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Structure of Phosphoglycerate Mutase from *M. Tuberculosis* – New Features. Peter Müller, Mike Sawaya, Sum Chan, Yim Wu, Inna Pashkova, Jeanne Perry, David Eisenberg, UCLA-DOE Institute for Genomics and Proteomics, 201 MBI, Box 95157, Los Angeles, CA, 90095-1570, peterm@mbi.ucla.edu

The open reading frame Rv0489 from *Mycobacterium tuberculosis* (*M Tb*) encodes for a cofactor dependent phosphoglycerate mutase, a member of a large family of highly conserved proteins, reversibly catalyzing the transfer of a phosphate group from C3 to C2 of phosphoglycerate. Low temperature data was collected at beamline 8.2.2 at the ALS in Berkeley, at a wavelength of 1.0000 Å (data reduction with DENZO and SADABS). The structure was solved with molecular replacement using the program GLRF and one homotetramer of the yeast Phosphoglycerate mutase (PDB-code 5PGM) as search model. Refinement with SHELXL gave rise to the following residual values: $R = 20.51\%$, $R_{\text{free}} = 25.65\%$ for data with $I > 4_{\text{I}}$ and $R = 21.93\%$, $R_{\text{free}} = 26.97\%$ for all data.

The enzyme crystallizes as a homotetramer in the monoclinic space group $P2_1$ with one tetramer in the asymmetric unit. This tetramer possesses pseudo 222 symmetry, violated by a helix-turn-helix segment from Asp 100 to Ser 119. The active site is highly conserved throughout the family and virtually identical in the structure of the yeast and the *M Tb* phosphoglycerate mutases. Especially the two catalytical histidine residues, which play a crucial role in the mechanism, are oriented very similarly in the two structures.

A striking feature in the amino-acid sequences of the phosphoglycerate mutases from *M Tb*, *Saccharomyces cerevisiae*, *Homo sapiens* and possibly several other organisms is a four-proline motif. In the structures of the *M Tb* and the yeast protein, the four proline residues form slightly less than one turn of a left-handed helix. This is not unlike the arrangement of some proline rich stretches found in other proteins that interact with SH3 domains.