



## Oxidative DNA Damage and the Importance of Measuring DNA Repair

Haim Moghim\*

Department of Chemical Engineering, University of Tehran, Tehran, Iran

### Description

Oxidative DNA damage is easily measured in human cells, but estimates of the background level of the most common (and potentially mutagenic) oxidized base, 8-oxaguanine; vary by an order of magnitude. Now, it seems obvious and is becoming widely accepted that DNA oxidation occurs during the preparation of samples for analysis by HPLC or GC-MS. Recent determinations by methods without this artefact indicate a true damage rate of ~1–5 8-oxaguanines/106 guanines. This relatively low level of damage reflects the presence of antioxidant defences and DNA repair in all cells. Reactive oxygen species are abundant as a by-product of respiration, but most are removed by antioxidant enzymes or scavengers such as glutathione (as well as dietary antioxidants such as vitamin C, carotenoids, flavonoids, etc.). The measured damage is in dynamic steady state; the input (regulated by antioxidants) is balanced by the output, i.e. DNA repair.

Cellular repair enzymes remove virtually all DNA damage before it is fixed; therefore repair plays a crucial role in preventing cancer. Repair studied at the transcriptional level correlates poorly with enzyme activity, and phenotypic assays are therefore required. In a biochemical approach, substrate nucleoids containing specific DNA lesions are incubated with cell extract; the regenerative enzymes in the extract cause ruptures at the sites of damage; and discontinuities are measured by comet analysis [1,2]. The nature of the substrate lesions determines the repair pathway to be explored. This *in vitro* DNA repair assay has been modified for use in animal tissues, specifically to study the effects of aging and nutritional interventions on repair. Recently, this assay was applied to different DNA repair-proficient and deficient *Drosophila melanogaster* strains. Most of

### ARTICLE HISTORY

Received: 02-Jan-2023, Manuscript No. EJMOAMS -23- 88089;  
Editor assigned: 05-Jan-2023, PreQC No. EJMOAMS -23- 88089 (PQ);  
Reviewed: 20-Jan-2023, QC No. EJMOAMS -23- 88089;  
Revised: 27-Jan-2023, Manuscript No. EJMOAMS -23- 88089 (R);  
Published: 03-Feb-2023

the applications of the recovery assay have been in human bio monitoring. Individual DNA repair activity may be a marker of cancer susceptibility; alternatively, high repair activity may result from induction of repair enzymes by exposure to DNA-damaging agents. Research to date has examined the effects of environment, diet, lifestyle and exercise in addition to clinical studies.

### The importance of measuring DNA repair

DNA is a molecule prone to damage by exogenous and endogenous sources with important implications for mutagenic and carcinogenic processes. Cells have repair systems that repair almost all damage before genome changes can occur; therefore, repair mechanisms play a critical role in cancer prevention [3,4]. Different pathways involving numerous groups of repair enzymes deal with different types of DNA damage, introduction of one or more bases followed by ligation and Single-Strand Breaks (SSBs) at sugar-phosphate bases; homologous recombination and non-homologous end joining deal with more severe Double-Strand Breaks (DSBs) in the sugar-phosphate base; Base Excision Repair (BER) deals with small base changes such as alkylation or oxidation; Nucleotide Excision Repair (NER), the most complex repair pathway, deals with bulky adducts of different molecules covalently bound to bases, covalent bonds between adjacent bases in the same chain (intra-strand cross-links), DNA-protein cross-links, and in the form of covalent bonds along a double helix (transverse inter-strand bonds); and finally, repair of transaction inconsistencies with incorrectly paired bases [5,6]. All of these pathways are likely to be regulated differently. For example, the enzymes that play a role in BER are thought to be constitutive because they deal with oxidized bases that are produced by the inevitable presence of reactive oxygen species (a by-product of respiration), while the

enzymes involved in NERs are more likely to be induced as they deal with lesions that are sporadically induced by exogenous agents (eg, dietary mutagens, UV) [7].

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