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OVERVIEW

With national healthcare costs now exceeding 40 trillion yen, preventive medicine is becoming increasingly important with the goal of extending healthy life expectancy. Aging is a risk factor for musculoskeletal diseases such as osteoporosis/sarcopenia/osteoarthritis, lifestyle-related diseases, cardiovascular disorders, and cancer. In recent years, it has become clear that aging changes in the body are not merely physical deterioration, but physiological activities that are actively regulated by molecular signals. This fact means that it is possible to prevent aging changes by intentionally manipulating molecules. With the goal of elucidating the mechanisms of aging, disease onset, and metabolic disorders, we have been studying aging regulators such as sirtuin genes and PAI-1 (Plasminogen Activator Inhibitor-1), gut microbiota, HIF (Hypoxia Inducible Factor Factor), etc., and have

been conducting functional evaluation and product development. We will continue to conduct research under two banners: regenerative medicine for age-related disorders and preventive medicine to delay aging itself.

RESEARCH CONTENTS

(1) Basic/clinical research on regenerative medicine using nanofibers as a carrier and cell therapy using mesenchymal stem cells

Technology to regenerate organs lost due to aging, trauma, or disease has been advancing rapidly in recent years. We are focusing on nanofibers as a next-generation regenerative medicine. Nanofibers are materials composed of extremely thin fibers less than 1 micron in diameter. We are developing nanofiber materials optimized as carriers of cells and growth factors to promote regenerative medicine. In Japan, ahead of the rest of the world, legislation has been established to ensure the safety of cell-based regenerative medicine, and cell therapy using mesenchymal stem cells is becoming increasingly popular. However, there are still many issues to be addressed, including the lack of evidence for cell therapy and tissue regeneration of sizes and sites that are difficult to overcome using current technology. We will continue our basic and clinical research to overcome these issues.

(2) Elucidation of the mechanisms of aging, disease onset, and metabolic disorders

In recent years, nicotinamide mononucleotide (NMN) has been attracting attention as a health food because it is expected to activate the longevity gene sirtuin and rejuvenate the body. For many years, we have focused on SIRT6, one of the sirtuin genes, and studied the aging mechanism of bone and cartilage tissue, and found that a decrease in SIRT6 activity with aging is a cause of osteoporosis and osteoarthritis. We will examine the effects of NMN on the aging process in the body, especially in bone and cartilage, and will examine the effect of PAI-1 (Plasminogen Activator Inhibitor-1), which is a marker of cellular senescence and induces cellular senescence on its own, on the aging process in the body. We found that SIRT6 and PAI-1 cross-talk and cause age-related changes, and that PAI-1 inhibition prevents postmenopausal osteoporosis and age-related muscle weakness.

(3) Specific Clinical Trial: Efficacy of PAI-1 Inhibition TM-5614 in the Treatment of FGF23-Associated Hypophosphatemic Rickets and Osteomalacia

FGF23 is a hormone produced mainly in bone cells and plays a central role in the physiological regulation of blood phosphorus levels. FGF23-associated hypophosphatemic rickets/osteomalacia is a rare disease caused by excessive production of FGF23. Recently, it has been shown that PAI-1 inhibition promotes the degradation of FGF23. We will promote a specific clinical study "Exploratory clinical study to investigate the efficacy and safety of TM5614 for congenital FGF23-related hypophosphatemic rickets and osteomalacia" using an orally available small molecule PAI-1 inhibitor TM-5614 to develop a novel therapeutic agent.

(4) Verification of the effect of oxygen nanobubble administration on hypoxemia

Through joint research with Gifu University, we have demonstrated that drinking oxygen nanobubble water prevents hypoxemia caused by respiratory depression under general anesthesia using beagle dogs. These results suggest that oxygen nanocapsule water may improve the ability to work under hypoxic conditions.

(5) Verification of antiviral effect of silver ionized water/effect on infectious diseases

We will verify the antiviral effect, its persistence, and concentration dependence of silver ionized water, which has been widely known for its antimicrobial effect in the past, and develop it for the purpose of countermeasures against COVID-19.

(6) Elucidation of aging control mechanism by intestinal bacteria

An enormous number of intestinal bacteria (several hundred trillion) inhabit the intestines. In recent years, attention has been paid to the functions of gut microbiota, and it has become clear that a variety of networks are organized between gut microbiota and organs. Our research focuses on the regulatory mechanism of skeletal tissues by intestinal bacteria. Proanthocyanidins, one of polyphenols, have been attracting attention for their antioxidant effects, but their large molecular weight means that they are rarely absorbed through the digestive tract. In collaboration with Tohoku University, we have found that oral intake of anthocyanidins changes the gut microbiota and prevents bone loss and obesity in a mouse ovariectomized model. The gut microflora, which changes with aging, is a cause of various diseases. We are analyzing the mechanism and approaching the prevention of aging of the locomotor organs from the gut.

Accepted papers

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