BIOGRAPHICAL SKETCH

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NAME: Sugio, Takeshi

eRA COMMONS USER NAME (credential, e.g., agency login): sugio.takeshi

POSITION TITLE: Special fellow

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE (if applicable)	END DATE MM/YYYY	FIELD OF STUDY
Kyushu University, Fukuoka	MD	03/2010	Medicine
Kyushu University, Fukuoka	PHD	03/2019	Hematology
Toranomon Hospital, Tokyo	Resident	03/2012	Internal Medicine
Kyushu University Hospital, Fukuoka	Fellow	03/2014	Hematology
Kyushu University Hospital, Fukuoka	Fellow	08/2021	Hematology
Stanford University, Stanford, California	Postdoctoral Fellow	present	Hematology/Oncology

A. Personal Statement

I am an M.D./Ph.D. physician-scientist and a postdoctoral fellow in the Division of Oncology at Stanford Medicine. Before transitioning to research, I practiced as a clinician for 10 years in Japan, specializing in hematopoietic stem cell transplantation (HSCT) and CAR-T therapy for relapsed/refractory (R/R) hematological malignancies. Working in a region with a high prevalence of HTLV-1 carriers, I treated numerous refractory cases, highlighting the urgent need for early detection and predictive strategies. This experience shaped my research focus and led to the development of my current proposal.

For the past eight years, my research has focused on T-cell lymphomas (TCL) and HSCT, with a particular emphasis on the tumor microenvironment. During my PhD, I developed a classification system based on microenvironmental gene expression signatures for TCL, which contributed to the design of a Phase II clinical trial evaluating PD-1 inhibitors for R/R TCL. This work was conducted under the supervision of Dr. Koichi Akashi, former Associate Professor at Dana-Farber Cancer Institute and Director of Kyushu University Hospital, and Dr. Takahiro Maeda, former Associate Professor at Brigham and Women's Hospital and current Professor of the Division of Precision Medicine at Kyushu University. In the Akashi lab, I played a key role in the initial setup, optimization, and maintenance of the Imaging Mass Cytometry (Hyperion) and CODEX. I identified that mast cell in intestinal tissue is associated with the favorable response to steroid therapy for gut GVHD using CODEX. This finding was presented in a webinar hosted by Akoya Biosciences (September, 2020) and were selected for a Plenary Session at the Annual Meeting of the Japanese Society of Cell Therapy (Feb, 2020), where I served as a second author. Additionally, I have specialized in clinical data analysis, contributing to statistical analyses for 20 papers, including four as first author. My current research is centered on investigating the role of mismatched HLA in the context of allogeneic HSCT and expanding my expertise in immunopeptidomics to better understand antigen presentation dynamics. Beyond my research contributions, I played a pivotal role in establishing a biobanking system for hematological malignancies, the Kyushu Clinical Sample NETwork (KCNET). My efforts included developing standardized protocols, implementing inventory management software, and leading the education of dedicated technicians, ensuring high-quality sample collection and processing to support translational research.

As a postdoctoral fellow, I have developed several computational pipelines, including SABER (immune repertoire analysis), QUARTZ (T/B-cell fraction in DNA mixtures), and CANARy-TF (tumor fraction by

copy number alterations). I also contributed to refining EPIC-Seq (epigenomics), and VirCAPP-Seq (viral genome detection). Furthermore, I established the wet-lab experimental system for cfRNA expression analysis, which was recently accepted for publication in Nature. QUARTZ has been filed as a U.S. Provisional Patent Application and is currently under evaluation for further patent proceedings. Additionally, CANARy-TF is currently being prepared for future patent filing. Leveraging my expertise in TCR analysis, I co-authored a Cancer Cell paper on cfDNA-based tumor and immune profiling in CAR-T therapy and served as co-first author on a New England Journal of Medicine paper detailing secondary TCL following CAR-T therapy.

In January 2022, the third daughter was born, and parental leave was taken from January to April 2022. As a result, eligibility for Pathway to Independence Awards (K99/R00) was extended by three months.

Building on my expertise in molecular biology, clinical hematology, and computational genomics, I am applying for a K99/R00 to advance my research independence. My mentor, Dr. Ash Alizadeh, provides an exceptional environment for lymphoma biology and liquid biopsy research. Additionally, my advisory committee. Building on my expertise in molecular biology, clinical hematology, and computational genomics, I am applying for a K99/R00 to advance my research independence. My mentor, Dr. Ash Alizadeh, provides an exceptional environment for lymphoma biology and liquid biopsy research. Additionally, my advisory committee —Dr. Mark Davis (President of the American Association of Immunologists and a pioneer in T-cell biology), Dr. Robert Tibshirani (Professor in the Department of Biomedical Data Science and an expert in statistical modeling), Dr. Akil Merchant (Director of the Spatial Molecular Profiling Shared Resource core facility at Cedars-Sinai Medical Center), and Dr. Lisa Wagar (Specialist in patient-derived organoid models for lymphoid tissues)—will support my scientific and career development. Their collective expertise will be instrumental in my successful transition to an independent investigator.

1. Sugio T, Nesselbush M, Shukla N, Garofalo A, Mutter J, Shahrokh Esfahani M, Alig S, Shi S, Noordenbos T, Hamilton M, Rossi C, Tian F, Liu C, Olsen M, Kang X, Russler-Germain D, Horwitz S, Kato K, Ito A, Yamagishi M, Fukuda T, Akashi K, Uchimaru K, Khodadoust M, Diehn M, Mehta-Shah N, Alizadeh A. Integrating Genomic & Transcriptomic Features for Noninvasive Detection, Characterization, and Monitoring of T-Cell Lymphomas. Blood. 2024 November 05; 144(Supplement 1):454-454. Available from: https://ashpublications.org/blood/article/144/Supplement%201/454/531506/Integrating-Genomic-amp-Transcriptomic-Features DOI: 10.1182/blood-2024-206518
2. Hamilton MP, Sugio T, Noordenbos T, Shi S, Bulterys PL, Liu CL, Kang X, Olsen MN, Good Z, Dahiya S, Frank MJ, Sahaf B, Mackall CL, Gratzinger D, Diehn M, Alizadeh AA, Miklos DB. Risk of Second Tumors and T-Cell Lymphoma after CAR T-Cell Therapy. N Engl J Med. 2024 Jun 13;390(22):2047-2060. PubMed Central PMCID: PMC11338600.
3. Sugio T, Kato K, Aoki T, Ohta T, Saito N, Yoshida S, Kawano I, Henzan H, Kadowaki M, Takase K, Muta T, Miyawaki K, Yamauchi T, Shima T, Takashima S, Mori Y, Yoshimoto G, Kamezaki K, Takenaka K, Iwasaki H, Ogawa R, Ohno Y, Eto T, Kamimura T, Miyamoto T, Akashi K. Mogamulizumab Treatment Prior to Allogeneic Hematopoietic Stem Cell Transplantation Induces Severe Acute Graft-versus-Host Disease. Biol Blood Marrow Transplant. 2016 Sep;22(9):1608-1614. PubMed PMID: 27220263.

B. Positions, Scientific Appointments and Honors

Positions and Scientific Appointments

2023 -	Special fellow, Leukemia Lymphoma Society
2023 - 2023	Overseas Research Fellowships, Japan Society for the Promotion of Science
2021 -	Postdoctoral Researcher, Stanford University, Stanford, CA
2021 -	Board Certified Instructor, Japanese Society of Hematology

2018 - 2021 Clinical Fellow, Kyushu University Hospital, Fukuoka
2017 - Board Certified Fellow, Japanese Society of Hematology
2013 - Board Certified Physician, Japanese Society of Internal Medicine

Honors

2023 - 2025 Special fellow, Leukemia Lymphoma Society, United States, Leukemia Lymphoma Society
2024 - 2024 The ASH Abstract Achievement Award, American Society of Hematology
2023 - 2023 Grant-in-Aid for JSPS Fellows, Japan Society for the Promotion of Science
2023 - 2023 JSH Young Investigator's Award, Japanese Society of Hematology
2023 The ASH Abstract Achievement Award, American Society of Hematology
2022 The ASH Abstract Achievement Award, American Society of Hematology
2020 Clinical Medical Research Award, Medical Care Education Research Foundation
2017 JSH International Symposium, Best presentation award, Japanese Society of Hematology

C. Contribution to Science

1. Developing of Disease Monitoring System and Identifying Immunologic Determinants of Lymphoma Progression for Personalized Treatment

   As a Ph.D. student, I conducted a study to reclassify the highly heterogeneous lymphoma subtypes, diffuse large B-cell lymphoma (DLBCL) and peripheral T-cell lymphoma, not otherwise specified (PTCL-NOS), using gene expression analysis. Notably, my analysis identified distinct classifications based on microenvironment-associated gene expression signatures for both lymphoma types, which also correlated with prognosis. Additionally, I played a major role in the planning and execution of a Phase II clinical trial evaluating a PD-1 inhibitor for relapsed and refractory PTCL. In my current lab at Stanford, I am performing multimodal analyses of cfDNA and cfRNA and developing comprehensive systems for disease monitoring and immune dynamics profiling.

   a. Sugio T, Nesselbush M, Shukla N, Garofalo A, Mutter J, Shahrokh Esfahani M, Alig S, Shi S, Noordenbos T, Hamilton M, Rossi C, Tian F, Liu C, Olsen M, Kang X, Russler-Germain D, Horwitz S, Kato K, Ito A, Yamagishi M, Fukuda T, Akashi K, Uchimaru K, Khodadoust M, Diehn M, Mehta-Shah N, Alizadeh A. Integrating Genomic & Transcriptomic Features for Noninvasive Detection, Characterization, and Monitoring of T-Cell Lymphomas. Blood. 2024 November 05; 144(Supplement 1):454-454. Available from: https://ashpublications.org/blood/article/144/Supplement%201/454/531506/Integrating-Genomic-amp-Transcriptomic-Features DOI: 10.1182/blood-2024-206518
   b. Miyawaki K, Kato K, Sugio T, Sasaki K, Miyoshi H, Semba Y, Kikushige Y, Mori Y, Kunisaki Y, Iwasaki H, Miyamoto T, Kuo FC, Aster JC, Ohshima K, Maeda T, Akashi K. A germinal center-associated microenvironmental signature reflects malignant phenotype and outcome of DLBCL. Blood Adv. 2022 Apr 12;6(7):2388-2402. PubMed Central PMCID: PMC9006269.

2. Identification of Prognostic Determinants for Hematopoietic Stem Cell Transplantation

   As a Ph.D. student, I retrospectively analyzed the data of patients with acute T-cell leukemia/lymphoma (ATLL) who received allogeneic stem cell transplantation (allo-HSCT). As a result, I identified that the CCR4 inhibitor, which was expected as pre-transplant therapy due to its high remission induction rate, induced lethal GvHD when it was used before allo-HSCT. The results of my study have led to a significant revision of the treatment strategy for ATLL and contributed to improved prognosis. During the clinical fellowship, I performed translational research on HSCT patients. I analyzed the function of mismatched HLA from two angles: 1) antigen-presenting function of mismatched HLA and 2) antigenicity of mismatched HLA. As a result, I found that 1) GVL effect is effectively induced in cases with matched mismatched HLA supertypes, dramatically lowering disease

recurrence, 2) mismatched HLA-B derived epitopes are associated with pre-engraftment immune reaction leading to engraft failure in cord blood transplantation. The results of these studies were significant for the development of new donor selection criteria. As a postdoctoral fellow, I conducted a retrospective analysis of the prognostic impact of PET-CT prior to HSCT for R/R lymphoma and identified that low TMTV is associated with better prognosis both in autologous and allogeneic hematopoietic stem cell transplantations. Moreover, For R/R B-cell lymphoma, I also performed retrospective analysis of Japanese registry data for patients treated with HSCT and made a prognostic index that can identify a subgroup of DLBCL patients who benefit from allo-HSCT.

a. Sugio T, Uchida N, Miyawaki K, Ohno Y, Eto T, Mori Y, Yoshimoto G, Kikushige Y, Kunisaki Y, Mizuno S, Nagafuji K, Iwasaki H, Kamimura T, Ogawa R, Miyamoto T, Taniguchi S, Akashi K, Kato K. Prognostic impact of HLA supertype mismatch in single-unit cord blood transplantation. Bone Marrow Transplant. 2024 Apr;59(4):466-472. PubMed PMID: 38238452.
b. Kato K, Sugio T, Ikeda T, Yoshitsugu K, Miyazaki K, Suzumiya J, Yamamoto G, Kim S, Ikegame K, Uehara Y, Mori Y, Ishikawa J, Hiramoto N, Eto T, Nakazawa H, Kobayashi H, Serizawa K, Onizuka M, Fukuda T, Atsuta Y, Suzuki R. Outcomes of allogeneic hematopoietic stem cell transplantation for relapsed or refractory diffuse large B-cell lymphoma. Bone Marrow Transplantation. 2023 December 15; 59(3):306-314. Available from: https://www.nature.com/articles/s41409-023-02156-4 DOI: 10.1038/s41409-023-02156-4
c. Sugio T, Baba S, Mori Y, Yoshimoto G, Kamesaki K, Takashima S, Urata S, Shima T, Miyawaki K, Kikushige Y, Kunisaki Y, Numata A, Takenaka K, Iawasaki H, Miyamoto T, Ishigami K, Akashi K, Kato K. Prognostic value of pre-transplantation total metabolic tumor volume on (18)fluoro-2-deoxy-D-glucose positron emission tomography-computed tomography in relapsed and refractory aggressive lymphoma. Int J Hematol. 2022 Oct;116(4):603-611. PubMed PMID: 35701707.
d. Sugio T, Kato K, Aoki T, Ohta T, Saito N, Yoshida S, Kawano I, Henzan H, Kadowaki M, Takase K, Muta T, Miyawaki K, Yamauchi T, Shima T, Takashima S, Mori Y, Yoshimoto G, Kamezaki K, Takenaka K, Iwasaki H, Ogawa R, Ohno Y, Eto T, Kamimura T, Miyamoto T, Akashi K. Mogamulizumab Treatment Prior to Allogeneic Hematopoietic Stem Cell Transplantation Induces Severe Acute Graft-versus-Host Disease. Biol Blood Marrow Transplant. 2016 Sep;22(9):1608-1614. PubMed PMID: 27220263.

3. Identification and Preclinical Validation of Novel Therapeutic Targets in Hematological Malignancies

During my Ph.D., we found that de novo purine synthesis-related genes, such as PAICS, were upregulated in DLBCL patients with poor prognoses. PAICS was further identified as a potential therapeutic target through CRISPR screening in AML. I validated the efficacy of PAICS inhibitors using multiple cell lines and PDX mouse models for both DLBCL and AML. Additionally, I assessed the efficacy and safety of KHK2823, a non-fucosylated fully human IgG1 monoclonal antibody targeting IL-3Ra, using PDX models for AML. I also contributed to research on leukemic stem cell metabolism, identifying molecules within the BCAA metabolism pathway as critical therapeutic targets for acute leukemia. Furthermore, I focused on BIRC5 as a novel therapeutic target in PTCL, where it was highly expressed in poor prognosis cases. I confirmed the efficacy of BIRC5 inhibition through in vitro gene modification (shRNA and CRISPR) and administration of BIRC5 inhibitors in PDX models generated via renal capsule transplantation of PTCL tumor tissues.

a. Kikushige Y, Miyamoto T, Kochi Y, Semba Y, Ohishi M, Irifune H, Hatakeyama K, Kunisaki Y, Sugio T, Sakoda T, Miyawaki K, Kato K, Soga T, Akashi K. Human acute leukemia uses branched-chain amino acid catabolism to maintain stemness through regulating PRC2 function. Blood Adv. 2023 Jul 25;7(14):3592-3603. PubMed Central PMCID: PMC10368855.
b. Yamauchi T, Miyawaki K, Semba Y, Takahashi M, Izumi Y, Nogami J, Nakao F, Sugio T, Sasaki K, Pinello L, Bauer DE, Bamba T, Akashi K, Maeda T. Targeting leukemia-specific dependence on the de novo purine synthesis pathway. Leukemia. 2022 Feb;36(2):383-393. PubMed PMID: 34344987.

c. Miyawaki K, Yamauchi T, Sugio T, Sasaki K, Miyoshi H, Osborne S, Taylor D, Ohshima K, Kato K, Maeda T, Akashi K. Paics Inhibition Is a Potential Therapeutic Strategy for MYC-Positive DLBCL. Blood. 2019 November 13; 134(Supplement_1):396-396. Available from: https://ashpublications.org/blood/article/134/Supplement_1/396/426231/Paics-Inhibition-Is-a-Potential-Therapeutic DOI: 10.1182/blood-2019-129613

d. Akiyama T, Takayanagi S, Maekawa Y, Miyawaki K, Jinnouchi F, Jiromaru T, Sugio T, Daitoku S, Kusumoto H, Shimabe M, Nishikawa S, Yamawaki K, Iijima K, Hiura M, Takahashi T, Kikushige Y, Iwasaki H, Akashi K, Tawara T. First Preclinical Report of the Efficacy and PD Results of KHK2823, a Non-Fucosylated Fully Human Monoclonal Antibody Against IL-3Rα. Blood. 2015 December 03; 126(23):1349-1349. Available from: https://ashpublications.org/blood/article/126/23/1349/104583/First-Preclinical-Report-of-the-Efficacy-and-PD DOI: 10.1182/blood.V126.23.1349.1349

4. Integrated Liquid Biopsy Approach for Monitoring Disease and Immune Dynamics in CAR-T Patients

   I performed a comprehensive multimodal analysis of plasma cfDNA from B-cell lymphoma patients treated with CAR19 therapies, leveraging my expertise in diverse liquid biopsy methodologies. Through this analysis, I identified high T-cell fraction in cfDNA post CART infusion as a favorable prognostic factor and discovered that CHIP-related mutations serve as a predisposing factor for secondary T-cell tumors following CAR-T therapy.

   a. Sugio T, Shahrokh Esfahani M, Jun S, Sworder B, Hamilton M, Hosoya H, Olsen M, Kang X, Liu C, Tian F, Miklos D, Kurtz D, Diehn M, Alizadeh A. Direct Method for Estimating the Fraction of T and B/Plasma Cell-Derived DNA. Blood. 2024 November 05; 144(Supplement 1):2223-2223. Available from: https://ashpublications.org/blood/article/144/Supplement%201/2223/531665/Direct-Method-for-Estimating-the-Fraction-of-T-and DOI: 10.1182/blood-2024-193441

   b. Hamilton MP, Sugio T, Noordenbos T, Shi S, Bulterys PL, Liu CL, Kang X, Olsen MN, Good Z, Dahiya S, Frank MJ, Sahaf B, Mackall CL, Gratzinger D, Diehn M, Alizadeh AA, Miklos DB. Risk of Second Tumors and T-Cell Lymphoma after CAR T-Cell Therapy. N Engl J Med. 2024 Jun 13;390(22):2047-2060. PubMed Central PMCID: PMC11338600.

Complete List of Published Work in My Bibliography:
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