

Electrochemical Detection of Lesions in DNA

Amie K. Boal and Jacqueline K. Barton*

*Division of Chemistry and Chemical Engineering, California Institute of Technology,
Pasadena, California 91125*

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Abstract:

Electrochemical DNA-based sensors that exploit the inherent sensitivity of DNA-mediated charge transport (CT) to base pair stacking perturbations are capable of detecting base pair mismatches and some common base damage products. Here, using DNA-modified gold electrodes, monitoring the electrocatalytic reduction of DNA-bound methylene blue, we examine a wide range of base analogues and DNA damage products. Among those detected are base damage products O4-methyl-thymine, O6-methyl-guanine, 8-oxo-guanine, and 5-hydroxy-cytosine, as well as a therapeutic base, nebularine. The efficiency of DNA-mediated CT is found not to depend on the thermodynamic stability of the helix. However, general trends in how base modifications affect CT efficiency are apparent. Modifications to the hydrogen bonding interface in Watson-Crick base pairs yields a substantial loss in CT efficiency, as does added steric bulk. Base structure modifications that may induce base conformational changes also appear to attenuate CT in DNA as do those that bury hydrophilic groups within the DNA helix. Addition and subtraction of methyl groups that do not disrupt hydrogen bonding interactions do not have a large effect on CT efficiency. This sensitive detection methodology based upon DNA-mediated CT may have utility in diagnostic applications and implicates DNA-mediated CT as a possible damage detection mechanism for DNA repair enzymes.

Full Text (Subscription May be Required):

<http://pubs.acs.org/cgi-bin/abstract.cgi/bcches/2005/16/i02/abs/bc0497362.html>