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Crystal Structure of the N-terminal Domain of the TyrR Transcription Factor Responsible for Gene Regulation of Aromatic Amino Acid Biosynthesis and Transport in E. coli K12

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TyrR is a somewhat enigmatic transcription factor involved in the regulation of at least eight, unlinked, widely spaced genes involved in aromatic amino acid biosynthesis and transport in the bacterium E. coli. It acts largely as an activator of amino acid transporters and repressor of biosynthetic genes, although in the case of tyrP it can act as either an activator or repressor, in a cofactor-dependent manner. Sequence alignments show that the central and C-terminal domains have a high level of identity to the σ54 bacterial enhancer binding protein family. Curiously, however, during the course of evolution TyrR seems to have lost the ability to utilise σ54 for transcription initiation, probably due to a seven-residue deletion corresponding to helix C3 in the central domain. TyrR uses the common housekeeping σ70 factor.

We have solved the structure of the N-terminal domain of TyrR (residues 1 - 190) to a resolution of 2.3 Å. This domain is involved with the activation functionality, non-ATP-dependent cofactor binding, and is the site of interaction with the C-terminal domain of the sigma subunit of RNA polymerase. The structure reveals a modular polypeptide comprising an ACT domain, connecting helix, PAS domain, and C-terminal helix. The dimer exhibits a large rigid body hinging of several of these domains between the protein chains. The structure is discussed with reference to other transcription regulatory proteins.

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