グローバルCOE特別セミナー

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演題：Shape matters: Ultrastructural analysis of Purkinje cell spines reveals a specific and highly asymmetrical organization, with significant influence on molecular signal integration.

日時：平成 20 年 6 月 4 日（水）
13 時 30 分～14 時 30 分

場所：東京大学医学部教育研究棟 13 階 第 6 セミナー室

概要：As the molecular mechanisms of synaptic plasticity are slowly revealed, it becomes increasingly obvious that what happens and where it happens cannot be dissociated. In this respect, the synaptic spine represents a highly adapted structure for cellular signaling because its constricted neck acts as a barrier to diffusion of cytoplasmic proteins and second messengers. In addition, the convoluted space inside the spine may create micro-domains with high density of reacting molecules, potentially influencing the speed of intermolecular reactions. We used three-dimensional reconstruction of electron micrograph from serially sectioned Purkinje cell dendrites and electron tomography to analyze the subcellular morphological features of the spine, at synapse between PC and parallel fibers. Specifically, we measured the shape and relative position in the spine of the post-synaptic density, the spine apparatus (smooth ER protruding into the spine) and the organelles that may impede molecular diffusion in the spine and dendritic shaft. This analysis showed that the PSD is systematically located on the side of the spine head rather than at the apex, irrespective of the spine shape and incidence angle of the parallel fiber. The morphology of the spine apparatus appeared to be optimized to maximize its surface facing the PSD and facilitate signal transduction. Similar evaluation in rat mutant devoid of spine apparatus demonstrated that this structure plays a central role as organizer of

spine morphology. The functional consequence of this specific cytoarchitecture on molecular signaling was evaluated using realistic reaction-diffusion models of Inositol-3-Phosphate signaling in reconstructed and synthetic spine morphologies. Our results suggest that in addition to receptor/enzyme distribution and kinetic, the relative position of spine apparatus and PSD has drastic consequences on the efficacy of molecular signal transmission within the spine and may thus directly affect induction of synaptic plasticity. This study suggests that the morphological organization of the PC-PF synapse has a profound influence on signaling and also provide a precise description of the various substructures for use in molecular-level simulation.