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COMMENTARY

Contribution to mitochondrial research in Brazil: 10th anniversary of the mitomeeting

Anibal E. Vercesi[1]* and Helena C.F. Oliveira[2]*

1 Faculty of Medical Sciences, State University of Campinas, 13083-970, Campinas, SP, Brazil
2 Biology Institute, State University of Campinas, 13083-970, Campinas, SP, Brazil

Abstract

This commentary introduces the subject, the context and the history of the Brazilian annually held meeting on Mitochondrial Research by the occasion of its 10th anniversary. Mitomeetings gather people interested in all aspects of mitochondrial biology in diverse species, including protists, animals, plants, and fungi.

Keywords: mitochondria; mitomeeting; mitochondrial research

This issue comprises communications, articles and mini-reviews authored by speakers of the 10th Mitomeeting, held in Guapé, MG (Brazil), April 27–30, 2017. Mitomeetings gather people interested in all aspects of mitochondrial biology in diverse species, including protists, animals, plants, and fungi.

The role of mitochondria is currently recognized as involving far more than ATP synthesis. These organelles are considered the fundamental regulators of cell survival and death. 50 years ago, mitochondria were thought to be the site of some metabolic pathways (citric acid cycle, fatty acid beta oxidation, and amino acids oxidation), oxidative phosphorylation and non-shivering thermogenesis; the latter limited exclusively to the brown adipose tissue. In the 1960s, the Nobel prize Peter Mitchell introduced the concept of coupling between respiration and phosphorylation through a transmembrane proton electrochemical potential (Mitchell, 1961). This potential is generated by the pumping of protons across the inner mitochondrial membrane while electrons flow through the respiratory chain. Proton pumping makes the matrix alkaline and negatively charged relative to the intermembrane space and provides energy for ATP synthesis by the ATP synthase. Increases in inner membrane permeability to protons disrupt the proton electrochemical potential and may be a key event in processes of mitochondrial pathophysiology.

In the 90's, the discovery of mitochondrial uncoupling proteins in plants changed completely the understanding of the function and evolutionary acquisition of these mitochondrial proteins (Vercesi et al., 1995). Further studies demonstrated that these proteins are, in fact, widely distributed in eukaryotic organisms and have functions other than thermogenesis, such as regulation of cellular redox signaling (Vercesi et al., 2006).

Progress in mitochondrial research has shown that mitochondria are versatile and dynamic organelles that can undergo fusion, fission, biogenesis and autophagic elimination to maintain mitochondrial network quality control in response to various cellular signals (Suárez-Rivero et al., 2016). One important breakthrough in the field of Mitochondrial Research was the delineation of how mitochondrial dynamics is linked to bioenergetics and signaling functions of the organelle. In general, fusion leads to increased respiration efficiency and resistance to stress-induced dysfunction while mitochondrial fission does the contrary (Wang et al., 2017).

Mitochondria participate in a multitude of essential cellular functions that depend on the production of ATP and reactive oxygen species (ROS). ATP is required to drive most cellular processes, while ROS can serve as important signaling molecules (Mailloux et al., 2014). Moreover, they contain their own genome, a 16.5 kb circular DNA molecule that encodes 13 peptides components of 4 of the 5 OXPHOS complexes (Anderson et al., 1981). Mutations in the mitochondrial DNA cause several human syndromes and accumulate during normal aging and in several complex

*Corresponding author: e-mail: anibal@unicamp.br (A.E.V.) and oliveira: ho98@unicamp.br (H.C.F)

diseases of great relevance in public health such as cancer, diabetes and neurodegeneration (Wallace, 2015). Mitochondrial dysfunction leads to a wide range of diseases and, in some cases, the diseases cause mitochondrial dysfunctions. Several different respiratory chain sites have the capacity to leak electrons to molecular oxygen and generate ROS. In addition, mitochondria also possess a cell death-regulatory machinery that includes highly regulated processes such as Ca^{2+} transporting systems and the membrane permeability transition pore (mPTP) (Figueira et al., 2013). The latter is regulated synergistically by mitochondrial ROS and Ca^{2+} levels. High levels of matrix Ca^{2+} stimulate ROS generation and mPTP opening, a key event in the mitochondrial cell death pathway, by both necrosis and apoptosis. A large body of evidence indicates that dysregulation of mitochondrial Ca^{2+} uptake and ROS production are responsible for the development and progression of many diseases such as cancer, cardiovascular, metabolic, and neurodegenerative diseases, and drug toxicity. Furthermore, unraveling the mechanisms underlying the regulation of mPTP may open new avenues to better understand longevity (Rottenberg and Hoek, 2017).

Another milestone in Mitochondrial Research was the identification of the mitochondrial calcium uniporter (MCU). The biochemical and functional existence of this channel was recognized for more than 50 years (De Luca and Engstrom, 1961), including its absence in fungi (Carafoli et al., 1970) and presence in trypanosomatids (Docampo and Vercesi, 1989). This latter knowledge was essential for the discovery of the molecular identity of the MCU in mammals. By comparing the mitoproteomes of mammals, fungi and trypanosomes, Perocchi et al. (2010) pinpointed the protein and then the gene, after which, through genetic engineering, the biological roles of this channel were revealed (Huang et al., 2013; Mammucari et al 2017).

Mitochondrial research has grown exponentially around the world as of the 1990's (Figure 1A). In Brazil, the same trend is observed from the year 2000 on (Figures 1C and 1D). Interestingly, Brazil occupies the 12th position in the word mitochondrial research bibliography (2.3%) (Figure 1B). The Brazilian bibliography citation profile also grows exponentially and shows an index of about 20 citations per item in recent years (Figure 1D). In the context of this positive scenario, a group of Brazilian scientists created a local annual meeting to discuss any mitochondria-related research topic, the Mitomeeting.

The first Mitomeeting, held in 2008, was organized by scientists from the Federal University of Rio de Janeiro (UFRJ), led by Pedro L. Oliveira and Marcus F. Oliveira, and a group from the State University of Campinas (Unicamp), led by Anibal E. Vercesi. This first meeting's format was very informal and had 21 participants. After 3 days of enthusiastic scientific discussions, the participants decided to keep an annual meeting to stimulate the interaction of senior and young investigators and thus create a Brazilian school for mitochondrial research. The name "Mitomeeting" was suggested by Milane de Souza Leite (Federal Rural University of Rio de Janeiro, UFRRJ), inspired by another

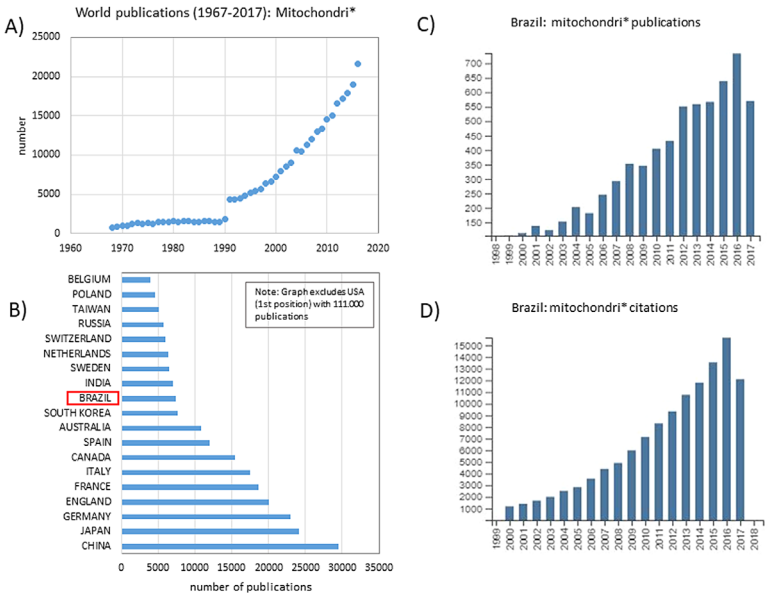


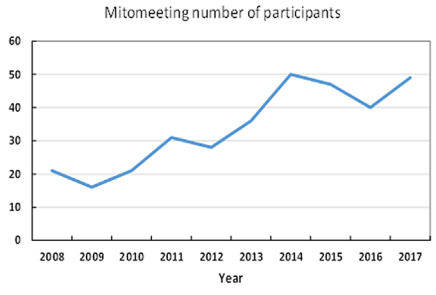
Figure 1 Results from Web of Science searches with the subject "Mitochondri*" over the last 50 years (1967–2017), categorized by year (A) and country (top 20) (B), and "Mitocondri* AND address: Brazil" by number of publications (C) and citations (D).

Table 1 Mitomeeting opening lectures: "Leopoldo DeMeis Conference"

Year	Invited speaker	Leopoldo DeMeis conference
2009	Francis Sluse, Université de Liege	UCP and UCP-homologues in Plants, Mammals and Protists: all under the same regulatory control
2010	Anibal E. Vercesi, University of Campinas	Evolution of the oxidative systems, coupling-uncoupling of respiration and oxidative phosphorylation, and Ca^{2+} transport
2011	Francis Sluse, Université de Liege	Mitoproteome of genetically hypertriglyceridemic mice
2012	Rafael Radi, Universidad de la República	Mitochondrial nitroxidative stress: opportunities for mitochondrial-targeted redox-based pharmacology
2013	Hatsubaro Masuda, Federal University of Rio de Janeiro	Sarcoplasmic reticulum ATPase: focus on enzyme phosphorylation by inorganic phosphate in the absence of calcium gradient
2014	Paulo Arruda, University of Campinas	A genetic view of life
2014	Hugo Aguilaniu, École Normale Supérieure de Lyon	Linking reproduction to diet-restriction-induced longevity in C. elegans
2015	Lício A. Velloso, University of Campinas	The control of body adiposity – mitochondria and beyond
2016	Iolanda M. Cuccovia, University of São Paulo	PUMP (plant uncoupling protein): The origin
2017	Maurício S. Baptista, University of São Paulo	Light modulates the mitochondrial-lysosomal axis

successful Brazilian scientific meeting of specialists in the field of arthropods and helminths, the "Arthromint." A few rules were incorporated over time, such as that all participants should present a 10- or 20-min talk, and that English should be the official language. The place was fixed in a well-preserved rural area of Guapé County, in the Brazilian State of Minas Gerais. Guapé is surrounded by beautiful touristic places including the Furnas Lake, Paredão Water Falls, Escarpas do Lago, and many local water fountains and streams. During the meeting breaks, it is possible to take a walk and watch birds, squirrel monkeys and eventually other wild animals. The nearby farm cattle yard is a must-visit to watch the milking of cows.

From the second meeting on, an opening lecture by a recognized specialist was established (Table 1). Since 2014, this opening lecture is named "Leopoldo DeMeis" in recognition of his valuable contribution to Biochemistry Research and Education in Brazil. The titles of these lectures provide a flavor of the variety of topics discussed every year (Table 1). The meeting has been held annually and the number of participants expanded from around 20 to about 50 in these 10 years (Figure 2), two thirds of them undergraduate and graduate students and post-docs. The Organizing Committee has been composed by José Roberto Meyer-Fernandes and Antonio Galina from UFRJ, Anibal E Vercesi, Leonardo R Silveira and Helena C F Oliveira from Unicamp, and Alicia Kowaltowski and Nadja Souza Pinto from the University of São Paulo (USP). From 2012 on, the Mitomeetings received the support of the Brazilian Society for Biochemistry and Molecular Biology (SBBq) through the contribution of the executive secretary Cynthia Bando in the Organizing Committee. The core Institutions responsible for the Mitomeetings are UFRJ, Unicamp and USP. However, along these years, members of many other national (including the south and northeast regions of Brazil) and international institutions have participated in Mitomeetings (Figure 2). Every year, at least one foreigner invited investigator participates. The Principal Investigators use their research



Institutions participants of the Mitomeetings (2008 - 2017)	
National Institutions	**International Institutions**
Fiocruz - Rio de Janeiro, RJ	Agilent Technology , USA
Instituto Ludwig - S. Paulo, SP	École Normale Supérieure de Lyon, France
Instituto Sírio-Libanês - S. Paulo, SP	Georgia University, USA
UENF - Campos dos Goytacazes, RJ	Harvard University, USA
UFAL - Maceió, AL	Michigan University, USA
UFCA - Cariri, Juazeiro do Norte, CE	Universidad de la República, Uruguay
UFMG - Belo Horizonte, Ouro Preto, MG	Université de Liege, Belgium
UFPE - Recife, PE	Université Laval, Canada
UFRGS - Porto Alegre, RS	University of Edinburgh, UK
UFRJ - Rio de Janeiro, RJ	
UFRRJ (Rural) - Rio de janeiro, RJ	
UFSC - Florianópolis, SC	
UFSCar - S. Carlos, SP	
Unesp - Botucatu, SP	
UNICAMP - Campinas, SP	
USP - S. Paulo, Ribeirão Preto, SP	

Figure 2 Number of participants and Institutions in Mitomeetings from 2008 to 2017.

grants (mainly from Brazilian research agencies Fapesp, Faperj and CNPq) to cover the meeting expenses. This has been the beginning of what we expect to be a successful advanced school for mitochondrial research in Brazil.

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