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MUTAGENIC POTENTIAL OF FREE RADICALS GENERATED FROM INFLAMMATORY LEUKOCYTES AND INHIBITION OF THE MUTAGENICITY BY FOOD FACTORS

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DNA mutations undoubtedly contribute to the onset of some life style-related diseases including cancer. Rapid and reliable methods to detect DNA mutations and to isolate mutants should have a great impact on this field. Activated inflammatory leukocytes are considered to play some important roles in carcinogenesis by generating reactive oxygen species (ROS). The purpose of the present study is to examine the relationship between leukocyte activation by TPA and mutagenesis. In order to examine the relationship between ROS from inflammatory leukocytes and the mutagenic potential, we co-cultured TPA-stimulated, differentiated HL-60 cells with Chinese hamster ovary cells (AS52) and conducted suppressive experiments to determine whether O2- generated from HL-60 cells is responsible for DNA mutations in AS52 cells. As the results, when AS52 cells were co-cultured with TPA-stimulated HL-60 cells, a significant increase in the frequency of mutants was observed when compared to those co-cultured with non-treated HL-60 cells or cultured alone. Treatment with SOD and diphenyleneiodonium (DPI), an NADPH oxidase inhibitor, resulted in a significant reduction in the rates of mutation. These results strongly support that O_2^- generated from HL-60 or subsequently produced ROS possesses a mutagenic potential. Moreover, some food phytochemicals, including auraptene (from citrus fruit), notably suppressed the mutation rate through attenuation of O_2^- generation in HL-60 cells, suggesting inhibition of O_2^- generation with some food phytochemicals can prevent mutagenesis, at least in AS52 cells. While further studies are required to elucidate the relationship between ROS production and chronic inflammation or carcinogenesis, the results of the present study

show that the AS52 cell line can be used to analyze the linkage between ROS production and mutagenesis, and to evaluate chemopreventive compounds. A novel bioassay system for measuring the mutagenicity of leukocyte-derived ROS and its suppressive food factors will be presented.