IMSUT Hospital

Department of Cell Processing and Transfusion

セルプロセッシング・輸血部

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Our department was established in 1990 to manage transfusion medicine and cell processing for hematopoietic stem-cell transplantation. In addition to transfusion related works, our department has been supporting the cell processing for translational studies preformed in IMSUT-Cell Resource Center (IMSUT-CRC), established in 1997. Our recent projects include the Research Cord Blood Bank (RCBB); the National BioResource Project (NBRP) supported by the Ministry of Education, Culture, Sports, Science and Technology; and umbilical cord derived mesenchymal stromal cells (UC-MSC). We have been studying the immunological effects of UC-MSC administration for treatment-resistant severe acute graft-versus host disease, acute cerebral injury, and radiation injury.

1. Transfusion medicine and related tests

Abe Y, Ogami K, Iwasawa N, Yokoyama K, Nagamura-Inoue T

Our department controls and supports transfusion medicine through blood typing, irregular antibody testing, and cross-matching tests on blood transfusion products including concentrated red blood cells, platelets, and frozen plasma. The blood type of some patients with hematopoietic disorders and post–stem cell transplantation is undetectable.

2. Cell Processing and quality tests for Hematopoietic stem cell transplantation (HSCT) and clinical trials.

Nagamura-Inoue T, Yokoyama K, Takahashi A, Ogami K, Miharu Y

For autologous peripheral blood stem cell transplantation (PBSCT), we perform apheresis for patients with myeloma and malignant lymphoma after mobilization by granulocyte colony-stimulating factor with or without the CXCR-4 inhibitor, Plerixafor. We test CD34-positive cells in the graft of PBSC, bone marrow, and cord blood as the quality tests for HSCT. We process the cells for clinical trials including collection (apheresis), cryo- preservation, and thawing with or without washing upon the requests.

3. Exploring the therapeutic application of UC-MSCs for severe acute graft-versus-host disease (aGVHD) and non-infectious pulmonary complications (NIPC) after hematopoietic stem cell transplantation

Huang X, Nagamura-Inoue T, Takahashi A, Hori A, Mori Y, Nagamura F, Yokoyama K

We investigated the immunosuppressive mechanisms of UC-MSCs on inflammatory cells. A phase I dose-escalation trial, IMSUT-CORD for steroid-resist-ant aGVHD using allogeneic umbilical cord-de-

rived mesenchymal stromal cells (IMSUT-CORD) have been safely completed (Int J Hematol. 2022 Nov; 116(5):754-769.). From 2022 to 2023, phase II clinical trial of NIPC treated with UC-MSCs have been implement- ed. We continued to prepare the next clinical trials of NIPC (phase III). We are investigating the mechanism of the effectiveness of UC-MSCs in severe aGVHD and NIPC in vitro and in vivo.

4. Study of therapeutic application of UC-MSCs to neurological injuries

Cho T, Sei K, Mori Y, Mukai T, Nagamura-Inoue T

Based on the efficacy of proof of concept using UC-MSCs for cerebral palsy by Mukai T et al, a clinical trial (Phase I/II) for cerebral palsy treated with UC-MSCs was implemented from 2021 to 2023, and completed safely. Nowadays, we investigated the efficiency of UC-MSCs for the treatment of acute encephalitis (AE) mimicking the infant viral encephalitis. We found the improvement of the neuron degeneration and part of behavior abnormalities in AE by intravenous injection of UC-MSCs. We also study the cerebral palsy (Periventricular leukoencephalopathy; PVL) rat model treated with UC-MSCs.

5. Research and Development of UC-MSCs (IMSUT-CORD) treatment for new application of UC-MSCs to acute radiation injury, ARDS, cleft palate, hemorrhagic arthropathy, and acceleration of engraftment of HSC

Sudo K, Hu D, Mori Y, Takahashi A, Miharu Y, Hori A, Nagamura-Inoue T

We have been exploring UC-MSCs (IMSUT-CORD) treatment for new application of UC-MSCs to acute radiation injury, cleft palate, hemorrhagic arthropathy, and acceleration of engraftment of using mice models in collaboration with companies.

6. The Research Cord Blood Cell Resource / National BioResource Project (NBRP)

Shibuya Y, Sakai R, Miharu Y, Takahashi A, Nagaya N, Nagamura-Inoue T

The Research Cord Blood bank / resource was established in 2004 and supported by the Ministry of Education, Culture, Sports, Science and Technology for the development of regenerative medicine, immunological cell therapy, infection research, modified gene cell therapy, and drug discovery. Since July 2012, this project has been incorporated into the National BioResource Project (NBRP). The research umbilical cord blood (CB) bank provides processed and cryopreserved CB units (nucleated cells, mononuclear cells, and CD34 + cells) to researchers worldwide via the RIKEN Bioresource Center. The website is at http://www.nbrp.jp/.

7. Institute of Medical Science, University of Tokyo, Cell Resource Center (IMSUT-CRC)

Takahashi A, Miharu Y, Hori A, Mori Y, Nagamura-Inoue T

To promote cell therapy in translational research, IMSUT-CRC was established in 1997 (originally called the Room for Clinical Cellular Technology, or RCCT). To date, the following projects have been implemented:1) CB cell processing for banking in the manner of the Tokyo Cord Blood Bank (1997–2008), 2) research cord blood bank (2004–), 3) dendritic cell therapies (1998–2001), 4) regenerative therapy of alveolar bone derived from bone marrow mesenchymal cells (2005–2011), 5) gene therapy for renal cancer (1998), 6) CB and UC-MSC banking (IMSUT-CORD; 2012–), 7) aAVC-WT1 cell therapy (2017–), and (8) dendritic cell (DC) therapy using DCs pulsed with neoantigen (2020–).

Visit our website: http: //www.ims.u-tokyo.ac.jp/dcpt/english/

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, Miharu 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