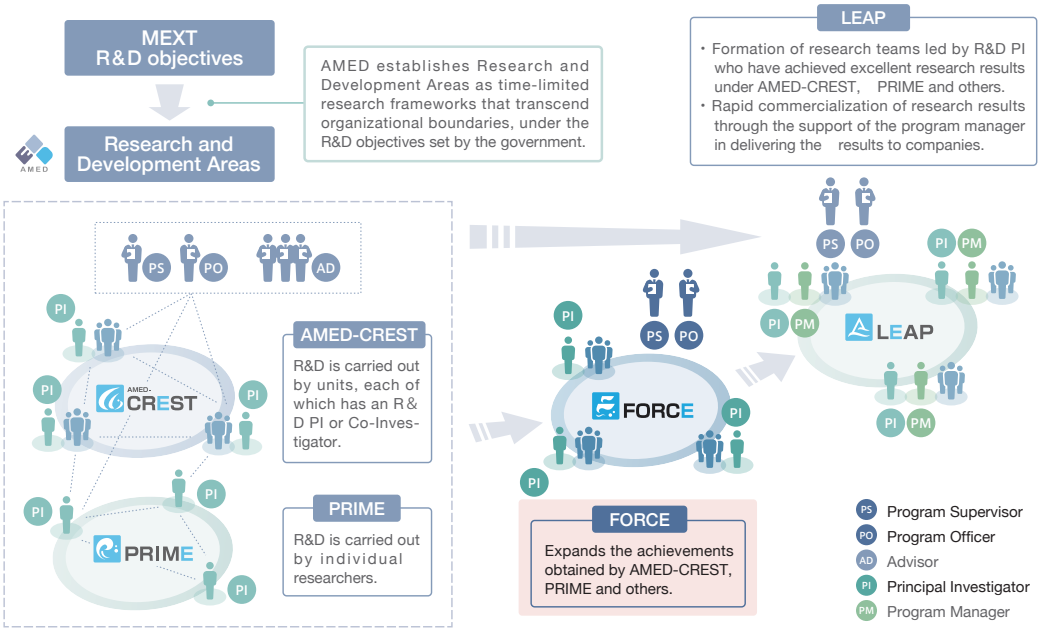
FORCE

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.



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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 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
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.

FORCE Started in 2025 · 7th period

The role of mother-to-child transmission of the microbiota in shaping IBD risk in offspring

KAMADA Nobuhiko
Specially Appointed Professor,
IFReC, The University of Osaka

It has been reported that early-colonizing gut microbiota plays an important role in the host's health not only during infancy but also in adulthood. On the other hand, disruption of the early-colonizing gut microbiota is believed to be associated with an increased risk of various diseases, including inflammatory bowel disease. This study focuses on the disruption of maternal resident microbiota -particularly oral microbiota - as a risk factor for disturbances in early-colonizing gut microbiota. The goal of this study is to unveil the relationship between oral bacteria acquired through mother-to-child transmission after birth and the risk of disease in children.

Elucidating the role of a B-cell pro-migratory factor in the pathogenesis of immune disorders

SUZUKI Kazuhiro
Professor, Immunology Frontier Research Center,
The University of Osaka

The migration of immune cells is essential not only for host defense but also plays a role in the pathogenesis of various diseases. We identified the COMMD3/8 complex as a signaling adaptor for chemokine receptors and demonstrated its critical role in B cell trafficking. In this project, we aim to translate findings from mouse models to human systems and elucidate the pathogenic role of the COMMD3/8 complex in immune disorders. Ultimately, our goal is to develop novel therapeutic strategies targeting immune cell migration for the treatment of immune-mediated diseases.

Elucidation of heart failure mechanisms induced by innate immune memory and exploration of therapeutic targets

FUJIU Katsuhito
Project Professor,
Graduate School of Medicine, The University of Tokyo

Basic research has suggested that heart failure imprints innate immune memory on hematopoietic stem cells in the bone marrow. Macrophages derived from these cells may lose their organ-protective functions, exacerbating heart failure, causing recurrence, and contributing to associated multi-organ diseases. This study aims to determine whether such immune memory exists in hematopoietic stem cells from human heart failure patients. We will also develop a novel diagnostic method capable of identifying pathological stem cells, laying the foundation for new strategies in heart failure diagnosis and treatment.

Diagnostic and therapeutic development for age-related diseases targeting senescent cells

MINAMINO Tohru
Professor, Department of Cardiovascular Biology and Medicine, Juntendo University Graduate School of Medicine

We have previously succeeded in developing a senolytic vaccine targeting senescence-associated antigens, and demonstrated that its administration leads to improvements in pathological aging phenotypes associated with age-related diseases. Building upon these findings, the present study aims to develop a diagnostic method for the accumulation of senescent cells and a novel anti-senescence therapy, both targeting senescence-associated antigens, with the ultimate goal of controlling the onset of age-related diseases that contribute to the gap between healthspan and lifespan.