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Editorial note

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Mitochondria are the most functionally diverse of cellular organelles. They coordinate cellular metabolism, bioenergetics, and an escalating list of signaling pathways associated with life and death decisions. This functional diversity relies on ion channels and transporters across the mitochondrial membranes, which mediate exchange of a long list of signaling molecules. The list includes metabolites, ions, lipids, nucleic acids, and even proteins.

This special issue on ion channels and transporters is in celebration of the life and career of one of the pioneers in the field: Kathleen (Casey) Kinnally. For anyone who was or is interested in mitochondrial ion channel recordings, Casey Kinnally is a giant among giants. She and a few others founded the field, but it is really Casey who has developed the field into the accepted body of work that exists today. Not only has she meticulously honed the techniques, but also she made us aware of the very existence of mitochondrial ion channels. She described many mitochondrial ion channels whose biophysical characteristics were not even imagined. She made us look at mitochondria in a new light; not just as the powerhouses of the cell, producing energy for cell processes, but as electrical beings, transferring ions across their membranes for purposes even now only partially uncovered. The findings seem as if they might only live in the fantasy world of our imaginings, but they are real: channels small enough to regulate levels of individual ions within organelle compartments; channels wide enough to transport proteins into the mitochondria; channels whose opening lead to cell demise. In case there is any remaining skepticism regarding their importance, the channels Casey described are now being found to regulate ischemic preconditioning, metabolic efficiency and cell growth, neurodegeneration, even, we think, memory formation in the mammalian brain.

Opening the issue, Starkov and collaborators present evidence of a putative new mitochondrial inner membrane channel regulated by magnesium (Starkov et al. 2016). The evidence waits to be corroborated by direct path clamping, and such was the case for a number of channel activities initially hinted and later identified by Casey and her collaborators. One of these channels was mPTP, whose initial discovery in the 70's was corroborated independently by Casey and Mario Zoratti almost two decades later. Advances in the molecular identification of mPTP needed yet another two decades. Mnatsakanyan and collaborators discussed these advances, highlighting the importance of the F_1F_0 ATP synthase c-subunit and a proposed uncoupling function that may impact cardiac development and synaptic efficacy (Mnatsakanyan et al. 2016). Studies of PTP regulation were extensive and predated its molecular identification, again, by decades. However, that is not to say we know everything. Hurst, Hoek, and Sheu reviewed the pathways for mitochondrial trafficking of calcium, highlighting its role in regulation of PTP (Hurst et al. 2016). Through the use of classical mitochondrial swelling assays, Baev, Negoda, and Abramov presented intriguing evidence that inorganic polyphosphates can induce PTP without addition of calcium (Baev et al. 2016). The authors propose that cytoplasmic polyP can be an

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Casey Kinnally and some of her previous post docs, from left to right, Evgeny Pavlov, Laurent Dejean, Sonia Martinez-Caballero, Liang Guo, and Pablo Peixoto at the 1st Symposium on Mitochondrial Ion Channels and Transporters

important contributor towards regulation of mitochondrial permeability transition and cell death. Other permeability pathways in the mitochondrial outer membrane are associated with cell death regulation, among which there is one formed by the lipid ceramide (here reviewed by the pioneer in its discovery, Marco Columbini) (Colombini 2016). The Mitochondrial Apoptosis-Induced Channel (MAC), discovered by Casey's group in 2001, forms a better-known pathway for cell death signals across the outer membrane. Peixoto and collaborators presented their findings on the mechanisms of action of small molecule inhibitors of MAC (Peixoto et al. 2015). A review by Martinez-Caballero describes import pathways important for biogenesis of mitochondrial proteins and the emerging pathways of DNA and RNA import (Campo et al. 2016), while McStay reviews the mechanisms of turnover of such channels and transporters (McStay 2016). Finally, Elustondo and colleagues reviewed the mechanisms of mitochondrial calcium uptake (Elustondo et al. 2016).

We thank all the contributors to this issue and everyone who attended the 1st Symposium on Mitochondrial Ion Channels and Transporters. We are indebted to Chief Editor, Dr. Daniel M. Raben, and the production team at JOBB. Casey now enjoys a sunny life in California, surrounded by her beloved family and grandkids.

The editors.

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