

IMSUT Hospital

IMSUT CORD

臍帯血・臍帯バンク

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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.

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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