PRESS RELEASE

Juntendo University

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Juntendo University research: Step forward towards treating hereditary deafness

(Tokyo, 31 May) **Researchers at Juntendo University report in the journal Human Molecular Genetics that a stem-cell technique may be used to develop a treatment of a common mutation-related type of deafness. The method involves reproducing cells occurring in the human inner ear where the researchers emphasize that "the pathological condition could be reproduced with iPS derived from a typical patient".**

Deafness is the most common sensory impairment in newborn children — about 1 child in 1000 is born with hearing loss, or develops it in early childhood. Half of these cases have a genetic cause; very often, this type of deafness is related to a mutation of a gene called 'gap junction beta 2 (GJB2)', which encodes a protein called 'connexin 26 (CX26)'. This protein occurs in cells in the cochlea, the part of the inner ear enabling hearing. One way of treating GJB2-related deafness would be to reproduce properly functioning cochlear cells and introduce them into the inner ear. Now, Kazusaku Kamiya from Juntendo University and colleagues have made an important step forward toward making this treatment possible: using a stem-cell technique, they succeeded in reproducing cochlear supporting cells, a type of cell known to contain CX26 proteins.

The researchers started from human induced pluripotent stem cells (iPSCs) — artificially generated cells that can differentiate into any other cell type of the human body. By applying a particular set of culture techniques, including exposure of the cultures to insulin, they were able to make their iPSCs produce CX26 protein. Further similarity to cochlear supporting cells was investigated by checking the occurrence of proteins expressed by other 'marker genes' typical for the cochlea. The cells themselves formed intercellular junctions — comprised in part of CX26 protein — characteristic of normal supporting cells in the cochlea.

Kamiya and colleagues also looked at the outcome of producing iPSCs starting from cells taken from patients with GJB2 deafness. The cells generated in this way differed from the healthy iPSCs: the intercellular junctions did not form as they should. It is this malformation that can be directly associated with hearing loss — in other words, the scientists reproduced the pathology of GJB2-related deafness.

It is worth stressing that the cochlea is anatomically complex, making traditional, invasive procedures like biopsies (for taking samples) or direct drug administration (for treatment) difficult as there is the risk of causing loss of hearing. The results of Kamiya and colleagues are therefore important in two ways. First, being able to reproduce cochlear supporting cells via the iPSC method may lead to a treatment of hereditary deafness in which malfunctioning cells are replaced by normally functioning ones. Second, reproducing the pathology by generating iPSCs derived from patients with GJB2 mutations is useful for testing drugs and for developing treatments for each occurring mutation. Quoting the scientists: "Such iPSC-derived cells should be particularly useful for drug screening and inner-ear cell therapies with genome editing targeting GJB2-related hearing loss and the pathological condition could be reproduced with iPS derived from a typical patient".

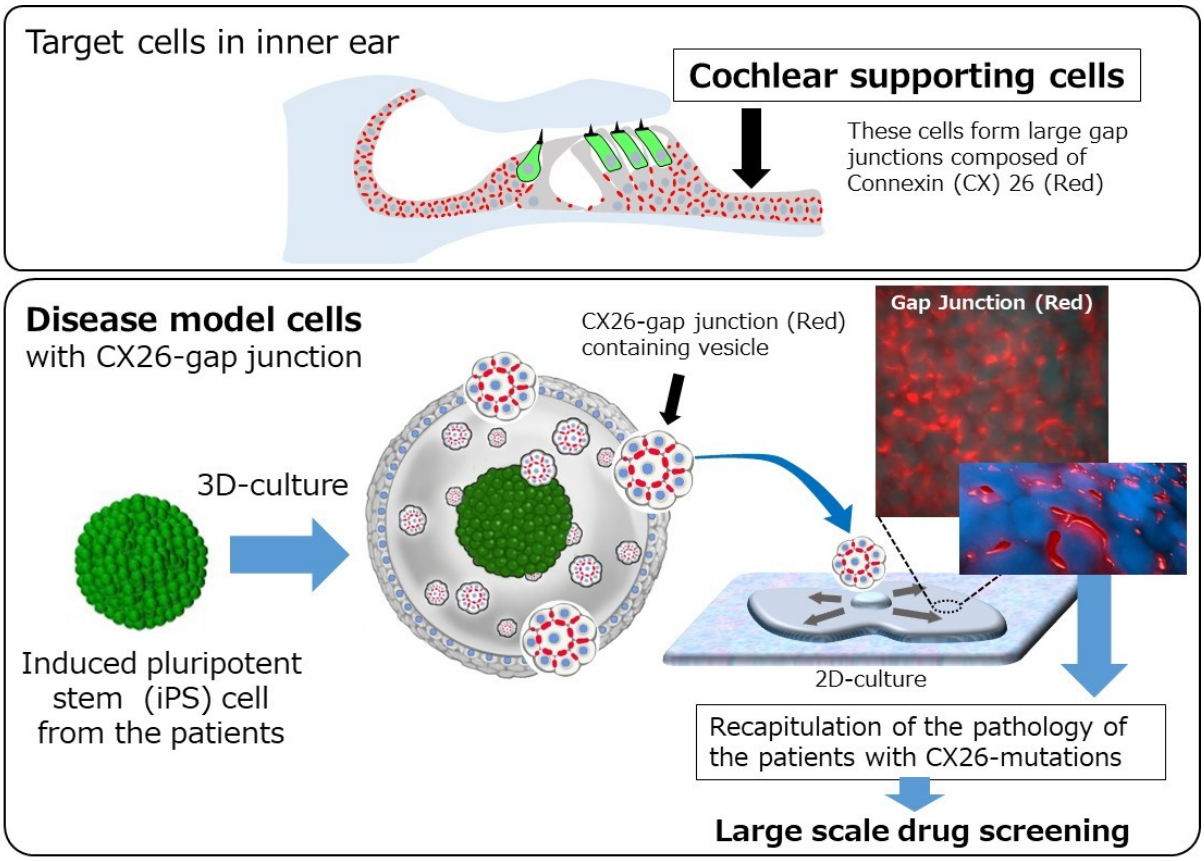

Illustration of the research described in this paper..

Background

Induced pluripotent stem cells (iPSCs)

Stem cells are cells that have the ability to differentiate — that is, become cells of a specialized type. An important attribute of a stem cell is its potency, indicating into what types of cells the stem cell can differentiate. So-called pluripotent stem cells (PSCs) can develop into organisms, because they can differentiate into cells of any of the three different germ layers characteristic of organisms.

An induced pluripotent stem cell (iPSC) is a PSC artificially generated from a non-PSC. The procedure for creating iPSCs was discovered in 2006 by Shinya Yamanaka (for which he received the 2012 Nobel Prize in Physiology or Medicine). iPSC generation is now a promising technique in the field of regenerative medicine: damaged or malfunctioning human cells can be replaced by cells regenerated using the iPSC technique.

Kazusaku Kamiya from Juntendo University and colleagues have now applied the iPSC technique to provide insights into a common type of deafness in newborns. They succeeded in creating cells functioning like cochlear supporting cells, a promising step forward to developing a replacement therapy for malfunctioning supporting cells. They also managed to produce cultures of iPSC-derived cells from patients with GJB2-related deafness; artificially reproducing the pathology is useful for drug testing and developing treatments.

Reference

Ichiro Fukunaga, Yoko Oe, Keiko Danzaki, Sayaka Ohta, Cheng Chen, Kyoko Shirai, Atsushi Kawano, Katsuhisa Ikeda & Kazusaku Kamiya. Modeling gap junction beta 2 gene-related deafness with human iPSC. Human Molecular Genetics Published online 17 May 2021.

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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.

History of Juntendo University

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 six undergraduate programs and three graduate programs, the university specializes in the fields of health science, health and sports science, nursing health care and sciences, and international liberal arts, 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.