

OCC Meeting Report: OCC 2004 World Congress

The 11th Annual Meeting of the Oxygen Club of California (OCC) on Oxidants and Antioxidants in Biology was held March 10–13, 2004, at Fess Parker's Doubletree Resort, in beautiful Santa Barbara, California, USA. The meeting was co-sponsored by the Linus Pauling Institute (LPI) and the Society for Free Radical Research International (SFRRI); The OCC's topics of interest are the research fields of reactive free radicals, oxidants and antioxidants within biological systems, and micronutrients in medicine, nutrition and health. One of its major goals is to enhance interaction between experts in these fields by providing meetings and discussion forums.

OCC meetings have been held for about a dozen years, with Lester Packer as the Founder and Honorary President of the OCC. In the beginning, these meetings were held under the name of the Bay Area Oxygen Club (BAOC) at the University of California at Berkeley. The BAOC meetings were co-sponsored by the National Foundation for Cancer Research (NFCR) and were held just prior to the Gordon Conference on Oxyradicals held in Southern California. Since 1996, the annual OCC meeting has been taking place in Santa Barbara, California. The LPI in Corvallis, Oregon is a co-sponsor and since 2003, the meetings have been held in alternate years in Santa Barbara, California and in Portland, Oregon, with their scientific programs designed to be complementary.

The 2004 meeting was dedicated to Dr Bruce Ames on the occasion of his 75th birthday. Dr Ames has made outstanding scientific contributions to the research areas of oxidative stress, gene regulation, mitochondrial dysfunction in the aging process, and the role of diet and micronutrients in cancer prevention and human health. All of these research fields were topics covered in the 57 presentations given at the 11th OCC meeting with all speakers dedicating their presentation to Dr Ames. In addition, a special issue of *Archives of Biochemistry and Biophysics* (Vol. 423 (1), March 1 issue, 2004, edited by Lester Packer, Enrique Cadenas, Balz Frei and Helmut Sies) with contributions by the scientific

community attending the OCC meeting has been dedicated to Dr Ames and was given to all OCC attendees. There was also a reception sponsored by Elsevier, the publisher of the Journal.

This year's meeting again was a full success, both scientifically and collegially. A formal announcement was made at the meeting that Dr Helmut Sies, Professor at the Institute for Biochemistry and Molecular Biology at the University of Duesseldorf, Germany, will be the new OCC president, succeeding Kelvin J.A. Davies from the University of Southern California, Los Angeles, California.

The conference started exactly on the day when news on diet, physical inactivity and obesity were national headlines for the day. A study by the Centers for Disease Control, conducted to identify and quantify the leading causes of death in the United States, found that about one third of all deaths in the U.S. can be attributed to preventable behavior such as tobacco, poor diet and physical inactivity. Poor diet and physical inactivity, both associated with obesity, are causing together almost as many deaths as tobacco smoking and secondhand exposure do (16.6% versus 18.1%, respectively), with a trend towards physical inactivity and poor diet taking the lead in a couple of years (Mokdad *et al.*, *JAMA*, March 10, 2004, Vol 291, No 10). Obesity is associated with inflammation and elevated oxidative stress and thus related to chronic disease development. In light of this, the conference's importance with regard to research on oxidants, antioxidants, oxidative stress, inflammation and associated diseases such as diabetes, cancer etc. became even more clear.

Preceding the official opening of the meeting, a round-table discussion was held on the safety of beta-carotene supplementation with an emphasis on the safety of supplementation in cigarette smokers. Two intervention trials published in 1996 (ATBC and CARET studies) showed increased lung cancer risks in smokers when supplemented with beta-carotene. Since then no further trials administering beta-carotene using pharmacological dosages have been conducted due to safety and

ethical reasons. However, epidemiological observational studies investigating dietary and blood data consistently show that high fruit and vegetable intake and high blood beta-carotene concentrations are inversely associated with lung cancer risk. It was discussed that when conducting subgroup analysis in the cohorts of smokers investigated in the ATBC and CARET studies, only current and heavy smoking was associated with increased relative risk for lung cancer. Concluding from this analysis, beta-carotene supplementation in conjunction with former smoking and light smoking does not seem to be increasing the risk for lung cancer. However, it was concluded that further research into details on current findings on all levels, in *in vitro*, animal and human studies, needs to be continued before clear recommendations on beta-carotene supplementation in smokers can be made.

The conference began with a keynote lecture given by the guest of honor, Bruce Ames on supplements in human health. Dr Ames emphasized that an optimum intake of micronutrients in the poor, young, obese and elderly of the U.S. population could increase overall health at little cost. This hypothesis is based on Dr Ames internationally highly respected contributions to the research fields of micronutrient deficiencies, DNA damage and chronic diseases, mitochondrial oxidative decay and aging. He presented research conducted in his laboratory which showed that feeding old rats high levels of mitochondrial metabolites such as acetyl carnitine and lipoic acid restored mitochondrial function and thus may ameliorate aging processes.

The meeting agenda covered eight sessions including the research fields of mitochondria, aging and neurodegeneration, micronutrients with a focus on vitamin E, vitamin C, flavanoids and phytoestrogens, coenzyme Q, lipoic acid, redox signaling and gene expression. Two half-day sessions were dedicated to a workshop reporting research on carotenoids and retinoids.

In the session on mitochondria, aging and neurodegeneration, Tory Hagen's work from the LPI was presented on the differences between two distinct subpopulations of cardiac mitochondria with regard to their response to oxidative stress. He showed that in old rats only mitochondria in the myofilaments had a significantly higher rate of oxidant production and a decline in mitochondrial ascorbate levels and glutathione redox status. This led his team to conclude that mitochondrial decay is not uniform under oxidative stress in the aging heart.

With regard to the micronutrient vitamin E, Angelo Azzi suggested in his presentation on gene regulation by tocopherols that vitamin E is not an antioxidant *in vivo*, but rather a signaling molecule, suggesting that vitamin E has mainly

"non-antioxidant" functions. He presented data from his laboratory on tocopherol dependent gene regulation grouping the genes into 5 categories. (1) Genes that are involved in the uptake and degradation of vitamin E; (2) Genes that are involved in lipid uptake and atherosclerosis; (3) Genes that modulate extracellular proteins; (4) Genes involved in inflammation; (5) Proteins that play a role in cell signaling and cell cycle control.

The activation of the pregnane X receptor which regulates a number of xenobiotics metabolizing enzymes like CYP3A4 by α -tocopherol and especially tocotrienols in cell cultures was reported by Regina Brigelius-Flohé. The finding was verified for α -tocopherol also *in vivo* which raised the question whether prolonged supplementation with high dosages of α -tocopherol might result in unwanted side effects like an interference with drug metabolism. Also, these observations can not be explained with a mere antioxidative function of vitamin E. However, in contrast to these statements that vitamin E is not (only) an antioxidant *in vivo*, a supplementation study presented by Maret Traber on oxidative stress induced by enduring exercise showed that vitamin E supplements decreased lipid peroxidation, a biomarker for oxidative stress. Overall, Dr Azzi's and Dr Brigelius-Flohé's comments on this issue were taken up by several presenters throughout the meeting and contributed nicely to a friendly scientific atmosphere of discussions among the participants.

Balz Frei presented a study conducted in his laboratory studying antioxidant effects of dietary flavanoids. His laboratory investigated the effect of apple consumption on antioxidant protection of human plasma after plasma has been incubated with a free radical initiator (AAPH). He and his colleagues found that apple extract did not protect plasma ascorbate from oxidation but significantly increased the half-life of urate and alpha-tocopherol, and increased lipid peroxidation lag time in human plasma. When apples were actually consumed, urate levels and plasma antioxidant capacity increased. From these results, his research group concluded that antioxidant protection of human plasma by apple consumption seems more likely to be based on an increase of plasma urate levels rather than on apple-derived antioxidant flavanoids.

Dr Roland Stocker started the session on coenzyme Q10 (ubiquinol 10) with a presentation on antioxidant activity of lipoprotein-associated ubiquinol 10. He reiterated that ubiquinol 10 represents the first line of defense in LDL particles against oxidation in synergism with α -tocopherol which is quantitatively the most abundant antioxidant in LDL particles. He showed that supplementation studies with

ubiquinol 10 in apolipoprotein E-deficient mice decreased the extent of atherosclerotic lesions. He suggested these results indicate that supplemental ubiquinol 10 can inhibit lipoprotein oxidation *in vivo* and thus may contribute to the inhibition of atherosclerosis development in humans.

There were many more sessions in the program, dense as always, and the interested reader is

referred to the website: www.oxyclubcalifornia.org where the conference program, the book of abstracts, and the conference photo can be viewed.

Marion Dietrich,
Regina Brigelius-Flohé and
Nesrin Kartal-Özer