March 25-26th, 2016

Sugiura Community Care Research Center, Kyoto University

2nd International Symposium on Regenerative Rehabilitation in Kyoto

報告書

Human Health Sciences, Graduate School of Medicine, Kyoto University
Center for iPS Cell Research and Application, Kyoto University
Kyoto University Hospital.

巻頭言 Foreword

京都大学医学研究科人間健康科学系専攻は、iPS細胞研究所および医学部附属病院と合同で第2回国際再生リハビリテーションシンポジウムin京都を3月25日(金)・26日(土)に開催しました。本国際シンポジウムには17名の国外参加者を含む計75名が参加しました(図)。

本国際シンポジウムの目的は、研究者、医師、リハビリテーション専門職が一堂に会し、再生医療を安全で効果的に実施するためのリハビリテーションについて議論を深めようとするものです。

シンポジウム1日目は、伊藤明良 京都大学医学研究科人間健康科学系専攻助教のオープニングリマークスに続き、中村雅也 慶應義塾大学医学部教授の基調講演、ヘザー・ロス ブレノー大学健康科学カレッジ准教授およびランディー・トロンボワー エモリー大学医学部助教の海外招待講演、さらに櫻井英俊 iPS細胞研究所准教授、田代祥一 慶應義塾大学医学部助教、南角学 京都大学医学部附属病院リハビリテーション部技師長による特別講演、最後にパネルディスカッションがありました。2日目には、本学における再生医療研究施設の見学(iPS細胞研究所、医学部附属病院先端医療機器開発・臨床研究センター、医学部附属病院リハビリテーション部)およびトロンボワー助教によるウェアラブル技術を用いたリハビリテーションのデモンストレーションを行いました。この2日間、日本ではまだあまり馴染みの少ない移植再生医療リハビリテーション分野という新しいテーマについて活発な議論が交わされ、シンポジウムは盛会のうちに終了しました。

京都大学医学研究科
人間健康科学系専攻
教授　黒木 裕士

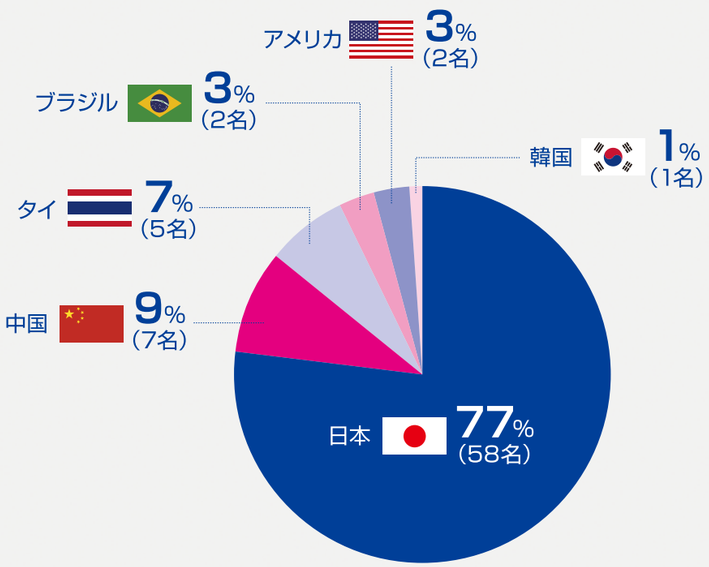
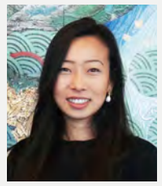


図. 国別参加者数

シンポジウムに参加して Travel award

Carolina Mie Kawagosi Onodera

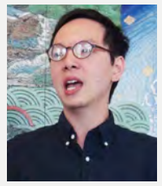
University of Campinas – UNICAMP, Brazil



シンポジウムに参加できて光栄です。この場で多くの事を学べました。リハビリテーションをどう活用するかについて学び、高度な研究に触れることができて非常に光栄です。

Kitsanapong Reaksudsan

Division of infection and immunity,
Walter and Eliza hall institute of medical research,
University of Melbourne, Australia



再生医療は、加齢や疾患、先天異常などで欠けた能力を、機能的な生きた細胞で修復もしくは代替する治療体系だと思います。それに対して、リハビリテーションはその治療体系を使って実用的な機能を獲得し、生活の質を高めることだと思います。このシンポジウムを通じて、リハビリテーションを統合させることで、再生医療のプロセスを加速できることが分かりました。しかし、まだやるべきことがあることもわかりました。リハビリテーションの効果を最大限に引き出すにはどうするか、評価法はどうするか、また、症状の改善だけでなく社会復帰や友達・家族・恋人との生活に本当に復帰できたかをどう評価するかなど、興味深い課題がたくさんあると思います。

Sasimol Udomruk

Department of Biochemistry, Faculty of Medicine,
Chiang Mai University, Thailand

まず、シンポジウムの皆さんに感謝します。日本へ来たのはこれが初めてです。私の専門は神経の変性です。私は神経変性を抑制することが大切で、それが出来れば神経の再生を促進できると考えていました。しかし、再生そのものも大切です。このシンポジウムを通じて、再生医療とリハビリテーションの統合について多くを学ぶことが出来ました。大変良い経験になりました。ありがとうございました。

Kanokwan Kulprachakarn

Faculty of Pharmacy, Payap University, Thailand

まず、このような素晴らしい機会を与えて下さったシンポジウムの皆さんに、厚く感謝したいと思います。京都へ来る前は再生リハビリテーションという単語も良く分からなかったのですが、ここでiPS細胞や再生医療とリハビリテーションの統合について理解することが出来ました。お招きいただき、ありがとうございました。

Orawan Wanachewin

Department of Biochemistry, Faculty of Medicine,
Chiang Mai University, Thailand

まずは、日本へ招待して頂き、再生医療とリハビリテーションについて学ぶ機会を与えて下さったコミッティーの皆さまに感謝します。リハビリテーションは再生医療と統合的に適用され、患者さんを共に治療する大きな可能性があると信じています。

Supranee Upanan

Department of Biochemistry, Faculty of Medicine,
Chiang Mai University, Thailand

まず、この機会を与えて下さったシンポジウムの皆さんと日本の皆さんに感謝いたします。日本は初めてで、得難い経験をさせて頂きました。シンポジウムでは、最先端の知見に非常に感銘を受けました。私の知らなかったことばかりで、また、タイにもこういったものはありません。研究の技術や機器類についても多くを学びました。日本は素晴らしいです。ありがとうございました。

プログラム | Program

Friday March 25, 2016

1:00 PM ~ 1:10
Room: Sugiura Hall

OPENING REMARKS
Akira Ito, PT, PhD
Department of Orthopaedic Surgery,
Kyoto University, Japan

1:10 PM ~ 2:10
Room: Sugiura Hall

KEYNOTE LECTURE
Regenerative medicine for spinal cord injury
Masaya Nakamura, MD, PhD
Department of Orthopaedic Surgery,
Keio University, Japan

2:10 PM ~ 2:15

BREAK

2:15 PM ~ 2:45
Room: Sugiura Hall

INVITED LECTURE 1
Intermittent hypoxia as a priming modality for CNS stem cells
Heather H. Ross, MPT, PhD
Department of Physical Therapy,
Brenau University, USA

2:45 PM ~ 3:15
Room: Sugiura Hall

INVITED LECTURE 2
Intermittent hypoxia as a plasticity-promoting primer of motor recovery after spinal cord injury
Randy D. Trumbower, MPT, PhD
Department of Rehabilitation Medicine,
Emory University, USA

3:15 PM ~ 3:25

BREAK

3:25 PM ~ 3:55
Room: Sugiura Hall

SPECIAL LECTURE 1
Cell therapy for muscular dystrophy by engraftable muscle stem cell derived from human iPSCs
Hidetoshi Sakurai, MD, PhD
Center for iPS Cell Research and Application, Kyoto University

3:55 PM ~ 4:25
Room: Foyer

POSTER SESSION & COFFEE BREAK

4:25 PM ~ 4:55
Room: Sugiura Hall

SPECIAL LECTURE 2
Combination therapy with cell transplantation and rehabilitation for chronic spinal cord injury
Syoichi Tashiro, MD, PhD
Department of Rehabilitation Medicine,
Keio University, Japan

4:55 PM ~ 5:15
Room: Sugiura Hall

SPECIAL LECTURE 3
Rehabilitation after cell transplantation in Kyoto University Hospital
Manabu Nankaku, PT, PhD
Kyoto University Hospital, Japan

5:15 PM ~ 5:55
Room: Sugiura Hall

DISCUSSION

6:00 PM ~ 7:00
Room: Foyer

RECEPTION

Saturday March 26, 2016

10:00 AM ~ 11:30
Room: Sugiura Hall

TOUR FOR REGENERATIVE MEDICINE & REHABILITATION FACILITIES OF KYOTO UNIVERSITY ***Need reservation**

11:30 AM ~ 12:10
Kyoto University Hospital

SEMINAR ON REHABILITATION OF SPINAL CORD INJURY
Instructor **Randy D. Trumbower, MPT, PhD**
Department of Rehabilitation Medicine,
Emory University, USA

12:10 PM ~ 12:30

CLOSING REMARKS

Keynote Lecture

Regenerative medicine for spinal cord injury using iPS cells

Masaya Nakamura MD, PhD
Professor, Department of Orthopaedic surgery, Keio University.

Spinal cord injuries (SCI) result in devastating loss of function, because spinal cord of human beings never regenerates after injury. People believed in this dogma for a long time. There is an emerging hope for regeneration-based therapy of the damaged spinal cord due to the progress of neuroscience and regenerative medicine including stem cell biology. Stimulated by the 2012 Nobel Prize in Physiology or Medicine awarded for Shinya Yamanaka and Sir John Gurdon, there is an increasing interest in the iPS cells and reprogramming technologies in medical science. While iPS cells are expected to open new era providing enormous opportunities in the biomedical sciences in terms of cell therapies for regenerative medicine, safety-related concerns for iPS cell-based cell therapy should be resolved prior to the clinical application of iPS cells. Especially, some previous reports indicated risk factors for the use of iPSCs, such as genetic and epigenetic abnormalities that could take place during reprogramming or maintenance in subsequent cell culture. Of particular relevance is the potential tumorigenicity and immunogenicity associated with iPSC-based cell therapy. In this symposium, I would like to summarize previous efforts in the field as well as the current status of iPSC-based cell therapy for repair of the damaged central nervous system (CNS), with a special emphasis on spinal cord injury (SCI).

Invited Lecture 1

Intermittent hypoxia as a priming modality for CNS stem cells

Heather H. Ross MPT, PhD
Associate Professor, Department of Physical Therapy, Brenau University, College of Health Sciences.

Heather Ross is an Associate Professor in the Department of Physical Therapy at the Brenau University College of Health Sciences. Her research interests are centered on the combinatorial approach of neural stem/progenitor cell therapies and rehabilitation strategies following neural insult. Specifically, Dr. Ross is studying whether progenitor cell transplant coupled with cell- and systemic-based modulation, including rehabilitation approaches, can synergize to optimally promote recovery following neural injury such as spinal cord injury and stroke. The work that will be presented will outline the rationale for the study of stem cells with regard to rehabilitation. The data presented will first focus on proof of concept experiments to determine whether systemic administration of intermittent hypoxia impacts stem cell biology at the tissue level. Pilot work on stem cell transplant and impact on respiratory recovery will be followed by preliminary findings on the impact of intermittent hypoxia on stem cell engraftment and functional recovery following neural insult.

Invited Lecture 2

Intermittent hypoxia as a plasticity-promoting primer of motor recovery after spinal cord injury

Randy D. Trumbower MPT, PhD
Director of Research, Department of Rehabilitation Medicine, School of Medicine, Emory University.

Spinal cord injury (SCI) disrupts connections between the brain and spinal cord, causing devastating loss of mobility and independence. Most injuries are incomplete, leaving intact at least some neural pathways to motor neurons that control movement. Although spontaneous plasticity in these spared pathways underlies some motor recovery, the extent of recovery is slow, variable and frustratingly limited. Thus, there is a critical need for new therapies that promote neuroplasticity and subsequently improve motor recovery in persons with SCI. One promising strategy is to induce additional spinal plasticity via repetitive exposures to modest bouts of low oxygen (repetitive acute intermittent hypoxia, rAIH). We recently demonstrated that rAIH, alone or in combination with walking training, stimulates motor recovery in persons with chronic, incomplete SCI. The fundamental hypothesis guiding this proposal is that rAIH elicits neuroplasticity, thereby facilitating motor recovery in persons with chronic, incomplete SCI. Detailed mechanistic studies of AIH-induced spinal respiratory and non-respiratory motor plasticity in rats provide a conceptual framework to advance our understanding and optimize functional benefits of rAIH in humans with SCI. The goal of this talk is to present a series of translational studies aimed at uncovering possible mechanisms of rAIH-induced motor plasticity and recovery after spinal cord injury.

Special Lecture 1

Cell therapy for muscular dystrophy by engraftable muscle stem cell derived from human iPSCs

Hidetoshi Sakurai MD, PhD
Associate professor, Center for iPS Cell Research and Application (CiRA), Kyoto University.

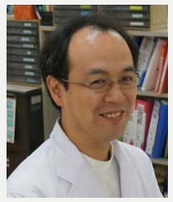
Cell therapy is one of desired method for treating intractable muscular diseases, such as Duchenne muscular dystrophy (DMD). Skeletal muscle contains a stem cell, called satellite cell, which has remarkable muscle regeneration potential and is considered as a good source of cell therapy. However, the clinical trials of cell therapy using adult satellite cells have never been succeeded mainly due to the difficulty of expansion of satellite cells with maintaining their regeneration potentials. Instead of adult satellite cells, generating satellite cells from induced pluripotent stem cells (iPSCs) would have advantage for application of cell therapy, because of their unlimited proliferation potentials. Here, we demonstrated the effective stepwise differentiation method from human iPSCs to engraftable muscle stem cells which can be isolated as Myf5 positive cells. To assess the regeneration potential, we transplanted the Myf5+ cells into immunodeficient DMD-model mice. The Myf5+ cells could be engrafted in more than one hundred of host myofibers and regenerate the diseased muscles with producing dystrophin. Moreover, we confirmed the functional recovery of cell transplanted DMD gastrocnemius by the assessment of the planterflex torque with electric stimulation. Taken together, we demonstrate that the transplantation of the human iPSC-derived muscle stem cells with step-wise differentiation can be effective for DMD with amelioration of muscle function. Our results facilitate to establish the cell therapy of muscular diseases using iPS cell-derived muscle stem cell.

Special Lecture 2

Combination therapy with cell transplantation and rehabilitation for chronic spinal cord injury

Syoichi Tashiro MD, PhD
Assistant professor, Department of Rehabilitation Medicine, Keio University.

Despite its remarkable effect on acute spinal cord injury (SCI), most of previous studies regarding neural stem/progenitor cell (NS/PC) transplantation therapy concluded only subclinical recovery is induced in chronic SCI. This is the major barrier for the realization of clinical application of cell-transplantation therapy for majority of SCI patients with chronic SCI. Although the potential importance of combination therapies involving cell transplantation and rehabilitation is widely recognized, there have been very few studies to date, all of which were limited in the acute and the sub-acute phase SCI. Here, we compared the therapeutic effects of each therapy using severe thoracic contusive SCI model mice separated into 4 groups: 1) combined; 2) transplantation; 3) training; and 4) control. NS/PCs were transplanted into lesion-epicenter at 49 days post injury (DPI). Partial body-weight supported bipedal-gait TMT was performed for two independent periods following different strategies: pre-training for all of SCI mice at 42–48 DPI, and intervention-training for mice in the groups with training at 52–105 DPI. Locomotor function was significantly improved in combined therapy group than the control group. While spinal conductivity and central pattern generator activity were improved by NS/PC transplantation, appropriate inhibitory motor control was improved by TMT respectively. Interestingly, neuronal differentiation of transplanted cells and maturation of central pattern generator were promoted synergistically in the combined therapy group in addition to independent effects observed in each single therapy. Combination therapy with NS/PC transplantation and TMT for chronic SCI induced significant functional recovery based on not only additive but also synergistical therapeutic mechanisms of each therapy.



Special Lecture 3

Rehabilitation after cell transplantation in Kyoto University Hospital

Manabu Nankaku PT, PhD
Chief physical therapist, Kyoto University Hospital.

Rehabilitation is the crucial methodology for complement of functional restoration following orthopaedic surgeries. Post-operative rehabilitation has mainly focused on evaluation and better understanding of pathological kinesiology of body malfunctions such as osteoarthritis to promote functional restorations. Considering the technological advancements in regenerative medicine, there are increasing needs to drive its progress in development of clinical application. Just as rehabilitation is important for recovery following surgeries or injuries, it is growingly recognized that combined approaches with optimal rehabilitation protocols are inevitable to maximize the efficacy of regenerative medicine technologies. In this talk, we will show part of our efforts for clinical application of rehabilitation in combination with regenerative medicine (「Rehabilitation program after mesenchymal stromal cell transplantation augmented by vascularized bone grafts for idiopathic osteonecrosis of the femoral head」 and 「An early low-invasive approach with bFGF-containing gelatin hydrogel to idiopathic osteonecrosis of the femoral head before the head collapse」), and share the future prospects of this emerging strategies.

アブストラクト | Poster abstract

Poster-1

Muscle-contraction training can enhance the efficacy of cell transplantation treatment for Duchenne Muscular Dystrophy (DMD)

Nana Takenaka-Ninagawa[1], Yuta Itoh[2], Keisuke Kawakami[3], Hidetoshi Sakurai[1].

[1]Center for iPS Cell Research and Application (CiRA), Kyoto University, [2]Faculty of Rehabilitation Science, Nagoya Gakuin University, [3]Oita University Faculty of Welfare and Health Sciences.

Muscle stem cell transplantation therapy is one of the hopeful therapies for intractable muscular diseases such as Duchenne muscular dystrophy (DMD). In adult skeletal muscles, satellite cells act as a stem cell with regenerating damaged myofibers. We have been investigating generation of muscle stem cells from human iPS cells. Although, a lot of reports showed effects of cell transplantation therapy toward DMD, the best way of cell transplantation into skeletal muscle and valid evaluating method to assess the efficacy of cell therapy have not been developed yet. Therefore we tried to establish the most stable and efficient method of cell transplantation in skeletal muscle by using human immortalized myogenic progenitor cell (Hu5/KD3), and the best way to assess the functional recovery of cell transplanted muscle of DMD model mice (DMD-null/NSG). Moreover, we are also trying to establish an effective rehabilitation programs to promote the effect of cell transplantation therapy toward DMD. These newly developed techniques could be a fundamental steps for establishment of cell therapy towards DMD patients.

Poster-3

Scaffold-free Bio 3D Conduits for the peripheral nerve regeneration

Junichi Tajino[1], Akira Ito[2], Hirofumi Yurie[2], Ryosuke Ikeguchi[2], Shizuka Akieda[3], Manami Tsuji[3], and Tomoki Aoyama[1].

[1]Department of Physical Therapy, Human Health Sciences, Graduate School of Medicine, Kyoto University, Japan, [2]Department of Orthopaedic Surgery, Graduate School of Medicine, Kyoto University, Japan, [3]Cyfuse Biomedical K.K., Japan.

Introduction: Functional restoration after the peripheral nerve injuries remains challenging. Although autologous nerve grafting (autograft) would be the gold standard, it has several shortcomings such as limited supply, sacrifice of the donor site function etc. Tube-like materials (nerve conduits) have been developed to bridge the disconnected nerves. However, synthetic materials don't match autografts in regenerative capacity. Nor they do in infectious safeness. To address these difficulties, we focused on Bio 3D printing technology that enables us to build biocompatible nerve conduits with no foreign materials.
Methods: F344–rnu/rnu rats with immune deficiency (9-10 wks old) were used in two groups (Conduit, Control). The right side sciatic nerve of each rat was bisected in the middle-thigh level and 5mm gap was created. For Conduit group, Bio 3D conduit solely made of human fibroblast was interposed between the nerve ends. For Control group, the cut nerve was left with no grafting. Eight weeks after the surgery, nerve regeneration and functional recoveries were evaluated.
Results and Discussion: Histological and morphometric evaluation showed enhanced nerve regeneration in Conduit group as well as greater recovery in electrophysiological and kinematical evaluation. Taken together, Bio 3D conduit might promote nerve regeneration after injury.

Poster-2

Assessment of therapeutic value of osteoarthritis rehabilitation by molecular biological and biochemical approach

Takashi Ohtsuki[1], Kanae Kumagishi[2,4], Akira Shinaoka[2], Keiichiro Nishida[2], Aiji Ootsuka[2], Kenichiro Sakata[3], Syunsuke Sakata[3], Kenji Kawamura[4], Satoshi Hirohata[1].

[1]Department of Medical Technology, Okayama University Graduate School of Health Sciences, [2]Department of Human Morphology, Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Okayama university, [3]Sakata Orthopedic Hospital, [4]Department of Physical Therapy, Kibi International university.

Backgrounds: Osteoarthritis is one of a major joint disease. Popular conservative therapies are physiotherapy and hyaluronan (HA) treatment. But, little was known about the impact of combined therapy. We compared the impact of combined therapy by molecular biological and biochemical analysis
Methods: The patients were divided 4 groups. Group 1 underwent physiotherapy (PT) alone as control. Group 2 underwent both PT and HA treatment. Group 3 underwent PT with Shaking board (SB) treatment. Group 4 underwent PT, SB and HA treatment. Urine collagen type II C-telopeptide (CTXII) was determined by Enzyme linked immunosorvent assay. Knee joint range of Motion (ROM), Visual analogue scale (VAS) and time up & go test (TUG) were measured. Shaking board GB 700 (OG Wellness, Okayama, Japan)
Results: CTXII concentration reduced in primary stage patients (Kellgren Lawrence grade I and II) but did not reduced in the progress stage (KL grade III-IV). CTXII concentration decreased in group 4.
Conclusion: Therapeutic impact was thought to be effective in the patients with the primary stage. The best therapy was PT with SB and HA treatment

Poster-4

Effect of low-intensity pulsed ultrasound after mesenchymal stromal cells injection to treat osteochondral defect

S. Yamaguchi[1,2], T. Aoyama[1], A. Ito[2,3], M. Nagai[4], J. Tajino[1], H. Iijima[1,2], X. Zhang[1], W. Kiyan[1], H. Kuroki[1].

[1]Department of Physical Therapy, Graduated of School Medicine, Kyoto University, Japan, [2]Japan Society for the Promotion of Science, Japan, [3]Department of Orthopaedic surgery, Gradate of School Medicine, Kyoto University, Japan, [4]Congenital Anomaly Research Center, Gradate of School Medicine, Kyoto University, Japan.

We investigated the effect of low-intensity pulsed ultrasound (LIPUS) treatment combined with mesenchymal stromal cell (MSC) injection for cartilage repair and subchondral bone reconstitution to treat rat knee osteochondral defect. An osteochondral defect was created on both femur grooves of Wistar rats (n=28). Four weeks later, bone marrow MSCs were injected into the right knee joint, and phosphate buffer saline were injected into the left knee as control. The rats were divided into 2 intervention groups: without or with LIPUS irradiation. Two days after injection, the rats with LIPUS were subjected to LIPUS treatment, 20 min/day, 5 days/week, to both knee joints. After 4 and 8 weeks intervention, the rats were euthanized, femora were removed for evaluation. Subchondral bone reconstitution was evaluated as bone volume (BV)/tissue volume (TV) by micro-computerized tomography analysis. Cartilage repair was evaluated histologically based on the Wakitani cartilage repair score. MSC injection improved the cartilage repair score and LIPUS irradiation improved BV/TV. Combination treatment promoted both cartilage repair and BV/TV improvement. Thus, MSC injection combined with LIPUS irradiation is more effective than either treatment alone in promoting concurrent cartilage repair and subchondral reconstitution.

Poster-5

Functional Assessment in Patients with Knee Osteoarthritis Treated by Different Preparation Protocols of Platelet Rich Plasma: Preliminary Data

Carolina Mie K. Onodera[1,2], Marco C. Uchida[1], Ricardo A. C. Sampaio[1], Priscila Y. S. Sampaio[1], Aline Urban Paffaro[2], José Fabio Fabio Santos Duarte Lana[2], Joyce M. A. Bizzacchi[2].

[1]Department of Adapted Physical Activity; School of Physical Education, University of Campinas, Campinas-SP, Brazil, [2]Hematology-Hemotherapy Center, University of Campinas, Campinas-SP, Brazil.

Background: Platelet-rich plasma (PRP) is an autologous therapy able to induce healing in soft tissue in Osteoarthritis (OA). The main objective of this study was to assess physical functioning comparing Platelet Poor Plasma (PPP), Platelet Rich Plasma Poor Leucocytes (P-PRP) and Platelet Rich Plasma Rich in Leucocytes (L-PRP) in knee OA treatment during a 3-month follow-up.
Methods: A total of 24 patients with knee OA (II, III, IV-Kellgren and Lawrence grading scale) were enrolled in this study. Patients were randomized in PPP, P-PRP, L-PRP groups. Outcome measures included Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC-function), 30 seconds chair test, usual walking speed, stair climb test. A paired t test was used to compare the differences between the pre and post interventions results in different groups.
Results: Our results demonstrated a statistically significant increase in functional tests ($p<0.05$) in groups treated with P-PRP and L-PRP when compared to PPP treatment; WOMAC scores showed no significant differences in any group after 3-month follow-up.
Conclusion: Our preliminary results suggest that P-PRP and L-PRP are promising to treat knee OA; in addition, functional tests could be more objective to detect differences in the treatment using PRP.

Poster-6

Electrical stimulation drives chondrogenesis of mesenchymal stem cells in the absence of exogenous growth factors

Hyuck Joon Kwon[1], Gyu Seock Lee[1], Honggu Chun[2].

[1]Department of Physical Therapy and Rehabilitation, College of Health Science, Eulji University, Gyeonggi, Korea, [2]Department of Bio-convergence Engineering, Korea University, Seoul, Korea.

Mesenchyme stem cells (MSCs) have high therapeutic potential for cartilage regeneration. We previously uncovered the role of ATP oscillations for prechondrogenic condensation in MSC chondrogenesis. In this study, we have tried to induce ATP oscillations which are crucial for prechondrogenic condensation in chondrogenesis by using electrical stimulation (ES) as a physical inducer. In this study, we found that ES generated ATP and calcium oscillations and induced MSCs to be condensed into the aggregation and subsequently differentiate into chondrocytes without addition of exogenous growth factors, displaying high expression levels of chondrogenic markers such as type II collagen, aggrecan and Sox9. The actions of ES for ATP oscillations and chondrogenesis depended on extracellular ATP signaling via $P2X_4$ receptor. In addition, ES induced the significant increase in expression of TGF-β1 and BMP2, and inhibition of either TGF-β or BMP signaling prevented the ES-induced upregulated expression of chondrogenic markers, which indicates that ES stimulates chondrogenesis via TGF-β and BMP signalings. However, inhibition of TGF-β signaling blocked ES-induced condensation, while inhibition of BMP signaling did not, which reveals that TGF-β signaling, but not BMP signaling, mediates ES-induced condensation. In conclusion, these findings advance our understanding of the effects of ES on chondrogenesis and their mechanisms of action, and contribute to developing electrotherapeutic strategies for cartilage repair using MSCs.

Poster-7

Exercise therapy for knee osteoarthritis

Hirotaka Iijima[1,2], Tomoki Aoyama[1], Akira Ito[2,3], Junichi Tajino[1], Shoki Yamaguchi[1,2], Momoko Nagai[4], Hiroshi Kuroki[1].

[1]Department of Physical Therapy, Human Health Sciences, Graduate School of Medicine, Kyoto University, Kyoto, Japan, [2]Japan Society for the Promotion of Science, Tokyo, Japan, [3]Department of Orthopaedic Surgery, Graduate School of Medicine, Kyoto University, Kyoto, Japan, [4]Congenital Anomaly Research Center, Graduate School of Medicine, Kyoto University, Kyoto, Japan.

Background: We have been researching the effects of physical activity including exercise intervention on articular cartilage-subchondral bone unit as well as functional performance, with the ultimate goal of developing effective and financially viable treatments in patients with knee OA. Recently, we conducted two researches from clinical and basic aspect using biological and epidemiological approaches as follows.
Methods and Results: [*STUDY1*]: Of 207 patients with radiographic Kellgren/Lawrence grade ≥1, 137 (66.2%) patients with knee OA were inactive (<5000 steps/day: sedentary lifestyle) due to knee specific impairment and other factors. Walking additional 1000 steps/day was associated with improved self-reported and performance-based physical function, particularly in patients with lower physical function. [*STUDY2*] We found that physiological level exercise intervention increases expression of bone morphogenetic proteins (BMPs) and prevents the progression of cartilage-subchondral bone lesions in a post-traumatic rat knee model (n = 60). Intraarticular injection of Gremlin-1, an inhibitor of BMPs, was likely to cancel the effects of physiological level exercise on cartilage-subchondral bone lesions, suggesting that exercise intervention may act as a disease-modifying therapy via increase of BMPs expression.
Conclusion: These findings indicate that increased physical activity might prevent osteoarthritic changes in knee joint as well as enhance functional improvement in patients with knee OA.

FIFTH ANNUAL SYMPOSIUM ON REGENERATIVE REHABILITAION
October 14-16th, 2016
Emory University, Atlanta, GA

スペシャルセミナー | Special Seminar

脊髄損傷リハビリテーションセミナー
Seminar on Rehabilitation of Spinal Cord Injury

Instructor : Randy D. Trumbower MPT, PhD
Director of Research, Department of Rehabilitation Medicine, Emory University, USA
Content : A demonstration on wearable technology for spinal cord injury rehabilitation
Venue : Rehabilitation Unit, Kyoto University Hospital

京都大学再生医療・リハビリテーション研究施設見学ツアー
Tour for Regenerative Medicine & Rehabilitation facilities of Kyoto University

---iPS細胞研究所
Center for iPS Cell Research andApplication (CiRA)
Tour guide
中内 彩香 Ayaka Nakauchi PhD
京都大学iPS細胞研究所国際広報室
サイエンスコミュニケーター
Science Communicator,
International Public Communications Office, CiRA

---先端医療機器開発・臨床研究センター (バイオ3Dプリンター)
Clinical Research Center for Medical Equipment Development (Bio 3D printer)

---京都大学附属病院リハビリテーション部
Rehabilitation Unit, Kyoto University Hospital