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Preface

Preface to special issue on nanoscale membrane organisations



The plasma membrane limits, protects and defines cell identity, separating two aqueous compartments: the cytoplasm from the extracellular space. However, cells need to transport nutrients, ions and waste products across their plasma membrane and also need to communicate with other cells. Cells intercommunicate using membrane receptors which transmit signals to the cytoplasm upon binding to their extracellular ligands. The extracellular ligands are soluble molecules or proteins embedded in the plasma membrane of other cells. In this way, the plasma membrane has a double function: (i) as a barrier, constituted by a lipid bilayer, and (ii) as a communication platform, provided by protein receptors anchored to the lipid bilayer. The distribution and organisation of membrane receptors within the membrane is not irrelevant to their function, since receptors not only transmit outside-in information, a process coined as signal transduction, in the plane perpendicular to the plasma membrane, but can also influence each other in a horizontal manner, a process that can lead to cooperativity phenomena.

A first model of plasma membrane organisation was proposed in 1972 by Singer and Nicolson who proposed that transmembrane proteins and lipids are homogeneously distributed and freely diffusing. This is known as the fluid mosaic model [1]. The validity of the fluid mosaic model was already challenged in the 1970s by Stier and Sackmann who proposed that the different chemico-physical properties of the lipids in the plasma membrane would make them to self-organise in microdomains thus breaking the homogenous landscape of the fluid mosaic model [2]. The most prominent lipid microdomains are formed by cholesterol and sphingolipids, which self-associate forming a liquid-ordered phase (lipid raft), and separate from common phospholipids, which form a lipid-disordered phase. Consequent with this heterogeneous distribution of lipids Simons and Ikonen proposed that membrane proteins would also distribute non-homogeneously and would have to partition either to the raft or to the non-raft phases [3]. The idea that membrane proteins are non-randomly distributed in membranes was supported by immuno-gold labelling electron microscopy studies on the distribution of receptors for immunoglobulins in mast cells [4]. However, the study of the distribution of antigen receptors in B and T lymphocytes [5,6] led to the idea that membrane proteins of the same type tend to concentrate in small areas of the membrane, forming oligomers of different size before the receptors are exposed to their extracellular ligands. Many receptors are now known to form nanometre-sized oligomers known as nanoclusters before ligand binding [5–9]. The distribution of membrane receptors in self-assembled nanoclusters is consequent with the general distribution of membrane proteins detected by electron microscopy and that led to the formulation of the protein island model in distinction, but not in contrast to, the lipid raft model [10]. Protein islands containing specific receptor nanoclusters

seem to be organised by the resident membrane proteins themselves, the different membrane lipids and the underlying cytoskeleton [11].

In this special issue of BBA – Molecular Cell Research entitled “Nanoscale Membrane Organisation and Signalling” we discuss new developments in our understanding of how membrane proteins and lipids are organised in biomembranes, with a focus on the plasma membrane and proteins involved in signalling. The idea for this special issue originates from an international symposium on “Nanoscale Membrane Organisation” that was organised by the excellence cluster BIOS of the University of Freiburg from the 24th to 25th October 2013; <http://www.bioss.uni-freiburg.de/cms/3055.html>.

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Balbino Alarcón was born in Almeria, Spain, in 1960. He finished his Master's degree at the University Autònoma of Madrid in 1982 and obtained his PhD in Biology in 1985 at the same university. Since 2002 he is Professor of Research of the National Research Council of Spain (CSIC) at the Center for Molecular Biology "Severo Ochoa" where he has been performing his studies as an independent researcher since 1990. His studies have focused on the elucidation of the earliest molecular mechanisms for signal transduction by the T cell antigen receptor (TCR) and on the characterization of novel intracellular ligands of the TCR. This has driven him to two important molecules: the adaptor Nck and the Ras-family GTPase RRas2 (TC21). Recently he has gained interest for the development of new therapies and this

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Michael Reth studied Biology at the University of Cologne, Germany, and received his PhD in 1981 in Immunology and Genetics. After a postdoc at Columbia University, New York, and a group leader position at the University of Cologne, he was appointed associate professor at the Max Planck Institute for Immunobiology in Freiburg, Germany, in 1989. In 1996 he was appointed full professor at the University of Freiburg and since 2007 is the founding director of the BIOS Centre for Biological Signalling Studies. Michael Reth has received a number of prizes, including the Gottfried-Wilhelm-Leibniz Prize 1995, the Schering-Plough Prize 2009, an ERC Advanced Grant 2012 and the Paul Ehrlich and Ludwig Darmstaedter Prize 2014. Currently, he works on the Nanoscale analysis of protein islands on B lymphocytes.



Wolfgang W. Schamel studied Biochemistry at the Free University of Berlin, Germany, and finished with his Diploma thesis at the Weizmann Institute in Israel in 1995. He started to work on transmembrane receptors and their arrangement on the plasma membrane during his PhD thesis at the Max Planck Institute of Immunology in Freiburg, Germany under the supervision of Michael Reth. In his postdoctoral training at the Center of Molecular Biology Severo Ochoa, Madrid, he studied the T cell antigen receptor (TCR) and showed that the TCR is co-expressed as single receptors and nanoclustered complexes. In 2002 he returned to the Max Planck Institute of Immunology in Freiburg with his own Emmy Noether junior group and was the coordinator of the large European Union project SYBILLA. In 2010 he

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