



# **FREE RADICAL BIOLOGY & MEDICINE**

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July 16 – 20, 2002  
René Descartes University, Paris, France

*Programme and Abstracts*



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**XIth Meeting of the Society for  
Free Radical Research International**

**Role of free radicals, oxidants and antioxidants, in  
molecular and cell biology and life processes.  
New development and techniques**

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#### URIC ACID DECREASE AND MALONEDIAL-DEHYDE CONTENT INDICATE OXIDATIVE STRESS IN THE COURSE OF CHEMOTHERAPY TREATMENT OF LEUKEMIA PATIENTS

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Plasma levels of antioxidants (uric acid), lipid peroxidation products (malonedialdehyde, MDA), and serum iron content were studied as markers of impaired antioxidant status in the course of cytostatic therapy of patients with acute myeloblastic leukemia (AML) and acute lymphoblastic leukemia (ALL). Patients with complete remission of AML and ALL appeared to have a significant decrease in plasma uric acid levels, indicating the consumption of uric acid as plasma antioxidant during the chemotherapy-induced oxidative stress. From normal before the treatment the uric acid values decreased to 60% of the normal values at the 4<sup>th</sup> day of the therapy. At the end of the treatment with cytostatics when leukocytes were lower than  $1.10^9/l$ , the uric acid values stayed below or within the lower limits of the normal range. At the early stage of the disease patients with AML and ALL having high number of blast cells in the blood (over  $30.10^9/l$ ) exhibited extremely high values of plasma uric acid content due to the high rate of tumor cell death (900  $\mu\text{mol/l}$  plasma uric acid content measured before therapy), masking the decrease during the cytostatic therapy as found for the rest of the AML and ALL patients with uric acid content below the norm at the end of their therapy. A correlation between uric acid consumption and an increase in the lipid peroxidation product MDA, consequence of the oxidative stress, was found for patients with complete remission of AML and ALL and AML and ALL patients with leukocyte levels lower than  $1.10^9/l$  but not for AML and ALL patients with leukocyte levels higher than  $30.10^9/l$ .

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#### THE EFFECT OF TRIBOMECHANICALLY ACTIVATED ZEOLITE (TMAZ) ON TOTAL ANTIOXIDANT STATUS OF HEALTHY INDIVIDUALS AND PATIENTS WITH MALIGNANT DISEASE

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Subject of study: Anticancer therapeutic protocols based on specific combination of various antioxidants are accepted. Here we present a new potential antioxidant: tribomechanically activated zeolite TMAZ as a product of nanotechnology. TMAZ significantly increases total antioxidant status (TAS) and lower free radicals in blood, measured by Free Radicals Analysis System (FRAS). We have performed both tests on patients with malignant disease as well as healthy individuals. TMAZ is gained in the process called tribomechanical micronization and activation (nano-

medicine-technology). **Patients, materials and methods:** Total antioxidant status. By measuring Total Antioxidant Status we followed overall activity of three antioxidant enzymes: Superoxid Dismutase (SOD), Glutathion Peroxidase (GPx) and Glutathion Reductase (GR). We used test system from Randox Laboratories Ltd., Crumlin, United Kingdom. Antioxidants in added sample cause inhibition of the radical (cation ABTS<sup>•+</sup>) to a degree that is proportional to their concentration. Test has been performed on 45 individuals; 22 healthy (10 male, 12 female), 18 patients with malignant disease (7 male, 11 female), all in the age of 40–70. 5 individuals were in the control group. FRAS is a system which is able to dose all types of hydroperoxide present in a biological sample via a simple, rapid, reliable and repeatable method using a mere drop of blood. We had 22 female patients and 24 male patients with malignant disease. **Summary:** Our results indicate that tribomechanically activated zeolite, clinoptilolite, is potentially a new antioxidant which seems to have bigger capacity than already known antioxidants. We have noticed that patients with malignant disease, who were taking TMAZ, have improved their general health condition. TMAZ significantly increases TAS values. **Conclusion:** TMAZ can be used as an adjuvans or roborans in any standard therapy of malignant disease, with the aim to improve the general health condition of patients and help them recover much easier and in a shorter period of time.

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#### OXIDATIVE STRESS SELECTIVE TARGETING IN HORMONALLY INDUCED EXPERIMENTAL CARCINOGENESIS

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The model of estradiol depended renal cancer in male Syrian hamsters is one of most popular model of tumorigenesis world wide. It has been postulated that this carcinogenesis is possibly inducted by semiquinone and quinone metabolites of 4-hydroxylation of estradiol and oxygen free radicals generated during red-ox cycling of these derivatives. The specificity of the targeting of the oxidative stress towards lipid and protein fraction in a model of estrogen-induced Syrian hamster nephrocarcinogenesis was evaluated. Thirty male Syrian hamsters were divided into two groups: group 1 (n = 16) was treated with estradiol given in one subcutaneous dose of 25 mg per animal. Group 2 (n = 14) did not receive hormone and served as a control group. The animals were sacrificed after four weeks and their kidneys were excised. The amount of oxidative stress modified proteins was significantly elevated as early as one month after the initial implantation of estradiol versus control group, while the stress did not affect lipids. The subcellular localization of the oxidative stress target was determined by the analysis of protein oxidation in subcellular fractions of kidney cells. : The analysis revealed a dramatic increase in level of carbonyl groups in microsomal fraction versus any other [13,77 vs.