



Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.



ELSEVIER

Contents lists available at ScienceDirect

BBA - Biomembranes

journal homepage: www.elsevier.com/locate/bbamem

Preface

Transporters in acidic organelles

Eukaryotic endomembrane systems include synaptic vesicles, secretory granules, lysosomes, Golgi apparatus and plant vacuole that contain the proton-pumping V-ATPase. Solute carrier-type secondary transporters utilize the electrochemical proton gradient established by the V-ATPase to store or release metabolites and inorganic ions into/from these organelles, playing a key role in a wide variety of biological functions. For instance, vesicular neurotransmitter transporters are responsible for vesicular storage of small-molecule neurotransmitters and play an essential role in the chemical transmission between neurons. Exporters in lysosomes supply amino acids and sugars formed in the lumen by degradation of macromolecules internalized by endocytosis and phagocytosis or sequestered by autophagy. Recent findings revealed unexpected links between the function of these transporters and various physiological and pathological processes such as organellar biogenesis, signaling pathways and inflammation. For instance, the SLC38A9 protein, one of the lysosomal amino acid transporters, acts as an amino acid sensor for mTORC1, playing a fundamental role in coordinating anabolic and catabolic processes in response to growth factors and nutrients. *SLC45A2*-encoded membrane-associated transporter protein (MATP) is a membrane protein in melanosomes and its functional defect initiates melanogenesis through increase in melanosomal pH (see relevant chapters). Consequently, suppression or activation of endomembrane transporters may perturb homeostasis and produce various pathological states. Drugs or genetic manipulation that controls their transport functions can be expected to have therapeutic effects. Based on such ideas, transporter research has been accelerating since entering this century, including the identification of novel transporters, the characterization of 3D structures, the association of endomembrane transporters with higher-order functions, the development of inhibitors and activators, and diverse clinical applications.

This special issue aims to overview the progress on the studies of transporters from endomembrane organelles, in particular those from secretory vesicles and lysosomes/vacuoles. It comprises 10 chapters. In the first chapter, Michael Collins and Michael Forgac update the structure and physiological functions of the mammalian vacuolar ATPase, which powers all organelles covered in this special issue. Then, Jacob Eriksen, Fei Li and Robert Edwards discuss the transport mechanism of vesicular glutamate transporters in the light of recent electrophysiological data and a transporter paralogue structure. Very recently, the Edwards and Stroud groups have made further progress and obtained by cryo-electron microscopy a 3D structure model at 3.8 Å resolution of the rat vesicular glutamate transporter 2 [1]. Charles M.

Thompson and Chih-Kai Chao discuss the interaction between inhibitors and VGLUT at the molecular level and provide clues to the development of new inhibitors. The results are not only useful for the development of specific inhibitors of other members of the SLC17 family, but also have general applicability to other transporter families. Drs. Hasuzawa and Moriyama and their colleagues comprehensively describe the recent achievements of two vesicular neurotransmitter transporters, the vesicular nucleotide transporter (VNUT) and the vesicular polyamine transporter (VPAT), respectively, and discuss the physiological functions and diseases in which each transporter might be involved. MATE transporter is a secondary active transporter existing in plasma membrane and plant vacuolar membrane, but strictly speaking, it is not necessarily energetically coupled with V-ATPase. The characteristic of this transporter is super-multi-substrate recognition. Drs. Ishitani and Nureki review the recent progress on the structure of MATE transporters and discuss the mechanism of substrate recognition. In another chapter, Drs. Huizing and Gahl provide a comprehensive overview of the set of lysosomal diseases caused by defective membrane transport, from their discovery and clinical features to the most recent progresses in diagnosis and therapy. Dr. Nagamori and his colleagues provide a comprehensive review of the expression, function and regulation of transporters involved in melanogenesis. Dr. Krantz and Dr. Shitan and their colleagues provide overviews of the general features and recent progress on transporters from *Drosophila* synaptic vesicles and higher plant vacuoles, respectively. We are convinced that this special issue will be useful not only for researchers and students working in these fields but also for scientists and clinicians working in a wide variety of areas where endomembrane organelles play an important role. Unfortunately, we could not include more chapters such as a vesicular transporter in *Plasmodium falciparum* because unexpected difficulties, including the Covid 19 pandemic, occurred during the preparation of this special issue.

Finally, we would like to express our sincere thanks to the authors and the editorial staff of BBA Biomembrane for their cooperation in publishing this special issue. Professor Howard Ronald Kaback at UCLA, who was a great leader of the transporter research, passed away on December 20, last year. We would like to express our respect and gratitude for his great contributions to transporter research.

Declaration of Competing Interest

The authors declare that they have no known competing financial

<https://doi.org/10.1016/j.bbamem.2020.183458>

Available online 27 August 2020

0005-2736/ © 2020 Elsevier B.V. All rights reserved.

interests or personal relationships that could have appeared to influence the work reported in this paper.

References

- [1] F. Li, J. Eriksen, J. Finer-Moore, R. Chang, P. Nguyen, A. Bowen, A. Myasnikov, Z. Yu, View D. Bulkley, Y. Cheng, R.H. Edwards, R.M. Stroud, Ion transport and regulation in a synaptic vesicle glutamate transporter, *Science* 368 (2020) 893–897, <https://doi.org/10.1126/science.aba9202>.

Yoshinori Moriyama^{a,*}, Bruno Gasnier^{b,*}

^a *Division of Endocrinology and Metabolism, Department of Internal Medicine, Kurume University Medical School, Japan*

^b *Université de Paris, SPPIN - Saints-Pères Paris Institute for the Neurosciences, Centre National de Recherche Scientifique, Unité Mixte de Recherche 8003, F-75006 Paris, France*

E-mail addresses:

yoshinori.moriyama@med.kurume-u.ac.jp (Y. Moriyama),
bruno.gasnier@parisdescartes.fr (B. Gasnier).

* Corresponding authors.