Electrically monitoring DNA repair by photolyase

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Cyclobutane pyrimidine dimers are the major DNA photoproducts produced upon exposure to UV radiation. If left unrepaired, these lesions can lead to replication errors, mutation, and cell death. Photolyase is a light-activated flavoenzyme that binds to pyrimidine dimers in DNA and repairs them in a reaction triggered by electron transfer from the photoexcited flavin cofactor to the dimer. Using gold electrodes modified with DNA duplexes containing a cyclobutane thymine dimer (T<>T), here we probe the electrochemistry of the flavin cofactor in *Escherichia coli* photolyase. Cyclic and square-wave voltammograms of photolyase deposited on these electrodes show a redox signal at 40 mV versus normal hydrogen electrode, consistent with electron transfer to and from the flavin in the DNA-bound protein. This signal is dramatically attenuated on surfaces where the π-stacking of the DNA bases is perturbed by the presence of an abasic site below the T<>T, an indication that the redox pathway is DNA-mediated. DNA repair can, moreover, be monitored electrically. Exposure of photolyase on T<>T-damaged DNA films to near-UV/blue light leads to changes in the flavin signal consistent with repair, as confirmed by parallel HPLC experiments. These results demonstrate the exquisite sensitivity of DNA electrochemistry to perturbations in base pair stacking and the applicability of this chemistry to probe reactions of proteins with DNA.

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