

# Annual Report



2024

## IMSUT Hospital

# IMSUT CORD

## 臍帯血・臍帯バンク

Clinical Professor Tokiko Nagamura-Inoue, M.D., Ph.D.  
 Professor Fumitaka Nagamura, M.D., Ph.D.  
 Project Assistant Professor Kazuhiro Sudo, Ph.D.

病院教授 博士(医学) 長 村 登紀子  
 教授 博士(医学) 長 村 文 孝  
 特任助教 博士(医学) 須 藤 和 寛

*Human umbilical cord blood (CB) and umbilical cord tissue (UC) are attractive sources of somatic stem cells for gene and cell therapies. Especially, the UC has been rapidly utilized as an abundant source of mesenchymal stromal cells (MSCs), which migrate toward inflamed or damaged tissue to reduce inflammation and support tissue repair. Both CB and UC can be provided as “off-the-shelf” cell products for immunotherapies and regenerative medicine. IMSUT CORD is the CB and UC-derived cell bank established in IMSUT hospital in 2016. The aim of IMSUT CORD is to collect, process /culture, cryopreserve, stock, and release CB- and UC-derived cells—including mesenchymal stromal cells (MSCs)—for clinical and research use. We have released CB and UC-derived MSCs to researchers under material transfer agreements to expedite translational studies. We have supplied UC-MSC products for clinical trials for severe acute graft-versus-host disease (GVHD; 2018–2020), COVID-19-related ARDS (2020–2022), cerebral palsy (PVL; 2021–2023), and noninfectious pulmonary complication after allogeneic hematopoietic stem cell transplantation NIPC; 2022–2023). Our main processing facility has been moved from IMSUT cell resource center to new IMSUT-HLC cell processing facility since 2021.*

### 1. Establishing a stable perinatal appendage-derived cell supply system as the source of allogeneic somatic stem cells for research and clinical use

Sudo K, Takahashi A, Hori A, Miharuru Y, Sakai T, Shibuya Y, Nagaya N, Ogami K, Mukai T, Nagamura F, Nagamura-Inoue T

Human umbilical cord blood (CB) and umbilical cord tissue (UC) are attractive sources of somatic stem cells for gene and cell therapies. CB and UC can be obtained noninvasively from donors. CB, a known source of hematopoietic stem cells for transplantation, has attracted attention as a new source of immune cells, including universal chimeric antigen re-

ceptor T cell therapy (CAR-T) and, more recently, universal CAR-natural killer cells. UC-derived mesenchymal stromal cells (UC-MSCs) have a higher proliferation potency than those derived from adult tissues and can be used anon-HLA restrictively. We have established a CB/UC bank at the IMSUT hospital (IMSUT CORD) to collect CB and UC tissue after informed consent from the mothers in collaboration with the obstetricians. After receiving them, we stock the UC-tissue, and to manufacture master cells and product cells for research and clinical use.

To maintain quality control, we have introduced the ISO 9001:2015 quality management standards in IMSUT CORD since 2018. We have transferred the manufacturing and testing technologies to the client companies, where they apply our techniques and

standards in their clinical trials including therapies for acute GVHD, cerebral palsy, and COVID-19 related acute respiratory distress syndrome (ARDS). The IMSUT CORD mission is to supply domestic UC-MSCs and CB as a source of allogeneic somatic stem cells in research and clinical use. We have supplied clinical-grade UC-MSC products for clinical trials including severe acute graft-versus-host disease (GVHD; 2018-2020), COVID-19-related ARDS (2020-2022), cerebral palsy (PVL) (2021-2023), and non-infectious pulmonary disease after allogeneic hematopoietic stem cell transplantation NIPS; 2022-2023),

after approval by the review board of IMSUT CORD and PMDA. We are currently preparing for a clinical trial for treating peripheral nerve injury using allograft bio3D conduit made with UC-MSC products with Kyoto University (AMED project 2022-2024). Since 2021, our main manufacturing location has been moved from the IMSUT-Cell Resource Center (IMSUT-CRC) to a new facility, the IMSUT-HLC Cell Processing Facility (IMSUT-HLC CPF), where the manufacturing license was obtained in 2023.

Visit our website: <https://plaza.umin.ac.jp/imsut-cord/>

### Publications

- 1) Iwai T, Ikeguchi R, Aoyama T, Noguchi T, Yoshimoto K, Sakamoto D, Fujita K, Miyazaki Y, Akieda S, Nagamura-Inoue T, Nagamura F, Nakayama K, Matsuda S. Nerve regeneration using a Bio 3D conduit derived from umbilical cord-Derived mesenchymal stem cells in a rat sciatic nerve defect model. *PLoS One*. 19(12): e0310711, 2024
- 2) Iwatake M, Nagamura-Inoue T, Doi R, Tanoue Y, Ishii M, Yukawa H, Matsumoto K, Tomoshige K, Nagayasu T and Tsuchiya T. Designer umbilical cord-stemcells induce alveolar wall regeneration in pulmonary disease models, *Frontiers in Immunology*, 15,1384718, 2024
- 3) Hori A, Takahashi A, Miharuru Y, Yamaguchi S, Sugita M, Mukai T, Nagamura F, and Nagamura-Inoue T. Superior migration ability of umbilical cord-derived mesenchymal stromal cells (MSCs) toward activated lymphocytes in comparison with those of bone marrow and adipose-derived MSCs, *Front Cell Dev Biol*. 12:1329218, 2024

## Center for Stem Cell Biology and Regenerative Medicine

# Division of Somatic Stem Cell Research

## 体性幹細胞研究分野

Associate Professor Tokiko Nagamura-Inoue, M.D., Ph.D.  
Project Assistant Professor Kazuhiro Sudo, Ph.D.

准教授 博士(医学) 長 村 登紀子  
特任助教 博士(医学) 須 藤 和 寛

*Somatic stem cells, which are derived from mesoderm, include mesenchymal stromal cells (MSCs), blood cells, and other mesenchymal tissues. MSCs exist in the interstitium of systemic organs; they have self-renewal ability, migrate to the sites of inflammation and tissue damage, and exert anti-inflammatory effects and tissue-repair ability. Among various somatic stem cells, we focused on umbilical cord blood (CB) and umbilical cord-derived MSCs (UC-MSCs) and we explored new immune and regenerative gene/cell therapies using CB and UC-MSCs. Another mission is to manage the IMSUT-HLC cell processing facility (IMSUT-HLC-CPF) for translational research. To achieve the high-quality processing and tests for UC-MSCs therapy, IMSUT-HLC-CPF obtained manufacturing license as the first national University in 2023.*

### Cord blood and umbilical cord-derived cells for immune-cell therapy and regenerative medicine

**Sudo K, Takahashi A, Hori A, Miharuru Y, Nagaya N, Mori Y, Ogami K, Nagamura-Inoue T**

We explored new immune and regenerative gene/cell therapies using umbilical cord blood (CB) and umbilical cord-derived MSCs (UC-MSCs) with high

quality and safety standards. For the high quality and safety standards

In addition, it is our mission to keep the IMSUT-HLC cell processing facility clean and functional to enable high-quality manufacturing for translation al gene and cell therapy. To achieve this mission IMSUT-HLC-CPF obtained manufacturing license for UC-MSCs therapy as the first national University in 2023.

### Publications

- 1) Iwai T, Ikeguchi R, Aoyama T, Noguchi T, Yoshimoto K, Sakamoto D, Fujita K, Miyazaki Y, Akieda S, Nagamura-Inoue T, Nagamura F, Nakayama K, Matsuda S. Nerve regeneration using a Bio 3D conduit derived from umbilical cord-Derived mesenchymal stem cells in a rat sciatic nerve defect model. PLoS One. 19(12): e0310711, 2024
- 2) Iwatake M, Nagamura-Inoue T, Doi R, Tanoue Y, Ishii M, Yukawa H, Matsumoto K, Tomoshige K, Nagayasu T and Tsuchiya T. Designer umbilical cord-stemcells induce alveolar wall regeneration in pulmonary disease models, Frontiers in Immunology, 15,1384718, 2024
- 3) Hori A, Takahashi A, Miharuru Y, Yamaguchi S, Sugita M, Mukai T, Nagamura F, and Nagamura-Inoue T. Superior migration ability of umbilical cord-derived mesenchymal stromal cells (MSCs) toward activated lymphocytes in comparison with those of bone marrow and adipose-derived MSCs, Front Cell Dev Biol. 12:1329218, 2024

