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Structural Studies of Human Mitochondrial Tryptophanyl tRNA Synthetase. Christopher J. Siemer, Charles W. Carter, Jr., Laurie S. Kaguni, Carol L. Farr, Biochemistry & Biophysics, Univ. of North Carolina, Chapel Hill, 101 Manning Dr., Chapel Hill, NC 27599 USA.

The role of aminacyl-tRNA synthetases as a link in the chain of protein synthesis constitutes a favorable target for antibacterial therapy. Bacterial Tryptophanyl (TrpRS) and Tyrosyl-tRNA (TyrRS) synthetases offer unique advantages in this regard because they differ from their eukaryotic counterparts in fundamental aspects of their catalytic mechanisms. However, it is necessary to avoid inhibition of the human mitochondrial counterparts, due to their inherent similarity to the corresponding bacterial enzymes. To begin to understand the structural differences between the bacterial and mitochondrial proteins, we report on the incomplete factorial screening and Hardin-Sloane optimization of human mitochondrial TrpRS, as well as diffraction data and progress toward a structure solution. Supported by NIGMS 48519