TMDU
東京医科歯科大学

# 6th TMDU International Summer Program

25—28 August 2014

# AGEING AND METABOLISM

## PROGRAM & ABSTRACT BOOK

Tokyo Medical and Dental University http://www.tmd.ac.jp/

6th TMDU International Summer Program (ISP2014) http://www.tmd.ac.jp/TMDU-e/isc/isp2014/

東京医科歯科大学

TOKYO MEDICAL AND DENTAL UNIVERSITY

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# Ageing and Metabolism

**PROGRAM & ABSTRACT BOOK**

# Contents

# ISP2014 SCHEDULE

| *Day / Time* | *Event* | *Venue* |
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## Monday, 25 August: Registration and Welcome Reception

**17:00-17:30** **Registration** — M&D Tower 2F Auditorium 1

**17:30-18:00** **Orientation**
MC: David Cannell
Introduction to ISP: Yoshihiro Ogawa (ISP2014 WG Chairperson, TMDU)
Program Schedule: Ikuko Morio (Director, International Exchange Center, TMDU)

**18:00-20:00** **Welcome Reception** — "Grill Saints"
MC: David Cannell

## Tuesday, 26 August: Lecture Course, Day 1

**9:00-9:10** **Opening Remarks** — M&D Tower 2F Auditorium 1
Keiji Moriyama (Dean, Graduate School of Medical and Dental Sciences)

**9:10-12:50** **Lecture Course 1**
**Chair:** Masayuki Yoshida / Shunsuke Minakuchi
＜ **Cardiovascular Metabolism and Ageing** ＞

***9:10-9:50*** Mitsuaki Isobe (TMDU)
Title: Role of Inflammation in Cardiovascular Remodeling: from Bench to Bed Side

***9:50-10:30*** Masayuki Yoshida (TMDU)
Title: Intravital Microscopy of Vascular Inflammation: an Emerging New Technique to Understand Development of Atherosclerosis

 **Coffee Break (15 min.)**

***10:45-11:25*** Yumiko Oishi-Tanaka (TMDU)
Title: Coordinated Regulation of Inflammation and Lipid Homeostasis in Macrophage

＜ **Dental Metabolism and Ageing** ＞

***11:25-12:05*** Yuichi Izumi (TMDU)
Title: Periodontal Medicine and Modern Periodontal Treatment

***12:05-12:50*** Junichi Furuya (Iwate Medical University, Japan)
Title: Oral Rehabilitation and Management of Elderly People in the Super-ageing Society of Japan

**12:50-14:30**  **Lunch Break**

**14:30-15:00** **Introduction to the University** — M&D Tower 2F Auditorium 1
Ikuko Morio (Director, International Exchange Center, TMDU)

**15:00-17:00** **Laboratory Visit**

**17:00-18:30** **Poster Session** — M&D Tower 2F Foyer
**Facilitator:** Akinori Kimura / Yuichi Izumi / Hiroshi Nishina

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## Wednesday, 27 August: Lecture Course, Day 2

**9:00-12:45** **Lecture Course 2** — M&D Tower 2F Auditorium 1

**Chair:** Hiroshi Nishina / Tetsushi Furukawa

＜ **Immunometabolism and Ageing** ＞

***9:00-9:40*** Shu Takeda (TMDU)
Title: Crosstalk between Bone and Other Organs

***9:40-10:20*** Takayoshi Suganami (TMDU)
Title: Chronic Inflammation and the Metabolic Syndrome

 **Coffee Break (15 min.)**

***10:35-11:20*** Peter Tontonoz (University of California, Los Angeles, U.S.A.)
Title: Integration of Lipid Metabolism and Inflammation by LXRs

＜ **Glucose Metabolism and Ageing** ＞

***11:20-12:05*** Domenico Accili (Columbia University, U.S.A.)
Title: Metabolic Regulation by the Liver

***12:05-12:45*** Akira Matsumoto (TMDU)
Title: “Borono-lectin” Based Strategies for Smart Drug Delivery Systems and Biosensing

**12:45-14:20**  **Lunch Break**

**14:30-16:30** **IEC Program** — M&D Tower 2F Auditorium 1

***14:30-15:00*** < Library Tour > — M&D Tower 3F Library

***15:00-16:30*** < Optional Program >
・Exposure to Japanese culture
・Guided walk in the TMDU neighborhood

**16:30-17:20**  **Free Time**

**17:20-17:30** **Commemorative Photograph** — M&D Tower 26F Faculty Lounge

**17:30-19:30** **Social Hour**
MC: David Cannell
ISP2014 Address: Yasuyuki Yoshizawa (President, TMDU)
Presentation of ISP2014 Certificate: Yasuyuki Yoshizawa (President, TMDU)
Presentation of Best Poster Award: Yoshihiro Ogawa (ISP2014 WG Chairperson, TMDU)

| *Day / Time* | *Event* | *Venue* |
|---|---|---|

## Thursday, 28 August: ISP Symposium 2014 "Ageing and Metabolism"

**9:00-9:10** **Opening Remarks** — M&D Tower 2F, Akio Suzuki Memorial Hall
Yoshihiro Ogawa (ISP2014 WG Chairperson, TMDU)

**9:10-13:00** **Symposium Chair**: Yoshihiro Ogawa / Koji Mitsubayashi

**＜ Cutting-edge Science of Ageing and Metabolism-1 ＞**

***9:10-9:50*** Emi Nishimura (TMDU)
Title: Mechanisms of Hair Graying and Hair Loss: Is There Any Tissue Aging Program?

***9:50-10:30*** Hitoshi Okazawa (TMDU)
Title: Comprehensive Phosphoproteome Analysis Unravels the Core Signaling Network that Initiates the Earliest Synapse Pathology in Preclinical Alzheimer's Disease Brain

 **Coffee Break (15 min.)**

***10:45-11:30*** Peter Tontonoz (University of California, Los Angeles, U.S.A.)
Title: Nuclear Receptor Control of Cholesterol Metabolism

**＜ Cutting-edge Science of Ageing and Metabolism-2 ＞**

***11:30-12:15*** Naoko Ohtani (Tokyo University of Science)
Title: Obesity-induced Gut Microbial Metabolite Promotes Liver Cancer via Senescence-associated Secretome

***12:15-13:00*** Domenico Accili (Columbia University, U.S.A.)
Title: The New Biology of Diabetes

**13:00-13:10** **Closing Remarks**
Yoshinobu Eishi (Vice Dean, Graduate School of Medical and Dental Sciences)

**13:10-14:30**  **Lunch Break**

**14:30-15:30** **Returning Procedure** — M&D Tower 2F, Auditorium 1

## Friday, 29 August: ISP Special Selection (Special Selection Participants only)

The TMDU Graduate School Entrance Examination will be held for ISP2014 Special Selection Participants.
Time and Place will be announced at the Registration on the first day of ISP2014

# Yasuyuki Yoshizawa

President
Tokyo Medical and Dental University

## Message from the President

Tokyo Medical and Dental University (TMDU) is a well-known institution for its dedication to the education of health care professionals and the pursuit of bioscience research. The guiding principle for our university is the mission statement, "*Cultivating Professionals with Knowledge and Humanity and Deploying those Professionals Domestically and Globally to Become a World-Leading Integrated Medical University.*" This powerful idea motivates our faculty and staff to help our students become world-leading health care professionals and bioscience researchers.

A critical part of our mission since the inception of our university over 80 years ago has been the teaching of international students, who I believe have helped the progress of medicine and dentistry in their home countries after returning to practice and teach. For our part, we have found the experience of educating international students to be invaluable in helping us appreciate different cultures and cultivate intellectual sympathy, which is increasingly necessary for medical professionals worldwide. Furthermore, it is a great honor and pleasure for us to learn 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 our three overseas education and research collaboration centers in Ghana, Chile, and Thailand, which we established in recent years. The purpose of these centers is to promote collaborative research and advance the professional development of medical and dental professionals in each local area. For example, we sponsor the exchange of students and faculty members with our partner institutions, support training programs, and manage other outreach activities with and through these research centers.

As an important part of our international activities based here in Japan, we are very pleased to be able to organize our sixth annual International Summer Program, ISP2014. The focus of this year is on the theme of ageing and metabolism. This summer school will provide good opportunities to summarize past successes and to look forward to future research on the topics of ageing and metabolism. I hope that you are as excited as we are about ISP2014. I am confident that this year's program will help you develop professionally, stimulate your academic curiosity, and encourage you to explore the unique features of our university.


## Junji Tagami

Executive Director / Executive Vice President of
Education and International Student Exchange
Tokyo Medical and Dental University


# Welcome to ISP2014

It is our great pleasure to welcome you to ISP2014, our sixth annual International Summer Program. A total of 136 young researchers and students have attended ISP over the last five years. This year we are welcoming 25 excellent young researchers and students from Asia to ISP.

The theme of ISP2014 is “Ageing and Metabolism”. We are happy to announce that our summer program will feature leading scientists from abroad and from Japan, who will offer lecture courses and a symposium over the course of three days. Other activities scheduled during ISP2014 include a library tour, laboratory visits, cultural programs, a poster session and various social events.

ISP2014 will also feature the “ISP Special Selection” program. First initiated in 2012, this program gives selected ISP participants the opportunity to apply for the entrance exam to a TMDU PhD program. The number of ISP participants who have been admitted to TMDU has reached a total of 28 since ISP 2009.

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 2013 QS Asian University rankings. Consequently, TMDU has kept first place in that category over the last four years. I believe TMDU is becoming increasingly attractive to promising students and young researchers from Asia and beyond, as evidenced by the 204 international students enrolled, primarily in our graduate schools, as of April 2014.

On behalf of the organizing committee, I would like to express our sincere gratitude to everyone who is participating in ISP2014. I am confident 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


## Mitsuaki Isobe

(Tokyo Medical and Dental University, Japan)


**Biodata**

Dr. Isobe is the Chair, and a Professor, of Cardiovascular Medicine at Tokyo Medical and Dental University. He received his medical degree and PhD degree in Medicine from The University of Tokyo. After finishing the residency program at Mitsui Memorial Hospital, he completed his research fellowship at the Massachusetts General Hospital in Boston where he published a paper in Science regarding development of immunological tolerance to cardiac allografts. He was an editorial board member of ATVB and Circulation Research. His research interests include transplantation immunology, heart failure, cardiomyopathy, myocarditis and vascular biology. He has published over 500 original articles in journals such as Cell, Science, Lancet and Nature Medicine. He served as a Chairman of the Japanese Heart Failure Society and has been a member of the board of trustees of Japanese Circulation Society since 2012.

**Lecture Course : Role of Inflammation in Cardiovascular Remodeling: from Bench to Bed Side**

**Abstract**


Inflammation is critically involved in the pathophysiology of cardiovascular remodeling. Recent investigations have revealed crucial roles of T cell-mediated immunity and inflammation in the development of atherosclerosis, cardiac allograft vasculopathy, and restenosis after stent implantation. Intracellular signals through T cell receptor cause activation of NFκB. The focus of our investigation is to clarify the pathophysiological role of NFκB in the development of occlusive arterial lesions. We used mice models including cardiac allograft vasculopathy after heart transplantation and wire-injured femoral arteries. Coculture of smooth muscle cells (SMC) and activated T cells from mice with cardiac allograft rejection resulted in proliferation of SMCs. Treatment of cardiac allografts or femoral artery with NFκB decoy gene transfected by either HVJ-liposome method or ultrasound-microbubble method attenuated development of intimal hyperplasia after heart transplantation or wire injury. These data indicate that NFκB are critically involved in the development of a variety of vascular remodeling through activation of SMCs. Based on these in vivo and in vitro data we developed translational research. Patients with coronary artery disease were treated with locally-delivered NFkB decoy after stent implantation. The results of 18 patients attest to the safety of this gene therapy and to the favorable results of prevention of restenosis after stenting. Treatment targeting inflammation through this molecule shows promise for the prevention of cardiac allograft vasculopathy and other vascular diseases.


## Masayuki Yoshida

(Tokyo Medical and Dental University, Japan)


**Biodata**

Masayuki Yoshida is Director of Life Science and Bioethics Research Center, Professor of Department of Life Science and Medical Ethics, and Chief of Department of Medical Genetics at Tokyo Medical and Dental University.

He graduated from Tokyo Medical and Dental University (TMDU) School of Medicine in Tokyo and completed a residency in Internal Medicine and Cardiology at TMDU Hospital. After his post-doctoral research fellowship in the Department of Pathology, Harvard Medical School, he went back to TMDU School of Medicine to work as an instructor in Molecular Medicine and then promoted to an Associated Professor in Medical Biochemistry. His main research field includes vascular biology, molecular biology, and atherosclerosis with a special interest in leukocyte-endothelial interaction.

He is also responsible for Department of Medical Genetics in our hospital, where novel genetic testing and counseling are provided.

**Lecture Course : Intravital Microscopy of Vascular Inflammation: An Emerging New Technique to Understand Development of Atherosclerosis**


**Abstract**

Although inflammation plays a crucial role in the pathophysiology of cardiovascular disease, it is not known how and when inflammatory cascade initiates its deteriorated process. We thus monitored the effect of high-fat diet (HFD) in the development of atherosclerosis in athero-prone artery of wild type mice. Compared to normal chow diet, where virtually no leukocyte interaction was observed, HFD for 4 weeks induced significant leukocyte recruitment to femoral artery. Flow cytometric analysis of peripheral blood revealed that the distinct population of leukocytes was increased during this early phase. We also found that chemokines plya a pivotal role in this process. Further, this technique was applicable to observing new phenotypes of genetically-engineered mice and screen compounds that are potentially useful in future therapeutic application. In this session, emerging potential of intravital microscopy will be discussed.


## Yumiko Oishi-Tanaka

(Tokyo Medical and Dental University, Japan)


**Biodata**

Dr. Yumiko OISHI-TANAKA graduated from Gunma University School of Medicine, earning her Medical Degree (M.D.) in 1998. After three years of clinical training as a cardiologist, she started focused research on the molecular mechanisms of metabolic syndrome as a PhD student in the Department of Cardiovascular Medicine, the University of Tokyo, and received her PhD in Medicine in 2006. She completed postdoctoral training in the laboratory of Dr. Christopher K. Glass at University of California, San Diego, in February 2013, followed by her tenure track faculty appointment at Medical research Institute, Tokyo Medical and Dental University in March 2013.

**Lecture Course : Coordinated Regulation of Inflammation and Lipid Homeostasis in Macrophage**


**Abstract**

Growing evidence has suggested that inflammation plays an important role in the onset of numerous diseases, including metabolic diseases. Recently, it has been recognized that macrophages synthesize varieties of bioactive lipids by responding various signals, characterized by the lipidomic analysis based on the mass spectrometry. Activated macrophages rapidly activate arachidonate cascade to produce inflammatory mediators such as leukotrienes and prostagrandins. On the other hand, the production of the anti-inflammatory omega-3 and -9 poly unsaturated fatty acids (ω-3,-9 PUFAs) significantly increases in the chronic phase of inflammation. By utilizing both molecular biology technique and bioinformatics, we found that the inflammatory activated NFκB kicks off both pro-inflammatory and anti-inflammatory signaling pathways. TLR4 activation rapidly, and transiently, inhibits Liver X receptor (LXR) signaling through NFκB, and subsequently activates Sterol regulatory element-binding protein (SREBP) by processing from the ER membrane. In the chronic phase of inflammation, LXR and SREBP work together to increase production of anti-inflammatory fatty acids, then actively resolve inflammation. Thus, transcriptional/signaling network between LXR and SREBP play an important role in regulation of the fatty acid synthesis to maintain homeostasis. These findings provide novel therapeutic strategies which target macrophage function to be stabilized by increasing anti-inflammatory fatty acids production.


## Yuichi Izumi

(Tokyo Medical and Dental University, Japan)


**Biodata**

Dr. Yuichi IZUMI has been Professor and Chair of the Department of Periodontology, Graduate School of Medical and Dental Sciences, Tokyo Medical and Dental University, since 2007. He graduated from the Faculty of Dentistry of TMDU in 1979 and received his PhD from the Graduate School of TMDU in 1983. He has worked as an Assistant Professor in education, research, and clinical practice, in the Department of Periodontology at TMDU (1983-1992), a Maître Assistant in the Department of Oral Physiopathology and Periodontology of University of Geneva (1987-1989), an Associate Professor (1992-1999) and Professor (1999-2007) in the Department of Periodontology of Kagoshima University Dental School. His research interests are etiology, host responses in periodontal diseases and periodontal medicine, periodontal regeneration by tissue engineering, clinical application of lasers in periodontics. He received Research Awards from AAP and IADR.

**Lecture Course : Periodontal Medicine and Modern Periodontal Treatment**


**Abstract**

Periodontitis is an inflammatory disease caused by periodontopathic bacteria harbored on root surfaces. It involves epithelial downgrowth and loss of tooth supporting structures such as gingiva, periodontal ligaments, root cementum and alveolar bone proper.

Recent studies suggest that periodontal pathogens may be associated with several systemic diseases such as, cardiovascular disease (CVD), diabetes mellitus (DM), aspiration pneumonia, preterm low birth weight (PLBW), and osteoporosis.

Epidemiological reports suggest that periodontitis is one of the key risk factors for the onset of CVD. Several studies have reported that periodontal bacteria were frequently detected in cardiovascular specimens. Previously, we revealed that patients with acute coronary syndrome showed significantly higher serum IgG titers to a strain of periodontopathic bacteria compared with patients with chronic coronary disease. Periodontopathic bacteria were also detected in a high percentage of specimens of diseased arteries from patients with Buerger disease or abdominal aortic aneurysm. Periodontopathic bacteria may play a crucial role in the development of CVD; however, the influence of these bacteria on the disease has not yet been studied in detail.

Periodontitis is closely related to DM. An increasing number of epidemiological studies suggests that periodontitis is associated with diabetes. To date, little evidence has been reported to indicate that diabetes and/or glucose intolerance have a significant cause-effect relationship with periodontal disease. In this regard, it is important to prove the effect of therapeutic approaches to periodontitis upon mitigation of glycemic control in diabetic patients. In our studies we revealed that effective glycemic control can improve bleeding on probing lesions in type 2 diabetic patients with periodontitis through ameliorating inflammation at the gingival sites of periodontal tissue.

Also, we evaluated the relevance of periodontal and general health conditions with Threatened Premature Labor (TPL) and Preterm birth in relation to serum cytokine levels and the composition of subgingival plaque. The TPL women revealed worsened periodontal conditions and elevated serum IL-8 and IL-1 levels compared to the non-TPL women.

The goal of the periodontal treatment is to arrest further periodontal destruction by eliminating soft and hard deposits which have accumulated on the root surfaces, and to create a new periodontal environment for easier cleaning of the root surfaces. In order to achieve this goal, soft and hard periodontal tissues have to be removed from the region. However, the ultimate goal of the periodontal treatment should be the regeneration of the periodontium that have been lost due to various reasons. A few regenerative techniques have been developed and introduced during the last two decades. One of them is Guided Tissue Regeneration using a barrier membrane. Another technique, that has been recently developed, is the application of enamel matrix derivative, and growth factors on the root surfaces.

This presentation reviews the relationship between periodontal pathogens and CVD, DM and PLBW, the modern periodontal therapy, new diagnostic system and examination will be introduced to guide further clinical and experimental investigations in the near future.


## Junichi Furuya

(Iwate Medical University, Japan)


**Biodata**

Dr. Junichi FURUYA is an associate professor of Prosthodontics and Oral Implantology at the Iwate Medical University (IMU) School of Dentistry. Since arriving at IMU in 2005, he has worked as a full-time faculty member in prosthodontics and gerodontology. Dr. Furuya received both his DDS in 1996 and PhD in 2000 from the Tokyo Medical and Dental University. While on sabbatical at Harvard School of Dental Medicine from 2013 to 2014, he joined the Department of Restorative Dentistry and Biomaterials Sciences as a visiting associate professor; he also served as a part-time faculty member of the Pre-Doctoral Teaching Practice at Harvard Dental Center.

Dr. Furuya's research interest is in clinical and basic research toward clarifying the relationships among ageing, oral function, and denture. He works as a prosthodontist at IMU Hospital Dental Center and is in charge of the Dysphagia Rehabilitation Clinic at IMU.

**Lecture Course : Oral Rehabilitation and Management of Elderly People in the Super-ageing Society of Japan**


**Abstract**

As of 2014, Japan has the highest ageing population in the world, and the number of elderly people with long-term care needs is rapidly increasing. Owing to their physical disabilities, most of these people have problems visiting dental clinics. Thus, it is very common for them to complain that they cannot eat what they want. In addition, their oral hygiene and oral function are mostly poor. Oral ingestion is particularly important for elderly people because it has a direct impact on their quality of life. It is, therefore, the responsibility of dental professionals in the super-ageing society of Japan to exploit the masticatory and swallowing ability of elderly people as much as possible through dental care including oral rehabilitation and management. In this lecture, clinical cases and researches will be reviewed to consider the importance of oral rehabilitation and management for elderly people.

Working within a super-ageing society now demands that the dental professionals modify their roles, such that they become a specialist for oral function of eating. Owing to the growing shortage of physicians in rural areas, dentists in Japan have had to assume responsibility for the eating ability of their patients. Aspiration pneumonia is caused by the aspiration of microbes in the saliva. It has been demonstrated that delivering professional oral hygiene care once a week was able to reduce the incidence of pneumonia in institutionalized elderly people. In terms of dysphagia rehabilitation, the dentist and dental hygienist can address the food texture, body posture, and swallowing methods to compensate for declined swallowing function. Mastication is also very important in bolus formation to achieve safety and smooth bolus passage through the pharynx, the enjoyment of eating, and efficient nutritive ingestion.

Dental practice for elderly patients with masticatory and swallowing disorders as a result of motor disturbances clearly presents greater difficulties than with healthy elderly patients. Therefore, additional practice-related dental skills and knowledge are required. However, dentistry should also strive to make dental techniques simpler and develop advanced technology to achieve labor-saving practical methods. It is particularly important that elderly people obtain good-quality dentures before they are no longer in a position to visit a dental clinic. This would allow elderly people in care institutions to receive the minimum necessary amount of dental care. Several studies have clarified that wearing dentures can improve the effects of dysphagia rehabilitation and thus help bolus transport during eating. However, little is known about the optimal design of dentures for elderly people with reduced oral functions. It is necessary for prosthetic dentistry to promote outstanding skills and knowledge in new areas. This can then lead to an elucidation of the proper role of prosthetic dentistry in a super-ageing society.


## Shu Takeda

(Tokyo Medical and Dental University, Japan)


**Biodata**

Shu Takeda was born in Tokyo Japan. He received M.D. and Ph.D. degrees from the University of Tokyo, Japan, in 1992 and 2002, respectively. He was an associate professor at Tokyo Medical and Dental University from 2004 to 2009 and at Keio University from 2009 to 2014 and returned to Tokyo Medical and Dental University as a professor of physiology and cell biology in 2014. He serves as the editor of Bone and on the editorial board of Journal of Bone and Mineral Metabolism. He received many awards including the President's Book Award and the Young Investigator Award from ASBMR and a research award from the Japanese Endocrine Society. His current research interests are molecular elucidation of the crosstalk between bone and other organs.

**Lecture Course : Crosstalk between Bone and Other Organs**

**Abstract**


It was believed that cytokines and hormones are main regulators of bone remodeling. However, this view has been challenged. Organ network has been shown to play a major role in homeostasis recently. Bone is not the exception.

Clinically, it is well known that head trauma accelerates fracture healing. Advances in molecular genetics revealed that neurons and neuropeptides, including sympathetic nervous system, are intimately involved in bone remodeling.

Semaphorin 3A (Sema3A) is a diffusible axonal chemorepellent that plays an important role in axon guidance. Previous studies have demonstrated that Sema3A is an osteo-anabolic autocrine and, accordingly, Sema3A-KO mice develop a low bone mass due to decreased bone formation. However, recently, we demonstrated that osteoblast-specific Sema3A-KO mice had normal bone mass, even though the expression of Sema3A in bone was substantially decreased. In contrast, mice lacking Sema3A in neurons had low bone mass similar to Sema3A-KO mice, indicating that neuron-derived Sema3A is responsible for the bone abnormalities independent of the local effect of Sema3A in bone. Indeed, sensory innervations of trabecular bone were significantly decreased in neuron-specific Sema3A-KO. Moreover, ablating sensory nerves reduced bone mass in wild-type mice, whereas it did not deteriorate low bone mass phenotype in neuron specific Sema3A-KO mice, further indicating the essential role of the sensory nervous system in normal bone homeostasis. Thus, we demonstrated that sensory nervous system is also a critical regulator of bone remodeling.

In this lecture, I would like to discuss novel regulators of bone remodeling.


## Takayoshi Suganami

(Tokyo Medical and Dental University, Japan)


**Biodata**

Dr. Takayoshi Suganami received his M.D. and Ph.D. from Kyoto University, Japan. He became an assistant professor (2003) and an associate professor (2011) in the Department of Molecular Medicine and Metabolism, Tokyo Medical and Dental University. Since 2013, he has been a professor in the Department of Organ Network and Metabolism, Tokyo Medical and Dental University. The focus of his laboratory is to elucidate the pathophysiologic role of chronic inflammation in the metabolic syndrome. His major research contributions include the molecular mechanisms underlying obesity-induced adipose tissue inflammation.

**Lecture Course : Chronic Inflammation and the Metabolic Syndrome**

**Abstract**


Metabolic syndrome is a constellation of visceral fat obesity, impaired glucose metabolism, atherogenic dyslipidemia, and blood pressure elevation, which increases the risk of atherosclerotic diseases. Evidence has accumulated indicating that obesity is associated with a state of chronic, low-grade inflammation, which may cause obesity-induced insulin resistance. Adipose tissue is an important endocrine organ that secretes a large number of bioactive substances or adipocytokines (adipokines). In obesity, unbalanced production of pro- and anti-inflammatory adipocytokines critically contributes to the development of many aspects of metabolic syndrome. In this regard, in addition to lipid-laden adipocytes, various stromal cells such as preadipocytes, endothelial cells, fibroblasts, and immune cells are also involved in the regulation of adipocytokines. We have provided evidence suggesting that the crosstalk between adipocytes and macrophages forms a vicious cycle that aggravates obesity-induced adipose tissue inflammation.

To store excessive energy as triglyceride is also a fundamental function of adipose tissue. In response to nutritional conditions, lipid metabolism in adipose tissue is tightly regulated by insulin and the sympathetic nervous system. When adipose tissue cannot meet the demand of storing excessive energy, triglyceride is accumulated in non-adipose tissues as ectopic fat, which may lead to insulin resistance in the liver and skeletal muscle and insufficient insulin secretion in the pancreas (lipotoxicity). Recent evidence also suggests that chronic inflammation in adipose tissue plays a role in this process. Our data indicates that interstitial fibrosis in adipose tissue may be a novel mechanism of ectopic lipid accumulation. In this lecture, we will discuss the recent progress about the role of chronic inflammation in the pathophysiology of the metabolic syndrome.


## Peter Tontonoz

(University of California, Los Angeles, U.S.A.)


**Biodata**

Peter Tontonoz received his B.A. from Wesleyan University and his M.D. and Ph.D. from Harvard Medical School.

Dr. Tontonoz is Professor of Pathology and Laboratory Medicine and a Howard Hughes Medical Institute Investigator at the University of California, Los Angeles. The focus of his laboratory is the control of gene expression by lipids and the role of nuclear receptors in lipid metabolism. His major research contributions include the delineation of role of PPAR and LXR in adipogenesis and atherosclerosis, and elucidation of mechanisms of crosstalk between metabolism, inflammation and immunity. Dr. Tontonoz is a recipient of the Richard Weitzman Award and the Gerald D. Aurbach Award from the Endocrine Society and the Jeffrey Hoeg Award for Basic Science and Clinical Research from the American Heart Association. Dr. Tontonoz serves on a number of editorial boards and is an Associate Editor of Molecular and Cellular Biology. He is the 2013-14 President of the American Society for Clinical Investigation.

**Lecture Course : Integration of Lipid Metabolism and Inflammation by LXRs**


**Abstract**

The fatty acyl composition of phospholipids determines the biophysical character of membranes and impacts the function of membrane proteins. We have defined a nuclear receptor pathway for the dynamic modulation of membrane composition in response to changes in cellular lipid metabolism. The Liver X Receptors (LXRs) are nuclear receptors that play central roles in the transcriptional control of lipid metabolism. LXRs function as nuclear “cholesterol sensors” that are activated in response to elevated intracellular cholesterol levels in multiple cell types. Ligand activation of LXRs preferentially drives the incorporation of polyunsaturated fatty acids into phospholipids through induction of the remodeling enzyme Lpcat3. Promotion of Lpcat3 activity ameliorates endoplasmic reticulum (ER) stress induced by saturated free fatty acids in vitro or by hepatic lipid accumulation in vivo. Conversely, Lpcat3 knockdown in liver exacerbates ER stress and inflammation. Mechanistically, Lpcat3 modulates inflammation both by regulating inflammatory kinase activation through changes in membrane composition and by affecting substrate availability for inflammatory mediator production. These results outline an endogenous mechanism for the preservation of membrane homeostasis during lipid stress and identify Lpcat3 as an important mediator of LXR effects on metabolism.


## Domenico Accili

(Columbia University, U.S.A.)


**Biodata**

Dr. Domenico Accili is Professor of Medicine, Russell Berrie Foundation Professor of Diabetes, and Director of the NIH-funded Diabetes Research Center at Columbia University College of Physicians & Surgeons. He also serves as an Attending Physician at Columbia-Presbyterian Hospital. A graduate of the University of Rome, his training in Internal Medicine was served at the University Hospital Gemelli, also in Rome. Following a Fogarty Fellowship in the Diabetes Branch of the National Institute of Diabetes and Digestive Kidney Diseases, he became Chief of the Section on Genetics and Hormone action of the National Institute of Child Health at the National Institutes of Health in Bethesda, Maryland. He joined the faculty at Columbia University in 1999.

Dr. Accili's research has delved into the pathogenesis of diabetes, the integrated physiology of insulin action and the mechanisms of pancreatic beta-cell failure. He is best known for the identification of a family of DNA-binding proteins that collectively regulate diverse pathophysiological processes, including liver glucose production, food intake, insulin production and adipogenesis. He has received numerous awards, including the 2003 Lilly Award for Outstanding Scientific Achievement by the American Diabetes Association. His work has been published in leading medical research journals. A member of several editorial boards, he also serves on numerous advisory panels for academia, government and industry. He is an elected member of the Association of American Physicians and the American Society for Clinical Investigation. His work is supported by the National Institutes of Health, the American Diabetes Association, the Russ Berrie Foundation, and the Brehm Coalition.

**Lecture Course : Metabolic Regulation by the Liver**

**Abstract**


Type 2 diabetes is caused by insulin resistance and pancreatic β-cell failure. Most diabetes prevention and outcome studies demonstrate that treatments for insulin resistance outperform those for β-cell dysfunction. Yet, with the exception of thiazolidinediones, treatment options for insulin resistance have remained unchanged since the 1940's. Our research focuses on the identification of hepatic signaling pathways that can be leveraged to treat insulin resistance. The diabetic liver overflows with glucose and atherogenic lipoproteins (VLDL triglycerides and small dense LDL, resulting in lower HDL) that are responsible for the microvascular (hyperglycemia-dependent) and macrovascular complications of diabetes (dyslipidemia-dependent). We have shown that key to insulin control of hepatic glucose production is the hormone's ability to regulate transcription factor Foxo. When Foxo is active, genes that promote gluconeogenesis and glycogenolysis are activated. Insulin inhibits Foxo, effectively shutting off glucose production. Interestingly, glucagon has the opposite effects on Foxo, suggesting a central role of this protein in hormonal regulation of glucose release. We have also recently discovered an additional dimension to insulin action through Foxo that may help explain the pathogenesis of altered lipid metabolism in the diabetic liver. We have shown that insulin, acting through Foxo, controls the composition of the bile acid pool, in such a way that the insulin-resistant state is associated with preferential synthesis of non-12α-hydroxylated (hydrophilic) bile acids. The latter turn out to be poor ligands for the bile acid receptor, FXR, leading to decreased intestinal cholesterol absorption and increased hepatic triglyceride synthesis. Both features contribute to a pro-atherogenic lipid profile, with elevated secretion of TG-rich lipoproteins from the liver. The key Foxo target in this process is the 12α-hydroxylase, Cyp8b1, indicating that strategies targeting this enzyme may help relieve excessive lipoprotein turnover and secretion in the insulin-resistant liver. Thus, our work provides evidence for a unifying mechanism mediated by Foxo that can be leveraged to reduce hepatic glucose production as well as excess CVD risk in type 2 diabetics.


## Akira Matsumoto

(Tokyo Medical and Dental University, Japan)


**Biodata**

Akira Matsumoto is an Associate Professor in the Institute of Biomaterials and Bioengineering at TMDU where he co-directs the Bioelectronics group with Prof. Yuji Miyahara. He eamed his B. Eng (1999) and Ph.D (2004) from the University of Tokyo. 2004-2005: Postdoctoral fellow in a group of Prof. David L. Kaplan at Tufts Univ. 2006-2009: Assistant Prof. in Dept. of Bioengineering at the University of Tokyo. With a background in polymer chemistry he has been interested in synthesis, design, functionalization and nano-/micro-fabrications of both synthetic and nature-derived polymers. His recent research also focuses on development of solid-state biosensors. Among other honors he has been awarded the Nakatani Award in 2012 (Nakatani Foundation of Electronic Measuring Technology Advancement) and TMDU Award for Excellence in Research.

**Lecture Course : "Borono-lectin" Based Strategies for Smart Drug Delivery Systems and Biosensing**

**Abstract**


Phenylboronic acid (PBA) derivatives readily complex with 1,2- and 1,3-cis-diol compounds, including those found in carbohydrates, through reversible boronate ester formation in an aqueous solution. Because of this property, PBA can be regarded as a synthetic (and thus remarkably stable) alternative to lectins or carbohydrate-binding proteins, often termed "boronolectin", whose binding specificity can be chemically tailored. Lorand and Edwards were the first to quantitatively reveal this fascinating property of PBA. Since the late 1960s, PBA compounds have been extensively studied as a ligand for affinity chromatography for the purification of polyol compounds including ribonucleic acids (RNA). Optical and electrical chemosensing applications, representatively those focusing on glucose detection, were the next-generation trend in this area of research, the first concept of which appeared in the early 1990s. Boronic acid compounds are compatible with human physiology, as exemplified by the fact that some of them have prevailed as chemotherapeutic agents and in other remedies. Meanwhile, PBA interacts with a variety of biological membranes including cells, viruses, bacteria and fungi through membrane-constituting carbohydrate moieties. To illustrate, some PBA functionalized synthetic polymers can specifically bind to glycoprotein of lymphocytes and induce their enhanced proliferation, a feature truly mimicking that of lectins and thus relevant for immunotherapy. These interactions can then rationalize the design of PBA-based synthetic ligands and the cell-targeting strategies for the purpose of drug delivery. To make them attractive as mediators of drug delivery application, PBA is able to undergo a dramatic inversion in the state of hydrophobicity depending on the degree of acid disassociation; it is strongly hydrophobic when uncharged but it turns into hydrophilic when anionically charged at pH values above its pKa. Since the PBA-diols interaction is a dynamic (equilibrium) event determined by the respective concentrations, these features leads to an ability to fine-tune or switch the stability of the complex, offering a new rationale for the design of environmental-sensitive materials and systems.

In this talk, I will describe some new aspects of the PBA (polymer)-based approaches toward diagnostic and therapeutic applications. The topics include PBA-mediated targeting to sialic acid (SA), an anionic monosaccharide that frequently occurs at the termini of the glycan chains, as techniques relevant to tumor diagnosis and treatment. Other unique PBA-based drug delivery systems, including those for siRNA and insulin, will also be summarized.

# Profiles and Abstracts of Symposium Speakers


## Emi K. Nishimura

(Tokyo Medical and Dental University, Japan)


**Biodata**

Dr. Emi Nishimura obtained her MD in 1994 and did her dermatology residency at Kyoto University Hospital. She then obtained her PhD in Shin-Ichi Nishikawa's laboratory at Kyoto University, studying melanocyte development, where she subsequently identified melanocyte stem cells. Dr. Nishimura did her post-doc training in David Fisher's lab at the Dana Farber Cancer Institute, Harvard Medical School, and extended her melanocyte stem cell research there. She then started her own research group as an Associate Professor at Hokkaido University, subsequently becoming Professor at Kanazawa University the following year. Her lab then moved to the Tokyo Medical and Dental University in 2009. She is currently a Professor in the Department of Stem Cell Biology within the Medical Research Institute of the Tokyo Medical and Dental University.

**Symposium Talk : Mechanisms of Hair Graying and Hair Loss: Is There Any Tissue Aging Program?**


**Abstract**

Multicellular organisms senesce with the expression of various aging phenotypes that are characterized by functional tissue decline and organismal changes with decreased regenerating capabilities. Hair loss and hair graying are typical aging phenotypes in mammals, but the underlying mechanisms of aging are still largely elusive in most tissues. In recent decades, some signaling pathways which determine organismal lifespan and molecules responsible for progeroid syndromes have been identified in some organisms, but the underlying cellular mechanisms of aging-associated hair changes remain unclear. Aging-associated somatic stem cell changes also have been reported in recent years, but the exact mechanisms underlying the expression of aging phenotypes and whether there is any tissue aging program are still largely unknown. We have studied the mechanisms of aging-associated hair graying and hair loss by focusing on adult stem cells. We previously identified melanocyte stem cells (McSCs) within the bulge-subbulge area of mouse hair follicles. That population is cyclically activated to self-renew and to provide mature melanocytes for hair pigmentation (Nishimura EK et al. 2002). Our chronological analysis of McSCs and hair follicle stem cells (HFSCs), which function as the niche cells for McSCs (Tanimura S et al. 2011), demonstrated that mouse hair follicles age through the defective renewal of McSCs and HFSCs. McSCs differentiate into pigment-producing melanocytes in the niche without renewing themselves under excessive genomic stress or with aging (Nishimura EK et al. 2005, Inomata K et al. 2009). Strikingly, HFSCs with a sustained DNA damage response also show characteristic fate changes which are clearly distinguished from cellular senescence and cell death. The stem cell fate changes with aging and the underlying tissue aging program based on the fate changes will be illustrated and discussed.


## Hitoshi Okazawa

(Tokyo Medical and Dental University, Japan)


**Biodata**

Dr. Hitoshi Okazawa is Professor and Chair at Neuropathology, Medical Research Institute, and Director of Center for Brain Integration Research, Tokyo Medical and Dental University. He graduated from Medical School, The University of Tokyo in 1984 and received his Ph.D. in 1991 from the Graduate School of Medicine, The University of Tokyo. There he discovered Oct-3;Oct-4;Oct-3/4, the key transcription factor for stemness of ES cells and generation of iPS cells. He worked as a staff scientist (BATIIa) at the Max-Planck Institute in Munich for research of neurotrophic factor receptors from 1991-1992, after which he served as Assistant Professor at Department of Neurology, The University of Tokyo in 1994, and Head of the Department of Molecular Neurotherapeutics, Tokyo Metropolitan Institute for Neuroscience in 2001. From 2003, he joined TMDU. His research is aimed at understanding the mechanisms of, and developing the therapeutics of, neurodegenerative diseases, including Alzheimer's disease, Huntington's disease and spinocerebellar ataxia. He established DNA damage repair as a common pathology in multiple neurodegenerative diseases and discovered PQBP1, a critical molecule to control brain size and intelligence. He is currently the leader of the innovative research field "Foundation of Synapse and Neurocircuit Pathology" supported by Japanese Government (MEXT). He received Narabayashi Prize, Japanese Society for Neurology in 2011.

**Symposium Talk : Comprehensive Phosphoproteome Analysis Unravels the Core Signaling Network that Initiates the Earliest Synapse Pathology in Preclinical Alzheimer's Disease Brain**


**Abstract**

Using high-end mass spectrometry, we screened phosphoproteins and phosphopeptides in four types of Alzheimer's disease (AD) mouse models and human AD postmortem brains. We identified commonly changed phosphoproteins in multiple models and also determined phosphoproteins related to the initiation of Aβ deposition in the mouse brain. After confirming that these proteins were also changed in human AD brains, we put the proteins on experimentally verified protein-protein interaction databases. Surprisingly most of the core phosphoproteins were directly connected, and they formed a functional network linked to synaptic spine formation. The change of the core network started at a preclinical stage even before histological Aβ deposition. Systems biology analyses suggested phosphorylation of specific proteins by over-activated kinases initiates synapse pathology. Interestingly, these proteins are directly connected in protein-protein interaction (PPI) databases. Two-photon microscopic observation revealed recovery of abnormal spine formation in the AD model mice by targeting a protein in the core PPI network or by inhibiting candidate kinases, supporting our hypothesis formulated based on phosphoproteome analysis.


## Peter Tontonoz

(University of California, Los Angeles, U.S.A.)


**Biodata**

Peter Tontonoz received his B.A. from Wesleyan University and his M.D. and Ph.D. from Harvard Medical School.

Dr. Tontonoz is Professor of Pathology and Laboratory Medicine and a Howard Hughes Medical Institute Investigator at the University of California, Los Angeles. The focus of his laboratory is the control of gene expression by lipids and the role of nuclear receptors in lipid metabolism. His major research contributions include the delineation of role of PPAR and LXR in adipogenesis and atherosclerosis, and elucidation of mechanisms of crosstalk between metabolism, inflammation and immunity. Dr. Tontonoz is a recipient of the Richard Weitzman Award and the Gerald D. Aurbach Award from the Endocrine Society and the Jeffrey Hoeg Award for Basic Science and Clinical Research from the American Heart Association. Dr. Tontonoz serves on a number of editorial boards and is an Associate Editor of Molecular and Cellular Biology. He is the 2013-14 President of the American Society for Clinical Investigation.

**Symposium Talk : Nuclear Receptor Control of Cholesterol Metabolism**


**Abstract**

The Liver X Receptors (LXRs) are nuclear receptors that play central roles in the transcriptional control of lipid metabolism. LXRs function as nuclear “cholesterol sensors” that are activated in response to elevated intracellular cholesterol levels in multiple cell types. Once activated, LXRs induce the expression of an array of genes involved in cholesterol absorption, efflux, transport and excretion. They also inhibit cholesterol uptake by inducing the ubiquitination and degradation of the LDL receptor. We identified IDOL (Inducible Degrader of the LDLR) an LXR-regulated E3 ubiquitin ligase that targets lipoprotein receptors for the LDLR, VLDLR and ApoER2 for degradation. IDOL directly binds to the cytoplasmic tails of lipoprotein receptors in conjunction with UBE2D enzymes, leading to clathrin-independent internalization and lysosomal degradation.

In addition to their function in lipid metabolism, LXRs modulate immune and inflammatory responses cell of both the innate and acquired immune systems. Synthetic LXR agonists promote cholesterol efflux and inhibit inflammation in vivo and inhibit the development of atherosclerosis in animal models. Loss of LXR expression in mice leads to pathologic lipid accumulation, atherosclerosis and the development of autoimmune disease. The ability of LXRs to integrate metabolic and inflammatory signaling makes them potentially attractive targets for intervention in human metabolic disease.


## Naoko Ohtani

(Tokyo University of Science, Japan)


**Biodata**

Dr. Naoko Ohtani is a Professor of Department of Applied Biological Science, Faculty of Science and Technology, Tokyo University of Science, since April of 2014. She graduated from the Faculty of Medicine of Kyoto Prefectural University of Medicine (KPUM) and received her Ph.D. from the Graduate School of the same university in 1995. She worked as an Assistant Professor in Kyoto Prefectural University of Medicine until 1998, and then as a post-doctoral fellow in the Paterson Institute for Cancer Research of University of Manchester until 2003. After coming back to Japan, she worked as an Associate Professor at The Institute of Genome Research of University of Tokushima until 2007, and a senior staff scientist at the Cancer Institute in Japanese foundation for Cancer Research until March of 2014. In April of 2014, she obtained the current position. Her research interests are the role of cellular senescence in vivo and obesity-associated liver carcinogenesis.

**Symposium Talk : Obesity-induced Gut Microbial Metabolite Promotes Liver Cancer via Senescence-associated Secretome**

**Abstract**


Naoko Ohtani, M.D., Ph. D.1,2,3

1, Department of Applied Biological Science, Faculty of Science and Technology, Tokyo University of Science, 2, Division of Cancer Biology, The Cancer Institute of Japanese Foundation for Cancer Research, 3,PRESTO, Japan Science Technology Agency Tokyo, JAPAN



Obesity has become more prevalent in most developed countries over the past few decades, and is increasingly recognized as a major risk factor for several common types of cancer. As the worldwide obesity epidemic has shown no signs of abating, better understanding of the mechanisms underlying obesity-associated cancer is urgently needed. Although several events were proposed to be involved in obesity-associated cancer, the exact molecular mechanisms that integrate these events have remained largely unclear. Here, we show that senescence-associated secretory phenotype (SASP) plays crucial roles in promoting obesity-associated hepatocellular carcinoma (HCC) development in mice (1,2). Dietary or genetic obesity induces alterations of gut microbiota, thereby increasing the levels of a bacterial metabolite that cause DNA damage. The enterohepatic circulation of the bacterial metabolites provokes SASP phenotype in hepatic stellate cells (HSCs), which in turn, secretes various inflammatory and tumour promoting factors in the liver, thus facilitating HCC development in mice after exposure to chemical carcinogen. Importantly, reducing gut bacteria efficiently prevents HCC development in obese mice. Similar results were also observed in mice lacking an SASP inducer or depleted of senescent HSCs, indicating that the induction of SASP by the gut bacterial metabolite in HSCs plays key roles in obesity-associated HCC development. Interestingly, moreover, signs of SASP were also observed in the HSCs in the area of HCC arising in patients with nonalcoholic steatohepatitis (NASH), implying that a similar pathway may contribute to at least certain aspects of obesity-associated HCC development in humans as well. These findings provide valuable new insights into the development of obesity-associated cancer and open up new possibilities for its control.


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## Domenico Accili

(Columbia University, U.S.A.)


**Biodata**

Dr. Domenico Accili is Professor of Medicine, Russell Berrie Foundation Professor of Diabetes, and Director of the NIH-funded Diabetes Research Center at Columbia University College of Physicians & Surgeons. He also serves as an Attending Physician at Columbia-Presbyterian Hospital. A graduate of the University of Rome, his training in Internal Medicine was served at the University Hospital Gemelli, also in Rome. Following a Fogarty Fellowship in the Diabetes Branch of the National Institute of Diabetes and Digestive Kidney Diseases, he became Chief of the Section on Genetics and Hormone action of the National Institute of Child Health at the National Institutes of Health in Bethesda, Maryland. He joined the faculty at Columbia University in 1999.

Dr. Accili's research has delved into the pathogenesis of diabetes, the integrated physiology of insulin action and the mechanisms of pancreatic beta-cell failure. He is best known for the identification of a family of DNA-binding proteins that collectively regulate diverse pathophysiological processes, including liver glucose production, food intake, insulin production and adipogenesis. He has received numerous awards, including the 2003 Lilly Award for Outstanding Scientific Achievement by the American Diabetes Association. His work has been published in leading medical research journals. A member of several editorial boards, he also serves on numerous advisory panels for academia, government and industry. He is an elected member of the Association of American Physicians and the American Society for Clinical Investigation. His work is supported by the National Institutes of Health, the American Diabetes Association, the Russ Berrie Foundation, and the Brehm Coalition.

**Symposium Talk : The New Biology of Diabetes**

**Abstract**


Until recently, type 2 diabetes was seen as a disease caused by an impairment of insulin's ability to promote glucose uptake and utilization in skeletal muscle and adipose tissue. With the advent of gene targeting technologies and large-scale genetic studies in humans, it has become increasingly clear that the pathophysiology of the disease is much more complex, and involves aspects of insulin action that had not been properly appreciated in the past. In our work, we have leveraged information derived from studies of the transcriptional sensor FoxO1 to glean new information on diabetes pathophysiology and its potential treatment. We have found that transcription factor FoxO1 mediates a surprisingly diverse subset of biological actions of insulin. In the liver, it mediates the effects of insulin (and glucagon) on glucose production, a process underlying a key abnormality in type 2 diabetes. In addition, FoxO1 links insulin action with triglyceride (TG) deposition, secretion and turnover, another important pathophysiological process related to the development of heart disease in diabetes. In the central nervous system, FoxO1 acts in key neuronal populations regulating appetite and peripheral metabolism, and bridges insulin with leptin signaling, providing a mechanistic foundation for the interaction between these two important metabolic hormones. Regardless of its causes, pancreatic β-cell failure is necessary for diabetes development, and is thought to involve changes in β-cell mass, possibly secondary to apoptosis. We have recently shown that this process is also regulated by FoxO1. The most striking finding is that FoxO1 is necessary to maintain β-cell differentiation. Using lineage-tracing experiments, we have shown that during diabetes development there is a gradual loss of FoxO1 function that correlates with β-cell dedifferentiation. We have suggested that treatment of β-cell failure should aim at restoring β-cell differentiation, and not at increasing β-cell mass. In summary, our studies have revealed new dimensions to the pathophysiology of diabetes, which we now hope to leverage to find new treatments for this condition.

# ISP2014 Participants

# ISP2014 Participants

## *Invited Participants*

(SS) : Special Selection Participant (GP) : General Participant

### Bangladesh

MD Shahid Sarwar
Southeast University
SS
Poster # 17

Mrityunjoy Biswas
NIPRO JMI Pharma Ltd.
SS
Poster # 2

### Bhutan

Tenzin Dorji
Jigme Dorji Wangchuck National Referral Hospital
GP
Poster # 10

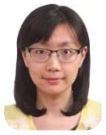
### Cambodia

Channvattey Lao
University of Health and Sciences
GP
Poster # 12

### P.R. China

Liang Ma
China Medical University
SS

Meng Jiang
Sichuan University
SS



Ridan Cao
Capital Medical University
SS
Poster # 1

Laiqing Xu
Sichuan University
SS

### India

Arun Kumar Rajendran
Amrita Centre for Nanosciences & Molecular Medicine
SS
Poster # 16

Sandeep Kumar Araveti
University of East, Philippines
SS

### Indonesia

Agustin Wulan Suci Dharmayanti
Jember University
GP
Poster # 20

### Iran

Mohammad Mehdi Movahednia
National University of Singapore
GP
Poster # 8

## Republic of Korea

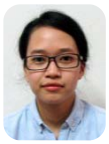
Joonwoo Chon

Sungkyunkwan University

GP

Poster # 11

## Laos



Thitsamay Luangxay

Mittaphab Hospital

SS

Poster # 11

## Malaysia

Joyce Chin

Ministry of Health Malaysia

GP

Poster # 9

## Mongolia

Tselmuun Chinzorig

Health Sciences University of Mongolia

GP

Poster # 5

## Myanmar

Khaing Myat Thu

University of Dental Medicine

GP

Poster # 4

## Nepal

Ashbita Pokharel

Tribhuvan University Teaching Hospital

GP

Poster # 3

## Pakistan

Tehseen Nawaz

University of Karachi

GP

Poster #19

## Taiwan

Yu-Yun Wu

Kaohsiung Medical University

SS

## Thailand

Soontaraporn Huntula

Siriraj Hospital

SS

Poster #15

Thanich Sangsuwannukul

ECC

SS

Poster #18

## Vietnam

Vu Tran Bao Chau

University of Medicine and Pharmacy at Ho Chi Minh City

SS

Mai Hang Nga

National Hospital of Odonto-Stomatology

SS

Vo Lam Thuy

University of Medicine and Pharmacy at Ho Chi Minh City

SS

# *TMDU Poster Session Participants*

Maierhaba Ailixiding

China

Poster # 6

Maria Jacinta Rosario Hernandez Romero

The Philippines

Poster # 13

Sahar Jameel Khunkar

Saudi Arabia

Poster #14

Kotaro Yoshioka

Japan

Poster # 7

# Abstracts of ISP2014 Poster Presentations

Poster
1

**Ridan Cao**

(Capital Medical University, China)

**Title: Effect of Sodium Hypochlorite Irrigation on Periapical Enterococcus faecalis Biofilm: An in Vitro Study**

**Abstract**

Purpose: The aim of this study was to develop a model system to study the structure of periapical biofilm comprising Enterococcus faecalis and evaluate the effect of sodium hypochlorite irrigation on it.

Methods: 51 human sound single-rooted premolars extracted for orthodontic reason were collected and divided randomly into 17 groups (n=3). The specimens were inoculated with 10ml Enterococcus faecalis（ATCC 29212）suspension adjusted to 108CFU/ml at 37° C for 1d, 2d and 7d and were then prepared for SEM and CLSM to examine the colonization and biofilm structure. The specimens incubated for 7days were also treated with sodium hypochlorite irrigations for 30s and saline solution (control group). Laser confocal scanning microscopy (CLSM) was used to examine the reduction of biofilm after treatment.

Result: It shows that the coverage (%) of the biofilm on the apical cementum increased with increasing incubation period. The assessment of 7d group ($p<0.05$) was significantly higher than those of the 1d and 2d groups and no significant difference was identified between the latter two groups. The 0.0291% sodium hypochlorite solution reduced the biofilm significantly and the 0.291% sodium hypochlorite solution removed the biofilm completely after 30-second treatment ($p<0.05$).

Conclusions: Enterococcus faecalis can form bacterial biofilm comprising dense bacterial aggregation composed of Enterococcus faecalis and amorphous matrix on the period of 7 days. The sodium hypochlorite irrigation seems to be a promising endodontic tool because it promotes the elimination of Enterococcus faecalis biofilm on root apical cementum.
KEYWORDS: Enterococcus faecalis, biofilm, sodium hypochlorite.

Poster
2

**Mrityunjoy Biswas**

(NIPRO JMI Pharma Ltd., Bangladesh)

**Title: Studies on Nutritional Analysis, Enzyme Activity and Partial Purification of Lectin from Typhonium Trilobatum (L.)**

**Abstract**

Typhonium trilobatum (L.) is a plant and belongs to the family Araceae. In this study the nutritional composition were determined by standard method. Rhizome and leaves were used for the investigation. The lipid content of rhizome was higher than that of leaves. Total protein and water soluble protein contents of rhizome were higher than that of leaves. In case of starch contents of leaves was higher than that of rhizome. Rhizome and leaves also contained some other nutrients such as total sugar, reducing sugar, non reducing sugar, and vitamin-C. The comparative amount of mineral present in Typhonium trilobatum was also studied. Iron content of leaves was slightly higher than that of rhizome. Calcium content of rhizome was higher than that of leaves. It was also a good source of zinc, manganese, potassium and led.

Enzyme activity was also determined from the rhizome of Typhonium trilobatum. The activities of amylase, cellulase, invertase and protease were 0.05466 ±0.03, 0.122 ± 0.005, 0.0588 ±0.001, and 0.452 ±0.002 mg/min/ml respectively. Among the enzyme activities, protease activity was higher than others.

Lectin was partially purified from the extract of Typhonium trilobatum using DEAE-Cellulose column chromatography. On the purity checking and molecular weight determination on SDS-PAGE and moved three bands. From this, it was assumed that the solution contained three lectins. A clear band may indicate a specific lectin and molecular weights were obtained as 19±1kDa, 40±1kDa and 90±1kDa respectively. These lectins agglutinated human ($o^{+ve}$) blood cells. The minimum concentration of hemaglutination activity assay was 15.4µg/ml. These lectins also showed slight toxicity towards brine shrimp nauplii, with the LC50 value of 94.90648. They also showed slight antibacterial activity against Escherichia coli. (123 µg/disc and 184.8 µg/disc).

Poster
3


## Ashbita Pokharel

(Tribhuvan University Teaching Hospital, Nepal)


**Title: Case Report of Diabetic Foot**


**Abstract**

In total, 15% of people with diabetes develop foot ulcer. 85% of the amputations are preceded by an ulcer and foot ulcer are highly susceptible to infection. Clinically, 3 distinct stages of diabetic foot infection may be recognized. Localized infection, spreading infection and severe infection. Localized infection refers to infection in ulcer bed or immediately surrounding skin. Sepsis has progressed to give signs of spreading infection emanating from the ulcer such as diffuse spreading erythema, edema, lymphangitis, lymphadenitis. Severe infection refers to ulcers with extensive deep soft tissue infection. The development of infection constitute a foot care emergency, which requires referral to specialized foot care team within 24 hours.CASE: 74 years male with type 2 Diabetes since 8 years presented with tender wound and swelling over bilateral foot for 1 week with HbA1C 14% (Ref <6.4%).There was bilateral pedal edema and dorsal pedis artery was feeble. Wound was about 5cm by 3.5cm in dorsal aspect of the left foot. It was superficial localized infection. Doppler showed biphasic flow in left common femoral, superficial femoral, and popliteal artery and monophasic flow in left anterior and posterior tibial artery with marked atherosclerotic change in bilateral lower limb vessels with thickening of wall and narrowing of lumen at places.

Poster
4

**Khaing Myat Thu**

(University of Dental Medicine, Myanmar)

**Title: In Vitro Study of Coronal Leakage of Four Temporary Filling Materials Immersed in Alcoholic Methylene Blue Dye**

**Abstract**

Introduction: Temporary restorative materials are placed in access cavity to provide the coronal seal of the root canal during multi-visits RCT. This in vitro study was designed to evaluate the coronal microleakage of four different temporary restorative materials commonly used in endodontics in Myanmar, viz., MD.Temp, Orafil, Caviton, Zinc oxide eugenol.

Materials and Methods: Forty-four extracted human premolars were selected, and access cavity was prepared. Pulp chambers were filled with wet cotton pellets leaving approximately 4 mm coronally. Forty teeth were randomly divided into four experimental groups equally. The remaining four teeth were equally divided into two control groups. Access cavities in each group were filled with one of the above tested materials, and immediately put into the water. Tooth surfaces except occlusal surface were then coated with nail varnish. Equal parts of 2% methylene blue and methylated alcohol were mixed to prepare a dye solution. Samples were immersed in dye for 10 days at 32 ± 2°C. Teeth were rinsed, dried, and sectioned mesiodistally and evaluated under a stereomicroscope at a magnification of 15X for linear dye penetration along cavity walls. Data were analyzed using Kruskal-Wallis and Tukey HSD tests.

Results: The lowest microleakage value was observed in MD.Temp and Orafil, and the highest in Zinc oxide eugenol(ZOE). Caviton was not statistically different from Orafil and ZOE, but significantly higher in microleakage than MD.Temp. Clinical Significance: ZOE which is dissolvable in alcohol was the least effective material for preventing microleakage, while MD.Temp and Orafil provided the best sealing in content of alcohol in this study.

Poster
5

**Tselmuun Chinzorig**

(Health Sciences University of Mongolia, Mongolia)

**Title: Preliminary Study on Health Impacts of Air Pollution at the Work Place of the School Of Dentistry, Health Sciences University of Mongolia**

**Abstract**

Tselmuun Ch.[1]; Purevdorj B.[2]
[1]Graduate Master student, School of Public Health, HSUM;
[2]Head, Department of Environmental Health Sciences, HSUM

Background: Air pollution has been one of the facts that affect our health. In a study of eight major Canadian cities, Health Canada found that approximately 5,900 deaths per year could be attributed to air pollution. The WHO estimates that within the air pollution particulate matter ($PM_{2.5}$) is the key reason that causes about 3% of mortality from cardiopulmonary disease, about 5% of mortality from cancer of the trachea, bronchus in worldwide.
School of Dentistry, Health Sciences University of Mongolia (HSUM) has moved to a location within the city of Ulaanbaatar with an ambient air quality peaking in the winter. Increasing indoor air pollution has been affecting negatively both the health and work productivity of the faculty, thus prompted us to conduct the present study.
Purpose: To evaluate air pollution impact to the faculty of the School of Dentistry, HSUM at the work place.

Methods: Totally 30 faculties were measured through Monday to Friday starting from 09:00 am to 17:00 pm. For measuring the personal exposure we have used TSI SidePak AM510 Aerosol Monitor and Dust Trak II Aerosol Monitor for environmental exposure. Descriptive statistics are used to describe data in the study.

Results: Personal Exposure of $PM_{2.5}$ among faculties at the School of Dentistry, HSUM was 0.830 (SD=0.286; TWA=0.105) $mg/m^3$, where as the indoor exposure of $PM_{2.5}$ were 2.005 (SD=1.277; TWA=0.252) $mg/m^3$.

Conclusion: The personal exposure of $PM_{2.5}$ among faculties at the School of Dentistry, HSUM are 40 times higher than the WHO air quality standard, which is 50 μg/m3 within 24 hours. Blood lead level test should be measured in order to determine influence of air pollutant to the general health and metabolism.

Poster
6

**Maierhaba Ailixiding**

(Tokyo Medical and Dental University, Japan)

**Title: Sirt6 Deficiency Accelerates Articular Cartilage Degeneration**

**Abstract**

Osteoarthritis (OA) is a chronic degenerative joint disorder characterized by articular cartilage destruction and osteophyte formation, and is prevalent in society as a major cause of disability.The risk factors identified by previous epidemiologic studies are limited to age 、 trauma history ,Occupation, Gender, Age and Obesity . Obesity and high body mass index are associated with a higher incidence of OA .Therefore, it has been hypothesized that one or more systemic facters are responsible for the correlation between obesity and OA.

Previously, we disclosed that the infrapatellar fat pad (IPFP) plays a pivotal role in the formation of osteophytes and functions as a secretory organ in response to a HFD .In this model, the initiation of OA change, such as osteophyte formation and articular chondrocyte apoptosis, occurs within three months of HFD with regard to the adipocyte hypertrophy and increased angiogenesis of IPFP. Among the seven mammalian sirtuin family members, sirtuin 6 (Sirt6) is localized to the nucleus and is involved in transcriptional silencing, genome stability, and longevity. Sirt6 is involved in the regulation of life span and ageing [13]. Sirt6 deficient mice exhibit features of premature aging, such as osteopenia and lordokyphosis, and die before 4 weeks of age due to lethal hypoglycemia.However, the role of Sirt6 in OA pathogenesis is poorly understood. This study sought to investigate the effects of Sirt6 deficiency on the aging of articular tissues in vivo. Furthermore, we investigated the role of Sirt6 in the development of HFD-induced OA by using a murine HFD-induced osteoarthritis model.

Poster
7

**Kotaro Yoshioka**

(Tokyo Medical and Dental University, Japan)

**Title: A New Class of Oligonucleotide Drug; DNA/RNA Heteroduplex Oligonucleotide for Highly Efficient Gene Silencing**

**Abstract**

Two major types of oligonucleotide drugs for gene silencing, short interfering RNA (siRNA) and RNase H active antisense oligonucleotides (ASOs), are being developed as therapeutic platforms orthogonal to small molecule and protein therapeutics. Despite progress in the design of new oligonucleotide chemical modifications, methods which improve potency of oligonucleotide drugs in animals are highly desirable. Here we developed a short DNA/RNA heteroduplex oligonucleotide (HDO) with a structure different from siRNA of double-stranded RNA and ASO of single-stranded DNA. When the DNA strand was used as 13-mer locked nucleotide acid (LNA) gapmer ASO targeting ApolipoproteinB (ApoB) mRNA and the RNA strand was conjugated with vitamin E (α-tocopherol) (Toc-HDO), it achieved the most efficacious gene silencing (estimated effective dose 50 [ED50], 0.038 mg/kg) in yet reported ASOs and could reduce serum LDL-cholesterol level much more effectively than ASO in the disease model mice of hyperlipidemia. We explored the utility of the systemic delivery to other tissues besides liver. In mouse model, high dose injection of Toc-HDO demonstrated remarkable progress in the efficacy of ASO in various organs such as kidney, lung, muscle, adrenal gland and adipose tissue. Within cells, the heteroduplex was unwound unexpectedly in cytosolic foci by cleavage of the RNA strand, and only the DNA strand was transferred into the nucleus. HDO technology comprises a novel concept of gene therapy with specific intracellular processing machinery, and development of this molecular design opens a new therapeutic field.

Poster
8

**Mohammad Mehdi Movahednia**

(National University of Singapore, Singapore)

**Title: Assessment of α-Tocopherol Photoprotective Ability against UV-mediated Oxidative Damage on Human Embryonic Stem Cells-derived Keratinocytes**

**Abstract**

Authors: M. Mehdi Movahednia, F. Karim Kidwai, Harish Handral, Cao Tong*.
Affiliation: Stem Cell Lab, Faculty of Dentistry, National University of Singapore.
Key words: Human embryonic stem cells, epidermal cells, Ultra violet, inflammatory cytokines, α-Tocopherol photoprotection.

Like all other organs, epidermis is affected by increasing the age of individuals. Photoaging is an important aspect of skin aging which correlates with the effect of long time sun exposure on skin. It is well known that ultra violet (UV) is responsible for reactive oxygen species (ROS) generation in sun-exposed skin and accumulation of generated ROS can overwhelm the cutaneous antioxidant defense ability, resulting in induction of oxidative stress. Therefore, reduction of UV induced oxidative stress and synergize cellular antioxidants by application of UV protectants on skin has been attracted lots of scientific attentions.
Upon introduction of reconstituted human skin models they heralded a representative epidermal cellular model in dermatology research. In order to wide application of these constructs in aging studies they need to be provided by source of cells with known background due to the fact that human epidermis aging is under influence of race, sex, age and donor life style. Variation in originated epidermal cells from individuals even among infants due to exposure to extrinsic stimuli in every donor during life-time and inherited systematic errors in epidemiological studies hampered obtaining objective results during aging researches and confounded the aim of these studies. In this study we utilized skin constructs populated with hESCs-derived cells as epidermal cellular model, and for the first time we will investigate the photoprotective effect of α-Tocopherol against two intensities of repetitive UV radiation with the of 10% and 20% of annual average of daily UV radiation in tropical region on these constructs. We found that α-Tocopherol exerts the maximum photoprotection ability at 100 μg/ml and this concentration showed the significance free radical scavenging in skin constructs with elimination of p16 expression at 10% tropical region UV exposure after 5 days. Investigation over expression of inflammatory cytokines at protein level revealed the high accumulation of these proteins under UV radiation in hESC-derived epidermal/dermal cells and significant reduction of expression under photoprotective concentration of α-Tocopherol. Generally, these data underscore the unique ability of hESC-derived cells as novel model in aging studies.

Poster
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**Joyce Chin**

(Ministry of Health Malaysia, Malaysia)

**Title: Role of Angiogenesis in Progression of Potentially Malignant Oral Lesion**

**Abstract**

NAME OF AUTHORS: J Chin, Kenneth YC Chew, SP Khoo

Objectives: It is well known that determining the severity and prognosis of potentially malignant lesion based on histological diagnosis alone can be complex and inaccurate. Researchers are trying to find a better indicator or marker to be able to aid the diagnosis; one such indicator is angiogenesis. Much research has been done on angiogenesis but the results vary although the specimens used were from the same site. Therefore, there is still uncertainty on the use of angiogenesis as a prognostic indicator. The aim of this research is to investigate the correlation between epithelial dysplasia and microvessel density (MVD) to understand their role in potentially malignant oral lesion

Methods: A total of 30 samples of Hematoxylin and Eosin-stained potentially malignant oral lesions were obtained. They were graded into mild epithelial dysplasia (n=18), moderate epithelial dysplasia (n=8) and severe epithelial dysplasia (n=4). The mean MVD was counted and correlated with the severity of epithelial dysplasia.

Results: There is no correlation between MVD and the severity of epithelial dysplasia.

Conclusions: Although angiogenesis is frequently over expressed in many potentially malignant oral lesions, there is no relationship seen in this research.

Poster
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## Tenzin Dorji

(Jigme Dorji Wangchuck National Referral Hospital, Bhutan)


**Title: Geriatric Care in Dentistry**


**Abstract**

Old age implies ages nearing or surpassing the average lifespan of human beings, and thus the end of the human life cycle.

Older people have limited regenerative abilities and are more prone to disease, syndromes and sickness than other adults. The medical study of this aging process I gerontology, and the study of disease that afflict the elderly is Geriatrics. Geriatrics is the branch of medicine that focuses on health promotion and the prevention and treatment of disease and disability in later life.

This population has unique problems that necessitate alterations in their treatment plans; they are more susceptible to plaque, root caries and oral cancer, they also use more medications, many of which can cause problems such as xerostomia and decreased saliva, altering host immune response and other inflammatory reaction. In these older adults, education, nutrition, counseling, regular dental care, compensatory home and professional care technique maybe required.

Geriatric dentistry is practically non-existent. Unless we as dentist begin to consider the active care of the aged an important endeavor.

“adding life to years” rather that “years to life”

Poster
11

**Joonwoo Chon**

(Sungkyunkwan University, Korea)

**Title: Development of Reinforced Poly Lactic Acid Composite Resin for Micro Surgery Bone Plate and Screw**

**Abstract**

Joon woo Chon[1], Dong June Chung[1*]
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Nowadays the medical field which operate surgery such as orthopedics, plastic surgery and maxillofacial surgery use metallic graft material for support mixture in the human body. The metallic graft materials led to foreign body reaction and infection in the human body. Furthermore, 2nd surgery to remove graft material is required. Biodegradable graft material is absorbed and released in the human body after degrade itself. But bone plate or screw for osteosynthesis which uses biodegradable graft material such as PGA (Poly glycolic acid), PLA (Poly lactic acid) and PLGA (Poly lactide-co-glycolide) has poor properties such as lower intensity than that of metallic graft materials. However we can expect that blending biodegradable polymer with natural polymer as fillers form 3D-network structure. This structures enhance its mechanical strength without any loss of biodegradable and biocompatible properties due to using natural polymer such as chitosan and hyaluronic acid.

Enhanced polymer composites would be used in not only graft material for auxiliary role as graft material, but also interference screw for ligament anastomosis. Furthermore, stent which using metallic material for internal medicine of heart can be replaced by this enhanced polymer composites.

PLA (Poly lactic acid) which use in common based on stereoregularity of L and D type has differential properties. In particular, PLLA (Poly-L-lactic acid) has good mechanical properties than other types of PLA due to its crystalline structure. Because of its structural properties, we can expect reinforced product after blending with natural polymers. Also natural polymer which has biocompatible and biodegradable can control graft material`s biodegradable rate.

In my research, I will approach the problem about reinforced material`s low mechanical properties and difficulty of control biodegradable with this concept.

Poster
12


## Channvattey Lao

(University of Health and Sciences, Cambodia)


**Title: Demographics, Diagnoses and Treatment of Patients Presenting to the Dental Clinic at the Khmer – Soviet Hospital in Phnom Penh, Cambodia**


**Abstract**

Background: The oral health of a nation is dependent on the knowledge of oral hygiene, proper levels of nutrition, fluorinated water and the availability of preventative and restorative dental care. In Cambodia, there is high incidence of dental caries that is thought to be secondary to pervasive poverty (1). According to the 2010 Cambodian Commune Database, an estimated 25.8% of the country's 14 million people are poor (2). Since many people have limited knowledge regarding dental health, they tend to seek out dental care only when they have an emergency. To make matters worse, especially in the rural provinces, people seek out non-professional dentists who lack adequate training, because they cost less than going to a professional dentist. (3).

In our study, we will seek to understand the demographics, diagnosis, and treatment of patients presenting to the Dental Clinic at the Khmer-Soviet Hospital in Phnom Penh.
Understanding how the poor in Cambodia utilize dental services may have direct influence on public policy on providing information, instituting water fluorination program, and managing resources in a country with limited resources.

Objective: To characterize the demographics, diagnosis and treatment of patients presenting to the Dental Clinic at the Khmer – Soviet Hospital in Phnom Penh, Cambodia to enable better procurement and distribution of limited resources.

Methods: Retrospective longitudinal cohort study of all patients who presented to the Dental Clinic of the Khmer – Soviet Hospital in Phnom Penh, Cambodia during the oneyear period from April 1, 2013 through March 30, 2014. The Dental Clinic has an annual census of over 5000 patients all of whom underwent standard triage screening.

Study Population: Our cohort will consist of patients presenting for care for any reason at the Dental Clinic of the Khmer-Soviet Hospital in Phnom Penh.

Setting: A large free dental clinic that has an annual census of over 5000 patients. All patients are entered in a log on arrival and completed when they are discharged. Patients are charged a nominal fee for service and that can range from $5 USD for a consultation, $5 USD for scaling, $10 USD for root canal, and up to more than a $1000 USD if they need an major operation.

Data Collection: All Dental Clinic patient encounters will be queried for the timeframe from April 1, 2013 through March 30, 2014. The query will be made from the log sheets from the clinic and for all encounters demographics including age, sex, home address, diagnosis, and treatment will be abstracted.

Statistical Analysis: Descriptive analysis will be used to analyze the data and will be recorded as means and standard deviations for continuous data, while percentages will be used for sex and geographic distribution. Comparisons between groups will be analyzed with t-tests for continuous data (age) and rank tests for non-parametric data.

Poster
13


## Maria Jacinta Rosario Hernandez Romero

(Tokyo Medical and Dental University, Japan)


**Title: Effect of Casein as a Model Pellicle Precursor Protein on In Vitro Dentin Remineralization**


**Abstract**

Pellicle precursor proteins (PPP) regulate tooth mineral processes but are often overlooked in vitro. Previously, we found that casein inhibits hydroxyapatite growth and precipitation on sound tooth surfaces, indicating its potential to be a PPP analogue. This study aims to investigate the effect of casein, when incorporated in artificial saliva (AS) solutions, with and without fluoride (F), on dentin remineralization. Bovine root dentin blocks were demineralized at pH 5.0 and remineralized for 28 days in AS with casein (0,10, 20, 50, 100 μg/ml) and F (0, 1 ppm). Mineral densities were obtained using transverse microradiography. Results analyzed using two-way ANOVA with Bonferroni post hoc revealed that surface mineral density of casein 0 μg/ml, F 1 ppm group which exhibited surface mineral precipitation was significantly greater ($p<0.001$) compared to the baseline and all other groups where surface precipitation was inhibited regardless of casein concentration. Mineral loss (ΔZ) was higher ($p<0.001$) in the baseline than the rest of the groups which were not significantly different from each other. Lesion depth recovery (LDR) was lower ($p<0.001$) for all F-containing groups, which exhibited laminations, compared to non-F groups. The laminated pattern of remineralization did not affect ΔZ but could have inhibited LDR. Based on these findings, we conclude that casein, regardless of concentration, inhibits mineral precipitation on tooth surfaces but does not inhibit dentin remineralization thus indicating its suitability to be a model PPP for in vitro studies. It can also be suggested that homogenous patterns of remineralization could lead to better LDR.

Poster
14

**Sahar Jameel Khunkar**

(Tokyo Medical and Dental University, Japan)

**Title: Formation and Characterization of Hypermineralized Zone beneath Dentin Lesion Body Induced by Topical Fluoride In-vitro**

**Abstract**

Objective: This in-vitro study found hypermineralized zone (Hyper-zone) with a higher mineral density than in sound dentin beneath dentin lesion body when the demineralized dentin lesion was treated by fluoride solution followed by remineralization treatment. Thus aim of this study is to characterize Hyper-zone and to investigate the mechanism of its formation.

Design: Demineralized bovine dentin specimens were treated by fluoride solutions (APF, NaF) and remineralized for 2-4 weeks. Then thin sections were prepared to characterize the Hyper-zone by transverse microradiography (TMR), energy dispersive x-ray analysis (EDS). Fractured specimen fragments were observed by scanning electron microscopy (SEM).

Results: TMR analysis revealed a higher mineral density at Hyper-zone than that of sound dentin (48 vol%) with ranging from 50 up to 61 vol% and the width ranging from 197 to 344 μm for 4-week specimens. SEM pictures at Hyper-zone showed no evident crystal-like deposits in dentinal tubules and no notable difference when compared to that in sound dentin. EDS analysis demonstrated higher concentrations of Ca and P at Hyper-zone than those in sound dentin, corresponding to the TMR profile whereas the magnesium (Mg) concentration was low at this zone.

Conclusions: During remineralization which followed the pre-demineralization and fluoride treatments, mineral regulators such as dentin phosphoprotein (DPP) and Mg, which are believed to play an important role in dentin mineral development, might be removed from the sound dentin area beneath the lesion body, creating active crystal growth sites for further mineral growth, resulting in Hyper-zone formation.

Poster
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**Soontaraporn Huntula**

(Siriraj Hospital, Thailand)

**Title: Effects of N-(2-propylpentanoyl) urea on Cortical Spreading Depression in Rats**

**Abstract**

This study aimed to investigate the effects of N-2(propylpentanoyl) urea (VPU) on development of cortical spreading depression (CSD) in male Wistar rats (200-300 g) using electrophysiology technique. The rats were anesthetized by urethane and then placed in stereotaxic frame. The scalps were cut open to expose the skulls and two burr holes were drilled on the right hemisphere. The anterior hole at frontal bone was to place glass microelectrode, whereas the posterior hole at the parietal bone was used for an application of solid KCl (3 mg). The animals were intraperitoneally injected of either 0.5% carboxymethyl cellulose (CMC) (1 ml/kg) or valproic acid (200 mg/kg) or VPU (70 mg/kg). CSD was induced by placing solid KCl onto the brain and observation was made for another 90 minutes. Variables regarding CSD wave included the area under the curve, amplitude, duration, number of peak and interpeak latency. The results showed that application of KCl resulted in series of depolarization activity for CSD. The development of these CSD wave was lower in presence of VPA and VPU. Such decrease was noted on frequency, amplitude and AUC of CSD and increased interpeak latency but duration showed no significant change. In addition, fos-immunohistrochemistry in both treated groups were significantly decreased in comparison to those of CMC group.

The present study demonstrated that VPA and VPU decrease CSD, VPU was found similar to parent compound. Therefore, future developed into a drug for the treatment of migraine.

Poster
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**Arun Kumar Rajendran**

(Amrita Centre for Nanosciences and Molecular Medicine, India)

**Title: Injectable Chitin-Poly(CaproLactone)/Nano Hydroxyapatite Composite Microgel for Craniofacial Bone Defects**

**Abstract**

R. Arunkumar[a], A. Sivashanmugam[a], K. P. Chennazhi[a], R. Jayakumar[a*]
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Injectable gel systems, for the purpose of craniofacial bone defect reconstruction has more advantages like, controlled flowability, adaptability to the defect site, increased handling properties when compared to the conventionally used materials such as grafts, bone powders and scaffolds. In this work, chitin-poly(caprolactone) (PCL) based injectable microgel has been developed by solvent regeneration along with incorporation of nano hydroxyapatite (nHAP). The prepared chitin-PCL microgel showed an excellent flowability and injectability property. The incorporation of nHAP increases the osteoconductivity as well as improved the mechanical properties of the microgel. The composite microgel was physico-chemically characterized using SEM, FTIR and Rheometer. The rheological studies include inversion test, temperature dependant visco-elastic changes, flow curve measurement and pH dependent rheological changes were studied. The results shows that composite microgel particles were 3-5 µm in size, and with the incorporation of nHAP, the elastic modulus of the gel was found to be increased. Further the protein adsorption and in vitro bio-mineralization of microgel was studied. The nHAP incorporated microgel showed enhanced protein adsorption and biomineralization. The cell culture studies were carried out using human Mesenchymal Stem Cells (hMSCs). It was found the cells were viable in the presence of microgel and also the composite microgel increased the cell migration. The nHAP composite microgel has been found to stimulate the differentiation of hMSCs to osteoblasts, with increase in alkaline phosphatase activity and mineralization, which proves the promising application for osteogenesis. Thus the composite microgel shows promising properties to be used as an injectable material for cranio-facial bone regeneration.

Poster
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**MD Shahid Sarwar**

(Southeast University, Bangladesh)

**Title: Evaluation of Serum Antioxidant, Trace Element and Macronutrient Status in Obese Individuals**

**Abstract**

Md. Shahid Sarwar[1], Tareek Adnan[2], Mohammad Safiqul Islam[2]
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[2]Department of Pharmacy, Noakhali Science and Technology University, Sonapur, Noakhali-3814, Bangladesh

Background: Obesity is associated with various health hazards and is becoming an epidemic worldwide. There are no available reported work regarding serum antioxidant vitamins, trace elements and macronutrients level in obese individuals.

Objective: The present study was conducted to determine serum antioxidant (vitamin A and E), trace elements (Zn, Fe), and macronutrients (Na, K, Ca) level in obese individuals.

Methods: We conducted this research as a case-control study with 100 obese and 100 non-obese subjects. Demographic, anthropometric and clinical data were collected at routine hospital visits. Obesity was determined by the body mass index (BMI). Serum antioxidant concentration was determined by RP-HPLC method, whereas serum trace elements and macronutrients were determined by flame atomic absorption spectroscopy (FAAS). Independent sample t-test and Pearson's correlation test was used for the statistical analysis using the statistical software package SPSS, version 16.0 (SPSS, Inc., Chicago, IL).

Results: This study found significantly lower level of antioxidant vitamins, trace elements, and macronutrients (except Na) in obese group than the control subjects ($P<0.05$). Pearson's correlation analysis revealed that there was negative correlation between BMI and Zn ($r=-0.097$, $p=0.338$); BMI and Fe ($r=-0.033$, $p=0.742$); BMI and Ca ($r=-0.129$, $p=0.200$); BMI and K ($r=-0.218$, $p=0.029$) in patient group.

Conclusion: Our study revealed that obese individuals have low serum concentration of antioxidant vitamin A and E, trace element Zn and Fe, macronutrient K and Ca but high serum concentration of Na than the non obese subjects.

Poster
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**Thanich Sangsuwannukul**

(ECC (Thailand), Thailand)

**Title: Muscarinic Receptor Activation Protects against Paraquat Neurotoxicity, and Upregulates α-Synuclein**

**Abstract**

Paraquat (PQ) is a widely used herbicide having similar structure to a neurotoxicant known to cause Parkinsonism ($MPP^+$), and is a putative risk of Parkinson's disease (PD). However, underlying mechanism of how PQ leads to PD is still on debate. Three major mechanisms have been proposed including redox cycling, mitochondrial impairment and up-regulation of a presynaptic protein, α-synuclein. Interestingly, dopaminergic neurons in substantia nigra pars compacta, the area mainly defected in Parkinsonism, have neuroprojection from brainstem cholinergic system implicating cholinergic influences on dopaminergic system. Therefore, the present study investigated the roles of muscarinic cholinergic receptors for PQ toxicity in dopaminergic neuronal SH-SY5Y cells.

The results demonstrated that pretreatment with muscarinic receptor agonists, carbachol and oxotremorine-M protected against PQ-induced apoptosis evidenced by attenuation of PQ-induced PARP proteolysis and p53 augmentations. This protection was reversed by atropine (muscarinic antagonist) indicating muscarinic activation protects against PQ neurotoxicity. Correspond to its apoptotic protection, carbachol increased level of α-synuclein which is a primary structural component of Lewy body, a pathological hallmark of PD, in carbachol and PQ co-exposure suggesting induction of α-synuclein may related to anti-apoptotic effect of muscarinic receptor activation. Furthermore, the α-synuclein induction was blocked by muscarinic antagonist indicating that the increment of α-synuclein by carbachol and PQ co-exposure was through muscarinic action. Collectively, this study showed that muscarinic receptor stimulation protects against PQ-induced apoptosis, and upregulation of α-synuclein may play a role in its protective effect.

Poster
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**Tehseen Nawaz**

(University of Karachi, Pakistan)

**Title: Clinical Diagnosis of Mycoplasmosis, and Detection of Mycoplasma in Lung Samples Obtained from Slaughtered Buffaloes in Karachi, Pakistan**

**Abstract**

Syed Khurram Fareed*, Tehseen Nawaz, Johar Hussain, Shakeel Ahmad Khan and Aqeel Ahmad
Department of Microbiology, University of Karachi, Karachi.

Mycoplasmosis is a most serious and economic disease of cattle and buffaloes due to its high morbidity and mortality. Bovine mycoplasmaosis a typical infection of these animals caused by different species of Mycoplasmas, such as M. bovis, M. bovigenetalium and M. arginini are important contributors to bovine respiratory diseases, arthritis, mastitis and genital disorders etc. Clinically 112 animals were examined for respiratory signs whereas 53 (47%) were showed nasal discharge, high temperature, coughing, watery and sunken eyes and weakness. On the other hand 87 lung samples (slaughtered animals) were studied for lesions and 39 (44%) samples were found pneumonic visually. Of the 39; 21 (54%) were found positive on the basis of cultural, morphological and biochemical characterization. Due to high cost of infection treatment, the animals sent to the slaughter house for slaughtering to fulfill the meat demand. While this slaughter causing a shear loss of superior germ plasm.

Poster
20

**Agustin Wulan Suci Dharmayanti**

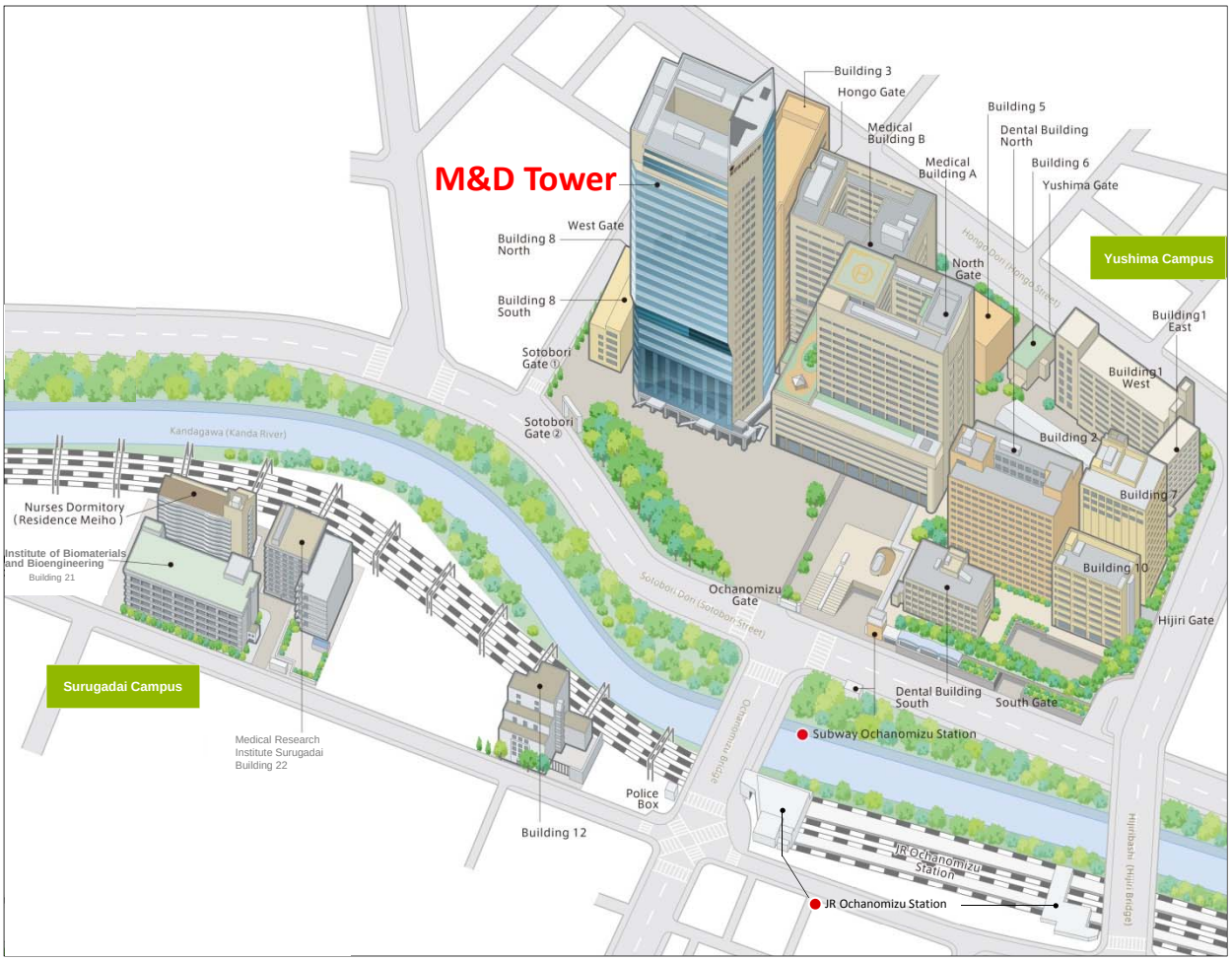
(Jember University, Indonesia)

**Title: Comparison Deoxypyridinoline Level in Serum and Saliva of Menopause Women**

**Abstract**

Aging is human physiology process. Effect of aging process occurs in almost human organs. One is in female reproductive organs by menstruation cycle cessation permanently or menopause. Menopause cause physiology changing that related ovarium dysfunction and resulting bone loss or osteoporosis. Bone loss due to osteoporosis is difficult to detect and only seen in late phase. Recently is developed diagnostic method that using body fluid, such serum and saliva. Serum is often used as disorders detection, however, this method is invasive. Saliva is non-invasive and easy for collecting. Deoxypyridinoline is pyridinium crosslink of type I collagen that is degraded before collagen is degraded. Deoxypyridinoline is most in bone and specific, because it is not re-metabolized in body. Developing of diagnostic tool is needed to determine early diagnostic and appropriate treatment. The aim of this study was to compare deoxypyridinoline level in serum and saliva of menopause women. This study was analytic observational. All procedures were approved by the Ethics Committee, Faculty of Dentistry, Universitas Gadjah Mada, Yogyakarta-Indonesia. Subjects of study were female who 45-50 years old. Saliva and serum were analyzed by Liquid Chromatography Mass Tandem Spectroscopy (LC MS/ MS) technique. The result showed that deoxypyridinoline level in serum was higher than saliva. Independent Ttest showed there was significant different between deoxypyridinoline level in serum and saliva. It can be concluded there was different of deoxypyridinoline in saliva and serum. Deoxypyridinoline can be used as bone resorption parameters.

Keywords: deoxypyridinoline, saliva, serum, menopause

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