

25th Annual Undergraduate Spring Symposium Seminar Speaker

Friday, April 21, 2023
3 p.m. ~ Chem 200

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Integrative Single-Molecule Studies of DNA Mismatch Repair

The DNA mismatch repair (MMR) system corrects these DNA synthesis errors that occur during replication. MMR is initiated by the highly conserved MutS and MutL homologs, which are both dimers and contain DNA binding and ATPase activities that are essential for MMR in vivo. MutS homologs initiate repair by binding to a mismatch and undergoing ATP-dependent conformational changes that promote its interaction with MutL homologs. This complex signals the initiation of excision and resynthesis of the newly synthesized DNA strand containing the incorrect nucleotide. We have been using a combination of atomic force microscopy (AFM), single-molecule fluorescence, coupled with biochemistry to characterize the stoichiometries and the conformational and dynamic properties of MutS and MutL homologs and their ATP-dependent assembly on DNA containing a mismatch. We correlate single-molecule fluorescence and ATPase data on *T. aquaticus* MMR proteins with AFM data on human proteins to generate a model of the initiation for DNA mismatch repair, starting from recognition of the mismatch by MutS (or MutS) to the ATP dependent assembly of MutS and MutL homologs on mismatch DNA. I will discuss how we have integrated AFM data on the human proteins with single-molecule fluorescence and biochemical data on *T. aquaticus* protein to arrive at the proposed model.