

Mihajlo B. SPASIĆ

Free radicals and cancer

INSTITUTE FOR BIOLOGICAL RESEARCH "SINIŠA STANKOVIĆ",
BELGRADE, YUGOSLAVIA

Naturally occurring antioxidants, such as vitamin E and selenium, have antimutagenic and radioprotective properties that need further examination with respect to long-term radiation effects. Modulation of endogenous antioxidants, such as superoxide dismutase, may be useful in specific radiotherapy protocols (1). It is well established that ionizing radiation induces the evolution of free radicals and other reactive species, (hydrated electrons and ions), in an organism due to ionization of aqueous medium. Among direct damaging effects to biomacromolecules, ionizing radiation induces free radical chain reactions, which lead to the appearance of non-functional derivatised molecules and thus disturbed physiological functions. Unappropriate antioxidative defense (AD) capacity for preventing formation and repair capacity for elimination of the damaged molecules results in pathological changes and fatal outcome. After millions of years of exposure to natural irradiation, living organisms have adapted so that low levels of radiation cause very little, if any harm. To examine molecular basis of such an adaptation, one of the main questions that should be answered is related to the role of reactive species in the regulation of biochemical i.e. physiological processes. A direct regulatory role of reactive oxygen species throughout their interaction with regulatory molecules such as tyrosine kinases or nuclear factor -kB was also reported (2).

Many tumor cells are in prooxidant status resulting from increased production of oxygen free radicals or decreased expression of antioxidant enzymes (3). Antioxidant molecules, such as glutathione and vitamin E and C as well as antioxidant enzymes such as superoxide dismutase, catalase and glutathione peroxidase, have been long believed to have protective and anticancer activities by scavenging excess of free radicals (4). New data suggest that another mechanism of action is possible. Redox modu-

lation of gene expression is well documented (5,6). Antioxidants may play protective role also through differential regulation of transcriptional activator activities (7). Redox regulation of the p53 tumor suppressor gene, which induces blocks in the cell cycle and prevents gene amplification (8), is obvious because the removal of reducing agents by dialysis completely inactivated p53 DNA binding activity (9).

In this volume, the Archive of Oncology has published some papers related to these problems. Vitamin E supplementation produces an improvement in the immune system and protection against disease other than cardiovascular disease such as prostate cancer (10). It will be extremely difficult to do trials that adequately probe the dose-effect curve for vitamin E for each condition that it might affect, or to do studies of all the possible combinations of other micronutrients that might act with vitamin E to improve its effectiveness. Data from clinical studies about level of vitamin E, in relation with other lipid components and effect of vitamin E supplementation may be very useful although far from being "complete". *In vitro* studies of the effect of ionization radiation on antioxidant enzymes in cell tissue cultures as well as protective effect of vitamin E gave more precise data but the relation with *in vivo* situation must be further verified. As Pryor said "Therefore, the scientific community must recognize that there never will be a time when the science is complete" (10), we may add that accumulation of data about free radicals in cancer through scientific papers, as in this volume of the Archive, puts us closer to determination of antioxidants' role *in vivo* and possible antioxidant use in therapy of cancer.

REFERENCES

1. Weiss JF, Landauer MR. Radioprotection by antioxidants. *Ann NY Acad Sci* 2000;899:44-60.
2. Spasić MB, Žunjić Z, Vujan S. *In vivo* regulation of biochemical processes by reactive species. *Vinca Bulletin* 3 1999; (Suppl.1):665-70.
3. Sun Y. Free radicals, antioxidant enzymes and carcinogenesis. *Free Radical Biol Med* 1990;8:583-99.
4. Simović M, Spasić MB, Michelson AM. Free radicals in human myocardial reperfusion injury. *Life Chem Rep* 1995;12:227-70.
5. Storz G, Tartaglia LA, Ames BN. Transcriptional regulator of oxidative stress-inducible genes: Direct activation by oxidation. *Science* 1990;248:189-94.
6. Allen F. Redox control of transcription: Sensors, response regulators, activation and repressors. *FEBS Lett* 1993; 332:203-7.
7. Sun Y, Oberley LW. Redox regulation of transcriptional activators. *Free Radical Biol Med* 1996;21:335-48.
8. Lane DP. p53 and human cancers. *Br Med Bull* 1994; 50:582-99.
9. Hupp TR, Meek DW, Midgley CA, Lane DP. Activation of the cryptic DNA binding function of mutant form of p53. *Nucleic Acids Res* 1993;21:3167-74.
10. Pryor WA. Vitamin E and heart disease: basic science to clinical intervention trials *Free Radical Biol Med* 2000;28:141-64.

Address correspondence to:

Prof. Dr Mihajlo B. Spasić, Department of Physiology,
Institute for Biological Research "Siniša Stanković", 29.
novembra 142, 11000 Belgrade, Yugoslavia

The manuscript received: 24. 11. 2000.

Accepted for publication: 27. 11. 2000.