COST Action CM1001 Strategic Group Meeting on

"Lipid peroxidation by-products in metabolic diseases"

The Hebrew University Faculty of Medicine, Ein-Kerem Campus, Jerusalem, Israel.

January 12-14, 2013

Organizers: Shlomo Sasson and Oren Tirosh

Meeting Summary:

The meeting included presentations from COST Action CM1001 members as well as Israeli scientists and of students on the involvement of advanced lipid peroxidation end products (ALEs) in the pathology and aetiology of chronic diseases. The meeting addressed cellular and molecular interactions that contribute to cell and organ damage and suggested strategies to prevent them. In addition, the meeting aimed at presenting advanced analytical methods for the determination of oxidized and covalently-modified proteins in cells and biological fluids.

Topic discussed:

Disease and pathologies: diabetes, non-alcoholic fatty liver disease, cancer and aging in the context of protein and lipid oxidation and adducts formation. Effects of diets (polyphenols, high fat diets, omega-3 fatty acids) on oxidative stress and the aetiology of chronic diseases were presented and discussed. The use and mechanism of action of active carbonyl scavengers (i.e., carnosine derivatives), and/or the use of activators of the endogenous antioxidant defence system (e.g., the proteasome activators) as therapeutically strategies were presented and discussed. Potentials of novel and advanced analytical methods for the identification and quantification of ALEs and oxidized and modified proteins were discussed following the presentation of several improved and innovative strategies.

Program:

Session 1: The roles of lipids in metabolic diseases and aging included presentations on diabetes and atherosclerosis:

Neven Zarkovic (HR): Lipid peroxidation and diabetic complications.

Gil Leibowitz (IL): Regulation of ER morphology and function in stressed β-cells.

Betul Catalgol (TR): Lipofuscin accumulation in aging and age related diseases.

Chantal Houee-Levin (FR): The control of the activity of NADPH oxidase by lipids.

Joseph Kanner (IL): Dietary advanced lipid oxidation end products are risk factors to human health: prevention by polyphenols.

Yael Riahi (IL): Role of lipid peroxidation in foam cell-induced damage in vascular endothelial cells.

Perinur Bozaykut (TR): The role of vascular antioxidant defences in response to dietary lipids and atherogenesis in hypercholesterolemic rabbit aorta.

Session 2: Analytical methods of carbonylated protein included state of the art presentations about analytical methods for ALEs evaluation and identification.

Corinne Spickett (UK): Challenges and successes in analysing adducts between proteins and phospholipid oxidation products.

Maria Fedorova (DE): Protein carbonylation by direct oxidation or in secondary reactions with products of lipid peroxidation – new analytical techniques.

<u>Session 3:</u> Highlight on WG3 discussed the modification of key cellular proteins and functional outcomes:

Efstathios Gonos (EL): Proteasome activation as a novel anti-aging strategy.

Bertrand Friguet (FR): Impairment of energy metabolism is associated with oxidative modifications of specific enzymes in senescent cells.

Oren Tirosh (IL): Diet-induced hepatosteatosis.

<u>Session 4:</u> Antioxidants and scavengers of lipid oxidation and peroxidation end-products :

Giancarlo Aldini (IT): The discovery of carnosine derivatives as selective and efficient sequestering agents of cytotoxic carbonyl species: from molecular design to preclinical studies.

Grzegorz Bartosz (PL): Prevention of protein damage by lipoxidation.

<u>Session 5:</u> Young investigators' presentations:

Karina Tveen Jensen (UK): Mass spectrometry and proteomic approaches to identifying protein oxidation.

Guy Cohen (IL): Impact of lipid peroxidation on pancreatic β-cell functions.

Ileana R. Leon (DK): Proteomics reveals the role of protein phosphorylation and acetylation in the regulation of dietary lipids metabolism.

Sarit Anavi (IL): Modulation of HIF1α response to hypoxia in fatty liver by lipid peroxidation.

In **<u>round table discussions</u>** we acknowledged that: (A) Lipid peroxidation and advanced lipid peroxidation-end products play important roles in the aetiology the chronic diseases on the background of metabolic dysfunctions (e.g., diabetes, hyperlipidemia). ALEs are not just by-products of the diseases, but also contribute to the pathology and progression of chronic diseases. (B) Tissue damage is also related to protein modification, to which the formation of lipids adducts, contributes greatly. Therefore, analytical methods should be developed for analysing whole cell and tissue protein and lipids oxidation profile, with special attention to the interaction of ALEs with key signalling proteins. Modern and advanced methods that were presented during the meeting may open the road to productive collaborations between the analytical and synthetic chemists and basic and clinical researchers in this COST Action.

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