CLINICAL SIGNIFICANCE OF OXIDATIVE DAMAGE TO DNA

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Reactive oxygen species (ROS) can cause oxidative damage to DNA which may be a major cause of various diseases such as cancer. Commonly used biomarkers of oxidative DNA damage include measure of 8-oxo 7,8-dihydro-2'-deoxyguanosine (8-oxodGua) and its corresponding base, 8-oxoGua. These modifications can be determined either in cellular DNA or in urine where their excretion represents the average rate of oxidative DNA damage in the total body.

In order to assess the role of oxidative DNA damage in cancer development we decided, for the first time, to analyse the broad spectrum of oxidative DNA damage biomarkers; urinary excretion of the base/nucleoside modification as well as the level of oxidative damage in cellular DNA and repair of the damage. It has been found that the levels of oxidative DNA damage were significantly higher while the concentrations of the antioxidant vitamins were significantly lower in colon and lung cancer patients than in control group. Moreover, the same direction of the changes has been found in patients with adenoma. This, in turn, suggests that the changes in aforementioned biomarkers of oxidative stress are characteristic for cancer development. Our work underscores the importantce of assessment of broad range of biomarkers in the interpretation of a meaning of oxidative stress in cancer development.

Age is a single the most important factor which may contribute to cancer development. There is a possibility that a common link of these pathological conditions is oxidative damage to DNA. We have demonstrated that the level of 8-oxodG in leukocytes' DNA showed statistically significant correlation with the age of the examined subjects (n = 256). Age-dependent decline in the concentration of vitamin C was also observed. On the basis of the presented correlative association between oxidative DNA damage parameters and age it seems reasonable to state that the damage may be one of the substantial factors in human ageing.

Given the plethora of, often contradictory, literature reports describing other pathological conditions in which levels of oxidative DNA damage have been increased, the lecture will critically address the extent to which significance of such damage is relevant for the pathogenesis of disease. Given the close link between ROS formation and oxidative DNA damage and the importance of DNA damage and mutation in carcinogenesis, it is very reasonable to link oxidative DNA lesions to cancer development. The involvement of oxidative DNA damage in the pathogenesis of other diseases is more elusive.