GENKI

Elucidation and Control of Biological Systems Leading to GENKI

Research and Development Objectives

Science of optimal health (“GENKI” in Japanese)
Elucidating and controlling life phenomena to maintain active and resilient bodies

Overview of Research and Development Areas

This research area redefines human life by moving beyond the conventional notion of “health = absence of disease” to embrace a new perspective: “GENKI.” While some people live vibrantly even with illness, others lack vitality despite being free from disease. “GENKI” thus represents a richness of human life that cannot be measured solely by the presence or absence of disease.
“GENKI” is understood as a state of body and mind supported by resilience—the power to live actively and flexibly throughout life. Its manifestations are diverse: vitality rooted in physical functions, vitality sustained by mood and mind, and vitality nurtured through human connections. This program seeks to comprehensively elucidate and scientifically define these dimensions of “GENKI.”
The central pillars of this exploration are nutrition and exercise, which interact with intrinsic factors such as immunity, metabolism, and neural function to shape “GENKI.” Research will be conducted across multiple levels, from molecules and cells to individuals and communities, establishing a foundation to visualize “GENKI” through interdisciplinary collaboration.
The outcomes will contribute to extending healthy life expectancy, reducing medical and caregiving burdens, and fostering the creation of new medical technologies and products. Ultimately, this initiative aims to establish “GENKI” as a globally recognized concept, sharing with the world a new future of health science originating from Japan.

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AMED-CREST Started in 2025 · 1st period

Elucidation and application of mitochondrial respiratory chain supercomplex dynamics regulation contributing to mental and physical GENKI



INOUE Satoshi
Director, Research Team for Aging Mechanism and Medical Science
Tokyo Metropolitan Institue for Geriatrics and Gerontology

Our project aims to elucidate the molecular mechanisms of mitochondrial respiratory supercomplex dynamics, which contributes to mental and physical GENKI as an essential intracellular regulatory system for energy production, and to develop GENKI-promoting strategies that enable to extend healthy longevity by improving exercise and recognition abilities. The molecular mechanisms of GENKI will be particularly clarified by utilizing state-of-the-art research technology originally developed or initiated by our members, including original animal and cell models, compounds, supercomplex dynamics analyzing system, and human resources from cohort studies and biobank led by Tokyo Metropolitam Institue for Geriatrics and Gerontology.

Decoding the cellular blueprint that shapes “GENKI” of skeletal muscle



UEZUMI Akiyoshi
Professor, Medical Institute of Bioregulation,
Kyushu University

The characteristic of skeletal muscle to be strengthened by exercise constitutes the basis for generating “GENKI.” This study comprehensively analyzes skeletal muscle adaptation to exercise, initiated by mesenchymal stromal cells acting as command centers and mediated through cellular interactions with satellite cells and myofibers. Furthermore, by integrating multimodal data from athlete cohorts, we aim to establish a research framework that seamlessly connects molecular to human levels, thereby elucidating the mechanisms underlying the formation of skeletal muscle “GENKI.”

Molecular Basis of Exercise Memory in Physical Resilience



ONO Yusuke
Professor, Institute of Molecular Embryology
and Genetics (IMEG), Kumamoto University

This study aims to demonstrate that past exercise habits (exercise history) lead to long-term potential adaptations in various organs, including skeletal muscle, thereby forming the basis for physical resilience. This acquired trait will be established as a novel concept of 'Exercise Memory', which contributes to inter-individual variability in aging trajectories and healthy lifespan. Elucidating the molecular mechanisms underlying exercise memory will offer strategies to promote and sustain a resilient physical state.

Decoding the Molecular Basis of “Vitality” via the Musculoskeletal–Neuro–Immune Axis



TAKAYANAGI Hiroshi
Professor, Graduate School of Medicine and Faculty
of Medicine, The University of Tokyo

This study focuses on the multi-organ network of the musculoskeletal, nervous, and immune systems to integratively elucidate the molecular basis of GENKI—a vigorous and resilient physical condition. By leveraging animal models and large-scale human cohort data, we will clarify the molecular mechanisms through which daily factors such as exercise and nutrition influence these networks and their interconnections. Furthermore, we aim to identify “vitality-promoting factors” and “vitality-suppressing factors,” thereby generating innovative insights that contribute to extending healthy life expectancy and preventing disease.

Study of lipid reprogramming toward healthy and active life



MURAKAMI Makoto
Professor,
Graduate School of Medicine, The University of Tokyo

In this research, we aim to approach “GENKI” from the perspective of lipids, an essential nutrient. Focusing on intracellular and extracellular metabolism of phospholipids and their metabolites, we will elucidate the molecular mechanisms underlying lipid reprogramming in response to dietary intake/fasting and exercise. By utilizing gene-manipulated mice for lipid metabolic enzymes, transporters and receptors and by developing intervention methods to facilitate the health and prevent the disease through artificial control of key metabolites, we will establish the scientific basis for maintaining an active and resilient physical state.

AMED-CREST Started in 2026 · 2nd period

Thyroid-bone marrow allostasis as a regulatory mechanism for Genki resilience



TAKUBO Keiyo
Chief, Department of Stem Cell Biology,
National Institute of Global Health and Medicine

Scientific vitality is more than the absence of disease or a subjective feeling of energy. It reflects physiological resilience, the capacity to maintain hematopoietic, immune, skeletal, and metabolic functions by reallocating resources in response to aging, nutrition, exercise, and environmental change. We will investigate how thyroid hormones and their related metabolites shape the bone marrow cell community through “thyroid–bone marrow allostasis.” By integrating molecular and cellular biology, mouse genetics, spatial and single-cell analyses, and studies of existing human samples, we aim to define its mechanisms and establish a minimally invasive index that detects early signs of declining vitality.

Adaptive Dynamics of “Genki” States



NISHIMURA Yukio
Project Leader,
Tokyo Metropolitan Institute of Medical Science

We subjectively assess our condition in terms of “GENKI,” a Japanese concept referring to one’s perceived level of physical and mental vitality. However, it remains unclear which biological states underlie this assessment and why it fluctuates. We define GENKI as an integrated biological state comprising brain activity, physiological responses, behavior, and psychological state. These components are longitudinally measured within individuals under daily-life and physical-load conditions and quantified using AI-based analyses. We further test the hypothesis that repeated adaptation to physical load enhances the level of GENKI.

Supersulfidation-Defined Skeletal Muscle Resilience as a Foundation for Healthy Aging



MOTOHASHI Hozumi
Professor,
Tohoku Univeristy Graduate School of Medicine

Skeletal muscle is a vital organ that supports not only motor function but also whole-body energy metabolism. In this study, we will test the hypothesis that supersulfidation of cysteine residues in proteins supports skeletal muscle resilience by stabilizing metal coordination, thereby maintaining metal homeostasis and protein function. Our goal is to redefine “vitality” from the perspective of sulfur metabolism and establish supersulfides as a new class of nutrients that contribute to the maintenance of health.

Developing methods to overcome a lack of vitality by elucidating the effects of nutritional, exercise, and environmental factors that determine individual differences in water metabolism and distribution



YAMADA Yosuke
Professor, Graduate School of Biomedical Engineering,
Tohoku University

Water in the human body is continuously circulating and moving between the intracellular and extracellular compartments, thereby supporting the functions of various organs. In this study, we reframe body water, which has traditionally been assessed primarily in terms of its quantity, from a dynamic perspective focusing on “water turnover” and “water distribution.” We aim to identify the nutritional, physical activity, and environmental factors that influence these processes and to elucidate their underlying molecular and physiological mechanisms. Ultimately, by appropriately regulating water turnover and distribution, we seek to develop novel approaches to enhance physical function and metabolism and help individuals recover from low-vitality states.

PRIME Started in 2025 · · ·

Sleep dependent mechanisms of vitality homeostasis



HASEGAWA Emi
Associate Professor, Graduate School of Pharmaceutical Sciences, Kyoto University

GENKI refers to a subjective sense of health, including motivation and vitality, and fluctuates daily with aging and lifestyle factors, though its underlying mechanisms remain unclear. Sleepiness, which affects GENKI, accumulates during wakefulness and is relieved by sleep. In this study, I aim to clarify the causal relationship between GENKI and sleepiness and to elucidate the molecular and neuroscientific mechanisms underlying the dynamics of GENKI. Furthermore, I will examine the potential for enhancing GENKI across the life course through sleep improvement via nutritional interventions.

Decoding Vitality Loss and Restoration from Lysosomes: Molecular Mechanisms of Lipotoxicity and Development of a Cross-Disease Monitoring Platform



MINAMI Satoshi
Specially Appointed Assistant Professor (Full time) , Graduate School of Medicine, The University of Osaka

The principal investigator has discovered that the root cause of “GENKI” decline lies in lysosomal damage induced by lipotoxicity, which disrupts cellular homeostasis. Building on this novel pathological foundation, the present study aims to redefine the process of GENKI loss at the molecular level by focusing on lysosomal dysfunction. We will elucidate the mechanisms by which lipotoxicity impairs lysosomal function, while simultaneously establishing a non-invasive, cross-disease biomarker platform to monitor lysosomal integrity. Through this approach, we seek to pioneer new diagnostic and therapeutic strategies toward the regeneration of “GENKI.”

Decoding the essence of “GENKI” through cross-organ effects of liver macrophages



MIYAMOTO Yu
Assistant Professor, Graduate School of Frontier Biosciences, The University of Osaka

The liver is a vital organ that generates metabolic energy and supports the function of multuple organs throughout the body. Therefore, maintaining proper liver function is considered essential for sustaining the overall physiological vitality of the organism. In this study, we focus on tissue macrophages and aim to elucidate how these immune cells support hepatic function and, consequently, influence the physiological activity of other organs. Furthermore, we seek to develop novel technologies to manipulate macrophages, with the ultimate goal of regulating hepatic homeostasis and enhancing systemic vitality.

Bioelectronic Wireless Implants for Gut-Brain Axis Modulation and Homeostatic Control of Gastrointestinal Function



YAMAGISHI Kento
Associate Professor, Institute of Engineering, Tokyo University of Agriculture and Technology

We aim to develop implantable wireless devices capable of both sensing and stimulation to achieve closed-loop control of gastrointestinal functions based on bidirectional gut-brain communication. By stabilizing gut activity disrupted by stress or disease, this research aims to uncover and modulate the underlying mechanisms that maintain systemic homeostasis and physiological resilience. Through this pioneering, interdisciplinary approach that integrates advanced engineering with medical science, we seek to establish a new framework for understanding and manipulating the biological basis of “GENKI” through gut-brain interactions.

Neural mechanisms for the creation and regulation of exercise motivation using whole brain imaging and opto-/chemo-genetics



YAMANAKA Ko
Associate Professor, Graduate School of Health and Sports Science, Juntendo University

This study aims to elucidate the neural basis of “exercise motivation,” conceptualized as an indicator of "GENKI." Whole-brain screening, neural activity recording, and optogenetic and chemogenetic approaches will be applied to clarify mechanisms underlying the regulation of exercise motivation. In addition, their involvement in recovery (resilience) from a stress-induced state of reduced vigor (loss of GENKI) will also be examined. The ultimate goal is to establish novel health-promoting interventions, including visualization of exercise motivation and the development of personalized, sustainable, tailor-made exercise programs.

Change of neural circuits to control skilled behaviors by aging and its recovery



YOSHIDA Yutaka
Professor,
Okinawa Institute of Science and Technology

Fine motor skills are fundamental to daily living. Impairments in these skills can significantly reduce both activity levels and quality of life. However, the precise neural circuits that govern fine motor control, as well as the effects of aging and cognitive changes on these circuits, remain poorly understood. The objective of this research is to elucidate the neural circuits underlying fine motor skills and to characterize age-related changes. We anticipate that this project will help identify strategies to promote the recovery of both structure and function in these circuits.

PRIME Started in 2026 ····· 2nd period

Organelle Network Dynamics Regulating Cellular Resilience States



AKI Sho
Project Researcher, Graduate School of Medicine, Osaka Metropolitan University

Within our cells, organelles such as mitochondria and the endoplasmic reticulum work together to support vital cellular functions. This study focuses on how organelle networks are dynamically reorganized in response to nutrition and lifestyle factors such as diet and exercise. We aim to uncover how this reorganization enables cells to withstand stress and maintain or recover their functions. By revealing these mechanisms, we seek to discover fundamental biological principles that support cellular resilience and ultimately contribute to our health and vitality.

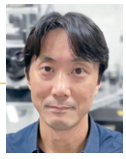
A Preconception Strategy to Promote Intergenerational Resilience via Uterine Microbiota and Metabolites



ICHINOSE Mari
Lecturer, The University of Tokyo, Graduate School of Medicine

Pregnancy imposes a dynamic physiological burden on both mother and infants, and breakdown of this homeostatic system can lead to maternal complications such as preeclampsia and, in the child, impaired postnatal adaptation to the external environment. This project tests the hypothesis that preconception uterine microbiota and their metabolites shape maternal “GENKI” through endometrial immune homeostasis and placental formation, which in turn nurtures the immune resilience of the next generation. Based on this hypothesis, we will identify metabolites that link mother and child, and establish a new, evidence-based preconception care strategy that supports lifelong health across generations.

Elucidation of molecular basis of “vitality” through esophageal homeostasis



IWAMURA Chiaki
Specially Appointed Associate Professor, Department of Immunology, Graduate School of Medicine, Chiba University

The esophagus is often regarded merely as a passage for food, yet esophageal dysfunction reduces not only food intake but also the enjoyment of eating. In this study, we define “GENKI” as the ability to enjoy meals comfortably and focus on esophageal homeostasis as its foundation. We will elucidate, at the cellular and molecular levels, how esophagus-adapted immune cell populations maintain homeostasis and how its disruption contributes to esophageal diseases, thereby providing a basis for developing new preventive and therapeutic strategies.

Elucidating Disease Resistance Through Alterations in Dendritic Cell Differentiation



KANAYAMA Masashi
Associate Professor,
Medical Research Laboratory, Institute of Science Tokyo

We all have a natural power to fight off the onset of illness, which we call "GENKI." Dendritic cells (DCs) play an essential role in "GENKI" by acting as the "conductors" of our immune system. In this study, we will explore how various daily stresses affect the differentiation pathways of DCs, and how alterations to this process impact "GENKI." Through this work, we would like to uncover the immunological mechanisms behind "GENKI" and develop new ways to measure and boost it.

Circadian rhythm synchronization via feeding rhythms and endocrine-metabolic homeostasis



KINOUCHI Kenichiro
Associate Professor,
Keio University School of Medicine

Circadian rhythms are crucial for maintaining homeostasis, and their desynchronization is implicated in pathologies including cancer, metabolic impairment, and sleep disorders. In this study, we define a state of synchronized rhythms as "Genki." Through omics and physiological fluctuation data analyses, we aim to clarify the role of feeding rhythm—a key factor in synchronizing peripheral circadian clocks—in both inter-organ synchronization and inter-individual (social) synchronization. Ultimately, we seek to generate knowledge that will serve as a foundation for building a society that maintains this state of Genki.

Identification of Sources of Offspring Vitality Cultivated During Pregnancy



KUSUYAMA Joji
Professor, Graduate School of Medical and Dental Science, Institute of Science Tokyo

We have established that the placenta functions as an information-transmitting organ that secretes bioactive molecules called placentokines to convey maternal lifestyle information to the offspring. Building on the concept that the foundation of lifelong health and vitality is established during fetal development, this study aims to elucidate how the placenta transmits maternal information that promotes offspring health to the next generation. We will identify the molecular and physiological events that generate this beneficial information and determine how they influence offspring development. Ultimately, we aim to develop a comprehensive “vitality package” encompassing pregnancy and childbirth to promote healthy mothers and children.

Elucidation of the Brain Lactate Shuttle Mechanism Supporting Exercise



SOYA Shingo
Assitant professor,
University of Tsukuba, Faculty of Medicine

In this study, we define “Genki” as the capacity to appropriately regulate physiological states in accordance with available energy resources and aim to elucidate the role of the underlying brain energy metabolism in sustaining physical activity, a key component of an active and vigorous life. Using our unique dual-color fiber photometry approach, we will visualize and analyze the dynamics of the brain lactate shuttle and its interactions with neuromodulatory signals during the progression from sustained exercise to exhaustion. Through these studies, we aim to uncover the brain energy-supply mechanisms that sustain “Genki” and the principles governing their regulation.

Trans-generational inheritance of gut resilience via the polyreactive IgA-mediated diet-gut microbiota-immunity axis



TAKAHASHI Daisuke
Associate Professor,
Keio University, Faculty of Pharmacy

Intestinal IgA is polyreactive, simultaneously retaining beneficial commensals and excluding pathogens. How a single IgA clone reconciles these opposing functions, and whether this capacity is handed down across generations, remain unknown. We recently showed that dietary soy drives the colonization of Limosilactobacillus reuteri and Muribaculum intestinale and elicits T follicular helper cell-dependent polyreactive IgA. Building on gnotobiotic mice colonized with these two species, this project identifies the molecular targets recognized by polyreactive IgA, traces how maternal milk IgA seeds the offspring gut and imprints their immune system through to the F2 generation, and tests whether the same axis operates in humans.

Elucidation of Innate Immune Epigenomic Memory Mechanisms Supporting Sensory Resilience



HATA Masayuki
Program-Specific Senior Lecturer,
Kyoto University

This study aims to elucidate how lifestyle factors, including sleep, physical activity, and diet, influence age-related changes in visual function and overall well-being. By integrating epidemiological and AI-based analyses with experimental studies, we will clarify the relationship between epigenomic memory established in the bone marrow innate immune system and sensory resilience, with the ultimate goal of developing new foundations for preventive and interventional strategies to extend healthy life expectancy.

Elucidation and Control of the Glucose Production System Generating “GENKI” during Exercise Based on the Technological Development of Dynamic Metabolic and Physiological Analyses



HORIUCHI Takahiro
Assistant Professor,
Tohoku University SiRIUS Institute of Medical Research

“GENKI” during exercise is supported by energy supply, including endogenous glucose production. Gluconeogenesis is a coordinated whole-body process in which gluconeogenic substrates supplied from tissues such as skeletal muscle and adipose tissue are converted into glucose in the liver. We aim to visualize “GENKI” using dynamic analytical approaches and to elucidate the systemic mechanisms of energy production during exercise. Furthermore, by controlling these mechanisms to enhance exercise capacity, we seek to develop new strategies to generate “GENKI.”

Large-scale brain activity dynamics underlying cognitive GENKI and their enhancement by exercise



MAKINO Yuichi
Project Lecturer, International Research Center for Neurointelligence, The University of Tokyo

The ability to sustain cognitive performance over extended periods is essential in many aspects of daily life. Using mouse models, we aim to elucidate the neural activity underlying this cognitive vitality ("cognitive GENKI"), from whole-brain dynamics to the cellular level. We will further identify exercise paradigms that enhance this neural activity, with the long-term goal of developing approaches to promote cognitive GENKI in everyday life.