Poster 1

Structural Analysis of Multi-functional Peptide Motifs Present in Human Bifunctional tRNA Synthetase

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Many cytoplasmic aminoacyl tRNA synthetases (ARSs) of higher eukaryoties exist as a multiprotein complex in the cell. Each of tRNA synthetases in this complex has an additional domain to the core enzyme that contributes to the assembly of this multi-tRNA synthetase complex. One of this complex, human bifunctional glutamyl-prolyl-tRNA synthetase (EPRS), contains three tandem repeats linking the two catalytic domains. These repeated motifs have been shown to be involved in protein-protein and protein-nucleic acid interactions. The single copy of the homologous motifs has also been found in several different aminoacyl-tRNA synthetase. In this work, we determined solution structure of repeat 1 (EPRS-R1) and the secondary structure of the whole appended domain containing all three repeated motifs in EPRS(EPRS-R123). And also we analyze the structural characteristics of these multifunctional peptide motifs. According to our results, EPRS-R1 consists of two helices (residues 679 to 699 and 702 to 721) arranged in a helix-turn-helix and EPRS-R123 is composed of three helix-turn-helix motifs linked by unstructured loop. When tRNA binding was titrated using ^{1}H-^{15}N HSQC, chemical shifts of several residues in each repeat are perturbed. However, the perturbed region in each repeat is not the same indicating that each repeat interacts with tRNA in different pattern, suggesting that each repeat in the appended domain is dynamically arranged to maximize contacts with tRNA. This indicates that each of the repeated motifs has a weak intrinsic affinity for tRNA or other synthetases but the repetition of the motifs may be required to enhance binding

affinity. Thus, the results of this work gave information on the RNA-binding mode of the multi-functional peptide motif attached to different ARSs and the functional reason for the repetition of this motif.