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EDITORIAL

Mitochondrial signalling, physiology and pathophysiology

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This issue contains five invited papers focused on the role of mitochondrial signalling in physiology and pathophysiology. Over the last 30 years many aspects of mitochondrial signalling, in particular Ca^{2+} signalling, have been elucidated. The contributions of these signalling mechanisms to the stimulus-metabolism coupling (i.e. their relevance to cell physiology) and to initiation of mitochondrial damage and cell death (i.e. their relevance to pathophysiology) have been substantially advanced. The last decade witnessed vigorous development of this research area. The reason for this was the discovery of the molecular identity of the mitochondrial Ca^{2+} uniporter (MCU) by the R. Rizzuto and V. Mootha research groups. This, in conjunction with the characterisation of other proteins (including MICU1, MICU2 and EMRE) regulating mitochondrial Ca^{2+} transport and forming a functionally efficient complex with MCU, provided researchers with the opportunity to test the importance of these mechanisms for a plethora of physiological responses and pathologically relevant conditions. The recent advancement of this research area is reviewed in this issue by C. Mammucari and colleagues. This authoritative review from the leading laboratory in this research field will be useful for scientists with interests in bioenergetics and mitochondrial physiology/pathophysiology.

Starting from the seminal studies of Otto Warburg, the association of pathophysiological development with the changes of cellular bioenergetics received considerable attention from cancer biologists, and "deregulation of cellular energetics" is now considered as one of the emerging hallmarks/enabling characteristics of cancer (reviewed in [1]). The discovery of the molecular components of the MCU complex allowed direct probing of the role of this mechanism in cancer biology. This important and rapidly developing subfield of mitochondrial pathophysiology is reviewed in this issue by A. Vultur and colleagues from the I. Bogeski laboratory. Novel and rapidly developing research areas are usually prone to contradictions and early synthesis, as provided by this review, will be beneficial to scientists interested in the interplay between cancer and bioenergetics.

The development of novel optical probes (based on fluorescent or bioluminescent proteins) stimulated studies into the interaction between the second messenger cascades. This subfield recently delivered a number of elegant studies defining the interaction between the cAMP and Ca^{2+} signalling cascades, including the discovery of SOcAMPS [2], the identification of direct interaction between adenylyl cyclase 8 and Orai1 channel [5]. In this issue, the mitochondrial cAMP production and a novel mechanism of the interaction between mitochondrial cAMP and Ca^{2+} signalling are discussed in the review by A. Spät and G. Szanda.

The recent advances in super-resolution microscopy provided opportunities to examine structure-function relationships and dynamics of mitochondria in live cells. An elegant example of the application of super-resolution microscopy (in this case of structured illumination microscopy) for the studies of mitochondrial cristae dynamics and junctions between the mitochondria and the endoplasmic reticulum is described in the invited experimental paper by B. Gottschalk and colleagues from the W. Graier laboratory. Notably, the paper describes interesting relationships between Ca^{2+} signals, OPA1, and the dynamics of mitochondrial cristae.

Studies of junctions between cellular organelles and signalling mechanisms operating in these junctions form one of the most dynamic and rapidly expanding research areas in modern cell biology (reviewed in [3]). Mitochondria are involved in the formation of junctions with a number of cellular organelles (including peroxisomes, lipid droplets, lysosomes/endosomes and the plasma membrane) but the ER is certainly one of their preferred junctional partners (e.g. [4] reviewed in [3]). The junctions between the mitochondria and the ER and signalling mechanisms operating in these junctions (particularly Ca^{2+} and ROS signalling) are the subject of the last review in this group of papers focused on mitochondrial signalling.

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