Seminar

Between energy conservation and energy dissipation: The dual life of mitochondrial ATP synthase

Speaker: Professor Paolo Bernardi

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Date and Time: Tuesday, November 29, 2016, 3:00 PM

Place: 1F Lecture Hall, Institute for Protein Research

Paolo Bernardi 教授は，ミトコンドリアのエネルギー変換・膜透過が専門の著名な研究者です.
European Bioenergetics Conference (EBEC2016)の Chair を務められました.
学会用務での来日の機会に，阪大でセミナーをして頂きます.
ふるってご参加頂けますようお願い致します.

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F_OF_1 ATP synthases convert the energy of a transmembrane H^+ gradient into ATP with remarkable efficiency [1]. We have recently discovered that in the presence of Ca^{2+} F_OF_1 ATP synthases can also form channels with the properties expected of the mitochondrial "permeability transition pore" (PTP, also called mitochondrial megachannel, MMC) in mammals [2], yeast [3] and drosophila [4]. Ca^{2+}-dependent PTP opening causes a large increase of permeability of the inner mitochondrial membrane, which has long been known to dissipate ion gradients and to cause detrimental effects on mitochondrial and cell function [5]. The molecular nature of the PTP had long been a mistery, as each of its candidate components (i.e. adenine nucleotide translocase, voltage-dependent anion channel, Pi carrier and peripheral benzodiazepine receptor) has been unequivocally ruled out by targeted gene deletion [5]. Our results show that channel activity can be seen in reconstituted systems with highly purified F_OF_1 ATP synthases, indicating that channel formation must occur within the enzyme complex. I will provide a brief account on the history of the permeability transition and present our recent results on the mechanism of channel formation as studied by site directed mutagenesis of key regulatory residues of F_OF_1 ATP synthases.

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2. Giorgio V, von Stockum S, Antoniel M, Fabbro A, Fogolari F, Forte M, Glick GD, Petronilli V, Zoratti M, Szabó I, Lippe G & Bernardi P (2013) Dimers of mitochondrial ATP synthase form the permeability transition pore. *Proc Natl Acad Sci U S A* **110,** 5887-5892.
3. Carraro M, Giorgio V, Šileikyte J, Sartori G, Forte M, Lippe G, Zoratti M, Szabó I & Bernardi P (2014) Channel Formation by Yeast F-ATP Synthase and the Role of Dimerization in the Mitochondrial Permeability Transition. *J Biol Chem* **289,** 15980-15985.
4. von Stockum S, Giorgio V, Trevisan E, Lippe G, Glick GD, Forte MA, Da-Rè C, Checchetto V, Mazzotta G, Costa R, Szabò I & Bernardi P (2015) F-ATPase of *D. melanogaster* Forms 53 Picosiemen (53-pS) Channels Responsible for Mitochondrial Ca^{2+}-induced Ca^{2+} Release. *J Biol Chem* **290,** 4537-4544.
5. Bernardi P, Rasola A, Forte M & Lippe G (2015) The Mitochondrial Permeability Transition Pore: Channel Formation by F-ATP Synthase, Integration in Signal Transduction, and Role in Pathophysiology. *Physiol Rev* **95,** 1111-1155.