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Novel Iron-Sulfur Cluster in *Pseudomonas aeruginosa* Adenosine Phosphosulfate Reductase. J. Chartron¹, K. S. Carroll², H. Gao^{2,3}, H. Chen², J.A. Leary³, C.R. Bertozzi², C.D. Stout¹; ¹Dept. of Molecular Biology, The Scripps Research Institute, La Jolla, CA, ²Depts. of Chemistry and Molecular and Cell Biology, Univ. of California, Berkeley; and ³Dept. of Chemistry and Molecular Cell Biology, Genome Center, Univ. of California, Davis.

APS reductase (APSr) catalyzes the first committed step in sulfur assimilation in pathogenic bacteria, including *Mycobacterium tuberculosis*, and is a promising target for drug development, as the enzyme does not occur in mammals. The thiosulfonate intermediate of APSr derived from adenosine 5'-phosphosulfate (APS) with sulfite attached to Cys256 has been crystallized anaerobically in the presence of excess APS. The structure was solved by Fe K-edge MAD and refined at 2.7 Å resolution. The asymmetric unit contains two tetramers; APS is bound in a deep active site cleft, but the C-terminal, thiosulfonated peptide is disordered. The [4Fe-4S] cluster is ligated by the unique Cys139-Cys140 motif within a helix, and by Cys228 and Cys231. The structure, and biochemical and spectroscopic experiments, support a two-step mechanism in which the thiosulfonate is reduced by thioredoxin at a site on the enzyme distal from the cluster. Features of the structure suggest a role for the cluster in conformational changes.