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

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
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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.

PRIME Started in 2025 — 1st period

Scientific Definition and Evaluation Methods for "Genki" Metabolic State Based on Adipose Progenitor Cells

ABE Ichitaro
Assistant Professor,
Graduate School of Medicine, The University of Tokyo

This research aims to define "GENKI" as a state where metabolic functions essential for life work appropriately and establish indicators for this condition. This research focuses on adipose progenitor cells, developing new indicators to assess "GENKI" metabolic states through comprehensive analysis of their metabolic characteristics and environmental responsiveness. The findings will contribute to developing nutrition and exercise-based products, creating medical technologies for maintaining physical function, and establishing personalized molecular nutrition approaches optimized for individuals through integrated multi-omics approaches.

Integrated understanding of “GENKI” at single-cell resolution through large-scale single-cell and multi-omics analysis

EDAHIRO Ryuya
Assistant professor, Graduate School of Medicine,
The University of Osaka

We aim to project physical function indices onto the immune cell single-cell scape and visualize “GENKI” at single-cell resolution through quantitative and qualitative analyses, thereby advancing our understanding of cellular characteristics. By leveraging an independent single-cell cohort with host genomic, metagenomic, and proteomic data, we will elucidate the molecular basis of immune cell states that constitute “GENKI” from multiple perspectives. Defining “GENKI” at single-cell resolution will enable the establishment of novel health indicators and a scientific foundation that contribute to the realization of a healthy and long-lived society.

Physiological characterization of vitality induced by mind–body correlation and application in disease models

KATAOKA Naoya
Lecturer,
Nagoya University Graduate School of Medicine

"GENKI," the vitality arising from the harmony of mind and body, is a crucial force that supports healthy longevity and recovery from illness. However, how physical activity and mental states influence this vitality remains largely unexplored. In this project, we analyze how different forms of exercise (voluntary or forced) and emotional states affect neural activity, physiological responses, immunity, and behavior. We will integrate these data to construct the "GENKI Index," a tool to visualize and quantify vitality, thereby clarifying its role and contributing to health prediction and novel exercise therapies.

Time and Space Regulation of Parathyroid Hormone Type 1 Receptor Signaling in Bone Metabolism

SANO Fumiya
Project Assistant Professor,
Graduate School of Science, The University of Tokyo

To promote bone health as a foundation for achieving 'GENKI,' this study aims to elucidate the bone metabolic mechanisms mediated by PTH1R. Using cryo-electron microscopy, molecular dynamics simulations, and high-speed atomic force microscopy, we will perform detailed analyses of the molecular dynamics of PTH1R. Furthermore, through structural analyses under in situ conditions, we will investigate the spatiotemporal regulatory mechanisms within cells. Building on these insights, our ultimate goal is to identify novel seeds for next-generation therapeutics.

Exploring the boundary between "Health" and immune disorders through granulocyte single-cell analysis

NISHIDE Masayuki
Lectuer, Graduate School of Medicine,
The University of Osaka

To maintain long-term health and well-being—what we call "GENKI"—our immune system, especially white blood cells, plays an essential role. Yet, when these cells become overactivated, they may attack the body's own tissues, leading to autoimmune and allergic diseases. Our research focuses on granulocytes such as neutrophils and eosinophils, the immune system's frontline defenders. By applying single-cell analysis to blood and tissue samples from patients with immune-mediated diseases, we aim to uncover the mechanisms that separate "GENKI" from immune breakdown, and identify novel biomarkers and develop targeted molecular therapies for precision medicine.

Unraveling strategies for cardiac resilience through sulfur redox metabolism

NISHIMURA Akiyuki
Project Associate Professor, National Institute for Physiological Sciences, The National Institutes of Natural Sciences

Supersulfides, which are sulfur metabolites containing catenated sulfur atoms, are involved in various biological processes, including energy metabolism. Imbalance in the levels of supersulfides and their metabolite, hydrogen sulfide, has been implicated in the development of heart failure. In this study, we aim to elucidate the effects of exercise and diet in maintaining a resilient heart that is resistant to aging and stress from the perspective of sulfur redox metabolism, and to establish novel preventive strategies that contribute to healthy longevity.

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
Lecturer, Department of Electrical Engineering and Information Systems, The University of Tokyo

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.