Executive Summary

Breakthrough discoveries and cutting-edge technologies in life science and clinical research area are driving our lives healthier and more sustainable.

Cross-interactions between various disciplines, such as clinical medicine, biology, chemistry, physics, informatics, and engineering are the key to deliver rapid advances in analytical methods, tools, and technologies, which are vital for attempts to decipher the rules of life. In addition, it is noteworthy that data science is becoming more and more important in the field of life science and clinical research, as researchers in this field are dealing with big data in various aspects. Multi-disciplinarity is crucial also in the process, where the outcomes of fundamental research turn into game changing innovations as a series of social applications; not only the technological robustness, understanding of various social aspects, such as social demands, market trend, legal requirements, economic viability, start-up company ecosystem, social acceptance of advanced technologies have to be assessed. An iterative interaction can be observed during the process in which social implementation of advanced technologies; application of new technologies derived from fundamental research often present new subjects that have to be addressed by further fundamental research.

Here we report the latest trends and topics in life science and clinical research area, ranging from basic to applied research activities, moreover, the social issues, such as science/technology policies, social demands, market trend, legal requirements, ethical issues, economic viability, start-up company ecosystem, social acceptance of advanced technologies are also assessed. The report mainly covers the recent topics in Japan with comprehensive comparison to global trends. During our analyses on the social aspects, we have identified that truly effective technologies/ solutions are much sought after, and more importantly, such solutions also have to be concurrently sustainable in various aspects. The word "sustainability" doesn't only mean to ensure the earth's natural systems which can support humanity's safe operation, but also includes the adequate/just use of medical/human/economic resources, which are also finite. The concept that combines the sustainability of earth's natural systems and human health is known as "Planetary Health" which was originally proposed by Horton et al., in the Lancet journal in 2014.

In many cases, the best efficacy and sustainability are contradicting each other; for example, using biomass fuels could reduce CO_2 emission from fossil resources, but at the same time it could squeeze the farmland for food production, possibly resulting in the destruction of natural forest with high biodiversity. In the case of medical treatment, cutting edge medications derived from advanced bioscience could provide cures for incurable disease, but the costs are often so high that only world's richest can afford them, widening the health inequalities by wealth. In many cases, several factors are so closely interrelated that it is almost impossible to have an intuitive solution that resolves the conflicting interests of best efficacy and sustainability. Thus, what we have to pursue is not the ultimate efficacy, but the better-balanced solution over the conflicting various interests. In order to see better- balanced solution, an objective evaluation of the solution from various aspects, including social impacts, needs to be made numerically.

In this 2023 edition, recent development in science/technology in each topic are detailed

in chapter two; in total 30 topics were categorized into 3 sections. The topics were carefully selected from the aspects of social impact, newly emerging, and fundamental. The "Health and Medical Care" section dedicated for research and development related to human health, sustainable bio-manufacturing related topics are described in the section of "Agriculture and Bioproduction", and emerging technologies serving for the advancement of both human health and bioproduction research area were outlined in the section of "Basic and Fundamental" section.

The following nine major global R&D trends were identified.

-"Omics technology", "Genome engineering (editing, synthesis, etc.)", "Protein and other structural prediction and design", "Gene therapy Genome editing therapy" "small molecule/ nucleic acid medicine", "digital medicine (medical devices, medical data infrastructure)", "environmentally friendly agriculture", "fermentation technology", "genome engineering (editing, synthesis, etc.)", "structural prediction and design of proteins, etc.", "Fermentation technology", "Breeding technology".

The results of the international comparison showed that the U.S. was overwhelmingly strong in all areas, from basic to applied, with Europe in a close second, and China rapidly increasing its presence and even surpassing the U.S. and Europe. Japan's presence in almost all areas of R&D was declining compared to Europe, the U.S., and China.

The areas of active R&D in Japan are as follows : "small molecule drug discovery", "stem cell therapy (regenerative medicine)", "gene therapy (*in vivo*/*ex vivo*)", "genome medicine", "cancer", "brain and nervous system", "immunology and inflammation", "biological clock and sleep", "organ connections", "microbial manufacturing", "plant manufacturing", "agricultural engineering", "structural analysis (biopolymers and metabolites)", and "optical imaging"

Based on the above, the following seven directions of R&D that are important for Japan have been identified.

1) Realization of individualized predictive medicine and health care
   - Acceleration of personalized medicine [health medicine & genome data integration], research and development of stratified "nutrition" and its social implementation, development of digital healthcare [medical devices, software], continuous promotion of infectious disease research [preparation for future pandemics].
2) Research and development of diverse drug discovery modalities
   - Advancement and integration of drug discovery modality technologies, development of technologies related to drug discovery process [AI, evaluation systems, etc.], exploration, identification and validation of therapeutic targets, development of GMP manufacturing technologies [vectors, cells, etc.]
3) Improving the sustainability of agricultural, food, and biotech production
   - Promote nature-positive R&D, development of technologies to reduce environmental impact, utilization of sustainable biomass, linkage of sustainability research with utilization of new biological functions
4) Advanced Measurement Technology / Development of Next Generation Biotechnology
   - Development of advanced measurement technologies [omics, imaging], development of data analysis technology [including AI], development of molecular, genetic, and cellular engineering technologies, expansion into applied fields [medicine, food and bio-

production].

5) Integrated understanding of life phenomena and elucidation of mechanisms
   - Cell-tissue-organ relationship, biological system interactions [immunology/neuron/metabolism, etc.], study of various organisms [microorganisms/plants/animals/humans], observation and analysis of multi-scale and multi-item dynamics
6) Establish R&D DX infrastructure [AI, data].
   - Establishment of data integration/utilization infrastructure, standardization, medical, health, agricultural and basic research data, training and retention of research DX-related human resources, further utilization of AI-related technologies [including generative AI]
7) Building an R&D Ecosystem
   - Establishment of an innovation ecosystem [academia/companies/start-ups], research and development based on the perspective of security (food, etc.), establishment of core facilities [development and common use of cutting-edge technology & equipment], collaboration between life science/clinical medicine and humanities/social sciences

Common to all these directions is the increasing importance of research utilizing data-driven approaches. Whereas in conventional research, a wide variety of data has been used to formulate equations deductively, in recent years the big data has increasingly been used in the form of making data-driven models in the way where the models are automatically generated from the data (data-driven). Data-driven model generation, as typified by deep learning, is an important technology in all situations involving life sciences and clinical research, as it is powerful for modelling phenomena that are difficult to describe explicitly using governing equations. As information science skills are essential for data-driven approaches, it is important to establish a system that can bring together researchers from different fields, including mathematics and informatics.

In addition, it has been said that the construction of an innovation ecosystem, including fostering of start-ups and venture companies, and the importance of human resource development are important in promoting these research and development systems, and it is important to continue to make strategic efforts based on Japan's systems and structures. The importance of strategic initiatives based on Japan's systems and structures will continue to be important.