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







# February 11<sup>th</sup>, 2017 Sugiura Community Care Research Center, Kyoto University

**3** International Symposium on Regenerative Rehabilitation in Kyoto



### 巻頭言

#### **Prefatory Note**

#### 開催の趣旨・概要

京都大学大学院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3回国際再生リハビリテーションシンポジウムin京都を2017年 2月11日(土)に開催しました。

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。今回のシンポジウムにおいても昨年開催された第2回国際再生リハビリテーションシンポジウムin京都と同様に、医師、研究者、理学療法士、作業療法士、アスレティックトレーナー、医療機器開発コーディネーター、大学院生、学部学生など、多職種の方々に参加いただきました。

シンポジウムは、伊藤明良(京都大学大学院医学研究科人間健康科学系専攻助教) の開会挨拶および再生リハビリテーションの概説から始まり、池谷真(京都大学iPS



of Medicine, Kyoto University,

Japan

細胞研究所准教授)による神経再生に向けた基礎的研究の講演、マイケル・モド (ピッツバーグ大学McGowan Institute for Regenerative Medicine准教授)による神経再生医療におけるリハビリテーションの併用効果解明に向けたトランスレーショナル研究の基調講演、そして池口良輔 (京都大学医学部附属病院リハビリテーション部准教授)による末梢神経再生医療における基礎および臨床研究の講演がありました。また、ポスターセッションでは多種多様な10演題が発表されました。最優秀ポスター賞を本シンポジウムから試験的に設けましたが、受賞ポスターの選定をよりオープンにするために、参加者および講演者による投票形式を採用しました。投票するポスターを選ぶ中で、プレゼンターと議論を交わす良い契機となったのではないでしょうか。さらに、本学が研究開発に係わり、再生リハビリテーションにおける補助機器としての応用が期待されている、「Honda歩行アシスト」のデモンストレーションも行いました。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。

#### Overview and aim of the symposium

We have hosted the 3rd International Symposium on Regenerative Rehabilitation in Kyoto on Saturday, February 11<sup>th</sup>, 2017 in accordance with Center for iPS Cell Research and Application (CiRA) and Kyoto University Hospital.

This symposium has been designed with the intention to foster multiple-discipline interactions between scientists, clinicians and rehabilitation specialists from around the world, focuses on the emerging field of Regenerative Rehabilitation. This novel and innovative approach integrates discoveries in regenerative medicine with rehabilitative regimens. Same as the past year, we had much participation of medical doctors, researchers, rehabilitation specialists, athletic trainers, medical industries, and graduate/under graduate students from wide varieties of backgrounds this time.

The agenda consisted of four lectures and poster session. Akira Ito, Assistant Professor of Human Health Sciences, Graduate School of Medicine, Kyoto University, made opening remarks and outlined the Regenerative Rehabilitation for icebreaking. Then three invited talks followed. Special Lecture 1 by Makoto Ikeya, Associate Professor of iPS Cell Research and Application, Kyoto University, focused on basic studies aiming at nerve regeneration; Keynote Lecture by Michel Modo, Associate Professor in the Department of Radiology & McGowan Institute for Regenerative Medicine at the University of Pittsburgh, on translational studies investigating synergistic effects of rehabilitation approaches with regeneration in nervous system; and Special Lecture 2 by Ryosuke Ikeguchi, Associate Professor, Department of Orthopaedic Surgery & Rehabilitation, Kyoto University Hospital, about basic and clinical studies for peripheral nerve regeneration. We had 10 presentations at the poster session. This time, we did a poster award competition that was selected by vote of participants and lecturers which allowed the selection to be more open. I am sure that was a good opportunity for each presenter to interact with others. Further, we had a demonstration of a gait-assist exoskeleton that Honda Motor Co., Ltd. and Kyoto University are jointly developing in hope of serving as a supportive device in Regenerative Rehabilitation. The symposium has successfully finished with active discussions and interactions on the Regenerative Rehabilitation, which has just arisen here in Japan.

## 講演者

#### **Presenters**

#### 開会挨拶・再生リハビリテーション概説 Opening Remarks・Outline of Regenerative Rehabilitation

#### 伊藤 明良

京都大学大学院医学研究科人間健康科学系 助教 Akira Ito PT, PhD Assistant Professor, Human Health Sciences, Graduate School of Medicine, Kyoto University, Japan



### 基調講演 Keynote Lecture

#### Michel Modo

Associate Professor, Department of Radiology & McGowan Institute for Regenerative Medicine, University of Pittsburgh Title:

Exploring synergistic effects of cell and physical therapy in stroke.





#### 特別講演1 Special Lecture 1

#### 池谷 真

京都大学iPS細胞研究所 准教授

Makoto Ikeya PhD Associate professor, Center for iPS Cell Research and Application (CiRA), Kyoto University.

Title:

Challenge towards neuroregeneration by using pluripotent stem cells



### 特別講演2 Special Lecture 2

#### 池口 良輔

京都大学医学部附属病院整形外科・リハビリテーション科 准教授

Ryosuke Ikeguchi MD, PhD Associate Professor, Department of Orthopaedic Surgery & Rehabilitation, Kyoto University Hospital

Rehabilitation and regeneration of peripheral nerve injury

## プログラム

#### **Program**

1:00 PM ~ 1:20

**OPENING REMARKS** 

Room: Sugiura Hall

Akira Ito PT, PhD

Department of Physical Therapy, Human Health Sciences, Kyoto University, Japan

 $1:20 \text{ PM} \sim 2:05$ 

**SPECIAL LECTURE 1** 

Room: Sugiura Hall

Challenge towards neuroregeneration by using pluripotent stem cells

Makoto Ikeya PhD

Center for iPS Cell Research and Application (CiRA), Kyoto University, Japan

2:05 PM ~ 2:10

BREAK

2:10 PM ~ 2:55

**KEYNOTE LECTURE** 

Room: Sugiura Hall

Exploring synergistic effects of cell and physical therapy in stroke

**Michel Modo PhD** 

Department of Radiology & McGowan Institute for Regenerative Medicine,

University of Pittsburgh, USA

2:55 PM ~ 3:30

**Coffee BREAK and Poster Session** 

Room: Foyer

 $3:30 \text{ PM} \sim 4:15$  **SPECIAL LECTURE 2** 

Room: Sugiura Hall

Rehabilitation and regeneration of peripheral nerve injury

Ryosuke Ikeguchi MD, PhD

Department of Orthopaedic Surgery & Rehabilitation, Kyoto University Hospital, Japan

4:15 PM ~ 5:30

**RECEPTION** 

Room: Foyer





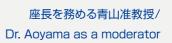


### 講演会場・質疑

#### **Snapshots**



会場/Lecture room





討議/D

討議/Discussion



会場スタッフ/Staff

## ポスター発表

#### **Poster Presentations**



1. 太治野氏のポスター発表 2. ポスターディスカッション 3. Kwon氏のポスター発表 4. ポスターディスカッション

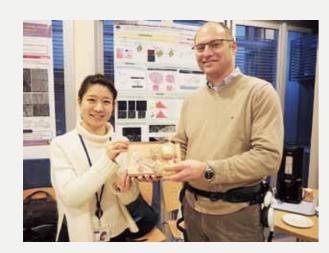
## 最優秀ポスター賞

### **Best Poster Award**

#### 竹中 菜々

京都大学iPS細胞研究所(CiRA)

Nana Takenaka-Ninagawa Center for iPS Cell Research and Application (CiRA), Kyoto University, Japan



今回のシンポジウムでは、骨格筋疾患に対する細胞 移植治療の有効性を示すデータを発表いたしました。 多くの方々に発表をお聞きいただけ、そして、有意義な ディスカッションができ、その上、最優秀ポスター賞に 選出していただけて、大変嬉しく思います。

次回の国際シンポジウムでは、さらに発展した内容 を報告できるように、引き続き頑張ります!

In this symposium, I had a presentation about efficacy of cellular therapy for a skeletal muscular disease. I was glad that I could discuss about my work with a lot of people. Besides, it is quite an honor that I was selected as a poster awardee!! I will continue to do my best to move forward with my research and look forward to seeing you with further progresses in the next symposium.

## Honda歩行アシスト デモンストレーション

### **Demonstration of Honda Walking Assist Device**

Instructor: Shihomi Kawasaki

Human health Sciences, Graduate School of Medicine, Kyoto University











### アブストラクト

#### **Lecture Abstracts**



Keynote Lecture

## Exploring synergistic effects of cell and physical therapy in stroke

Michel Modo PhD

Associate Professor, Department of Radiology & McGowan Institute for Regenerative Medicine, University of Pittsburgh

Stroke remains an acute neurological injury with very limited treatment options, especially in its chronic phase. We have investigated the use of intracerebral implantation of human neural stem cells for the treatment of stroke and evaluated their efficacy in a battery of behavioral tests. This approach has recently founds its clinical translation, with a phase I trial demonstrating safety and a phase II trial currently investigating indications of efficacy in patients with chronic stroke. A key question that has arisen is whether physical therapy often given to patients with stroke will work synergistically with cell therapy. To investigate this issue, we are evaluating in a preclinical model of stroke if both therapies will produce equivalent recovery and if there is a synergistic benefit by combining both approaches. It is hope that the results of these experiments will guide the design of future clinical trials and ensure an optimal treatment for patients with stroke.



Special Lecture 1

## Challenge towards neuroregeneration by using pluripotent stem cells

Makoto Ikeya PhD

Associate Professor, Center for iPS Cell Research and Application (CiRA), Kyoto University

When neurotmesis occurs and the gap is too long to be sutured, transplantation treatment should be taken. Autologous nerve grafting from other parts is commonly used to connect the gap, but excision of nerve bundles from other parts may have a risk. As an alternative treatment, nerve conduits have been also studied for many years. Although 3D-constructed tubule made from adult fibroblasts in addition to the biodegradable materials have been tried as a constituent material of the nerve conduit, other materials or cell types could be applied to improve the quality. One of the possible candidates is cells differentiated from induced pluripotent stem cells (iPSCs), since theoretically iPSCs are ultimately expandable and HLA-homozygous iPSCs project is now ongoing. Recently, we have succeeded to induce mesenchymal stem cells (MSCs) from iPSCs through neural crest cell (NCC) lineage under defined conditions. We are now trying to adopt this induction protocol to xeno-free conditions and mostly done. In this presentation, I will show the potential application of the xeno-free MSCs to the regeneration of the locomotive organ. We are still on the way but happy to discuss about our recent data.



Special Lecture 2

## Rehabilitation and regeneration of peripheral nerve injury

Ryosuke Ikeguchi MD, PhD

Associate Professor, Department of Orthopaedic Surgery & Rehabilitation, Kyoto University Hospital

Peripheral nerve injury is a common traumatic disorder that severely affects patient activities of daily living. Recent developments in nerve reconstruction procedures have resulted in reduced patient disability following peripheral nerve injuries. After peripheral nerve surgeries, rehabilitation is essential for both motor nerve and sensory deficits to restore functional improvement. In the case of acute sharp-cut trauma, the injured peripheral nerve should be explored and repaired by primary neurorrhaphy as soon as possible. Acute laceration of the peripheral nerve should be treated by nerve grafting because of the unrepairable nerve gap. In other cases, such as nerve root avulsion in brachial plexus injury, in which nerve repair or grafting is impossible, neurotization (nerve transfer) should be considered. As an alternative to autologous nerve grafting we use Bio 3D printing technology and create a completely biological, tissue-engineered, and scaffold-free Bio 3D conduit. Here we present our nerve reconstruction and nerve injury rehabilitation program case series. In addition, we also present the peripheral nerve regeneration through the scaffold-free Bio 3D conduit.

## アブストラクト

#### **Poster Abstracts**

#### Poster-1

## Application of iPSC-derived Mesenchymal Stromal Cell (MSC) toward Treating Muscular Disease

Nana Takenaka-Ninagawa<sup>1</sup>, Yuta Itoh<sup>2</sup>, Makoto Ikeya<sup>1</sup>, Kim Jin Sol<sup>1</sup>, Rukia Ikeda<sup>1</sup>, Hidetoshi Sakurai<sup>1</sup>

<sup>1</sup>Center for iPS Cell Research and Application (CiRA), Kyoto University, Japan

<sup>2</sup>Faculty of Rehabilitation Science, Nagoya Gakuin University, Japan

Mesenchymal stromal cell (MSC) is well known as a multipotent progenitor for osteogenic, chondrogenic and adipogenic lineage, and is also found in skeletal muscles. Recent studies reported that although they normally act as supportive cells on skeletal muscle homeostasis with producing collagen VI, they are also the responsive cells for fibrosis and fatty degeneration in diseased muscle. Moreover, mutations of Coló genes, which are specifically expressed in MSC but not in muscle, cause a severe muscle disorder, Ullrich congenital muscular dystrophy (UCMD). Therefore, we assumed that collagen VI positive MSC could be a cell source of cell therapy for UCMD. However MSC isolated from adult tissues are quite limited in expansion. To overcome such hurdle, we plan to use iPSC-derived MSC for future cell therapy of UCMD. In this symposium, I'll introduce our recent results which demonstrate that human iPSC-derived MSC could ameliorate the phenotype of UCMD model mice (COL6KO/NSG).

#### Poster-3

## Research for the appropriate stimulation after mesenchymal stromal cells injection to treat osteochondral defect

<u>Shoki Yamaguchi</u><sup>1</sup>, Tomoki Aoyama<sup>2</sup>, Akira Ito<sup>2</sup>, Momoko Tanima-Nagai<sup>3</sup>, Junichi Tajino<sup>2</sup>, Hirotaka lijima<sup>2</sup>, Xiangkai Zhang<sup>2</sup>, Wataru Kiyan<sup>2</sup>, Hiroshi Kuroki<sup>2</sup>

<sup>1</sup>Department of Physical Therapy, School of Nursing and Rehabilitation Sciences at Odawara, International University of Health and Welfare, Japan

<sup>2</sup>Department of Physical Therapy, Human Health Sciences, Graduate School of Medicine, Kyoto University, Japan

<sup>3</sup>Congenital Anomaly Research Center, Graduate School of Medicine, Kyoto University, Japan

The purpose of this study was to research for appropriate follow up treatment after mesenchymal stromal cell (MSC) injection for osteochondral defects in rat knee joint. Allogenic MSCs were injected in the rat knee joint with chronical osteochondral defect. We assessed the effect of exercise and low-intensity pulsed ultrasound (LIPUS) irradiation after MSC injection for the cartilage repair score. MSC injection is effective in stimulating cartilage regeneration on osteochondral defects 4 weeks after injection. Exercise performed after MSC injection could promote cartilage repair in rat osteochondral defect model. On the contrary, LIPUS irradiation after MSCs injection might not promote the cartilage regeneration. Although, the subchondral bone reconstruction was evaluated by measuring the bone volume/ tissue volume in the repaired area of osteochondral defect, LIPUS irradiation might promote subchondral bone reconstruction. This study suggested that exercise and LIPUS intervention might bring the promotion effect of the regeneration in the different tissue. It may become more effective treatment by combining each intervention.

#### Poster-2

## Electrical stimulation induces direct reprogramming of dermal fibroblasts into chondrocytes

Gyu Seock Lee<sup>1</sup>, Hyuck Joon Kwon<sup>1</sup>

<sup>1</sup>Department of Physical Therapy and Rehabilitation, College of Health Science, Eulji University, Gyeonggi, Korea

We previously reported that electrical stimulation drives chondrogenesis of mesenchyme stem cells even in the absence of exogenous growth factors. In the previous study, we noticed that electrical stimulation induce MSC chandrogenesis more effectively than chandrogenic growth factors such as TGF betas and BMPs. Therefore, in this study, we have investigated whether electrical stimulation would be able to induce direct reprogramming of dermal fibroblasts into chondrocytes because dermal fibroblast can be easily obtained in comparison to stem cells. We found that electrical stimulation induced human adult dermal fibroblasts to be condensed into the aggregation without addition of exogenous growth factors. qPCR analysis showed that electrical stimulation not only enhanced gene expression of chondrogenic markers such as Col2a1, aggrecan and Sox9, but also reduced gene expression of fibroblast markers such as Col1a1 and Col1a2. Moreover, immunostaining and alcian blue staining also confirmed that electrical stimulation increased significantly expression of Col2 and glycosaminoglycan. These findings would contribute to developing electrotherapeutic strategies for cartilage regeneration. Further studies would be required to elucidate the role of electrical stimulation for cell reprogramming and chondrogenesis.

#### Reference]

Hyuck Joon Kwon, Gyu Seock Lee, Honggu Chun., Electrical stimulation drives chondrogenesis of mesenchymal stem cells in the absence of exogenous growth factors. *Scientific Reports* 6, 39302 (2016)

#### Poster-4

Effects of Mesenchymal Stem Cells In Treating Patients With Knee Osteoarthritis and Role of Rehabilitation –a Systematic Review of Clinical study-

<u>Hirotaka lijima</u><sup>1,2</sup>, Takuya Isho<sup>1,3</sup>, Hiroshi Kuroki<sup>1</sup>, Tomoki Aoyama<sup>1</sup>

<sup>1</sup>Department of Physical Therapy, Graduate School of Medicine, Kyoto University, Kyoto, Japan

<sup>2</sup> Japan Society for the Promotion of Science, Tokyo, Japan

<sup>3</sup>Rehabilitation Center, Fujioka General Hospital, Gunma, Japan

This systematic review aimed to examine the effects of mesenchymal stem cells (MSCs) in treating patients with knee osteoarthritis (OA) and the role of rehabilitation program on the MSC treatment. Data were collected from randomized controlled trials (RCTs) and non-RCTs that comparing the effects of MSC treatment on clinical symptom and structural outcomes in patients with knee OA. For each electronic database, the endpoint was September 2016. The literature research was performed by two independent examiners. In total, 32 studies were included. Of 32 studies, 23 (71.9 %) studies used MSC intra-articular injection, and the other studies used arthroscopic MSC implantation or those combined with high tibial osteotomy. MSC treatment had high effect sizes in improving knee pain and quality of cartilage, however treatment had a low effect size in increasing cartilage volume. Rehabilitation programs described in the included studies were weight-bearing schedule (37.5 %) and range of motion exercise (28.1 %). However, other information about rehabilitation program such as muscle strength exercise, physical therapy modalities, and preoperative rehabilitation were poor. Although there is an accumulated in vitro evidence that physiological mechanical stimuli promotes MSC differentiation into chondrocyte and extracellular matrix synthesis, rehabilitation program after MSC treatment was insufficient. We believed that establishment of effective rehabilitation protocol is essential in developing regenerative medicine.

#### Poster-5

## Mechanical unloading causes subchondral osteoclast activation resulting in thinning of articular cartilage

Masato Nomura<sup>1</sup>, Naoyoshi Sakitani<sup>1</sup>, Hiroyuki Iwasawa<sup>1,2</sup>, Yoshio Wakimoto<sup>1</sup>, Shoko Takano<sup>1</sup>, Yuta Kohara<sup>1</sup>, Shunsuke Shimaya<sup>1</sup>, Hideki Moriyama<sup>1</sup>

<sup>1</sup>Department of Rehabilitation Science, Graduate School of Health Sciences, Kobe University, Japan

<sup>2</sup>Department of Rehabilitation, St. Marianna University School of Medicine, Japan

Articular cartilage is a highly mechano-responsive tissue. A well-established association exists between mechanical overloading and osteoarthritis, which is characterized by cartilage and subchondral bone alterations. However, the effects of reduced loading on articular cartilage and subchondral bone is still poorly understood. Herein, we investigated the morphological and metabolic responses of articular cartilage and subchondral bone to decreased mechanical stress in vivo, using mouse model of hindlimb unloading by tail suspension. After joint unloading, the thickness of knee cartilage was decreased and subchondral bone atrophy with concomitant marrow expansion predisposed osteoclast activity at bone surface to invade into cartilaginous layer. MMP13 activities were distributed at the bone surface corresponding to the lower edges of articular cartilage. Given that osteoclasts have shown to be capable of expression of MMPs and cartilage matrix resorption, these findings support the concept that the thinning of articular cartilage by mechanical unloading is the result of cartilage matrix degradation and resorption by osteoclasts. Increased RANKL/OPG ratio in chondrocytes at deep zone of cartilage after unloading may partly contribute to subchondral osteoclast activation. Our results should help quide better understanding of crosstalk between articular cartilage and subchondral bone under unloading condition

#### Poster-7

## ER Manipulation: A promising therapeutic intervention for protein aggregation diseases

<u>Arisa Yamashita</u><sup>1</sup>, Takamitsu Nakatsuru<sup>1</sup>, Hiroki Saito<sup>1</sup>, Yuri Hiraki<sup>1</sup>, Tetsuo Yamazaki<sup>1</sup>

<sup>1</sup>Department of Molecular Cell Biology and Medicine, Graduate School of Biomedical Sciences, Tokushima University, Japan

Intracellular accumulation of protein aggregates is associated with various neuromuscular degenerative diseases, including amyotrophic lateral sclerosis. At present, no effective therapeutic strategy is available for this spectrum of disease. We recently demonstrated that formation of aberrant protein aggregates can be prevented by tethering aB-crystallin, a chaperone protein, to the endoplasmic reticulum (ER) membrane. To elucidate the underlying mechanisms, we isolated binding partners of the ER-tethered aB-crystallin, and identified two ER transmembrane proteins of unknown function, tentatively designated as ABER1 and ABER2, respectively. ABER1 repressed aggregate formation mediated by the R120G aB-crystallin mutant. In contrast, ABER2 enhanced the aggregation of the mutant. We thus have concluded that the microenvironment surrounding the ER membrane can be a novel therapeutic target to overcome protein aggregation diseases, and that ABER1 and ABER2 are most likely candidates to manipulate to ensure the preventive effects on protein aggregates.

#### Poster-6

Remobilization after 8 weeks of joint immobilization repairs the cartilage surface structure but aggravates site specific degeneration of chondrocyte

Momoko Tanima-Nagai<sup>1</sup>, Tomoki Aoyama<sup>2</sup>, Hiroshi Kuroki<sup>2</sup>

<sup>1</sup>Congenital Anomaly Research Center, Kyoto University Graduate School of Medicine, Japan

<sup>2</sup>Department of Physical Therapy, Human Health Sciences, Graduate School of Medicine, Kyoto University, Japan

Within synovial joints, articular cartilage acts as low friction and wear resistant. The pathological changes were reported in animal models of osteoarthritis and joint immobilization including cartilage surface fibrillation or chondrocyte degeneration. These structural alteration lead mechanical, biochemical, cellular and molecular abnormalities in joint tissue. Previous reports using rat immobilization model indicated that joint immobilization causes various degeneration of articular cartilage such as thinning, softening, and surface illegality.

In this study, we investigated that how cartilage changes with remobilization after joint immobilization by using scanning electron microscope (SEM) and transmission electron microscope (TEM). The surface was even and smooth consisted of collagen fibrillar structures were observed in the control group (ctrl) using SEM. After immobilization, the knobby surfaces consisted of a cross-linking fiber network or the leafy and split surfaces were observed at site specifically. With 8 weeks remobilization after then, fiber structure similar to the ctrl was observed again. On the other hand, the degenerated chondrocyte morphology such as cyst formation was observed using TEM. This results showed that the remobilization intervention after immobilization has a negative effect on the chondrocyte at site specific, although has a positive effect on the collagen fiber of cartilage surface.

#### Poster-8

#### Investigating Multiple Influence of Gravitation

<u>Junichi Tajino</u><sup>1</sup>, Akira Ito<sup>2</sup>, Momoko Tanima-Nagai<sup>3</sup>, Shoki Yamaguchi<sup>2</sup>, Hirotaka lijima<sup>2</sup>, Wataru Kiyan<sup>2</sup>, Tomoki Aoyama<sup>1</sup> and Hiroshi Kuroki<sup>2</sup>

<sup>1</sup>Department of Development and Rehabilitation of Motor Function, Graduate School of Medicine

<sup>2</sup>Department of Motor Function Analysis, Graduate School of Medicine, Kyoto University, Kyoto, Japan

<sup>3</sup>Congenital Anomaly Research Center, Graduate School of Medicine, Kyoto University, Kyoto, Japan

Since every life on Earth has evolved under the Earth's gravity, altered gravitational stimuli has multiple biological influences. In terms of physical abilities, impairments due to less loading, which are the consequences of inactivity or bedrest are of great interest. Using Hindlimb Unloading and artificial gravity by animal centrifuge, we investigate how various gravitational stimuli affects the physical conditions of rats. As to walking, two-week Hindlimb Unloading evokes gait distortion with their knee and ankle extended throughout the gait cycle, while centrifugation at twice of the normal gravity for 1 hour a day attenuates this alteration. Unloading also diminishes spatial learning ability. In an object-recognition task, unloaded rats show as similar interest in familiar object as new object, which supposed to draw more attention. That implies they do not learn from the environment. Meanwhile centrifugation ameliorates this learning deficits. However, the benefits of centrifugation might be restricted within a certain range of intensity. Centrifugation at 2.5 times of the normal gravity results less preventive effects from those alterations. Further, intermittent centrifugation affects a circadian rhythm of activity and causes transient drop of deep body temperature. We will keep these investigations to pursue the effects of gravitational stimuli on physical functions

#### Poster-9

Three-dimensional models of the segmented human fetal brain generated by magnetic resonance imaging

Yutaka Yamaguchi<sup>1</sup>, Momoko Tanima-Nagai<sup>2</sup>, Shigehito Yamada<sup>1,2</sup>

<sup>1</sup>Human Health Sciences, Kyoto University Graduate School of Medicine, Kyoto, Japan

<sup>2</sup>Congenital Anomaly Research Center, Kyoto University Graduate School of Medicine, Kyoto, Japan

The understanding of embryonic development leads to an elucidation of the basic human body structure and congenital anomaly. In recent years, advances in imaging technology have permitted us to obtain more detailed images of the human fetus in a nondestructive and noninvasive manner. However, there is no report that the segmentation is performed for each region of the developing brain using magnetic resonance image (MRI). In this study, we set original landmarks and attempted to create a three-dimensional (3D) models of the developing brain which were reconstructed using MRI. Besides, we confirmed the validity of landmark by comparing our results and the several histological serial sections from the Kyoto Collections. We succeeded in registering a maximum of nine landmarks on MR images and reconstructing 19 sequential models of the regionalized developing brain. The same morphological characteristics were observed on both histological serial sections and MRI. These results will be useful for clinical diagnosis of living fetuses in utero and understanding the growth process of each region of the brain.

#### Poster-10

Postpartum radiographic changes in pelvic morphology and its relation with symptoms of pregnancy-related symphysis pain

Xiang Ji<sup>1</sup>, Masaki Takahashi<sup>2</sup>, Saori Morino<sup>2</sup>, Hirotaka lijima<sup>1</sup>, Mika Ishihara<sup>3</sup>, Mirei Kawagoe<sup>1</sup>, Yoko Hatanaka<sup>4</sup>, Fumiko Umezaki<sup>4</sup>, Mamoru Yamashita<sup>4</sup>, Tomoki Aoyama<sup>1</sup>

<sup>1</sup>Human Health Sciences, Graduate School of Medicine, Kyoto University, Kyoto, Japan

<sup>2</sup>School of Science for Open and Environmental Systems, Graduate School of Science and Technology, Keio University, Japan <sup>3</sup>Pilates Studio Wohl, Aichi, Japan

<sup>4</sup>Kishokai Medical Corporation, Aichi, Japan

The etiology of pregnancy-related pubic symphysis pain (PSP) is usually considered as the change in pelvic biomechanics during pregnancy. However, the morphological changes that occur during puerperium remains unknown. Our study investigated the radiographic changes on conventional X-ray films, indicated a 'closure' alteration in the pelvic cavity diameter 1-month postpartum with a significant decrease in the distance between bilateral furthest lateral points of acetabular margins (delivery day 239.1 mm vs 1 month postpartum 237.0 mm) and shortened pubic symphysis separation (delivery day 7.9mm vs 1 month postpartum 6.5mm). However, difference in radiographic diameters between groups with and without rapid recovery during postpartum was not clearly evident.

