Structure of MRG15 reveals a Novel Fold and provides Insights into its Biological Functions

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MRG15(MORF4 related gene on chromosome 15) and MORF4 (mortality related gene on chromosome 4) belong to a newly identified protein family which share high sequence homology. Recently, the MRG proteins have been shown to function in transcription regulation (histone modification). We determined the crystal structures of the C terminal domains of MRG15 (MRG15C) and MORF4 (MORF4C) to 2.2 Å and 3.0 Å resolution, respectively.. A structure homology search with the DALI algorithm indicates that MRG15C and MORF4C have a novel protein fold with no obvious similarity to those of other proteins of known structures. The proteins are mainly consisted of α-helices and form homodimer in both solution and structures. Structure analysis and multiple sequence alignment indicate that there are a negatively charged hydrophilic patch at the C-terminal and a hydrophobic pocket at the dimeric interface both of which are composed of several highly conserved residues. These structural locations could be putative binding sites for other proteins or substrates. Biochemical assays indicate that the hydrophilic patch might be involved in binding with PAM14. Additionally, we have also obtained a 2.3 Å resolution diffraction data for the N-terminal domain (1-90 amino acids) of MRG15(MRG15N) which shows limited similarity to Chromo domain. Structure determination of MRG15N is ongoing. Analysis of these structures will shed new light on the biological functions of MRG15 protein and other members of the MRG protein family.

Keywords: MRG15, novel fold, chromo domain