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Oxysterols

Oxysterols are oxygenated forms of cholesterol or its precursors. They have traditionally been considered as intermediates in bile acid and steroid hormone biosynthesis or as autoxidation products in tissues, especially under conditions of oxidative stress. However, more recent data show that oxysterols are not only intermediary waste products or disease products, but also have many important and specific biological activities.

They can act as transport forms of cholesterol and have several distinct receptor functions, being ligands to nuclear receptors as well as to G protein-coupled receptors. In this function, they are involved in lipid homeostasis and regulation of cholesterol biosynthesis, and are important in diverse fields, such as neuroscience and immunology. Analysis of oxysterols is therefore important but also challenging since they have low abundance in biological systems, much lower than cholesterol, and are difficult to handle.

Oxyphytosterols are plant-derived relatives of oxysterols, and also have biological activities. At one time their precursors, phytosterols, were considered as food alternatives or supplements with protective functions against cholesterol excess but they may also themselves give overload problems and unwanted activities. This is a subject of much debate and many opinions.

In this edition, the diverse functions of oxysterols, sterols and phytosterols are discussed in mini reviews and new discoveries reported in research communications. The latter concern not only the biological activities but also the analytical problems regarding oxysterols and their down-stream metabolites, and the chemical synthesis of authentic standard compounds. Particular attention is paid to the oxysterol receptors, LXRα and β (liver X receptors α and β) and their diverse actions in biology and medicine. Other topics include methodological aspects, highlighting separations and derivatizations for mass spectrometric analysis.

This special edition of BBRC on oxysterols was initiated in preparations for last year's meeting in Swansea, UK, of the European Network for Oxysterol Research (ENOR), which was established in 2010. At this meeting we had the pleasure to have the grandfather of both steroid research and biological mass spectrometry present, Jan Sjövall, who by the way was mentor for one of us (W.G.) and who recruited the other one of us (H.J.) to our once common department. The special issue is composed of papers presented at the conference as well as contributions by eminent scientists in the field unable to attend. Together they account for 30 reports. We have arranged them such that some reviews appear first to introduce the field, research papers then extend specific subjects, and other reviews summarize the knowledge, with the end message highlighting an altered opinion on medical food advice.

In the following synopsis of the special edition we mention only one author per chapter, either the corresponding author or the first author, although we are aware that there are, in most cases, many co-authors to each article. The first section of the special edition is devoted to LXRs and other oxysterol receptors. The issue opens with a review of the mechanism of action of LXRs by J.-Å. Gustafsson and is followed by articles discussing actions of LXRs by D. Trompier and by A. Oumeddour. In subsequent papers I. Preuss discusses the transcriptional regulation of the oxysterol G protein-coupled receptor EBI2 (Epstein–Barr virus induced gene 2), H. Roberg-Larsen reviews the involvement of oxysterols in Hedgehog signalling and V.M. Olkkonen describes a vertebrate model for the study of OSBP (oxysterol-binding protein)-related proteins involved in development and metabolism.

The second section of this edition concentrates on the biological activity of oxysterols and related molecules. S.A.M. Khalifa describes how dendrogenin A and B, two newly discovered alkylaminooxysterols, promote proliferation of adult neural stem cells. F. Gosselet reviews the effects of oxysterols on the blood brain barrier, N. Noguchi reviews the functions of 24S-hydroxycholesterol in brain, and V. Leoni reviews cholesterol metabolism in Huntington's disease. Oxysterols formed by autoxidation mechanisms are linked to the pathogenesis of disease, this topic is discussed in relation to inflammatory disease by N. Miyoshi and to atherosclerotic plaques by S. Khatib. The involvement of oxysterols in mixed mode cell death is discussed by T. Nury and their effects on adipose tissue mesenchymal stem cells by D. Levy.

The analysis of oxysterols is challenging. This is largely on account of their low level in comparison to cholesterol and the tendency of cholesterol itself to be oxidised in air to oxysterols, generating artefacts with an identical structure to those present endogenously. Sterols other than cholesterol are also difficult to analyse in mammalian systems. An important analytical consideration, often overlooked or forgotten, is pre-analytical storage. This is a topic discussed by C. Helmschrodt. Papers discussing the quantification of oxysterols in plasma or serum with respect to familial combined hyperlipidemia and chronic hepatitis C virus infection are presented by L. Baila-Rueda and T. Ikegami, while Y. Saito discusses 7-hydroxycholesterol and plasma lipid peroxidation.

Novel analytical methods for vitamins D, sterols, oxysterols and steroids are discussed by J. Abdel-Khalik, S. Matysik, P.J. Crick and by K. Rigdova. The analysis of oxysterols in brain of the cholesterol 24-hydroxylase knock out mouse is described by A. Meljon, while the in vivo consequence of cholesterol 24-hydroxylase inhibition in rat retina is described by C. Fourgeux. Conclusive identification of any oxysterol requires comparison to an authentic standard and M. Voisin describes the one step synthesis of 6-oxocholestan-3β,5α-diol for this purpose.

The final section of this special edition is devoted to oxysterols in food, phytosterols and oxyphytosterols, also known as phytos-

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terol oxidation products (POPs). Y. O'Callaghan reviews the recent literature on POPs highlighting that POPs are formed in food storage and preparation, while M. Rodriguez-Estrada discusses 7-ketocholesterol formation in food systems. Y. Kharrassi determines the sterol composition of argan oil and shows that two of the natural phytosterols present modulate the expression of LXRs in microglial BV2 cells. H.F. Schött measures POPs in plasma and cardiovascular tissue. Finally the contentious issue of plant sterols as food supplements is commented on by O. Weingärtner giving one side's view on the argument. The issue of food recommendations and possible use of phytosterols for health purposes is a sensitive subject with shifting opinions over time.

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