Press Release

Keio University

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Keio University School of Medicine
Keio University Regenerative Medicine Research Center

World's First Clinical Study of iPSC-Derived Neural Progenitor Cell Therapy for Subacute Spinal Cord Injury Supports Long-Term Safety Through Up to Four Years of Follow-up

Hideyuki Okano and Masaya Nakamura of Keio University, along with their research team, have continued the long-term follow-up study of participants enrolled in the clinical study, "Regenerative medicine for spinal cord injury at subacute stage using human induced pluripotent stem cell-derived neural stem/progenitor cells." Okano is Director and Professor of the Keio University Regenerative Medicine Research Center; Nakamura is Professor and Chair of the Department of Orthopaedic Surgery at Keio University School of Medicine. The team has now compiled follow-up results of up to four years after transplantation. No tumor formation or serious adverse events attributable to the transplanted iPSC-NS/PCs were observed, providing further support for the long-term safety of this therapy.(see Notes 1, 2)

This study was the world's first clinical transplantation of iPSC-NS/PCs into the injured human spinal cord. The present findings provide additional evidence supporting the safety of this therapeutic approach. Furthermore, improvements in motor function and the proportion of patients achieving improvement in AIS grade at 52 weeks exceeded those observed in a historical control cohort*. These findings support the further development of spinal cord cell transplantation using iPSC-NS/PCs for patients with severe spinal cord injury and may also contribute to the future development of regenerative therapies for a broad range of central nervous system disorders.

These findings, integrating the results of the initial one-year clinical study and the subsequent long-term follow-up study, were published online in *Nature Medicine* on July 21, 2026 (British Summer Time).

1. Background

From 2020 to 2025, the world's first clinical study, "Regenerative medicine for spinal cord injury at subacute stage using human induced pluripotent stem cell-derived neural stem/progenitor cells," was conducted. Four patients underwent transplantation of iPSC-NS/PCs, followed by one year of post-transplant follow-up.

Because transplanted immature cells are expected to engraft and remain in the body for an extended period, long-term safety assessment is essential. Therefore, the research team initiated a separate follow-up study, "Observational study beyond one year after transplantation of human induced pluripotent stem cell-derived neural stem/progenitor cells for spinal cord injury," to continue monitoring the long-term safety of the participants.

Clinical Study: "Regenerative medicine for spinal cord injury at subacute stage using human induced pluripotent stem cell-derived neural stem/progenitor cells"

Study organization

- **Principal Investigator:**

Hideyuki Okano, Professor, Department of Physiology, Keio University School of Medicine (study initiation–2024)
Masaya Nakamura, Professor, Department of Orthopaedic Surgery, Keio University School of Medicine (2024–)

- **Principal Clinical Investigator:** Masaya Nakamura, Professor, Department of Orthopaedic Surgery, Keio University School of Medicine
- **Cell Manufacturing Facility:** National Hospital Organization Osaka National Hospital
- **Medical Institution Conducting the Cell Transplantation:** Keio University Hospital
- **Collaborating Medical Institution:** National Hospital Organization Murayama Medical Center

Study overview

- **Objective:** To evaluate the safety of iPSC-NS/PC transplantation, with exploratory assessment of efficacy.
- **Participants:** Patients with subacute complete traumatic spinal cord injury (neurological level C3/C4–T10; 14–28 days after injury; American Spinal Injury Association [ASIA] Impairment Scale [AIS] grade A; see Note 3).
- **Target enrollment:** Four patients.
- **Transplanted cells:** iPSC-NS/PCs differentiated at the National Hospital Organization Osaka National Hospital from the clinical-grade iPSC stock established by the Center for iPS Cell Research and Application (CiRA), Kyoto University. The iPSC-NS/PCs were cryopreserved at Keio University Hospital, then thawed and recovery-cultured after informed consent was obtained before transplantation.
- **Clinical trial registration:** jRCTa031190228.

Follow-up Study: "Observational study beyond one year after transplantation of human induced puluripotent stem cell-derived neural stem/progenitor cells for spinal cord injury"

Study organization

- **Principal Clinical Investigator:** Masaya Nakamura, Professor, Department of Orthopaedic Surgery, Keio University School of Medicine

Study overview

- **Objective:** To evaluate the long-term safety of iPSC-NS/PC transplantation in the four participants enrolled in the initial clinical study.
- **Institutional Review Board approval:** Keio University School of Medicine Ethics Committee (Approval No. 20221199).

2. Results, Significance, and Future Perspectives

In the long-term follow-up study, all four participants were evaluated for 2–4 years after transplantation. No tumor formation or serious adverse events attributable to the transplanted iPSC-NS/PCs were observed, and no participant showed any obvious deterioration in neurological function. These findings further support the long-term safety of iPSC-NS/PC transplantation.

With regard to the exploratory efficacy evaluation, the median improvement in the International Standards for Neurological Classification of Spinal Cord Injury (ISNCSCI; see Note 4) total motor score was 7 points at 24 weeks and 13 points at 52 weeks after transplantation. These improvements exceeded the median improvements observed in a historical control cohort* that met eligibility and exclusion criteria comparable to those of the present study (5 and 7 points at Weeks 24 and 52, respectively, in the available-case analysis, and 4 and 4 points, respectively, in the last-observation-carried-forward [LOCF] analysis). Furthermore, 2 of the 4 transplanted participants (50.0%) improved from AIS grade A to AIS grade C or better, compared with 12.0% in the available-case analysis and 15.4% in the LOCF analysis of the historical control cohort.

iPSC-NS/PCs are thought to exert therapeutic effects by differentiating into neurons and glial cells and engrafting at the injury site, as well as by secreting neurotrophic factors that promote repair of the injured spinal cord. However, engraftment of the transplanted cells could not be confirmed directly in this study. In addition, because the study included only four participants and lacked a concurrent control group, the efficacy of this therapeutic approach should be confirmed in future clinical trials.

These findings are expected to contribute to the further development of iPSC-NS/PC transplantation toward its clinical application.

* Historical control cohort: Patients meeting eligibility and exclusion criteria comparable to those of the present study were identified from the Japan Single-Center Study for Spinal Cord Injury Database (JSSCI-DB) at the Spinal Injuries Center (Fukuoka, Japan; Ideta, Sakai, Maeda, et al.) for comparative analysis.

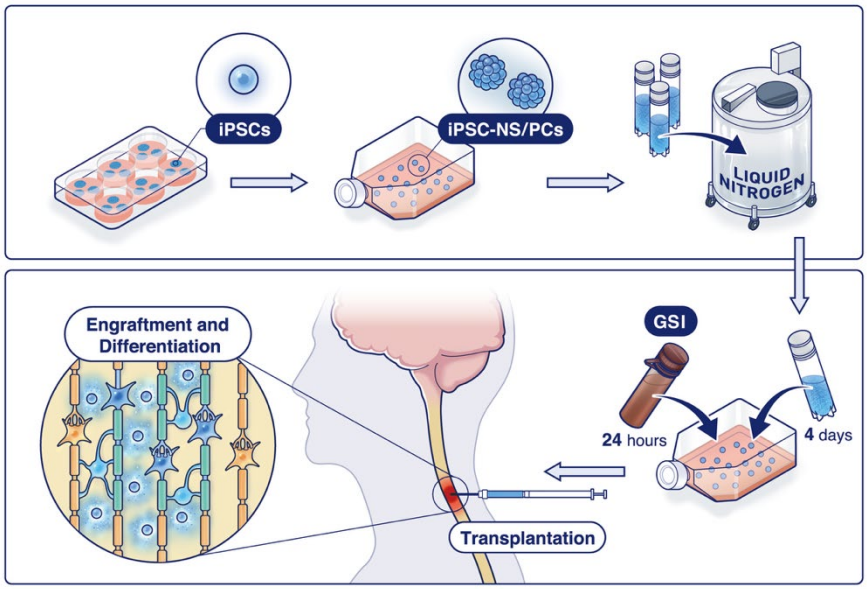

Figure 1. Overview of the study

Human iPSC-NS/PCs were manufactured under Good Manufacturing Practice (GMP) conditions and cryopreserved until use. Four days before transplantation, the cells were thawed and recovery-cultured, followed by treatment with a γ-secretase inhibitor (GSI) 24 hours before transplantation. Under ultrasound guidance, 2×10^6 iPSC-NS/PCs were slowly injected into the epicenter of the injured spinal cord. The transplanted iPSC-NS/PCs are expected to engraft at the injury site, differentiate into neural cells, and promote repair of the injured spinal cord.

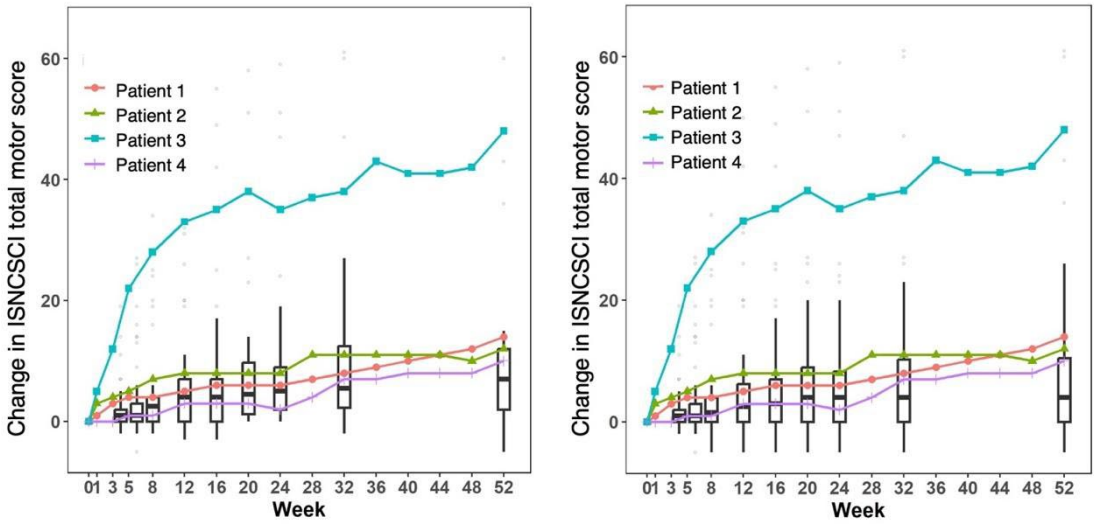

Figure 2. Changes in motor function during the first year after transplantation

The four transplanted participants are shown as colored lines, and the distribution of the historical control cohort is presented as box-and-whisker plots. The center line indicates the median, the box represents the interquartile range (25th–75th percentiles), the whiskers extend to the minimum and maximum values excluding outliers (within 1.5 times the interquartile range), and the gray dots indicate outliers.
Left: Comparison of the four transplanted participants with the historical control cohort using the available-case analysis.
Right: Comparison of the four transplanted participants with the historical control cohort using the last-observation-carried-forward (LOCF) analysis.

3. Funding

This study was supported by the Japan Agency for Medical Research and Development (AMED) through the Research Center Network for Realization of Regenerative Medicine Program ("Regenerative Medicine for Spinal Cord Injury and Stroke Using iPSC-Derived Neural Stem/Progenitor Cells"), the Research Project for Practical Applications of Regenerative Medicine ("Development of Rehabilitation Therapy Accompanying Spinal Cord Regeneration Therapy"), the Research Project for Practical Applications of Regenerative Medicine ("Clinical Study of Transplantation of iPSC-Derived Neural Stem/Progenitor Cells for Subacute Spinal Cord Injury"), and by designated donations to the Department of Orthopaedic Surgery, Keio University School of Medicine.

4. Publication

Title: An iPSC-derived neural progenitor cell therapy for subacute spinal cord injury: a phase 1 trial with long-term follow-up
Authors: Keiko Sugai, Osahiko Tsuji, Kanehiro Fujiyoshi, Masahiro Ozaki, Takayuki Abe, Tsuneo Kohzuki, Hiroki Okawara, Tomonori Sawada, Miho Sumida, Ema Yoshioka, Tomoko Shofuda, Shioko Kawashima, Ryo Yamaguchi, Munehisa Shinozaki, Naoko Takasu, Narihito Nagoshi, Toshiki Okubo, Jun Kohyama, Takeshi Maeda, Yoshiyuki Yato, Yonehiro Kanemura, Shinya Yamanaka, Masaya Nakamura, and Hideyuki Okano
Journal: *Nature Medicine* (online)
DOI: 10.1038/s41591-026-04549-6

Glossary

(Note 1) Induced pluripotent stem (iPS) cells:
Induced pluripotent stem (iPS) cells are pluripotent stem cells generated by introducing a small number of factors into mature somatic cells, such as skin or blood cells, followed by

cell culture. They have the ability to differentiate into virtually any cell type in the body and to proliferate almost indefinitely.

(Note 2) Neural stem/progenitor cells (NS/PCs):
Neural stem/progenitor cells (NS/PCs) are immature cells of the nervous system. They possess the capacity for self-renewal and can differentiate into the major cell types of the nervous system, including neurons and glial cells.

(Note 3) American Spinal Injury Association (ASIA) Impairment Scale (AIS):
The ASIA Impairment Scale (AIS) is an internationally accepted system for classifying the severity of spinal cord injury. In general, AIS A indicates complete loss of motor and sensory function in the sacral region, AIS B indicates preservation of sensory but not motor function in the sacral region, AIS C indicates that some motor function is preserved below the level of injury, and AIS D indicates that motor function below the level of injury is preserved to the extent that movement against gravity is possible.

(Note 4) International Standards for Neurological Classification of Spinal Cord Injury (ISNCSCI) total motor score:
The ISNCSCI total motor score is an internationally standardized measure of motor function after spinal cord injury. Muscle strength is graded on a 6-point scale (0–5) in 20 key muscle groups (five in each upper and lower limb). The total motor score ranges from 0 to 100, comprising a maximum of 50 points for the upper extremities and 50 points for the lower extremities.

*Please direct any requests or inquiries to the contacts listed below in advance of any press coverage.
*This news release has been sent to the MEXT Press Club, Science Press Club, MHLW Press Club, MHLW Hibiya Club, and the science desks of other media outlets.

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