3SDA-01 動物の発生における PAR/aPKC 細胞極性システムの計測に基づいた数理モデル化**Measurement-based mathematical modeling of PAR/aPKC-dependent cell polarization in animal development**

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Asymmetric protein localization functions as a source of positional information in cells and embryos during animal development. However, quantitative aspects-how molecular reactions control protein dynamics for pattern formation remains largely unexplored. We succeeded in detecting single molecules of polarity protein PAR-2 in living *C. elegans* embryos. The dissociation and association rate constants of PAR-2 proteins with the cell cortex were changed along the anterior-posterior axis. A mathematical model, in which all parameter values were determined by *in vivo* measurements, reproduced the asymmetric localization. In this study, we demonstrated that bi-stable polarity system is maintained by phosphorylation and oligomerization of PAR-2 proteins in *C. elegans* embryos.

3SDA-02 気管繊毛の運動と 3 次元構造解析**Ciliary motion and the three-dimensional structure in mouse respiratory cilia**

Hironori Ueno (*Mol. func. and life sci., Aichi Univ. of Edu.*)

Mucociliary clearance of the tracheal lumen is an important component of lung defense. However, the axonemal structure that achieves effective ciliary motion and the mechanisms by which cilia generate directional flow are unknown. In this study, we examined individual ciliary motion with 7-9 nm spatial precision using quantum dots. Moreover, we analyzed the conformational change in each dynein head of outer dynein arm by cryo-electron tomography and image processing. Most of two heads were in the same form and tightly packed in the non-nucleotide condition, whereas they are dissociated and alternatively moves in different ways in the presence of nucleotide. It probably contributes force generation of ciliary dynein in axoneme during fast ciliary motion.

3SDA-03 非侵襲 *in vivo* 技術を用いたマウス内の好中球における高速小胞輸送解析**A non-invasive technique for the *in vivo* tracking of high-speed vesicle transport in mouse neutrophils**

Kenji Kikushima, Sayaka Kita, Hideo Higuchi (*Dept. Physics, Grad. Sch. Sci., Univ of Tokyo*)

Neutrophils play an essential role in the innate immune response. We developed a new non-invasive technique for the *in vivo* imaging of neutrophils labeled with quantum dots, up to 100 μ m below the skin surface of mice. The quantum dots were endocytosed into vesicles in the neutrophils, allowing us to track the vesicles at 12.5 msec/frame with 15-24 nm accuracy. Most intriguingly, the vesicles containing quantum dots were transported at higher speed than the *in vitro* velocity of a molecular motor such as kinesin or dynein. This is the first report in which non-invasive techniques have been used to visualize the internal dynamics of neutrophils. In this symposium, I'll report recent progress in the molecular mechanism of the vesicle transport in the neutrophil.

3SDA-04 Real-time high-resolution cardiac imaging *in vivo*

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To explore the molecular mechanisms of cardiac muscle contraction under physiologic conditions, we directly imaged the motions of single sarcomeres in the beating mouse heart *in vivo* at high spatial and temporal resolution. The Z-lines were labeled with α -actinin-GFP (as in rat neonatal cardiomyocytes) via infection of adenoviruses, and sarcomere lengths were measured by using a spinning disk confocal microscope at ~100 fps (resolution in the XY plane, ~20 nm). We successfully imaged sarcomeric motions, simultaneously with electrocardiogram and left ventricular pressure. Likewise, we imaged Ca^{2+} waves / transients in the cardiomyocytes of the isolated mouse heart. At the meeting, we will discuss how cardiac muscle contraction is organized at the molecular level *in vivo*.

3SDA-05 筋収縮の数理モデルとその心臓シミュレーションへの応用について**A numerical model of cross-bridge cycling and its application to a beating human heart**

Takumi Washio¹, Kazunori Yoneda², Akihito Takahashi¹, Seiryu Sugiura¹, Toshiaki Hisada¹ (¹Grad. Sch. of Fron. Sci., University of Tokyo., ²Fujitsu Ltd.)

Numerical modeling of cross-bridge cycling is an important issue to utilize numerous experimental molecular scale findings for understanding organ scale functionalities of muscle. In this talk, we propose a simple state-transition model, which includes a cooperative property with its neighboring units and the two stage head-rotation mechanism proposed by Huxley and Simons (1971 model). First, we show that typical experimental results in the myofibril level, such as the pCa-force relationship, the tension responses for quick release and stretch, and for oscillatory length change, can be reproduced with this model. Second, we examine how the features in the cross-bridge model are related with the performance of pumping human heart by multiscale numerical simulations.

3SEA-01 ガングリオシドクラスターを介したアルツハイマーアミロイド β タンパク質のフォールディングと凝集**Ganglioside Cluster-Mediated Folding and Aggregation of Alzheimer's Amyloid beta-Protein**

Katsumi Matsuzaki (*Grad. Sch. Pharm. Sci., Kyoto Univ.*)

The aggregation of A β is considered to be the key step in the development of Alzheimer's disease. We propose the following mechanism of A β aggregation in membranes. A β specifically binds to a GM1 cluster, changing its conformation from a random coil to an α -helix-rich structure. At A β /GM1 ratios of between ~0.013 and ~0.044, the helical species and aggregated beta-sheets (~15 mer) coexist. However, the beta-structure is stable and does not form larger aggregates. At A β /GM1 values above ~0.044, the beta-structure is converted to a second, seed-prone beta-structure. Amyloid fibrils formed in solution are almost nontoxic, whereas fibrils formed in lipid rafts are cytotoxic and have different morphologies and secondary structures.