

I. How can you choose the fate of iPSCs and stem cells, Regeneration or Carcinogenesis? A hypothetical insight.

Seno M¹

Abstract

It is nowadays taken granted that induced pluripotent stem cells (iPSCs) are available for the regeneration therapy since iPSCs differentiate into any kind of phenotypes. If iPSCs can choose their fate in every way of differentiation why they do not choose cancer phenotype. As a body develops for one fertilized egg, embryonic stem cell must choose every phenotype of tissues such as blood, neuron, lung, liver, pancreas and so on depending on the stages. And sometimes the cells get cancer. So do iPSCs because iPSCs are almost equivalent to embryonic cells. Then how can the safety of the regeneration therapy be maintained with iPSCs? When inducing the differentiation of iPSCs it is considered important to choose the proper conditions of culture such as 3D-platform for embryoid, supplement of cytokines and growth factors, inhibition of signaling and so on. On the other hand, several conditions have been reported to induce cancer stem cells. The cancer inducing conditions are possibly summarized as the factors chronically exposed to iPSCs. It is further worthwhile noticing that the conditions do not appear to induce mutations but affecting the epigenetics. Collectively, to secure the safety of regeneration therapy, it appears the best way to avoid the conditions to induce cancer stem cells. Further insights in details will be discussed in the lecture.

II. Modelling human beta cell development with pluripotent stem cells

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Abstract

Type 1 Diabetes (T1D) is an autoimmune disease characterized by destruction of the pancreatic beta cells and loss of insulin. Using the Edmonton protocol, donor-derived islets seeded into the liver successfully restore glycemia in 58% of T1D patients. However, donor scarcity, risks associated with immunosuppressants and poor engraftment limit this therapeutic application to a small number of patients. To overcome these challenges, the developmental potential of human embryonic stem cells and human induced pluripotent stem cells is being harnessed to produce surrogate islets in vitro. We and others have been able to mimic human embryonic development and generate pancreatic progenitors (PP) that have the ability to mature into insulin-producing beta-like cells both in vitro and in vivo. Transplantation of pancreatic progenitors in the kidney capsule of immunodeficient mice leads to formation of islet-like structures that secrete human insulin. However, there are some limitations to the use of pancreatic progenitors for the treatment of T1D. First and foremost, their safety as the PP population can be heterogenous and highly proliferative, which might lead to formation of cellular outgrowth or teratoma after transplantation. Second, while insulin-producing cells develop in vivo 6 weeks after transplantation, restoration of normoglycemia occurs ~5 months later, suggesting that these “early” insulin-producing cells are immature, or poorly connected to the host vasculature. We have been addressing these two limitations and developed approaches to 1) improve safety by identifying markers to purify the PP populations and 2) accelerate functionality by improving vascularization at the time of transplantation.

These lectures were delivered in the Plenary Session of NCRM NICHE 2020. NCRM NICHE (www.ncrmniche.org) is a day of commemorative events to celebrate the inaugural Anniversary of Nichi-In Centre for Regenerative Medicine (NCRM), conducted every year since 2006 in the month of October. NCRM NICHE provides a platform that augments the interaction of scientists and clinicians. It enables them to exchange ideas in order to arrive at synergies while working towards a common goal of discovering clinically applicable solutions for diseases without a definitive treatment to yield relief to numerous patients. Conducted in India till 2016, it has been conducted in Japan from 2017 onwards. NCRM NICHE has two components: 1. Active Knowledge Gaining (AKG) events which refer to any knowledge gaining activity in which the participant plays an active role before and during the event instead of being a passive listener to a lecture by a speaker or a conversation among third parties. AKG events of NCRM NICHE include a. Fujio Cup Quiz (FCQ); and b. Inter Disciplinary Conclave (IDC); 2. Passive Knowledge Gaining (PKG) events which refer to an event, where there is no mandatory preparation by the participants before the event. During the event, they have to merely be a passive listener to others either delivering a lecture or interacting among third parties. PKG events of NCRM NICHE include Lectures & Orations. NCRM NICHE 2020 was conducted as a Virtual event on the 18th of October, 2020.

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