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Abstracts

10th Joint Seminar on Biomedical Sciences

15-17 November, 2017

Tokyo, Japan

Symposium

1. Accurate Graft Positioning during Total Arch Replacement with Open Stent Graft Using Aortic Endoscopy

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Background: In cases of synthetic vascular replacement of the complete aortic arch using an open stent graft (OSG) for the treatment of aortic arch aneurysm, and if such a procedure would be attempted, there is concern for cerebral or spinal infarction due to embolization of plaque or thrombi inside the aneurysm. We therefore reviewed the achievement of accurate positioning by introducing the OSG into the aorta under endoscopy and hereby report the results. **Methods:** The subjects were 11 patients who underwent the procedure between April 2015 and April 2017; age was 66.6 ± 9.4 years, and sex ratio was 10 males and 1 female. During the procedure, a unilateral axillary artery and unilateral femoral artery were exposed, a midline incision of the sternum was made, the ascending aorta was perfused, and blood was removed from the upper and lower vena cava. At a rectal temperature of 28℃ , selective antegrade cerebral perfusion of the right brachiocephalic artery (BCA), the left common carotid artery (LCA) and the left subclavian artery (LSCA) was made. LSCA was ligated, and an endoscope was introduced from the peripheral transected part while the circulation was stopped, and after observing the shape of the aorta, the plaque inside the aorta and the condition of the peripheral implantation site, the OSG was inserted in the target aorta. After stump formation, conventional vascular replacement of the aortic arch was performed. **Results:** Post-operative CT showed no cases of type 1b endoleak, no additional procedures were necessary and no complications. **Conclusions:** Aortic endoscopic aid under circulatory arrest is very useful for the OSG method.

2. Tips for Precise Laparoscopic Liver Resection

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Background: Liver resection has been demonstrated as the preferable initial treatment for patients with resectable liver tumor. Since 1990's, we have suggested that the laparoscopic liver resection (LLR) can provide favorable outcome with early postoperative recovery in selected patients received Minor LLRs, such as left lateral sectionectomy or partial hepatectomy in antero-lateral region of the liver. Development of instruments and technical refinement with effective usage of maginified-caudal endoscopic view, have contributed to overcome limitation of LLR. With accumulation of our experience, advanced liver procedures, such as hepatectomy for tumor located postero-superior region of the liver or anatomy oriented resections including Major LLRs have been utilized by totally laparoscopic approach. **Surgical technique:** All fundamental technique to perform LLR,

such as maintenance of operative field, choice and appropriate use of instruments, isolation and division of vessels, control hemostasis could be learned in Minor LLRs. Hilar dissection of hepatic inflow vessels is performed in anatomical liver resection. In our concept, individual isolation approach is used for hemi-hepatectomy, and Glissonean pedicle approach is used for anatomical hepatectomy smaller than hemi-hepatectomy. As well as technical standardization, surgical simulations using recent modalities, such as 3D-CT, intraoperative contrast enhancement US and Indocyanine green fluorescence imaging, can help to have periopearative decision in disease diagnosis, trocar insertion and liver parenchymal transection. **Results:** Two hundred fifty patients received LLR. No severe postoperative morbidity above Clavien-Dindo Grade IIIb except one patient developed cerebral infarction, was observed. **Conclusion:** We believe that benefits of LLR are not only minimally invasiveness, but also precise performance of surgery. The accumulation of contrivance in each Minor fundaments leads to major progress for reliable LLR.

3. Reversible Axonal Damage Is Remarkable in Acutely Worsening Symptoms of Compression Myelopathy; Analysis of Cerebrospinal Fluid Samples

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Background: We determined levels of biomarkers reflecting damage to axon, myelin, astrocyte, and neuron in the cerebrospinal fluid (CSF) of patients with worsening symptoms of compression myelopathy. **Methods:** From 2011 to 2015, we collected 69 samples of CSF from patients before spinal surgery for acutely worsening compression myelopathy (AM, 20), chronic compression myelopathy (CM, 20), and lumbar canal stenosis (LCS; control group 29). We measured levels of pNF-H and tau (reflecting axonal damage), MBP (reflecting demyelination), S100b (reflecting astrocyte damage), and NSE (reflecting neuronal damage). Change of neurological function was determined using a JOA score for cervical myelopathy. **Results:** Significantly higher levels of pNF-H

(pg/ml) were detected in the CSF of AM (1907.8 ± 730.4) compared with those in either CM (198.6 ± 124.5) or LCS (462.9 ± 635.1) group (P<0.01). Significantly higher levels of tau were detected in the CSF of AM compared with CM (P<0.05). On the other hands, the level of MBP, S100b were not significantly different between the three groups. By contrast, the levels of NSE in AM and CM were significantly lower than those in LCS (P<0.01). In the neurological outcome, a positive correlation between pNF-H and recovery of JOA score was observed (y=0.0072x+51.85; r=0.381). **Conclusion:** The present results suggest that axonal damage is remarkable compared with demyelination, astrocytic, and neuronal damage in AM. Better clinical outcome in AM patients with high CSF levels of pNF-H indicates axonal damage in the spinal cord is reversible, and the levels of pNF-H can be predictive of good surgical outcome for patients with AM.

4. The Challenge in Renal Transplantation for Small Children Less than 15 kg

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Background: Renal transplantation in small children has the risk for early graft loss due to hypoperfusion and vascular thrombosis compared with adults. To achieve successful outcome of renal transplantation in small children, careful management must be needed. **Methods:** We examined 46 pediatric patients (24 boys and 22 girls) who received a live donor renal transplant at our center between March 2009 and May 2017. The outcomes such as s-Cr (mg/dl) after transplantation, graft survival rate and patient survival rate were evaluated. **Results:** In recipients, age was 4.5 ± 2.0 years old, and weight/height were 11.7 ± 2.2 kg and 89.5 ± 9.3 cm. Donors were only relatives and the age was 38.1 ± 7.9 years old. All but one had immediate graft function and the time of initial urine after reperfusion was 22 (interquartile range12-49) minutes. S-Cr were 0.42 ± 0.35 at post-operative day (POD) 1, 0.27 ± 0.08 at POD 7 and 0.29 ± 0.09 at POD 28. The

patient survival rate and graft survival rate at 1 and 5 years post-transplant were 100%/97.8% and 97.0%/94.8%, respectively. One recipient lost the graft due to vascular thrombosis and transplant nephrectomy was performed at 1 day post-transplant. Patient death was shown in one cases because of bacterial pneumonia at 6 months after transplantation. The others still had well-functioning graft at end of the observation. **Conclusion:** The short- and long-term outcome of pediatric transplantation in small children was excellent.

5. Flavonoid Glycosides from Japanese Camellia Oil Cakes and Their Inhibitory Activity against Advanced Glycation End-Products Formation

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Background: The Japanese Camellia (*Camellia japonica* L.; Japanese name: Tsubaki) is one of most well-known species in genus *Camellia*, Theaceae family. The seeds are used as oil materials in food and cosmetics industries. Oil cakes are obtained as by-products during seed oil production, and most of them are unutilized. Advanced glycation end-products (AGEs) are produced from the carbonyl groups of the reducing sugars reacting with the free amino groups of proteins. Inhibition of AGEs formation is paid attention as a potential therapy for many aging-related diseases. In this study, we reported the isolation and structural elucidation of flavonoid glycosides from oil cake of *C. japonica* seeds, as well as their AGEs formation inhibitory activities. **Methods:** The oil cakes were extracted with hot water. Isolation and separation was carried out by column chromatography and preparative HPLC. Structural elucidation was achieved by analysis of spectroscopic data, including 1D and 2D NMR, and MS. Chemical profiling of the oil cake extract was characterized by HPLC-PDA analysis. Anti-AGEs activity was carried out by D-ribose-BSA assay and GA/MGO/GO-HSA assay. **Results:** Phytochemical investigation resulted in the isolation and structural elucidation of thirteen flavonoid glycosides, including four novel compounds. The extract and isolated compounds exhibited potent inhibitory activities against AGEs formation. The extract and the major compound 7 also inhibited AGEs formation between HSA and three intermediates, GA/GO/MGO. Moreover, the extract and 7 decreased the GA-HSA enhanced expression of MIP-1β mRNA in differentiated U937 cells. **Conclusions:** The extract and its flavonoid glycoside constituents from the oil cakes of *C. japonica* seeds possessed potential usability as health materials against AGE-associated chronic diseases.

6. Steroidogenic Acute Regulatory Protein-Related Lipid Transfer Domain Containing 10 Promotes Lipid Accumulation and Lipid Droplet Formation in the Liver of Nonalcoholic Steatohepatitis (NASH) Model Mouse

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Nonalcoholic steatohepatitis (NASH) is characterized by lipid accumulation with inflammation and fibrosis in the liver. STARD10 is a member of the START domain-containing lipid transfer protein family. We have previously shown that STARD10 is highly expressed in the liver. When fed a high fat diet, *Stard10* knockout (*Stard10*^{-/-}) mice accumulated significantly less cholesterol and triglycerides (TG) in the liver than wild type (WT) mice. The purpose of this study was to clarify the role of STARD10 in lipid accumulation associated with NASH in the liver. We examined the effect of STARD10 disruption on lipid accumulation in the liver of NASH model mice that were induced by choline-deficient L-amino acid-defined diet (CDAA). *Stard10*^{-/-} mice fed CDAA gained weight and epididymal fat in a manner similar to WT mice. However, the liver of *Stard10*^{-/-} mice was smaller in size and the area of lipid droplet (LD) in hepatocytes of *Stard10*^{-/-} mice was significantly smaller than those of WT mice. Gene expression levels of proinflammatory cytokines and fibrosis marker genes were significantly lower in the liver of *Stard10*^{-/-} mice compared with WT mice, suggesting that STARD10 regulates these genes through the promotion of lipid accumulation. Lysophosphatidylcholine acyltransferase 1 (LPCAT1) is an enzyme which catalyzes the conversion of lysophosphatidylcholine to

phosphatidylcholine (PC). We found that the STARD10 plays a role in promoting LD formation through the interaction with LPCAT1. We confirmed the colocalization of STARD10 and LPCAT1 at the LD membrane and their interaction. In conclusion, our study indicated that STARD10 is involved in fine-tuning the balance between PC and TG to promote LD formation in the liver through the interaction with LPCAT1.

7. Quantification of Repolarization Reserve for the Risk Prediction of Drug-Induced Arrhythmia

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A number of drugs under development and in clinical use turned out to induce arrhythmia and were withdrawn from the market. Drug-induced arrhythmia is mainly accounted for by block of one type of repolarizing K^+ currents in cardiac myocyte called I_{Kr}. However, the risk of drug-induced arrhythmia differs among various I_{Kr} blockers because normal repolarization of membrane potential in myocyte is determined by multiple and redundant mechanisms. Currents other than I_{Kr} can compensate the blocked I_{Kr}. This compensation for repolarization is called repolarization reserve. The vaguely defined concept was used only for a qualitative explanation to account for different risks among drugs. Aiming at utilizing the concept of repolarization reserve for the accurate prediction of drug-induced arrhythmia, in the present study, we developed a method for quantification of repolarization reserve. We redefined repolarization reserve as a source of repolarization currents that are activated during prolonged depolarization. By using human ventricular myocyte simulation models, we searched a novel quantification method based on this definition. We calculated a new quantitative index of repolarization reserve by simulating action potential (AP) clamp with prolonged AP waveforms and the human ventricular myocyte models. The calculated index quantitatively accounted for prolongation of action potential duration (APD) under various conditions in cardiac myocytes. We also confirmed that the quantified repolarization reserve could be used to predict the prolongation of APD by different drugs. The proposed index for repolarization reserve is expected to contribute to further understanding of APD prolongation.

Therefore, our method may contribute to efficient developments of safe drugs by predicting the risk of drug-induced arrhythmia.

8. Active Learning in Toho University Faculty of Medicine

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Background: It is said that medical education in Japan is biased toward mastery of knowledge and education on skills and attitudes is inadequate. After the ECFMG statement in 2010, we have transformed from process-based education to outcome-based education that clearly shows the learning objectives. Clinical practice has improved both quality and quantity, and also in pre-clinical practice education, students are required to study memorization (knowledge) themselves. In the classes, it is required to think themselves, discuss and present themselves based on that knowledge. That is, gradually but active learning on skills and attitudes has come to be carried out. **Contents:** Even at Toho University, some lessons are focused on students thinking, discussing, and presenting themselves rather than acquiring knowledge. Active learning classes are being developed in humanity education (whole-human medical personnel education), which are being conducted from 1st to 6th year, integrated social medicine practice and clinical reasoning PBL tutorial classes. In this presentation, we will introduce the active learning class in our university. **Conclusion:** Active learning is progressing not only in our university but also in medical school in Japan. Further improvement is also required at our university so as not to miss the trend of medical education of the world.

Poster

1. Pathogenic Role of Resistin in Rheumatoid Arthritis

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Background: Adipose tissue synthesizes and releases physiologically active molecules that are known as adipokines. Resistin, an adipokine, has been widely studied the regulation of glucose homeostasis and insulin sensitivity. Moreover, resistin also plays an important role of inflammation. We previously reported that serum level of resistin correlated with the disease activity of rheumatoid arthritis (RA). However, the pathogenic role of resistin has not been elucidated. In this study, we examined the stimulatory effect of resistin on fibroblast-like synoviocytes (FLSs) form RA patients. **Methods:** Expression of resistin and the receptor, adenylyl cyclase-associated protein 1 (CAP1), in the synovial tissue from RA and osteoarthritis (OA) was examined by immunohistochemistry. FLSs were incubated with resistin for 18 hours. Then, total RNA was extracted, and the gene expression profile was analyzed by RNA sequencing. Concentration of chemokines in the culture supernatant was determined by enzyme-linked immunosorbent assay (ELISA). Expression of CAP1 was examined by RT-PCR and Western blotting. To verify signaling of resistin via CAP1, we transfected siRNA for CAP1 before stimulation with resistin. **Results:** Resistin and CAP1 was abundantly expressed in the RA synovial tissue. Resistin expression was minimal in the OA synovium. Double immunofluorescence staining revealed that CD68-positive macrophages expressed resistin in RA synovium. CAP1 was expressed by cadherin-11-positive FLSs in RA. RT-PCR and Western blotting showed that *in vitro* cultured FLSs also expressed CAP1. RNA sequencing revealed that expressions of 18 genes, including 7 chemokines (CXCL1, CXCL2, CXCL3, CXCL5, CXCL6, CXCL8 and CCL2), from RA FLSs were increased more than 2 folds by stimulation with resistin. Production of CXCL8 and CCL2 in the culture supernatant of FLSs was increased by resistin. Transfection with CAP1 siRNA suppressed resistin-induced CXCL8 production by FLSs. **Conclusion:** Resistin might play an important role in the pathogenesis of RA via upregulation of chemokine production in the synovial tissue.

2. SATB1 Deficiency in Mice Leads to Sjögren's Syndrome-Like Autoimmune Exocrinopathy

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Sjögren's syndrome (SS) is a chronic autoimmune disease in which the patient's lymphocytes infiltrate and destroy the lachrymal and salivary glands. However, the molecular mechanism of SS pathogenesis is poorly understood. SATB1 (Special AT-rich sequence binding protein-1) is a genome organizer that regulates chromatin structure and gene expression. SATB1 conditional knockout (SATB1cKO) mice, in which SATB1 gene is specifically deleted in hematopoietic cells are autoimmune prone with age caused at least in part by defective thymic central tolerance (Kondo M., Tanaka Y. et al, J. Immunol. 196: 563-572, 2016). Furthermore, we uncovered SS-like symptoms developed in young SATB1cKO mice. In this study, we analyzed the detail of the SS-like symptoms in SATB1cKO mice. We found that mononuclear cell infiltration into salivary gland and production of saliva was significantly lower even at young age (4 weeks) in SATB1cKO mice. Female mice manifested with an earlier onset of the disease than male mice, suggesting that female mice are more susceptible to SS. Interest-

ingly, these young SATB1cKO mice did not produce some autoantibodies which are increasing in elder SATB1cKO mice and in patient with SS. In addition, we did not observe mononuclear cell infiltration into other organs and immune-complex-mediated glomerulonephritis in young SATB1cKO mice. These results indicate that young SATB1cKO mice may be useful as a new animal model for the SS. We discuss the scheme of autoimmune disease progression especially the early stage of SS.

3. Extent of Bacterial Contamination of Electronic Warm Water Bidet Toilets in a University Hospital Setting

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Background: Bidet toilet seats feature electric toilet seats with a nozzle spraying warm water to the genitalia, anal, and perianal area. In recent years, installation of bidet toilets within hospitals in Japan has raised concerns regarding potential for cross-contamination by antimicrobial resistant bacteria from patients who are hospitalized over an extended period. **Methods:** All 292 electronic bidet toilets at a university hospital were sampled for contamination. Swabs for culture were used to sample water-jet nozzles, and seats. Following incubation, colonies were identified, and antimicrobial susceptibility testing was performed. Identification of antimicrobial resistant bacteria including methicillin-resistant *Staphylococcus aureus* (MRSA), and extended-spectrum β-lactamase (ESBL) producers was performed. Pulsed field gel electrophoresis (PFGE) was also performed on the isolates. **Results:** Of the 292 bidet toilet seats sampled, warm water nozzles of 254 (86.9%) were found to be contaminated by one or more of the following organisms: *S. aureus*, *Streptococcus* sp., *Enterococcus* sp., Enterobacteriaceae, and non-Enterobacteriaceae gram-negative bacteria. *S. aureus* was recovered from one water-jet nozzle and 9 toilet seats of which MRSA was found in a water-jet nozzle, and a toilet seat. Both nozzle and seat of the same toilet were contaminated with a CTX-M-9 group ESBL-producing *Escherichia coli* with an identical PFGE band pattern. *Pseudomonas aeruginosa* was isolated from 6 water-jet nozzles, and *Acinetobacter* species was isolated from 7 water-jet nozzles, and toilet seat. Of the gram-

negative isolates recovered from samples, the organism with the highest frequency of isolation was *Stenotrophomonas maltophilia* which was recovered from 39 toilets. **Conclusion:** Warm-water nozzles of bidet toilets are contaminated with a wide range of bacteria making it a potential vehicle of cross-infection. In the hospital setting, shared use of bidet toilets must consider the clinical background of the patient. Based on our findings, these devices must be part of the risk management program and include steps for monitoring and disinfection.

4. Electropharmacological Effects of Antibiotic Azithromycin in *Microminipigs*: Propose of New Potential Mechanisms for Lethal Arrhythmia Leading to Sudden Death

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Background: Azithromycin has been reported to increase the cardiovascular risk and sudden cardiac death in the patients with high baseline risk, which raised concerns for its arrhythmogenic potential. Although azithromycin suppresses I_{Na}, I_{Kr}, I_{Ks}, I_{CaL} and I_{K1} in the heart, its electropharmacilogical effect leading to the onset of lethal arrhythmias is not fully investigated. **Methods:** Using an extraordinary small size of miniature pigs; *microminipigs*, weighing approximately 10 kg (male, n=4), we examined electropharmacological effects of azithromycin in doses of 0.3, 3 and 30 mg/kg under the halothane anesthesia, which were intravenously infused over 10 min with an interval of 20 min. **Results:** The low dose did not alter any of the cardiovascular variables. The middle dose significantly shortened the QT interval and QTc for 10-30 min, whereas it tended to increase the heart rate for 10-20 min. The high dose significantly decreased the mean blood pressure for 5-15 min, prolonged the QRS width at 15 min but shortened the QT interval at 15 min, whereas it tended to increase the

heart rate for 5-15 min. **Conclusion:** Prolongation of the QRS width by the high dose indicates that azithromycin may suppress ventricular I_{Na} *in vivo*, which may unmask Brugada electrocardioghraphic genotype in susceptible patients. Meanwhile, abbreviation of the QTc by the middle dose might cause potentially lethal, short QT-related, cardiac arrhythmia syndrome.

5. JNK Signaling Dynamics Controls Cytokine Expressions

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JNK (c-jun N-terminal kinase) plays key roles in inflammatory response. Therefore dysregulation of JNK is known to cause neurodegenerative diseases or malignant transformation of cells. Previous studies reported that transient JNK activation causes survival response, while sustained JNK activation is responsible for apoptosis. However, how JNK signaling controls multiple cellular functions is unclear because information of JNK activity in live cells is missing. Here, we focused on the relationship between JNK signaling dynamics and downstream gene expression. To understand JNK signaling dynamics, we visualized JNK activity in HeLa cells by using a novel FRET reporter. We then applied repetitive IL-1β (10 ng/ml) stimulation to the cells to analyze the regulation of JNK activity. In the repetitive IL-1β stimulation experiment, the amplitude of JNK activity became higher when stimulation pulses were given at low frequency, but not at high frequency. To understand the relationship between JNK dynamics and downstream gene expressions, we determined IL-6 and IL-8 mRNA expressions by periodic IL-1β stimulation. JNK activity could be varied depending on the temporal patterns of IL-1β stimulation. IL-1β-dependent activation of IL-6 and IL-8 were suppressed in the presence of JNK inhibitor SP600125 (20 μM). When the expression of IL-6 and IL-8 were induced by repetitive IL-1β pulse stimulation, the mRNA expression levels were increased in proportional to the frequency but not to the total exposure time of the IL-1β stimulation. Our data clearly indicate that JNK is dynamically regulated in living cells, and the temporal pattern of JNK activity determines downstream cytokine expression.

6. Amitriptyline May Have Possibility to Induce Brugada Syndrome Rather than Long QT Syndrome

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Background: Amitriptyline is a tricyclic antidepressant that is known to induce long QT syndrome; however, its potential to induce Brugada syndrome is less studied. We qualitatively and quantitatively analyzed the potential of amitriptyline to induce these lethal syndromes by using the halothane-anesthetized dogs (n=6). **Methods:** Amitriptyline was intravenously administered in doses of 0.1, 1 and 10 mg/kg over 10 min with 20 min interval between each dose, which would provide approximately 1, 10 and 100 times higher plasma concentrations than a therapeutic one, respectively. **Results:** The low dose hardly altered any of the cardiovascular variables. The middle dose increased the heart rate, cardiac output and left ventricular contractility, but decreased the total peripheral vascular resistance and left ventricular end-diastolic pressure, whereas it did not alter any of the electrocardiographic variables. The high dose decreased the mean blood pressure and left ventricular contractility; suppressed atrioventricular nodal and intraventricular conduction; shortened the repolarization period without altering the J-T_{peak}c and T_{peak}-T_{end}; and prolonged the effective refractory period, providing post-repolarization refractoriness in addition to the enhancement of the middle dose-induced cardiovascular effects. **Conclusion:** Amitriptyline at up to 100 times its therapeutic concentration may not be associated with the onset of long QT syndrome, but may induce Brugada syndrome.

7. A Novel Drug Candidate for Atrial Fibrillation: Cardiovascular Effects of M201-A in Canine Models

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Background: Most of antiarrhythmic drugs for atrial fibrillation alter the electrophysiological profile of both atrium and ventricle. M201-A is a 1,4-benzothiazepine derivative that inhibits both $I_{K,ACh}$ and I_{Kur} which were known to be selectively expressed in atrium. In this study, we simultaneously assessed the pharmacological and adverse effects of M201-A using 2 types of *in vivo* canine models. **Methods:** [Exp. 1] We administered M201-A in doses of 0.03, 0.3 and 3 mg/kg i.v. over 10 min to the halothane-anesthetized dogs to evaluate its cardiohemodynamic and electrophysiological effects (n=4). [Exp. 2] We administered M201-A in doses of 1 and 3 mg/kg i.v. over 10 min to the chronic atrioventricular block dogs to assess its torsadogenic potential (n=4). **Results:** [Exp. 1] The low dose did not alter any of the cardiovascular variables. The middle dose prolonged the QTc without altering the other variables. The high dose increased the mean blood pressure, shortened the AH interval and prolonged the QTc and atrial effective refractory period without altering the other variables including the ventricular effective refractory period. [Exp. 2] Both doses prolonged the QTc, but did not alter QT interval, short-term variability of repolarization or the number of ventricular contractions. No torsade de pointes was detected during the experimental period. **Conclusion:** These results indicate that M201-A exhibits preferable pharmacological characters, i.e. high atrial specificity and lack of proarrhythmic potential, as a novel drug candidate for atrial fibrillation. Further studies using persistent atrial fibrillation model would be helpful to test its efficacy against atrial fibrillation.

8. Pharmacological Effects of Mongolian Medicinal Plant *Adonis mongolica* on Cardiovascular System

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Background: *Adonis mongolica* (Ranunculaceae) is one of endemic plants in Mongolia and has been used as a medicinal herb in Mongolian traditional medicine to treat patients with congestive heart failure showing tachycardia and edema. Although the plant has been empirically used, the precise information regarding its cardiovascular profile is still limited. **Methods:** We assessed the cardiohemodynamic and electrophysiological profile of the water-soluble extract of *Adonis mongolica* using the guinea-pig *in vivo* model (n=4) and in vitro preparation (n=4-17). In addition, the onset mechanism of the extract-induced effects on the heart was pharmacologically analyzed (n=4-5). **Results:** The extract exerted the positive chronotropic and inotropic, negative dromotropic, and vasopressor effects in addition to the proarrhythmic action, which were similar to the cardiovascular profile of cardiac glycosides. Also, liquid chromatography-mass spectrometry analysis showed that water-soluble extract of *Adonis mongolica* contained eight kinds of cardiac glycosides. **Conclusions:** These results indicated that cardiac glycosides in the water-soluble extract of *Adonis mongolica* may explain currently observed various cardiovascular

effects.

9. Asian Dust and Pediatric Emergency Visits Due to Bronchial Asthma and Respiratory Diseases in Nagasaki, Japan

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Background: The adverse health effects of Asian dust on the respiratory system of children are unclear. We hypothesized that Asian dust events may lead to increased visits by children to emergency medical centers due to bronchial asthma and respiratory diseases including bronchial asthma. **Methods:** We used anonymized data on children receiving primary emergency treatment at Nagasaki Municipal Primary Emergency Medical Center, Japan between March 2010 and September 2013. We used Light Detection and Ranging (LIDAR) data to assess Asian dust exposure and performed time-stratified case-crossover analyses to examine the association between Asian dust exposure and emergency visits. The main analysis was done with data collected from March through May each year. **Results:** The total number of emergency visits was 756 for bronchial asthma and 5,421 for respiratory diseases, and the number of "Asian dust days" was 47 during the study period. In school children, Asian dust events at lag3 and lag4 were associated with increased emergency visits due to bronchial asthma with odds ratios of 1.837 (95% Confidence Interval, 1.212-2.786) and 1.829 (95%CI, 1.179-2.806), respectively. Asian dust events at lag0, lag1 and lag2 were significantly associated with respiratory diseases among preschool children with odds ratios of 1.244 (95%CI, 1.128-1.373), 1.314 (95%CI, 1.189-1.452) and 1.273 (95%CI, 1.152-1.408), respectively. These associations were also significant when the results were adjusted for meteorological variables and other air pollutants. **Conclusions:** The study findings suggested that Asian dust exposure increased emergency visits by children.

10. Characteristics of Outpatients with Medically Unexplained Symptoms at a University Hospital, Considering Age

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Background: Diseases characterized by severe pain and other disorders exhibit so-called medically unexplained symptoms (MUS). The characteristics of patients with MUS are largely unexplained. In this presentation, the characteristics of a series of new patients with MUS, treated at a Japanese university hospital, are discussed. **Methods:** Patients who visited the Department of Psychosomatic Medicine, Toho University, Omori Medical Center, between January and December of 2015, were enrolled. We evaluated the following, considering age as a factor; correlation between MUS and sex, academic background, chief complaints, reasons for visiting the medical center, diagnosis, symptoms, presence or absence of a referral form, continued treatment after the first visit, and marital status at the time of the respective examination. **Results:** Of the patients studied, 70% displayed MUS; 10% were defined as having functional somatic symptoms and 70% had somatization associated with a mood or anxiety disorder. Digestive symptoms were reported in 30% of patients, headaches occurred in 25%, and unusual sensations in 20%. In patients of a younger age, there was no correlation between MUS and the patients' academic background, reason for visiting the medical center, referral form, marital history, or medical history after the first visit to the medical center. However, a positive correlation did exist between MUS and the reason for visiting the medical center, referral form, and medical history after the first visit. **Conclusion:** Many patients that present with MUS, regarding age, were referred to us from other hospitals and continued to receive medical services at the university hospitals. We concluded that patients who were difficult to diagnose or treat were referred the Department of Psychosomatic Medicine at Japanese university hospitals; therefore, these hospitals must prevent mistaken diagnoses by conducting effective psychological treatment and thorough medical examinations.

11. Glucocorticoid Therapy Causes Contradictory Changes of Serum Wnt Signaling-Related Molecules in Systemic Autoimmune Diseases

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Background: The objective of this study was to investigate the clinical significance of the Wnt/β-catenin signaling pathway in glucocorticoid-induced osteoporosis. **Methods:** A total of 91 patients with systemic autoimmune diseases who received initial glucocorticoid therapy with prednisolone (30-60 mg daily) were prospectively enrolled. We measured serum levels of N-terminal peptide of type I procollagen (P1NP), tartrate-resistant acid phosphatase isoform 5b (TRACP-5b), sclerostin, Dickkopf-1 (Dkk-1), and Wnt3a before starting glucocorticoid therapy and every week for four weeks after its initiation. The effect of dexamethasone on expression of sclerostin and Dkk-1 by cultured normal human osteoblasts (NHOst) was evaluated by RT-PCR and ELISA. **Results:** Serum levels of sclerostin and Dkk-1 increased significantly by one week and then decreased from the second week onward. Serum Wnt3a tended to decrease and serum P1NP showed a significant decrease. However, TRACP-5b was significantly elevated from the first week of treatment onward. *In vitro* study, dexamethasone increased Dkk-1 mRNA expression in cultured NHOst, but sclerostin mRNA was not detected. Dexamethasone also increased Dkk-1 protein production by osteoblasts, whereas sclerostin protein was not detected. **Conclusion:** Bone formation might be impaired at least in the first week of the initiation of glucocorticoid therapy by increase of the serum Wnt signaling inhibitors, however, their reductions in the subsequent weeks were contradictory to the maintained suppression of the bone formation markers after glucocorticoid therapy for patients with systemic autoimmune diseases.

12. Epstein-Barr Virus Infection and Epstein-Barr Virus Nuclear Antigen 1 Variants in the Synovial Tissue of Rheumatoid Arthritis

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Background: Epstein-Barr virus (EBV) infection causes various malignant tumors, such as B cell lymphoma and epithelial cell cancer. Previous reports showed a certain variant of EBV nuclear antigen 1 (EBNA-1) may trigger development of the malignant cells. It was also reported that EBV infection may play a role of RA, however, underlying mechanisms remains unknown. Moreover, mutation of EBV in RA patients has not been examined. We then investigated EBNA-1 in the synovial tissue of RA. **Methods:** One hundred twenty-eight RA and 98 osteoarthritis (OA) patients undergoing joint surgery at the Toho University Omori Medical Center were enrolled. Synovial tissues were collected during surgery under sterile condition. Informed consent was obtained from all the patients. DNA was extracted from the synovial tissues. The EBNA-1 gene was determined by nested PCR. The amplicons were detected by performing electrophoresis. Nucleotide sequence of the PCR product was determined. HLA DRB1 genotyping was also performed. **Results:** EBV DNA was more frequently detected in the synovial tissue from RA (32.8%; 42 of 128) than OA (15.3%; 15 of 98) (p<0.01, chi-squared test). The sequence of EBNA-1 revealed Japanese prototype (V-Val subtype) in 35 of the 42 RA (83.3%) and 13 of the 15 OA (86.7%). Although four other subtypes were also detected in small number of patients, there were no significant differences between RA and OA. Frequency of HLA-DRB1*0405, *0410, *1001 (shared epitope: SE) was significantly higher in RA (55.5%) than OA (30.6%). Proportion of EBV-positive tended to be higher in SE-positive (39.4%; 28 of 71) than SE-negative (24.6%; 14 of 57), although it is not statistically significant. **Conclusion:** EBV might be an environmental risk factor for development or chronic synovitis of RA. However, nucleotide mutations of EBNA-1 may not contribute it.

13. Multimodal Team Approach to Failed Back Surgery Syndrome with Spinal Cord Stimulation

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Background: Failed back surgery syndrome (FBSS) is a condition in which improvement of symptoms is poor or worse after of spinal surgery. In the pain clinic, one of the innovative treatment is spinal cord stimulation therapy (Spinal Cord Stimulation: SCS), but evaluation methods have not been established. **Methods:** From September 2015, team intervention was performed on five lumbar FBSS patients who underwent SCS. As an effect judgment of SCS, in addition to the degree of improvement of pain by our department, the gait function was evaluated in the Department of Rehabilitation. **Results:** After SCS, 4 cases obtained pain relief, and also showed reduction of QOL-disability and improvement of intermittent claudication. Only one case described no change of pain score but showed highly improvement of gait performance. Numerical Rating Score (NRS) as a change (median ± SD) before surgery/three months after surgery: $7.8 ± 2.9/2.8 ± 1.9$, 6 min walking test as walk function: $334 ± 119/394 ± 81$ (m), Walking maximum speed: $77 ± 19/85 ± 23$ (m/min). Roland-Morris Disability Questionnaire (RMDQ) and Oswestry Disability Index were showed a reduction in daily living disorders in all patients. **Conclusion:** Comprehensive assessment focused not only on pain assessment but also on walking ability and daily living is effective for scientific demonstration of SCS.

14. Alteration in Plasma and Striatal Levels of D-Serine after D-Serine Administration with or without Nicergoline: an *in vivo* Microdialysis Study

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Background: D-Serine (D-Ser), a co-agonist of *N*-methyl-D-aspartate receptor (NMDAR), is effective for treating schizophrenia. In the present study, we investigated changes in plasma and striatal D-Ser levels in Sprague-Dawley (SD) rats after intraperitoneal D-Ser administration alone or together with nicergoline (Nic), a commercial cerebral ameliorating drug, using *in vivo* microdialysis (MD) to explore the pharmacological function of Nic. **Methods:** Phosphate-buffered saline (PBS) or Nic (0, 1.0, or 3.0 mg/kg) followed by D-Ser (5.0, 10.0, 20.0, and 50.0 mg/kg for PBS or 20.0 mg/kg for Nic) was administered intraperitoneally to male SD rats, and the profiles of D-Ser levels in plasma and striatal MD samples were examined by high-performance liquid chromatography (HPLC) with fluorescence detection. The area under the curve (AUC) for the MD and plasma samples was also calculated and statistically compared among the groups. **Results:** AUC values of D-Ser were increased in a D-Ser dose-dependent manner in plasma samples, while a proportional increase in the AUC values of striatal MD samples was only observed in D-Ser doses up to 20.0 mg/kg. The Nic co-administered group showed a significant increase in the AUCs of plasma D-Ser in a Nic dose-dependent manner, but the AUCs in striatal D-Ser were significantly decreased with increasing Nic doses, suggesting that Nic may prevent excess D-Ser from penetrating the central nervous system (CNS). **Conclusion:** Nic may prevent an excessive distribution of exogenous D-Ser, such as that from a dietary origin, into the CNS to suppress an excitatory neurotransmission through NMDAR.

15. Analyses of Endogenous Metabolites in Serum from at-Risk Mental State Subjects

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Background: It has recently been reported that the levels of some endogenous compounds were altered in serum of patients with schizophrenia as compared with those of healthy controls,[1] and these compounds may be expected as biomarkers for schizophrenia. Schizophrenia reaches the onset as a prodrome via psychotic at-risk mental state (ARMS), however, there have been few

reports on the serum concentrations of endogenous compounds in ARMS phase. In the present study, serum concentrations of endogenous compounds, L-tryptophan (L-Trp), L-kynurenine (L-KYN), 5-hydroxytryptamine (5-HT), D-, L-lactate, glucose, between ARMS and healthy subjects were compared. **Methods:** Written informed consent was obtained from all subjects prior to participation, and the protocol was approved by both of the ethics committee in the Faculty of Pharmaceutical Sciences (No. 26-4) and the Faculty of Medicine (No.26012), Toho University. ARMS subjects (6 males and 8 females) and healthy volunteers (8 males and 17 females) were recruited with their informed consent. Glucose was measured using a commercial kit, glucose CII-test Wako. All compounds except glucose were determined by HPLC with fluorescence detection or LC-MS/MS. **Results:** Although there were no significant differences of serum levels of 5-HT, L-KYN, glucose, and D-, L-lactate between ARMS subjects and healthy controls, the serum levels of L-Trp, a precursor of L-KYN and 5-HT, were significantly increased in the ARMS subjects $(p = 0.010)$. **Conclusion:** The present results are consistent with previous report describing that the levels of serum L-Trp were significantly increased in patients with schizophrenia[1] and suggested some association between L-Trp and onset of schizophrenia. In addition, the correlation between levels of these compounds in serum and clinical scores of ARMS subjects are also presented.

Reference: 1) Fukushima T. *et al*. *PLoS One*. 2014 9(7): e101652.

16. Quick and Easy Preparation Method for Kampo Formula Decoctions (Part 4): IPCD Method for Rhubarb and Aconite Root

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Background: The immersing powdered crude drugs (IPCD) method has been developed as a quick, easy and high-yielding method for preparing decoctions. Given that the extraction process is different from the conventional decoction method, the safety of this method should be carefully examined. In the present study, the amounts of the diester alkaloids of aconite root, the tuberous root of Aconitum carmichaeli, and sennoside A of rhubarb, the rhizome of Rheum palmatum, were determined in the IPCD immersion. Both of these compounds have strong physiological activities and have been suggested to be decomposed during the decoction process. **Methods:** The amounts of marker compounds in the IPCD immersion prepared from processed or unprocessed aconite root or rhubarb were measured and compared with those prepared using the conventional decoction method. **Results:** The amount of sennoside A extracted with the IPCD method was 1.1-fold increased compared with that from theconventional method. No diester alkaloids were detected in the IPCD immersion prepared from processed aconite root, whereas for unprocessed aconite root, the amount of diester alkaloids extracted from the IPCD immersion was 8.8-fold higher than that from the conventional decoctions. **Conclusion:** The IPCD method can be safely used on rhubarb or well-processed aconite root under the same conditions as other less-powerful crude drugs, whereas precautions are required for unprocessed aconite root.

17. Application of AMSAT to Kampo Examination: Prescription Decision of Yokukansan and Kousosan

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Background: Prescription of Kampo medicines is decided by patterns from four examinations, including Inspection, Listening and smelling, Inquiry, and Palpation. Prescription decision of Kampo medicines is always difficult for whom not being a Kampo medical specialist. Thus, we paid attention to the application of "Auto Mastic System for Analysis Therapy" (AMSAT), which can visualize the function of the whole body, to Kampo examination. Herein, we reported the application of AMSAT in prescription decision of Yokukansan and Kousosan, which are representative Kampo medicines for the treatment of mental illness. **Methods:** We chose patients who com-

plained about anxiety and frustrating, and whose prescriptions were Yokukansan (also include Yokukansan-Kachinpihange) (16 patients) and Kousosan (6 patients) in Kichijoji-Touhou Clinic. We checked their body function through "BASE" and "Colloidal-Shift". BASE is used for checking the function of whole body, and Colloidal-Shift is used for checking the hardness of cytoplasm. **Results:** In all cases, Colloidal-Shift showed from yellow to red color at their head. The patients, who were prescribed Kousosan, showed stress level at 1-2. On the other hand, 8 out of 16 cases, who were prescribed Yokukansan, showed the highest stress level at 4, and BASE showed blue color at their head. This observation was not found in the cases of Kososan. Among five re-visit patients, who were prescribed Yokukansan, they were found improvement of the stress level, and BASE was showed from blue to green or yellow at their head. This indicted the possibility of that therapeutic improvement by Yokukansan may be observed through AMSAT. **Conclusion:** AMSAT maybe a useful tool for prescription decision of Yokukansan against mental illness.

18. Identification of Caffeoylquinic Acid Derivatives as Protein Tyrosine Phosphatase 1B Inhibitors from *Artemisia princeps*

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Background: PTP1B ubiquitously expressed in classical insulin targeted tissues, and has received extensive attention as important target enzyme for the treatment of insulin resistance diseases, as the PTP1B plays critical roles in negatively regulating insulin- and leptin-signaling cascades. These have led to an intense interest in developing PTP1B inhibitors as potential therapies for diabetes. *Artemisia princeps* Pamp. (Asteraceae), is widely distributed in Asian. It is used in traditional medicines for the treatment of inflammation, gastric ulcer, and many circulatory disorders. The aim of the present study is discovery of novel natural PTP1B inhibitors from *A. princeps.* **Methods:** The aerial parts of *A. princeps* were extracted with MeOH and then separated with multiple column chromatography and semi-preparative HPLC, which led to the isolation of ten caffeoylquinic acid derivatives. The chemical structures of these compounds were determined by NMR and MS spectra. The potentials of compounds as PTP1B inhibitors were evaluated by enzyme kinetic, molecular docking simulation, inhibitory selectivity against other PTPs (e.g., SHP-1, SHP-2, VHR and TC-PTP). **Results:** All isolated compounds exhibited above 60% inhibition of PTP1B at 100 μM. These compounds inhibited PTP1B in a concentration dependent manner, and their IC_{50} values were determined by regression analyses. Among them, chlorogenic acid **(3)** was the most potent (IC_{50} 11.13 μM). Further investigation demonstrated that **3** is a noncompetitive inhibitor by kinetic analysis, and molecular docking simulation. **3** also showed inhibitory selectivity between PTP1B and omologous PTPs (SHP-1, SHP-2, and VHR). **Conclusions:** Chlorogenic acid from *A. princeps* is a natural PTP1B inhibitor and might be potentially valuable for further investigation of anti-diabetic effect.

19. Simultaneous Quantification of Surfactants in Environmental Samples by LC-MS

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Background: Recently, surfactants are more frequently synthesized in larger quantities. Even after water treatment, a part of these compounds ends up in surface waters. Although there is no evidence for accumulation, the determination of surfactants is important for environmental analysis. In this study, we developed a simultaneous determination method for cationic surfactants (CS), anionic surfactants (AS) and nonionic surfactants (NS) in river water, sediment and shellfish using liquid chromatography mass spectrometry (LC-MS). **Methods:** Standard solutions were prepared ranging between 250-2000 ppb for AS, 0.9-18 ppb for CS and 200-800 ppb for NS. For analysis, LC-MS with electrospray ionization in positive and negative modes was used. The column used was a Shodex MSPak GF-310. A gradient elution method was used with acetonitrile. In selected-ion monitoring (SIM), $[M]^+$, $[M]^-$ and $[M+Na]^+$ were used for detection of AS, CS and NS, respectively. Solid phase extraction (SPE) was used as pre-treatment to separate surfactants from sample matrix. For validation, among other, recovery after SPE treatment using standards was determined. Environmental samples were collected from Kisarazu-shi, Chiba-ken. **Results and Conclusion:** 3 CS, 4 AS and 14 NS compounds are simultaneously determinable with the developed method. Validation showed poor

range for 1 NS, while recovery was positive for the rest. CS and AS ions, [M]⁺ and [M]⁻, were detected by ESI⁺ and ESI⁻ at retention times between 9 and 13 min and between 26 and 31 min, respectively. The sodium adduct ions [M+Na]⁺ of NS were detected by ESI⁺ at the retention times between 8.5 and 29.5 min. Surfactants were successfully extracted with the SPE method and showed possible accumulation of CS in sediment and Asari shellfish.

20. Concentration of PAHs in the Excrement of Annelids

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Background: Polycyclic aromatic hydrocarbons (PAHs) occurred in any combustion processes and derived from fossil fuels diffuse in the environment. Some of PAHs are mutagens, carcinogens, or endocrine disruptors and hence it is important to grasp the kind and amount of hazardous PAHs and to recognize their movement in the environment. In a previous study, we measured PAH concentrations in sediments and in benthos and their excrements, which were collected from the Yoro tidal flat in Japan. In the course of the study, we found interesting phenomena, bioaccumulation and biodegradation of PAHs in the excrement of an annelid, *Marphysa sanguinea*. In the present study, to clarify the bioaccumulation feature of PAHs in the excrement of *M. sanguinea*, we analyzed the PAH concentrations in sediment, excrements after excreted by annelid, and excrements in annelid's body. **Methods:** Samples; sediments, annelids and excrements; were collected in the Yoro tidal flat (Ichihara, Chiba, Japan). These samples were pretreated by acetone extraction, alkaline decomposition, and hexane extraction, and purified by silica gel column chromatography. Concentration of PAHs in samples was measured by gas chromatograph-mass spectrometer (GC-MS). Phenanthrene, anthracene, fluoranthene, pyrene, chrysene, benzo[*b*]fluoranthene, benzo[*a*]pyrene, and perylene were selected as target compounds. Deuterium-labeled PAHs were used as surrogate standards for determining the recovery rates of PAHs in the sample preparation procedure. *p*-Terphenyl-d_{14} was used as an internal standard. **Results and Conclusion:** PAH concentrations of samples, sediments and excrements of annelids, significantly differed according to the sampling date and location. The excrement of annelid contained PAHs at concentrations approximately 8 to 200 times that found in the sediments. These results indicate that the accumulation of PAHs is usually occurred in the excrements of *Marphysa sanguinea*.

21. Biodegradation of PAHs by Microorganisms Isolated from the Excrement of *Marphysa sanguinea*

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Background: Polycyclic aromatic hydrocarbons (PAHs) are ubiquitous environmental pollutants generated during the incomplete combustion of organic materials. Since PAHs are potential mutagens, carcinogens, or endocrine disruptors, it is important that they are degraded effectively. In our previous studies, we discovered an interesting phenomenon in which PAHs showed rapid degradation in the excrement of *Marphysa sanguinea*. To clarify the mechanism underlying the rapid degradation of PAHs in the excrement of *M. sanguinea*, pyrene (Pyr)-degrading microorganisms were isolated and examined their abilities to degrade PAHs *in vitro*. **Methods:** Excrements of *M. sanguinea* were collected in the Yoro tidal flat (Ichihara, Chiba, Japan), and Pyr-degrading microorganisms were isolated from the excrement using a selected medium containing Pyr as the sole carbon source. Isolates cultured on the agar plates containing 50 mg L⁻¹ Pyr and incubated at 28℃ for 7 days. Then, the colonies of isolates were suspended into a liquid medium without Pyr. Samples were extracted from the medium with 1 mL of hexane and acetone after 0, 3, 8, 10 days, and the concentrations of Pyr in samples were monitored by gas chromatograph-mass spectrometer (GC-MS). GC-MS analyses were performed on a Shimadzu GC-2010 equipped with a capillary column (Rtx-5MS, 30 m length, 0.25 mm diameter). **Results and Conclusions:** Pyr levels were gradually decreased in the media in which these microorganisms were cultured. Approximately 20-70% of the Pyr was removed after 9 days of incubation and 1-hydroxypyrene, a Pyr metabolite, was detected in the media. The Pyr degradation ratio of individual microorganisms in the media was lower than that in the excrement; thus, these microorganisms likely comprise a part of a Pyr-degrading consortium in PAH-polluted environments.

22. Needs Survey of Faculty Members at Educational and Research Institutions on Child-Raising and Elderly Care

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Background: Toho University have put effort into support activities on child-raising and elderly care throughout female physician supports and promotion activities of gender equality. Our university adopted many kinds of support systems such as dispatch program of research support staff, and sick child care services prior to other universities in Japan. However, there are still many issues to keep a good balance among work and child-raising and elderly care. In Japan, female researchers account for only a small portion in the overall faculty members. Our university was adopted "Program to supporting research activities of female researchers" with two institutions in 2015, and this opportunity enables us to facilitate female researches supports. Three institutions conducted a needs survey on child-raising and elderly care, and the present poster shows results of Toho University. The purpose of the survey was to clarify things necessary for good balance between work and home life. **Methods:** The survey was conducted in 2017, and 833 faculty members participated. They were asked to answer self-completed anonymous questionnaires (41questions) that included demographic data and needs for child-raising and elderly-care using a three or four-point scale. **Results:** The response rate was 26.9% (224 faculty members), and 37.5% (84 faculty members) were female. The highest response rate was 42.4% among the age group of 41-50 years old. One hundred and seventy-five (78.1%) were married, 154 (68.7%) have more than one child, and 56 (25%) have a family with needed long-term care. Female subjects feel that there are "needs" regarding child-raising and elderly-care rather than male subjects (independent t-test). Also, the results suggest understandings of family members and workplaces are placed great significance on child-raising as well as child care support systems such as a nursery school and a parental leave. Moreover, the results suggest understandings and actual support of family members and

understandings of workplaces are placed great significance on elderly care. Finally, results of independent t-tests showed that more female subjects feel very difficult balancing their family and job especially in child-raising of school children and elderly care.

23. Supporting Activities for Women Researchers in Toho University

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Toho University started as the Imperial Women's Medical College in 1926. It has since laid the foundation for Japanese women to receive higher education in medicine and biological science. The University has produced many talented women researchers including Dr. Katsuko Saruhashi who established the Saruhashi Award to give to women who made their distinguished research results. The University has been still developing the educational system for highly-skilled medical professionals such as doctors, pharmacists, nurses, and others engaged in the natural science field. According to the Basic Law on Science and Technology promulgated in 1995, Japan has settled on a concrete 5-year support plan for women researchers. In 2008, the University set up the support office for women, and established the program to help "junior doctors on training" who tend to leave their workplaces, influenced by the idea of "All or None." In 2009, under the initiative of "Promoting Role Models to Support Female Researchers" of the Ministry of Education, Culture, Sports, Science and Technology (MEXT), the University started the "day care center for children with infections," a "discount coupon for babysitting services" and a temporary staffing service sending an "assistant" to women researchers handling both a career and raising children. In 2015, the University collaborated with Chiba University and National Institutes for Quantum and Radiological Science and Technology to form a tripartite project for supporting female researchers. Adopted in "the Program to Support the Research Activ-

ities of Female Researchers of MEXT," this is now the core of a Consortium. In April, 2017, we renamed into "the Center for Diversity and Inclusion" to make our efforts known more widely.