


SHIGEKI YAGYU MD. PhD

Assistant Professor/Department of Pediatrics

Kyoto Prefectural University of Medicine, Kyoto, Japan



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CORE COMPETENCIES

- General Pediatrics
- Pediatric Hematology
- Pediatric Oncology
- Immunology
- Immunotherapy
- Molecular Biology
- Molecular Cloning
- Gene & Cell Therapy

BOARD CERTIFICATE

- Japanese Society of Pediatrics (23427)
- Japanese Society of Hematology (231739)
- Japanese Board of Cancer Therapy (09101035)

MEDICAL LICENSURE

Full medical license (Japan)
No. 408311

SUMMARY

Physician Scientist –Pediatric Oncologist – Gene & Cell Therapy

Disciplined and confident pediatric oncologist with Japanese medical license and Board Certification in Pediatrics, Hematology, and Oncology. Dynamic physician scientist with extensively detailed research experience in the field of molecular and cellular biology. Expertise in the basic science of pediatric oncology, focusing on the development of novel cell and gene therapy for hematologic/solid malignancies.

QUALIFICATION

- Work in a broad range of pediatric department including general pediatrics, pediatric hematology/oncology, immunology, and stem cell transplantation, working with and leading teams in the delivery of high standard of pediatric patients care.
- Managing basic and translational researches in the development of adoptive cell therapy, gene therapy, and molecular-based diagnosis for cancers, with over 30 publications in the peer-reviewed journals and 4 patent applications in the field of adoptive cell therapy.

PROFESSIONAL EXPERIENCE

- 2015-** **Assistant Professor**
Department of Pediatrics, Graduate School of Medical Science, Kyoto Prefectural University of Medicine, Kyoto, Japan
- 2013-2015** **Postdoctoral Associate**
Center for Cell and Gene Therapy, Baylor College of Medicine, Houston, TX, USA
- 2011-2012** **Assistant professor**
Department of Pediatrics, Graduate School of Medical Science, Kyoto Prefectural University of Medicine, Kyoto, Japan
- 2009-2011** **Attending Doctor**
Division of Pediatrics, Kyoto Prefectural University of Medicine, North Medical Center, Kyoto, Japan

RESIDENCIES AND FELLOWSHIP

- 2005-2009** Fellow in Pediatric Hematology/Oncology/Immunology branch, Department of Pediatrics, Kyoto Prefectural University of Medicine, Kyoto, Japan
- 2003-2005** Fellow in the Department of Pediatrics, Kyoto City Hospital, Kyoto, Japan
- 2001-2003** Resident in the Department of Pediatrics, Otsu Municipal Hospital, Otsu, Japan
- 2000-2001** Resident in the Department of Pediatrics, Kyoto Prefectural University of Medicine, Kyoto, Japan

EDUCATION

- 2005-2009** Ph.D. in the field of Child Health and Human Medicine, Graduate School of Medical Science, Kyoto Prefectural University of Medicine
- 1994-2000** MD, Kyoto Prefectural University of Medicine,

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AWARDS AND RECOGNITION

- Oct. 2011 **Best Poster Award**
43rd Congress of the International Society of Pediatric Oncology,
- May 2015 **Meritorious Abstract Travel Award**
18th Annual Meeting of American Society of Gene and Cell therapy
- Nov 2017 **Academic Award**
Japanese Society of Pediatric Hematology Oncology
- Feb 2019 **Merit Award**
2nd International Cancer Research Symposium of Training Plan for Oncology Professionals

RESEARCH GRANTS

- 2018-2021 Japan Agency for Medical Research and Development, Japan Cancer Research Project, Practical Research for Innovative Cancer Control
- 2017-2019 Grant in Aid for Scientific research (17K07224) from the Ministry of Education, Culture Sports, Science, and Technology of Japan
- 2016-2018 The Mother and Child Health Foundation Research Grant
- 2015 Kyoto innovative medical technology research and development Research Grant
- 2015-2016 Gold ribbon Research Grant
- 2013-2014 The Rotary International Foundation Global Grant Scholarship
- 2012-2013 Grant in Aid for Scientific research (22790994) from the Ministry of Education, Culture Sports, Science, and Technology of Japan
- 2009-2010 Grant in Aid for Scientific research (22790994) from the Ministry of Education, Culture Sports, Science, and Technology of Japan

PATENT APPLICATION

1. WO2011126048 A1, PCT/JP2011/058722
Method for detecting genetic aberrations of neuroblastoma using sample derived from body fluid
2. JP2016-242054, PCT/JP2017/43629
A genetically-modified chimeric antigen receptor T cells having cytotoxic effect
3. 2019-103074
A genetically-modified chimeric antigen receptor T cells targeting ALK
4. PCT/JP2019/029942
Method for manufacture of CAR expressing immune cells

CURRENT RESEARCH INTEREST

1. Comprehensive analysis of cancer immunotherapy for the improvement of the efficacy and safety of adoptive T cell therapy.
2. Clinical application of cancer immunotherapy, including adoptive cell therapy (chimeric antigen receptor T cells, NK cell therapy).
3. Development of genetically-engineered immune cells targeting pediatric solid tumors.
4. Gene therapy for pediatric malignancy, including oncolytic virotherapy.
5. Molecular genetics of pediatric solid tumors.
6. Establishment of liquid biopsy for early diagnosis of pediatric solid tumors.

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PUBLICATION

1. Nakagawa N, Kikuchi K, **Yagyu S**, Miyachi M, Iehara T, Tajiri T, Sakai T, Hosoi H. Mutations in the RAS pathway as potential precision medicine targets in treatment of rhabdomyosarcoma. *Biochem Biophys Res Commun*. 2019 (19)30415-2.
2. Tomoyasu C, Kikuchi K, Kaneda D, **Yagyu S**, Miyachi M, Tsuchiya K, Iehara T, Sakai T, Hosoi H. OBP-801, a novel histone deacetylase inhibitor, induces M-phase arrest and apoptosis in rhabdomyosarcoma cells. *Oncol Rep*. 2018 in press
3. Otabe O, Kikuchi K, Tsuchiya K, Katsumi Y, **Yagyu S**, Miyachi M, Iehara T, Hosoi H. MET/ERK2 pathway regulates the motility of human alveolar rhabdomyosarcoma cells. *Oncol Rep*. 37(1):98-104. 2017
4. **Yagyu S**, Iehara T, Tanaka S, Gotoh T, Misawa-Furihata A, Sugimoto T, London WB, Hogarty MD, Teramukai S, Nakagawara A, Hiyama E, Maris JM, Hosoi H. Serum-Based Quantification of *MYCN* Gene Amplification in Young Patients with Neuroblastoma: Potential Utility as a Surrogate Biomarker for Neuroblastoma. *Plos One* 11(8) e0161039.
5. Iehara T, **Yagyu S**, Tsuchiya K, Kuwahara Y, Miyachi M, Tajiri T, Sugimoto T, Sawada T, Hosoi H. Residual tumor in cases of intermediate-risk neuroblastoma did not influence the prognosis. *Jpn J Clin Oncol*. 46(7):661-6.
6. **Yagyu S**, Hoyos V, Del Bufalo F, Brenner MK. Multiple mechanisms determine the sensitivity of human-induced pluripotent stem cells to the inducible caspase-9 safety switch. *Mol Ther. Methods Clin Dev* 16003. 2016
7. Del Bufalo F, Manzo T, Hoyos V, **Yagyu S**, Caruana I, Jacot J, Benavides O, Rosen D, Brenner MK. 3D modeling of human cancer: A PEG-fibrin hydrogel system to study the role of tumor microenvironment and recapitulate the in vivo effect of oncolytic adenovirus. *Biomaterials*. 84:76-85 2016.
8. Hoyos V, Del Bufalo F, **Yagyu S**, Ando M, Dotti G, Suzuki M, Bouchier-Hayes L, Alemany R, Brenner MK. Mesenchymal Stromal Cells for Linked Delivery of Oncolytic and Apoptotic Adenoviruses to Non-small-cell Lung Cancers. *Mol Ther*. 23(9):1497-506. 2015
9. **Yagyu S**, Hoyos V, Del Bufalo F, Brenner MK. An Inducible Caspase-9 Suicide Gene to Improve the Safety of Therapy Using Human Induced Pluripotent Stem Cells. *Mol Ther*. 23(9):1475-85. 2015
10. Ninomiya S, Narala N, Huye L, **Yagyu S**, Savoldo B, Dotti G, Heslop HE, Brenner MK, Rooney CM, Ramos CA. Tumor indoleamine 2,3-dioxygenase (IDO) inhibits CD19-CAR T cells and is downregulated by lymphodepleting drugs. *Blood*. 125(25):3905-16. 2015
11. Hatsuse M, Taniguchi-Yoshihara K, **Yagyu S**, Fuchida S, Okano A, Murakami S, Shimazaki C. Successful treatment with pseudo-autologous blood stem cell transplantation for an adolescent-onset multiple myeloma who relapsed after allogeneic bone marrow transplantation. *Rihsho Ketsueki* 56(4) 428-31, 2015
12. Yoshida H, Miyachi M, Sakamoto K, Ouchi K, **Yagyu S**, Kikuchi K, Kuwahara Y, Tsuchiya K, Imamura T, Iehara T, Kakazu N, Hojo H, Hosoi H. PAX3-NCOA2 fusion gene has a dual role in promoting the proliferation and inhibiting the myogenic differentiation of rhabdomyosarcoma cells. *Oncogene*. 33(49):5601-8. 2014
13. Ando M, Hoyos V, **Yagyu S**, Tao W, Ramos CA, Dotti G, Brenner MK, Bouchier-Hayes L. Bortezomib sensitizes non-small cell lung cancer to mesenchymal stromal cell-delivered inducible caspase-9-mediated cytotoxicity. *Cancer Gene Ther*. 21(11):472-82. 2014
14. Farzad L, Cerullo V, **Yagyu S**, Bertin T, Hemminki A, Rooney C, Lee B, Suzuki M. Combinatorial treatment with oncolytic adenovirus and helper-dependent adenovirus augments adenoviral cancer gene therapy. *Mol Ther Oncolytics*. 1:14008. 2014.
15. Sugimoto T, Gotoh T, **Yagyu S**, Kuroda H, Iehara T, Hosoi H, Ohta S, Ohira M, Nakagawara A. A *MYCN*-amplified cell line derived from a long-term event-free survivor among our sixteen established neuroblastoma cell lines. *Cancer Lett*. 331(1):115-21. 2013
16. Hiramoto N, Kobayashi Y, Nomoto J, Maruyama D, Watanabe T, Tochigi N, Furuta K, Takeda K, Chuman H, **Yagyu S**, Hosoi H, Tobinai K. Ewing sarcoma arising after treatment of diffuse large B-cell lymphoma. *Jpn J Clin Oncol*. 43(4):417-21. 2013
17. Fujiki A, Imamura T, Sakamoto K, Kawashima S, Yoshida H, Hirashima Y, Miyachi M, **Yagyu S**, Nakatani T, Sugita K, Hosoi H. All-trans retinoic acid combined with 5-Aza-2'-deoxycytidine induces *C/EBPα* expression and growth inhibition in MLL-AF9-positive leukemic cells. *Biochem Biophys Res Commun*. 428(2):216-23. 2012

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18. **Yagyu S**, Iehara T, Gotoh T, Miyachi M, Katsumi Y, Kikuchi K, Tsuchiya K, Osone S, Kuroda H, Sugimoto T, Sawada T, Hosoi H. Preoperative analysis of 11q loss using circulating tumor-released DNA in serum: a novel diagnostic tool for therapy stratification of neuroblastoma. *Cancer Lett.* 309(2):185-9. 2011
19. Katsumi Y, Iehara T, Miyachi M, **Yagyu S**, Tsubai-Shimizu S, Kikuchi K, Tamura S, Kuwahara Y, Tsuchiya K, Kuroda H, Sugimoto T, Houghton PJ, Hosoi H. Sensitivity of malignant rhabdoid tumor cell lines to PD 0332991 is inversely correlated with p16 expression. *Biochem Biophys Res Commun.* 413(1):62-8. 2011
20. Kimoto T, Inoue M, Tokimasa S, **Yagyu S**, Iehara T, Hosoi H, Kawa K. Detection of MYCN DNA in the cerebrospinal fluid for diagnosing isolated central nervous system relapse in neuroblastoma. *Pediatr Blood Cancer.* 56(5):865-7. 2011
21. Miyachi M, Tsuchiya K, Yoshida H, **Yagyu S**, Kikuchi K, Misawa A, Iehara T, Hosoi H. Circulating muscle-specific microRNA, miR-206, as a potential diagnostic marker for rhabdomyosarcoma. *Biochem Biophys Res Commun.* 400(1):89-93. 2010
22. Miyachi M, Kakazu N, **Yagyu S**, Katsumi Y, Tsubai-Shimizu S, Kikuchi K, Tsuchiya K, Iehara T, Hosoi H. Restoration of p53 pathway by nutlin-3 induces cell cycle arrest and apoptosis in human rhabdomyosarcoma cells. *Clin Cancer Res.* 15(12):4077-84. 2009
23. Misawa A, Tanaka S, **Yagyu S**, Tsuchiya K, Iehara T, Sugimoto T, Hosoi H. RASSF1A hypermethylation in pretreatment serum DNA of neuroblastoma patients: a prognostic marker. *Br J Cancer.* 100(2):399-404. 2009
24. **Yagyu S**, Gotoh T, Iehara T, Miyachi M, Katsumi Y, Tsubai-Shimizu S, Kikuchi K, Tamura S, Tsuchiya K, Imamura T, Misawa-Furihata A, Sugimoto T, Sawada T, Hosoi H. Circulating methylated-DCR2 gene in serum as an indicator of prognosis and therapeutic efficacy in patients with MYCN nonamplified neuroblastoma. *Clin Cancer Res.* 14(21):7011-9. 2008
25. Kikuchi K, Tsuchiya K, Otabe O, Gotoh T, Tamura S, Katsumi Y, **Yagyu S**, Tsubai-Shimizu S, Miyachi M, Iehara T, Hosoi H. Effects of PAX3-FKHR on malignant phenotypes in alveolar rhabdomyosarcoma. *Biochem Biophys Res Commun.* 365(3):568-74. 2008
26. **Yagyu S**, Morimoto A, Kakazu N, Tamura S, Fujiki A, Nakase Y, Iehara T, Hosoi H, Kuroda H. Late appearance of a Philadelphia chromosome in a patient with therapy-related acute myeloid leukemia and high expression of EVI1. *Cancer Genet Cytogenet.* 180(2):115-20. 2008
27. Hosoi H, Iehara T, Tsuchiya K, Misawa A, Miyaji M, **Yagyu S**, Koizumi M, Nishimura T, Tokiwa K, Iwai N, Yanagisawa A, Sugimoto T. Continuous remission in an infant with chest wall malignant rhabdoid tumor after relapse. *J Pediatr Surg.* 42(10):E9-12. 2007
28. Yasuno T, Yamasaki A, Maeda Y, Fujiki A, **Yagyu S**. Atopic dermatitis and transient hypogammaglobulinemia of infancy improved simultaneously. *Pediatr Int.* 49(3):406-8. 2007
29. **Yagyu S**, Kuroda H, Fujiki A, Tamura S, Iehara T, Morimoto A, Hosoi H, Sugimoto T, Imashuku S. Successful non-T-cell-depleted HLA-haploidentical 3-loci mismatched bone marrow transplantation. *Eur J Haematol.* 74(6):529-32. 2005
30. Okuda T, Takeda K, Fujita Y, Nishimura M, **Yagyu S**, Yoshida M, Akira S, Downing JR, Abe T. Biological characteristics of the leukemia-associated transcriptional factor AML1 disclosed by hematopoietic rescue of AML1-deficient embryonic stem cells by using a knock-in strategy. *Mol Cell Biol.* 20(1):319-28. 2000