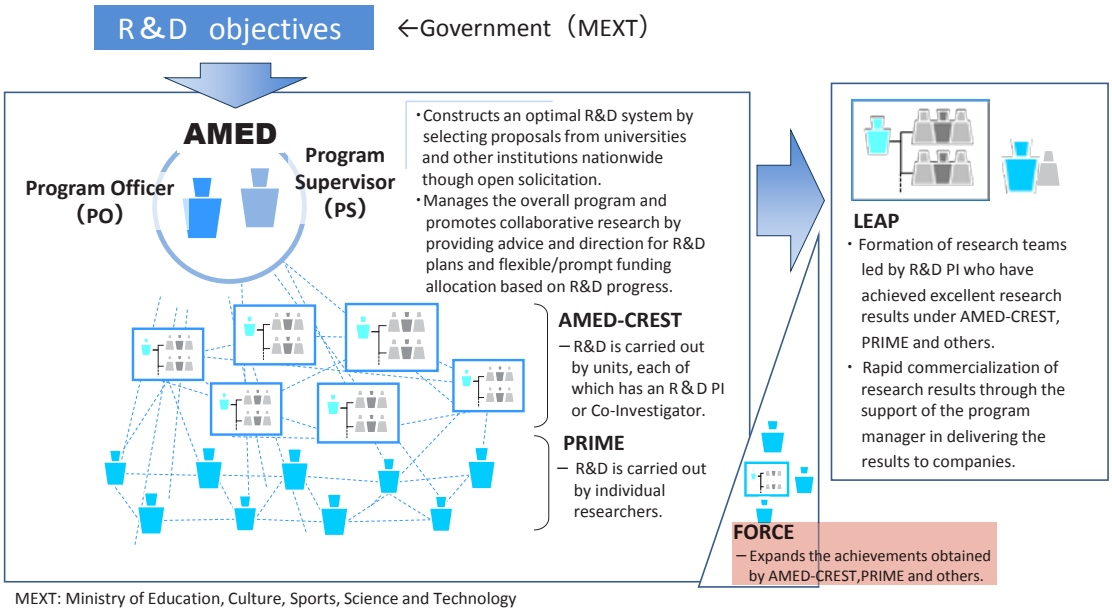
FORCE

Objectives/Characteristics

- Step-type (Frontier Outstanding Research for Clinical Empowerment, FORCE) program promotes prospective R&Ds which can lead to large developments, among research accomplishments obtained from terminated AMED-CREST , PRIME and other projects. FORCE program aims to verify correlations between their achievements and target diseases and to validate generated analytical methods, devices, and instruments, by using human clinical samples.
- Purpose 1, Correlations with human diseases:
  - Elucidation of correlations between the object of R&Ds (e.g., proteins, genes, metabolites, biological phenomena) and specific diseases, and researches for their potentials toward medical treatments to narrow down target diseases.
  - Establishment of novel/improved model systems for target diseases.
- Purpose 2, Analytical methods, devices, and instruments:
  - Verification of versatility and effectiveness of analytical methods, devices, and instruments based on experimental results under various conditions including human clinical samples.
  - Improvement and optimization of analytical technologies and methods.



MEXT: Ministry of Education, Culture, Sports, Science and Technology

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R&D Period and R&D Costs

Program	R&D Period	Annual R&D Costs (direct cost)
FORCE	Up to two years	Up to 20 million yen

FORCE Started in 2023 · 5th period

Pathological significance of cardiomyocyte DNA damage in human heart failure

KOMURO Issei
Project professor,
The University of Tokyo Hospital

Heart failure is a serious disease that, along with cancer, threatens the lives of many people worldwide. The disruption of the heart's response mechanism to mechanical stimuli is the essence of heart failure pathogenesis, and we have identified DNA damage as a central molecular mechanism. This study aims to elucidate the molecular mechanisms by which DNA damage causes heart failure and to develop a long-awaited pathogenesis-based therapeutic agent for heart failure.

Study on regulation of intestinal immunity and epithelial barrier in humans

TAKEDA Kiyoshi
Professor,
Osaka University Graduate School of Medicine

We have analyzed human intestinal microbiota and microbiota-derived metabolites to identify changes in patients with inflammatory bowel disease (IBD), and have analyzed the effects of these changes at the in vivo level using a mouse model of intestinal inflammation. In this project, we aim to elucidate the pathophysiology of human IBD by developing the pathophysiology of IBD clarified by the analysis of "human intestinal microbiota and metabolites – mouse model" into "human intestinal microbiota and metabolites - human intestinal mucosal cells".

Development of a microfluidic device system for analyzing the single immune cell function and its application to diagnosis of anti-tumor activity

TAMIYA Eiichi
Specially appointed professor,
SANKEN, Osaka University

Using biosensing and microfluidic device technology, we can identify the function of each cell, investigate the relationship between these cell function and various diseases, and characterize the genomic traits of individual cells by isolating each cell and linking each cell to genetic analysis. We aim to elucidate the relationship between cell function and disease. Using the developed chip, we seek to investigate whether single-cell GZMB activity evaluation can be used to predict the efficacy of ICT treatment in lung cancer. Our goal is to enhance the efficiency of cancer immunotherapy and contribute significantly to the comprehension of anti-tumor immune responses.

Development of innovative therapies for ischemic diseases targeting vascular endothelial stem cells

NAITO Hisamichi
Professor, Graduate School of Medical Sciences,
Kanazawa University

Regulation of angiogenesis is critical to overcome ischemic diseases. We priviously reported that vascular endothelial stem cells are important for angiogenesis and vascular repair. In this study, we analyze human samples to clarify the cellular heterogeneity of vascular endothelial cells, including vascular endothelial stem cells. In addition, we aims to develop new therapeutic targets by clarifying the correlation between endothelial cell heterogeneity and ischemic diseases.

FORCE Started in 2024 · 6th period

Autophagy activation by AUTACs for treatments of neurodegenerative diseases

ARIMOTO Hirokazu
Professor,
Tohoku University

Autophagy is an intracellular degradation mechanism that is also involved in the removal of debris that have accumulated in the cell. The AUTACs we are studying are compounds that selectively degrade specific harmful substances. We will work with clinicians to develop AUTACs effective in human-patient-derived cells, primarily for the remediation of neurodegenerative diseases.

Development of a new method for evaluating diagnostic and therapeutic efficacy using multi-parametric single-nanoparticle analysis

ISHII Ken
Professor,
The Institute of Medical Science, The University of Tokyo

We have invented a novel flow cytometry technology to develop high-resolution single nanoparticle analysis and sorting techniques for extracellular particles, such as exosomes and viruses, which have traditionally been analysed in bulk. By analysing microparticles in biological samples, including exhaled breath condensate, this study aims to develop new methods for disease diagnosis and treatment evaluation, ultimately proposing single-particle biology as an alternative to single-cell biology.

Mechanism of liver tumor-promoting microenvironment formation by gut microbial factors and its application to prognosis prediction, prevention, and treatment

OHTANI Naoko
Professor,
Graduate School of Medicine, Osaka Metropolitan University

Treatments for non-viral, metabolic dysfunction-associated liver diseases and hepatocellular carcinoma (HCC) are still underway, and even immune checkpoint inhibitors have shown limited efficacy for them. We focus on the gut-liver axis-mediated impact of gut microbiota and microbiota-related factors on the liver microenvironment. In this study, we aim to uncover mechanisms underlying the non-viral HCC progression and identify potential biomarkers and molecular targets. Additionally, we focus on improving the gut barrier function, which could contribute to preventing liver cancer progression.

Elucidation of correlations between lymphoma and dysfunction of inter-organelle lipid transport

NAKATSU Fubito
Associate Professor, Graduate School of Medical and Dental Sciences, Niigata University

Lipids shape the structure of cellular membranes, including the plasma membrane and organelle membranes, and are responsible for numerous crucial physiological functions. We have studied the regulation and operational mechanisms of inter-organelle lipid transport at membrane contact sites, where cellular membranes are closely apposed. The goal of this research is to investigate whether the malfunction of inter-organelle lipid transport contributes to human malignant lymphoma pathology using clinical specimens, and to elucidate the pathogenesis using model mice and in vitro analyses.