

HEALTHY LONGEVITY GLOBAL COMPETITION

2023 Catalyst Awardees

Sponsor: Agency for Medical Research and Development of Japan

Development of nucleic acid therapeutics with built-in DDS

Principal Investigator	YOSHIOKA Kotaro, PhD, MD
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Co-Investigator(s)	None

PROJECT DESCRIPTION

Nucleic acid therapeutics are rapidly advancing as a new class of molecular-targeting drugs following antibody therapies. However, two main challenges remain: inadequate drug delivery to target tissues and risk of nucleic acid-induced toxicity. To overcome these challenges, Dr. Kotaro Yoshioka has developed a novel double-stranded oligonucleotide technology, overhanging heteroduplex oligonucleotide (ODO) that enables inherent nucleic acid-based drug delivery system (DDS). The ODO technology enables much more efficient drug delivery to target tissues and higher safety compared to conventional nucleic acid therapies, resulting in an expansion of the therapeutic window by more than 10-fold.

Leveraging rapid development of nucleic acid therapeutics for clinical application, this innovation is able to make rapid contributions toward extending healthy lifespan through groundbreaking curative treatments for debilitating diseases. In addition, the versatility of this ODO-technology, applicable to diverse effects such as gene expression suppression or upregulation and splicing regulation, holds promise for addressing a wide range of challenging pathology. Consequently, this ODO-technology provide the substantial potential for societal contributions to various diseases, spanning from life-threatening diseases such as cancer to neurodegenerative disorders like Alzheimer's disease and mental health conditions like depression.

In this project, we aim to elucidate the correlation between nucleic acid molecular structure and interdisciplinary characteristics through the utilization of novel molecular techniques, including nanoscale nucleic acid chemical modification design and atomic-level analysis of target molecules. Subsequently, development of DDS-intrinsic nucleic acid molecules tailored to individual target organs will be undertaken in a progressive and novel manner.

Development of prognosis prediction model and disease-modifying therapy by integrating multilevel bioinformatics and MRI

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Co-Investigator(s)	SAIKI Shinji, MD, PhD SAKO Wataru, MD, PhD

PROJECT DESCRIPTION

With the aging of society, the number of patients with neurodegenerative diseases, especially Parkinson's disease (PD), for which aging is a risk factor, continues to increase. Phenotypes of PD vary widely, especially in prognosis. Accurate prognosis prediction is vital for patients and their families for prospects. We would like to work on research aimed at (1) identification of factors that influence prognosis, (2) creation of models that enable

prognosis prediction based on these factors, and (3) intervention aimed at improving prognosis through multilevel bioinformatics that adds a time component to spatial omics analysis of genes, diffusion-weighted/structural/functional MRI, metabolome, and miRNA transcriptome, as well as clinical information such as non-motor symptoms including cognitive functions. Especially for studies aiming to improve prognosis, we will search for possible intervention points in elucidating the mechanisms at the pathway level and also examine the validity using cultured cells, iPS cells derived from cases with PD, and animal models. Ultimately, a double-blind, randomized controlled trial is planned to intervene on the identified factors, aiming to approve the drug as a disease-modifying drug. This study would bring us closer to achieving healthy longevity for elderly patients with PD, whose number is growing with the arrival of an aging society, and to enhance their well-being by extending the length of time, they can walk on their own two feet.