UNIVERSITY OF CALIFORNIA, SAN FRANCISCO

BERKELEY • DAVIS • IRVINE • LOS ANGELES • RIVERSIDE • SAN DIEGO • SAN FRANCISCO SANTA BARBARA • SANTA CRUZ

University of California, San Francisco **Prepared: 4/15/2024**

CURRICULUM VITAE

Name: **Carolyn Sangokoya, MD, PhD**
Position: Assistant Professor
Department of Pathology
School of Medicine

Address: UCSF Medical Center
Department of Pathology
505 Parnassus Ave
Room M580, Box 0102
San Francisco, CA 94143-0102
Email: carolyn.sangokoya@ucsf.edu

Sangokoya Lab
Regenerative Medicine Building
35 Medical Center Way
Room 1033, Box 0525
San Francisco, CA 94143-0525

EDUCATION

1999-2003	Stanford University	A.B.	Human Biology (conc: Molecular Genetics)	ADVISOR Virginia Walbot, PhD
2004-12	Duke University School of Medicine	M.D.	Medicine, Medical Scientist Training Program (MSTP)	Nancy Andrews, MD, PhD
2006-11	Duke University Graduate School	Ph.D.	Genetics and Genomics	Jen-Tsan Ashley Chi, MD, PhD
2012-2021	University of California, San Francisco		Physician-Scientist Pathway	Abul Abbas, MBBS
2012-14	University of California, San Francisco	Resident	Anatomic Pathology	Patrick Treseler, MD, PhD
2014-15	University of California, San Francisco	Fellow	Liver/GI Pathology	Linda Ferrell, MD
2014-15	University of California, San Francisco	Fellow	Surgical Pathology	Linda Ferrell, MD
2015-21	University of California, San Francisco	Postdoc	Stem Cell Biology	Robert Blelloch MD, PhD

LICENSES AND CERTIFICATION

2014-present Medical licensure, California, #A131780
2015 Board Certification, Anatomic Pathology, American Board of Pathology

PRINCIPAL POSITIONS HELD

2023-present	University of California, San Francisco	Assistant Professor	Pathology
2021-2023	University of California, San Francisco	Instructor	Pathology

HONORS AND AWARDS

1999	National Merit Scholarship	Baton Rouge Magnet High School
2000	Dean's Award for Academic Excellence	Stanford University
2001	Dean's Award for Academic Excellence	Stanford University
2002	Dean's Award for Academic Excellence	Stanford University
2007	Fellow, Aspen Health Forum	The Aspen Institute
2009	Graduate Student Conference Travel Fellowship	Duke University Graduate School
2010	Keystone Symposia Student Travel Fellowship	Keystone Symposia
2010	Fuqua/Coach K Leadership Conference	Duke University
2012	Dean's Recognition Award (for outstanding performance as medical student)	Duke University School of Medicine
2014	USCAP Annual Meeting Stowell Orbison finalist (outstanding trainee abstract)	US & Canadian Academy of Pathology
2015	USCAP Annual Meeting Stowell Orbison finalist (outstanding trainee abstract)	US & Canadian Academy of Pathology
2015	Eli & Edythe Broad Regeneration Medicine and Stem Cell Fellowship	University of California, San Francisco

2016	F32 Ruth L. Kirschstein Postdoctoral Individual National Research Service Award	NIH/NICHD
2017	UCSF Program for Breakthrough Biomedical Science Independent Postdoctoral Research Award	University of California, San Francisco
2018	Trainee award, UCSF Center/Reproductive Sci Symposium	University of California, San Francisco
2021	K08 Mentored Clinical Scientist Research Career Development Award	NIH/NICHD
2021	John A. Watson Faculty Scholar	School of Medicine, University of California, San Francisco
2022	Young Physician-Scientist Award	American Society for Clinical Investigation
2022	Gordon Research Conference Travel Award "Post-Transcriptional Gene Regulation"	Gordon Research Conferences
2022	Career Award for Medical Scientists	Burroughs Wellcome Fund
2023	UCSF Liver Center Pilot Feasibility Grant	UCSF Liver Center, NIH-NIDDK

PROFESSIONAL ACTIVITIES

MEMBERSHIPS

2012-present United States and Canadian Academy of Pathology (USCAP)
2015-present Rodger C. Haggitt Gastrointestinal Pathology Society
2015-present Hans Popper Hepatopathology Society
2020-present International Society for Stem Cell Research (ISSCR)
2020-present Society for Developmental Biology
2024-present American Society for Investigative Pathology (ASIP)

SERVICE TO PROFESSIONAL ORGANIZATIONS

International Society for Stem Cell Research
2021-2023 ISSCR Early Career Scientist Committee
2023-present ISSCR Education Committee
Gordon Research Conference "Post-Transcriptional Gene Regulation" 2022
2022 GRS Session Chair, "RNA Processing and Disease"

SERVICE TO PROFESSIONAL PUBLICATIONS

2010-2012 Ad-hoc reviewer (with Jen-Tsan Ashley Chi): *Public Library of Science*
2015-2024 Ad-hoc reviewer (with Robert Blelloch): *Cell*, *Science*, *Nature Cell Biology*, *PNAS*, *Genome Research*, *Cell Reports*, *Nature Methods*, *EMBO*

INVITED PRESENTATIONS - INTERNATIONAL

2011 Keystone Symposium: MicroRNAs and Human Disease (Banff, AB, Canada)
2013 Keystone Symposium: Noncoding RNAs in Development and Cancer (Vancouver, BC, Canada)
2021 International Society for Stem Cell Research (ISSCR), Platform Presentation (Virtual2021) "Illuminating Post-Transcriptional Regulation of Pluripotent Cell State Transition and Fate at Single Cell Resolution" 6/24/21 (San Francisco, CA)
2022 International Society for Stem Cell Research (ISSCR), 2022 Early Career Group Leader Luncheon: invited as co-moderator (with Dr. Valentina Greco (Yale)) 6/15/22
2022 International Society for Stem Cell Research (ISSCR), Next Generation of Leaders Representative and invited as Panelist for event "A Global Discussion on Equity, Diversity, and Inclusion: with directors of stem cell institutes and centers, heads of stem cell societies and networks. 6/17/22 (San Francisco, CA)
- spoke on perspectives/experience as founder and director of UCSF Women Physician Scientists group

2023 International Society for Stem Cell Research (ISSCR), Featured Moderator for Webinar: Part 2 of "Equity, Diversity, and Inclusion in Action"- co-sponsored by NYSCF. March 28, 2023 (virtual)

INVITED PRESENTATIONS - NATIONAL

2008 National MD-PhD Student Annual Research Conference (Keystone, CO)
2014 United States and Canadian Academy of Pathology, Annual Meeting (San Diego, CA)
2015 United States and Canadian Academy of Pathology, Annual Meeting (Boston, MA)
2019 NICHD Career Planning and Networking Workshop for Developmental Biologists (Bethesda, MD)
2021 NIH/NICHD NCTRI "Stem Cells in Reproduction" Meeting. Platform Presentation (NIH/Virtual)
2022 Joint Meeting American Society for Clinical Investigation Young Physician Scientist Award (Chicago, IL)
2022 Gordon Research Conference- Post-Transcriptional Gene Regulation (Newry, ME)
2023 Joint Meeting American Society for Clinical Investigation Young Physician Scientist Award (Chicago, IL)
2024 Joint Meeting American Society for Clinical Investigation Young Physician Scientist Award (Chicago, IL)

INVITED PRESENTATIONS – REGIONAL AND OTHER INVITED PRESENTATIONS

2013-14 UCSF Mechanisms of Disease Conference, Department of Pathology
2018-19 UCSF Center for Reproductive Sciences Symposium
2022 University of Utah Pathology Research Interest Mentoring Program, 6/9/22 (host: Dr. Kim Evason)
2022 Stanford Department of Pathology and Institute of Stem Cell Biology 12/1/22 (hosts: Dr. Tom Montine, Dr. Ravi Majeti)
2022 Yale Department of Lab Medicine Grand Rounds 12/13/22 (host: Dr. Brian Smith)
2022 UCSF International Women's Day "Women in Science: Moving Forward in Academic Science, Engineering, and Medicine" 3/8/22 invited as organizer (UCSF Committee on Status of Women)
2023 University of Chicago Department of Pathology Grand Rounds 2/9/23 (host: Dr. Scott A. Oakes)
2024 UCSF Women Physician-Scientists Supergroup Panel "Ins and Outs of Starting A Lab" 2/16/24
2024 UCSF International Women's Day, "Women in Science: Moving Forward in Academic Science, Engineering, and Medicine" 3/8/24 invited as moderator+panelist (UCSF Committee on Status of Women)

CONTINUING EDUCATION AND PROFESSIONAL DEVELOPMENT ACTIVITIES (abridged)

2022 United States and Canadian Academy of Pathology, Annual Meeting (Los Angeles, CA)
2022 Hans Popper Hepatopathology Society Companion Meeting (Los Angeles, CA)
2022 Inclusive Mentoring Training Course, UCSF School of Medicine
2023 USCAP - Tutorial in Pathology of the GI Tract, Pancreas and Liver (Palm Springs, CA) 36 CME
2023 United States and Canadian Academy of Pathology, Annual Meeting (New Orleans, LA)
2023 Hans Popper Hepatopathology Society Companion Meeting (New Orleans, LA)

RESEARCH AND CREATIVE ACTIVITIES

RESEARCH AND CREATIVE ACTIVITIES SUMMARY

My most significant contributions to science thus far are in the basic study of microRNA functions in cellular stress response, cellular iron homeostasis, and translational methods in the RNA isolation from clinical materials. My post-doctoral studies have centered on post-transcriptional regulation in pluripotent stem cell biology. Seeking greater independence as a physician-scientist, I have also built a small focus on posttranscriptional regulation in human liver development and disease during residency and fellowship training as well as during my postdoctoral studies. Due to space restrictions, an abbreviated list is below:

As an Assistant Professor in the Department of Pathology at the University of California, San Francisco, I am a physician-scientist, pathologist, and stem cell biologist with expertise in RNA biology who leverages genome engineering, quantitative cell biology, single-cell technologies, and imaging for innovation and discovery. My broader scientific mission is to discover and build molecular tools to re-engineer and re-wire cell fates for innovation in regenerative medicine. My clinical/translational mission is to advance human liver pathobiology research and diagnostics for cell-based regenerative therapies and precision-based medicine.

Post-transcriptional regulation and microRNA function in pluripotent stem cell biology

We demonstrate that the miR-290/302 target Profilin-2 regulates many aspects of pluripotent stem cell (PSC) biology, defining an axis of post-transcriptional control, endocytosis, and signal transduction that is essential for stem cell growth, cell cycle control, and early differentiation (1). We continue to explore the role of post-transcriptional control mechanisms in cell fate decisions (2). I contributed several new methods for quantitative cell biology at single-cell resolution within the context of stem cell biology, including those for measuring endocytosis/endosomal uptake (3) and using targeted CRISPR-based deletions to interrogate the specific impacts of microRNA binding sites (1).

Role: Developed project, performed experiments, co-wrote papers.

1. **Sangokoya C**, and R Blelloch. MicroRNA-dependent inhibition of PFN2 orchestrates ERK activation and pluripotent state transitions by regulating endocytosis. Proc Natl Acad Sci. 2020 Aug25;117(34):20625-20635. PMID:32788350
2. **Sangokoya C**, and R Blelloch. Coordinate control of PFN2 by RNA-binding proteins regulate cell fate. (manuscript in preparation)
3. **Sangokoya, C.** Measuring Endocytosis and Endosomal Uptake at Single Cell Resolution. Methods Mol Biol. 2022 2490:57-67 PMID: 35486239

MicroRNA function in cellular iron homeostasis

Ferroportin (FPN) is the only known cellular iron exporter in mammalian cells and plays a critical role in the maintenance of both cellular and systemic iron balance. During iron deprivation, the translation of FPN is repressed by iron regulatory proteins (IRPs), which bind to the 5' untranslated region (UTR), to reduce iron export and preserve cellular iron. This study used functional genomic methods to identify differential expression and characterize the role of microRNAs in cellular iron homeostasis in human primary cells and cell lines. Here, we reported a novel iron-responsive mechanism for the post-transcriptional regulation of FPN, mediated by miR-485-3p, which is induced in human cell lines and primary cells during iron deficiency and represses FPN expression by directly targeting the FPN 3'UTR (1). These findings support a model that includes both IRPs and microRNAs as iron-responsive post-transcriptional regulators of FPN. The involvement of microRNA in the iron-responsive regulation of FPN offers additional stability and fine-tuning of iron homeostasis within different cellular contexts.

Role: Conceived/developed study, performed majority of experiments, analyzed data, co-wrote/edited paper.

1. **Sangokoya C**, Doss JF, Chi JT. Iron-responsive miR-485-3p regulates cellular iron homeostasis by targeting ferroportin. PLoS Genet. 2013 Apr;9(4):e1003408. doi: 10.1371/journal.pgen.1003408. Epub 2013 Apr 4. PMID: 23593016; PMCID: PMC3616902.

Post-transcriptional regulation in human liver development and disease

In a series of studies, I have learned and applied methods for the unbiased efficient capture of small RNAs from formalin-fixed paraffin-embedded (FFPE) liver tissue samples, allowing for the performance and coordination of unbiased high-throughput RNA sequencing from clinical liver tissue samples with immunohistochemistry and RNA in-situ hybridization. As a resident, using resources in UCSF Pathology, I designed eight tissue microarrays (TMAs) from FFPE patient liver tissues ranging from fetal liver to different etiologies of cirrhosis, tested the ability of these TMAs to demonstrate robust expression of control and specific microRNAs by quantitative PCR, microRNA in situ hybridization, and immunohistochemistry, and identified differential spatial localization of microRNAs within liver parenchyma (1-2). Now with my own laboratory, I am leveraging RNA ---in the form of spatial transcriptomics--- at a tool to establish the in situ landscape of both liver zonation and cellular iron homeostasis directly in human liver tissue at single-cell resolution. My vision is to be able to develop RNA signatures in liver biopsy tissue and add this lens to our ancillary toolbox to better inform metabolic status and assess early steatotic liver disease pathology

Role: Developed project, performed experiments, analyzed data, presented posters/abstracts.

1. **Sangokoya C** et al. Expression of the Iron-Regulating MicroRNA miR-485-3p in Hepatic cirrhosis. Laboratory investigation; a journal of technical methods and pathology. 2014 February; 94:427.
2. **Sangokoya C** et al. MicroRNA In Situ Hybridization Analysis of MIR-485-3p and MiR-122 Expression in Human Liver Development and Disease. Laboratory investigation; a journal of technical methods and pathology. 2015 February; 95:423A.

MicroRNA function in cellular stress response

MicroRNAs are essential for fine-tuning physiological functions and responding to changing environments and stress conditions. We demonstrate a role for microRNA in the regulation of oxidative stress response in erythroid cells and the functional consequences of dysregulated microRNA expression in Sickle Cell Disease (SCD) pathobiology (1). Homozygous Sickle Cell (HbSS) erythrocytes are known to have reduced tolerance for
oxidative stress, yet the basis for this phenotype has remained unknown. Here we use erythrocyte microRNA expression profiles to identify a subset of HbSS patients with higher miR-144 expression and more severe anemia. In our study we revealed that in K562 erythroid cells and primary erythroid progenitor cells, miR-144 directly regulates NRF2, a transcription factor and central regulator of cellular response to oxidative stress, and modulates the oxidative stress response. We further demonstrate that increased miR-144 is associated with the reduced NRF2 levels, decreased glutathione regeneration, and attenuated antioxidant capacity found in HbSS erythroid progenitor cells, thereby providing a mechanism for the reduced oxidative stress tolerance and increased anemia severity seen in HbSS patients.

Role: Developed project to identify functional and clinical relevance of miR-144 in mature erythrocytes, identified and characterized oxidative stress response narrative experimentally, designed/produced unique oxidative stress-related reporter constructs subsequently used in other studies and publications in the lab (2), co-wrote paper.

1. **Sangokoya C**, Telen MJ, Chi JT. MicroRNA miR-144 modulates oxidative stress tolerance and associates with anemia severity in sickle cell disease. Blood. 2010 Nov 18;116(20):4338-48. doi: 10.1182/blood-2009-04-214817. PMID: 20709907; PMCID: PMC2993631.
2. Lamonte G, Tang X, Chen JL, Wu J, Ding CK, Keenan MM, **Sangokoya C**, Kung HN, Ilkayeva O, Boros LG, Newgard CB, Chi JT. Acidosis induces reprogramming of cellular metabolism to mitigate oxidative stress. Cancer Metab. 2013 Dec 23;1(1):23. doi: 10.1186/2049-3002-1-23. PMID: 24359630; PMCID: PMC4178214.

Translational methods from clinic to bench: erythrocyte microRNA profiling in anemia disorders

Approaches to study of the molecular basis for phenotypic heterogeneity in SCD in the past have used candidate genes, quantitative trait loci, and genome-wide association studies to identify DNA-based genetic variants associating with particular phenotypes. These approaches required large sample sizes in order to detect significant associations. We developed a novel approach employing the use of erythrocyte microRNA expression profiles (1) from easily accessible peripheral blood shown to demonstrate abundant, diverse, and disease-specific microRNA expression profiles in a pilot study where samples from normal erythrocytes or from anemia disorders grouped into their respective types simply based

on microRNA expression (1). Since erythrocytes do not contain DNA or larger RNAs, the RNA extracted from these cells is enriched for microRNAs, thus only a small amount is needed for robust analysis. Erythrocytic microRNA expression can give insight into the total molecular picture of the life of the red blood cell and further illustrate temporal, developmental, stress-responsive, and otherwise functionally meaningful relationships. The use of erythrocytic microRNA expression profiles is thus a tool which can be used to further identify novel disease modifiers and potential therapeutic targets. We published a key protocol paper (1) and applied these methods in large and small scale form in the study of anemia disorders including paroxysmal nocturnal hemoglobinuria (2) and Sickle Cell Disease (3). These methods were used in profiling microRNA expression over HbSS erythroid progenitor cell development in (3).

Role: Performed experiments, analyzed data, edited papers.

1. **Sangokoya C**, LaMonte G, Chi JT. Isolation and characterization of microRNAs of human mature erythrocytes. Methods Mol Biol. 2010;667:193-203. doi: 10.1007/978-1-60761-811-9_13. PMID: 20827535; PMCID: PMC4347925.
2. Chi JT, **Sangokoya C**, de Castro CM. MicroRNA Expression in Red Blood Cells from Patients with PNH. Blood. 2007 November; 110(11):3675
3. **Sangokoya C**, Telen MJ, Chi JT. MicroRNA miR-144 modulates oxidative stress tolerance and associates with anemia severity in sickle cell disease. Blood. 2010 Nov 18;116(20):4338-48. doi: 10.1182/blood-2009-04-214817. PMID: 20709907; PMCID: PMC2993631.

NCBI/MyBibliography List of Publications:
https://www.ncbi.nlm.nih.gov/myncbi/carolyn.sangokoya.1/bibliography/public/

PEER REVIEWED PUBLICATIONS

1. **Sangokoya C**, Blelloch R. MicroRNA-dependent inhibition of PFN2 orchestrates ERK activation and pluripotent state transitions by regulating endocytosis. Proc Natl Acad Sci U S A. 2020 Aug 11. PMID: 32788350
2. **Sangokoya,** C, Doss JF, and JT Chi. Iron-Responsive miR-485-3p Regulates Cellular Iron Homeostasis by Targeting Ferroportin. PLoS Genetics 9.4 (2013): e1003408.
3. **Sangokoya C,** Telen MJ, and JT Chi. MicroRNA miR-144 modulates oxidative stress tolerance and associates with anemia severity in sickle cell disease. Blood. 2010 Nov 18;116(20):4338-48. PMID: 20709907
4. LaMonte G, Tang X, Chen JL, Wu J, Ding CK, Keenan MM, **Sangokoya** C, Kung HN, Ilkayeva O, Boros LG, Newgard CB, and Chi, JT. Acidosis induces reprogramming of cellular metabolism to mitigate oxidative stress. *Cancer Metab* 1(2013): 23.
5. Hao K, Niu T, **Sangokoya C,** Li J, and X Xu. SNPkit: an efficient approach to systematic evaluation of candidate single nucleotide polymorphisms in public databases. Biotechniques. 2002 Oct 33(4):822, 824-6, 828 passim. PMID: 12398191

BOOKS AND CHAPTERS

1. **Sangokoya C**, LaMonte G, and JT Chi. Isolation and characterization of microRNAs of Human Mature Erythrocytes MicroRNAs and the Immune System: Methods in Molecular Biology. 2010, 667:193-203. PMID: 20827535
2. **Sangokoya C.** Measuring Endocytosis and Endosomal Uptake at Single Cell Resolution. Epiblast Stem Cells: Methods in Molecular Biology Series (2022) Vol. 2490. PMID: 35486239

OTHER PUBLICATIONS

1. **Sangokoya C.** MicroRNA Function in Cellular Stress Response. PhD Dissertation, Duke University, University Program in Genetics and Genomics (2011)

2. Chi JT, **Sangokoya C**, de Castro CM. MicroRNA Expression in Red Blood Cells from Patients with PNH. Blood. 2007 November; 110(11):3675

3. **Sangokoya C** et al. MicroRNA In Situ Hybridization Analysis of MIR-485-3p and MiR-122 Expression in Human Liver Development and Disease. Laboratory investigation; a journal of technical methods and pathology. 2015 February; 95:423A.

4. **Sangokoya C** et al. Expression of the Iron-Regulating MicroRNA miR-485-3p in Hepatic cirrhosis. Laboratory investigation; a journal of technical methods and pathology. 2014 February; 94:427.

SIGNIFICANT PUBLICATIONS

1. **Sangokoya C**, Blelloch R. MicroRNA-dependent inhibition of PFN2 orchestrates ERK activation and pluripotent state transitions by regulating endocytosis. Proc Natl Acad Sci U S A. 2020 Aug 11. PMID: 32788350

   Co-conceived, developed, and performed experiments, co-wrote paper. These findings define a previously unknown axis of post-transcriptional control, endocytosis, and signal transduction important for stem cell biology

2. **Sangokoya C,** Telen MJ, and JT Chi. MicroRNA miR-144 modulates oxidative stress tolerance and associates with anemia severity in sickle cell disease. Blood. 2010 Nov 18;116(20):4338-48. PMID: 20709907

   Developed methods for isolation and characterization of microRNA expression in human erythrocytes (red blood cells) for novel study of cellular stress response (oxidative stress) and hematologic diseases (anemias).

3. **Sangokoya,** C, Doss JF, and JT Chi. "Iron-Responsive miR-485-3p Regulates Cellular Iron Homeostasis by Targeting Ferroportin." PLoS Genetics 9.4 (2013): e1003408.

   Conceived and developed novel study using functional genomic methods to characterize the role of microRNAs in cellular iron homeostasis in human primary cells and cell lines.