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Preface

Foreword to 2014 Aquaporins Special Issue

This special issue of BBA contains a fascinating collection of 16 short reviews on the aquaporin water channels. We must thank Susanna Törnroth-Horsefield from Lund University for identifying the topics and authors and succeeding in the very difficult task of guiding the assignments to completion. The 16 reviews include eight dealing with biochemical and biophysical aspects of aquaporin function and eight dealing with aquaporin function in whole organisms, including humans. Readers should be interested in both groups, as several reviews are interrelated.

These come at a time when major efforts by dozens of laboratories have advanced the water channel field from the physical phenomenon of osmotic water permeability to an advanced field with atomic resolution structures, biophysical analyses of pure proteins reconstituted into defined lipid bilayers, identification of mutant phenotypes, and even development of potential therapeutics. Coming ten years after a Nobel Prize, the reviews will remind the readers that although the field is advanced, it is still not complete.

This foreword provides an opportunity to revisit notable early work. I feel it is particularly fitting to acknowledge the 1970 report in this same journal (R.L. Macey and R.E.L. Farmer. Inhibition of water and solute permeability in human red cells. *Biochim Biophys Acta* 211: 104–106, 1970). By establishing that transport of water and transport of solutes can be pharmacologically disassociated with organomercurial sulfhydryl reagents, Macey and Farmer correctly predicted the existence of the membrane channel, now known as aquaporin-1 (AQP1).

Identification of the large aquaporin protein family followed, and aquaporins are believed to exist in all life forms. The aquaporin polypeptides contain two tandem repeats each comprised of three transmembrane spans and a functional motif, Asn-Pro-Ala (NPA). The genetic relationships among 1700 aquaporin sequences were compared (reviewed by Abascal et al.) showing marked conservation among orthologs. It should be noted that the identity of the ancient three transmembrane protein still remains a mystery.

Important roles of the multiple aquaporins in the kidney were soon recognized (reviewed by Kortenoeven and Fenton). Molecular understanding of the multiple physiological processes, such as constitutive and vasopressin-regulated renal concentration, now exists. Pathophysiological processes such as syndrome of inappropriate anti-diuretic hormone (SIADH) and nephrogenic diabetes insipidus are direct consequences of defects in AQP2 expression. Mechanisms of aquaporin regulation are analyzed (reviewed by Day et al.) and the identities of potential interaction partners are discussed (reviewed by Sjöhamn and Hedfalk).

The biology of aquaporins in the brain is of particularly large importance (reviewed by Badaut et al.). AQP4 in perivascular astroglial endfeet plays a pivotal role in maintaining the blood barrier. Moreover, AQP4 has been implicated in the pathogenesis of cerebral edema and epileptic seizures. The AQP4 surface antigen is apparently targeted by antibodies in plasma of patients with neuromyelitis optica and provides a new method for establishing the diagnosis. High-resolution electron crystallography has yielded an important explanation for how double-layer membranes are formed as found in glial lamellae surrounding vasopressin secretory neurons (reviewed by Tani and Fujiyoshi).

Aquaporins are also present in other normal tissues as well as pathological tissues. Multiple aquaporins play physiological roles in eye (reviewed by Schey et al.). Secretion and absorption of aqueous humor, secretion of tears, maintenance of lens and corneal transparency, and signal transduction in retina all involve aquaporins. Clinical defects are being actively investigated. Aquaporins provide normal physiological functions in salivary glands and pancreas, and AQP5 has been implicated in xerostomic conditions, pancreatic insufficiency and even diabetes (reviewed by Delporte). Studies of mutant mice connected mutations in the gene encoding AQP11 to polycystic changes in the kidney, and defects in the gene encoding AQP12 to severe pancreatitis (reviewed by Ishibashi et al.). Although not known to be the site of primary mutations, aquaporin expression is disordered in certain cancer specimens and may contribute to angiogenesis and tumor edema (reviewed by Ribatti et al.).

Helminthic and protozoan parasites each bear aquaporins. It is believed that they play interesting physiological and pathophysiological roles (reviewed by Song et al.). Parasitic aquaglyceroporins exhibit metalloid transport, explaining therapeutic benefits of antimonials and arsenicals (reviewed by Mukhopadhyay et al.). Relevant to host defense against pathogens, aquaporins facilitate transmembrane diffusion of hydrogen peroxide (reviewed by Bienert and Chaumont). *Saccharomyces cerevisiae* yeast contains two aquaporins that confer resistance to freezing and spore formation and a functional aquaglyceroporin required for osmoregulation (reviewed by Ahmadpour et al.).

Plants deploy aquaporins with the greatest degree of complexity, and most plant genomes contain at least 30 different genes encoding aquaporins. Aquaporin-mediated processes known in plants include hydraulic turgor, nutrient transport in roots and leaves, and germination of seeds (reviewed by Li et al.). Furthermore, while mammalian physiologists are still debating whether aquaporins transport carbon dioxide, it has been well established in plants where it drives photosynthesis (reviewed by Kaldenhoff et al.).

Much important information is presented in these 16 reviews, but we are still left seeking the answers to other questions relating to aquaporins. This special issue of BBA documents fascinating discoveries of aquaporins ranging from etiology of clinical disease to growth of food crops. Given the rapid pace of contemporary research, it seems safe to predict that additional aquaporin breakthroughs will continue to be made.

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1. Diversity and evolution of membrane intrinsic proteins. Abascal F, Irisarri I, Zardoya R.
2. Renal aquaporins and water balance disorders. Kortenoeven ML, Fenton RA.
3. Aquaglyceroporins: Generalized metalloid channels. Mukhopadhyay R, Bhattacharjee H, Rosen BP.
4. Unraveling aquaporin interaction partners. Sjöhamn J, Hedfalk K.
5. Plant aquaporins: Roles in plant physiology. Li G1, Santoni V1, Maurel C2.
6. The role of mammalian superaquaporins inside the cell. Ishibashi K, Tanaka Y, Morishita Y.
7. Aquaporins in the eye: Expression, function, and roles in ocular disease. Schey KL, Wang Z, L Wenke J, Qi Y.
8. Aquaporins and membrane diffusion of CO2 in living organisms. Kaldenhoff R, Kai L, Uehlein N.
9. Parasite aquaporins: Current developments in drug facilitation and resistance. Song J, Mak E, Wu B, Beitz E.
10. Water channel structures analysed by electron crystallography. Tani K, Fujiyoshi Y.
11. Human aquaporins: Regulators of transcellular water flow. Day RE, Kitchen P, Owen DS, Bland C, Marshall L, Conner AC, Bill RM, Conner MT.
12. Yeast reveals unexpected roles and regulatory features of aquaporins and aquaglyceroporins. Ahmadpour D, Geijer C, Tamás MJ, Lindkvist-Petersson K, Hohmann S.
13. Aquaporins in cancer. Ribatti D, Ranieri G, Annese T, Nico B.
14. Aquaporin-facilitated transmembrane diffusion of hydrogen peroxide. Bienert GP, Chaumont F.
15. Aquaporins in salivary glands and pancreas. Delporte C.
16. Aquaporin and brain diseases. Jerome Badaut,; Andrew M Fukuda; Amandine Jullienne; Klaus G Petry.

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