

Foreword

Lipid signalling: cellular events and their biophysical mechanisms

This Special Issue of FEBS Letters contains most of the contributions presented at the 'Workshop on Lipid Signalling: Cellular Events and their Biophysical Mechanisms', held at the Juan March Foundation (Madrid, Spain) on May 20–22, 2002.

The last decade has witnessed the discovery of a large number of lipid molecules that play specific roles in cell signaling. Ceramide, sphingosine phosphate, lysophosphatidic acid and others have joined the previously known phosphatidylinositol derivatives, diglyceride, phosphatidic acid, platelet activating factor and numerous eicosanoids in their roles as metabolic regulators. Thus, phospholipids and sphingolipids, in addition to their structural involvement in membranes, are now viewed as important reservoirs of lipid second messengers.

Current research in this field includes studies in at least three areas, namely cell biology, biochemistry and biophysics, but sometimes unfortunately without the desirable degree of interaction among them. From the point of view of cell physiology, lipid signals have been found to mediate an amazing variety of processes, from cell activation to apoptosis, including ion channel regulation, intracellular membrane trafficking and membrane adhesion. Simultaneously, metabolic studies of these substances have led to significant advances in understanding the mechanism and regulation of biosynthetic and degradative enzymes, notably phospholipases A2, C and D, sphingomyelinases and CTP:phosphocholine cytidyltransferase. Finally, recent biophysical studies have led to important discoveries as a result of solving the structure of some of the involved enzymes (e.g. PIP3 kinase, PI-phospholipase C), in the behavior of lipid signals in bilayers (e.g. ceramide segregation into domains and rafts), or in the regulation of important enzymes through membrane physical properties (e.g. PI-specific phospholipase C), that may provide the molecular foundation for an understanding of critical lipid-mediated cellular processes.

Moreover, the genomic revolution has been impressive and innovative for the biological sciences and as difficult as it was, it only had to deal with a finite number of genes, estimated to a range from 30 000–50 000 for humans. The proteomics revolution is now upon us, and the number of discrete proteins is enormous and certainly not finite. Proteins come in many forms: they are acylated, acetylated, phosphorylated, and ubiquitinated and exist as preproteins and proproteins, and

they can be altered in subtle manners by interaction with other proteins. The metabolomics revolution is next, but the number of distinct metabolites is astronomical. Even if one just thinks of the lipid metabolites, the number of unique structures is difficult to fathom. It is clear that the next decade will enlighten us with numerous novel and new lipids and will identify diverse new functions for them. Certainly the last decade has shifted the interest in lipids from just their traditional roles in energy storage and membrane structure to a more central role in all of cell signaling.

Our workshop focused on LIPIDS, both their biophysical and cellular aspects. Our hope was to share the parallel evolution of biophysical approaches to understanding the physical parameters of lipids and the structural parameters of the proteins that make or interact with them. Then, we hoped to integrate this information with our evolving knowledge of the cellular and physiological actions of a variety of lipids as they interact with cellular proteins and with other lipid assemblies. During the course of the workshop, we considered a vast array of proteins that degrade lipids, that transfer lipids, and that synthesize lipids and the cellular responses of activation, proliferation, differentiation, inflammation, and apoptosis. We heard the latest results from both the biophysical and the cellular directions and most importantly, the interplay of both. The papers that follow provide a view of the often separate sphingolipid and phospholipid fields that were brought together in the meeting. We all greatly benefited from excellent discussions that were fostered by the intimate atmosphere provided by the Juan March Foundation venue.

The Guest Editors (and workshop organizers) would like to dedicate this issue of FEBS Letters to Mr. Andrés González, Director of the Centre for International Meetings on Biology (Juan March Foundation), on the occasion of his retirement. Mr. González has been instrumental in developing the Juan March Centre for International Meetings on Biology into such an outstanding organization for convening truly international, broad, but intimate meetings on molecular and cell biology.

Edward A. Dennis
Isabel Varela-Nieto
Alicia Alonso
Guest Editors