

Biochemical requirements for enzymatic perchlorate reduction: What makes a perchlorate reductase a perchlorate reductase?

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In canonical dissimilatory perchlorate reducing bacteria (DPRB), the first step in the perchlorate respiratory pathway is catalyzed by PcrA, an enzyme in a monophyletic sub-group of the Nar nitrate reductase superfamily. To understand the biochemical basis for perchlorate reduction by PcrA, we purified, kinetically characterized, and solved the X-ray crystal structure of the enzyme from the model DPRB *Azospira suillum* PS. *A. suillum* PcrA has a much lower K_m for perchlorate compared to the homologous NarG protein from *E. coli*, suggesting that these two enzymes have adapted to either access (PcrA) or exclude (NarG) the low concentrations of perchlorate found on Earth. Mutagenesis and structural analysis of PcrA suggest that key residues in the active site function as a “gate” that traps reactive catalytic intermediates. Based on our findings, we propose a mechanism for PcrA, refine a model of the genetic determinants of perchlorate reduction in the NarG superfamily, and discuss implications for the newly postulated cryptic and symbiotic perchlorate reduction metabolisms.