Electrostatic Potential of AaRS Navigates tRNA on its Pathway to the Binding Site

Mark Safro, Dmitry Tworowski, Anna Feldman, *Department of Structural Biology, Weizmann Institute of Science, 76100 Rehovot, Israel.* E-mail: Mark.Safro@weizmann.ac.il

In the first stage of diffusion-controlled enzymatic reaction, aminoacyl-tRNA synthetases (aaRSs) interact with cognate tRNA's forming nonspecific encounters. The aaRSs catalyzing the same overall aminoacylation reaction vary greatly in subunit organization, structural domain composition and amino acid sequence. The diffusional association of aaRS and tRNA was found to be governed by long-range electrostatic interactions when negative potential of tRNA fits to the patches of positive potential produced by aaRS: one patch for each tRNA molecule. Considering aaRS as a molecule with anisotropic reactivity and based on the Smoluchowski's theory, the reaction conditions for tRNA-aaRS diffusional encounters are formulated. The significance of multipole electrostatic potential components to the tRNA steering process is conditioned by subunit organization of aaRS. Enzymatically relevant domains appeared to be nonessential for field sculpturing at long distances. On the other hand, set of complementary domains exerts primary control on the aaRS's isopotential surface formation. Subdividing the aaRS's charged residues into native, conservative and non-conservative subsets we evaluated the contribution of each group to long-range electrostatic potential. Surprisingly, the electrostatic potential landscapes generated by native and non-conservative subsets are fairly similar, thus suggesting the non-conservative subset being specifically developed for efficient tRNA attraction.

Keywords: tRNA, aminoacyl-tRNA synthetase, recognition