Stanford

# Yusuke Nakauchi

Postdoctoral Research Fellow, Stanford Cancer Center

## Bio

### BIO

My research projects aim to investigate the biology of human leukemia. I believe my research will contribute to clarify the disease pathogenesis of leukemia and help identify the critical cells to target to both prevent the development of de novo leukemia and halt relapse.

### HONORS AND AWARDS

- 60th ASH Abstract Achievement Award (Oral Presentation), American Society of Hematology (2018)
- Stanford University School of Medicine, the Dean's Postdoctoral Fellowship, Stanford University (2016)
- Overseas Award, Nakayama Foundation for Human Science (2014)

### BOARDS, ADVISORY COMMITTEES, PROFESSIONAL ORGANIZATIONS

- Associate Member, The American Association for Cancer Research (2015 - present)
- Associate Member, The American Society of Hematology (2015 - present)
- Member, The Japanese Society for Immunology (2011 - present)
- Member, The Japanese Society of Hematology (2006 - present)
- Member, The Japanese Society of Internal Medicine (2006 - present)

### PROFESSIONAL EDUCATION

- Doctor of Philosophy, The University of Tokyo (2014)
- Doctor of Medicine, Asahikawa Medical College (2005)

### STANFORD ADVISORS

- Ravindra Majeti, Postdoctoral Faculty Sponsor

### LINKS

- Majeti Lab, Stanford University School of Medicine: http://majetilab.stanford.edu
- The Institute of Medical Science, The University of Tokyo: http://stemcell-u-tokyo.org/en/sct/
- Asahikawa Medical University: http://www.jimu.asahikawa-med.ac.jp/english/index.html

# Research & Scholarship

## CURRENT RESEARCH AND SCHOLARLY INTERESTS

From 2005 to 2010, my work as a clinical hematology fellow allowed me to experience first-hand how scientific advances that started in a laboratory can transform the lives of patients. While many of my patients were cured of their disease with allogeneic hematopoietic stem cell transplantation, underscoring the importance of anti-tumor immunotherapy in eradicating leukemia, I witnessed face-to-face their suffering from the long-term consequence of graft-versus-host disease (GVHD). This experience was ultimately what drove me to engage in research to discover novel therapies. For this reason, I embarked on a PhD program in 2010 to design antibody therapy to (i) target GVHD and (ii) target hematological malignancies. Under the mentorship of Professor Hiromitsu Nakauchi at the University of Tokyo, an international leader in hematopoiesis, I developed allele-specific anti-human leukocyte antigen (HLA) monoclonal antibodies for severe GVHD caused by HLA-mismatched hematopoietic stem cell transplantation (Nakauchi et al., Exp Hematol, 2015). This study was the first to find that anti-HLA antibodies can be used therapeutically against GVHD. That success gave me the motivation and confidence to further my research beyond targeting GVHD, to targeting leukemic stem cells through my current postdoctoral fellowship in the laboratory of Professor Ravindra Majeti, Department of Hematology at Stanford University.

Many people suffer from leukemia each year, but we still don't know how to completely cure it. Recent advances in sequencing technologies have tremendously improved our understanding of the underlying mutations that drive hematologic malignancies, although, the reality is that the majority of the mutations are not easily "druggable" and the discovery of these mutations has not yet made a significant impact in patient outcomes. I view this perhaps the most crucial challenges facing a translational cancer researcher like myself. My current research is a major step toward my long term goal to make personalized medicine a reality for patients with acute myeloid leukemia (AML) and other hematologic malignancies. Although my research is focused on targeting Ten-Eleven Translocation methylcytosine dioxygenase-2 (TET2) mutations, I anticipate it will lead to a better understanding of the cell context requirement for TET2 mutations in AML and help identify the critical cells to target to both prevent the development of de novo leukemia and halt relapse. It may also prove of value to understanding of the biology of a range of other cancers.

# Publications

## PUBLICATIONS

- **Azacitidine and Ascorbate Inhibit the Competitive Outgrowth of Human TET2 Mutant HSPCs in a Xenograft Model of Pre-Leukemia**
  Nakauchi, Y., Thomas, D., Sharma, R., Corces, M., Reinisch, A., Cruz, D., Koehnke, T., Karigane, D., Fan, A., Majeti, R.
  AMER SOC HEMATOLOGY.2018
- **Hematopoietic Stem Cells** *Harrison's Principles of Internal Medicine (Japanese 5th Edition)*
  Nakauchi, Y., Nakauchi, H.
  MEDSI.2017; 19: 89e1-4
- **Effective treatment against severe graft-versus-host disease with allele-specific anti-HLA monoclonal antibody in a humanized mouse model.** *Experimental hematology*
  Nakauchi, Y., Yamazaki, S., Napier, S. C., Usui, J., Ota, Y., Takahashi, S., Watanabe, N., Nakauchi, H.
  2015; 43 (2): 79-88 e1 4
- **Concurrent administration of intravenous systemic and intravitreal methotrexate for intraocular lymphoma with central nervous system involvement** *INTERNATIONAL JOURNAL OF HEMATOLOGY*
  Nakauchi, Y., Takase, H., Sugita, S., Mochizuki, M., Shibata, S., Ishiwata, Y., Shibuya, Y., Yasuhara, M., Miura, O., Arai, A.
  2010; 92 (1): 179-185
- **Enasidenib drives human erythroid differentiation independently of isocitrate dehydrogenase 2.** *The Journal of clinical investigation*
  Dutta, R., Zhang, T. Y., Köhnke, T., Thomas, D., Linde, M., Gars, E., Stafford, M., Kaur, S., Nakauchi, Y., Yin, R., Azizi, A., Narla, A., Majeti, et al
  2020
- **Use of polyvinyl alcohol for chimeric antigen receptor T-cell expansion.** *Experimental hematology*
  Nishimura, T., Hsu, I., Martinez-Krams, D. C., Nakauchi, Y., Majeti, R., Yamazaki, S., Nakauchi, H., Wilkinson, A. C.
  2019

- **An Engineered Cell-Traceable Model of Reticular Dysgenesis in Human Hematopoietic Stem Cells Linking Metabolism and Differentiation**
  Wang, W., Awani, A., Reich, L., Nakauchi, Y., Thomas, D., Dever, D. P., Porteus, M., Weinacht, K. G.
  AMER SOC HEMATOLOGY.2018

- **IDH1 Mutant AML Is Susceptible to Targeting De Novo Lipid Synthesis Independent of 2-Hydroxyglutarate and Has a Distinct Metabolic Profile from IDH2 Mutant AML**
  Thomas, D., Nakauchi, Y., Wu, M., Zheng, M., Sinha, S., Dill, D., Peltz, G., Majeti, R.
  AMER SOC HEMATOLOGY.2018

- **Large-Scale Clonal Analysis Resolves Aging of the Mouse Hematopoietic Stem Cell Compartment.** *Cell stem cell*
  Yamamoto, R., Wilkinson, A. C., Ooehara, J., Lan, X., Lai, C. Y., Nakauchi, Y., Pritchard, J. K., Nakauchi, H.
  2018; 22 (4): 600–607.e4

- **Establishment of a Therapeutic Anti-Pan HLA-Class II Monoclonal Antibody That Directly Induces Lymphoma Cell Death via Large Pore Formation.** *PloS one*
  Matsuoka, S., Ishii, Y., Nakao, A., Abe, M., Ohtsuji, N., Momose, S., Jin, H., Arase, H., Sugimoto, K., Nakauchi, Y., Masutani, H., Maeda, M., Yagita, et al
  2016; 11 (3): e0150496

- **A Safeguard System for Induced Pluripotent Stem Cell-Derived Rejuvenated T Cell Therapy** *STEM CELL REPORTS*
  Ando, M., Nishimura, T., Yamazaki, S., Yamaguchi, T., Kawana-Tachikawa, A., Hayama, T., Nakauchi, Y., Ando, J., Ota, Y., Takahashi, S., Nishimura, K., Ohtaka, M., Nakanishi, et al
  2015; 5 (4): 597-608

## PRESENTATIONS

- Novel Strategy to Treat Graft-versus-Host Disease with Allele-Specific Anti-HLA Monoclonal Antibody - 18th Annual Winter Meeting of the Korean Society of Blood and Marrow Transplantation (2/14/2014 - 2/15/2014)
- Novel Therapeutic Approach To Graft-Versus-Host Disease With Allele-Specific Anti-HLA Monoclonal Antibody - 55th American Society of Hematology Annual Meeting and Exposition (12/7/2013 - 12/10/2013)
- TET2 Disruption Alters Human Hematopoietic Stem/ Progenitor Cells Differentiation and Self-Renewal