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EDITORIAL

Herve Duclohier · Yves Pichon

Ion channels: from biophysics to disorders

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Foreword

Biological membranes have been known for a long time to be permeable to ions and small molecules. This permeability reflects the function of specialized membrane proteins within the hydrophobic lipid bilayer. Some of these proteins, the ion channels, have received special attention, being responsible for the ionic currents underlying nerve and muscle excitability as first demonstrated by Hodgkin and Huxley (1952) for the squid giant axon. Since then, the nature of these ion channels and their mode of operation have been the object of intense research, and half of the 2003 Nobel Prize in chemistry was awarded to Roderick MacKinnon who unveiled, using X-ray crystallography, the 3D structure of a bacterial voltage-dependent potassium channel (Jiang et al, 2003). At the same time, an increasing number of reports have indicated that these same ion channels are involved in a variety of diseases called channelopathies. Furthermore, molecular biology has shown that the number of genes coding for ion channels is much higher than initially expected from electrophysiological recordings of the ionic currents, and the precise functions of the proteins encoded by these genes often remain to be discovered.

Whereas it is still possible to discuss these different aspects at specialized meetings, the need for a broader view of this constantly moving field was becoming apparent. In this context, we organized, with the help of the British and French Biophysical Societies, an informal meeting entitled: ''Ion Channels: from Biophysics to Disorders'', which was held in Rennes (France) in May 2003 [1].

This special issue of the *European Biophysics Journal* assembles the contributions of the participants who volunteered to take part in this follow-up of the meeting. Special care has been taken to present the results in a way that would be comprehensible by non-specialists.

The first set of papers deals with model channels. In his contribution on artificial porous systems, C.L. Bashford summarizes the results of his investigations on the role of surface charges as a basic determinant of the conductance, selectivity, and fluctuation of the conducting states of ion channels. L. Whitmore and B.A. Wallace illustrate how one can extract from the peptaibol database the salient features of these peptide molecules related to their propensity to form ion channels. The third paper of this set is by H. Duclohier and illustrates how the bending of the transmembrane helices formed by three peptaibol molecules (alamethicin, trichotoxin, and antiamoebin) is correlated with different patterns of activity as recorded electrophysiologically using planar lipid bilayers. In the last contribution of this set, P. Llanos, M. Henriquez, J. Minic, K. Elmorjani, D. Marion, G. Riquelme, J. Molgo, and E. Benoit indicate that wheat endosperm proteins form ion pores when incorporated into giant liposomes.

The second set of papers concerns emerging studies on the essential structural features of ion channels. In the first paper, D. Doyle summarizes some of the lessons or common structural themes that can be drawn after 5 years of crystallographic studies of ion channels, in particular from the inwardly rectifying bacterial potassium channel KirBac1.1. The second contribution, by J. Holyoake, C. Domene, J.N. Bright and M.S.P. Sansom, compares, using modelling and simulation studies, the

H. Duclohier (✉) · Y. Pichon
Interactions Cellulaires et Moleculaires,
UMR 6026 CNRS-Universite de Rennes I,
Batiment 13, Campus de Beaulieu, 35042 Rennes, France
E-mail: herve.duclohier@univ-rennes1.fr

H. Duclohier
Institut de Physiologie et Biologie Cellulaires,
UMR 6487, Pole Biologie-Sante,
40 Avenue du Recteur Pineau,
86022 Poitiers, France

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properties of KcsA, a pH-gated potassium channel, in the closed and open configurations. In the last paper of this set, P.T.F. Willamson, B.H. Meier and A. Watts review structural and functional studies of the nicotinic acetylcholine receptor using solid-state NMR.

One crucial question for the biologist is to understand how ion-channel genes are expressed in the cell, namely how transcriptional, pre-translational and post-translational mechanisms can result in subtypes and isoforms with unique functional signatures. These specific points are reviewed by J.K.J. Diss, S.P. Fraser, and M.B.A. Djamgoz in the case of voltage-gated Na^+ channels.

The next set of three papers illustrates the complexity of ion-channel function in cells and its links to the metabolism. Analysing the kinetics of the currents induced by Kv2.1 and HEAG channel genes injected into *Xenopus* oocytes, D. Wray shows that different parts of the intracellular domain of the proteins play an important role in the activation of these voltage-dependent channels. In the next contribution, J.C. Herve, I. Plaisance, J. Loncarek, F. Duthe, and D. Sarrouilhe investigate the role of phosphorylation on the junctional uncoupling in rat myocytes (i.e. on the permeability of the junctional channels made by connexin43). The next paper, by L. Liu, M.L. Roberts and A.R. Rittenhouse, is devoted to an electrophysiological study of the phospholipid metabolism required for the inhibition of N-type calcium channels of sympathetic neurons by oxotremorin, the classical agonist of muscarinic M1 receptors.

Some of the physiological roles of ion channels are highlighted in three papers. The first paper, by Y. Pichon, L. Prime, P. Benquet and F. Tiaho, deals with various aspects of the physiological role of ion channels in the nervous system with special emphasis on invertebrate nervous systems. In the second paper, L. Prime and Y. Pichon illustrate how a combination of ligand-gated ion channels supports the fictive swimming behaviour of *Xenopus* tadpoles. In the last paper of this series, J.M. Dubois and B. Rouzaire-Dubois discuss recent results suggesting that ion channels may have an important role in cell volume control.

The last contribution, by J.Y. LeGuennec, P. Besson, and S. Roger, concerns the properties of the sodium channels that have recently been shown to be present in breast cancer cells, as examined with the patch-clamp technique.

References

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