# Yang Zhou, Ph.D.

Assistant Professor of Molecular Microbiology & Immunology Division of Biology and Medicine, Brown University

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## **ACADEMIC APPOINTMENTS AND EDUCATION -**

10/01/2021-present Assistant Professor (Tenure-Track)

Department of Molecular Microbiology and Immunology Division of Biology and Medicine, Brown University

Providence, RI

04/29/2022-present Adjunct Assistant Professor

Department of Biomedical and Pharmaceutical Sciences

University of Rhode Island

07/01/2014-9/30/2021 Assistant Professor (Research)

Department of Molecular Microbiology and Immunology Division of Biology and Medicine, Brown University

Providence, RI

09/01/2011-6/30/2014 Associate Research Scientist

Section of Pulmonary, Critical Care and Sleep Medicine

Department of Internal Medicine

Yale University School of Medicine, New Haven, CT

2010-2011 Postdoctoral Associate

Section of Pulmonary and Critical Care Medicine

Department of Internal Medicine

Yale University School of Medicine, New Haven, CT

Mentor, Jack A. Elias, M.D.

2005-2010 Ph.D. in Biochemistry and Molecular Biology

The University of Texas Health Sciences Center

Houston, TX

Advisor, Michael R. Blackburn, Ph.D.

2001-2005 B.S. in Biochemistry

Nanjing University, Nanjing, China

#### **RESEARCH INTERESTS** -

My primary research interests are directed towards understanding the immunopathogenesis of lung injury and repair. I have interrogated the roles of adenosine signaling, EGFR signaling, and chitinase-like proteins in a variety of lung diseases including asthma, chronic obstructive pulmonary disease (COPD), and pulmonary fibrosis. My future research plans are aimed at understanding 1) Role of innate immunity in the pathogenesis of fibrotic lung diseases, and nanoparticle delivery systems as therapeutics to treat related disorders; 2) Pathogenesis of abnormal pulmonary vascular remodeling and the development of pulmonary hypertension; 3) Innate Type 2 immune responses in normal pulmonary homeostasis and injury and repair; 4) Novel host genes and cellular pathways modulating respiratory viral infections. My long-range research goals are to identify the immune and cellular responses that mediate lung injury and repair responses and to identify specific molecular targets that can be targeted in the treatment of related disorders.

# AWARDS AND HONORS —

2024	American Heart Association Transformational Project Award
2024	American Thoracic Society Research Award
2024	CALA Junior Investigator Award
2022, 2023	Dean's Research Bonus Program Award
2013-2014	American Thoracic Society Abstract Scholarship Award
2011	American Thoracic Society/Hermansky-Pudlak Syndrome Network Research Award
2010	President's Research Scholarship, The University of Texas Health Science Center
2010	Graduate Student Education Committee, The University of Texas
2009	Dean's Research Award, University of Texas-Houston Medical School
2008-2009	Biochemistry and Molecular Biology Retreat Oral Presentation, UT Health
2008-2009	GSBS Young Investigator Travel Award, UT Health
2009	Keystone Symposia Scholarship, Keystone Symposia of Asthma and Fibrosis
2008	American Thoracic Society Genentech/Novartis Award
2005	Outstanding Graduate Award, Nanjing University
2003-2005	Honors awarded, Nanjing University

### **FUNDING** -

## **Ongoing Research Support**

AHA 24TPA1277918 Zhou, PI

07/1/24--06/30/27

American Heart Association, Total Award Amount (including indirect cost): \$299,398.24 The goal of this research project is to understand what could lead to the damage that are found in Pulmonary Hypertension(PH), and its relationship to a protein known as CHI3L1. This

research proposal will expand on our findings by understanding the function of CHI3L1, and it regulates the functions of immune cells. If successful, we will possibly find new targets to treat tissue damage that is found in PH.

ATS 23-24PHP11 Zhou, PI

07/1/24--07/1/26

American Thoracic Society, Total Award Amount (including indirect cost): \$80,000

We will use our newly developed mouse model that develops spontaneous lung fibrosis to understand important interactions that occur between a fully matured immune system and elements of Hermansky-Pudlak Syndrome pathology. Experiments proposed in this project will investigate the cellular and molecular mechanisms and plausible targets to treat HPS-associated lung disease.

R01 HL146498 Zhou, PI

03/22/20--02/28/25

NIH-NHLBI, Total Award Amount (including indirect cost): \$2,043,028

Targeting CHI3L1 and its receptors in Hermansky-Pudlak Syndrome-associated lung disease Experiments proposed in this project will investigate CHI3L1 biology in pale ear mouse models of pulmonary fibrosis with phenotypes similar to human HPS disease. Targeting this pathway may benefit patients with HPS and other forms of pulmonary fibrosis including Idiopathic Pulmonary Fibrosis (IPF).

R01HL146498-S1

Zhou, Pl

09/1/23--02/28/25

NIH-NHLBI, Total Award Amount (including indirect cost): \$220,569

Research Supplement to Promote Diversity in Health-Related Research

We hypothesize that citrus pectin-PLGA nanoparticles will target and inhibit Galectin-3 leading to a marked reduction in the expression of profibrotic markers in pulmonary fibrosis mouse models.

T32 HL134625 Zhou, multi-PI (Harrington, Levy, Rounds, multi-PI)

03/01/22-02/28/27

NIH-NHLBI, Total Award Amount (including indirect cost): \$3,186,405

Brown Respiratory Research Training Program

The overall goal of this training program is to provide predoctoral candidates and postdoctoral fellows training in the pathobiology and/or outcomes, prevention, and epidemiology as it relates to pulmonary/ critical care/ sleep disorders.

#### **Pending Research Support**

U54 GM115677

Zhou, multi-PI (Fedulov, multi-PI)

08/01/24-07/31/25

NIH-NIGMS, Total Award Amount (including indirect cost): \$100,000

Advance-CTR Pilot Project: Targeting human genes for epigenetic editing in lung fibrosis In this project, we propose to combine my expertise in lung fibrosis pathogenesis with Dr. Fedulov's expertise in epigenetic editing, to custom-design fusion proteins that work gene-specifically to modulate epigenetic setpoint of gene promoters and test the protective effect of CXCL11 demethylation in lung fibrosis.

### **Completed Research Support**

PR211855

Zhou, Co-investigator (Lee, PI)

03/01/22-02/28/24

Department of Defense, Total Award Amount (including indirect cost): \$318,628

Bispecific targeting of CHI3L1 and PD-1/PD-L1 axis as a novel therapeutic strategy for idiopathic pulmonary fibrosis

This project aims to determine the specific role of CHI3L1 as a major driver of profibrotic microenvironment and to evaluate the therapeutic efficacy of a bispecific CHI3L1-PD-1 monoclonal antibody as an agent to block or reverse pulmonary fibrosis.

P20 GM103652 Zhou, multi-PI (Meenach, multi-PI) 06/01/21-05/31/23

NIH-NIGMS, Total Award Amount (including indirect cost): \$37,500

Cardiopulmonary Vascular Biology COBRE Pilot Project: Development of Cell Membrane-Coated Nanoparticles for the Treatment of Pulmonary Fibrosis and Related Diseases

The objective of this proposal is to develop and validate novel particle-based therapeutics based on cell membrane-coated nanoparticle (CMCNP) for the attenuation of pulmonary fibrosis and related diseases.

P01 HL114501 Zhou, Co-investigator (Choi, PI, Elias, PI of Project 2) 04/01/21 - 06/30/23NIH-NHLBI, Total Award Amount (including indirect cost): \$1,625,000 Distinct and Overlapping Pathways of Fibrosis and Emphysema in Cigarette Smokers

This project will determine the differential roles of Chi3l1 and its receptors in COPD and IPF.

P20 GM 103652 Zhou, PI of Project 3 (Rounds, Harrington, PI) 07/20/18-01/31/21 NIH-NIGMS, Total Award Amount (including indirect cost): \$666,705

Cardiopulmonary Vascular Biology COBRE Project 3: CHI3L1 and its Receptors in Vascular Remodeling and Pulmonary Hypertension Associated with Pulmonary Fibrosis

These studies will determine whether CHI3L1 and its receptor systems are therapeutic targets to treat vascular remodeling and PH in pulmonary fibrosis.

Zhou, multi-PI (Shea, multi-PI) U54 GM115677

03/01/17 - 02/28/18

NIH-NIGMS, Total Award Amount (including indirect cost): \$75,000

Advance-CTR Pilot Project: Chitinase 3-like 1 and its receptors in pulmonary fibrosis

5P20 GM 103652-02 Zhou, Pilot PI (Rounds, Harrington, PI) 1/1/15 - 6/30/15

NIH-NIGMS, Total Award Amount (including indirect cost): \$50,000

Cardiopulmonary Vascular Biology Cobre Pilot Project: Chitinase 3-like-1 in Pulmonary Hypertension Associated with Interstitial Lung Disease

American Thoracic Society

Zhou, Pl

11/01/2011 - 10/31/2014

Total Award Amount (including indirect cost): \$80,000

Chitinase-3 Like 1 as a Biomarker and Therapeutic Target in Hermansky-Pudlak Syndrome Associated Pulmonary Fibrosis

1 UH2 HL 123876-01 Zhou, Co-investigator (Chupp, Elias, PI) 07/01/14 - 06/30/19 NIH-NHLBI, Total Award Amount (including indirect cost): \$3,700,000

Pre-Clinical Development of Novel Anti-YKL-40 Biologic to Treat Severe Asthma

In this proposal, our multidisciplinary team in translational research, genomics, drug development, and immunology will complete the pre-clinical development of humanized monoclonal antibodies against YKL-40.

1U01 HL 108638-01 Zhou, Co-investigator (Elias, PI) 7/1/11 – 6/30/16

NIH-NHLBI, Total Award Amount (including indirect cost): \$3,238,180

YKL-40 in Idiopathic Pulmonary Fibrosis and Kidney Transplantation

This grant is designed to evaluate circulating YKL-40 as a biomarker for disease progression in IPF and urinary YKL-40 as a predictor of delayed graft function after renal transplantation. These studies will also evaluate the utility of YKL-40 as a therapeutic target in both disorders.

## **Mentee Funding:**

F31 HL174078, Ruth L. Kirschstein National Research Service Award (NRSA) Individual
Predoctoral Fellowship to Carmelissa Norbrun
16 percentile, pending
T32 HL134625, Brown Respiratory Research Training Program to Parand Sorkhdini

2024-present

T32 GM139793, Interdisciplinary Training in Pharmacological Sciences to Carmelissa Norbrun

2021-2023

Undergraduate Teaching and Research Fellowship to Kiran Klubock-shukla	2024
Undergraduate Teaching and Research Fellowship to Ashley Choi	2022
Undergraduate Teaching and Research Fellowship to Selena Sheth	2022
Undergraduate Teaching and Research Fellowship to Erika Nakajima	2020
Undergraduate Teaching and Research Fellowship to Phillip Yang	2018
Undergraduate Teaching and Research Fellowship to Daniel Yang	2017
Undergraduate Teaching and Research Fellowship to Tung Nguyen	2016

# **PUBLICATIONS –**

My Bibliography at PubMed:

http://www.ncbi.nlm.nih.gov/sites/myncbi/1luOfpcwskV5g/bibliography/40350446/public/?sort=date&direction=ascending

# Papers as a Tenure-track Assistant Professor (Brown University):

All work was performed in the Zhou lab unless specifically stated otherwise.

**Key:** <sup>G</sup>, graduate student at Brown working in the Zhou lab; <sup>T</sup>, technician in the Zhou lab; <sup>U</sup>, undergraduate working in the Zhou lab; <sup>R</sup>, rotating graduate student working in the Zhou lab; <sup>P</sup>, postdoc working in the Zhou lab.

**39.** Ashley Hernandez-Gutierrez <sup>U</sup>, Sonoor Majid <sup>U</sup>, Adam Eberle <sup>U</sup>, Ashley Choi <sup>U</sup>, Parand Sorkhdini <sup>P</sup>, Dongqin Yang <sup>T</sup>, Alina Xiaoyu Yang <sup>G</sup>, Carmelissa Norbrun <sup>G</sup>, Chuan Hua He, Changmin Lee, Chun Geun Lee, Jack A. Elias, **Yang Zhou**\*, Phospholipid Scramblase-1 Regulates Innate Type 2 Inflammation in Mouse Lung via CRTH2-dependent Mechanisms. *Journal of Clinical Investigation*, 2023 Aug 1;133(15):e169583

<sup>\*</sup> denotes corresponding authorship

**Importance in the field:** This work was initially started when I was affiliated with the Elias lab, and has been one of the projects in my independent lab. Exaggerated Type 2 immune responses play critical roles in the pathogenesis of a variety of diseases including asthma, allergy, and pulmonary fibrosis. Recent studies have highlighted the importance of innate type 2 immune responses and innate lymphoid 2 cells (ILC2s) in these disorders. However, the mechanisms that control the development of pulmonary innate type 2 responses (IT2IR) and the recruitment and/or activation of ILC2 cells are poorly understood. Our studies demonstrate that PLSCR1 plays an essential role in the pathogenesis of ILC2 responses, providing new, critical insights into biology and disease pathogenesis and identifying novel targets that can be manipulated in attempts to control IT2IR in chronic diseases such as asthma.

**38.** Andrea Gonsalves, Parand Sorkhdini <sup>P</sup>, Jasmine Bazinet, Moez Ghumman, Dinesh Dhamecha, **Yang Zhou**, Jyothi U. Menon, Development and characterization of lung surfactant – coated nanoparticles to improve lung retention for sustained pulmonary drug delivery, *Biomaterials Advances*, *2023 Jul;150:213430*.

**Importance in the field:** This is a collaborative work between the Zhou lab and the Menon lab at URI. Lung cancer is often diagnosed at an advanced stage where tumors are usually inoperable and first-line therapies are inefficient and have off-targeted adverse effects, resulting in poor patient survival. Here, we report the development of an inhalable poly lactic-co-glycolic acid polymer-based nanoparticle (PLGA-NP) formulation with a biomimetic Infasurf lung surfactant (LS) coating, for localized and sustained lung cancer drug delivery. In the Zhou lab, we performed *in vivo* studies to demonstrate greater retention of LS-coated NPs in the lungs of C57BL/6 WT mice compared to uncoated NPs. The overall results confirm that LS coating is a unique strategy for cloaking polymeric NPs to potentially prevent their rapid lung clearance and facilitate prolonged pulmonary drug delivery.

**37.** Xiuna Sun <sup>P</sup>, Erika Nakajima <sup>U</sup>, Carmelissa Norbrun <sup>G</sup>, Parand Sorkhdini <sup>P</sup>, Alina Xiaoyu Yang <sup>G</sup>, Dongqin Yang <sup>T</sup>, Corey E. Ventetuolo, Julie Braza, Alexander Vang, Jason Aliotta, Debasree Banerjee, Mandy Pereira, Grayson Baird, Qing Lu, Elizabeth O. Harrington, Sharon Rounds, Chun Geun Lee, Hongwei Yao, Gaurav Choudhary, James R. Klinger, **Yang Zhou**\*, Chitinase 3-Like-1 Contributes to the Development of Pulmonary Vascular Remodeling in Pulmonary Hypertension, *JCI Insight*, 2022 Aug 11;e159578

Importance in the field: The relationship between CHI3L1 and pulmonary vascular remodeling is not well understood. Our work showed that: 1) In human subjects with variable types of PH, circulating levels of serum CHI3L1 were associated with worse hemodynamics and correlated directly with mean pulmonary artery pressure and pulmonary vascular resistance; 2) In all 3 mouse models of pulmonary vascular disease, pulmonary hypertensive responses were mitigated in CHI3L1 null mice and accentuated in transgenic mice that overexpress CHI3L1; 3) CHI3L1 alone was sufficient to induce pulmonary arterial smooth muscle cell proliferation, inhibit pulmonary vascular endothelial cell apoptosis, and induce endothelial-to-mesenchymal transition. These studies demonstrate that CHI3L1 and its receptors play an integral role in pulmonary vascular disease pathobiology and may offer a novel target for the treatment PAH and PH associated with fibrotic lung disease.

**36.** A.A. Howell, C.J. Versoza, G. Cerna, T. Johnston, S. Kakde, K. Karuku, M. Kowal, J. Monahan, J. Murray, T. Nguyen, A. Sanchez Carreon, E. Song, A. Streiff, B. Su, F. Youkhana, S. Munig, Z. Patel, M. So, M. Sy, S. Weiss, **Y. Zhou**, and S.P. Pfeifer. Complete Genome Sequence of the Cluster P Mycobacteriophage Phegasus. *Microbiol. Resour. Announc.* 4 August 2022.

**Importance in the field:** This is a collaborative work between the students and instructors of Phage Hunters at Brown and Dr. Pfeifer's team at Arizona State University. We characterized the complete genome of the cluster P mycobacteriophage Phegasus. Its 47.5-kb genome contains 81 protein-coding genes, 36 of which could be assigned a putative function. Phegasus is most closely related to two subcluster P1 bacteriophages, Mangethe and Majeke, with an average nucleotide identity of 99.63% each.

**35.** Yueming Cao <sup>U</sup>, Jahnavi Rudrakshala <sup>U</sup>, River Williams <sup>U</sup>, Shade Rodriguez <sup>R</sup>, Parand Sorkhdini <sup>P</sup>, Alina X. Yang <sup>G</sup>, Miles Mundy <sup>R</sup>, Dongqin Yang <sup>T</sup>, Amy Palmisciano, Thomas Walsh, Cesar Delcompare, Tanis Caine, Luca Tomasi, Barry S. Shea, **Yang Zhou**\*. CRTH2 Mediates Pro-fibrotic Macrophage Differentiation and Promotes Lung Fibrosis, *American Journal of Respiratory Cell and Molecular Biology*, 2022 Aug;67(2):201-214.

Highlighted in Editorial: CRTH2 in Pulmonary Fibrosis: Friend or Foe?, in American Journal of Respiratory Cell and Molecular Biology.

Importance in the field: This work was an Advance-CTR project between the Zhou lab and Dr. Shea, who was at Rhode Island Hospital. Our previous studies demonstrate that high serum and lung levels of CHI3L1 can be detected and are associated with poor survival in patients with IPF. We hypothesize that CHI3L1 interacts with its receptor CRTH2 to stimulate M2 macrophage differentiation and the development of pulmonary fibrosis. Here we used genetically modified murine pulmonary fibrosis models to investigate the role of CRTH2 on M2 macrophage differentiation and fibrosis development, and primary human PBMC cell culture from normal and IPF patients to detect the difference in the responses to CHI3L1 stimulation and CRTH2 inhibition. These studies support targeting CHI3L1-CRTH2 pathway as a promising therapeutic approach in IPF and that the sensitivity of blood monocytes to CHI3L1 induced M2 differentiation may serve as a biomarker that predicts responsiveness to CHI3L1 or CRTH2 based interventions.

**34.** Suchitra Kamle, Bing Ma, Chang Min Lee, Gail Schor, **Yang Zhou**, Chun Geun Lee, Jack A Elias, Host chitinase 3-like-1 is a universal therapeutic target for SARS-CoV-2 viral variants in COVID-19, *Elife*, 2022 Jun 23;11:e78273

**Importance in the field:** This is a collaborative work between us and my former labmates in the Elias lab. We demonstrate that CHI3L1 augments epithelial cell infection by pseudoviruses that express the alpha, beta, gamma, delta, or omicron S proteins and that the CHI3L1 inhibitors anti-CHI3L1 and kasugamycin inhibit epithelial cell infection by these VOC pseudovirus moieties. Thus, CHI3L1 is a universal, VOC-independent therapeutic target in COVID-19.

**33.** Suh-Young Lee, Chang-Min Lee, Bing Ma, Suchitra Kamle, Jack A Elias, **Yang Zhou\***, Chun Geun Lee, Targeting Chitinase 1 and Chitinase 3-Like 1 as Novel Therapeutic Strategy of Pulmonary Fibrosis. *Front Pharmacol.* 2022 Mar 17;13:826471. \*co-corresponding author.

**Importance in the field:** This is an invited review article discussing specific roles and regulatory mechanisms of CHIT1 and CHI3L1 in profibrotic cell and tissue responses as novel therapeutic targets of pulmonary fibrosis.

**32.** Md Golam Jakaria, Parand Sorkhdini <sup>P</sup>, Dongqin Yang <sup>T</sup>, **Yang Zhou**, Samantha A. Meenach, Lung Cell Membrane-Coated Nanoparticles Capable of Enhanced Internalization and Translocation in Pulmonary Epithelial Cells, *International Journal of Pharmaceutics*, Volume 613, 5 February 2022

Importance in the field: This is a collaborative work between the Zhou lab and the Meenach lab at URI. Cell membrane-coated nanoparticles (CMCNP), which involve coating a core nanoparticle (NP) with cell membranes, have been gaining attention due to their ability to mimic the properties of the cells, allowing for enhanced delivery and efficacy of therapeutics. Two CMCNP systems comprised of an acetalated dextran-based NP core loaded with curcumin (CUR) coated with cell membranes derived from pulmonary epithelial cells were developed. The CMCNP internalized into and translocated across an in vitro pulmonary epithelial monolayer significantly more than the control NP. Blocking endocytosis pathways reduced the transcytosis of NP, indicating a relationship between endocytosis and transcytosis. These newly developed CMCNP have the potential to be used in pulmonary drug delivery applications to potentially enhance NP internalization and transport into and across the pulmonary epithelium.

**31.** Suchitra Kamle, Bing Ma, Chuan Hua He, Bedia Akosman, **Yang Zhou**, Chang-Min Lee, Wafik S El-Deiry, Kelsey Huntington, Olin Liang, Jason T Machan, Min-Jong Kang, Hyeon Jun Shin, Emiko Mizoguchi, Chun Geun Lee, Jack A Elias. Chitinase 3-like-1 is a therapeutic target that mediates the effects of aging in COVID-19. JCI Insight. 2021 Nov 8;6(21):e148749.

**Importance in the field:** This is a collaborative work between us and my former labmates in the Elias lab. These studies demonstrate that CHI3L1 is a potent stimulator of ACE2 and SPP, that this induction is a major mechanism contributing to the effects of aging during SC2 infection, and that CHI3L1 co-opts the CHI3L1 axis to augment SC2 infection.

**30.** Moez Ghumman, Dinesh Dhamecha, Andrea Gonsalves, Lauren Fortier, Parand Sorkhdini P, **Yang Zhou\***, Jyothi U. Menon. Emerging Drug Delivery Strategies for Idiopathic Pulmonary Fibrosis Treatment. European Journal of Pharmaceutics and Biopharmaceutics, 2021 Jul;164:1-12. \*co-corresponding author.

**Importance in the field:** This review was written by us and researchers in the Menon lab at URI, providing an update on promising strategies for the delivery of anti-fibrotic agents, along with an overview of key therapeutic targets as well as relevant emerging therapies currently being evaluated for IPF treatment.

**29.** Pamela Velazquez-Diaz <sup>U</sup>, Erika Nakajima <sup>U</sup>, Parand Sorkhdini <sup>P</sup>, Ashley Hernandez-Gutierrez <sup>U</sup>, Adam Eberle <sup>U</sup>, Dongqin Yang <sup>T</sup>, **Yang Zhou**\*. Hermansky-Pudlak Syndrome and Lung Disease: Pathogenesis and Therapeutics. Frontiers in Pharmacology, 2021 Mar 18;12:644671.

**Importance in the field:** This was an invited review that summarized the findings in the field of Hermansky-Pudlak Syndrome and lung fibrosis. This is related to the current project of understanding the immune regulations of Hermansky-Pudlak Syndrome and lung disease.

**28.** Christine A. Byrum, Christopher A. Korey, Zachary Jordan, **Yang Zhou**, Sarah Taylor, Joas Alfajardo, and Veronique Delesalle, Complete Genome Sequence of the Cluster F1 Mycobacteriophage KingMidas. Microbiology Resource Announcements. 10.1128/MRA.01557-19, 2020.

**Importance in the field:** This is a collaborative work between the students and instructors of Phage Hunters at Brown and Dr. Byrum at College of Charleston. Subcluster F1 bacteriophage KingMidas was isolated from soil collected in Providence, Rhode Island, using Mycobacterium smegmatis mc2155 as the host. The genome is 57,386 bp and contains 105 predicted proteincoding genes but no transfer-messenger RNAs or tRNAs. This siphovirus has an icosahedral head, with a genome 99.1% identical to that of F1 mycobacteriophage Scottish.

**27.** Keshava Rajagopal, Andrew J Bryant, Sandeep Sahay, Nancy Wareing, **Yang Zhou\***, Lavannya M Pandit, and Harry Karmouty-Quintana. Idiopathic Pulmonary Fibrosis (IPF) and pulmonary hypertension: Heracles meets the Hydra. British Journal of Pharmacology. bph.15036, January, 2021.

**Importance in the field:** This was a review article written by me and colleagues who are interested in studying pulmonary hypertension associated with IPF. In this review, we summarize existing therapies from the perspective of molecular mechanisms underlying lung fibrosis and vasoconstriction/vascular remodeling and discuss potential future targets for pharmacotherapy.

# Papers as a Research-track Assistant Professor (Brown University) and Postdoc (Yale):

- **26.** Junsuk Ko, Tingting Mills, Jingjing Huang, Ning-Yuan Chen, Tinne C J Mertens, Scott D Collum, Garam Lee, Yu Xiang, Leng Han, **Yang Zhou**, Chun Geun Lee, Jack A Elias, Soma S K Jyothula, Keshava Rajagopal, Harry Karmouty-Quintana, Michael R Blackburn. Transforming Growth Factor β1 Alters the 3'-UTR of mRNA to Promote Lung Fibrosis. J Biol Chem, 294 (43), 15781-15794 2019 Oct 25. PMID 31488543
- **25. Zhou Y\***, He CH, Yang DS, Nguyen T, Cao Y, Kamle S, Lee CM, Gochuico BR, Gahl WA, Shea BS, Lee CG, Elias JA. Galectin-3 Interacts with the CHI3L1 Axis and Contributes to Hermansky-Pudlak Syndrome Lung Disease. Journal of immunology (Baltimore, Md. : 1950). 2018; 200(6):2140-2153. NIHMSID: NIHMS933354. \*corresponding author

**24.** Murray LA, Habiel DM, Hohmann M, Camelo A, Shang H, **Zhou Y**, Coelho AL, Peng X, Gulati M, Crestani B, Sleeman MA, Mustelin T, Moore MW, Ryu C, Osafo-Addo AD, Elias JA, Lee CG, Hu B, Herazo-Maya JD, Knight DA, Hogaboam CM, Herzog EL. Antifibrotic role of vascular endothelial growth factor in pulmonary fibrosis. JCI insight. 2017; 2(16).

- **23.** Lee CM, He CH, Nour AM, **Zhou Y**, Ma B, Park JW, Kim KH, Dela Cruz C, Sharma L, Nasr ML, Modis Y, Lee CG, Elias JA.IL-13Rα2 uses TMEM219 in chitinase 3-like-1-induced signalling and effector responses. Nat Commun. 2016 Sep 15;7:12752. doi: 10.1038/ncomms12752.
- **22.** Peng X, Moore M, Mathur A, **Zhou Y**, Sun H, Gan Y, Herazo-Maya JD, Kaminski N, Hu X, Pan H, Ryu C, Osafo-Addo A, Homer RJ, Feghali-Bostwick C, Fares W, Gulati M, Hu B, Lee CG, Elias JA, Herzog EL. Plexin C1 deficiency permits synaptotagmin 7-mediated macrophage migration and enhances mammalian lung fibrosis. FASEB J. 2016 Sep 8. pii: fj.201600373R
- **21. Zhou Y**, Herzog EL, He CH, Peng X, Lee CM, Nguyen TH, Gulati M, Gochuico BR, Gahl WA, Lee CG, and Elias JA. Chitinase 3-like-1 and its receptors in Hermansky-Pudlak syndrome-associated lung disease. J Clin Invest. 2015 Aug 3;125(8):3178-92
- **20.** Kang MJ, Yoon CM, Kim BH, Lee CM, **Zhou Y**, Dhamija A, Boffa D, West AP, Shadel G, Ting J, Kaminski N, Kim WJ, Lee CG, Oh YM, Elias JA. Suppression of NLRX1 in Chronic Obstructive Pulmonary Disease. *Journal of Clinical Investigation*, 2015; 125(6):2458-62
- **19. Zhou Y**, Peng H, Sun H, Tang C, Gan Y, Peng X, Chen X, Mathur A, Hu B, Montgomery RR, Shaw AC, Homer RJ, Lee CM, Lee CG, Elias JA and Herzog EL. Chitinase 3-like 1 Suppresses Injury and Promotes Fibroproliferative Responses in Mammalian Lung Fibrosis. co-first author. *Science Translational Medicine*, 2014 Jun 11;6(240):240ra76.
- **18.** Lee CM, Park JW, Cho WK, **Zhou Y**, Han B, Yoon PO, Chae JW, Elias JA, and Lee CG. Modifiers of TGF-β1 effector function as novel therapeutic targets of pulmonary fibrosis. *Korean J Intern Med.* 2014;29(3):281-290.
- **17.** He CH, Lee CG, Dela Cruz CS, Lee CM, **Zhou Y**, Ahangari F, Ma B, Herzog EL, Rosenberg SA, Li Y, Nour AM, Parikh CR, Schmidt I, Modis Y, Cantley L, Elias JA. Chitinase 3-like 1 Regulates Cellular and Tissue Responses via IL-13 Receptor α2. *Cell Reports*. 2013 Aug 29;4(4):830-41. doi: 10.1016/j.celrep.2013.07.032. Epub 2013 Aug 22.
- **16. Zhou Y**, Kang MJ, Jha BK, Silverman RH, Lee CH, and Elias JA. Role of RNase L in Viral PAMP/Influenza Virus and Cigarette Smoke-induced Inflammation and Remodeling. *Journal of Immunology*. 2013 Sep 1;191(5):2637-46.
- **15. Zhou Y**, Lee JY, Lee CM, Cho WK, Kang MJ, Koff JL, Elias JA, Lee CG. Amphiregulin, an EGFR Ligand, Plays an Essential Role in the Pathogenesis of TGF-β-induced Pulmonary Fibrosis. *Journal of Biological Chemistry*. 2012 Dec 7;287(50):41991-2000.
- **14.** Lee CG, Herzog E, Ahangari F, **Zhou Y**, Gulati M, Lee CM, Peng X, Feghali-Bostwick C, Jimenez SA, Varga J, Elias JA. Chitinase1 is a Biomarker for and Therapeutic Target in

Scleroderma- Interstitial Lung Disease that Augments TGF-β1 Signaling. *Journal of Immunology*. 2012 Sep 1;189(5):2635-44.

- **13.** Lee CG, Dela Cruz CS, Ma B, Ahangari F, **Zhou Y**, Haliban R, Sznol M, Elias JA. Chitinase-like Proteins in Lung Injury, Repair and Metastasis. *Proceedings of the American Thoracic Society*. 2012 May;9(2):57-61.
- **12.** Matsuura H, Hartl D, Kang MJ, Dela Cruz CS, Koller B, Chupp GL, Homer RJ, **Zhou Y**, Cho WK, Elias JA, Lee CG. Role of Breast Regression Protein (BRP)-39 in the Pathogenesis of Cigarette Smoke-Induced Inflammation and Emphysema. *Am J Respir Cell Mol Biol*. 2010 Jul 23.

## Papers as a Graduate Student (UT Health):

- **11.** Le TT, Karmouty-Quintana H, Melicoff E, Le TT, Weng T, Chen NY, Pedroza M, **Zhou Y**, Davies J, Philip K, Molina J, Luo F, George AT, Garcia-Morales LJ, Bunge RR, Bruckner BA8, Loebe M, Seethamraju H, Agarwal SK, Blackburn MR. Blockade of IL-6 Trans signaling attenuates pulmonary fibrosis. J Immunol. 2014 Oct 1;193(7):3755-68.
- **10.** Carbonaro DA, Jin X, Wang X, Yu XJ, Rozengurt N, Kaufman ML, Wang X, Gjertson D, **Zhou Y**, Blackburn MR, Kohn DB. Gene Therapy/Bone Marrow Transplant in ADA-deficient Mice: Roles of Enzyme Replacement Therapy and Cytoreduction. *Blood*. 2012 Nov 1;120(18):3677-87.
- **9.** Ma W, Ortiz-Quintero B, Rangel R, Mckeller MR, Herrera-Rodriguez S, Suh WK, Mak TW, **Zhou Y**, Blackburn MR, Martinez-Valdez H. Coordinate Activation of Inflammatory Gene Networks, Alveolar Destruction and Neonatal Death in AKNA Deficient Mice. *Cell Research*. 2011 Nov;21(11):1564-77.
- **8. Zhou Y**, Schneider DJ, Morschl E, Song L, Pedroza M, Karmouty-Quintana H, Le T, Sun CX, Blackburn MR. Distinct Roles for the A2B Adenosine Receptor in Acute and Chronic Stages of Bleomycin-induced Lung Injury. *Journal of Immunology*. 2011 Jan 15;186(2):1097-106.
- **7.** Lu Q, Harrington EO, Newton J, Radin G, Casserly B, Warburton R, **Zhou Y**, Blackburn MR, Rounds S. Adenosine Protection of Pulmonary Edema Acts Through Both Transporter- and Receptor 2-mediated Endothelial Barrier Enhancement. *American Journal of Physiology Lung Cellular and Molecular Physiology*. 2010 Jun;298(6):L755-67.
- **6. Zhou Y**, Murthy JN, Zeng D, Belardinelli L, Blackburn MR. Alterations in Adenosine Metabolism and Signaling in Patients with Chronic Obstructive Pulmonary Disease and Idiopathic Pulmonary Fibrosis. *PLoS One*. 2010 Feb 16;5(2):e9224
- **5.** Schneider DJ, Lindsay JC, **Zhou Y**, Molina JG, Blackburn MR. Adenosine and Osteopontin Contribute to the Development of Chronic Obstructive Pulmonary Disease. *FASEB J.* 2010 Jan;24(1):70-80

**4. Zhou Y**, Mohsenin A, Morschl E, Young HWJ, Molina JG, Ma W, Sun CX, Martinez-Valdez H, Blackburn MR. Enhanced Airway Inflammation and Remodeling in Adenosine Deaminase Deficient Mice Lacking the A2B Adenosine Receptor. *Journal of Immunology*. 2009. 182(12): 8037-8046.

- **3. Zhou Y**, Schneider DJ, Blackburn MR. Adenosine Signaling and the Regulation of Chronic Lung Disease. *Pharmacology & Therapeutics*. 2009. 123(1):105-116.
- **2.** Zaynagetdinov R, Ryzhov S, Goldstein AE, Yin H, Novitskiy SV, Goleniewska K, Polosukhin VV, Newcomb DC, Mitchell D, Morschl E, **Zhou Y**, Blackburn MR, Peebles RS, Biaggioni I, Feoktistov I. Attenuation of Chronic Pulmonary Inflammation in A2B Adenosine Receptor Knockout Mice. *American Journal of Respiratory Cell Molecular Biology*. 2009 Jun 25.

# Paper as an Undergraduate Student (Nanjing University):

**1.** Liang Y, **Zhou Y**, Shen PP. NF-kappaB and Its Regulation on the Immune System. *Cell Mol Immunol*. 2004 Oct;1(5):343-50.

## Patents:

Jack A. Elias, Yang Zhou, Suchitra Kamle, Chun Geun Lee, METHODS AND COMPOSITIONS RELATING TO ANTI-CHI3L1 ANTIBODY REAGENTS FOR THE TREATEMENT OF FIBROSIS, PCT/US2019/060288

Jack A Elias, Yang Zhou, Chun Geun Lee, METHODS FOR THE DIAGNOSIS AND TREATMENT OF PULMONARY FIBROSIS IN SUBJECTS WITH HPS US61/984,253

### **Book Chapter:**

Yang Zhou, Katherine E. Cox-Flaherty, and James R. Klinger, Pulmonary Vascular Disorders, NOVA Science Publishers, ISBN: 978-1-53619-458-6, Chapter 9 Pulmonary Hypertension in Obstructive Sleep Apnea and Interstitial Lung Disease

### **Book Review:**

Immunosenescence (Kobo eBook), by Andreas Thiel

ISBN-13: 9783034602198

Publisher: Springer

## **TEACHING EXPERIENCE -**

### **Teaching at Brown University**

BIOL 0190R Phage Hunters, I Co-Instructor Student evaluations (scale: 1=high, 5=low)

Fall 2014: 20 students

2014-2016

Fall 2015: 20 students (Course: 1.12; Instructor 1.29) Fall 2016: 20 students (Course: 1.6; Instructor 1.53)

BIOL 0190S Phage Hunters, II Co-instructor 2015-2016

Course Head 2018-present

Student evaluations (scale: 1=high, 5=low)

Spring 2015: 20 students (Course: 1.18; Instructor 1.18) Spring 2016: 20 students (Course: 1.5; Instructor 1.44) Spring 2018: 20 students (Course: 1.42; Instructor 1.0) Spring 2019: 20 students (Course: 1.67; Instructor 1.20)

Student evaluations: Brown inverted the scale (scale: 1=low, 5=high)

Spring 2020: 11 students (Course: 4.71; Instructor 4.71)

Spring 2021 (remote Summer 2021): 21 students (Course: 4.25; Instructor 4.28)

Spring 2022: 23 students (Course: 4.80; Instructor 4.70) Spring 2024: 19 students (Course: 4.69; Instructor 4.69)

**Brown University Guest Lectures** 

Introduction to Pathobiology Research

BIOL-1950/1960: Independent Research

BIOL-2980: Independent Research

2019-present
2014-present
2020-present

#### MENTORING EXPERIENCE -

# **Brown University: Zhou Lab Mentees**

Current positions for former mentees are listed in **bold**.

#### **Postdoctoral Associates**

Parand Sorkhdini, PhD, Postdoctoral Research Associate Dec 2020 – present

Xiuna Sun, MD, Visiting Scholar

July 2018-July 2019

Currently **Associate Professor** at the First Affiliated Hospital of Dalian Medical University

**Graduate Students** 

Alina Yang, PhD student, Pathobiology PhD student Feb 2021 - present

Carmelissa Norbrun, TSGP PhD student March 2022-present

**Undergraduate Students** 

Kiran Klubock-shukla, Undergraduate at Brown Sep 2022-present

Gabriel Martinez, Leadership Alliance Student

Currently **student** at CUNY John Jay College of Criminal Justice

June 2024-Aug 2024

Nicholas Ristic, Undergraduate at Brown Sep 2022-May 2024 Currently Research Assistant at Yale University Ashley Choi, Undergraduate at Brown Sep 2021-May 2023 Currently Medical Student at the Medical University of South Caroline Esha Kataria, Undergraduate at Brown Sep 2021- May 2023 Currently Global Markets Analyst at RBC Selena Sheth, Undergraduate at Brown Sep 2021- May 2023 Currently **student** at Brown Adam Eberle, Undergraduate at Brown June 2020-May 2022 Currently Clinical Research Intern at Barrow Neurological Institute Erika Nakajima, Undergraduate at Brown Sep 2018-May 2021 Currently medical student at U of Toronto Ashley Hernandez-Gutierrez, Undergraduate at Brown Sep 2018- May 2021 Currently medical student at U of Southern California Pamela Velazquez-Diaz, Leadership Alliance Student June 2020-August 2020 Currently Public Health PhD student at University of Puerto Rico-Humacao Campus Claire Chung, Undergraduate at Brown May 2018-June 2019 Currently student at Brown Sonoor Majid, Leadership Alliance Student June 2019-August 2019 Currently **PharmD student** at University of Nebraska Chenxi Sun, Visiting Summer Student June 2019-August 2019 Currently **BS student** at College of William and Mary Phillip Yang, Undergraduate at Brown May 2018-May 2019 Currently student at Brown Tung Nguyen, Undergraduate at Brown August 2014-May 2017 Currently MD/PhD student at the University of Wisconsin-Madison Jahnavi Rudrakshala, Undergraduate at Brown June 2015-May 2017 Currently **medical student** at Tulane University Daniel Yang, Undergraduate at Brown August 2015-May 2018 Currently **medical student** at Brown

Yueming Cao, Undergraduate at Brown

June 2015-May 2018

Currently **Medical Resident** at Yale University School of Medicine

River Williams, Leadership Alliance Student

June 2016-August 2016

Currently MPH student at George Washington University

**Technicians** 

Dongqin Yang Jan 2019-present

**Brown Rotation Graduate Students** 

Lisa Ramos-Rodriguez, Pathobiology PhD student

Wenqing Yuan, Rotating PhD student

Shade Rodriguez, Rotating PhD student

Miles Mundy, Rotating PhD student Pathobiology Graduate Program

Sep 2023-Dec 2023

Feb 2024-April 2024

Feb 2022-April 2022

Dec 2019-March 2020

**Brown University: Thesis Committee Mentees** 

Kalindu Perera, PhD student at URI	March 2022-present
Andrea Gonsalves, PhD student at URI	August 2020-Dec 2023
Valeriia Syrovatska, Biotechnology master student	Sep 2022- Jan 2023
Kayla Campbell, PhD student Pathobiology Graduate Program	Sep 2018-Sep 2020
Joyce Lee, Undergraduate at Brown	Sep 2021-May 2022
Nicolas Renton, Undergraduate at Brown	Sep 2018-May 2019
Lillian Dominguez, Undergraduate at Brown	August 2015-May 2017
Edgar Garcia-Lopez, Undergraduate at Brown	August 2015-May 2017
Alex Blum, Undergraduate at Brown	May 2015-June 2016

**Further Undergraduate Advising** 

First- and Second-Year undergraduates for 20 students

Concentration-declared undergraduates for 2 students

2017-present
2016-present

#### RESEARCH COMMUNICATION -

### **Invited seminars (National and International)**

Shanghai Children's Medical Center, Shanghai Jiaotong University, July 2023

Multi-COBRE Seminar Series, University of Nevada, Brown University and University of Mississippi Medical Center, 12/13/2022

University of Colorado, Anschutz Medical Campus, 09/22/2022

Michael R. Blackburn, PhD, and the Many Faces of Adenosine, 06/24/2022

Multi-COBRE Seminar Series, University of Louisville, Brown University and University of Mississippi Medical Center, 8/10/2021

CPM Seminar series, the University of Texas Health Science Center at Houston, Oct 2019 Jinan University, Guangzhou, China, Nov 2016

Yale monthly fibrosis meeting. New Haven, CT May 2014

Brown Pulmonary Research Seminar Series. Providence, RI March 2014

NIAID, National Institute of Health. Bethesda, MD Dec 2009

Center for Infectious & Inflammatory Diseases, Institute of Biosciences and Technology, Texas A&M Health Science Center, Houston, TX October 2009

Department of Pulmonary Medicine, the University of Texas M.D. Anderson Cancer Center, Houston, TX May 2009

## **Invited seminars: Internal**

**CPVB COBRE Seminar June 2023** 

Leadership Alliance Summer Research in Progress, Webinar/online symposium, 6/23/2020

Rhode Island IDeA Symposium, Webinar/online symposium, 6/12/2020

MMI seminar, Brown University, Jan 2020

CPVB COBRE EAC meeting, Oct. 24, 2019

CPVB C OBRE EAC meeting, Nov. 2018

Advance CTR Seminar, March 2018

Bench to Bedside Series, Brown Pulmonary Research Conference, Rhode Island Hospital, 11/13/2017

Rhode Island Hospital Pulmonary Conference, Providence RI, March 2017

CPVB COBRE Seminar July 2016

CPVB COBRE Seminar Oct 2015

Molecular Microbiology and Immunology Seminar Series, Nov 2014

7<sup>th</sup> Yale Fibrosis Symposium. November 2013

6th Yale Fibrosis Symposium. November 2012

Department of Immunobiology, Yale University School of Medicine, March 2012

# **International and National Conference Speaking Engagements**

International Respiratory Medicine Conference 2024. 06/28/2024

Aspen Lung Conference. 06/05/2024

American Thoracic Society International Conference. 5/18/24

Hermansky-Pudlak Syndrome network conference. 4/6/2024

Changan International Forum on Vascular Biology, Virtual. 05/18/2023

Hermansky-Pudlak Syndrome network conference. 4/1/2023

International Respiratory Medicine Conference 2023. 02/12/2023

Aspen Lung Conference, 06/11/2022

Hermansky-Pudlak Syndrome network conference 4/2/2022

Hermansky-Pudlak Syndrome network conference 3/20/2021

Hermansky-Pudlak Syndrome network conference 3/09/2019

Hermansky-Pudlak Syndrome network conference March 2018

Hermansky-Pudlak Syndrome Network Conference March 2012, 2013, 2014, 2015, 2016.

American Thoracic Society International Conference. 2008

### PROFESSIONAL SERVICE -

#### **Brown University service**

Graduate Council of Brown University (2022-present)

Pathobiology Graduate Program Diversity, Equity and Inclusion Committee (2022-2023)

Member, the Advisory Committee on Honorary Degrees, Brown University (2017-2019)

Pathobiology Graduate Program Admission Committee (2015)

Pathobiology Retreat Poster Judge (2022, 2014)

#### **Grant review**

Ad Hoc, Lung Injury Repair Remodeling (LIRR) study section (2024)

Worldwide Cancer Research (2023)

Small Business' Respiratory Sciences ZRG1 CVRS B 11 (2023)

Respiratory Sciences Special Emphasis Panel ZRG1 RCCS-B (11) B (2023)

Respiratory Sciences Special Emphasis Panel [ZRG1 CVRS-B (11) B] (2022)

VA Merit BL/CS Merit Review Subcommittee for PULM (2021)

CVRS-J11 SBIR/STTR Study Section (2021)

External Ad Hoc reviewer for British Lung Foundation (2020)

Panelist, Florida Department of Health Biomedical Research Program (2014-2018)

External Ad Hoc reviewer for PSI Foundation (2018)

CPVB COBRE Pilot Project review panel (2018-present)

CPVB COBRE Junior Investigator Project review panel (2021)

## Service to the research community

ATS-RCMB Grant Writing Seminar Series, 2023

Chinese American Lung Association Organization Committee, 2023

Session Chair, Gordon Research Conference on lung injury, repair, development, Aug 2023

Panelist, ATS RCMB webinar, Oct 2022

Frontiers in Pharmacology (Associate Editor)

Pharmacological Research (Associate Editor)

Experimental and Clinical Sciences (Associate Editor)

#### Journal Ad hoc reviewer for:

Scientific Reports, American Journal of Respiratory Cell and Molecular Biology, Frontiers in Pharmacology, Journal of Respiratory Biology and Translational Medicine, Thorax, Phsiological Reports, Journal of Molecular Cell Biology, eLife, Journal of Experimental Medicine, British Journal of Pharmacology, Immune Network, Hepatology, Cells, Toxics, Respiratory Research, Pharmacological Research, Journal of Cellular Physiology, Autophagy, Pulmonary Circulation, LUNG, Archives of Toxicology, Physiological Reports, Disease Models & Mechanisms, Current Molecular Medicine, Molecular Genetics and Metabolism, Molecular Immunology, Neoplasma, Journal of Ethnopharmacology, PLoS One, Journal of Biological Regulators & Homeostatic Agents, Clinical and Experimental Pharmacology and Physiology, Cellular and Molecular Life Sciences, International Immunopharmacology, Cellular & Molecular Immunology, European Journal of Inflammation

## PROFESSIONAL SOCIETIES

2023-present American Heart Association

2011-present Hermansky-Pudlak Syndrome Network

2008-present American Thoracic Society

#### PROFESSIONAL DEVELOPMENT

Boston Biomedical Innovation Center (B-BIC) Skills Development Center-Pitch for Any	Occasion
	2019
Advance-CTR Mentoring Training Program	2019
Boston Biomedical Innovation Center (B-BIC)-The Art and Science of Slide Design	2019
Teaching Certificate, Sheridan Center at Brown	2014