東京医科歯科大学

TOKYO MEDICAL AND DENTAL UNIVERSITY

International Summer Program 2012

26—29 August 2012

Brain and Mind: Neuroscience Up-to-date

PROGRAM & ABSTRACT BOOK

Contents

ISP2012 SCHEDULE

Day / Time	*Event*	*Venue*
Sunday, 26 August: Registration and Welcome Reception		
17:00–17:30	**Registration**	M&D Tower 2F Auditorium 1
17:30–18:00	**Orientation** MC: Kevin Cleary (TMDU) Introduction to ISP: Hidehiro Mizusawa (ISP2012 WG Chairperson, TMDU) Program Schedule: Ikuko Morio (Director, International Exchange Center, TMDU)	
18:00–20:00	**Welcome Reception** MC: Kevin Cleary (TMDU)	"Grill Saints"
Monday, 27 August: Lecture Course, Day 1		
9:00–9:10	**Opening Remarks** Junji Tagami (Dean, Faculty of Dentistry, TMDU)	M&D Tower 2F Auditorium 1
9:10–12:55	**Lecture Course 1 "Neuroscience Research Methods"** Chair: Kohichi Tanaka (TMDU) / Itsuki Ajioka (TMDU)	
9:10–9:50	Sumio Terada (TMDU) Title: Microscopic and spectroscopic dissections of cytosolic and cytoskeletal protein dynamics in neurons	
9:50–10:30	Yuriko Sugiuchi (TMDU) Title: Neural mechanisms for generating rapid eye movements: Electrophysiological and anatomical study in systems neurophysiology	
	 **Coffee Break, 15 min**	
10:45–11:30	Atsushi Iriki (RIKEN Brain Science Institute) Title: Neurobiology of primates' cognitive niche-construction	
11:30–12:15	Takeo Yoshikawa (RIKEN Brain Science Institute) Title: Genetic approaches of schizophrenia research from human and animal models	
12:15–12:55	Masahiko Shimada (TMDU) Title: Contemporary orofacial pain management	
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14:30–15:00	**Introduction to the University** Ikuko Morio (Director, International Exchange Center, TMDU)	M&D Tower 2F Auditorium 1
15:00–17:00	**Mini-Lectures & Laboratory Visit**	
17:00–18:30	**Poster Session** Supervisor: Takashi Ono (TMDU)	M&D Tower 2F Foyer

Day / Time	*Event*	*Venue*

Tuesday, 28 August: Lecture Course, Day 2

9:00–12:45	**Lecture Course 2 "Research on Neurological Disease-Mental Illness"** Chair: Hitoshi Okazawa (TMDU) / Masato Taira (TMDU)	M&D Tower 2F Auditorium 1
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9:40–10:20	Kohichi Tanaka (TMDU) Title: Genetic animal models of neuropsychiatric disorders	
	 **Coffee Break, 15 min**	
10:35–11:20	Don W. Cleveland (Ludwig Institute for Cancer Research, UC San Diego, USA) Title: Understanding ALS: from mechanism to therapy	
11:20–12:05	Shinsuke Shimojo (California Institute of Technology, USA) Title: Crossmodal Interactions – Attention and synchrony	
12:05–12:45	Toru Nishikawa (TMDU) Title: Molecular basis of schizophrenia	
12:45–14:30	**Lunch Break**	
14:30–16:30	**IEC Program**	
14:30–15:00	**Library Tour**	M&D Tower 3F Library
15:00–16:30	**Optional Programs** ・Exposure to Japanese culture ・Guided walk in the TMDU neighborhood	
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17:20–17:30	**Commemorative Photograph**	M&D Tower 26F Faculty Lounge
17:30–19:30	**Social Hour** MC: Kevin Cleary (TMDU) ISP2012 Address : Takashi Ohyama (President, TMDU) Presentation of ISP2012 Certificates: Hajime Karasuyama (Associate Managing Trustee / Planning and International Exchange, TMDU)	

Day / Time	*Event*	*Venue*

Wednesday, 29 August: ISP Symposium 2012 "Brain and Mind"

9:00–9:10	**Opening Remarks** Yasuhito Yuasa (Dean, Faculty of Medicine, TMDU)	M&D Tower 2F Akio Suzuki Memorial Hall
9:10–13:05	**Morning Session** Chair: Hidehiro Mizusawa (TMDU) / Kei Watase (TMDU)	
9:10– 9:50	Hitoshi Okazawa (TMDU) Title: Pathomechanisms of Intellectual Disabilities linked to a new RNA splicing protein, PQBP1	
9:50–10:35	Don W. Cleveland (Ludwig Institute for Cancer Research, UC San Diego, USA) Title: Mechanism and therapy in neurodegenerative disease: ALS and beyond	
	 **Coffee Break, 15 min**	
10:50–11:30	Hidehiro Mizusawa (TMDU) Title: Spinocerebellar ataxia type 31: A new RNA disease	
11:30–12:15	Shinsuke Shimojo (California Institute of Technology, USA) Title: Sensory substitution, crossmodal plasticity, and the third kind of "qualia"	
12:15–12:55	Masato Taira (TMDU) Title: Neural mechanisms for navigation: Comparison between the medial parietal region and the parahippocampal gyrus	
12:55–13:05	**Closing Remarks** Ikuko Morio (Director, International Exchange Center, TMDU)	
13:05–14:30	**Lunch Break**	
14:30–15:30	**Returning Procedure**	

Thursday, 30 August: ISP Special Selection (Special Selection Participant only)

9:00–10:00	Written Examination	Building 1 West 6F Department of Dentistry Seminar Room
10:00–13:00	**Lunch Break**	
13:00–	Oral Examination	

Takashi Ohyama

President
Tokyo Medical and Dental University

Message from the President

Tokyo Medical and Dental University (TMDU) is unique in the respect that all of our divisions are related to education of health care professionals and/or the pursuit of bioscience research. As shown by our university mission, “Cultivating Professionals with Knowledge and Humanity”, all of the faculty and staff at TMDU have been doing their best to help our students become world-class health care professionals and/or bioscience researchers.

An important part of our history, which has now passed the milestones of 80 years as a dental school and 50 years as a medical school, has been the precious experience of teaching many international students, who I believe have helped advance the level of medicine and dentistry in their home countries after returning to practice and teach. On our side, we have found the experience of educating international students to be invaluable in helping us appreciate different cultures and cultivate intellectual sympathy. Furthermore, it is a great honor and pleasure for us to know that our international student alumni have continually encouraged their friends, colleagues and students to join us in our academic endeavors.

In terms of international outreach, we are especially proud of three overseas education/ research collaboration centers — in Ghana, Chile, and Thailand — which we founded in recent years. At these centers we aim to promote collaborative research and to advance the professional development of medical and dental professionals in each local area. For example, we exchange students and faculty members with our partner institutions, sponsor training programs and support other outreach activities.

As an important part of our international activities based here in Japan, we are very pleased to be able to organize our fourth International Summer Program, ISP2012, which this year focuses on the increasingly important area of neuroscience. I hope that your experience at ISP2012, in addition to helping you develop professionally, will pique your academic curiosity and encourage you to explore the unique features of our university.

Kikuo Ohno

Trustee, Vice-President for
Planning and International Exchange
Tokyo Medical and Dental University

Welcome to ISP2012

It is our great pleasure to welcome you to ISP2012, our fourth annual International Summer Program. We are very pleased to report that this year we accepted 25 excellent young researchers and students from Asia to ISP.

ISP2012's theme is "Brain and Mind: Neuroscience Up-to-date". The three days of ISP2012 will feature lecture courses taught by leading scientists from overseas and Japan, a symposium, and many other events, including a library tour, mini-lectures, laboratory visits, cultural programs, a poster session and social events. In addition, this year we are initiating the "ISP Special Selection" in which selected students will have the opportunity to apply for entrance to a TMDU PhD program on the fourth day of ISP.

The topics to be presented at ISP2012 include research methods in neuroscience and current research on neurological diseases, mental illnesses, pain management and related areas. Clinically-oriented basic research, which is critically important for the development of clinical applications for medical treatment, will also be presented in the lecture courses.

At TMDU we are putting a great deal of effort into not only educating our students, at both the undergraduate and graduate levels, but also into the promotion of interdisciplinary research in medical and dental science. As a reflection of these efforts, it was recently reported that TMDU topped the category of citations per paper in the 2012 QS Asian University rankings. In addition, TMDU is becoming increasingly attractive to promising students and young researchers from Asia and beyond, and we had 211 international students in 2011.

On behalf of the organizing committee, I would like to express our sincere gratitude to all of our participants in ISP2012. I am sure that this program will yield many fruitful results and will also help build bridges of friendship between all of the participants.

Profiles and Abstracts of Lecture Course Speakers

Sumio Terada

(Tokyo Medical and Dental University)

Biodata

Prof. TERADA, Sumio is a Professor in the Department of Neuroanatomy and Cellular Neurobiology, the Center for Brain Integration Research at Tokyo Medical and Dental University. Prof. Terada started his career as a resident in surgery at Saitama Medical School Hospital after his graduation from the University of Tokyo, Faculty of Medicine in 1989. He then joined the Division of Medical Sciences at the University of Tokyo Graduate School as a PhD candidate in 1991, obtained his degree in 1996, and joined the faculty as an assistant professor and then as a lecturer in the Department of Cell Biology and Anatomy between 1993 and 2005. Since 2005, he has been in his present position at TMDU and his research field has been in the cytoskeletal dynamics, the intracellular transport mechanism of cytosolic proteins and the development of new spectroscopic techniques. In 2002, Prof. Terada received the 2nd Japan Neuroscience Society Young Investigator Award.

Lecture Course: Microscopic and spectroscopic dissections of cytosolic and cytoskeletal protein dynamics in neurons

Abstract

Neuronal cells such as neurons and glial cells are atypical and asymmetric in their morphology; both of them having long processes. They have to endure the burden of energy-consuming long-distance intracellular transport, and develop specialized cytoskeletal structures. Both intracellular transport and cytoskeletal dynamics are inseparably interrelated, and essential for cellular homeostasis and function. In neurons, these cytoskeletal protein transport and dynamics have been investigated as a slow axonal transport study. This lecture will explain its brief history with special reference to microscopic and spectroscopic techniques that we have experienced.

Based on the classic pulse labeling studies, especially regarding cytoskeletal proteins on slow axonal transport, Lasek's group proposed the cytoskeletal polymer sliding theory as a possible slow axonal transport mechanisim. They considered the polymer sliding as a prerequisite for slow axonal transport of other general cytosolic proteins, and further claimed "structural hypothesis" that defines the polymer sliding for other cytosolic proteins to ride piggy-back. On the other hand, Ochs's group insisted "unitay hypothesis" that can explain various slow axonal transport rates with a single putative motor origin. They speculated that the variation of the transport rates might reflect (1) the different affinity between cytosolic-protein cargoes and a putative motor molecule and/or (2) the changing interaction beween transporting complex and intraaxonal environments. "Unitary hypothesis" is based on the cytoskeletal subunit transport theory, because the moving cytoskeletal proteins pulse-labeled were contained mainly in the biochemcally soluble fractions. Following studies implicated that the motor molecule for slow transport is Kinesin-1, the same motor for fast axonal tranport of membranous organelles. These lines of evidence justified the "unitary hypothesis" over the "structural hyphthesis" but the dispute between polymer sliding and subunit transport theories has not fully been resolved yet.

In this lecture, I will address the controversies and their possible solutions, mainly based on our experimental evidences.

[References]

1) Lasek RJ et al.: J Cell Biol 99, 212s-221s, 1984. 2) Tytell M et al.: Science 214, 179-181, 1981. 3) Lasek RJ: J Cell Sci Suppl 5, 161-179, 1986. 4) Ochs S: A unitary concept of axoplasmic transport based on the transport filament hypothesis. In "Recent advances in myology: Proceedings of the third international congress on muscle diseases," 189-194 (Excerpta Medica, Amsterdam, 1975). 5) Ochs S: J Physiol 253, 459-475, 1975. 6) Okabe S et al.: J Cell Biol 121, 375-386, 1993. 7) Takeda S et al.: J Cell Biol 127, 173-185, 1994. 8) Terada S et al.: Science 273, 784-788, 1996. 9) Terada S et al.: Cell 103, 141-155, 2000. 10) Yabe JT et al.: J Cell Sci 112, 3799-3814, 1999. 11) Xia CH et al.: J Cell Biol 161, 55-66, 2003. 12) Wang L et al.: Nat Cell Biol 2, 137-141, 2000. 13) Wang L, Brown A: Mol Biol Cell 12, 3257-3267, 2001. 14) Yan Y, Brown A: J Neurosci 25, 7014-7021, 2005. 15) Yuan A et al.: J Neurosci 29, 11316-11329, 2009. 16) Terada S et al.: EMBO J 29, 843-854, 2010

Yuriko Sugiuchi

(Tokyo Medical and Dental University)

Biodata

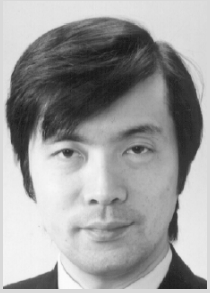
Yuriko Sugiuchi is an Associate Professor in the Department of Systems Neurophysiology at Tokyo Medical and Dental University. She started basic research in neurophysiology in the Department of Physiology (Prof. Yoshikazu Shinoda) when she was a medical student. After her graduation from the School of Medicine at TMDU, she was also trained in neuro-otology in the Department of Otorhinolaryngology and continued her basic research on the vestibular and cerebellar systems. Since 1996, she has been in the Department of Physiology and her main research field has been in the oculomotor system. She received the 23rd Barany Society Young Investigator Award in Paris in 2004. Dr. Sugiuchi has been a member of the editorial board of "Vestibular Reseach" since 2007.

Lecture Course: Neural mechanisms for generating rapid eye movements: Electrophysiological and anatomical study in systems neurophysiology

Abstract

Neuroscience covers very wide range of fields from basic science to clinical application and from molecular biology to whole animal study. The final goal of neuroscience is to understand the way how the brain works. This lecture will introduce some of classical basic methods (electrophysiological and anatomical methods) for analyzing functions of the mammalian central nervous system, using an example of the oculomotor system for understanding neural mechanisms of motor control that our group has been investigating in higher mammals. These methods are basic techniques that are indispensable for understanding other brain functions in systems neuropnysiology in general.

The fovea is the centeral part of the macula of the retina, and is responsible for our central, sharpest vision. In primates, when something interesting suddenly appears somewhere in the visual field, the line of sight moves very quickly, in order to orient the fovea towards the visual target and obtain precise visual information. This kind of eye movement is called saccadic eye movements (saccades). Regarding the neural mechanisms for generating saccades, many lesion and stimulation studies have shown that the superior colliculus plays important roles from long time ago. But the output pathways from the superior colliculus to extraocular muscles remain undetermined. Since the discovery of some neurons in the brainstem that showed characteristic activity patterns related to saccades in the monkey, some hypothetical neural circuits have been postulated to operate mainly from engeneering points of view. This hypothetical diagram for the neural circuits has been widely accepted, but it is lacking in experimental evidences. Our group has been addresssing this issue for the last ten years. In this lecture, I will discuss neural circuits for generating and suppressing saccades revealed by electrophysiological and anatomical methods.



Atsushi Iriki

(RIKEN Brain Science Institute)

Biodata

IRIKI, Atsushi received his Ph.D. in Neuroscience from Tokyo Medical and Dental University in 1986. He held research associate positions at Tokyo Medical and Dental University and then at The Rockefeller University. He joined the faculty of Toho University Medical School as an assistant professor and then as an associate professor in Physiology (1991-1999). In 1999, he returned to Tokyo Medical and Dental University as a full professor and chairman in Cognitive Neurobiology. Since 2004, Prof. Iriki has been the Head of Laboratory for Symbolic Cognitive Development at RIKEN Brain Science Institute. He is a visiting professor of University College London, an adjunct professor of Keio University, and a research professor of Kyoto University.

Lecture Course: Neurobiology of primates' cognitive niche-construction

Abstract

The evolution of the human lineage has involved a continuous process of addition of new kinds of cognitive capacity, including those relating to the manufacture and use of tools and the establishment of linguistic faculties. The dramatic expansion of the brain that accompanied such additions of new functional areas would have supported such continuous evolution. Extended brain functions would have driven rapid and drastic changes in the hominin ecological niche, which in turn demanded further brain resources to adapt to it. In this way, primate ancestors have constructed a novel niche in each of the ecological, cognitive and neural domains, whose interactions accelerated their individual evolution through a process of 'triadic niche construction'. The brain's functional characteristics seem to play a key role in this triadic interaction.

Expansion (or increase in capacity) of organs as an adaptive response to ecological pressures seems to be a general biological and evolutionary tendency to make the phenotypic system robust—the brain will not be an exception. Multi-sensory integration and coordinate transformation for the control of reaching movements in the inhabited space is an essential function of the nervous system, for which evolution finally endowed primates with a well-developed parietal cortex. Such neural enhancement (construction of the neural niche) happened to enable the processing of abstract information, detached from actual physical constraint, by applying and re-using existing principles for spatial information processing to realize novel mental functions (construction of the cognitive niche)—ultimately leading to language. Purposeful manipulation of the body image in space, required for tool use, would have accelerated interactive links between the neural and cognitive niches—tool use requires transformation of various bodily and spatial coordinates, as well as logical and sequential relations of action components.

Tools represent materialized cognitive brain functions. They have been created one after another and incorporated into primate habitats as constituent elements (construction of the ecological niche). A primate-modified environment puts pressure on succeeding generations to adapt to it, perhaps by acquiring further resources for the relevant organs. Epigenetically induced plasticity (including developmental or learning mechanisms) would participate in such processes—and this is a subject for future biological investigations. In this way, extra genomic information could be transmitted between generations via mutual interactions among ecological, neural and cognitive domains of niches, which may have contributed to primates' evolutionary processes (that is, 'triadic niche construction'). Primates', and eventually humans', higher cognitive activity can therefore be viewed holistically as one component in a terrestrial ecosystem.

Takeo Yoshikawa

(RIKEN Brain Science Institute)

Biodata

Dr. Takeo Yoshikawa graduated from Osaka University School of Medicine in 1984. He then took up clinical residential training in the Faculty of Neuropsychiatry at Tokyo Medical and Dental University (TMDU). Prof. Yoshikawa obtained his PhD degree from TMDU in 1991. In 1992, he became an assistant professor at National Institute for Physiological Sciences in Japan. From 1993 to 1997 he worked for the National Institute of Mental Health, (NIH) in the U.S. as a visiting scientist, engaging in the genetic analysis of bipolar disorder. After he came back to TMDU and worked as a psychiatrist, he moved to RIKEN Brain Science Institute and opened the "Laboratory for Molecular Psychiatry" in 1999. Since then, his laboratory has mainly studied schizophrenia from a genetic perspective. Recently his laboratory began to study iPS cells from schizophrenia and autism. He is an editorial board member of several international scientific journals, including Biological Psychiatry.

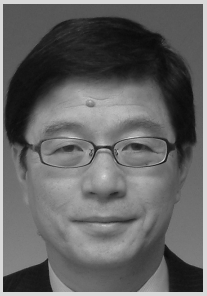
Lecture Course: Genetic approaches of schizophrenia research from human and animal models

Abstract

Schizophrenia is one of the two major, adult-onset mental illnesses and the outcome is debilitating. Its prevalence is about 1%, irrespective of geographical area and era, and therefore it is not a rare disease. However, the precise etiology of the disease has remained elusive. Recently, "GABA hypothesis of schizophrenia" has been proposed, mainly from the findings that the expression levels of multiple GABA-related genes are down-regulated in the postmortem brains from schizophrenia, compared to those from controls. We performed a Genome-Wide Association Study (GWAS) of schizophrenia in the Japanese population. By scrutinizing the data, we noticed the accumulation of association signals from GABA-related genes. Therefore, we decided to perform a replication study. First, we selected 384 tag SNPs (single nucleotide polymorphism) from 25 GABA-related genes and we then genotyped them using 1,500 patients with schizophrenia and 1,500 controls. Among the 25 genes, 11 genes were replicated. These results suggest that the GABAergic system may underlie the genetic architecture of schizophrenia in the Japanese as one of iB primary causes. In the next step, we examined whether schizophrenia-like behavioral phenotypes can be seen in model mice. The mice were doubly hetero-knocked out of the genes encoding Gad67 and Gad65 (wHT KO), both encoding GABA-synthesizing enzymes. The mice showed dampened prepusle inhibition (see next paragraph), increased aggression in a social interaction test and enhanced sensitivity to a hallucinogenic drug, methamphetamine. These results imply that also in mice a deteriorated GABAergic function may lead to human schizophrenia-like phenotypes. The transcript expression analyses using GeneChips detected the altered expression levels of genes that were identified by the aforementioned GWAS. Collectively, our results point to the view that genomic polymorphisms of GABA-related genes are located around one of the central genetic causes of schizophrenia in the Japanese population, by interacting directly/indirectly with other susceptibility genes.

As an alternative approach, the search for genetic basis for "endophenotype" is also promising. Deficits in prepulse inhibition (PPI) are a biological marker for mental disorders including schizophrenia. To unravel the mechanisms that control PPI, we performed quantitative trait loci (QTL) analysis, on 1010 F2 mice derived by crossing C57BL/6 (B6) animals that show high PPI with C3H/He (C3) animals that show low PPI. We detected 6 major loci for PPI. A promising candidate on the chromosome 10-QTL was Fabp7 (fatty acid binding protein 7, brain), a gene predominantly expressed in neural stem/progenitor cells in developmental stage. Fabp7-deficient mice indeed showed decreased PPI. A quantitative complementation test proved Fabp7 as a PPI-QTL gene. Disruption of Fabp7 attenuated neurogenesis in vivo. Human FABP7 showed genetic association with schizophrenia.

Finally, I would like to discuss a potential link between the GABAergic system and aberrant lipid metabolism in terms of schizophrenia pathology.



Masahiko Shimada

(Tokyo Medical and Dental University)

Biodata

Masahiko Shimada is a Chair and Professor of Orofacial Pain Management, Graduate School, Tokyo Medical and Dental University. His research interests fall mainly in the field of Dental Anesthesiology and Orofacial Pain, with current research focusing on neuropathic pain and atypical odotalgia. He graduated from the Faculty of Dentistry of Tokyo Medical and Dental University in 1980, and received his Ph.D from the Graduate School of Tokyo Medical and Dental University in 1984. Prof. Shimada was a visiting Professor at Johns Hopkins University from 1990 to 1992. He worked at Department of Dental Anesthesiology, Okayama University as a Chair and Professor from 1992 to 2006, where he focused his research in the field of biological responses to medical aggression. Prof. Shimada has been at Tokyo Medical and Dental University since 2006. He has been the Director of the Tokyo Medical and Dental University Dental Hospital since 2008 and President of The Japanese Dental Society of Anesthesiology since 2009.

Lecture Course: Contemporary orofacial pain management

Abstract

The objective of this presentation is to introduce the Orofacial Pain Clinic, of the University Hospital of Dentistry, Tokyo Medical and Dental University.

The diseases and symptoms we manage in the Orofacial Pain Clinic are pain, abnormal sensation, sensory paralysis and motor paralysis.

In particular, we manage all forms of pain in the oral and maxillofacial region, including intractable pain related to dental treatment such as neuropathic pain, atypical odontalgia, atypical facial pain and so on.

Prior to treatment, obtaining a comprehensive pain history of the pain problem is an important part of the clinical assessment process. The clinician must inquire about localization, quality, intensity, duration, frequency, triggering factors, improving factors and associated signs and symptoms. A careful pain description is important since several orofacial conditions are diagnosed only upon specific pain features.

Based on physical examination and laboratory tests, diagnosis is performed.

The causes of chronic pain are generally divided into three kinds of pain; nociceptive pain, neuropathic pain and psychogenic or psychiatric pain.

The pain caused by nerve injury is difficult to be control with medications such as anti-inflammatory agents and antibiotics. Medications recommended to use for the neuropathic pain are antidepressants, calcium channel a2-d ligands, topical anesthesia, opioid agonists tramadol and so on[1]. In our clinic, many medicines such as antidepressants, anticonvulsants, and anti-anxiety medications are usually used in the treatment of these patients, together with cognitive-behavioral treatment. The Kampo, a form of Japanese traditional medicine, and acupuncture therapy are also used. In addition, we provide photo dynamic therapy and AC iontophoresis.

The Transdermal drug delivery can be enhanced by chemical and physical enhancement systems; iontophoresis is one of the physical enhancement systems with electrical energy [2,3]. Two electrodes are placed apart from each other on the skin, and charged drugs are transported through the skin by the principle of electrophoresis.

Direct current (DC) is normally used in iontophoresis, but it often causes skin irritations, burns and inflammation. In order to avoid these inferiorities of DC iontophoresis, we clinically apply the alternating current (AC) iontophoresis in our department, with 4% lidocaine hydrochloride as treatment for neuropathic pain in the oral and maxillofacial region.

Atypical odontalgia is a poorly understood chronic pain disorder that presents as a persistent pain in apparently normal teeth and adjacent oral tissues. In addition, atypical facial pain is a persistent pain in the face or intraoral region that does not fit into the diagnostic criteria associated with specific orofacial pain disorders. At the Orofacial Pain Clinic, we have applied acupuncture, pharmacotherapy and psychotherapy so on for 915 patients with atypical odontalgia or atypical facial pain.

(Reference)

[1] RH. Dworkin, AB. et al "Recommendations for the pharmacological management of neuropathic pain: an overview and literature update," Mayo Clin Proc., vol. 85 no. 3 Suppl., pp. S3-14, 2010.

[2] N. Higo, "Recent trend of transdermal drug delivery system development," Yakugaku Zasshi, vol. 127, no. 4, pp. 655-62, 2007.

[3] Y. N. Kalia, A. Naik, J. Garrison, and R. H. Guy, "Iontophoretic drug delivery," Adv Drug Deliv Rev., vol. 56, no. 5, pp. 619-658, 2004.

Itsuki Ajioka

(Tokyo Medical and Dental University)

Biodata

Itsuki Ajioka obtained his PhD from Tokyo Institute of Technology in 2001 by studying on how mature liver hepatocytes proliferate. After that, he started to study cerebral cortical development by focusing on neurogenesis and neuronal differentiation as a JSPS research scholar (2001-2002) and later as an Instructor in the Department of Anatomy at Keio University School of Medicine (2002-2005). Then, he did his second post-doc training by studying on eye development and retinoblastoma at St. Jude Children's Research Hospital in the US (2005-2009) and was appointed as a tenure-track faculty (Assistant Professor) at Keio University. Subsequently, he was appointed as an Associate Professor of the Center for Brian Integration Research (CBIR) at TMDU (2009-). His major concern is to understand how cell cycle regulation is coordinated with brain development and how cell cycle deregulation leads to brain disorder.

Lecture Course: Deregulation of cell cycle on brain disorder

Abstract

Neurons are generated from multi-potent progenitor cells (neural stem cells) during development. Once the daughter cells generated from neuronal progenitors initiate neuronal differentiation program, they become post-mitotic and non-dividing cells. This idea was suggested one century ago by Ramon y Cajal, Nobel Prize winner of 1906, and was experimentally supported by using radioactive thymidine analog, called as "neuronal birth-date study", by Richard Sidman in the 1950s. Although post-mitotic neurons are believed to be in quiescent state (G0 phase) of cell cycle until neurons die, neurons re-enter cell cycle and undergoes S phase in patients of neurodegenerative diseases such as Alzheimer's disease and Parkinson's disease. In addition, when neurons cultured *in vitro* are forced to re-enter the cell cycle, they undergo cell death following S phase progression. Based on these facts, some researchers support the hypothesis that the cell cycle re-entering of neurons is the cause of cell death associated with neuronal degeneration.

Although neurons are believed to be non-dividing cells, neuronal tumors are not rare. RB1 is the first tumor suppressor gene cloned from the family with retinoblastoma and suppresses the transcription of the genes important for S phase progression by binding to E2F transcription factors. By using in vitro cell culture system, the molecular mechanisms of Rb pathway have been extensively revealed during the past 25 years. However, *in vivo* study has been difficult to perform because of the complicated compensations and redundancies among the Rb family members (Rb, p107, p130). Recently, we have carefully investigated the role of each Rb family member for retinal development by generating Rb-single (Chx10-Cre; RbLox/+; p107-/-; p130-/-), p107-single (Chx10-Cre; RbLox/Lox; p107+/-; p130-/-), and p130-single (Chx10-Cre; RbLox/Lox; p107-/-; p130+/-) mice and unexpectedly discovered that differentiated p107-single horizontal neurons, one of the retinal interneurons, proliferate and form tumors with maintaining the feature of differentiated neurons including neurites and synapses. This was the first demonstration that differentiated neurons can proliferate and form cancer while maintaining their differentiated state including neurites and synaptic connections.

Thus, neurons can proliferate in a certain situations. However, the mechanisms of how neurons are protected from cell division in general and how Rb family-deficient neurons overcome this protection and form tumors are still unknown.

In this lecture, I would like to introduce the role of cell cycle regulation in brain development. Also, I would like to introduce our recent research that addressed the mechanisms by which differentiating neurons can proliferate after the loss of Rb family members.

Kohichi Tanaka

(Tokyo Medical and Dental University)

Biodata

KOHICHI TANAKA, M.D., Ph.D.

Professor, Laboratory of Molecular Neuroscience Medical Research Institute Tokyo Medical & Dental University

In 1984 Prof. Tanaka received his M.D. degree from Niigata University. From 1984 to 1986 he was an Assistant Professor at Saga Medical University. After receiving his Ph.D. degree in Medicine in 1990 from Niigata University, he served as a Postdoctoral Fellow at RIKEN. In 1993 Prof. Tanaka became a section chief at the National Institute of Neuroscience. From 1998 he has been a Professor at the Laboratory of Molecular Neuroscience of the Medical Research Institute of Tokyo Medical & Dental University .

Lecture Course: Genetic animal models of neuropsychiatric disorders

Abstract

Despite massive research efforts, the pathogenesis and pathophysiology of neuropsychiatric disorders remain largely unknown. Although modeling of human neuropsychiatric disorders in animals is challenging, animal models are necessary for understanding disease pathophysiology and for developing the treatments. This lecture will cover the validation and use of animal models of neuropsychiatric disorders. Neuropsychiatric disorders focused will include obsessive-compulsive disorder (OCD) and glaucoma.

There is a growing body of evidence implicating an increased ratio of excitation/inhibition in the pathophysiology of neuropsychiatric disorders, including schizophrenia, OCD, autism and glaucoma. Glutamate is the primary excitatory neurotransmitter in the mammalian central nervous system. In order to ensure normal neurotransmission, the extracellular glutamate concentration is controlled mainly by glial glutamate transporters GLT1 and GLAST. We generate animal models for neuropsychiatric disorders, in which a ratio of excitation/inhibition is increased by genetic down-regulation of glial glutamate transporters. Downregulation of glial glutamate transporters results in decreased uptake of glutamate and elevated glutamate overstimulates glutamate receptors.

I will show how glutamate transporters GLT1 conditional knockout mice (GLT1 cKO mice) exhibit physical tics and compulsive grooming behavior leading to facial hair loss and skin lesions; these behavioral abnormalities are considered as autism spectrum disorders (ASDs) and OCD-like behaviors. In contrast, GLT1 cKO mice do not show increased anxiety-like behavior, other OCDs-like behavior, or ASDs-like impaired social behavior. Electrophysiological studies reveal increased excitatory neurotransmission during repetitive stimulation of cortico-striatal synapses. Furthermore, treatment of memantine, an open channel blocker of NMDA-type glutamate receptor, rescues excessive grooming and physical tics. These findings demonstrate glutamatergic hyperactivity in cortico-striatal synapses due to the dysfunction of GLT1, a finding that is important for the pathogenesis of compulsive-repetitive behaviors.

I also show that mice deficient in the glutamate transporters GLAST demonstrate spontaneous retinal ganglion cell (RGC) and optic nerve degeneration despite exhibiting normal intraocular pressure (IOP). In GLAST-deficient mice, both glutamate excitotoxicity and oxidative stress contribute to RGC degeneration. These mice are the first animal models of normal tension glaucoma (NTG) that offer a powerful system for investigating mechanisms of neurodegeneration in NTG. Next, we investigated whether GLAST mutations play roles in human glaucoma phenotypes. We identified two novel missense mutations that decreased a capacity for glutamate uptake. These results suggest that heterozygous mutations in GLAST can lead to decreased glutamate uptake, which can contribute to RGC loss in some glaucoma patients. Furthermore, arundic acid that enhances GLAST expression can rescue RGC death in GLAST heterozygous mice, suggesting that enhancing the function of GLAST may be useful for the treatment of glaucoma.

Thus, useful animal models can serve as essential tools for examining the etiology and treatment of neuropsychiatric disorders.

Don Cleveland

(The Ludwig Institute and Department of Cellular and Molecular Medicine,
University of California at San Diego, USA)

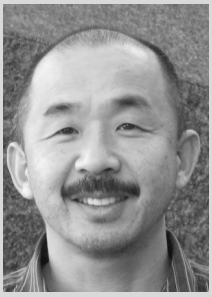
Biodata

Dr. Don Cleveland is Professor and Chair of the Department of Cellular and Molecular Medicine at the University of California at San Diego and a member of the Ludwig Institute for Cancer Research. He initially purified and determined the properties of tau, which accumulates aberrantly in Alzheimer's disease. He uncovered the mechanisms underlying the major genetic forms of Amyotrophic Lateral Sclerosis (ALS) and demonstrated the disease to be non-cell autonomous. He has developed gene silencing therapies for ALS and Huntington's diseases. Dr. Cleveland has been elected to the National Academy of Sciences and the American Academy of Arts and Sciences and has won the Wings Over Wall Street MDA Outstanding Scientist and The Sheila Essey Prize from the American Academy of Neurology.

Lecture Course: Understanding ALS: from mechanism to therapy

Abstract

The genes whose mutation is now known to cause the major neurodegenerative diseases are widely or ubiquitously expressed. This is true for each of the genes now known to cause the fatal, adult motor neuron disease Amyotrophic Lateral Sclerosis (ALS). Unifying features of inherited and sporadic ALS are errors in RNA processing, including cytoplasmic misaccumulation in ALS and frontal temporal dementia (FTD) of TDP-43, an RNA/DNA binding protein and the likely sequestration of one or more RNA binding proteins onto a large hexanucleotide expansion within an intron of the pre-mRNA encoded by the C9orf72 gene. Modeling in mice has demonstrated that one inherited form is caused by mutation in superoxide dismutase (SOD1). Disease mechanism is through an acquired toxicity unrelated to dismutase activity. Toxicity is non-cell autonomous, with mutant SOD1 within motor neurons and oligodendrocytes driving disease onset, while damage within neighboring astrocytes and microglia accelerates disease progression. These findings have validated therapies to slow disease progression, including cell replacement through injection of stem cell derived astrocytic progenitors and infusion of DNA antisense oligonucleotides (ASOs) that direct destruction of SOD1 mRNA widely within the non-human primate nervous system. A final approach is through use of an Adeno-Associated Virus (AAV9) that can cross the blood brain barrier and transduce astroctyes in adult mice. A single peripheral administration of AAV9 encoding an shRNA to SOD1 mRNA slows disease progression, doubling survival after onset.



Shinsuke Shimojo

(California Institute of Technology, USA)

Biodata

For his Biodata, please refer to Prof. Shimojo's Symposium Talk abstract on p24.

Lecture Course: Crossmodal Interactions – Attention and synchrony

Abstract

Crossmodal interactions are important because they provide bases of adaptive behaviors in the daily environment. More theoretically, they are critical for a better understanding of interplays between top-down vs. bottom, conscious vs. subconscious, and sensory vs. motor processes. In this lecture, I will raise over a dozen of big questions about crossmodal interactions (as listed below), to which I can find at least partial empirical answers from my own and other laboratories. They will provide us with a balanced overview of this quickly expanding field on one hand, and locate it in broader biological (i.e. Nature vs. Nurture) as well as computational (i.e. Modularity notion) contexts.

<14 Big Questions (& partial answers) about Crossmodal Interactions>

Q1. Are sensory modalities segregated both anatomically and functionally?

A: Not completely. More vigorous interactions at earlier levels than what used to be believed.

Q2. Are their relationship (connections) flexible?

A: Very flexible, as indicated in early sensory plasticity in animals, as well as sensory substitution studies in humans.

Q3. Is there single clock across sensory modalities, or rather multiple clocks?

A: Evidence for both, depending on what psychophysical paradigm to use.

Q4. Does vision affect other modalities?

A: Of course yes, with the McGurk and the Ventriloquism effects as classical examples, which has led to the common notion that the human is a vision-dominant species.

Q5. Can other modality affect vision? For example, can audition affect vision?

A: According to the latest findings, yes. It necessitates some theoretical modification on the above-mentioned notion that the human is vision-dominant.

Q6. Can audition affect vision, not only quantitatively, but also qualitatively (i.e. in structure of percept)?

A: Yes, the "double flash" illusion would be the strongest evidence.

Q7. Is this auditory "capture" of visual percept really due to early sensory pathways (as opposed to cognitive or selection bias)?

A: Yes, according to various psychophysical control experiments and fMRI/EEG evidence.

Q8. Can a role of one modality in crossmodal interaction be replaced by another modality?

A: This may sound like an odd question, but the answer is mostly yes, and it points to the generality of crossmodal integration mechanisms.

Q9. Can crossmodal synchrony/temporal order modifiable?

A: Yes, via sustained adaptation/aftereffect.

Q10. Are transient signals critical for crossmodal integration(, thus this is what common among cross- and within-modal cases)?

A: Seemingly yes, related to Q8 above.

Q11. What determines ambiguity solving in crossmodal perception?

A: Attention and timing (synchrony) are critical.

Q12. Can crossmodal adaptation/aftereffect occur without contingent exposure?

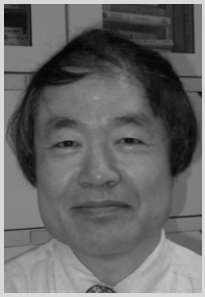
A: Yes, according to the crossmodal temporal rate adaptation findings.

Q13. Computationally, can the Bayesian (maximum likelihood) model explain everything?

A: Mostly, but not quite. The above-mentioned "double flash" (Q6) and the non-contingent adaptation (Q12) may be notable exceptions.

Q14. Does crossmodal integration provide a perceptual basis for perceptual metaphor (and thus, language)?

A: Yes, there are accumulated pieces of evidence for intrinsic crossmodal mapping, which in turn provides a basis for spatial metaphor (such as "up" and "down" both in spatial and tonal domains).



Toru Nishikawa

(Tokyo Medical and Dental University)

Biodata

Toru Nishikawa received his M.D. and Ph.D. from Tokyo Medical and Dental University in 1977 and 1985, respectively. After his residency at the Psychiatry Section of the Tokyo Medical and Dental University Hospital of Medicine and postdoctoral research training at the National Institute of Neuroscience, Japan, and Synthelabo-L.E.R.S, France, and service as section chief at the National Institute of Neuroscience, he was appointed director of Department of Mental Disorder Research at the Institute in 1994. Since 1999, he has been professor and chair of the Department of Psychiatry and Behavioral Sciences of the Graduate School of Medical and Dental Sciences, Tokyo Medical and Dental University Graduate School. He has served on numerous scientific committees and boards in various fields of psychiatry.

Lecture Course: Molecular basis of schizophrenia

Abstract

Schizophrenia is a major brain disorder that has high prevalence, approximately 0.8 % regardless the regions in the world, and a wide variety of long lasting or recurrent symptoms and which often produces serious disability in patients. The rate of complete recovery with intact individual functioning and social ability and of suicide in schizophrenic patients has been estimated fewer than 20 % and about 10 %, respectively. These difficulties prompt us to clarify the biological mechanisms of schizophrenia and to develop more effective therapies for its intractable symptoms. However, as other psychiatric disorders, the lack of apparent neuropathological changes in schizophrenic brains brings a rough road to the investigations in these research fields.

In the present lecture, successful understandings by pharmacological approaches of the molecular basis of schizophrenia and their applications to the development of a novel pharmacotherapy for its treatment-resistant symptoms in our and other laboratories will be introduced and discussed.

A body of evidence has been accumulated indicating that disturbances in dopaminergic and glutamatergic neurotransmission, which play pivotal roles in expression and regulation of mental functions, may be implicated in the pathophysiology of schizophrenia. Thus, the agents that enhance activity of dopamine synapse such as amphetamines, cocaine and L-DOPA (for Parkinson's disease) cause schizophrenia–like positive symptoms, mainly hallucinations and delusions. Moreover, the hallucinatory-paranoid states in schizophrenic patients and induced by these dopamine agonists are improved by antipsychotic drugs that are potent blockers (antagonists) for the D2 type dopamine receptor in a manner in proportion to their potencies for the D2 receptor. On the other hand, the agents that block (antagonize) the glutamate transmission via the NMDA (N-methyl-D-aspartate) type glutamate receptor (NMDA receptor antagonists) elicit schizophrenia-like symptoms, not only positive but also negative, and cognitive deficits, the latters of which are resistant to current antipsychotic drugs and include restrictions in the range and intensity of emotional expression (affective flattening), in the fluency and productivity of thought and speech (alogia), and in the initiation of goal-directed behavior (avolition). In support of these hypotheses, schizophrenic patients have been reported to be much more sensitive to dopamime agonists and NMDA receptor antagonist than healthy volunteers.

We have demonstrated that blockade of the NMDA receptor augments dopamine release in the cerebral cotex, bridging the dopamine and glutamate pathology in schizophrenia. Also, we have found that the facilitation of NMDA receptor functions attenuate the animal models of intractable schizophrenic symptoms. Indeed, the agents enhancing NMDA receptor activities have been documented to ameliorate negative and cognitive disturbances in schizophrenic patients. In addition, we have identified in mammalian brains the presence of D-serine (a D-amino acid) that facilitates NMDA receptor functions and is required for physiological activation of the receptor, while D-amino acids had been believed to be uncommon in mammalian tissues. We, therefore, are currently investigating the molecular and cellular mechanisms of D-serine signaling as the new targets for the development of NMDA receptor regulating drugs and their possible defects in schizophrenia.

Profiles and Abstracts of Symposium Speakers

Hitoshi Okazawa

(Tokyo Medical and Dental University)

Biodata

Neurologist and Neuroscientist. 1984: MD, graduated from The University of Tokyo, School of Medicine. After becoming a staff member of the Department of Neurology, The University of Tokyo, Prof. Okazawa received his PhD degree in 1991 due to the discovery of Oct-3/4:Oct-4:Oct-3 (Cell1990; EMBO J 1991), which is now well known as a key regulator of ES cell and the most important factor for generating iPS cells. After working at the Max Planck Institute for Psychiatry as a staff scientist, he became an assistant professor in the Department of Neurology of The University of Tokyo and started research on polyglutamine diseases. He then expanded the research to include mental retardation and microcephaly, after the discovery of polyglutamine binding protein-1 (PQBP1) (Hum Mol Genet 1999; Neuron 2002). In 2001 he becane the Head, Tokyo Metropolitan Institute for Neuroscience. From 2003, he was named Professor and Chairman, Neuropathology, Tokyo Medical and Dental University.

Symposium Talk: Pathomechanisms of Intellectual Disabilities linked to a new RNA splicing protein, PQBP1

Abstract

We previously discovered a novel gene, polyglutamine tract-binding protein-1 (PQBP1) as a mediator of polyglutamine disease pathology (Waragai et al., Hum Mol Genet 1999; Okazawa et al., Neuron 2002). PQBP1 interacts with multiple polyglutamine diseases proteins including ataxin-1 and huntingtin. PQBP1 possesses a unique C-terminal domain (CTD) and a WW domain (WWD) conserved beyond species (C. elegans, Drosophila and Arabidopsis). PQBP1 interacts with a component of U5 spliceosome, U5-15kD via CTD and another RNA binding protein WBP11/NpwBP/SIPP via WWD. Mass spectrometry analysis revealed that PQBP1 is transiently involved in spliceosome at the critical step for exon-intron junction recognition.

European Consortium of X-linked Mental Retardation/ Intellectual Disability (MR/ID) identified that PQBP1 is a causative gene for non-syndromic ID and syndromic ID including Renpenning syndrome, Golabi-Ito-Hall syndrome and Sutherland-Haan syndrome. Recent analyses revealed the patient frequency among population is comparable to Rett syndrome, indicating the clinical significance of PQBP1.

We have investigated PQBP1 via multiple approaches, and found interacting partner molecules of PQBP1 (Waragai et al., BBRC 2000; Okazawa et al., Neuron 2002), revealed an intrinsically unstructured nature of CTD (Takahashi et al., BBA 2009, 2010), and made various animal models. Drosophila mutant of PQBP1 showed a defect in learning acquisition, which is caused by reduced expression of NR1 subunit of NMDA receptor in projection neurons (Tamura et al., J Neurosci. 2010). Correspondingly, a knockdown mouse model of PQBP1 showed anxiety-related cognitive impairment and reduced expression of NR1 (Ito et al., Hum Mol Genet 2009). An HDAC inhibitor, PBA, recovered these phenotypes in both models. Meanwhile, overexpression of PQBP1 causes delayed degeneration of spinal motoneurons in mouse (Okuda et al., Hum Mol Genet 2003) and lifespan shortening in Drosophila.

We recently generated conditional KO mouse models of PQBP1, and performed systemic analysis of gene expression profiles. I will talk about new mechanisms underlying PQBP1-linked ID unraveled through these analyses.

Don Cleveland

(The Ludwig Institute and Department of Cellular and Molecular Medicine,
University of California at San Diego, USA)

Symposium Talk: Mechanism and therapy in neurodegenerative disease: ALS and beyond

Abstract

The great cell biologists of the 19th century, especially Virchow and Bernard, established the pivotal idea that individual cells function autonomously, while being part of the whole organism. Since then the major neurodegenerative diseases have traditionally been considered mechanistically cell autonomous, meaning that damage within a selective population of affected neurons alone suffices to produce disease. Most of the genes whose mutation is now known to cause the major neurodegenerative diseases are widely or ubiquitously expressed, however, including superoxide dismutase (SOD1) whose mutation causes an inherited form of the fatal, adult motor neuron disease ALS. Modeling in mice has demonstrated that disease mechanism is through an acquired toxicity unrelated to dismutase activity. Use of selective gene excision or viral encoded siRNA has demonstrated that toxicity is non-cell autonomous, with mutant SOD1 within motor neurons and oligodendrocytes driving disease onset, while damage within neighboring astrocytes and microglia accelerates disease progression.

These findings have validated therapies to slow disease progression, including cell replacement through injection of stem cell derived astrocytic progenitors. Another approach now in trial is suppression of mutant SOD1 expression following infusion of DNA antisense oligonucleotides (ASOs) that direct destruction of SOD1 mRNA widely within the non-human primate nervous system. Moreover, because non-cell autonomous toxicity is likely to be generally true in neurodegenerative disease, ASO infusion to target catalytic degradation of specific mRNAs may prove to be a broadly applicable therapeutic approach. For example, polyglutamine expansion in the widely expressed huntingtin protein is the sole cause of Huntington's disease (HD). Infusion into rodents or non-human primates of ASOs targeting huntingtin mRNA effectively lowers huntingtin levels in the striatum and cortex, the primary brain targets of HD pathology. Transient infusion of ASOs into already symptomatic HD mouse models not delays disease progression, but mediates a sustained reversal of disease phenotype that persists for much longer than the huntingtin knockdown. Rather than requiring continuous treatment, these findings establish a feasible therapeutic strategy for sustained HD disease reversal from a "Huntingtin holiday" produced by transient ASO therapy.

Finally, a unifying feature of many neurodegenerative diseases has come from the cytoplasmic misaccumulation of TDP-43, an RNA/DNA binding protein. This is especially so in ALS and in Frontal Temporal Dementia (FTD) Discovery that mutations in TDP-43 cause dominantly inherited ALS and that TDP-43 is misaccumulated in essentially all instances of sporadic ALS has initiated a paradigm shift in defining disease mechanism. So what does TDP-43 do in the nervous system? TDP-43 has binding sites on mRNAs from 6,304 genes, and loss of nuclear TDP-43 (that is seen in neurons of sporadic ALS patients) affects the levels of >600 mRNAs and splicing patterns of 965 mRNAs. RNAs whose levels are most depleted by reduction in TDP-43 are derived from genes with very long introns and which encode proteins involved in synaptic activity, providing a basis for neuronal vulnerability to loss of TDP-43 function. Finally, TDP-43 enhances splicing of an intron within the 3' untranslated region of its own mRNA thereby triggering nonsense mediated RNA degradation, thereby providing a mechanism by which cytoplasmic aggregation will drive runaway synthesis of TDP-43 following any initiating insult that reduces nuclear TDP-43 activity.

Hidehiro Mizusawa

(Tokyo Medical and Dental University)

Biodata

Hidehiro Mizusawa, MD, PhD, is Professor and Chair of the Department of Neurology and Neurological Sciences of the Graduate School of Medical and Dental Sciences of Tokyo Medical and Dental University, where he is also Director of the Center for Brain Integration Research, Director of the School of Medicine, Vice Director of the Medical Hospital, and Associate Managing Trustee for Research. He graduated with an MD in 1976 from the Faculty of Medicine of Tokyo University, where he received his PhD in 1983. After training in internal medicine and neurology at the Tokyo University Hospital and related institutes, he became a Junior Assistant Professor of the Department of Neurology of Tokyo University in 1982. He then joined the Department of Neurology of Tsukuba University as a Senior Assistant Professor in 1984, becoming an Associate Professor there in 1990. He then moved to Tokyo Medical and Dental University as Professor and Chair of the Department of Neurology in 1996. He has long been a core member of the Research Committee on Ataxic Disorders and of the Advisory Board of the National SCA/MSA Patients' Association. He is also serving as Leader of the Strategic Research Program for Brain Science, Field E, Ministry of Education, Culture, Sports, Science and Technology, Japan and since 2010 has been President of the Japanese Society of Neurology.

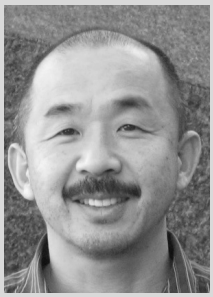
Symposium Talk: Spinocerebellar ataxia type 31: A new RNA disease

Abstract

Hereditary ataxias consist of autosomal dominant (AD), autosomal recessive (AR) and X-linked recessive forms of ataxia in which the cerebellum, brainstem, spinal cord and other parts of the nervous system are affected by neurodegeneration. AD and AR ataxias comprise more than 30 diseases, frequencies of which are quite different among various ethnicities. In Japan, for example, most cases are AD and there has not yet been a case of Friedreich's ataxia, which is the most common ataxia in Caucasians. Spinocerebellar ataxia type 3 (SCA3), SCA6, SCA31 and DRPLA are the four most common ataxias in Japan. SCAs 6 and 31 are pure cerebellar ataxias, while SCA3 and DRPLA are multiple system-involved ataxias. Approximately 20 years ago, we began a linkage analysis of pure cerebellar ataxias in Japan and found a 19p-linked locus that turned out to be of SCA6. The remaining cases were linked to a 16q locus that turned out to be of SCA31.

In SCA31, MRI reveals almost pure cerebellar atrophy with preserved brainstem and cerebrum. The neuropathology of SCA31 is characterized by a peculiar halo-like amorphous material around degenerating Purkinje cells (PCs). The mutation is a complex penta-nucleotide repeat containing (TGGAA)n, (TAGAA)n and (TAAAA)n inserted in an intron shared by two different genes, BEAN and TK2, transcribed in mutually opposite directions. The transcripts create RNA foci in the SCA31 PC nuclei, though their pathogenic significance is unknown. In order to clarify its pathogenesis, we established cultured cell models with these repeat insertions. We found that only the nucleotide sequences containing (UGGAA)n, corresponding to the mutation transcribed in BEAN-direction, formed RNA foci and showed significant toxicity revealed by LDH and MTS assays, whereas other repeats did not. We also demonstrated that serine/arginine-rich splicing factor 1 (SFRS1), the splicing factor essential for any living cell and binds with (UGGAA)n in vitro, co-localized with RNA foci. In human SCA31 cerebella, the RNA foci were more in the morphologically preserved PCs than those in atrophic PCs. According to these findings, it is suggested the formation of RNA foci containing (UGGAA)n may be a hallmark of the SCA31 neurodegeneration, which potentially affects the nuclear SFRS1 level. SCA31 is considered one of a growing number of neuromuscular diseases with RNA-mediated gain-of-function mechanism such as myotonic dystrophies type 1 & 2, SCA8, SCA10 and fragile X-tremor ataxia syndrome. Further studies are necessary to find molecular targets for effective therapies of SCA31.

Based on our study of the SCA31 mutation in large European cohorts of SCA families in addition to a Japanese one, (TAAAA)n is the original pentanucleotide with polymorphic but small 8 to 21 repeats in both Caucasians and Japanese. However, large (TGGAA)n repeats associated with SCA31 and (TAGAA)n are exclusively found in Japanese whereas (TACAA)n, (GAAAA)n, (TAACA)n and (TGAAA)n pure expansions exclusively in Caucasians'. There may be some evolutional mechanisms regarding the Japanese and Caucasian expansions at the SCA31 locus.



Shinsuke Shimojo

(California Institute of Technology, USA)

Biodata

Shinsuke Shimojo is an experimental psychologist/cognitive neuroscientist, with long-standing interests in visual psychophysics and their applications to cross-modal plasticity, human emotion, preferences, and decision making. He received his BA and MA degrees from the University of Tokyo ('78, '80), and Ph.D. from Massachusetts Institute of Technology ('85). He is currently Gertrude Baltimore Professor in Experimental Psychology in Division of Biology/Computation and Neural Systems at California Institute of Technology (Caltech). His laboratory at Caltech has been applying quantitative psychophysical techniques to understand human implicit and social behaviors, with technical applications of eye tracking, fMRI, EEG, TMS and tDCS. He is the author of several popular books, and also one of the regular columnists at ASAHI WEBRONZA, Science & Environment Section (in Japanese language).

Symposium Talk: Sensory substitution, crossmodal plasticity, and the third kind of "qualia"

Abstract

"Qualia" to some philosophers refers to the absolute, unique and subjective quality of a conscious sensory experience, which may not be "explained away" by any sort of neurophysiological account or model. Whereas we do not endorse to the opinion that the qualia is the "hard" (i.e. impossible in principle) problem for science, we also agree that the current visual perceptual sciences failed to explain the "absolute, unique and subjective quality of conscious sensory experiences." In this context, we may be able to find significant insights in the latest progresses in sensory substitution since they raise fundamental questions, such as what precisely are the basic characteristics of "vision-like" sensory processing.

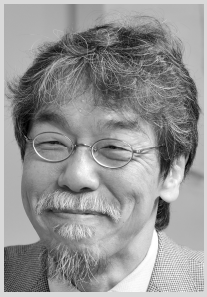
The "vOICe" is one of the currently available visual substitution devices based on auditory inputs, primarily for blind people. It translates video inputs (X- and Y-axes) into auditory parameters (time and pitch, respectively). There are several "super users" who claim "visual" experiences. Moreover, at least one of them showed neural activity in higher-level visual cortical areas in fMRI, when engaged in a shape discrimination task relying on this device.

In principle, we may come up with a brief list of psychophysical & neuroscientific criteria to acquire new "visual" experiences, and I will describe some data that our laboratory recently obtained along this line.

The psychophysical results suggest that some aspects of perceptual constancy (such as orientation or shape) can be attained by the vOICe training in sighted subjects, but that the post-training performance is mainly based on top-down cognitive strategy, rather than the typical, vision-like, automatic processes. To make it more automatic and effortless, dynamic sampling, i.e. sensory feedback from self action, turned out to be critical. Our fMRI data, albeit preliminary, indicate V3 activation.

All these results, as well as the vast majority of the literature on sensory substitution, have been base on the assumption that before training, the participants can perform the task only at the baseline chance level. It turned out not to be true, due to some intrinsic (synesthetic) mapping across modalities. Texture discrimination is the best example so far in our case with the vOICe, where untrained sighted subjects can grossly outperform the chance level and training does not necessarily add much.

Considering all these findings together, qualia, if still want to use such a word, should be understood with regard to adaptive behavior. Consequently, the subjective sensory experience which is acquired via excessive training/experiences with the sensory substitution device is not entirely "visual," nor "auditory." Instead, it may be characterized best as "the third kind of qualia."



Masato Taira

(Tokyo Medical and Dental University)

Biodata

Masato Taira is a Professor in the Department of Cognitive Neurobiology at Tokyo Medical and Dental University (TMDU). His specialty is neurophysiology. After receiving a Ph.D. in basic research for the neural mechanisms for mastication with Prof. Yoshio Nakamura at TMDU, Dr. Taira got a postdoctoral fellow position at Tokyo Metropolitan Institute of Neuroscience and then moved to Nihon University School of Medicine. During this time, he started a single unit recording from the parietal cortex of an awake monkey and revealed the cortical mechanisms for visual control of hand manipulation movement. He studied abroad as visiting assistant professor with Prof. Apostolos Georgopoulos at The Johns Hopkins University and the University of Minnesota, concentrating his studies on the primary motor cortex (*Science*, 1993). Since he returned to Japan in 1994, he has been studying the function of the parietal cortex by the single unit recording in animal and a functional MRI in human, and published papers concerning neural mechanisms for stereopsis (*Science*, 2002) and navigation (PNAS, 2006) with his collaborators.

Symposium Talk: Neural mechanisms for navigation: Comparison between the medial parietal region and the parahippocampal gyrus

Abstract

When we drive to our office, we can take the correct route subconsciously, making a turn or going straight at each intersection. This phenomenon suggests that we may have an internal list of what we have to do at a given location (route knowledge) in our brain. Lesion and neuroimaging studies of humans suggest that the medial parietal region (MPR), including the retrosplenial and posterior cingulate cortices, is critically involved in navigation based on route knowledge. On the other hand, it is well known that the place which codes the location of an animal is in the hippocampus and the hippocampus is also suggested to be involved in navigation. In this study, we recorded a single unit activity from the monkey MPR and the parahippocampal gyrus (PG) while the monkey navigated in an virtual environment.

We found that many neurons in MPR showed significant responses to the monkeys' movements in the virtual environment. Many of their responses were associated with a specific movement at a specific location (navigation neurons). We also found some navigation neurons whose responses to the same movement at the same location were modulated depending on the route. We further investigated the visual responses of those neurons when the monkeys were shown animations of the navigation route. We observed that the responses of some neurons reduced when the monkeys viewed the preferred field in the segmented animation or in the still image. In PG, we also found that many neurons became active during the navigation task. In those, there were neurons responded to the instruction slides which indicated the destination. We further found the neurons responding to the scene at the middle point of route, which looks like the place cell in the hippocampus.

Thus, these results suggest that neurons both in MPR and PG play a critical role in navigation. MPR neurons may be involved in route-based navigation by integrating location information and self-movement information, however, PG neurons may encode the location information along the route.

Abstracts of Mini-Lectures

Mini-Lecture 1. Department of Cell Biology
"Optogenetics of Signalling Molecules in Neurons" (Professor Takao Nakata)

Abstract

We are investigating spatiotemporal regulation of cell signaling in neurons. For this purpose, we developed photoswitchable signaling molecules by making various hybrids of animal and plant proteins. We express these proteins in neuronal cells and photostimulate them, and monitor downstream signallings. Our approach enables us to elucidate how information is processed in signalling cascade in living cells.

Mini-Lecture 2. Department of Medical Biochemistry
"Potential roles of the tumor suppressor Hippo pathway in brain" (Professor Yutaka Hata)

Abstract

The Hippo pathway is a newly emerging tumor suppressor signaling cascade. It was originally discovered in Drosophila, but it is well conserved in mammals. The dysfunction of the pathway is very frequently detected in human cancers including glioblastoma, increases cancer metastasis and invasiveness, and results in poor prognosis. We are currently trying to find out the compounds that activate the pathway, which may be beneficial for cancer therapy. Recent studies have revealed that the pathway is important to regulate the balance between differentiation and cell proliferation in neural, intestinal, and mesenchymal stem cells and ES cells, and to modulate iPS induction. The pathway is also involved in the inflammatory cytokine signalings and tissue overgrowth such as cardiac hypertrophy under pressure overload. Given the versatile roles of the pathway and that the pathway is implicated in dendrite growth in Drosophila neurons, the Hippo pathway is speculated to be implicated in physiological and pathophysiological processes in human brain. I will give a brief overview on the Hippo pathway and our drug screening, and discuss the potential roles of the Hippo pathway in brain.

Mini-Lecture 3. Molecular Genetics Division, Center for Brain Integration Research
"Mouse models for cerebellar ataxia" (Associate Professor Kei Watase)

Abstract

Ataxia is a neurological condition that consists of gross lack of coordination of muscle movements and often originates from dysfunction of cerebellum. Our group has been trying to clarify molecular pathogenesis of spinocerebellar ataxias (SCAs), a group of hereditary neurodegenerative diseases, using genetically-engineered mutant animal models. Here I discuss the molecular basis of ataxias as well as generation of mouse models of human ataxias. In the lab, we are also planning to show some behavioral analysis of knockin mouse models of SCA6.

Mini-Lecture 4. Department of Neurology and Neurological Science
"Gene Therapy with New Class of Oligonucleotide Drug for Neurologic Diseases"
(Professor Takanori Yokota)

Abstract
The antisense oligonucleotides (ASOs) and small interfering RNA (siRNA) are both recognized therapeutic agents for the silencing of specific genes at the post-transcriptional level, but their potency and safety make them insufficient for universal clinical application. Here we developed a new class of exceptionally potent ASOs that are hybridized with complementary RNA (cRNA) and conjugated with a ligand. Within target cells, RNase H cleaves the cRNA from the double-stranded ASO (dsASO) leaving the single-strand ASO. The another key approach for the clinical application of ASOs is the development of delivery systems. Previously, we hypothesized that the best in vivo carrier for siRNA would be a molecule that is essential for target tissue cells, but which cannot be synthesized by the cells themselves. Vitamins meet these requirements, and the least toxic, fat-soluble vitamin is vitamin E (V.E). Therefore, we directly conjugated V.E to siRNA and obtained a substantial reduction in the expression of an endogenous gene in mouse liver and brain. When conjugated with V.E, the ASO was more effectively delivered to the mouse liver and in vivo gene silencing was 1,000-fold greater than with V.E-siRNA. We believe that our development of ligand-conjugated dsASOs opens up a new horizon for human gene therapy through synthetic oligonucleotides, and now try to apply our innovation to neurologic diseases including Alzheimer disease and multiple sclerosis.

Mini-Lecture 5. Department of Neurosurgery
"Functional neuroimaging study for malignant brain tumor" (Lecturer Tadashi Nariai)

Abstract
We have been using various functional neuroimaging technique such as MRI or PET to investigate the pathophysiology of neurosurgical disorders and to establish an appropriate treatment strategy for them. Focus of the present lecture will be put mainly on the field of malignant brain tumor. PET molecular imaging research using multiple tracers to evaluate the proliferative potential of malignant tumor will be introduced. Our clinical and basic trial in seeking for better outcome of patients with malignant glioma will also be introduced.

Mini-Lecture 6. Department of Pharmacology and Neurobiology
"Microglia and neuroinflammatory/neurodegenerative disease" (Assistant Professor Hironao Saegusa)

Abstract
In the neurodegenerative disease like Alzheimer's, Parkinson's and Huntington's disease, cumulative evidences indicate that short term activation of the microglia in the afflicted area is effective for repairing the damages. However, chronic (long term) activation of the microglia worsens the inflammation and induce degeneration. Thus, controlling the microglial activation states (enhance neuro-protective nature and reduce neuro-destructive nature) would be the excellent way to improve the disease conditions. In our lab, we are conducting studies identifying the molecules which will control the activation sates of microglia.

Mini-Lecture 7. Department of Physiology and Cell Biology

1)"Mitochondrial quality control and autophagy" (Assistant Professor Atsushi Tanaka)

2)"Denervation-induced muscle atrophy" (Graduate Student Pham Nguyen Quy)

Abstract

Autophagy is the major intracellular degradation system by which cytoplasmic materials are delivered to and degraded in the lysosome. For the maintenance of cellular homeostasis, recent studies on autophagy serve lines of evidence of its importance. We provide a short lab-tour followed by brief introductions of our recent progress in elucidating the mechanism and physiological significance of autophagy; 1) Mitochondrial autophagy (mitophagy) in the pathobiology of Parkinson's disease, 2) The mechanism of mTORC1 activation in denervation-induced muscle atrophy.

Mini-Lecture 8. Department of Systems Neurophysiology

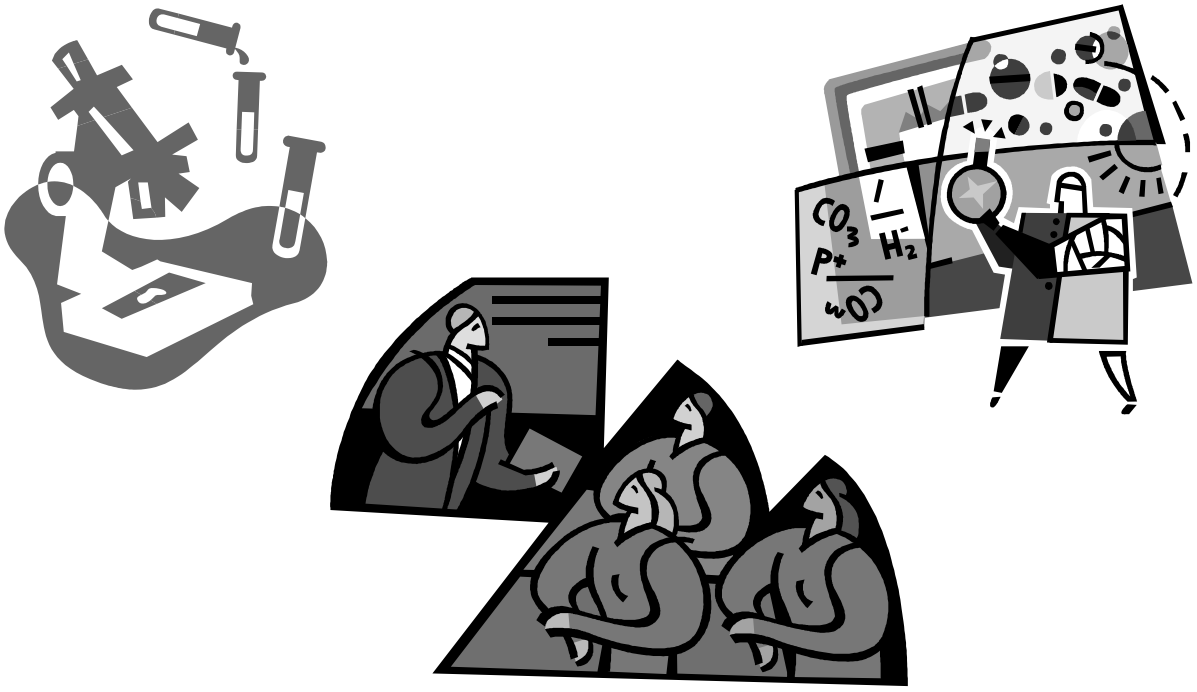
1)"Cerebellar compartmentalization" (Professor Izumi Sugihara)

2)"Neural organization of saccade generation and suppression" (Lecturer Yoshiko Izawa)

3)"Roles of the superior colliculus in control of eye movements" (Assistant Professor Mayu Takahashi)

Abstract

We are going to briefly show current research topics in our department. Dr. Sugihara's group has clarified the fine compartmentalization in the mammalian cerebellum in relation to molecular expression patterns and axonal projections. Dr. Izawa's group examined oculomotor pathways in the brain stem, and further investigated the higher order control of eye movements and visual fixation by the frontal eye field in trained monkeys. Dr. Takahashi will talk about neural mechanisms of eye movement controlled by the superior colliculus. The program includes three Mini-Lectures and lab tours.



ISP2012 Participants

ISP2012 Participants

Invited Participants

Bangladesh

Muhammad Shahdaat Bin Sayeed

University of Asia Pacific

Poster #19

P.R. China

Huijia Guo

Guilin Medical University

Poster #7

Yajun Hu

Guilin Medical University

Poster #16

FuYing Li

Guilin Medical University

Poster #6

Lian Liu

Peking University Third Hospital

Poster #1

JinDong Song

Guilin Medical University

Poster #3

Xiaoyin Xu

China Medical University

Poster #8

Zhenlei Yang

Guilin Medical University

Poster #11

India

Mohd Saif

Indian Institute of Technology

Poster #2

Shilpa Sankara Pandian

University of Madras

Pavethy Nath Velusamy

University of East

Republic of Korea

Ji-a Park

Seoul National University

Laos

Syxiong Bisayher

Mahosot Hospital

Poster #12

Malaysia

Kai Wey Goh

University Tunku Abdul Rahman

Myanmar

Chaw Kyi Tha Thu

Shwe Gone Dine Specialist Hospital

Poster #18

Taiwan

Po-jen Chien

Taipei Medical University

Poster #17

Thailand

Boosana Kaboosaya

Chulalongkorn University

Poster #4

Supak Ngamsom

Mahidol University

Suteera Viboonyasek

Chulalongkorn University

Poster #13

Woranan Wongmassang

Mahidol University

Varunya Chantadul

Mahidol University

Vietnam

Su Tran Minh Le

University of Medicine and Pharmacy
Ho Chi Minh City

Poster #9

Ngoc Trang Nguyen Vo

University of Medicine and Pharmacy
Ho Chi Minh City

Anh Phi Phan

Hospital of Blood Transfusion and Hematology

Poster #14

Private Expense Participants

Malaysia

Phee Phee Chia

University Tunku Abdul Rahman

TMDU Poster Session Participants

Wanping Aw

Singapore

Poster #5

Ye Changchang

P.R. China

Poster #10

Sun Weinan

P.R. China

Poster #15

Pham Nguyen Quy

Vietnam

Poster #20

Abstracts of ISP2012 Poster Presentations

Poster No.

1

Lian Liu

(Peking University Third Hospital, P.R. China)

Title: Molecular mechanism for the anticancer effect of Su-Mu

Abstract

Su-Mu（or Caesalpinia sappan L）is a traditional Chinese medicine which is reported to inhibit the proliferation of tumor cells and induce apoptosis. Previous study of the purified Su-Mu components shows that, haematein (brazilein) and Brazil hematoxylin (Brazilin) have significant inhibitive effects on proliferation of a variety of tumor cells.

A variety of quinone and ketone compounds, including vitamin K and its derivatives, block cancer cell cycle progression and induce apoptosis and autophagic cell death by inhibiting CDC25A and B, which are cell cycle related phosphatases. Su-Mu on the one hand contains substances that are structurally similar to vitamin K naphthoquinones , on the other hand acts on the coagulation-fibrinolysis system and has antibacterial and antitumor activity, which is very similar to vitamin K's biology effect. Does Su-Mu also anticancer by inhibiting CDC25A / B just as vitamin K?

I configured the Su-Mu extracts of water, ethanol, ethyl acetate, hydroxylamine to different concentrations and compared their antiproliferative activities by reacting against cultured HeLa cells and measuring OD values after the reaction. The experiments revealed that with the concentrations of the extracts increasing, cell viability or survival rate decreased. Su-Mu extracts are abundant in polyphenols. According to the published structures of these polyphenols, I suggested that Su-Mu might exert its anticancer effect through inhibition of the phosphatases CDC25A and CDC25B that control the cell cycle progression.

Then I purified recombinant CDC25A and CDC25B, and reacted the several batches of Su-Mu extracts of different solvent combinations against CDC25A / B and also measured OD values after the reaction to detect the enzymatic activities. My experiment revealed that Su-Mu extracts indeed inhibit CDC25A/B activities. So I concluded that the inhibition effect of Su-Mu on hela cells may be related to its inhibition effect on CDC25A/B.

Poster No.
2

Mohd Saif
(Indian Institute of Technology, India)

Title: Role of insulin in Memory Formation and in Alzheimer's

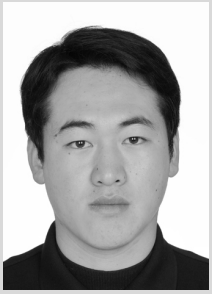
Abstract

Alzheimer's disease is the most common cause of dementia. It is degenerative disease of the brain that leads to both memory loss and behavioural change.In recent years Alzheimer's has been considered to be a neuroendocrine disorder, even referred to by some as type 3 diabetes because it harbours elements of both type 1 and type 2 diabetes. Since there is both a decrease in production of insulin and resistance to insulin receptor. Insulin resistance leads to decrease in brain insulin.

Insulin helps to regulate process such as neuronal survival, energy metabolism and plasticity. It also controls neurotransmitter release process at the synapses and activate signalling pathways associated with learning and long term memory. Novel research demonstrates that impaired insulin signalling may be replicated in Alzheimer disease. Analyzing various braak stages of Alzheimer disease neurodegeneration found that insulin expression was inversely propotional to the braak stage with 80% decrease in no. of receptors.
Neurotoxins coined amyeloid beta-derived diffusible ligand(ADDL`S) a molecule generated by proteolytic cleavage of the amyloid precursor protein. While monomeric ADDL is not neurotoxic the peptide exhibits a marked toxic gain of function upon self association.

In healthy brains, insulin binds to receptor at synapse resulting in the memory formation .ADDL disrupt this mechanism of communication by binding to the synapse and changing its shape thereby causing dysfunction.Because shape of the synapse is altered, insulin cannot effectively bind, disrupting signal transduction and resulting in insulin resistance.ADDL have been shown to reduce the plasticity of the synapse, potentiate synapse loss, cause oxidative damage and result in Alzheimer disease type tau hyperphosphorylation.

Poster No.
3



JinDong Song
(Guilin Medical University, P.R. China)

Title: Pathologic study on the expression of the matrix metal proteinase II in the patients' brain Sol cytoma lump body

JinDong Song (宋金東), Min Zheng

Abstract

To explore whether the expression of MMP-2 is along with the brain sol cytoma malignant degree markup we collected 45 patients in Affiliated Hospital of Guilin Medical University. ① The control group contains 15 cases of brain tissue from normal patients with cerebral contusion, in which male 8 and female 7 examples. ② The control group is constitute by 30 tumors from patients' brain sol cytoma lump body, in which male 18 and female 12 examples. According to WHO central nervous system tumor classification, this material includes Pilocytic Astrocytoma 8 examples (WHO Grade Ⅰ) ; Fibrillar Astrocytoma 7 examples (WHO Grade II); Anaplastic Astrocytoma 11 examples (WHO Grade Ⅲ); Glioblastoma Multiforme 4 examples (WHO Grade Ⅳ). So we divide them into low grade gliomas (WHO Grade I/II, total 15 examples) and high grade gliomas (WHO Grade Ⅲ/Ⅳ, total 15 examples). With mouse anti-person matrix metal proteinase-2 monoclonal antibody (MAB-0244) treat 45 patients' tissue, analysis by the immunity method and extract mRNA, examines the different expression of MMP-2 among these groups. Although the MMP-2 expresses in normal cerebral contusion tissue, the rate and intensity of masculine gender expression in high grade gliomas are higher than in low grade gliomas significantly, the low grade gliomas is higher compared with the cerebral contusion.

Poster No.
4

Boosana Kaboosaya
(Chulalongkorn University, Thailand)

Title: Success of microvascular free flap in reconstruction of maxillofacial defect : Retrospective study of 50 patients

Abstract

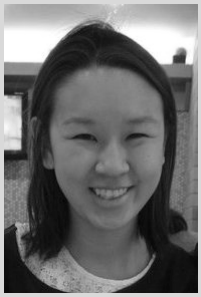
Purpose: The aim of this study was to retrospectively review our experience in microvascular free flap for the reconstruction of head and neck defects following extirpation of head and neck benign tumor and cancer.

Method: A total of 50 patients, 55 times of operations underwent microvascular free flap between January 2002 to April 2010. An overall descriptive analysis was carried out by collecting data from in-patient records including types of pathology, types of microvascular free flap, causes of reconstruction, times of operation, post-operative complications, length of hospitalization and Success rate of microvascular free flap reconstruction.

Results: There were 30 men and 20 women in our study cohort, with the age ranging from 18 to 70 (mean 46.58). The most common types of pathology were Squamous cell carcinoma 42 percent and Ameloblastoma 36 percent. The most common types of microvascular free flap were Radial forearm free flap 49.09 percent, Fibular free flap 25.45 percent and Deep circumflex iliac artery free flap 21.82 percent. The most common causes of reconstruction were long span defect 56.36 percent, poor soft tissue bed 43.64 percent. Times of operation were between 5.15 to 13.00 hours (mean 8.18 hours). Most common post-operative complication was flap dehiscence 36 percent. Length of hospitalization was range from 7 to 85 days (mean 18.18 days). The success rate of microvascular free flap reconstruction in our school was 96.36 percent.

Conclusion: The microvascular free flap is one of beneficial methods for the reconstruction in oral and maxillofacial regions. Even though the operations need good surgical skill or time consuming, our 8 years' experience demonstrated a great success.

Poster No.
5



Wanping Aw
(Tokyo Medical and Dental University)

Title: Effects of coffee intake on gene expression in diet-induced obese mice

Wanping Aw[1,2], Kenji Egashira[2], Shoko Takahashi[2], Hiroshi Tanaka[1] and Hisanori Kato[2].

Abstract

[1]Graduate School of Biomedical Science, Biomedical Science PhD Program, Tokyo Medical and Dental University, Japan [2]Graduate School of Agricultural and Life Science, University of Tokyo, Japan

Coffee has been associated with a decreased risk of developing type II diabetes by various epidemiological studies. It is a rich source of natural products, including caffeic acid and chrologenic acid which have been reported to have anti-diabetic or anti-obesity effects. However, active ingredients and underlying mechanisms behind this phenomenon are still poorly understood.

In order to investigate the underlying the benefits of coffee, we performed a study in mice fed a high-fat diet with added coffee and analyzed gene expression in muscle tissue using cDNA microarray.
8 week old male C57BL6 mice were raised for 9 weeks on either a normal diet (ND group), a high fat diet (HF group), or a high fat diet with 2% freeze-dried caffeinated coffee (HFCC group), or a high fat diet with 2% freeze-dried decaffeinated coffee (HFDC) or high fat diet with 2% freeze-dried green unroasted caffeinated coffee (HFGC). Mice were subjected to each diet ad libitum. Primary measurements were body weight, food intake, fecal lipids, mesenteric fat and epididymal fats. Coffee intake suppressed body weight gain as well as fat accumulation in obese mice induced by high fat diet. Muscle was excised from sacrificed mice and equal amounts of cDNA were extracted to form a pool of cDNA. Pooled cDNA for each group was then used in microarray using Affymetrix GeneChip Mouse Genome 430 2.0. We report that Ras-related associated with diabetes (Rrad) and suppressor of cytokine signaling 3(Socs3) gene expression was up regulated in the HF group but significantly down regulated in HFCC, HFDC, HFGC and ND groups. Interestingly, the relative mRNA expression level of Socs3 was also significantly down regulated in HFGC groups as compared to being up regulated in the HF group.
The down regulation of these genes by coffee consumption may be contributing factors to the benefits of coffee.

Poster No.
6

FuYing Li
(Guilin Medical University, P.R. China)

Title: Magnesium concentration in the cerebrospinal fluid of mice and its response to changes in serum

Fu-Ying Li, Li-Yuan Sun
Department of Pothophysiology, Guilin Medical University

Abstract

Magnesium (Mg) is essential for cell functions such as the transport of calcium and potassium ions, and modulates signal transduction, energy metabolism, and cell proliferation. Although mice have been used as models of various neurological diseases of humans, and for investigating the therapeutic effects of Mg, neither the normal concentration of Mg in cerebrospinal fluid (CSF), nor its response to alteration of the serum level of Mg has yet been reported. The present study investigated the normal Mg concentration in the CSF of C57BL/6J (B6) and ICR mice and its response to elevation of the serum Mg level in B6 mice. In B6 mice, the normal Mg concentration in the CSF was 0.89 ± 0.11 mM, being lower than that in serum, which was 1.38 ± 0.12 mM, whereas in ICR mice the corresponding values were 1.00 ± 0.12 mM and 1.10 ± 0.09 mM, respectively. No significant alteration was found in the CSF of B6 mice injected intraperitoneally with Mg, even though the serum Mg concentration was significantly increased.

Poster No.

7

Huijia Guo

(Guilin Medical University, P.R. China)

Title: The change of T peak to T end interval in hypertensive patients with left ventricular hypertrophy

Huijia Guo, Jianyi Zhang

Department of Cardiology, Affiliated Hospital of Guilin Medical University, Guilin 541001

Abstract

Objective: To explore the clinical significance of T peak to T end interval (TpTe interval) in hypertensive patients with Left Ventricular Hypertrophy(LVH).

Methods: Three hundred and thirteen patients with primary hypertension (EH) were randomly selected and divided into LVH group and non LVH (NLVH) group according to the left ventricular mass index (LVMI) determined by echocardiogram, which were hospitalized in Department of Cardiology, Affiliated Hospital of Guilin Medical University between October 2010 and June 2011. Differences and Correlation Analysis of TpTe interval, TpTec, QT interval, QTc, QRS duration, LVMI, left ventricular internal diameter end-diastolic (LVIDd), inter ventricular septal thickness (IVST) and left ventricular posterior wall thickness（LVPWT） were compared between the two groups. The relationship of different grades of hypertension with TpTe interval, and the relationship of TpTe interval with different LVH patterns were analysised.

Results: ① Compared with NLVH group, Tp Te interval(100.0±23.3)vs(85.3±14.1)ms, TpTec（108.6± 26.7) vs（91.4±15.4)ms, QTc(435.0±23.6) vs (420.0±23.5)ms, QRS duration(105.3±22.3) vs (95.6± 16.1)ms were significant longer [all P<0.01], and the LVMI(142.8±29.3）vs (82.5±19.0）ms, LVIDd（58.9 ±7.5）vs (47.6±6.5)ms, IVST(9.7±1.0) vs（8.8±1.2）ms, LVPWT（9.4±1.1）vs（8.5±1.1）ms were significant higher in the LVH group[P<0.01]. There was no significant difference of QT interval in the two groups. ②The TpTe interval was compared among different LVH patterns : the eccentric hypertrophy group > the concentric hypertrophy group > the concentric remodeling group>the normal left ventricle group ; ③TpTe interval,TpTec were positively related with LVMI(r=0.43,0.44),LVIDd(r=0.41,0.43),(P<0.05).

Conclusions: TpTe interval can be a new ECG index to detect the damage of the target organ in EH patients with LVH.

Poster No.

8

Xiaoyin Xu

(China Medical University, P.R. China)

Title: Natural plant products and extracts that reduce immunoexcitotoxicity-associated neurodegeneration and promote repair within the central nervous system

Abstract

Neural disorder is an impairment of the brain or central nervous system. A narrower use of the term refers to a disorder of brain function that affects emotion, learning ability and memory and that unfolds as the individual grows. Our understanding of the pathophysiological and biochemical basis of a number of neurological disorders has increased enormously over the last three decades. Parallel with this growth of knowledge has been a clearer understanding of the mechanism by which a number of naturally occurring plant extracts, as well as whole plants, can affect these mechanisms so as to offer protection against injury and promote healing of neurological tissues. Curcumin, quercetin, green tea catechins, balcalein, and luteolin have been extensively studied, and they demonstrate important effects on cell signaling that go far beyond their antioxidant effects. The effect of these compounds on immunoexcitotoxicity is a common mechanism in a number of neurological disorders. By suppressing or affecting microglial activation states as well as the excitotoxic cascade and inflammatory mediators, these compounds dramatically affect the pathophysiology of central nervous system disorders and promote the release and generation of neurotrophic factors essential for central nervous system healing. So these compounds provide a new method to heal CNS injury in clinic.

Poster No.
9

Su Tran Minh Le

(Ho Chi Minh City University of Medicine and Pharmacy, Cho Ray Hospital, Vietnam)

Title: Microvascular decompression for the treatment of hemifacial spasm: Short term results of 30 cases between 2009 and 2012

Abstract

Objective: Microvascular decompression for the treatment of hemifacial spasm has been accepted at many neurosurgical centers all over the world. In this study, we present the short term surgical results of 30 patients treated with this method.

Method: We present the surgical results of 30 cases treated with microvascular decompression for hemifacial spasm (performed between 2009 and 2012). Among 30 patients, 80% was female, 20% was male, the average age of symptom onset was 45.4, the mean preoperative duration of symptom was 5.3 years.100% patients had typical onset of symptoms. The left side spasm was dominent (60%). We had one case (3.3%) with bilateral spasm. All patients were followed up by monthly reexaminations or with questionaires on the telephones. The average time of follow up was 6 months.

Results: At discharge, 18 patients (60%) were spasm free, 6 patients (20%) had decrease of symtoms and 6 patients (20%) complained no changes. At the average time of monitoring, 19 patients were spasm free. We had one case (3.3%) suffered from facial paralysis, one case (3.3%) with facial paralysis and deafness postoperatively.

Conclusion: Microvascular decompression brings good outcomes for the patients with hemifacial spasm (63.3% of patients were spasm free, 16.7% had decrease of spasm). Deafness and facial paralysis were the main postoperative complications (6.7%) which is caused by damaging the VII,VIII cranial nerves or the labyrinthine artery intraoperatively.

Poster No.
10

Ye Changchang
(Tokyo Medical and Dental University)

Title: The role of antibodies against periodontal pathogen on preterm low birth weight

Abstract

Objective: Several studies suggested that periodontal disease is a risk factor of preterm low birth weight (PLBW). We hypothesize periodontal pathogen infection might enhance thrombosis through molecular mimicry with TLRVYK on beta-2 glycoprotein I, which was a target molecule in anti-phospholipid syndrome. The purpose of this study was to examine the effect of periodontal infection on pregnancy outcome.

Material and Methods: 95 pregnant women, including 47 threaten premature labor (TPL) and 48 healthy subjects, participated in this study. Periodontal examinations were performed and presence of periodontopathic bacteria was examined using PCR. Molecular mimicry between TLRVYK peptides and homologous peptides on the bacteria was examined by ELISA, using rabbit polyclonal antibodies specific for the respective peptides (SIRVYK on A. actinomycetemcomitans, TLRIYT on P. gingivalis, TLALYK on T. denticola). Serum C-reactive protein, anti-TLRVYK and anti-SIRVYK antibodies were measured using ELISA.

Results and Conclusion: Among the rabbit antibody specific for the bacterial homologous peptides, only anti-SIRVYK antibody reacted with TLRVYK peptides. Concentration of anti-SIRVYK antibody had a higher tendency in TPL patients than in healthy subjects. Serum antibody concentration against-TLRVYK was significantly correlated with serum anti-SIRVYK antibody. Multivariable analysis showed that anti-SIRVYK antibody concentration was associated with diagnosis of TPL. Out of subjects, 19 had PLBW, and ordinal logistic regression analysis revealed that past smoking, presence of P.gingivalis and diagnosis of TPL were significantly correlated with PLBW. The presence of P.gingivalis might be a risk factor for PLBW. Anti-SIRVYK antibody reacted with TLRVYK which might be associated with TPL.

Poster No.
11

Zhenlei Yang
(Guilin Medical University, P.R. China)

Title: Effectiveness of nerve growth factor in treatment of acute cerebral ischemia in rats

Abstract

Exogenous nerve growth factor (NGF) can goes through a rat's blood brain barrier. Mainly distributed in the basal forebrain、cerebellum.、dentate nucleus、hippocampus、the prefrontal cortex、olfactory bulb and the area around brain ventricle. Clinical studies show that, effectiveness of exogenous NGF in the acute phase of cerebral infarction is better than in the therapeutic recovery.

By establishing damage model of middle cerebral artery occlusion/reperfusion in rats, using transmission electron microscope observe acute period after intraperitoneal injection of NGF, watch the ultrastructural changes in brain ischemia injury area ,and determinate the quantity of synaptophysin in the brain tissue .Then explore the efficacy and its possible mechanism of ischemic Cerebral damage when make intraperitoneal injection with NGF.

Some people found that, in the acute stage of cerebral ischemia, intraperitoneal injection of NGF can reduce the ischemic injury in the rat brain, possibly by up-regulating the expression of synaptophysin
But there are still a lot of uncertainty we need to verify.

Also, in recent years, music therapy and traditional Chinese medicine in clinical application are more and more widely. Do they have any certain meanings on neurological rehabilitation? So, if convenient, I want to have a study.

Poster No.
12

Syxiong Bisayher
(Mahosot Hospital, Laos)

Title: Human immunodeficiency virus testing among patients with tuberculosis and patients suspected to have HIV infection at Mahosot Hospital, from 2008 to 2009

Bisayher S, Vidhamaly S, Sayavong B, Nanthavong P, Vongphacdy V, Sihalath V, Soukhaseum H

Abstract

Introduction: Human immunodeficiency virus (HIV) infection is the most important risk factor for developing tuberculosis. WHO has recommended that all TB patients should be testing for HIV by voluntary counseling and testing such as patient initiated procedure (opt in). The Ministry of health has stated a policy on TB/HIV collaboration between TB and HIV program at Mahosot Hospital on 2008. The purpose of this study is to determine the seroprevalence and the HIV testing rate among TB patients and patients whom suspected HIV infections.

Methods: A retrospective review of the case records of all patients diagnosed with TB and patients suspected HIV infections from January 2008 to December 2009, at the Pneumology department, at Mahosot Hospital, Lao PDR. Medical records of the patients with TB were reviewed and a standardized case record form was used to collect the data, used the Epidata 3.1 for data input and Stata 8.2 for data analyze. HIV serology was done by the double quick test: DETERMINE® HIV-1/2 and UNI-GOLD® Recombigen HIV. ELISA for confirmation if unconformity.

Results: A total of 954 patients were recorded and diagnosed with TB and suspected HIV infection during the 2 years study period. Eight patients whose HIV positivity was already known were excluded. The mean age of the remaining 946 patients was 39.5±16.7years. HIV testing was performed in 458 (48.4%) patients, with whom 66(14.4%) were seropositivity. Univariate analysis showed that the reproductive age (15-49), male gender, divorce and patient with HIV suspected were all significantly associated with seropositivity ($p<0.002$). Multivariate analysis showed that three factors were independently associated with seropositivity such as follow : age of 25-34 years (OR=2,5, CI 95%=1,1-3,8), divorce (OR=3,02; CI 95%=1,4-4,6) and patient with HIV suspected (OR=2,1; CI 95%=1,3-2,9).

Conclusion and Recommendation: TB is a common initial manifestation of HIV infection. Despite the recommendations for HIV testing in all patients with TB, the frequency of HIV testing were low, with less than 50% of patients being tested at our hospital. The prevalence of TB and HIV co-infection were look like high. It is necessary to increase the rate of HIV testing among all TB patients.

Poster No.
13

Suteera Viboonyasek
(Chulalongkorn University, Thailand)

Title: Effect of chronic treatment of dihydroergotamine on cortical spreading depression

Viboonyasek, S., Bongsebandhu-phubhakdi, S., Srikiatkhachorn, A.
Department of Physiology, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand

Abstract

Medication overuse headache (MOH) refers to a chronic headache condition which is caused by overuse of analgesics or anti-migraine drugs. The mechanism by which chronic consumption of drugs leads to MOH is still unknown. Our previous study has found that chronic analgesic exposure led to an increase in neuronal excitability of the cortex. Ergot alkaloid is anti-migraine drugs which can lead to MOH. This study was designed to investigate of dihydroergotamine (DHE) overuse can also increase cortical excitability whether using cortical spreading depression (CSD) model.

Adult male Wistar rats were treated with DHE (100 µg/kg-BW/day, intraperitoneally) for acute, 7, 14 and 28 days. DMSO was given to the control rats. CSD was induced in all groups by topical application of 3mg solid KCl on parietal cortex. Electrocorticogram was continuously monitored for 1 hour. The measured parameters were frequency, amplitude, interpeak latency, and area under the curve of the depolarization waves.

The results showed that single dose DHE did not alter CSD, whereas chronic administrations affected cortical depolarization. The amplitude was significantly increased in DHE-14days (30.49+2.49mV) and DHE-28days (31.18+2.27mV) as compared with controls (26.32+3.48mV, 24.8+4.1mV for DHE-14, 28days, P=.035 and .005, respectively). There were no difference in frequency, interpeak latency and area under the curve.

These findings indicate that the chronic exposure of DHE can increase neuronal excitability of the cortex. This study, therefore, confirms the hypothesis of an increased cortical excitability as a mechanism of increasing headache frequency in MOH.

Poster No.
14

Anh Phi Phan
(University of Medicine and Pharmacy, Vietnam)

Title: Effects of Berberin and Palmatin on Rat's Hippocampus

Phan Phi Anh, Vo Phung Nguyen, Tran Hung
School of Pharmacy - University of Medicine and Pharmacy Ho Chi Minh City

Abstract

Introduction:
Alzheimer's disease (AD) is a neurodegenerative disease and causes memory loss and dementia, which mostly affects the elderly population (Francis et al., 1993). Cognitive impairment in AD is caused mainly by death of cholinergic neurons in hippocampus and basal forebrain area (Kopelman and Corn, 1988). A deficit of acetylcholine in an AD brain is well known (Wilcock et al., 1982). These findings lead us to search for agents that have the efficacy on process of learning and memory was evaluated on scopolamine-induced amnesia rat, and increase acetylcholine level in the brain.

Materials and methods:
(1) Animals and surgery
Male Sprague–Dawley rats (200–250 g), were individually housed with food and water available ad libitum and subjected to a reverse cycle 12 : 12 h dark : light.
Rat were anesthetized with thiopental (40 mg/kg, i.v.), placed in a stereotaxic frame and implanted with guide cannulas into the hippocampus (stereotaxic coordinates: AP = -3.0 mm; ML = ± 2.6 mm; DV = 3.6 mm from Bregma). The animals were allowed at least 4 days post-operative recovery before behavioral testing commenced.
(2) Methods:
Berberine at the doses of 15 μmol/l and 30 μmol/l and palmatin at the doses of 60 μmol/l were administered for 5 days on scopolamine (intrahippocampus) induced memory impairment in rat. Memory and learning were evaluated by using the Morris water maze. Acetylcholine/Acetylcholinesterase levels were measured by Amplex Red Kit.
(3) Data and statistical analysis:
Results are expressed as means ± SEM. Data analysis using the Mann-Whitney U test to assess pairwise differences between the groups. P values less than 0.05 were considered to be statistically significant. Calculations were performed using Minitab statistical software version 14.0.

Results and discussion:
The berberin given intrahippocampal at the dose of 15, 30 μmol/l or palmatin with dose of 60 μmol/l, abolished the amnesic effect of scopolamine in water maze test, and increased acetylcholine level in the brain when compared with control group. The activities of berberin and palmatin on scopolamine –induced amnesia rat are not significantly different with galantamine, an acetylcholinesterase inhibitor, has been used in the treatment of AD.

Poster No.
15

Sun Weinan
(Tokyo Medical and Dental University)

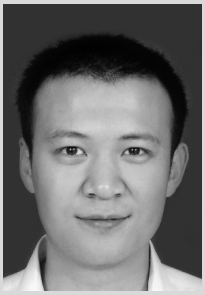
Title: The role glial glutamate transporters in cortical spreading depression

Abstract

Cortical spreading depression (CSD) is a depolarization wave in the cerebral gray matter characterized by massive ion translocation, neuronal swelling and silencing of brain electrical activity. In the clinic, strong electrophysiological evidence now exists that CSD occurs abundantly in patients with migraine, stroke, subarachnoid hemorrhage and traumatic injury, implicating CSD as a pathophysiological mechanism for these acute neurological disorders. Despite the clinical relevance of CSD in neurological disorders, mechanisms of CSD remain unclear.

Glutamate is a major excitatory neurotransmitter in the mammalian central nervous system and its increase in extracellular space is involved in acute neurological disorders. Glial glutamate transporters play a critical role in the control of extracellular glutamate concentration. Therefore, I hypothesize that the impaired activity of glial glutamate transporter may decrease the threshold of CSD induction and increase the rate of CSD propagation. To address this, I have recorded direct current potential from the frontal and parietal cortex in response to the chemical stimulation of the visual cortex in the mice deficient of the glial glutamate transporter GLT1. Through the application of a series of concentration of potassium chloride to stimulate the visual cortex, I determined the threshold and velocity of propagation of CSD and compared them between control and GLT1 mutant mice. GLT1 mutant mice show a reduction in CSD threshold and an increase in CSD velocity compared to control mice. These results suggest that GLT-1 prevents the incidence of OCD. The activators of GLT1 may potentially treat acute neurological disorders by curtailing CSD.

Poster No.
16



Yajun Hu

(Guilin Medical University, P.R. China)

Title: FoxO1 and TORC2 gene regulation of the biological activity of the pancreatic islet beta cells and the relationship between the two genes

Abstract

Objective: Through the intervention of the application of different concentrations of glucose and small molecules interfering RNA (small interfering of RNA of SiRNA) technology regulation of Pancreatic β cell lines of NIT - 1 cells FoxO1 and TORC2 gene expression observed FoxO1 and TORC2 gene regulation of Pancreatic β cells Proliferation and apoptosis, the detection of Protein expression changes Provide a theoretical basis to Promote the diagnosis and treatment of Pancreatic β cell Proliferation and Prevent apoptosis gene in the diabetic state.

Methods: 1) Optimize transfection conditions, access to effective SiRNA to fragment. By the manual design synthesis of three Pairs TORC2SiRNA (TORC2SiRNA - 1, TORC2SiRNA -2, TORC2SiRNA -3) and one Pair of negative control of SiRNA SiRNA to optimize transfection conditions with fluorescently labeled negative control. Transfection conditions, in accordance with the best three Pairs transfection TORC2SiRNA by Nanotechnology - based, SBI's purefection™ Transfection Reagent. Liposomes to NIT-1 cells 24 hours after transfection by Western blot analysis, the interference effect of the gene, screening best TORC2SiRNA sequence. 2) Use different concentrations of glucose intervention. NIT-1 cell lines in accordance with 1 × 106 / well in 6-well culture Plates and cultured for 48 hours were added to the medium of different concentrations of sugar, divided into four groups: Group 1 in accordance with the different concentration of glucose in RPMI1640 medium 5.6mmol / L, 11.1mmol / L, and 16.7mmol / L, 27.6mmol / L and cultured for 120 hours.3 Intervention 3.FoxO1siRNA and TORC2SiRNA. Filter out the optimal transfection conditions of different glucose concentrations 24 hours after the intervention, respectively FoxO1, intervention in 24 hours or 48 hours of TORC2 of small interfering RNA. 4 the application of four methods of experimental monitoring and assessment: the ① MTT method for the determination of cell survival and growth; ② radioimmunoassay determination of the level of insulin secretion; ③ Hoechst 33258 immunofluorescent nuclear staining observed apoptosis; ④ by Western - blot technique, the detection of different interventions under the conditions of intracellular AKT, FoxO1, TORC2 gene Protein expression.

Result: (1) Transfected with fluorescently labeled negative control of SiRNA 24 hours after observed under fluorescence microscope cell fluorescence color when SiRNA concentration of 160Pmol / L, and SBI Purefection™ Nanotechnology - based Transfection Reagent. Transfection reagent in accordance with volume (v: v) ratio of 4:1 mixed transfection is the best cell viability.

(2) By MTT cell Proliferation was detected: FoxO1 application FoxO1siRNA inhibition of gene expression, cell Proliferation levels, significantly higher than the normal control group; the contrary, the application of high concentrations of glucose intervention in high- expression the FoxO1 genes will significantly inhibits cell Proliferation ($P<0.05$).

(3) Those detected by radioimmunoassay of insulin secretion: the FoxO1 application FoxO1siRNA inhibition of gene expression levels of insulin secretion was significantly higher than the normal control group; the contrary, high expression of FoxO1 gene, the inhibition of insulin secretion ($P<0.05$).

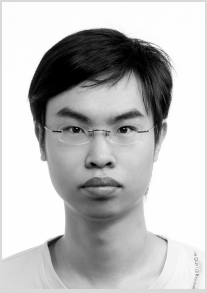
(4) Immunofluorescent nuclear staining to detect apoptosis: application FoxO1siRNA inhibition of the FoxO1 gene expression, decreased cell apoptosis was significantly lower than the normal control group; the contrary, high expression of FoxO1 gene, Promotes cell apoptosis ($P<0.05$).

(5) Immune Western blotting detection of Protein expression: ① Application FoxO1siRNA inhibit FoxO1 gene expression, the TORC2 Protein expression was reduced with decreasing FoxO1 expression, lower than the untransfected FoxO1siRNA group; AKT, Protein exPression was no significant change. ② The TORC2SiRNA inhibits TORC2 gene expression, The FoxO1 Protein expression with the TORC2 Protein expression was reduced to decrease.

Conclusion: Using purefection™ Nanotechnology - based Transfection Reagent. Transfection reagent referral guide FoxO1siRNA import NIT-1 cells can be specific, efficient inhibition of NIT-1 cells of FoxO1 expression, with low cytotoxicity, method of operation is simple. Inhibit the FoxO1 gene expression, Promote cell Proliferation, apoptosis, and stimulate insulin secretion, but also can reduce TORC2 gene expression; high expression of FoxO1 can inhibit NIT-1 cells Proliferation and Promote apoptosis and reduce insulin secretion. Inhibit TORC2 gene expression, the FoxO1 gene expression was also reduced.

KEY WORDS: islet NIT-1 cells; SiRNA; FoxO1; TORC2; Cell Proliferation; apoptosis

Poster No.
17



Po-jen Chien
(Taipei Medical University, Taiwan)

Title: Fiber-optic sensor of D-lactate

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Abstract

Previous research has found that D-lactate abnormally raise in urine from kidney injured rats. It seems that D-lactate might have potential to be a new biomarker of kidney injured. However, the common analysis method of D-lactate is so time-consuming that it is hard to research the D-lactate concentration meaning in human. The purpose of this study is to building a system that can detect the concentration of D-lactate in short time.

D-lactate dehydrogenase is the enzyme which can transform D-lactate and NAD+ to pyruvate and NADH. NADH has fluorescent characteristic that it absorbs 355 nm light and release 491 nm fluoresce. So, we can calculate the concentration of NADH in sample by detecting the NADH fluorescence intensity. Then, the NADH concentration can be deliberated to the concentration of D-lactate.
In this study, there is a plastic film which attached D-lactate dehydrogenase on the detection tip of system. The light resource on the detection site is UV-LED which is used to excite NADH, the UV-light would pass the band-pass filter and through the fiber to the detection site. The detection site also can receive the NADH fluoresce and the NADH fluoresce would through the fiber to the computer. The data will transfer to the computer to calculate the concentration of D-lactate. In this study, the established system shows quickly reaction of D-lactate concentration detection. Besides, the precision and accuracy of this detection system also have good performance.

By this system conception, the detection of D-lactate could be much more convenient and the research of D-lactate concentration in human or in food industry meaning can be quickly promoted.

Poster No.
18

Chaw Kyi Tha Thu
(Shwe Gone Dine Specialist Hospital, Myanmar)

Title: Evaluation of risk factors for hypertension in Kalaw Township, Myanmar

Abstract

Background: Hypertension or high blood pressure is a chronic medical condition in which the blood pressure in the arteries is elevated. Hypertension is the one of the common non-communicable diseases in Myanmar and it is a preventable disease. This study was done by "cross-sectional analysis" during the residential field training from 25th April to 15th May, 2009. Criteria of systolic blood pressure 140 mmHg and above, and diastolic blood pressure 90 mmHg and above, regardless of the age of the respondent were used for recording the hypertension status.

Aim: The present study was designed to determine the prevalence of hypertension among the people lived in Kalaw Township, Shan State, Eastern Myanmar.

Methods----Based on "Community based cross sectional analytical survey", we collected the data including age, sex, weight, height, waist circumference, hypertension status, personal habit, dietary habit, socioeconomic status and physical activity using structured questionnaires and standard measuring procedures in 150 respondents with "House to house inter-collection" method.

Results: Among the factors, obesity, increased salt intake and alcohol drinking are the common factors relating to hypertension.

Conclusion: Hypertension is a major risk factor for stroke, myocardial infarction (heart attacks), heart failure, aneurysms of the arteries, peripheral arterial disease and is a cause of chronic renal disease. Dietary and lifestyle changes can improve blood pressure control and decrease the risk of associated health complications. Therefore, we suggest that giving proper and efficient health education to people who living in rural areas is very important to reduce the hypertensive patients in Myanmar.

Poster No.
19

Muhammad Shahdaat Bin Sayeed
(University of Asia Pacific, Bangladesh)

Title: Effects of Nigella sativa seeds on memory, cognition and attention of elderly volunteers

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Abstract

Nigella sativa seed is investigated for a potential role in reducing widespread cognitive decline. Traditionally Nigella sativa seeds have reputations for improving memory conditions in different countries and there are several evidences of memory enhancement because of N. sativa seeds as carried out in mice model. Present study was conducted by randomized, placebo controlled & double blinded way to investigate the effects on impaired memory of elderly peoples. Forty aged participants divided in four different groups were introduced with three different dosages of N. sativa seeds and placebo for sixty days. Results of the study indicated the positive modulation effects on verbal, visual & spatial memory conditions due to N. sativa. In accordance of time the cognitive capability boosted in different dosed groups compared with placebo. Tests also provide evidence on capacity of attentiveness and the capability of execution power enhanced in all groups except placebo controlled group in time and dose dependent way.

Poster No.
20

Pham Nguyen Quy
(Tokyo Medical and Dental University)

Title: Proteasome-dependent activation of mTORC1 is essential for autophagy suppression and muscle remodeling following denervation

Abstract

Drastic protein degradation occurs during muscle atrophy induced by denervation, fasting, immobility, and various systemic diseases. While the ubiquitin–proteasome system is highly upregulated in denervated muscles, the involvement of autophagy and protein synthesis has been controversial. Here we report that autophagy is rather suppressed in denervated muscles even under autophagy-inducible starvation condition. This is due to a constitutive activation of mammalian target of rapamycin complex 1 (mTORC1). We further reveal that denervation-induced mTORC1 activation is dependent on the proteasome, which is likely mediated by amino acids generated from proteasomal degradation. Protein synthesis and ribosome biogenesis are paradoxically increased in denervated muscles in an mTORC1-dependent manner. Furthermore, mTORC1 activation plays an anabolic role against denervation-induced muscle atrophy. These results suggest that denervation induces not only muscle degradation but also adaptive muscle response in a proteasome- and mTORC1-dependent manner.