Plenary Lectures
Academic Education Lectures
Named Lectures

Plenary Lecture 1

(March 21, 10:00～10:45, Room A)

PL1

Electron Tomography or the Challenge of Doing Structural Biology *in situ*

Baumeister, Wolfgang (*Max-Planck-Institute of Biochemistry, Germany*)

Electron cryotomography enables the structural analysis of non-repetitive pleomorphic structures, such as organelles or even whole cells providing unprecedented insights into their supramolecular organization. In conjunction with subtomogram classification and averaging molecular structures can be studied *in situ*, i.e. in their functional cellular environments. Recent developments such as the targeted micromachining of cells embedded in amorphous ice using correlative LM-EM techniques and focused ion beam technology open up new windows of opportunity for studying cellular ultrastructure. Studies of ribosomes and proteasomes *in situ* and of neurotoxic aggregates will illustrate the potential of this new approach to structural cell biology.

References:

1) *Lučić, V., Rigort, A., Baumeister, W.*: Cryo-Electron Tomography: The Challenge of Doing Structural Biology In Situ (Review). J. Cell Biol. **202**, 407-19 (2013).
2) *Brandt, F., S.A. Etchells, J.O. Ortiz, A.H. Elcock, F.U. Hartl and W. Baumeister*: The native 3D organization of bacterial polysomes. Cell. **136**, 261-271 (2009).
3) *Ortiz, J.O., F. Brandt, V.R.F. Matias, L. Sennels, J. Rappsilber, S.H.W. Scheres, M. Eibauer, F.U. Hartl and W. Baumeister*: Structure of hibernating ribosomes studied by cryoelectron tomography *in vitro* and *in situ*. J. Cell Biol. **190**, 613-621 (2010).
4) *Villa, E., Schaffer, M., Plitzko, J.M., Baumeister, W.*: Opening Windows into the Cell: Focused-Ion-Beam Milling for Cryo-Electron Tomography, Current Opinion in Structural Biology 23:1-7 (2013).
5) *Fitting Kourkoutis, L., J.M. Plitzko and W. Baumeister*: Electron microscopy of biological materials at the nanometer scale. Ann. Rev. Mat. Sci. 42 (2012).

Plenary Lecture 2

(March 21, 10:45～11:30, Room A)

PL2

Structural physiology studied by cryo-electron microscopy

Fujiyoshi, Yoshinori (*Cellular and Structural Physiology Institute (CeSPI), and Graduate School of Pharmaceutical Sciences, Nagoya University, Japan*)

I am personally interested in molecular mechanisms, how education and experiences during human development influence the ability and personality of the adult. To challenge such a difficult question, structural and functional studies of membrane proteins are important, and thus I named this research field structural physiology. I would like to discuss mainly three topics of cell adhesive-channels. First, as an exceptional feature specific to AQP4 among 13 water channel isoforms, characteristic orthogonal arrays were observed and the array formation of AQP4 was regulated by the N-terminal palmitoylation of either Cys13 or Cys17, which was revealed by structure analysis of AQP4 2D-crystals [JMB 355, 628-39 (2006)] and subsequent freeze-fracture studies [BBA 1778, 1181-9 (2008)]. Large numbers of AQP4 molecules with cell adhesive-function are expressed in the glial lamellae of hypothalamus at which important brain functions such as thermo-, osmo- and glucose-sensory systems are thought to be carried out. For example, AQP4 might therefore be responsible for the pressure regulation in brain. The second topic is gap junction intercellular communication channels that allow a wide variety of solutes to pass through, and have critical roles in biologically important processes, such as, cardiac development, fertility, immune system and electrical signaling in the nervous system. The structures of connexin-26 were analyzed by electron crystallography [PNAS, 104 10034-9 (2007)] as well as X-ray crystallography [Nature 458, 597-602 (2009)], and we proposed plug gating model as a gating mechanism of the gap junction channel. As the third topic, we recently analyzed structure of claudin by X-ray crystallography and proposed a paracellular channel model [Science 344, 304-7 (2014)].

Plenary Lecture 3

(March 22, 10:30～11:15, Room A)

PL3

Receptors, Neurons, and Circuits: The Biology of Mammalian Taste

Zuker, Charles S. (*Howard Hughes Medical Institute and Columbia University, USA*)

The taste system is one of our fundamental senses, responsible for detecting and responding to sweet, bitter, umami, salty, and sour stimuli. In the tongue, the five basic tastes are mediated by separate classes of taste receptor cells each finely tuned to a single taste quality. In the cortex, each taste quality is represented in its own separate cortical field, revealing the existence of a gustotopic map in the brain. We study the logic of taste coding as a platform to understand how our brain creates an internal representation of the outside world and transforms sensory signals at the periphery into percepts, actions and complex behaviors.

Plenary Lecture 4

(March 22, 11:15～12:00, Room A)

PL4

Neural Map Formation in the Mouse Olfactory System

Sakano, Hitoshi (*School of Medicine, University of Fukui, Japan*)

In the mouse olfactory system, odorants are detected with ~1,000 different odorant receptor (OR) species expressed in the cilia of olfactory sensory neurons (OSNs). Each OSN in the olfactory epithelium (OE) expresses only one functional OR gene in a mutually exclusive and mono-allelic manner. Furthermore, OSNs expressing the same OR species converge their axons to a specific location in the olfactory bulb (OB) forming a glomerular structure. Because a given OR responds to multiple odorants and a given odorant activates multiple OR species, the odor information detected in the OE is topographically represented as the pattern of activated glomeruli in the OB[1].

A remarkable feature of axonal projection in the mouse olfactory system is that ORs play an instructive role in projecting OSN axons to the OB. For dorsal-ventral (D-V) projection, anatomical location of OSN cells within the OE regulates both OR gene choice and expression levels of axon guidance molecules, thus indirectly correlating the OR identity to the glomerular location along the D-V axis[2]. In contrast, anterior-posterior (A-P) projection is totally independent of the positional information of OSN cells, but instead dependent on the expressed OR species[3]. We have recently found that A-P targeting is regulated by the agonist-independent baseline activity of ORs using cAMP as a second messenger[4]. OR-derived cAMP signals also regulate the expression of glomerular segregation molecules for the map refinement through local sorting of OSN axons[5]. Unlike A-P projection molecules, glomerular segregation molecules are regulated by stimulus-driven neuronal activity[4].

Here, we discuss the recent progress in the neural map and circuit formation in the mouse olfactory system.

References

1) *Mori, K. and Sakano, H.*: Ann. Rev. Neurosci. 34, 465 (2011).
2) *Takeuchi, H., et al.*: Cell 141, 1056 (2010).
3) *Imai, T., et al.*: Science 325, 585 (2009).
4) *Nakashima, A., et al.*: Cell 154, 1314 (2013).
5) *Serizawa, S., et al.*: Cell 127, 1057 (2006).

Plenary Lecture 5

(March 23, 10:30～11:30, Room A)

PL5

Molecular Dissection of Autophagosome Formation in Yeast

Ohsumi, Yoshinori (*Integrated Research Institute, Tokyo Institute of Technology, Japan*)

Autophagy is well a conserved degradation process of cytoplasmic constituents in the lysosome/vacuole. Recently it is getting clear that autophagy plays important roles in so many physiological events and is related to diseases. More than 26 years ago we first found autophagy in yeast induced by nutrient starvations by light microscopic observation. Taking advantage of the yeast system, we started genetic approach to dissect the process, and successfully isolated many autophagy-defective mutants. Subsequent identification of ATG genes revealed unique set of genes involved in membrane dynamics during autophagy. These genes were mostly conserved in mammals and plants and most other eukaryotes. These findings triggered a vast of autophagy research in various organisms. We know now that 18 *ATG* genes are essential for starvation-induced autophagy in yeast. They consist of six functional units, namely the Atg1 protein kinase and its regulators, the PI3 kinase complex, the Atg2-Atg18 complex, the membrane protein Atg9, and two unique ubiquitin-like conjugation systems. Then we have been focusing to elucidate the structure and function of each Atg protein. Atg proteins function concertedly in membrane dynamics during the formation of autophagosome. Recent studies on the Atg proteins, especially early steps of the PAS assembly will be presented. In addition recent physiological roles of autophagy in yeast will be discussed.

Academic Education Lecture 1

(March 21, 14:00～14:45, Room A)

EL1

Kinesin Superfamily Molecular Motors, KIFs: Intracellular Transport, Regulation of Higher Brain Function, and Development and Diseases

Hirokawa, Nobutaka (*Graduate School of Medicine, The University of Tokyo, Japan*)

Academic Education Lecture 2

(March 21, 14:45～15:30, Room A)

EL2

Integrative research on bio-system bridging from single molecules to organ

Yanagida, Toshio (*Graduate School of Frontier Biosciences, Osaka University, Japan*)

S. Hagiwara Memorial Lecture

(March 23, 13:30～14:15, Room A)

NL1

The role of cortical areas MT/MST in short-latency ocular tracking

Kawano, Kenji (*Graduate School of Medicine, Kyoto University, Japan*)

Whenever we move around in the environment, the observer's movements activate the vestibular organs and are then compensated by the vestibulo-ocular reflexes (VORs). However, the VORs are not always perfect and the visual acuity is severely impaired if the images of interest on the retina move excessively. Recent studies revealed three distinct visual tracking eye movements with ultra-short latencies (~60 ms in monkeys), which are thought to help reduce the residual visual disturbances. One of these eye movements is 'ocular following', which deals with the visual stabilization problems confronting the observer who looks off to one side. Two other eye movements, 'disparity vergence' and 'radial-flow vergence', deal with the binocular fusion problems of the observer who looks in the direction of heading.

To understand the neural mediation of these tracking eye movements, we focused on the role of the middle temporal (MT) and medial superior temporal (MST) areas within the superior temporal sulcus (STS) of the monkey's cortex, since these areas are known to contain many neurons that respond vigorously to visual motion with directional selectivity and others that are sensitive to binocular disparity or to the patterns of optic flow experienced by the moving observer. We recorded single unit activities and made focal chemical lesions in these areas in monkeys. The results were consistent with the hypothesis that the MT/MST areas are primary sites for initiating all three visual tracking eye movements at ultra-short latencies.

S. Tawara Memorial Lecture

(March 23, 14:15～15:00, Room A)

NL2

Intracellular Ca^{2+} in striated muscle: measurement and physiological significance

Kurihara, Satoshi (*The Jikei University School of Medicine, Japan*)

Intracellular Ca ion (Ca^{2+}) plays a pivotal role in muscle contraction. In the present Tawara Memorial Lecture, I will present the intracellular Ca^{2+} concentration change measured with the Ca^{2+} sensitive photoprotein aequorin in mammalian cardiac muscles, and will discuss the molecular mechanism of the length-dependent change of tension in cardiac muscle (the Frank-Starling law of the heart). If the papillary muscle of the rat or ferret was stretched from a shorter length to the length to produce maximal tension (Lmax), tension was increased without a change in the peak Ca^{2+} signal (Ca^{2+} transient, CaT). However, the relaxation time was prolonged and the decay time of CaT was shortened. If muscle length was quickly shortened from Lmax to a shorter length during a twitch contraction, tension was promptly decreased and then re-developed. In response to quick release, the CaT showed a transient increase (hump) in the falling phase. The magnitude of the hump was correlated with the magnitude of tension reduction rather than with muscle length. If the preparation was treated with 2,3-butanedione monoxime, tension disappeared, but the CaT was not greatly affected. In the 2,3-butanedione monoxime-treated preparation, quick release did not induce a hump in the CaT. Thus, the change in muscle length affects the Ca^{2+} affinity of the Ca^{2+}-binding protein troponin through cross-bridge attachment and detachment. The measurement of the intracellular Ca^{2+} concentration is essential for understanding the molecular mechanism of cardiac muscle contraction.