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EDITORIAL

Membrane Protein Folding & Lipid Interactions: Theory & Experiment

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The notion that membrane proteins play a crucial role in numerous aspects of cellular functioning (and dysfunctioning) is as popular as are the complaints that we do not know enough about their structure, assembly, and performance within the native environment of the lipid bilayer. Both of these ideas were at the forefront of the discussion that occurred at a recent Telluride Science Research Workshop, where a number of experimentalists and theoreticians got together to swap ideas about their research and to try and figure out the points of common interest, of complementary approaches and most of all, to attempt an identification and formulation of relevant questions and challenges. The ideas that are the fruit of this discussion, and that became enriched by numerous other contributors, are presented in this Special Issue of the *Journal of Membrane Biology*, entitled "Membrane Protein Folding & Lipid Interactions: Theory & Experiment."

A quick glance through the issue will immediately reflect one of the most dramatic advancements in the field over recent years, namely the full penetration of computational methodology into the field. The approaches range from micro-second atomistic simulations [1] to coarse-grained studies [2] and implicit modeling [3]. The scale of the processes under study also varied from determining the pathway of proton transfer in AHA2 proton pump [4] to the induction of bilayer curvature by surface-bound priscidin peptides [5]. The folding of transmembrane α-helices, which is of fundamental importance for membrane protein assembly, was studied in the context of both lipid bilayer [6] and translocon-like pores [7]. Several studies demonstrated how computational and experimental approaches can be integrated to gain insights into the mechanism of interfacial interactions of diphtheria toxin [8] and to validate spectroscopic tools for determining membrane penetration [9]. The significance of computational studies is further highlighted by two reviews, one specifically dedicated to describing molecular motions associated with the functioning of the voltage-sensing domains [10], while the other is dedicated to reviewing multiple applications of a novel membrane representation termed highly mobile membrane mimetic (HMMM), resulting in an efficient sampling of lipid–protein interactions at atomic resolution [11].

Several papers are dedicated to the membrane actions of antimicrobial and other host-defense peptides [1–3, 5], including modulation of membrane activity of novicidin by the phospholipid ether linkages [12]. Bacterial toxins—another traditional subject for exploring lipid–protein interaction—are represented by studies of pore assembly of perfringolysin O [13], thermodynamics of the insertion and refolding of diphtheria toxin translocation domain [14], and lipid nanodisc-based methodology to study inserted bacterial toxins [15]. Structural motifs involved in membrane pore formation by bacterial toxins are reviewed and compared to those involved in mitochondrial outer membrane permeabilization by Bcl-2 proteins during apoptosis [16]. And finally, the role of membrane proteins in pathogenesis is explored through studies of *Staphylococcus epidermidis* biofilms [17] and analysis of energetic consequences of pathogenic mutations in misfolding-prone α-helical membrane proteins, revealing important implications for future therapeutic design and personalized medicine [18]. These collected studies show the potential power of a joint

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computational and experimental focus on understanding problems of membranes and their associated membrane protein structure and function.

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