

Research Works

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● *Handbook of Dietary Phytochemicals, 1st ed. 2021.*

Xiao Jianbo (EDT), Sarker Satyajit D. (EDT), Asakawa Yoshinori (EDT),

This book summarizes recent advances in the chemistry, bioactivity, nutrition, and functional aspects of dietary phytochemicals, as well as the health and functional aspects of foods rich in phytochemicals. Consisting of forty-four chapters, it discusses the different chemical types of phytochemicals in our diets and food and presents data collected from animal or human experiments that are directly related to human health. Each chapter covers the chemistry, epidemiological study, bioavailability, bioactivity (animal experiments) function in humans and safety, as well as products on the market. Moreover, the more than 200 figures make it easy to grasp the main findings in each area.

● *In vitro Evaluation of The Effects of Cadmium on Endocytic Uptakes of Proteins into Cultured Proximal Tubule Epithelial Cells.*

Fujihiro H, Yamamoto H, Otera N, Oka N, Jinno M, Himeno S. *Toxics*. 2020;8(2):24. Published 2020 Apr 1. doi:10.3390/toxics8020024

Cadmium (Cd) is an environmental pollutant known to cause dysfunctions of the tubular reabsorption of biomolecules in the kidney. Elevated levels of urinary excretion of low-molecular-weight proteins such as β_2 -microglobulin (β_2 -MG) have been used as an indicator of Cd-induced renal tubular dysfunctions. However, very few studies have examined the direct effects of Cd on the reabsorption efficiency of proteins using cultured renal cells. Here, we developed an in vitro assay system for quantifying the endocytic uptakes of fluorescent-labeled proteins by flow cytometry in S1 and S2 cells derived from mouse kidney proximal tubules. Endocytic uptakes of fluorescent-labeled albumin, transferrin, β_2 -MG, and metallothionein into S1 cells were confirmed by fluorescence imaging and flow cytometry. The exposure of S1 and S2 cells to Cd at 1 and 3 μ M for 3 days resulted in significant decreases in the uptakes of β_2 -MG and metallothionein but not in those of albumin or transferrin. These results suggest that

Cd affects the tubular reabsorption of low-molecular-weight proteins even at nonlethal concentrations. The in vitro assay system developed in this study to evaluate the endocytic uptakes of proteins may serve as a useful tool for detecting toxicants that cause renal tubular dysfunctions.

● *Requirement of zinc transporter ZIP10 for epidermal development: Implication of the ZIP10-p63 axis in epithelial homeostasis.*

Bum-Ho Bin, Jinhyuk Bhin, Mikiro Takaishi, Koh-Ei Toyoshima, Saeko Kawamata, Kana Ito, Takafumi Hara, Takashi Watanabe, Tarou Irié, Teruhisa Takagishi, Su-Hyon Lee, Haeng-Sun Jung, Sangchul Rho, Juyeon Seo, Dong-Hwa Choi, Daehee Hwang, Haruhiko Koseki, Osamu Ohara, Shigetoshi Sano, Takashi Tsuji, Kenji Mishima, Toshiyuki Fukada, Proc Natl Acad Sci USA, 2017,Nov.14;14(46):12243-12248.doi:10.1073/pnas.1710726114.

Skin tissues, in particular the epidermis, are severely affected by zinc deficiency. However, the zinc-mediated mechanisms that maintain the cells that form the epidermis have not been established. Here, we report that the zinc transporter ZIP10 is highly expressed in the outer root sheath of hair follicles and plays critical roles in epidermal development. We found that ZIP10 marked epidermal progenitor cell subsets and that ablating Zip10 caused significant epidermal hypoplasia accompanied by down-regulation of the transactivation of p63, a master regulator of epidermal progenitor cell proliferation and differentiation. Both ZIP10 and p63 are significantly increased during epidermal development, in which ZIP10-mediated zinc influx promotes p63 transactivation. Collectively, these results indicate that ZIP10 plays important roles in epidermal development via, at least in part, the ZIP10-zinc-p63 signaling axis, thereby highlighting the physiological significance of zinc regulation in the maintenance of skin epidermis.

● *Facilitation of IKr current by some hERG channel blockers suppresses early afterdepolarizations.*

Furutani K, Tsumoto K, Chen IS, Handa K, Yamakawa Y, Sack JT, Kurachi Y. J Gen Physiol. 2019 Feb 4;151(2):214-230. doi: 10.1085/jgp.201812192.

Fatal cardiac arrhythmias are caused by some, but not all, drugs that block human ether-a-go-go-related gene (hERG) potassium channels. Currently, all new drug candidates are tested against hERG and those that block are generally neglected at the early stage of drug development process without the further assessments. This assay triages a remarkably large number of cardiac safe drugs, and the inadequacy of current hERG screening is a major

impediment to drug development. In this manuscript, I show that safe blockers facilitate channel opening in ventricular myocytes and provide a repolarization reserve to suppress arrhythmias.

● *Effect of intervention by a pharmacist after implementation of inpatient pharmaceutical service.*

Kawasumi H, Ogawa Y, Ienaga T, Isobe K, Saito T, Hakuno H. The 141st Annual Meeting of the pharmaceutical Society of Japan (Hiroshima) March 27, 2021

We investigated the content of active interventions and questions and answers conducted in each ward from April 2016 to March 2019. The rate of change due to active intervention increased from 72.0% to 79.8%. The rate of changes made by the active intervention of pharmacists is increasing year by year, and it is considered that more effective intervention has become possible. Most of the questions and answers were about injectable drugs, but the number is decreasing year by year, and it is thought that the ward activities so far have deepened the understanding of injectable drugs of other occupations.

● *Physiological roles of zinc transporters: molecular and genetic importance in zinc homeostasis.*

Hara T, Takeda TA, Takagishi T, Fukue K, Kambe T, Fukada T. *J Physiol Sci*. 2017 Mar;67(2):283-301. doi: 10.1007/s12576-017-0521-4. Epub 2017 Jan 27.

Zinc (Zn) is an essential trace mineral that regulates the expression and activation of biological molecules such as transcription factors, enzymes, adapters, channels, and growth factors, along with their receptors. Zn deficiency or excessive Zn absorption disrupts Zn homeostasis and affects growth, morphogenesis, and immune response, as well as neurosensory and endocrine functions. Zn levels must be adjusted properly to maintain the cellular processes and biological responses necessary for life. Zn transporters regulate Zn levels by controlling Zn influx and efflux between extracellular and intracellular compartments, thus, modulating the Zn concentration and distribution. Although the physiological functions of the Zn transporters remain to be clarified, there is growing evidence that Zn transporters are related to human diseases, and that Zn transporter-mediated Zn ion acts as a signaling factor, called "Zinc signal". Here we describe critical roles of Zn transporters in the body and their contribution at the molecular, biochemical, and genetic levels, and review recently reported disease-related mutations in the Zn transporter genes.

● *Structure-activity relationships of talaumidin derivatives: Their neurite-outgrowth promotion in vitro and optic nerve regeneration in vivo.*

K. Harada, K. Zaha, R. Bando, R. Irimaziri, M. Kubo, Y. Koriyama, Y. Fukuyama. *Eur. J. Med. Chem.* **148**, 86-94 (2018).

(-)-Talaumidin (**1**), a 2,5-biaryl-3,4-dimethyltetrahydrofuran lignan, shows potent neurotrophic activities such as neurite-outgrowth promotion and neuroprotection. Previously, we found that (-)-(1*S*,2*R*,3*S*,4*R*)-stereoisomer **2** exhibited more significant activity than did the natural product talaumidin (**1**). However, the preparation of optically active (-)-**2** requires a complicated synthetic route. To explore new neurotrophic compounds that can be obtained on a large scale, we established a short step synthetic route for talaumidin derivatives and synthesized fourteen analogues based on the structure of (-)-**2**. First, we synthesized a racemic compound of (-)-**2** (**2a**) and assessed its neurotrophic activity. We found that the neurotrophic property of racemic **2a** is similar in activity to that of (-)-**2**. Using the same synthetic methodology, several talaumidin derivatives were synthesized to optimize the oxy-functionality on aromatic rings. As a result, bis(methylenedioxybenzene) derivative **2b** possessed the highest neurotrophic activity. Furthermore, examination of the structure-activity relationships of **2b** revealed that the 2,5-diphenyl-tetrahydrofuran structure was an essential structure and that two methyl groups on THF ring could enhance neurotrophic activity. In addition, compounds **2a** and **2b** were found to induce mouse optic nerve regeneration *in vivo*.

● *Synthesis of 2'-C,4'-C-methyleneoxy-bridged thymidine derivatives and properties of modified oligonucleotides.*

Osawa T, Kim H, Shoji M, Saijo M, Dohi M, Ito Y, Obika S, Hari Y. *J Org Chem.* 2019 Nov 1;84(21):13336-13344.doi: 10.1021/acs.joc.9b01496.

2',4'-Bridged nucleic acid (2',4'-BNA) analogues are used for therapeutic oligonucleotides, owing to their excellent hybridizing ability with complementary RNA and high resistance toward enzymatic degradation. We developed 2',4'-BNA analogues with oxygen atoms at 6'-positions (e.g., EoNA and EoDNAs) and demonstrated that the presence of 6'-oxygen atoms in the bridge structure could show positive effect on the properties of the modified oligonucleotides. Herein, we designed and synthesized 7'-methyl derivatives of methyleneoxy-bridged 2'-deoxyribonucleic acid (MoDNA), possessing a five-membered bridge with 6'-oxygen atom via radical cyclization for the bridge construction. The synthesized monomers were incorporated into the oligonucleotides by solid-phase oligonucleotide synthesis. The MoDNA-modified oligonucleotides showed high affinity toward single-stranded RNA and double-stranded DNA, as well as excellent resistance toward nuclease compared with the corresponding natural oligonucleotide.

● *Acetylation of the influenza A virus polymerase subunit PA in the N-terminal domain positively regulates its endonuclease activity.*

Hatakeyama D*, Shoji M, Ogata S, Masuda T, Nakano M, Komatsu K, Saitoh A, Makiyama K, Tsuneishi H, Miyatake A, Takahira M, Nishikawa E, Ohkubo A, Noda T, Kawaoka Y, Ohtsuki S, Kuzuhara T*; FEBS J. 2021 Jul 16. doi: 10.1111/febs.16123.

We reported that the PA subunit of influenza A virus RNA polymerase is acetylated, resulting in accelerated endonuclease activity. The partial recombinant protein of the PA N-terminal region containing the endonuclease domain was acetylated, which facilitated its endonuclease activity. The K19 was identified as a candidate acetylation target. Substitution of the K19 with glutamine, a mimic of the acetyl-lysine, enhanced its endonuclease activity; this point mutation also accelerated influenza A virus RNA polymerase activity in the cell. PA acetylation is suggested to be important for the regulation of the endonuclease and RNA polymerase activities of the influenza A virus.

● *Renoprotective effects of a factor Xa inhibitor: fusion of basic research and a database analysis.*

Horinouchi Y, Ikeda Y, Fukushima K, Imanishi M, Hamano H, Izawa-Ishizawa Y, Zamami Y, Takechi K, Miyamoto L, Fujino H, Ishizawa K, Tsuchiya K, Tamaki T. Sci Rep. 2018 Jul 18;8(1):10858. doi: 10.1038/s41598-018-29008-2.

Renal tubulointerstitial injury, an inflammation-associated condition, is a major cause of chronic kidney disease (CKD). Levels of activated factor X (FXa), a blood coagulation factor, are increased in various inflammatory diseases. Therefore, we investigated the protective effects of an FXa inhibitor against renal tubulointerstitial injury using unilateral ureteral obstruction (UUO) mice (a renal tubulointerstitial fibrosis model) and the Food and Drug Administration Adverse Events Reporting System (FAERS) database. The renal expression levels of FX and the FXa receptors protease-activated receptor (PAR)-1 and PAR-2 were significantly higher in UUO mice than in sham-operated mice. UUO-induced tubulointerstitial fibrosis and extracellular matrix expression were suppressed in UUO mice treated with the FXa inhibitor edoxaban. Additionally, edoxaban attenuated UUO-induced macrophage infiltration and inflammatory molecule upregulation. In an analysis of the FAERS database, there were significantly fewer reports of tubulointerstitial nephritis for patients treated with FXa inhibitors than for patients not treated with inhibitors. These results suggest that FXa inhibitors exert protective effects against CKD by inhibiting tubulointerstitial fibrosis.

● *Xanthone glucoside from an insect pathogenic fungus *Conoideocrella luteorostrata* NBRC106950.*

Tatsuro Yoneyamaa , Miki Iguchia, Kento Yoshiia, Abdelsamed I. Elshamya,b ,

Sayaka Banc, Masaaki Nojia and Akemi Umeyamaa. Natural Product Research, DOI: 10.1080/14786419.2021.1883607.

Insect pathogenic fungi which belong to the order Hypocreales, such as Cordyceps and Conoideocrella species produce its fruiting body or perithecium from host insects. Conoideocrella luteorostrata (which belongs to the order Hypocreales, the family Clavicipitaceae) primarily parasite on scale insects. Insect pathogenic fungi produce an interesting variety of metabolites, but not many of them have been studied and reported so far, given the existence of about 500 species worldwide. From these reasons, we have focused on the isolation of new compounds and bioactive compounds from Cordyceps. (Grudniewska et al. 2014; Umeyama et al. 2014; Ganaha et al. 2016)

In this manuscript, we report the isolation and structural elucidation of a new 1,6-dihydroxy- 8-methyl-3-O-(4-O-methyl- β -D-glucopyranosyl) xanthone (1). There are few reports of glucose glucoside methylated at the hydroxy group of C-40 position, limited to examples from some entomopathogenic fungi and other species.

● *Total synthesis of (\pm)-spirotenuipesine A, a promoter of neurotrophic factor secretion from glial cells.*

Yanagimoto, Tsuyoshi; Yamada, Sayo; Kasai, Yusuke; Yamamoto, Hirofumi; Kubo, Miwa; Fukuyama, Yoshiyasu; Imagawa, Hiroshi, Tetrahedron Letters (2021), 64, 152723.

Naturally occurring (+)-spirotenuipesines A and B are known to promote the biosynthesis of neurotrophic factors in glial cells. Therefore, these compounds can be expected to constitute promising drug leads for neurodegenerative diseases such as Alzheimer's disease. In order to obtain sufficient amts. for biol. evaluation, (\pm)-spirotenuipesine A was synthesized via a stereoselective Ireland-Claisen rearrangement as a key step. A culture medium of 1321N1 cells treated with the obtained synthetic racemic compound showed differentiation-inducing activity against PC12 cells, resulting in a morphological change.

● *Survey on Accumulated Drug Information by Pharmaceutical Companies about Crushed or Simply Suspended Internal Medicines.*

Shiro ISHIDA, Japanese Journal of Drug Informatics, Vol.20, No.4, 2019, pp.220-226.

Objective : We conducted a survey on drug information accumulated by pharmaceutical companies about the adequacy of applications of crushed or simple suspended internal medicines through enteral feeding tube, examination method to confirm adequacy and inquiry from medical institutions to pharmaceutical companies about the adequacy of these methods.

Methods : We sent a questionnaire to 162 pharmaceutical companies that sell internal

medicines to collected information. The survey was conducted from May 1, 2016 to March 31, 2017.

Results: The questionnaire response rate was 61% (99 companies responded). Eighty and 90 percent of the companies possessed information about the drug crushing methods and simple suspension methods used for administration of internal medicines, respectively. The type of information and the examination methods used varied among the companies, was very limited, and was often limited to new drugs. The information acquisition rate about crushing methods was 69.3% in original examination methods of pharmaceutical companies. On the other hand, 90.3% of the information about simple suspension methods was obtained by the unified method of Hand Book of Simple Suspension Method.

Conclusions: In the future, medical practice and patients will benefit if examination methods to confirm the adequacy of crushing and administration through feeding tubes are commonly and consistently obtained by pharmaceutical companies. Furthermore, it would be very useful for information of crushing methods and simple suspension methods to be included in package inserts and interview forms.

● *Synthesis of the methyl analog of 2'-O,4'-C-ethylene-bridged 5-methyluridine via intramolecular radical cyclization and properties of the modified oligonucleotides.*

Yuta Ito, Norika Tsutsui, Takashi Osawa, Yoshiyuki Hari. *J. Org. Chem.* 2019 Jul 19;84(14):9093-9100.doi:10.1021/acs.joc.9b01035.

The synthesis of 6'*S*-Me-2'-O,4'-C-ethylene-bridged 5-methyluridine (6'*S*-Me-ENA-T) was achieved using visible light-mediated stereoselective radical cyclization as a key step. This is the first example of a method for constructing a 2',4'-bridged structure from a 4'-carbon radical intermediate. The 6'*S*-Me-ENA-T monomer was successfully incorporated into oligonucleotides, and their properties were examined. The oligonucleotides containing 6'*S*-Me-ENA-T exhibited a highly selective hybridization affinity toward single-stranded RNA and an excellent enzymatic stability, compared to the corresponding LNA- and ENA-modified oligonucleotides.

● *Metallothioneins regulate the adipogenic differentiation of 3T3-L1 cells via the insulin signaling pathway.*

Kadota Y, Toriuchi Y, Aki Y, Mizuno Y, Kawakami T, Nakaya T, Sato M, Suzuki S. *PLoS One.* 2017 Apr 20;12(4):e0176070.doi: 10.1371/journal.pone.0176070. eCollection 2017.

Knockout of metallothionein (MT) genes contributes to a heavier body weight in early life and the potential to become obese through the intake of a high fat diet (HFD) in mice. It has thus been suggested that MT genes regulate the formation of adipose tissue,

which would become the base for later HFD-induced obesity. We evaluated the fat pads of mice during the lactation stage. The fat mass and adipocyte size of MT1 and MT2 knockout mice were greater than those of wild type mice. Next, we assayed the ability of small interfering RNA (siRNA) to silence MT genes in the 3T3-L1 cell line. The expressions of MT1 and MT2 genes were transiently upregulated during adipocyte differentiation, and the siRNA pretreatment led to the suppression of the expression of both MT mRNAs and proteins. The MT siRNA promoted lipid accumulation in adipocytes and caused proliferation of post-confluent preadipocytes; these effects were suppressed by an inhibitor of phosphatidylinositol 3-kinase (LY294002). In addition, MT siRNA promoted insulin-stimulated phosphorylation of Akt, a downstream kinase of the insulin signaling pathway. Enhanced lipid accumulation in 3T3-L1 cells resulting from MT-gene silencing was inhibited by pretreatment with an antioxidant, N-acetylcysteine, used as a substitute for antioxidant protein MTs. These results suggest that interference in MT expression enhanced the activation of the insulin signaling pathway, resulting in higher lipid accumulation in 3T3-L1 adipocytes.

● *Optically Active 2,7,10,15-Tetrahydroxytetraphenylene: Clathrates with Both Enantiomers of 1-Phenylethylamine and Their Stability.*

Kaku, H.; Mitarai, A.; Okamoto, N.; Tanaka, K.; Ichikawa, S.; Yamamoto, T.; Inai, M.; Nishii, T.; Horikawa, M. and Tsunoda, T. Eur. J. Org. Chem 2018,48, 6991-6999. doi: 10.1002/ejoc.201801422

2,7,10,15-Tetrahydroxytetraphenylene (THTP) was synthesized in two steps by the homo-coupling reaction of 2,2'-dibromo-5,5'-dimethoxybiphenyl. Optical resolution of racemic THTP was achieved by complexation with (S)-1-phenylethylamine in toluene to afford (S,S)-THTP in good yield. (R,R)-THTP was also obtained using (R)-1-phenylethylamine. In the course of these studies, (S,S)-THTP constituted an inclusion compound even with (R)-1-phenylethylamine. Both complexes were characterized by X-ray structural analyses and the thermal analyses (DSC and TGA). The hydrogen bonding networks of the complex with (R)-1-phenylethylamine are more complicated than those of the complex with (S)-1-phenylethylamine. The thermal analysis suggests that the complex with (S)-1-phenylethylamine is a less stable clathrate than the complex with (R)-1-phenylethylamine.

● *Identification and Characterization of Daurichromenic Acid Synthase Active in Anti-HIV Biosynthesis.*

Iijima M, Munakata R, Takahashi H, Kenmoku H, Nakagawa R, Kodama T, Asakawa Y, Abe I, Yazaki K, Kurosaki F, Taura F. DOI: 10.1104/pp.17.00586

Daurichromenic acid (DCA) synthase catalyzes the oxidative cyclization of grifolic acid to produce DCA, an anti-HIV meroterpenoid isolated from *Rhododendron dauricum*. We identified a novel cDNA encoding DCA synthase by transcriptome-based screening from young leaves of *R. dauricum*. The gene coded for a 533-amino acid polypeptide with moderate homologies to flavin adenine dinucleotide oxidases from other plants. The primary structure contained an amino-terminal signal peptide and conserved amino acid residues to form bicovalent linkage to the flavin adenine dinucleotide isoalloxazine ring at histidine-112 and cysteine-175. In addition, the recombinant DCA synthase, purified from the culture supernatant of transgenic *Pichia pastoris*, exhibited structural and functional properties as a flavoprotein. The reaction mechanism of DCA synthase characterized herein partly shares a similarity with those of cannabinoid synthases from *Cannabis sativa*, whereas DCA synthase catalyzes a novel cyclization reaction of the farnesyl moiety of a meroterpenoid natural product of plant origin. Moreover, in this study, we present evidence that DCA is biosynthesized and accumulated specifically in the glandular scales, on the surface of *R. dauricum* plants, based on various analytical studies at the chemical, biochemical, and molecular levels. The extracellular localization of DCA also was confirmed by a confocal microscopic analysis of its autofluorescence. These data highlight the unique feature of DCA: the final step of biosynthesis is completed in apoplasmic space, and it is highly accumulated outside the scale cells.

● *Genetic knockout and pharmacologic inhibition of NCX1 attenuate hypoxia-induced pulmonary arterial hypertension.*

Nagata A, Tagashira H, Kita S, Kita T, Nakajima N, Abe K, Iwasaki A, Iwamoto T. *Biochem Biophys Res Commun.* 2020 Aug 27;529(3):793-798. doi: 10.1016/j.bbrc.2020.06.045.

The Na⁺/Ca²⁺ exchanger type-1 (NCX1) is a bidirectional transporter that is controlled by membrane potential and transmembrane gradients of Na⁺ and Ca²⁺. Vascular smooth muscle NCX1 plays an important role in intracellular Ca²⁺ homeostasis and Ca²⁺ signaling. We found that NCX1 was upregulated in the pulmonary arteries of mice exposed to chronic hypoxia (10% O₂ for 4 weeks). Hence, we investigated the pathophysiological role of NCX1 in hypoxia-induced pulmonary arterial hypertension (PAH), using NCX1-heterozygous (NCX1^{+/-}) mice, in which NCX1 expression is reduced by half, and SEA0400, a specific NCX1 inhibitor. NCX1^{+/-} mice exhibited attenuation of hypoxia-induced PAH and right ventricular (RV) hypertrophy compared with wild-type mice. Furthermore, continuous administration of SEA0400 (0.5 mg/kg/day for 4 weeks) to wild-type mice by osmotic pumps significantly suppressed hypoxia-induced PAH and

pulmonary vessel muscularization, with a slight reduction in RV hypertrophy. These findings indicate that the upregulation of NCX1 contributes to the development of hypoxia-induced PAH, suggesting that NCX1 inhibition might be a novel approach for the treatment of PAH.

● *Synthesis of the Common Monomeric Unit of Uroleuconaphins and Viridaphins via Hauser–Kraus Annulation.*

Kei Kitamura, Hinano Kanagawa, Chiharu Ozakai, Taichi Nishimura Hayato Tokuda, Tetsuto Tsunoda, Hiroto Kaku, *Synthesis* 2021; 53(09): 1629-1635 DOI: 10.1055/a-1334-6982

A stereoselective synthesis of a pyranonaphthoquinone derivative found in aromatic polyketide-derived aphid pigments is reported herein. This approach features the anionic [4+2]-annulation of phthalides with a carbohydrate-derived optically active enone. Additional synthetic steps provide access to the monomer fragment of uroleuconaphins and viridaphins. The optimization for a facile preparation of phthalides bearing sulfonyl or cyano groups are also studied.

● *Internalization of Clostridium botulinum C2 toxin is regulated by cathepsin B released from lysosomes.*

Nagahama M, Kobayashi K, Ochi S, Takehara M. *Toxins (Basel)*. 2021 Apr 9;13(4):272. doi: 10.3390/toxins13040272.

Clostridium botulinum C2 toxin is a consisting of actin ADP-ribosyltransferase (C2I) and C2II binding components. Activated C2II (C2IIa) binds to receptors and forms oligomer. C2IIa oligomer assembles with C2I and contributes to the transport of C2I into the cytoplasm. C2IIa induces lysosomal exocytosis, extracellular release of the acid sphingomyelinase (ASMase), and ASMase-induced endocytosis of C2 toxin. Here, we reveal that C2 toxin requires the lysosomal cysteine protease cathepsin B (CTSB) during endocytosis. Cysteine protease inhibitor E64 blocked C2 toxin-induced cell rounding, and inhibited the C2IIa-promoted ASMase activity. C2IIa induced the release of CTSB. CTSB knockdown suppressed cytotoxicity of the toxin. Together, CTSB is important for internalization of C2 toxin into cells.

● *Influenza A virus nucleoprotein is acetylated by histone acetyltransferases PCAF and GCN5*
Influenza A virus nucleoprotein is acetylated by histone acetyltransferases PCAF and GCN5.

Hatakeyama D, Shoji M, Yamayoshi S, Yoh R, Ohmi N, Takenaka S, Saitoh A, Arakaki Y, Masuda A, Komatsu T, Nagano R, Nakano M, Noda T, Kawaoka Y, Kuzuhara T. *J. Biol. Chem.* 293(19): 7126-7138. (2018) doi: 10.1074/jbc.RA117.001683.

RNA of the influenza virus interacts with its nucleoprotein (NP), whose function

corresponds to that of eukaryotic histones. NP regulates viral replication and has been shown to undergo acetylation by the cAMP-response element (CRE)-binding protein (CBP) from the host. However, whether NP is the target of other host acetyltransferases is unknown. Here, we show that influenza virus NP undergoes acetylation by the two host acetyltransferases GCN5 and P300/CBP-associated factor (PCAF) and that this modification affects viral polymerase activities. Western blot analysis with anti-acetyl-lysine antibody on cultured A549 human lung adenocarcinoma epithelial cells infected with different influenza virus strains indicated acetylation of the viral NP. A series of biochemical analyses disclosed that the host lysine acetyltransferases GCN5 and PCAF acetylate NP in vitro MS experiments identified three lysine residues as acetylation targets in the host cells and suggested that Lys-31 and Lys-90 are acetylated by PCAF and GCN5, respectively. RNAi-mediated silencing of GCN5 and PCAF did not change acetylation levels of NP. However, interestingly, viral polymerase activities were increased by the PCAF silencing and were decreased by the GCN5 silencing, suggesting that acetylation of the Lys-31 and Lys-90 residues has opposing effects on viral replication. Our findings suggest that epigenetic control of NP via acetylation by host acetyltransferases contributes to regulation of polymerase activity in the influenza A virus.

● *Arsenic Secondary Methylation Capacity Is Inversely Associated with Arsenic Exposure-Related Muscle Mass Reduction.*

Md. Khalequzzaman Sarker, Selim Reza Tony, Abu Ebrahim Siddique, Md. Rezaul Karim, Nazmul Haque, Zohurul Islam, Md. Shofikul Islam, Moriom Khatun, Jahidul Islam, Shakhawoat Hossain, Zahangir Alam Saud, [Hideki Miyataka](#), Daigo Sumi, Aaron Barchowsky, Seiichiro Himeno and Khaled Hossain International Journal of Environmental Research and Public Health 2021, 18(18), 9730.

Skeletal muscle mass reduction has been implicated in insulin resistance (IR) that promotes cardiometabolic diseases. We have previously reported that arsenic exposure increases IR concomitantly with the reduction of skeletal muscle mass among individuals exposed to arsenic. The arsenic methylation capacity is linked to the susceptibility to some arsenic exposure-related diseases. However, it remains unknown whether the arsenic methylation capacity affects the arsenic-induced reduction of muscle mass and elevation of IR. Therefore, this study examined the associations between the arsenic methylation status and skeletal muscle mass measures with regard to IR by recruiting 437 participants from low- and high-arsenic exposure areas in Bangladesh. The subjects' skeletal muscle mass was estimated by their lean body mass (LBM) and serum creatinine levels. Subjects' drinking water arsenic concentrations

were positively associated with total urinary arsenic concentrations and the percentages of MMA, as well as inversely associated with the percentages of DMA and the secondary methylation index (SMI). Subjects' LBM and serum creatinine levels were positively associated with the percentage of DMA and SMI, as well as inversely associated with the percentage of MMA. HOMA-IR showed an inverse association with SMI, with a confounding effect of sex. Our results suggest that reduced secondary methylation capacity is involved in the arsenic-induced skeletal muscle loss that may be implicated in arsenic-induced IR and cardiometabolic diseases

● *Internalization of Clostridium botulinum C2 toxin is regulated by cathepsin B released from lysosomes.*

Nagahama M, Kobayashi K, Ochi S, Takehara M. *Toxins* (Basel). 2021 Apr 9;13(4):272. doi: 10.3390/toxins13040272.

Clostridium botulinum C2 toxin is a consisting of actin ADP-ribosyltransferase (C2I) and C2II binding components. Activated C2II (C2IIa) binds to receptors and forms oligomer. C2IIa oligomer assembles with C2I and contributes to the transport of C2I into the cytoplasm. C2IIa induces lysosomal exocytosis, extracellular release of the acid sphingomyelinase (ASMase), and ASMase-induced endocytosis of C2 toxin. Here, we reveal that C2 toxin requires the lysosomal cysteine protease cathepsin B (CTSB) during endocytosis. Cysteine protease inhibitor E64 blocked C2 toxin-induced cell rounding, and inhibited the C2IIa-promoted ASMase activity. C2IIa induced the release of CTSB. CTSB knockdown suppressed cytotoxicity of the toxin. Together, CTSB is important for internalization of C2 toxin into cells.

● *1,3,9-Triaza-2-oxophenoxazine: An Artificial Nucleobase Forming Highly Stable Self-Base Pairs with Three Ag^I Ions in a Duplex.*

Fujii A, Nakagawa O, Kishimoto Y, Okuda T, Nakatsuji Y, Nozaki N, Kasahara Y, Obika S. *Chemistry – A European Journal*. 2019 Jun 4;25(31):7443-7448. doi:10.1002/chem.201900373.

Metal-mediated base pairs (MMBPs) formed by natural or artificial nucleobases have recently been developed. The metal ions can be aligned linearly in a duplex by MMBP formation. The development of a three- or more-metal-coordinated MMBPs has the potential to improve the conductivity and enable the design of metal ion architectures in a duplex. This study aimed to develop artificial self-bases coordinated by three linearly aligned Ag^I ions within an MMBP. Thus, artificial nucleic acids with a 1,3,9-triaza-2-oxophenoxazine (9-TAP) nucleobase were designed and synthesized. In a DNA/DNA duplex, self-base pairs of 9-TAP could form highly stable MMBPs with three Ag^I ions. Nine equivalents of Ag^I led to the formation of three consecutive 9-TAP

self-base pairs with extremely high stability. The complex structures of 9-TAP MMBPs were determined by using electrospray ionization mass spectrometry and UV titration experiments. Highly stable self-9-TAP MMBPs with three Ag^I ions are expected to be applicable to new DNA nanotechnologies.

● *Prophylactic administration of granulocyte colony-stimulating factor in epirubicin and cyclophosphamide chemotherapy for Japanese breast cancer patients: a retrospective study.*

Takumi Sakurada, Sanako Bando, Yoshito Zamami, Kenshi Takechi, Masayuki Chuma, Mitsuhiro Goda, Yasushi Kirino, Toshimi Nakamura, Kazuhiko Teraoka, Masami Morimoto, Akira Tangoku, Keisuke Ishizawa. *Cancer Chemother Pharmacol.* 2019 Nov;84(5):1107-1114.

Purpose: Epirubicin and cyclophosphamide (EC) therapy, a major chemotherapy for patients with early-stage breast cancer, has a low risk (< 10%) of febrile neutropenia (FN). However, data used in reports on the incidence rate of FN were derived primarily from non-Asian populations. In this study, we investigated the FN incidence rate using EC therapy among Japanese patients with breast cancer and evaluated the significance of prophylactic administration of granulocyte colony-stimulating factor (G-CSF).

Methods: We evaluated medical records of patients with early-stage breast cancer who had been treated with EC therapy as neoadjuvant or adjuvant therapy between November 2014 and July 2018.

Results: The incidence rate of FN was 23.9%. In patients who received G-CSF as primary prophylaxis, FN expression was completely suppressed. The incidence rate of severe leucopenia/neutropenia, emergency hospitalization, and the use of antimicrobial agents were low in patients receiving primary prophylaxis with G-CSF compared with those not receiving G-CSF (27.3% vs. 64.8%, 9.1% vs. 27.3%, and 27.3% vs. 71.6%, respectively). Furthermore, in all patients who received primary prophylaxis with G-CSF, a relative dose intensity > 85% using EC therapy was maintained.

Conclusion: The incidence of FN in EC therapy among Japanese patients was higher than expected, EC therapy appears to be a high-risk chemotherapy for FN, and prophylactic administration of G-CSF is recommended. Maintaining high therapeutic intensity is associated with a positive prognosis for patients with early breast cancer, and prophylactic administration of G-CSF is likely to be beneficial in treatment involving EC therapy.

● *Macrocyclization Using RCM Reactions. Synthesis of Simple Metacyclophanes and Synthetic Efforts toward Platycaryinol, a 15-Membered Aromatic Ether.*

Nakashima, Katsuyuki; Matsunaga, Hatsuna; Ito, Masako; Minami, Hiroshi; Aiba,

Akihito; Fujisaki, Norihiro; Tori, Motoo, *Natural product communications* (2016), **11**(8), 1135-1142

Preparation of 13- to 19-membered carbocycles (metacyclophanes) from 1,3-disubstituted benzene derivs. was successfully carried out using the ring closing metathesis (RCM) reaction, but similar starting materials having di-Ph ether did not cyclize to 15-membered compds., whose ground state conformations were calculated and discussed. Several attempts to cyclize to form platycaryinol were also described.

● *Pentacyclic triterpenoids, fuscotorunones A and B, with ϵ -caprolactone in ring E from *Fuscoporia torulosa*.*

Noji M., Yoneyama T, Nishihama K, Elshamy AI, Hashimoto T, Umeyama A. *Phytochemistry*. 2021 Jul;187:112748. doi: 10.1016/j.phytochem.2021.112748. Epub 2021 Apr 8. PMID: 33839519

Fuscoporia torulosa (Pers.) (Hymenochaetaceae) is a mushroom forming woody fruiting body on living or dead trees. Two curious pentacyclic triterpenoids, fuscotorunones A and B, each of which has a unique ϵ -caprolactone in ring E, were isolated from the fruiting bodies of *F. torulosa*. The structures of fuscotorunones A and B were elucidated using MS analyses, IR spectrum and extensive 2D-homo and heteronuclear NMR data interpretation. Furthermore, a predicted biosynthetic pathway from 2,3-oxidosqualene to fuscotorunones A and B in *F. torulosa* is proposed.

● *Chemical Composition of Intergeneric Hybrids between*

Ligularia and Cremanthodium Collected in Sichuan Province of China.

Yasuko Okamoto, Arisa Fukui, Takuya Hashida, Kosuzu Shiojiri, Chiaki Kuroda, Motoo Tori, Xun Gong, and Ryo Hanai, *Natural Product Communications*, November, 2019, 14(11), pp.1-5.

Two intergeneric hybrids between *Ligularia nelumbifolia* and *Cremanthodium stenoglossum* were examined with respect to the chemical composition of root extracts and the sequences of neutral DNA regions. The DNA data showed that the direction of hybridization was different between the individuals. Eremophilane sesquiterpenes were found in both hybrids and deduced to have come from their *Cremanthodium* parents, because sesquiterpenes were detected in *C. stenoglossum* but not in *L. nelumbifolia*.

● *Antibiotic prescriptions for Japanese outpatients with acute respiratory tract infections (2013-2015).*

Koyama T., Hagiya H., Teratani Y., Tatebe Y., Ohshima A., Adachi M., Funahashi T., Zamami Y., Tanaka HY., Tasaka K., Shinomiya K., Kitamura Y., Sendo T., Hinotsu S., Kano MR., A retrospective observational study. *J Infect Chemother*. 2020. Jul;26(7):660-666. doi: 10.1016/j.jiac.2020.02.001.

Appropriate antibiotic prescriptions for outpatients with acute respiratory tract infections (ARTIs) are urgently needed in Japan. We aimed to determine antibiotic prescription rates, and the proportions of antibiotic classes prescribed for Japanese patients with ARTIs. We analysed health insurance claims data over 2013–2015 among Japanese patients aged <75 years and determined the following indicators: 1) visit rates for patients with ARTIs and antibiotic prescription rates per 1000 person-years, and 2) proportion of visits by antibiotic-prescribed patients with ARTIs. Both the visit rates and antibiotic prescription rates for ARTIs were high in this Japanese cohort. The proportion of antibiotic prescriptions exceeded that recommended in the clinical guidelines.

● *Different murine-derived feeder cells alter the definitive endoderm differentiation of human induced pluripotent stem cells.*

Shoji M., Minato H., Ogaki S., Seki M., Suzuki Y., Kume S., Kuzuhara T.#.

#corresponding authors. PLoS ONE. 2018 Jul 26;13(7):e0201239, DOI: 10.1371 / journal.pone.0201239.

We show that the efficiency of definitive endoderm (DE) differentiation from hiPSCs cultured on MEFs was higher than that of hiPSCs cultured on SNLs. The expression levels of mRNA and/or proteins of the DE marker genes in DE cells differentiated from hiPSCs cultured on MEFs were significantly higher than those cultured on SNL. Interestingly, the expression of non-coding hXIST exon 4 was up-regulated in hiPSCs cultured on MEFs, in comparison to that in hiPSCs cultured on SNLs. The mRNA expression of hXIST exon 4, LEFTY1, and LEFTY2 was higher in hiPSCs cultured on MEFs than in those cultured on SNLs.

● *Serum vitamin D in patients with mild cognitive impairment and Alzheimer's disease.*

Ouma S, Suenaga M, Hatip FF, Hatip-Al-Khatib I, Tsuboi Y, Matsunaga Y, Brain Behav.. 2018 Feb 9;8(3):e00936. doi: 10.1002/brb3.936.

Objectives: To determine the relevance of Mini-Mental State Examination (MMSE), serum 25-hydroxyvitamin D (25(OH)D₃), and 1,25(OH)2D₃ concentrations to mild cognitive impairment (MCI) and various stages of Alzheimer's disease (AD).

Materials and methods: The study included 230 participants (>74 years) allocated to three main groups: 1-healthy subjects (HS, n = 61), 2-patients with MCI (n = 61), and 3-patients with Alzheimer's disease (AD) subdivided into three stages: mild (n = 41), moderate (n = 35), and severe AD (n = 32). The cognitive status was evaluated using MMSE. Serum 25 (OH)D₃ (ng/ml) and 1,25(OH)2D₃ concentrations (pg/ml) were determined by competitive radioimmunoassay.

Results: MMSE scores and 25(OH)D₃ were decreased in MCI and all stages of the AD in both genders. MMSE variability was due to gender in HS (11%) and to 25(OH)D₃ in MCI (15%) and AD (26%). ROC analysis revealed an outstanding property of MMSE in diagnosis of MCI (AUC, 0.906; CI 95%, 0.847-0.965; sensitivity 82%; specificity, 98%) and AD (AUC, 0.997; CI 95%, 0.992-1; sensitivity, 100%; specificity, 98%). 25(OH)D₃ exhibited good property in MCI (AUC, 0.765; CI 95%, 0.681-0.849; sensitivity, 90%; specificity, 54%) and an excellent property in diagnosis of AD (AUC, 0.843; CI 95%, 0.782-0.904; sensitivity, 97%; specificity, 79%). Logistic analyses revealed that, in MCI, MMSE could predict (or classify correctly) with 97.6% accuracy (Wald, 15.22, β, -0.162; SE, 0.554; OR = 0.115:0.039-0.341; p = .0001), whereas 25(OH)D₃ with 80% accuracy (Wald, 41,013; β, -0.213; SE, 0.033; OR = 0.808: 0.757-863; p = .0001). 25(OH)D₃ was the only significant predictor for the severe AD and contributed to MMSE variability. Age and gender were significant predictors only in the moderate AD. In patients with MCI, 25(OH)D₃ and 1,25(OH)2D₃ were correlated men, but in case of the AD, they were correlated in women.

Conclusions: MMSE and serum 25(OH)D₃ concentrations could be useful biomarkers for prediction and diagnosis of MCI and various stages of the AD. The results support the utility of vitamin D supplementation in AD therapy regimen.

● *Arsenite suppresses IL-2-dependent tumoricidal activities of natural killer cells.*

Sumi D, Tsuyama H, Ogawa T, Ogawa M, Himeno S., *Toxicology and Applied Pharmacology*, 2020 Feb 1;412:115353. doi: 10.1016/j.taap.2020.115353.

Chronic exposure to arsenic causes cancers in various organs including the skin, liver, lung, and bladder in humans, but the mechanisms of the multi-organ carcinogenicity of arsenic remain unknown. Natural killer (NK) cells play important roles in the immune surveillance and elimination of tumor cells. Although accumulating evidence has indicated that arsenic has immunosuppressive properties, little is known about the effects of arsenic on the tumoricidal functions of NK cells. We examined the effects of arsenite on the cytotoxic activities of human and mouse NK cells toward target tumor cells. Exposure of human NK-92 cells and primary mouse NK cells to sublethal doses of arsenite reduced the IL-2-activated cytotoxic activities toward human K562 cells and murine YAC-1 cells, respectively. NK cells recognize target cells via integrated signals from both activating and inhibitory receptors and induce apoptosis of target cells via a granzyme/perforin system. We found that exposure of NK-92 cells to arsenite diminished the IL-2-activated down-regulation of the inhibitory receptors, KIR2DL2 and KIR2DL3, and the up-regulation of granzyme B and lymphotoxin-α. The IL-2-activated increases in secretion of interferon-γ and IL-10 were also slightly reduced

by arsenite. Thus, arsenite suppressed the IL-2-activated cytotoxic activity of NK cells by disrupting multiple pathways required for the recognition and killing of target tumor cells. Our findings provide new insights into the roles of NK cell-mediated tumor immunity in cancer development by arsenic.

● *Metallothioneins regulate the adipogenic differentiation of 3T3-L1 cells via the insulin signaling pathway.*

Kadota Y, Toriuchi Y, Aki Y, Mizuno Y, Kawakami T, Nakaya T, Sato M, Suzuki S. 2017 PLoS One. 12, (4), e0176070. PMID: 28426713.

Knockout of metallothionein (MT) genes contributes to a heavier body weight in early life and the potential to become obese through the intake of a high fat diet (HFD) in mice. It has thus been suggested that MT genes regulate the formation of adipose tissue, which would become the base for later HFD-induced obesity. We evaluated the fat pads of mice during the lactation stage. The fat mass and adipocyte size of MT1 and MT2 knockout mice were greater than those of wild type mice. Next, we assayed the ability of small interfering RNA (siRNA) to silence MT genes in the 3T3-L1 cell line. The expressions of MT1 and MT2 genes were transiently upregulated during adipocyte differentiation, and the siRNA pretreatment led to the suppression of the expression of both MT mRNAs and proteins. The MT siRNA promoted lipid accumulation in adipocytes and caused proliferation of post-confluent preadipocytes; these effects were suppressed by an inhibitor of phosphatidylinositol 3-kinase (LY294002). In addition, MT siRNA promoted insulin-stimulated phosphorylation of Akt, a downstream kinase of the insulin signaling pathway. Enhanced lipid accumulation in 3T3-L1 cells resulting from MT-gene silencing was inhibited by pretreatment with an antioxidant, N-acetylcysteine, used as a substitute for antioxidant protein MTs. These results suggest that interference in MT expression enhanced the activation of the insulin signaling pathway, resulting in higher lipid accumulation in 3T3-L1 adipocytes.

● *Identification and classification of innexin gene transcripts in the central nervous system of the terrestrial slug *Limax valentianus*.*

Sadamoto H, Takahashi H, Kobayashi S, Kondoh H, Tokumaru H. PLoS One. 2021 Apr 15;16(4):e0244902. doi: 10.1371/journal.pone.0244902. eCollection 2021.

Intercellular gap junction channels and single-membrane channels have been reported to regulate electrical synapse and the brain function. Innexin is known as a gap junction-related protein in invertebrates and is involved in the formation of intercellular gap junction channels and single-cell membrane channels. Multiple isoforms of innexin protein in each species enable the precise regulation of channel function. In molluscan species, sequence information of innexins is still limited and the

sequences of multiple innexin isoforms have not been classified. This study examined the innexin transcripts expressed in the central nervous system of the terrestrial slug *Limax valentianus* and identified 16 transcripts of 12 innexin isoforms, including the splicing variants. We performed phylogenetic analysis and classified the isoforms with other molluscan innexin sequences. Next, the phosphorylation, N-glycosylation, and S-nitrosylation sites were predicted to characterize the innexin isoforms. Further, we identified 16 circular RNA sequences of nine innexin isoforms in the central nervous system of *Limax*. The identification and classification of molluscan innexin isoforms provided novel insights for understanding the regulatory mechanism of innexin in this phylum.

● *Clostridium perfringens* α -toxin impairs granulocyte colony-stimulating factor receptor-mediated granulocyte production while triggering septic shock.

Takehara M, Seike S, Sonobe Y, Bandou H, Yokoyama S, Takagishi T, Miyamoto K, Kobayashi K, Nagahama M. *Commun Biol.* 2019 Jan 31;2:45. doi: 10.1038/s42003-019-0280-2.

During bacterial infection, granulocyte colony-stimulating factor (G-CSF) is produced and accelerates neutrophil production from their progenitors. This process, termed granulopoiesis, strengthens host defense, but *Clostridium perfringens* α -toxin impairs granulopoiesis via an unknown mechanism. Here, we tested whether G-CSF accounts for the α -toxin-mediated impairment of granulopoiesis. We find that α -toxin dramatically accelerates G-CSF production from endothelial cells in response to Toll-like receptor 2 (TLR2) agonists through activation of the c-Jun N-terminal kinase (JNK) signaling pathway. Meanwhile, α -toxin inhibits G-CSF-mediated cell proliferation of Ly-6G⁺ neutrophils by inducing degradation of G-CSF receptor (G-CSFR). During sepsis, administration of α -toxin promotes lethality and tissue injury accompanied by accelerated production of inflammatory cytokines in a TLR4-dependent manner. Together, our results illustrate that α -toxin disturbs G-CSF-mediated granulopoiesis by reducing the expression of G-CSFR on neutrophils while augmenting septic shock due to excess inflammatory cytokine release, which provides a new mechanism to explain how pathogenic bacteria modulate the host immune system.

● *A metallo-DNA nanowire with uninterrupted one-dimensional silver array.*

Jiro Kondo, Yoshinari Tada, Takenori Dairaku, Yoshikazu Hattori, Hisao Saneyoshi, Akira Ono, Yoshiyuki Tanaka *Nat Chem.* 2017 Oct;9(10):956-960. doi: 10.1038/nchem.2808. Epub 2017 Jul 3.

The double-helix structure of DNA, in which complementary strands reversibly hybridize to each other, not only explains how genetic information is stored and

replicated, but also has proved very attractive for the development of nanomaterials. The discovery of metal-mediated base pairs has prompted the generation of short metal-DNA hybrid duplexes by a bottom-up approach. Here we describe a metallo-DNA nanowire-whose structure was solved by high-resolution X-ray crystallography-that consists of dodecamer duplexes held together by four different metal-mediated base pairs (the previously observed C-Ag-C, as well as G-Ag-G, G-Ag-C and T-Ag-T) and linked to each other through G overhangs involved in interduplex G-Ag-G. The resulting hybrid nanowires are 2 nm wide with a length of the order of micrometres to millimetres, and hold the silver ions in uninterrupted one-dimensional arrays along the DNA helical axis. The hybrid nanowires are further assembled into three-dimensional lattices by interactions between adenine residues, fully bulged out of the double helix.

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● *A Concise Total Synthesis of Dehydroantofine and the Antimalarial Activity against Chloroquine-Resistant Plasmodium falciparum.*

Yamasaki N, Iwasaki I, Sakumi K, Hokari R, Ishiyama A, Iwatsuki M, Nakahara M, Higashibayashi S, Sugai T, Imagawa H, Kubo M, Fukuyama Y, Ōmura S, [Yamamoto H.](#) Chem. Eur. J. 2021 Mar 22;27(17):5555-5563. doi: 10.1002/chem.202100032. Epub 2021 Feb 26. PMID: 33482050.

On the basis of a novel regioselective azahetero DA reaction as a key step, the total synthesis of dehydroantofine has been achieved. This synthetic procedure was

accomplished in 9 steps from 3,5-dichloro-2*H*-1,4-oxazin-2-one in 30.3% overall yield. Moreover, dehydroantofine and the synthetic intermediate were applied to the procurement of (±)-antofine and *seco*-dehydroantofine, which facilitated the SAR study of dehydroantofine. Our SAR study with chloroquine-sensitive and -resistant *P. falciparum* showed that the azatriphenylene framework in dehydroantofine is important to ensure potent antimalarial activity, and demonstrated that dehydroantofine is a promising candidate for the development of a novel antimalarial agent.

● *Marylosides A-G, Norcycloartane Glycosides from Leaves of Cymbidium Great Flower 'Marylaurencin'*

Yoneyama, T., Iseki, K., Noji, M., Imagawa, H., Hashimoto, T., Kawano, S., Baba, M., Kashiwada, Y., Yahagi, T., Matsuzaki, K., Umeyama, A. *Molecules*. 2019 Jul 9;24(13):2504.doi: 10.3390/molecules24132504.

Seven novel norcycloartane glycosides, maryloside A-G (**1-7**), were isolated from the leaves of *Cymbidium* Great Flower 'Marylaurencin', along with a known norcycloartane glycoside, cymbidoside (**8**). These structures were determined on the basis of mainly NMR experiments as well as chemical degradation and X-ray crystallographic analysis. The isolated compounds (**1-6** and **8**) were evaluated for the inhibitory activity on lipopolysaccharide (LPS) and interferon- γ (IFN- γ)-stimulated nitric oxide (NO) production in RAW 264.7 cells. Consequently, **1** and **3** exhibited moderate activity.

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● *Synthesis of pyrone-annulated 2-oxabicyclo[3.3.1]nonanes by palladium-catalyzed cyclization of 4-hydroxy-2-pyrones with allylic bisacetates.*

Yoshida, M.; Shibata, M.; Mukae, S.; Kinoshita, K.; Matsumoto, K.; Hirokane, T., *Tetrahedron Letters*, 60, 151262 (2019). DOI: 10.1016/j.tetlet.2019.151262.

Cyclization of 4-hydroxy-2-pyrones with allylic bisacetates by a palladium catalyst is described. Pyrone-annulated 2-oxabicyclo[3.3.1]nonane derivatives were regioselectively produced from the reaction of 4-hydroxy-2-pyrones with 1,4-diacetoxy-2-cyclohexene at high temperature. The reaction would proceed via a migration of the π -allylpalladium intermediate.

■ Human Life Sciences

□ Food-Nutritional Sciences

● *Biphenyl increases intracellular Ca^{2+} concentration in HL-60 cells.*

Tomoko Inubushi, Mayumi Sugimoto, Haruka Kunimi, Haruka Hino, Atsushi Tabata, Naohiro Imura, Abe Shin, Tulji Akihiko, Yasuno Oyama, Norio kamemura. *Fundam.Toxicol. Sci*, Vol 5(3), 2018, pp.99-103.

Biphenyl is a universal intermediate agent such as a protectant in various production activities. Biphenyl is currently used as a postharvest application in foreign countries and, maintains the safety and quality of agricultural products. However, the risk of Biphenyl is argued in Japan. The toxic effect of Biphenyl is studied in animals, and is reported the influence in liver and kidney especially. However, the toxic effect of biphenyl is currently not well understood on blood cells, and the mechanism of cytotoxicity is unclear. We examined the toxicity of biphenyl on HL60 cells, a human promyelocytic leukemia, by performing flow cytometry analysis with fluorescent probes. Biphenyl at 100 μ M or greater significantly increased cell lethality and the intensity of the side scatter on HL60 cells. Moreover, biphenyl at 30 μ M or greater increased intracellular Ca^{2+} in a concentration-dependent manner. The free Ca^{2+} enters into the cells from extracellular fluid.

An increase in intracellular Ca^{2+} on cells may be one of several causes induced cytotoxicity by biphenyl.

● *Ubiquitin ligase Cbl-b and inhibitory Cbln peptides.*

Nikawa T, Ishidoh K. *Biochim Biophys Acta Proteins Proteom*. 2020 Nov;1868(11):140495. doi: 10.1016/j.bbapap.2020.140495.

This review focuses on the Cbl-b muscle atrophy-associated ubiquitin ligase and its inhibitors. Herein, the role of E3 ubiquitin ligase-associated muscle atrophy genes (atrogenes), including MAFbx-1/agrogin-1 and MuRF-1, as well as another ubiquitin ligase, Cbl-b and its inhibitors, is discussed. Cbl-b plays an important role in unloading

muscle atrophy caused by spaceflight and in bedridden patients: Cbl-b ubiquitinated and induced the degradation of IRS-1, a key intermediate in the IGF-1 signaling. Furthermore, a pentapeptide (DGPYMP), inhibited Cbl-b-mediated IRS-1 ubiquitination. This peptide-based Cbl-b inhibitor Cblin and its homologous peptides in foods presumably affect muscle atrophy under such conditions.

●Tomoharu Kawano, Satoshi Numata, Akio Kuroda, Tetsuyuki Yasuda, Kazuyuki Miyashita, Fumie Sakamoto, Naoto Katakami, Takaaki Matsuoka, Munehide Matsuhisa and Seiichi Hashida, *Development of a simultaneous detection method for GAD and IA-2 antibodies*, Research Bulletin of Tokushima Bunri University, Vol.99, Mar, 2020, pp.1-8.

Detection of pancreatic islet-associated autoantibodies (GAD antibody, IA-2 antibody) is useful for diagnosis of type 1 diabetes and prediction of onset. However, since each antibody has a high positive rate depending on age of onset and duration of disease, single antibody detection may misidentify positive individuals. Therefore, a simultaneous detection method for GAD and IA-2 antibodies was developed and reported. The simultaneous detection method was verified using model serum (24 specimens) prepared from positive serum and serum of diabetic patients (28 specimens). For detection of GAD and IA-2 antibodies, an ultra-sensitive ELISA (ICT-EIA) method was used. In model serum, the measured/expected ratio was 71 - 136% with a predictive value of 24/24 (100%) by the simultaneous detection method. Further, this method showed higher values of sensitivity (57.1%) and specificity (100%) in sera of type 1 diabetic patients compared to single measurement of GAD antibody and IA-2 antibody. Furthermore, the predictive value for positive and negative obtained by two independent measurements was 28/28 (100%). Specimens that were positive for either one or two antibodies could be judged as positive using this simultaneous detection method, indicating its usefulness.

●*In vitro and in vivo evaluation of antioxidant activity of Petasites japonicus Maxim. flower buds extracts.*

Hiemori-Kondo M, Nii M. Biosci Biotechnol Biochem. 2020 Mar;84(3):621-632. doi: 10.1080/09168451.2019.1691913.

The antioxidant activity of *Petasites japonicus* flower buds was examined. Antioxidants in the 80% ethanol extract were investigated using online HPLC-DPPH and were identified as caffeic acid, 3-*O*-caffeoylquinic acid, fukinolic acid, 3,4-di-*O*-caffeoylquinic acid, 3,5-di-*O*-caffeoylquinic acid, and 4,5-di-*O*-caffeoylquinic acid using LC-MS. Fukinolic acid was the most active compound based on its activity and abundance.

Administering the extracts orally to ICR mice prior to iron injection significantly suppressed plasma TBARS production. Moreover, TBARS and triglyceride concentrations in the plasma of C57BL/6 mice fed with a high fat diet were also significantly decreased by the extract. The results suggest that antioxidative compounds in *P. japonicus* can be used in the management of oxidative stress.

● Lin WL, Mizobuchi M, Kawahigashi M, Nakahashi O, Maekawa Y, Sakai T. , *Functional kupffer cells migrate to the liver from the intraperitoneal cavity*. Biochem Biophys Rep. 2021 Aug 17;27:101103.

We established a method of KC transplantation by intraperitoneal (i.p.) injection using EGFP-expressing cells (EGFP-KCs) and normal KCs. The novel method is easier and less invasive than conventional methods so that it is not only technically advantageous but also ethically preferable for experiments using animals. KC injection decreased the KC number at 24 h and then recovered the KCs at 10 days to a normal level. Additionally, recovery to the normal level by KC injection was observed in mice with KC depletion induced by GdCl₃. These results suggest that a regulatory mechanism exists for controlling the number of KCs.

● *Weight and cardiometabolic risk among adolescents in Agano city, Japan: NICE EVIDENCE Study-Agano 1.*

Sakiko Yoshizawa Morikawa, Kazuya Fujihara, Yasunaga Takeda, Mariko Hatta, Chika Horikawa, Masahiro Ishizawa, Masahiko Yamamoto, Tomonobu Shiraishi, Hajime Ishiguro, Takaho Yamada, Yohei Ogawa, Hirohito Sone. Asia Pac J Clin Nutr. 2020;29(4):856-866. doi: 10.6133/apjcn.202012_29(4).0022.

Background and objectives: Pediatric obesity is associated with clustered cardiometabolic risk and the future incidence of cardiovascular disease. However, few studies have determined the effect of pediatric obesity in Asia, where obesity is less common than in Western countries. We aimed to clarify whether weight status including underweight and slightly overweight is associated with metabolic risk factors in Japanese adolescents.

Methods and study design: We performed a cross-sectional analysis of 2241 adolescents aged 13-14 years. Participants were classified as underweight, normal weight, slightly overweight, overweight, or obese according to the International Obesity Task Force. The clustered cardiometabolic risk (Z-CMR) was estimated by summing standardized sex-specific Z scores of mean arterial pressure (MAP), non-high-density lipoprotein cholesterol (non-HDL-C), and HbA_{1c}.

Results: Linear regression analysis showed that MAP, non-HDL-C, and Z-CMR were higher in the slightly overweight, overweight, and obese groups than in the normal weight group after adjusting for confounders. Compared with the normal weight group, the slightly

overweight, overweight, and obese groups had higher prevalence of high BP [odds ratios (ORs): 1.38 (95% CI, 1.03, 1.85); 2.63 (1.77, 3.91); and 2.39 (1.57, 3.64), respectively]. Compared with the normal weight group, underweight boys, but not girls, had a lower prevalence of high Z-CMR [OR=0.20 (0.05, 0.84)].

Conclusions: Adolescents classified as slightly overweight had higher levels of BP, serum lipids, and clustered cardiometabolic risk than those classified as normal weight. This observation showed significant associations between weight status and cardiometabolic risk factors during adolescence even in East Asians.

● Ritsuyo Nakagawa, *Area activation activities by development of new agricultural product in Mugi-Town, Tokushima Prefecture for the purpose of local production for local consumption in 2018-2021.*

Tokushima Bunri University (R.Nakagawa is a leader.) cooperated with the meeting for the activation of agriculture and area from 2018. Specifically, we made the Mugi-Town rice cake wheat a raw material and developed products. A nutritional ingredients label was performed taking advantage of the food nutritional department and enlightened on necessity of a dietary fiber. In 2021 rice cake Mugi pasta of noodles is commercialized firmly. The planted acreage of the wheat was 15a in 2018, but increased 20 times to 3ha in 2021. The developed goods root as local specialties of Mugi-Town.

● *Association of increased renal Cyp24a1 gene expression with low plasma 1,25-dihydroxyvitamin D levels in rats with streptozotocin-induced diabetes.*

Tajiri M, Nakahashi Q, Kagawa T, Masuda M, Ohminami H, Iwano M, Takeda E, Taketani Y, Yamamoto H.J Clin Biochem Nutr. 2020 Jan;66(1):49-56. doi: 10.3164/jcfn.19-79.

Decreases in plasma vitamin D concentrations have been reported in diabetes, although the mechanism involved in this decrease is unclear. Here, we investigated the association between Cyp24a1, a vitamin D catabolic enzyme, and abnormalities in vitamin D metabolism in streptozotocin-induced diabetes rats, an animal model of type 1 diabetes. Plasma 1,25-dihydroxyvitamin D [1,25(OH)₂D] levels were significantly lower in streptozotocin-induced diabetes rats and renal Cyp24a1 mRNA expression levels were increased. Western blotting analysis of streptozotocin-induced diabetes rats kidney tissues with anti-CYP24A1 antibody showed a strong signal around 40 kDa, which differs from the predicted 50-55 kDa molecular weight for full-length Cyp24a1 and could represent the Cyp24a1-splicing variant that lacks exons 1 and 2. We observed high levels of renal Cyp24a1-splicing variant mRNA expression in streptozotocin-induced diabetes rats. We also confirmed transcriptional up-regulation of endogenous Cyp24a1 mRNA expression through glucocorticoid receptors by

glucocorticoid in opossum kidney proximal cells. Taken together, our results indicated that high Cyp24a1 expression levels may play a role in the decrease of plasma 1,25(OH)₂D levels in streptozotocin-induced diabetes rats. High plasma corticosterone levels in diabetes may affect transcriptional regulation to promote increases in Cyp24a1 expression.

●Ayano N, Tomoko I, Junko M, Naoko O, Seiichi H. *Nutrient ingestion and vegetable intake among Tokushima junior high school students*, Technical bulletin of Tokushima Bunri University Vol 98, Sep. , 2019,9-19.

The diabetes mortality rate in 2017 in Tokushima Prefecture was the highest in the country at 19.8 persons per 100,000 people. This study aimed to investigate whether the first signs of diabetes in junior high school students appear based on their dietary intake. The study of the development of symptoms is linked to the prevention of lifestyle-related diseases, such as diabetes. Subjects included junior high school students (338 male, 383 females) of Tokushima prefecture, whose nutrient intake was investigated using the brief-type self-administered diet history questionnaire. Three consultation periods were held, across six schools, from June to July 2013, July 2014, and November to December 2015. Both male and female students were found to have low energy intake, with many showing potassium, calcium, iron, vitamin B₁, and dietary fiber deficiency, with one individual showing excess intake of salt. In terms of ingestion, students had low intake of potatoes, legumes, fruits, and eggs. As for the intake of vegetables, about 80 percent students (both men and women) had an intake lower than the target of 350g. The results suggest students must consume a variety of foods to meet their nutrient requirements.

●Yoko TSUMAKI, Yoko TORII, Kentaro SAKAI, *Effect of Histidine and Carnosine on Degranulation in RBL-2H3*, Bulletin of Hiroshima Jogakuin University, Vol.66, Feb., 2019, pp.33-42.

Most food allergies are caused by immunoglobulin epsilon (IgE)-dependent immediate immune responses. Upon ingestion of allergens that act as antigens, antigen-specific IgE antibodies are produced in the body, and sensitization is established through the binding of IgE antibodies to high affinity IgE receptors on mast cells. When the same allergen invades again, owing to the acquired immune sensitivity, it binds to the specific IgE antibodies, thereby degranulating histamine and serotonin. Histamine is one of the several compounds responsible for causing allergic symptoms, and is synthesized via histidine decarboxylation by histidine decarboxylase (HDC). As it is one of the essential amino acids, the body obtains this compound through its diet. In this study, the influence of high levels of histidine on the synthesis and the degranulation of histamine

were examined. L-histidine and a dipeptide of L-histidine, L-carnosine, were added to RBL-2H3 cells (rat basophil leukemia model) at a final concentration of 0.5 mM or 1 mM and incubated for 3 hours. After incubation, degranulation was induced via antigen-antibody reaction using IgE antibodies in combination with antigens or A23187, a calcium ionophore. The β -hexosaminidase release rate (%), a degranulation index, was calculated. Expression of the HDC gene was also detected using the reverse transcription polymerase chain reaction (RT-PCR) technique. The results indicate that the induction of degranulation was promoted by the addition of L-histidine, particularly by L-carnosine. However, the expression of the HDC gene was reduced due to the addition of L-histidine or L-carnosine. Thus, induction of degranulation was found to be promoted when histidine or carnosine levels were high, indicating the possibility that L-histidine and L-carnosine are potential causes of allergic symptoms. However, the mechanisms involved in the stimulation of histamine synthesis and induction of degranulation that subsequently reduced HDC gene expression remain unclear. Hence, further research is needed to clarify these stimulatory mechanisms and explore the potential for preventing the onset and exacerbation of allergic symptoms by adjusting the quantity of histidine obtained through the diet.

● *Functional kupffer cells migrate to the liver from the intraperitoneal cavity.*

Wen-Ling Lin, Mizuki Mizobuchi, Mina Kawahigashi, Otoki Nakahashi, Yuuki Maekawa, Takashi Sakai. *BB Reports* 2021 Sept; 27:101103.

<https://doi.org/10.1016/j.bbrep.2021.101103>.

We established a method of KC transplantation by intraperitoneal (i.p.) injection using EGFP-expressing cells (EGFP-KCs) and normal KCs. The novel method is easier and less invasive than conventional methods so that it is not only technically advantageous but also ethically preferable for experiments using animals. We demonstrated that KCs migrated to the liver following i.p. Injection. Engraftment in the liver was not observed for peritoneal macrophages (pMPs). This suggests that KCs migrate to the liver via a sorting mechanism. KC injection decreased the KC number at 24 h and then recovered the KCs at 10 days to a normal level. Additionally, recovery to the normal level by KC injection was observed in mice with KC depletion induced by GdCl₃. These results suggest that a regulatory mechanism exists for controlling the number of KCs.

□ Childhood Education

● Matsumoto, Y., Ishimoto, Y., & Takizawa, Y. , *Examination of the effectiveness of Neuroscience-Informed Child Education (NICE) within Japanese School Settings*, Child and Youth Service Review, 118. <https://doi.org/10.1016/j.chidyouth.2020.105405>.

<https://doi.org/10.1016/j.chidyouth.2020.105405>

Mental health services using evidence-based practices within school systems can provide accessible care to schoolchildren, thereby promoting both their mental health and well-being. Because a meta-analysis of cognitive-behavioral oriented school interventions found small treatment effects, and research has shown implementation difficulties in Japanese schools, ways to improve intervention effectiveness and feasibility should be explored.

The present study examined the efficacy and feasibility of a neuroscience-informed child education (NICE) developed by the authors in a Japanese school context. In a program group, homeroom teachers voluntarily conducted an eight-session NICE during 20-minute after-class periods. In an information group, teachers applied the approach and skills in daily class management. Students (63 first graders; 6-7 years old) completed questionnaires regarding their class adjustment and social support awareness at three-time points under the supervision of their teachers, whereas teachers assessed students' behaviors, including total difficulties and prosocial behavior. The trial revealed significant changes in the class adjustment, social support awareness, and prosociality, but not in the behavior difficulties. This study highlights the efficacy and feasibility of the neuropsychological approach that may enhance mental health services in Japanese schools.

● N.Ikeno, J.Watanabe, K.Mihashi, *Examination of Educational Methodology for the teaching of Drama(4) : Citizenship Education and Drama*. The 52rd Annual Conference on National Association for the Study of Educational Methods, Roundtable ④, Kyushu university, 2016,10.1.-10.2.

In this presentation we discuss the relationship between citizenship education and Drama. Research that bridges citizenship education and drama research has progressed in both Japan and England. Based on the 2015 article by Professor Davies (University of York), who gave the interim summary, we discuss the relationship between the new image of what it means to be a citizen and drama by looking ahead to the current situation where various images of citizens dynamically intersect such as the search for empowered education with the introduction of voting rights for 18-years-olds and advocating for GCED by UNESCO.

● A.Niyu, *The using of the plaster figure drawing for creating different kinds of art works, The sensory method transforms art works*. Research Bulletin of Tokushima Bunri University Vol. 96, September 2018, pp.151-160.

In this article, we will look at a new approach to plaster figure drawing. I have

developed a sensory method that is different from the conventional visual method required by many colleges of art for entrance examinations. I examined how it changes and influences the artists' works. I had workshops with many artists in Tokushima, Japan and Taiwan. I tried a sensory method in many ways by using senses other than sight. For instance, I covered the figure with a cloth and had them draw by touch or had them draw by intuition. After that, we tried to create new art works using this method with a focus on senses.

As a result. Many art works changed into creative spiritual and profound ones by the synergy between the sensory drawing method and the artists' intentions, ideas, and concepts of art works. The details of the effects of the sensuous plaster figure drawing on art as follows. (1)Sensory plaster figure drawing breaks through old molds, allowing new works to be born.(2)Both abstract and concrete art works were created, (3)It helps the artist to visualize oneself objectively, resulting in a growth of both the artist and this/work.

●Keiko Aizu, Kasumi Mikami, Ryoko Tsuchiya, Mayumi Shimizu, Naoki Oka, Yoshiko Nishizawa, *Educational Method for Developing Assessment Skills of Nursing Students*. Open Journal of Nursing, Vol.8, No.8, August 2018. DOI: 10.4236/ojn.2018.88039.

This study aimed to verify the effects of a new instructional method to structure knowledge. The research hypothesis was that “Structured knowledge improves assessment skills of students”. Fifty-five second-year undergraduate students volunteered to participate in this study. They were randomized into either a group that received instructional intervention (n = 19; intervention) or a group that did not (n = 36; non-intervention). The results of the concept map drawing task showed that post-test structural knowledge scores were significantly higher for the intervention, than the non-intervention group (p < 0.001). Post-test scores of the intervention group for assessment skills regarding “nursing problems and factors” were significantly better than pre-test scores (p < 0.001), and significantly higher than those for the non-intervention group (p < 0.01). The educational intervention in this study seemed to augment the ability to identify nursing problems, although we did not teach assessment strategies. The intervention seemed to confer structured knowledge with explicit conditions for applicability.

●Chikako OKAYAMA, *A Study on the Actual Condition of Mutual Recognition of Childcare Supporters and Parents*, Journal of Child Studies, vol.99, Oct.,2020,pp.13-21. The purpose of this study is to understand the motivation and efficacy of childcare supporters, and the awareness of parents who are raising children toward childcare

supporters. An interview survey was conducted and analyzed in order to understand expectations. Furthermore, we compared and examined the mutual recognition between childcare supporters and parents who are raising children.

As a result, it was found that the relationship of trust between parents and childcare supporters is based on the "child-rearing experience" of the childcare supporters. Furthermore, the childcare supporters have a negative consciousness, in contrast to the high expectations of parents.

● *Response Format, Not Semantic Activation, Influences the Failed Retrieval Effect.*

Tanaka, S., Miyatani, M., & Iwaki, N., *Frontiers in Psychology*, 2019 Apr 4; 10:599. doi: 10.3389/fpsyg.2019.00599.

In educational settings, tests are mainly used to measure the extent to which learners' knowledge and skill have been acquired. However, the act of taking a test also promotes learning itself. In particular, making errors on tests (i.e., searching for erroneous information) promotes learning. This is called the "failed retrieval effect" (FRE) and has been the subject of considerable study. Previous research shows that enhanced learning does not occur if feedback correcting an error is delayed. This is attributed to the relative absence of activated information. In this study, we manipulated both the amount of information to be retrieved prior to learning and the delay time until feedback is given to investigate their effects on learning. As a result, even when multiple incorrect answers were given to increase the degree of semantic activation, learning was not promoted beyond that found with traditional procedures that rely on only one incorrect response. The timing of feedback (immediate, short-delay, long-delay) also did not impact FRE. However, the manipulation of response format for erroneous information resulted in degraded performance when responses were typed and feedback was delayed. Based on this result, we suggested that the failed retrieval effect was not affected by semantic activation at the time of retrieval but was affected by response format. Moreover, the processing necessary for typing may affect FRE under the delayed feedback condition.

□ Psychology

● Chiharu Obata, Fumiko Nakajima, Hiroshi Aoki, *A Survey to Determine University-aged Stalker Victims*, *Research Bulletin of Tokushima Bunri University*, Vol.99, Mar., 2020, pp.27-34.

This paper will examine and report the results of a survey that was conducted to get a more accurate idea of the number of young stalker victims in Tokushima Prefecture. According to the National Police Agency, the number of young victims is on the rise. 40% of victims are in their 20s. Because many stalking incidents go unreported, Tokushima Prefectural Police conducted a joint survey of university students in Tokushima

prefecture, to determine the actual number of stalker victims. Results indicate that one in seven students has been the victim of a stalker.

●Yukihiro DONAKA, *Psychological Study of the Arousing the Imagination of Art Appreciation*, Research Bulletin of Tokushima Bunri University, Vol.102, Sep.,2021,pp.67-76.

The arts weaved by people, such as music, paintings, and dancing, have not only been appreciated and enjoyed, but also functioned to liberate the spirit or save the soul. Nowadays, it can be said that art therapy occupies an important position in the framework of psychotherapy. In this study, after overviewing of the relationship between art and psychotherapy, I conducted a survey to verify the effect of painting appreciation on human thinking. As a result, it was suggested that the image of the thought content was expanded and the episodic memory of the past became clearer by using the painting as a medium.

●Hiroyuki FUKUMOTO, *Attempts to focus on unfinished business when using “the Blue door & the Red door technique” and “the empty chair technique” : Discussion based on the case of so-called on-going counseling case*, Journal of Japanese Clinical Gestalt Therapy, Vol.6, Sep.,2021, pp.55-65.

The client in his late thirties male who repeatedly leaves and changes jobs at the workplace. He lost self confidence in building relationships with others and had a weakened self-image. He began to be aware of the so-called "the age of forty" and wanted to be able to settle in the workplace and build a stable life from now on. And he came to the Psychological Counseling Room of the University I work for. I conducted a counseling session aimed to restore self-affirmation by focusing on the client's past regrets and unfinished business. However, he had many regrets that were serious experiences, and pulling them out made him confused. In this paper, I attempted to focus on the theme of regret by incorporating “the Blue door & the Red door” technique and “the empty chair technique”.

●Kotaro Harada, *Which of perceived fairness and perceived rationality is predominant as a priority cue and verbal framing effect in risky choice?*, The Japanese Journal of Interpersonal Communication, The Japanese Society of Interpersonal Communication, (in press).

According to Ambiguity – ambivalence hypothesis (Wang, 2008), it is suggested that the priority cue and the secondary cue are used for decision making in risky choices, and that verbal framing effect in risky choices will appear when decision making using the priority cue is not accomplished. This study examined which of perceived fairness and perceived rationality was predominant as the priority cue, and examined verbal

framing effect in the live-or-death problem which Mai et al. (2020) used. 139 students completed one of four problems varied with Sure/Risky and Positive/Negative. Perceived rationality was predominant over perceived fairness as the priority cue in decision making. Verbal framing effect did not appear. The relation between perceived rationality and perceived fairness was considered by comparing to the relation between justice and fairness in philosophy.

● Chieko Kishi , Rie Takeuchi , Taizou Nagahama, Katsuyuki Yamasaki, *Class practice using the flipped classroom and its effect -Through a class on " School Health Care " for university students-* , Research bulletin of Tokushima Bunri University 100(0), pp.29-35, 2020.

The current research aimed to examine the changes in students' evaluations from the classes in 2014, 2015, and 2016 before introducing flip classes (N = 184) to the ones in 2017 and 2018 after it (N = 94). The classes were "School Health Care", given to the first- and second-year undergraduates. The five-point Likert type of questionnaire was administered to both students who took traditional lecture-based classes before the introduction of flipped classes and students who took the flipped classes. The data from the questionnaire were analyzed using one-way repeated measure analyses of variance. This study suggested that learners prefer the flipped classroom approach to the traditional lecture-based approach. It is underscored that the flipped classroom was rated more positively than the traditional classroom on the comprehensive class evaluation [F (1,276) = 8.24, p < 0.05] .

● *Development of a low energy small electron gun to study electron transport in hydrogen negative ion source plasmas.*

Yoshikatsu Matsumoto, Masashi Kisaki, Katsuhiko Shinto, Haruhisa Nakano, Mamiko Sasao, and Motoi Wada, Rev. Sci. Instrum. 91, 013333 (2020); doi: 10.1063/1.5128609

We developed a small-size electron gun capable of producing electrons with kinetic energy less than few tens of eV to investigate the slowing down and transport mechanisms of electrons in hydrogen negative ion source plasmas. The maximum extractable beam current density reached 36 $\mu\text{A}/\text{cm}^2$ for 1 eV beam energy in a preliminary experiment. Although the present electron current density is still insufficient compared with our target value, 1 mA/cm², we have found some hints to realize larger beam current density from the electron gun through this study. The measured beam profile along the electron beam axis has shown that the electron beam could travel approximately 7 mm from the electron gun in vacuum. The Particle-In-Cell (PIC) simulation explained the measured beam profile well and indicated that the electron beam has an energy spread as small as 0.1 eV compared to the 1 eV mean energy. The PIC simulation showed a discrepancy from the measurement in the dependence of the electron beam current on the beam extraction voltage of the electron

gun. It implies that we should introduce a more realistic filament structure inside the electron gun in the PIC simulation in order to study the transport of low energy electrons more precisely.

●Tatsuo Nakatsu, *About narrative characteristics to be seen in the Baum Test*, Studies in clinical application of drawings, Vol.31, 2016, pp.88-103.

The Baum Test that Koch,K. (1957) systematized can infer the current conscious or unconscious contents of mind from a drawn tree-picture. In this study, 30 university students who participated were interviewed after this test, and the narrative account which they provided was analyzed by M-GTA (Kinosita, Y. 2007). As a result, it was found that the narrative theme (The Dominant story) to influence the life of the respondent was often included in their account. It became clear that The Baum Test has possibility to show not only current mental state but also life story (The Identity) of a drawer.

●Haruo OKABAYASHI , *The Formation of Mutual Understanding in Conversation: An Embodied Approach*, International Scholarly and Scientific Research & Innovation 11(3) 2017, 563-569.

The mutual understanding in conversation is very important for human relations. This study investigates the mental function of the formation of mutual understanding between two people in conversation using the embodied approach. Forty people participated in this study. They are divided into pairs randomly. Four conversation situations between two (make/listen to fun or pleasant talk, make/listen to regrettable talk) are set for four minutes each, and the finger plethysmogram (200 Hz) of each participant is measured. As a result, the attractors of the participants who reported “I did not understand my partner” show the collapsed shape, which means the fluctuation of their rhythm is too small to match their partner’s rhythm, and their cross correlation is low. The autonomic balance of both persons tends to resonate during conversation, and both LLEs tend to resonate, too. In human history, in order for human beings as weak mammals to live, they may have been with others; that is, they have brought about resonating characteristics, which is called self-organization. However, the resonant feature sometimes collapses, depending on the lifestyle that the person was formed by himself after birth. It is difficult for people who do not have a lifestyle of mutual gaze to resonate their biological signal waves with others’. These people have features such as anxiety, fatigue, and confusion tendency. Mutual understanding is thought to be formed as a result of cooperation between the features of self-organization of the persons who are talking and the lifestyle indicated by mutual gaze. Such an entanglement phenomenon is called a nonlinear relation. By this research, it is found

that the formation of mutual understanding is expressed by the rhythm of a biological signal showing a nonlinear relationship.

●Akinari HAYASHI, Kumiko KOZAWA, Seiji MABUCHI, Tomoko MURAMATSU, Noriko NAKAMURA, Masamichi NODA, Takahiro SASAKI, Ritsuko TSUGAWA, Hiroshi URATA, Satoru WATANABE, *The Interim Report of the Map Project at Rorschach Centenary Congress*, Journal of Japan Rorschach Society for the Comprehensive System, Oct., 2020, Vol24(1), pp.51-57.

The Rorschach test will reach its 100th anniversary in 2021. In this memorable year, the International Society of the Rorschach and Projective Methods will be held Centenary Congress at the University of Geneva Medical School in Switzerland. For this event, the ISR Board is planning the Map Project that how did Hermann Rorschach's "Psychodiagnostik" and 10 cards spread, and develop into the world. Research for this Map Project revealed that in Japan, the Department of Psychiatry, Kyoto Imperial University imported "Psychodiagnostik" in March 1923. It was also found that there are four first editions of "Psychodiagnostik" in Japan. Of these four books, only the first edition in the International Research Center for Japanese Studies has 10 cards.

□Media Design

●*Dental Caries in Children Under Five Years of Age In Mongolia.*

Mizuho Nishino, Bazar Amarsaikhan, Nanayo Furumoto, Saki Hirao, Hiroko Bando, Akemi Nakagawa, Sukhbaatar Nonmineral, Begzsuren Bolorchimeg and Masami Fujimoto, *Int J Environ Res Public Health*, 2020 Jul 1;17(13):4741.

During the Japan International Cooperation Agency (JICA) partnership program in Mongolia, six times between October 2017 and October 2019, education for caries prevention, a questionnaire of daily oral health behavior, and an oral examination for parents and children aged 0–5 years old were done. The target parent population were middle socio-economic class families. In total, there were 2223 participants. The caries prevalence measured in October 2017, January, April, and October 2018, and April and October 2019, was 78.0% (95% CI: 74.2–81.4); 79.4% (73.7–84.4); 80.8% (76.2–84.9); 76.4% (70.1–82.0); 89.3% (85.3–92.6); and 82.6% (79.3–85.6), respectively. Compared to October 2017, in October 2019, the deft of three years old was significantly decreased ($p < 0.01$) and that of four years old was also decreased ($p = 0.085$). For the prevention of early childhood caries (ECC), daily oral health behaviors are important. In 2019, compared with the percentage of 0–5 years old in 2017, the frequency of tooth cleaning per day, parents cleaning after children, and parents watching during children's tooth

cleaning were significantly increased ($p < 0.01$). Unfortunately, the frequency of sugary—snack intake per day showed an increased tendency ($p < 0.05$). The baby teeth decayed, extracted and filled (def) index at three and/or four years old in October 2019 was correlated with the childrens' background characteristics, such as parent educational attainment, frequency of sweets intake, frequency of daily tooth cleaning, and parental cleaning of children's teeth. The effects of the JICA program were recognized.

● Yoshio Kaji, Junji Kawata, and Shoichiro Fujisawa, *Educational Effect of Participation in Robot Competition on Experience-Based Learning*, Journal of Robotics and Mechatronics, Vol.31, No.3, Jun., 2019, pp.383 - 390.

In recent years, instructional robot materials have often been used in robotics and engineering education. We use LEGO Mindstorms which is an educational robot development kit in its curriculum. In this subject, students are taught basic subjects such as robot mechanisms, robotic control, and programming. To enhance the subject's educational effects, the students are set the objective of entry into a robot competition. In the subject, the students are grouped into teams comprising two or three members to undertake the aforementioned task, with the objective of improving their communication skills and problem-solving capacities. The effects of participation in the robot competition were observed in the improved performances in the robot competition implemented in a class held after the SMART competition. In the questionnaire survey conducted at the end of the subject, the upper-class students, in particular, conveyed favorable views on the use of LEGO Mindstorms and participation in the robot competition. On comparing the realized educational effects on the first- and third-year students, positive effects were confirmed in both groups.

● Taizou NAGAHAMA, Ryuichi MIZOGUCHI, *Activation of Library Utilization Through Collaboration Between Students and Faculty: Research on Project-Based Active Learning*, The 14th "Distinctive Education and Research" All-Academic Presentation, Tokushima Bunri University, Sep, 2021.

The purpose of this study is to implement project-based active learning in a university library and to investigate the effects of active learning and students' lecture attitude on the change of students' basic and general competency. The results showed that students' lecture attitude had a positive impact on their basic and general competency. And that active learning had a positive impact on their basic and general competency. In addition, the prior learning of active learning had a positive impact on students' basic and general competency.

● Terumi KOJIMA, Naho KAWAUCHI, Yasunori SHINOHARA, Nanayo FURUMOTO,

Attempt to re-educate the piano for nursery teachers -Application development for online piano lessons-, Japan Society of Research on Early Childhood Care and Education, 73rd convention in Nara University of Education, May 2020.

Many Nursery Teachers feel that they are not good at playing the piano. This is related to the low level of satisfaction in childcare regarding musical expression. Furthermore, the results suggest that it is related to the satisfaction level of childcare in general. Therefore, the authors thought that reducing the sense of weakness in piano accompaniment skills would increase satisfaction with childcare.

We developed a smartphone-based online piano lesson application as a way for childcare providers to learn without feeling psychologically or time-consuming.

● *Flood damage and continued childcare of nursery schools in Nagano Prefecture due to the heavy rain event by Typhoon Hagibis in October 2019.*

Shingo YAMASHIRO, Susumu NAKANO, Junko KANAI and Masayuki HASEGAWA, Journal of Japan Society of Civil Engineers, Ser. F6 (Safety Problem), 2020 Vol.76, Issue 2 Pages I_1-I_8, Published: 2020, Released: February 05, 2021

The Typhoon Hagibis in October 2019 caused flood damage in various places in Nagano pre-fecture. Four nurseries were flooded in Nagano City and Chikuma City. We interviewed the city staff and nursery school staff about the disaster situation and childcare continuity. Furthermore, we carried out flood inundation analysis of the Chikuma River and analyzed the inundation process. Nursery schools need rules to close before a typhoon arrives. And six types of resources are required for the nursery school to resume services. In this case, “building” and “supporter” were the key resources.

□ Architectural Design

● Takao MORITA, *Text Analysis on Evacuation in Automobiles and on Planning of Shelters in the 2016 Kumamoto Earthquake*, Regional Community Facilities Planning and Design, AIJ, Vol.36, Jul., 2018, pp.185-194.

About 50% refugee in Kumamoto Prefecture fled from their houses into automobiles when Kumamoto Earthquake was generated on April 17 2016. The purpose of this study was to analyze the reason why they did not flee into shelters but why they fled into automobiles and slept there. The analysis method was a statistical analysis of a result of the questionnaire survey and newspaper article about evacuations. The computer software KH Coder was used for categorization and co-occurrence network analysis of newspaper article. Safety against an earthquake was biggest important

factor. People thought living in automobile was comparatively safe. Privacy was second important factor.

□ Human Life Sciences

● Yoshihiko FUJITA, *Inspection of DNA Typing in the United States and Measure*, ACTA CRIM. JAPON, Vol.84(5), Oct., 2018, pp.130-134.

As a result of examining the information of 65,493 individuals registered in DNA database of the Arizona Department of Public Safety (DPS) Crime Laboratory, 9 of 13 STR loci matched in 122 pairs, 10 STR loci matched in 20 pairs, 11 STR loci matched in 1 pair (brothers), and 12 STR loci matched in 1 pair (brothers). It is considered that inspection using an Identifiler Kit and the like is necessary for performing DNA typing using a Profiler Kit in Japan, because 9 STR loci matched for DNA typing between 2 apparently unrelated individuals in the United States. In addition, it was reported that no match was found for 9 STR loci used for DNA typing in the Profiler Kit among 1,200 unrelated Japanese individuals. Although the Devil's proof (*probatio diabolica*) is a difficulty here (e.g., absence of evidence is not evidence of absence), it is necessary to increase the number of samples to examine this issue further. To avoid false accusations, investigations must be made certainly and steadily without relying on the myth of the infallibility of DNA typing.

● Junko IKEZOE, Suguru MORI, Rie NOMURA, *A fundamental study on transfer housing to uplands for prevention of natural disaster as reconstruction of urban planning in advance :A case study of Nankai Trough Earthquake*. Japan Society for Urbanology, VOL.51, pp.201-209, 2018

In the Great East Japan Earthquake, many houses were damaged by tsunamis, and some villages were relocated to higher ground as a whole. Similar damages are expected to be caused by the Nankai Trough earthquake, which is likely to occur in the near future. In this study, we conducted a questionnaire survey on the plan of relocating housing to higher ground for the pre-disaster community planning in 139 municipalities where tsunami inundation is expected due to the Nankai Trough earthquake. The survey details include whether or not there is a plan to relocate housing, and if there is such a plan, progress of the plan. For those municipalities having such plans, interviews were also made for more details.

● Kinugawa Akemi, *Looking for Mme Grès's creating secrets, by making a replica of one of her most beautiful dresses*, Osaka Shoin Woman's University Graduate School of

human sciences, Jan., 2015, pp.4-7.

Madam Grès's clothing-making technique are created by a unique pleating technique, which are comfortable to wear and suitable for the person's physique. They are different from ready-made clothes that were cut from cloth and sewn together. The purpose of this study was to clarify her spirit and technique, pass it on to young people involved in clothing, and give it back to society through the replica production of the costumes made by Madam Grès, which is called *The Last Couturier* at the end of the last century, by verifying it concretely. It was found that it was significant to make clothes is to carefully select the material for creating the design, that is, the quality of the fabric. Furthermore, it was clear that handicrafts, that is, craftsmanship, completes beautiful clothes.

●Rie TAKEUCHI, Chieko KISHI, Taizou NAGAHAMA, *An Examination of Yogo Practice to Develop Independence of Will and the Spirit of Inquiry in Children Through Qualitative Analysis Using SCAT*, Journal of Japanese Association of Yogo Teacher Education, Vol.25, No.1, 2021 (in print).

It is essential to develop independence of will and the spirit of inquiry in children survive society in the future. Therefore I took up *Yogo* practice about the health education and performed a qualitative study to clarify a method and requirements to develop independence of will and the spirit of inquiry children. In analysis, the next conclusion was provided using 'Steps for Coding and Theorization' by Otani.

In order to grow children's independence of will and the spirit of inquiry it is important for them to be aware of their health issues and challenges through the sense of the bodies such as the grasp of the actual situation or experience.

In addition, it is also important to make this practice a familiar and necessary one so that children may place it in life, find a solution voluntarily and search a better method.

Furthermore, it is necessary for children to do activities for creating new values and to wrestle measures voluntarily in cooperation at home and to be aware that they themselves are main constituent bodies who make their rich lives.

And it is shown that stimulating children's growth both in mind and body through actual practice leads them to take healthful action willingly.

■ Health and Welfare

□ Nursing

● *Usefulness of PRO-CTCAE and its Impact on QOL in Breast Cancer Patients Receiving EC Therapy.*

Hiromi Arahori, Kazuya Kondo, Yoshie Imai, Takae Bando, Aki Takahashi, Hirokazu Takechi, Hiroaki Inoue, Masami Morimoto, Soichiro Sasa, February 2021.

The 35th Annual Conference of the Japanese Society of Cancer Nursing, Feb.27-Apr.26, 2021, online.

https://jscn.or.jp/entry/c_movie/user_abst_detail.php?menu=6&cate=2&lid=25

The Common Terminology Criteria for Adverse Events (CTCAE), published by NCI, is a tool for assessing adverse events associated with drug therapy. In recent years, it has been pointed out that there are differences between CTCAE evaluations performed by medical professionals and patients' own evaluations, and PRO-CTCAE was developed. The aim of this study was to clarify the usefulness of PRO-CTCAE and its impact on quality of life over time in breast cancer patients receiving EC therapy.

● *Urinary tract obstruction by endometrial cyst, surgically treated in two cases.*

Shirakawa A, Yamamoto S, Fukui R, Azuma K. International Federation of Fertility Societies. International Meeting 2015 on April 26-29, 2015, Yokohama.

We report two rare cases with urinary tract obstruction by endometriosis lesion. Case 1. A 43-years-old woman visited our clinic complaining low back pain occurring in menstrual period. Cystectomy and ureterectomy were carried out. The pathological examination of ureter revealed its stenosis caused by

Endometriosis lesion. Case 2. A 29-years old woman was referred to our hospital with uterine myoma, adenomyosis and left ovarian cyst with a history of infertility. She had to receive cystectomy, adhesiolysis and nephrectomy. We experienced two rare cases of ureter obstruction due to endometriosis, the one was able to preserve kidney, the other was not.

● Kaoru Furukawa, Chiaki Moriwaki, *Development of the child-rearing ability assessment tool for mothers at high risk for abusing their children*, Japanese Journal of Maternal Health, Vol.61, Apl,2020, pp.151-158

Objectives: We aimed to prepare an assessment questionnaire of the child-rearing ability for mothers at high risk for abusing their children, and verify the reliability and validity of the questionnaire in an attempt to prevent child abuse.

Methods: We conducted interviews among public health nurses to clarify constructive concepts of the child-rearing ability of mothers at high risk for abusing their children, and used the interview results to prepare a prototype child-rearing ability assessment tool for such mothers. We then conducted a survey of public health nurses across Japan using the prototype assessment tool. Valid responses from 667 public health nurses

were included in the analysis. We confirmed the construct validity of our questionnaire with an exploratory factor analysis and evaluated the reliability of the tool via internal consistency with Cronbach's coefficient α .

Results: Based on the exploratory factor analysis, we developed an assessment tool consisting of five factors: involvement with children and emotional control, ability to continue child-rearing, ability to learn child-rearing that suit each child, ability to perform basic daily activities, and the ability to at least protect the child's life. The questionnaire consisted of 38 items.

● Keiko Imoto, Kayoko Kamada, Sumiko Yoshinaga and Hiroko Ooka, *Survey on Health Management and lifestyle habits of nursing students*, Research Bulletin Of Tokushima Bunri University, Vol.102, Sep., 2021, pp.15-24.

The purpose of this study is to clarify the circumstances of health management and lifestyle habits of nursing students and to obtain suggestions for student support aimed at changing behavior in order to protect health. We conducted a web questionnaire created with Google Forms for nursing students and received responses from 242 people. Regarding health management, interest in food was low, and respondents skipped breakfast; overall, the situation was not desirable. Regarding lifestyle habits, respondents had not established regular exercise habits, and approximately one in five students went to bed at 2 AM or later, showing the need for improvement in this area.

● *Paradoxical development of polymyositis-like autoimmunity through augmented expression of autoimmune regulator (AIRE)*

Nishijima H, Kajimoto T, Matsuoka Y, Mouri Y, Morimoto J, Matsumoto M, Kawano H, Nishioka Y, Uehara H, Izumi K, Tsuneyama K, Okazaki IM, Okazaki T, Hosomichi K, Shiraki A, Shibutani M, Mitsumori K, Matsumoto M. *J Autoimmun.* 2018 Jan;86:75-92. doi: 10.1016/j.jaut.2017.09.006. Epub 2017 Sep 18. PMID: 28931462

Autoimmunity is prevented by the function of the autoimmune regulator [AIRE (Aire in mice)], which promotes the expression of a wide variety of tissue-restricted antigens (TRAs) from medullary thymic epithelial cells (mTECs) and from a subset of peripheral antigen-presenting cells (APCs). We examined the effect of additive expression of human AIRE (huAIRE) in a model of autoimmune diabetes in NOD mice. Unexpectedly, we observed that mice expressing augmented AIRE/Aire developed muscle-specific autoimmunity associated with incomplete maturation of mTECs together with impaired expression of Aire-dependent TRAs. This led to failure of deletion of autoreactive T cells together with dramatically reduced production of regulatory T cells in the thymus. In peripheral APCs, expression of costimulatory molecules was augmented. We suggest that levels of Aire expression need to be tightly controlled for maintenance of immunological

tolerance. Our results also highlight the importance of coordinated action between central tolerance and peripheral tolerance under the common control of Aire.

●Kayoko KAMADA, Michiko FUKUSHIMA, *The Status of Continuation of Professional Duties in Home Nursing Station Managers*. J.Jpn.Soc.Nurs.Health Care, Vol.22, No.1:38-46, 2020.

Purpose: The purpose of this study was to clarify the status of continuation of professional duties of home nursing station (ST) managers, and to obtain suggestions for investigating issues and specific support in the continuation of professional duties.

Methods: Semi-structured interviews using an interview guide were conducted on study participants who were working at STs in Prefecture A, and had worked continuously as a manager for at least three years at the time of the survey. Verbatim transcripts were prepared from the recorded interview contents. Parts related to the status of continuation of professional duties in ST managers were extracted from the transcripts in semantic units and coded. Categories were then made.

Results: There were 10 study participants, all of whom were women with ages ranging from the 40s to 70s. The status of professional duties in ST managers consisted of six major categories: "began working with dreams and goals", "difficulty opening and operating an ST", "work with a direct nature", "results obtained from experience", "mastery of how to be a manager" and "creation of an ST."

Discussion: The status of professional duties in ST managers involves seeking revenue while making efforts to improve the quality of home nursing as the person responsible for the ST. It has the characteristics of receiving direct assessments from patients and their families and of being taken on wholeheartedly, while also pursuing the dreams and goals of home nursing envisioned at the time of or before taking up the position.

●Hitoe Kanai, *A New Edition of Introduction to Nightingale's Theory of Nursing: Reading the "Notes on Nursing" from a Modern Perspective*, Gendaisha, 2019, 277p.

This is a revised and updated edition of "Introduction to Nightingale's Theory of Nursing" (1993). The essence of Nightingale's philosophy is based on the principle of nursing, which has not changed over time. One of the main concepts is "All disease is a reparative process". This point needs to be interpreted with the help of the latest findings in the life sciences in order to make it relevant today. This book explains the ideal state of nursing by making extensive use of life science knowledge. In this sense, this book is a new way of reading the "Notes on Nursing" from a modern perspective.

●Sayoko Kusaka, Masami Nishiuchi, Eriko Okada, Kaoru Wakayama,

Route and treatment environment joint work to survive it which a patient caught by continuation of the radiation therapy after the breast preservation operation, Japan Red Cross medicine Vol. 71 first ,2019, p.208.

The purpose of this study was to clarify the reasons for the continuation of radiotherapy in patients after breast-conserving surgery. As the result, seven categories, "decision to survive", "burden of mind and body with radiotherapy", "thought to fulfill the role", "danger of daily life maintenance and recurrence", "appreciation to support and treatment environment received from others", "substantiality and utilization of economic support system", and "secondary effect by receiving radiotherapy" were extracted. These results suggest that the patients after breast-conserving surgery have a strong desire to continue outpatient radiotherapy, and that they are grateful for the environment that has helped them to survive and to support their treatment.

● *Consideration of Safety Management When Using Pepper, a Humanoid Robot for Care of Older Adults.*

Misao Miyagawa, Yoshihiro Kai, Yuko Yasuhara, Hirokazu Ito, Feni Betriana, Tetsuya Tanioka, Rozzano Locsin, *Intelligent Control and Automation* > Vol.11 No.1, February 2020. DOI: 10.4236/ica.2020.111002

Pepper, a humanoid robot, is 1.2 m in height and is designed to move its limbs. There are risks of the older adults experiencing falling and collision accidents when they interact with Pepper. When physical interaction happens between a humanoid robot and human beings, potential harmful physical contact might occur. The aim of this report was to examine the safety management aspects when using Pepper, a humanoid robot for the care of older adults. The older adults' reactions to Pepper's functions cannot be predicted. Hence, it is necessary to clarify methods to guarantee its safety in advance and to increase the safety and properties of the robots. The benefits of introducing support robots such as Pepper for aging medical and nursing care settings are obvious. Therefore, engagement in robot development while considering both the risks and benefits is critical. Our academic initiatives have just begun. Through information exchange among researchers, users, engineers, and law specialists, we need to identify latent and prominent risks in situations where Pepper and the older adults interact and deepen our examination of measures against such risks.

● Sawa Fujita, Norimi Okawa, Ayumi Mori, Akiko Fukawa, Mami Syouji, Toshiko Morishita, *Development of nursing care guidelines that support the empowerment of cancer patients in the transition to at-home care*, J.K.W.U.Acad.Nurs. Vol. 43 , No. 2 , 2018, pp.102~110.

The purpose of this study was to develop nursing guidelines that support the

empowerment of cancer patients in the transition to at-home care. Existing literature was reviewed to identify problems expected to be faced by cancer patients at acute hospitals who require support in the transition to at-home care, as well as the types of support available to them. Nursing care guidelines were drafted based on this review. The authors and five certified nurse specialists in cancer nursing examined the drafted guidelines, which support the empowerment of cancer patients in the transition to at-home care, and finalized them.

● Kaoru Furukawa, Chiaki Moriwaki, *Development of the child-rearing ability assessment tool for mothers at high risk for abusing their children*, Japanese Journal of Maternal Health.vol.60.no.4,2020,pp151-158

Objectives : We aimed to prepare an assessment questionnaire of the child-rearing ability for mothers at high risk for abusing their children, and verify the reliability and validity of the questionnaire in an attempt to prevent child abuse.

Methods : We conducted interviews among public health nurses to clarify constructive concepts of the child-rearing ability of mothers at high risk for abusing their children and used the interview results to prepare a prototype child-rearing ability assessment tool for such mothers. We then conducted a survey of public health nurses across Japan using the prototype assessment tool. Valid responses from 667 public health nurses were included in the analysis. We confirmed the construct validity of our questionnaire with an exploratory factor analysis and evaluated the reliability of the tool via internal consistency with Cronbach's coefficient.

Results : Based on the exploratory factor analysis, we developed an assessment tool consisting of five factors : involvement with children and emotional control, ability to continue child-rearing, ability to learn child-rearing that suit each child, ability to perform basic daily activities, and the ability to at least protect the child's life. The questionnaire consisted of 38 items.

● *Changes in range of motion due to physical restraining on the non-paralyzed side of the body in stroke patients.*

Minagawa T, Tamura A, Yokoi Y. Japanese Academy of Neuroscience Nursing, 2019. Dec.30; 6(1): 15-22.

Data collected in a previous study on acute stroke patients were analyzed. The range of motion of the elbow joint of two groups of 10 patients each was compared. In the restrained group, the wrist on the nonparalyzed side was secured to the bed with an 8-cm restraining band; in the control group, it was not. The control group was similar to the restraint group in gender, nonparalytic side, disease, treatment, and NIHSS score at admission. First, changes from day 1 or 2 to day 6 of restraint were checked. They

also compared the restraint group to the control group; comparing day 1 to day 6, elbow flexion was significantly lower in the restraint group. A comparison of the restraint and control groups showed that elbow flexion in the restraint group decreased significantly after approximately one week, indicating that the range of motion of the joint was already restricted. These results indicate that the range of elbow motion was significantly decreased in the acute stroke patients who underwent wrist restraint from the first measurement to approximately one week after the second.

● Chie Namitomi, Hitomi Maeda, *Effects of outpatient nurse intervention for COPD patients using home oxygen therapy: Comparison between the effects of instruction at home and at the outpatient department by outpatient nurses*, The Journal of Japan Society for Respiratory Care and Rehabilitation, vol.29 No2, Dec.2020, pp276-281.

The author compared and studied the case where outpatient nurses gave instructions to individual COPD patients aged 65 years or older who were undergoing home oxygen therapy at an outpatient department and the case where they conducted visiting care while giving instructions. It was found that the difference in intervention causes no significant difference in acute exacerbation, but the patients receiving visiting care obtained more information regarding disease conditions and treatments, including “the knowledge of diseases” and “medicines,” and daily life, including “self-management” and “exercise” through LINQ. Since the patients receiving instructions during visiting care obtained necessary information for self-management, visiting nurses are required to put the information obtained by patients to practical use so that they can self-monitor, in order to prevent the acute exacerbation of COPD patients.

● Hiroko Ooka, *Analysis of factors related to fundamental competencies for nurses working at university hospitals*. The journal of the Japan Academy of Nursing Administration and Policies. Vol.21.no.2.2017, pp87-97.

The purpose of this study is to identify primary factors contributing to the fundamental competencies of working nurses by conducting a self-administered anonymous questionnaire consisting of the following factors: individual attributes, nursing, education, and experience, feelings of self-esteem, career maturity, and fundamental competencies for working persons. The questionnaires were distributed to 1,220 nurses working at two national university hospitals located in Shikoku from June to August 2014. Some 1,142 responses were received (a response rate of 93.6%), out of which 997 valid responses were selected for the study (81.7%). The average age of the respondents was 33.65 ± 10.48 years, with an average of 9.52 ± 9.01 years of nursing experience. Multiple regression analysis results revealed that the following factors are important for enhancing the fundamental competencies of working nurses: career

maturity, feelings of self-esteem, nursing practice, one job status or position, role models, advisors or people one can consult, and involvement in training that requires giving presentations. We observed an especially strong association with career maturity, which suggests that career maturity is the most significant factor for enhancing the fundamental competencies of working nurses.

● Tamae SAHARA, Tsuyako HOSOKAWA, *The Process of Building Relationships among Members of a Nursing Practicum*, J Jpn Aca Health Behav Sci, Vol.35(1), 2020, pp.52-62.

The purpose of this study was to clarify the process of building relationships among members of a nursing practicum group. The participants consisted of nursing students from the 4th grade. Semi-structured interviews were conducted with 11 students who had completed their clinical nursing practicum. The data were analyzed using M-GTA. The core category representing the process of building relationships among nursing practicum group members is “acquire my location within the group.” Students began building relationships by “approach the group members to get along,” after which they “grasp members characteristic” and “accept the members’ roles.” Students who performed their role as expected by members “help each other and become best friends.” On the other hand, they are caring for other members severely and are tired of being led to “A bad relationship with members.”

Conclusion: The process by which nursing practicum students build relationships with their group members is the process through which they “acquire my location within the group” by caring for members appropriately and performing their expected roles.

● Nakamura N, Yakushijin Y, Kanamaru T, Tani H, Ideno K, Nakai, *A Development and validity testing of the revised diabetes self-care inventory for children and adolescents*. Diabetologia International.10(2)117-125, 2018.

The aims of this study were to modify and subsequently test the validity of the revised diabetes self-care inventory (R-DSCI) for children and adolescents, and to construct the diabetes self-care model on the R-DSCI, HbA1c, duration of diabetes and age. The final version of the R-DSCI was composed of 41 items. Eight factors, which explained 40.9% of the variance, were identified using the varimax method; Cronbach's alpha for the 41 items was 0.79. The R-DSCI should be useful for clinicians and researchers to assess the self-management in children and adolescents.

● Isako UETA, Hiroko OTA, Miho ONO, Sanae ASANO, Chiemi ONISHI, Yoshie IMAI, Masato NISHIMURA, Akiko ABE, *Exploring the Psychological Adjustment of Female Cancer Survivors in Terms of Femininity*, Shikoku Medical Journal, Vol.76(1-2), Apr. 2020, pp.73-82.

The purpose of this study is to explore the psychological adjustments female cancer

survivors undergo with respect to their femininity. Semi-structured interviews were performed with 29 female cancer survivors in their 20s to 50s. Qualitative descriptive study data was interpreted. Six categories were generated as psychological adjustments utilized by female cancer survivors: "I like the way I am"; "I am charming as a woman"; "I live independently as a woman"; "I am expanding my life as a woman"; "I can feel connected with someone"; and "I have graduated from pessimism." These could be interpreted as psychological adaptations that reflect feminine emotions and reflect the strength and resilience of female cancer survivors.

● *Trends in investigator-initiated clinical studies at a university hospital after enforcement of the 2018 Clinical Trials Act in Japan.*

Sato Y, Sakaguchi S, Takechi K, Chuma M, Yagi K, Kane C, Goda M, Hamano H, Aoe Y, Nokihara H, Kubo Y, Hashimoto I, Yanagawa H. *Biol Pharm Bull.* 2022;45(3):374-377. doi: 10.1248/bpb.b21-00753.

In April 2018, the Clinical Trials Act pertaining to investigator-initiated clinical trials was passed in Japan. The purpose of this study was to investigate activity in investigator-initiated clinical studies before and after enforcement of the new Clinical Trials Act. This was done by analysing the records of the Ethics Committee of Tokushima University Hospital, which reviews studies based on the Japanese government's Ethical Guidelines for Medical and Health Research Involving Human Subjects prior to the Clinical Trials Act, and records of the Certified Review Board established at Tokushima University under the Clinical Trials Act in 2018. The number of new applications to these two review boards during fiscal years 2015-2017 (pre-Act) and fiscal years 2018 and 2019 (post-Act) were used as an indicator of activity in investigator-initiated clinical studies. The number of new applications to the Ethics Committee was 303, 261, 316, 303, and 249 in 2015, 2016, 2017, 2018, and 2019, respectively. The data show that the total number of new interventional studies decreased from 50.3 in average in 2015-2017 (pre-Act) to 42 in 2018 and 40 in 2019 (post-Act), respectively. These results suggest that fewer interventional studies were started following enforcement of the new Clinical Trials Act. To confirm this trend and identify contributing factors, further studies are required. In addition, possible way, such as broader contribution of clinical research coordinators, to promote clinical studies in the new Clinical Trials Act era should be examined.

● Takeyo Yamada, Chiaki Moriwaki, *Literature review of fatigue among pregnant women in Japan.* Research Bulletin of Tokushima Bunri University, Vol.101, March 2021, pp.35-41.

In this study, we focused on the “feeling of fatigue” during pregnancy. Fatigue among pregnant women is often overlooked as a minor problem that occurs during pregnancy, and it is often not medically regarded as a problem. To improve the health and comfort of women during pregnancy, we conducted a literature review to understand the actual situation of the feeling of fatigue. Using the online version of the Japan Medical abstracts society, we analyzed 21 publications regarding fatigue in pregnant women. More than 90% of pregnant women feel tired during the entire duration of their pregnancy. The cause of fatigue in pregnant women is often thought to be due to the pregnancy itself, and most pregnant women spend their pregnancy feeling tired. We suggest that it is important to understand the actual condition underlying pregnant women’s feelings of fatigue after the second trimester, identify the factors that exacerbate fatigue during pregnancy, and assess the relationship between the identified factors and the feelings of fatigue.

Keywords: pregnant women, fatigue, literature review

□ Human Welfare

● *Totally Conservative Integration Method for the General Three-body Problem and Its Lagrangian Solutions.*

Yukitaka Minesaki, *The Astrophysical Journal*. 2019 Feb.; 873(1):4. doi:[10.3847/538-4357/ab03cc](https://doi.org/10.3847/1538-4357/ab03cc)

In this paper, we design a precise integration method with a variable time step for the general three-body problem that maintains all the conserved quantities. Our method is based on a logarithmic Hamiltonian leapfrog with chain vectors proposed by Mikkola & Tanikawa and features an energy-preserving parameter. Although the proposed method is merely second-order accurate, it can precisely trace some periodic orbits. This is not possible with generic geometric eighth-order numerical integrators and the logarithmic Hamiltonian leapfrog approach. Further, similar to logarithmic Hamiltonian leapfrog, our method is analytically shown to have Lagrangian solutions. Prior to the presented integration method, no integration method was known to preserve all the conserved quantities, in addition to presenting triangular Lagrangian solutions. Because our method is implicit, it requires an iteration method. Therefore, the proposed approach seems to be computationally intensive. However, our method is less computationally burdensome than a generic explicit eighth-order symplectic method. © 2019. The American Astronomical Society. All rights reserved.

●Kazusa MIYAHARA, *Introduction of Active Learning to the Class "Basics of Consultation Support and Specialist Jobs" Which is a Subject of the National Examination for Social Workers, and Evaluation Thereof*, Research Bulletin of Tokushima Bunri University, Vol.101, March 2021, pp.29-34.

In this paper, the author reports an example in which active learning was introduced to a class, entitled "Basics of Consultation Support and Specialist Jobs." The class teaches one of the specialist subjects of the Japanese National Examination for Social Workers. The class is also one of the subjects of a social worker training course, which has been knowledge-oriented to date.

●*Relationship among Eating Behavior, Effortful Control, and Personality Traits in Japanese Students: Cross-sectional Study.*

Katsumasa Momoi, Kumiko Ohara, Katsuyasu Kouda, Tomoki Mase, Chiemi Miyawaki, Tomoko Fujitani, Yoshimitsu Okita, Rumiko Murayama, Harunobu Nakamura. Journal of Advances in Medicine and Medical Research, 18(8), BJMMR.29729 PP.1-9

In this study, we investigated the relationships among eating behavior, personality, and effortful control in Japanese university students. Participants were 576 Japanese university students (422 males and 154 females). Participants completed a questionnaire measuring effortful control, Big Five personality traits, and eating behaviors. Our results indicate that eating behaviors are associated with both effortful control and the Big Five personality traits. However, the direction of the associations of effortful control and Big Five personality traits with restrained eating differed from the associations of effortful control and personality with emotional eating and external eating.

●*Evaluation of renal function in the advanced stage with Duchenne muscular dystrophy.*

Takahiro Motoki, Yuko Shimizu-Motohashi, Isao Saito, Hirofumi Komaki, Kaori Aibara, Toshihiro Jogamoto, Yuko Tezuka, Mika Kawabe, Kei Makino, Koji Nagatani, Katunori Tatara, Kozue Kuwabara, Chiya Kikuchi, Mitumasa Fukuda, Eiichi Ishii, Mariko Eguchi, Muscle & Nerve Volume61, Issue2 February 2020 pp192-197.

With improved treatments, patients with Duchenne muscular dystrophy (DMD) can survive far beyond adolescence. However, advanced-stage DMD patients are at risk of developing renal dysfunction. In this study, long-term renal function outcomes and associated risk factors in advanced stage DMD were analyzed. Fifty-one patients were classified into three different age groups (<20, 20-29, and ≥30 years of age), and cystatin C (CysC) levels were compared among groups. Median serum CysC levels were 0.74 mg/L, 0.63 mg/L, and 0.76 mg/L in the age groups of <20, 20-29, and ≥30 years,

respectively ($P = .003$). Five of the nine patients in the ≥ 30 years age group showed elevated serum CysC and decreased cardiac function compared with the other four in the group ($P = .014$). Our results indicate an association between cardiac and renal dysfunction in patients with advanced-stage DMD.

□ Physical Therapy

● *Intramuscular adipose tissue in the quadriceps is more strongly related to recovery of activities of daily living than muscle mass in older inpatients.*

Akazawa N, Kishi M, Hino T, Tsuji R, Tamura K, Hioka A, Moriyama H.

Journal of Cachexia, Sarcopenia and Muscle. 2021 Aug;12(4):891-899. doi: 10.1002/jcsm.12713. Epub 2021 May 16. PMID: 33998169; PMCID: PMC8350216.

Background: The relationship between intramuscular adipose tissue at admission and recovery of activities of daily living (ADL) remains unclear. This study aimed to examine the relationship between intramuscular adipose tissue in the quadriceps at admission and recovery of ADL in older inpatients.

Methods: This prospective study included 404 inpatients aged ≥ 65 years (54.7% female). Recovery of ADL during hospital stay was assessed using the Barthel Index (BI) score at discharge, BI score change, and BI efficiency. Higher BI at discharge, BI score change, and BI efficiency indicate more improvement in ADL. Intramuscular adipose tissue and muscle mass of the quadriceps were assessed using echo intensity and muscle thickness on ultrasound images, respectively. Multiple regression analysis was performed to identify factors independently associated with BI score at discharge, BI score change, and BI efficiency. The independent variables were BI score at admission, echo intensity and muscle thickness of the quadriceps, age, sex, number of medications, C-reactive protein concentration, updated Charlson Comorbidity Index score, Food Intake Level Scale, Geriatric Nutritional Risk Index score, days from onset disease, length of hospital stay, number of units of rehabilitation therapy, and subcutaneous fat thickness of the thigh.

Results: The medians (inter-quartile range) of the BI score at discharge, BI score change, and BI efficiency were 60.0 (35.0-80.0), 10.0 (0.0-25.0), and 0.11 (0.00-0.37), respectively. The median (inter-quartile range) of the length of hospital stay (days) and days from onset disease were 58.0 (39.0-92.0) and 79.0 (49.0-112.0), respectively. Quadriceps echo intensity was independently and significantly associated with the BI score at discharge ($\beta = -0.13$, $P < 0.01$), BI score change ($\beta = -0.23$, $P < 0.01$), and BI efficiency ($\beta = -0.21$, $P < 0.01$). Quadriceps thickness was not independently and

significantly associated with the BI score at discharge ($\beta = -0.02$, $P = 0.68$), BI score change ($\beta = -0.02$, $P = 0.79$), and BI efficiency ($\beta = 0.03$, $P = 0.67$).

Conclusions: Our study indicates that greater intramuscular adipose tissue in the quadriceps at admission is more strongly related to worse recovery of ADL than less muscle mass in older inpatients. Greater intramuscular adipose tissue in the quadriceps in older inpatients is considered to be a predictor of worse recovery of ADL, and intervening for greater intramuscular adipose tissue may be important for improving ADL in older inpatients.

● *A new method for characterizing hand dysfunction in cervical spondylotic myelopathy: a preliminary study.*

Spinal Cord. 2016 Mar;54(3):221-5.

T Akutagawa, T Tani, K Kida, N Tadokoro, H Enoki, Y Nagano, M Ikeuchi

Study design: A case-control investigation.

Objectives: The objective of this study was to quantitatively study impaired ability to appropriately adjust pinch strength while holding a small object in patients with cervical spondylotic myelopathy (CSM).

Setting: Kochi Medical School Hospital, Japan.

Methods: The subjects consisted of 19 CSM patients who had frequent episodes of failing to grasp and hold small objects in their daily life (Group A), 13 CSM patients who did not experience such episodes (Group B) and 16 healthy subjects (Control Group). We continuously measured the dynamic internal pressure of a pneumatic rubber object called a blower pinched by the subject, following two different sets of instructions: (1) pinching with eyes open and with the minimal strength required to prevent dropping; and (2) maintaining a constant pinch strength at given levels with eyes closed.

Results: Compared with the other two groups, Group A subjects used a significantly ($P < 0.01$) greater pinch strength to avoid dropping the blower held with eyes open and showed a significantly ($P < 0.01$) greater deviation in pinch strength from the baseline values with eyes closed. These tendencies in Group A showed a significant correlation with the tactile perception threshold of the digits ($P < 0.01$) but not with impairment of rapid repetitive movements of the digits that reflects spasticity.

Conclusion: Our technique applied to CSM patients helps assess functional integrity primarily, if not exclusively, of the fasciculus cuneatus mediating the feedback signals from proprioceptive and cutaneous receptors in the digits, which are otherwise difficult to evaluate quantitatively.

● *Foot Tapping Test as Part of Routine Neurologic Examination in Degenerative Compression Myelopathies: A Significant Correlation between 10-sec Foot-tapping*

Speed and 30-m Walking Speed.

Hayato Enoki, Toshikazu Tani, Kenji Ishida

Affiliations expand

PMID: 31440678 PMCID: PMC6698509 DOI: 10.22603/ssrr.2018-0033

Free PMC article

Introduction: Leg spasticity in degenerative compression myelopathy causes impairment of fast and rapid repetitive movements, which tends to appear despite the disproportionate paucity of clinical weakness. As clinically useful measures used to quantify the slowness of voluntary leg movements in this pathological condition, we compared the foot tapping test (FTT) with the simple walking test, which is now considered the gold standard in this field.

Methods: We compared the FTT with the simple walking test, the grip-and-release test, and the functional scales of Nurick and the Japanese Orthopedic Association (JOA) in 77 patients with cervical compression myelopathy and 56 age-matched healthy subjects. The FTT was conducted on both sides separately, and the subject, while being seated on a chair, moved his/her toes up and down repeatedly to tap the floor as fast and as vigorously as possible for 10 sec with his/her heels planted on the floor.

Results: The number of 10-sec foot tapping in the patient group significantly correlated with the Nurick grades ($r = -0.566$; $P < 0.0001$), the JOA scores ($r = 0.520$; $P < 0.0001$), and the grip-and-release rates ($r = 0.609$; $P < 0.0001$). It also significantly correlated with the 30-m walking time ($r = -0.507$; $P < 0.0001$) and the number of steps taken ($r = -0.494$; $P < 0.0001$). Assessments of wheelchair-dependent patients and side-to-side comparison, in which the simple walking test plays no role, revealed significantly fewer FTT taps in wheelchair-bound patients than in the ambulatory patients and a significant trend for cervical compression myelopathy to dominantly affect the upper and lower limbs on the same side.

● Ryohei Hirose, Yukio Yanagisawa, Hiroshi Tateishi, *Examination of factors affecting postoperative hospital stay in elderly abdominal surgery patients*, Shikoku Rigaku Ryohoshikai Gakkaishi, Vol.42 Mar., 2020, pp.128-129.

The prevalence of gastrointestinal cancer is high and surgical therapy is the main treatment. But there is no guideline about progression of postoperative rehabilitation of abdominal surgery. The aim of this study was to investigate factors affecting the length of hospital stay after abdominal surgery in elderly patients. As a result of the research, preoperative laboratory data (ALB, HGB, GNRI), walking speed and 6-minute walking distance were significantly lower and rate of preoperative sarcopenia and postoperative transvenous analgesia were significantly higher in the extended hospital stay group.

The length of hospital stay after abdominal surgery may be affected preoperative physical condition and postoperative pain management method.

● *Increased total body extracellular-to-intracellular water ratio in community-dwelling elderly women is associated with decreased handgrip strength and gait speed.*

Akemi Hioka, Naoki Akazawa, Naomi Okawa, Shinji Nagahiro. *Nutrition*, 2021 Jun;86:111175. doi: 10.1016/j.nut.2021.111175. Epub 2021 Jan 29.

Objective: As the extracellular-to-intracellular water (ECW/ICW) ratio of the thigh is negatively associated with knee extension strength or gait speed in the elderly, an increase in the total body ECW/ICW ratio in the elderly is considered to be related to a decrease in physical function. However, these relationships have not been properly investigated. The aim of this study was to investigate the relationship of handgrip strength and gait speed with the total body ECW/ICW ratio in community-dwelling elderly women.

Methods: The present study used a cross-sectional design. We enrolled 71 community-dwelling women, ≥ 65 y of age, who could independently perform activities of daily living. The total body ECW/ICW ratio was measured using bioelectrical impedance analysis. Relationships between the total body ECW/ICW ratio and grip strength and gait speed were assessed using Pearson's correlation coefficient. Additionally, stepwise multiple regression analysis was used to identify the factors that were independently associated with handgrip strength and gait speed. The independent variables considered were the total body ECW/ICW ratio, age, body mass index, number of medications, presence of pain, and a history of certain conditions.

Results: The results indicated that an increased total body ECW/ICW ratio in community-dwelling elderly women was associated with a decreased handgrip strength and gait speed. Furthermore, the total body ECW/ICW ratio was significantly, independently associated with handgrip strength even after adjusting for confounding factors.

Conclusion: These findings suggest that the total body ECW/ICW ratio may indicate health conditions in community-dwelling elderly women.

● Yoshitsugu Kondo, Sachiko Chikahisa, Tetsuya Shiuchi, Noriyuki Shimizu, Daisuke Tanioka, Haruo Uguisu, Hiroyoshi Séi. *Sleep profile during fasting in PPAR- α knockout mice*. *Physiology & Behavior*, Volume 214, 2020, DOI: 10.1016/j.physbeh.2019.112760

Peroxisome proliferator-activated receptor alpha (PPAR α) is a transcription factor that belongs to the nuclear receptor family and plays an important role in regulating gene expression associated with lipid metabolism. PPAR α promotes hepatic fatty acid

oxidation and ketogenesis in response to fasting. Because energy metabolism is known to affect sleep regulation, manipulations that change PPAR α are likely to affect sleep and other physiological phenotypes. In this study, we examined the role of PPAR α in sleep/wake regulation using PPAR α knockout (KO) mice. Sleep, body temperature (BT), locomotor activity, arterial pressure (AP) and heart rate (HR) were recorded in KO mice and wild-type (WT) controls under ad libitum-fed conditions and 24-hour food deprivation (FD). KO and WT mice were identical in basal sleep amount, BT, mean AP and HR, although KO mice showed enhanced sleepiness (enhanced EEG slow-wave activity). In response to FD, KO mice showed a large drop in wakefulness and locomotor activity at the end of the dark phase, whereas WT mice did not. Similarly, AP and HR, which were suppressed by FD, decreased more in KO than in WT mice. Compared to WT mice, KO mice showed a reduced concentration of plasma ketone bodies and decreased mRNA expression of the ketogenic enzyme gene Hmgcs2 in the liver and brain under FD conditions. These results suggest that PPAR α and/or lipid metabolism is involved in the maintenance of wakefulness and locomotor activity during fasting in mice.

● *Abnormal Gait Movements Prior to a Near-Fall in Individuals Following Stroke.*

Osada Y, Motojima N, Kobayashi Y, Yamamoto S. Archives of Rehabilitation Research and Clinical Translation. Vol 3 (4), 2021, in press. doi: 10.1016/j.arrct.2021.100156

This study provides interesting kinetic and kinematic data for understanding what occurs during the last gait cycle before a near-fall in individuals with stroke. However, there are various reasons for near-falls, with abnormal movements commonly observed in the last cycle before the near-falling gait cycle, including decreased gait velocity, prolonged total cycle time, and excessive mediolateral movement of the CoM. This is useful knowledge for providing walking assistance and for preventing falls after stroke.

● Kouhei OHNISHI, Yasuyuki MORII, *How does the motivation of learning based on the explanation to others differ depending on the assumed explanation receiver ?*, Journal of Kibi International University, Vol.6, 2020, pp.21-25.

A questionnaire survey was conducted on 180 vocational school students to examine how the motivation of learning assuming explanations to others differs depending on the attributes of the explanation receivers. Depending on the amount of knowledge about the learning content of the receivers, three assumed receiver groups were set up: experts (professors of the university), amateurs (junior freshmen), and unspecified others.

The results showed that the junior freshmen assumed group had a higher score for the identification motivation that links the value and importance of learning to themselves

than the professors assumed group. These results were discussed in relation to the effects of explaining expectancy, the self-deterministic theory of motivation, and the metacognitive strategies of learning.

● *Isolated congenital left ventricular diverticulum in an elderly patient that was identified because of an incidental finding during a complete medical checkup.*

Sakabe K, Fukuda N, Fukuda Y, Wakayama K, Nada T, Morishita S, Shinohara H, Tamura Y. Int J Cardiol. 2008 Apr;125(2):e30-e33

Congenital left ventricular diverticulum is a rare cardiac malformation in an elderly patient. We presented an asymptomatic elderly patient, evaluated because of an incidental finding of a left ventricular anatomic change on chest computed tomography during a complete medical checkup. The diagnosis of isolated congenital left ventricular diverticulum was confirmed by echocardiography and cardiac catheterization.

● Haruo Uguisu, *About community activities*, Shikoku Physical Therapist Association Trade Journal, Vol.40,2018,31-37.

The knowledge and skills of physical therapists can meet the needs of the Japanese people not only in the field of rehabilitation based on stage-specific models for common diseases, but also in the fields of prevention, health promotion, sports, school health, and industry.

I hope that as many physical therapists as possible will carry out practical activities in the community instead of working only in the hospital. We strongly believe that the accumulation of our activities in the community will increase the recognition of physical therapists in society.

● Ebisudani T, Hashida S, Yanagisawa Y, et al., *Effects of branched-chain amino acids intake on energy metabolism during and after skeletal muscle electrical stimulation*. Research Bulletin of Tokushima Bunri University,2018.96(102)57-64.

This study aimed to clarify the effect of pre-treatment intake of branched chain amino acids (BCAA) on energy metabolism during electrical stimulation (ES). Blood lactate concentration, blood pressure, heart rate and muscle soreness (DOMS) was measured. BCAA intake showed a significant decrease in blood lactate concentrations compared to placebo. DOMS on the next day and the 2nd day was significantly lower after BCAA intake. It was suggested that the intake of BCAA, can be a source of energy during ES as it is during regular exercise, and can possibly inhibit protein degradation and promote protein synthesis.

□ Oral Health Sciences

● *Compositional and histological comparison of carbonate apatite fabricated by dissolution-precipitation reaction and Bio-Oss®.*

Fujisawa K, Akita K, Fukuda N, Kamada K, Kudoh T, Ohe G, Mano T, Tsuru K, Ishikawa K, Miyamoto Y., *J Mater Sci Mater Med.* 2018 Jul 21;29(8):121. doi: 10.1007/s10856-018-6129-2. PMID: 30032409

Carbonate apatite (CO₃Ap) is an inorganic component of bone. This study aimed to compare the composition and tissue response to of CO₃Ap (CO₃Ap-DP) fabricated by the dissolution-precipitation reaction using calcite as a precursor and Bio-Oss®, which is widely used in orthopedic and dental fields as a synthetic bone substitute. X-ray diffraction and Fourier transform infrared results showed that CO₃Ap-DP and Bio-Oss® were both B-type carbonate apatite with low crystallinity. The average sizes of CO₃Ap-DP and Bio-Oss® granules were 450 ± 58 and 667 ± 168 μm, respectively, and their carbonate contents were 12.1 ± 0.6 and 5.6 ± 0.1 wt%, respectively. CO₃Ap-DP had a larger amount of CO₃ than Bio-Oss® but higher crystallinity than Bio-Oss®. When a bone defect made at the femur of rabbits was reconstructed with CO₃Ap-DP and Bio-Oss®, CO₃Ap-DP granules were partially replaced with bone, whereas Bio-Oss® remained at 8 weeks after implantation. CO₃Ap-DP granules elicited a significantly larger amount of new bone formation at the cortical bone portion than Bio-Oss® at 4 weeks after the implantation. The results obtained in the present study demonstrated that CO₃Ap-DP and Bio-Oss® showed different behavior even though they were both classified as CO₃Ap. The CO₃ content in CO₃Ap played a more important role than the crystallinity of CO₃Ap for replacement to bone and high osteoconductivity.

● Hiromi Nakae, Masami Yoshioka, Satsuki Yabuchi, Tokiko Doi, Natsumi Fujiwara, Hiroki Iga, Daisuke Hinoide, *Nurses' Perceptions of Oral Health Care at a Recovery Hospital in Tokushima Prefecture : Results of a Questionnaire Survey.* *Journal of the Shikoku Public Health Association*, Vol.62, No.1, February,2017, pp.95-99.

A questionnaire survey was conducted on nurses in 18 hospitals in Tokushima Prefecture in order to understand the current status of daily oral care provided by nurses. As a result, we analyzed the relationship between the presence or absence of a sense of burden in oral care, the presence or absence of worries, and the reasons for worries. As a result, the group with a sense of burden had significantly more worries about "not having enough time for oral care" and "dealing with halitosis" than the group without a sense of burden.

● *Validity of Peer Evaluation for Team-Based Learning in a Dental School in Japan.*

Keisuke Nishigawa, Rika Hayama, Katsuhiko Omoto, Kazuo Okura, Toyoko Tajima, Yoshitaka Suzuki, Maki Hosoki, Mayu Ueda, Miho Inoue, Omar Marianito Maningo Rodis, Yoshizo Matsuka. Dent Educ. 2017 Dec;81(12):1451-1456. doi: 10.21815/JDE.017.106.

The aim of this study was to determine the validity of peer evaluation for team-based learning (TBL) classes in dental education in comparison with the term-end examination records and TBL class scores. Examination and TBL class records of 256 third- and fourth-year dental students in six fixed prosthodontics courses from 2013 to 2015 in one dental school in Japan were investigated. Results of the term-end examination during those courses, individual readiness assurance test (IRAT), group readiness assurance test (GRAT), group assignment projects (GAP), and peer evaluation of group members in TBL classes were collected. Significant positive correlations were found between all combinations of peer evaluation, IRAT, and term-end examination. Individual scores also showed a positive correlation with group score (total of GRAT and GAP). From the investigation of the correlations in the six courses, significant positive correlations between peer evaluation and individual score were found in four of the six courses. In this study, peer evaluation seemed to be a valid index for learning performance in TBL classes. To verify the effectiveness of peer evaluation, all students have to realize the significance of scoring the team member's performance. Clear criteria and detailed instruction for appropriate evaluation are also required.

● *There is an Association between Gingival Inflammation and Obesity in Japanese Male Adolescents*, Doi T, Fukui M, Sakamoto H, Nakae H, Yoshioka M, Komoda J, Rodis Omar, Hinode D, Journal of Oral Health and Biosciences 33 (2) : 33 ~ 38, 2021
Abstract : Background: There are few studies showing the association between obesity and

gingivitis in young male adolescents. The aim of this study is to investigate the association between gingivitis and obesity in addition to life style habits among male high school students.

Materials and Methods: The participants in this study were 1,027 1st-year male high school students (15-16 years old) in Tokushima Prefecture, Japan. Regular health checkup and oral examination were performed. Items regarding oral health behavior and eating habits were investigated through a self-reported questionnaire. Binomial logistic regression analysis was used to analyze the cross-sectional data. Moreover, 513 students who were recalled after two years were divided into 2 groups according to changes of BMI (<25 or ≥25) and their gingival condition, were investigated.

Results: Binomial logistic regression analysis showed that gingival inflammation was significantly associated with obesity (OR=1.78, 95% CI: 1.08-2.95) in addition to malalignment and plaque accumulation. From this longitudinal study, a significant improvement of gingival conditions was observed in the improved group (McNemar's test, $p < 0.05$) whereas no difference was observed in the non-improved group.

Conclusions: These results indicate that gingival inflammation was associated with obesity.

Furthermore, improvement in the management of obesity might be effective for the prevention of gingival inflammation.

● Sogawa Y, Yoshioka M, Fukui M, Nakamura S, Abe M, Hinode D., *Effectiveness of professional oral health care on oral mucositis in patients undergoing autologous hematopoietic stem cell transplant*. J Dent Health. 2019 ;69: 125–30

The aim of this study is to investigate the preventive effect of professional oral health management (POHM) on oral mucositis (OM) in patients undergoing autologous hematopoietic stem cell transplant. Thirty-three patients who were diagnosed with multiple myeloma or malignant lymphoma and received autologous hematopoietic stem cell transplant at Tokushima University Hospital from November 2004 to June 2013 were enrolled in this study. These results suggest that the duration of severe OM is related with the day of fever and the prescription days of drugs. Furthermore, POHM might be effective for the prevention of severe OM in patients undergoing autologous hematopoietic stem cell transplant.

● Kenji OKA, Chihiro SHINOHARA, Susumu ABE, Chie MIHARA, Toshinori OHKAWA, Fumiaki KAWANO. *Clinical practice examination using patient robot (SIMROID®) at Tokushima University Hospital*. The 39th General and Scientific Meeting of the Japanese Dental Education Association Program book 2020:81(#P-13).

Trainee dentists at Tokushima University Hospital were evaluated for their clinical attitude and ability using interactive patient simulation system (SIMROID) on completion of their training. Trainee dentists considered treatment techniques such as preparation, impression and filling better than physical pain, discomfort, treatment safety and clean area for patients. SIMROID is a full-body model robot patient with a realistic appearance and reactions including expression, movement and speech. SIMROID is expected usefulness in developing the communication and considerate skills for patients and in evaluating treatment attitudes and clinical skills as a practice test.

● Masanori NAKANO, Ichiro FUJISAWA, Ruri OHKUMA, Masami YOSHIOKA, Hiromi NAKAE, Keisuke NISHIGAWA, Yuka SOGAWA, Shigemasa TOMIOKA, Kenji

FUJISAWA, *Examination of the evaluation method of the swallowing questionnaire by scoring*, The Japanese Journal of Dysphagia Rehabilitation Vol.24(3), 2020, pp.240-246. In this study, our new method for scoring and evaluating the answer choices was devised and compared with the conventional Seirei dysphagia screening questionnaire. The sensitivity and specificity of the Seirei dysphagia screening questionnaire by scoring were almost the same as those of the conventional assessment method in which the presence of dysphagia was suspected if at least one answer in severe symptoms was given. In the general elderly population, scores were found to be significantly higher after 75 years of age, providing basic data for the development of screening tools to assess impaired swallowing function.

● *Association between Oral Health Status and Diabetic Nephropathy-Related Indices in Japanese Middle-Aged Men.*

Masami Yoshioka, Yoshifumi Okamoto, Masahiro Murata, Makoto Fukui, Shizuko Yanagisawa, Yasuhiko Shirayama, Kojiro Nagai, Daisuke Hinode, J Diabetes Res. 2020 Jun 7;2020:4042129. doi: 10.1155/2020/4042129.

Oral health status is known to be associated with lifestyle-related diseases such as diabetes and chronic kidney disease. In Japan, around 40% of hemodialysis cases are patients with diabetic nephropathy. The aim of this study was to clarify the association between oral health status and diabetic nephropathy-related indices in Japanese middle-aged men. Sixty-six men (age range: 55-64 years) with ≥ 20 remaining teeth and who received public medical checkups and oral examinations were enrolled. We examined correlations of age, body mass index, HbA1c, HDL-C, LDL-C, neutral fat, serum creatinine, and the estimated glomerular filtration rate (eGFR) with the number of remaining teeth or the community periodontal index (CPI) score (periodontal pocket < 4 mm: 0, 4-6 mm: 1, ≥ 6 mm: 2). A positive correlation between the CPI score and serum creatinine and a negative correlation between CPI score and eGFR (Spearman's rank correlation coefficient, $r = 0.459$, $p < 0.01$, and $r = -0.460$, $p < 0.01$, respectively) were observed. The mean eGFR in the CPI score 0 group was significantly higher than that in the CPI score 1/2 group (82.6 vs. 70.7, Student's t-test, $p < 0.01$). Logistic regression analysis using eGFR as a dependent variable and age, CPI score, body mass index, HbA1c, and neutral fat as independent variables suggested that low eGFR (<60) could be attributed to CPI score (OR = 3.169, 95% CI: 1.031-9.742, $p = 0.044$). These results suggest a possible association between periodontal status and renal function in Japanese middle-aged men. Periodontal condition is controlled by oral prophylaxis, and periodontal disease and chronic kidney disease have some common risk factors. Thus,

periodontal management can contribute to the prevention of severe chronic kidney disease.

■ Policy Studies

□ Policy Studies

● Hiroyuki FURUYA, *National Defence and the Economy in Adam Smith*, in *The Economic Thought of War and Peace*, Atsushi Komine, ed. (Kyoto: Koyo Shobo, March 2020), Chapter 2: pp. 52–74.

This paper seeks to examine Adam Smith’s argument of how commercial civilisation, or the civilising force of commerce, gave rise to the social division of labour and consequently to the changes of political economy, arms and wars, as well as how Smith treated the issue of national security, liberty and economic growth in a century dubbed the ‘Second Hundred Years’ War’ between Britain and France.

● Satoshi HASHIMOTO, *A Study on Liabilities for Administrators under Bankruptcy in Closely Connected Society with IoT and Cloud from the Viewpoint of Contract Theory*, *IPJSJ Journal*, Vol.59, No.1, Jan.2018, pp.189-198

IoT is one of embedded systems and bases on distributed system including cloud computing. Devices used in IoT have characteristics including long-term application, unification between hardware and software, and purification for devices. IoT system may make us difficult to maintain securities on networks. During bankruptcy, the trustees of the concerned company face a dilemma regarding the protection of personal data managed by the bankrupt businesses between creditors and data subjects under liquidation since during liquidation, it is not clear whether such data belong to the creditors or the data subjects. Particularly in the case of this system, trustees find it difficult to obtain an overall view of the personal data managed by the bankrupt firm. This paper discusses a course of action on a burden of responsibilities for administrators under bankruptcies in Closely Connected Society with IoT and Cloud Computing from

the viewpoint of Contract Theory. Especially this paper focuses on the relationship between power of receivers and incentive for activities of administrators.

● Makoto Hirono, *Demographic change, human capital accumulation, and sectoral employment*, Journal of Economics, 2021, Vol132, pp165-185.

Many studies examine the relationship between aging and economic growth; however, only a few theoretical studies find a possible non-linear relationship. Thus, this study theoretically investigates the impact of population aging on economies. We construct a three-period overlapping generations model with two sectors: non-education and education. We assume that learning-by-doing effects compound as the share of employment increases and improves productivity. Both adults and old agents consume non-education goods and services, while only adults demand education services for their children to gain human capital. Our results demonstrate that whether an increase in life expectancy positively or negatively influences income growth per capita depends on the productivity of the non-education and education sectors.

● Ken-ichi KANEKO, Tomoya HIRANO, Michio YAMAGISHI, Yu KASHIWAGI, Kazuo FUNATO, *Kinematic and kinetic characteristics of 180-degree change-of-direction in 4 male youth high-school soccer players*, Journal of Training Science for Exercise and Sport, Vol.33, No.1, 2021, pp.51-59.

This study seeks to analyze the kinematic and kinetic characteristics in a 180-degree change-of-direction test, and examine their relationship with the 180-degree change-of-direction time in male youth soccer players. The study involved 11 youth soccer players. The 180-degree change-of-direction test was modified from the 505 agility test and conducted. First, the players started to run at 0m position, until 15m position, and returned to the 10m position as fast as possible. The kinematic and kinetic data were collected from a three-dimensional motion analysis system (200Hz) and three force platforms (1,000Hz). Consequently, compared with the ground reaction force (GRF) of the second foot (SF) and the turn foot (TF), the highest GRF was observed in the two steps before the change-of-direction (FF). In addition, there was a correlation between the horizontal impulse of the FF and the horizontal displacement of the center-of-gravity-velocity (COGV) during the TF contact. Therefore, it is suggested that the horizontal impulse of the FF is related to the movement time of the change-of-direction phase. Conversely, at the 180-degree change-of-direction time, it was suggested that it is important to lower the center-of-gravity and increase the horizontal impulse of the TF take-off.

● Toyota MATSUMURA, *How to walk the Policy Sciences*, Printed by Designeg co.Ltd. in 2021.

For freshman students enrolled in the Faculty of Policy Sciences, This book is to help understand the all subject of "Policy Sciences ". There is a international travel guidebook called "How to Walk the Earth". The book provides information on countries / regions such as currency, transportation, inns, and gourmet food of all of the world. As same as this book, I tried to explain why spelled out with “s” after the word “science”, what is the relationship between economics and legal science, which are specialized subjects that students will study.

●Tomokuni MIZUNOUE, Zhao Tong, *An Event History Analysis of Chinese Online P2P Platforms*, ICCS Journal of Modern Chinese Studies Vol.12(1) 2019, pp.19-36.

This paper analyzes the activities of trading sites that play an intermediary role in China's P2P Internet finance, which has experienced rapid growth in just ten years. Specifically, we conducted an event history analysis on the occurrence of problems in platforms using panel data from January 2016 to April 2018 for each PF collected and aggregated by Chinese P2P internet finance portals. As a result, the impact of the Chinese government regulations on platform became clear. Secondly, the dummy variable group, which was thought to be a signal of the health of the platform, had almost no significant impact.

●Atsushi SAITO, *A study of Recall Responsibility and the Risk Absorption Theory of the Prime Contractor in Modularization and Parts Commonization*, Journal of Japan Association for the Comparative Studies of Management, Vol. 39, Oct, 2021, pp.104-123.

In the Japanese automobile industry, a pyramidal, multi-level subcontracting structure has been formed. Initially, it was believed that within this structure, the prime contractor bears the risk of economic fluctuations to the subcontractors. However, in the Japanese automobile industry, the prime contractor and the subcontractor have been collaborating on research and development in automobile production, and as a result, the subcontractor has been gaining power. This is why subcontractors are becoming more powerful, and this is also why prime contractors are absorbing the risk of economic fluctuations from subcontractors. For this paper, I researched the subcontractors that are cooperating with Toyota Motor Corporation.

In recent years, intensifying global competition and the increasing use of electronics in automobiles have promoted modularization and commonality of parts in automobiles. Toyota Motor Corporation, as the main contractor, and its subcontractors have been collaborating on research and development for modularization and commonality of parts as in the past. However, the modularization and commonality of parts has led to an increase in the number and scale of recalls. Once a recall occurs, Toyota, as the prime contractor, often imposes heavy recall responsibilities on its subcontractors. In other

words, in the midst of modularization and commonality of parts, Toyota may not absorb the risk of economic fluctuations from its subcontractors.

●Eiji TOKOZAKURA, *The impact of “Place attachment” and “Connection with the community” on Organizational commitment – The case of company M–*, Japan Telework Society, VOL.17, NO.1, 2019, pp.5-12.

This study mainly analyzes the impact of Personal attachment to place (hereinafter called "Place attachment") and Connection between company and community (hereinafter called "Connection with the community") on organizational commitment. The empirical analysis was conducted on 350 employees working for the Call center company whose head office is located in the Tokyo metropolitan area and has multiple offices in rural areas. The results were as follows. It turned out that in Place attachment, "Preference" had positive impact on the emotional commitment. In addition, it was found out that within Connection with the community, "Public-private partnership" and "Social contribution" had positive effects on both emotional and utilitarian commitments. In other words, the results of this empirical analysis suggest that Place attachment and Connection with the community are important factors to improve the retention rate of corporate employees.

■Music

□Music

●Sayaka CHIBA, [Actual report] *Supervision of music therapy internship -Implementation of community music therapy and analysis*. Research bulletin of Tokushima Bunri University, Vol.88, Sep., 2014, pp.103-108.

This paper focuses on “Community Music Therapy (CoMT)”, one of the methods of music therapy such as Creative Music Therapy, Neurological Music Therapy and so on. The purpose of implementation of CoMT was to make a connection for other people as social participation through attending music activities based on leading by music therapists. Participants were adults and elderly invited to join from the community of Tokushima city. For the purpose of CoMT, participants planned and discussed with leading by music therapists the performance program, genre of music and type of instruments. Each time they participated, the motivation increased and their discussion and performance skills improved. According to a questionnaire on the last day, the participants expressed their feelings better than before attending CoMT. In addition to

the content of implementation of CoMT, the last half of this paper participant's analyzes how arrangements are easy to perform for participants who haven't had experience with performing and learning music skills.

● Takashi MATSUOKA, (Composition) *"Daybreak (Atarasii Asani)" for orchestra*, world premiere on June 2. 2021 in Tokyo Opera City Concert Hall, Orchestra Project 2020 (Postponed performance), TOKYO SYMPHONY ORCHESTRA, Conductor: Kousuke TSUNODA, 2fl, 2ob, 2cl, 2bn, 4hr, 2trp, 3trbn, 1tuba, 3perc, 1celesta 1hp, Vn I, Vn II, Vla, Vc, Db, p59, 15 min.

The theme is to live anew. The music is composed of prologo, pastorale, sedotto, inquieto, penitenziale, con grazia, redento, con anima, pacificamente, affettuoso, armonioso, grato, epilogo.

● Giuseppe MARIOTTI, *Beneficial daily technical exercises for University piano students*, Technical bulletin of Tokushima Bunri University (88), pag. 63-83, 2014-09. <https://ci.nii.ac.jp/naid/110009840425>

Piano playing is a very complex motor act that requires an enormous degree of coordination and comprehensive daily training. The pianist's technical training is usually separate from the musical training, and consists mostly of exercises that contain several repetitions of brief note patterns. Those patterns are intended to overcome deficiencies in the structure of the hand, like a limited span between fingers, or to master recurring difficult passages of the piano literature. In the typical school environment, those technical exercises are chosen from the several available piano methods.

However, the conceptions of most methods are well over one century old and based on antiquated assumptions. For example, most methods focus excessively on the increase of fingers' muscles strength. This misconception leads to very inefficient and time-wasting practicing strategies with deplorable results like muscle soreness and pain, tendinitis and even focal dystonia. The vast majority of high school and university piano students in Japan are affected by those playing-related musculoskeletal disorders.

Many research projects on musicians' sensorimotor system have amply demonstrated that the main requisite for a proficient piano technique is movement coordination instead of finger strength. This is confirmed by the empirical description that eminent pianists give of their extraordinary technique.

The daily exercises presented here were developed and tested over a 5-year span, and are based on recent neuroscience research. The exercises are rather simple and short, and have a moderate melodic sense in order to avoid monotony. They are newly created,

or adapted from historical sources, and are targeted to piano students of high school and university grade. These exercises have shown to be useful in the improvement of students' auditory-sensorimotor skills, and they can lead to a better music making.

■ ■ Junior College

□ Music

● Shigetani, M., Hiraoka, R., Imura, S., Arase, T., Kondo, A., & Tanida, N., *Effects of music therapy on pain relief and relaxation of hospice patients*. Poster session presented at the meeting of the 15th World Congress of Music Therapy, Tsukuba, Japan, 2017, July.

In order for Japanese hospice music therapy to be acknowledged as one alternative intervention of complementary health approaches, more quantitative research done by music therapists is needed. This study evaluated the effects of music therapy on pain and relaxation in 52 hospice patients.

■ ■ Kagawa Campus

■ Pharmaceutical Sciences at Kagawa Campus

□ Pharmacy

● *Preparation and Stability of Liposomal Resveratrol.*

Kazutaka Atobe, Chika Nagao, Yoshihisa Kato, The 36th Annual Meeting of the Academy of Pharmaceutical Science and Technology Japan. 2021/05/13~15.

Resveratrol has been reported to have anti-oxidant, anti-inflammatory, and anti-cancer effects. However, due to its low bioavailability, it is not effective in oral administration. Therefore, we investigated the inclusion of resveratrol in liposomes. When the lipid membrane containing resveratrol was hydrated with saline solution, little resveratrol was encapsulated. On the other hand, when the liposome was hydrated with a cyclodextrin solution, a liposome solution with a resveratrol concentration of 9.3 ug/mL could be prepared. When the lipid membrane was hydrated with cyclodextrin solution

dissolved in resveratrol, the resveratrol concentration was about 30 ug/mL.

● *Fracture risk increased by concurrent use of central nervous system agents in older people: Nationwide case-crossover study.*

Ohara E, Bando Y, Yoshida T, Ohara M, Kirino Y, [Iihara N.](#), Res Social Adm Pharm. 2021; 17(6):1181-1197. doi: 10.1016/j.sapharm.2020.09.007

BACKGROUND: Multiple medication use among older patients is reported to increase fracture risk. But this association is unclear in different subgroups and has not been confirmed by a case-crossover study, which can eliminate measurable and unmeasurable time-invariant confounders.

OBJECTIVE: To estimate the fragility fracture risk associated with concurrent use of multiple central nervous system (CNS) agents in older patients using a case-crossover design.

METHODS: This study targeted almost all patients aged ≥ 65 years in Japan who incurred fragility fractures from May 2013 to September 2014, based on the National Database of Health Insurance Claims and Specific Health Checkups of Japan (NDB Japan). Conditional logistic regression analysis estimated the risk of fragility fracture associated with the daily number of CNS agents, including subgroup analyses stratified by sex, age, and fracture location.

RESULTS: For 446,101 patients, the adjusted odds ratios (ORs) of fragility fracture increased almost linearly with number of CNS agents; 0, 0-1, 1-2, 2-3, 3-4, 4-5, and >5 : OR reference, 1.21 (95% confidence interval, 1.18-1.23), 1.40 (1.35-1.46), 1.58 (1.49-1.67), 1.89 (1.74-2.05), 1.80 (1.60-2.03), and 1.90 (1.61-2.23; trend $p < 0.001$), respectively. A similar trend was observed for several subgroups, especially in males and those aged ≥ 85 years, showing marked linearity.

CONCLUSIONS: The increased risk of fragility fracture associated with the use of multiple CNS agents was robust in older people in Japan.

● *Investigation of Successful Eyedrop Instillation Rates and Analysis of Drop Positions Using High-speed Digital Video Recording System.*

[Hiroaki Ikeda](#) , Ayane Takamoto, Junko Ikeda, Kiyotaka Kohno, [Akira Nakatsuma](#), [Tadakazu Tokumura](#), Kumiko Mori, [Naomi Iihara](#), [Hitoshi Houchi](#), [Masaki Ninomiya](#), Yakugaku Zasshi, 140, 1455-1462 (2020), PMID: 32999129. DOI: 10.1248/yakushi.20-00136

We investigated the success rates of eyedrop instillation and the distance between the cornea and the dropper tip in 100 volunteers using high-speed digital video recording. The success rate of the first instillation was 70%. When the eye was arbitrarily divided into 9 sections, most of the drop sites were the iris or the center of the eye. The distance

between the dropper tip and cornea was 2.62 cm. These results indicate that the generally recommended distance is usually followed. The successful instillation rate based on the distance from the dropper tip to the cornea was 77% at 1.6 cm and 54.9% at 4.8 cm.

● *Kanechlor 500-mediated changes in serum and hepatic thyroxine levels primarily occur in a transthyretin-unrelated manner.*

Yoshihisa Kato, Sekihiro Tamaki, Koichi Haraguchi, Shin-Ichi Ikushiro, Yukiko Fujii, Chiho Ohta, Kazutaka Atobe, Osamu Kimura, Tetsuya Endo, Nobuyuki Koga, Shizuo Yamada, Masakuni Degawa, *J Appl Toxicol.* 2019, Dec; 39(12): 1701-1709. doi:10.1002/jat.3895. Epub 2019 Sep 9.

The effects of Kanechlor-500 (KC500) on the levels of serum total thyroxine (T_4) and hepatic T_4 in wild-type C57BL/6 (WT) and its transthyretin (TTR)-deficient (TTR-null) mice were comparatively examined. Four days after a single intraperitoneal injection with KC500 (100 mg/kg body weight), serum total T_4 levels were significantly decreased in both WT and TTR-null mice. The KC500 pretreatment also promoted serum [125 I] T_4 clearance in both strains of mice administrated with [125 I] T_4 , and the promotion of serum [125 I] T_4 clearance in WT mice occurred without inhibition of the [125 I] T_4 -TTR complex formation. Furthermore, the KC500 pretreatment led to significant increases in liver weight, steady-state distribution volume of [125 I] T_4 , hepatic accumulation level of [125 I] T_4 , and concentration ratio of the liver to serum in both strains of mice. The present findings indicate that the KC500-mediated decrease in serum T_4 level occurs in a TTR-unrelated manner and further suggest that KC500-promoted T_4 accumulation in the liver occurs through the development of liver hypertrophy and the promotion of T_4 transportation from serum to liver.

● *The prospective mathematical idea satisfying both radiation hormesis under low radiation doses and linear non-threshold theory under high radiation doses.*

Katsuhito Kino. *Genes Environ.* 2020 Feb 3;42:4. doi: 10.1186/s41021-020-0145-4.

It has yet to be determined whether or not the probability of developing cancer due to radiation exposure levels of low doses is proportional to the dose. Herein, for radiation hormesis occurring at low doses, mathematical models using functions that take a mountain-like shape having two inflection points are considered. The following perspectives were obtained: (i) When the probability of developing cancer decreases at radiation levels above the natural background dose, the radiation hormesis effect occurs up to ~ 12.4 mSv. (ii) When there is a proportional relationship at ≥ 750 mSv, the radiation hormesis effect occurs up to ~ 225 mSv. Thus, by performing studies at the

molecular and cellular levels for radiation doses at ≤ 16.8 or 307 mSv, it is possible to investigate carcinogenesis resulting from low radiation doses.

● *FxRIamide regulates the oscillatory activity in the olfactory center of the terrestrial slug *Limax*.*

Yamanaka A, Kobayashi S, Matsuo Y, Matsuo R, Peptides. 2021 Jul; 141, 170541.

DOI: 10.1016/j.peptides.2021.170541.

The terrestrial slug *Limax* acquires odor-aversion memory. The procerebrum is the secondary olfactory center in the brain of *Limax*, and functions as the locus of the memory formation and storage. The change in the local field potential oscillation in the procerebrum reflects the information processing of the learned odor. However, it is not fully understood what factors, intrinsic or extrinsic in the procerebrum, alter the oscillatory activity and how it is regulated. In the present study, we found that FxRIamide (Phe-x-Arg-Ile-NH₂), which was previously identified as a myomodulatory peptide in the gastropod *Fusinus ferrugineus*, downregulates the oscillatory frequency of the local field potential oscillation in the procerebrum of *Limax*. FxRIamide peptides were encoded by two distinct transcripts, which exhibit partially overlapping expression patterns in the brain. Immunohistochemical staining revealed a scattered distribution of FxRIamide-expressing neurons in the cell mass layer of the procerebrum, in addition to the ramified innervation of FxRIamidergic neurons in the neuropile layers. Down-regulation of the oscillatory frequency of the local field potential was explained by the inhibitory effects of FxRIamide on the bursting neurons, which are the kernels of the local field potential oscillation in the procerebrum. Our study revealed the previously unidentified role of FxRIamide peptides in the network of interneurons of *Limax*, and these peptides may play a role in the mnemonic functions of the procerebrum.

● *Expression and Regulation of Tal2 during Neuronal Differentiation in P19 Cells.*

Takanobu Kobayashi, Yakugaku Zasshi. 2017;137(1):61-71.doi:10.1248/yakushi.16-00176.

T-cell acute lymphocytic leukemia 2 (Tal2) is a gene encoding a member of the basic helix-loop-helix transcription factor family, which is essential for the normal development of the mouse brain. We found that Tal2 was induced during neural differentiation in P19 cells, which are pluripotent mouse embryonal carcinoma cells that differentiate into the neural lineage upon both exposure to all-trans retinoic acid (atRA) and the formation of cell aggregation. Tal2 expression during neural differentiation in P19 cells was detected within 3 h after induction with atRA and retinoic acid receptor α (RAR α). The atRA-RAR α complex is known to bind to a

characteristic retinoic acid response element (RARE) located in the promoter of target genes. We found a RARE-like element in the intron of Tal2. We also found a TATA-box-like element in the 5' region. The TATA-box-like element functioned as a core promoter, and TATA-box binding protein bound to this element upstream of Tal2 in P19 cells. The RARE-like element responded to atRA signaling that activated the transcription, and RAR α was bound to this element in the intron of Tal2 in P19 cells. Furthermore, the interaction between these elements on Tal2 was confirmed in a chromatin immunoprecipitation assay. Because the neural differentiation of P19 cells mimics in part the development of the nervous system, P19 cells are useful for studying the mechanism underlying the role of Tal2 in neural differentiation. Further work is underway to clarify the function of Tal2 in neural differentiation using the differentiation system of P19 cells.

● *Levetiracetam treatment influences blood-brain barrier failure associated with angiogenesis and inflammatory responses in the acute phase of epileptogenesis in post-status epilepticus mice.*

Itoh K, Ishihara Y, Komori R, Nochi H, Taniguchi R, Chiba Y, Ueno M, Takata-Tsuji F, Dohgu S, Kataoka Y. Brain Res. 2016 Dec 1;1652:1-13. doi: 10.1016/j.brainres.2016.09.038.

Our previous study showed that treatment with levetiracetam (LEV) after status epilepticus (SE) termination by diazepam might prevent the development of spontaneous recurrent seizures via the inhibition of neurotoxicity induced by brain edema events. In the present study, we determined the possible molecular and cellular mechanisms of LEV treatment after termination of SE. To assess the effect of LEV against the brain alterations after SE, we focused on blood-brain barrier (BBB) dysfunction associated with angiogenesis and brain inflammation. The consecutive treatment of LEV inhibited the temporarily increased BBB leakage in the hippocampus two days after SE. At the same time point, the LEV treatment significantly inhibited the increase in the number of CD31-positive endothelial immature cells and in the expression of angiogenic factors. These findings suggested that the increase in neovascularization led to an increase in BBB permeability by SE-induced BBB failure, and these brain alterations were prevented by LEV treatment. Furthermore, in the acute phase of the latent period, pro-inflammatory responses for epileptogenic targets in microglia and astrocytes of the hippocampus activated, and these upregulations of pro-inflammatory-related molecules were inhibited by LEV treatment. These findings suggest that LEV is likely involved in neuroprotection via anti-angiogenesis and anti-inflammatory activities against BBB dysfunction in the acute phase of

epileptogenesis after SE.

● *Design and concise synthesis of novel vitamin D analogues bearing a functionalized aromatic ring on the side chain.*

Toshie Fujishima, Takuro Komatsu, Yuri Takao, Wataru Yonamine, Tsutomu Suenaga, Hiroaki Isono, Masayuki Morikawa, Keisuke Takaguchi, *Tetrahedron*. 2019 Feb; 75(8): 1098-1106. doi: 10.1016/j.tet.2019.01.019.

Five novel vitamin D analogues (2a, 2b, 3a, 3b and 4) bearing an aromatic side chain have been designed and synthesized in a convergent manner. The requisite CD-ring synthons (10a–c) were prepared from C22 aldehyde (5) using four- or five-step procedures. Using turbo-Grignard reagents allowed aromatic side chains with a polar functional moiety to be installed in a single step with excellent yields. A preliminary biological evaluation using bovine thymus vitamin D receptor (VDR) suggested that incorporating a carboxylic acid instead of the C25-hydroxy group had a positive effect on the VDR affinity compared with the corresponding esters.

● *Retinoic Acid Prevents Dendritic Cells from Inducing Novel Inflammatory T Cells That Produce Abundant Interleukin-13.*

Aya YOKOTA-NAKATSUMA, *Yakugaku Zasshi*. 2017;137(12):1491-1496. doi: 10.1248/yakushi.17-00153.

We found that dendritic cells in mesenteric lymph nodes (MLN-DCs) from vitamin A (VA)-deficient mice induced a distinct inflammatory Th2-cell subset that produced abundant IL-13 and expressed receptors for homing to skin and inflammatory sites but not to the intestine. IL-6 induced the differentiation of this subset from naive CD4⁺ T cells upon activation with antibodies against CD3 and CD28, and retinoic acid (RA) receptor antagonists enhanced this induction. Oral administration of an antigen to VA-deficient mice failed to induce immune tolerance but primed strong IL-13-dependent IgG1 responses and IgE responses that caused skin allergy. These results suggest that MLN-DCs possess the latent ability to induce IL-13-producing inflammatory Th2 cells and that RA prevents them from inducing IL-13-dependent allergic or inflammatory responses to orally administered antigens.

● *Ultrasensitive detection of proteins and sugars at single-cell level.*

Watabe, S., Morikawa, M., Kaneda, M., Nakaishi, K., Nakatsuma, A., Ninomiya, M., Yoshimura, T., Miura, T., Ito, E., *Commun Integr Biol*. 9(1) e1124201,2016.

Each cell produces its own responses even if it appears identical to other cells. To analyze these individual cell characteristics, we need to measure trace amounts of molecules in a single cell. Nucleic acids in a single cell can be easily amplified by polymerase chain reaction, but single-cell measurement of proteins and sugars will

require de novo techniques. In the present study, we outline the techniques we have developed toward this end. For proteins, our ultrasensitive enzymelinked immunosorbent assay (ELISA) coupled with thionicotinamide-adenine dinucleotide cycling can detect proteins at subattomoles per assay. For sugars, fluorescence correlation spectroscopy coupled with glucose oxidase-catalyzed reaction allows us to measure glucose at tens of nM. Our methods thus offer versatile techniques for single-cell-level analyses, and they are hoped to strongly promote single-cell biology as well as to develop noninvasive tests in clinical medicine.

● *Induction of PD-L1 by Nitric Oxide via JNK Activation in A172 Glioblastoma Cells.*

Yoshimitsu Kiriya, Anna Tani, Minako Kadoya, Ryoko Okamoto, and Hiroshi Nochi, Biol. Pharm. Bull., 2020 Jun; 43(6), 1020-1022. doi: 10.1248/bpb.b20-00087. Epub 2020 Mar 20.

Glioblastoma comprises 54% of all the gliomas derived from glial cells and are lethally malignant tumors of the central nervous system (CNS). Glioma cells disrupt the blood-brain barrier, leading to access of circulating immune cells to the CNS. Blocking the interaction between programmed cell death 1 (PD-1) and programmed cell death 1 ligand 1 (PD-L1) enhances T-cell responses against tumor cells, and inhibition of the PD-1/PD-L1 pathway is used as immunotherapy for cancer, including glioblastoma. Nitric oxide (NO) has multiple physiological roles, such as immune modulation and neural transmission in the CNS. Moreover, it has both tumor-promoting and tumor-suppressive functions. We examined the effects of NOC-18, an NO donor, on the expression of PD-L1 in A172 glioblastoma cells. NOC-18 increased PD-L1 expression in A172 glioblastoma cells. Moreover, this increase is regulated via the JNK pathway.

● *Laser Desorption Ionization-Mass Spectrometry of Linear Diphenylenes Encapsulated in Crystalline Sponge.*

Ohara, Kazuaki; Hayashi, Yukako; Yamaguchi, Kentaro, Bulletin of the Chemical Society of Japan (2020), 93(8), 963-968. Language: English, Database: CAPLUS

Three linear diphenylene compds. having one, two, and three double bonds, resp., were encapsulated in a nano-porous coordination complex called "cryst. sponge" (CS). The presence of these diphenylene compds. in CS was confirmed by single-crystal X-ray structure anal. and NMR spectroscopy. In CS, CH- π and π - π interactions between the pyridyl group of the triazine ligand in the CS framework and the Ph group of the diphenylene compds. were detd. on the basis of the geometrical orientation in the nanopore. After the single-crystal X-ray structure anal., the same single crystal was subjected to imaging mass spectrometry (IMS). Mol. ion peaks were almost equally detected in all regions of the target plate where the CSs were present and the search for

hotspots was no longer necessary. At the same time, ion peaks derived from the triazine ligand and its metal complex, which are components of the CS framework, were clearly obsd. CSs have been shown to be effective matrixes for laser desorption ionization of trace linear conjugate compds.

● *Retinoic acid and GM-CSF coordinately induce retinal dehydrogenase 2 (RALDH2) expression through cooperation between the RAR/RXR complex and Sp1 in dendritic cells.*

Yoshiharu Ohoka, Aya Yokota-Nakatsuma, Naoko Maeda, Hajime Takeuchi, Makoto Iwata, PLoS One. 2014 May 2;9(5):e96512 doi:10.1371/ journal.pone. 0096512. eCollection 2014.

Retinoic acid (RA)-producing dendritic cells (DCs) play critical roles in gut immunity. Retinal dehydrogenase 2 (RALDH2) encoded by *Aldh1a2* is a key enzyme for generating RA in DCs. Granulocyte-macrophage colony-stimulating factor (GM-CSF) potently induces RALDH2 expression in DCs in an RA-dependent manner, and RA alone weakly induces the expression. However, how GM-CSF and RA induce RALDH2 expression remains unclear. Here, we show that GM-CSF-induced activation of the transcription factor Sp1 and RA-dependent signaling via the RA receptor (RAR)/retinoid X receptor (RXR) complex contribute to *Aldh1a2* expression. The RAR antagonist LE540 and the Sp1 inhibitor mithramycin A inhibited GM-CSF-induced *Aldh1a2* expression in fms-related tyrosine kinase 3 ligand-generated bone marrow-derived DCs (BM-DCs). ERK and p38 MAPK inhibitors suppressed GM-CSF-induced nuclear translocation of Sp1 and *Aldh1a2* expression. Sp1 and the RAR α /RXR α complex bound to GC-rich Sp1-binding sites and an RA response element (RARE) half-site, respectively, near the TATA box in the mouse *Aldh1a2* promoter. The DNA sequences around these sites were highly conserved among different species. In the presence of RA, ectopic expression of RAR α /RXR α and Sp1 synergistically enhanced *Aldh1a2* promoter-reporter activity. GM-CSF did not significantly induce *Aldh1a2* expression in plasmacytoid DCs, peritoneal macrophages, or T cells, and the *Aldh1a2* promoter in these cells was mostly unmethylated. These results suggest that GM-CSF/RA-induced RALDH2 expression in DCs requires cooperative binding of Sp1 and the RAR/RXR complex to the *Aldh1a2* promoter, and can be regulated by a DNA methylation-independent mechanism.

● *Informatics framework of traditional Sino-Japanese medicine (Kampo) unveiled by factor analysis.*

Okada T, Afendi FM, Yamazaki M, Chida KN, Suzuki M, Kawai R, Kim M, Namiki T, Kanaya S, Saito K. J Nat Med. 2016 Jan;70(1):107-14.doi: 10.1007/s11418-015-0946-0.

Kampo, an empirically validated system of traditional Sino-Japanese medicine, aims to treat patients holistically. This is in contrast to modern medicine, which focuses in principle on treating the affected parts of the body of the patient. Kampo medicines formulated as combinations of crude drugs are prescribed based on a Kampo-specific diagnosis called *Sho* (in Japanese), defined as the holistic condition of each patient. Therefore, the medication system is very complex and is not well understood from a modern scientific perspective. Here, we show the informatics framework of Kampo medication by multivariate factor analysis of the elements constituting Kampo medication. First, the variation of Kampo formulas projected by principal component analysis (PCA) indicated that the combination patterns of crude drugs were highly correlated with *Sho* diagnoses of Deficiency and Excess. In an opposite way, partial least squares projection to latent structures (PLS) regression analysis could also predict Deficiency/Excess only from the composed crude drugs. Secondly, to chemically verify the correlation between Deficiency/Excess and crude drugs, we performed mass spectrometry (MS)-based metabolome analysis of Kampo prescriptions. PCA and PLS regression analysis of the metabolome data also suggested that Deficiency/Excess could be theoretically explained based on the variation in chemical fingerprints of Kampo medicines. Our results show that factor analysis of Kampo concepts and of the metabolomes of Kampo medicines enables interpretation of the complex system of Kampo. This study will theoretically form the basis for establishing traditionally and empirically based medications worldwide, leading to systematically personalized medicine.

● *Identification and classification of innexin gene transcripts in the central nervous system of the terrestrial slug *Limax valentianus*.*

Sadamoto H, Takahashi H, Kobayashi S, Kondoh H, Tokumaru H. PLoS One. 2021 Apr 15;16(4):e0244902. doi: 10.1371/journal.pone.0244902.

Intercellular gap junction channels and single-membrane channels have been reported to regulate electrical synapse and the brain function. Innexin is known as a gap junction-related protein in invertebrates and is involved in the formation of intercellular gap junction channels and single-cell membrane channels. Multiple isoforms of innexin protein in each species enable the precise regulation of channel function. In molluscan species, sequence information of innexins is still limited and the sequences of multiple innexin isoforms have not been classified. This study examined the innexin transcripts expressed in the central nervous system of the terrestrial slug *Limax valentianus* and identified 16 transcripts of 12 innexin isoforms, including the splicing variants. We performed phylogenetic analysis and classified the isoforms with

other molluscan innexin sequences. Next, the phosphorylation, N-glycosylation, and S-nitrosylation sites were predicted to characterize the innexin isoforms. Further, we identified 16 circular RNA sequences of nine innexin isoforms in the central nervous system of *Limax*. The identification and classification of molluscan innexin isoforms provided novel insights for understanding the regulatory mechanism of innexin in this phylum.

● *The effect of the leak conductance parameter on the dynamics of a mathematical model of pre-Bötzinger complex pacemaker neurons: period-doubling bifurcation and chaotic activity.*

Shirahata T. *Advanced Studies in Theoretical Physics*. Vol. 15, 2021, no. 5, 257-266.

doi: 10.12988/astp.2021.91652

The present article presents results of a numerical simulation of a mathematical model of pre-Bötzinger complex pace

maker neurons, which is described by a system of nonlinear ordinary differential equations. A controlling parameter of the present study was leak conductance contained in the pre-Bötzinger complex pacemaker neuron model. In addition, we numerically investigated the effect of variation of that parameter on the dynamics of the model. Numerical simulation results indicated that an increase in leak conductance changes the dynamical state of the model, such that a period-1 spiking state → a period-2 spiking state → a period-4 spiking state → a chaotic spiking state → a chaotic bursting state → a periodic bursting state.

● *Leishmanicidal phenolic compounds derived from *Dalbergia cultrata*.*

Mori-Yasumoto, K.; Hashimoto, Y.; Shirota, O.; Sekita, S.; Agatsuma, Y.; Satake, M.; Fuchino, H.; Yasumoto, K.; Satake, M.; Sekita, S., *Natural product research* 2020, 1-9.

Leishmaniasis is a protozoan tropical infection that is estimated to be more than 0.3 million new cases occur annually worldwide. A novel phenolic compound, cultratin A (1), was isolated as a leishmanicidal constituent from the timber of *Dalbergia cultrata*, along with three known neoflavanoids (2, 3, 4), two benzofurans (5, 6), and two phenolic compounds (7, 8). Their structures were determined using spectral methods. Among them, a new compound (1) and 4-(S)-methoxydalbergione (2) showed effective leishmanicidal activities (IC₅₀: 2.0 and 2.6 μM, respectively), while compound 8 showed moderate activity (IC₅₀: 11 μM). The cytotoxicity of compounds 1 and 2 was also weaker than that of the other compounds.

● *Metallothioneins regulate the adipogenic differentiation of 3T3-L1 cells via the insulin signaling pathway.*

Kadota Y, Toriuchi Y, Aki Y, Mizuno Y, Kawakami T, Nakaya T, Sato M, Suzuki S. 2017., PLoS One. 12, (4), e0176070. PMID: 28426713

Knockout of metallothionein (MT) genes contributes to a heavier body weight in early life and the potential to become obese through the intake of a high fat diet (HFD) in mice. It has thus been suggested that MT genes regulate the formation of adipose tissue, which would become the base for later HFD-induced obesity. We evaluated the fat pads of mice during the lactation stage. The fat mass and adipocyte size of MT1 and MT2 knockout mice were greater than those of wild type mice. Next, we assayed the ability of small interfering RNA (siRNA) to silence MT genes in the 3T3-L1 cell line. The expressions of MT1 and MT2 genes were transiently upregulated during adipocyte differentiation, and the siRNA pretreatment led to the suppression of the expression of both MT mRNAs and proteins. The MT siRNA promoted lipid accumulation in adipocytes and caused proliferation of post-confluent preadipocytes; these effects were suppressed by an inhibitor of phosphatidylinositol 3-kinase (LY294002). In addition, MT siRNA promoted insulin-stimulated phosphorylation of Akt, a downstream kinase of the insulin signaling pathway. Enhanced lipid accumulation in 3T3-L1 cells resulting from MT-gene silencing was inhibited by pretreatment with an antioxidant, N-acetylcysteine, used as a substitute for antioxidant protein MTs. These results suggest that interference in MT expression enhanced the activation of the insulin signaling pathway, resulting in higher lipid accumulation in 3T3-L1 adipocytes.

● *Direct interaction of SNARE complex binding protein synaphin/complexin with calcium sensor synaptotagmin 1.*

Hiroshi Tokumaru 1, Chigusa Shimizu-Okabe, Teruo Abe, Brain Cell Biol 2008.,Dec; 36(5-6):173-89.doi: 10.1007/s11068-008-9032-9. Epub 2009 Jan 9.

Although the binding of synaphin (also called complexin) to the soluble N-ethylmaleimide-sensitive factor attachment protein receptor (SNARE) complex is critical for synaptic vesicle exocytosis, the exact role of synaphin remains unclear. Here, we show that synaphin directly binds to synaptotagmin 1, a major Ca²⁺ sensor for fast neurotransmitter release, in a 1:1 stoichiometry. Mapping of the synaphin site involved in synaptotagmin 1 binding revealed that the C-terminal region is essential for the interaction between these two proteins. Binding was sensitive to ionic strength, suggesting the involvement of charged residues in the C-terminus region. Mutation of the seven consecutive glutamic acid residues (residues 108-114) at the C-terminal region of synaphin to alanines or glutamines resulted in a dramatic reduction in synaptotagmin 1 binding activity. Furthermore, a peptide from the C-terminus of synaphin (residues 91-124) blocked the binding of synaptotagmin 1 to synaphin, an

effect that was abolished by mutating the consecutive glutamic acid residues to alanine. Immunoprecipitation experiments with brain membrane extracts showed the presence of a complex consisting of synaphin, synaptotagmin 1, and SNAREs. We propose that synaphin recruits synaptotagmin 1 to the SNARE-based fusion complex and synergistically functions with synaptotagmin 1 in mediating fast synaptic vesicle exocytosis.

● *Hollow and Solid Spheres Assembled from Functionalized Macrocycles Containing Adamantane.*

M. Tominaga, N. Kunitomi, K. Ohara, M. Kawahata, T. Itoh, K. Katagiri, K. Yamaguchi, *J. Org. Chem.* 84 (9), 5109–5117 (2019). Apr 2019, DOI: 10.1021/acs.joc.9b00069.

An adamantane-based macrocycle possessing eight hydroxyl groups was synthesized. Functionalized macrocycles containing methyl and methoxycarbonylmethyl groups were prepared. From X-ray analysis, the macrocyclic backbone in all crystals had a nearly hexagonal shape with a cavity, and these macrocycles could be arranged into different tubular structures dependent on the substituents. In acetone, macrocycle formed stable hollow spherical aggregates with multilayer membranes. In contrast, macrocycle exhibited no production of self-assembled materials in chloroform. The addition of hexane into the solution caused the generation of solid spheres and their fused network aggregates, which were finally transformed into crystals owing to the solvent effects.

● *Traceable stimulus-dependent rapid molecular changes in dendritic spines in the brain.*

Kazuya Kuboyama, Takafumi Inoue, Yuki Hashimoto, Takuya Itoh, Tohsuke Suzuki, Aya Tetsuzawa, Yosuke Ohtsuka, Ryo Kinoshita, Ren Takara, Tohru Miyazawa, Pooja Gusain, Masanobu Kano & Maki K. Yamada, *Scientific Reports* volume 10, Article number: 15266 (2020), DOI: 10.1038/s41598-020-72248-4

Dendritic spines function as microcompartments that can modify the efficiency of their associated synapses. Here, we analyzed stimulus-dependent molecular changes in spines. The F-actin capping protein CapZ accumulates in parts of dendritic spines within regions where long-term potentiation has been induced. We produced a transgenic mouse line, AiCE-Tg, in which CapZ tagged with enhanced green fluorescence protein (EGFP-CapZ) is expressed. Twenty minutes after unilateral visual or somatosensory stimulation in AiCE-Tg mice, relative EGFP-CapZ signal intensification was seen in a subset of dendritic spines selectively in stimulated-side cortices; this right-left difference was abolished by NMDA receptor blockade. Immunolabeling of α -actinin, a PSD-95 binding protein that can recruit AMPA receptors,

showed that the α -actinin signals colocalized more frequently in spines with the brightest EGFP-CapZ signals (top 100) than in spines with more typical EGFP-CapZ signal strength (top 1,000). This stimulus-dependent in vivo redistribution of EGFP-CapZ represents a novel molecular event with plasticity-like characteristics, and bright EGFP-CapZ in AiCE-Tg mice make high-CapZ spines traceable in vivo and ex vivo. This mouse line has the potential to be used to reveal sequential molecular events, including synaptic tagging, and to relate multiple types of plasticity in these spines, extending knowledge related to memory mechanisms.

● *Control over multiple molecular states with directional changes driven by molecular recognition.*

Hirao, T.; Kim, D-S.; Chi, X.; Lynch, V-M., Ohara, K.; Park, J-S.; Yamaguchi, K.; Sessler, J-L. Nat. Commun., 2018, 9, 823. DOI: 10.1038/s41467-018-03220-0

Recently, ligand–metal coordination, stimuli-responsive covalent bonds, and mechanically interlinked molecular constructs have been used to create systems with a large number of accessible structural states. However, accessing a multiplicity of states in sequence from more than one direction and doing so without the need for external energetic inputs remain as unmet challenges, as does the use of relatively weak noncovalent interactions to stabilize the underlying forms. Here we report a system based on a bispyridine-substituted calix[4]pyrrole that allows access to six different discrete states with directional control via the combined use of metal-based self-assembly and molecular recognition. Switching can be induced by the selective addition or removal of appropriately chosen ionic guests. No light or redox changes are required. The tunable nature of the system has been established through a combination of spectroscopic techniques and single crystal X-ray diffraction analyses. The findings illustrate a new approach to creating information-rich functional materials.

■ Health and Welfare

□ Radiological Technology

● Morimoto M, Takeuchi K, Asahara M. *Evaluation of Image Rotation Processing in Digital X-ray Imaging*, Medical Imaging and Information Sciences, Vol.36(1), 2019, p.p.10-15.

The image rotation processing in the digital X-ray image is useful in performing the rotation processing of less than 90 degrees, however, the influence on the image quality

has not been clarified. The aim of this research is to evaluate the influence of image rotation processing on image quality of digital X-ray image using physical evaluation and image evaluation. An original digital X-ray image was taken at 0 degrees. Images were taken after increasing the inclination angle at 5 degree intervals, up to 45 degrees. We measured the processed modulation transfer functions (processed MTFs) and normalized noise power spectrum (NNPS) as the physical evaluation. We measured Contrast-Detail (C-D) curve and inverse of Image Quality Figure (IQF_{inv}) using CDRAD phantom as the image evaluation. Compared with the original image, the processed MTFs increased as the rotation angle increased in the arbitrarily rotated image, and the NNPS increased. The C-D curve was not influenced by the extent of rotation, and it made no difference to IQF_{inv} ($p > 0.05$) either. The result showed that the effects of the image rotation on clinical X-ray image differs depending on the structure of radiographed objects.

● *Implementation of a Remotely Controlled FPD System for X-ray Imaging in an Advanced Isolation Room*

Iizuka.A, Yamauchi.M, Fukagawa.K, Yamato.M

Japanese journal of infection Prevention and Control. 2020 Vol.35(1):37-42

Abstract

Our medical institution is a designated center for the treatment of patients with infectious diseases such as Ebola virus disease (EVD), which was a major epidemic in West Africa beginning in 2014. We set up an advanced isolation room containing a flat-panel detector (FPD) system that was used for the X-ray imaging of a patient suspected to have EVD. The FPD system appeared to be very useful from the viewpoint of performing early image examinations, obtaining a diagnosis, and preventing the spread of the virus. However, it is very difficult and complicated for staff wearing full personal protective equipment to operate the personal computer (PC) of an FPD system from within the advanced isolation room. Therefore, we constructed a remotecontrol system in which all PC operations of the FPD system could be performed in a separate room, without the need for staff to wear full personal protective equipment. We consider that a remotely controlled FPD system would be advantageous for operating medical equipment in an advanced isolation room, particularly from the viewpoint of infection control. Key words: Institution for Specific Infectious Diseases, advanced isolation ward, X-ray photography, remote-control system for PC of flat-panel detector system.

● *Comparison between Variance and Edge Methods for Measuring Image Resolution Properties in Digital Mammography.*

Yukiko Matsubayashi, Mizuki Hamano, Rie Ishii, Kaoru Kitagawa, Mie Ishii, Taizo

Sanada, Akira Yoshida, Nihon Hoshasen Gijutsu Gakkai Zasshi. 2021;77(2):182-190.
doi:10.6009/jjrt.2021_JSRT_77.2.182.

PubMed Abstract

We studied the image resolution properties in digital mammography using the variance and edge response function methods. The associated measurements were made using a polymethylmethacrylate phantom of 0-40 mm thickness while maintaining the incident dose to the detector constant, as well as with and without using the phantom but by varying the level of exposure to the detector. The results obtained using the two methods were compared on the object plane of the mammography unit with compensation for the magnification and rejection of the scattered radiation. In this unit, the imaging process of resolution enhancement may be performed according to the phantom thickness, shape of test device, exposure level, and so on. The modulation transfer function values of the variance method were slightly higher than those of the edge method, approximately 6% at 2 cycles/mm and 8% at 4 cycles/mm without resolution enhancement processing. We concluded that the variance method is more suitable than the edge method for the constancy test or quality control because of its lower coefficient of variation.

● *Effect of quantitative values on shortened acquisition duration in brain tumor ¹¹C-methionine PET/CT.*

Masatoshi Morimoto , Nobuyuki Kudomi , Yukito Maeda , Takuya Kobata , Akio Oishi ,
Keisuke Matumoto , Toshihide Monden , Takanobu Iwasaki , Katsuya Mitamura ,
Takashi Norikane , Yuka Yamamoto and Yoshihiro Nishiyama, EJNMMI physics 8 , Article number
34 (2021)

Background: The amount of signal decreases when the acquisition duration is shortened. However, it is not clear how this affects the quantitative values. This study aims to clarify the effect of acquisition time shortening in brain tumor PET/CT using ¹¹C-methionine on the quantitative values.

Method: This study was a retrospective analysis of 30 patients who underwent clinical ¹¹C-methionine PET/CT examination. PET images were acquired in list mode for 10 min. PET images of acquisition duration from 1 to 10 min with 1-min step were reconstructed. We examined the effect on the quantitative values of acquisition duration. We placed a volume of interest to include the entire tumor and regions of interest in the shape of a large crescent in the contralateral hemisphere in 5 contiguous axial slices as normal tissue. Quantitative values examined were maximum, peak, and mean standardized uptake values (SUV_{max}, SUV_{peak}, SUV_{mean}), metabolic tumor volume (MTV), and maximum tumor to normal tissue ratio

(TNRmax), with each duration compared to that with 10 min.

Results: SUVmax, MTV, and TNRmax showed the highest values due to the effects of statistical noise when the acquisition time was 1 min. These values were stable when the acquisition duration was > 6 min. SUVpeak and SUVmean showed mostly consistent values regardless of duration.

Conclusions: SUVmax, MTV, and TNRmax are affected by acquisition time. If the acquisition duration was > 6 min. the fluctuation could be suppressed within 5% in these quantitative values. However, SUVpeak was suggested to be a robust index regardless of the acquisition duration.

●Kunihiko Katagiri, *Study on the role of radiological technologists and improvement of medical quality -Possibility of contribution to medical care by self evaluation of technologists.*

Abstract of Doctoral Thesis,

In recent years, with the advancement of medical care, it has been suggested that there is a need for team medical care by a tandem of physicians, nurses, and radiological technologists (hereinafter referred to as ‘technologists’) in hospitals. What is the role of technologists in the improvement of medical care quality and how should they contribute to it? Research into these questions has not necessarily been sufficient. We put forward the following three propositions in this paper. Technologists are in a unique position and play a role that can further contribute to medical care (Proposition 1); a technologist’s self-awareness regarding their studies and career formation affects improvements in the quality of medical care (Proposition 2); and technologists are aware of the fact that proactive communication within medical facilities can contribute to improvements in working efficiency (Proposition 3). With regard to the first proposition, we analyzed operating room data etc using social network analysis software to visualize the position of technologists in hospitals. In addition, we interviewed medical professionals to investigate the role and potential of technologists. With regard to the second and third propositions, the methods of verifying the propositions consisted of quantitative analysis (regression analysis) of responses of 101 technologists to self-evaluation questionnaires and qualitative analysis of interviews of medical professionals. Verification of the propositions revealed the following. The role of technologists is unclear, but there is potential for utilizing their core strengths. We found that the technologists recognized that there are benefits to lifelong learning. Furthermore, the technologists felt that while in-hospital communication was poor, workplace learning could lead to better work performance. In conclusion, we established that there is potential for technologists to contribute to the improvement of medical care quality by utilizing their current strengths and striving for lifelong learning and in-hospital communication is improved.

●*Research on Utilization of LCD Monitors substitute for Light Box about Hard-copy Diagnosis in an Emergency by Using Receiver Operating Characteristic Analysis.*

Kazuhiro Takeuchi, Yoshitaka Matsumura, Hiroki Akane, and Akihiro Miki, Jpn. J. Radiol. Technol., Vol.75, No.5, May, 2019, pp.438-445

The creation of the business continuity plan (BCP) for disaster key hospitals were mandated on March 31, 2017. The creation of BCP must take countermeasures assuming damage at all levels. In Japan, a light box is no longer being used by a shift to soft-copy diagnosis. However, supposing the hospital network failure occurred, we assumed the film diagnosis was necessary for radiological examination images. The purpose of this study is to investigate whether the film diagnosis using a medical monitor with high luminance (410, 800 cd/m²) instead of the light box is inferior or not to a monitor diagnosis (410 cd/m²) in detect pulmonary nodules. Ten radiological technologists participated in the observer tests for detection of nodules, respectively. In each observer test, radiological technologists marked their confidence levels for diagnosis of pulmonary nodules. The detection performance of radiological technologists was evaluated by ROC analysis. The average AUC value (area under the ROC curve) in detecting pulmonary nodules with monitor (410 cd/m²) and film (410 cd/m²), film (800 cd/m²) were 0.770 and 0.754, 0.806 respectively. There was no statistically significant difference between monitor (410 cd/m²) and film (410, 800 cd/m²) for detection of pulmonary nodules (P=0.32, 0.09). Therefore, we believe that the film diagnosis can be used for the medical monitor instead of the light box when film operation in case of a disaster inevitable.

● *Comparison Between Prone and Upright Imaging of the Inferior Wall Using ²⁰¹TlCl Myocardial Perfusion SPECT.*

Koji Nakaya, Masahisa Onoguchi, Yoshihiro Nishimura, Keisuke Kiso, Hideki Otsuka, Yoshifumi Nouno, Takayuki Shibutani and Eisuke Yasuda, *Journal of Nuclear Medicine Technology* December 2017, 45 (4) 304-308.

Because it suppresses attenuation artifacts from the diaphragm, prone SPECT is suitable for evaluating the cardiac inferior wall. A solid-state dedicated cardiac camera allows upright imaging, which can also be used to avoid attenuation artifacts from the diaphragm. We compared prone and upright imaging for inferior wall evaluation using ²⁰¹TlCl myocardial perfusion SPECT (MPS). In comparison with upright imaging, prone imaging has a higher rate of suppression of attenuation artifacts from the diaphragm. However, this difference does not seem to affect the images visually. Therefore, upright and prone imaging can be used interchangeably to evaluate the inferior wall.

● *Assessment of the cut-off value of quantitative liver-portal vein contrast ratio in the hepatobiliary phase of liver MRI.*

Takatsu Y, Nakamura M, Shiozaki T, Narukami S, Yoshimaru D, Miyati T, Kobayashi S., *Clinical Radiology*, 76 (2021) 551.e17e551.e24. <https://doi.org/10.1016/j.crad.2021.03.015>

<https://doi.org/10.1016/j.crad.2021.03.015>

AIM: To calculate the quantitative liver-portal vein contrast ratio (Q-LPC) cut-off value based on tumour detectability by using receiver operating characteristic (ROC) curves.

MATERIALS AND METHODS: Seventy-four patients with tumours (46 men and 28 women; age, 71± 8.1 years), who underwent liver magnetic resonance imaging (MRI) using gadolinium-ethoxybenzyl-diethylenetriamine pentaacetic acid (Gd-EOB-DTPA) were enrolled. Some patients were found to have multiple tumours. In total, 102 tumour images were evaluated for quantitative liver-spleen contrast ratio (Q-LSC) and Q-LPC 10 minutes after the administration of Gd-EOB-DTPA. Q-LPC and Q-LSC were compared to assess the cut-off values and usefulness. The ROC curve was evaluated using the method for continuously distributed test results, with a free scale of 50 mm. A score of ≥30 out of 50 points was considered good. Cut-off values of Q-LPC and Q-LSC were then calculated. The areas under the ROC curve (AUCs) were also examined and compared.

RESULTS: The AUC-ROC for Q-LPC was 0.858 (95% confidence interval [CI], 0.783–0.933).

The cut-off value was determined to be at 1.462. Sensitivity was 0.747, and specificity was 0.852 at the cut-off value. The AUC-ROC for Q-LSC was 0.710 (95% CI, 0.597–0.822). The cut-off value was at 1.543, the sensitivity was 0.560, and the specificity was 0.778 at the cut-off value.

A significant difference was noted between the AUCs ($P=0.0016$).

CONCLUSION: Q-LPC can be used for hepatobiliary phase MRI evaluation.

● Yoshihiro NISHIMURA, Yu HACHISUKA, Sadatoshi YASUDA, *Development of the Ultrasonic Examination Learning Support System Using Projection Mapping Method with Abdominal X-ray CT Image*, Journal of the Japan Association of Radiological Technologists Education Vol.12 No.1 p.21-26, 2021

We have newly developed a projection mapping method for the purpose support for ultrasonic examination training. With the probe operation of ultrasonography, the observation field of view is narrow and it is difficult to grasp the positional relationship of the abdominal organs.

This method projects an abdominal X-ray CT image on the surface of the abdominal phantom, which is an ultrasonic simulator, and operates the probe with reference to this projected image. When the students were given ultrasonic training by this method, the average value of the comprehension level of the probe investigation for delineating the target organ improved by 1.8 points out of a maximum of 4 points, showing a good value of 3.8 points. By using this learning support system, it was thought that the student's understanding of ultrasonic examination training could be improved.

□ Clinical Engineering

● Akari Goto, Kunihiro Ishihara, *Identification and Evaluation of Coagulation Promoters on Surface of Medical Materials*, International Journal of Engineering and Applied Sciences (IJEAS). ISSN: 2394-3661, Volume-8, Issue-4, April 2021.

During hemodialysis treatment, many problems such as residual blood, thrombocytopenia, coagulation in the blood circuit occur due to the patient's blood contacting with various materials. Then in this paper, we will propose to evaluate the thrombin activity caused by contact between blood and material as an evaluation method of the antithrombotic medical material.

In the previous study, as the objective of elucidation of the blood coagulation mechanism, thrombin-like activity remained on the surface of the medical materials was measured and compared in order to evaluate the difference of materials for the blood coagulation activation which is caused in the case of the blood contacting the medical materials outside the living body.

In the previous study, thrombin-like activity is confirmed for five kinds of materials such as polystyrene, polymethylpentene, polypropylene, tetrafluoroethylene, perfluoroalkoxyethylene and glass. In the present study, it was clarified that the coagulation promoter adsorbed on the surface of the material was thrombin due to the experiment using anti-thrombin antibody.

● Keisuke Hayashi, Takashi Hitosugi, Yoshifumi Kawakubo, Norihisa Kitamoto, Takeshi Yokoyama, *Influence of measurement principle on total hemoglobin value*, BMC Anesthesiol. 2020 Apr 7;20(1):81.

Background: Total hemoglobin (tHb) measurement is indispensable for determining the patient's condition (hemorrhagic vs. ischemic) and need for blood transfusion.

Conductivity- and absorbance-based measurement methods are used for blood gas analysis of tHb. For conductivity-based measurement, tHb is calculated after converting blood conductivity into a hematocrit value, whereas absorbance measurement is based on light absorbance after red blood cell hemolysis. Due to changes in plasma electrolytes and hemolysis, there is a possibility that conductivity- and absorbance-based measurement methods may cause a difference in tHb.

Methods: In this study, test samples with controlled electrolyte changes and hemolysis were created by adding sodium chloride, distilled water or hemolytic blood to blood samples collected from healthy volunteers, and tHb values were compared between both methods.

Results: Conductivity-based measurement revealed reduced tHb value (from 15.49 to 13.05 g/dl) following the addition of 10% sodium chloride, which was also reduced by the addition of hemolysate. Conversely, the addition of distilled water significantly

increased tHb value than the expected value. In the absorbance method, there was no significant change in tHb value due to electrolyte change or hemolysis.

Conclusions: We have to recognize unexpected conductivity changes occur at all times when tHb is measured via conductivity- and absorbance-based measurement methods. The absorbance method should be used when measuring tHb in patients with expected blood conductivity changes. However, when using this method, the added contribution of hemoglobin from hemolytic erythrocytes lacking oxygen carrying capacity must be considered. We recognize that discrepancy can occur between conductivity- and absorbance-based measurement methods when tHb is measured.

●Kunihiko ISHIHARA, *Study on sound pressure level and acoustic damping ratio of one dimensional sound field*, Transaction of Japan Society of Mechanical Engineers, Vol.86, No.891, 2020, pp.1-14. DOI: 10.1299/transjsme.20-00250

In heat exchangers, as a tube bank is set in a duct the alternative vortices occur behind a tube bank and the vortex shedding frequency increases with the flow velocity when the boiler is operated. High level sound is suddenly generated when the vortex frequency comes close to the acoustic natural frequency of the duct. This is generally called the self-sustained tone. The effective countermeasure is required in the design stage. In recently, it was clarified that the perforated plate suppresses the high level sound. Then in this paper, the acoustic experiments will be conducted by using the three different sizes of the ducts and perforated plates. The acoustic damping obtained by these experiments and analyses is compared. As a result, it was clarified that the acoustic damping ratio becomes smaller with larger of dimensional ratio.

●Makoto Kashino, Kunihiko Ishihara, *Investigation on optimum position relation between fan and filter in development of deodorization equipment*, The Japanese Journal Of Medical Instrumentation, Vol.90, Oct,2020, pp.438-446.

In hospitals, odor has often been a problem. The deodorization equipment will be developed as countermeasures. First, we examined the optimal position of the fan sending air to the filter efficiently. Using a duct and a triangular prism equipments, three wind velocities, V1(inlet side), V2(outlet side), and V3(before passing through the filter) were measured. The filter was fixed and the height of the fan was changed. Static pressure was measured on the wall at the same height as the position of V3. The flow rate was calculated from the wind velocity and the cross sectional area. The CFD was performed to visualize the airflow inside the triangular prism equipment. V2 became high as the fan moved closer to the filter. In triangular prism, the law of conservation of mass was satisfied when the fan was at 305 mm apart from the floor. Similar results were obtained with a triangular prism device using CFD. However, it was different from

the experimental results. The cause of this is unknown at this time. This is a topic for the future. Experimental results suggest that the closer the fan is to the filter, the more flow rate will pass through the filter.

● Satoru Kudo, Kunihiko Ishihara, *Analysis of the effect of local albumin concentration in dialyzer estimated from sieving coefficient of albumin on internal filtration flow rate*, The journal of Japanese Society for Technology of Hemopurification, Vol.28, Dec., 2020, pp.136-146.

The current dialyzers, which are called high-performance membranes, have high water permeability and solute-removal capacity, but exhibit albumin leakage. Albumin is involved in the local filtration flow rate because it produces oncotic pressure. It is useful for estimating the therapeutic effects to estimate the internal filtration flow rate obtained by calculating the local filtration flow rate. Many studies have estimated the internal filtration flow rate; however, to the best of our knowledge, simulations considering albumin leakage have not been reported. Moreover, why albumin leakage can be ignored remains unclear. The local albumin concentration is expected to change not only because of concentration and dilution but also because of albumin leakage. Here, a numerical calculation was performed to examine the effect of albumin leakage on the internal filtration flow rate.

We found that a larger SC led to a smaller absolute value of the local filtration flow rate; however, the difference was very small when SC was ≤ 0.1 . Because the SC of the dialyzer currently used in clinical practice is approximately 0.01, It is not necessary to consider the effect of albumin leakage on the internal filtration flow rate.

● Mizuho Tagashira, Takafumi Nakagawa, *Discrimination Method for Vascular Stenosis by Acoustic Analysis of Dialysis Shunt Sound*, Transactions of Japanese Society for Medical and Biological Engineering, Volume 59 Issue 1, 2021, pp.31-39.

In this paper, we present a method for facilitating the diagnosis of vascular stenosis in hemodialysis treatments. Sensory evaluation based on vascular sounds is usually used to identify vascular stenosis. However, skilled clinical judgement is required for this work. We applied the Mahalanobis-Taguchi Method to the assessment of vascular abnormalities. Mel-frequency cepstral coefficients, histogram kurtosis, and autocorrelation coefficients are used as features. The difference between normal and abnormal sounds is measured by Mahalanobis distance (MD). The performance of this method is estimated for 60 vascular sounds, with correct results obtained at a rate of 87% for abnormal sounds. The proposed method provides better discrimination than sensory evaluation. In addition, the relative change in MD values along the auscultation positions is similar to the result achieved by sensory evaluation.

●Tomokazu Nagasawa, Yoshifumi Kawakubo, Keisuke Hayashi, Masanobu Tsurumoto, Norihisa Kitamoto, Masanori Tsukamoto, Takeshi Yokoyama, Comparing Data Analysis for Hemodynamic Monitoring in the Vigileo and LiDCORapid Models, International Journal of New Technology and Research (IJNTR)ISSN:2454-4116, Volume-3, Issue-9, September 2017 Pages 114-120.

Currently, the standard method of cardiac output monitoring is to use a Swan-Ganz catheter. This catheter can lead to complications, and therefore the benefits over risks are being analyzed. In order to have a continuous monitoring of cardiac output or circulatory dynamics in a less invasive form, two different devices were developed. The first device that was developed is the Vigileo monitor (Vigileo) (Edwards Lifesciences corporation, CA, USA) and the second device is the LiDCORapid (Lidcolimited, London, UK). The comparison analysis of the cardiac output was measured between the Vigileo and LiDCORapid. A blood pressure calibrator made by BIO-TEK INSTRUMENTS called BIO-TEK601A was used for the artificial pressure source. Aortic pressure (Ao) and radial artery pressure (Rd) was obtained through the BIO-TEK601A. The CO was displayed from the data that was divided into each model, gender, age and input waveform. For statistical evaluation of the experimental data, Mann-Whitney U-test or Wilcoxon Signed rank sum test were used. The CO results from the Vigileo model were less dependent on the Ao or Rd pressure compared to the LiDCORapid model. The Vigileo was determined to have less variability with CO results compared to the LiDCORapid model.

■ Science and Engineering

□ Nano Material and Bio Engineering

● *Development of analysis system for Candida glabrata infection using nematode.*

Junki Takeba, Koichi Mita, Atsushi Maeda, Takayuki Mizuno, and Masanori Bun-ya Proceedings of 71st SBJ Annual Meeting. (Okayama) 2019, 284, 3Ep06

In this study, we showed that a *C. glabrata-C. elegans* infection model was established in the *C. elegans* N2 strain by statistical analysis of viable cell count, fluorescence observation, and survival rate in *C. elegans*. It was clarified that the nematode infertility strain gave similar results to the N2 strain, suggesting that the *C. glabrata* infection model could be analyzed using the infertility strain

● *VHF Plasma CVD Synthesis of Photochromic ZnO Nanoparticles.*

Hiroshi Kajiyama, Shin Kuboyama, Atsushi Otomo, Hiroki Uyama, Toshihiro Matsuura¹, Shuhei Inoue, Yukihiro Matsumura, Keiji Takata, Kentaro Tomita, Kiichiro Uchino, MRS Adv., <http://dx.doi.org/10.1557/adv.2019.80>.

A photochromic (PC) ZnO nanoparticle is synthesized for the first time by using a VHF plasma enhanced CVD apparatus. It changes from transparent to PC states by UV irradiation; by heat treatment, it changes back to transparent. There is a threshold temperature for the PC phase. The Debye-Waller factor of Zn atoms is specifically large for the photochromic ZnO. The nanoparticle contains carbon as impurity. The effects of C-O bonds on the ZnO structure and the density of states (DOS) are simulated based on a density functional theory. It is obtained that the structure is slightly distorted and that a sufficient DOS for photochromic light absorption is formed in the band gap.

● *Development of Eu²⁺ and Mn²⁺ co-activated silicate phosphor for plant cultivation light source.*

Kunimoto T., Fujita Y, Kajiyama H, Honma T, Kawaguchi H, Ishigaki T, Ohmi K, Ohshima K, Miyazaki D, Saito Y, Hara S, Sakurai T, Okubo S, Ohta H, Japanese Journal of Applied Physics (2019) 58 SFFD03. DOI: 10.7567/1347-4065/ab09cc
Various light sources for plant production have been developed to establish a completely controlled factory. We propose a pulse light source using Xe discharge. For the rapid growth of the plant, an intense light covering the absorption spectral region of chlorophyll is demanded, and periodic irradiation is also required because the photosynthetic reaction has a certain period. In this study, Sr₃MgSi₂O₈:Eu,Mn phosphor powders with various Eu and Mn content, which show two emission peaks in the absorption region of photosynthetic pigment and phytochrome, were synthesized, and were analyzed using X-ray diffraction, photoluminescence and electron spin resonance spectroscopy. It was found that the exchange-coupled Mn-Mn and Eu-Mn pairs lead the rapid decay of Mn emission and efficient energy transfer from Eu and Mn ions, respectively. A plasma tube array panel using the phosphor was also fabricated and the similar emission spectrum of Sr₃MgSi₂O₈:Eu,Mn is obtained under vacuum-UV excitation in comparison to the UV excitation.

● *Nonlinear piezoresistance coefficients of semiconductors.*

Kazunori Matsuda, Hiroki Uyama, and Kazuo Tsutui Journal of Applied Physics 126, 225701(2019), doi:10.1063/1.5121884

The inconsistency of symmetry relationship in nonlinear piezoresistance coefficients, which is long-standing puzzle, is resolved by taking into account the complex relation between piezoresistance coefficients and piezoconductance coefficients. The procedure

to obtain correct nonlinear piezoresistance coefficients in theory according to the coordinate transformation of tensors is suggested.

● *What are the elements of motivation for acquisition of conditioned taste aversion?*

Koichi Mita, Akiko Okuta, Ryuichi Okada, Dai Hatakeyama, Emi Otsuka, Miki Yamagishi, Mika Morikawa, Yuki Naganuma, Yutaka Fujito, Varvara Dyakonova, Ken Lukowiak, Etsuro Ito, *Neurobiology of Learning and Memory*. Volume 107, January 2014, Pages 1-12. DOI: 10.1016/j.nlm.2013.10.013

The pond snail *Lymnaea stagnalis* is capable of being classically conditioned to avoid food and to consolidate this aversion into a long-term memory (LTM). Previous studies have shown that the length of food deprivation is important for both the acquisition of taste aversion and its consolidation into LTM, which is referred to as conditioned taste aversion (CTA). Here we tested the hypothesis that the hemolymph glucose concentration is an important factor in the learning and memory of CTA. One-day food deprivation resulted in the best learning and memory, whereas more prolonged food deprivation had diminishing effects. Five-day food deprivation resulted in snails incapable of learning or remembering. During this food deprivation period, the hemolymph glucose concentration decreased. If snails were fed for 2 days following the 5-day food deprivation, their glucose levels increased significantly and they exhibited both learning and memory, but neither learning nor memory was as good as with the 1-day food-deprived snails. Injection of the snails with insulin to reduce glucose levels resulted in better learning and memory. Insulin is also known to cause a long-term enhancement of synaptic transmission between the feeding-related neurons. On the other hand, injection of glucose into 5-day food-deprived snails did not alter their inability to learn and remember. However, if these snails were fed on sucrose for 3 min, they then exhibited learning and memory formation. Our data suggest that hemolymph glucose concentration is an important factor in motivating acquisition of CTA in *Lymnaea* and that the action of insulin in the brain and the feeding behavior are also important factors.

● *HTLV-1 viral oncoprotein HBZ contributes to the enhancement of HAX-1 stability by impairing the ubiquitination pathway.*

Yuka Tanaka, Risa Mukai, Takayuki Ohshima. *J Cell Physiol*. 2021 Apr; 236(4): 2756-2766. doi: 10.1002/jcp.30044. Epub 2020 Sep 7.

Human T-cell leukemia virus type 1 (HTLV-1) is an oncogenic retrovirus that causes adult T-cell leukemia (ATL). The viral protein HTLV-1 basic leucine-zipper factor (HBZ), which is constitutively expressed in all ATL patient cells, contributes toward the development of ATL; however, the underlying mechanism has not been elucidated yet. Here, we identified HS-1-associated protein X-1 (HAX-1) as a novel binding partner of

HBZ. Interestingly, HAX-1 specifically associated with HBZ-US, but not HBZ-SI, in the cytoplasm. HBZ suppressed the polyubiquitination levels of HAX-1 protein by inhibiting the association HAX-1 with F-box protein 25 (FBXO25), which is a member of the SCF E3 ubiquitin ligase complex, and promoted the stabilization of HAX-1 levels. In fact, the protein levels of HAX-1 were significantly increased in HTLV-1 infected and the overexpressing HBZ in uninfected T-cell lines. Enhanced HAX-1 correlated well to suppression of caspase 9 processing, suggesting that HBZ may contribute to the enhancement of antiapoptotic function for HAX-1. Our results revealed a role for HBZ on HAX-1 stabilization by abrogating the ubiquitination-mediated degradation pathway, which may play an important role in understanding the potential mechanisms of HTLV-1 related pathogenesis.

● *Tissue-mimicking Materials for various kind of Phantoms.*

Kazuishi Sato; Masaki Suzuki; Tomoji Yoshida; Toshio Kondo; Takuya Kubo; Kohei Hamachi; Mashiko Taniguchi, 2019 IEEE International Ultrasonics Symposium (IUS). DOI: 10.1109/ULTSYM.2019.8925807

We present a tissue-mimicking material for the phantom of medical diagnostic instruments. Accurate testing of an instrument by phantoms requires a tissue-mimicking material that has the acoustic velocity, density, and attenuation defined in the International Electrotechnical Commission (IEC) standard, and furthermore the tissue-mimicking material must be stable over time. To achieve the material with the desired acoustic velocity, density, and attenuation, we have developed a new swollen segmented polyurethane gel. To realize the gel with low attenuation, we have discussed liquid composition of the gel. Acoustic properties of binary mixtures of tetraethylene glycol dimethyl ether with 1-ethyl-3-methylimidazolium dicyanamide, 1-butthyl-3-methylimidazolium dicyanamide, and 1-ethyl-3-methylimidazolium thiocyanate have been experimentally investigated.

□ Mechanical Engineering

● *Experimental observations on the optimal layout of orientation blocks for safe road crossing by the visually impaired.*

Tomoyuki Inagaki , Shoichiro Fujisawa, Kazuya Takahashi, Norihiro Ikeda, Kiyohito Takeuchi, Hiroshi Ogino, and Satoru Kobayakawa, IATSS Research 41, pp. 82-88, June 2017. <http://dx.doi.org/10.1016/j.iatssr.2017.06.005>

For this paper, in order to examine in greater detail the desirable position of orientation blocks relative to TWSI, the authors conducted an experiment using totally blind

subjects to evaluate conditions on a 10 m walk that simulated an actual crossing. The results, based on observations of the trajectories walked by participants in the experiment and interviews eliciting their subjective evaluations, showed that separating orientation blocks and blister tactile blocks by about 8–12 cm is effective in constraining lateral deviation at a point 5 m from the start of crossing and that an 8 cm separation was desirable in order to maintain an effective reduction of mental stress while crossing.

● *Development of an Adjustable Lift Cart using Linear Equation Mechanism (Design and Prototyping of an Experimental Model).*

Mineo HIGUCHI, Daisuke YOKOTE, Junji KAWATA, Isao MATSUMOTO, Jiro MORIMOTO, Shoichiro FUJISAWA, Design Engineering, Vol.56, No.6, pp.287-302, 2021.

Lift carts of the type in which the loading platform is lifted up and down by human power are widely used. In the operation of such conventional lift carts, the cart's horizontal movement and the load's vertical movement on the cart's loading platform must be operated separately. This paper presents a novel adjustable lift cart with a function that lifts the loading platform up or down to a desired height while it is moved horizontally by human power. The loading platform of the adjustable lift cart moves forward and upward (or downward) as if it is on a virtual ramp. The adjustable lift cart's structure joins the left and right wheels of the cart to a differential gear whose output is coupled with a Continuously Variable Transmission (CVT) that raises the loading platform up and down. We call this mechanism, which consists of a CVT and a differential gear, "a linear equation mechanism". In this paper we first propose the concept of a novel adjustable lift cart and explain how our linear equation mechanism can be applied to it. Second, we illustrate a mechanism of the CVT that consists of a roller and wheels and derive the CVT's ratio. Finally, we explain the design of an experimental model of the adjustable lift cart and show experiment results.

● *Effect of Nitrification Restraint of Outflowing Water from Waste Treatment Plants on Nori Aquaculture.*

Machi Miyoshi, WET2019, p.23, 2019.

Seaweed is important for the food and feed industries, and has potential uses as a biofuel feedstock and nutrient scrubber for bioremediation applications. Among the effects of declining fishery resources, the discoloration of nori (*Pyropia yezoensis*) in aquaculture is serious in coastal areas of the Seto Inland Sea, Japan. Therefore, a program aiming to restore these fishery resources has been proposed. Nitrification restraint treatment was applied to outflows from sewage treatment plants in Shido Bay,

located in Bisan Seto, in order to prevent damage to nori aquaculture. Near the water outlet, desalination had the effect of releasing the water, but salinity was restored to 30 psu within a few meters from the outlet. Total nitrogen and chlorophyll-a concentrations did not increase around aquaculture spaces far from the waste treatment plant outlet. The effect of restraining the nitrification of water likely did not affect nori production because of dilution and diffusion by seawater. Thus, we propose an appropriate management method based on a numerical simulation of the water flow in the inner bay.

□ Electronic Engineering and Information Science

● Ikunori KOBAYASHI, *A Bidirectional Course Questionnaire System for Promoting Reflection and Self-assessment*, Journal of University Education Research, Vol.18, 2021, pp.1-12 (in Japanese).

This report introduces a new system of course questionnaires that has been in use since the 2019 school year at Tokushima Bunri University. The system is used not only for course evaluations by students, but also to promote reflections on and self assessments of their study. Teachers using the system for course evaluation are expected to promote the updating of teaching content and methods. The report describes the design concept and some functions and introduces parts of the questionnaire results utilizing the system.

● *An Extended Pulse Position Modulation for Visible Light Communication with Flicker Suppression.*

Hiroyuki Nakayama, Jiro Morimoto, International Conference on Imaging, Sensing, and Optical Memory (ISOM2018), pp.121-122, October 2018.

Visible Light Communication (VLC) is a simple and safe method of data communication that uses visible light. In this technique, dimming control and flicker are considered together with communication efficiency, because illumination and communication are performed simultaneously in many cases. In this paper, a novel transmission technique that achieves high communication efficiency, low flicker and wide dimming control range is proposed. Low-complexity encoding and decoding algorithms are also provided.

● *Securing IoT Sensor Networks Based on LoRa.*

Shoichiro Seno, Akinori Furuya and Hiroyuki Nakayama, International Symposium on Imaging, Sensing, and Optical Memory (ISOM) 2020, We-C-01, Nov 2020.

IoT sensor networks based on LoRa are being deployed increasingly thanks to its relatively wide range. As LoRa becomes popular, security threats like traffic analysis and localization will impose a major issue. This paper proposes a new security measure called address randomization in addition to standardized encryption and message authentication.

■ Literature

□ Cultural Property

● Shin'ichi SHIMIZU, *Social Changes and the Protection of Cultural Heritages in Post-war Japan*, 34th International Symposium on the Conservation and Restoration of Cultural Property “Reconstruction Process” and Cultural Heritage, National Institute for Cultural Properties, Tokyo, March 2012, pp.181-193.

In Japan, the Law for the Protection of Cultural Property was enacted after the Second World War, during the post-war reconstruction period when democratization and peace policies were vigorously promoted. The country thereafter faced a rapid loss of cultural heritage when high economic growth brought a rise in land development and changes in lifestyles, but the situation prompted civil society, local and public organizations, and the government, to implement various activities and measures for the protection of cultural heritage. The effects of sudden social changes on cultural heritage can hardly compare in seriousness with the impacts of conflicts and natural disasters, but they nevertheless posed a serious threat in terms of the fact that the wave of changes spread throughout the country and destroyed people's lifestyles and thoughts, as well as cultural traditions.

Let us examine the effects that rapid social changes had on traditional culture in post-war Japan, how these changes transformed people's ways of thinking, and how their thinking was later reflected in cultural property protection policies. Reviewing the history of cultural heritage protection and sharing Japan's experience from this perspective could perhaps contribute to promoting international exchanges and cooperation with rapidly growing countries in East and Southcast Asia in the area of cultural heritage protection.

In the following sections, the division of post-war time periods conforms to generally accepted stages of development of Japan's economy, but historical events are not mentioned if they are not conceived as having a clear relevance to cultural heritage

protection policies. Additionally, because the objective of this paper is to provide a perspective on the trends of the times and social events, it does not delve into personal achievements and efforts that helped form the ideological foundation of cultural heritage protection.

●Susumu UENO, *The Shikoku Pilgrimage and its temples – An investigation of Shikoku pilgrimage temples in Kagawa prefecture*, *The Shikoku Henro and Pilgrimages of the World* No.5, Mar., 2020, pp.22-30.

In the paper I will examine the actual state of Shikoku pilgrimage temples during the Edo period by looking at the results of investigations about temples in Kagawa prefecture, which are being carried out as part of the process to obtain World Heritage Site status for the Shikoku pilgrimage. Above all, I will study the characteristics of Shikoku pilgrimage temples by focusing on specific aspects of such buildings as the Daishido and Chado (tea hut). The building of tea huts and the reconstruction of the Daishido acted as a space to welcome pilgrims at the Shikoku pilgrimage temples during the late Edo period, and we can see the character of these temples to accept a large number of unspecified people.

□Japanese Literature

●Hiroaki NAKAYAMA, *Kiyoshi Kanzaki and Postwar Japan: His Challenge to the Literary Assumptions*, *Japanese Literature*, January (Nihon Bungaku) Vol. 67-1, No. 775 2018.1, pp.42-52.

Kiyoshi Kanzaki (1904-1979) is a literary critic known for his pioneering study of Meiji literature in the early Showa Period. His critical style was very unorthodox because he collected a great amount of data and carefully conducted field research before interpreting the texts. He also applied this empirical method to the analysis of the High Treason Incident or the construction of modern women's history which leads to his inquiry about the relation between prostitution and the U.S. military bases in postwar Japan. His transdisciplinary interest in such a variety of topics provides an important clue to reviewing and challenging our literary assumptions.

●Hiroaki NAKAYAMA, *Meiji Bungaku Danwa-kai (Symposium on Meiji Literature) and The History of Literature: The History of Scholarship/the Power of Discourse*, *Modern Japanese Literary Studies (Nihon Kindai Bungaku)* No. 98, 2018.5, pp.116-131.

"Symposium on Meiji Literature" is an organization that was founded in 1933. One of the fundamental starting points for the academic study of modern Japanese literature, it sponsored academic presentations and bibliographical research into individual authors, held

interviews with elderly literary figures, and systematically collected books and other necessary materials. The aim of this paper is to rethink the concept of the "history of literature." To that end, I have surveyed the journal published by this organization and other relevant materials, examining them from the perspective of the "history of scholarship," which allows me to shed an objective light on the study of literature. As an example of the power of "discourse," I focus

particularly on a series of recorded remarks made by Kinoshita Naoe, following the ways in which historical materials concerning the "High Treason Incident" were unearthed, and the opportunities and modes they provided for connecting historical discourse to "literature." In addition, I trace this organization's influence on Ito Sei' *Nihon Bundanshi* (History of the Japanese Literary Scene), and consider the possibilities for historical narrative when it is stimulated by methods of listening to mil recording "discourse."

● Tago T, Kaneko K, Tsuchioka D, Ishii N. (2018), *Adjustment movement to baseballs tossed at different velocities in baseball batting*, Proceedings of the 36th international conference on biomechanics in sports pp.382-385.

The purpose of this study was to compare shifts in the centre of gravity (CG) when balls were tossed at different velocities, in order to obtain data for coaching purposes. The subjects were 10 experienced university baseball players. The subjects batted basic toss up ball toward the centre field, both fastballs and slowballs. Data were collected using 2 high-speed cameras. The movement timing and velocity of the center of gravity were computed. Batting motion was divided into three phases. The mean times in the 1st phase and 3rd phase were approximately the same for both fast and slow balls, but both the time and distance by which the CG moved in the 2nd phase were significantly greater for slow balls than for fast balls.

● Yūsuke SHIMODA, *A Note on the Fragments of Ryōkan's Handwritten Travel Journal: Reading the Part of Suma*, Japanese Literature, December 2019, Vol.68-12, No.798, pp.46-49.

Ryōkan's handwritten travel journal lost most of its text, leaving only four fragments. This work is not just practical record, it has literary features, which are further enhanced by elaboration. It is important as a work of the time when Ryōkan was searching for his own way of life.

□ English-American Language and Culture

