東京医科歯科大学

TOKYO MEDICAL AND DENTAL UNIVERSITY

International Summer Program 2011

28-31 August 2011

Organ/Tissue Development and Regeneration

Fundamentals and Clinical Applications

PROGRAM & ABSTRACT BOOK

Contents

ISP 2011 PROGRAM

Date/Time	*Event*	*Venue*

Sunday, 28 August: Registration and Welcome Reception

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

17:30-18:00 **Orientation**
MC: Kevin Cleary (TMDU)
Welcome Address: Kikuo Ohno (Trustee, Planning and International Exchange, TMDU)
Introduction to ISP2011: Tetsuya Taga (ISP2011 Chairperson, TMDU)
Program Schedule: Ikuko Morio (Director, International Exchange Center, TMDU)

18:00–20:00 **Welcome Reception** — "Grill Saints"
MC: Kevin Cleary (TMDU)

Monday, 29 August: Lecture Course, Day 1

9:00–9:10 **Opening Remarks** — M&D Tower 2F Auditorium 1
Junji Tagami (Dean / Faculty of Dentistry, TMDU)

9:10-12:50 **Lecture Course 1**
Chair: Akira Yamaguchi (TMDU) / Tetsuya Taga (TMDU)

9:10–9:50 Sachiko Iseki (TMDU)
Title: Can we learn from developmental mechanism to regenerate tissue?

9:50–10:35 Jing Xiao (Dalian Medical University, P.R. China)
Title: Progress of postnatal dental stem cells in tooth generation in China


Coffee Break, 15 min

10:50–11:30 Akira Yamaguchi (TMDU)
Title: Roles of BMP, Notch and CCN3 in osteoblast differentiation and bone regeneration

11:30–12:10 Tetsuya Taga (TMDU)
Title: Stem cell regulatory signals: Basics and examples from the central nervous system

12:10–12:50 Hiroshi Asahara (TMDU)
Title: Systems approach to reveal molecular network regulating musculoskeletal diseases and development

12:50–14:30 Lunch Break

14:30–14:50 **Introduction to the University** — M&D Tower 2F, Auditorium 1
Ikuko Morio (Director, International Exchange Center, TMDU)

14:50–16:20 **Campus Tour**

16:20–18:10 **Laboratory Visit, Part 1**

18:10–19:30 **Poster Session** — M&D Tower 2F, Foyer
Supervisor: Emi Nishimura (TMDU)

Tuesday, 30 August: Lecture Course, Day 2

9:00–12:55 **Lecture Course 2** — M&D Tower 2F, Auditorium 1
Chair: Ichiro Sekiya (TMDU) / Kenji Yasuda (TMDU)

9:00–9:40 Ichiro Sekiya (TMDU)
Title: Mesenchymal stem cells derived from synovium: their properties and clinical application for cartilage regeneration

9:40–10:25 Johan Hyllner (Cellartis, Sweden)
Title: Pluripotent stem cells for drug discovery and regenerative medicine via collaborative partnerships between industry and academia

Coffee Break, 15 min

10:40–11:25 Noriko Osumi (Tohoku University, Japan)
Title: The neural crest and its derived cells in contribution to craniofacial development and regenerative medicine

11:25–12:10 Minoru Ueda (Nagoya University, Japan)
Title: Stem cell based cytokine therapy: A new era for regenerative medicine

12:10–12:55 Ian Wilmut (The University of Edinburgh, United Kingdom)
Title: Cloning, stem cells and regenerative medicine

12:55–14:15 Lunch Break

14:15–16:05 **Laboratory Visit, Part 2**

16:05–17:30 **Optional Program**
•Exposure to Japanese culture
•Guided walk in the TMDU neighborhood

17:30–19:30 **Social Hour** — M&D Tower 26F, Faculty Lounge
MC: Kevin Cleary (TMDU)
ISP2011 Address: Kikuo Ohno (Trustee, Planning and International Exchange, TMDU)
Presentation of ISP2011 Certificates: Takashi Ohyama (President, TMDU)

Date/Time	*Event*	*Venue*

Wednesday, 31 August: ISP Symposium 2011

9:00–9:10 **Opening Remarks** — M&D Tower 2F, Akio Suzuki Memorial Hall
Yasuhito Yuasa (Dean, Faculty of Medicine, TMDU)

9:10–12:35 **Morning Session**
Chair: Sachiko Iseki (TMDU) / Emi Nishimura (TMDU)

9:10– 9:45 Masayuki Yoshida (TMDU)
Title: Socio-biological interface of research ethics

9:45–10:25 Noriko Osumi (Tohoku University, Japan)
Title: Neural crest stem cells: Origins and applications

10:25–11:00 Emi Nishimura (TMDU)
Title: Regulation of stem cells by stem cells


Coffee Break, 15 min

11:15–11:55 Johan Hyllner (Cellartis, Sweden)
Title: Pluripotent stem cells for drug discovery and regenerative medicine via collaborative industrial partnerships in Europe

11:55–12:35 Ian Wilmut (The University of Edinburgh, United Kingdom)

12:35–12:45 **Closing Remarks**
Ikuko Morio (Director, International Exchange Center, TMDU)

12:45–14:30 Lunch Break

14:30–17:30 **PhD Program Admission-related Activities**

Takashi Ohyama

President
Tokyo Medical and Dental University

Message from the President

First of all, I would like to state my appreciation for the kind messages and generosity exhibited by people all over the world in the aftermath of the Great Tohoku Earthquake. The aid and support provided by our friends in the international community has inspired and humbled us, and we will always be grateful for the help we received in our time of need. I also greatly appreciate your decision to attend the International Summer Program 2011 despite the uncertainty that must accompany any trip to Japan.

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

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

In terms of international outreach, we are especially proud of three overseas education / research collaboration centers — in Ghana, Chile, and Thailand — which we founded in recent years. At these centers we aim to promote collaborative research and advance the professional development of medical and dental professionals in each local area. In the past year we have finalized our student and faculty exchange agreement with the Universidad de Chile, and have opened a Research and Education Collaboration Center at Chulalongkorn University in Thailand. We look forward to the continued exchanges of scholarly knowledge and personnel via these centers, as well as through our other international partner institutions throughout the world.

As an important part of our international activities based here in Japan, we are very pleased to be able to organize our third International Summer Program, ISP2011. I hope that your experience at ISP2011, in addition to helping you develop professionally, will pique your academic curiosity and encourage you to explore the unique features of our university.

Kikuo Ohno

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

Welcome to ISP2011

It is our great pleasure to welcome you to ISP2011, our third annual International Summer Program. We are also very pleased to report that we accepted 24 excellent young researchers and students from Asia to ISP2011.

The theme of ISP2011 is "Organ/Tissue Development and Regeneration – Fundamentals and Clinical Applications." ISP2011 features lecture courses, taught by leading scientists from overseas and Japan, a symposium, and many other events including campus tours, laboratory visits, cultural programs, a poster session and social events throughout the three days of the ISP.

The topics presented in the area of restorative medical treatment include replacement of lost stem cells, promotion of tissue repair with various growth factors, repair of lost tissue or organs, modulation of inflammation and immunological response, and related therapies. Clinically oriented basic research, which is critically important for the development of clinical applications of restorative medicine, will also be presented in the lecture courses.

As you are no doubt aware, a terrible earthquake, followed by a dreadful tsunami, struck northern Japan this March. In addition, nuclear power plant accidents in Fukushima prefecture, about 300 kilometers from Tokyo, have created an atmosphere of great uncertainty. We are very grateful for the wonderful amount of support we have received from overseas to help the residents in the affected areas. Considering this situation, it was doubtful whether we would be able to hold ISP this summer, but of course we made every effort to ensure that we could hold it as planned. On behalf of the organizing committee, I express sincere gratitude to all participants in ISP2011. I am sure that this program will yield many fruitful results and also build a bridge of friendship among all participants.

Profiles and Abstracts of Lecture Course Speakers

Sachiko Iseki

(Tokyo Medical and Dental University)

Biodata

Sachiko Iseki, DDS, PhD, has been a professor in the Department of Molecular Craniofacial Embryology at Tokyo Medical and Dental University (TMDU) Graduate School since 2008. After she finished her PhD course at TMDU, she worked in the Department of Human Anatomy (later changed to Department of Human Anatomy and Genetics) at the University of Oxford in the UK, from 1994-1996 and from 1997-2000, and studied the function of fibroblast growth factor (FGF) signaling in skull development. As a research associate at TMDU she continued to work on craniofacial morphogenesis including cell lineage analysis, palate development and FGF signaling function. Currently she is trying to apply the mechanism of hard tissue formation to regenerative medicine.

Lecture Course: Can we learn from developmental mechanism to regenerate tissue?

Abstract

The ultimate goal of regenerative medicine is to replace lost or damaged tissues, which requires three important factors: cell source, scaffolds and biological active factors that provide the appropriate environment for regeneration. It is very important to have a coordinated combination of these factors for successful regeneration. Regeneration of bone tissue has been extensively studied, especially in aging societies such as Japan. Since the skeleton continues to remodel itself throughout life, it is therefore reasonable to assume that there will be enough cell sources available when bone regeneration or formation is necessary. Yet, if the defect is beyond a critical limit, it cannot heal without treatment to stimulate bone formation. There have been many ways of inducing bone regeneration and formation proposed such as cell transplantation techniques and supply of an inorganic scaffold. Currently, besides bone autografts and allografts, rhBMP2 or rhBMP7 are the only approved biological materials for use in stimulating bone formation in humans, although these materials are not yet permitted in Japan.

It is suggested that tissue regeneration go through, at least in part, developmental steps. Theoretically, if the regeneration follows normal developmental steps, regeneration could be perfectly achieved in both morphology and function. The trunk skeleton is derived from mesodermal tissue while the tissue origin of craniofacial skeleton is either cranial neural crest or mesoderm. Most of the trunk skeleton is formed by endochondral ossification whereas cranial bones mainly develop by intramembranous ossification. The importance of fibroblast growth factor (FGF) signaling in skeletal development has been demonstrated by identifying autosomal dominant mutations in their receptors, FGFRs, in osteo-chodrodysplastic disorders and craniosynostosis defined as early closure of one or more of the cranial sutures. Gene targeting technique in mice has also revealed the involvement of Fgf/Fgfr signaling in skeletal development. Among four Fgfrs, Fgfr1, Fgfr2 and Fgfr3 are expressed in osteoblasts and their expression pattern suggests that each Fgfr functions in different stages of osteoblast differentiation. However, this phenomenon has not been yet clearly demonstrated. We have been taking an approach to apply the ligands to mouse fetal skull bones to study Fgf/Fgfr signaling function in osteogenesis and learned that different FGF ligands work differently on osteoblast differentiation.

Currently, we are trying to apply the data from these fetal experiments to bone regeneration study in adults. In this lecture, I would like to address the question if we can apply what we learn from developmental process to regenerative medicine in terms of bone regeneration.

Jing Xiao

(Dalian Medical University, P.R. China)

Biodata

Dr. Jing Xiao is presently the Chief Professor of the Department of Oral Biology and the Deputy Director of Scientific & Technical Administration at Dalian Medical University in China. Dr. Xiao received her DDS at Dalian Medical University (1991) and her PhD at Tokyo Medical and Dental University (1999). Dr. Xiao then worked at the University of Southern California (USA) as a post-doctoral fellow (2000-2003) and as a foreign researcher at the Japan Society for the Promotion of Science (JSPS, 2004-2006). Dr. Xiao is a member of the Chinese Oral Biology & Medicine Committee and Oral Pathology Committee. Her current research projects focus on the mechanism of signaling pathway in orofacial development and regeneration.

Lecture Course: Progress of postnatal dental stem cells in tooth generation in China

Abstract

Postnatal dental stem cells have been successfully isolated from dental and periodontal tissues due to their obvious self-renewal and multilineage differentiation capacity. Studies by several Chinese research groups have shown that these cells are ideal candidates for dental reconstruction.

Dental pulp stem cells (DPSC), combined with scaffold materials, can be induced to form dentin- pulp complex. Periodontal ligament stem cells (PDLSC) can be differentiated to a variety of periodontal cells, and can form a periodontal ligament-cementum-like composite structure in vivo. Combined swine stem cells from apical papilla (SCAP) with the root-shaped HA/TCP scaffold, and PDLSC with collagen membrane, respectively, can then be implanted in alveolar sockets, and renewable biological roots can be regenerated. The study may be refined so as to help transition the biological root to further clinical application.

Akira Yamaguchi

(Tokyo Medical and Dental University)

Biodata

Dr. Akira Yamaguchi received his DDS degree from Tokyo Dental College in 1974 and his PhD degree from Tokyo Medical and Dental University in 1980. He became an Assistant Professor of Department of Oral Pathology at the School of Dentistry of Showa University in 1980, and was promoted to Associate Professor in the same department in 1988. He was then a visiting Assistant Professor at Washington University School of Dentistry and St. Louis University School of Medicine (1985-1988) and was Professor of Oral Pathology at the Nagasaki University Dental School from 1998 to 2004. Dr. Yamaguchi joined the Graduate School of Medical and Dental Sciences at Tokyo Medical and Dental University as a Professor in the Oral Pathology Department in 2004. Dr. Yamaguchi's current research interests are 1) molecular mechanism of bone formation and regeneration, and 2) the mechanism of bone destruction by oral cancer.

Lecture Course: Roles of BMP, Notch and CCN3 in osteoblast differentiation and bone regeneration

Abstract

Osteoblasts originate from common progenitors, which are capable of differentiating into other mesenchymal cell lineages such as chondrocytes, myoblasts and adipocytes. Various hormones and cytokines regulate osteoblast differentiation of mesenchymal progenitors to osteoblasts. Among these, bone morphogenetic proteins (BMPs) are the most potent inducers and stimulators of osteoblast differentiation. BMPs are important local factors that regulate Runx2, which is an essential transcription factor for osteoblast differentiation. Although Notch signaling is involved in a variety of cellular functions including cell proliferation, differentiation and apoptosis, it often exerts a dual effect on the regulation of cell differentiation in various cell types; some groups have reported that Notch signal stimulated osteoblast differentiation, but others have demonstrated the inhibitory effects of Notch signaling on osteoblast differentiation. These contradictory effects might be caused by interaction of other molecules with BMP and Notch signaling.

We identified CCN3 (NOV) as a highly up-regulated gene during bone repair by microarray analysis. We demonstrated that CCN3 associated with BMP-2, and attenuated BMP signal by suppressing phosphorylation of Smad1/5/8 and the expression of Id1 and Id2. We reported that CT-domain of CCN3 associated with EGF repeat of Notch, and CCN3 binding to Notch activated its signaling by stimulating the expression of cleaved Notch1 (NICD), mRNAs for Hes1 and Hey1, and promoter activities of Hes1 and Hey1. These results indicate that CCN3 exerts inhibitory effects on BMP-2-induced osteoblast differentiation by interacting with BMP (BMP antagonist) and Notch signaling pathways (Notch ligand). In a bone regeneration model in mice, CCN3 up-regulated in the early phase of bone regeneration associating with up-regulation of NICD and phosphorylated Smad1/5/8. We generated CCN3 transgenic mice using 2.3 kb Col1a1 promoter (osteoblast specific promoter), and they exhibited osteopenia due to decreased bone formation rate. In contrast, CCN3-deficient mice showed no particular changes in their skeleton. We are now investigating the bone repair in these CCN3 mutant mice. Collectively, CCN3 is involved in osteoblast differentiation and bone regeneration as a modulator interacting with BMP and Notch signaling.

References:

1. Komori T, et al.: Targeted disruption of Cbfa1 results in complete lack of bone formation owing to the maturation arrest of osteoblasts. Cell 89:755-764,1997.
2. Yamaguchi A, et al.: Regulation of Osteoblast Differentiation Mediated by BMPs, Hedgehogs and Cbfa1. Endocrine Reviews 21:393-411, 2000.
3. Nobuta M, et al.: Critical regulation of BMP-induced osteoblastic differentiation by Delta1/Jagged1-activatedNotch1 signaling. J Biol Chem280:15842-15848, 2005.
4. Minamizato T, et al.: CCN3/NOV inhibits BMP-2-induced osteoblast differentiation by interacting with BMP and Notch signaling pathways. Biochem Biophys Res Commun 354:567-573, 2007.
5. Yamaguchi A, et al: Regulation of osteoblast differentiation mediated by BMP, Notch, and CCN3/NOV. Jap Dent Sci Rev 44:48-56, 2008.

Tetsuya Taga

(Tokyo Medical and Dental University)

Biodata

Tetsuya Taga graduated from Kyoto University's Faculty of Science in 1982. During his PhD study at Osaka University Medical School he contributed to the purification and molecular cloning of interleukin-6 (IL-6), followed by characterization of the IL-6 receptor. Dr. Taga then discovered the signal-transducing receptor component of the IL-6 receptor complex, i.e., gp130, which later was found to be a common signaling component of the IL-6 family of cytokines, providing new insights into the cytokine signaling and function (Taga et al., Cell 1989; PNAS 1992; Annu. Rev. Immunol. 1997). In 2000, Dr. Taga received the Thompson ISI Citation Laureate Award, recognizing him as one of the top ten Japanese scientists authoring multiple and influential papers in a wide range of research, e.g. from chemistry to astrophysics, between 1981 and 1998.

Since becoming a full professor in 1996, his research has expanded to the elucidation of the mechanisms by which stem cells are regulated, partly because gp130 plays a role in stem cell regulation. His major focus has been on neural stem cells (Science 1999; PNAS 2001; Stem Cells 2006), hematopoietic stem cells (Mol. Cell. Biol. 2003; J. Exp. Med. 2004) and cancer stem cells (PNAS 2004). Particular attention is given to cell-external cues such as cytokines (Mol. Cell. Biol. 2007, 2008) and cell-intrinsic programs including chromatin modification (Dev. Cell 2001; Development 2003), taking cross-interactions of regulatory signals into consideration.

Positions held:

1989- Assistant Professor, Inst. Molecular and Cellular Biology, Osaka University
1996- Associate Professor, Inst. Molecular and Cellular Biology, Osaka University
1996- Professor, Medical Research Institute, Tokyo Medical and Dental University
2000- Professor, Inst. Molecular Embryology and Genetics, Kumamoto University
2001-2006, 2008- Director, Inst. Molecular Embryology and Genetics, Kumamoto University
2008- Professor, Medical Research Institute, Tokyo Medical and Dental University

Lecture Course: Stem cell regulatory signals: Basics and examples from the central nervous system

Abstract

The fate of stem cells is regulated by (i) cell-external cues such as the microenvironment called niche, that contains, for instance, extracellular matrix and cytokines, as well as (ii) cell-intrinsic programs including DNA methylation, histone acetylation, and histone methylation. This lecture starts from an overview of the basic ideas in this subject, and then proceeds to a discussion of theoretical considerations.

In the latter part of the lecture, basic scientific questions regarding how neural stem cell fate is regulated will be addressed. Neurons, astrocytes, and oligodendrocytes are the three major cell types in the brain and they develop from neural stem cells. We have demonstrated that leukemia inhibitory factor (LIF), a member of the interleukin-6 family of cytokines, and bone morphogenetic protein 2 (BMP2), a member of the BMP family of cytokines, synergistically act on neural stem/progenitor cells to induce differentiation of mature astrocytes which express glial fibrillary acidic protein (GFAP). In neural stem/progenitor cells stimulated by LIF and BMP2, their respective downstream transcription factors STAT3 and Smad1 form a complex in the nucleus with a transcriptional co-activator, p300. This complex is suggested to be important for astrogliogeneis and lead to transcriptional activation of the gene for GFAP.

Interestingly, BMP2 induces expression of negative regulatory helix-loop-helix (HLH) proteins such as Hes5, Id1 and Id3, which leads to inhibition of neuronal differentiation by suppressing transcriptional activity of neurogenic basic-HLH transcription factors such as neurogenin. Furthermore, an oligodendrocyte differentiation-inducing transcription factor, Olig2, inhibits the activity of an astrocyte differentiation-inducing transcription factor, STAT3. Taken together with some other findings, it is suggested that the cell-fate in the developing brain is determined in part by cross-interactions among transcriptional regulatory signals.

It has long been an interesting question why astrocyte differentiation is prevented in the mid-gestational brain, where neurogenesis is predominant. As described above, astrocyte differentiation is dependent on STAT3. There exists a STAT3 recognition element in the promoter region of the astrocyte specific GFAP gene. A cytosine residue in this element is highly methylated in neural stem/progentir cells in a mid-gestational stage but becomes demethylated as the brain develops. This methylation was found to inhibit STAT3 binding to its recognition element, suggesting that DNA methylation is a critical determinant in the developmental stage-dependent regulation of astrocytic differentiation.

Fibroblast growth factor 2 (FGF2) promotes proliferation of neural precursors while it inhibits their differentiation. We recently found that FGF2 signaling and Wnt signaling cooperate together, via inactivation of glycogen synthase kinase 3beta (GSK3beta) and subsequent induction of cyclin D1 expression, to induce proliferation of neural precursor cells. The inactivation of GSK3beta is unexpectedly involved in the inhibition of neurogenesis by cooperating with a Notch pathway.

In conclusion, these findings suggest that cross-interactions among transcriptional regulatory mechanisms are important for the cell-fate determination in the developing brain.

Hiroshi Asahara

(Tokyo Medical and Dental University)

Biodata

Dr. Hiroshi Asahara is a Professor in the Department of Systems BioMedicine at Tokyo Medical and Dental University. After graduating from Okayama University Medical School, he was trained as an Orthopedic Surgeon, and his career as a researcher led him to be a postdoctoral fellow at Harvard Medical School and a staff scientist at Salk Institute, under Prof. Marc Montminy. Dr. Asahara then started his own lab as Assistant Professor at Scripps Research Institute, USA, and then became Department Head at the National Research Institute for Child Health and Development, Japan. At Tokyo Medical and Dental University he is tasked with the responsibility to construct a new department in the Faculty of Medicine, with the mission to encode the molecular network regulating human development and regeneration by combining multiple post-genomic systems approaches. Based on a novel strategy and database, he and his lab are trying to uncover molecular mechanisms of limb development and are also identifying the critical pathway to regulate inflammatory diseases, including rheumatoid arthritis.

Lecture Course: Systems approach to reveal molecular network regulating musculoskeletal diseases and development

Abstract

We created a whole-mount in situ hybridization (WISH) database, termed EMBRYS <http://embrys.jp>, containing the expression data of 1520 transcription factors and cofactors expressed in E9.5, E10.5, and E11.5 mouse embryos – a highly dynamic stage of skeletal myogenesis. This approach implicated 43 genes in regulation of embryonic myogenesis, including a transcriptional repressor, the zinc-finger protein RP58 (also known as Zfp238). Knockout and knockdown approaches confirmed an essential role for RP58 in skeletal myogenesis. Cell-based high-throughput transfection screening revealed that RP58 is a direct MyoD target. Microarray analysis identified two inhibitors of skeletal myogenesis, Id2 and Id3, as targets for RP58-mediated repression. Consistently, MyoD-dependent activation of the myogenic program is impaired in RP58 null fibroblasts and downregulation of Id2 and Id3 rescues MyoD's ability to promote myogenesis in these cells. Our combined, multi-system approach reveals a MyoD-activated regulatory loop relying on RP58-mediated repression of muscle regulatory factor (MRF) inhibitors.

We applied our systems approaches to other locomotive tissues research including cartilage and tendon tissue, and revealed a novel molecular network regulating joint cartilage development and homeostasis via miRNA-140 (Genes and Development, 2010; Arthritis and Rheum, 2009) and tendon development by Mkx (PNAS, 2010).

Based on these findings and tools, we are now trying to understand the molecular pathway which enables regeneration in the musculoskeletal system and the attenuation of chronic inflammatory diseases.

Ichiro Sekiya

(Tokyo Medical and Dental University)

Biodata

Ichiro Sekiya is a Professor in the Cartilage Regeneration section at Tokyo Medical and Dental University. His residency and knee surgery training were completed at Tokyo Medical and Dental University. He started basic research for regulation of cartilage-specific transcription factor with Prof. Masaki Noda in his graduate school days. Dr. Sekiya studied abroad as a postdoctoral fellow with Prof. Darwin Prockop in New Orleans, concentrating his studies on the chondrogenesis of bone marrow stem cells. Since he returned to Japan in 2002, he has been studying stem cell biology and cell therapy for cartilage regeneration with Prof. Takeshi Muneta and more than 10 graduate students. He received the New Investigator Recognition Award by the US Orthopaedic Research Society in 1998 and the Japan Orthopaedic Association Award in 2002. Dr. Sekiya has published more than 90 publications in international journals, and joined the editorial board of "Stem Cells" in 2008. Based on his basic research, he started clinical study for cartilage regeneration with synovial stem cells four years ago.

Lecture Course: Mesenchymal stem cells derived from synovium: their properties and clinical application for cartilage regeneration

Abstract

Injuries to articular cartilage have a limited capability for intrinsic repair because articular cartilage is avascular and relatively hypocellular. Mesenchymal stem cells (MSCs) are an attractive cell source for cartilage regeneration. Our in vivo chondrogenic assay demonstrated that synovial and bone marrow MSCs had a higher chondrogenic ability than adipose and muscle MSCs. Human synovial MSCs expanded more in human serum than in FBS, and the opposite results were obtained in bone marrow MSCs. Our strategy for cartilage regeneration is the transplantation of synovial MSCs.

Current cell therapy for cartilage regeneration requires invasive procedures. We have developed a novel implantation procedure with synovial MSCs. (1) The knee is positioned so that the cartilage defect faces upward. (2) Synovial MSC suspension is slowly dripped onto the cartilage defect. (3) The knee is held stationary for several minutes or hours until most cells adhere to the cartilage defect. According to our in vitro and in vivo studies, more than 60% of the cells adhered to the cartilage defect in 10 minutes, and promoted cartilage regeneration.

We are currently doing clinical trials for cartilage defects. All patients have their cartilage defects filled with synovial MSCs arthroscopically. Favorable results are obtained by MRI imaging in many cases, and also by second look arthroscopies and biopsies, although the number of patients who undertake these invasive examinations is still limited. Our method is advantageous because no periosteal coverage or scaffold is required and transplantation is possible arthroscopically.

Johan Hyllner

(Cellartis, Sweden)

Biodata

Johan Hyllner is at present Chief Scientific Officer (CSO) at Cellartis. Hyllner has profound industrial experience in biotech company build-up and high level management. Before joining Cellartis, Hyllner was the CSO of Vitrolife AB, Sweden, a company listed on the Stockholm stock exchange. He has also been the CEO of a successful biotech company in the toxicity testing area (SQC AB) and a Research Fellow at Hoffman-LaRoche (Nutley, NJ, USA). Hyllner earned his PhD degree in Zoophysiology at Gothenburg University in 1994 and has published more than 50 full length scientific publications in international journals and books.

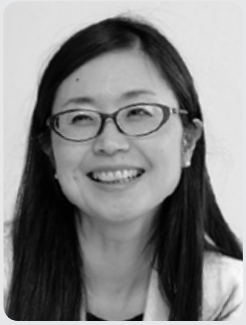
Lecture Course: Dendritic cells: Control of immunity and tolerance

Abstract

Human pluripotent stem cells have the ability to proliferate indefinitely and to differentiate into virtually any human cell type, making it possible to generate large quantities of partially or terminally differentiated human cells. Recent technical advancements now enable the culturing of human pluripotent stem cells under standardized feeder-free conditions which allows for cost efficient and robust large scale cell production. Human pluripotent stem cell based technologies are progressing rapidly and several ground-breaking discoveries have been made during the last few years, with the discovery of induced human pluripotent stem cells in the Yamanaka Laboratory in Japan being one of the absolutely most important findings. Such scientific achievements are now being transformed into products and services addressing both the in vitro and in vivo markets.

However, in order to speed up developments in this area it is clear that collaborative partnerships between academic institutions, pharmaceutical enterprises, and biotechnology companies are needed. Since this research field is relatively young, the necessary development activities include a substantial amount of basic research and validation studies, but commercial challenges exist. Thus, collaborations involving partners from different disciplines are instrumental for scientific and commercial success. This approach has been acknowledged in Europe by the European Commission in its design of the 6th and 7th Framework Programs which stimulate and finance large international collaborative projects. Several countries such as Japan, USA, Sweden, and the UK also have bilateral agreements with the aim of funding joint efforts in this area. One such example is a program that fosters multidisciplinary bioscience research between Japan and Sweden. The funding is provided by JST (Japan Science and Technology Agency) and the Swedish organizations Vinnova and SSF. One grant within the last call was recently announced and awarded to Professors Kenji Yasuda (Tokyo Medical and Dental University) and Anders Lindahl (Göteborg University, Sweden) to develop novel cardiotoxicity testing tools based on pluripotent stem cells. It is clear that such international partnerships between expert researchers will speed up the advancement in the field.

Recent progress in the area of pluripotent stem cells for drug discovery and regenerative medicine will be described in more detail. These advancements will be illustrated using recent original research data from collaborative partnerships from EU sponsored programs that Cellartis has taken part in.



Noriko Osumi

(Tohoku University)

Biodata

Dr. Noriko Osumi graduated from the Faculty of Medicine of Tokyo Medical and Dental University and subsequently earned a PhD from the university. A Professor at Tohoku University School of Medicine since 1998, she was recently chosen as one of the 25 Distinguished Professors at Tohoku University. Dr. Osumi serves on various governmental committees such as ethical issues, grant system development, and career paths for young scientists, and was chosen as the youngest member of Japanese Council Japan, on which she has served since 2005. Dr. Osumi's research interest covers broad areas such as pre- and postnatal development of the brain and craniofacial region, and the behavior of animals as models of psychiatric diseases. More specifically, she is recently eager to understand regulatory mechanisms of neurogenesis and maintenance of neural stem cells at cellular and molecular levels both in embryonic and postnatal stages. Her lab has deep expertise in manipulating embryos and imaging brain cells. Furthermore, Dr. Osumi has translated two books into Japanese: Essential Developmental Biology, by Jonathan Slack, and The Birth of the Mind, by Gary Marcus. She is a representative of CREST project (2005-2010) supported by JST (Core Research for Evolution of Science and Technology, a project of the Japan Science and Technology Agency) and Global COE project (2007-2012) supported by MEXT (Global Center of Excellence, through the Ministry of Education, Culture, Sports, Science and Technology).

Lecture Course: The neural crest and its derived cells in contribution to craniofacial development and regenerative medicine

Abstract

The neural crest is a transient tissue formed in between the ectodermal epithelium and neural plate during the process of neural tube formation in early embryonic development. Neural crest-derived cells (NCDCs) escape from the neural crest, proliferate rigorously, migrate into almost the entire body, and at their terminal tissues differentiate into various cell types including neurons and glial cells of sensory, autonomic and enteric nervous systems, endocrine cells such as the adrenal medulla, and melanocytes in the skin. In the craniofacial region, NCDCs give rise to meninges covering the brain, bone and cartilage of the face, dentine and cement of teeth, and smooth muscles and pericytes of the blood vessels, in addition to above mentioned cell types. It is now known that NCDCs also contribute to the anterior part of the eye such as the iris stroma, where they penetrate back into the brain to become pericytes. Because of such a wide contribution to development, the neural crest is sometimes called as “the fourth germ layer.” The neural crest is only found in vertebrate, suggesting its significance in evolution. Recently, the importance of NCDCs has been revisited since they are resident in adult tissues such as the gut, heart, and iris, as “quiescent stem cells,” and thus can potentially be taken out from the body and used as “tissue stem cells” for regeneration therapy. In this lecture, I would like to take you into the promenade to understand these mysterious NCDCs in regard with their origin and unique character.

References:

1. Matsuo, T. *, Osumi-Yamashita, N. *, Noji, S., Ohuchi, H., Koyama, E., Myokai, F., Matsuo, N., Taniguchi, S., Doi, H., Iseki, S., Ninomiya, Y., Fujiwara, M., Watnabe, T. and Eto, K.: A mutation in the Pax-6 gene in rat small eye is associated with migration defect of midbrain crest cells. Nat Genet. 3(4), 299-304, 1993. (*Equally contributed□
2. Osumi-Yamashita, N., Ninomiya, Y., Doi, H. and Eto, K.: The contribution of both forebrain and midbrain crest cells to the mesenchyme in the frontonasal mass of mouse embryos. Dev Biol. 164(2), 409-419, 1994.
3. Imai, H., Osumi-Yamashita, N., Ninomiya, Y. and Eto, K.: Contribution of early-emigrating midbrain crest cells to the dental mesenchyme of the mandibular molar tooth in rat embryos. Dev Biol. 176(2), 151-165, 1996.
4. Osumi-Yamashita N., Ninomiya, Y., & Eto K.: Craniofacial embryology in vitro. Int J. Devel Biol 41, 187-194, 1997.
5. Tomita, Y., Matsumura, K., Wakamatsu, Y., Matsuzaki, Y., Shibuya, I., Kawaguchi, H., Ieda, M., Kanakubo, S., Shimazaki, T., Ogawa, S., Osumi, N., Okano, H. and Fukuda, K.: Cardiac neural crest cells contribute to dormant multipotent stem cells in the mammalian heart. J Cell Biol. 170(7), 1135-1146, 2005.
6. Kanakubo, S., Nomura, T., Yamamura, K., Miyazaki, J., Tamai, M., and Osumi, N.: Abnormal migration and distribution of neural crest cells in Pax6 heterozygous mutant eye, a model for human eye diseases. Genes Cells. 11(8), 919-933, 2006.
7. Le Douarin, N. Kalcheim, C.: The Neural Crest (Developmental and Cell Biology Series). 2nd Ed. Cambridge University Press, 2009.
8. Cordero, D.R., Brugmann, S., Chu, Y., Bajpai, R., Jame, M., Helms, J.A.: Cranial neural crest cells on the move: their roles in craniofacial development. Am J Med Genet A, 155(2), 270-279, 2011.
9.Kikuchi, M., Hayashi, R., Kanakubo, S., Ogasawara, A., Yamato, M., Osumi, N. and Nishida, K.: Neural crest-derived multipotent cells in the adult mouse iris stroma. Genes Cells. 16(3), 273-381, 2011.

Minoru Ueda

(Nagoya University)

Biodata

Dr. Minoru Ueda received his DDS degree from Tokyo Medical and Dental University in 1978 and his PhD degree in medical science from Nagoya University in 1982. He was appointed Professor and Chair of Oral and Maxillofacial Surgery at Nagoya University School of Medicine in 1994, Visiting Professor of Stem Cell Engineering at Institute of Medical Science, University of Tokyo in 2003, and Visiting Professor at Korea University Ansan Hospital, Korea in 2011. In 1999 Dr. Ueda became Chairman of the scientific advisory board at Japan Tissue Engineering, Inc., the first tissue engineering company to commercialize cultured skin. Dr. Ueda received the "2004 President's Award" from the Science Council of Japan for his contribution to the development of tissue engineered skin and cartilage. Dr. Ueda is a former President of the Japanese Tissue Engineering Society and the Asian Tissue Engineering Society, and served as Vice-President of the Tissue Engineering International & Regenerative Medicine Society.

Lecture Course: Stem cell based cytokine therapy: A new era for regenerative medicine

Abstract

INTRODUCTION

Regenerative medicine using stem cells is a promising tool in a new clinical platform for a whole spectrum of intractable diseases.

On the other hand, there have been extensive investigations into tissue healing by the exogenous application of various growth factors. However, the results of utilizing growth factors at a single dose, multiple doses, or the combined application of multiple factors, with the expectation of synergistic effects, have not yet been confirmed clinically.

Mixed growth factors secreted from stem cells may have an ideal combination which can improve damaged tissue condition. We hypothesized that stem cell cultured conditioned media which contains such factors would enhance tissue and organ regeneration through endogenous cell migration and organogenesis.

BONE

We aimed to establish a new bone regeneration therapy by using stem cell cultured conditioned media. Mesenchymal stem cell cultured conditioned media (MSC-CM) were extracted from basal media (BM) cultured hMSCs. Cell proliferation and migration of rMSCs increased significantly from culturation in hMSCs-CM. The expressions of osteogenetic-related genes in rMSCs cultured in each CM were significantly higher than in BM. In animal study, collagen sponge / hMSC-CM group had well-formed bone compared with the control groups. Moreover, these groups confirmed an equal newly formed bone compared with PRP / hMSCs group.

SPINAL CORD

We report here that dental pulp stem cells from human exfoliated deciduous conditioned medium (SH-CM), when administrated into the acute phase of damaged rat spinal cord, significantly recovered hind-limb locomotors functions. SH-CM strongly suppressed apoptosis of neurons, astrocytes and oligodendrocytes, and preserved neuronal filaments and myelin sheaths after the code injury. SH-CM regenerated both corticospinal tract and raphe spinal serotonergic (5-HT) axons beyond the epicenter. Taken together, our data demonstrate significant benefits of SH-CM based regeneration therapy for treatment of SCI. In the acute phase, factors secreted from SHEDs would protect injured spinal cord from severe neural damages in non-cell autonomous manner; subsequently, specifically self-differentiated neural stem cell into the oligodendorocytes contributed functional recovery by promoting re-myelination of damaged axons in cell autonomous manner.

STROKE

We investigated the influence of intranasal administration of SHED-derived conditioned medium (SH-CM) after permanent MCAO (pMCAO). After adult male Sprague-Dawley rats were subjected to pMCAO(day 0), SHEDs were transplanted into the brain 24 hours after pMCAO (day 1) (SHED group), and SH-CM (SH-CM group) was intranasally administrated from day 3 to day 15 on a daily basis. Evaluation of motor function and infarct volume were measured. Neurogenesis and vasculogenesis were determined with immunochemical markers on day 6 and day 16 after pMCAO. Evaluation of motor function showed significant recovery and a decrease in infarct volume for both SHED and SH-CM groups as compared with the control group. SHED group and SH-CM group have more positive signals with doublecortin, neurofilament, NeuN and RECA-1 in peri-infarct area than control group. The migration of neuronal progenitor cells (NPCs) with doublecortin from subventricular zone (SVZ) to the peri-infarct area was observed on day 6 and 16 and NPCs of migration on day 6 were more prominent.

CONCLUSIONS

The findings of these studies indicated that stem cells cultured conditioned media contained enhancers for the migration and organogenesis of endogenous stem cells, and that this process enhanced tissue regeneration without cell transplantation. We can open a new era for regeneration medicine.

Ian Wilmut

(The University of Edinburgh, United Kingdom)

Biodata

Professor Sir Ian Wilmut was the founding director of the MRC Centre for Regenerative Medicine at the University of Edinburgh and formerly head of the Department of Gene Expression and Development at the Roslin Institute. Prof Wilmut is best known for his pioneering work in the science of cloning. In 1996, he led the team that created the first animal to be cloned from an adult cell, Dolly the sheep. He has since become an international expert on cloning techniques, stem cell technologies, and stem cell research ethics. The research of Professor Wilmut's lab explores novel ways of being able to change the fate of adult somatic cells and therapeutic uses of stem cells to treat degenerative and genetic diseases.

Lecture Course: Cloning, stem cells and regenerative medicine

Abstract

Important new opportunities for research and therapy are being provided by the emerging methods for changing the fate of cells. New methods will make it possible to derive progenitor or terminally differentiated cells of many lineages by simple treatment of patient somatic cells. The availability of these populations holds out the promise of providing important new clinical treatments in three ways which will be reviewed by considering research in the Centre in Edinburgh and elsewhere.

First, it will be possible to identify drugs that are able to prevent the symptoms of some inherited degenerative diseases, such as ALS (motor neuron disease). New methods of producing stem cells make it possible to produce from a patient cells that are equivalent to those early in their life. If the patient has an inherited disease their cells may be compared with equivalent cells from a healthy donor in a search for differences associated with the disease and in this way identify molecular mechanisms that cause inherited diseases. In turn this will make it possible to identify the first drugs that prevent the effect of the abnormality. In principle many other inherited diseases may be studied in this way including schizophrenia and causes of sudden heart failure. In addition, similar cells lines will be used for more effective safety testing of new drugs and so reduce the frequency of late withdrawal of new drugs. This has the potential to increase the efficiency of drug development and reduce the costs involved.

A second opportunity will take advantage of the fact that in some cases it will be possible to prompt dormant stem cells in the patient's own tissue to repair or replace cells that no longer function normally. Cultures of cells in the laboratory will be used to identify compounds that are able to stimulate appropriate activity of the cells. In this way re-myelination of neurones has been achieved during culture of tissue slices.

Thirdly, some diseases will be treated by transplantation of cells or tissues into the patient to replace those that are lost or not functioning appropriately. Effective therapy by this means depends upon being able to produce large numbers of cells of the required type that function appropriately and either are immunologically matched to the patient or are accompanied by immunological treatment to prevent rejection. A number of clinical trials of cell therapy are in progress at present.

It is likely that new treatments will be introduced gradually over a period of decades as greater biological knowledge and technical understanding are gain from continuing research. All of these approaches depend upon understanding the developmental biology of specific tissues and being able to produce stem cell populations at the required stage of development and selected genotype.

Profiles and Abstracts of Symposium Speakers

Masayuki Yoshida

(Tokyo Medical and Dental University)

Biodata

Masayuki Yoshida 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.

He completed his post-doctoral research fellowship at Department of Pathology, Harvard Medical School. His scientific theme included pathophysiology of vascular endothelium during atherosclerosis and inflammation. In particular, he discovered a novel signal transduction pathway of E-selectin, an adhesion molecule inducibly expressed on the surface of endothelial cells upon leukocyte adhesion. After returning to TMDU School of Medicine in 1996, he was appointed as an instructor in Molecular Medicine and then promoted to an Associate Professor in Medical Biochemistry.

In 2006, he became a professor and was tasked with managing a new research center for life science and bioethics (BERC) where he is responsible for ethical management of both clinical and basic research. During BERC's first 5 years, it held several international symposiums to directly connect researchers and scientists in the field of research ethics and guidelines. The Center's hands-on methods have helped researchers at TMDU significantly improve the quality of reseach protocols in TMDU. From 2010, Prof. Yoshida has led BERC as Director and further expands his commitment to create an environment to conduct good medical research.

Positions held:

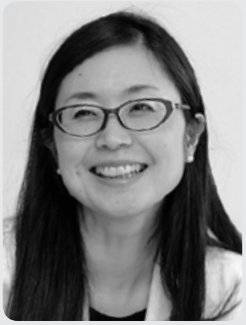
1988 — 1992: Resident, Div. Int. Med, Tokyo Medical and Dental University
1991 — 1991: Research Fellow, Medical Institute of Bioregulation, Kyushu University
1992 — 1996: Research Fellow, Department of Pathology, Harvard Medical School
1996 — 1999: Instructor, Medical Research Institute, Tokyo Medical and Dental University
1999 — 2002: Associate Professor, Medical Research Institute, Tokyo Medical and Dental University
2002 — 2006: Associate Professor, Department of Medical Biochemistry, Tokyo Medical and Dental University
2006 — Present: Professor, Life Science and Bioethics Research Center, Tokyo Medical and Dental University
2009 — Present: Member, the Committee for Basic and Clinical Research, Tokyo Medical and Dental University

Symposium Talk: Socio-biological interface of research ethics

Abstract

Even though many researchers think it is important, ethical considerations sometimes remain detached or marginalized from central discussions of scientific research projects. Nonetheless, the ethical soundness of the researcher is a critically important aspect to insure the validity of any research project. In the scientific research field, samples of human tissues and organs have been collected for many years, with a huge amount of new samples being added each year. Specimens correlated with certain diseases have proven enormously useful in scientific research. Needless to add, new methods in molecular biology and genetics enable us to obtain more information from these samples. These remarkable progresses in science also have the effect of pouring a sense of uncertain into the community. In other words, the more scientific use we make of human biological materials, the greater our concerns about ethical issues become. To provide ethical standards to conduct these studies, numerous statements, guidelines, and regulations have been issued worldwide, including in Japan. However, due to the highly complex nature of recent clinical studies, it is not easy to identify the guidelines that govern one's research project.

I would like to emphasize core principles underlying scientific as well as ethical integrity and the application of these principles to a range of issues in scientific research, especially focusing on the research ethics situation at TMDU.



Noriko Osumi

(Tohoku University)

Symposium Talk: Neural crest stem cells: Origins and applications

Abstract

The neural crest is a transient tissue of the vertebrate embryo. It originates from a dorsal part of the neural tube, i.e., the primordium of the central nervous system. Neural crest-derived cells (NCDCs), which emigrate from the neural tube to various places in the embryo, have a character of stem cells as giving rise to many different cell types and tissues including neurons and glial cells of sensory, autonomic and enteric nervous systems, endocrine cells such as the adrenal medulla, and melanocytes in the skin. NCDCs born in the cranial region give rise to meninges covering the brain, bone and cartilage of the face, dentine and cement of teeth, and smooth muscles and pericytes of the blood vessels. In addition, NCDCs contribute to the anterior part of the eye such as the iris stroma, penetrate back into the brain to become pericytes. Importantly, NCDCs persist in various locations of the postnatal organism such as the gut, heart, and iris. We can take these NCDCs out from a rodent and let them expand and differentiate into many types of cells in vitro, suggesting the best possible source of tissue stem cells for future use in medical applications. Simultaneously, I would like to point out in this symposium a potential dark side of neural crest stem cells as the seed of various cancers, e.g., melanoma, pheochromocytoma, neuroblastoma, various types of glioma, and probably more.

References:

1. Matsuo, T. *, Osumi-Yamashita, N. *, Noji, S., Ohuchi, H., Koyama, E., Myokai, F., Matsuo, N., Taniguchi, S., Doi, H., Iseki, S., Ninomiya, Y., Fujiwara, M., Watnabe, T. and Eto, K.: A mutation in the Pax-6 gene in rat small eye is associated with migration defect of midbrain crest cells. Nat Genet. 3(4), 299-304, 1993. (*Equally contributed)
2. Osumi-Yamashita, N., Ninomiya, Y., Doi, H. and Eto, K.: The contribution of both forebrain and midbrain crest cells to the mesenchyme in the frontonasal mass of mouse embryos. Dev Biol. 164(2), 409-419, 1994.
3. Imai, H., Osumi-Yamashita, N., Ninomiya, Y. and Eto, K.: Contribution of early-emigrating midbrain crest cells to the dental mesenchyme of the mandibular molar tooth in rat embryos. Dev Biol. 176(2), 151-165, 1996.
4. Osumi-Yamashita N., Ninomiya, Y., & Eto K.: Craniofacial embryology in vitro. Int J. Devel Biol 41, 187-194, 1997.
5. Tomita, Y., Matsumura, K., Wakamatsu, Y., Matsuzaki, Y., Shibuya, I., Kawaguchi, H., Ieda, M., Kanakubo, S., Shimazaki, T., Ogawa, S., Osumi, N., Okano, H. and Fukuda, K.: Cardiac neural crest cells contribute to dormant multipotent stem cells in the mammalian heart. J Cell Biol. 170(7), 1135-1146, 2005.
6. Kanakubo, S., Nomura, T., Yamamura, K., Miyazaki, J., Tamai, M., and Osumi, N.: Abnormal migration and distribution of neural crest cells in Pax6 heterozygous mutant eye, a model for human eye diseases. Genes Cells. 11(8), 919-933, 2006.
7. Le Douarin, N. Kalcheim, C.: The Neural Crest (Developmental and Cell Biology Series). 2nd Ed. Cambridge University Press, 2009.
8. Cordero, D.R., Brugmann, S., Chu, Y., Bajpai, R., Jame, M., Helms, J.A.: Cranial neural crest cells on the move: their roles in craniofacial development. Am J Med Genet A, 155(2), 270-279, 2011.
9. Kikuchi, M., Hayashi, R., Kanakubo, S., Ogasawara, A., Yamato, M., Osumi, N. and Nishida, K.: Neural crest-derived multipotent cells in the adult mouse iris stroma. Genes Cells. 16(3), 273-381, 2011.

Emi Nishimura

(Tokyo Medical and Dental University)

Biodata

Dr. Emi Nishimura obtained her MD in 1994 and did her dermatology residency in Kyoto University Hospital. She then obtained her PhD in Shin-Ichi Nishikawa's lab 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 in the Dana Farber Cancer Institute, Harvard Medical School, and extended her melanocyte stem cell research there. She then started her own group as an Associate Professor at Hokkaido University, subsequently becoming Professor at Kanazawa University the following year. Her lab then moved to 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 TMDU.

Symposium Talk: Regulation of stem cells by stem cells

Abstract

In most stem cell systems, the organization of the stem cell niche including the niche cells and the anchoring matrix required for stem cell maintenance are largely unknown. Melanocyte stem cells (MSC) and hair follicle stem cells (HFSC), which are originally derived from a completely different developmental origin, are located in the bulge area of mammalian hair follicles.1,2 Our previous studies indicated that the niche plays dominant role in MSC fate determination1, while the identity of niche cells, the underlying mechanisms and the correlation with HFSCs remain unclear. We recently found that collagen XVII (COL17A1/BP180/BPAG2), a hemidesmosomal transmembrane collagen, is highly expressed in hair follicle stem cells (HFSCs) and is required for the maintenance not only of HFSCs but also of melanocyte stem cells (MSCs), which do not express Col17a1 but directly adhere to HFSCs. Mice lacking Col17a1 show premature hair graying and hair loss. Analysis of Col17a1 null mice revealed that COL17A1 is critical for the self-renewal of HFSCs through maintaining their quiescence and immaturity, potentially explaining the mechanism underlying hair loss in human COL17A1 deficiency. Interestingly, Col17a1 null mice show defective TGF-β production by HFSCs and targeted TGF-b type II receptor (Tgfbr2) deficiency in the melanocyte lineage causes incomplete maintenance of melanocyte stem cell immaturity and results in premature hair graying.3 These data demonstrate that the TGF-b signaling pathway is the critical niche factor that regulate melanocyte stem cell immaturity and quiescence. Finally, forced expression of COL17A1 in basal keratinocytes, including HFSCs, in Col17a1 null mice rescues MSCs from premature differentiation and restores TGF-β signaling, demonstrating that HFSCs function as a critical regulatory component of the MSC niche.4 The regulation of somatic stem cells by different types of stem cells in a specialized tissue organization might be a recurring strategy for somatic stem cell maintenance.

References:

1. Nishimura, E.K. et al. Nature. 416(6883):854-60, 2002.
2. Nishimura, E.K., et al. Science. 307(5710):720-724, 2005.
3. Nishimura, E.K., et al. Cell Stem Cell, 6(2):130-40, 2010.
4. Tanimura S., et al. Cell Stem Cell, 8;(2):177-187, 2011.
5. Inomata K., et al. Cell. 137(6):1088-1099, 2009.

Johan Hyllner

(Cellartis, Sweden)

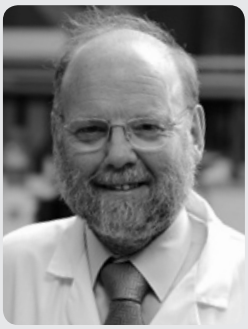
Symposium Talk: Pluripotent stem cells for drug discovery and regenerative medicine via collaborative industrial partnerships in Europe

Abstract

The industrial exploitation of human pluripotent stem cell based technologies is progressing rapidly, and the scientific achievements made during the past decade are now being transformed into products and services addressing both the in vitro and in vivo markets. The great interest in these technology developments is illustrated by the fact that most of the major pharmaceutical companies have, to various degrees, either internal or external stem cell programs. It is also evident that collaborative partnerships between major pharmaceutical enterprises, biotechnology companies, and academic institutions seem to be the most preferred route forward. The complexity of the field of human pluripotent stem cells requires substantial amount of basic research and validation studies but also technical and commercial challenges need to be addressed.

Cellartis is a biotech company with a strong focus on human pluripotent stem cells and their use for drug discovery and regenerative medicine. The company has developed a product line including stem cell derived-hepatocytes, cardiomyocytes, and mesenchymal stem cells as well as associated products such as antibodies, tools, and culture media. In addition, based on its long standing experience in the human pluripotent stem cell platform, Cellartis represents an excellent partner for customized stem cell programs including LMW compound screening and projects addressing regenerative medicine challenges.

Recent progress in industrial use of pluripotent stem cells for drug discovery and regenerative medicine will be described in more detail. These advances will be exemplified using original research data from collaborative industrial partnerships were Cellartis has been involved. Presently, Cellartis collaborates in two cell therapeutic programs with major industrial partners. One program is led by Novo Nordisk A/S (Denmark) with the aim to cure diabetes and the second program, led by Mitsubishi Tanabe Pharma (Japan), is focused on finding treatments for Parkinson's disease.



Ian Wilmut

(The University of Edinburgh, United Kingdom)

Symposium Talk:

Professor Wilmut's abstract will be available at ISP2011.

ISP2011 Participants

ISP2011 Invited Participants

Invited Participants

B

Od Bayarsaikhan

Mongolia

Poster #9

Health Sciences University of Mongolia

H

Moe Htet

Myanmar

Poster #19

Moe Dental Clinic

J

Fariba Taba Jahan

Bangladesh

Poster #4

Marks Dental College

Ripa Jamal

Bangladesh

Poster #18

University of Dhaka

K

Siwen Kang

P.R. China

China Medical University

Saranthorn Kanokvijitsilp

Thailand

Chulalongkorn University

Asmatullah Khan

Pakistan

Poster #12

Helper's Eye Hospital

Boyun Kim

Republic of Korea

Seoul National University

Sophannary Kong

Cambodia

University of Health Sciences

Tejaswini Vaman Kulkarni

India

Poster #1

L

Lina Lim

Cambodia

University of Health Sciences

N

Mya Nandar

Myanmar

West Yangon General Hospital

O

Buyan-Ochir Orgil

Mongolia

Poster #17

Health Sciences University of Mongolia

P

Wattage Kathya Leoni Perera

Sri Lanka

Poster #16

University of Peradeniya

R

Dordia Anindita Rotinsulu

Indonesia

Poster #6

Bogor Agricultural University

S

Manish Subedi

Nepal

Poster #8

Subidha Hospital

Weinan Sun

P.R. China

Poster #13

China Medical University

Didi Wahyudi Syukur

Indonesia

Poster #14

DentCo Dental Clinic

T

Linh Thuy Ta

Vietnam

Poster #2

Ho chi minh City Eye Hospital

Sze Jun Tan

Malaysia

Poster #11

Universiti Sains Malaysia

Tien Kim Quynh Tran

Vietnam

Poster #7

HCMC Society of Dental Implantology

W

Wenqian Wang

P.R. China

China Medical University

Ting Wang

P.R. China

The Affiliated Hospital of Medical College QingDao University

Xin Wang

P.R. China

Poster #3

Beijing Stomotological Hospital

TMDU Poster Session Participants

Li Min

P.R. China

Poster #5

Tokyo Medical and Dental University

Pham Anh Vu Thuy

Vietnam

Poster #10

Tokyo Medical and Dental University

Gamaralalage Amodini Rajakaruna

Sri Lanka

Poster #15

Tokyo Medical and Dental University

Ilnaz Hariri

Iran

Poster #20

Tokyo Medical and Dental University

Abstracts of ISP2011 Poster Presenters

Poster No.
1

Tejaswini Vaman Kulkarni

(India)

Title: Studies on Gelatin

Research is in progress

Poster No. 2

Linh Thuy Ta

(Hohchiminh City Eye Hospital, Vietnam)

Title: Assessment of the disturbances of contrast sensitivity and color vision before and after treatment in optic neuritis

Abstract

Purpose: To describe the types and changings of color vision defects and contrast sensitivity disturbances present in the acute phase of the disease and 6 weeks / 3 months into recovery in the optic neuritis patients.

Methods: Patients meeting strict eligibility criteria were seen within 14 days of the onset of symptoms and then at regular follow-up visits. At the first, 6-week, and 3-month visits, spatial vision (acuity, contrast sensitivity) and color vision were measured. We used the Farnsworth-Munsell 15 hue test and the Functional Acuity Contrast Test in this research.

Results: Color vision defect percentage was 76.6% in the acute phase, 53.3% at the 6-week point and 20% at the 3-month point. In the acute phase, most patients with low vision acuity show mixed red-green (RG) color defects while ones with medium acuity showed blue-yellow (BY) color defects. However, all three types of color defects were present in every time of assessment. Contrast sensitivity defect percentage was 93.3% in the acute phase, 73.3% at the 6-week point and 60% at the 3-month point. Overall, the most common defects were medium-high spatial frequency defects, followed by all-spatial frequency defects, medium spatial frequency defects and high spatial frequency defects. There was only one patient with low-medium spatial frequency defect at the acute phase and the 6-week visit. In the recovery period (6 weeks and 3 months after treatment), there were some patients with disturbance in color vision or contrast sensitivity although their decimal vision acuity measured 10/10.

Conclusion: Contrary to common clinical wisdom, optic neuritis is not characterized by selective RG defects. Its types can shift time over time. Contrast sensitivity defects are in a wide variety yet happen most around medium spatial frequency. Thus, color and contrast sensitivity defect types cannot be used for differential diagnosis of optic neuritis. In order to follow the patients's recovery process, ophthalmologists should not only assess vision acuity but also measure color vision and contrast sensitivity.

Keywords: optic neuritis, contrast sensitivity, color vision, Farnsworth test, Functional Acuity Contrast Test (FACT).

Note: The research has not finished yet so I only have data to the 3-month point at present.

Poster No.
3

Xin Wang

(Beijing Stomatological Hospital, P.R. China)

Title: Apply GBR technique in auto-transplantation cases

Abstract

Objective:

Auto-Transplantation is a new technique for the treatment of complicated crown-root fracture and residual crown and root. It can limit the shrinkage of gingival and alveola. Also, it can provide a delicate esthetic restoration for the patients.

But it also has some weak points as a treatment, and it is thus necessary to increase the effectiveness of osteoblast propagation. Through hard work with many passages about the treatments, we applied GBR technique in auto-transplantation for the first time. For the observation about the cases, we found no alveolar & gingival shrinkage.

Methods:

10 cases of appliance of GBR technique in auto-transplantation and complicated crown-root fracture were observed. There was almost no resorption of bone and gums. Also, the PDL could be reconstructed. 6 months later, the bone and PDL were repaired completely.

Here are the steps of the operation:

1. Taking a "before" X-ray picture
2. Local anesthesia flap extraction in the micro-damage area
3. Place the fracture line to the margin of gum level and reverse 180 º
4. Put the cologne membrane over the gap between the root alveolar
5. Fix the teeth to neighboring teeth and suture
6. 4-weeks later, take an X-ray and do the restoration
7. 24-weeks: Return Visit

Results:

- Better aesthetic restoration for the patients and complete repair of the alveolar PDL.
- No looseness and no gum resorption
- X-ray shows improved recovery of the alveolar

Discussion:

The case shows the reconstruction of the PDL and alveolar.
A better aesthetic restoration for the patients, especially for the complicated crown-root fracture, is possible.

Poster No. 4

Fariba Taba Jahan

(Marks Dental College, Bangladesh)

Title: Syndecan-1 expression in different stages of oral squamous cell carcinoma

Abstract

Objectives:

Oral squamous cell carcinoma (SCC) is one of the most common malignancies worldwide, but its exact pathogenesis is still unknown. Syndecan-1, a transmembrane heparan sulfate proteoglycan, modulates cell proliferation, adhesion, migration and angiogenesis. Malignant epithelial cells often down-regulate their own syndecan-1 production, and are capable of inducing aberrant syndecan-1 expression in stromal cells. The aim of this study was to evaluate the variations in syndecan-1 expression in different stages of oral SCC.

Study design:

A cross-sectional study.

Study setting and period:

From February 2011 to September 2011.

Participants:

120 histologically diagnosed oral squamous cell carcinoma patients were selected for the study.

Methods:

Surgical specimens containing normal or hyperplastic epithelium, epithelial dysplasia, carcinoma in situ and invasive SCC were examined for syndecan-1 by immunohistochemistry.

Poster No.
5

Li Min

(Tokyo Medical and Dental University)

Title: Characterization of human induced pluripotent stem cell (hiPSC)-derived cardiomyocytes (CMs)

Abstract

Purpose:

Drug-induced long QT syndrome is a common reason for withdrawal of late-stage clinical development products. Although the use of human cells is expected to improve prediction of drug safety, it is difficult to obtain satisfactory amounts of cardiac myocytes from healthy humans. In order to examine if human induced pluripotent stem (iPS) cells could be used for drug safety tests, cardiac myocytes were generated from human iPS cells and their properties were characterized using electrophysiological approaches.

Methods and Results:

Embryoid bodies (EBs) from human iPS cells (201B7) were formed in ultra-low attachment dishes. After about 20 days of differentiation, some EBs (5 %) began to beat spontaneously at 1.0 ±0.1 Hz (n=9). Single cells isolated from beating EBs also beat spontaneously at similar rates 0.91 ±0.07 Hz (n=9). Using patch clamp technique, diverse shapes of action potentials (APs) resembling sino-atrial nodal, atrial or ventricular cardiomyocytes were recorded. In a fraction of beating cells, If currents were recorded by voltage-clamp recording. 5 mM Cs+ dramatically inhibited If currents and moderately reduced beating rates. Atrial or ventricular like APs were elicited by current injection into quiescent cells where 0.2 mM Ba2+ depolarized resting membrane potential and prolonged AP duration, suggesting functional expression of IK1 channels.

Conclusion:

We have succeeded in obtaining human iPS cell-derived cardiomyoytes. These cells generated diverse shapes of APs, and exhibited If and IK1 current activities. These results might contribute to developments for more predictable pre-clinical cardiac drug safety tests.

Poster No. 6

Dordia Anindita Rotinsulu

(Bogor Agricultural University, Indonesia)

Title: The use of animals in stem cell research as a therapy of human cardiovascular diseases

Abstract

The use of laboratory animals has long been an essential part of biomedical research, including for stem cell research. Research in stem cell biology and regenerative medicine covers a broad spectrum of basic and translational studies, in which the use of animals has been and remains paramount. Animal-based research is at the center of both "proof-of-principle" experiments for cell-based interventions and the safety and efficacy tests required for approval of clinical trials. This poster provides the review of the current status of animal models for stem cells research as a therapy of cardiovascular diseases.

Animal models that are used in stem cells research as a therapy of cardiovascular diseases include rodents, canine, porcine, and primates. A few animal model studies have shown that mobilized haematopoietic stem cells after myocardial infarction can differentiate into cardiomyocytes. Improvement in cardiac function has been reported. Animal model studies also showed that transplanted endothelial progenitor cells improve cardiac function after myocardial infarction, lead to better preservation of capillary density, and incorporate into sites of neovascularisation.

One of the most fundamental future challenges is to determine how appropriate animal models are to the human condition they are designed to represent. The comparatively short life span and fast growth of some animals makes it difficult to make claims about the longevity and effectiveness for humans of cell based therapies tested in rodents alone. Therefore, continuing extensive animal work to prepare for human application should be done in the future.

Keywords: stem cells, animal models, cardiovascular diseases

Poster No.
7

Tien Kim Quynh Tran

(HCMC Society of Dental Implantology, Vietnam)

Title: Role of the interactions between gingival fibroblasts and endothelia cells in gingival regeneration

Abstract

Introduction: Clinical observations and research show that regeneration of gingival is faster than that of cicatrization of skin. However, the mechanisms that originate this difference are not yet established clearly. This research aims to study the interactions between human gingival fibroblasts and endothelial cells and the consequences of interactions of angiogenesis in the regeneration.

Materials and Methods: Gingival fibroblast obtained from the blood of healthy people were isolated during the extraction of third molars and cultivated in EGM environment with or without artificial lesions. This region is used for cultivating HUVECs (human umbilical vein endothelial cells) on Matrigel.

Angiogenesis capabilities were evaluated by measurement of the surrounding structure of tubular that corresponded to the formation of capillaries in vivo and with the help of neutral antibodies (anti FGF-2 and VEGF).

The expression and secretion of FGF-2 (basic fibroblast growth factor) and VEGF (vascular endothelial growth factor) were studied by immunohistology and ELISA (enzyme-linked immune sorbent assay).

Results: We observed a significant augmentation of perimeter tubule with environment incubated with the intact and lesser fibroblast. The perimeter obtained with the lesser fibroblast are bigger than that obtain with intact fibroblast. ($p<0.05$)

Conclusion: Our results suggests that human gingival fibroblasts secrete FGF-2 and VEGF, factors that stimulate angiogenesis, in order promote regeneration in the gingival lesions. This secretion can explicate, at least to some extent, the fast regeneration of gingival lesions.

Poster No. 8

Manish Subedi

(Subidha Hospital Private Limited, Nepal)

Title: Development and validation of bioanalytical methods of enalapril maleate

Abstract

Enalapril maleate is an angiotensin converting enzyme inhibitors developed for the treatment of CHF, angina, renovascular hypertension, diabetic nephropathy and post MI cases. For the assay of enalapril maleate in human plasma, a new reversed-phase high performance liquid chromatography method has been developed. The instrumentation consisted of RP-HPLC of Shimadzu, solvent delivery system LC 20 AD, autosampler 20 AC, UV visible detector and the analytical column Luna 5 μmC18 (2)100A of size 250X4.6 mm. After the development of bioanalytical method the final mobile phase was composed of acetonitrile: buffer (50 mM, pH 3.5), in the ratio of 25:75, the final pH of the mobile phase was 4.5 adjusted with 10% v/v orthophosphoric acid. The equipment settings were flow rate 1.5 ml/min, oven temperature 37 °C and wavelength 239 nm. Under these conditions the retention time of propanolol hydrochloride (IS) 5 ng/ml and enalapril maleate was 3.0 and 5.8 minutes respectively. The method was validated for accuracy, recovery, precision, and linearity within a day and between day analysis and calibration curve. The LOQ was 2 ng/ml and the %RSD and accuracy deviation were 6.75 and 9% at this concentration. The LOD was found to be 1.5 ng/ml. The calibration curve was found to be linear at concentrations 4-20 ng/ml with coefficient of regression (r) to be 0.9998 and mean %RSD of 13.0

Keywords: angina, hypertension, diabetic nephropathy, RP-HPLC, bioanlytical method, validation, internal standard, enalapril maleate, propanolol hydrochloride

Poster No. 9

Od Bayarsaikhan

(Health Sciences University of Mongolia, Mongolia)

Title: Determination of folate and vitamin B12 in human serum and complete blood count parameters in women of child-bearing age in Mongolia

Abstract

Background: We were prompted to conduct the present pilot study in order to increase the public and professional awareness of the protective role of folic acid against NCL/P in Mongolia, and because of the necessity of preventive health promotion to decrease occurrence and recurrence of congenital anomalies as well as the absence of current clinical diagnostic methods in determining the level of folate in human serum of women of childbearing age.

Purpose: To determine folate and vitamin B12 levels in human serum and complete blood count parameters in women of child-bearing age.

Methods: 360 questionnaires were sent to three medical schools of Ulaanbaatar within the period of 2009-2010. Participants were female students between 17 and 28 years of age. Based on the questionnaires, 60 volunteers free of habitual smoking, alcohol drinking, anti-folate drugs, supplements, pregnancy, HIV, HbsAg, and Anti HCV were selected for the final laboratory blood tests. Fasting specimens of venous blood collected to analyze biochemical (GOT, GPT) and complete blood count (CBCs) were taken. The folic acid and cyanocobalamin were determined by Folate III CalSet I,II, Precicontrol Anemia, Vitamin B12 CalSet I, II, precicontrol anemia diagnostic kit, Germany.

Results: Biochemical and complete blood count showed: red blood cell (RBC) concentration was 4.59± 0.25 (M/μL), hemoglobin (Hgb) was 13.6± 0.89 (g/dL), mean corpuscular volume (MCV) was 84.05±0.25 (fL), hematocrit (HCT) was 38.5± 2.22 (%). The human serum folate was 7.78±2.71 ng/ml, serum B12 was 710.81±233.32 pg/ml. Comparison of folate and vitamin B12 in human serum with complete blood count parameters of childbearing-age women revealed significant statistical differences ($p < 0.05$).

Keywords: folic acid, cyanocobalamin, folic acid deficiency, hematology, cleft lip and palate

Poster No.
10

Pham Anh Vu Thuy

(Tokyo Medical and Dental University)

Title: Factors affecting oral malodor in periodontitis and gingivitis patients

Abstract

The aim of this study was to examine the association between oral health status, the presence of BANA-positive bacteria and oral malodor in 137 periodontitis and 80 gingivitis patients. Oral malodor was measured by organoleptic test and Oral Chroma. Oral examination including the assessment of decayed teeth, periodontal status and tongue coating was conducted. The presence of N-benzoyl-DL-arginie-2-napthylamide (BANA) positive bacteria in subgingiva, tongue coating and saliva was evaluated by BANA test. The Pearson correlation was used to detect the association between oral health status, BANA test parameters and oral malodor. Stepwise multiple regression analysis was employed to assess the predictors of oral malodor. In the periodontitis group, there were significant correlations of oral malodor with decayed teeth, periodontal parameters and tongue coating. Among BANA test parameters, the highest correlation of oral malodor was found with BANA-Subgingiva, followed by BANA-Tongue coating and BANA-Saliva ($p<0.01$). The predictors of oral malodor were dental plaque and BANA-Subgingiva. In the gingivitis group, on the other hand, the significant correlations of oral malodor were found with plaque index, bleeding on probing and tongue coating. Among BANA test parameters, the highest correlation of oral malodor was found with BANA-Tongue coating, followed by BANA-Saliva and BANA-Subgingiva ($p<0.01$). The predictors of oral malodor were dental plaque, bleeding on probing, tongue coating, BANA-Tongue coating and BANA-Saliva. This study suggested that dental plaque, bleeding on probing, tongue coating and BANA-positive bacteria contributed to oral malodor, but with different degrees in the periodontitis and gingivitis patients.

Poster No. 11

Tan Sze Jun

(University Sains Malaysia)

Title: Immunologic properties and osteogenic potential of undifferentiated stem cells from human exfoliated deciduous teeth (SHED)

Abstract

Stem cells from human exfoliated deciduous teeth (SHED) are highly proliferative, clonogenic cells capable of differentiating into osteoblasts and inducing bone formation. It is a potential alternative for stem cell bone regeneration therapy. However, stem cell therapy carries risk of immune rejection mediated by inflammatory cytokines of human defense system. This preliminary research studies the interaction between SHED and the immune system by determining the inflammatory cytokines profile and osteogenic potential of SHED. Human fetal osteoblasts (hFOb) cell line and isolated SHED were cultured and total RNA was extracted, followed by reverse transcription cDNA synthesis. Semi-quantitative reverse transcription PCR and Multiplex PCR was performed to detect expression levels of OPG/RANKL and TNF-, IL-1β, IL-6, IL-8 and TGF-β in both cell types. Analysis showed that SHED expressed significantly lower amounts of IL-1β, IL-6, and IL-8 compared to hFOB. IL-1β is a potent bone-resorbing factor, while IL-6 and IL-8 induce osteoclastogenesis and osteolysis respectively. SHED did not express TNF-α which stimulates osteoclastic activity. SHED demonstrated high OPG/RANKL ratio, in contrast with low OPG/RANKL ratio in marrow stem cells described in previous studies. Our findings suggest that SHED may have improved immunomodulatory profile in terms of promoting relatively lower inflammatory reaction during transplant and enhancing bone regeneration. In conclusion, SHED is an ideal source of osteoblasts to be used in bone regeneration therapy. Further studies on the immunomodulatory properties of SHED-derived osteoblasts are necessary to enable stem cell therapy in immunocompetent hosts.

Poster No. 12

Asmatullah Khan

(Helper's Eye Hospital, Pakistan)

Title: The ATP-Binding cassette transporter gene, VMD2 gene and macular diseases: A combined wet-lab and insilico analysis for future work-up

Abstract

The efforts of the Human Genome Project are providing new tools and opportunities for medical advances. The identification of new genes is increasing our understanding not only of single-gene disorders, but also of complex disease processes such as cardiovascular diseases, diabetes, cancer, Alzheimer's disease and infection. Further, the identification of mutations in disease genes could lead to improved clinical diagnostic interventions, make prognostic projections, and enable other pre-symptomatic or carrier testing of family members.

Genomic DNA maps and sequences are a means to an end. The end is to use this information to understand biological phenomena. At the heart of most applications of mapping and sequencing is the search for altered DNA sequences. These may be sequences involved in an interesting phenotypic trait, an inherited disease, or a non-inherited genetic disease due to a DNA change in somatic cells. In case of complex diseases the use of intermediate phenotypes has helped in understanding new pathogenetic pathways.

Our strategy could be based upon detecting mutations in ABCR gene by using PCR-SSCP- sequencing system. After DNA extraction, promoter regions and the intron-exon boundaries of ABCR gene will be amplified. SSCP will be carried out as described in the literature. DNA samples found mutated on SSCP will be subjected for DNA sequencing. This study will help us decipher the genetic architecture of AMD in Pakistani population. This study will be the first genetic study done in the field of ophthalmology in Pakistan. It will open new avenues for future genetic studies in this field.

Poster No.
13

Weinan Sun

(China Medical University, P.R. China)

Title: The function of TRPV4

Abstract

Transient receptor potential vanilloid 4 (TRPV4), also known as OTRPC4, VRL-2, VR-OAC, and TRP12, is a member of the vanilloid subfamily of transient receptor potential channels (TRP) initially identified as a channel activated by hypotonicity-induced cell swelling. TRPV4 channels are the thermosensitive, polymodal, non-selective cation channels that are modestly permeable to ca2+ with a permeability ratio Pca/PNa between 1 to 10.

In general, all mammalian TRPV4 homologues are similar in length and share a high degree of sequence identity (95% - 98%). The human TRPV4 gene is localized on chromosome 12q23-q24.1 and TRPV4 protein consists of 871 amino acids with at least three ankyrin repeats in NH2.

Expression of TRPV4 protein has been demonstrated in a broad range of tissues, including lung, spleen, kidney, testis, fat, brain, cochlea, skin, smooth muscle, liver, and vascular endothelium. So its function is comprehensive.

Poster No. 14

Didi Wahyudi Syukur

(DentCo Dental Clinic, Indonesia)

Title: Violation of United Nations Convention on Biological Diversity in the mechanism of Global Influenza Surveillance Network-World Health Organization In Indonesia

Abstract

Indonesia has many microbial resources, including bacteria and viruses that are from the many diseases that exist in Indonesia as it is a tropical country. This phenomenon has attracted international researchers to do some research directly by staying in Indonesia or indirectly by taking specimens to their home countries. As a result, many specimens have been sent from Indonesia to other countries, not only for scientific reasons, but also for commercial benefit. For example, there was an international researcher who registered his research finding as purely his own achievement after using an original specimen from Indonesia.

This research took a case of exploitation of H5N1 virus from Indonesia which was done by the World Health Organization (WHO) through the mechanism of the Global Influenza Surveillance Network (GISN). The case was then analyzed by using the United Nations Convention on Biological Diversity (UNCBD). This analytical descriptive research with a juridical normative approach used a literature review and interviews with experts as a method to collect the data of research.

The result showed that there was a violation of UNCBD by GISN-WHO: (1) There was no Material Transfer Agreement (MTA) used when sending specimens from Indonesia to WHO, (2) Commercialization of the vaccine by WHO as it sold the vaccine without any compensation for the affected country, and (3) There was no fair and equitable sharing of the benefits between the donor country and WHO.

Poster No.
15

Gamaralalage Amodini Rajakaruna

(Tokyo Medical and Dental University)

Title: Localization of porphyromonas gingivalis and tannerella forsythia in diseased gingival and subgingingival granulation tissues using novel monoclonal antibodies

Abstract

Objectives: Recent publications have reported an association between periodontopathic bacteria and peripheral and central vascular diseases. However none of these studies show clear histological evidence with detection of bacteria in diseased gingiva or in vascular sites. Therefore our objectives were to develop monoclonal antibodies (mAbs) specific for P. gingivalis and T. forsythia and to locate these bacteria in the gingival tissues.

Methods: mAbs were prepared in the conventional method and specificity and cross reactivity were confirmed with ELISA and immunohistochemistry (IHC) using rat liver infected with 36 species of bacteria commonly present in human body. IHC was done to locate these bacteria in gingival/subgingival granulation tissues collected from 102 patients. The results were confirmed with real-time PCR. Immuno-fluorescence double staining was done to detect intracellular positivity.

Results: Both mAbs gave positive reactions only with respective bacteria infected rat liver sections. Out of 102 cases P. gingivalis was located in 53 (65%) and T. forsythia in 66 (80%) extracellularly in IHC. P. gingivalis was detected in 59 (72%) and T. forsythia in 76 (93%) in real time PCR. The correlation between the density of bacteria lgenomes and their respective IHC grading gave values < 0.001 for both the species.

Conclusion: The produced mAbs could be used as specific and reliable tools to locate P. gingivalis and T. forsythia in human tissue sections that are formalin fixed and paraffin embedded. Also these bacteria may exist intracellularly in squamous epithelial cells of diseased gingival tissues in patients with chronic periodontitis and aggressive periodontitis.

Poster No. 16

Wattage Kathya Leoni Perera

(University of Peradeniya, Sri Lanka)

Title: Periodontal healing response in a group of Sri Lankan smokers following a phase of non-surgical periodontal therapy

Abstract

Introduction: The fact that tobacco smoking is a strongly predicted risk factor for development and progression of periodontal disease is well established. Studies with adjusted plaque levels among smokers and non-smokers report greater probing depths, clinical attachment loss and bone loss in smokers when compared to non-smokers. However smokers benefit from periodontal therapy although clinical improvements have been found to be less than those for non-smokers.

Aims and objectives: This study was carried out to compare the periodontal treatment response in smokers compared to a group of non-smokers.

Materials and methods: The study sample consisted of 200 male patients between ages 30-60 years, who underwent periodontal treatment at the Division of Periodontology, Teaching Dental Hospital in Faculty of Dental Sciences, University of Peradeniya, Sri Lanka. The study was ethically approved and the sample included an equal number of smokers (test group) and non-smokers (control group), who were carefully selected according to the selection criteria of the study and they were followed-up to carry out a standard phase of non-surgical periodontal treatment. The smoking status of the subjects was elicited by means of a standardized, pre-tested questionnaire and all patients underwent a standard phase of non-surgical periodontal treatment, having subjected them to a thorough periodontal assessment, diagnosis and treatment planning. Clinical periodontal parameters were compared among the test and control groups before and after periodontal treatment. Periodontal treatment response was evaluated by comparing pre- and post-treatment clinical parameters.

Results: When the pre-treatment and post-treatment periodontal parameters were compared between the two groups, there was a highly significant improvement in non-smokers than smokers with regard to plaque levels, probing pocket depths (PPD) of less than 9mm, grade I tooth mobility and experiencing tooth loss (P=0.000, Mann-Whitney U test). However, the rest of the parameters (PPD of greater than 9mm, grade II & III mobility and furcation involvement) did not show statistically significant differences between the two groups after periodontal treatment.

Conclusion: Smokers showed an overall poor periodontal healing response following a standard phase of non-surgical periodontal treatment compared to non-smokers. This was in spite of smokers having better plaque control than non-smokers at the time of their presentation for treatment. This may implicate a lowered potential in periodontal regeneration in smokers than non-smokers, which could be well attributed to the hindered immune responses in tobacco smokers affecting periodontal healing responses.

Poster No.
17

Buyan-Ochir Orgil

(Health Sciences University of Mongolia, Mongolia)

Title: Screening of Heart Diseases in Children in Rural Areas of Mongolia

Abstract

Background: Diagnosis and treatment of pediatric heart diseases in developing countries is a major challenge. Accurate data for the prevalence of heart diseases in the pediatric population in rural areas of Mongolia were unavailable due to the nomadic style of life of the people in the region.

Objective: The purpose of our project was to assess the prevalence of heart diseases in a rural pediatric population in Mongolia.

Methods: Echocardiography screening for heart diseases was performed in 7 rural prefectures including Nalaikh, Baganuur, Bulgan, Hovsgol, Orkhon, and Selenge aimags from 2003 to 2007. Children of age from 0 to 18 years old were included in this study.

Results: 635 individuals were involved in screening. The highest number of patients was in age group from 10 to 15 years old (42.6%). The median age of all patients with congenital heart diseases (CHD) was 9 years 2 months (IQR, 4 to 18 years). Ventricular septal defect, atrial septal defect, and patent ductus arteriosus were the most common lesions. The average prevalence of CHD was 0.59 children per 1000 children.

Conclusion: We emphasize the importance of health screening in children in rural areas in Mongolia. The significantly low level of the cardiac diseases in Mongolia as compared to Western countries is due to early death, especially in newborn period. These deaths occur due to poor cardiovascular care and the low chance of early surgical treatment for children in the rural population.

Poster No. 18

Ripa Jamal

(Dhaka University, Bangladesh)

Title: A study of iodine nutrition status in consumed household salt and urinary iodine

Abstract

Background: In most previous surveys or studies, iodine nutrition status has been assessed on school-age children and also on men and women of childbearing age. But no study has been done specifically on adolescent girls aged 12-18 years, a large percentage of whom get married and enter into pregnancy, thus perpetuating malnutrition through generations.

Objective: The study was carried out to assess the iodine nutrition status of college girls aged 16-18 years. This was done by determining the level of salt iodine, which they were consuming in their households, and also their urinary iodine excretion (UIE), which is an indicator of biochemical iodine deficiency.

Methodology: In total, 459 students, randomly selected from 3 women's colleges, were surveyed. One day before the survey, the students were provided with small polythene packets to bring salt from their homes. Next day, salt and a random urine sample were collected from each student. The salt and urine samples were analyzed in the laboratory of the Institute of Nutrition and Food Science (ICCIDD). Salt iodine was determined by the titrimetric method, and urinary iodine was estimated by the ammonium per sulfate digestion on micro plate (APDM) method.

Results: The median urinary iodine (MUI) level was 269 mcg/L, and distribution analysis showed that 15.3% of the students had biochemical iodine deficiency (urinary iodine <100 mcg/L). The highest percentage (16.2%) of deficiency was observed among girls aged 16 years. The mean iodine value of salts consumed in the household level was 49 ppm (as per law, 15 ppm iodine should be present at household level). However, some salt samples contained no iodine. Only 8.1% of the salt samples contained iodine in the range of 10 to 20 ppm. More than 34% of the salt samples contained iodine greater than the standard factory level (45 to 50 ppm). Iodine in salt was reflected by a urinary iodine excretion. The average level of iodine was found 3 times higher than it should be, which is reflected in the MUI.

Conclusion: The findings suggest that a large percentage of the study population was not consuming the standard level of iodine from their household salt intake. Salt factories should thus be more careful and sincere about mixing iodine properly in household salts. Higher salt iodine corresponds to higher urinary iodine.

Acknowledgements: The study was supported by the International Council for Control of Iodine Deficiency Disorders, Bangladesh, Institute of Nutrition and Food Science, University of Dhaka, and Department of Biochemistry and Molecular Biology, University of Dhaka, Dhaka.

Poster No.
19

Moe Htet

(Moe Dental Clinic, Myanmar)

Title: Variation among dentists on shade selection

Abstract

Introduction: Because traditional shade matching is subjective and dependent on illumination, the surrounding environment and the receiver's eyes, consistency is difficult to achieve. Considerable variations could exist among dentists, and some are unable to duplicate even their own shades selection from one time to another. This indicates that the shade matching systems currently employed are unreliable and not consistent for all the dentists and the dental technicians. The purpose of this investigation is to determine inter-examiner variation on tooth shade selection among dental practitioners, and the consistency of two commercially available dental shade guides with different shade organization.

Materials and Methods: Five dental students, two males and three females, who have fair complexion and good dental health status with Class I normal occlusion and tooth alignment, were selected. Shades of their anterior teeth were measured by twenty dentists who have been practicing as general dental practitioners for at least 5 years. Shade measurement was carried out at a standard daylight, using two commercial shade guides, Ivoclar Chromoscop and Vitapan 3D-Master.

Results: For both shade guides, higher agreement between the inter-examiners was found in the selection of base shade, either hue or value. Both shade guides are more consistent in selection of shade for teeth with brighter or lighter color than that with dark color (low value or high chroma).

Clinical significance: The use of a shade tab is a subjective approach that still remains the most common practice, although it contains uncertainties because of individual variations in the perception of color. Until an objective approach or digital type shade guide is widely available for dental practitioners, the use of multiple conventional shade guides and the obtaining of second or third opinions could be helpful to record the shade of teeth to the nearest value.

Poster No.
20

Ilnaz Hariri

(Tokyo Medical and Dental University)

Title: Effects of structural orientation on local refractive indices of human enamel and dentin by optical coherence tomography

Abstract

Optical coherence tomography (OCT) is a promising tool for the study of dental hard tissues. Human enamel is composed almost entirely of arranged arrays and densely packed hydroxyapatitie (HAp) crystals, while the underlying dentin can be described as a complex structure of organic components, inorganic components incorporated into HAp crystals, and water dentinal tubules as the main structural components. The aim of this study was to use a swept source (SS-) OCT system with a hand-held probe (Panasonic Health Care, Japan) at the laser center wavelength 1310 nm to evaluate refractive index (n) of human enamel and dentin obtained in relationship to structural orientation of enamel prisms and dentinal tubules. Optical path length and real thickness were measured using SS-OCT images and used to calculate the n. It was shown that the refractive index of human enamel was not significantly affected by the orientation of enamel prisms (n = 1.63). However, in dentin, different orientations of dentinal tubules led to different values (n = 1.55, range: 1.49~1.60). The variations among different biological samples and different regions were more remarkable for dentin. The results of this study may contribute to a better understanding of the interaction of the tissue with light and provide useful information for the accurate measurement of enamel and dentin thickness by OCT.