

【Moonshot Goal 2】

R&D Concept of “Realization of ultra-early disease prediction and intervention by 2050.”

February 2020

Ministry of Education, Culture, Sports, Science and Technology

1. Moonshot Goals

Within the Moonshot Goals (decided on January 23rd, 2020, by Plenary session of Council for Science, Technology and Innovation), the Ministry of Education, Culture, Sports, Science and Technology (“MEXT”), with Japan Science and Technology Agency (“JST”) as a research and development promotion agency, will undertake research and development activities for achieving of the following Goal.

<Moonshot Goal>

“Realization of ultra-early disease prediction and intervention by 2050”

- Establishment of a system for disease prediction and evaluation of pre-symptomatic states through integrated analysis of the entire functional network between human organs, and suppression and prevention of disease onset, by 2050.
- Establishment of a strategy that enables the conversion of a pre-symptomatic state to a healthy state, by clarification of functional changes in human physiology along life course considering the comprehensive network between organs, by 2050.
- Identification of disease-related network structures and establishment of innovative prediction and intervention methods by 2050.
- Understanding of the comprehensive network between human organs by 2030.

2. Direction of research and development

Based on the discussion and proposal made in the Moonshot International Symposium (held in December 17, 18, 2019), direction of research and development at present is shown as follows.

(1) Area and field to promote challenging R&D

Particularly considering Japan's decreasing birthrate and aging population, it is important to increase healthy lifespan expectancy. To do this, it is necessary to go a step further than the conventional approach of treating the disease after the onset and start an innovative research program with the new concept of disease prevention by identification at extremely early disease stage or before becoming symptomatic.

To realize ultra-early disease prediction and intervention, it is necessary to promote R&D on the technologies as shown in Fig.1 (observation, manipulation, measurement, analysis, database creation), and advance understanding of the comprehensive network between human organs through integrating these technologies. In these research fields and areas, challenging R&D should be promoted.

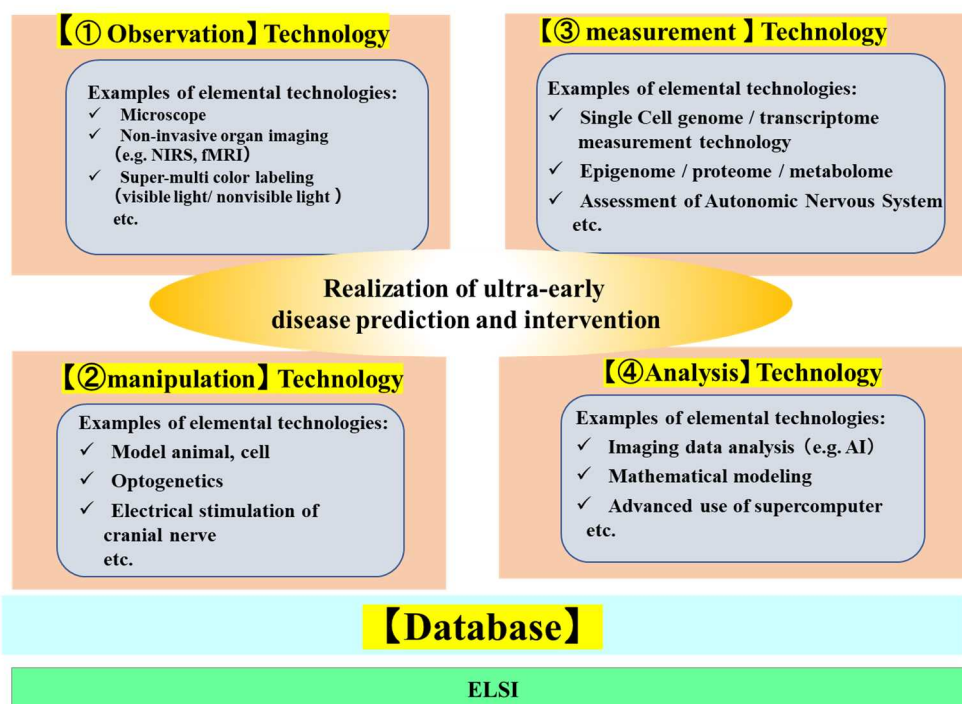


Fig.1 Main fields and areas of R&D required for realization of ultra-early prediction and intervention.

(2) Research subject for realization of MS Goal

The image in Fig.1 is the area and field for challenging R&D to be promoted under the Moonshot Research & Development Program. R&D that contribute to the achievement of this MS goal "realization of ultra-early disease prediction and intervention by 2050" should proceed. In order to have the most effective and efficient countermeasure, the most cutting edge scientific trends shall be researched and used for R&D.

And in concrete terms, the aim is to perform an integrated analysis of the networks between organs and based on this develop a system that simulates these networks. Development of such a system will also contribute to predicting and preventing diseases at an early stage.

In conducting R&D, various sources and types of knowledge and ideas will be adopted, stage gates will be established. And evaluation will be conducted to promote R&D to achieve Goal.

In addition, from the viewpoint of smoothly implementing research results in society, a system that enables researchers in various fields to participate in ethical, legal, and social issues will be considered.

(3) Direction of research and development for realization of the Goals

○ By 2030

Understanding of the comprehensive network between human organs by 2030.

○ By 2050

Establishment of a system for disease prediction and evaluation of pre-symptomatic states through integrated analysis of the entire functional network between human organs, and suppression and prevention of disease onset, by 2050.

Establishment of a strategy that enables the conversion of a pre-symptomatic state to a healthy state, by clarification of functional changes in human physiology along life course considering the comprehensive network between organs, by 2050.

Identification of disease-related network structures and establishment of innovative prediction and intervention methods by 2050.

Understanding of the comprehensive network between human organs by 2030.

In order to realize ‘ultra-early disease prediction and intervention’, first of all, we need a comprehensive understanding of the network between human organs. In addition, we need to establish a database containing comprehensive information about the network between all organs at the cellular level. Finally, it is necessary to develop and commercialize ultra-early disease prediction and intervention technologies based on a simulation system. Therefore, we aim at understanding the comprehensive network between human organs by 2030. Fig. 2 shows how to proceed with R&D to achieve the Moonshot Goal by realizing the ambitious R&D plan.

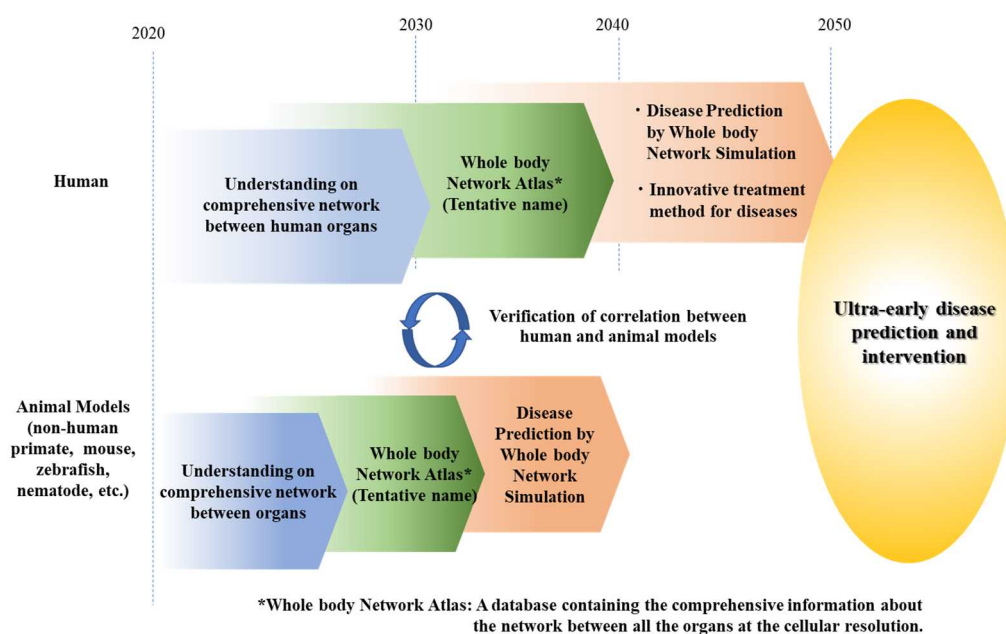


Fig.2 R&D process toward the realization of ultra-early prediction and intervention

<Reference : Analysis for realization of the Goals>

Summary of content which is analyzed in the Initiative Report presented in Moonshot International Symposium is shown, as follows:

(1) Structure of research fields and technologies

The MS goal will be driven by data research, which has rapidly increased its presence in recent years, and develop and use innovative basic technologies (observation, manipulation, measurement, analysis) to increase understanding of health and disease and ultimately detect and prevent disease onset early through analyzing the comprehensive networks between organs. Ambitious R&D is required.

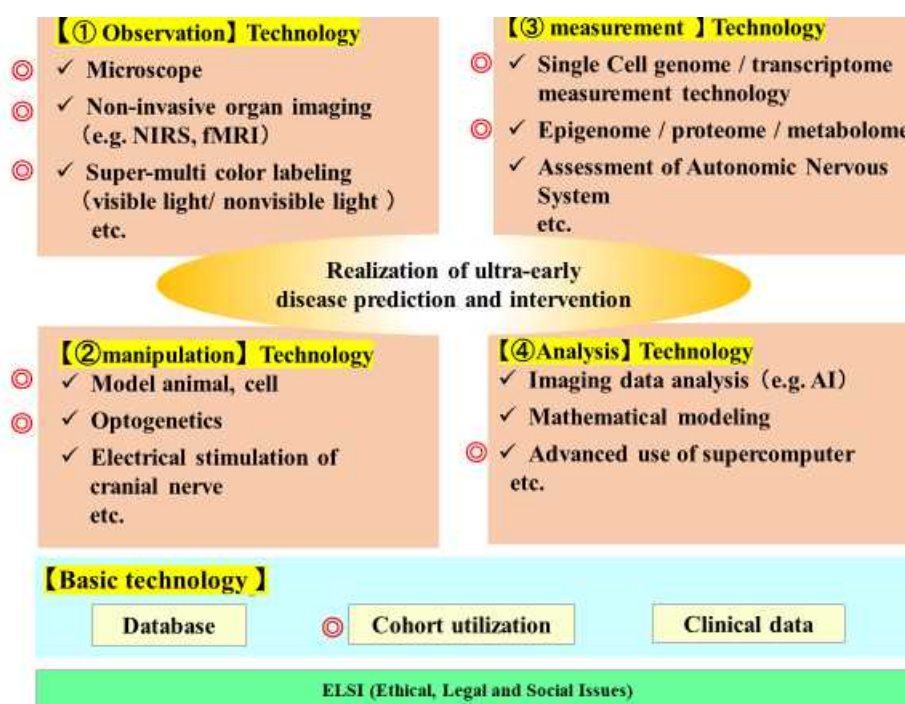


Fig. 3 Structure of research fields and technologies mainly related to ultra-early prediction and intervention

In Fig. 3, the strength areas of Japan are indicated by double circles. In general, Japan holds a leading position in various core technologies and life phenomena research, that lead to health and medical technology improvements. Regarding databases and clinical data, there is a world shortage of these assets, and they are in particular demand in Japan. However, regarding cohort usage, a relatively large cohort composed of super elderly persons only exists in Japan, and Japan

has the world’s largest scale and highest quality genome cohort.

By expanding these advantages and performing strategic integration, we expect to create results with great impact.

(2) R&D trends in related fields

Here we describe existing large scale projects that are relevant to MS goal.

① Large US projects『Brain Initiative』

- In April 2013 the former US president Mr. Barack Obama announced the “Brain Research through Advancing Innovative Neurotechnologies (BRAIN) Initiative”, and the project started in 2014.
- The project mission is the “development and application of technology for understanding human brain function”. The project is aimed at the development and application of new technologies to elucidate how the brain functions through the interaction of individual brain cells and neural circuits. It also aims to elucidate the complex relationship between the brain and behavior that enables the recording, processing, use, storage, and withdrawal of a large amount of information.

Table1. Overview of the US Brain Initiative

Research area	Participating research institutions	Implementation period and Budget etc.
1. Technology development by utilizing the results of nerve and brain research	• Federal government agency NIH, NSF, DARPA, IARPA, FDA, DOE	• From 2014 to 2025 • Approx. \$430 million in FY2019
2. Brain function visualization by promoting dynamic imaging	• Private foundation, research institute, and private company	• 21st Century Cures Act will contribute to approx. \$ 1.5 billion in FY2017-FY2026
3. Brain function research	National Photonics Initiative, Brain & Behavior Foundation, Simmons Foundation, The Kavli Foundation, Allen Institute for brain, Janelia Research Campus, Salk Institute for Biological Studies, Google, GlaxoSmithKline, GE, etc.	• Budget in FY2019 includes \$120 million under this bill
4. An integrated understanding of brain function and behavior		
5. Promotion of use to patients		

- ② Large European Union research project 『Human Brain Project』
- The Human Brain Project started in 2013 as EU-FET (Future and Emerging Technologies) .
 - Its purpose are: — integration of brain science, information and communication technology, and medical treatment
 - construction of ICT integrated infrastructure research platform, and data integration.
 - Experimental basic research has been performed to provide data for this purpose.

Table2. Overview of EU Human Brain Project

Research area	Participating research institutions	Implementation period and Budget etc.
1.Mouse Brain Organization 2.Human Brain Organization 3.Systems and Cognitive Neuroscience 4.Theoretical Neuroscience 5.Neurominformatics Platform 6.Brain Simulation Platform 7. High-Performance Analytics and Computing Platform 8.Medical Informatics Platform 9.Neuromorphic Computing Platform 10.Neurorobotics Platform 11.Central Services 12. Ethics and Society	<ul style="list-style-type: none"> • EU-FET (Future and Emerging Technologies) Flagship program 112 organizations in 24 countries • In Japan, Okinawa Institute of Science and Technology and RIKEN participate in this project. 	<ul style="list-style-type: none"> • From 2013 to 2023 • \$11 billion / 10 years

- ③ Large Japan research project『Brain/MINDS』
(Brain Mapping by Integrated Neurotechnologies for Disease Studies)
- The purpose is to map brain structures and functions at various levels and to improve the efficiency and sophistication of primate (marmoset) genetic manipulation technology and optical system technology. In addition, through these technologies, the project will elucidate the whole aspect of neural

circuits that perform higher-order functions in the brain of primates at the neuron level, and to contribute to overcome mental and neurological diseases and enhance information processing technology.

Table3. Overview of Japan 『Brain/MINDS』

Research area	Participating research institution	Implementation period and Budget etc.
<ul style="list-style-type: none"> • Acquisition and aggregation of image data such as schizophrenia / depression / dementia / Parkinson's disease / autism • Comparison with human disease image data / Correspondence between differences and similarities between humans and monkeys • Identification of neural circuits important for human mental activity • Development of translatable indicators for brain behavior linked to humans • Elucidation of the brain and neural circuit using marmoset 	<p>【Representative organization】</p> <ul style="list-style-type: none"> • RIKEN • Kyoto Univ. • Keio Univ. <p>【Clinical Research Group】</p> <ul style="list-style-type: none"> • The Univ. of Tokyo • Kyoto Univ. • Tokyo Medical and Dental University <p>etc.</p>	<ul style="list-style-type: none"> • From FY 2014 to FY 2024 • Government budget: 3,225 million JPY (FY2019)

④ International project 『Human Cell Atlas』

- The purpose is to categorize and catalog the type, state, and lineage of all human cells.
- The project aims to construct a map of human cells including cell types, 3D locations, geographical and racial differences, using a single-cell transcriptome in all major human tissues.
- Advances in measurement technology allowed this project to start. (single-cell analysis made the detailed profiling of each cell possible)

Table 4. Overview of International Project 『Human Cell Atlas』

Research area	Participating research institution	Implementation period and Budget etc.
<ul style="list-style-type: none"> • Sample adjustment / analysis technology of Brain / Immune / Gastrointestinal (Gastrointestinal) / Skin / Tissue • Software tools, etc. 	<p>The United States globally directs this project.</p> <ul style="list-style-type: none"> • UK EMBL-EBI, US Broad Institute, US UCSC, Genomics Institute, etc. • In Japan, RIKEN participate. 	<ul style="list-style-type: none"> • From 2017 • Supported by the various public and private projects, directed by the Zuckerberg Foundation.

(3) Strengths of Japan, trends in global research community

Table5 shows how Japan currently compares with other major nations in research and technical areas that are relevant to this Working Group. In basic research Japan has established its strengths in:

- “Brain and neuroscience”

Japan is a world leader in this field. For many years Japan has carefully maintained both human resource and research resource among universities and research institutes. As a result, physiological technologies for analyzing the nervous system were developed to a high standard. Forming cross-functional research groups for integrated research was also beneficial to pursue specific areas and new academic interests. In recent years, Japan’s “marmoset (primate) brain clarification project” was internationally recognized especially for investigating functional brain molecules through sedated animal analysis. -

“Optics / Imaging” and “Bioimaging”

Japan’s leading position is exemplified by successful development of small organic moleculebased probes for imaging – a fruit of historical strength in synthetic organic chemistry. In addition, Japan is a pioneer in the area of imaging technologies such as PET, MRI, and NMR. For example, fMRI, an important tool that directly measures the blood flow in the brain to observe brain activity, was invested in Japan.

-“Data analysis and artificial intelligence (AI) “

Regarding measurement data analysis, basic research such as medical image processing is active in Japan, but there are restrictions on the data that can be handled and the absolute number of participating researchers is

insufficient. Historically, Japan’s researchers were quite active in this field making considerable contributions. However, in recent times, the amounts of financial investment in other countries have been greatly surpassing that of Japan. Consequently, at present, Japan is not in a position to claim Data analysis and AI as its strength. Strategically promoting this field is essential for the future.

Table 5. International comparison of related research and technical fields

Country, Region	Phase	Brain and neuroscience		Optics Imaging		Bioimaging		Data analysis (AI)	
		Current status	Trend	Current status	Trend	Current status	Trend	Current status	Trend
Japan	Basic research	◎	→	◎	→	◎	↘	○	↗
	Applied research	○	→	○	→	○	→	△	→
US	Basic research	◎	→	◎	↗	◎	→	◎	↗
	Applied research	◎	→	○	↗	◎	→	◎	↗
EU	Basic research	○	→	◎	→	◎	→	○	↗
	Applied research	○	→	◎	→	◎	→	○	↗
China	Basic research	△	↗	○	↗	○	↗	◎	↗
	Applied research	△	↗	△	↗	○	↗	◎	↗

(Source) Panoramic View of the Systems and Information (2019)

(Note 1) Phase

Basic research phase: Range of basic research by universities, national laboratories, etc.

Applied research/development phase: Range of technology development (including development of prototypes)

(Note 2) Current level

*Absolute evaluation, not a relative evaluation based on the current level in Japan.

◎: Particularly remarkable activities and results

○: Remarkable activities and results

△: No remarkable activities or results

×: No activities or results.

(Note 3) Trend

↗ : Upward trend → : Maintaining current level ↘ : Downward trend