Executive summary

Here we provide Panoramic View Report 2021, for life science and clinical research field. This report guides you to show the latest development of science and technology related to biological and medical science, ranging from basic to applied research and partly experimental development. The report mainly covers the recent topics in Japan, with comprehensive comparison to worldwide trends.

The topics and research areas argued in this report are carefully chosen following our criteria: i) basic research topics which could contribute to applied biological/medical research in the future. ii) transformative technological developments that are applicable in wide range of science. Research topics which could be applied to the society are listed as much as possible.

As we identified that development in science/technology and the social activity are mutually influencing each other, we provided the analysis on the influence from the society to scientific development in chapter one. This includes the overview of the research strategies and the dramatic changes in research system/facility observed in advanced countries, mainly in the US and Europe.

The detailed descriptions of recent development in science/technology in each topic are illustrated in chapter two; in total 36 topics are categorized into 5 sections, reflecting the direction of their applications.

In this field, knowledge found in basic research and seeds of new technologies are applied in a small pretrial followed by social implementation with larger scale. However, this is not a linear model, but it is important to have a cycle in which its significance and effects are verified in society, new issues are set, hypotheses are extracted, and the results are returned to basic research (Fig. S1).

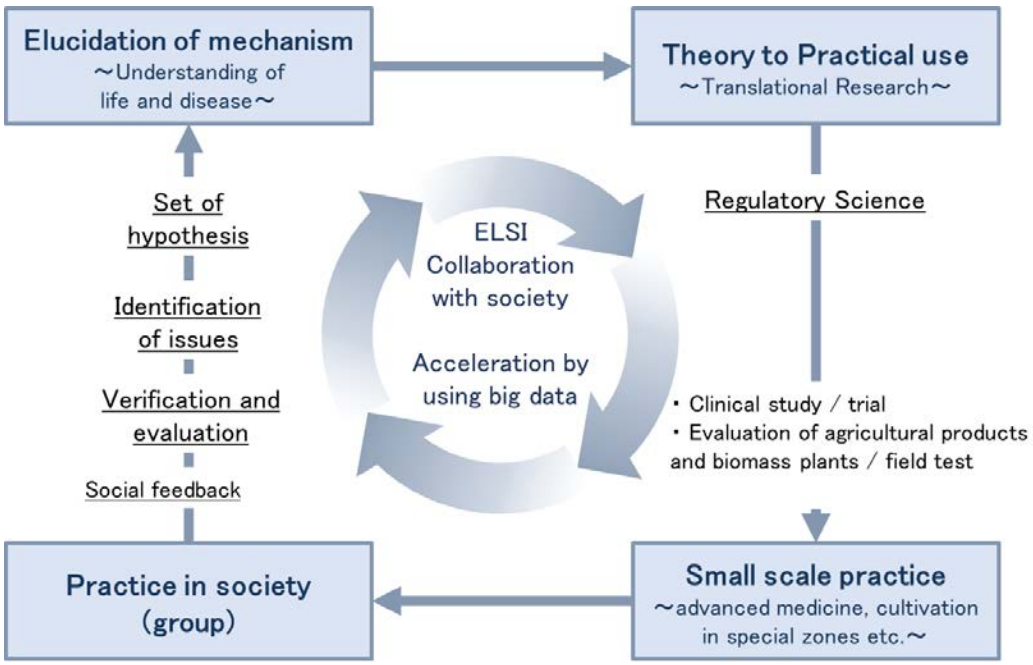

Figure S1. Iterative research ecosystem

The pandemic of COVID-19 has highlighted the problems such as delays in digital transformation. One of the benefits of digital transformation is the increase of added value. It is necessary to strongly recognize the importance of increasing added value by promptly collecting information (data) and differentiating the outcome of research and development. Solving social issues requires a "data-driven" approach to discover principles in a wide variety of data in society, but this is not necessarily a deterministic world, but a stochastic world that sometimes cannot be anticipated logically. Therefore, in addition to "pursuit of inevitability" to explore the mechanism, "control of contingency" to reduce errors is required through the utilization of statistics, AI, and new mathematics. This applies not only to the solution of social issues but also to basic research. In addition, the consent by society is required for data utilization, and research outcome must be returned to society for autonomous life of citizens (autonomous society). Strengthening the relationship between science and society, e.g. by tackling ELSI, is indispensable to establish the cycle to return the social feedback to basic research after social implementation. It is required for universities to change their mind and to promote cross-sectional research and mobilization of human resources, considering the risks associated with science and technology.

In addition to the recent COVID-19 issues, the trends in global policies on science and technology can be summarized as follows. In health and medical field, "genome based medical treatment and precision medicine", "cancer", "brain and neuroscience", "drug discovery: cancer immunotherapy, central nervous system, infectious diseases", "cell therapy and gene therapy" and "human cell landscape" are commonly prioritized. Reflecting this trend, an increase papers on "cancer" and "neuroscience" is observed in Europe and the US. In food and agriculture field, in addition to international issues such as climate change and bioeconomy, researches have been conducted under the keywords of "sustainability", "circularization" and "smart" in response to technological progress in genome editing and AI. In the field of bio-based material production, research and development based on synthetic biology are accelerating mainly in theUS, the UK and China.

Considering these circumstances, CRDS extracted 36 R&D areas from the perspectives of socio-economic impact, emerging potential and basis, and summarized trends, topics, and international benchmarks individually in the 36 areas.. The differences from the previous version are as follows;

- Considering the trend of bioeconomy, we expanded food/agriculture and bio-production field, and added “plant-based material production”, “plant-derived materials”, “plant factory” and “forestry”.
- Considering the progress of digital transformation, we emphasized the IT and robotics fields, and added "healthcare IoT", "AI/in silico drug discovery", "plant factory", "measurement x AI", "Brain Machine Interface (BMI)", etc.
- Research in the field of biology (life science/medical science) is significantly subdivided, but the trend of research is targeting complex systems, and there is an increase in issues that

cannot be solved without interdisciplinary research. We added "organ-organ association" since nervous system, immunity, digestive system, metabolism, etc. are strongly linked (neuroimmunity, immunity and microbiome in gastrointestinal tract, cancer metabolism, etc.). We also added "trans-scale imaging" because it is necessary to collaborate beyond discipline such as biology, chemistry, physics, informatics, and engineering.

From a bird's-eye view, we analyzed the major technological and research trends (changes and progress) over the past few years as follows;

- Emergence of new drug discovery/diagnostic modalities such as nucleic acid vaccine, protein knockdown drug discovery, modified immune cell therapy, optical molecule manipulation/control, therapeutic application (digital therapy), nucleic acid biomarker (liquid biopsy)
- Advances in the application of genome editing technology to the medical and food fields
- The rise of single-cell omics and the progress of understanding of life and diseases at the single-cell level
- Progress in understanding of life systems and functional evaluation using organoids
- Improvement of the spatio-temporal resolution of the analysis by the progress of imaging technology such as cryo-EM and optical imaging. Improvement of genome analysis capability by long-read NGS
- Spread of digital technologies such as AI/machine learning and BMI/cybernics to society. Advances in research automation by robotics, etc.

From the perspective of international benchmarks, the US is overwhelmingly strong from basic research to applications in all areas, and Europe also shows an overall presence, especially on biomedicine in the UK and measurement technology in Germany. Japan has strength in "macromolecular drug", "regenerative/stem cell medicine ", "plants/agriculture", "plant factories", "fisheries", "livestock", "chronobiology", "brain/neuroscience", " organ-organ association ", "extracellular vesicles", "chemical biology", "optobiology", "synthetic biology", "structural analysis", "optical imaging", "trans-scale imaging" in basic research. It has also strengths in " regenerative/stem cells medicine", "plant-derived materials", "plants/agriculture", "plant factories", "fisheries", "forestry" and "extracellular vesicles" in applied research.

While the circulatory system of basic research, applied research and experimental development is working in the US, it seems that there are environmental (structural) problems in Japan that prevent moving toward the construction and promotion of such a system. In R&D, of course, what to do is important, but how to promote research beyond the existing organization will become more important in the future. Therefore, we investigated the innovation ecosystem. In the medical R&D field in Boston in the US and London, Cambridge and Oxford in the UK, and in the agricultural R&D field in the Food Valley in the Netherlands, knowledge and technology are integrated at the world's leading universities, and a wide variety of people from startups, support

organizations and major companies are gathering together to create innovation.
From the survey of cutting-edge researches in emerging fusion fields in Europe and the US, interdisciplinary research under-one-roof is successfully conducted as a research system that creates new science and technology. By integrating high-tech equipment such as microscopes, mass spectrometers, and flow cytometers into the core facilities and assigning dedicated staff, it is possible to provide a wide range of expertise and efficient access to the equipment. On the other hand, in Japan, the development of core facilities has been delayed, making it difficult to proceed with research using high-tech equipment. This has led to a slowdown in the number of treatises in life sciences and clinical medicine as well as its diminished presence, especially in emerging fusion fields.

Based on the above-mentioned bird's-eye view of research and development, 7 global research directions and the challenges for Japan under these directions are set from the perspective of socio-economic impact and emergence（new trends in science and technology）for the next 10 years（Fig. S2）.

AI/data-driven research is becoming important in common with these challenges. It is important to build a system that encourages researchers from different fields e.g. mathematics, informatics, to gather.. There is a need for collaboration between MDs who understand diseases and PhDs in health and medical field, and between agricultural scientists and plant scientists in the field of agriculture.

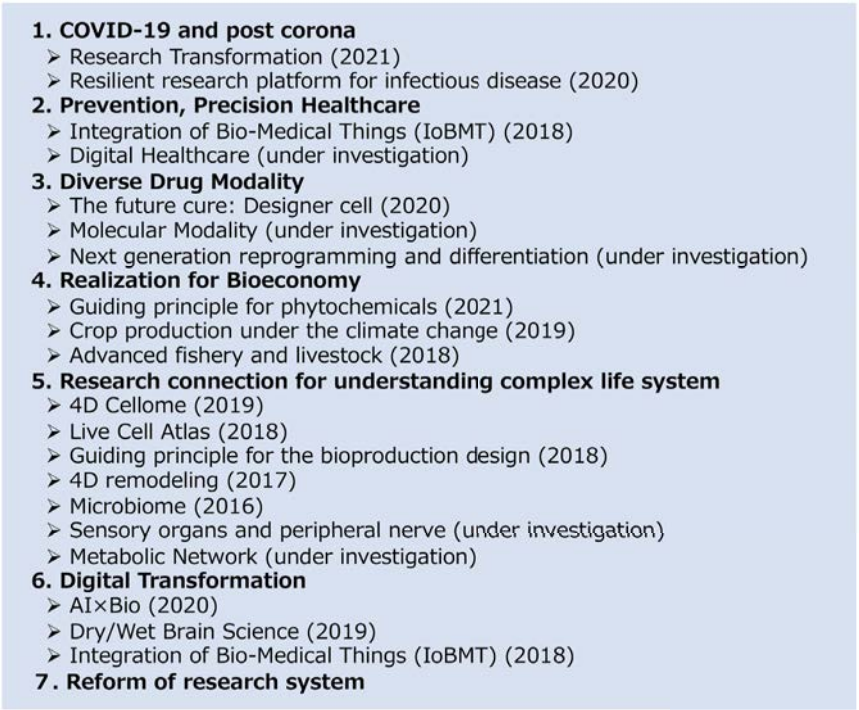

Fig. S2. Future directions and challenges for Japan

In the innovation creation process, the change from the conventional linear model to the concurrent model in which basic/applied research and commercialization proceed in parallel is accelerating. In the case of AI and genome editing technology, new discoveries and knowledge at the basic research phase are directly linked to practical use in a short period of time. Here, the role of startups, that they act as catalysts for converting the knowledge accumulated by society into value, is important. In Japan as well, there is an urgent need for universities and national research institutes to build an innovation ecosystem to promote research and development in cooperate with companies, governments, entrepreneurs and investors.