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**Crystal Structure of an Archaeal Peptidyl-tRNA Hydrolase from *Thermoplasma acidophilum*.** Jerzy Osipiuk<sup>a</sup>, Elena Evdokimova<sup>b</sup>, Alexei Savchenko<sup>b</sup>, Aled Edwards<sup>b</sup>, Andrzej Joachimiak<sup>a</sup>, <sup>a</sup>Argonne National Laboratory, Biosciences Div., Structural Biology Center & Midwest Center for Structural Genomics, Argonne, IL 60439, <sup>b</sup>Univ. of Toronto, Structural Genomics Consortium, Toronto, Canada.

The mechanism of mRNA translation by ribosomes is far from being perfect. Abnormal termination of translation which may take place before stop codon occur with frequency of  $3 \times 10^{-4}$  per codon. As a result, release of premature peptidyl-tRNA happens quite frequently. In the absence of peptidyl-tRNA hydrolases (PTHs), this may lead to accumulation of the premature translation termination products peptidyl-tRNA in cells, decrease in availability of acylatable tRNAs and also may cause cell death. Peptidyl-tRNA hydrolases cleave a premature peptidyl residue from a tRNA and therefore allow tRNA and peptide recycling in protein synthesis.

The PTHs are divided into two classes, the first type is found in all bacteria and some eukaryotes and the second type of PTHs is found in eukaryotes and archaea. The two classes of PTHs show comparable hydrolytic activities. However, they do not share neither amino acid sequence nor structural similarity. Very recently, the structure of C-terminal part of human PTH, responsible for the enzymatic activity, was published (De Pereda et al, 2004). This protein shows sequence similarity to archeal PTHs.

In this report, we describe the first structure of ancestral peptidyl-tRNA hydrolase from archaeon *Thermoplasma acidophilum* (Ta-PTH). The Ta-PTH structure was solved at 1.95Å resolution using single wavelength anomalous diffraction. The structure shows structural similarity to the human homologue. However, a considerable movement of the loop forming part of the active site (83-92 residues) was observed in the Ta-PTH structure. This movement may be relevant to the substrate locking prior to its hydrolysis and the catalysis. Interestingly, the structure suggests a possible dual way of enzyme-tRNA interaction, where only one of substrate orientations leads to placing peptidyl residue in active site of the enzyme.

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