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ORIGINAL ARTICLE – CANCER RESEARCH

Meeting report of the 14th Japan–Korea joint symposium on cancer and aging research: current status of translational research and approaches to precision medicine

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Abstract

Purpose The 14th Japan–Korea joint symposium on cancer and aging research was held at an auditorium of Saga University, Japan, May 31–Jun 2, 2018. Participants presented 31 oral and 21 poster presentations, two lectures at a luncheon seminar, plus special lectures from two Korean Emeritus Professors and founders of our joint symposia. The essential parts of the lectures are reviewed here.

Results This Symposium was called Japan–Korea, because the host country comes first. Our symposia are organized every 18 months and the program includes keynote and plenary lectures, and oral and poster presentations. (1) Subjects related to cancer development at this symposium were: prostate cancer progression, molecules activating GSK3β, suppressing the activation of cancer stem cells, profiling human B cell receptor repertoires, and hereditary gastrointestinal cancer syndrome. (2) Subjects related to treatment were: G-quadruplex ligands for glioma stem cells, tankyrase inhibitor for colorectal cancer, and eradication of ATL. (3) Cancer prevention subjects were: physical adsorption of EGCG to cell membrane, inhibition of immune evasion of cancer cells with EGCG, and prevention with antidiabetic agents. (4) Aging subjects were life span extension with Toll-like receptor 5 vaccine and reversal of senescence with inhibitors of ATM and ROCK. (5) The results of epidemiology focused on aldehyde dehyrogenase-2 and alcohol consumption.

Conclusion The 14th symposium demonstrated the cutting-edge of presentations with discussion of numerous ideas by the participants.

Keywords PAK4 · EGCG · G-quadruplex · ATL · KRAS

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Introduction

The first Korea–Japan Symposium on Chemoprevention was organized at an auditorium of Kang-nung National University in 1996 by three research groups headed by Prof. Sang Chul Park from Seoul National University College of Medicine, Prof. In Kyoung Lim from Ajou University College of Medicine and Director Hirota Fujiki from Saitama Cancer Center Research Institute. Since then, we have regularly organized joint symposia on cancer and aging, because human cancer development is closely associated with aging. It was a great pleasure for us to celebrate the first Joint Symposium of Korea–Japan–Germany in Gyeongju, Korea in 2012, with the successful collaboration of Prof. Otmar D. Wiestler, the previous Chairman of the German Cancer Research Center (DKFZ) in Heidelberg. We regularly publish meeting reports (2000, 2001, 2003, 2006, 2008, 2013, 2015) in *Journal of Cancer Research and Clinical Oncology* (Table 1), since most participants are editorial members of this journal, and our meeting reports have received numerous requests for downloads. From the beginning of our symposia, we identified two aims: Promotion of active poster presentations by young scientists and students in English, and Personal contact with participants during the symposia, including excursions associated with the history of our nations. Since our joint symposia have continued over 20 years, young scientists from early symposia are now Professors.

Author (ES), the main organizer of this symposium and his colleagues set two purposes: (1) The vital continuation of the symposia with organizers consisting of both senior and active scientists, and (2) Presentation of internationally competitive scientific results. The 14th symposium began with opening remarks delivered by President of Saga University Prof. Kohji Miyazaki, who talked about the development of the Medical Faculty of Saga University and historical figures born in Saga Prefecture, including Shigenobu Ookuma, who was Prime Minister of Japan and founded Waseda University in Tokyo. We had 31 oral and 21 poster presentations that focused on genetic changes related to carcinogenesis, cancer treatment therapeutic strategy, cancer stem cells, and aging control within the framework of translational research and precision medicine (Fig. 1). The participation of 55 active researchers showed the gender equity of our scientific activity: 21 females and 34 males (Fig. 2). For the educational sessions for students, two Korean Emeritus Profs, Sang Chul Park and In Kyoung Lim, gave distinguished lectures featuring Korean philosophy and wisdom. One of the most important symposium features has always been diligent discussion between scientists of both nations in a relaxed environment: The symposia have given us the opportunity to become familiar with various research results during these 20 years. This strong motivation in science encourages participants to move on to further steps in international academic society.

Table 1 Seven meeting reports of previous Korea–Japan joint symposia published in *Journal of Cancer Research and Clinical Oncology* (2000−2015)

Titles	Authors	JCRCO
The Seoul Symposium of the *Journal of Cancer Research and Clinical Oncology* regulation of aging and carcinogenesis	In Kyoung Lim, Sang Chul Park Hirota Fujiki	126: 418–423, 2000
Japan–Korea Cancer Research Symposium: investigation on the balanced cooperation of cancer cells with the human body	Sang Chul Park, In Kyoung Lim Nam-Sun Paik, Tadashi Yamamoto Yasuhito Yuasa, Kei Nakachi Hirota Fujiki	127: 692–695, 2001
Korea–Japan, JCRCO and UICC Joint Symposium on cancer and aging research: Molecular epidemiological and translational studies	Sang Chul Park, Yasuhito Yuasa In Kyoung Lim, Tadashi Yamamoto Sataro Goto, Kei Nakachi	129: 252–257, 2003
The seventh Korea–Japan Joint Symposium on cancer and aging research: molecular targets in cancer and aging research	Sang Chul Park, In Kyoung Lim Gou Young Koh, Young-Joon Surh, Yun-Sil Lee, Hirota Fujiki Tadashi Yamamoto, Yasuhito Yuasa, Naoki Maruyama, Sataro Goto	132: 339–342, 2006
Friendship in research: The Japan–Korea Symposia on cancer and aging	Hirota Fujiki, Sang Chul Park In Kyoung Lim, Yasuhito Yuasa	134: 813–817, 2008
The eleventh Korea–Japan–Germany Joint Symposium on cancer and aging research	Eung-Gook Kim, Hiroyuki Seimiya, Junho Chung, Jöerg Hoheisel, In Kyoung Lim, Hirota Fujiki, Sang Chul Park	139: 901–904, 2013
Highlights of the Twelfth Japan–Korea Joint Symposium on cancer and aging research	Masami Suganuma, Tae Jun Park Eisaburo Sueoka, Keisuke Iida Yoichi Tanaka	141:1953–1961, 2015

Fig. 1 The proceedings of the 14th Joint Symposium

Keynote and plenary lectures, oral presentations, posters and special lectures

Plenary session I with five keynote lectures focusing on prostate cancer progression with p21-activated kinase 4, cancer prevention with antidiabetic agents, RAS degradation via signal transduction, G-quadruplex ligands for glioma stem cells, and tumor-suppressive function of wild-type KRAS, chaired by Drs. Atsumasa Komori and Junho Chung.

Dr. Eung-Gook Kim, Department of Biochemistry, College of Medicine, Chungbuk National University studied the role of p21-activated kinase 4 (PAK4) in prostate cancer progression. Deregulation of androgen receptor (AR) signaling pathway plays a key role in prostate cancer progression, including invasion, metastasis and chemoresistance. AR-independent signaling is also involved in progress to castration-resistant prostate cancer (CRPC). Dr. Kim's group defined the role of cAMP response element binding protein (CREB) and Slug transcription factors in prostate cancer progression. PAK4 mediates the activation of these transcription factors in a distinct way: PAK4 directly activated Slug via phosphorylation, but CREB indirectly activated via CREB-regulated transcriptional co-activator (CRTC1). The inhibition of two PAK4-CREB and PAK4-Slug axes may provide a new method for therapeutic intervention of CRPC.

Dr. Yohei Shirakami, Department of Gastroenterology, Gifu University Graduate School of Medicine, reported the effects of biguanide metformin (MET) and tofogliflozin (TOFO) on the development of obesity-related liver tumorigenesis. Treatments with MET and TOFO (sodium glucose cotransporter-2 inhibitor), significantly suppressed the development of hepatic neoplastic lesions in obese and

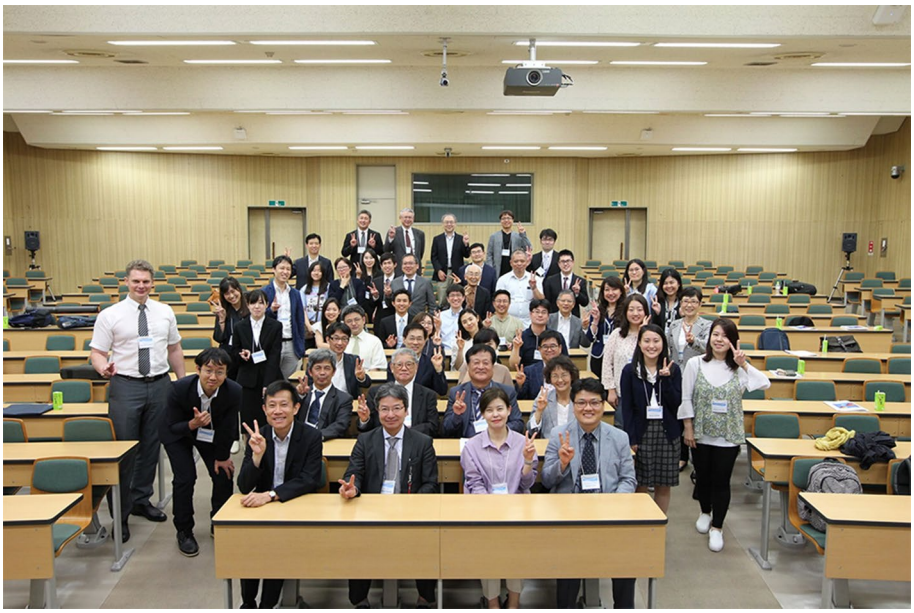

Fig. 2 The group picture of the 14th Japan–Korea joint symposium on cancer and aging research in the auditorium of Saga University

diabetic mice, which were previously treated with diethylnitrosamine. Treatments with MET reduced the phosphorylated form of Akt (a serine/threonine-specific protein kinase) and mTOR (mammalian target of rapamycin) proteins in the liver. The results showed that MET suppresses the early phase of obesity-related liver carcinogenesis by regulating adipokine imbalance and PI3K (phosphoinositide 3-kinase)/Akt/mTOR signaling, and TOFO suppresses it by attenuating chronic inflammation and hepatic steatosis.

Dr. Kang-Yell Choi, Department of Biotechnology, Yonsei University emphasized the interaction of two transforming pathways in colorectal cancer (CRC): Wnt (wingless)/β-catenin and RAS–extracellular signal-regulated kinase (ERK). Both β-catenin and RAS levels showed high increases in the tissue of CRC patients. In addition, epidermal growth factor receptor (EGFR) is overexpressed in human CRCs. The results suggested that inhibition of both Wnt/β-catenin and EGFR–RAS–ERK pathways could be an ideal treatment of human CRC. Dr. Choi's group screened the small molecules that activate glycogen synthase kinase 3β (GSK3β)—a serine/threonine protein kinase - and induce phosphorylation and subsequent polyubiquitin-dependent proteasomal degradation of both β-catenin and RAS. These small molecules effectively suppressed the activation of cancer stem cells.

Dr. Hiroyuki Seimiya, Cancer Chemotherapy Center, Japanese Foundation for Cancer Research, reported his original work on targeting G-quadruplex (G4), which is a four-stranded nucleic acid structure formed at guanine-rich sequences, such as the telomeric repeats. G4s are widely distributed through the genome and can affect various intracellular events. G4 stabilization by small compounds called G4 ligands preferentially inhibit the growth of glioma stem cells, and glioma stem cells are highly sensitive to G4 ligands, such as telomestatin and its synthesized derivative 6OTD. As a potential pharmacodynamic biomarker, immunofluorescence intensities of the nuclear G4 foci were enhanced by G4 ligands. These ligands inhibited both in vitro transcription and translation of mRNA that contained G4-forming sequences, indicating that G4s in both DNA and RNA are promising targets for cancer therapy.

Dr. Gloria H. Su, Herbert Irving Comprehensive Cancer Center, Columbia University Medical Center, New York, kindly attended. KRAS is the most frequently mutated oncogene (~95%) in pancreatic ductal adenocarcinoma, and Dr. Su's group previously reported that loss of the wild-type KRAS allele is associated with metastasis in pancreatic tumorigenesis. To find out about the wild-type KRAS allele function and its underlying mechanisms in the context of mutant KRAS, they restored the wild-type KRAS allele in a doxycycline inducible manner in two pancreatic cancer cell lines that had undergone loss of the wild-type allele. The wild-type KRAS allele has a tumor-suppressive role in the context of the mutant KRAS allele in pancreatic tumorigenesis through inhibition of YAP1 nuclear translocation.

Plenary session II chaired by Drs. Tetsuo Mashima and Eung-Gook Kim, featured four lectures concerning life span extension with a vaccine of Toll-like receptor 5, oxidative DNA damage and repair in cancer and aging, reversal of senescence with screened inhibitors, and role of senescent cells in aging-related pigmentation.

Dr. Kyung A Cho, Department of Biochemistry, Chonnam National University Medical School, reported the first trial on the lifespan extension of mice with a mucosal Toll-like receptor 5 (TLR5) stimulating vaccine. Dr. Cho's group conducted a new antiaging intervention by activating

immunosenescence with a mucosal vaccine, that can directly stimulate TLR5 signaling. Stimulation of the mucosal vaccine at 650 days of age in mice extended both mean and maximum lifespans of mice of both sexes, and also improved a wide range of healthspan parameters for more than 2 years, including hair color and loss, rectal prolapse frequency, eye lens opacity, bone mineral density and cognitive activity. TLR5-dependent immune stimulation will likely be a new tool for extending lifespan and healthspan in humans.

Dr. Yusaku Nakabeppu, Medical Institute of Bioregulation, Faculty of Medical Sciences, Kyushu University, reviewed his extensive data on oxidative DNA damage and repair. Accumulation of 8-oxo-7,8-dihydroguanine (GO) that originated from 8-oxo-7,8-dihydro-2′-deoxygunanosine 5′-triphosphate (8-oxo-dGTP) in cellular genomes results in mutation or programmed cell death, and can be minimized by the action of numerous enzyme combinations, including oxidative nucleotide hydrolase MutT homolog-1 (MTH1) with 8-oxo-dGTPase, OGG1 (8-oxoguanine glycosylase) with GO DNA glycosylase, and MutY homolog with adenine DNA glycosylase. Cancer cells were here exposed to high oxidative stress levels and accumulated a high level of 8-oxo-dGTP in their nucleotide pools. Transgenic expression of human MTH1 efficiently prevents neurodegeneration under oxidative stress by avoiding GO accumulation in mitochondrial genomes of neurons and/or nuclear genomes of microglia.

Dr. Young-Sam Lee, Well-Aging Research Center, Daegu Gyeongbuk Institute of Science and Technology (DGIST), aimed at reversal of senescence to rejuvenate organisms or alleviating age-related pathology. Dr. Lee first presented a hypothesis that the altered physiology in aged cells can be restored by modulating protein kinase activity, and the compounds that reverse senescence can be determined by performing high-throughput screening. Ataxia telangiectasia mutated (ATM) inhibitor and rho-associated, coiled-coil-containing protein kinase (ROCK) inhibitors were identified as effective agents for this process. Attenuation of the age-related kinase activation by screened inhibitors of ATM and ROCK reduced phosphorylation of the substrate protein, which induced functional recovery of lysosomes or mitochondria, where the substrate is located.

Dr. Tae Jun Park, Department of Biochemistry, Ajou University School of Medicine, investigated the role of senescent cells in skin aging-related pigmentation. The cutaneous aging process is influenced by an important extrinsic factor which modifies the pigmentary system: Senescent fibroblasts accumulated at the sites of age-related pigmentation in vivo. Phenotype switching of the cells resulted in the repression of stromal-derived factor 1 (SDF1) under promoter methylation, and the SDF1 deficiency appeared to be a potent stimulus for the melanogenic process that contributes to the uneven pigmentation. Aged pigmented skin contains an increasing proportion of senescent fibroblasts, providing a new therapeutic paradigm, possibly a stroma-targeting therapy for pigmentary disorders.

Plenary session III chaired by Drs. Yoshimitsu Akiyama and Kyung A Cho, was four lectures related to aldehyde dehyrogenase-2 and alcohol consumption, cyclin-dependent kinases–cyclin complex, target of rapamycin complex 1, and tankyrase inhibitors for colorectal cancer.

Dr. Keitaro Matsuo, Division of Cancer Epidemiology and Prevention, Aichi Cancer Centre Research Institute, presented epidemiological studies on gene–environment interaction between aldehyde dehyrogenase-2 (ALDH2) polymorphisms and alcohol consumption, since the International Agency for Research on Cancer has provided convincing evidence for alcohol increasing the risk of cancer in various human organs. The single nucleotide polymorphism (SNP) in ALDH2, (Glu504Lys) has strong phenotypic changes in acetaldehyde metabolism, and the minor Lys-allele shows reduced oxidation capacity leading to reduced tolerability to acetaldehyde. The dataset from Dr. Matsuo's epidemiological study, and the Hospital-based Epidemiologic Research Program at Aichi Cancer Center (HERPACC) established in 1988, revealed their findings on esophageal, head and neck, gastric and bladder cancers and compared them with breast and colorectal cancers.

Dr. Kyungtae Kim, Research Institution, National Cancer Center in Korea, spoke about a central thema: that oscillation of cyclin-dependent kinases (CDKs)—cyclin complex gears cells to grow and divide. It is well established that many of the cyclins and CDK_S have been identified as causative factors for tumorigenesis. Although numerous evidence has been reported in relation to carcinogenesis, molecular mechanisms of the highest active complex CDK1-cyclin B, and the physiological negative regulators for the over-active CDK1-cyclin B, are still remain to be elucidated. Dr. Kim discussed the discovery of the potential negative regulator of the CDK1-cyclin B and its operation in carcinogenesis.

Dr. Jung Min Han, College of Pharmacy, Yonsei University, studied the amino acid-sensing mechanism to develop a new strategy for treatment of human diseases. Leucyl-tRNA synthetase (LRS) forms specific interaction with the recombination activating gene D (RagD), and then initiates the Rag GTPase cycle through the GTP hydrolysis of RagD. Sestrin2, which is the other leucine sensor, acts as an "OFF" switch of leucine-dependent Rag-mTORC1 (mechanistic target of rapamycin complex 1) signaling by controlling GTP hydrolysis of RagB. Dr. Han's group developed a new mTORC1 inhibitor that specifically blocks the leucine-sensing function of LRS by interfering in its interaction with RagD, without affecting its catalytic activity. This new mTORC1 inhibitor effectively suppressed the activity of cancer-associated *MTOR* mutants, as well as the growth of rapamycin- or mTOR kinase inhibitor-resistant cancer cells.

Dr. Tetsuo Mashima, Division of Molecular Biotherapy, Cancer Chemotherapy Center, Japanese Foundation for Cancer Research, identified tankyrase inhibitors as cancer stem cell-targeting agents. Tankyrase inhibitors showed stronger an antiproliferative effect on colorectal cancer stem-like CD44(+) cells than on CD44(–) cells, and decreased CD44(+) cell population. Mechanistically, tankyrase positively regulates Wnt/β-catenin signaling pathways by destabilizing Axin (an inhibitor of the Wnt signaling pathway), a negative regulator of β-catenin in colorectal cancer cells, and tankylase inhibitors similarly downregulate Wnt/β-catenin signaling in CD44(+) and CD44(–) cells. It is important to note that tankylase inhibitors suppressed the expression of a subset of stemness-related genes in CD44(+) cells.

Plenary session IV chaired by Drs. Keitaro Matsuo & Tae Jun Park, was four lectures about physical adsorption of (–)-epigallocatechin gallate (EGCG) to cell membrane, profiling human B cell receptor repertoires, inhibition of immune evasion of cancer cells with EGCG, and hereditary gastrointestinal cancer syndrome in Japan.

Dr. Hiroshi Yoshikawa, Department of Chemistry, Saitama University, is interested in the mechanism of green tea catechins interacting with cell membrane. (–)-Epigallocatechin gallate (EGCG) and (–)-epicatechin gallate (ECG) with a galloyl moiety showed stronger interaction with lipid membranes than (–)-epicatechin (EC) and (–)-epigallocatechin (EGC) without a galloyl moiety. The catechin–membrane interaction is dominated by the electrostatic and cation-π interactions between galloyl catechins and quaternary amine groups. The incubation of cell-sized vesicles with 1 μM galloyl catechins significantly increased the bending stiffness of membrane by a factor of more than 60, while those without galloyl moiety showed no detectable influence. Thus, this insight contributes to understanding of the physical and generic functions of green tea catechins in human cancer prevention.

Dr. Junho Chung, Seoul National University, College of Medicine, presented recent results obtained by next generation sequencing, which allow a massive increase in capacity to sequence genomes. Dr. Chung's group successfully constructed a database of human B cell receptor (BCR) repertoire from convalescent patients who had recovered from severe fever with thrombocytopenia (SFTS) and middle east respiratory syndrome (MERS). After this, the algorithms for analyzing the diversity, enrichment pattern, and accumulation of somatic hypermutation in BCR repertoire were developed. By in silico analysis, Dr. Chung's group selected clones of interest and prepared recombinant antibodies using a mammalian transient expression system. Currently they are investigating the clinical value of BCR repertoire-profiling in autoimmune disease patients.

Dr. Masami Suganuma, Department of Strategic-research, Graduate School of Science and Engineering, Saitama University, presented two subjects. First, AXL receptor tyrosine kinase (AXL) of TAM (Tyro3, AXL and Mer) family is a key stimulator of cell softening and motility. Knockdown of AXL with AXL-targeted siRNA (siAXL) increased cell stiffness, resulting in inhibition of motility in human lung cancer cells. Treatment with siAXL and EGCG showed different stiffening patterns, suggesting that the mechanism of siAXL is slightly different from that of EGCG. Dr. Suganuma's second report was about anti-cancer immunity of green tea catechins. EGCG inhibited the expression of programmed cell death-ligand 1 (PD-L1) on lung cancer cells induced by interferon-γ. Oral administration of green tea extract in drinking water reduced the PD-L1 levels in mouse lung tumors induced by a tobacco-specific nitrosamine, 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK), and also inhibited tumorigenesis. EGCG has the potential to stimulate anti-cancer immunity for cancer cells.

Dr. Hidetaka Eguchi, Diagnostics and Therapeutics of Intractable Diseases, Juntendo University, Graduate School of Medicine, reported on hereditary gastrointestinal cancer syndromes (HGICS), such as Lynch syndrome (LS) and familial adenomatous polyposis. Dr. Eguchi's group began a project on identification of the causative mutations of the HGICS in 2013 using a multi-panel sequencing technique, followed by whole-exome sequencing. They identified 28 LS patients with mutations of class 4/5 pathogenicity: 11 *MLH1*, 13 *MSH2*, 3 *MSH6*, and I *EPCAM*+*MSH2* whole deletion patients. The somatic mutation profile of the patient's cancer showed the tendency of the C>T transition at the CpG site compared with the non-CpG site, in accordance with the defects of the methyl-CpG-binding domain protein 4 (MBD4).

Luncheon seminar featuring two presentations about a comprehensive approach for the eradication of adult T-cell leukemia–lymphoma (ATL) in Japan, and also a novel therapeutic strategy for ATL by targeting aberrant DNA methylation. This was chaired by Dr. Masami Suganuma. Due to the tight schedule of the oral presentation, the organizers kindly arranged to give their lectures during lunch time.

Dr. Eisaburo Sueoka, Department of Clinical Laboratory Medicine, Faculty of Medicine, Saga University, reviewed his main subject, ATL, which is an aggressive hematological malignancy caused by human T-lymphotropic virus type I (HTLV-1). The south-western part of Japan including Saga Prefecture is one of the rare HTLV-1 endemic areas. After HTLV-1 infection, T lymphocytes acquire malignant phenotypes through multi-step carcinogenesis. Dr. Sueoka's group found similarly and differentially hypermethylated positions specific to HTLV-1-infected T cells by comprehensive DNA methylation analysis. The accumulation of DNA methylation at these sites correlated strongly with ATL development and progression.

Dr. Tatsuro Watanabe, Department of Drug Discovery and Biomedical Sciences, Faculty of Medicine, Saga University, talked about DNA demethylating agents, that inhibit cell growth and induce apoptosis accompanied by decreased DNA methylation at the long interspersed nuclear element-1(LINE-1) repeat region in HTLV-1-infected cell lines, both in vitro and in xenograft mouse model. Thus, DNA demethylation therapy will be a new, and probably effective, approach to prevent disease development and progression in ATL.

Poster presentations were an important part of this Symposium for young students and research fellows, chaired by Dr. Tatsuro Watanabe. 21 posters were displayed and poster presenters gave short oral presentations and answered questions in English. The subjects included cellular senescence, mechanisms of carcinogenesis, targeting cancer stem cells with green tea catechins, liquid biopsy for clinical application and a new strategy of antibody therapy using bispecific antibodies. It was a fruitful opportunity for young students to talk personally with senior Professors and learn how to write better manuscripts. We accepted this system from the beginning in 1996, and realized that short conversations between senior Professors and young students could produce a lot of new ideas. That is one royal road of education.

Oral presentation I with five lectures, chaired by Drs. Yohei Shirakami and Hong Seok Kim.

Dr. Yoshimitsu Akiyama, Department of Molecular Oncology, Tokyo Medical and Dental University, reported on changes in histone modification by SET-related histone–lysine *N*-methyltransferase (SETDB2) overexpression in gastric cancer. The expression of SETD7 and SETDB2 were frequently reduced or overexpressed in primary gastric cancers (GCs). SETDB2 expression was suppressed when several epigenetic drugs were used to treat SETDB2-positive GC cells. The treatment of GC cells with epigenetic drugs reduced cell growth through up-regulation of p21 and p27. The SETDB2 overexpression is related to increased histone H3K9me3, and it contributed to GC progression. The molecular mechanism of how the drugs affect SETDB2 expression is now being studied.

Dr. Eunhee Kim, Department of Biological Sciences, Chungnam National University, has been on her sabbatical at the Medical Institute of Bioregulation, Kyushu University, Japan, for six months, in the lab of Prof. Yusaku Nakabeppu. Dr. Kim's group performed the functional study of a death protein, Fas-associated factor 1 (FAF1), regarding its disease relevance, such as Parkinson's disease (PD), and identified FAF1 as a substrate of Parkin, since FAF1 promotes α-synuclein accumulation, demonstrating the presence of Parkin-FAF1-α-synuclein-signaling pathway. FAF1 increased dopaminergic neuronal necrosis as well as apoptosis upon oxidative stress. Dr. Kim's group screened FAF1 inhibitory compounds and developed a compound targeting FAF1 (CTF), a first-in-class molecule whose phase I clinical study has recently been completed.

Dr. Atsumasa Komori, Clinical Research Center, National Hospital Organization Nagasaki Medical Center, reported on the molecular dissection of the human hepatic fibrogenesis based on liver transcriptome. Utilizing in-house biorepository resources and public domain data base, Dr. Komori's group confirmed transcriptome-based universal core gene expression in human hepatic fibrogenesis, which had also been detected among hepatitis C virus (HCV)-, hepatitis B virus (HBV)-, and non-alcoholic fatty liver disease (NAFLD)-associated advanced fibrosis. This reverse translational study revealed the role of cholangiocytes as a possible pacemaker in the fibrosing inflammatory milieu, associated with the liver-specific biology of fibrosis.

Dr. Alexandre Loukanov, Graduate School of Science and Engineering, Saitama University, discussed the design, synthesis and principle of operation for an artificial anticancer nanomachine, consisting of two main components: light-powered nanoconverter and biorecognition element. The specificity of cancer cells was achieved by conjugation of the nanoconverter to oligonucleotide aptamer, which reacts with membrane DNA binding proteins of cancer cells. Future studies with nanomachine may find three functions: specificity of cancer cells can be increased by screening of specific aptamers, the nanoconverter ability to generate reactive oxygen species (ROS) may be enhanced by introducing metal chelate complexes, and toxicity to healthy cells can be decreased with endonuclease inhibitors.

Dr. Somdet Srichairatanakool, Department of Biochemistry, Faculty of Medicine, Chiang Mai University, Thailand, participated in this Symposium, for the first time, to establish scientific collaboration between Korea and Thailand. Guava is a tropical fruit, and guava seeds are by-products from the processing of fruit-based products in the beverage and juice industry. Dr. Somdet's group found that guava seed oil (GSO) contained mainly linoleic acid (ω6 fatty acid) and vitamin E derivatives, such as α-tocopherols and β-tocotrienols. GSO exhibited no toxicity in human hepatoma cell line (Hep G2) cells, or in peripheral blood mononuclear cells. In addition, GSO was not toxic to mouse or rat models. Therefore, GSO is as a consumable natural product and functional food with powerful antioxidant capacity.

Oral presentation II with five lectures, chaired by Drs. Hisataka Eguchi and Eunhee Kim.

Dr. Naoko Aragane, Division of Hematology, Respiratory Medicine and Oncology, Department of Internal Medicine, Saga University, reported on circulating tumor DNA and tumor progression. Dr. Aragane's group conducted a prospective multicenter observational study to determine whether a mutation of epidermal growth factor receptor gene (*EGFR*) T790M, would be detected at acquired resistance to

1st generation EGFR tyrosine kinase inhibitors (EGFR–TKI) with circulating tumor DNA (ctDNA). The frequency of T790M detection with ctDNA increased in tumor progression, and T790M was frequently detected with ctDNA isolated from non-small cell lung cancer patients with distant metastasis but not with local progression.

Dr. Yun-Il Lee, Well-Aging Research Center, Companion Diagnostics and Medical Technology Research Group, Daegu Gyeongbuk Institute of Science and Technology (DGIST), talked about drug repositioning for Parkinson's disease treatment. Overexpression of parkin provides protection against cellular stress and prevents dopamine cell loss in several animal models of Parkinson's disease. A high-throughput screen using a luciferase construct harboring the promoter identified hydrocortisone and liquiritigenin, respectively, as parkin and IDUNA (E3 ubiquitin ligase) inducers. They found that hydrocortisone stimulated parkin expression via CREB pathway, and liquiritigenin mediated IDUNA induction by estrogen receptor activation. The results indicate a potential therapeutic and/or preventive strategy for Parkinson's disease.

Dr. Tomotaka Ugai, Division of Cancer Epidemiology and Prevention, Aichi Cancer Center Research Institute, reported on the association of body mass index (BMI), smoking and alcohol with multiple myeloma mortality in Asians. During an average 12.7 years of follow-up, Dr. Ugai's group identified a total of 428 deaths from multiple myeloma (MM) for both sexes. A statistically significant increase in the risk of MM mortality was observed for the highest category of BMI at baseline (≥ 27.6 kg/m^2), compared with 22.6–25.0 kg/m^2 (HR = 1.42, 95% CI 1.02–1.98). However, this dose-dependent association was observed only among women. The results indicated that excess body mass increases the risk of MM mortality among Asian population, especially Asian women.

Dr. So-Yoon Won, Department of Biochemistry, College of Medicine, Chungbuk National University, reported that p21-activated kinase 4 (PAK4) is a key survival factor for Parkinson's disease (PD) neurons. PAK4 activity markedly decreased in postmortem brain tissue from PD patients and in rodent models of PD, and PAK4 immunoreactivity was found in rat and human dopaminergic neurons in brain tissue, but was not found in microglia or astrocytes. Expression of constitutively active PAK4S445N/S474E (caPAK4) protected dopaminergic neurons in both the 6-hydroxydopamine and α-synuclein in rat models of PD, and also preserved motor functions. The PAK4-CRTC1 (cAMP response element binding protein-regulated transcription co-activator 1) S215—signaling pathway may, therefore, be a useful therapeutic target in PD.

Dr. Hong Seok Kim, Department of Molecular Medicine, College of Medicine, Inha University, reported that MAPK phosphatase 1 (MKP-1) is a redox-regulated master controller of monocyte function and macrophage phenotype in atherosclerosis. The mitogen-activated protein kinase (MAPK) pathway has a critical role in the regulation of macrophages function and plasticity, and MKP-1 has been found to be the main counter regulator of MAPK signaling in monocytes and macrophages. An MKP-1 deficiency in monocytes and macrophages promotes and accelerates the formation of atherosclerotic lesions by hyper-sensitizing monocytes to chemokine-induced recruitment, predisposing macrophages to M1 polarization. On the other hand, overexpression of MKP-1 protects macrophages against metabolic stress-induced dysfunction, indicating that MKP1 is a master regulator of macrophage phenotype and function.

Special lectures—for students and young scientists

In 1984, three young biochemists; Dr. Sang Chul Park, Dr. In Kyoung Lim and Dr. Hirota Fujiki, met for the first time, at the International Cancer Symposium of the Korea Cancer Center Hospital and Research Institute in Seoul: They then cherished their scientific friendships. When they began directing their own research departments, they organized the first joint symposium in 1996 with the support of the Japan–Korea Basic Scientific Cooperation Program. Over 20 years, these three scientists participated in fourteen symposia with their young colleagues and students, who have been promoted to higher positions. In addition, numerous active scientists outside of these institutions found great interest in the symposia. This type of symposia creates a familiar environment including a Confucian salutation ("Rei 礼" in Japanese), mutual respect, learning and teaching among the participants, which increases scientific motivation. Todays organizer invited eminent Profs. Park and Lim to give special lectures to young scientists.

Prof. Sang Chul Park, Chair Prof. at Chonnam National University, gave a lecture to young scientists on "New Horizon of Life requests Changes." He introduced recent astonishing achievements in science and technology of BT and IT, which could foster revolutionary changes in human lives and extent of lifespan in the near future. Prof. Park illustrated the new trend of active centenarians who still work and even compete in athletics. As Prof. Park said, "Live long and prosper" is becoming a truth for human kind. Therefore, it is urgent and essential that everyone should be prepared for this new era. And Prof. Park strongly emphasized that scientists should make mission: Do our best for the coming unprecedented society with an attitude of "Not being afraid of change, but being afraid of no-change (不怕變 怕不變)." Finally, Prof. Park invited all the members to Gwangju, the City of Love and Memory, his home town, in 2019 for our next meeting.

Prof. In Kyoung Lim talked about the "Desirable attitude to be a sound scientist" to encourage graduate students working on their theses. Prof. Lim's lecture focused on: Observe with keen eyes, Communicate with colleagues as often as you can, Do lab work during the day and read articles at night, Have a wide study scope, and Believe in God. Prof. Lim said that the first attitude to being a good scientist is to use keen eyes to observe biological changes. The 2nd attitude is listening to senior colleagues' advice with open heart and following their experience before doing your own project. The 3rd attitude is to work with your own hands and head in a day time and read articles at night. The 4th attitude is to attend seminars and lecture on diverse subjects in your institute, do not narrow down your study subject before deciding your own research field. This attitude can expand your knowledge as well as the way of scientific thinking. The 5th attitude is to rely on the Creator in Universe and try to keep a Holy Spirit.

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Compliance with ethical standards

Conflict of interest We declare no conflicts of interest.

Ethical approval This article does not include any studies of humans or animals performed by any of the authors.