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Juntendo University Corporate Communications
Keio University

Juntendo University and Keio University: T cells provide a non-invasive solution for neurological research

(Tokyo) Researchers in Japan report that neural stem cells derived from readily available T cell-derived iPSCs provide a neurological disease model when cultured in a novel protocol developed by them. The findings are important for the treatment of Parkinson's disease and are published in *Stem Cell Reports*, February 2016.

Neurological disease research, such as on Parkinson's disease, relies on animal models and immortalized neural cell lines because the central nervous system of patients is not accessible for invasive examination. Cultured neural stem cells could provide an alternative that is closer to the biology of the patient in question. However, due to the epigenetic memories of iPSCs, efficient preparation of neural stem cells requires human induced pluripotent stem cells (iPSCs) usually derived from skin fibroblasts harvested from patient skin biopsies, which can lead to bleeding, scarring and infection. Now researchers from a collaboration of universities and institutions in Japan have demonstrated the potential efficacy of a less invasive alternative.

"T cells can be obtained non-invasively, are easily stored and efficiently reprogrammed, and might therefore be an ideal source of patient-specific iPSCs," explain Juntendo University's Wado Akamatsu and Keio University's Hideyuki Okano, and colleagues in their latest report. However the snag is that the source of stem cells seems to affect what cells they are likely to differentiate into. T cells are a type of lymphocyte or white blood cell and the researchers obtained very few neural cells from T cell-derived iPSCs cultured in standard embryoid bodies compared with the usual fibroblast-derived iPSCs.

To encourage differentiation into neural cells, the researchers tried converting the iPSCs directly into neural stem cells as neurospheres – culture systems of free-floating neural cells - instead of embryoid bodies that contain cells of other germ layers. By using this protocol, T cell-derived iPSCs efficiently differentiated into neural cells as well as fibroblast-derived iPSCs. Neurospheres generated from T cell-derived iPSCs were differentiated into neurons and various neuronal subtypes in similar quantities to those from fibroblast-derived iPSCs.

Furthermore, the researchers confirmed that iPSCs derived from the T cells of patients suffering from juvenile Parkinson's disease (PARK2) exhibited impaired mitochondrial phenotypes that the team had previously reported using the fibroblast-derived iPSCs derived from this patient.

"These results strongly support that the hiPSCs derived from T-cells can be used as a model of neurological disease by using our differentiation protocol," state Wado Akamatsu and Hideyuki Okano and colleagues in their latest report.

Background

Induced pluripotent stem cells

Induced pluripotent stem cells (iPS cells or iPSCs) are pluripotent stem cells that can be induced from somatic cells by cellular reprogramming. The original set of reprogramming factors (so-called as Yamanaka factors) are the genes Oct4 (Pou5f1), Sox2, cMyc, and Klf4. So far, it has been reported that each of these factors can be functionally substituted by other transcription factors, miRNAs, small molecules, or proteins.

Embryoid bodies

These are three-dimensional aggregates of embryonic pluripotent stem cells. They contain the cells from all three germ layers and are readily scalable because they form in suspension making them useful for culturing large yields of cells. In contrast, the neurosphere culture used by Okano, Akamatsu and collaborators are similar structures but comprising neural cells.

Parkinson's disease

In Parkinson's disease (PD), mutation of a specific gene is the cause of PD (familial PD [FPD]) in approximately 10% of PD patients, whereas the other 90% of patients are called sporadic PD. Particularly, understanding the causes of sporadic PD may require statistical approaches that require large numbers of cell lines, further raising the demand for less invasive approaches to gathering neural cell models.

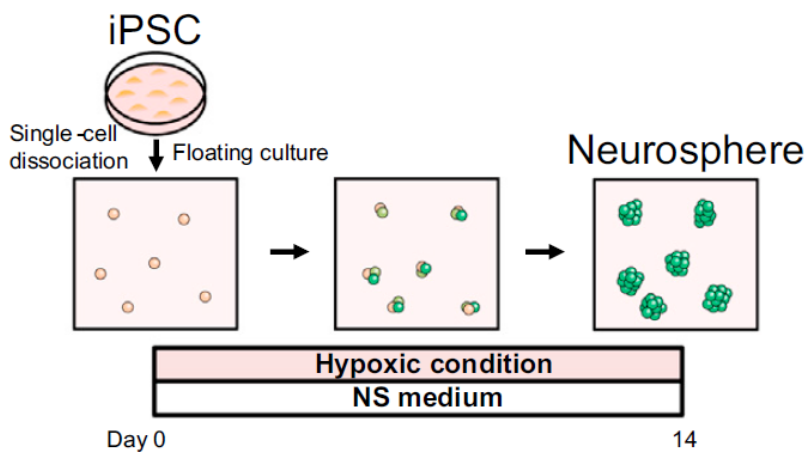
Reference

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Figure 3A



A schematic representation of the direct neurosphere converting method (dNS method).

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About Juntendo University

Mission Statement

The mission of Juntendo University is to strive for advances in society through education, research, and healthcare, guided by the motto “Jin – I exist as you exist” and the principle of “Fudan Zenshin - Continuously Moving Forward”. The spirit of “Jin”, which is the ideal of all those who gather at Juntendo University, entails being kind and considerate of others. The principle of “Fudan Zenshin” conveys the belief of the founders that education and research activities will only flourish in an environment of free competition. Our academic environment enables us to educate outstanding students to become healthcare professionals patients can believe in, scientists capable of innovative discoveries and inventions, and global citizens ready to serve society.

About Juntendo

Juntendo was originally founded in 1838 as a Dutch School of Medicine at a time when Western medical education was not yet embedded as a normal part of Japanese society. With the creation of Juntendo, the founders hoped to create a place where people could come together with the shared goal of helping society through the powers of medical education and practices. Their aspirations led to the establishment of Juntendo Hospital, the first private hospital in Japan. Through the years the institution’s experience and perspective as an institution of higher education and a place of clinical practice has enabled Juntendo University to play an integral role in the shaping of Japanese medical education and practices. Along the

way the focus of the institution has also expanded, now consisting of four undergraduate programs and three graduate programs, the university specializes in the fields of health and sports science and nursing health care and sciences, as well as medicine. Today, Juntendo University continues to pursue innovative approaches to international level education and research with the goal of applying the results to society.

About Keio University

Mission Statement

Keio University is not merely a place for academic pursuit. Its mission is to be a constant source of honorable character and a paragon of intellect and morals for the entire nation and for each member to apply this spirit to elucidate the essence of family, society, and nation. They will not only articulate this essence in words, but also demonstrate it in their actions, and by so doing make Keio a leader of society.

About Keio University School of Medicine

Formally founded in 1917, Keio University School of Medicine is regarded as one of Japan's top medical schools. Its long-standing reputation for excellence stems from its unique history and its leading role in promoting the practice of advanced Western medicine in Japan. The school's leadership in this area is evidenced by the fact that it has produced two presidents of the Japan Medical Association and one of the two Japanese who have been presidents of the World Medical Association. The School of Medicine has established a formidable reputation in the international medical community, not only for its hospital — the largest university hospital in Japan — but also for its promotion of excellence in medical research through the prestigious annual Keio Medical Science Prize.

As it approaches its centenary, the school will build on its past achievements to play a leading role in addressing such global problems as rapidly ageing populations. The construction of a new state-of-the-art hospital building will be key to promoting 'Keio Medicine', an important feature of which is the unique interdisciplinary team approach to patient-oriented medical care currently being realized at Keio.