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Keio University School of Medicine
Keio University Hospital

Clinical Research on First-In-Human Clinical Trial of Transplantation: Regenerative Medicine Using iPSC Cell-Derived Neural Stem/Progenitor Cells to Treat Complete Subacute Spinal Cord Injury

A group at Keio University Hospital has successfully transplanted human iPSC cell-derived neural stem/progenitor cells (iPSC-NS/PCs) into the first participant of a clinical study on regenerative medicine using iPSC-NS/PCs for subacute spinal cord injury (SCI).

1. Research Background

After receiving approval from the Ministry of Health, Labour and Welfare in 2019, the Keio University School of Medicine and Keio University Hospital prepared to start a clinical study into regenerative medicine using iPSC-NS/PCs for subacute spinal cord injury.

But after research began in December 2020, recruitment was suspended due to the COVID-19 pandemic. The group has now successfully transplanted iPSC-NS/PCs into the study's first participant. Details of the clinical research are outlined below.

Organization & Contacts

<u>Contact for scientific queries:</u>	Professor Hideyuki Okano, Keio University School of Medicine
<u>Principal investigator:</u>	Professor Masaya Nakamura, Keio University School of Medicine
<u>Host institution:</u>	Keio University Hospital
<u>Partner institution:</u>	National Hospital Organization Murayama Medical Center

Outline

- Objectives:** The primary objective is to assess the safety of hiPSC-NS/PC transplantation in patients with subacute SCI. The secondary objective is to obtain preliminary evidence of its impact on neurological function and quality-of-life outcomes.
- Condition:** Subacute spinal cord injury (C3/4-Th10 level, within 14–28 days post-injury)
- Target Sample Size:** 4 patients
- Cells:** iPSC-NS/PCs were prepared at a Good Manufacturing Practice-grade cell processing facility at Osaka National Hospital using a clinical-grade integration-free hiPSC line established by the iPSC Stock Project organized by the Kyoto University Center for iPSC Cell Research and Application (CiRA). Cells are cryopreserved at Keio University Hospital.

2. Cell Transplantation

(1) Implementation Details

Location: Keio University Hospital

Date: December 2021

Surgeons: Dr. Masaya Nakamura and three other doctors from the Department of Orthopedic Surgery

(2) Surgical Procedure & Results

Surgeons approached the damaged spinal cord from the back with the patient in a prone position under general anesthesia. After confirming the epicenter of the spinal cord injury using an ultrasound probe, the membrane covering the spinal cord was cut open to expose the damaged site. Approximately 2 million iPSC-NS/PCs (20 μ l as the cell suspension volume) were then transplanted into the epicenter of the injury.

3. Research Significance and Future Development

This surgery is the world's first transplantation of human iPSC-NS/PCs for spinal cord injury. In order to prioritize the safety of the research participant, the number of cells to be transplanted was determined based on the number of cells for which the research team was able to confirm safety in their non-clinical study conducted with small animals. So although there is a possibility that therapeutic efficacy may be observed, the primary objective of this clinical study was to first and foremost confirm the safety of the transplanted cells and method of transplantation.

An independent data monitoring committee¹ will evaluate the safety of the study based on data obtained up to about three months after the first transplant. If the independent data monitoring committee decides that the study can continue, the group expects to conduct transplantations for the study's second, third, and fourth participants.

As a result, patient recruitment for a subsequent trial is currently suspended and is expected to resume around April 2022.

¹ **Independent Data Monitoring Committee:** A committee comprised of individuals with the expertise required to evaluate the clinical trial who conduct objective, neutral evaluations of interim data throughout the trial. The committee operates independently of the research group and provides the group with appropriate advice to ensure the safety of participants and the ethical and scientific validity of the clinical research.

4. Notes

This study is supported by the Research Center Network for Realization of Regenerative Medicine (Centers for Clinical Application Research on Specific Disease/Organ), Grant No. JP21bm0204001), and the Research Project for Practical Applications of Regenerative Medicine from the Japan Agency for Medical Research and Development (AMED), Grant No. JP20bk0104017 and JP21bk0104120.

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*We have sent this news release to the MEXT Press Club, Science Press Club, MHLW Press Club, MHLW Hibiya Club, and society and education departments of other media outlets.

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