第495回 難研セミナー
第68回 難治疾患共同研究拠点セミナー

下記により難研セミナーを開催しますので、多数御来聴下さい。

記

日　時：　H25年3月21日（木）17 :00 ～19 :00

場　所：　M&Dタワー2F　共用講義室1

演　者：　Prof. Paolo Bernardi

(University of Padova, Italy)

演　題：　The mitochondrial permeability transition pore: A mystery solved?

要　旨：

The molecular nature of the mitochondrial permeability transition pore (PTP), a key effector of cell death, remains undefined. The PTP is regulated by matrix cyclophilin (CyP) D, which also binds the lateral stalk of the F_OF_1 ATP synthase. I will show that CyPD binds the OSCP subunit of the enzyme at the same site as the ATP synthase inhibitor benzodiazepine (Bz) 423; that Bz-423 sensitizes the PTP to Ca^{2+} like CyPD itself; and that decreasing OSCP expression by RNA interference increases the sensitivity of the PTP to Ca^{2+}. Purified dimers of the ATP synthase, which did not contain VDAC or adenine nucleotide translocator, were reconstituted into lipid bilayers. In the presence of Ca^{2+}, addition of Bz-423 triggered opening of a channel whose currents were typical of the mitochondrial megachannel, the PTP electrophysiological equivalent. Channel openings were inhibited by the ATP synthase inhibitor AMP-PNP (γ-imino ATP, a non hydrolyzable ATP analog) and by Mg^{2+}/ADP. The demonstration that the PTP forms from dimers of the F_OF_1 ATP synthase solves a long-lasting issue in cell biology and readily accommodates key pathophysiological effectors of the permeability transition. Our findings suggest a dual function for complex V, ATP synthesis and PTP formation. The enzyme of life appears therefore to also be the molecular switch that signals the presence of fully depolarized, dysfunctional mitochondria to stimulate cell death and/or mitophagy.

連絡先：　病態細胞生物学分野　清水　重臣（内線 4797）

共　催：　発生再生生物学分野　仁科　博史（内線 4658）