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Single-Molecule Studies of EF-Tu Accommodation and Proofreading Mechanism

Delivery of aminoacyl-tRNA to the ribosome during translation is assisted by elongation factor thermal unstable (EF-Tu). During this process the EF-Tu ternary complex detects the correct codon and initiates delivery at the cost of GTP. Although the translation process is meticulously monitored, errors can occur such as when assisting factors have mutations. Localized mutations EF-Tu, more specifically eukaryotic homolog eEF1A, have been linked to various health issues such as Huntington's disease, ADHD, epilepsy, intellectual disability, and depression; however, as factors of EF-Tu's mechanism is highly debated, it is not well understood how these mutations contribute to these diseases. To observe and understand EF-Tu's mechanism and conformational changes, mutations at D81 were introduced into the GTP binding pocket and will be observed using single-molecule studies, such as FRET and FIRMS, to determine the conformational changes and interactions with the ribosome. Ternary complex formation and GTPase activity will also be assessed to determine the effect of the mutations on enzymatic activity. Once the single molecule studies have been analyzed, we can survey antibiotics to test their effects on mutant EF-Tu function and conformation to help gather useful information for the further development of these antibiotics.