IARO 2024

THE 2ND INTERNATIONAL SYMPOSIUM

June 19, 2024

**VENUE: THE UNIVERSITY OF TOKYO,
ITO INTERNATIONAL RESEARCH CENTER**

https://www.iaro.link/

The 2nd International Symposium of International Anti-aging and Regenerative Medicine Organization (IARO)

June 19, 2024 (Wed)

Ito International Research Center B2F, The University of Tokyo

Welcome Message

Dear Participants,

Welcome to the "IARO 2024 The 2nd International Symposium." As the Chairman of the International Anti-aging and Regenerative Medicine Organization (IARO), it is my great honor to host this significant event. Today, we bring together distinguished researchers at the forefront of regenerative medicine and anti-aging therapy to discuss the latest advancements and innovative technologies.

Our goal is to develop new treatments that extend healthy lifespans and improve the quality of life. In today's program, experts from various fields will share valuable insights and explore new possibilities for the future of medicine.

I hope this symposium proves to be a meaningful and rewarding experience for all of you.

Sincerely,
Dr. Tatsuya Yamasoba
Chairman of IARO / Director of Tokyo Teishin Hospital /
Professor Emeritus of the University of Tokyo

PROGRAM

11:00 **Opening Ceremony and Greetings**

Dr Tatsuya Yamasoba
Chairman of IARO / Director of Tokyo Teishin Hospital / Professor Emeritus of the University of Tokyo

Dr Somarch Wongkhomthong
Former CEO of Bangkok Dusit Medical Services (BDMS)

Seminar, 25 minutes including Q&A

11:20-11:45 **Aquatic Animal Stem Cells Hold the Future of Regenerative Medicine**

Chee-Wee LEE, Ph.D.

11:45-12:10 **Advances in Exosomes, Senolytics, Heart and Kidney Treatments**

Kampon Sriwatanakul, M.D., Ph.D.

12:10-12:35 **Approach to the Next-Generation Cell Processing Facility That is Energy-Saving, Labor-Saving, and Highly Productive, Achieved by Non-Woven Fabric Automatic Culture System**

Shunmei Chiba, M.D., Ph.D.

12:35-13:35 Lunch

13:35-14:00 **Decidualization and Angio-myogenesis Potentials of Placental Choriodecidual Membrane-Derived MSCs**

Thai-Yen Ling, Ph.D.

Stem Cell and Its Derivatives in Aging Disease Treatment

Rita Yen-Hua Huang, Ph.D.

14:00-14:25 **Uncovering the Relationship Between Aging and Cancer Passenger Mutations Through Liquid Biopsy**

Tomohiro Umezu, Ph.D.

14:25-14:50 **The New IARO Laboratory at Mahidol University**

Pongrama Ramasoota, DVM, Ph.D.

～Short break 15min～

15:05-15:30 **The Future of Medicine iPSC Technology Will Usher In**

Koji Tanabe, Ph.D.

15:30-15:55 **Immunotherapy for Cancer Using iNKT Cell and Next Generation NKT Therapy With Drug Delivery System**

Taehun Hong, Ph.D.

15:55-16:20 **Problems of Speech and Swallowing in Human Beings, the Additional Solutions with Regeneration, Instead of Just Anti-Aging**

Koichi Tsunoda, M.D., Ph.D.

Aging of the Olfactory System: Pathophysiology and Treatment Strategies

Kenji Kondo, M.D., Ph.D.

16:20-16:45 **Ultra-Low Dose Computed Tomography Combined with Artificial Intelligence for Enhanced Health Screening: A Nexus of Evidence, Innovation and Integrative Medicine**

Richard H. Kaszynski, M.D., Ph.D.

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Aquatic Animal Stem Cells Hold the Future of Regenerative Medicine

Chee-Wee LEE, Ph.D.

Principal Scientist & Technology Advisor- Temasek Polytechnic, Singapore
Co-Director- Centre for Aquaculture, Innovation & Education, Nanyang Technological University, Singapore
Associate Professor- Department of Physiology, Yong Loo Lin School of Medicine, National University of Singapore, Singapore
Associate Professor- School of Chemistry, Chemical Engineering & Biotechnology, College of Engineering, Nanyang Technological University, Singapore

Aquatic organisms, sculpted by millions of years of evolutionary pressure, possess a remarkable capacity for regeneration, often surpassing that of their terrestrial counterparts. Their unique adaptations, including scarless healing and diverse stem cell populations, offer a treasure trove of potential for regenerative medicine. This presentation explores two groundbreaking applications of marine-derived biomaterials that leverage this innate regenerative prowess.

Firstly, we delve into the use of coral-derived biomaterials as bone graft substitutes. Their porous structure, similar in composition to human bone, provides an ideal scaffold for bone tissue integration and growth. Moreover, their biocompatibility minimizes adverse immune responses, a common challenge with traditional bone grafts. This approach promises to enhance bone regeneration, reduce complications, and provide a sustainable source of biomaterial for orthopaedic procedures.

Secondly, we examine the burgeoning field of aquatic animal stem cell research and its implications for tissue engineering. Derived from sources as diverse as fish skin, marine sponges, sea cucumbers, and axolotls, these stem cells possess remarkable plasticity, capable of differentiating into various cell types. Their rapid proliferation and inherent resilience to environmental stressors make them ideal candidates for regenerative therapies with lower production costs. Results with tilapia spleen derived mesenchymal cells will be presented. By combining these potent stem cells with coral scaffolds, researchers are developing innovative solutions for complex tissue reconstruction, including advanced skin grafts, with the potential to revolutionize wound care and burn treatment.

Beyond these specific applications, aquatic-derived biomaterials offer several advantages over traditional mammalian sources. Their enhanced biosecurity reduces the risk of disease transmission, while their ethical sourcing circumvents the controversies associated with embryonic stem cells. Additionally, the evolutionary distance between aquatic animals and humans may lead to reduced immunogenicity and a lower risk of rejection in transplantation.

While the potential of aquatic-derived biomaterials is vast, translating these advancements into clinical practice requires addressing challenges in production and standardization. These include optimizing isolation and culture techniques, ensuring consistent quality control, and scaling up production to meet clinical demands. Nevertheless, ongoing research and development in this field promise to unlock the full potential of marine-derived biomaterials, paving the way for a new era of regenerative medicine that harnesses the power of the ocean to heal and restore human tissues.

Advances in Exosomes, Senolytics, Heart and Kidney Treatments

Kampon Sriwatanakul, M.D., Ph.D.

Chairman- National Health Charter of Thailand
General Manager- Wellness Group, Royal Thai Wellness Association
Chairperson- Thailand Wellness Tourism Network
Advisor- Thai Association for Anti-Aging and Regenerative Medicine

We are entering an evolution in cellular medicine. As these bio pharmaceuticals are becoming more understood, the treatment applications continue to advance and improve.

Exosomes are Nano-sized vesicles, containing biomolecules that are secreted by virtually every cell type in the body. In cell biology, a vesicle is a self-contained structure consisting of fluid enclosed by an outer membrane called the lipid bilayer. Basically, an exosome is a vesicle which is like a tiny bubble that stores, and transports materials, protein, DNA, and RNA of the cells that secrete them. Growing evidences indicate that many of the observed therapeutic outcomes of stem cell-based therapy are due to paracrine effects rather than long-term engraftment and survival of transplanted cells. Given their ability to cross biological barriers and mediate intercellular information transfer of bioactive molecules, extracellular vesicles or exosomes are being explored as potential cell-free therapeutic agents.

Senolytics are a relatively new class of treatments that focuses on the removal of senescent cells. Senescent stem cells comprise a small number of total cells in the body, but they secrete pro-inflammatory cytokines, chemokines, and extracellular matrix proteases, which together form the *senescence-associated secretory phenotype or SASP.* The resulting SASP is thought to significantly contribute to aging and cancer and thus Senolytics and removal of SASP is a potential strategy for promoting health and longevity.

Senolytic cell therapy is a new therapy that aims in physically removing these senescent stem and somatic cells from the blood stream without the use of drugs

Natural Killer T (NKT) cells are a subset of T cells that have both innate and adaptive immune functions. They recognize glycolipid antigens presented by the CD1d molecule on antigen-presenting cells. The idea of using NKT cells for senescent cell therapy revolves around their ability to recognize and eliminate abnormal or aged cells. By targeting senescent cells, NKT cells could potentially help mitigate age-related inflammation and tissue dysfunction, thereby promoting healthy aging.

Traditional treatments for Cardiovascular Disease and Chronic Kidney Disease often struggle to significantly enhance a patient's quality of life. For those suffering from Cardiovascular Disease, conventional approaches involve long-term medication use to manage symptoms and underlying causes, as well as surgical interventions such as bypass surgery or angioplasty. Kidney patients typically have fewer treatment options compared to heart patients.

We are offering an integrative medical alternative to traditional medication and surgical approaches. In a hospital catheter lab, patients can receive specialized stem cells delivered directly to the heart and both kidneys. This innovative treatment has successfully benefited hundreds of patients, offering hope for those seeking a less invasive and more effective solution.

Approach to the Next-Generation Cell Processing Facility That is Energy-Saving, Labor-Saving, and Highly Productive, Achieved by Non-Woven Fabric Automatic Culture System

Shunmei Chiba M.D., Ph.D.

CEO- FullStem Co., Ltd.
Member of the Clinical Cultivator System Committee- The Japanese Society for Regenerative Medicine

Ahead of other countries, Japan has been implementing regenerative medicine under the Law for Ensuring the Safety of Regenerative Medicine. In this environment, central kitchen-type contract cell processing facilities have made it possible for many clinics to provide regenerative medicine widely. However, in cell processing facilities using the conventional manual labor method, if high productivity is desired, a large facility and space that can accommodate a large number of workers and a large number of culture equipment are required. In order to maintain the production environment, the cleanliness of the air must be maintained at all times, and the larger the space, the higher the electricity and running costs for appropriate air condition, leading to a negative spiral. The largest source of contamination in cell processing is humans, and since there is a physical limit to the amount of manual labor, there is no qualitative or quantitative development potential for cells in a large facility with many labors.

Naturally, the first step is expected to be to achieve high productivity through the use of automated culture system, and mass culture techniques and devices developed for the production of vaccines and antibodies will be introduced. In reality, they are not suitable for stem cell culture and are not commercially available device with high practicality in terms of quality and quantity.

We are the only company in the world that possesses automated culture technology utilizing non-woven fabric as a scaffold for stem cells, and similar technology itself does not exist because cells cultured on non-woven fabric cannot be peeled off by others. Nonwoven fabrics have the largest culture area of all cell scaffold materials, which enables space-saving and high-density culture that cannot be achieved with other scaffold materials and culture techniques. The three-dimensional environment composed of intricate fibers creates an environment close to nature, as if the cells existed in vivo, and the cell aging phenomenon of hypertrophy in culture is suppressed.

We would like to report on the application of this non-woven automated cell culture system to next-generation cell processing facilities, while explaining the cell processing technology using this system.

Decidualization and Angio-myogenesis Potentials of Placental Choriodecidual Membrane-Derived MSCs

Thai-Yen Ling, Ph.D.

Associate Professor and Director- Department and Graduate Institute of Pharmacology College of Medicine, National Taiwan University

Our studies demonstrated a distinctive type of MSCs derived from the placental choriodecidual membrane, termed pcMSCs, characterized by the expression of estrogen receptor (ER) and progesterone receptor (PR). In vitro studies revealed that pcMSCs exhibit remarkable decidualization potential when stimulated by estrogen/progesterone or agents such as cAMP/ Medroxyprogesterone 17-acetate (MPA), resulting in the secretion of decidualization biomarkers, including prolactin (PRL) and insulin-like growth factor-binding protein-1 (IGFBP-1). Furthermore, pcMSCs demonstrate pro-angiogenic and muscle regeneration properties, showing therapeutic effects in a critical limb ischemia (CLI) mouse model. Treatment with pcMSCs led to improved blood perfusion, reversal of muscle atrophy, and fibrosis within two weeks. Muscle repair was evident through satellite cell activation and enhanced protein expression in the muscle regeneration pathway post pcMSCs treatment. Taken altogether, these findings show the decidualization and angio-myogenesis potentials of pcMSCs for application in clinical use.

Stem Cell and Its Derivatives in Aging Disease Treatment

Rita Yen-Hua Huang, Ph.D.

Distinguished Professor- Department of Biochemistry and Molecular Cell Biology, International PhD Program in Cell Therapy and Regenerative Medicine, College of Medicine, Taipei Medical University

The utilization of stem cells and their derivatives in the treatment of aging-related diseases represents a promising frontier in advanced cell and gene therapy (CGT). Stem cells, including induced pluripotent stem cells (iPSCs) and mesenchymal stem cells (MSCs), possess the remarkable ability to differentiate into diverse cell types or secrete beneficial derivatives (secretome or exosome), providing potential solutions for age-related degenerative conditions. Furthermore, the systematic safety of CGT in clinical applications is garnering increased attention. This speech delves into the therapeutic potential of stem cells and their derivatives in addressing systemic safety and aging-related diseases, with a specific focus on the treatment of infertility-related premature ovarian insufficiency (POI) and its associated circadian rhythm disorder.

Uncovering the Relationship Between Aging and Cancer Passenger Mutations Through Liquid Biopsy

Tomohiro Umezu, Ph.D.

Associate Professor- Department of Molecular Pathology, Tokyo Medical University

Co-author:
Masahiko Kuroda

Senior Professor-Department of Molecular Pathology, Tokyo Medical University

Organisms age due to internal factors such as aging and stress, as well as external factors like ultraviolet radiation and chemicals. Advances in science have elucidated the molecular mechanisms of this aging process, and the definition of aging has become increasingly clear. Recently, senolytic drugs targeting senescent cells that accumulate in the body with age have also been introduced. However, there are still many unknowns regarding the relationship between "aging necessary for maintaining homeostasis" and "aging that causes diseases," and understanding these relationships is essential for the practical application of anti-aging treatments.

Furthermore, it is known that aging and cancer are closely related, and the accumulation of genomic mutations with aging has been confirmed to increase the risk of cancer development. This is a significant social issue, especially in Japan, where the aging population is rapidly growing. In this context, we aim to elucidate the involvement of "genomic damage" accumulated due to aging in the development of cancer.

With the spread of NGS and gene analysis technologies, cancer genomic medicine has significantly advanced, and cancer panel testing is now conducted within insurance coverage. Genomic analysis from cancer tissue as well as liquid biopsy panel diagnostics have become practical. Since determining driver genes that serve as molecular targets for cancer treatment is crucial, mutation analysis of driver genes, which are directly involved in cancer development and proliferation, has been the focus. However, recent findings have shown that not only driver genes but also mutations in passenger genes and non-coding regions are important in tumor development. Passenger mutations, reflecting the genetic diversity acquired during the evolution of cancer cells, provide crucial information about cancer progression.

In this study, we investigated the biological significance of genomic damage, including passenger mutations accumulated with aging, with the aim of applying this knowledge to next-generation cancer diagnosis, prognosis monitoring systems, and novel targeted therapies. From the perspective of early cancer diagnosis, we attempted to detect these mutations from circulating cell-free DNA (cfDNA) in the blood. To comprehensively analyze passenger mutations scattered throughout the genome, we have also developed a signature analysis for these mutations. In this symposium, we will introduce our analysis pipeline for detecting genomic mutations from plasma cfDNA and present the latest data.

The New IARO Laboratory at Mahidol University

Pongrama Ramasoota, DVM, Ph.D.

Director- Center of Excellent for Antibody Research (CEAR), Faculty of Tropical Medicine, Mahidol University

After the MOU between Dean of Faculty of Tropical Medicine (FTM), Mahidol University (MU) and Dr. Sakura Sousa, Director of International Anti-Aging and Regenerative Medicine Organization (IARO) was signed in 2023. The collaboration between FTM, MU and IARO has been extensively expanded. Research on anti-aging product like Nicotinamide mononucleotide (NMN) has been started. The anti-aging marker detection such as telomere length measurement using Q RT-PCR & Aging related cytokines (IL-1 β , IL-6, IL-8, and TNF- α) detection using Bio-plex system, has been started. The licensing plan for commercialization of therapeutic antibody against Dengue virus has been started. And the plan for production of INKT cell and other IPSC cell at FTM, MU has been started. So, since March 2024, the new IARO Laboratory has been built at 12th floor, 50th year Anniversary building, FTM. MU. Two rooms of the total 50 Square Meters was rented and renovated by IARO. One room is the main laboratory equipped with two Cell processing (CPC) machine, Safety cabinet, freezer and liquid nitrogen tanks. The other room can be used as office and refrigerator to keep cleaned products. Both rooms have equipped with Electronic cleaned air system.

The main mission of the new IARO Laboratory at Mahidol University is;

1. Using CPC machine to Produce NKT cell for Senescent cell reduction and also to produce IPSc and Exosome for regenerative medicine.
2. Checking quality and tested the produced INKT, IPSC cells and Exosome.
3. Telomere length measured using Realtime Q PCR.
4. Detection of Aging related cytokines (IL-1 β , IL-6, IL-8, and TNF- α) using Bio-plex system.
5. Rapid detection of multiple pathogens using Novel DNA Micro-Array system.
6. Research and development of therapeutic antibody against dengue virus and other diseases.
7. Production of therapeutic and diagnostic monoclonal antibody (MAb) using novel single cell MAb production of the Cytomine® System (UK).

With our great hope to help peoples to live better life using our cutting edge therapeutic and Anti-Aging products that being proved by the world class research. The IARO Laboratory at Mahidol University will keep on trying our best to find new innovation to help peoples.

The Future of Medicine iPSC Technology Will Usher In

Koji Tanabe, Ph.D.

Founder&CEO- I Peace, Inc.

At I Peace, we are constantly considering how to swiftly bring about a world where iPSC technology genuinely improves and saves lives. The Nobel Prize-winning iPSC technology has an extraordinary ability to reprogram aged cells into a youthful state, promoting longevity, personalized medicine, drug discovery, and autologous transplantation. Our vision extends to a future where individuals routinely receive and preserve their iPSCs at birth, envisioning iPSC technology as a source of joy and relief for millions enduring suboptimal quality of life, pain, and despair. We are committed to promptly realizing this vision, striving to ensure universal access to iPSCs for clinical treatment and rejuvenation.

Our dedication to advancing iPSC technology stems from my tenure as a graduate student in Dr. Yamanaka's lab at Kyoto University. Over eight years, I had the privilege of collaborating with esteemed colleagues and contributing to several journal publications and patents, including the seminal first human iPSC paper as a second author, which significantly influenced my trajectory.

As the application of iPSC technology expands, so does recognition of its bottleneck—the exorbitant cost of producing clinical-grade iPSCs ($1M per person), making it inaccessible to many. Additionally, there is a scarcity of organizations capable of producing high-quality, clinical-grade iPSCs. I firmly believe that the transformative impact of any scientific field is magnified when basic research findings are leveraged by industry. Merely automating conventional iPSC induction processes falls short of our aspirations. Leveraging our expertise, we have pioneered a proprietary automation system capable of annually producing thousands of clinical-grade iPSCs, drastically reducing production costs and broadening accessibility. Recently, we also succeeded in establishing a system for efficiently generating iPSC-derived somatic cells. These mass-produced iPSC-derived cell products are valuable for personal care and drug screening. These innovations envision a future where individuals routinely possess and utilize their own iPSCs from birth. It has been an exhilarating journey from a mere vision and ambition in 2015 to our current standing. We will present the future of regenerative medicine and rejuvenation therapy brought by iPSC technology.

Immunotherapy for Cancer Using iNKT Cell and Next Generation NKT Therapy With Drug Delivery System

Taehun Hong, Ph.D.

Research & Development Manager- Ambicion Co., Ltd.
Research Fellow- Department of Bioengineering, The University of Tokyo
Adjunct Assistant Professor- Department of Molecular Pathology, Tokyo Medical University

Co-authors:
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The University of Tokyo

Introduction Among the numerous challenges associated with aging, carcinogenesis stands out as one of the most devastating and fearsome issues. Despite the development of various antitumor drugs, many patients still lack a complete cure, while others suffer from severe side effects. Immunotherapy using immune checkpoint inhibitors (ICIs) has emerged as a promising approach for cancer treatment in recent years due to its low toxicity and ability to engage autoimmune cells in self-cure. However, the instability of treatment effects in individual patients has hindered the achievement of satisfactory outcomes in many cases. In this study, we propose a novel immunotherapy approach based on the activation of NKT cells, independent of cancer type and patient characteristics. To implement this approach, we utilized a Drug Delivery System (DDS) to create a nano-carrier that effectively delivers RK-163 to dendritic cells in the lymph nodes adjacent to the tumor. This delivery mechanism activates the NKT cells and enhances the immune system's ability to attack cancer cells. Our method demonstrated successful suppression of 4T1 breast cancer growth, even in cases which showed resistance to conventional ICIs. Furthermore, it prolonged the survival of 4T1 tumor-bearing mice by five-fold. By implementing DDS into the NKT activation method, we aimed to inhibit cancer growth in a cost-effective and simple manner for those cancers that cannot be effectively treated with traditional immuno-cancer therapies.

Keywords immunotherapy for cancer; NKT cell activation; RK-163; Drug Delivery System; Immune checkpoint inhibitors.

Problems of Speech and Swallowing in Human Beings, the Additional Solutions with Regeneration, Instead of Just Anti-Aging

Koichi Tsunoda, M.D., Ph.D.

Department of Artificial Organs & Medical Creations/Otolaryngology National Hospital Organization Tokyo Medical Center

Last 40 Years, I developed many novel therapies for voice problems with satisfactory evidence to every citizen. With that, I simultaneously took care with phono-surgery for voice problems of professional voice users including many top actors and singers in Japan.

In contrast to other mammals, evolution has brought humans the long and flexible vocal tract needed for speech. The human adult larynx is located in and has descended through the neck, resulting in an effective articulatory system that has enabled the ability to communicate through speech. As a result, humans must elevate the larynx and move it anteriorly while swallowing to prevent aspiration. The vocal folds themselves also participate in prevention of aspiration during swallowing by closing the glottis. When aspiration does occur, action of the true and false vocal folds operates as part of the cough mechanism to expel foreign bodies (water, food). Laryngeal elevation and glottal closure are indispensable for human beings.

Anatomically and physiologically, atrophy of extrinsic and intrinsic laryngeal muscles due to aging gradually weakens the functions of laryngeal elevation and glottal closure, which causes hoarseness and aspiration. This results not only from glottal incompetence, but also from lower position of the larynx and increased difficulty to elevate it. Surgical solutions require strengthening the atrophic intrinsic and extrinsic laryngeal muscles. Many techniques involving injections inside intrinsic laryngeal muscles, and laryngeal elevation surgery have been developed but have disappeared.

In 1998, I developed a surgical solution for insufficient glottal closure for phonation and aspiration called autologous transplantation of fascia into the vocal folds (ATFV), that was within the new conception of regenerative medicine. We observed histological changes and cell proliferation activity after ATFV, suggesting that fibroblasts transplanted into the fascia do not degenerate but survive and proliferate in human Reinke‘s space. However, for Wermer’s syndrome, transplantation of fascia leading to regeneration of vocal fold tissue, using a mechanism like stem-cell transplantation, was not effective. That might have been caused by the aged state of the stem-cells transplanted. Reproducible/promotable tissue transplantation is necessary.

Considering the swallowing function in the elderly, injection of reproducible/promotable stem-cells into atrophic vocal folds may produce improvements for glottal incompetence and injections into laryngeal elevation muscles may produce improvements for laryngeal elevation in swallowing. This technique, which prevents scar formation in the surrounding tissues, would be preferable to invasive surgical incisions.

In combination with these simple injections of stem-cells into weakened muscles, drawing in the jaw during swallowing (easier laryngeal elevation by shortening the distance between the oral cavity and the larynx) and maintaining speech as self-rehabilitation (training to reinforce the glottal closure) may prevent future problems of aspiration in the elderly. Furthermore, if velopharyngeal dysfunction (weakened changes of soft-palate elevation for phonation and swallowing) is recognized, injection into the muscle of soft-palate elevation with suitable training (training to reinforce the soft-palate elevation) is necessary.

Before those solutions, it is necessary to individually evaluate swallowing and phonatory functions as a medical check-up. To rejuvenate aged senses and muscles with a view to improving an individual’s life as they age is important. For that, a novel medical check-up program is needed to maintain and enhance quality of life, not only for speech and hearing, but also for the function of the nose for smelling.

Keywords: Human; Phonation; swallowing; glottal closure, vocal fold, laryngeal elevation; intrinsic/extrinsic laryngeal muscles; injections of reproducible/promotable tissue; prevention of aspiration

Aging of the Olfactory System: Pathophysiology and Treatment Strategies

Kenji Kondo, M.D., Ph.D.

Professor- Department of Otorhinolaryngology Head and Neck Surgery, The University of Tokyo

The sense of smell is involved in appreciating the smell of food, wine, flowers, or perfume, as well as in the physical safety by detecting gas leaks and foul odors. The worldwide spread of COVID-19 has resulted in a large number of patients with olfactory dysfunction, which has made not only medical professionals but also the general public aware of the importance of the sense of smell. Compared to vision and hearing loss, olfactory dysfunction has been neglected in the past because it is less socially disabling, but patients with olfactory dysfunction have difficulties in many aspects of daily life.

The pathophysiology of olfactory loss can be divided into two main categories: conductive olfactory loss and sensorineural olfactory loss. The former is typically caused by rhinosinusitis, which mechanically obstructs nasal airflow and prevents odorants from reaching the olfactory mucosa. This pathophysiology can be treated by treating the underlying disease. On the other hand, sensorineural loss is caused by dysfunction/degeneration of the olfactory neuroepithelium and the olfactory neural pathway. Sensorineural olfactory loss is difficult to treat and there is currently no evidence-based medication.

Age-related olfactory dysfunction is one of the major categories of sensorineural olfactory dysfunction. Our recent research aims to elucidate the pathophysiology of age-related olfactory dysfunction and to develop effective methods to prevent/treat it. Previous animal studies have shown that aging is associated with a decrease in the number of olfactory neurons in the olfactory mucosa, as well as the degeneration of supporting tissues such as olfactory glands and supporting cells. The decrease in the number of olfactory neurons appears to be due to a decrease in the proliferation of basal cells, which are stem cells, in both normal and injured mucosal conditions. The accumulation of lipid peroxide in the olfactory mucosa with aging suggests that oxidative stress is one of the factors contributing to age-related degeneration of the olfactory mucosa. These studies suggest that treatment to reduce oxidative stress in the nasal cavity may be useful in preventing age-related olfactory loss, and drugs that stimulate basal cell proliferation may be candidates for the treatment.

In addition to these findings in sensorineural tissues, we also found that the metabolic capacity of olfactory mucus and LCN15, a specific protein of olfactory mucus, decreases with age. These molecular mechanisms potentially involved in olfactory perception may also be a future therapeutic target for sensorineural olfactory dysfunction.

Ultra-Low Dose Computed Tomography Combined with Artificial Intelligence for Enhanced Health Screening: A Nexus of Evidence, Innovation and Integrative Medicine

Richard H. Kaszynski, M.D., Ph.D.

Executive Director- Advanced Medicine Center, SENSHIN CLINIC
Director, Stanford Solutions, Stanford University School of Medicine

The integration of artificial intelligence (AI) with medical imaging technologies is revolutionizing diagnostic accuracy and patient safety in health screening. In the present lecture, we introduce a pioneering system that combines Ultra-Low Dose Computed Tomography (ULD-CT) with advanced diagnostic AI, presenting the world's first screening system specifically designed for comprehensive health screening. This innovative system capitalizes on the reduced radiation exposure of ULD-CT while leveraging AI's capability to enhance image analysis, thereby mitigating the traditional limitations associated with lower-dose CT scans. The present ULD-CT + AI system employs a series of state-of-the-art AI algorithms enabling the identification and evaluation of clinical radiographic features with high precision. The AI component not only compensates for the potential decrease in image quality due to reduced radiation but also enhances detection rates of subtle pathological changes, which are often missed in standard imaging protocols.

The AI algorithm supports real-time analysis, providing immediate feedback that is essential for early disease detection and management. The implementation of this system in a clinical setting has demonstrated a significant reduction in radiation exposure—up to 93% compared to conventional CT scans—without compromising diagnostic accuracy. This reduction is vital for population-based screenings, particularly in high-risk groups where repeated imaging may be necessary. Preliminary studies using the present combination of ULD-CT + AI have shown promising results in detecting early-stage diseases, including cancers and vascular disorders, which are often asymptomatic in their initial stages. By enabling earlier detection and intervention, our system has the potential to improve patient outcomes significantly and reduce healthcare costs associated with late-stage treatments. The ULD-CT + AI system represents a significant advancement in medical imaging technology. It exemplifies how AI can transform health screening, making it safer, faster, economical and more accurate. Future studies and broader implementations are planned to further validate the effectiveness and adaptability of this system across various clinical scenarios.

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