Introduction to Regenerative Medicine

The ACCJ and EBC applaud the Japanese government's efforts to amplify the cutting edge regenerative medicine research being done in Japan.[1-2] Translating these new innovations into commercial applications will require much more thought and attention to regulatory processes. Japan has an opportunity to lead the world in the commercial application of regenerative medicine; however, there are several aspects to the current approach that will require further attention.

Regenerative Medicine is a medical practice to repair or replace dysfunctional or diseased tissues and organs with new functional tissue. Regenerative Medicine is expected to pave the way for new approaches to the treatment of disease that heretofore have been considered incurable by traditional treatment options including surgery and medication, and to overcome the chronic shortage of donor organs, tissues and cells, especially in Japan.[3] To bring these promising new therapeutic options to patients quickly, Japan has already taken action to address a number of outstanding medical and commercial issues.

Japan's new regenerative medicine law enacted in November 2014 clarifies pre-existing regulatory ambiguities in guidelines and classifies cell types into three categories based on their risks. The regulations and classifications governing autologous and allogeneic therapies will need to be calibrated to the level of risk involved and simultaneously should consider the proof of concept and pre-existing clinical research data. The strictness of rules governing cell therapies should reflect the gradation in risk when moving along a continuum from autologous cells which originate from the same patient, to allogeneic cells which require a matching donor and which hold the promise of providing a large number of patients with accelerated new regenerative medicine treatments using pre-qualified cell stocks and cell banks.[4]

It is widely recognized that the therapeutic efficacy and result of using pure cell populations versus crude cell samples sometimes differ significantly.[5-9] Depending on the goal of cell quality and clinical need, the required level of purity of therapeutic cells can differ. In regenerative medicine, as with the gradation in risk with cell source and types of therapies, the need for purity of sample should also be viewed as a gradation moving from autologous to allogeneic cells. Purity requirements should give consideration for maximizing safety and efficacy and mitigating the risk of graft-versus-host disease (GVHD), rejection, and unexpected effect of crude cells. For both autologous cell therapies and allogeneic donor cell therapies when using ESC and iPSC-derived cells, there is the additional need to minimize the potential risk of tumor formation from rare contaminating stem cells and undifferentiated cells.[10-11] Maximizing the purity of cell samples becomes increasingly important as these risks increase.

In the cell processing stage, in addition to cell quality and biosafety, operator safety also needs to be considered. These prevention mechanisms include conduction of regular reviews of the biosafety in laboratory settings, as well as strict guidelines to follow for both laboratory and operating room procedures. A fundamental objective of any biosafety program is the containment of potentially harmful biological agents. For regenerative medicine, containment also protects biological samples from outside contamination, whereby ensuring the highest purity of cell samples for therapeutics applications.

Despite Japan's world leading basic research in the science and medical fields, Japan's efforts to translate and commercialize regenerative treatments has been slow in comparison to Western countries and even Korea.[12] Japan has recognized the pressing need to streamline its development, regulatory and commercialization

pathways in order to bring innovative treatment solutions to patients as quickly as possible.

The Japan Revitalization Strategy which was revised and published on June 24, 2014 calls for the creation of a control tower for medical R&D. This strategy document also noted, "a bill to revise the Pharmaceutical Affairs Act, in order to accelerate the approval of medical devices and regenerative medicine products, was enacted in November 2013, along with the Act on the Safety of Regenerative Medicine." A key objective of these new laws is to promote the swift and safe commercialization of regenerative medicine technologies.[13]

In sync with the Japan Revitalization Strategy, the Ministry of Economy, Trade and Industry (METI) vision for the commercialization of regenerative treatments includes the creation of opportunities for companies to collaborate in packaging of devices, consumable supplies and services for the overall production, process and delivery of cells for regenerative therapies. Cell therapies, however, often utilize special medical devices and instruments in clinical and hospital settings.

To ensure the smooth commercialization of new cell therapies, there is a real need for a clear regulatory pathway for the review, approval and reimbursement of instruments, devices, consumable supplies and reagents used in clinical and hospital settings for characterization, isolation and quality control. It is important that this regulatory pathway be created in tandem with the regulatory pathway now being envisioned and developed for the production, processing and transport of cell and tissue products. Without clear regulatory pathways for the approvals of both devices and cells for regenerative therapies, commercialization for many therapies may not be possible.

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