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Analysis of 8-Hydroxydeoxyguanosine as a Marker of Oxidative Stress

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To evaluate the role of oxidative stresses in carcinogenesis induced by environmental agents and life style, we measured the 8-hydroxydeoxyguanosine (8-OH-dG) levels in animal organ DNA and in human urine. Cadmium (Cd) and diesel exhaust particles (DEP), increased 8-OH-dG in rat testis and lung DNA, respectively. In these experiments, an decrease of 8-OH-dG repair activity was also observed. These results indicate that oxidative DNA damage accumulates by impaired repair activity and is involved in the carcinogenic mechanisms of Cd and DEP. In the experiments related to life style, we investigated the effects of forced and spontaneous exercise on the levels of 8-OH-dG in the DNA of rat organs. Forced exercise increased the 8-OH-dG levels in the heart, lung, and liver DNA of the rat, but spontaneous exercise reduced them. Recently, we established a method for urinary 8-OH-dG analysis by HPLC-ECD. After analyses of 318 samples, we found that moderate physical exercise, such as sports, reduced the urinary 8-OH-dG level, while cigarette smoking, severe labor conditions, such as day and night shift work and physical labor, low meat intake and low BMI (<22) increased its level. These results suggest that the measurement of 8-OH-dG in cellular DNA and urine is a useful marker of oxidative stress, which may induce cancer.

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S1-3

Role of oxidative DNA damage by environmental chemicals in carcinogenicity and reproductive toxicity.

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Reproductive impairment in wildlife and humans induced by environmental chemicals is a growing problem. Reproductive toxicity is considered to involve not only endocrine disruption but also genetic damage. In fact, a number of carcinogens exhibit reproductive toxicity. We found that the carcinogenicity of various chemicals is closely associated with the extent of DNA damage. Thus, such chemicals may show reproductive toxicity through DNA damage and apoptosis. Here we discuss the role of oxidative DNA damage induced by various environmental chemicals in relation to their carcinogenicity and reproductive toxicity.

We investigated the mechanism of DNA damage using ^{32}P 5'-end labeled DNA fragments obtained from the human c-Ha-*ras*-1 protooncogene and *p53* and *p16* tumor suppressor genes. The site specificity of DNA damage was analyzed using the Maxam-Gilbert method. We measured the content of an indicator of oxidative DNA damage, 8-oxo-7,8-dihydro-2'-deoxyguanosine (8-oxodG), with an electrochemical detector coupled to HPLC.