東京大学 グローバル COE 特別セミナー

東京大学大学院 理学系研究科 生物化学専攻

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演題： Role and function of the scaffolding protein ENH1, a PDZ-LIM protein, in the heart

日時：平成 22 年 12 月 16 日（木）14:00ー15:00

場所：東京大学理学部 3 号館 3F 303 号室

Proteins called PDZ-LIM proteins are characterized by the combination of two interaction modules, a PDZ domain (named for proteins PSD-95, DLG, ZO-1) and one to three LIM domains (named for the proteins LIN-1, Isl-1, MEC-3). PDZ-LIM proteins are important scaffolding proteins connecting cytoskeletal structures to signaling proteins, transcription factors or ion channels. The PDZ-LIM proteins are important for the heart development, immune response, and prevention of cancer.
ENH1 (PDLIM5) is a PDZ-LIM protein mainly expressed in the brain and in the heart. ENH1 binds PKCβ through its LIM domains. The PDZ domain of ENH1 binds to cytoskeletal proteins, actin and α-actinin. ENH gene encodes for at least four splice variants ENH1 is the only variants with one PDZ and three LIM domains. The other variants, ENH2, ENH3 and ENH4, lack any LIM domains. Recently, we found that ENH1 promotes cardiomyocytes hypertrophy. Interestingly, the LIM-deficient splice variant ENH4 has the opposite effect: ENH4 prevents cardiomyocytes hypertrophy. Thus, ENH splice variants have opposite roles in the heart. Our results suggest that ENH1 favors cardiac hypertrophy whereas LIM-deficient splice-variants prevent cardiac hypertrophy.
We have identified ENH1 as a binding partner of the Protein Kinase D (PKD) in cardiomyocytes. PKD is an essential kinase in the development of cardiac hypertrophy.
In addition, we found that ENH1 anchors PKD to CaV1.2, the pore subunit of the L-type calcium channel in cardiomyocytes. We have shown that both ENH1 and PKD are essential for the regulation of the cardiac L-type calcium channel upon stress stimulation. Therefore, ENH1 may play a central role in the adaptive changes during heart hypertrophy linking stress-sensing and signaling.

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