

Pediatric Center for Pulmonary & Vascular Biology – 2019 Annual Report

Introduction

The Center for Pulmonary and Vascular Biology (PVB) provides a programmatic research home for pediatric faculty and trainees pursuing basic research in pulmonary biology and vascular biology. The Center's mission is to expand the basic understanding of lung and vascular diseases, striving to gain new knowledge that will ultimately lead to new diagnostic, prophylactic, and therapeutic strategies. The science being pursued is focused on lung and vascular development and responses to inflammation, metabolic stress and injury.

The Center provides a valuable resource for investigative endeavors in pulmonary biology and vascular biology across the UT Southwestern campus. This is represented by active collaborations between PVB faculty and other UT Southwestern faculty in the Departments of Internal Medicine, Cell Biology, Physiology, Pharmacology and Molecular Genetics, and by participation of PVB faculty in numerous training grants across the campus.

Notably, since 2009 Dr. Shaul in PVB and Dr. Lance Terada in the Division of Pulmonary and Critical Care Medicine in the Department of Internal Medicine have codirected an NIH T32 program to support postdoctoral research training in lung biology and disease at UT Southwestern. The T-32 award was successfully renewed in 2014.



Philip Shaul, M.D.
Professor,
Vice Chair of Research

Faculty

The Pediatric PVB faculty are basic scientists and physician-scientists from four pediatric divisions working in partnership.



Philip W. Shaul, M.D.
Professor, Vice Chair of Research
Director, Center for Pulmonary and Vascular
Biology. Director, Physician-scientist
Training Program in Pediatrics
Associates First Capital Corporation
Distinguished Chair in Pediatrics



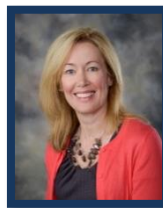
Michelle Gill, M.D., Ph.D.
Associate Professor of Pediatric,
Immunology and Internal Medicine
Division of Pediatric Infectious Disease



Rashmin C. Savani, M.B.Ch.B.
Professor and Division Director, Neonatal
and Perinatal Medicine
Associate Director, Center for Pulmonary
and Vascular Biology
The William Buchanan Chair in Pediatrics



Chieko Mineo, Ph.D.
Associate Professor, Center for Pulmonary
and Vascular Biology



Jessica Moreland, M.D.
Professor of Pediatrics and Microbiology
Division Chief, Pediatric Critical Care
Medicine
Thomas Fariss Marsh, Jr. Chair in Pediatrics



Anastasia Sacharidou, Ph.D.
Instructor, Center for Pulmonary and
Vascular Biology

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Honors / Awards

Best Pediatric Specialists in Dallas, *D Magazine*

- Michelle Gill
- Jessica Moreland

Texas Super Doctor, *Texas Monthly*

- Rashmin Savani

Michelle Gill

- Appointed Assistant Director, Medical Scientist Training Program (MSTP)

Anastasia Sacharidou

- Promotion to Instructor

Rashmin Savani

- Lifetime Achievement Award – Marquis Who's Who

Invited Lectures

Michelle Gill

- American Academy of Allergy, Asthma & Immunology (AAAAI), San Francisco, CA, February 2019
 - *"Lung Innate Immunity: At the Frontlines of Host Defense"*
- American Academy of Allergy, Asthma & Immunology (AAAAI), San Francisco, CA, February 2019
 - *"Immunophenotype Mapping of Human Dendritic Cells in the Context of Respiratory Virus Exposure"*
- American Thoracic Society (ATS), Dallas, TX, May 2019
 - *"Lung Innate Immunity: At the Frontlines of Host Defense"*

Chieko Mineo

- HDL Workshop, Boston, MA, May 2019
 - *"SR-BI in Atherosclerosis: A new Paradigm for an Old Story"*

Rashmin Savani

- Federation of European Biochemistry Societies, 7th Advanced Lecture Course, Porto Hellis, Greece, April 2019
 - *"Matrix Pathobiology, Signaling & Molecular Targets"*
- International Perinatal Collegium, Porto Carras, Greece, July 2019
 - *"Title?"*
- 36th Annual Advances in Therapeutics and Technology: Critical Care of Neonates, Children and Adults Snowbird, Utah, March 2019
 - *"Title?"*
- Innovations in Neonatal Care and BPD in the 21st Century, Austin, TX, August 2019
 - *"Title?"*

Philip Shaul

- European Society for Cardiology, PCSK9 Forum, Paris, France, September 2019
 - *"Endothelial LDL Transcytosis in Atherosclerosis"*
- The Hartwell Foundation, Annual Biomedical Research Meeting, Dallas, TX, September 2019
 - *"Preventing Obesity-induced Diabetes"*

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Conference Presentations

Pediatric Academic Societies Meeting, Baltimore, Maryland, April 2019

Murthy K, **Savani R**, Grover T, Logan JW, Zaniletti I, **Yallapragada S**, Rose R, Wymore E, Engle W, Vyas-Read S, Nelin L, Garfield C, Michelson K, Natarajan G, Kiger J, Porta N, Mikhail M, Touch S, Ibrahim J, Lagatta J.

- Platform Presentation: *“Nasogastric Versus Gastrostomy Tube Feedings in Regional NICU Graduates: Inter-Center Variation and 30-Day Readmission Risks”*

Wan-Huen P, NedreLOW J, Miao D, Truelove A, Charless M, Gist C, Antonisse H, **Savani R**.

- Poster Presentation: *“Regional Collaborative Efforts to Implement Best Practice Guidelines Improve Newborn Admission Temperatures in Multi-level NICUs and Mother Baby Units (MBUs) in North Texas”*

Savani R, Longoria C, Ibrahim J, Liao J, Cheong N, Nozik-Grayck E.

- Poster Presentation: *“Neonatal Extracellular Superoxide Dismutase (EC-SOD) Knockout Mice Have NLRP3 Inflammasome Activation, Increased Inflammation and Worse Alveolarization in Room Air that is Exaggerated with Hyperoxia Exposure”*

Savani R, Longoria C, Cheong N, Liao J, Toelg C, Luyt L, Turley E.

- Poster Presentation: *“Hyaluronan Binding Peptide Treatment to Block Inflammasome Activation and Prevent Bronchopulmonary Dysplasia”*

Jagarapu J, **Kapadia V**, **Mir I**, **Kakkilaya V**, Carlton K, Fokken M, Brown LS, Hall-Barrow J, **Savani R**.

- Poster Presentation: *“TeleNICU: Extending the Reach of Level IV Care and Optimizing the Triage of Patient Transfers”*

Mir I, **Chalak L**, **Savani R**, **Rosenfeld C**.

- Poster Presentation: *“Placental Clearance not Synthesis Modulates Increases in Circulating Fetal Pro-inflammatory Cytokines in Neonates with Maternal Chorioamnionitis (Chorio) With and Without Birth Asphyxia (BA)”*

Vyas-Read S, Cuna A, Logan JW, DiGeronimo R, Engle W, Grover T, Hysinger E, Coghill C, Leeman K, Mikhail M, Natarajan G, Padula M, Porta N, Rose R, **Savani R**, Touch S, Truog W, Wymore E, **Yallapragada S**, Zhang H, Nelin L, Murthy K, Lagatta J.

- Poster Presentation: *“Short-Term Outcomes in the Newly Re-Defined BPD: Findings from The Children’s Hospitals Neonatal Consortium”*

Education and Training

The primary teaching activities of the PVB faculty occur at the laboratory bench where residents, clinical pediatric subspecialty fellows, graduate students, and Ph.D. postdoctoral fellows are trained in pulmonary biology research and vascular biology research.

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Research Activities

The overall goal of the Shaul-Mineo laboratory is to identify mechanisms in endothelial cells that govern cardiovascular and metabolic health and disease. The disorders that they study include thrombosis (blood clotting), atherosclerosis, obstructive vascular disease (stenosis), hypertension and type 2 diabetes. Dr. Sacharidou has made major discoveries regarding a common cause of thrombosis and processes that underlie type 2 diabetes. Their ultimate goal is to identify new targets for therapies to combat cardiovascular and metabolic disorders.

Dr. Michelle Gill, whose research centers on evaluating the role of dendritic cells in pediatric respiratory viral infections, partners with Dr. Rebecca Gruchalla and the Division of Pediatric Allergy and Immunology to study asthma pathogenesis. By defining how dendritic cell function is affected in patients with asthma, they hope to better understand how to interrupt, and eventually design strategies to prevent the deleterious immune responses associated with the clinical symptoms of asthma.

Dr. Jessica Moreland focuses her research on better understanding the cell biology of inflammation with a specific interest in neutrophil biology. Her laboratory studies neutrophil priming by infectious and inflammatory stimuli, with a specific interest in Toll-like receptor signaling, and the role of NADPH oxidase in pro- and anti-inflammatory signaling. The Moreland laboratory studies both primary human neutrophils from healthy donors and from patients, and also utilizes a murine model of the systemic inflammatory response syndrome (SIRS) and multi-organ dysfunction syndrome (MODS).

Dr. Rashmin Savani's laboratory studies the pathogenesis of bronchopulmonary dysplasia and development of novel therapies for this devastating disorder of preterm infants. With over 20 years' experience in the biology of the glycosaminoglycan hyaluronan and its receptors, they have developed the expertise and tools, including antibodies, peptides, cDNAs, knockout and transgenic mice, that allow examination of this system in angiogenesis, inflammation and lung development, as well as in responses to injury. Specific mechanistic studies of the role of hyaluronan in the activation of nitric oxide production and of the NLRP3 inflammasome are being pursued.

Current Grant Support

Michelle Gill

Grantor: University of Wisconsin, Madison
Title of Project: Immunologic Approaches to Reduce Asthma
Role: Co-Investigator (PI: R Gruchalla)
Dates: 08/2018 – 07/2019

Grantor: Benaroya Research Institute at Virginia Mason
Title of Project: Title??
Role: Co-Investigator
Dates: 02/2019 – 01/2020

Chieko Mineo

Grantor: University of Kentucky College of Medicine
Title of Project: Mechanism of Adrenal Insufficiency as a Risk Factor for Sepsis
Role: Principle Investigator
Dates: 09/2017 – 08/2019

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Grantor: NIH-National Institutes of Health
Title of Project: Endothelial SR-BI and Metabolic Health
Role: Principle Investigator
Dates: 08/2015 – 06/2020

Grantor: NIH-National Institute of DDK Diseases
Title of Project: Endothelial Basis of Obesity-induced Insulin Resistance
Role: Principle Investigator
Dates: 07/2016 – 06/2020

Grantor: American Heart Associate Southwest Affiliate
Title of Project: Molecular Basis of Maternal Hypertension in the Antiphospholipid Syndrome
Role: Principle Investigator
Dates: 07/2018 – 06/2020

Grantor: NIH-National Heart, Lung and Blood Institute
Title of Project: Molecular Basis of Pregnancy Complications in the Antiphospholipid Syndrome
Role: Principle Investigator
Dates: 08/2018-05/2023

Philip Shaul

Grantor: NIH-National Heart, Lung and Blood Institute
Title of Project: Dichotomous Role of Endothelial SR-B1 in Atherosclerosis
Role: Principle Investigator
Dates: 12/2016 – 11/2020

Grantor: American Heart Association Inc
Title of Project: Endothelial Regulation of Insulin Sensitivity
Role: Principle Investigator
Dates: 01/2019 – 12/2020

Grantor: NIH-National Heart, Lung and Blood Institute
Title of Project: Endothelial Estrogen Receptor Alpha and Cardiometabolic Disease
Role: Principle Investigator
Dates: 06/2019 – 04/2023

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Peer-Reviewed Publications

1. Altman MC, **Gill MA**, Whalen E, Babineau DC, Shao B, Liu AH, Jepson B, Gruchalla RS, et al. [Transcriptome networks identify mechanisms of viral and nonviral asthma exacerbations in children.](#) *Nat Immunol.* 2019 May;20(5):637-651. PMID: 30962590
2. Cui Z, Liao J, Cheong N, Longoria C, Cao G, DeLisser HM, **Savani RC.** [The Receptor for Hyaluronan-Mediated Motility \(CD168\) promotes inflammation and fibrosis after acute lung injury.](#) *Matrix Biol.* 2019 May;78-79:255-271. PMID: 30098420
3. Garantziotis S, **Savani RC.** [Hyaluronan biology: A complex balancing act of structure, function, location and context.](#) *Matrix Biol.* 2019 May;78-79:1-10. PMID: 30802498
4. Ghosh D, Peng J, Brown K, Sirsi S, **Mineo C, Shaul PW**, Hoyt K. [Super-Resolution Ultrasound Imaging of Skeletal Muscle Microvascular Dysfunction in an Animal Model of Type 2 Diabetes.](#) *J Ultrasound Med.* 2019 Oct;38(10):2589-2599. PMID: 30706511
5. Goleva E, Babineau DC, **Gill MA**, et al. [Expression of corticosteroid-regulated genes by PBMCs in children with asthma.](#) *J Allergy Clin Immunol.* 2019 Mar;143(3):940-947.e6. PMID: 30059697
6. Hook JS, Cao M, Potera RM, Alsmadi NZ, Schmidtke DW, **Moreland JG.** [Nox2 Regulates Platelet Activation and NET Formation in the Lung.](#) *Front Immunol.* 2019 Jul 5;10:1472. PMID: 31338092
7. **Huang L**, Chambliss KL, et al, **Mineo C, Shaul PW.** [SR-B1 drives endothelial cell LDL transcytosis via DOCK4 to promote atherosclerosis.](#) *Nature.* 2019 May;569(7757):565-569. PMID: 31019307
8. Kakkilaya V, Wagner S, Mangona KLM, Steven Brown L, Jubran I, He H, **Savani RC**, Kapadia VS. [Early predictors of continuous positive airway pressure failure in preterm neonates.](#) *J Perinatol.* 2019 Aug;39(8):1081-1088. PMID: 31089256
9. Mandell EW, **Savani RC.** [Ceramide, Autophagy, and Apoptosis Mechanisms of Ventilator-induced Lung Injury and Potential Therapeutic Targets.](#) *Am J Respir Crit Care Med.* 2019 Mar 15;199(6):687-689. PMID: 30372122
10. **Mineo C.** [A Novel Proangiogenic Function of Fsp27 in Endothelium: You Only Live Thrice?](#) *J Am Heart Assoc.* 2019 Jun 4;8(11):e013042. PMID: 31433705
11. Peng J, Vongpatanasin W, **Sacharidou A**, et al, **Mineo C, Shaul PW.** [Supplementation With the Sialic Acid Precursor N-Acetyl-D-Mannosamine Breaks the Link Between Obesity and Hypertension.](#) *Circulation.* 2019 Dec 10;140(24):2005-2018. PMID: 31597453
12. Potera RM, Cao M, Jordan LF, Hogg RT, Hook JS, **Moreland JG.** [Alveolar Macrophage Chemokine Secretion Mediates Neutrophilic Lung Injury in Nox2-Deficient Mice.](#) *Inflammation.* 2019 Feb;42(1):185-198. PMID: 30288635
13. Rodriguez A, Trigatti BL, **Mineo C**, Knaack D, et al. [Proceedings of the Ninth HDL \(High-Density Lipoprotein\) Workshop: Focus on Cardiovascular Disease.](#) *Arterioscler Thromb Vasc Biol.* 2019 Dec;39(12):2457-2467. PMID: 31597448
14. Zhang M, Wang T, Sirianni R, **Shaul PW**, Xie Y. [Identifying genes with tri-modal association with survival and tumor grade in cancer patients.](#) *BMC Bioinformatics.* 2019 Jan 8;20(1):13. PMID: 30621577