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Editorial

Biophysics meets membrane-active peptides

Once a typical field for organic chemists, peptide science has long overcome this frontier and is expanding into new scientific and technological areas. The idea that membrane lipids may mediate receptor–ligand interactions, the emergence of new anti-microbial peptides, and the potential of cell-penetrating peptides for therapeutic applications have granted membrane-active peptides the attention of a large community of scientists. Among them, the biophysicists: people keen on a quantitative understanding of the physical principles that govern the interactions between peptides and lipids as well as peptide–peptide interactions in lipid environments at the molecular level. For a better control of variables and a deeper insight into these molecular events, model systems such as lipid vesicles are often used. A correlation with *in vivo* studies is often aimed, but the complexity involved in cell membranes makes this task quite hard and difficult to accomplish. To help each other through the challenges of the biophysics of membrane-active peptides, more than 120 researchers gathered in a workshop in Lisbon (Portugal) in spring 2007, inspired by a similar meeting in Berlin two years earlier. The participation of both predoctoral and senior researchers and people covering a wide range of techniques, from in silico to *in vivo*, helped formulate new problems and seek new solutions, thus improving the state of the art.

In this issue, methodical aspects, the structure and function of peptides exhibiting fusogenic, membrane-translocating or membrane-permeabilising behaviour, as well as their interaction with model membrane systems and their effects on a cellular level are presented. Among them, the reader will find integrative reviews as well as some of the best communications presented at the meeting.

With a new approach for the quantification of binding of flexible peptides and unstructured proteins to membranes, Teif *et al.* [1] provide an important contribution on how unstructured clusters of basic residues bind. The paper makes a novel advance in dealing with the corrections to the binding affinities arising from conformational constraints.

A molecular dynamics simulation of transmembrane helical fragments of the EGF receptor inserted into several lipid bilayers by Rog *et al.* [2] shows that peptide tilt and loss of helical structure could constitute a new type of response to lipid bilayer mismatch.

Two other papers by Hesselink *et al.* [3] and Duarte *et al.* [4] elucidate the structural properties of short peptides encompassing the seventh transmembrane fragment of V-ATPase and the relevance of the sequences for the function of the proton pump as potential drug target.

A methodical review by Domingues *et al.* [5] aims at introducing the reader to light-scattering techniques to monitor peptide-induced aggregation processes of lipid vesicles. The potential of steady-state fluorescence as a fast and inexpensive methodology to study protein–protein interactions in lipid membranes is reviewed by M. Ribeiro *et al.* [6], and P. Matos *et al.* [7], who present the application of potential-sensitive fluorescent probes to get insight into the mode of peptide action on biomembranes by monitoring surface, dipole, and transmembrane potentials.

On the basis of their prediction of and experimental approaches to different protein domains related to membrane insertion, Lins *et al.* [8] suggest that tilted peptides could have a general role in mediating insertion into and translocation of proteins across membranes.

With the prediction of the short peptides able to induce optimal *in vitro* fusion of SIV and HIV-2 isolates, Lorin *et al.* [9] introduce a method which could be used also to predict the minimal fusion peptide of other viruses.

NMR studies by Sarzedas *et al.* [10] in membrane-mimetic systems demonstrate that a small peptide (145–164) of the fusion-catalysing vesicular stomatitis virus (VSV), glycoprotein G, undergoes pH-dependent structural changes with a prevalence of β-structure at fusogenic pH, which is in accordance with the β-hairpin structure of the sequence in the full-length protein.

With conformational investigations of the fusogenic motif of the bindin-derived peptide B18, Rocha *et al.* [11] contribute to answering the question whether the α-helical or the β-sheet structure represents the fusogenic conformation.

With their molecular dynamics simulation studies of two HIV fusion-inhibiting peptides used in clinical trails, do Canto *et al.* [12] present an interesting contribution to our understanding of the ability of the compounds to be soluble in water and to interact efficiently with cell membranes.

Vieira *et al.* [13] report, in their clinically oriented study on possible side reactions at the cellular level, that the peptidic HIV-1 entrance inhibitor T-20 does not affect the functional properties of erythrocytes and lymphocytes.

The review by Lebleu [14] provides a comprehensive overview of the problems and promises using arginine-rich cell-penetrating peptides to improve the bioavailability of oligonucleotides.

Tae *et al.* [15] present an interaction study of the cell-penetrating TAT-peptide with planar phospholipid monolayers, using Langmuir–Blodgett techniques, Brewster angle microscopy (BAM), and X-ray reflectivity, which demonstrate deep penetration of the peptide into the hydrophobic region of zwitterionic lipids but surface adsorption at high negative surface charge densities.

Tünneman *et al.* [16] provide new information and corroborate earlier observations on the cell penetration ability and cytotoxicity of oligoarginine sequences.

Uptake studies by Chugh *et al.* [17] with the arginine-poor pVEC peptides and transportan into plant cells corroborate the applicability of the concept of cell-penetrating peptides to plant tissues.

Studies on the cell-penetrating peptide, pep1, showing a dependence of membrane-translocating ability or membrane-permeabilising activities on the local concentration at the membrane are reviewed by Heriques *et al.* [18].

In their study on members of the LAH4 family of cationic linear antibiotics, Marquette *et al.* [19] describe the pH-dependent aggregation of histidine-containing sequences to micellar structures that act on lipid bilayers in a detergent-like manner.

DallaSerra *et al.* [20] demonstrate that the antimicrobial lipodepsipeptides, Fuscopeptins form channels in both biological and model membranes.

Applying the methods of ellipsometry, laser scanning microscopy, and z-scan fluorescence correlation spectroscopy to monitor the effect of the anti-microbial peptides cryptdin-4 and magainin upon bilayers, Miszta *et al.* [21] find pronounced structure-dependent differences in the mode of action of the two peptides.

An investigation of the structure of the cationic peptide NK-2 at the air–liquid interface, complemented with conformational studies in aqueous solution and in membrane-mimetic environments, confirms a structural change and surface positioning which is known to be associated with anti-microbial activity [22].

Spectroscopic studies have been performed by Morgera *et al.* [23] to determine the role of β-sheet and α-helical structures of β-defensin peptides in their interaction with membranes and their anti-microbial effect.

NMR-spectroscopic studies by Appelt *et al.* [24] demonstrating different structures of cyclic arginine- and tryptophan-rich hexpapeptides with comparable activity provide a valuable contribution to future building-block approaches for the design of antibiotics.

With their structural and binding studies of antibacterial lycotoxin peptides identified in the venom of a spider, Adão *et al.* [25] aim at understanding the basis of activity and selectivity as one step in the development of lyxotoxin-based antibiotics.

Finally, activity studies with *E. coli* mutant strains were performed by Junkes *et al.* [26] to identify, at the cellular level, the interaction partners that are involved in the pronounced cyclisation-induced activity and selectivity increase of arginine- and tryptophan-rich hexapeptides.

As guest editors of this edition and organisers of the Lisbon workshop we would like to take the opportunity to thank all those who have contributed to organising the meeting and who provided generous support: The University of Lisbon, the Lisbon Science Museum, the Portuguese Society of Biochemistry, the Portuguese Biophysical Society, the Leibniz Institute of Molecular Pharmacology (Berlin), the European Peptide Society, the Biophysical Society (USA), IUPAB, IUBMB, Fundação Luso-Americana (Portugal), EBSA, FEBS, Polymer Laboratories, LOT Oriel Europe, Avanti Polar Lipids, Inc., NIMA Technology, Schering AG, Bachem and EZBiolab.

To continue the successful series of such specialised meetings focussed on peptide–membrane biophysics, the next workshop on 'Biophysics of Membrane-Active Peptides' is scheduled for 2009, to be organised by Prof. Anne Ulrich in Karlsruhe, Germany.

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Guest Editors

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