

W0365

Recognition of D-tyrosine by Tyrosyl-tRNA Synthetase. Eric A. First¹, Anita Sheoran¹, Jason Manning¹, Charles W. Carter², Laurie Betts³, ¹Dept of Biochemistry & Mol Biology, LSU Health Sciences Center, Shreveport, LA, ²Dept of Biochemistry & Biophysics and ³Dept of Pharmacology, Univ. of North Carolina, Chapel Hill, NC.

Tyrosyl-tRNA synthetase is able to catalyze the transfer of both L- and D-tyrosine to the 3' end of tRNA^{Tyr}. Pre-steady state kinetic analysis indicates that *Bacillus stearothermophilus* tyrosyl-tRNA synthetase binds D-tyrosine with an 8-fold lower affinity than that of L-tyrosine ($K_d^{D-Tyr} = 102 \mu\text{M}$) and exhibits a 3-fold decrease in the forward rate constant ($k_3^{D-Tyr} = 11 \text{ s}^{-1}$) for the activation reaction. These observations suggest that the side chain and carboxyl moieties of L- and D-tyrosine bind to tyrosyl-tRNA synthetase in similar orientations. We have crystallized tyrosyl-tRNA synthetase in complex with D-tyrosine. Analysis of the diffraction pattern at 1.9 Å resolution indicates that the orientations of L- and D-tyrosine differ by 180°. In agreement with the kinetic analysis, binding of the side chain, amino moiety, and one carboxylate oxygen atom is similar for L- and D-tyrosine. These results suggest that tyrosyl-tRNA synthetase can be used to incorporate D-tyrosine during protein synthesis.



We thank SER-CAT for access to beamline 22-ID. This research was supported by NIH GM 06870 to E.A.F.