

University of California, San Francisco
CURRICULUM VITAE

Name: Stephen L Nishimura, MD

Position: Professor, Step 4
Pathology
School of Medicine

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EDUCATION

1977 - 1978	Colgate University, Hamilton, NY		
1979 - 1981	Wesleyan University, Middletown, CT	BA	Chemistry
1983 - 1988	University of Vermont College of Medicine	MD	Medicine
1988 - 1991	University of California San Francisco	Pathology and Laboratory Medicine	
1991 - 1995	University of California San Francisco	Molecular and Cell Biology	
1997 - 1997	Armed Forces Institute of Pathology, Washington, DC	Pulmonary Pathology	

LICENSES, CERTIFICATION

2010	Medical license (G8337)		
1994	Diplomat of the American Board of Pathology, Anatomic and Clinical Pathology		

PRINCIPAL POSITIONS HELD

1981 - 1983	Research Assistant in Neuropharmacology	Memorial Sloan-Kettering	Neurology, Cancer Center, NY
1984 - 1984	Research Fellowship in Pharmacology	University of Vermont	Pharmacology
1986 - 1987	Post-Sophomore Fellowship in Pathology	University of Vermont	Pathology

1988 - 1991	Resident in Anatomic Pathology and Laboratory Medicine	University of California at San Francisco	Anatomic pathology and Laboratory Medicine
1991 - 1991	Chief Resident in Pathology	San Francisco General Hospital	Pathology
1991 - 1991	Post-Doctoral Research Fellow	University of California	Medicine
1995 - 1995	Clinical Instructor in Pathology	San Francisco General Hospital	Pathology
1995 - 1998	Adjunct Assistant Professor in Pathology	University of California	San Francisco
1998 - 2003	Assistant Professor in Pathology in Residence	University of California	San Francisco
2003 - 2009	Associate Professor in Pathology in Residence	University of California	San Francisco
2009 - present	Professor in Residence	University of California	San Francisco
2009 - 2010	Acting Chief of Pathology	San Francisco General Hospital	Pathology
2014 - 2015	Acting Chief of Pathology	San Francisco General Hospital	Pathology
2016 - 2017	Interim Chief of Pathology	Zuckerberg San Francisco General	Pathology
2017 - present	Chief of Pathology	Zuckerberg San Francisco General	Pathology
2018 - present	Professor of Pathology	University of California	San Francisco

OTHER POSITIONS HELD CONCURRENTLY

1997 - 2000	Consultant, Cancer Genomics	Chiron Corporation, Emeryville, CA	
2003 - 2003	Consultant, Pulmonary Pathology	Actelion Pharmaceuticals Ltd.	Build 1 Clinical Trial

2013 - 2015 Scientific Advisory Board

CSA Medical

HONORS AND AWARDS

- 1991 Research Fellowship, Department of Pathology, University of California at San Francisco
- 1992 College of American Pathologists Foundation Scholar
- 1993 National Research Service Award (CA09335)
- 1995 Clinical Investigator Award (KO8 CA63148)
- 1998 ACS Institutional Award
- 1998 American Lung Association, Research Grant
- 1998 Edward Livingston Trudeau Scholar
- 1998 American Lung Association
- 1999 American Heart Association, Grant in Aid
- 2000 UCSF Academic Senate Award
- 2000 UCSF, REAC Award
- 2000 Hellman Family Award for Early-Career Faculty
- 2001 Selected Speaker, Gordon Research Conference on MMPs
- 2002 Independent Scientist Award (NIH)
- 2005 Selected Speaker, Gordon Research Conference on Integrins
- 2006 Invited Speaker, University of Alabama, Cell Biology
- 2007 Invited Speaker, Gordon Conference, Tissue repair and injury, Colby-Sawyer College, NH

KEYWORDS/AREAS OF INTEREST

Lung, Airway Remodeling COPD, Pulmonary Fibrosis, Lung Cancer, Airway epithelium, Cell Proliferation, Integrins, TGF-b, Cytokines, Angiogenesis, Vasculogenesis, Surgical Pathology, Lung Pathology

CLINICAL ACTIVITIES

CLINICAL ACTIVITIES SUMMARY

Surgical Pathology Attending: I have attended on the surgical pathology service at SFGH between 8 and 26 weeks/year for the past 20 years. When on service, I supervise 3-4 residents, fellows and medical students.

Currently, I attend on the general pathology service at SFGH for 12-16 weeks a year. During this time I oversee residents, medical students and fellows.

My subspecialty interest is pulmonary pathology and I am responsible for pulmonary pathology at the SFGH all year.

PROFESSIONAL ACTIVITIES

MEMBERSHIPS

- 1992 - present American Society of Investigative Pathology
- 1993 - 2001 Cancer and Leukemia Group B
- 1993 - present UCSF/Mt Zion Cancer Center
- 1993 - present Thoracic Oncology Research Group, UCSF
- 2001 - present American Thoracic Society
- 2012 - present College of American Pathologists
- 2013 - present American Society for Biochemistry and Molecular Biology

SERVICE TO PROFESSIONAL PUBLICATIONS

- 2012 - 2017 Journal of Biologic Chemistry (Ad hoc reviewer; 1 papers in 5 years)
- 2012 - 2017 Oncogene (Ad hoc reviewer, 2 papers in 5 years)
- 2012 - 2017 American Journal of Respiratory Cell and Molecular Biology (Ad hoc reviewer 5 papers in 5 years)
- 2012 - 2017 Experimental Cell Research (Ad hoc reviewer, 1 paper in 5 years)
- 2012 - 2017 American Journal of Pathology (Ad hoc reviewer, 5 papers in 5 years)
- 2012 - 2017 Journal of Cell Science (2 papers in five years)
- 2012 - 2017 Journal of Molecular Biology (1 paper in 5 years)
- 2012 - 2017 Journal of Epithelial Biology (1 paper in 5 years)
- 2012 - 2012 Matrix Biology (1 paper in 5 years)
- 2013 - 2013 PLoS Computational Biology (1 paper 5 years)
- 2014 - 2014 Chest (1 paper in 5 years)
- 2014 - 2014 American Journal of Physiology (1 paper in 5 years)

2012 - 2017 Journal of Cell Biology 1 Paper in 5 years)
 2012 - 2017 Cell Reports (4 papers in 5 years)
 2011 - present Associate Editor, PLOSone
 2015 - 2015 European Journal of Cell Biology (1 Paper in 5 years)
 2012 - 2017 PLOSone, (5 Papers in 5 years)
 2015 - 2017 American Journal of Pathology (1 Paper)
 2016 - 2017 PNAS (2 papers)
 2017 - 2017 Journal of Pathology (2 Papers)
 2018 - 2018 Thorax (1 paper)

INVITED PRESENTATIONS - INTERNATIONAL

2001	Gordon Conference on Matrix Metalloproteases, Il Ciocco, Italy	
2007	Gordon Conference on Tissue Repair and Regeneration, Colby-Sawyer College, NH	
2010	Co-Chair International Blood-Brain-Barrier Consortium, Bend, Oregon	
2012	American Thoracic Society, San Francisco, CA	
2013	Keytone Conference, Dendritic Cells, Keystone Colorado	
2016	American Thoracic Society, San Francisco	Speaker
2017	FASEB meeting ; TGF-beta super family signaling in development and disease, Lisbon, Portugal	Speaker

INVITED PRESENTATIONS - NATIONAL

2001	Oregon Health Sciences Center, Portland Or.
2002	University of New Mexico, Cancer Center
2005	Gordon Research Conference on Fibronectin and related molecules, Ventura, CA
2006	University of Alabama, Cell Biology program
2007	Gordon Conference on Tissue repair and injury, Colby Sawyer College, NH
2008	NIH workshop on cerebral vascular malformations, Bethesda, MD
2008	University of Vermont Lung Center, Burlington, VT
2010	NIH, Epithelial plasticity, Special meeting, Bethesda, MD

2011 Genentech, South San Francisco, CA
2011 MedImmune, Gaithersburg, MD
2012 American Thoracic Society, San Francisco, CA
2013 UC Innovation Award presentation , South San Francisco
2014 UC Centers for Accelerated Innovation Award, UCLA

INVITED PRESENTATIONS - REGIONAL AND OTHER INVITED PRESENTATIONS

2001 UCSF, Pathology and Laboratory Medicine Grand Rounds
2002 Stanford University Department of Pathology
2003 Neurosurgery Grand Rounds, UCSF
2003 Thoracic Oncology Program Retreat
2004 Program Project Retreat, UCSF
2005 Thoracic Oncology Program Retreat
2006 Program Project Retreat, UCSF
2006 Thoracic Oncology Program Retreat
2007 Deans's research conference, SFGH, UCSF
2009 Thoracic Oncology Program Retreat
2010 Department of Experimental Medicine
2010 Thoracic Oncology Retreat
2010 Pulmonary Research Retreat, UCSF
2013 UCOP Proof of Concept Technology and Innovation retreat2
2013 Pulmonary Research Retreat, UCSF
2014 UCSF Liver Center Mini-symposium, Fibrosis
2017 Dean's Seminar, UCSF, ZSFG
2017 Catalyst 2 Project Presentation, UCSF
2017 Genentech, Seminar Speaker
2018 Antibody Technology Resource Center, Symposium,
Speaker
2019 ImmunoX, Ignite

CONTINUING EDUCATION AND PROFESSIONAL DEVELOPMENT ACTIVITIES

2000 Mechanisms of Disease, weekly pathology conference
1997 Pulmonary Clinical Case Conference, SFGH

- 2006 Amercian Thoracic Society, Moscone Center, San Francisco
- 2010 Pulmonary Clinical Case Conference, UCSFAmercian Thoracic Society, Moscone Center, San Francisco
- 2016 Amercian Thoracic Society, Moscone Center, San Francisco

GOVERNMENT AND OTHER PROFESSIONAL SERVICE

- 2006 - 2006 Hellman Family selection committee
- 2007 - 2007 Wellcome Trust, Ad Hoc reviewer
- 2008 - 2008 Wellcome Trust, Ad Hoc reviewer
- 2009 - 2009 NIH, NIDA-Special emphasis panel-Genes and environment initiative
- 2010 - 2010 NIH, NHLBI, Ad-Hoc reviewer
- 2010 - 2010 Blood Brain Barrier international consortium, Co-chair, Bend, Oregon
- 2010 - 2010 NIH, Epithelial plasticity, Special meeting, Bethesda, MD
- 2011 - 2011 Grant reviewer, Biotechnology and Biologic Sciences Research Council, Ad hoc reviewer
- 2011 - 2011 University of Vermont, School of Medicine, Environmental Lung Health Program External Advisory Committee
- 2012 - 2012 NIH, Lung, Cellular, Molecular Immunology study section, Ad Hoc reviewer
- 2013 - 2013 NIH, Lung, Cellular, Molecular Immunology study section, Ad Hoc reviewer
- 2015 - 2016 Wellcome Trust, Ad hoc reviewer

UNIVERSITY AND PUBLIC SERVICE

SERVICE ACTIVITIES SUMMARY

I attend on the general surgical pathology service providing 24/7 attending coverage approximately 14 weeks/year.

This year, I have assumed the role of Interim Chief of Pathology at SFGH, in place of the current Chief, who has stepped down. My new duties include involve weekly meetings and presentations to the service chiefs regarding the state of the department and the leadership and coordination of all aspects of the clinical service. I currently supervise all aspects of the clinical service including the cytology, autopsy and surgical pathology service.

UNIVERSITY SERVICE

UC SYSTEM AND MULTI-CAMPUS SERVICE

- 2012 - 2012 Out-licensing of humanized monoclonal anti-avb8 antibodies Inventor
- 2016 - 2016 Out-licensing of anti-integrin antibodies Inventor

UCSF CAMPUSWIDE

2003 - 2003	Department of Medicine Search Committee	Member
2005 - 2015	Cancer Committee, SFGH	Member
2009 - 2009	Department of Medicine Search Committee	Member
2009 - 2009	Department of Medicine Search Committee	Member
2011 - 2011	Faculty search committee, Pathology	Chair
2015 - present	SFGH research committee	Chair (co-)
2017 - present	Department of Laboratory Medicine Search Committee	Member
2017 - present	Subcommittee on Clinical Research Billing, ZSFG	Chair
2017 - present	Department of Medicine Search Committee	Member
2018 - present	Department of Medicine Search Committee	Member

SCHOOL OF MEDICINE

1995 - 1998	Attending Autopsy and Surgical Pathologist, SFGH, and UCSF 4 months/year
1998 - 2000	Attending Autopsy and Surgical Pathologist, SFGH, 3 months/year
2000 - 2002	Attending Autopsy and Surgical Pathologist, SFGH, 5 months/year
2002 - 2002	Attending Autopsy and Surgical Pathologist, SFGH, 2 months/year
1998 - 1998	Tumor Board, representing pathology, every other week
1997 - 1997	Multidisciplinary pulmonary teaching Conference, every week
1999 - 1999	Interstitial Lung Disease Multidisciplinary Conference, every week
2000 - 2000	SFGH Cancer Committee
2010 - 2011	Acting Chief of Pathology, SFGH
2014 - 2015	Acting Chief of Pathology, SFGH
2016 -	Interim Chief of Pathology, ZSFG

DEPARTMENTAL SERVICE

2002 - 2002	Department of Pathology Faculty Search Committee	
2008 - 2008	Department of Pathology Faculty Search Committee	
2009 - 2009	Department of Pathology Faculty Search Committee	
2011 - 2012	Department of Pathology Faculty Search Committee	Chair

2016 - 2017	Department of Pathology Faculty Search Committee	Chair
2017 - present	Resident clinical competency committee	Member
2018 - 2018	Department of Pathology Faculty Search Committee	Chair
2018 - present	Clinical Research Grants Program, Review Committee	Chair

COMMUNITY AND PUBLIC SERVICE

2018 - present	Santa Fe Indian School, San Fe New Mexico	Mentor to High School Science Students
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CONTRIBUTIONS TO DIVERSITY

CONTRIBUTIONS TO DIVERSITY

Statement of commitment to diversity:

I have been committed to diversity and social justice my entire life. As the son of two Japanese-American internee's during WWII, I am acutely aware of the insidious nature and effects of bias. One of the most satisfying facets to working at ZSFG is being part of a hospital system that values diversity in both its staff and patient population.

In my laboratory, I have mentored numerous members of underrepresented populations, including members of the LBGT community, and ethnic minorities. I am committed to promoting women in science and in academic medicine. In the pathology department, it is my vision is to promote a multicultural and tolerant work environment free of bias.

TEACHING AND MENTORING

TEACHING SUMMARY

Over the past 20 years, my teaching interests and efforts have steadily increased and diversified. My efforts can be divided into teaching of house staff/fellows; teaching of medical students; teaching of graduate students and faculty and teaching of post-doctoral fellows and undergraduate students. Some of the most rewarding teaching that I am involved in revolves around the medical student pathology course. Through the years I have organized a medical student course (Advances in Medical Sciences), given numerous lectures, teaching basic aspects of lung pathology and airway biology. I focus the lectures so that they integrate pathology with immunology, histology, anatomy and with the introduction to clinical medicine course. I am now leading laboratories and small group teaching sessions, both in the old and new curriculum. In lectures, I try to provide a comprehensive base of information that is scientifically and clinically rigorous while at the same time being comprehensible to students with a wide range of scientific and clinical experience. In laboratories, I try to encourage critical thinking and provoke thoughtful discussion and peer-to-peer learning. This, I hope, will improve the transfer of information and will help the students place pathology and pathogenesis into a context relevant to patient care.

I am involved in the teaching of pulmonary fellows. I represent pathology for the weekly pulmonary conference and participate in case discussions. While this is a "working conference" focused mainly on the pulmonary fellows, the audience also includes medical attendings, residents, medical students, undergraduate observers and nurse practitioners. Patients are presented and the differential diagnosis is discussed, the salient pathologic

features are pointed out, and therapeutic measures are entertained.

As a surgical pathologist I supervise and provide formal and informal teaching to medical students and pathology residents around the microscope. These sessions included daily “sign-outs” where diagnoses are rendered for current cases. They also include consultations for second opinions of cases and consensus conferences. The audience may vary between one to four residents and medical students. Formal teaching includes monthly teaching sessions for pathology residents designed to hone frozen section technical and diagnostic skills. As interim chief of pathology, I have redesigned and organized the resident teaching curriculum to include formal teaching sessions in cytology, surgical pathology, neuropathology, placental pathology and frozen section diagnosis. I also have started the ZSFG pathology consensus conference which is attended by the surgical pathology attendings, resident, students and fellows. The purpose of this conference is to increase diagnostic accuracy, provoke critical discussion and opinions, standardize wording and grading schemes, and to teach residents and fellows the thought process of rendering diagnoses and communicating those diagnoses accurately and effectively to clinicians.

As a researcher, I am involved in frequent teaching sessions concerning my research interests. These are mostly informal 1-1 sessions with students and fellows where I teach student basic molecular and cellular biology, statistical analysis, critical thinking and hypothesis generation and testing. I have given courses in international meetings, most recently the American Thoracic meeting in 2016. I have supervised undergraduates from UC Berkeley (Ran Chang, Ahmed Ellatma), recent college graduates (Stephanie Gline, Tyren Barker, Kate McNelly, Royce Ma, Michelle Levine, Andrew Bondesson), and post-doctoral fellows Drs. Dez-hi Mu, David O’Connell, Lars Fjelbirkeland, Jun Araya, Jennifer Marcovics., Hideya Kitamura, Sangeeta Somanath, Robert Seed, Oliver Brand, Shunsuke Minagawa, Mitsuo, Hashimoto, Harusuke Yanagisawa, Naoki Takasaka, Catherine Moermans, Saburo Ito, Anthony Cormier). Through didactic teaching and daily discussions, I have acted as a mentor and am closely involved in trainee’s career development. I have completed the UCSF Faculty mentoring course. I lead weekly lab meetings, which are informal presentations of information pertinent to our research. I also participate in several multicenter research forums where members of my lab present research findings twice yearly.

FORMAL TEACHING

	Academic Yr	Course No. & Title	Teaching Contribution	School	Class Size
	1997 - 2016	Pulmonary Organ Block	Lecturer	Medicine	All
	1997 - 2016	Organ Blocks	Lab leader	Medicine	60
	2016 - present	Bridges	Lecturer	Medicine	All
	2016 - present	Bridges	Small group leader	Medicine	12-16

INFORMAL TEACHING

1995 - 2014 Over the course of my career at UCSF, I have been continuously involved in the informal training of medical, graduate students and fellows in various departments at UCSF and other Universities. These informal activities center around research methodology, hypothesis testing, preparation of manuscripts and presentation of research findings. These interaction take place through email exchanges, phone conversations and face-to-face meetings at UCSF and at scientific meetings. I spend approximately 2 hrs/day with lab members going over their results, demonstrating techniques and teaching them theory, methodology and statistical analysis.

MENTORING SUMMARY

I consider mentorship to be an integral part of my mission at UCSF. I have recently taken and complete the course in mentoring at UCSF. I have many former students that are in academic positions around the world.

PREDOCTORAL STUDENTS SUPERVISED OR MENTORED

Dates	Name	Program or School	Mentor Type	Role	Current Position
2015 - present	Ahmed Ellatma	UC Berkeley	Research/Scholarly Mentor, Project Mentor, Career Mentor	PI	Junior at UCB

POSTDOCTORAL FELLOWS AND RESIDENTS MENTORED

Dates	Name	Fellow	Mentor Role	Faculty Role	Current Position
2000 - 2000	Karin Chang	Cornell University (So)		Supervised Summer Work	Chicago Medical School-last known
2002 - 2002	Stephanie Gline	Wesleyan University(graduate.)		Supervised post-baccalaureate work	Post-doctoral fellow, University of California San Francisco

Dates	Name	Fellow	Mentor Role	Faculty Role	Current Position
1999 - 2000	David O'Connell	Post-doctoral Fellow		Research Supervisor	Head Student Fellowships, Trinity College, Dublin, Ireland
1999 - 2003	Dezhi Mu	Post-doctoral Fellow		Research Supervisor	Associate Professor, Hospital of W. China, Medical University, Chengdu, CHN
2000 - 2003	Lars Fjellbirkeland	Post-doctoral Fellow		Research Supervisor	Dept of Internal Medicine, University of Oslo, Norway
2004 - 2004	Jun Araya	Post-doctoral Fellow		Research Supervisor	Associate Professor, Jikei University, Tokyo < Japan
2005 - 2005	Cedric Govaerts	Post-doctoral Fellow		Co-Mentor	Researcher, University of Brussels, Belgium
2007 - 2007	Jennifer Markovics	Post-Doctoral Fellow		Research Supervisor	Researcher, Celgene, Mission Bay, San Francisco, UCSF
2008 - 2008	Hideya Kitamura	Post-doctoral Fellow		Research Supervisor	Assistant Professor, Jikei University, Tokyo < Japan

Dates	Name	Fellow	Mentor Role	Faculty Role	Current Position
2008 - 2008	Thomas Arnold	Post-doctoral Fellow	Co-Mentor/Clinical Mentor	Co-Mentor	Post-doctoral Fellow, Department of Physiology, UCSF
2010 - 2010	Sangeeta Somanath	Post-doctoral Fellow		Research Supervisor	Instructor, University of Texas,
2010 - 2010	Shunsuke Minagawa	Post-doctoral Fellow		Research Supervisor	Assistant Professor, Jikei University, Tokyo
2012 - 2014	Mitsuo Minagawa	Post-doctoral Fellow		Research Supervisor	Assistant Professor, Jikei University
2012 - 2012	Oliver Brand	Post-doctoral Fellow		Research Supervisor	Fellow, Manchester University, UK
2012 - 2012	Haruhiro Yanagisawa	Post-doctoral Fellow		Research Supervisor	Nishimuura Lab, UCSF
2013 - 2013	Rob Seed	Post-doctoral Fellow		Research Supervisor	Fellow, University of Leeds, UK
2013 - 2013	Anthony Cormier	Post-doctoral Fellow		Research Supervisor	Nishimuura Lab, UCSF
2014 - 2016	Catherine Moermans	Post-doctoral Fellow		Research Supervisor	Assistant Professor, University of Liege, Belgium
2015 - 2016	Naoki Takasaka	Post-doctoral Fellow	Research/Scholarly Mentor	Research Supervisor	Nishimura Lab, UCSF

Dates	Name	Fellow	Mentor Role	Faculty Role	Current Position
2014 - 2015	Ran Cheng	Undergraduate Student Volunteer	Research/Scholarly Mentor, Career Mentor	Supervisor	Graduate student, Department of Biology Stanford University
2013 - 2015	Kate McKnelly	Research Assistant	Research/Scholarly Mentor, Career Mentor	Supervisor	Graduate Student, Chemistry, UC Irvine
2013 - 2015	Royce Ma	Research Assistant	Research/Scholarly Mentor, Career Mentor	Supervisor	Graduate Student Immunology, Baylor University
2014 - 2015	Michelle Levine	Research Assistant	Research/Scholarly Mentor, Career Mentor	Supervisor	Medical Student, Rocky Vista University College of Osteopathic Medicine, CO
2014 - 2015	Han Li	Volunteer	Research/Scholarly Mentor, Career Mentor	Supervisor	Icahn School of Medicine at Mt. Sinai
2014 - 2016	Andrew Bondesson	Research Assistant	Research/Scholarly Mentor, Career Mentor	Supervisor	Graduate Student, Immunology, University of WA
2016 -	Saburo Ito	Post-doctoral Fellow	Research/Scholarly Mentor	Supervisor	Post-Doctoral Fellow, UCSF

FACULTY MENTORING

Dates	Name	Position while Mentored	Mentor Type	Mentoring Role	Current Position
2004 - 2012	Tomoki Hashimoto	Assistant/Associate professor		Career and research advice	Professor

Dates	Name	Position while Mentored	Mentor Type	Mentoring Role	Current Position
2007 - 2012	Jun Araya	Assistant professor		Career and research advice	Associate Professor
2007 - 2012	Roland Bainton	Assistant professor		Political and research advice	Associate Professor
2008 - 2012	Jianlong Lou	Assistant Professor		Career navigation	Assistant Professor
2012 - 2012	Bradley Stohr	Assistant Professor		Career navigation	Assistant Professor
2015 - 2017	Sarah Umetsu	Clinical Instructor	Career Mentor	Assigned Career Mentor	Assistant Clinical Instructor
2016 - present	Rebecca Wolsky	Assistant Clinical Professor	Career Mentor	Career and research advice	Assistant Clinical Instructor
2017 - present	Ursula Lang	Clinical Instructor	Career Mentor, Co-Mentor/Clinical Mentor	Career and research advice	Clinical Instructor
2017 - present	Alicia Calderon Bhambra	Clinical Instructor	Co-Mentor/Clinical Mentor	Career Advice	Clinical Instructor
2017 - present	Dianna Ng	Assistant Clinical Professor	Career Mentor, Co-Mentor/Clinical Mentor	Career Advice	Assistant Clinical Instructor

RESEARCH AND CREATIVE ACTIVITIES

RESEARCH AND CREATIVE ACTIVITIES SUMMARY

Our laboratory addresses a central biologic question: What are the basic mechanisms underlying the propagation of signals that initiate, sustain and modulate inflammation and fibrotic responses? Integrins are one of the central biologic sensors and transducers of such signals. Integrins are a large group of heterodimeric type I transmembrane receptors for the extracellular matrix that directly mediate adhesive interactions guiding inflammatory cell recruitment, and trafficking. At the same time, integrins generate and transduce signals bidirectionally across the cell membrane to influence gene expression guiding key biologic processes in the inflammatory and fibrotic response, and during tumor progression. There is a wide agreement that integrins carry out these functions through conformational changes in response to ligand binding. But, there are polar viewpoints as how integrins change conformations to allow maximal ligand binding and signal transduction. One hypothesis, supported by crystal structures of integrins with and without bound peptide ligand, proposes

that integrins are always bent. Another hypothesis, the “switchblade” hypothesis, proposes that integrins change from a bent “inactive” conformation to an extended “active” form that has maximal ligand binding properties. This hypothesis is supported by low-resolution electron microscopy (EM) studies where integrins are bent without and extended with bound ligand. We have produced recombinant integrin $\alpha\text{v}\beta\text{8}$ that is fully functional and exceptionally well suited to structural interrogations of the integrin activation mechanism. Typically a promiscuous repertoire of ligands binds to each integrin with different affinities, which are usually in the μM to mM range, which suggests ligand-specific conformational effects. An exception is $\alpha\text{v}\beta\text{8}$ which binds preferentially to one ligand, latent transforming growth factor- β (L-TGF- β), with exceptionally high affinity (pM to nM range) suggesting a highly specialized function of $\alpha\text{v}\beta\text{8}$. Binding of $\alpha\text{v}\beta\text{8}$ to L-TGF- β triggers activation of TGF- β which in turn triggers a diverse range of immunologic and fibrotic pathologic processes. Using a low resolution electron microscopic technique, negative stain EM, $\alpha\text{v}\beta\text{8}$ is almost always in an extended “active” conformation with and without binding to L-TGF- β . This observation suggests that $\alpha\text{v}\beta\text{8}$ does not undergo the major “bent” to “extended” conformational changes upon binding of its natural ligand, L-TGF- β . This unique property makes $\alpha\text{v}\beta\text{8}$ well suited for a high-resolution structural determination of the integrin “extended” form. Furthermore, it allows us to dissect the structural basis of TGF- β activation by $\alpha\text{v}\beta\text{8}$, which will have immediate translational potential to target integrin-mediated TGF- β activation in lung disease.

Our recent data using an antibody-assisted approach in single particle electron cryo-microscopy (cryo-EM) demonstrates game-changing progress in integrin structural biology by determining sub-nanometer resolution structures of an integrin in the extended active state. In a recently awarded RO1 grant, we have assembled a collaborative UCSF research team, consisting of international leaders in integrin biology (Nishimura), CryoEM (Cheng) and antibody engineering (Marks), we aim to test our central hypothesis that the integrin $\alpha\text{v}\beta\text{8}$ head domain in the extended conformation is poised to bind to L-TGF- β with high affinity. We plan to determine structures of $\alpha\text{v}\beta\text{8}$ alone, with L-TGF- β bound, and finally, in a low-affinity conformation stabilized by allosteric inhibitory monoclonal antibodies. We will use cryo-EM to gain atomic insights into both the conformational changes that regulate integrin activation and integrin-mediated TGF- β activation.

As a pathologist, I am also keenly interested in the down stream effects of TGF- β pertinent to homeostasis and how perturbation of homeostatic set points leads to fibrosis and cancer progression. As a pulmonary pathologist, I am most keenly interested in these process in the lung and how TGF- β can be therapeutically targeted. Towards this end, we have rationally improved and created highly-specific antibodies to $\alpha\text{v}\beta\text{8}$. One clone C6D4 was created from a number of engineering stages, including epitope selection, chain shuffling, yeast display, random mutagenesis and mammalian cell production. This antibody shows activity in targeting TGF- β activity in syngeneic lung cancer models where it inhibits lung metastasis. Treatment with C6D4 appears to have tumor immunomodulatory activity and modifies suppressive arms of the immune response. We also have a long-standing research program investigating the cell biology of chronic obstructive pulmonary disease. This program investigates epithelial-mesenchymal-immune cell interactions in airway development and disease. Our interest in this area began with the identification of the integrin $\alpha\text{v}\beta\text{8}$ as a potent inhibitor of airway epithelial proliferation, which led us to identify a novel mechanism of TGF- β activation. We have defined the epithelial and mesenchymal contributions to TGF- β activation and have surprisingly found that a major compartment for $\alpha\text{v}\beta\text{8}$ -mediated activation of TGF- β is in subepithelial airway fibroblasts where it might play a major role in regulating the reciprocal trophic interactions between airway epithelial and the surrounding fibroblast sheath during human airway development/pathology. These spatially restricted reciprocal interactions guide the proper differentiation of airway cell types during development. In COPD, a chronic lung disease where

airway remodeling is an important pathologic component, we hypothesized that chronic epithelial injury could lead to aberrant "reactivation" of these normally highly regulated epithelial-mesenchymal trophic interactions. Indeed, we have reported that squamous metaplasia of airway epithelium, a common change in smokers, leads to increased airway epithelial secretion of IL-1 β . Increased IL-1 β acts on adjacent fibroblasts to induce α v β 8 surface expression and α v β 8-mediated activation of TGF- β , which feeds into a self amplifying loop of TGF- β activation. We have defined the regulation of β 8 expression and function of α v β 8-mediated activation in COPD using human in vitro and in vivo systems. Our work in COPD has immediate therapeutic implications; selective inhibition of α v β 8 would bypass the undesirable systemic effects of global TGF- β inhibition. One of our early generation engineered high affinity Mabs has been used in preclinical mouse models to test for efficacy in treating COPD phenotypes. To test this Mab we developed a human ITGB8 BAC rescue mouse expressing a single integrated copy of ITGB8 expressed appropriately to rescue the lethal *itgb8* null phenotype. We recently reported that the B5 antibody that blocks airways disease in several different pre-clinical models using the ITGB8 humanized mice. We have out-licensed the B5 Mab to MedImmune/AstraZeneca and is in early clinical development and we have out-licensed other research tools to Millipore.

Another focus of our research is to understand the cellular interactions required for vessel formation in the central nervous system (CNS). Towards that goal, we have investigated the cell-type specific roles that cell adhesion receptors play in CNS vessel formation. For CNS vessels to become fully competent, interactions of endothelial cells with other cell types are likely required. Genetic evidence has implicated that the recruitment of pericytes/smooth muscle cells is important for proper cerebral vessel development. In vitro studies have pointed toward astrocytes as another putative cell-type required for proper cerebral endothelial development. However, the molecular basis of the reciprocal signaling between CNS endothelial cells and these other cell types is poorly understood. We have previously determined that integrin α v β 8, identified as being essential for murine cerebral vascular development, is expressed by astrocytes and not by endothelial cells or smooth muscle cells. That the integrin β 8 subunit knock-out mice die at late gestation of cerebral hemorrhage is the first genetic evidence to support a role for astrocytes in cerebral vascular development and suggests that α v β 8 acts directly through mediating adhesive cell-cell interactions between astrocytes and endothelial cells or indirectly through another pathway. Our data support an indirect mode of action of α v β 8 since our data suggests that that α v β 8 is the major molecular mediator of TGF- β activation in vivo. Furthermore, despite exhaustive efforts, we have no evidence that α v β 8 mediates cell-cell adhesion. TGF- β is a likely candidate molecule to provide instructional cues and to orchestrate proliferation and differentiation events between endothelial cells and mesenchymal cell types. TGF- β is essential to normal cerebral vasculogenesis since loss of function of the endothelial receptors for active TGF- β , endoglin and Alk-1, lead to hereditary hemorrhagic telangiectasia (HHT) in humans and a similar cerebral hemorrhagic disorder in mice. Because TGF- β is ubiquitously expressed in tissues almost entirely in an inactive (latent) state, the α v β 8-dependent conversion of latent to active TGF- β could be a major point in the regulation of TGF- β function in CNS vessel development. Future work will include cell biologic work to gain mechanistic insight into TGF- β activation in neural tissues and cell biologic and genetic approaches to understand the role of non-endothelial cells in CNS vasculogenesis. Towards that end we have generated neural-cell specific "knock-in" mice to to rescue the β 8 knock-out lethal phenotype.

In summary, the major theme of our research is to understand how the functions of integrins, and cytokines are orchestrated to achieve proper development and to achieve homeostatic regulation and how alterations in the orchestration of these molecules influences neoplasia and wound healing.

Most significant recent publications:

I have chosen a spectrum of publications that represent the three different aspects of my experimental work. These are: airway biology, vascular neurobiology and structural biology.

Airway Biology:

A manuscript "Selective Targeting of TGF- β activation in treating fibroinflammatory airway disease" represents 12 years of work in my laboratory. It includes developing a therapeutic monoclonal antibody for treatment of airway disease, efficacy studies in three mouse models of airway disease, and an in-depth structural, biochemical and structural biologic examination of the mechanism of action of the antibody.

Minagawa S, Lou J, Seed RI, Cormier A, Wu S, Cheng Y, Murray L, Tsui P, Connor J, Herbst R, Govaerts C, Barker T, Cambier S, Yanagisawa H, Goodsell A, Hashimoto M, Brand OJ, Cheng R, Ma R, McKnelly KJ, Wen W, Hill A, Jablons D, Wolters P, Kitamura H, Araya J, Barczak AJ, Erle DJ, Reichardt LF, Marks JD, Baron JL, Nishimura SL. Selective targeting of TGF- β activation to treat fibroinflammatory airway disease. *Sci Transl Med.* 2014 Jun 18; 6(241):241ra79. PMID: 24944194. PMCID: PMC4341974

Other significant recent contributions to epithelial biology that I have made over the past 15 years are represented by:

Hideya Kitamura, Stephanie Cambier, Sangeeta Somanath, Tyren Barker, Shunsuke Minagawa, Jennifer Markovics, Amanda Goodsell, Jean Publicover, Louis Reichardt, David Jablons, Paul Wolters, Arthur Hill, James D. Marks, Jianlong Lou, Jean Francois Pittet, Jack Gauldie, Jody Baron, Stephen L. Nishimura, Mouse and human lung fibroblasts regulate dendritic cell trafficking, airway inflammation and fibrosis, through integrin $\alpha\beta 8$ -mediated activation of TGF- β , *J Clin Investigation*, 2011 Jul 1;121(7):2863-75

Jun Araya, Stephanie Cambier, Jennifer A. Markovics, Paul Wolters, David Jablons, Arthur Hill, Walter Finkbeiner, Kirk Jones, V. Courtney Broaddus, Dean Sheppard, Andrea Barczak, Yuanyuan Xiao, David J. Erle, Stephen L. Nishimura, Squamous metaplasia amplifies pathologic epithelial-mesenchymal interactions in COPD, 2007, *J. Clin. Investigation*, Nov 1;117(11):3551-3562

Mu, Dezhi, Cambier, S, Baron, JL, Munger, J, Sheppard, D, Broaddus, VC, Nishimura, SL, The integrin $\alpha\beta 8$ mediates epithelial homeostasis through the MT1-MMP-dependent activation of TGF- β *J. Cell Biol.* 2002, Apr, 157(3),493-507

Cambier, S, Mu D, O'Connell, D, Liu, W-H, Travis, W, Broaddus, VC, Nishimura, SL, The integrin $\alpha\beta 8$ negatively regulates the growth of airway epithelium, *Cancer Res.* 2000 Dec 15;60(24):7084-93.

These publications represent the first papers describing the function of the integrin $\alpha\beta 8$ in the lung and define a novel pathway of integrin-mediated activation of TGF- β . Furthermore, these papers define a novel mechanism of epithelial homeostasis with broad implications to airway remodeling and cancer pathogenesis. In these studies, I functioned as the principal investigator and was responsible for experimental design and interpretation. I performed initial pilot studies and then taught and supervised post-doctoral fellows, students and technical personnel. I forged the collaborative relationships and oversaw the writing of the manuscript.

Vascular neurobiology: Two publications in the field of neural vascular biology highlight our interest in cell biology, gene regulation and human genetics.

Cambier S, Gline S, Mu D, Collins R, Araya J, Dolganov G, Einheber S, Boudreau N, Nishimura SL. Integrin $\alpha(v)\beta 8$ -mediated activation of transforming growth factor- β by perivascular astrocytes: an angiogenic control switch. *Am J Pathol.* 2005 Jun; 166(6):1883-94. PMID: 15920172. PMCID: PMC1602409

This paper provides the first mechanistic evidence for a CNS-specific mechanism of vessel development involving paracrine interactions between astrocytes and endothelial cells.

Su, Hua; Kim, Helen; Pawlikowska, Ludmila; Kitamura, Hideya; Shen, Fanxia; Cambier, Stephanie; Markovics, Jennifer; Lawton, Michael; Sidney, Steve; Bollen, Andrew; Kwok, Pui-Yan; Reichardt, Louis; Yang, GY; Young, William; Nishimura, Stephen. Reduced Expression of Integrin $\alpha\beta 8$ is Associated with Brain Arteriovenous Malformation (BAVM) Pathogenesis, *Am J Pathol.* 2010 Feb;176(2):1018-27

Structural Biology: Our lab has developed an interest in integrin structure. In particular, we are interested in sorting out the structural biology of integrin-TGF- β interaction. Our contributions to this area are highlighted by:

Gline SE, Cambier S, Govaerts C, Nishimura SL. A 50-A separation of the integrin alpha v beta 3 extracellular domain C termini reveals an intermediate activation state. *J Biol Chem.* 2004 Dec 24; 279(52):54567-72. PMID: 15475365

Minagawa S, Lou J, Seed RI, Cormier A, Wu S, Cheng Y, Murray L, Tsui P, Connor J, Herbst R, Govaerts C, Barker T, Cambier S, Yanagisawa H, Goodsell A, Hashimoto M, Brand OJ, Cheng R, Ma R, McKnelly KJ, Wen W, Hill A, Jablons D, Wolters P, Kitamura H, Araya J, Barczak AJ, Erle DJ, Reichardt LF, Marks JD, Baron JL, Nishimura SL. Selective targeting of TGF- β activation to treat fibroinflammatory airway disease. *Sci Transl Med.* 2014 Jun 18; 6(241):241ra79. PMID: 24944194. PMCID: PMC4341974

RESEARCH AWARDS - CURRENT

1. 1R01HL134183-01	PI (MPI: Contact PI)	15 % effort	Nishimura (PI)
NIH		07/04/2016	4/30/2020
Structural mechanism of integrin-mediated TGF- β activation		\$ 338,183 (Total) direct/yr 1	\$ 1,353,622 total

AIM 1: Determine the atomic structure of the ectodomain of $\alpha\beta 8$ integrin without bound ligand. AIM 2: Dissect the mechanism of integrin $\alpha\beta 8$ high-affinity binding and activation of L-TGF- β . AIM 3: Determine structures of the $\alpha\beta 8$ ectodomain in different functional conformational states stabilized by Fabs.

Conception, oversight, execution.

2. 24RT-0020	PI	5 % effort	Nishimura (PI)
University of California Tobacco-Related Disease Research Program (University of California)		08/31/2015	07/30/2018
Airway inflammation in the evolution of airway fibrosis		\$ 125,000 direct/yr 1	\$ 375,000 total

AIMs To determine the causative role of DCs in cigarette smoke (CS)-induced airway remodeling; To determine the mechanisms leading to DC influx and egress around airways: 2-photon microscopy of living lung sections; To confirm the relevance of the $\alpha\beta 8$ /TGF- β -*ccr6/ccl20* axis to human airway biology

Conception, oversight, execution.

3. Catalyst Plus	PI	0 % effort	Nishimura (PI)
UCSF		07/01/2017	06/30/2018
Targeting <i>avb8</i> integrin, with a monoclonal antibody to prevent activation of TGF beta in cancers and fibrosis		\$ 100,000 direct/yr 1	\$ 100,000 total

To bring new therapeutic and companion diagnostic antibodies forward toward clinical development

Conception, oversight, execution

RESEARCH AWARDS - PAST

1. 01HL090662	PI		Nishimura (PI)
NIH		09/01/2009	08/31/2011
Role of squamous metaplasia in airway wall thickening		\$ 250000 direct/yr 1	\$ 750000 total

Conception, oversight, execution.

2. 2RO1- HL63993-01	PI		Nishimura (PI)
NIH		7/1/2009	6/30/2014
Integrin avb8 Inhibits Airway Epithelial Cell Growth			
Specific Aim 1: To test the hypothesis that the increased $\beta 8$ expression in COPD is mediated by response to inflammatory cytokines and alterations in HDAC activity. Specific Aim 2: To test the hypothesis that increased integrin $\alpha\beta 8$ expression on airway epithelial cells and lung fibroblasts in COPD leads to increased activation of TGF- β . Specific Aim 3: To test the hypothesis that increased integrin $\alpha\beta 8$ mediated activation of TGF- β in COPD leads to alterations in airway epithelial and fibroblast functions involved in airway remodeling.			

Conception, oversight, execution.

3. NS-44155	Project 4		Young (PI)
NIH		09/1/2009	03/31/2014
Integrative studies of brain vascular malformations (project 4)		\$ 125,000 (Nishimura Project) direct/yr 1	\$ 625000 total
Aim 1: will explore the mechanisms of transcriptional regulation of $\beta 8$. Aim 2: to correlate $\beta 8$ expression, and downstream angiogenic signaling in BAVM and control tissues with allelic variation. Aim 3: to directly test the respective roles of $\alpha\beta 8$ and TGF- β signaling in CNS vascular integrity			

Conception, oversight, execution.

4. The use of a multi-sample bead mill homogenizer to efficiently process biological specimens			
UCSF Academic Sentate		\$12,000 total	\$12,000 total
Mouse smoking machine		\$ 35,000 direct/yr 1	\$ 35,000 total

5. 1R01HL113032-01	PI	12.7 % effort	Nishimura (PI)
NIH/NHLBI		04/01/2012	03/31/2017
Role of genetic variation in TGF-beta overactivation in COPD		\$ 312,973 direct/yr 1	\$ 1,334,063 total

Project goals: AIM1) To discover all common genetic variants in and around ITGB8 associated with increased B8 expression; AIM2) To test common genetic variants in ITGB8 for association with COPD and lung phenotypes; AIM3) To test the hypothesis that genetic variation in ITGB8 leads to increased ITGB8 expression; and AIM4) To test the hypothesis that genetic variation in ITGB8 leads to altered airway disease susceptibility.

Conception, oversight, execution.

6. U54HL119893	PI	5 % effort	Nishimura (PI)
University of California/NIH NHLBI Center for Accelerated Innovation		09/01/2014	08/31/2016
Selective targeting of TGF- β activation for airway remodeling with engineered monoclonal antibodies		\$ 100,000 direct/yr 1	\$ 200000 total
AIMs) To optimize glycosylation of anti- β 8 antibody clone B5 and related antibodies; To create optimized anti- β 8 antibodies for immunohistochemical detection; To create novel neutralizing anti- β 8 antibodies Overlap: None			
Conception, oversight, execution.			

PEER REVIEWED PUBLICATIONS

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3. Nishimura, S. L., Recht, L. D., Pasternak, G. W. Biochemical Characterization of High Affinity 3H-Opioid Binding; Further Evidence for Mul Sites. *Mol. Pharm.* 25:29-37, 1983.
4. Ling, G. S. F., Spiegel, K., Nishimura, S. L., Pasternak, G. W. Dissociation of Morphine's Analgesic and Respiratory Depressant Actions. *Eur. J. Pharm.* 86:487-488, 1983.
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- expression of intact and secreted forms of the receptor. *J Biol Chem.* 1994 Mar 4; 269(9):6940-8. PMID: 8120056
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 11. Breuss JM, Gallo J, DeLisser HM, Klimanskaya IV, Folkesson HG, Pittet JF, Nishimura SL, Aldape K, Landers DV, Carpenter W, et al. Expression of the beta 6 integrin subunit in development, neoplasia and tissue repair suggests a role in epithelial remodeling. *J Cell Sci.* 1995 Jun; 108 (Pt 6):2241-51. PMID: 7673344
 12. Ramos DM, Chen BL, Boylen K, Stern M, Kramer RH, Sheppard D, Nishimura SL, Greenspan D, Zardi L, Pytela R. Stromal fibroblasts influence oral squamous-cell carcinoma cell interactions with tenascin-C. *Int J Cancer.* 1997 Jul 17; 72(2):369-76. PMID: 9219848
 13. Milner, R., Frost, E., Nishimura, S., Delcommenne, M., Streuli, C., Pytela, R., ffrench-Constant, C., Expression of avb3 and avb8 integrin during oligodendrocyte precursor differentiation in the presence and absence of axons, *Glia*, 1977, 21:350-360.
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BOOKS AND CHAPTERS

1. Nishimura, S.L., Broaddus, V.C., Asbestos-related pleural diseases, (Chapter), *Chest Clinics of North America* 1998;19(2):311-29
2. Nishimura, S.L., Finkbeiner, W., Pulmonary Pathology, (Chapter), in *Textbook of Respiratory Medicine*, Murray and Nadel, Eds., 4th Ed..

SIGNIFICANT PUBLICATIONS

1. Hideya Kitamura, Stephanie Cambier, Sangeeta Somanath, Tyren Barker, Shunsuke Minagawa, Jennifer Markovics, Amanda Goodsell, Jean Publicover, Louis Reichardt, David Jablons, Paul Wolters, Arthur Hill, James D. Marks, Jianlong Lou, Jean Francois Pittet, Jack Gauldie, Jody Baron, Stephen L. Nishimura, Mouse and human lung fibroblasts regulate dendritic cell trafficking, airway inflammation and fibrosis, through integrin $\alpha\beta 8$ -mediated activation of TGF- β , *J Clin Investigation*, 2011 Jul 1;121(7):2863-75.

I served as the PI of this study which is the first to define a role for lung fibroblasts in directing pathologic inflammation. I was the main contributor to the design and conception of all of experiments and supervised the post-docs who performed the studies.

2. Hashimoto M, Yanagisawa H, Minagawa S, Sen D, Goodsell A, Ma R, Moermans C, McKnelly KJ, Baron JL, Krummel MF, Nishimura SL. A Critical Role for Dendritic Cells in the Evolution of IL-1 β -Mediated Murine Airway Disease. *J Immunol*. 2015 Apr 15; 194(8):3962-9. PMID: 25786688. PMCID: PMC4390519

I served as PI of the study and oversaw all aspects of the project and wrote the manuscript.

3. Hashimoto M, Yanagisawa H, Minagawa S, Sen D, Ma R, Murray LA, Tsui P, Lou J, Marks JD, Baron JL, Krummel MF, Nishimura SL. TGF- β -Dependent Dendritic Cell Chemokinesis in Murine Models of Airway Disease. *J Immunol*. 2015 Aug 1; 195(3):1182-90. PMID: 26109638. PMCID: PMC4506848

I served as PI and oversaw all aspects of the study.

4. Brand OJ, Somanath S, Moermans C, Yanagisawa H, Hashimoto M, Cambier S, Markovics J, Bondesson AJ, Hill A, Jablons D, Wolters P, Lou J, Marks JD, Baron JL, Nishimura SL. Transforming Growth Factor- β and Interleukin-1 β Signaling Pathways Converge on the Chemokine CCL20 Promoter. *J Biol Chem*. 2015 Apr 27. PMID: 25918170. PMCID: PMC4505537

I served as PI and oversaw all aspects of the study.

5. Minagawa S, Lou J, Seed RI, Cormier A, Wu S, Cheng Y, Murray L, Tsui P, Connor J, Herbst R, Govaerts C, Barker T, Cambier S, Yanagisawa H, Goodsell A, Hashimoto M, Brand OJ, Cheng R, Ma R, McKnelly KJ, Wen W, Hill A, Jablons D, Wolters P, Kitamura H, Araya J, Barczak AJ, Erle DJ, Reichardt LF, Marks JD, Baron JL, Nishimura SL. Selective targeting of TGF- β activation to treat fibroinflammatory airway disease. *Sci Transl Med*. 2014 Jun 18; 6(241):241ra79. PMID: 24944194. PMCID: PMC4341974

I served as PI and oversaw all aspects of the study.

PATENTS ISSUED OR PENDING

1. INTEGRIN α V β 8 NEUTRALIZING ANTIBODY (US Provisional Application No. 61/305,749 filed February 18, 2011, and US Provisional Application No. 61/428,814, filed December 30,2010)
2. ANTIBODIES THAT BIND INTEGRIN α V β 8 (US Provisional Application, filed Aug 17, 2011)
3. IMPROVED ALPHA-V BETA-8 ANTIBODIES (US Provisional Application, filed June 17, 2014)
4. Neutralizing monoclonal antibodies to integrin avb8 for immunotherapy (US Provisional Application, filed September 29, 2016).

ACADEMIC LEADERSHIP

Co-chair of the ZSFG research committee. Have played a leadership role in organizing, facilitating planning, dissemination of information and programming the planned new research building at ZSFG.