Substitution Correlation in sequences of Transcriptional Factors from MerR Family and their Binding Sites

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The MerR family of bacterial transcriptional regulators contains a number of proteins responsible for heavy metal resistance phenotypes: MerR, CueR, HmrR, ZntR, CadR, PbrR, and GolS. Their homologs comprise several closely related subfamilies inside the MerR family. Previous studies have shown that these proteins act as transcriptional activators in form of dimers [1, 2]. The activated genes encode heavy metal ion efflux and other heavy metal detoxification systems. The structure of such proteins is formed by N-terminal DNA binding helix-turn-helix (HTH) domain, antiparallel coiled coil facilitating dimerization and small C-terminal metal ion binding domain [3]. The list of metals includes mercury, copper, zinc, lead, cadmium, silver and gold. The palindromic binding sites of these transcriptional factors are situated between the −35 and −10 boxes of the activated promoters. Meanwhile the spacers of these promoters have length of 19-20 b.p. comparing to average of 16-17 b.p [4]. The distance between the promoter boxes shortens upon the regulator binging providing the access of RNA polymerase.

In this work we study the correlation between the substitutions of amino acids in the helix-turn-helix domains and the substitutions of base pairs in the binding sites. We identified 1516 transcriptional factors from the heavy metal associated subfamilies of the MerR family in RefSeq database encoded in complete genomes. Binding sites inside the spacers of putative promoters were identified for 768 of these proteins using positional weighted matrices (PWMs). This correlation provides additional information on specificity of protein-DNA interaction for MerR family transcriptional factors comparing to conservation of nucleotides and amino acids usually represented by sequence logos.

This is joint work with Mikhail Gelfand

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