S010 Oxidative Damage to DNA

Steffen Loft, Pernille H. Danielsen, Lotte Risom, Lykke Forchhammer, Elvira V. Bräuner and Peter Møller
Institute of Public Health, Department of Environmental Health, University of Copenhagen, Denmark

Oxidative stress-induced damage to DNA includes a multitude of lesions, many of which are mutagenic and have multiple roles in cancer and aging. Many lesions have been characterised by MS-based methods after extraction and digestion of DNA. These preparation steps may cause spurious base oxidation, which is less likely to occur with methods, such as the comet assay, which are based on nicking of the DNA strand at modified bases, but offer less specificity. The European Standards Committee on Oxidative DNA Damage has concluded that the true levels of the most widely studied lesion, 8-oxo-7,8-dihydro-2'-deoxyguanosine (8-oxodG), in cellular DNA is between 0.5 and 5 lesions per 10^6 dG. Base excision repair of oxidative damage to DNA can be assessed by nicking assays based on oligos with lesions or the comet assay or in case of e.g. OGG1 responsible for repair of 8-oxodG by genotyping. Products of repair in DNA or the nucleotide pool, such as 8-oxodG, excreted into the urine can be assessed by MS-based methods and generally reflects the rate of damage. Experimental and population based studies indicate that many environmental exposure, including particulate air pollution, causes oxidative damage to DNA, whereas diet rich in fruit and vegetables or antioxidant supplements may reduce the levels and enhance repair. Urinary excretion of 8-oxodG, genotype and expression of OGG1 have been associated with risk of cancer in cohort settings, whereas altered levels of damage, repair or urinary excretion in case-control settings may be a consequence rather than the cause of the disease.