the growth of $\Delta nrdD$ mutants in aerobic and anaerobic zone-of-growth inhibition assays. (D) Titration of hydroxyurea in the $\Delta nrdD$ mutant. O.D. was measured 8 hours after inoculation. Error bars represent SD. * Student's *t*-test indicates $p < .01$ compared to wild-type TIGR4 treated with the same concentration of hydroxyurea (HU) $n = 3$. (E) Manganese increases replication of the $\Delta nrdD$ mutants but cannot rescue them from hydroxyurea stress. Replication measured 8 hours after inoculation and normalized to that of the $\Delta nrdD$ mutant without 1 mM of HU and/or 250 μ M of manganese. Error bars represent SEM $n = 3$. * Student's *t*-test indicates $p < .01$ compared to the $\Delta nrdD$ mutant without metal stress; ND = Student's *t*-test indicates no difference.

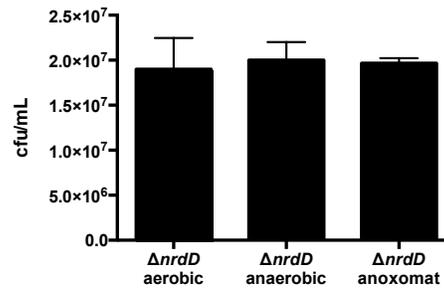
Supplemental Figure 2. Potential binding configuration for copper in NrdF (A) The structural alignment of *E. coli* NrdF (pdb: 3N37) (cyan) to a Phyre model of TIGR4 *S. pneumoniae* NrdF (green) bound to manganese (magenta), as predicted by using PyMOL (Bennett-Lovsey et al., 2008; Boal et al., 2010). (B) Binding affinities of specific amino acids for various metals (Furia, 1972).

Supplemental Figure 1

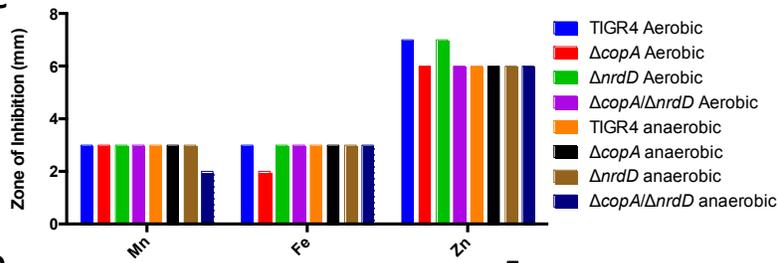
A

TIGR4 Gene	Real Time Fold Increase $\Delta copA$ w/Cu vs. $\Delta copA$ w/o Cu
SP_1179 (<i>nrdH</i>)	2.33
SP_1713 (<i>nrdR</i>)	2.02

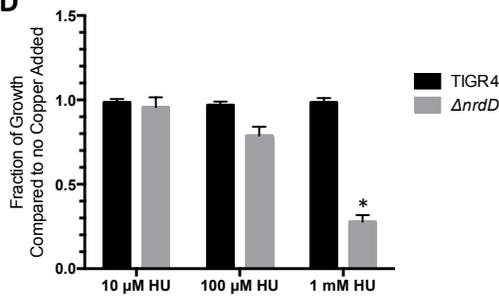
B



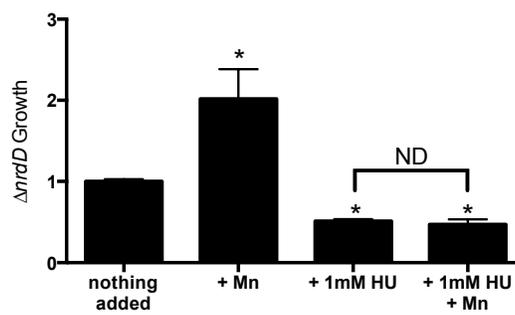
C



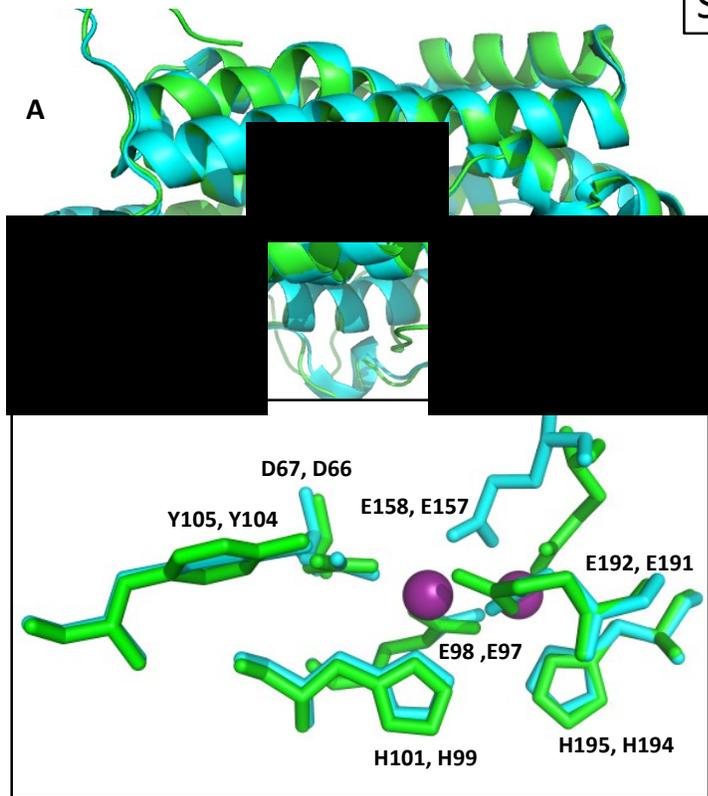
D



E



Supplemental Figure 2



(*E. Coli* NrdF, Modeled *S.Pneumoniae* NrdF)
Manganese metal cofactor