Structure and Function of Unusual Archaeal Serly-tRNA Synthetases

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Aminoacyl-tRNA synthetase establish the genetic code by attaching particular amino acid to the 3' ends of tRNAs bearing the cognate anticodons. Sequence comparisons reveal two major types of seryl-tRNA synthetases (SerRS): a canonical form found in most organisms and a divergent type of SerRS found only in certain methanogenic archaea. On the sequence level, these atypic, methanogenic enzymes are characterized by alterations in two regions involved in tRNA binding. First, the N-terminal module of atypical SerRS has no detectable sequence homology to the N-terminal tRNA recognition domain of canonical SerRS, which is composed of an extended a-helical coiled coil and is shorter in size. Second, a sequence region referred to as the motif 2-loop in canonical SerRS, where it is involved in major groove recognition of approaching tRNA, is shortened significantly in atypical SerRS. Together, these differences imply a distinct, yet unknown, mechanism of tRNA recognition in methanogenic SerRSs. Besides, motif 2-loop is a part of the catalytic site what raises questions how these SerRSs determine the amino acid specificity.

To analyse this mechanism at atomic level we have determined X-ray crystal structure of atypical SerRS. Crystals diffracted well beyond 2.1Å resolution. The structure revealed a novel and unique RNA-binding fold of N-terminal domain in methanogenic SerRSs. The co-crystal structures of the enzyme in complex with the (pseudo-) substrate serine and AMPNP and a stable thio-analogue of seryl adenylate allowed an understanding of the catalytic mechanism and the structural basis of amino acid specificity of the unique non-canonical SerRS family.

Keywords: seryl-tRNA synthetases , RNA-binding domain, amino acid specificity