Functional Discoveries from Crystal Structures of Proteins from *M. tuberculosis*

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Less than 50% of the gene products encoded in complete genome sequences can be annotated with firm biochemical functions. A primary goal of structural genomics then is to use protein structures for the discovery of function. Here we present some of the varied outcomes from crystal structure analyses of a selection of proteins from *Mycobacterium tuberculosis* which we have undertaken in the context of a laboratory-scale structural genomics project.

For two proteins, Rv1170 (MshB) and Rv3710 (LeuA), functions were known, but the crystal structures revealed metal and substrate binding sites from adventitious binding of ions or small molecules in the crystal. For Rv3853, which was annotated as the methyltransferase MenG, the crystal structure showed clearly that this function was incorrect. A fourth protein, Rv1347c, proved to be a CoA-dependent acyltransferase of the GCN5 family, but the crystal structure and associated bioinformatic analyses suggested a role in siderophore biosynthesis instead of the annotated function of antibiotic resistance. Finally, PAE2754, of previously unknown function, was found to be a metal-dependent nuclease that was representative of a large family of related proteins with major implications for TB biology [1].

[1] Arcus V.L., Backbro K, Roos A., Daniels E.L., Baker E.N., *J. Biol. Chem*., 2004, **279**, 16471.

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