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Electron trap for DNA-bound repair enzymes: A strategy for DNA-mediated signaling

Eylon Yavin[†], Eric D. A. Stemp[†], Valerie L. O'Shea[‡], Sheila S. David[‡], and Jacqueline K. Barton^{†,§}

[†]Division of Chemistry and Chemical Engineering, California Institute of Technology, Pasadena, CA 91125; and [‡]Department of Chemistry, University of Utah, Salt Lake City, UT 84112

Despite a low copy number within the cell, base excision repair (BER) enzymes readily detect DNA base lesions and mismatches. These enzymes also contain [Fe₄S₄] clusters, yet a redox role for these iron cofactors had been unclear. Here, we provide evidence that BER proteins may use DNA-mediated redox chemistry as part of a signaling mechanism to detect base lesions. By using chemically modified bases, we show electron trapping on DNA in solution with bound BER enzymes by electron paramagnetic resonance (EPR) spectroscopy. We demonstrate electron transfer from two BER proteins, Endonuclease III (EndoIII) and MutY, to modified bases in DNA containing oxidized nitroxyl radical EPR probes. Electron trapping requires that the modified base is coupled to the DNA π -stack, and trapping efficiency is increased when a noncleavable MutY substrate analogue is located distally to the trap. These results are consistent with DNA binding leading to the activation of the repair proteins toward oxidation. Significantly, these results support a mechanism for DNA repair that involves DNA-mediated charge transport.

base excision repair | DNA charge transport | iron sulfur clusters

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