Stanford

Siddhartha Jaiswal

Assistant Professor of Pathology

NIH Biosketch available Online

CLINICAL OFFICES

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Bio

BIO

Siddhartha Jaiswal is a recent faculty recruit to Stanford in the Department of Pathology. He is no stranger to the Farm, having also obtained undergraduate, medical, and doctorate degrees at Stanford. His thesis work in Irv Weissman's lab focused on understanding the role of the innate immune signaling ligand, CD47, in macrophage tumor immunosurveillance. This work formed the rationale for the therapeutic targeting of CD47 in human cancer, which is currently in clinical trials at Stanford and elsewhere.

Dr. Jaiswal subsequently completed residency and fellowship training in pathology at the Massachusetts General Hospital and Harvard Medical School. As a post-doctoral fellow at the Broad Institute, he identified a common, pre-malignant state for blood cancers by reanalysis of large sequencing datasets. This condition, termed "clonal hematopoiesis", is characterized by the presence of stem cell clones harboring certain somatic mutations, primarily in genes involved in epigenetic regulation of hematopoiesis. Clonal hematopoiesis is prevalent in the aging population and increases the risk of not only blood cancer, but also cardiovascular disease and overall mortality. Understanding the biology of these mutations and how they contribute to the development of cancer and other age-related diseases is the current focus of work in his lab.

CLINICAL FOCUS

- Transfusion Medicine
- Genomics and Molecular Pathology
- Clinical Pathology

ACADEMIC APPOINTMENTS

- Assistant Professor, Pathology
- Member, Bio-X
- Member, Cardiovascular Institute
- Member, Stanford Cancer Institute

HONORS AND AWARDS

- EvansMDS Discovery Research Award, Evans Foundation (2018)
- Transatlantic Network of Excellence, Foundation Leducq (2018)
- Career Award for Medical Scientists, Burroughs Wellcome Fund (2016)
- BroadIgnite Scholar, Broad Institute of MIT and Harvard (2016)
- Paul E. Strandjord Young Investigator Award, ACLPS (2014)
- Firestone Medal for Excellence in Research, Stanford University (2000)
- Phi Beta Kappa, Stanford University (2000)

PROFESSIONAL EDUCATION

- Board Certification: Clinical Pathology, American Board of Pathology (2017)
- Fellowship: Massachusetts General Hospital Emergency Medicine Residency (2013) MA
- PhD Training: Stanford University School of Medicine Registrar (2010) CA
- Fellowship, Harvard Medical School , Transfusion Medicine (2013)
- Residency, Massachusetts General Hospital , Clinical Pathology (2014)
- PhD, Stanford University School of Medicine , Immunology (2010)
- MD, Stanford University School of Medicine (2010)
- BS, Stanford University , Biological Sciences (2000)

PATENTS

- Siddhartha Jaiswal, Irving L. Weissman, Ravindra Majeti, Mark P. Chao. "United States Patent 8562997 B2 Methods of treating acute myeloid leukemia by blocking CD47", The Board Of Trustees Of The Leland Stanford Junior University, Oct 22, 2013

LINKS

- Google Scholar Profile: https://scholar.google.com/citations?hl=en&user=xvEYvfUAAAAJ&view_op=list_works&gmla=AJsN-F6kuCVHiYZ1RP7tWJmNSh0fVlEr9RM3FWu1CH1QTfKOGXYPrmH4Dwsq957bmYNf-NtvrMrAUEatfFuV0pk2KbVN_lbHwoLhGHhn96QiIgI5zl3lP64
- Lab Website: https://www.jaiswallab.org
- Twitter: https://twitter.com/jaiswalmdphd

Research & Scholarship

CURRENT RESEARCH AND SCHOLARLY INTERESTS

Somatic Mutations in Aging

Aging is associated with an increased incidence of cancer and several other diseases. As a post-doctoral fellow, Dr. Jaiswal identified a common age-related disorder of the blood characterized by the acquisition of certain somatic mutations in hematopoietic stem cells (Jaiswal et al., NEJM 2014). These mutations allow stem cell clones to expand relative to normal stem cells; this clonal expansion is termed "clonal hematopoiesis of indeterminate potential", or CHIP (Steensma et al., Blood 2015).

The most commonly found mutations in CHIP are in genes involved in epigenetic regulation (DNMT3A, TET2, ASXL1). CHIP is very rare in the young, but becomes common with aging. Between 10-30% of the elderly have a clonal mutation meeting the definition of CHIP. Those with CHIP are at markedly increased risk of developing hematological malignancies such as myelodysplastic syndrome, acute myeloid leukemia, and lymphoma.

Surprisingly, CHIP is also associated with increased risk of atherosclerotic cardiovascular disease, and this relationship is thought to be causal based on mouse models (Jaiswal et al., NEJM 2017). Mechanistically, the mutations in CHIP lead to increased expression of inflammatory gene modules in mature immune cells such as macrophages. These immune effector cells are derived from the mutated hematopoietic stem cells in the marrow, hence they also harbor the CHIP-related mutations.

These observations suggest that somatic mutations in hematopoietic stem cells that arise during aging may have a variety of effects on health. The lab seeks to understand the biology and clinical impact of these mutations, as described in the projects below.

PROJECTS

- Using human population genetics to learn the health associations of clonal hematopoiesis.
- Mechanistic studies on the role of DNA methylation in clonal expansion of stem cells and dysregulated inflammation.
- Characterization of hematopoietic and immune cell subsets from humans with CHIP.
- Identification of novel therapeutics to treat CHIP and/or its associated diseases.

Teaching

COURSES

2019-20

- Biology and Disease of Hematopoiesis: IMMUNOL 223 (Win)

STANFORD ADVISEES

Postdoctoral Faculty Sponsor

Hind Bouzid, Shaneice Mitchell, Daniel Nachun

Doctoral Dissertation Advisor (AC)

Kameron Rodrigues

GRADUATE AND FELLOWSHIP PROGRAM AFFILIATIONS

- Immunology (Phd Program)

Publications

PUBLICATIONS

- **PPM1D-truncating mutations confer resistance to chemotherapy and sensitivity to PPM1D inhibition in hematopoietic cells** *BLOOD*
  Kahn, J. D., Miller, P. G., Silver, A. J., Sellar, R. S., Bhatt, S., Gibson, C., McConkey, M., Adams, D., Mar, B., Mertins, P., Fereshetian, S., Krug, K., Zhu, et al
  2018; 132 (11): 1095–1105

- **Clonal Hematopoiesis and Risk of Atherosclerotic Cardiovascular Disease.** *The New England journal of medicine*
  Jaiswal, S., Natarajan, P., Silver, A. J., Gibson, C. J., Bick, A. G., Shvartz, E., McConkey, M., Gupta, N., Gabriel, S., Ardissino, D., Baber, U., Mehran, R., Fuster, et al
  2017; 377 (2): 111–21

- **Clonal hematopoiesis of indeterminate potential and its distinction from myelodysplastic syndromes** *BLOOD*
  Steensma, D. P., Bejar, R., Jaiswal, S., Lindsley, R. C., Sekeres, M. A., Hasserjian, R. P., Ebert, B. L.
  2015; 126 (1): 9-16

- **Age-Related Clonal Hematopoiesis Associated with Adverse Outcomes** *NEW ENGLAND JOURNAL OF MEDICINE*
  Jaiswal, S., Fontanillas, P., Flannick, J., Manning, A., Grauman, P. V., Mar, B. G., Lindsley, R. C., Mermel, C. H., Burtt, N., Chavez, A., Higgins, J. M., Moltchanov, V., Kuo, et al
  2014; 371 (26): 2488-2498

- **CD47 Is Upregulated on Circulating Hematopoietic Stem Cells and Leukemia Cells to Avoid Phagocytosis** *CELL*
  Jaiswal, S., Jamieson, C. H., Pang, W. W., Park, C. Y., Chao, M. P., Majeti, R., Traver, D., van Rooijen, N., Weissman, I. L.
  2009; 138 (2): 271-285

- **Clonal haematopoiesis: connecting ageing and inflammation in cardiovascular disease.** *Nature reviews. Cardiology*
  Jaiswal, S., Libby, P.
  2019

- **It's in the blood.** *Nature medicine*
  Jaiswal, S.
  2019; 25 (8): 1184

- **Clonal Hematopoiesis of Indeterminate Potential Reshapes Age-Related CVD JACC Review Topic of the Week** *JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY*
  Khetarpal, S. A., Qamar, A., Bick, A. G., Fuster, J. J., Kathiresan, S., Jaiswal, S., Natarajan, P.
  2019; 74 (4): 578–86

- **Clonal Hematopoiesis Crossroads of Aging, Cardiovascular Disease, and Cancer: JACC Review Topic of the Week** *JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY*
  Libby, P., Sidlow, R., Lin, A. E., Gupta, D., Jones, L. W., Moslehi, J., Zeiher, A., Jaiswal, S., Schulz, C., Blankstein, R., Bolton, K. L., Steensma, D., Levine, et al
  2019; 74 (4): 567–77

- **Connections Between Clonal Hematopoiesis, Cardiovascular Disease, and Cancer: A Review.** *JAMA cardiology*
  Calvillo-Arguelles, O., Jaiswal, S., Shlush, L. I., Moslehi, J. J., Schimmer, A., Barac, A., Thavendiranathan, P.
  2019

- **Clonal hematopoiesis: Pre-cancer PLUS.** *Advances in cancer research*
  Silver, A. J., Jaiswal, S.
  2019; 141: 85–128

- **Biological implications of clonal hematopoiesis.** *Experimental hematology*
  Luis, T. C., Wilkinson, A. C., Beerman, I., Jaiswal, S., Shlush, L. I.
  2019

- **CHIPping Away at the Pathogenesis of Heart Failure** *JAMA CARDIOLOGY*
  Libby, P., Jaiswal, S., Lin, A. E., Ebert, B. L.
  2019; 4 (1): 5–6

- **Loss-of-Function Mutations in Dnmt3a and Tet2 Lead to Accelerated Atherosclerosis and Convergent Macrophage Phenotypes in Mice**
  Rauch, P. J., Silver, A. J., Gopakumar, J., McConkey, M., Sinha, E., Fefer, M., Shvartz, E., Sukhova, G., Libby, P., Ebert, B. L., Jaiswal, S.
  AMER SOC HEMATOLOGY.2018

- **Clonal Hematopoiesis Somatic Mutations in Blood Cells and Atherosclerosis** *CIRCULATION-GENOMIC AND PRECISION MEDICINE*
  Natarajan, P., Jaiswal, S., Kathiresan, S.
  2018; 11 (7): e001926

- **Predicting progression to AML** *NATURE MEDICINE*
  Sellar, R. S., Jaiswal, S., Ebert, B. L.
  2018; 24 (7): 904–6

- **Clonal Hematopoiesis Associated With Adverse Outcomes After Autologous Stem-Cell Transplantation for Lymphoma** *JOURNAL OF CLINICAL ONCOLOGY*
  Gibson, C. J., Lindsley, R. C., Tchekmedyian, V., Mar, B. G., Shi, J., Jaiswal, S., Bosworth, A., Francisco, L., He, J., Bansal, A., Morgan, E. A., LaCasce, A. S., Freedman, et al
  2017; 35 (14): 1598-?

- **Clonal hematopoiesis** *SEMINARS IN HEMATOLOGY*
  Jan, M., Ebert, B. L., Jaiswal, S.
  2017; 54 (1): 43-50

- **Clonal Hematopoiesis and Atherosclerosis.** *The New England journal of medicine*
  Jaiswal, S., Natarajan, P., Ebert, B. L.
  2017; 377 (14): 1401–2
- **Clonal Hematopoiesis and Blood-Cancer Risk** *NEW ENGLAND JOURNAL OF MEDICINE*
  Yan, B., Ban, K., Chng, W.
  2015; 372 (11): 1071-1071
- **Mutations in G protein beta subunits promote transformation and kinase inhibitor resistance** *NATURE MEDICINE*
  Yoda, A., Adelmant, G., Tamburini, J., Chapuy, B., Shindoh, N., Yoda, Y., Weigert, O., Kopp, N., Wu, S., Kim, S. S., Liu, H., Tivey, T., Christie, et al
  2015; 21 (1): 71-75
- **MDS Is a Stem Cell Disorder After All** *CANCER CELL*
  Jaiswal, S., Ebert, B. L.
  2014; 25 (6): 713-714
- **Janus-like opposing roles of CD47 in autoimmune brain inflammation in humans and mice** *JOURNAL OF EXPERIMENTAL MEDICINE*
  Han, M. H., Lundgren, D. H., Jaiswal, S., Chao, M., Graham, K. L., Garris, C. S., Axtell, R. C., Ho, P. P., Lock, C. B., Woodard, J. I., Brownell, S. E., Zoudilova, M., Hunt, et al
  2012; 209 (7): 1325-1334
- **The CD47-signal regulatory protein alpha (SIRPa) interaction is a therapeutic target for human solid tumors** *PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA*
  Willingham, S. B., Volkmer, J., Gentles, A. J., Sahoo, D., Dalerba, P., Mitra, S. S., Wang, J., Contreras-Trujillo, H., Martin, R., Cohen, J. D., Lovelace, P., Scheeren, F. A., Chao, et al
  2012; 109 (17): 6662-6667
- **Calreticulin Is the Dominant Pro-Phagocytic Signal on Multiple Human Cancers and Is Counterbalanced by CD47** *SCIENCE TRANSLATIONAL MEDICINE*
  Chao, M. P., Jaiswal, S., Weissman-Tsukamoto, R., Alizadeh, A. A., Gentles, A. J., Volkmer, J., Weiskopf, K., Willingham, S. B., Raveh, T., Park, C. Y., Majeti, R., Weissman, I. L.
  2010; 2 (63)
- **Macrophages as mediators of tumor immunosurveillance** *TRENDS IN IMMUNOLOGY*
  Jaiswal, S., Chao, M. P., Majeti, R., Weissman, I. L.
  2010; 31 (6): 212-219
- **CD47 Is an Adverse Prognostic Factor and Therapeutic Antibody Target on Human Acute Myeloid Leukemia Stem Cells** *CELL*
  Majeti, R., Chao, M. P., Alizadeh, A. A., Pang, W. W., Jaiswal, S., Gibbs, K. D., van Rooijen, N., Weissman, I. L.
  2009; 138 (2): 286-299
- **Hematopoietic Stem and Progenitor Cells and the Inflammatory Response** *6th International Cancer Vaccine Symposium*
  Jaiswal, S., Weissman, I. L.
  BLACKWELL PUBLISHING.2009: 118–121
- **Expression of BCR/ABL and BCL-2 in myeloid progenitors leads to myeloid leukemias** *PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA*
  Jaiswal, S., Traver, D., Miyamoto, T., Akashi, K., Lagasse, E., Weissman, I. L.
  2003; 100 (17): 10002-10007