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Dynamics of DNA Mismatch Repair[1] JULIE COATS, YUYEN LIN, IVAN RASNIK, Emory University — DNA mismatch repair protects the genome from spontaneous mutations by recognizing errors, excising damage, and re-synthesizing DNA in a pathway that is highly conserved. Mismatch recognition is accomplished by the MutS family of proteins which are weak ATPases that bind specifically to damaged DNA, but the specific molecular mechanisms by which these proteins recognize damage and initiate excision are not known. Previous structural investigations have implied that protein-induced conformational changes are central to mismatch recognition. Because damage detection is a highly dynamic process in which conformational changes of the protein-DNA complexes occur on a time scale of a few seconds, it is difficult to obtain meaningful kinetic information with traditional ensemble techniques. In this work, we use single molecule fluorescence resonance energy transfer (smFRET) to study the conformational dynamics of fluorescently labeled DNA substrates in the presence of the mismatch repair protein MutS from *E. coli* and its human homolog MSH2/MSH6. Our studies allow us to obtain quantitative kinetic information about the rates of binding and dissociation and to determine the conformational states for each protein-DNA complex.

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