BIOGRAPHICAL SKETCH

NAME	POSITION TITLE
Rama K. Mallampalli, M.D.	Division Chief, Pulmonary, Allergy, and Critical Care Medicine, UPMC Endowed Professor of Medicine Department of Medicine, University of Pittsburgh
eRA COMMONS USER NAME (credential, e.g., agency login) MALLAMPALLI	

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	YEAR(s)	FIELD OF STUDY
Northland College, Ashland, WI	BS	1980	Biology and Chemistry
Univ. of Wisconsin Medical School, Madison, WI	MD	1984	Medicine

A. PERSONAL STATEMENT

My research is in the area of pulmonary epithelial molecular and cell biology as it relates to inflammation. My laboratory is internationally recognized in the area of lipid metabolism and proteolysis as it relates to ALI/ARDS. I initially built my research program in the area of ARDS and surfactant lipids during my tenure as a faculty member at the University of Iowa (1991-2009) and then shifted my focus to ubiquitin-mediated degradation at the University of Pittsburgh (2009-present). I am also highly committed to training and education, having successfully trained nearly seventy predoctoral, graduate, post-doctoral students, clinical fellows, and junior faculty, many of whom who have obtained F32s/NRSAs, K-series awards, and developed independent NIH R01 funded research programs.

B. POSITIONS AND HONORS

Professional Appointments

1984-1987 Resident, Hennepin County Medical Center, Minneapolis MN
1987-1988 Chief Resident, Internal Medicine, Hennepin County Medical Center, Minneapolis, MN
1988-1991 Fellow, Pulmonary Division, University of Iowa Hospitals and Clinics, Iowa City IA
1991-1992 Associate, Pulmonary and Critical Care Division, University of Iowa, Iowa City IA
1992-1998 Assistant Professor, Pulmonary Diseases and Critical Care, University of Iowa, Iowa City IA
1998-2003 Associate Professor, Pulmonary Diseases and Critical Care, University of Iowa, Iowa City IA
1992-2009 Staff Physician, Veterans Affairs Medical Center, Iowa City, IA
2003-2009 Professor of Medicine and Biochemistry, Pulmonary Diseases and Critical Care, University of Iowa, Iowa City, IA
2007-2009 Chair, Research and Development Committee, VA Medical Center, Iowa City, IA
2008-2009 Associate Chair for Promotions, Department of Medicine, University of Iowa
2009-present Professor and UPMC Endowed Chair in Acute Lung Injury, Division of Pulmonary, Allergy, and Critical Care Medicine, Dept. of Medicine, University of Pittsburgh School of Medicine
2009-present Inaugural Director, University of Pittsburgh Acute Lung Injury Center of Excellence,
2010-present Professor, Department of Cell Biology and Physiology, University of Pittsburgh
2009-2013 Pulmonary Division Chief, Veteran's Affairs Pittsburgh Healthcare System, Pittsburgh, PA
2013-2015 Vice Chair for Research, Department of Medicine, University of Pittsburgh
2015-present Division Chief, Pulmonary, Allergy and Critical Care Medicine, Department of Medicine, University of Pittsburgh

Awards and Other Professional Activities

Summa Cum Laude, Northland College
Clinician Scientist Award, American Heart Association, (Declined)
Clinical Investigator Award (K08), National Institutes of Health, NICHD, (Declined)
Elected Member, Society for Pediatric Research (SPR), 1997-2010
Established Investigator, American Heart Association
Career Investigator, American Lung Association
MERIT Review, Veteran's Administration

FIRST Award, National Institutes of Health, NHLBI
Member, ATS/ National American Lung Assoc. Grant Review Committee, *Study Section B, 2*000-2009
Member, National American Heart Assoc. Study Section on *Lung, Resuscitation & Respiration*, 2001-03,
NIH /CSR *Special Emphasis Panels* (*ZRG1*), 2001, 2003, 2004
NIH/CSR NRSA Fellowship Review Panel (*ZRG1 F10*), 2005
Elected Member, American Society for Clinical Investigation (ASCI), 2005
Editorial Boards/ Editorships/Panels: *J. Biol. Chem., Am. J. Respir. Crit. Care Med., Am. J. Physiol*., *Am. J. Cancer Biol., J Epithelial Biol. Pharm*.
Consulting Editor, *Journal of Clinical Investigation*
ALA Research/National Scientific Advisory Committee (2008-10)
Elected Co-organizer, FASEB Conference on *Lung Epithelium in Health and Disease* (2008-10)
Elected Member, Association of American Physicians (AAP), 2011
NIH/NHLBI/NIAID Program Project Review Committee, Consultant, 2001, 2006, 2009, 2010, 2011, 2014-15
Lead Organizer, 2012 Pittsburgh International Lung Conference on Acute Lung Injury: "*New Mechanisms, Future Therapies, and the Translation to Clinical Care"*
Permanent Member, NIH /CSR *Lung Injury, Remodeling, and Repair Study Section* (*LIRR*), 2005-11, '13
Veterans Administration Merit Review Subcommittee for Respiration, 2013
American Thoracic Society (ATS) Recognition Award for Scientific Accomplishments, 2014
Pitt Innovator Award, University of Pittsburgh, 2014
Harrington Scholar-Innovator, Harrington Discovery Institute, 2016
Permanent Member, NHLBI Program Project Review Committee [HLBP] 2014-19.

C. Contributions to Science

My laboratory has made landmark contributions in three areas:

1. Ubiquitin-mediated Proteolysis and Small Molecule Discovery. The primary goal of my research is in the molecular behavior of orphan ubiquitin E3 ligases and how they might impact regulatory proteins in sepsis and pneumonia. My current activity investigates the discovery, characterization, and biological role of E3 ligases belonging to the Skp-Cullin1-F box (SCF) family that control site-specific ubiquitination and disposal of target proteins involved in innate immunity, inflammation, and cellular lifespan. We have discovered a new model of innate immunity that led to our synthesis of a *first-in-class* genus of ubiquitin E3 ligase (F box) inhibitors that modulate proteolysis thereby inhibiting inflammation in preclinical models of ALI and multi-organ failure. This work is rapidly moving through the FDA milestone pipeline for eventual therapeutic application in clinical trials for subjects with respiratory illness.

a. Chen BB, Coon TA, Glasser JR, McVerry BJ, Zhao J, Zhao Y, Zou C, Ellis, B, Sciurba FC, Zhang Y, **Mallampalli RK**. A combinatorial F box protein directed pathway controls TRAF stability to regulate inflammation. ***Nature Immunol***. 2013 May;14(5):470-9. PMCID: PMC3631463

b. Weathington NM, **Mallampalli RK**. Emerging therapies targeting the ubiquitin proteasome system in cancer. ***J Clin Invest***. 2014 Jan 124(1):6-12. *doi: 10.*1172/JCI71602. PMID:24382383. (PMCID: PMC387125; doi. 10.1172/JCI71602) (*Invited Review).*

c. Chen BB, Glasser JR, Coon TA, Zou C, Miller HL, Fenton M, McDyer JF, Boyiadzis M, **Mallampalli RK**. F box protein FBXL2 targets cyclin D2 for ubiquitination and degradation to inhibit leukemic cell proliferation. ***Blood***. 2012 Mar 29;119(13):3132-41. PMCID: PMC3321873

d. Zou, C., Li, J., Chen, W., Chen, Y., Xiong, S., Snavely, C., Chen, B.B., and **Mallampalli, R.K.** Morf4l1 mediates apoptosis in experimental pneumonia. ***Science Transl. Med****. (In Press)* 2015.

2. **Cardiolipin as a new Damage-Associated Molecular Pattern (DAMP)**. A second, more recent and untapped area of interest is based on our discovery that the mitochondrial-specific lipid, cardiolipin, is a unique cellular damage signal and important mediator of pneumonia. We uncovered a totally new paradigm for pneumonia. Pneumonia patients had increased levels of a toxin, cardiolipin, which reproduces this disorder when given to mice. From clues in a rare disease, we discovered that a pump normally removes cardiolipin from lung fluid but is degraded in pneumonia. We believe this is a transformative discovery that could lead to non-antibiotic therapies in this illness.

a. Ray NB, Durairaj L, Chen BB, McVerry BJ, Ryan AJ, Donahoe M, Waltenbaugh AK, O'Donnell, CP, Henderson, FC, Etscheidt CA, McCoy DM, Agassandian M, Hayes-Rowan EC, Coon TA, Butler PL,

Gakhar L, Mathur SN, Sieren JC, Tyurina YY, Kagan VE, McLennan G, **Mallampalli RK.** Dynamic regulation of cardiolipin by the lipid pump, ATP8b1 determines the severity of lung injury in experimental pneumonia. ***Nature Med.*** 2010 Oct;16(10):1120-7. NIHMSID: NIHMS229578

b. Chen BB, Coon TA, Glasser JR, Zou C, Ellis B, Das T, McKelvey AC, Rajbhandari S, Lear T, Kamga C, Shiva S, Li C, Pilewski JM, Callio J, Chu CT, Ray A, Ray P, Tyurina YY, Kagan VE, **Mallampalli RK**. E3 ligase subunit Fbxo15 and PINK1 kinase regulate cardiolipin synthase 1 stability and mitochondrial function in pneumonia. ***Cell Rep.*** 2014 Apr 24;7(2):476-87. doi: (*Cell Press*).

c. Balasubramanian, K., Maeda, A. Lee, J.S., Mohammadyani, D., Tyurin, V.A., Tyurina, Y.Y., Ray, P., Klein-Seetharaman, J., **Mallampalli, R.K**., Bayir, H., Fadeel B., and Kagan V.E.. Dichotomous roles for externalized cardiolipin in extracellular signaling: Promotion of phagocytosis and attenuation of innate immunity. ***Science Signaling***. *(In Press)* 2015.

d. Zhao J, Wei J, Mialki RK, Mallampalli DF, Chen BB, Coon TA, Zou C, *__Mallampalli RK__, *Zhao Y. F-box protein FBXL19-mediated ubiquitination and degradation of the receptor for IL-33 limits pulmonary inflammation. ***Nature Immunol***. 2012 Jun 3;13(7):651-8. PMCID: PMC3643313 **co-senior authors.*

3. Surfactant Metabolism. A third focus is to investigate the fundamental molecular regulation of enzymes needed for production of major phospholipids of animal membranes and of lung surfactant, including phosphatidylcholine (PC). PC levels are tightly controlled, in part, by the rate-regulatory enzyme cytidylyltransferase (CCT) and the remodeling enzyme lysophosphatidylcholine acytransferase (LPCAT). Our laboratory was the first to discover a physiological role for (1) reversible phosphorylation and (2) ubiquitin/calpain mediated proteolysis in governing CCT enzymatic behavior in any system. In models of inflammatory lung injury, surfactant PC biosynthesis is impaired because CCT and LPCAT activity decrease as a result of post-translational enzyme modification. Interestingly, we identified that LPCAT also triggers histone palmitoylation, a new epigenetic mark that affects inflammatory gene expression.

a. Chen BB, Coon TA, Glasser JR, **Mallampalli RK**. Calmodulin antagonizes a calcium-activated SCF ubiquitin E3 ligase subunit, FBXL2, to regulate surfactant homeostasis. ***Mol Cell Biol***. 2011 May;31(9):1905-20. PMCID: PMC3133224

b. Han S, **Mallampalli RK**. Sizing up surfactant synthesis. ***Cell Metab.*** 20:195-196, 2014.

c. **Mallampalli RK**, Salome RG, Bowen SL, Chappell DA. Very low-density lipoproteins stimulate surfactant lipid synthesis in vitro. ***J Clin Invest***. 1997 Apr 15;99(8):2020-9. PMCID: PMC508027 10.1164/rccm.201304-0754PP. PMCID: PMC3827704; doi. 10.1164/rccm.201304-0754PP

d. Chen, W., Xiong, S., Li J., Li, X., Liu, Y., Zou, C., and **Mallampalli, R.K**. The ubiquitin E3 ligase SCF- FBXO24 recognizes acetylated nucleoside diphosphate kinase A to regulate its degradation. ***Mol. Cell Biol.*** 2015 35(6):1001-13.

Complete List of Published Work in MyBibliography:
http://www.ncbi.nlm.nih.gov/sites/myncbi/rama.mallampalli.1/bibliography/40768428/public/?sort=date&direction=ascending

D. RESEARCH PROJECTS ONGOING

"Mechanisms of Lung Phospholipid Homeostasis by F Box Proteins"
Principal Investigator: R. K. Mallampalli, M.D. Agency: NIH/NHLBI
Type: NHLBI R01 HL097376-06 Period: Apr 2014 to Mar 2018
This award is limited to investigation of the *in vivo* effect of Fbxo3 in sepsis (AIM 1), BC-1261 in sepsis models (AIM 2) and role of Fbxo3 in a sepsis cohort (AIM 3).

"Septic Lung Injury and Surfactant"
Principal Investigator: R. K. Mallampalli, M.D. Agency: NIH/NHLBI
Type: NHLBI R01 HL098174-05 Period: Feb 2010 to Jan 2017
This award is limited to investigation of the effect of GSK-3 (AIM1) and its turnover (AIM 2) on surfactant.

"F box-Induced Acute Lung Injury and Parkin"
Principal Investigator: R.K. Mallampalli, M.D. Agency: NIH/NHLBI
Type: NHLBI R01 HL096376-03 Period: Apr 2016 to Mar 2021

This award is limited to investigation of the effect of Parkin degradation on mitochondria (AIM1) and small molecule stabilizers of Parkin in ALI (AIM 2).

"Regulation of F box Proteins in Acute Lung Injury"
Principal Investigator: R. K. Mallampalli, M.D. Agency: NIH/NHLBI
Type: NHLBI R01 HLHL081784-08 Period: Jul 2014 to Jun 2019
This award is limited to investigation of F box proteins on NALP7 (AIM 1) and drug design of a dual anti-inflammatory anti-microbial (AIM 2) in ALI models.

"Cardiolipin as a Novel Mediator of Acute Lung Injury".
Principal Investigator: R. K. Mallampalli, M.D. Agency: NIH/NHLBI
Type: NHLBI P01 HL114453-01A1 Period: Feb 2014 to Jan 2019
This Program Project Grant investigates the molecular regulation of cardiolipin on mitochondrial function and innate immunity. It studies FBXO15 and Pink1 (Project 1), and provides the PPG with administrative, lipidomic, biorepository, and imaging support (Cores A-D).

"SCF-based Ubiquitin E3 Ligases in the Pathobiology of Pneumonia"
Principal Investigator: R. K. Mallampalli, M.D. Agency: Veterans Administration
Type: Merit Review Award Period: Sept 2014 to Oct 2017
This award is limited to investigation of the molecular regulation of FBXL2-FBXO3 (AIM1), and FBXO3 analysis in VAPHS patients (AIM3). Aim 2 on FBXO3 drug inhibition was administratively withdrawn.

"A New Genus of Ubiquitin-Based Anti-inflammatories for COPD"
Principal Investigator: R. K. Mallampalli, M.D. Agency: NIH/NHLBI
Type: CADET II 1UH2HL123502-02 Period: Jul 2014 to Jun 2016
This award is limited to investigation of synthesis and testing of F box inhibitors (UH2), and its evaluation of pharmacokinetic and pharmacodynamics to IND status in COPD models.

"Novel F box Anti-inflammatories for COPD"
Principal Investigator: R. K. Mallampalli, M.D. Agency: NIH/NHLBI
Type: Flight Attendant Medical Research Institute (FAMRI) Period: Jul 2014 to Jun 2017
This award is limited to investigation of effects of an activated inflammasome/MMP inflammation pathway in COPD (Aim 1) and anti–inflammatory actions of an F box inhibitor BC-1261 (Aim 2).

"Translational Training Program In Pulmonary Biology and Medicine"
Director: R. K. Mallampalli, M.D. Agency: NIH/NHLBI
Type: 2T32 HL007563-26 Period: Jul 2014 to Jun 2018
This award is limited to training clinical pulmonary post-doctoral fellows in biomedical research.

"Targeting a Ubiquitin E3 Ligase in Acute Lung Injury"
Principal Investigator: R. K. Mallampalli, M.D. Agency: Bayer Pharma AG, Germany
Type: Grant for Targets Program Period: Oct 2013 to Sept 2015
This is a pilot award is limited to investigation of anti–inflammatory actions of an F box inhibitor BC-1261

"Fbxo3 Targeted Anti-inflammatories for Bronchitis and *E3 Therapeutics, Inc.*"
Principal Investigator: R. K. Mallampalli, M.D. Agency: Coulter Foundation
Type: Pilot Program Period: Jul 2014 to Dec 2015
This is a pilot award is limited to investigation of anti–inflammatory actions of an F box inhibitor in bronchitis to support its commercialization and tech transfer.