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Evaluation of DNA Oxidation and Chemical DNA Damage Using Electrochemiluminescent Enzyme/DNA Microfluidic Array

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Abstract : DNA damage from metabolites of lipophilic drugs and pollutants, generated by enzymes, represents a major toxicity pathway in humans. These metabolites can react with DNA to form either 8-oxo-7,8-dihydro-2-deoxyguanosine (8-oxodG), which is the oxidative product of DNA or covalent DNA adducts, both of which are genotoxic and hence considered important biomarkers to detect cancer in humans. Therefore, detecting reactions of metabolites with DNA is an effective approach for the safety assessment of new chemicals and drugs. Here we describe a novel electrochemiluminescent (ECL) sensor array which can detect DNA oxidation and chemical DNA damage in a single array, facilitating a more accurate diagnostic tool for genotoxicity screening. Layer-by-layer assembly of DNA and enzyme are assembled on the pyrolytic graphite array which is housed in a microfluidic device for sequential detection of two type of the DNA damages. Multiple enzyme reactions are run on test compounds using the array, generating toxic metabolites in situ. These metabolites react with DNA in the films to cause DNA oxidation and chemical DNA damage which are detected by ECL generating osmium compound and ruthenium polymer, respectively. The method is further validated by the formation of 8-oxodG and DNA adduct using similar films of DNA/enzyme on magnetic bead biocolloid reactors, hydrolyzing the DNA, and analyzing by liquid chromatography-mass spectrometry (LC-MS). Hence, this combined DNA/enzyme array/LC-MS approach can efficiently explore metabolic genotoxic pathways for drugs and environmental chemicals.

Keywords : biosensor, electrochemiluminescence, DNA damage, microfluidic array
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