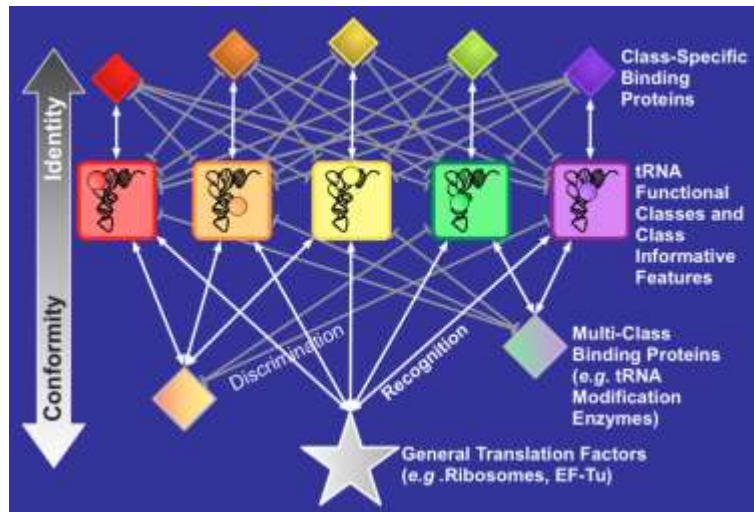


"Evolution of the tRNA interaction Network in Bacteria and Eukaryotes"



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3:00 – 4:00 PM
Science 2, room 109
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Interactions among biological macromolecules underlie practically all functions in cells. Yet we cannot generally predict the structural basis of protein-protein/protein-RNA interactions from genomic data, in part because the structural features that underlie macromolecular interactions are not strictly conserved. If we can find new ways to learn the "shape code" of macromolecular interactions directly from genomic data, we will better understand how interaction networks originate and evolve, with potential applications from metagenomics to biomedicine. We have developed an information theoretical approach to predict interaction-determining features in tRNA from the genome sequence of any cell or organelle. The "identity elements" estimated by our models target tRNAs to interact with specific proteins for biogenesis and function. I will demonstrate potential applications of our models by showing results from three studies. First, we used our models to create phylogenomic classifiers that robustly assign alphaproteobacterial genomes into trusted clades, despite factors like base content convergence that confound standard methods. Second, our models predict the most rapidly evolving sites in *Drosophila* tRNA, where they occur in a rapidly evolving and structurally coherent ion-binding pocket, and mediate with the transfer of interaction-determining features from one functional tRNA-aminoacylation system to another, an evolutionary transfer of interaction-determinants that occurred independently at least three times between the same two enzyme systems during diversification of *Drosophila*. Third, we applied our models to predict the mostly highly divergent tRNA-protein interaction determinants between humans and a human parasite, which led to the discovery of a potential chemotherapeutic hit that specifically inhibits the parasitic enzyme with no activity against its human ortholog. In summary, interaction-determining features have complex evolutionary dynamics that are phylogenetically informative and likely underdeveloped as targets against pathogens.