

Meeting Report

Japan-Korea Joint Seminar: Asian Aging Core for Longevity 2008 in Nagasaki

-Toward the establishment of an Asian Aging Research and Education Center-

September 4th to 6th, 2008 at Huis Ten Bosch, Nagasaki, Japan

Isao Shimokawa^{1*}, Sang Chul Park², Nozomu Mori³, Eun Seong Hwang⁴

¹⁾ Department of Investigative Pathology, Unit of Basic Medical Science, Graduate School of Biomedical Sciences, Nagasaki University

²⁾ Department of Biochemistry and Molecular Biology, Aging and Apoptosis Research Center, Seoul National University College of Medicine

³⁾ Department of Anatomy and Neurobiology, Unit of Basic Medical Science, Graduate School of Biomedical Sciences, Nagasaki University

⁴⁾ Department of Life Science, University of Seoul

*Corresponding author

Isao Shimokawa,

Department of Investigative Pathology,

Unit of Basic Medical Science,

Graduate School of Biomedical Sciences,

Nagasaki University

12-4 Sakamoto 1-chome, Nagasaki City

852-8523 Japan

Phone: +81-95-819-7051 Fax: +81-95-819-7052

e-mail: shimo@nagasaki-u.ac.jp

The Japan-Korea Joint Seminar, an academic activity of Asian Aging Core for Longevity (AACL), was held 4 to 6 September 2008 in Nagasaki, Japan. The three days of the seminar included great scientific sessions, special lectures, and poster presentations from students and young investigators' showcasing 20 abstracts. As well, there were multiple networking opportunities. The over 50 attendees, mostly from Japan and Korea, were involved in lively discussions of topics associated with aging research (Figure 1). Views were also exchanged on strategies to expand the activities of AACL to other Asian countries.

1. Meeting report

The main purpose of the seminar was to facilitate lectures by leading biomedical gerontology research scientists from Japan and Korea, and to enable students, young investigators, and clinicians to gain knowledge and to discuss various topics. Some topics from the seminar are highlighted below; the final program and abstracts can be downloaded from <http://www.med.nagasaki-u.ac.jp/pathlgy1/AACL2008/index.html>.

On the afternoon of September 4th, the session entitled "Molecular and genetic basis of brain aging and neurodegenerative diseases" was opened by *Dr. Nozomu Mori* (Nagasaki University, Japan) who overviewed the roles of the NAD-dependent histone deacetylases (HDAC) family in the regulation of longevity and brain aging. *Dr. Mori* focused on the potential involvements in deacetylation of cytoplasmic tubulin by HDAC6 (HDAC Class II) and SIRT2 (HDAC Class III) in neuronal aging. *Dr. Inhee Mook-Jung* (Seoul National University (SNU), Korea) demonstrated a significant role

for the disruption of intracellular calcium homeostasis and the subsequent expression of receptors for advanced glycation end products (RAGE) and β -site amyloid precursor protein (APP)-cleaving enzyme 1 (BACE1) in the pathogenesis of Alzheimer's disease (AD). A new immunotherapy for AD was introduced by *Dr. Takeshi Tabira* (National Institute of Longevity Science, Japan). Active immunization with amyloid β was seen to have serious side effects such as subacute meningoencephalitis. *Dr. Tabira* reported a tissue amyloid plaque immuno-reactive antibody that potentially slows the decline of cognitive functions by reducing the amyloid burden without eliciting inflammation or hemorrhage in the brain.

The pathogenesis of prion diseases was also highlighted. Accumulation of mutant prion proteins (PrP) produced by point mutation of the gene or by post-translational modification could be a cause of prion diseases. Normal and soluble PrP play a role in autophagy. *Dr. Yong-Sun Kim* (Hallym University, Korea) introduced *Drosophila* models of Gerstmann-Straussler-Scheinker (GSS) syndrome, a prion disease. Flies genetically engineered to express mutant mouse PrP lost motor control and showed deposition of insoluble PrP. *Dr. Noriyuki Nishida* (Nagasaki University) challenged the central hypothesis of the pathogenesis of prion diseases. He suggested that insoluble PrP are not responsible for the infectivity of prion diseases. He presented a drug-discovery strategy for therapy of conformational diseases. The relevance of citrullinated proteins and calcium-dependent peptidylarginine deiminases to the pathogenesis and diagnosis of neurodegenerative diseases were discussed by *Dr. Eun-Kyoung Choi* (Hallym University). *Dr. Shinji Fushiki* (Kyoto Prefectural University) demonstrated the effects on brain development and disorders in later life of environmental exposure to low-doses of chemicals early in the developmental process.

In the session entitled “Genome instability and cellular senescence”, held on the morning of September 5th, *Dr. Jae-Yong Lee* (Hallym University) suggested that suppression of FoxO3a, one of the mammalian orthologs of DAF-16 in nematodes, by IGF-1 signaling and subsequent reduction of anti-oxidative and DNA repair mechanisms, causes cellular senescence. In parallel with this finding, *Dr. Masatoshi Suzuki* (Nagasaki University) provided evidence that the IGF-1 signaling pathway was activated in senescent cells. *Dr. In Kwon Chung* (Yonsei University, Korea) emphasized a role for RLIM, a RING H2 zinc finger protein with intrinsic ubiquitin ligase activity, in the regulation of a telomeric protein TRF1 that inhibits access of telomerase at telomere termini. RLIM is involved in the degradation of TRF1 and promotes maintenance of telomere. His colleague, *Mi Kyung Kim*, presented data about a TRF1-interacting protein NUB1, which stabilizes TRF1 protein and promotes telomere shortening in cultured cells. *Dr. Eun Seong Hwang* (University of Seoul, Korea) demonstrated that nicotinamide increased replicative lifespan in cultured human cells, probably through reduced mitochondrial respiration and ROS production. In this setting, SIRT1 and GAPDH seemed to have roles. *Dr. Naoaki Ishii* (Tokai University, Japan) presented a great report showing that a mutation of the gene encoding subunit of complex II in the electron transport chain (SDHC) caused overproduction of superoxide, leading to excessive apoptosis, premature aging, and carcinogenesis in nematodes and fibroblasts. The work also extended to conditional transgenic mice.

In the afternoon of the second day, two sessions on epidemiological and socio-medical aspects of human aging focused on the possibility of the application of experimental outcomes for promotion of a healthier lifespan in human and for establishing sound societies. *Dr. Sang Chul Park* (SNU) proposed a novel approach,

designated as “Confident Aging”, to deal with medical and socio-cultural needs of elderly people. He emphasized the importance of medical and social systems that provide total support for elderly people to live long lives with dignity. *Dr. Nobuyoshi Hirose* (Keio University, Japan) indicated a decline in the speed of the mortality rate in an over-105 year-old population, and suggested the utilization of the population, called semisupercentenarians, for analysis of properties of human longevity as well as longevity genes. *Dr. Toshiro Takezaki* (Kagoshima University, Japan) introduced the field work conducted by his study team in islands in the south-western part of Kagoshima Prefecture, an area in which the residents show great longevity. *Dr. Kozo Matsubayashi* (Kyoto University, Japan) discussed comprehensive community-based geriatric assessment and intervention for elderly people, based on his activities in Southeast Asian countries. *Dr. Youngtae Cho* (SNU) presented unique data suggesting that people in Korea affected with leprosy had a longer life expectancy, even if those people had been socioeconomically disadvantaged. *Dr. Takahiro Maeda* and *Isao Shimokawa* (Nagasaki University) introduced the island areas of Nagasaki Prefecture where the elderly population is increasing at a higher speed than in mainland urban areas. They mentioned the potential of these island areas and the southwestern parts of Korea, which also have isolated island and peninsular areas, as places suitable for joint international studies on molecular epidemiology and intervention in the aging processes in human.

In the morning of September 6th, anti-aging intervention and related issues were featured. In the first session entitled “Biomarker of aging and animal models for longevity and progeria”, *Dr. Masanori Hosokawa* (Aichi Human Service Center, Japan) overviewed animal models and the concept for aging research. He presented the traits of

a unique mouse model of accelerated senescence, the SAM strain of mice. He also showed data indicating that mitochondrial dysfunction partly contributed to premature aging in SAM mice. *Dr. Cheol Koo Lee* (Korea University, Korea) presented data of transcriptome of calorie restriction (CR) in yeast, suggesting increased mitochondrial function by CR. *Dr. Manabu Tsuda* (Tokyo Metropolitan University, Japan) presented data about premature death in a thioredoxin (Trx)-2 mutant line of *Drosophila*. The Trx-2 mutant was hypersensitive to oxidative stress, while Trx-2-overexpressing flies resisted oxidative stress. He suggested the importance of Trx for protection against oxidative stress and in the regulation of lifespan. *Dr. Takahiro Shimizu* (Tokyo Metropolitan Institute of Gerontology (TMIG), Japan) presented heart muscle-specific Mn-SOD deficient mice that had excess formation of superoxide in mitochondria and developed cardiac failure; by contrast, SOD mimesis prevented cardiac dysfunction.

In the session that followed, *Dr. Naoki Makino* (Kyushu University, Japan) suggested that improved insulin sensitivity by pioglitazone in OLETF rats, an obese diabetic model, restored cardiac telomerase activity and induced cardiac remodeling. Finally, *Dr. Naoki Maruyama* (TMIG) introduced his distinct work about the discovery of SMP 30, a biomarker of senescence, and subsequent functional analyses that finally revealed the gluconolactonase activity of SMP30, the loss of which leads to a deficiency of vitamin C, an antioxidative agent. He also gave a warning about the recent common use of supplements, some lacking scientific evidence, by introducing a Chinese saying “Too much is too short” (or “Too much is half”).

In addition to the above described sessions, a special lecture was given by *Dr. Kyu-Won Kim* (SNU) on developmental analysis of the blood brain barrier. This inspired an interest in the listeners about research into the aging brain from the viewpoint of the

dysfunction of the blood brain barrier. Indeed, a recent hypothesis of the pathogenesis of AD is closely related to this topic. Another special lecture, this one by *Dr. Byoung Pal Yu* (University of Texas Health Science Center in San Antonio, USA), suggested future directions for Asian aging research and education. As well, by reviewing the historical circumstances of aging research groups during 1970 – 1980 in the United States, the importance of a center or institute of networked research groups was highlighted.

In summary, most Korean aging research groups specialize in molecular biology of neurodegenerative diseases and cellular senescence. By contrast, Japanese groups researching biomedical gerontology tend to focus on the basis of aging in mammals including human. Thus, the two countries' research groups complement each other.

2. Asian Aging Core for Longevity (AACL)

Japan and Korea are facing medical and social problems caused by an increase in their elderly populations. Other Asian countries including China and India, both with huge populations, are also predicted to undergo rapid demographic changes. As life scientists, we realize the necessity and the significance of international academic activities to promote research and the education of students and young scientists well-grounded in biomedical gerontology.

Since 2001, the Japan Society of Biomedical Gerontology and the Korean Society of Gerontology have been conducting exchange programs for young investigators to present their papers at annual meetings. The exchange program has provided opportunities for researchers in both countries to enjoy friendly relations. However, we

have not yet established systemic educational programs related to basic as well as translational aging research.

AACL, as proposed by *Dr. Mori* and *Shimokawa* at Nagasaki University (Nagasaki, Japan) in 2006, is an international collaborative project that promotes research and education of biomedical gerontology in Asia. At the first meeting of the AAACL, held in Ioujima, Nagasaki in 2006, the core members from Japan, Korea, and China agreed to promote the academic activity of AAACL, centered on Nagasaki University Graduate School of Biomedical Sciences (Figure 2). Since then, Nagasaki University has concluded an agreement for academic cooperation with Seoul National University, Hallym University, and Pusan National University in Korea. Discussion is now underway toward an agreement with the Capital University of Medical Sciences (Beijing, China).

The aims of AAACL are as follows; 1) promotion of aging research among core and cooperating institutions, 2) education of students and young researchers, 3) establishment of a regional center for biomedical gerontology and geriatrics at Nagasaki University. The activities to accomplish these aims include collaborative research, exchange programs for researchers and students, seminars and workshops, a credit exchange system for students, and the publishing of textbooks or handbooks on aging. To continue these activities, we have been seeking grants from the Japan Society for the Promotion of Sciences and the Korea Science & Engineering Foundation.

Several international research projects are currently under way. An example is “Molecular analysis of aging-dependent sarcopenia”, a collaborative work between research groups from Nagasaki University and Seoul National University. We have also agreed to hold the 3rd international seminar of AAACL in 2010 in Seoul. Our

international and interdisciplinary network contributes to the promotion of young gerontologists and geriatricians who will work towards achieving a healthier lifespan for people domiciled in Asian countries.

Acknowledgments

The seminar was supported by 1) the Nagasaki University: president's discretionary fund for promotion of internationally academic activity, 2) Nagasaki University, the Global COE program: the Global Strategic Center for Radiation Health Risk Control, and 3) the Shoin Human Science Foundation.

Figure Legends

Figure 1. Participants at the Japan-Korea Joint Seminar: AACL 2008 in Nagasaki (September 4th - 6th, Huis Ten Bosch, Nagasaki, Japan)

Figure 2. Main research groups in Asian Aging Core for Longevity (AACL). The official agreement on academic cooperation including the activities of AACL was concluded between Nagasaki University and Seoul National University (SNU), Hallym University, and Pusan National University (PNU). Other research groups have also been involved in the activities of AACL: UOS; University of Seoul, CUMS; Capital University of Medical Science, Beijing, TMIG; Tokyo Metropolitan Institute of Gerontology, and NILS; the National Institute of Longevity Science. Aichi, Aichi Human Service Center.

Figure 1.



Figure 2.

