

Center for Cell Therapy

1. Staffs and Students (April, 2010)

Director	Tomohiro Morio (Department of Pediatrics)
Vise Director	Michiko Kajiwara (Department of Blood Transfusion Medicine)
Product manager	Norio Shimizu (Division of Virology, Medical Research Institute)
Quality control manager	Michiko Kajiwara (Chief administrator)
Technicians	Shizuko Minegishi, Atsushi Ohyama
Technicians (From Collaborative Research)	Takashi Kosaka
Clerical Assistant	Akiko Hoshikawa, Ayako Tsuji

2. Purpose of Education

Our center is the first ISO9001:2000(2008)-certified cell processing center in Japan. We provide assistance to prepare standard operation procedure (SOP) and offer on-the-job training for cell processing/manipulating procedures and that for quality assurance at the center.

3. Research Subjects

1. Development of innovative techniques for quality assurance of cell products
2. Development of a novel measure for rapid and sensitive detection of multiple pathogens
3. Clinical study on *ex-vivo* expanded donor T-cell infusion for patients who underwent hematopoietic stem cell transplantation (HSCT)
4. Study on *ex vivo*-activated cord blood T-cells for various conditions post-cord blood stem cell transplantation.
5. Development of short tandem repeat method as a molecular ID for personal identification
6. Research on a regeneration system of the cartilage bone from the synovial membrane (Department of Orthopedic Surgery)
7. Basic research on neuroregeneration and its clinical application (Department of Neurology and Neurological Science)
8. Development of novel peptide-pulsed dendritic therapy for adult T-cell leukemia (Department of Immunotherapeutics)

4. Clinical Services

Our center has four independent cell processing rooms (class 10,000 clean rooms) and has received ISO9001:2000(2008) certificate. All the rooms are equipped with a bio-safety cabinet. The hardware as well as software used in our center fulfills all the guidelines that are required for the preparation of cell products of clinical grade.

The cell products prepared in our centers include

- #1 *Ex-vivo* expanded T-lymphocytes
- #2 Synovium-derived mesenchymal stem cells
- #3 Bone marrow-derived mesenchymal stem cells
- #4 Processed peripheral blood stem cells

The center offers our novel detection system for 12 different viruses in rapid and sensitive manner for the doctors in our medical hospital. We also measure virus loads of the detected virus using a real time PCR system. We measured 1,488 samples in year 2010 in total.

5. Publications

Original articles

1. Inoue H, Takada H, Kusuda T, Goto T, Ochiai M, Kinjo T, Muneuchi J, Takahata Y, Takahashi N, **Morio T**, Kosaki K, Hara T. Successful cord blood transplantation for a CHARGE syndrome with CHD7 mutation showing DiGeorge sequence including hypoparathyroidism. *Eur J Pediatr*. 2010;169:83-94.
2. Oba D, Hayashi M, Minamitani M, Hamano S, Uchisaka N, Kikuchi A, Kishimoto H, Takagi M, **Morio T**, Mizutani S. Autopsy study of cerebellar degeneration in siblings with ataxia-telangiectasia-like disorder. *Acta Neuropathol*. 2010;119:513-20.
3. Albert MH, Bittner TC, Nonoyama S, Notarangelo LD, Burns S, Imai K, Espanol T, Fasth A, Pellier I, Strauss G,

- Morio T**, Gathmann B, Noordzij JG, Fillat C, Hoenig M, Nathrath M, Meindl A, Pagel P, Wintergerst U, Fischer A, Thrasher AJ, Belohradsky BH, Ochs HD. X-linked thrombocytopenia (XLT) due to WAS mutations: Clinical characteristics, long-term outcome, and treatment options. *Blood*. 2010; 115(16):3231-8.
4. Okamoto K, Iwai Y, Oh-Hora M, Yamamoto M, **Morio T**, Aoki K, Ohya K, Jetten AM, Akira S, Muta T, Takayanagi H. IkappaBzeta regulates T(H)17 development by cooperating with ROR nuclear receptors. *Nature*. 2010;464:1381-5.
 5. Shin MJ, Shim JH, Lee JY, Chae WJ, Lee HK, **Morio T**, Park JH, Chang EJ, Lee SK. Qualitative and quantitative differences in the intensity of Fas-mediated intracellular signals determine life and death in T cells. *Int J Hematol*. 2010;92:262-70.
 6. Seki M, Kimura H, Mori A, Shimada A, Yamada Y, Maruyama K, Hayashi Y, Agematsu K, **Morio T**, Yachie A, Kato M. Patient Report: Prominent eosinophilia but less eosinophil activation in a patient with Omenn syndrome. *Pediatr Int*. 2010;52:e196-9.
 7. Takagi M, Shinoda K, Piao J, Mitsui N, Takagi M, Matsuda K, Muramatsu H, Doisaki S, Nagasawa M, **Morio T**, Kasahara Y, Koike K, Kojima S, Takao A, Mizutani S. Autoimmune lymphoproliferative syndrome-like disease with somatic KRAS mutation. *Blood*. [Epub ahead of print 2010 Nov 9.]
 8. Asai E, Wada T, Sakakibara Y, Toga A, Toma T, Shimizu T, Imai K, Nonoyama S, **Morio T**, Kamachi Y, Ohara O, Yachie A. Analysis of mutations and recombination activity in RAG-deficient patient. *Clin. Immunol*. [Epub 2010 Dec 4.]
 9. Sugita S, **Shimizu N**, Watanabe K, Katayama M, Horie S, Ogawa M, Sugimoto Y and Mochizuki M. Diagnosis of bacterial endophthalmitis by broad-range quantitative PCR. *Br J Haematol*. Jul 31, 2010 [Epub ahead of print].
 10. Miyanaga M, Sugita S, **Shimizu N**, **Morio T**, Miyata K, Maruyama K, Kinoshita S, Mochizuki M. A significant association of viral loads with corneal endothelial cell damage in cytomegalovirus anterior uveitis. *Br. J. Ophthalmol*. 2010; 94:336-40.
 11. Nagasawa M., Ogawa K., Nagata K., **Shimizu N**. Serum granulysin as a possible biomarker of NK cell neoplasm. *Br J Haematol*. 2010; 148(5):812-4.
 12. Zhang Y, Ohyashiki JH, **Shimizu N**, Ohyashiki K. Aberrant expression of NK cell receptors in Epstein-Barr virus-positive gammadelta T-cell lymphoproliferative disorders. *Hematology*. 2010; 15(1): 43-7.
 13. Kariya Y, Hamatake M, Urano E, Yoshiyama H, **Shimizu N**, Komano J. Dominant-negative derivative of EBNA1 represses EBNA1-mediated transforming gene expression of Epstein-Barr virus infection independent of rapid loss of viral genome. *Cancer Sci*. 2010; 101(4):876-81.
 14. Iwata S, Wada K, Tobita S, Gotoh K, Ito Y, Demachi-Okamura A, **Shimizu N**, Nishiyama Y, Kimura H. Quantitative Analysis of Epstein-Barr Virus (EBV)-Related Gene Expression in Patients with Chronic Active EBV Infection. *J Gen Virol*. 2010; 91(Pt1):42-50.
 15. Yamanaka Y, Tagawa H, Takahashi N, Watanabe A, Guo Y-M, Iwamoto K, Yamashita J, Saitoh H, Kameoka Y, **Shimizu N**, Ichinohasama R, and Sawada K. Aberrant overexpression of microRNAs activate AKT signaling via down-regulation of tumor suppressors in natural killer-cell lymphoma/leukemia. *Blood*. 2010; 114(15): 3265- 75.
 16. Miyagawa Y, Kiyokawa N, Ochiai N, Imadome K, Horiuchi Y, Onda K, Yajima M, Nakamura H, Katagiri Y, Okita H, **Morio T**, **Shimizu N**, Fujimoto J. and Fujiwara S. Ex vivo expanded cord blood CD4 T lymphocytes exhibit a distinct expression profile of cytokine-related genes from those of peripheral blood origin. *Immunology*. 2010; 128(3):405-19.
 17. Chan KK, Shen L, Au WY, Yuen HF, Wong KY, Guo T, Wong ML, **Shimizu N**, Tsuchiyama J, Kwong YL, Liang RH, Srivastava G. Interleukin-2 induces NF-kappaB activation through BCL10 and affects its subcellular localization in natural killer lymphoma cells. *J Pathol*. 2010; 221(2):164-74.
 18. Shimaya M, Muneta T, Ichinose S, Tsuji K, I. **Sekiya I**. Magnesium enhances adherence and cartilage formation of synovial mesenchymal stem cells through integrins. *Osteoarthritis and cartilage*. 2010;18: 1300-9.
 19. Miyamoto T, Muneta T, Tabuchi T, Matsumoto K, Saito H, Tsuji K, **Sekiya I**. Intradiscal transplantation of synovial mesenchymal stem cells prevents intervertebral disc degeneration through suppression of matrix metalloproteinase-related genes in nucleus pulposus cells in rabbits. *Arthritis Res Ther*. 2010; 12(6):R206.PDF
 20. Xu H, Miki K, Ishibashi S, Inoue J, Sun L, Endo S, **Sekiya I**, Muneta T, Inazawa J, Dezawa M, Mizusawa H. Transplantation of neuronal cells induced from human mesenchymal stem cells improves neurological functions after stroke without cell fusion. *J Neurosci Res*. 2010; 88(16):3598-609.
 21. Nimura A, Muneta T, Otabe K, Koga H, Ju YJ, Mochizuki T, Suzuki K, **Sekiya I**. Analysis of human synovial and bone marrow mesenchymal stem cells in relation to heat-inactivation of autologous and fetal bovine serums. *BMC Musculoskelet Disord*. 2010; 11:208.