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Down-regulation of Manganese Superoxide Dismutase Gene Expression by Vitamin C in Cultured Pheochromocytoma Cells

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ABSTRACT

Epidemiological studies have revealed the beneficial effects of vitamin C consumption on cancer prevention because reactive oxygen species have been linked to the process of carcinogenesis. Severe reduction of manganese superoxide dismutase (MnSOD) activity has been noticed in many human and experimental tumors. The present study evaluates the effect of ascorbate (vitamin C) on changes of SOD in cultured pheochromocytoma (PC-12) cells. Incubation of PC-12 cells with vitamin C at different concentrations for 2 days (short-term) caused a dose-dependent decrease of both the activity and mRNA level of MnSOD. Similar phenomena were also observed after a 7-day (long-term) incubation. Both activity and mRNA level of MnSOD were reduced by long-term vitamin C supplementation in a dose-dependent manner. These results showed that MnSOD was down-regulated after supplementation with an antioxidanted. These findings are compatible with those of previous reports in which MnSOD decreased in some tumors. (N. Taipei J. Med. 2000; 2:245-250)

INTRODUCTION

Superoxide dismutases (SODs) are key enzymes in the cellular defense against oxidative damage caused by free radicals.[1] Superoxide free radicals are normal byproduct of metabolism, being generated by oxidative phosphorylation and photosynthesis.[2] Oxidative damage caused by free radicals results in the breakdown of biological macromolecules and thus contributes to adverse conditions such as aging, cancer, and a variety of degenerative diseases.[3] SODs catalyze the breakdown of toxic superoxide radicals into hydrogen peroxide and molecular oxygen, thus providing protection against oxidative damage.[4]

Vitamin C (ascorbic acid) is one of the most powerful natural antioxidants. Vitamin C is water soluble and is found in high concentrations in many tissues; human plasma contains about 60 μmol ascorbate/L.[5,6] Upon reaction with reactive oxygen species, ascorbic acid is oxidized in 2 one-electron steps to dehydroascorbate via the ascorbyl free radical.[7] Dehydroascorbate is recycled back to ascorbate by the dehydroascorbate reductases.[8] As a scavenger of reactive oxygen species, ascorbate has been shown to be ef-

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