

Pediatric Center for Pulmonary & Vascular Biology – 2022 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, Population and Data Sciences, and Molecular Genetics, and by participation of PVB faculty in numerous training grants across the campus. PVB researchers also have active collaborations with faculty in the Department of Biomedical Engineering at UT Dallas.

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 co-directed an NIH T32 program to support postdoctoral research training in lung biology and disease at UT Southwestern. Beginning in 2020 the T-32 was successfully awarded for years 11 to 15.



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

Faculty

The Pediatric PVB faculty are basic scientists and physician-scientists from 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



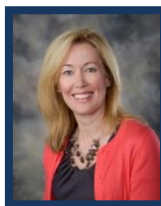
Chieko Mineo, Ph.D.
Professor, Center for Pulmonary and
Vascular Biology



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



Anastasia Sacharidou, Ph.D.
Instructor, 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

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Honors / Awards

Best Pediatric Specialists in Dallas, *D. Magazine*

- Jessica Moreland, M.D.

Associate Editor, Proteoglycans Research

- Rashmin C. Savani, M.B.Ch.B.

National Science Committee, Innovations Fund, March of Dimes

- Rashmin C. Savani, M.B.Ch.B.

Texas Super Doctor, *Texas Monthly*

- Rashmin C. Savani, M.B.Ch.B.

Vice Chair, Executive Committee, Texas Collaborative for Healthy Mothers and Babies, (TCHMB)

- Rashmin C. Savani, M.B.Ch.B.

Invited Lectures

Rashmin Savani, M.B.Ch.B.

- Johns Hopkins University Clinic K12 Glycoscience Training Program Seminar Series, Cleveland, OH, February 2022
 - *“RHAMM as a target in COVID-19”*
- Federation of European Biochemistry Societies, (FEBS) - 8th Advanced Lecture Course, Crete, Greece, May 2022
 - *“Matrix Pathobiology, Signaling & Molecular Targets”*
- International Perinatal Collegium, Reykjavik, Iceland, June 2022
 - *“The Hyaluronan Receptor RHAMM is Critical for Toll-Like Receptor 7, Influenza A and SARS-CoV2-- Mediated Increases in Lung Cytokines and Inflammation”*
- Proteoglycans Gordon Conference, Andover, NH, July 2022
 - *“The Hyaluronan Receptor RHAMM is Critical for Toll-Like Receptor 7, Influenza A and SARS-CoV2-- Mediated Increases in Lung Cytokines and Inflammation”*
- Matrix Biology Europe, Florence, Italy, September 2022
 - *“Novel therapeutic approaches to combat SARS-CoV-2 inflammation”*
- 8th Annual Pediatric Research Forum for Medical Students, Orlando, FL, Keynote Speaker, September 2022
 - *“A Life Journey to Prevent Bronchopulmonary Dysplasia”*

Phil W. Shaul, M.D.

- 4th Gulf Coast Vascular Research Consortium, Shreveport, LA, March 2022
 - *“Probing the Endothelium in Human Coronary Artery Disease”*
- Annual Meeting of the Endocrine Society, Atlanta, GA, June 2022. Presidential Plenary Presentation
 - *“Endothelial Estrogen Receptor Signaling in Cardiometabolic Health and Disease”*
- UT Tyler School of Medicine, Science and Society Symposium, Tyler, TX, September 2022
 - *“Seeking Uncommon Strategies to Prevent Common Diseases”*
- UT Tyler School of Medicine, Biomedical Research Center Seminar, Tyler TX
 - *“Macrophage-to-endothelial Cell Crosstalk in Atherosclerosis”*

Conference Presentations

Annual Gulf Coast Vascular Research Consortium Meeting, Shreveport, LA, March 2022

Yu L, Huang L, Chu H, Peng J, **Sacharidou A**, Weinstock A, Fisher EA, **Mineo C**, **Shaul PW**

Abstract, *“Monocyte-to-endothelial cell crosstalk by 27-hydroxycholesterol promotes monocyte vascular recruitment and thereby advances atherogenesis.”*

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Peng J, Yu L, Oh D, Kohler JJ, Holland WL, **Shaul PW**, Mineo C

Abstract, *“Liver-specific inhibition of sialic acid biosynthesis improves systemic glucose homeostasis in mice.”*

Shaul PW

Moderator, Session 6

Pediatric Academic Societies, Denver, CO, April 2022

Savani RC

Abstract Poster, *“The Hyaluronan Receptor RHAMM is Critical for Toll-Like Receptor 7- and SARS-CoV-2-Mediated Increases in Lung Cytokines and Inflammation”*

Annual Meeting of the Endocrine Society, Atlanta, GA, June 2022

Peng J, Yu L, Oh D, Kohler JJ, Holland WL, **Shaul PW**, Mineo C

Abstract, *“Liver-specific inhibition of sialic acid biosynthesis improves systemic glucose homeostasis in mice.”*

Shaul PW

Poster Judge

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. Drs. Mineo and Shaul are active in the Genes, Development and Disease Graduate Program, participating in qualifying exam and thesis committees. Dr. Shaul gives lectures in the Molecular Metabolism and Metabolic Diseases (3MD) Graduate Track.

Research Activities

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 nicotinamide adenine dinucleotide phosphate 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).

With an overarching focus on endothelial cell biology, Dr. Sacharidou has made major discoveries regarding a common cause of thrombosis (blood clotting). She has also discovered and continues to characterize a new kinase for Akt kinase, which is critical to the cardiovascular protection afforded by HDL cholesterol. Dr. Sacharidou has additionally pursued a number of projects determining how mechanisms in endothelial cells govern the role of the skeletal muscle in normal glucose homeostasis and in type 2 diabetes.

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Dr. Rashmin Savani's laboratory studies the pathogenesis of bronchopulmonary dysplasia and the 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 have been pursued. This year studies have also focused on the role of hyaluronan and its receptors in the cytokine storm generated by activation of TLR7 responses as a model of SARS-CoV-2 infection, and the use of therapeutic agents to block the activation of this pathway in innate immunity.

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. The basic processes they study are focused on how endothelial cells respond to extracellular cues. Their ultimate goal is to identify new targets for therapies to combat cardiovascular and metabolic disorders.

Current Grant Support

Chieko Mineo

Grantor: UT Southwestern Synergy Grant Award

Title of Project: Endothelial Basis of Thrombotic Diathesis in Rheumatoid Arthritis

Role: Co-Principal Investigator

Dates: 04/2022 – 03/2023

Grantor: NIH-National Heart, Lung and Blood Institute

Title of Project: Molecular Basis of Pregnancy Complications in the Antiphospholipid Syndrome

Role: Principal Investigator

Dates: 08/2018 – 05/2023

Grantor: American Heart Assoc National Ctr

Title of Project: Endothelial Basis of Thrombotic Diathesis in Rheumatoid Arthritis

Role: Principal Investigator

Dates: 07/2022 – 06/2025

Grantor: NIH-National Heart, Lung and Blood Inst

Title of Project: Endothelial Estrogen Receptor Alpha and Cardiometabolic Disease

Role: Co-Investigator

Dates: 07/2019 – 04/2024

Grantor: NIH-National Heart, Lung and Blood Inst

Title of Project: Unraveling ApoE4 Promotion of Cardiometabolic Disease

Role: Co-Investigator

Dates: 07/2020 – 04/2024

Jessica Moreland

Grantor: NIH-National Inst of Allergy Infect Dis

Title of Project: Bacterial lipoprotein mediated activation of neutrophils: implications for pediatric sepsis

Role: Co-Investigator

Dates: 07/2022 – 06/2023

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Grantor: NIH-National Inst of Child Health & Human Dev

Title of Project: Toll-like receptor signaling mechanisms underlying neutrophil inflammatory phenotypes: implications for organ dysfunction in pediatric sepsis

Role: Co-Investigator

Dates: 04/2022 – 05/2023

Grantor: NIH-National Inst of Allergy Infect Dis

Title of Project: Role of staphylococcal lipoproteins in neutrophil extracellular trap formation: implications in pediatric sepsis

Role: Co-Investigator

Dates: 07/2021 – 06/2022

Rashmin Savani

Grantor: Mallinckrodt Pharmaceuticals, Inc.

Title of Project: RHAMM-Based Peptides to Block NFkB and NLRP3 Inflammasome Activation

Role: Principal Investigator

Dates: 09/2020 – 01/2023 (Managed by Dr. J. Gattineni 09/2022 - 01/2023)

Philip Shaul

Grantor: NIH-National Heart, Lung and Blood Institute

Title of Project: Unraveling ApoE4 Promotion of Cardiometabolic Disease

Role: Principal Investigator

Dates: 07/2020 – 04/2024

Grantor: NIH-National Heart, Lung and Blood Inst

Title of Project: Unraveling ApoE4 Promotion of Cardiometabolic Disease
Administrative Supplement

Role: Principal Investigator

Dates: 05/2021 – 04/2024

Grantor: NIH-National Heart, Lung and Blood Institute

Title of Project: Molecular Basis of Pregnancy Complications in the Antiphospholipid Syndrome

Role: Co-Investigator

Dates: 08/2018 – 05/2023

Grantor: NIH-National Heart, Lung and Blood Inst

Title of Project: Endothelial Estrogen Receptor Alpha and Cardiometabolic Disease

Role: Principal Investigator

Dates: 07/2019 – 04/2024

Grantor: NIH-National Heart, Lung and Blood Inst

Title of Project: Training Program in Lung Biology and Disease

Role: Co-Program Director

Dates: 04/2020 – 04/2025

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Peer-Reviewed Publications

1. Avena P, Casaburi I, Zavaglia L, Nocito MC, La Padula D, Rago V, Dong J, Thomas P, **Mineo C**, Sirianni R, **Shaul PW**. [27-Hydroxycholesterol Binds GPER and Induces Progression of Estrogen Receptor-Negative Breast Cancer](#). *Cancers (Basel)*. 2022 Mar 16;14(6):. PMID:35326671
2. Chuo J, Makkar A, Machut K, Zenge J, Jagarapu J, Azzuqa A, **Savani RC**. [Telemedicine across the continuum of neonatal-perinatal care](#). *Semin Fetal Neonatal Med*. 2022 Oct;27(5):101398. PMID:36333212
3. Garantziotis S, **Savani RC**. [Proteoglycans in Toll-like receptor responses and innate immunity](#). *Am J Physiol Cell Physiol*. 2022 Jul 1;323(1):C202-C214. PMID:35675639
4. Kinnare N, Hook JS, Patel PA, Monson NL, **Moreland JG**. [Neutrophil Extracellular Trap Formation Potential Correlates with Lung Disease Severity in COVID-19 Patients](#). *Inflammation*. 2022 Apr;45(2):800-811. PMID:34718927
5. Mahmood B, Murthy K, Rintoul N, Weems M, Keene S, Brozanski B, DiGeronimo R, Haberman B, Hedrick H, Gien J, Seabrook R, Ali N, Chapman R, Daniel J, Harrison A, Johnson Y, Porta NFM, Uhing M, Zaniletti I, Grover TR, Children's Hospitals Neonatal Consortium. [Predicting treatment of pulmonary hypertension at discharge in infants with congenital diaphragmatic hernia](#). *J Perinatol*. 2022 Jan;42(1):45-52. PMID:34711937
6. Mikhael M, Cleary JP, Zaniletti I, Truog WE, Ibrahim J, DiGeronimo R, Cuna A, Kiehl MJ, Coghill CH, Vyas-Read S, Yallapragada S, Engle WA, **Savani RC**, Murthy K, Lagatta JM, Children's Hospitals Neonatal Consortium (CHNC) Severe BPD Focus Group. [Chronic lung disease in full-term infants: Characteristics and neonatal intensive care outcomes in infants referred to children's hospitals](#). *Pediatr Pulmonol*. 2022 Sep;57(9):2082-2091. PMID:35578392
7. Nichols BE, Hook JS, Weng K, Ahn C, **Moreland JG**. [Novel neutrophil phenotypic signature in pediatric patients with type 1 diabetes and diabetic ketoacidosis](#). *J Leukoc Biol*. 2022 Apr;111(4):849-856. PMID:34342036
8. Vyas-Read S, Logan JW, Cuna AC, Machry J, Leeman KT, Rose RS, Mikhael M, Wymore E, Ibrahim JW, DiGeronimo RJ, Yallapragada S, Haberman BE, Padula MA, Porta NF, Murthy K, Nelin LD, Coghill CH, Zaniletti I, **Savani RC**, Truog W, Engle WA, Lagatta JM. [A comparison of newer classifications of bronchopulmonary dysplasia: findings from the Children's Hospitals Neonatal Consortium Severe BPD Group](#). *J Perinatol*. 2022 Jan;42(1):58-64. PMID:34354227
9. Yu L, Peng J, **Mineo C**. [Lipoprotein sialylation in atherosclerosis: Lessons from mice](#). *Front Endocrinol (Lausanne)*. 2022;13():953165. PMID:36157440
10. Wu CH, Guo L, Hao D, Wang Q, Ye X, Ito M, Huang B, **Mineo C**, **Shaul PW**, Li XA. [Relative adrenal insufficiency is a risk factor and endotype of sepsis - A proof-of-concept study to support a precision medicine approach to guide glucocorticoid therapy for sepsis](#). *Front. Immunol*. 2022 13:1110516. PMID: 36713379