Committee Symposium

Committee Symposium 1

Current Status and Issue of Research Ethics

(March 21, 8:30～10:00, Room B)

CS01-1 Roles of Academia and Research Society in Ethical Education for Young Scientists

Kurata, Kiyoshi Dept Physiol, Hirosaki Univ Grad Sch Med, Hirosaki Japan

CS01-2 Pitfalls in modern scientific research: neglectfulness and ethics

Takeda, Sen Univ.Yamanashi. Fac.Med.

CS01-3 What we can do not to repeat fraudulence in science

Honma, Sato Dept. Chronomedicine, Grad.Sch Med, Hokkaido Univ. Sapporo, Japan

CS01-4 Misconduct and university management

Takata, Kuniaki Gunma Univ, Maebashi, Japan

Committee Symposium 2

Brain structures from physiological viewpoints; brain functions from anatomical viewpoints

(March 21, 8:30～10:00, Room F)

CS02-1

Regulation of telencephalic development through glycogen

Gotoh, Hitoshi (*Kyoto Pref. Univ. Med., Kyoto, Japan*)

Cellular metabolism has reported to be involved in cell proliferation and differentiation. Mammalian embryos faces 'nutritional shift' on their birth because of the separation from placental energy supply. However, it remains unclear how the cellular metabolism is changed and maintained in the brain. Glycogen is a branched polysaccharide and act as energy stores that rapidly supply energy depending on the demand. Glycogen is reported to be present in developing brain, however, the function of glycogen in the developing brain remains unclear. In order to analyze the function of glycogen in the central nervous system, we first analyzed localization of glycogen in the developing telencephalon. We found that glycogen particles are abundantly present in the border of ventral/dorsal telecephalon. GLAST-positive glial lineage cells but not neuronal cells have glycogen inside the cell. Further, we found that quantity of glycogen is dramatically decreased after birth. In addition, glycogen phosphorylase, a glycogen degrading enzyme, is activated as compared with that of embryonic stage. To analyze its functions, we injected inhibitors of glycogen phosphorylase, and found that inhibition of glycogen phosphorylase lead to decreased cell proliferation. In primary cultured astrocytes, p21cip, a cell cycle inhibitor, was upregulated and cells were arrested at G1-S phase upon glycogen phosphorylase inhibition. These results suggest that glycogen is a energy source that is required for maintaining cell proliferation upon transition of embryonic to postnatal stage.

(COI: No)

CS02-2

Molecular mechanism underlying development of the cerebral cortex -Roles of Dpy19 family-

Watanabe, Keisuke (*Div Neurobiol Anat, Niigata Univ*)

The mammalian cerebral cortex has been evolutionarily expanded and acquired a distinct six-layer structure. However, developmental mechanisms specific to this area are poorly understood. Recently, we have revealed that a multi-transmembrane protein Dpy19L1 is required for proper migration of glutamatergic neurons in the developing cortex. In mammals, Dpy19 family consists of four members (Dpy19L1-L4), which have been revealed to be associated with human diseases. However their functions during development have been unclear. In this study, we examined roles of Dpy19 family members in the developing cerebral cortex. Dpy19L1, Dpy19L3 and Dpy19L4 showed distinct expression patterns in the developing cortex. Furthermore, we have generated Dpy19L1, Dpy19L3 and Dpy19L4 mutant mice. A large number of Dpy19L1 homozygotes displayed postnatal lethality. Some Dpy19L1 knockout mice are viable, but smaller in size. Cortical layer formation was apparently normal in Dpy19 knockout brains. Interestingly, Dpy19 homozygotes showed weaker fear responses to predator odours, compared with that of wild-type and the heterozygous mice. Furthermore, we examined molecular functions of Dpy19 protein. Dpy19 is predicted to have multi-transmembrane domains, but lacks any predicted functinal domains. Our in vitro studies suggest a possible association of Dpy19L1 with the endoplasmic reticulum and microtubules. These results suggest important roles of Dpy19L1 in cortical development and innate fear responses.

(COI: No)

CS02-3

Changes of brain function and structure involved in functional recovery after brain damage

Higo, Noriyuki (*Systems Neurosci Sect, Human Tech Res Inst, AIST, Tsukuba, Japan*)

The central nervous system has the capacity for functional recovery following the damage. We previously reported that motor training after lesioning of the primary motor cortex (M1) induces recovery of dexterous hand movements including precision grasp in macaque monkeys (Murata et al., 2008). To clarify the neuronal bases underlying the functional recovery of dexterous movements after M1 lesion, we measured brain activity during performing a precision grasp task using positron emission tomography (PET). The PET imaging analysis revealed overactivity of the ventral premotor cortex (PMv) during the early post-recovery period (the period just after recovery) and increased functional connectivity within M1 during the late post-recovery period (the period at several months after recovery). The causal role of these areas in motor recovery was confirmed by means of pharmacological inactivation by muscimol during each recovery period. We also investigated the structural changes of neurons in the corresponding areas during the functional recovery using histochemical analysis; gene expression of growth-associated protein-43 (GAP-43) was increased in both the PMv during the early-post recovery period and the perilesional M1 during the late-post recovery period, suggesting that GAP-43-mediated structural changes of presynaptic axon terminals occurred in these areas. These findings indicate that in both the remaining primary motor and premotor cortical areas, time-dependent plastic changes, both functional and structural, are involved in functional recovery from the motor deficit caused by the M1 lesion.

(COI: No)

CS02-4

Type 1 metabotropic glutamate receptor regulates experience-dependent maintenance of mature synaptic connectivity in the visual thalamus

Narushima, Madoka[1]; Uchigashima, Motokazu[2]; Harada, Takeshi[3]; Hashimoto, Kouichi[4]; Aiba, Atsu[3]; Watanabe, Masahiko[2]; Miyata, Mariko[1,5]; Kano, Masanobu[6] (*[1]Dept Physiol, Sch Med, Tokyo Women's Medical Univ, Tokyo, Japan; [2]Dept Anatomy, Grad Sch Med, Hokkaido Univ, Sapporo, Japan; [3]Lab Animal Resources, CDBIM, Fac. Med, Univ. Tokyo, Tokyo, Japan; [4]Dept Neurophysio, Grad Sch Biomed & Health Sci, Hiroshima Univ, Hiroshima, Japan; [5]PRESTO, JST, Kawaguchi, Japan; [6]Dept Neurophysiol., Grad Sch Med, Univ Tokyo, Tokyo, Japan*)

In the dorsal lateral geniculate nucleus (dLGN), retinogeniculate (RG) synapses undergo formation and elimination during development and mature by postnatal day 20 (P20). Afterwards, visual experience is critical to maintenance of established RG synapses since one week of visual deprivation from P20 triggered remodeling of RG synaptic connectivity. In contrast to synapse formation and elimination phases, molecular basis of experience-dependent maintenance remained poorly understood. We found that expression of type 1 metabotropic glutamate receptor (mGluR1) increased in the dLGN after eye opening. In mGluR1 knock-out (KO) mice, formation and elimination of RG synapses was normal by P20 but the synapses were remodeled in the mice older than P28. Visual deprivation (p20-28) could not induce the remodeling in the KO mice. Importantly, in wild-type mice, pharmacological blockade of mGluR1 in the dLGN after P21 triggered remodeling of RG synapses and activation of mGluR1 in the dLGN rescued visual deprivation-induced remodeling. These results suggest that mGluR1 is required for the experience-dependent maintenance to conserve mature RG connectivity.

(COI: No)

Committee Symposium 3

Symposium by the Committee on the Promotion of Gender Equality

(March 21, 12:00～13:00, Room G)

CS03-1 Find the pride, joy and appreciation in life and work

Tokuda, Nobuko Grad. Sch. Med. Yamaguchi Univ., Yamaguchi, Japan

CS03-2 Changing times, Changing gender roles : Who do we want female researcher to be

Miyata, Mariko Tokyo womens medical univ.

Committee Symposium 4

Functional architecture of localization and integration of subcellular Ca^{2+} signaling

(March 21, 14:00～17:00, Room C)

CS04-1

Piezo1 integration of vascular architecture with physiological force

Beech, David J; Li, Jing; Hou, Bing (*Div Cardiovasc Res, Sch Med, Univ Leeds*)

Endothelial cells are strikingly sensitive to shear stress, a frictional force caused by blood flow. Vascular development depends on it, production of nitric oxide is strongly promoted by it, the location and size of atherosclerotic plaques depend on differences in shear stress imposed by vascular architecture, and shear stress-induced migration is pivotal in angiogenesis and wound healing. The nature of the sensor has nevertheless been elusive. We recently revealed a key player (Li et al 2014 Nature doi: 10.1038/nature13701). Piezo1 was important for normal shear stress-evoked calcium signalling and non-selective cationic current in endothelial cells. Piezo1 disruption in the mouse was embryonic lethal just at the time when vascular maturation was required from embryonic day 9.5. Lethality reflected specific requirement for endothelial Piezo1 because endothelial-specific disruption of Piezo1 led to endothelial cells which were present but which did not remodel to form mature vascular architecture. Adult haploinsufficient Piezo1+/- mice showed disturbed phosphorylation of endothelial nitric oxide synthase and reduced alignment of endothelial cells to the direction of blood flow. Downstream of Piezo1-dependent calcium signalling was protease (calpain) activation and spatial reorganization of endothelial cells to the polarity of the applied force. Piezo1 is suggested to have major significance in vascular biology and to be critical for the development of complex life.Supported by the Medical Research Council, Wellcome Trust, the British Heart Foundation, and Cancer Research UK. The author declares no conflict of interest.

(COI: No)

CS04-2

Genetically-encoded tools to optically control and image Ca^{2+} dynamics

Nagai, Takeharu (*ISIR, Osaka Univ, Japan*)

In living organism, Ca^{2+} is one of the most versatile second messenger to control biological processes such as muscle contraction, hormonal secretion and apoptosis induction. Its spatial and temporal dynamics has key roles to regulate these physiological phenomena. To reveal such dynamics, variety of Ca^{2+} indicators had been developed. They enabled noninvasive visualization of Ca^{2+} dynamics, provided meaningful information for research in wide range of biological field. However, for deeper understanding of relationship between the spatiotemporal Ca^{2+} dynamics and the following response, development of tools to manipulate intracellular Ca^{2+} level have been desired. For this, we developed a genetically-encoded photoactivatable Ca^{2+} releaser called PACR. That is composed of a Ca^{2+}+ binding protein and a light-sensitive protein LOV2 derived from phototoropin. Affinity of PACR for Ca^{2+} was decreased during irradiation of blue light but increased after the irradiation. Thus reversible and repeatable manipulation of Ca^{2+} concentration is possible without damages to living specimens. By using PACR, we succeeded nucleus specific temporal Ca^{2+} increase in HeLa cells and excitation of specific neuron in freely moving *C. elegans* by blue light irradiation. This useful tool is expected to contribute on researches to reveal the role of Ca^{2+} dynamics in complex biological phenomena. In addition to this manipulation tool, I would like to introduce cyan and orange color variants of bright luminescent Ca^{2+} indicators, which can be used compatibly with optogenetic actuators including PACR.

(COI: No)

CS04-3

Cellular processes mediated by a lipid-metabolizing enzyme diacylglycerol kinase (DGK) family

Goto, Kaoru (*Yamagata Univ. Sch. Med., Japan*)

Diacylglycerol kinase (DGK) phosphorylates a lipid second messenger diacylglycerol (DG) to phosphatidic acid and is involved in a variety of pathophysiological cellular responses through the metabolism of DG. DGK consists of a family of isozymes, each of which has a unique character in terms of regulatory mechanism, binding partner, and subcellular localization. Of DGKs, DGKzeta localizes primarily to the nucleus in various cell types. Under pathological conditions, DGKzeta translocates from the nucleus to the cytoplasm in hippocampal neurons in animal models of excitotoxicity. DGKzeta cytoplasmic translocation is shown to recapitulate in acute hippocampal slices exposed to oxygen-glucose deprivation (OGD), in which NMDA receptor-mediated Ca influx triggers this phenomenon. What is the functional implication of cytoplasmic translocation of DGKzeta? The transcription factor p53 plays a crucial role in coordinating the cellular responses to various stresses, such as apoptotic cell death. We found that DGKzeta physically interacts with p53. In addition, cytoplasmic DGKzeta is revealed to attenuate p53-mediated cytotoxicity against DNA damage by facilitating cytoplasmic anchoring and degradation of p53 through a ubiquitin-proteasome system. Concomitantly, decreased levels of nuclear DGKzeta engender down-regulation of p53 transcriptional activity. These findings suggest that DGKzeta cytoplasmic translocation is a protective stress response and attenuates p53-mediated cytotoxicity under stress conditions.

(COI: No)

CS04-4

Ca^{2+}- and Calmodulin-mediated regulation of receptor-operated cation currents of TRPC6 channels

Mori, Masayuki X[1]; Hirano, Mitsuru[1]; Hase, Hideharu[1]; Itsuki, Kyohei[2]; Inoue, Ryuji[3]; Mori, Yasuo[1] (*[1]Dept SynBiol, Grad Sch Engr, Kyoto Univ, Kyoto, Japan; [2]Sch Dent. Kyushu Univ, Fukuoka; [3]Sch Med, Dept Physiol, Fukuoka Univ. Fukuoka*)

Calmodulin (CaM) contributes a variety of ion channels gating regulation in response to cellular Ca2+ ([Ca2+]i) changes. However, the information is still missing about the molecular basis of CaM-mediated regulation of mammalian TRP channels which generate receptor-operated cation (Ca2+ and Na+) currents (ROC). To accumulate of Ca2+ and CaM roles in TRP channels, we first characterized the Ca2+ regulation in TRPC6 channels. The decay of the ROC of TRPC6 was delayed by chelation with EGTA or BAPTA, thus suggesting a global Ca2+ mechanism. We then examined CaM binding to the C-terminal region of TRPC6 by Ca2+-dependent FRET system. FRET due to CaM binding to the C-terminal region of TRPC6 demonstrated a bell-shape response curve with respect to [Ca2+]i. This Ca2+-dependence was a unique compared to those of IQ-domain of voltage-gated Ca or Na channels. The bell-shape response changed to a simple grow by a mutation in either N- or C-lobe domain of CaM. Intriguingly, the mutant in the N-lobe of CaM delayed the decay of receptor-operated currents of TRPC6, indicating the lobe-specific function. From these results, the Ca2+-dependent regulation of TRPC6 can be explain by the bell-shape response curve of CaM binding which is probably caused by a competitive binding between the both lobes of CaM. Our results provide a unique molecular basis for CaM to terminate ion channel activity, which may play critical roles at the down-stream of vasoconstrictors and growth factors.

(COI: No)

CS04-5

Imaging Intraorganellar Ca^{2+} at Subcellular Resolution Using CEPIA

Suzuki, Junji[1]; Kanemaru, Kazunori[1]; Ishii, Kuniaki[2]; Ohkura, Masamichi[3]; Okubo, Yohei[1]; Iino, Masamitsu[1] (*[1]Dept. Pharmacol., Grad. Sch. Med., Univ. Tokyo, Tokyo, Japan; [2]Dept. Pharmacol., Grad. Sch. Med., Yamagata Univ., Yamagata, Japan; [3]Brain Sci. Inst., Saitama Univ., Saitama, Japan*)

The endoplasmic reticulum (ER) and mitochondria accumulate Ca^{2+} within their lumens to regulate numerous cell functions. However, determining the dynamics of intraorganellar Ca^{2+} has proven to be difficult. We generated a family of genetically-encoded Ca^{2+} indicators, named calcium-measuring organelle-entrapped protein indicators (CEPIA), which can be utilized for intra-organellar Ca^{2+} imaging. CEPIA, which emit green, red or blue/green fluorescence, are engineered to bind Ca^{2+} at intra-organellar Ca^{2+} concentrations. They can be targeted to different organelles and may be used alongside other fluorescent molecular markers, expanding the range of cell functions that can be simultaneously analyzed. The spatiotemporal resolution of CEPIA makes it possible to resolve Ca^{2+} import into individual mitochondria while simultaneously measuring ER and cytosolic Ca^{2+}. We have used these imaging capabilities to reveal differential Ca^{2+} handling in individual mitochondria. Thus, CEPIA enable to study the physiological functions of intraorganellar Ca^{2+} dynamics.

(COI: No)

CS04-6

Local calcium signaling in neuronal development and remodeling

Emoto, Kazuo (*Dep Biol, Grad Sch Sci, Univ of Tokyo, Japan*)

Nervous system development relies on a balance between progressive and regressive events. After progressive events such as axon/dendrite outgrowth and synapse formation, neurons refine their connections through regressive events such as pruning of axons and dendrites. Thus, proper dendrite pruning critically depends on local activation of the elimination machinery in unwanted dendrites, but our understanding of locally acting mechanisms involved in this process remains incomplete. We have been working on how neurons can selectively eliminate unnecessary dendritic branches using Drosophila sensory neurons as a model system, and found that compartmentalized calcium transients in dendritic branches act as temporal and spatial cues to trigger pruning. By performing long-term in vivo imaging, we show that calcium transients occur in dendritic branches, but not in the soma or axon which exhibits no pruning, at ~3 hours prior to branch elimination. The compartmentalized calcium transients are induced in part by a local increase of dendritic excitability, which thereby activates calcium influx via voltage-gated calcium channels (VGCCs); blockade of VGCC activity impairs dendrite pruning. Further genetic analyses suggest that the calcium-activated protease calpain functions downstream of the calcium transients to promote dendrite pruning. Our findings reveal the importance of compartmentalized sub-dendritic calcium signaling in spatio-temporally selective elimination of dendritic branches.

(COI: No)

Committee Symposium 5

Japan-Korea Joint Symposium - Towards FAOPS2019

Morphological and Physiological Approaches to Synaptic Transmission

(March 22, 9:00～10:30, Room E)

CS05-1

Cellular mechanisms for mossy fiber input-induced heterosynaptic plasticity at direct cortical synapses in the hippocampal CA3 pyramidal cells

Lee, Suk-Ho; Hyun, Jung Ho; Eom, Kisang; Lee, Kyu-Hee; Ho, Won-Kyung (*Department of Physiology, Seoul National University College of Medicine, Seoul, Korea*)

A short high frequency stimulation of mossy fibers (MFs) induces long-term potentiation (LTP) of direct cortical or perforant path (PP) synaptic inputs in the hippocampal CA3 pyramidal cells (CA3-PCs). However, the cellular mechanism underlying this heterosynaptic modulation remains elusive. We found that high frequency MF inputs downregulate Kv1.2 in the CA3-PCs, and that the downregulation of Kv1.2 results in specific enhancement of PP-EPSPs. The NEURON simulation based on the known ion channel distributions on apical dendrites of CA3-PCs suggests that a concerted action of passive normalization of synaptic inputs and polarized distributions of ionic channels underlie a preferential generation of dendritic Na^+-spikes at distal apical dendrites, where PP inputs arrive. Accordingly, 10 nM tetrodotoxin, which specifically suppresses dendritic Na^+-spikes, brought back the enhanced PP-EPSPs to the baseline level. These results indicate that activity-dependent downregulation of Kv1.2 in CA3-PCs mediates MF input-induced heterosynaptic LTP of direct cortical synaptic inputs through preferential generation of Na^+-spikes at distal apical dendrites of a CA3-PC.

(COI: No)

CS05-2

Activity-dependent Homeostatic Plasticity of Hippocampal Mossy Fiber-CA3 Circuit

Lee, Kea Joo (*Korea Brain Research Institute, Daegu, Korea*)

Network activity homeostatically alters synaptic efficacy to constrain neuronal output. However, it is unclear how such compensatory adaptations coexist with synaptic information storage, especially in established networks. Here, we demonstrate that in mature hippocampal neurons in vitro, network activity preferentially regulated excitatory synapses within the proximal dendrites of CA3 neurons. These homeostatic synapses exhibited morphological, functional, and molecular signatures of the specialized contacts between mossy fibers of dentate granule cells and thorny excrescences (TEs) of CA3 pyramidal neurons. In vivo TEs were also selectively and bidirectionally altered by chronic activity changes. TE formation required presynaptic synaptoporin and was suppressed by the activity-inducible kinase, Plk2. These results implicate the mossy fiber-TE synapse as an independently tunable gain control locus that permits efficacious homeostatic adjustment of mossy fiber-CA3 synapses, while preserving synaptic weights that may encode information elsewhere within the mature hippocampal circuit.

(COI: No)

CS05-3

Physiological approaches to study presynaptic motor proteins in vesicle reuse pathways

Mochida, Sumiko (*Dept Physiol, Tokyo Med Univ, Tokyo, Japan*)

Myosins II and VI are actin-based cytoskeletal motors that drive actin dynamics and membrane transport at brain synapses, however, the molecular mechanism linking variation in neural activity to synaptic vesicle (SV) resupply is unknown. We combined genetic knockdown and direct physiological measurement of synaptic transmission from paired superior cervical ganglion neurons to show that myosins IIB and VI work individually in vesicle reuse pathways, having distinct dependency and time constants with physiological action potentials (AP) frequency. Myosin VI resupplied the readily releasable pool (RRP) with slow kinetics independently of firing rates but acted quickly within 50 ms after AP. Under high frequency AP firing, myosin IIB resupplied the RRP with fast kinetics in a slower time window of 200 ms. Myosin IIB-mediated SV resupply follows dynamin-1-mediated endocytosis, while myosin VI-mediated SV resupply follows dynamin-3-mediated endocytosis. Collectively, our findings show how myosins work in appropriate vesicle reuse pathways associated with specific firing patterns. This work was supported by #25290025 grants-in-aid for Scientific Research B and for Exploratory Research.

(COI: No)

CS05-4

Cellular and molecular mechanisms of synaptic circuit pruning and plasticity

Watanabe, Masahiko (*Hokkaido Univ. Grad. Sch. Med., Sapporo, Japan*)

Initial synaptic circuits formed by genetic programs are stero-typed with redundant and overlapping connections. After birth, activation of postsynaptic neurons refines immature circuits into mature ones in an activity-dependent manner. In this process, two forms of synapse refinement, i.e., synapse pruning and circuit plasticity, occurs efficiently and simultaneously during the early postnatal period called critical period. In the synapse pruning, active synapses are strengthened, while less active ones are eliminated. By critical period plasticity, projection fields of active afferents expand at the expense of those of less active ones. Through these refinements, neural circuits acquire functional topography, in which early life history of individual animals and humans is reflected. We have so far studied cellular and molecular mechanisms of synaptic refinement using gene-manipulated mice. In the symposium, I will introduce that molecules involving activity-dependent intracellular Ca^{2+} dynamics regulate the synapse pruning, such as NMDA receptors for barrel formation in the somatosensory cortex and P/Q-type Ca^{2+} channels and mGluR1 for climbing fiber and parallel fiber elimination in cerebellar Purkinje cells. On the other hand, glutamate transporters controlling extracellular glutamate concentrations magnify the circuit plasticity mediating the expansion of active circuits and reciprocal shrinkage of inactive ones.

(COI: No)

Committee Symposium 6

Recent Development of Physical Therapy Research on Motor Control

(March 22, 16:00～17:30, Room D)

CS06-1

Posture-movements and cognition of bodily information

Takakusaki, Kaoru (*Ctr Brain Funct & Med Eng, Asahikawa Med Univ.*)

Are we aware of the existence of our body and the motion of every part of the body during movements? A "loss of the awareness or the knowledge of the body" would deprive not only capability to achieve adaptive movements but also willingness and orientation. Real-time sensory signals during movements always inscribe our body information into the brain through visual, auditory, somatosensory and vestibular pathways. Sensory signals acting on the brainstem and the limbic system call "attention" and alter "emotional state", respectively. In addition those acting on cerebral cortex produce "body schema". The information (attention, emotional state and body schema) of the body is always updated like ever-changing scenes. The information provides us orientation and knowledge of embodiments that can be utilized for motor programing that occurs at the supplementary motor area (SMA) and premotor area (PM) as initial and restraint conditions. Body schema, which is constructed in the temporal and parietal association cortices, can be particularly essential in this process. The motor program includes that for volitional-guided precise movements and that for postural control of whole body that precedes the movement onset. Possibly, the former is achieved by the corticospinal projection and the latter can be accomplished by the cortico-reticular and the reticulospinal projections.

(COI: No)

CS06-2

Implicit adjustment of postural control strategy with a real-time feedback movable footplate

Kawashima, Noritaka (*Research Inst., NRCD, Saitama, Japan*)

Postural control relies on multisensory processing and its interaction to automatic control system which dominantly involves quick-responded reflex and vestibular system. Such control system enables us to maintain seemingly-unstable bipedal posture without special attention. Additional cortical demand would be increased when one faced to uncertain surroundings or unstable ground surface. We recently developed a real-time feedback movable footplate in order to get a better understanding of human postural control and to find a novel approach for the improvement of postural instability due to aging and disorders. In my talk, I will firstly show the results obtained from healthy subjects, which aimed to clarify postural responses due to augmented/reduced postural sway realized by established real-time feedback system. The results clarify that the real-time feedback has a potential to modulate the interaction between spinal reflex excitability and cortical command during upright standing. Then, I will show the preliminary results obtained from patients in order to discuss potential advantages of our developed system for the improvement of postural disorder.

(COI: No)

CS06-3

Meso-limbic system as a meta-learning center for motor recovery after neuronal damage

Nishimura, Yukio (*Dept Develop Physiol, Nat Inst Physiol Sci, Okazaki, Japan*)

It is generally believed that depression impedes functional recovery after neuronal damage such as spinal-cord injury. The ventral striatum is generally considered to regulate motivation, and not to be involved in the direct control of movements. However, it was found the activity of the VSt increased in association with activation of the motor cortex during recovery from spinal cord injury . This fact suggests that the interaction between VSt and motor cortex plays an important role for the reorganization of motor circuits after the SCI. Nevertheless, the causal relationship of the VSt for the motor recovery remains unclear. Here we show that the VSt plays crucial role in more direct control of dexterous finger movements by modulating the oscillatory activity of the motor cortex during the early stage of the recovery course. We found that high frequency oscillatory activity (200-400 Hz) of the VSt became enhanced and causally influences the activity of sensorimotor cortices during early stage of recovery. Reversible inactivation of the VSt caused severe deficit of the finger dexterity and diminished high frequency oscillatory activity of sensorimotor cortices during early stage of recovery. Our results first demonstrate that the VSt up-regulates the activity of sensorimotor cortices and can work as a meta-learning center for the recovery of motor functions after the neuronal damage.

(COI: No)

CS06-4

Interaction between gastrocnemius muscle weakness and moderate running exercise on rat knee joint cartilage

Ozawa, Junya (*Fac.Rehab.Hiroshima Int Univ., Hiroshima, Japan*)

Objective: Therapeutic exercises are used for symptomatic relief in patients with osteoarthritis of the knee. However, the interaction between ankle muscle dysfunction and exercise of the knee joint structure has not been studied.
Design: Gastrocnemius muscle weakness was induced by intramuscular injection of botulinum toxin type A (BTX) in skeletally mature rats. Moderate treadmill running (12 m/min for 60 min) was applied for 6 weeks in rats with and without BTX. Untreated animals were used as controls. Kinematic features of the hindlimb during locomotion were investigated by 3D motion analysis. Serum biomarkers of cartilage metabolism were investigated by ELISA. Cartilage thickness and chondrocyte density in the tibial plateau of the knee joint were also calculated histometrically.
Results: The gastrocnemius muscles were severely atrophied by BTX injection. Gastrocnemius muscle dysfunction was confirmed by locomotion analysis as an increased maximal dorsiflexion angle during the stance phase. Biomarker analysis revealed that 6 weeks of moderate running exercise facilitated the anabolic response of type II collagen. However, running-induced anabolism was significantly counteracted by BTX injection. In addition, thinning of the cartilage layer and a reduction in the chondrocyte density was also found in the BTX-injected rat knee after running for 6 weeks.
Conclusions: Exercise is proposed to have a positive effect on joint homeostasis. However, ankle muscle weakness may alter the mechanical environment of the knee and impair the integrity of joint cartilage with moderate exercise.
(COI: No)

CS06-5

Stimulation of functional recovery via the mechanisms of neurorepair by S-nitrosoglutathione and motor exercise following focal cerebral infarction in rats

Sakakima, Harutoshi; Matsuda, Fumiyo; Yoshida, Yoshihiro (*Sch. Health Sci. Med. Kagoshima Univ. Kagoshima, Japan*)

Ischemic stroke is major cause of neurological disability and big burden on the family and society. Physical exercise and pharmacological agents following stroke induce neurophysiological and neuroanatomical plasticity, leading to the recovery of function. In this session, we talk about the protective effects of physical exercise on neurovascular unit, including neurons, astrocytes, pericytes and extracellular matrix. Furthermore, we talk whether neurovascular protective agent, S-nitrosoglutathione (GSNO) in combination with motor exercise exerts a synergistic effect in stimulating the mechanisms of neurorepair, leading to accelerated and enhanced functional recovery following stroke. GSNO invokes anti-inflammatory effects on post-injury events mainly through the down regulation of the expression of NF-kB, adhesion molecules, cytokines, and inducible nitric oxide synthase. Stroke was induced by middle cerebral artery occlusion and reperfusion in adult male rats. Endurance exercise training reduced infarct volume, alleviated neurological deficits, enhanced expression of neurotrophic factor, promoted angiogenesis, and decreased apoptosis cell death. Combination of GSNO and exercise showed reduced infarction, decreased neuronal cell death, enhanced neurotrophic factors, and improved neurobehavioral functions. The protective effect of GSNO and exercise was blocked by the inhibition of Akt activity. GSNO and exercise aid functional recovery by stimulating neurorepair mechanisms.
(COI: No)

Committee Symposium 7

Neural mechanisms of acupuncture analgesia

(March 22, 17:30～19:00, Room D)

CS07-1

Recent advances in anatomical studies on the descending pain control systems

Senba, Emiko (*Osaka Yukioka College of Health Science, Osaka, Japan*)

Clinically relevant long-term pain relieving effects of acupuncture (AP) can be seen in a proportion of patients with chronic pain, such as chronic low-back pain. However, the mechanisms behind such effects are still obscure. It has been demonstrated that electro-AP-induced analgesia in experimental animals was antagonized by naloxone or methysergide, indicating the involvement of opioid peptides and serotonin (5-HT), i.e. descending pain inhibitory system. Stress-induced analgesia (SIA) and the activation of diffuse noxious inhibitory control (DNIC) may also contribute to the AP-induced analgesia. It has been demonstrated that the rostral ventromedial medulla (RVM) plays key roles in endogenous pain control system and AP can activate RVM neurons, thus inducing analgesia.Therefore, in this symposium, I'll focus on the detailed anatomy of the descending inhibitory system. Neurons in the RVM are divided into ON-, OFF- and neutral cells. 5-HT neurons belong to neutral cells. About 50% of RVM projection neurons, that project to spinal dorsal horn, are serotonergic. GABA containing RVM neurons have been considered to be local interneurons, but about 40% of RVM projection neurons were shown to be GABAergic. GABA synthesis in the RVM and superficial dorsal horn is a critical component in the descending inhibition. Recently it has been demonstrated that GABA synthesis in these neurons is suppressed in animals suffering chronic inflammatory and neuropathic pain. This suppression seems to be mediated by epigenetic regulation of GAD transcription. We have recently demonstrated that physical exercise can prevent this down-regulation.
(COI: No)

CS07-2

Mechanisms underlying descending modulation of spinal and medullary nociceptive neurons

Iwata, Koichi; Katagiri, Ayano; Shinoda, Masamichi (*Dept. Physiol, Sch Dent, Nihon Univ, Tokyo, Japan*)

It is well known that peripheral nociceptive inputs come up to the spinal and medullary dorsal horn, and those are sent to the higher central nervous system via medial and lateral ascending pathways. The activities of nociceptive neurons in these ascending pathways are modulated by the descending modulation system. Descending inhibitory system is well known to be involved in inhibition of responses of spinal and medullary nociceptive neurons via descending serotoninergic or noradrenergic system. Rostral Ventral Medulla (RVM) is known to be a key nucleus involving in descending modulation of nociceptive neurons. Furthermore, activities of nociceptive neurons are enhanced via RVM neurons associated with peripheral nerve injury or inflammation. There are 3 groups of neurons involving in modulation of the nociceptive neurons in the RVM, ON cells, OFF cells and neutral cells. ON cells are involved in the enhancement of nociceptive neurons, OFF cells are inhibition and neutral cells are not involved in modulation of nociceptive neurons. Though these 3 types of RVM neurons are thought to be involved in modulation of spinal and medullary nociceptive neurons, detail mechanisms underlying descending modulation of nociceptive neurons are not fully understood. In this symposium, known mechanisms underlying descending modulation system via RVM will be presented, and the modulation of nociceptive neurons under pathological conditions will be discussed.
(COI: No)

CS07-3

Chronic stress and pain

Kiyama, Hiroshi (*Grad.Sch.Med. Nagoya Univ., Nagoya, Japan*)

Patients suffering from cryptogenic symptoms, such as chronic fatigue syndrome (CFS) and fibromyalgia syndrome (FMS), display chronic widespread pain (hyperalgesia and/or allodynia) and multiple symptoms, including severe fatigue, sleep disturbance, malaise and cognitive dysfunction. Among these symptoms the abnormal pain sensation could be the most serious, however its pathophysiology remains unknown. We used a multiple continuous stress (CS) model in rat, which were housed in a cage with a low level of water (1.5 cm in depth) for 5 days. Using the von Frey and Randall Seritto tests, the model rat showed the mechanical allodynia at plantar skin and mechanical hyperalgesia at the anterior tibialis (i.e. muscle pain). Although no signs of inflammation and injury incidents were observed in both the plantar skin and leg muscles, microglial accumulation and activation were observed in L4-L6 dorsal horn of CS rats. To evaluate an implication of microglia in pain, minocycline was intrathecally administrated. Minocycline significantly attenuated CS-induced mechanical hyperalgesia and allodynia. Although the mechanism underlying the local activation of microglia remains obscure, these results indicated that activated microglia were involved in the development of abnormal pain in CS animals, suggesting that the pain observed in CFS and FMS patients may be partly caused by a mechanism in which microglial activation is involved.
(COI: No)

CS07-4

What is the biological significance of emotion in pain and its regulation?

Kato, Fusao (*Dept Neurosci, Jikei Univ Sch Med*)

According to the definition by Charles Darwin (1872), emotion is automatic responses to events in an organism's environment that help it to survive. Primordial sensory sensations, such as taste, olfaction and nociception, are often the detectors of aversive, potentially harmful events closely related with survival, and thus with the emotion. In addition to the neural connections that allow avoiding on-going harmful situations (withdrawal reflex, e.g.), the suffering function of the pain is thought to have evolved so that it enables the organism to alter its behavioral program through neural plasticity after the aversive experience. The capsular part of the central nucleus of the amygdala receives direct nociceptive information from the spinal cord via the spino-parabrachio-amygdaloid (SPA) pathway, in addition to the indirect thalamocortical pathway. This SPA pathway has been identified to be essential in the nociception-emotion link and its plasticity. Unlike acute pain that has pro-survival beneficial functions, the chronic pain, characterized by its potent suffering aspect, is pathological and of no biological significance. In human patients, chronic pain is strongly linked with aberrantly elevated spontaneous activities in brain areas involved in emotion, such as the amygdala. In animal models of chronic pain, a robust synaptic potentiation has been described in the amygdala. On the basis of our electrophysiological and functional MRI studies in rodent models of chronic pain, we argue that the amygdala would be an important target of the chronic pain therapies.

(COI: No)

CS07-5

Neural mechanisms of anti-nociceptive effect induced by gentle skin stimulation

Hotta, Harumi (*Dept Auton Neurosci, Tokyo Metropol Inst Gerontol, Tokyo, Japan*)

Somato-sympathetic reflexes induced by noxious stimuli are involved in pathogenesis of chronic pain, therefore their managements are of clinical importance. In anesthetized rats, skin touch can suppress somato-cardiac sympathetic C reflex induced by excitation of unmyelinated C-afferent fibers of the plantar nerve. The effect was dependent on texture in contact with skin: a disc having orderly arranged microcones (similar to a fingertip), but not a flat disk, was effective. Similarly, in conscious humans, microcones, but not flat disc, suppressed noxious heat-induced somato-cardiovascular responses. To clarify further mechanisms, we compared effects between touch with and without microcones. Tactile perception or glucose metabolism in the somatosensory cortices (measured by positron emission tomography) was not different between two different touch. However, the metabolism of anterior cingulate cortex was higher during touch with microcones. Among three different types of low-threshold mechanoreceptive fibers of skin, $A\delta$;- and C-fibers, but not $A\beta$-fibers, showed greater excitations during touch with microcones. The inhibitory effect of somato-cardiovascular reflexes by microcone was abolished following intrathecal application of naloxone into the lumber spinal cord. We suggest that excitation of low-threshold $A\delta$ and C afferents releases spinal opioids, resulting in the inhibition of nociceptive transmission into the sympathetic nerves. Such spinal mechanisms apart from cognition may help to explain relief of chronic pain by gentle somatic stimulation, such as Japanese acupuncture.

(COI: No)

CS07-6

Role of anterior cingulate cortex in descending antinociceptive effects produced by acupuncture stimulation

Toda, Kazuo (*Integr Sensory Physiol, Nagasaki Univ, Nagasaki, Japan*)

It is well-known that descending inhibitory mechanisms are strongly involved in acupuncture analgesia.This descending inhibition is the most powerful analgesic mechanism in the CNS. Generally, descending pathways project to the spinal cord from various pain suppression centers as revealed by neuroanatomical studies.These centers include the periaqueductal gray matter (PAG), nucleus raphe magnus (NRM) and other areas in the ventromedial medulla. On the other hand, it is recently reported that the anterior cingulate cortex (ACCX) is involved in emotional pain perception and modulating pain sensation. Indeed, nociceptive responses can be recorded non-somatotopically in the rat and these responses are well modulated under physiological disturbance, such as, stress. Anatomical studies also indicate that there are dense descending projections from the ACCX to the PAG. Because the PAG is a key link in the descending analgesic system projecting to the spinal cord through the NRM, it can be assumed that the ACCX is concerned with the control of the descending analgesic system activated by acupuncture stimulation. However, there are no available data concerning the response properties and the role of the ACCX neurons following acupuncture stimulation. The present study shows that acupuncture stimulation can predominantly provoke inhibitory effects on the spontaneous activities of descending ACCX neurons. Since it is reported that a majority of the functional connection between ACCX and PAG is inhibitory, disinhibition of the PAG is closely related to produce descending acupuncture analgesia.

(COI: No)

Committee Symposium 8

Japan-Germany Joint Symposium

New bridge between Germany and Japan for basic medical sciences

(March 23, 9:00～10:30, Room E)

CS08-1

Anatomische Gesellschaft and Japanese Association of Anatomists (JAA): a long lasting relationship between anatomists of both societies: past, present and future

Paulsen, Friedrich P. (*Department of Anatomy II, Friedrich Alexander University Erlangen-Nuremberg*)

In 1870, the new Japanese Government had decided the implementation of the German Medical curriculum. Thus, many Japanese studied medicine in Germany or worked as medical doctors in Germany. This was interrupted by World War II, whereupon both countries were faced with severe destruction. Nevertheless, based on the old connections, Japanese students started coming back to Germany comparatively soon thereafter. Here, the German Departments of Anatomy played a crucial role. The talk will describe some of these old connections and will highlight successful collaborations between Japanese and German Anatomists such as those between Yutaka Sano and Wolfgang Bargmann or between Chihiro Yokochi and Johannes Rohen. The Chihiro and Kiyoko Yokochi Fund that is open to young German anatomists, but still needs collaborations with Departments of Anatomy in Japan, will be introduced and explained as an easy option for exchange of young researchers from Germany with Departments of Anatomy in Japan. Moreover, the talk will give an overview about research areas and current themes in Departments of Anatomy across Germany to provide JAA members with an idea of how anatomy is currently organized and working in Germany. Finally, a major intention of the talk will be to present the Anatomische Gesellschaft and its members as an attractive partner for JAA, and to stimulate, once again, a deeper connection between anatomists of both societies.

(COI: No)

CS08-2

My teachers in Japan and Germany -glycine oder das Glyzin-

Sato, Kohji (*Sch.Med.Hamamatsu Univ., Shizuoka, Japan*)

Here, I want to present the audience my three teachers in Japan and Germany. The first teacher is Prof. Keiya Tada. He was a former professor of the department of pediatrics, Tohoku Univ.. He devoted his life to studying congenital metabolic disorders, especially, hyper-glycinemia, which is manifested by very high concentrations of glycine in blood, etc and very sever symptoms including seizures. He found that the glycine cleavage enzyme is defected in the patients. As this disease has very severer neurological symptoms compared with other metabolic disorders, he asked me to investigate where the glycine cleavage enzyme is in the CNS. To do this, I went to the departmemt of Anatomy in Osaka Univ.. There, I met the second teacher, Prof. Masaya Tohyama. He is a specialist of neuroanatomy. I learned immunohistochemical technique and found that the glycine cleavage enzyme is specifically expressed in astorcytes. After that, I learned in situ hybridization technique and investigated the distributions of glycine receptors. From that point, I decided to deeply investigate the glycinergic system. After getting PhD degree in Osaka Univ., I joined the department of neurochemistry, Max-Planck institute, Frankfurt. There I met the third teacher, Prof. Heinrich Betz, who had cloned many glycine receptors. In his laboratory, I studied glycine transporter regulation via phosphorylation. Through above-mentioned stories, I want to show the audience what the glycinergic system is and my sweet memories with the teachers in Japan and Germany.

(COI: No)

CS08-3

Membrane biophysics: Quantitative understanding of neural signaling

Sakaba, Takeshi (*Grad Sch Brain Science, Doshisha Univ*)

In the past 15 years, we have examined the mechanism of transmitter release at the large nerve-terminal called the calyx of Held located in the brainstem, Ca-uncaging method, which has been introduced first by Almers, Neher and Zucker and others for studying Ca-secretion coupling in secretory cells, has been used for determining the Ca-dependence of neurotransmitter release and synaptic vesicle replenishment at the large central synapse. More recently, in collaboration with German scientists, we extended the study using super-resolution microscopy (STED), molecular genetics (the use of KO and Ki mice) and biochemistry, to understand the molecular mechanisms of neurotransmitter release. Also, in order to compare the properties among different types of synapses, we are currently running the collaborative program among Japanese and European synaptic physiologists. Such an effort is important for obtaining the basic principle of synaptic transmission in a quantitative manner.The study was supported by Core-to-Core Program A. Advanced Research Networks.

(COI: No)

Committee Symposium 9

Japan-China Joint Symposium - Towards FAOPS2019

Recent Advances in Organellar Morphology and Physiology

(March 23, 13:30～15:00, Room E)

CS09-1

Polar body genome transfer for preventing the transmission of inherited mitochondrial diseases

Sha, Hongying; Wang, Tian; Ji, Dongmei; Zhang, Helen L; Chen, Dawei; Cao, Yunxia; Zhu, Jainhong (*Dept Neurobiol, Inst Brain Sci, Sch Basic Med Sci, Fudan Univ, Shanghai, China*)

Inherited mitochondrial DNA (mtDNA) diseases transmit maternally and cause severe phenotypes. Since no effective treatment is available, nuclear genome transfer between patients' and healthy eggs to replace mutant mtDNAs holds promises. Since polar body contains very few mitochondria and share same genomic scale as oocyte, here we perform polar body transfer to prevent the transmission of inherited mtDNA variants. We compare the value of different germline genome transfer, i.e., spindle-chromosome transfer (ST), first polar body transfer (PB1T), pronuclear transfer (PNT), and second polar body transfer (PB2T), to exchange mtDNA genotype in a mouse model. Reconstructed embryos support normal fertilization and produce live offspring. Strikingly, genetic analysis confirms polar body generated-offspring possesses minimal donor mtDNA carry-over compared with spindle-chromosome (low/medium carry-over) and pronuclear (medium/high carry-over) transfer. All PB1T offspring contains undetectable mtDNA heteroplasmy level (0%), which is significantly lower than ST offspring (5.53% ± 1.43%). PB2T infants possessed 1.7% ± 2.8% mtDNA carry-over on average, which is significantly lower than PNT infants (23.7% ± 11.1%). Importantly, all F2 PB1T progeny still harbors undetectable heteroplasmy level. Our preclinical model demonstrates polar body transfer, especially PB1 transfer, which circumvent the possibility of mtDNA heteroplasmy in offspring, holds great potential in preventing the transmission of inherited mtDNA diseases.

(COI: No)

CS09-2

Mitochondrial DNA damage and disease

Zhang, Xiuying; Zhou, Deshan (*Cap.Med.Univ.Sch.Med., Beijing, China*)

Human mtDNA is a 16, 569 bp, plasmid-like circular DNA molecule that encodes 13 gene products required for electron transport and oxidative phosphorylation. Increased ROS production by mitochondria is likely to damage mtDNA and impair mitochondrial function leading to their inability to completely reduce molecular oxygen and further injury to the mitochondria. The lack of protective histone and reduced fidelity of DNA replication and abundant DNA repair mechanisms make mitochondrial genome more sensitive to the attacks of free radicals produced in mitochondria, or other DNA damaging agents. Mitochondrial DNA (mtDNA) is 10 to 20 times more vulnerable to oxidative damage and subsequent mutations than nuclear DNA. Only base excision (BER) and perhaps single strand break repair (P-PARP) are functioning in mitochondria. Neil1 and OGG1 are two major repair enzymes for mtDNA. In the studies of alcoholic liver disease, we found that ethanol feeding in IL-6 KO mice induced significant mtDNA deletions that were associated with the loss of the mitochondrial membrane potential, greatly diminished levels of cytochrome c oxidase subunit-I synthesized in the mitochondria, along with diminished ATP and mtDNA repair enzymes levels. Thus oxidative injury that was fairly well tolerated in WT mice fed ethanol had highly deleterious effects in IL-6 KO mice. In these experiments we have shown that IL-6 is necessary to provide cell cycle checkpoints via induction of p21 and p53, and stimulate the transcription of DNA repair enzymes.

(COI: No)

CS09-3

Ion channels in perinuclear endoplasmic reticulum membrane

Maruyama, Yoshio (*Dept Cell Physiol, Grad Sch Med, Tohoku Univ, Sendai, Japan*)

Finishing *in situ* identification of ion channels in the cell membrane, patch-clampers intend the same in the organelle membranes including those in the endoplasmic reticulum (ER) or the nucleus. Then immediately we face to a critical problem; how one can say that our membrane preparation keeps its normal orientation without contamination of the plasma membrane, and is suited to every patch-clamp technique. We discuss it in the section of making preparation while showing its shape.

I demonstrate the presence of some ion channels in the peri-nuclear ER membrane in mammalian exocrine gland cells, mouse pancreatic acinar cells. I show that 1) Maxi-K^+ channels, its expression depending animal age, 2) anion-channels balancing the electroneutrality, 3) water-channels regulating compartment volume by osmosis, and 4) unknown other channels.

Applying capacitance measurements to the preparation, I show that a rise in the compartment Ca^{2+} increases membrane capacitance, an indicator of the membrane area. It suggests that the rise connects adjacent compartment together.

I propose a scenario of the peri-nuclear ER shape change (compartment change). As cell s up-growing proceeds, their ATP content increases. The Ca^{2+} pump in the ER (SERCA) functions and consequently leads to the increase in compartment Ca^{2+} concentration. Then it activates Maxi-K^+ channels and Cl^- channels, which together trigger the water osmosis. Meanwhile the compartment Ca^{2+} connects the neighbor compartment together. Thus, the area and volume of the ER extend for the protein formation and storage.

(COI: No)

CS09-4

Ultrastructural analyses of the formation of autophagic isolation membrane in mammalian cells

Waguri, Satoshi (*Fukushima Med. Univ. Sch. Med., Fukushima, Japan*)

Recent findings have suggested that autophagic isolation membrane (IM) originates from a domain of endoplasmic reticulum (ER) called "omegasome". However, its fine structure and detailed positional relationships to the ER and IM during autophagosome formation remain unclear. In the present study, we used *Atg3*-deficient mouse embryonic fibroblasts (MEFs) expressing a marker of omegasome, GFP-tagged double FYVE domain-containing protein 1 (GFP-DFCP1), and found that GFP-DFCP1 was localized on tubular or vesicular elements adjacent to the IM rims by correlative light and electron microscopy and immuno-electron microscopy. Moreover, we developed a fixation protocol for electron microscopy (EM) using a mixture of paraformaldehyde, glutaraldehyde, and osmium tetroxide as a primary fixative, for clear-cut detection of IM and associated vesicular or tubular structures. By EM analyses including serial ultra-thin sections and electron tomography, we observed a cluster of thin tubular structures between the IM edges and ER, part of which were continuous with IM and/or ER. These IM-associated tubular structures (IMATs) were observed in several cell lines and MEFs deficient for *Atg5*, *Atg7*, or *Atg16L1*, but not in *FIP200*-deficient cells, suggesting that they are relevant to earlier events in autophagosome formation. Taken together, our findings indicate that IMATs represent a part of omegasome during completion steps of autophagosome formation.

(COI: No)

Committee Symposium 10

Future prospect of anatomical, pharmacological, and physiological journals

(March 23, 13:30～15:00, Room J)

CS10-1 JPhysS's way to go as an international scientific journal in Physiology

Ishikawa, Yoshihiro CVRI, Yokohama City Univ Sch Med, Yokohama, Japan

CS10-2 Anatomical Science International: past, present and future

Yorifuji, Hiroshi Grad. Sch. Med. Gunma Univ., Maebashi, Japan

CS10-3 New Platform from International Pharmacological Sciences

Fukunaga, Kohji Dept Pharm, Grad Sch Pharm Scis, Tohoku Univ, Japan