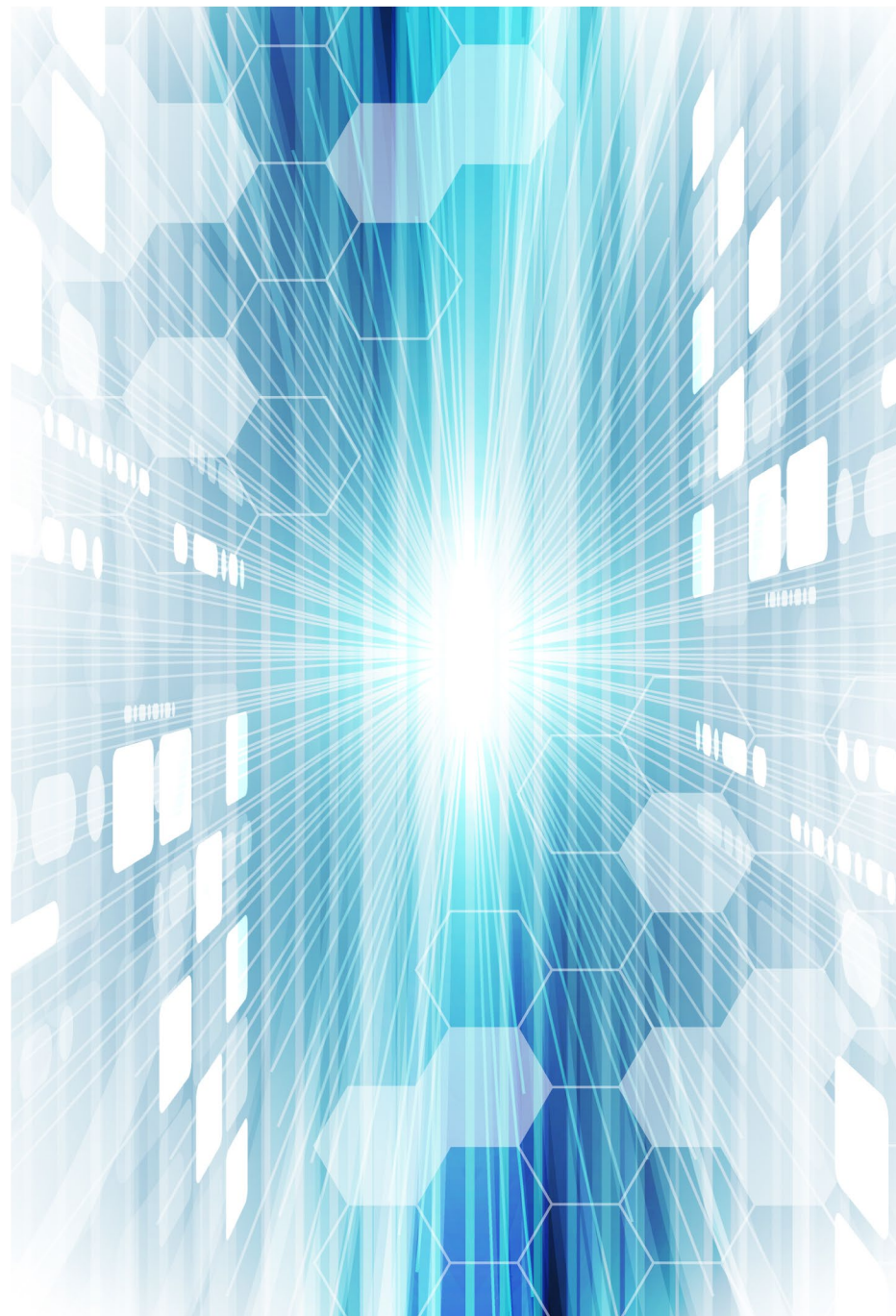


October 12th, 2018

Proposals for Realizing Social Implementation of Regenerative Cell Medicine

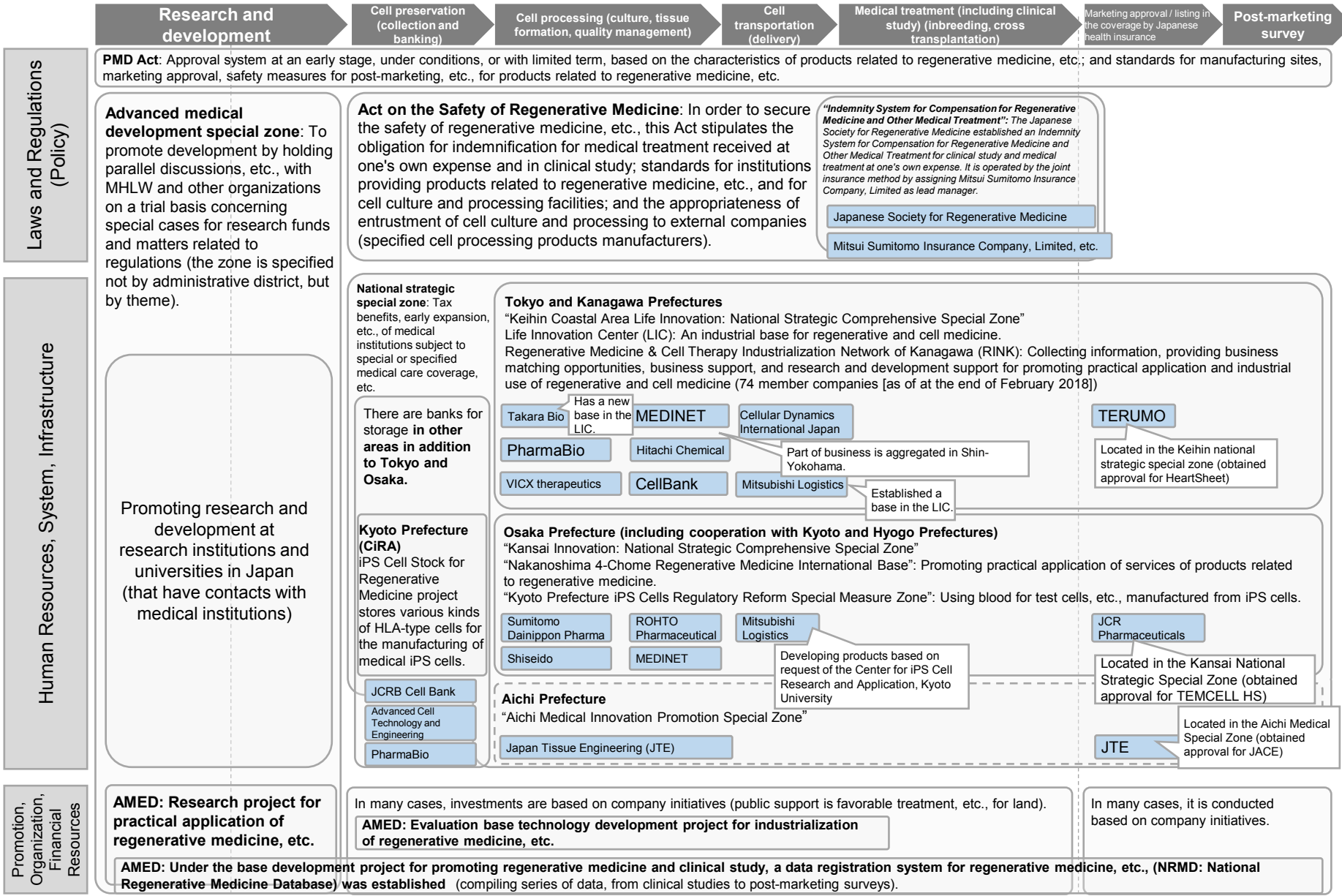


For discussion and review



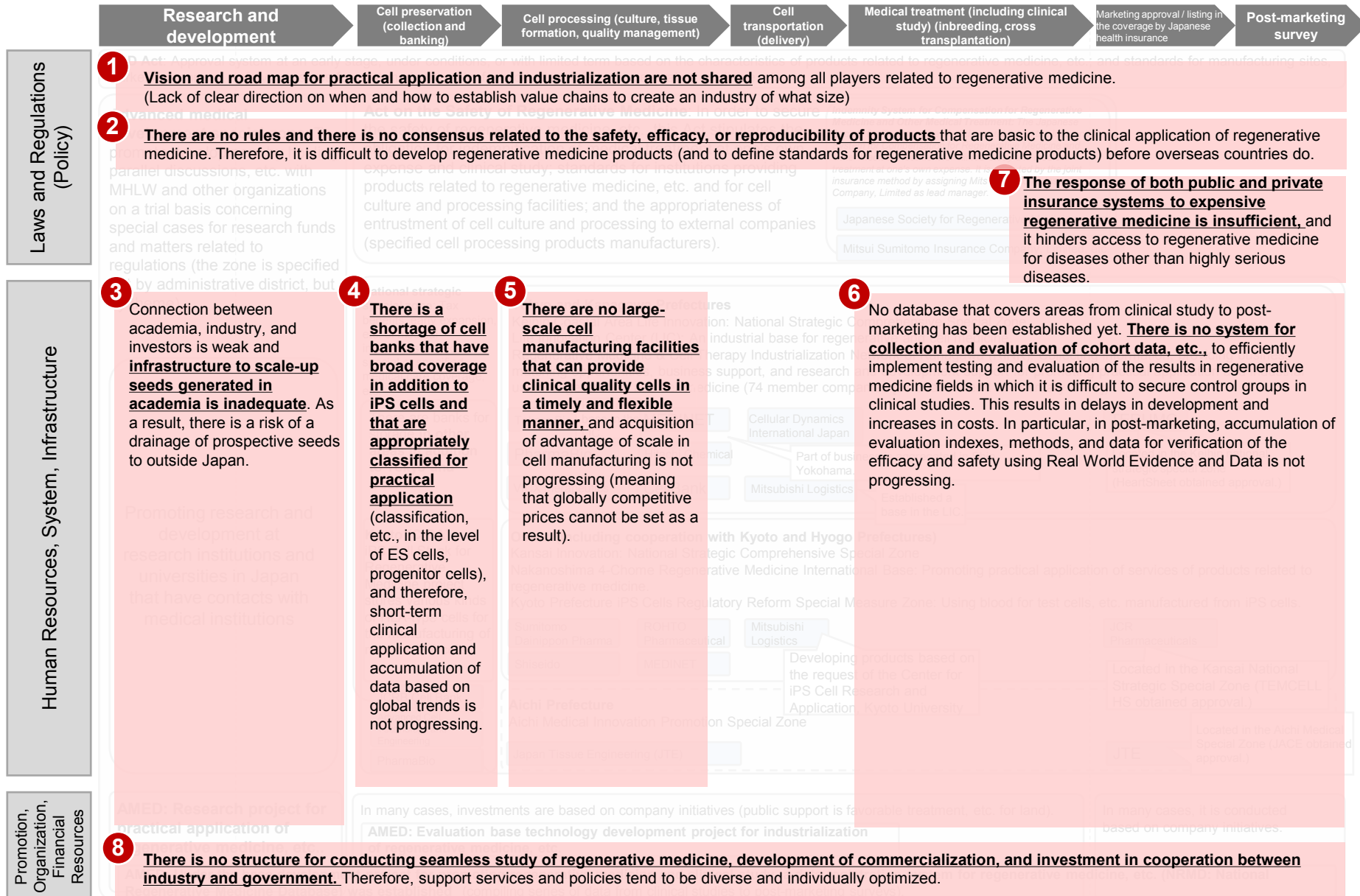
Laws and Regulations; Human Resources, System, Infrastructure; and Promotion, Organization, Financial Resources for Each Value Chain

Example of players



Major Gaps in Practical Application of Regenerative Medicine

Example of players



Proposals for Realizing Social Implementation of Regenerative Cell Medicine (1/8)

- 1** **Vision and road map for practical application and industrialization are not shared** among all players related to regenerative medicine.
(Lack of clear direction on when and how to establish value chains to create an industry of what size)

Overseas activities

- Proposal of the House of Commons, Science and Technology Committee in UK: “**Regenerative Medicine Fifteenth Report of Session 2016–17**”
- Proposal of the National Cell Manufacturing Consortium in US: “Achieving Large-Scale, Cost-Effective, Reproducible Manufacturing of High-Quality Cells A Technology Roadmap to 2025”

Proposal (1)

All players related to regenerative medicine share problem awareness and design procedures for industrialization of regenerative medicine. During the process, establish an eco-system so that the process of Production → Medical Treatment → Follow-up after medical treatment can be provided via a one-stop system in consideration of the characteristics of handling live cells in regenerative medicine.

- Share problem awareness through preparation and use of this map.
- Coordinate the above by cooperation with local bases and aim to form a local promotion system.
- Speed up increases in scale and commercialization through development of incubation programs and VC participation.
- Eventually, lead these activities to discussion with relevant government agencies (MHLW, METI, MEXT) and to development of relevant laws and regulations so that the roadmap for regenerative medicine can be re-defined nation-wide.

Proposals for Realizing Social Implementation of Regenerative Cell Medicine (2/8)

- 2** There are no rules and there is no consensus related to the safety, efficacy, or reproducibility of products that are basic to the clinical application of regenerative medicine. Therefore, it is difficult to develop regenerative medicine products (and to define standards for regenerative medicine products) before overseas countries do.

Overseas activities

- (UK) Catapult determined the safety standards as consensus between relevant persons without waiting for establishment of the science.
- (USA) Standards for safety, efficacy, and reproducibility have not been established by consensus between relevant persons, and therefore the situation is disturbing the activities for practical application.

Proposal (2)

Establish rules and consensus for “manufacturing” in regenerative medicine that comprehensively involve relevant players from study to practical application (academia, industry, and government) concerning regenerative medicine, as “living matter.”

- In consideration of the characteristics of “living matter” that are different from previous drugs, which are “inanimate objects,” establish a system to flexibly set and re-define safety, efficacy, and reproducibility for each disease.
- Evaluate conformity to ICH after accumulating data on regenerative medicine products and submit a proposal.
- Formulate rules and establish consensus to secure quality on both the shipping side and timing and the receiving side and timing during the transportation of cells.
- Encourage relevant players based on the initiative of the government and formulate rules and establish consensus.

Proposals for Realizing Social Implementation of Regenerative Cell Medicine (3/8)

- 3** Connection between academia, industry, and investors is weak and **infrastructure to scale-up seeds generated in academia is inadequate**. As a result, there is a risk of a drainage of prospective seeds to outside Japan.

Overseas activities

- (UK) Three organizations, BBSRC, EPSRC, MRC, cooperated and formed the UK Regenerative Medicine Platform. It accumulates and shares knowledge and know-how held by individual players in the Platform and thereby supports the seamless transfer of seeds of regenerative medicine from the search phase to clinical and commercial applications.
- (Canada) The Centre for Drug Research and Development (CDRD) cooperates with over 50 universities and research institutions, proactively discovers and evaluates seeds (including regenerative medicine) based on the opinions, etc., of KOL, and supports commercialization of prospective seeds.

Proposal (3)

Establish a network of incubation and acceleration programs by designing research and commercialization plans and by cooperation between Life Science Parks in order to promote the commercialization of research results of universities, etc. (“Japanese BioHub”).

- Create opportunities to design the best fast-to-market strategies by including the perspectives of all players (regulations, industry, etc.) related to regenerative medicine in the commercialization plan of research in the university in anticipation of the goal.
(Integrate research plan review from the external perspective and events, such as business competition, etc., into the regular research and development process.)
- Cooperate with pitch contests and other events sponsored by the Life Science Park in addition to public offices and local government.
- Provide mentoring support by overseas major healthcare VC.
- Provide advice from the clinical and commercialization perspectives in the Health Park and provide spaces that can respond even to PoC.

Proposals for Realizing Social Implementation of Regenerative Cell Medicine (4/8)

- 4** There is a shortage of cell banks that have broad coverage in addition to iPS cells and that are appropriately classified for practical application (classification, etc., in the level of ES cells, progenitor cells), and therefore, short-term clinical application and accumulation of data based on global trends is not progressing.

Overseas activities

- (EU) EBiSC provides clinical grade cell banks and associated services at multiple bases, including in the UK and Germany, etc. Under the initiative of pharmaceutical companies, consortiums that promote the use of drug discovery of cell medicine strongly support commercialization of cell medicine in Europe, such as the creation of disease models using genome editing and provision, etc., of differentiation lineage, in addition to cell banks.
- (UK) UK Stem Cell Bank holds and manages various kinds of human ES cell strains.
- (USA) WiCell holds human ES cell strains of National Stem Cell Bank, etc., and iPS cell strains have also been expanded recently. In addition, the California Institute of Regenerative Medicine (CIRM) has an iPS cell bank for research purposes in six disease fields, such as Alzheimer's disease, etc.
- (Australia) Genea Biocells has 150 or more human ES cell strains.

Proposal (4)

Establish under government initiative a large-scale cell bank network that covers iPS, ES, and MSC cells and is based on their future use in business.

- Establish cell banks in multiple bases in Japan based on common quality and safety standards.
- Classify cells in the cell bank by direction of differentiation and by use.
- Establish logistics and storage infrastructure in order to achieve smooth provision of cells to peripheral clinical institutions.
- Promote use and commercialization of drug discovery related to cell medicine by providing relevant services, such as creation of disease models, etc.

Proposals for Realizing Social Implementation of Regenerative Cell Medicine (5/8)

- 5** **There are no large-size cell manufacturing facilities that can provide clinical quality cells in a timely and flexible manner**, and acquisition of advantage of scale in cell manufacturing is not progressing (meaning that globally competitive prices cannot be set as a result).

Overseas activities

- (UK) Catapult established cell manufacturing facilities that are available for many products in urban hubs of major cities, including London, Cambridge, and Oxford.
- (Canada) CCRM built a GMP facility, the Centre for Cell and Vector Production (CCVP), with public support (scheduled to start operation in October 2018). It is close to advanced medical institutions and research institutions and is responsible for the manufacturing of various cell products at an early stage of development.
- (Australia) CTM CRC conducts pilot manufacturing of various kinds of cell species.
- (USA) CMaT created a roadmap for stable manufacturing and supply of cell products of MSC, T cells, and iPS cells.

Proposal (5)

Establish large-size cell manufacturing facilities that can manufacture iPS, ES, and MSC cells and can deliver them to peripheral facilities.

- Initial investment for start-up of future industry using a structure of a semipublic “Japanese Catapult.”
- Provide modular-type and prefabricated facilities for which the equipment and interior can be tailored based on the needs of tenants.
- Consider the use of research facilities in each Health Park.

Proposals for Realizing Social Implementation of Regenerative Cell Medicine (6/8)

6 No database that covers areas from clinical study to post-marketing has been established yet. **There is no system for collection and evaluation of cohort data, etc.**, to efficiently implement testing and evaluation of the results in regenerative medicine fields in which it is difficult to secure control groups in clinical studies. This results in delays in development and increases in costs. In particular, in post-marketing, accumulation of evaluation indexes, methods, and data for verification of the efficacy and safety using Real World Evidence and Data is not progressing.

Overseas activities

- Parts of integration and analysis of cohort data are conducted by academia, and types of diseases and study endpoints are visible to a limited extent.
 - Example: Collecting and analyzing data of overall survival and progression-free survival in patients with stage 4 melanoma or advanced pancreatic cancer.

Proposal (6)

Consolidate large-scale cohort data that include medical data (health checkups, electronic charts, and other individual data from birth), lifelogs, and genomic data.

- Establish a concept of “Internet Cohorts” into which data that can be collected from web services and wearables, etc., is also integrated.
- Promote PoC, such as remote and virtual clinical study, etc., using the aforementioned data (in fields other than regenerative medicine) (including promotion of use of data of patients in special zones).
- Establish verification systems of efficacy and safety in post-marketing using Real World Data.
- Update measurement indices and methods of outcome and cost-effectiveness from the perspective of medical economy specializing in regenerative medicine (establishing an approach to substituting or complementing QALY index, etc., that are usually used).

Proposals for Realizing Social Implementation of Regenerative Cell Medicine (7/8)

- 7** **The response of both public and private insurance systems to expensive regenerative medicine is insufficient**, and it hinders access to regenerative medicine for diseases other than highly serious diseases.

Overseas activities

- There are no cases in which special drug prices and reimbursement are applied; however, the introduction of a system to cover expensive medical care, such as risk-sharing agreements, etc., is being considered.

Proposal (7)

Establish “two-tier” and “three-tier” insurance structures through joint projects by regenerative medicine players, insurance companies, and government-affiliated agencies, in the Health Parks specialized in regenerative medicine.

- Define and collect endpoint data and data necessary for calculating cost-effectiveness of regenerative medicine.
- Implement pilot programs and measure effects on specific patient cohorts.

Proposals for Realizing Social Implementation of Regenerative Cell Medicine (8/8)

8 There is no structure for conducting seamless study of regenerative medicine, development of commercialization, and investment in cooperation between industry and government. Therefore, support services and policies tend to be diverse and individually optimized.

Overseas activities

(UK) Catapult operates facilities through collaborative investment by both government and private sectors and supports practical application. In addition, it has built and is managing UK preclinical research databases, and has visualized an overall view of pipelines in the pre-clinical stage related to cells and genes. It leads activities to secure the diversity of research (cell species subject to the research, etc.), including private investors, by releasing the visualized information.

Proposal (8)

Provide funds that are seamless with a system to achieve public-private fusion-type innovation.

- Build and operate a local system to achieve innovation using diversified and professional activities of private factors based on the coordinated functions of public institutions.
- Establish a public and private fund for regenerative medicine in which multiple funding sources are combined to enable provision of continuous and seamless funds for public research.
- Invest and operate semi-public business through a “Japanese Catapult” program at important bases on the value chain (cell banks, manufacturing, etc.).

Cooperation



A.T. Kearney



Kanagawa Prefectural Government



Shonan Health Innovation Park

[Disclaimer]

The information contained in this document is current as of October 12, 2018. Shonan Health Innovation Park cannot guarantee its completeness, reliability and accuracy beyond this date.

Shonan Health Innovation Park reserves the right to make revisions to this document based on future surveys, discussions and reviews.